ABSTRACTS OF THE 28th ANNUAL MEETING OF THE ITALIAN SOCIETY OF URO-ONCOLOGY (SIUrO)

URO-ONCOLOGIA: MULTIDISCIPLINARIETÀ E REALTÀ CLINICA

12-14 April, 2018, Milan, Italy

Milan Marriott Hotel, Via Giorgio Washington 66, 20146 Milan, Italy

Honorary Chair: Riccardo Valdagni

Italian Society of Uro-Oncology

Italian Society of Uro-Oncology (SIUrO)

President: Riccardo Valdagni, Milan, Italy

Board

PRESIDENT: Riccardo Valdagni
VICE PRESIDENT: Sergio Bracarda
PAST PRESIDENT, SECRETARY GENERAL & TREASURER: Giario N. Conti
INCOMING PRESIDENT: Alberto Lapini

Advisors

Vincenzo Altieri
Marco Borghesi
Luigi F. Da Pozzo
Roberto Sanseverino
Enrico Bollito
Renzo Colombo
Cinzia Ortega
Vittorio Vavassori

Elected Scientific Committee

Orazio Caffo, Giovanni Pappagallo

Congress Scientific Committee

Barbara Avuzzi
Michelangelo Fiorentino
Tommaso Prayer-Galetti
Federico Lanzi
Cinzia Ortega
Mimma Rizzo
Giuseppe Sanguineti
Riccardo Valdagni

Scientific Secretariat
Società Italiana di Urologia Oncologica (SIUrO)
Via Dante 17 – 40126 Bologna, Italy
Tel: +39051349224 – Fax: +39051349224
e-mail: congresso@siuro.it – web: www.siuro.it

Organizing Secretariat
Overgroup
Via Pagliari, 4–26100 Cremona, Italy
Tel: +39037223310 – Fax: +390372569605
e-mail: info@overgroup.eu

Referees of Abstracts

B. AVUZZI, *Milan, Italy*
E. BOLLITO, *Turin, Italy*
R. BORTOLUS, *Aviano, Italy*
S. BRACARDA, *Arezzo, Italy*
R. CECCARELLI, *Bologna, Italy*
R. COLOMBO, *Milan, Italy*
G. N. CONTI, *Como, Italy*
M. FIORENTINO, *Bologna, Italy*
F. LANZI, *Siena, Italy*
A. LAPINI, *Florence, Italy*
C. ORTEGA, *Alba, Italy*
G.L. PAPPAGALLO, *Treviso, Italy*
M. RIZZO, *Trento, Italy*
G. SANGUINETI, *Rome, Italy*
V. SCATTONI, *Milan, Italy*
R. VALDAGNI, *Milan, Italy*
V. VAVASSORI, *Bergamo, Italy*
N. ZAFFARONI, *Milan, Italy*

2

RELATIONSHIP BETWEEN TESTOSTERONE LEVELS AND PROSTATE CANCER IN PATIENTS AFFECTED BY ATYPICAL SMALL ACINAR PROLIFERATION

Lucio Dell'Atti, Guevar Maselli, Luca Leone, Simone Scarcella and Andrea Benedetto Galosi

Institute of Urology, University Hospital "Ospedali Riuniti", Ancona, Italy

Background/Aim: Atypical small acinar proliferation (ASAP) is a diagnosis that occurs in about 1-5% of prostate biopsies. The guidelines recommend immediate repeat biopsy within 3-6 months after the initial diagnosis of ASAP (1). The current literature does not support the usefulness of clinical markers on predicting patients with ASAP that are more likely to progress to prostate cancer (PCa) (2). In many observational studies, high levels of testosterone have long been considered to be possible risk factors for PCa. However, recent studies show that PCa has often been associated with low testosterone levels (3). It is therefore important to define whether in the early stages of prostate carcinogenesis there is a relationship between testosterone levels and PCa. The present retrospective study, we wished to analyze the relationship between serum testosterone levels and the diagnosis of PCa after the first prostate biopsy in patients affected by ASAP. *Materials and Methods:* The medical records of 327 patients diagnosed with ASAP in an initial transrectal ultrasound-guided prostate biopsy (TRUSBx) for suspicious PCa were retrospectively reviewed. Patients with a history of biopsy, surgical treatment for prostatic disease, neoadjuvant therapy, and incomplete clinical data were excluded from our study. A total of 143 patients, mainly men, referred for erectile dysfunction in our andrology clinics, were eligible for this study. TS levels were measured preoperatively and also, patients have undergone prostate biopsy due to PCa suspicion. All patients enrolled in the study signed a consent form. TRUSBx was performed using an ultrasound machine equipped with a 5-9 MHz multi-frequency convex probe "end-fire". Three experienced urologists performed a 14-core biopsy scheme, as first intention. This biopsy scheme was changed based on TRUS findings concerning the size of the prostate and the possible suspicious regions, and varied from 8 cores from a small prostate to 18 cores for large prostatic glands. The decision for a second biopsy was based on ASAP diagnosis in the initial biopsy. The second biopsy was performed within 3-6 months from the first one. *Results:* All patients had a second biopsy and were suitable for further analysis. Pre-biopsy TS ranged widely from 153 to 968 ng/dl (median=462 ng/dl). TS levels were less than 299 ng/dl in 29 (20.3%), 300-399 ng/dl in 47 (32.9%), and equal to or greater than 400 ng/dl in 67 (46.9%) patients. Thus, low and normal TS groups were composed of 29 (20.3%) and 114 (79.3%) patients, respectively. There was no statistically significant association between pre-biopsy clinicopathologic parameters and pre-biopsy TS levels. The diagnosis of the second biopsy was ASAP in 36 patients (25.2%) and PCa in 52 patients (36.4%). The comparison between PCa patients and those with negative or an ASAP result in the second biopsy showed that men with cancer had significantly higher levels of TS ($p<0.001$). The cancer rate was 37.9% (50/132) in men whose biopsies involved more than 8 cores and was 18.2% (2/11) in those with 8 cores only. Finally, the rate of cancer detection was 24.2% (7/29) in low TS patients and 39.5% (45/114) in eugonadal patients ($p<0.002$). The Gleason score (GS) was assigned as follows: among patients with TS level ≤300 ng/dl, 57.1% (4/7) had a low GS, 28.6% (2/7) had a moderate GS, and 14.3% (1/7) had a high GS; among patients with TS level >300 ng/dl, 53.4% (24/45) had a low GS, 33.3% (15/45) had a moderate GS, and 13.3% (6/45) had a high GS. These findings were not statistically significant ($p=0.623$). *Discussion and Conclusion:* According to our current knowledge, this is the first study to examine the TS level as a clinical predictor in identifying the risk of PCa progression in patients with ASAP. In literature, few studies reported an association between high-grade intra-prostatic neoplasia diagnosis and TS levels at the second biopsy in terms of cancer progression, but not between ASAP and TS levels (2, 3). Our experience prompts that eugonadal patients may have higher risk for PCa diagnosis on re-biopsy after ASAP than hypogonadal. This reliable biomarker is inexpensive, reproducible, and serves to avoid prostate biopsies, which are associated with significant morbidity including pain, bleeding, and infectious complications. However, further studies are required to define the complex mechanism between androgen hormones and genetic factors in PCa etiology.

1 Leone L, Lacetera V, Montironi R, Cantoro U, Conti A, Sbrollini G, Quaresima L, Mariani L, Muzzonigro G and Galosi AB: Biopsy follow-up in patients with isolated atypical small acinar proliferation (ASAP) in prostate biopsy. Arch Ital Urol Androl *86*: 332-325, 2014.

2 Fiamegos A, Varkarakis J, Kontraros M, Karagiannis A, Chrisofos M, Barbalias D and Deliveliotis C: Serum testosterone as biomarker for second prostatic biopsy in men with negative first biopsy for prostatic cancer and PSA>4 ng/ml, or with PIN biopsy result. Int Braz J Urol *42*: 925-931, 2016.

3 Khera M, Crawford D, Morales A, Salonia A and Morgentaler A: A new era of testosterone and prostate cancer: from physiology to clinical implications. Eur Urol *65*: 115-123, 2014.

3

MANAGEMENT OF SYNCHRONOUS BILATERAL CLEAR RENAL CELL CARCINOMA: OUR EXPERIENCE AND REVIEW OF THE LITERATURE

Simone Scarcella, Lucio Dell'Atti,
Guevar Maselli and Andrea Benedetto Galosi

Institute of Urology, University Hospital "Ospedali Riuniti", Ancona, Italy

Background/Aim: According to the latest European Association of Urology Guidelines not only tumors smaller than 4 cm but also larger than 4 cm are treatable with nephron-sparing techniques and the oncologic outcomes seem to be similar between partial nephrectomy and radical nephrectomy cohorts. In addition it has been confirmed that patients losing a renal unit for RCC surgery are at higher risk for developing renal insufficiency and to die of non-cancer-related causes, such as cardiovascular events, compared to patients undergoing nephron-sparing techniques. Identifying multifocality and bilaterality of RCC in adult patients is of major importance due to its influence on surgical strategy, timing, and treatment modality used (1, 2). Managing these patients can be demanding due to clinical matters from diagnostic, prognostic and therapeutic perspectives: it is difficult to discriminate benign from malignant tumors only with imaging techniques considering small renal masses ≤4 cm. Multifocality is a relative contraindication to partial nephrectomy, and the role of biopsy in evaluation of renal masses remains controversial (2). We present a case report of an adult man affected by synchronous bilateral clear renal cell carcinoma, his surgical management and follow-up. *Case Report:* A 69-year-old Caucasian man underwent chest and abdomen computed tomography (CT) scan due to incidentally detected suspicious bilateral renal masses during a routine abdominal ultrasound in order to investigate possible cause of recurrence of urinary infection. His past medical history showed hypertension, dilated cardiomyopathy, atrial fibrillation, and severe chronic obstructive pulmonary disease (COPD). Laboratory findings were within normal limits, except for microscopic hematuria. Urine cytology was negative for malignancy. The CT scan revealed two solid enhancing lesions of the right kidney, one with maximum diameter of 43 mm, partially exophytic in the upper renal pole, and another lesion of 10 mm, completely endophytic, in the middle renal position. Furthermore, on the left kidney CT scan showed one solid enhancing lesion of 18 mm, partially exophytic, in the lower renal pole (Figure 1). However, there was no evidence of vascular invasion or lymphadenopathy. An ultrasound guided biopsy of the bigger mass was then performed and the histological examination showed a renal tumor with papillary and tubular aspects, and clear cytoplasm cells compatible with clear cell renal carcinoma. The patient, considering the severe COPD and the cardiovascular comorbidities, was then scheduled for an open nephron-sparing surgery (NSS). The surgery technique was performed using an intra-operative ultrasonography to identify intrarenal lesions and remove with a clampless procedure all renal masses. The patient was discharged after 5 days without post-operative complications. The definitive histopathological examination confirmed the diagnosis of clear renal cell carcinoma with growth aspects of papillary carcinoma (CK 7^{-}, CD 10^{+}, Vimentin^{+}, RCC^{+}). A whole-body CT was repeated every six months for two years, and no recurrence was documented preserving a renal function unchanged. *Discussion and Conclusion:* In the last decade NSS has largely supplanted the radical approach for the treatment of small renal masses. NSS for patients with sporadic ipsilateral renal tumors shows excellent long-term oncological outcomes and in the current era of expanding indications for NSS also patients with multiple renal tumors should be considered treatable with conservative techniques. Indeed, the coexistence of both bilateral and multifocal disease is rare, but several surgical case series have reported rates of bilaterality or multifocality of 4-5% and 6-13%, respectively (1, 2). The presence of multiple,

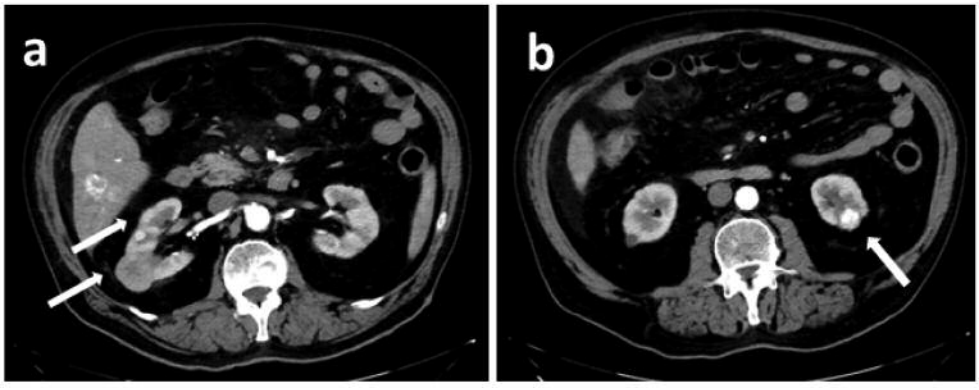


Figure 1. *Abdomen computed tomography scan.*

bilateral renal masses continue to be an unresolved clinical problem as shown in conflicting reports on therapeutic strategy and pathological aspects in these patients. Blute and colleagues observed a significantly higher rate of local recurrence in patients with bilateral nonhereditary renal masses compared to those treated for unilateral RCC, and these patients were classified in high-risk category (3). Although many investigators have reported excellent oncologic outcomes of patients with multifocal RCC treated by radical nephrectomy, the real clinical impact of tumor multifocality and bilaterality on cancer-specific survival is not completely understood, probably due to the low prevalence of multifocal RCC. However, recent data demonstrating the adverse effects of radical nephrectomy for small renal tumors on long-term renal function have further underlined the need to avoid radical resection in favour of partial nephrectomy for tumors <4 cm. Renal surgery for multifocal bilateral renal masses can be technically demanding and possibly associated with higher rates of intraoperative and postoperative complications but most renal units may be saved during repeated interventions. Furthermore, NSS provides low long-term haemodialysis rates and a favourable prognosis, which is comparable to patients with unilateral RCC. The surgical treatment of synchronous bilateral RCC represents a challenge for both long-term tumor control and renal function. Facing limited alternatives for this patient cohort, repeat nephron-sparing interventions to the fullest possible extent, is a better alternative to radical treatment. With this goal surgeons should always attempt NSS, whenever technically feasible.

1 Boorjian SA, Crispen PL, Lohse CM, Leibovich BC and Blute ML: The impact of temporal presentation on clinical and pathological outcomes for patients with sporadic bilateral renal masses. Eur Urol *54*: 855-863, 2008.
2 Klatte T, Wunderlich H, Patard JJ, Kleid MD, Lam JS, Junker K, Schubert J, Böhm M, Allhoff EP, Kabbinavar FF, Crepel M, Cindolo L, De La Taille A, Tostain J, Mejean A, Soulie M, Bellec L, Bernhard JC, Ferriere JM, Pfister C, Albouy B, Colombel M, Zisman A, Belldegrun AS and Pantuck AJ: Clinicopathological features and prognosis of synchronous bilateral renal cell carcinoma: an international multicentre experience. J Urol *100*: 21-25, 2007.
3 Blute ML, Itano NB, Cheville JC, Weaver AL, Lohse CM and Zincke H: The effect of bilaterality, pathological features and surgical outcome in non hereditary renal cell carcinoma. J Urol *169*: 1276-1281, 2003.

4
ARE ULTRASONOGRAPHIC MEASUREMENTS A RELIABLE PARAMETER TO CHOOSE A TREATMENT WITH TESTICULAR-SPARING SURGERY?

Lucio Dell'Atti, Paola Fulvi, Guevar Maselli and Andrea Benedetto Galosi

Institute of Urology, University Hospital "Ospedali Riuniti", Ancona, Italy

Background/Aim: The use of scrotal ultrasonography in the evaluation of urologic diseases, such as infertility, orchitis or trauma increased the detection of non-palpable testicular masses. Recent reports have shown that characteristics, such as the dimensions of lesions (≤1.5 cm), are critical for the management of small testicular masses, since they comprise an important parameter for the assessment of testiclular-sparing surgery (TSS) safety (1). The aim of this study was to analyze the dimensional characteristics between the testicular masses detected during ultrasonographic (US) study and their post-operative dimensions reported in definitive histological diagnosis. We further evaluated whether the US measurements are a relevant parameter to improve identification of testicular lesions amenable to treatment with TSS. *Materials and Methods:* This retrospective study was conducted in two academic referral centers between June 2006 and December 2016. A total of 77 patients who underwent radical orchiectomy or TSS for non-palpable testicular mass suspected for malignant neoplasm, were included to the study. Preoperative US studies were also carried out in all patients to evaluate the diameters, volume, and sonographic characteristics of the testicular lesions and the contralateral testes. US study was performed using a machine equipped with a 7-12 MHz multi-frequency linear probe. Testicular lesions were examined in at least two planes in the long and transverse axis, and calculated using the size (maximum diameter) of the mass. All patients underwent inguinal orchiectomy or testicular exploration (for masses ≤1.5 cm) through an inguinal approach under spinal anesthesia. All testicular masses were submitted to definitive histological examination including immunohistochemistry and were reviewed by a dedicated uro-pathologist. *Results:* The mean age at the time of diagnosis was 32.4 (22-74) years. In our study, scrotal pain was the first most common indication for US study in patients with incidentally discovered non-palpable testicular lesions (41.5%), followed by infertility (33.8%), scrotal mass (16.9%), and atrophy of testis (7.8%). Of the 77 patients studied, 75 had bilateral testes, 1 had only the right testis and 1 had only the left testis. The predominant finding was a hypoechoic mass (55/77; 71.4%). The vast majority of all malignant masses appeared markedly hypoechoic (44/49; 89.8%); moreover, this differed significantly from benign lesions (11/28; 39.3%, $p<0.001$). Calcified lesions were significantly associated with benignity (9/7; 77.8%, $p<0.002$). Of all 37 patients in whom TSS was accomplished, 15 had benign and 22 had malignant lesions. TSS was performed with no significant intra- and

postoperative complications, and all patients were discharged within 2 days after surgery. The mean maximum lesion diameter of the affected testicle determined by an US study preoperatively was 14.1 (7-24) mm and controlateral testicle was normal according to sonography in all cases. The mean maximum lesion determined by pathologist postoperatively was 13.4 (5-20) mm. Tumor lesions estimated by US study were more accurate in benign tumors. The capacity of sonography in estimating the dimensions of benign tumor was 94%, compared to 86% of malignant tumors, with no significant difference between seminal and non-seminal germ cell tumor. *Discussion and Conclusion:* In the past, all intratesticular lesions were theoretically treated with radical orchiectomy; however, to date, a TSS is supported especially for bilateral and/or multiple lesions or in monorchid patients. The advantages of TSS comprise the improvement of the patient's overall quality of life, endocrine function, fertility, and the avoidance of the negative cosmetic effects of radical orchiectomy (2). However, the indications for TSS as conservative treatment of testicular cancer are still controversial, especially for patients with normal contralateral testis (1, 2). There are few published data on the correlation between sonographic findings and the histological size of testicular tumors. Shtricker *et al*. reported that an US measurement of malignant testicular lesions underestimates the lesion size in 25% of the patients. Therefore, this evaluation can have a serious impact on the decision of TSS (3). According to the authors' opinion underestimation might be due to the inability of US to depict the peripheral layers of the malignancy tumor that are of clinical significance. However, the results of the present study indicate that a quantitative estimation of tumor diameter by sonography is an accurate method for detecting and measuring testicular masses in order to obtain an elective TSS.

1 Dell'Atti L: Efficacy of ultrasound-guided testicle-sparing surgery for small testicular masses. J Ultrasoud *19*: 29-33, 2015.

2 De Stefani S, Isgrò G, Varca V, Pecchi A, Bianchi G, Carmignani G, Derchi LE, Micali S, Maccio L and Simonato A: Microsurgical testis-sparing surgery in small testicular masses: seven years retrospective management and results. Urology *79*: 858-862, 2012.

3 Shtricker A, Silver D, Sorin E, Schreiber L, Katlowitz N, Tsivian A, Katlowitz K, Benjamin S and Sidi AA: The value of testicular ultrasound in the prediction of the type and size of testicular tumors. Int Braz J Urol *41*: 655-660, 2015.

7

PATTERN OF FAILURE IN POST-OPERATIVE PROSTATE CANCER BY MEANS OF PSMA-PET/CT

Rosario Mazzola[1], Berardino De Bari[2], Sergio Fersino[3], Dario Aiello[3], Fabiana Gregucci[3], Niccolo' Giaj-Levra[3], Alba Fiorentino[3], Francesco Ricchetti[3], Stefano Cavalleri[4], Matteo Salgarello[5] and Filippo Alongi[3]

[1]Division of Radiation Oncology, Sacro Cuore Don Calabria Cancer Care Center, Negrar, Verona, Italy; [2]Radiation Oncology, Centre Hospitalier Régional Universitaire Jean Minjoz, Besançon, France; [3]Urology, Sacro Cuore Don Calabria Cancer Care Center, Negrar, Verona, Italy; [4]Nuclear Medicine, Sacro Cuore Don Calabria Cancer Care Center, Negrar, Verona, Italy; [5]University of Brescia, Brescia, Italy

Background/Aim: Gallium-68-prostate-specific membrane antigen (^{68}Ga-PSMA) ligand positron emission tomography/computed tomography (PET/CT) has been advocated as an alternative to Choline PET/CT, as it seems to be more accurate in identifying macroscopic relapses, also at lower levels of rising PSA. Compared to the available literature, ^{68}Ga-PSMA PET/CT could allow a novel definition of the pattern of relapse in prostate cancer (PCa) patients, allowing a better tailoring of radiotherapy indication and volumes. The aims of this study were: i) to describe the pattern of relapse in PCa patients presenting with a biochemical relapse following surgery +/- adjuvant radiotherapy or androgen deprivation therapy (ADT) by using ^{68}Ga-PSMA PET/CT; ii) to evaluate whether nodal relapses patients identified with an early ^{68}Ga-PSMA PET/CT were located within the pelvic clinical target volume (CTV) defined by the Radiation Therapy Oncology Group (CTVRTOG); iii) to assess the impact of some clinical and therapeutic variables on the pattern of relapse of these patients. *Materials and Methods:* Forty patients received a ^{68}Ga-PSMA-PET/CT for a biochemical failure and 32/40 showed positive findings. All of them had received prior radical prostatectomy (RP). Post-operative radiotherapy had been delivered in 11/32 patients (34%), while other 11 patients (34%) had received ADT after surgery. The sites of recurrence and the impact of clinical and therapeutic variables on the pattern of relapse were reported. Also, the number of patients relapsing inside and/or outside the pelvic irradiation fields according to the RTOG guidelines (CTVRTOG), was analyzed. *Results:* Median PSA level before ^{68}Ga-PSMA PET/CT was 0.59 ng/ml (range=0.1-1.47 ng/ml). All patients had previously undergone RP +/- lymphadenectomy (between October 2002 and January 2017). Median number of removed lymph nodes was 9 (range=0-30). Ten out of 32 patients were referred to ^{68}Ga-PSMA-PET/CT for a biochemical recurrence following RP only (32%), while 11/32 patients received a ^{68}Ga-PSMA-PET/CT in the setting of biochemical recurrence following RP and salvage radiotherapy (34%), and 11/32 patients during

salvage ADT after RP (34%). In total, 8/32 patients (25%) presented with a ^{68}Ga-PSMA-PET/CT positive lymph node failure inside the CTVRTOG, 22/32 patients (68.75%) outside the CTVRTOG and 2/32 patients (6.25%) had nodal relapses, which occurred both inside and outside of the CTVRTOG. Overall, 36 positive lymph node lesions were identified: 23/36 nodal relapses (63%) were identified within the CTVRTOG and/or at the lomboaortic level. To cover 95% of these 23 relapses, a hypothetical CTV should encompass the nodal regions of the CTVRTOG as well as the paraaortic lymph node level up to T12- L1. Relapses outside the CTVRTOG were statistically more frequent than those inside the CTVRTOG (12/36 *vs*. 24/36, p=0.0095). Of the 24 patients presenting with a solely nodes relapse (75%), 8/24 (33%) positive lymph node recurrences were inside the CTVRTOG and 16/24 outside the CTVRTOG (66%, Pearson's chi-squared test p=0.04). The risk of presenting a relapse outside the CTVRTOG was not statistically different between the patients with only one positive lymph node compared to patients presenting with more than one positive ^{68}Ga-PSMA-PET/CT nodes (Pearson's chi-squared test p=0.53). *Conclusion:* In this preliminary analysis, the type of treatment seems to influence the pattern of relapse of PCa patients. In our population of post-operative patients, most of the recurrences appeared outside the CTVRTOG. ^{68}Ga-PSMA-PET/CT seems to be a useful tool to evaluate patients in this setting, as it allows an early identification of nodal or bone metastases and/or relapses outside the standard irradiated volumes.

8
PSMA PET/CT IN PATIENTS WITH LOW-LEVEL OF PSA AFTER RADICAL PROSTATECTOMY

Filippo Alongi[1], Berardino De Bari[2], Dario Aiello[3], Rosario Mazzola[3], Sergio Fersino[3], Fabiana Gregucci[3], Pierpaolo Alongi[4], Maurizio Nicodemo[5], Stefano Cavalleri[6] and Matteo Salgarello[7]

[1]Division of Radiation Oncology, Sacro Cuore Don Calabria Cancer Care Center, Negrar, Verona, Italy;
[2]Division of Radiation Oncology, Centre Hospitalier Régional Universitaire Jean Minjoz, Besançon, France;
[3]Division of Radiation Oncology, Sacro Cuore Don Calabria Cancer Care Center, Negrar, Verona, Italy;
[4]Division of Nuclear Medicine, Nuclear Medicine, Ospedale Giglio, Cefalù, Palermo, Italy;
[5]Division of Medical Oncology, Sacro Cuore Don Calabria Cancer Care Center, Negrar, Verona, Italy;
[6]Division of Urology, Sacro Cuore Don Calabria Cancer Care Center, Negrar, Verona, Italy;
[7]Division of Nuclear Medicine, Sacro Cuore Don Calabria Cancer Care Center, Negrar, Verona, Italy

Background/Aim: Recently, Gallium-68-prostate specific membrane antigen (^{68}Ga-PSMA) ligand positron emission tomography/computed tomography (PET/CT) has been increasingly evaluated as a potential alternative to Choline PET/CT, as it seems to be more accurate in the identification of macroscopic relapses at lower levels of prostate-specific antigen (PSA). The aim of the present study was to evaluate the impact of ^{68}Ga-PSMA-PET/CT in decision-making strategy for patients with relapsing prostate cancer (PC) presenting a second biochemical relapse after radical prostatectomy (RP) and salvage radiation therapy (RT) or salvage androgen deprivation therapy (ADT). *Materials and Methods:* Forty patients who had undergone prostatectomy were analyzed. Thirteen out of 40 were addressed to ^{68}Ga-PSMA-PET/CT for a biochemical relapse after RP, 14/40 after a salvage RT, and 13/40 after salvage ADT. The PSA level ranged between 0.1 and 1.62 ng/ml (median=0.51 ng/ml). The impact of additional data obtained from ^{68}Ga-PSMA-PET/CT on the decision-making process in a multidisciplinary tumor board was studied. *Results:* Thirty-one out of 40 evaluated patients showed positive findings at ^{68}Ga-PSMA-PET/CT (77.5%). Among them, 5 were positive in the prostatic bed, 9 in the pelvic nodes, 12 in nodes outside the pelvis, and 8 at bone level. Specifically, 9 patients presented two different sites of relapse (22.5%). In our experience, ^{68}Ga-PSMA-PET/CT data changed the therapeutic approach in 28 patients (70%) of all the study population. Six patients were candidates to no treatments before ^{68}Ga-PSMA-PET/CT; of them, 3 finally received SBRT, and 1 SBRT+ADT. In 66.6% of these patients, ^{68}Ga-PSMA-PET/CT changed the treatment. ^{68}Ga-PSMA-PET/CT had also an impact on patients who already had an indication for local treatments. Eleven patients at ^{68}Ga-PSMA-PET/CT had an indication for RT on prostatic bed and pelvic irradiation. Based on the results of ^{68}Ga-PSMA-PET/CT, 4 received also a boost on the positive pelvic nodes identified at ^{68}Ga-PSMA-11 (HBED-CC) PET/CT, 1 finally received SBRT and 1 palliative bone RT. *Conclusion:* ^{68}Ga-PSMA-PET/CT can be a useful tool in the restaging of post-RP, RT or ADT patients presenting biochemical relapse of PC, and it could change the decision-making process for up to 70% of these patients. Some important limitations of this study that could influence the external applicability of the results were, the small size of the study population, and the monocentric nature of the study surely. The lack of comparison of other standard imaging modalities could potentially be considered a bias; however, the available literature supports our indications of the superiority of ^{68}Ga-PSMA-PET/CT in terms of accuracy in this setting (1-3). Prospective, larger series are needed to establish the correct role of this very promising tool in the staging and therapeutic approach of PC patients.

1 Afshar-Oromieh A, Zechmann CM, Malcher A, Eder M, Eisenhut M, Linhart HG, Holland-Letz T, Hadaschik BA, Giesel FL, Debus J and Haberkorn U: Comparison of PET imaging with a (68)Ga-labelled PSMA ligand and ^{18}F-choline-based PET/CT for the diagnosis of recurrent prostate cancer. Eur J Nucl Med Mol Imaging *41*: 11-20, 2014.
2 Bluemel C, Krebs M, Polat B, Linke F, Eiber M, Samnick S, Lapa C, Lassmann M, Riedmiller H, Czernin J, Rubello D, Bley T, Kropf S, Wester HJ, Buck AK and Herrmann K: ^{68}Ga-PSMA-PET/CT in patients with biochemical prostate cancer recurrence and negative ^{18}F-choline-PET/CT. Clin Nucl Med *41*: 515-521, 2016.
3 Perera M, Papa N, Christidis D, Wetherell D, Hofman MS, Murphy DG, Bolton D and Lawrentschuk N: Sensitivity, specificity, and predictors of positive ^{68}Ga–prostate-specific membrane antigen positron emission tomography in advanced prostate cancer: A systematic review and meta-analysis. Eur Urol *70*: 926-937, 2016.

11

SALVAGE IMAGE-GUIDED MULTIPLE RE-IRRADIATION FOR LOCALLY RECURRENT PROSTATE CANCER WITH HIGH-PRECISION TECHNOLOGY: PROOF OF CONCEPT AND CLINICAL OUTCOMES

Stefania Volpe[1], Barbara Alicja Jereczek Fossa[1], Dario Zerini[1], Damaris Patricia Rojas[1], Cristiana Fodor[1], Andrea Vavassori[1], Paola Romanelli[1], Sabrina Vigorito[2], Elena Rondi[2], Stefania Comi[2], Raffaella Cambria[2], Federica Cattani[2], Samantha Dicuonzo[1], Paolo De Marco[2], Giuseppe Beltramo[3], Gennaro Musi[4], Ottavio De Cobelli[4], Giulia Marvaso[1] and Roberto Orecchia[1]

[1]Radiation Oncology Department, European Institute of Oncology, Milan, Italy;
[2]Department of Medical Physics, European Institute of Oncology, Milan, Italy;
[3]Radiation Oncology Department, CyberKnife Center CDI, Milan, Italy;
[4]Department of Urology, European Institute of Oncology, Milan, Italy

Background/Aim: Although androgen deprivation therapy (ADT) is widely recognized as a mainstay in the treatment of recurrent prostate cancer (PCa), newer data suggest that focal approaches (*e.g.* radiotherapy (RT), or high intensity focused ultrasound) may be considered in adequately selected patients. The aim of the current study was to present the technical feasibility and clinical outcomes of multiple external beam RT (EBRT) for low-burden locally recurrent PCa on a series of patients treated at a tertiary care center. *Materials and Methods:* Retrospective analysis of an updated series of patients who received multiple (>3 EBRT courses to prostate/prostate bed) re-EBRT with stereotactic image-guided technique and hypofractionated RT. Eight patients received three EBRT courses, 2 of them were candidates to subsequent forth EBRT following further local recurrence. No alternative focal approaches were considered. Two patients received surgery as a primary treatment modality; 6 were treated with EBRT +/- ADT. Local relapse was assessed by multiparametric magnetic resonance imaging (MRI) and/or choline positron emission tomography (PET). The presence of local recurrence was confirmed histologically in 4 cases (in other cases with univocal PET, MRI and PSA findings, all suggestive of recurrence, biopsy was not required). All patients had been evaluated for toxicity from previous EBRT per Radiation Therapy Oncology Group (RTOG)/ European Organization for Research and Treatment of Cancer (EORTC) criteria. Biochemical control was assessed according to 2006 Phoenix definition. Dosimetric constraints were based on previously published institutional experience on PCa re-RT. Previous treatment plans were retrieved for each patient. Computed tomography (CT) simulation EBRT sessions were performed with full bladder and empty rectum, according to oral and written instructions handed over during the first visit (water intake of 500 ml 30 minutes before CT scan and treatment; enema the day before CT simulation and low-fiber diet during radiation treatment). Gross tumor volumes (GTVs) were limited to the site of relapse; planning target volume margins were achieved expanding the GTVs of 3 mm posteriorly, and of 5 mm in any other direction. Clinical data and radiological of the primary and recurrent tumor were retrospectively collected from electronic medical records; treatment plans were retrieved for each patient using iPlan Net 3.0.0 (Brainlab, Munich, Germany) and Cyberknife MultiPlan® System for treatment planning (Accuray, Sunnyvale, CA, USA). *Results:* Mean age at second re-EBRT was 68 years [standard deviation (SD)=7.2 years]; all patients had a good performance status according to Karnofsky and Eastern Cooperative Oncology Group scoring system. At diagnosis, 4 cases were classified as high-risk PCa, 3 as intermediate and 1 as low per National Comprehensive Cancer Network 2017. Median follow-up time from diagnosis was 168.5 months [interquartile range (IQR)=144.2-203.1 months] for the whole cohort. In the non-surgical scenario (6 patients), mean PSA at the time of first and second relapse was 5.2 ng/ml (SD=3.7) and 5.3 ng/ml (SD=4.4), respectively. Median follow-up time from the third RT was 12 months (IQR=3.1-42.5); follow-up time from the forth RT course were 17 and 6 months. Biochemical progression-free intervals after the first and the second EBRT-course were 74 months (IQR=59.3-133.6) and 33 months (IQR=20.8-53.1), respectively. Biochemical and radiological response was registered in all patients; at present, 7/8 patients are free of disease. Overall toxicity profile was

good; no severe acute or late genitourinary or gastrointestinal events were recorded. *Conclusion:* Multiple-course re-EBRT with high precision technology and image guidance can be proposed as a possible salvage therapy for locally recurrent, low-burden PCa recurrence in adequately selected patients. Some room for further dose escalation is suggested. Additionally, re-EBRT may be regarded as an option for avoiding/deferring ADT in carefully selected patients. Larger series and longer follow-up are warranted to assess the potential of multiple re-RT in the setting of local salvage therapies for PCa.

12
HIGH-GRADE PLEOMORPHIC SARCOMA OF THE BLADDER: A RARE TUMOR IN UROLOGY

Valerio Olivieri[1], Luca Bellei[1], Massimo Massarelli[1], Massimo Ollino[1], Sandro Guglielmetti[1], Renzo Orlassino[2], Valentina Fortunati[2], Valter Pezzuto[2], Chiara Eberspacher[3] and Scipio Annoscia[1]

[1]Division of Urology, Ivrea Hospital, Turin, Italy; [2]Division of Pathology, Ivrea Hospital, Turin, Italy; [3]Division of General Surgery, Hospital Policlinico Umberto I, Rome, Italy

Background/Aim: Pleomorphic sarcoma is a rare tumor of the urinary tract, reported in limited literature. It commonly arises in men with a mean age of 60 years as a slow growing painless mass. Despite clinical presentation, it may change according to its primitive localization: macroscopic hematuria or irritative urinary symptoms are not unusual manifestations of this neoplasm. Herein, a case report of a 75-year-old patient who has been diagnosed with this rare tumor is presented. *Case Report:* A 75-year-old Caucasian male presented to our hospital with history of lower urinary tract symptoms (dysuria, urgency, hesitancy, terminal dribble) and recent gross hematuria. The patient did not give history of urolitiasis, flank pain or previous hematuria. No family history for urothelial cancer was referred during anamnesis. The patient was affected by benign prostatic hyperplasia and abdominal aortic aneurysm while on medication with acetylsalicylic acid. Many of these symptoms were initially attributed to prostatic disease; however, several episodes of symptomless gross hematuria of one month of duration were also reported. The patient was previously treated by general practitioner with empirical antibiotics for suspected urinary tract infection, though without any changes in clinical symptoms. General and systemic examination was unremarkable and no abnormalities were found during digito-rectal exploration, which revealed an enlarged soft gland without any suspicion of prostatic carcinoma or prostatitis. Ambulatory ultrasonography also revealed a voluminous endophytic mass of the bladder: no hydro-ureteronefrosis was described. The patient subsequently underwent to abdominal contrast-enhanced computed tomography that showed an 8-cm heterogeneously enhancing bladder mass at the dome and entirely left wall (Figures 1 and 2) with involvement of terminal left ureter (Figure 3). A mild left hydro-ureteronefrosis was also described. Anyway, no visceral or bone metastasis were reported. Cystoscopy revealed a broad-based tumor occupying almost the whole of the urinary bladder except for the right wall and trigone: both ureteric orifices were identified during endoscopic procedure. Due to the size of the mass, an open surgical procedure was preferred by performing cystotomy and complete excision of the bladder tumor. *Results:* The tumor was histologically diagnosed as pleomorphic sarcoma of the bladder with myxoid areas coexisting (Figure 4); muscular invasion was also confirmed. For accurate pathological diagnosis of undifferentiated pleomorphic sarcoma, immunohistochemistry was necessary for analyzing proliferation rate antigen Ki67, mitotic index, and immunophenotypic profile. Our results showed a Ki67 proliferative index of 50%, 85 mitotic counts per 10 high power fields and, immunophenotypic study showed that the tumor was positive for vimentine and CD68, though negative for Pan Cytokeratin (PanCK), desmin, and actin. *Discussion:* The majority of the bladder tumors described in the literature originates from the epithelium, while mesenchymal tumors account for fewer than 5% of all bladder tumors: liposarcoma, leiomyosarcoma, fibrosarcoma and angiosarcoms are present some variants of these tumors (1). Pleomorphic sarcoma is also reported among them. Etiology is not yet understood, although there is an association with pelvic radiation and systemic chemotherapy for other malignancies. Moreover, the rarity of the disease makes it difficult to assess the biological behavior of these tumors, which appear aggressive with a high-risk of local recurrence and metastasis. In this case, radical cystectomy was offered to the patient. This surgical approach plus adjuvant systemic chemotherapy has been reported in the literature (2, 3) as the best standard treatment for this neoplasm. Our patient refused any surgical treatment, thus, chemotherapy alone was administered after re-evaluation by a multidisciplinary tumor board. The patient was sent to a specialized center for the treatment of rare tumors in order to start the therapy and establish an appropriate follow-up. Transurethral resection of the bladder and histological analysis are both useful in characterizing this mesenchymal tumor. However, only immunohistochemistry is helpful for an accurate pathological diagnosis, since it is necessary in order to separate pleomorphic sarcoma from sarcomatoid urothelial carcinoma. Pleomorphic sarcoma is usually non-reactive for cytokeratin but it is often reactive for vimentin, α-1-antichymotrypsin, and CD68. To date, radical cystectomy plus adjuvant chemotherapy seems to be the best standard of

care; however, the rarity of cases limits the comparisons of the efficacy between different therapeutic strategies. Therefore, more studies enrolling a large number of patients are necessary for the development of therapeutic guidelines.

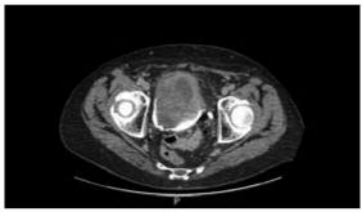


Figure 1. *Abdominal computed tomography of pleomorphic sarcoma; axial scan.*

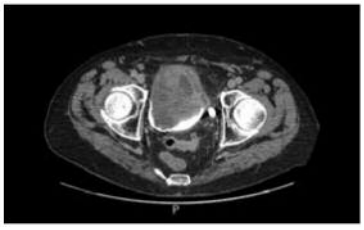


Figure 2. *Abdominal computed tomography of pleomorphic sarcoma; axial scan.*

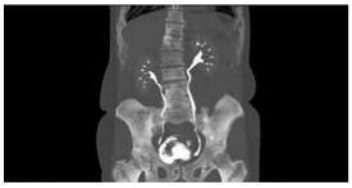


Figure 3. *Computed tomography of pleomorphic sarcoma; longitudinal scan.*

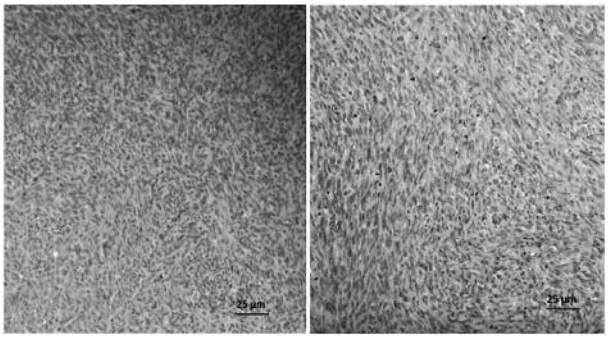


Figure 4. *High-grade pleomorphic sarcoma of the bladder. Hematoxylin-eosin (H/E) original magnification 10×.*

1 Povo-Martín I, Gallego-Vilar D, Bosquet-Sanz M, Miralles-Aguado J, Gimeno-Argente V, Rodrigo-Aliaga M and Gallego-Gómez J: Malignant fibrous histiocytoma of the bladder. A literature review. Actas Urol Esp *34*: 378-385, 2010.

2 Gunia S, May M, Koch S and Erbersdobler A: Is radical oncosurgery justified for the treatment of primary malignant fibrous histiocytoma of the urinary bladder? Report of two cases and analyses of disease-specific survival rates based on a review of the literature. Urol Int *86*: 261-268, 2011.

3 Katayama K, Fukumoto R, Hayashi T, Matsuoka A, Fujimoto N, Koide T and Kasugai T: A case of myxofibrosarcoma of the bladder. Hinyokika Kiyo *58(6)*: 291-293, 2012.

13
ABIRATERONE ACETATE PLUS RADIOTHERAPY IN OLIGOPROGRESSIVE METASTATIC CASTRATION RESISTANT PROSTATE CANCER PATIENT: A CASE REPORT

Giulia Poti[1], Serena Macrini[1], Silvana Giacinti[1], Francesca Romana Di Pietro[1], Maurizio Valeriani[2], Maria Bassanelli[1], Anna Maria Aschelter[1] and Paolo Marchetti[1]

[1]Division of Oncology, Sant'Andrea Hospital-Sapienza University, Rome, Italy;
[2]Institute of Radiation Oncology, Sapienza University, Sant'Andrea Hospital, Rome, Italy

Background: To date, several options for systemic treatment of metastatic castration resistant prostate cancer (mCRPC) exist (chemotherapy, androgen-receptor (AR)-axis-targeted therapy, bone-seeking-targeted radionuclide therapy). Likewise, a variety of palliative radiotherapy (RT) options are available in mCRPC. Therefore, search for new combination strategies of the aforementioned therapeutic options has become increasingly interesting. Abiraterone acetate (AA) is a selective CYP17A1 inhibitor approved for mCRPC patients who experienced or not disease progression after prior chemotherapy. This drug presents a good safety profile and improves overall survival and quality of life (1). *Case Report:* A 59-year-old patient underwent radical prostatectomy for a Gleason Score 9 (5+4) prostate cancer (pT3b pN0 pMx) with positive surgical margins, and bicalutamide (150 mg daily) was administered. Prostate-specific antigen (PSA) level was 20 ng/ml. After 15 months, a biochemical recurrence occurred and therapy was shifted to total androgen blockade with bicalutamide 50 mg daily plus leuprolin 3.75 mg, and salvage RT was performed. Five months after bipolar androgen therapy start, positron emission tomography (PET)-computed tomography (CT) scan showed progression in the bones. PSA level was 47 ng/ml.

Thus, a 3-weekly docetaxel-based chemotherapy (75 mg/m^2) was prescribed. After 6 months of therapy, PSA value decreased to 0.14 ng/ml (nadir) and CT scan demonstrated a partial response according to response evaluation criteria in solid tumors. Nine months after the onset of chemotherapy, PSA levels increased up to 27 ng/ml, and a PET-CT scan showed new hepatic metastasis. Thus, patient started AA plus prednisone (10 mg daily) with a biochemical response after 4 months, while PET-CT showed one pathologic uptake in back bone. Stereotactic ablative RT was performed on bone lesion and AA/prednisone treatment was continued. Complete blood count, PSA, PET-CT scan and bone scan were tested periodically. After 11 months of AA/prednisone, PET-CT revealed a stable disease without any new lesions. Patient is asymptomatic with a good performance status and therapy is ongoing. *Conclusion:* In this case of an oligoprogressive mCRPC (defined as 3 to 5 tumor sites progressing disease where all other sites are controlled by systemic drug), the addition of a local RT approach allowed the ongoing systemic treatment to continue. A local control strategy, *e.g.* RT, may be a valid therapeutic option to delay progression and to improve clinical benefits of oligometastatic/oligoprogressive mCRPC patients.

1 Emmenegger U, Cheng S, Zukotynski K and Cheung P: 840TiP Stereotactic ablative radiotherapy (SABR) for oligoprogressive metastatic castration-resistant prostate cancer (mCRPC) during abiraterone therapy: A phase I study. Ann Oncol 28(Suppl 5), 2017.

15
CYTOREDUCTIVE PROSTATE RADIOTHERAPY IN OLIGOMETASTATIC PROSTATE CANCER: A SINGLE CENTER ANALYSIS OF TOXICITY AND CLINICAL OUTCOME

Giulia Riva[1], Giuia Marvaso[1], Matteo Augugliaro[1], Dario Zerini[1], Cristiana Fodor[1], Gennaro Musi[2], Ottavio De Cobelli[2], Roberto Orecchia[3] and Barbara Alicja Jereczek-Fossa[1]

[1]Department of Radiotherapy, European Institute of Oncology, Milan, Italy; [2]Department of Urology, European Institute of Oncology, Milan, Italy; [3]Scientific Direction, European Institute of Oncology, Milan, Italy

Background/Aim: The current standard treatment of metastatic prostate cancer (mPCa) is androgen deprivation therapy (ADT) with or without anti-androgen and chemotherapy. Recently a large case series showed that local therapy (*e.g.* radiotherapy, RT; surgery) may improve tumor outcome prediction. The aim of this study was to define the role of a local RT treatment in the mPCa setting. *Patients and Methods:* We retrospectively reviewed data of patients with PCa and bone oligometastases, treated in our Institution with ADT, followed by cytoreductive prostate-RT with or without RT. Biochemical and clinical failure (BF, CF), overall survival (OS) and RT-toxicity were studied. *Results:* Twenty patients treated with ADT and external-beam RT on primary, between June 2008 and March 2016, were identified. Median age was 64.1 years, median Gleason score was 8, and median initial prostate-specific antigen (PSA) level was 14.7 ng/ml. The median number of bone metastases was 1 (range=1-4). All cases were discussed on the multidisciplinary tumor board. All patients but four were treated also for bone metastases. RT on primary with moderately and extremely hypofractionated regimes started after 8.6 months (range=2-51.7) from ADT initiation. After a median follow-up of 26.9 months (range=10.3-55.5) 18 patients are alive. Twelve patients showed BF after a median time of 23 months (range=14.5-104) and CF after a median of 23.6 months (range=15.3-106.1) from the start of ADT. The most common site of recurrence was bone. Three patients became castration resistant starting a new therapy, median time to castration resistance was 31.03 months (range=29.9-31.5 months). According to Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer (RTOG/EORTC), only one patient developed acute Grade 3 genitourinary toxicity. No late Grade>2 adverse events were observed. *Conclusion:* Prostate RT in oligometastatic patients is safe and offers long-lasting local control. When compared to ADT alone, RT on primary tumor seems to improve biochemical control and long-term survival. Further research is warranted towards the evaluation of RT on primary tumors and oligometastases, and to the definition of the optimal dose, timing, and combination with systemic therapy.

16
TARGETED SEQUENCING APPROACH FOR PROSTATE CANCER USING ION TORRENT PERSONAL GENOME MACHINE (PGM™) PLATFORM

Alessandra Mangolini[1], Miriam Servello[1], Cristian Bassi[2], Lucio Dell'Atti[3], Roberta Gafà[4], Christian Rocca[1], Martina Bandi[1], Giovanni Lanza[4], Carmelo Ippolito[1], Massimo Negrini[2] and Gianluca Aguiari[5]

[1]Division of Urology, University Hospital "St. Anna", Ferrara, Italy; [2]Department of Morphology, Surgery and Experimental Medicine, Section of Pathology, Oncology and Experimental Biology, University of Ferrara, Ferrara, Italy; [3]Institute of Urology, University Hospital "Ospedali Riuniti", Ancona, Italy;

[4]Department of Morphology, Surgery and Experimental Medicine, Section of Pathological Anatomy and Biomolecular Diagnostic, University Hospital "St. Anna", Ferrara, Italy;
[5]Department of Biomedical and Specialty Surgical Sciences, Section of Biochemistry, Molecular Biology and Medical Genetics, University Hospital "St. Anna", Ferrara, Italy

Background: Prostate cancer (PCa) is the second most common cancer in men, accounting for 15% of all diagnosed cancers (1). Currently, screening for PCa is one of the most controversial topics in the urological literature. In fact, PCa screening has led to a reduction in advanced disease and disease-specific mortality. However, many cases of overdiagnosis by using prostate-specific antigen (PSA) test were observed, leading to harmful treatments for patient quality of life. Therefore, the primary objectives of screening and early detection are: reduction in mortality and at least, a maintained satisfactory quality of life. Radical treatment, such as surgery and radiotherapy, can negatively impact long-term quality of life causing sexual, urinary, and bowel dysfunction. Moreover, androgen deprivation therapy used in short or long-term treatment can induce different side effects including loss of muscle mass, sexual problems, adverse metabolic sequelae, and increased cardiovascular risk. Many patients with screening-detected localized PCa will not benefit from definitive treatment and 45% of them are candidates for deferred management (active surveillance and watchful waiting) (2). The key point is the need to discriminate "latent" PCa from "lethal" PCa and subsequent over-diagnosis and over-treatment. Therefore, other biomarkers for a more accurate prognosis in PCa are needed. *Materials and Methods:* Tissue samples were collected form 48 patients (23 GS6, 11 GS7, 11 GS8 and 3 GS9) with pathologically confirmed PCa, who underwent curative radical prostatectomy, between 2010 and 2012. After 5 years of follow-up, patients were stratified into two groups (Table I) according to their prognosis (benign, n=25; poor, n=23). To confirm Gleason score (GS) and tumor cellularity, all formalin-fixed paraffin-embedded (FFPE) tumor tissue samples were stained with hematoxylin and eosine (H&E) and evaluated by genitourinary pathologist. Selected samples (both tumor and normal tissues from the same patient) were cut into 8×10 μm sections. One 4-μm thick section was stained with H&E to confirm tumor cellularity. Genomic DNA (gDNA) was extracted using the QIAmp FFPE tissue kit (Qiagen, Germantown, MD, USA) according to the manufacturer's instructions. gDNA was quantified by a Qubit® 2.0 Fluorometer (Thermo Fisher Scientific, Waltham, MA, USA) using Qubit® dsDNA HS Assay Kit. Libraries were prepared from 10 ng of gDNA using the Ion AmpliSeq™ On-Demand Panel (PC Panel). The PC Panel was designed using AmpliSeq.com program by selecting target regions of 16 genes (APC, AR, ATM, CDK12, CHD1, COL5A1, FOXA1, MED12, KMT2D, OR5L1, PIK3CA, PTEN, RB1, SPOP, TP53, ZFHX3), which are the more frequently mutated in PCa (cBioPortal database). The panel consisted of two DNA primer pools (pool 1: 337 amplicons, pool 2:331 amplicons) capable to amplify coding regions of maximum 150 bp to ensure optimal amplification. Overall, gDNA was subjected to library preparation according to the Ion Ampliseq Librery kit Plus (Thermo Fisher Scientific, Waltham, MA, USA). Target regions were initially amplified (20 PCR cycles) with a multiple PCR and the amplicons produced from pool 1 and pool 2 were combined and partially digested. Amplicons were then subjected to ligation of barcoded adapters and purified. Before sequencing, libraries were quantified using the Agilent™ 2100 Bioanalyzer™ (Agilent Genomics, Santa Clara, CA, USA) and diluted to 100 pM. Barcoded libraries, combined for maximizing chip use, labor and costs, were subjected to emulsion PCR using OneTouch™ Instrument and enriched by the OneTouch™ ES Instrument using the Ion PGM™ Hi-Q View™ OT2 Kit, following the manufacturer's instructions. Finally, sequencing was performed on the Ion PGM with the Ion PGM™ Hi-Q View™ Sequencing Kit (Thermo Fisher Scientific, Waltham, MA, USA), loading barcoded samples into a 316 v.2 BD chip (3). Sequencing data analysis was conducted by using Torrent Suite software v. 5.0 (Thermo Fischer Scientific, Milan, Italy). The alignment against a reference genome (hg19) was performed using the Torrent Mapping Alignment Program after low-quality reads removal and adapter sequences trimming. The Variant Caller (VC) plug in was used to identify variations from the reference sequence. To identify pathogenic variations, mutations that did not affect the protein coding regions were filtered out. All identified variants were visually confirmed by the Integrative Genome viewer (IGV). Genomic Evolutionary Rate Profiling (GERP) tools were used to predict the effect of missense mutations on the protein and calculate their conservation scores. *Results:* All 48 tumor and matched normal samples were sequenced. All target genes of the PC Panel were covered and the minimum coverage was 500×. Despite this high coverage, 5/48 FFPE samples revealed at least 50 amplicons with coverage between 500× and 100× and 20 amplicons with a coverage lower than 100×, suggesting that lower quality of gDNA could affect sequencing results. The PC Panel design had a high performance with high copy number of all amplicons except for the AMPL 7153036487 region, encoding AR gene (start 66765084-end 66765219, 136 bp), which was missing from the sequencing in all samples. The VC plug-in reported a total of about 3000 mutations (80% single nucleotide variants, SNVs and 20% indels), but they were successively filtered for coverage and mutation frequency. In fact, all variants with coverage lower than 100× and mutation frequency less than 8-10% were not considered. Moreover, results from normal and tumor tissue were

compared and variants present in both samples were excluded. Finally, a total of 95 variants were selected for annotation (92 SNVs, 2 indels, and 1 duplication). The 95 variants were found in 14 genes of the PC Panel, while no variants were annotated in two genes (OR5L1, CDH1). Analyzing the variant distribution between the selected genes, we found that KMT2D, AR, ATM, TP53, FOXA1, and CDK12 are the most frequently mutated genes in more than 50% of our cohort. MED12, ZFHX3, SPOP, and APC genes showed variants in about 30% of tumor samples, while the lower mutation frequency was observed in PTEN, RB1, COL5A1 and PIK3CA genes (Table II). Moreover, by matching gene mutations with the follow-up of patients, we observed that the gene variant frequency is different between patients with benign or poor prognosis. In fact, the mutation frequency is increased in ATM, ZFHX3, SPOP, APC, RB1, and TP53 in patients with poor prognosis, while variants present in KMT2D, COL5A1, AR, and CDK12 are decreased in the same population (Table III). No substantial variations were shown for the rest of the genes. *Discussion and Conclusion:* NGS analysis is a powerful approach to detect genomic lesions in PCa starting from low amount of DNA also in critical condition (FFPE Tissues). Our results are in line with data reported in the comprehensive databases published online indicating that PC Panel could individuate tumor variants that are involved in PCa in an efficiently manner. Moreover, some of the annotated variants were already known as recurrent in PCa and they were studied for their clinical implication in initiation, progression and pharmacological impact of PCa. Data from the two groups of patients indicated that "PC Panel" could individuate genome variations typical of PCa progression also in early disease stages. Importantly, somatic mutation in ATM, SPOP, TP53, and KMT2D, which are associated with PCa progression, may be also identified in patients with low Gleason score. In fact, it is known that PTEN and TP53 lesions are more frequently mutated in patients with advanced disease and, likely, the co-localization with SPOP mutations is associated with poor prognosis (4). Moreover, mutation in SPOP gene may promote a more aggressive clinical behavior by increasing genome instability. In conclusion, targeted sequencing approach could increase the possibility to distinguish the patient risk profile improving PCa management strategies.

1 Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM and Forman D: Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer *136*: E359-356, 2015.

2 Albertsen, P.C. Observational studies and the natural history of screen-detected prostate cancer. Curr Opin Urol *25*: 232, 2015.

3 Rothberg JM, Hinz W, Rearick TM, Schultz J, Mileski W, Davey M, Leamon JH, Johnson K, Milgrew MJ, Edwards

Table I. *Cohort of patients with prostate cancer.*

	Gleason Score			
	6	7	8	9
Patient (n)	23	11	11	3
Years (mean)	71.4	73.3	71.6	70.7
Benigne prognosis (n)	18	5	2	0
Poor prognosis (n)	5	6	9	3

Table II. *Variant distribution in the analyzed cohort.*

Genes	Patients with gene mutations	
	(n)	%
KMT2D	33	68.8
AR	31	64.6
ATM	29	60.4
TP53	28	58.3
FOXA1	28	58.3
CDK12	27	56.3
MED12	22	45.8
ZFHX3	22	45.8
SPOP	16	33.3
APC	19	39.6
PTEN	14	29.2
RB1	11	22.9
COL5A1	9	18.8
PIK3CA	8	16.7

Table III. *Variant distribution in the analyzed cohort considering 5 years of follow-up.*

Genes	Number of patients with gene mutations	
	Benign prognosis	Poor prognosis
PTEN	7	7
ATM	12	17
KMT2D	19	14
MED12	11	11
ZFHX3	9	13
PIK3CA	5	3
FOXA1	15	13
SPOP	5	11
APC	8	12
COL5A1	6	3
RB1	5	7
TP53	12	16
AR	17	14
CDK12	15	12

M, Hoon J, Simons JF, Marran D, Myers JW, Davidson JF, Branting A, Nobile JR, Puc BP, Light D, Clark TA, Huber M, Branciforte JT, Stoner IB, Cawley SE, Lyons M, Fu Y, Homer N, Sedova M, Miao X, Reed B, Sabina J, Feierstein E, Schorn M, Alanjary M, Dimalanta E, Dressman D, Kasinskas R, Sokolsky T, Fidanza JA, Namsaraev E, McKernan KJ, Williams A, Roth GT, Bustillo J: An integrated semiconductor device enabling non-optical genome sequencing. Nature *475*: 348-352, 2011.

4 Barbieri CE, Demichelis F, Rubin MA: The lethal clone in prostate cancer: Redefining the index. Eur Urol *66*: 395-397, 2014.

17
NEW TECHNOLOGIES IN RADIOTHERAPY FOR PROSTATE CANCER: FEASIBILITY, DOSIMETRIC ASPECTS AND CLINICAL RESULTS IN PATIENTS WITH AT LEAST 5-YEAR FOLLOW-UP

Antonella Sicilia, Luca Eolo Trodella, Rolando Maria D' Angelillo, Michele Fiore, Aurelia Lurato, Alessia Carnevale, Carlo Greco, Marianna Miele, Pasquale Trecca, Lucio Trodella and Sara Ramella

Division of Radiotherapy, Campus Bio-Medico of Rome University, Rome, Italy

Background/Aim: Radiotherapy (RT) for prostate cancer has been constantly evolving over the last few decades, improving overall survival, cancer-specific and time progression of the disease. Different studies have shown a strong association between survival and RT doses (≥76 Gy). Advanced RT techniques such as modulated intensity (IMRT) and modulated intensity dynamic volumetric therapy (VMAT) facilitate and allow higher doses, minimizing the side effects on healthy surrounding tissues. *Patients and Methods:* A total of 261 prostate cancer patients referred to our institution for radical treatment, from January 2010 to December 2014, have been reviewed. Dosimetric comparison between IMRT and VMAT was made to evaluate the constraints (dose limits) for the organs at risk (OARs) in the district: the rectum, the bladder, the femoral heads, and the penile bulb. In addition, toxicity was assessed (according to CTCAE version 4.02 scale), progression-free survival (PFS) and overall survival (OS). Progression disease has been evaluated from a clinical point of view, through laboratory and radiological examinations. *Results:* Patients (49 at low-risk, 101 at intermediate-risk, and 111 at high-risk) were treated with radical RT for a total dose of 80 Gy (the pelvis was included in the volume of treatment in 57 patients). Of those, 208 were treated with IMRT technique and 53 with VMAT technique. Average age of patients was 72 years (range=42-86 years). Median PSA was 7.47 ng/ml and the minimum follow-up was 30 months. Dosimetric data showed that VMAT technique achieved better compliance with constraints for OARs, reducing the percentage of patients that deviated from dose limits. No patient exhibited Grade 2 Gastrointestinal (GI) and Genitourinary (GU) toxicity. G2 GI and G2 GU toxicity was reported in 13.5% and 5.7% of patients, respectively, at 5 years. PFS at 5 years was 82% for low- and intermediate- risk patients and 81% for high-risk patients. At 5 years, OS of the entire cohort was 93.2%. OS of the population by risk class stratification, at 5 years, can be summarized as follows: at 100% low-risk; in the intermediate-risk of 90% and in the high-risk of 93%. *Conclusion:* Reviewing our patients with at least 5-year follow-up, low acute and late toxicity was observed. This evidence could support the adoption of further dose escalation mainly in high-risk patients.

19
CLINICAL AND PLASMATIC MARKERS OF VISCERAL ADIPOSE TISSUE ACTIVITY DO NOT CORRELATE WITH GLEASON PATTERNS 4 AND 5 DETECTION AT PROSTATE BIOPSY

Vincenzo Serretta[1], Cristina Scalici Gesolfo[1], Alberto Abrate[1], Simone Siracusano[1], Marco Vella[1], Fabrizio Di Maida[1], Alchiede Simonato[1], Antonina Cangemi[2] and Elisabetta Barresi[3]

[1]Section of Urology, Department of Surgical, Oncological and Stomatological Sciences, University of Palermo, Palermo, Italy;
[2]Section of Oncology, Department of Surgical, Oncological and Stomatological Sciences, University of Palermo, Palermo, Italy;
[3]Department of Human Pathology, University of Palermo, Palermo, Italy

Background/Aim: The correlation between prostate cancer (PCa) and obesity remains controversial, mainly based on the association of body mass index (BMI) with pathology after surgery. BMI has a low correlation with adipose tissue distribution and activity. The aim of the study was to relate BMI, visceral adiposity index (VAI), a novel marker of fat tissue activity, and the plasmatic levels of leptin, adiponectin and matrix metalloproteinase-3 (MMP-3), biomarkers of adipose tissue function, with the detection of Gleason patterns 4 and 5 at biopsy. *Materials and Methods:* Consecutive patients with PCa detected at 12-core transrectal biopsy performed due to elevated PSA levels and/or positive digital rectal examination were enrolled. BMI and waist circumference (WC) were obtained at the time of biopsy. Blood samples were collected immediately before biopsy to evaluate the plasmatic levels of triglycerides (TG), high density lipoproteins (HDL), adiponectin, leptin and MMP-3.

The Visceral Adiposity Index (VAI) was obtained as described in literature according to the following formula: WC/[39.68 + (1.88×BMI)] × TG/1.03×1.31/HDL. *Results:* 149 patients harboring PCa with median values of PSA, BMI, and VAI of 10.0 ng/ml, 27.6 kg/m^2, and 4.6 respectively, were entered. Gleason patterns 4 or 5 were detected in 68 (45.6%) patients; in 15 (41.7%), 31 (44.9%) and 22 (50.0%) among normal weight, overweight and obese patients, respectively (p=0.55). The statistical analysis did not show any significant correlation between BMI (p=0.56), VAI (p=0.35), the plasmatic levels of leptin (p=0.18), adiponectin (p=0.68), MMP-3 (p=0.49) and the detection of Gleason patterns 4 and 5 at biopsy. A statistically significant association emerged only with older age (p=0.017) and higher PSA values (p=0.02). *Conclusion:* Although high-risk PCa has been reported to be more frequent in patients with elevated BMI, we did not detect any correlation between clinical markers of obesity (BMI or VAI) and diagnosis of an aggressive PCa at biopsy. Moreover, we found no association between the plasmatic levels of leptin, adiponectin and MMP-3, biomarkers of visceral fat activity, and the presence of Gleason pattern 4 and 5. However, for this specific population we cannot exclude the protective effect of the Mediterranean diet, life-style, and other environmental factors against the development of aggressive prostate tumors induced by obesity and metabolic syndromes.

GSTU Foundation, Palermo, Italy for the laboratory kits supply and the statistical support.

20

RENAL ADVERSE EVENTS IN ADVANCED CANCER PATIENTS TREATED WITH TARGETED THERAPY: A RETROSPECTIVE ANALYSIS AND CORRELATION WITH SURVIVAL

Michela Roberto[1], Maria Bassanelli[1], Alessia Nave[2], Silvana Giacinti[1], Giulia Poti[1], Claudia Fofi[2], Anna Maria Aschelter[1], Paolo Menè[2] and Paolo Marchetti[1]

[1]Department of Clinical And Molecular Medicine, Division of Oncology, Sapienza University of Rome, Rome, Italy; [2]Division of Nephrology, Sapienza University of Rome, Rome, Italy

Background: The anti-VEGF monoclonal antibody (bevacizumab), the mammalian target of rapamycin (mTOR) inhibitors (everolimus and temsirolimus), and the anti-VEGFR tyrosine-kinase inhibitors (anti-VEGF TKIs) represent effective treatment options for several metastatic solid tumors. As described in literature, these targeted agents may cause renal toxicity. Although renal adverse events are most often mild in severity, may sometimes lead to treatment discontinuation. It is known that VEGF is fundamental to the maintenance of renal function. Therefore, it is possible that using multi-kinase-targeted therapies (TTs) might disorganize normal glomerular function, leading to kidney injuries. However, the most frequently reported manifestations are any grade of both proteinuria and creatinine increase, which may regress after TTs dose adjustment. The exact incidence of renal toxicities and TTs-related mechanism of action are still unknown. A multidisciplinary evaluation with an early nephrological intervention may be useful to manage patients more carefully, prevent treatment discontinuation and to improve survival. *Patients and Methods:* Patients affected with several advanced stage tumors (6 breast, 22 kidney, 5 colon, 1 neuroendocrine pancreas), treated with targeted therapy and subjected to nephrological evaluation from December 2013 to January 2017 at our Institution, were enrolled in this study. Renal toxicities were graded according to the Common Terminology Criteria for Adverse Events version 4.0. Time to renal failure (TRF) was calculated as the time from starting TTs to the first renal event, defined as a value of creatininaemia ≥001.5 mg/dl and/or proteinuria >1000 mg/24 h. SPSS software v.24, was used for statistical analysis. *Results:* According to TTs class, in total 34 Patients were grouped as followed: i) 11 (32.4%) anti-VEGF (bevacizumab); ii) 14 (41.2%) VEGF-TKI (sunitinib, sorafenib, pazopanib, axitinib); iii) 9 (26.4%) mTOR inhibitors (temsirolimus, everolimus). With a median follow-up of 25 months, 23 (67.6%) patients reported a renal event including 14 (60%) of grade 2 (3 proteinuria, 11 hypercreatininaemia) and 6 (26%) of grade 3 (4 proteinuria, 2 hypercreatininaemia) (Figure 1). None grade 4 event or death for toxicity occurred. Twenty-two patients discontinued TTs for toxicity. After 1 month, toxicity regressed in 8 (23.5%) patients which resumed treatment at lower dosage with good tolerability. However, 14 (41.1%) finally stopped TTs for persistent proteinuria and/or hypercreatininaemia. Overall, the median time of TTs treatment was 15 months and the median TTRF was 5±10 months. The median TTRF occurred significantly later in patients treated with anti-VEGF *versus* VEGF-TKI or mTOR inhibitors (12.0 *vs*. 4.5 or *vs*. 4.5 months, respectively; p=0.004). Moreover, median overall survival (OS) of patients who experienced a renal event was better compared to patients who did not report renal events [53 *vs*. 42 months, hazard ratio, (HR)=0.57, 95% confidence interval (CI)=0.17-1.87; p=0.3] (Figure 2). *Conclusion:* There is some evidence that side effects may be used as biomarkers of response to anti-angiogenic agents (1). Previous studies have evidenced interdependence between the occurrence of toxicity (*i.e*. hypertension) in patients receiving anti-VEGF-TKI and outcomes. The results of our study suggest that the detection of renal side effects may be associated with a better survival. Indeed, a risk reduction of about 40%, as described by an HR=0.57 for OS, between patients with renal events compared to those without, was clinically relevant. However,

this association failed to reach statistical significance, possibly due to the limited sample size. Surely, a careful onco-nephrology intervention should lead to an early toxicity regression and treatment continuation, resulting from longer response to TTs and better outcome. However, further, larger studies are needed to confirm these results.

1 Dienstmann R, Braña I, Rodon J and Tabernero J: Toxicity as a biomarker of efficacy of molecular targeted therapies: focus on EGFR and VEGF inhibiting anticancer drugs. Oncologist *16(12)*: 1729-1740, 2011.

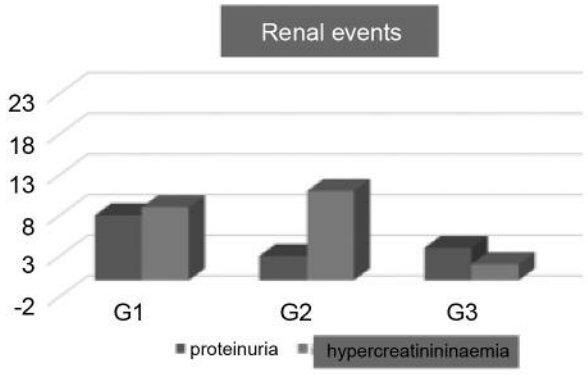


Figure 1. *Renal Adverse Events reported according to CTCAE classification.*

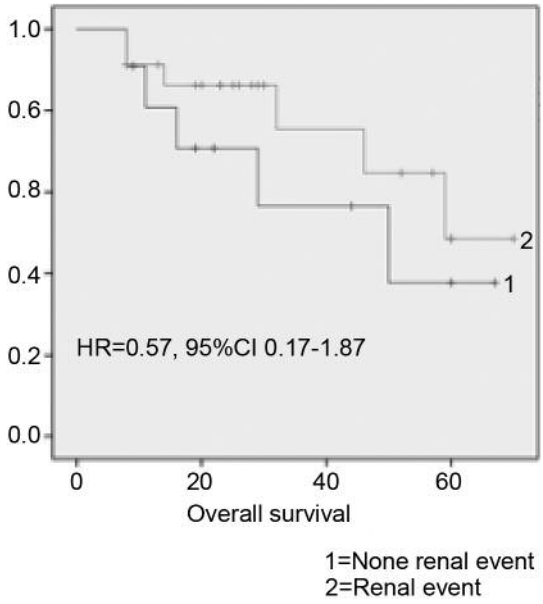


Figure 2. *Kaplan-Meier survival curve of patients who did or did not experience renal events.*

21
CAN THE BODY MASS INDEX HAVE AN IMPACT ON OUTCOMES IN MEN TREATED BY ROBOTIC RADICAL PROSTATECTOMY?

Lucio Dell'Atti, Luca Leone, Erica Palagonia, Lorenzo Montesi and Andrea Benedetto Galosi

Institute of Urology, University Hospital "Ospedali Riuniti", Ancona, Italy

Background/Aim: Obesity is associated with an increased risk of advanced aggressive disease and death from prostate cancer (1). Several large studies have shown that higher body mass index (BMI) is related with higher grade tumors, increased risk of biochemical recurrence, positive surgical margins (PSM), and capsular incision after radical prostatectomy (RP) (2). However, many of these studies are limited by small sample size (1, 2). In this study we estimated the impact of BMI on operative time (OT), estimated blood loss (EBL), length of hospital stay (LOS), complications and pathologic outcomes in patients who underwent robot-assisted radical prostatectomy (RARP) *versus* open RP. *Materials and Methods:* We retrospectively reviewed a series of 677 patients who underwent RARP [Group 1 (G1)] or open RP [Group 2 (G2)] at two tertiary academic referral centers between 2013 and 2016. Excluding patients with BMI≤30 kg/m^2 and those who had undergone neoadjuvant hormonal therapy left 181 patients for analysis. Operations were performed either transperitoneally with modified Montsouris approach (G1:121 patients) or extraperitoneally (G2:60 patients). Prostatectomy specimens were examined by dedicated genitourinary pathologists. Intraoperative parameters evaluated were: OT, EBL, complications, nerve sparing status, and pelvic lymph node dissection (PLND). Postoperative data were PSM, Gleason score (GS), pathological stage (pT), tumor volume (TV), LOS, and postoperative complications (PCs). *Results:* The groups were statistically comparable for age, PSA, GS biopsy and clinical stages. Pelvic lymphadenectomy was performed in 61.2% of G1 and 83.3% of G2, whereas nerve sparing was performed in 86% of G1 and 91.6% of G2. The mean number of PLND per patient was 12.1 in G1 and 14.3 in G2. Mean OT was significantly greater (p<0.01) in G1 at 216±32 min *versus* 178±93 min in G2. Mean EBL in G1 and G2 patients were 279.20±227.20 ml and 879.09±386.06 ml, respectively (p<0.01). The comparison of mean LOS, 3.12±1.24 days in G1 and 4.53±1.34 days in G2 (p<0.01). Pathological data analysis did not demonstrate a significant difference in PSM between G1 (20.6%) and G2 (21.6%) (p=0.32). The factors that could affect the PSM, such a GS and pT, were evenly distributed amongst the two groups. Overall the TV was 0.9±0.85 cc in obese patients. TV was statistically significant when related to GS [odds ratio (OR)=37%, p<0.001], extraprostatic extension (OR=30%,

p=0.008), and lymph node positivity (OR=35.5%, p=0.002). There was no correlation between surgical technique used and PCs. *Discussion and Conclusion:* Obese men have higher rates of co-morbid diseases including, but not limited to hypertension, coronary artery disease, and diabetes mellitus. In our cohort of patients affected by prostate cancer, obese men tended to have an elevated ASA (American Society of Anesthesiologists) score, but did not reach statistical significance (p=0.283). Pelvic surgery in general is more technically challenging in obese patients, because the pelvic fatty tissue may compromise the pelvic space and hinder the surgeon's visualization, increasing the time required for surgical dissection and intraoperative complications. Therefore in literature, obesity has been associated with 30% higher odds of OT, EBL, LOS and PSM (3). In this study, nerve sparing, a factor that may affect PSM, was performed in equal numbers between the two groups (p=0.14), and pathological data analysis did not demonstrate a significant difference in PSM. The overall PCs experienced by patients with high BMI in the different techniques were similar (p=0.21). These results suggest that obese patients with prostate cancer can undergo RARP safely and with similar oncologic outcomes comparable to open RP.

1 Gu X, Araki M and Wong C: Does elevated body mass index (BMI) affect the clinical outcomes of robot-assisted laparoscopic prostatectomy (RALP): a prospective cohort study. Int J Surg *12*: 1055-1060, 2014.
2 Castle EP, Atug F, Woods M, Thomas R and Davis R: Impact of body mass index on outcomes after robot assisted radical prostatectomy. World J Urol *26*: 91-95, 2008.
3 Freedland SJ, Terris MK, Presti JC Jr, Amling CL, Kane CJ, Trock B and Aronson WJ: Obesity and biochemical outcome following radical prostatectomy for organ confined disease with negative surgical margins. J Urol *172*: 520-524, 2004.

22
URETERAL CARCINOMA PRESENTING WITH SINGLE SUPRACLAVICULAR LYMPHNODE METASTASIS

Valerio Olivieri[1], Luca Bellei[1], Massimo Massarelli[1], Massimo Ollino[1], Sandro Guglielmetti[1], Renzo Orlassino[1], Valentina Fortunati[1], Chiara Eberspacher[2] and Scipio Annoscia[1]

[1]Division of Urology, Ivrea Hospital, Ivrea, Turin, Italy; [2]Division of General Surgery, Hospital "Policlinico Umberto I", Rome, Rome

Background/Aim: Primary transitional cell carcinomas of the ureter frequently develop distant metastasis to lungs, bones and brain. Moreover, according to their localization, these tumors are generally associated with regional lymph node metastases that impact the overall survival. Paraaortic, paracaval, ipsilateral common iliac or pelvic lymph nodes are more commonly involved, while others are very rarely involved. We report the case of a supraclavicular single lymph node metastasis as the onset of a ureteral carcinoma in an old female patient. *Case Report:* A 78-year-old female patient presented to our facility for flank pain poorly responsive to non-steroidal anti-inflammatory drug therapy. The patient has suffered for several months but pain intensified during last weeks. No episodes of gross hematuria, fever or irritative symptoms of micturition were referred during anamnesis; however, many episodes of urolithiasis with spontaneous expulsion of urinary stones were reported by the patient. On physical examination the abdomen was soft with Giordano's test a mildly positive on right flank. Moreover, a fixed supraclavicular lymph node on left side was identified during medical inspection, initially suspicious for metastasis coming from aerodigestive tract tumor. In contrast with this hypothesis, no symptoms of weight loss, melaena, haematemesis or dyspepsia were referred. An ambulatory ultrasound showed a voluminous right renal pelvis without visualizing homolateral parenchyma, both elements suggestive for pelvic junction pathology. Due to the discovery of suspicious supraclavicular lymph node and in exclusion of concurrent right upper tract urolithiasis, the patient underwent a total body contrast-enhanced computerized tomography (CT). The exam revealed a voluminous right hydronephrosis without visualizing iodinate contrast excretion, highly suggestive for ureteropelvic junction pathology. No signs of urinary stones in the right ureter were described. The scan also revealed a 2-cm bladder thickening on right ureteric orifice with secondary upper tract dilatation. Moreover, the middle-distal right ureter was described as thickened with inhomogeneous contrast enhancement, tenaciously adhering to psoas muscle without a clear cleavage plane. Pelvic lymph nodes were negative, while aortocaval were increased in dimension and strongly suspicious for urothelial metastatic spread originating from ureter. No hydronephrosis, on the contrary, was highlighted on left side and no signs of other metastases were identified on liver, lung or bone. Lymphadenopaty with enlarged lymph nodes in the left head-neck region, in detail a diameter of 37 mm in supraclavicular one and 23 mm in the posterior jugular region one, was reported. Cytology resulted positive for atypical cells. For this reason the patient was enrolled for a biopsy of the left supraclavicular node in order to confirm the urothelial origin of the metastatic involvement. *Results:* Pathological examination concluded on the urothelial metastatic involvement of lymph node. Moreover, few days before the surgical

procedure, the patient also presented swelling and severe pain in the left leg. Suspecting a deep vein thrombosis, the patient underwent a color-Doppler examination, which confirmed the thrombosis in deep femoral vein; hence, low weight heparin was administered. In consideration of the general performance status, the poor prognosis, the neoplastic staging, the presence of multiple metastases, and the deep vein thrombosis as an expression of a paraneoplastic syndrome, no surgical or chemotherapeutic therapies were possible and patient received only pain palliation therapy. *Discussion and Conclusion:* Upper tract carcinoma is a common cancer of the urogenital system. It often presents with painless gross hematuria, weight loss, asthenia, or flank pain due to homolateral hydronephrosis; however, in some cases these symptoms can be missing so that the diagnosis is delayed with a strong impact on cancer progression and patient's prognosis. The involvement of lymph nodes has been reported in the literature as a variable strongly associated with tumor grading and staging. Genitourinary tract tumors may be linked with lymph node involvement, but they rarely spread to cervical nodes. Metastases to head-neck region are extremely rare and only few reports have been published (1, 2), all with poor prognosis. Moreover, the most frequent metastasis location in these cases is supraclavicular lymph node, probably by hematogenous way. However, because of the very few cases reported in literature, it is also hard to establish the most effective therapeutic strategies, which seem to be palliative radiotherapy and chemotherapy (3). In our case, owing to rapid disease progress, the patient died 2 months after diagnosis. In conclusion, genitourinary tumors have been shown to rarely metastasize to head-neck region. Few cases of this unusual metastasis are described in the literature, confirming that unexpected lymph node metastasis can be seen in ureteral tumor. For this reason the work-up of new head or neck lesions in a patient with a history of urothelial cancer should include metastases as part of the differential diagnosis.

1 Hessan H, Strauss M and Sharkey FE: Urogenital tract carcinoma metastatic to the head and neck. Laryngoscope *96(12)*: 1352-1356, 1986.

2 Hunt JL, Tomaszewski JE and Montone KT: Prostatic adenocarcinoma metastatic to the head and neck and the workup of an unknown epithelioid neoplasm. Head Neck *26(2)*: 171-178, 2004.

3 Pynnonen MA, Gillespie MB, Roman B, Rosenfeld RM, Tunkel DE, Bontempo L, Brook I, Chick DA, Colandrea M, Finestone SA, Fowler JC, Griffith CC, Henson Z, Levine C, Mehta V, Salama A, Scharpf J, Shatzkes DR, Stern WB, Youngerman JS and Corrigan MD: Clinical practice guideline: evaluation of the neck masses in adults. Orolaryngol Head Neck Surg *157(2_suppl)*: S1-S30, 2017.

23

CRYOSURGICAL HEMIABLATION FOR LOW AND INTERMEDIATE RISK OF PROSTATE CANCER: 4 YEARS OF FUNCTIONAL AND INITIAL ONCOLOGICAL OUTCOMES

Giovanni Silecchia, Luigi Cormio, Oscar Selvaggio, Rocco Di Brina and Giuseppe Carrieri

Division of Urology, University of Foggia, Foggia, Italy

Background/Aim: Currently there are many different options for the treatment of prostate cancer, particularly for the low and intermediate risk variety from D'Amico risk classification (1). According to the latest European Association of Urology (EAU) guidelines, there are different types of standard treatments for low- and intermediate- risk prostate cancer including Cryoablation therapy. The goal of surgery is to eradicate the disease by preserving continence and sexual potency when possible (2). The aim of this study was to determine safety and success of cryo-hemiablation of prostate cancer in terms of early functional recovery of erectile function, urinary continence, perioperative/postoperative complications and good oncological control. *Materials and Methods:* We performed a retrospective analysis of 45 patients who underwent focal hemiablation for biopsy proven unilateral prostate cancer (<T2b). All patients underwent an entry-staging biopsy. Potency was defined as the ability to penetrate quantified pre- and post-operatively as a score > 3 for International Index of Erectile Function (IIEF)-5 question 2. All patients underwent to post-operatively stress-test to evaluate onset of stress incontinence. Serum prostate-specific antigen (PSA) was sampled every 3 months for the first 2 years, then every 6 months for 5 years, and every 1 year for 10 years. Biochemical failure was defined according to the Phoenix criteria of PSA rising >2 ng/ml of nadir (3). All patients with biochemical failure underwent to target biopsy. Local recurrence was defined as prostate cancer in treated lobe; tumor progression was defined as prostate cancer in non-treated lobe. Complications were scored using the Clavien-Dindo scale. Every patient had signed a specific informed consent. This study was carried out in agreement with applicable laws and regulation good clinical practice and ethical principles as described in the Declaration of Helsinki in1975 and revised in Tokyo in 2008. *Results:* From February 2013 to September 2017, 45 patients meeting inclusion criteria underwent entry-staging biopsy, and then were treated with cryo-hemiablation of prostate. Patients' characteristics and pathological features are reported in Table I. Median follow-up was 21,72 months, though in this study we reviewed data from 1-year follow-up. Concerning erectile function, 84.4% (38/45) of patients had IIEF-5 question 2>3 pre-operatively; at 3 months post-operative this rate has remained unchanged. No urinary stress incontinence was reported by any patient,

and all stress tests resulted negative for urine leakage. There were no major complications registered (Clavien-Dindo>3), either intraoperatively or postoperatively. Biochemical failure was registered in 4 patients at 1 year; all of them underwent saturation biopsy with diagnosis of cancer progression, and then radical cryoablation of prostate with actually undetectable PSA. At 4 years of follow-up no patient showed distant metastasis. *Discussion and Conclusion:* Our study, although retrospective, highlights the feasibility and safety of the cryo-hemiablation of prostate cancer, which guarantees preservation of both sexual power and urinary continence in a highly selected group of patients. From an oncological point of view, to assess its efficacy there is a need for longer follow-up. Cryo-hemiablation of prostate cancer preserves both urinary continence and erectile function. Currently, given the short follow-up no oncological conclusions could be drawn in this paper.

Table I. *Demographics and pre-operative characteristics.*

Age	
Years (range)	74.7 (61-83)
Race	n (%)
Caucasian	45 (100)
Pretreatment clinical stage	n (%)
T2b	45 (100)
Gleason score in entry biopsy	n (%)
3+3	25 (55.5)
3+4	13 (29)
4+3	7 (15.5)
PSA pre-operative biopsy	n (%)
<10	36 (80)
>10	9 (20)
Entry staging biopsy	n (range)
Median cores positive	3 (1-5)
	n (%)
Unilateral cancer	45 (100)
	n (%)
Preoperative urinary continence	45 (100)
Potency (IIEF-5 question 2>3)	38 (84.4)
Mean follow-up (months)	21.72

IIEF, International index of erectile function.

24
IMPACT OF BEDSIDE ASSISTANT DURING ROBOT ASSISTED RADICAL PROSTATECTOMY ON PERIOPERATIVE AND CLINICAL OUTCOMES

Mario Salvatore Mangano[1], Claudio Lamon[1], Francesco Beniamin[1], Alberto De Gobbi[1], Matteo Ciaccia[1], Giuseppe Battistella[2] and Luigino Maccatrozzo[1]

[1]Urology Unit, Ca'Foncello Hospital, Treviso, Italy; [2]Epidemiology Unit, Ca'Foncello Hospital, Treviso, Italy

Background/Aim: It is believed that the outcome of robotic surgery during Robot Assisted Radical Prostatectomy (RARP) for prostate cancer depends not only on the experience of the console surgeon, but also of the bedside assistant (1). The bedside assistant is a fundamental member of the robotic team and assumes numerous roles during surgery, such as placing clips for hemostasis, providing visibility by clearing the surgical field from blood, passing instruments and sutures, and removing tissues (2); by virtue of physical proximity, the assistant acts as the robotic console surgeon's link to the patient. The goal of the study was to analyze the impact of the bedside assistant's experience during RARP. *Materials and Methods:* All consecutive RARPs without bilateral pelvic lymphadenectomy performed from January 2017 to September 2017 were sourced from a prospectively maintained database. All cases were performed by a single surgeon, who was beyond his learning curve during the entire period of the study. He was supported by 2 bedside assistants (randomly distributed throughout the series, based on availability): one with relevant experience (who was involved in the whole learning curve), one basically inexperienced. The following patients' parameters were documented and analyzed: age, body mass index (BMI), previous abdominal surgery, prostate volume (by transrectal ultrasonography), pre-operative prostate-specific antigen (PSA) levels, and bioptic grading. Surgical outcomes analyzed included skin-to-skin operative time and estimated blood loss; clinical outcomes included length of hospital stay and time to catheter removal; the oncological outcome was represented by positive surgical margin rate. Statistical analysis was performed using Mantel-Haenszel chi-square test. *Results:* Sixty-five RARPs were identified: 33 RARPs (50.8%) were performed with the experienced bedside assistant, 32 (49.2%) with the novice one. The variables thought to influence the difficulty of surgery were similar between the two groups: age (66 *vs.* 66, p=0.87), BMI (27.2 *vs.* 27, p=0.76), previous abdominal surgery (19 *vs.* 18, p=0.91), prostate volume (40 *vs.* 37, p=0.09); there was also no difference in pre-operative PSA (5.2 *vs.* 5.0, p=0.77) and bioptic grade (p=0.33). As far as outcomes are concerned, there were no statistically significant differences between experienced and novice assistant in terms of operative time (190 *vs.* 205 min, p=0.83), blood loss (260 *vs.* 270 ml, p=0.91), length of stay (5 *vs.* 5 days, p=0.70), days of catheterization (12 *vs.* 12, p=0.90), positive surgical margin rate (27.3% *vs.* 31.2%, p=0.37). *Discussion and Conclusion:* The experience of the bedside assistant had no influence on perioperative and postoperative course following RARP. The high experience of the console surgeon is probably the explanation for the absence of differences in evaluated outcomes between the two considered bedside assistants. Consequently, given a highly experienced primary surgeon, a less experienced assistant can be safely incorporated into the procedure. However, it is difficult to evaluate the safety and

confidence that the console surgeon feels when he works with a skilled rather than an inexperienced bedside assistant. The experience of the console surgeon as bedside assistant and the standardization of every step of the procedure remain crucial and indispensable factors for the success of robotic surgery (3).

1 Nayyar R, Yadav S, Singh P and Dogra PN: Impact of assistant surgeon on outcomes in robotic surgery. Indian J Urol *32(3)*: 204-209, 2016.
2 Yuh B: The bedside assistant in robotic surgery--keys to success. Urol Nurs *33(1)*: 29-32, 2013.
3 Thiel DD, Lannen A, Richie E, Dove J, Gajarawala NM and Igel TC: Simulation-based training for bedside assistants can benefit experienced robotic prostatectomy teams. J Endourol *27(2)*: 230-237, 2013.

25
INCIDENCE OF PATHOLOGICAL HIGH GRADE AND STAGE DISEASE IN PATIENTS WITH A BIOPTIC DIAGNOSIS OF MICROFOCAL ADENOCARCINOMA OF THE PROSTATE: A MULTICENTER STUDY

Alberto Abrate[1], Cristina Scalici Gesolfo[1], Daniele Romagnoli[2], Federico Mineo Bianchi[2], Amelio Ercolino[2], Nicola Pavan[3], Guglielmo Mantica[4], Andrea Romagnoli[4], Carlo Terrone[4], Carlo Pavone[1], Vincenzo Serretta[1], Marco Vella[1], Eugenio Brunocilla[2], Andrea Gregori[5], Virginia Varca[5], Alberto Diminutto[6], Salvatore Siracusano[6], Andrea Lissiani[3], Angelo Porreca[7], Riccardo Schiavina[2] and Alchiede Simonato[1]

[1]Department of Surgical, Oncological And Stomatological Sciences, Section of Urology, University of Palermo, Palermo, Italy;
[2]Department of Urology, University of Bologna, St. Orsola-Malpighi Hospital, Bologna, Italy;
[3]Department of Urology, University of Trieste, Trieste, Italy;
[4]Department of Urology, IRCCS AOU San Martino, University of Genoa, Genoa, Italy;
[5]Department of Urology, ASST Rohdense, G. Salvini Hospital, Garbagnate Milanese, Milan, Italy;
[6]Department of Urology, University of Verona, Policlinico G. B. Rossi, Verona, Italy;
[7]Department of Urology, Abano Policlinic Hospital, Padua, Italy

Background/Aim: The introduction of active surveillance aimed to reduce overtreatment in patients with clinically localized low-risk prostate cancer (PCa). According to the European Association of Urology (EAU), patients with a clinically confined PCa (T1–T2), Gleason score (GS)=6 at biopsy, ≤3 biopsy cores involved with cancer, with 50% of each core involved with cancer, and PSA <10 ng/ml, are eligible for active surveillance (1). However, these tumors may have very different biological behavior and their treatment remains controversial. The aim of the current study was to investigate the incidence of unfavorable features [defined as the diagnosis of prostate cancer with International Society of Urologic Pathologists (ISUP) Grade ≥3 and/or stage ≥pT3a] in microfocal prostate cancer (miPCa) patients having undergone radical prostatectomy (RP). *Patients and Methods:* This is a multicenter retrospective study that included male patients having undergone RP after a diagnosis of miPCa at prostate biopsy, from 2006 to 2016. miPCa was defined as a single positive focus ≤3 mm. The population was stratified according to the D'Amico risk classification. The incidence of ISUP grade ≥3 and stage ≥pT3a overall were calculated within the three classes. The ability of the preoperative variables to predict unfavorable characteristics was investigated. *Results:* Overall 427 patients were included: 313 (73.3%), 79 (18.5%), and 35 (8.2%) patients were classified as low-, intermediate- and high-risk according to the D'Amico risk classification. Mean age was 65.1±6.6 years. Pre-bioptic PSA and prostate specific antigen density (PSAD) were 8.78 ng/ml and 0.19, respectively. Overall 155 (36.3%) patients were upgraded after RP. Unfavorable characteristics were found in 123 (28.9%), 66 (53.7%) of which were previously classified as low-risk patients. One hundred and two of 313 (32.6%) low-risk patients were upgraded after radical prostatectomy: an ISUP Grade ≥3 PCa was diagnosed in the 38.2% of them (29, 5, and 5 patients with ISUP Grade 3, 4, and 5, respectively). Moreover 78 (18.2%) patients had an extraprostatic extension of the cancer (pathological stage ≥pT3a). Interestingly, it is notable that one (0.2%) patient, previously diagnosed with a GS 6 PCa, was definitively classified as pT0 after RP. The receiver operating characteristic (ROC) curve analysis demonstrated that PSA, PSAD, clinical stage, and D'Amico risk classification had an AUC value of 0.660, 0.697, 0.600, and 0.645, respectively, to predict the risk of unfavorable features. The PSAD had the best predictive ability, but significantly higher than clinical stage only (p=0.01). *Discussion and Conclusion:* According to recent literature only ISUP Grade ≥3 was considered as unfavorable (2). Moreover the population included was stratified according to D'Amico risk classification. In line with the results previously shown in literature (3), overall we found that the 28.9% of the patients included, finally, had unfavourable pathological characteristics. Patients with miPCa detection at prostate biopsy have a significant potential risk of ISUP Grade 3 and pT3 cancer at definitive histological examination after RP. PSA, PSAD, and the D'Amico risk classification could be helpful in the decision making process to indicate active surveillance or treatment.

1 Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, De Santis M, Fossati N, Gross T, Henry AM, Joniau S, Lam TB, Mason MD, Matveev VB, Moldovan PC, van den Bergh RCN, Van den Broeck T, van der Poel HG, van der Kwast TH, Rouvière O, Schoots IG, Wiegel T and Cornford P: EAU-ESTRO-SIOG guidelines on prostate cancer. Part 1: Screening, diagnosis, and local treatment with curative intent. Eur Urol *71*: 618-629, 2017.
2 Epstein JI, Zelefsky MJ, Sjoberg DD, Nelson JB, Egevad L, Magi-Galluzzi C, Vickers AJ, Parwani AV, Reuter VE, Fine SW, Eastham JA, Wiklund P, Han M, Reddy CA, Ciezki JP, Nyberg T and Klein EA: A contemporary prostate cancer grading system: A validated alternative to the Gleason score. Eur Urol *69*: 428-435, 2016.
3 Guttilla A, Zazzara M, Zattoni F, Zazzara M, Zattoni F, Novara G, Zanin M, Gardiman M, Ficarra V and Zattoni F: Histopathological characteristics of microfocal prostate cancer detected during systematic prostate biopsy. BJU Int *116*: 202-206, 2015.

26
BUILDING A HEALTH PROMOTING ACTIVE SURVEILLANCE: A QUALITATIVE STUDY ON PROSTATE CANCER PATIENTS' PERCEPTIONS

Julia Paola Menichetti Delor[1], Letizia De Luca[1], Paola Dordoni[1], Simona Donegani[1], Riccardo Valdagni[2] and Lara Bellardita[1]

[1]Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[2]Prostate Cancer Program; Department of Radiation Oncology 1; Department of Oncology and Hematology; Università degli Studi di Milano, Milan, Italy

Background/Aim: Active surveillance (AS) has been evolved in the last years as a protocolled monitoring alternative for low-risk prostate cancer (PCa) patients, able to avoid the possible risks of unnecessary radical treatments (1). For these patients, finding a meaning to move in a health promoting direction during AS can be particularly relevant. It can help them not only reduce the risks for further health problems that usually raise in the old age, but, even more, be equipped to face at best eventual future radical treatments (2). Furthermore, health promotion activities have been demonstrated to have the potential to promote quality of life of PCa patients (3), which is a key issue for patients on AS. There is a need of studies to explore whether and how AS can increase interest among PCa patients for maintaining and also promoting their overall health and well-being. This study aimed to explore perceptions of PCa patients on AS, concerning their health promotion. *Materials and Methods:* In this qualitative study, the explored areas followed a semi-structured track: 1) shared representations of views/meanings of health promotion and prioritization of conceptual areas, 2) barriers and facilitators for promoting health during AS, 3) open needs for health promotion. Twenty-four men with low-risk PCa enrolled in the Prostate Cancer Research International AS (PRIAS) protocol, in one of the PRIAS European Centers, with different age range and with different time period from enrollment were involved. Each group comprised 6 participants, all recorded, transcribed, and analyzed. A thematic analysis approach with an inductive approach was used, allowing the themes and names for themes to flow from the data. *Results:* PCa patients described their efforts for health promotion during AS being challenged by mental, age-related, informational, and organizational issues. Health promotion was firstly described as a mental effort to enjoy the present, without living space to PCa worries and without thinking too much forward to the future. For participants, being older and having to manage physical and mental struggles related to age was particularly relevant for their health promotion activities during AS, and they reported a need to care particularly for their older age. Furthermore, promoting their health during AS was hard because of the lack of reliable information; they reported a need to build a personalized knowledge on health promotion in AS, adapted to their individual needs. Finally, for them, taking care and promoting their health strictly depended on taking control and responsibility on the AS pathway and on the overall care process. *Conclusion:* Findings of this study may help healthcare professionals and healthcare organizations to build a "health promoting AS".

1 Eggener SE, Mueller A, Berglund RK, Ayyathurai R, Soloway C, Soloway MS, Abouassaly R, Klein EA, Jones SJ, Zappavigna C, Goldenberg L, Scardino PT, Eastham JA and Guillonneau B: A multi-institutional evaluation of active surveillance for low risk prostate cancer. J Urol *189(1)*: 1635-1641, 2009.
2 Champ CE, Francis L, Klement RJ, Dickerman R and Smith RP: Fortifying the treatment of prostate cancer with physical activity. Prostate Cancer *2016*: 9462975, 2016.
3 Menichetti J, Villa S, Magnani T, Avuzzi B, Bosetti D, Marenghi C, Morlino S, Rancati T, Van Poppel H, Salvioni R, Valdagni R and Bellardita L: Lifestyle interventions to improve the quality of life of men with prostate cancer: A systematic review of randomized controlled trials. Crit Rev Oncol Hematol *108*: 13-22, 2016.

27
HOW DO PATIENTS ON ACTIVE SURVEILLANCE COPE WITH CANCER? A 3-YEAR FOLLOW-UP STUDY

Paola Dordoni[1], Maria Francesca Alvisi[1], Julia Menichetti[1], Letizia De Luca[1], Fabio Badenchini[1], Teresa Di Florio[1], Tiziana Magnani[1], Cristina Marenghi[1], Tiziana Rancati[1], Riccardo Valdagni[2] and Lara Bellardita[1]

[1]Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[2]Department of Oncology and Hemato-oncology, Radiation Oncology 1, Prostate Cancer Program, University of Milan, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Background/Aim: The diagnosis of cancer can trigger consequences of life adjustment and emotional reactions. Men diagnosed with low- or very low-risk, potentially indolent, prostate cancer (PCa), who choose active surveillance (AS), could find hard to adjust their lives and to "live with an untreated cancer" (1, 2). For this reason, coping strategies are important in cancer management and particularly on the AS management. The most used coping strategies' categorization for cancer patients samples summarized five different coping: 1) fighting spirit is the tendency to confront and actively face the illness; 2) anxious preoccupation is the tendency to experience the illness as an event source of marked anxiety; 3) fatalism is the tendency to have a resigned and fatalistic attitude towards the illness; 4) hopelessness/helplessness is the tendency to adopt a pessimistic attitude about the illness; 5) avoidance is the tendency to avoid direct confrontation with illness-related issues. Understanding how PCa patients drive their coping strategies after diagnosis might contribute to a better support of the whole cancer experience. However, few studies addressed the role of coping during AS (3). The present study aimed to investigate coping strategies in men at the entrance on AS, and whether these strategies statistically and clinically changed during the first 3-year follow-up period. *Materials and Methods:* The Mini-Mental Adjustment to Cancer (Mini-MAC) was used to measure coping styles. Data were collected from patients enrolled in the Prostate cancer Research International: Active Surveillance (PRIAS) Quality of Life (QoL) study, at entrance in AS protocol (T0). Follow-up measures were collected at three time-points: 10

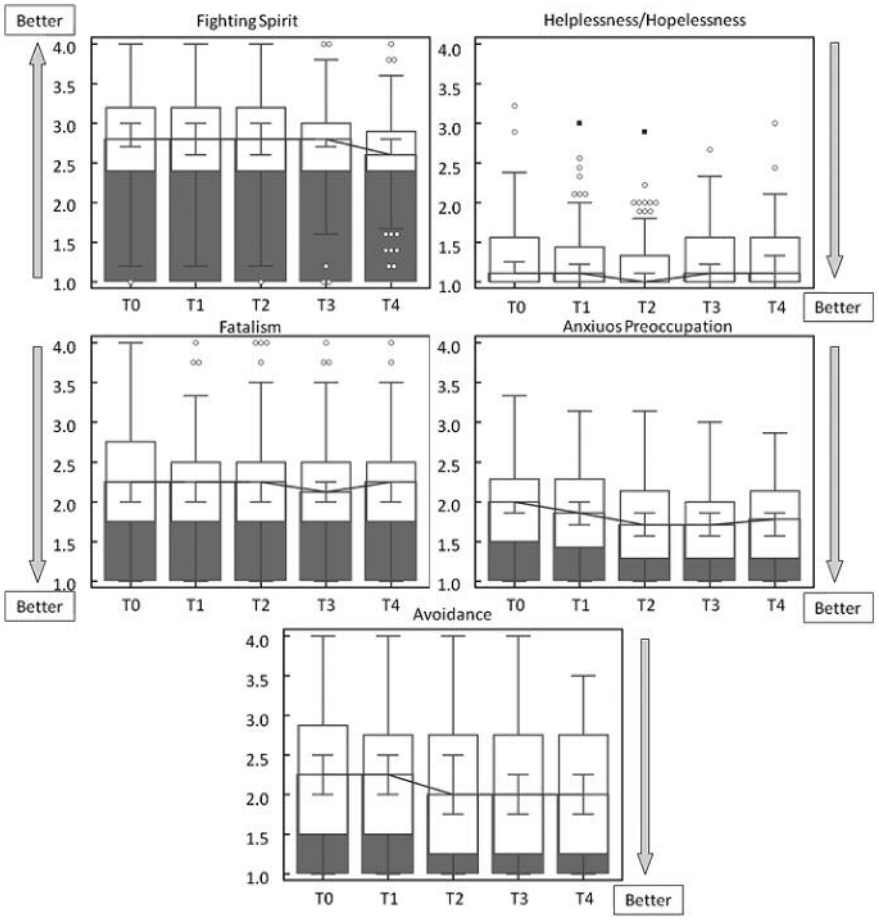


Figure 1. *Distributions of Mini-Mac subscales over time.*

Table I. *Descriptive analyses of Mini-MAC subscales for each follow-up.*

	Time	N	Mean	SD	Min	25° Percentile	Median	75° Percentile	Max
Fighting spirit	T0	418	2.8	0.6	1	2.4	2.8	3.2	4
	T1	312	2.8	0.5	1	2.6	2.8	3.2	4
	T2	249	2.8	0.6	1	2.4	2.8	3.2	4
	T3	201	2.7	0.6	1	2.4	2.8	3	4
	T4	159	2.6	0.6	1	2.4	2.6	3	4
Helplessness/ hopelessness	T0	418	1.4	0.5	1	1	1.2	1.7	3.22
	T1	312	1.4	0.5	1	1	1.2	1.6	3.89
	T2	249	1.3	0.4	1	1	1.1	1.6	3.33
	T3	201	1.4	0.4	1	1	1.1	1.7	2.67
	T4	159	1.3	0.4	1	1	1.2	1.7	3
Fatalism	T0	418	2.3	0.7	1	1.75	2.3	2.8	4
	T1	312	2.3	0.7	1	1.75	2.3	1.8	4
	T2	249	2.2	0.7	1	1.75	2.3	2.8	4
	T3	201	2.2	0.6	1	1.75	2.3	2.5	4
	T4	159	2.2	0.6	1	1.75	2.3	2.5	4
Anxious preoccupation	T0	418	2.0	0.6	1	1.57	2.0	2.3	4
	T1	312	1.9	0.6	1	1.57	1.9	2.3	3.57
	T2	249	1.8	0.6	1	1.43	1.9	2.3	3.43
	T3	201	1.8	0.6	1	1.29	1.8	2.1	3.29
	T4	159	1.8	0.5	1	1.29	1.9	2.1	3.14
Avoidance	T0	418	2.3	0.8	1	1.75	2.3	3	4
	T1	312	2.3	0.7	1	1.75	2.3	2.8	4
	T2	249	2.1	0.8	1	1.5	2.0	2.8	4
	T3	201	2.1	0.8	1	1.5	2.3	2.8	4
	T4	159	2.1	0.7	1	2	2.0	2.8	4

SD, Standard deviation; T0, entrance in AS protocol; T1, 10 months after the diagnostic biopsy; T2, 12 months from diagnosis; T3, 24 years from diagnosis; T4, 48 years from diagnosis.

Table II. *Clinically significant differences in Mini-MAC subscales between enrolment in AS and 3 years follow-up.*

	T4-T0≥1 (154 patients with T0 and T4)		T4-T0≤-1 (154 patients with T0 and T4)		Net coping improvement (%)
	N	%	N	%	
Fighting spirit	11	7	8	5	2
Helplessness/hopelessness	6	4	3	2	-2
Fatalism	11	7	16	10	3
Anxious preoccupation	3	2	8	5	3
Avoidance	7	5	28	18	12

months after the diagnostic biopsy (T1), after receiving the histological report of the first re-biopsy with AS criteria were confirmed (T2, 12 months from diagnosis), and once every year (T3, T4). Mini-MAC score range from 1 to 4, with 4 indicating the presence of coping. Specifically, a fighting spirit is a positive style of coping, while high scores in the other subscales negatively impact coping. Descriptive analyses were performed to identify the greatest presence of specific coping strategies (cut off >2.5). Friedman tests were used to detect statistically significant changes over time. Changes ≥1 point (or ≤-1) were considered as clinically relevant. *Results:* Between September 2007 and September 2017, 418 patients completed Mini-MAC at T0; of these, 154 completed also T4. The median age was 64.9 years, the

median PSA at diagnosis was 5.4 ng/ml, and 61% of patients had a partner. Descriptive analyses of Mini-MAC at every follow-up are presented in Table I. At enrolment in AS, 73% of patients had high fighting spirit (>2.5), high helplessness/hopelessness was almost negligible (3%), 31% of patients reported fatalism over 2.5 points, anxious preoccupation was present only in the 16% of cases, and avoidance was elevated in 35% of patients. Fighting spirit, anxious preoccupation and avoidance showed a statistically significant slight reduction with time, (p=0.028, p<0.001, p=0.002, respectively). The trend of the five coping strategies as a function of follow-up time is shown in Figure 1. When considering clinically significant changes between T0 and T4, net improvement was measured in avoidance, with 5% of patients increasing their avoidance and 18% decreasing it. Details on clinically significant changes are reported in Table II. *Discussion and Conclusion:* At baseline, the majority of patients were shown to adopt and maintain good coping strategies through first three years, with low levels of anxiety preoccupation and helplessness. Indeed high fighting spirit and low fatalism suggested that patients were motivated to care their health "fighting against cancer" and had scarce tendency to resigned and fatalistic attitude towards the illness. As regards avoidance and fighting spirit, limited changes over time were revealed. Patients slightly decreased avoidance thoughts and behaviors in terms of cancer (*i.e.* distracting themselves when thoughts about illness come into heads) during the first three years. This period could be seen as a functional adaptation towards "life on AS". Men on AS may perceive an increasing control over their cancer and comfort with the AS protocol over time. Even though our findings revealed that good coping strategies are adopted at the entrance of AS, clinicians have to be aware that psychological interventions may support men anxiety particularly during the first year. In conclusion, our study suggests that AS does not seem to challenge patients' coping strategies, nor at entrance nor at the first 3-year follow-up.

1 Bellardita L, Rancati T, Alvisi MF, Villani D, Magnani T, Marenghi C, Nicolai N, Procopio G, Villa S, Salvioni R and Valdagni R: Predictors of health-related quality of life and adjustment to prostate cancer during active surveillance. Eur Urol *64*: 30-36, 2013.

2 Alvisi MF, Dordoni P, Rancati T, Avuzzi B, Badenchini F, De Luca L, Magnani T, Marenghi C, Menichetti J, Villa S, Zollo F, Valdagni R and Bellardita L: Facing untreated prostate cancer on active surveillance: who is at risk for increased anxiety 10 months after diagnosis? In preparation.

3 Bellardita L, Valdagni R, van den Bergh R, Randsdorp H, Repetto C, Venderbos LD, Lane JA and Korfage IJ: How does active surveillance for prostate cancer affect quality of life? A systematic review. Eur Urol *67*: 637-645, 2015.

28
A PARTIAL RESPONSE IN A POORLY DIFFERENTIATED RENAL CELL CARCINOMA PATIENT TREATED WITH PAZOPANIB

Francesca Romana Di Pietro, Michela Roberto, Maria Bassanelli, Silvana Giacinti, Giulia Poti, Serena Macrini, Anna Maria Aschelter and Paolo Marchetti

Department of Clinical and Molecular Medicine, Division of Oncology, Sapienza University of Rome, Rome, Italy

Background: Renal cell carcinoma (RCC) is the most common renal tumor and the 80% of RCC have been classified as clear-cell subtype. All other subtypes are grouped as non-clear cell RCC, which include papillary (type I and type II), chromophobe, and various other entities. The 5-year relative survival rate in metastatic RCC (mRCC) is about 11.6% (1, 2). *Case Report:* We report the case of a 79-year-old male, who underwent a left nephrectomy and splenectomy for a poorly differentiated (Furhman grade 3) RCC with a component of clear cells and type II papillary cells (pT3a, pN0, pMx, stage III according to the American Joint Committee on Cancer 2010), in October 2016. At preoperative evaluation, an abdomen computed tomography (CT) scan, showed a neoformation of 50 mm on the left kidney with intralesional vascularization. However, a postoperative body CT-scan showed multiple lung metastases, with an infiltrating lesion, localized into the left chest wall, extended to the midaxillary line for about 49×51×90 mm in dimension. Moreover, this lesion involved the 2th and 3th coasts. Some lymphadenopathy satellites at the level of the left internal mammary chain and ilo-mediastinal lymph nodes were reported. It was also observed an osteolytic secondary lesion with solid component that infiltrated the 4th lumbar vertebra and extended into the 4th-5th lumbar neuroforamen and inside the vertebral canal. According to the Memorial Sloan Kettering Cancer Centre/International Metastatic RCC Database Consortium (MSKCC/IMDC) score criteria, the patient was considered as poor-risk for: Karnofsky performance status 50%, 3 months of time from diagnosis to treatment, hemoglobin 12 g/dl, platelets count 425.000 mm^3, and neutrophils count 6000 mm^3 (3). In January 2017, the patient underwent palliative radiotherapy on symptomatic 4th-5th lumbar vertebra (8Gy, single dose); 2th-3th left coast (8 Gy, single dose). Considering the stage of the disease, the histology, the prognostic factors and comorbidities (hypertension, previous heart attack and diabetes mellitus) we decided to start first-line treatment with pazopanib at dosage of 800 mg daily. After the first cycle, patient experienced a grade 3 hypertension according to Common Terminology Criteria for Adverse Events (CTCAE); the treatment was interrupted and anti-hypertensive treatment with ACE-inhibitor and calcium-antagonist was prescribed. One month

later, in May 2017, hypertension resolved to grade 1 and pazopanib was resumed at lower dose level of 400 mg daily. In July 2017, a CT scan showed a partial response: volumetric reduction of the chest solid tissue, determining the osteolysis of the III left coast, with a maximum current thickness of 20 mm *versus* 45 mm. The lymphadenopathies at the level of the left internal mammary chain were also reduced with a shorter maximum axis of few millimeters. Whereas, solid tissue determining osteolysis of 4th lumbar vertebra was stable. In addition to the instrumental response, a good control of the pain, previously reported at the lumbar column and the lower left limb, was obtained with the combination of opioids and radiotherapy. Currently the treatment is still ongoing, with good tolerability and symptom control. *Discussion and Conclusion:* In this case, pazopanib showed activity in poorly differentiated and mixed histology RCC with poor risk features.

29

LINAC-BASED STEREOTACTIC RADIATION THERAPY FOR LOCALIZED PROSTATE CANCER: 4-YEAR FOLLOW-UP UPDATE ON TOXICITY AND SURVIVAL

Giuseppe Roberto D'Agostino, Lucia Di Brina, Ciro Franzese, Davide Franceschini, Cristina Iftode, Stefano Tomatis, Angelo Tozzi, Fiorenza De Rose, Pierina Navarria and Marta Scorsetti

Radiotherapy and Radiosurgery, Humanitas Clinical and Research Hospital, Rozzano, Milan, Italy

Background/Aim: Stereotactic Body Radiation Therapy (SBRT) is a promising treatment modality for the management of localized prostate cancer. Several studies argue for a low alpha/beta ratio for prostate cancer, even lower than the value of the surrounding healthy tissues. For this reason, prostate cancer may be more sensitive to large fraction sizes of radiotherapy and resistant to small fraction sizes. Several studies have clinically confirmed this hypothesis, showing comparable results to standard fractionation by delivering only four or five high dose fractions to cure localized prostate cancer. This study updates our previously reported experience (1) on the efficacy and toxicity of a Linac-based SBRT in patients with low- or intermediate-risk prostate cancer, exploring the potential correlation between toxicity, biochemical recurrence-free survival (BRFS) and clinico-pathological characteristics. *Materials and Methods:* Biopsy confirmed prostate cancer patients were enrolled, provided that they had the following characteristics: initial prostate-specific antigen (PSA) <20 ng/ml, Gleason Score <8, International Prostate Symptom Score <8. The treatment schedule was 35 Gy in 5 fractions, delivered every other day, with volumetric modulated arcs and flattening filter-free beams. Treatment plans were designed and optimized according to the RapidArc technique, with one or two full arcs. All plans were optimized and delivered on a TrueBeam Linac (Varian Medical Systems, Palo Alto, CA, USA), choosing 10 MV flattening filter-free photon beams. Treatment delivery was image-guided. Before each radiation fraction delivery, cone beam computed tomography (CBCT) was carried out to verify the correct position and requested conditions (full bladder, empty rectum). Toxicity was recorded according to Common Terminology Criteria for Adverse Events CT-CAE criteria v3.0. Biochemical failure was calculated according to the Phoenix definition. BRFS was calculated in months from SBRT. *Results:* Between February 2011 and March 2015, 90 patients were enrolled (53 low-risk, 37 intermediate-risk, according to the NCCN criteria). The median age was 71 years (range=48-82). The median initial PSA was 6.98 ng/ml (mean=7.18, range=2.7-17.0). According to the International Society of Urological Pathology-World Health Organization (ISUP-WHO) 2016 grading system, 57 patients (63.3%) were Grade Group (GG) 1, 22 patients (24.5%) were GG2 and 11 patients (12.2%) GG3. Acute toxicity was mild, with 32.2 patients presenting a G1 urinary toxicity and 32.2% of patients presenting a G2 urinary toxicity, mainly represented by urgency, dysuria and stranguria. A rectal G1 toxicity was found in a 15.5% of patients, while a rectal G2-toxicity was recorded in 6.6% of patients. Urinary late toxicity was G1 in 48.9% of cases, G2 in 2.2%. A G1 late proctitis was recorded in 18.0 % of patients. A statistically significant correlation was found between the genito-urinary (GU) toxicity and the clinical target volume (p=0.0025), men with a prostate volume greater than 60 cc (as measured at simulation CT-scan) resulting at higher risk for GU toxicity >G1 [odds ratio=1.04, 95% confidence interval (CI)=1.01-1.07]. At a median follow-up of 48 months (range=10-67) all patient are still alive. Four-year biochemical recurrence-free survival (BRFS) was 94.2% for the whole study population, four biochemical failures were recorded (GG 1: 1 case, GG 2: 1 case, GG 3: 2 cases). Choline positron emission tomography (PET) revealed a local recurrence (GG1), 2 cases of distant metastases (GG2: 1, GG3:1), 1 case with both local recurrence and bone metastasis (GG3). Four-year-BRFS was therefore 97.7 % for the subgroup of GG1 patients, 95.0% for GG2 patients, 72.9% for GG3 patients (p=0.028). Cox regression analysis showed a Hazard Ratio of 3.67 (95% CI=1.07-12.55, p=0.037) of biochemical failure for GG3 patients compared to GG1 and GG2. *Conclusion:* This study updates our previously published experience on SBRT in prostate cancer. After a 4-year follow-up our analysis suggests that SBRT may be considered as a valid therapeutic option for low- and intermediate- risk prostate cancer patients, warranting an adequate control of disease, with mild toxicity profiles. It also

confirms that among the intermediate-risk patients, those with a GG 3 disease bear a worse prognosis and are at major risk of biochemical failure after SBRT.

1 D'Agostino G, Franzese C, De Rose F, Franceschini D, Comito T, Villa E, Alongi F, Liardo R, Tomatis S, Navarria P, Mancosu P, Reggiori G, Cozzi L and Scorsetti M: High-quality linac-based stereotactic body radiation therapy with flattening filter free beams and volumetric modulated Arc therapy for low-intermediate risk prostate cancer. A mono-institutional experience with 90 patients. Clin Oncol *28(12)*: e173-e178, 2016.

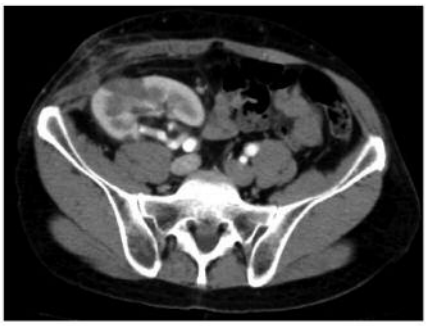


Figure 1. *Computed tomography abdomen of the lesion, at 3 months.*

30

SAFETY AND EFFICACY OF MICROWAVE THERMAL ABLATION FOR SMALL RENAL MASS ON PATIENT WITH RENAL TRANSPLANTATED: A CASE REPORT

Giovanni Silecchia[1], Luigi Cormio[1], Oscar Selvaggio[1], Matteo Gravina[2], Luca Macarini[2] and Giuseppe Carrieri[1]

[1]Division of Urology, University of Foggia, Foggia, Italy; [2]Division of Radiology, University of Foggia, Foggia, Italy

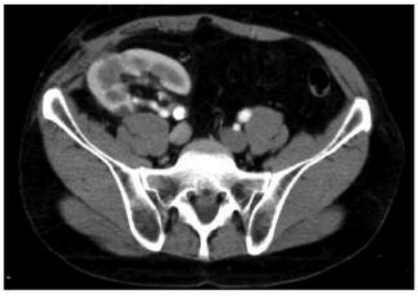


Figure 2. *Computed tomography abdomen of the lesion, at 18 months.*

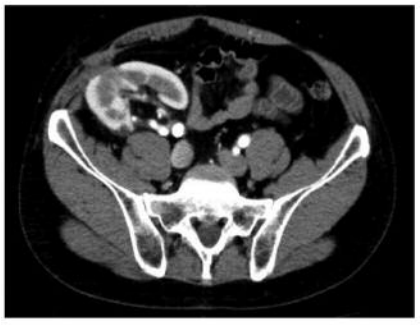


Figure 3. *Computed tomography abdomen of the lesion, at 3 years.*

Background/Aim: Management of renal cell carcinoma (RCC) in renal transplanted patients represents a clinical dilemma: the oncological outcomes must be weighted against the renal function preservation. Microwave thermal ablation (MWTA) technique is used in selected cases for the treatment of small RCC (1, 2). The aim of this case report is to evaluate safety, and functional and oncological outcomes of MWTA in the treatment of RCC in a patient who had previously undergone renal transplantion. *Case Report:* We present a case of a 48-year-old male patient, who had undergone right renal transplantation for chronic renal disease stage II according to the Kidney Disease Outcomes Quality Initiative (K-DOQI) classification, secondary to glomerulonephritis from IgA deposits or Berger's disease, in February 2000. In February 2014, follow-up abdominal ultrasonography showed occasional findings: "at the limit of 1/3 upper and 1/3 average of the right kidney transplanted with a rounded image of about 2.5 cm protruding from the renal profile, uneven in the presence of some hypoechogenic/anechogenic areas in its interior, with delicate profiles, surrounded by thin hypoechoic lobe". Computed tomography (CT) chest and abdomen confirmed the renal lesion, which exhibited homogeneous density and enhancement after endovenous medium contrast. In April 2014, after urological evaluation, a MWTA of the renal mass with positioning, under ultrasonography control, of 1 antenna and 2 cycles of 10 minutes each, was performed. The follow-up included CT abdomen-pelvis at 3 (Figure 1), 6, 12, 18 months (Figure 2), 2, and 3 years (Figure 3). The definition of incomplete treatment was the persistence of the lesion contrast enhancement (CE) at the end of the scan; the definition of relapse, in according to the European Association of Urology (EAU) guidelines, was the appearance of the CE to the 6-month control CT. *Results:* The case did not showed incomplete treatment and local relapse or secondarisms (confirmed with no enhancement within resolved tumor mass) at the CT abdomen-pelvis with contrast medium at 3, 6, 12, 18 months and 2, 3 years. No immediate and late post-operative

complications were recorded, nor any change in serum creatinine levels in the immediate and subsequent follow-up. *Discussion and Conclusion:* Although the standard treatment for a renal cancer found in a kidney transplant has been transplant nephrectomy for many years due to the perception of a worse prognosis in these immunocompromised patients (3), our study shows that percutaneous MWTA for these small tumors is effective and can be safely performed. This therapeutic option can help avoid graft removal and a return of the patient to hemodialysis, which is associated with a substantially reduced life expectancy (4). The use of MWTA, in selected cases, could represent the tailored treatment for renal trasplantated patients, reducing the risk of renal failure and achieving satisfying oncological results. The procedure is easy to perform, with few or none peri- and post-operative complications, well tolerated and accepted by the patient and represents a feasible therapeutic option in small renal masses. In addition, percutaneous technique is easier to perform in a superficial organ such as a transplanted kidney.

1 Brace CL: Microwave tissue ablation: biophysics, technology, and applications. Crit Rev Biomed Eng *38*: 65-78, 2010.
2 Floridi C, De Bernardi I, Fontana F, Muollo A, Ierardi AM, Agostini A, Fonio P, Squillaci E, Brunese L, Fugazzola C and Carrafiello G: Microwave ablation of renal tumors: state of the art and development trends. Radiol Med *119*: 533-540, 2014.
3 Ribal MJ, Rodriguez F, Musquera M, Segarra J, Gulrado L, Villavicencio H and Alcaraz H. Nephron-sparing surgery for renal tumor: a choice of treatment in an allograft kidney. Transplant Proc *38(5)*: 1359-1362, 2006.
4 Rao PS, Schaubel DE, Jia X, Li S, Port FK and Saran R: Survival on dialysis post-kidney transplant failure: results from the Scientific Registry of Transplant Recipients. Am J Kidney Dis *49(2)*: 294-300, 2007.

31
MODELING PROSTATE-CANCER RESPONSE FOR PATIENTS TREATED WITH EXTERNAL BEAM RADIATION THERAPY-ANDROGEN DEPRIVATION THERAPY: CALCULATION OF RADIOSENSITIVITY AND REPOPULATION PARAMETERS

Domenico Gabriele[1], Matteo Tamponi[2], Angelo Maggio[3], Michele Stasi[3], Maurizio Conti[4], Giovanni Battista Meloni[4] and Pietro Gabriele[5]

[1]Radiation Oncology Unit, Sassari University Hospital, Radiation Oncology, Sassari University, Turin, Italy;
[2]Health Physics Service, Heath Physics Service, ATS Sardinia, Sassari, Italy;
[3]Medical Physics, Candiolo Cancer Institute- FPO, IRCCS, Candiolo, Turin, Italy;
[4]Radiology Institute University of Sassari, Radiology Institute, Sassari, Italy;
[5]Radiotherapy, Candiolo Cancer Institute-FPO, IRCCS, Candiolo, Turin, Italy

Aim: The aim of this work was to examine the short-term outcome of patients treated by means of fractionated external beam radiation therapy (EBRT) delivered once a day, with or without androgen deprivation therapy (ADT), expressed as 5-year biochemical recurrence free survival (BCFS), based on clinical data available until now. Also, radiosensitivity to fractionation and accelerated repopulation parameters were evaluated considering the patient risk class and the use of ADT. *Materials and Methods:* Twenty-six data sets reporting the 5-year BCFS, dose scheduling, ADT, and clinical variables, were reviewed, for overall 17949 prostate cancer patients, treated with a dose of 1.80 to 7.25 Gy per fraction and overall treatment time (OTT) from 1 to 10 weeks. Fifteen groups of patients were built and studied taking into account the risk-class and the use of ADT as inclusion criteria. First, the bootstrap-based cross-validated dose-response curve at standard dose scheduling was calculated for each patient group, using three different models evaluating the D50 and g50 parameters with their 95% confidence interval (CI). Then, the a/β parameter was evaluated for each group of patients, based on the dose-response curves, using non-standard dose scheduling with three hypotheses: (i) no dependence on OTT, (ii) dependence only on OTT difference, and (iii) dependence on OTT. The accelerated proliferation during the EBRT, the time parameters expressing the accelerated tumor cell repopulation (d prolif) and the time delay before the onset of proliferation (T prolif) parameters and their bootstrap-based cross-validated 95% CI and median value were also determined. No-linear constrained least square minimization and statistical evaluation has been performed using R version 3.3.3 software (The R Project for Statistical Computing, http://www.r-project.org). *Results:* The bootstrap-based cross-validated median values of D50 and g50 of the dose-response curve at standard dose scheduling were lower for low-risk patients (57 Gy and 1.7, respectively), high for high-risk patients (68 Gy and 1.9, respectively), and median for intermediate-risk patients (61 Gy and 1.8, respectively). For intermediate- and high-risk ADT-treated patients, D50 and g50 median values were 65 Gy and 1.9, higher than those of the corresponding groups including also patients not treated with ADT, equal to 61 Gy and 1.4. With hypothesis (i), for each patient group, the bootstrap-based cross-validation median value of the a/β parameter was within the range of 0.8-2.6 Gy, $p<0.05$, standard error of the estimate (SEE) <10% and the amplitude of the bootstrap-based cross-validation 95% CI <1.5 Gy. When using ADT, for patients of intermediate- and high-risk, median a/β was lower (1.1 Gy, 95% CI=0.7-2.0) compared to

the respective patient group including also patients not treated with ADT (a/β=1.7 Gy, 95% CI=1.0-2.2 Gy). The SEE associated to the evaluation of the equivalent dose in 2 Gy (EQD2) did not improve for any groups when assuming dependence on OTT or on OTT difference, compared to the hypothesis (i); the reduction was almost always less than 0.3 Gy (range=0.0-0.5). With hypotheses (ii) and (iii), a/β increased, as well as the amplitude of the bootstrap-based cross validation 95% CI. The bootstrap-based cross validation median values of the d prolif parameter were always within the range of 0.0-0.3 Gy/day with the median T prolif >20 days and <40 days. *Conclusion:* Diverse short-term responses of prostate cancer to EBRT and ADT were evaluated as 5-year BCFS expressed in function of dose scheduling for patients of different risk groups, treated or not with ADT. The present results suggest that the values of a/β are low for each class of risk; the use of ADT seems to reduce median a/β for intermediate- and high-risk patients. Results showed that it is not convenient to consider any dependence on OTT in EQD2 evaluation. Also, the bootstrap-based cross-validation median values of d prolif and T prolif were obtained for different groups of prostate cancer patients; these values could be used to evaluate some prolonged unscheduled gaps occurring during treatment.

33

EVALUATION OF OUTCOMES AFTER STEREOTACTIC HYPOFRACTIONATED RADIOTHERAPY FOR PROSTATE CANCER

Giancarlo Beltramo[1], Giovanni Longo[2], Cristina Locatelli[3], Isa Bossi Zanetti[1], Achille Bergantin[1], Anna Stefania Martinotti[1], Irene Redaelli[1], Paolo Bonfanti[1], Andrea Bresolin[1], Livia Corinna Bianchi[1], Matteo Maggioni[2] and Guido Dormia[2]

[1]Cyberknife Center, Centro Diagnostico Italiano, Milan, Italy;
[2]Department of Urology, San Carlo Borromeo Hospital, Milan, Italy;
[3]Department of Oncology, San Carlo Borromeo Hospital, Milan, Italy

Background/Aim: In accordance with the new radiobiological knowledge concerning prostate cancer, several randomized trials support the use of high doses of radiation. Hypofractionated stereotactic radiotherapy schedules are now proposed as a suitable approach in patients with localized prostate cancer. We retrospectively report collected data from a cohort of localized prostate cancer patients treated with Cyberknife (CK) Stereotactic Body Radiotherapy Treatment (SBRT) in our Center. *Patients and Methods:* From July 2007 to 2016, a retrospective analysis was carried out on 217 consecutive patients with a median age of 75 years (range=52-86), median prostate volume of 75.6 cc (range=37.03-163.16), and clinically localized prostate cancer. Cyberknife was used to deliver fiducial-based image-guided hypofractionated SBRT. The majority of patients 116 (53%) were low-risk, 60 patients (28%) were intermediate-risk, and 41 patients (19%) were high-risk (according to the National Comprehensive Cancer Network criteria). Pre-treatment prostate-specific antigen (PSA) ranged from 1.51 to 51 ng/ml (median=8.51 ng/ml). Seventeen (41%) of 41 high-risk patients received androgen deprivation therapy (ADT), that was not administered to any low-/intermediate-risk patient. Computed tomography and magnetic resonance imaging were used for treatment planning in all patients. The course of radiotherapy consisted of 38 Gy over 4 fractions (9.5 Gy/fraction) given daily to the planning target volume (PTV), which was defined as the clinical target volume (CTV) on prostate (plus at least 1 cm extension in seminal vesicles in intermediate- and high-risk patients) expanded 3 mm in all directions, except posteriorly (2 mm). Heterogeneous dose planning was used; dose was normalized to the 75% isodose line in order for the prescription dose to cover at least 95% of PTV. Real-time intrafractional motion tracking was used. Radiation therapy oncology group (RTOG) toxicity grades were assigned for genitourinary and gastrointestinal symptoms. *Results:* With a median follow-up of 61 months (range=12-120), the 6-year actuarial PSA relapse-free survival rate was 94.4% (confidence interval=90.8%-98.2%) with 98.2% for low-risk, 94.5% for intermediate-risk, and 85.6% for high-risk. In total 23 (10.5%) patients died during the follow-up for unrelated causes, only one (0.5%) died for prostate cancer with bone metastases. The patterns of PSA response showed a gradual decline with a PSA nadir below 1.0 ng/ml, 12 months after the radiation treatment. The majority of patients did not report any early genitourinary (53.5%) or gastrointestinal (79.3%) toxicities. Limited acute urinary symptoms (frequency, dysuria, urgency, hesitancy, and a nocturia) were common: 46.5% of patients reported grade I or II toxicity, no one experienced grade III or worse symptoms. Moreover, 20.3% of patients reported grade I or II acute gastrointestinal symptoms, such as diarrhea, constipation, and proctitis, while only one patient experienced a grade III acute proctitis. Grade IV rectal toxicity was not observed. Regarding late toxicity, 78.3% of patients experienced grade 0 genitourinary toxicity, 18% experienced grade I or II symptoms, while 3% reported grade III toxicity (most of them after repeated urologic instrumentation, in two patients, urethral dilatation was required for bulbar urethral stricture). In one patient (0.5%) a grade IV bladder fistula was observed. The median time from CK course of radiotherapy completion to the occurrence of late grade III-IV genitourinary toxicity was 29 months

(range=18-45). The majority of patients (95%) did not experienced late gastrointestinal toxicity, only Grade I or II symptoms were observed in 10 patients (4.6%), while grade III or higher was not reported. *Discussion and Conclusion:* Our preliminary data confirm that Cyberknife SBRT represents a non invasive method for the definitive treatment of localized prostate cancer with results not inferior to standard fractionated radiotherapy in terms of biochemical control rates at up to 6 years and early and late toxicities. Long-term follow-up is needed in order to evaluate the maintenance of biochemical and clinical outcomes and late toxicity results.

34
MAGNETIC RESONANCE IMAGING-GUIDED CONTOURING IN STEREOTACTIC BODY RADIATION THERAPY IN LOCALIZED DISEASE PROSTATE CANCER: PRELIMINARY RESULTS OF A PHASE-II STUDY

Alessandro Magli[1], Eugenia Moretti[2], Marika Guernieri[2], Rossano Girometti[3], Mauro Urpis[4], Margherita Crespi[5], Tino Ceschia[1], Marco Andrea Signor[1], Claudio Foti[5], Paolo Scalchi[5] and Marco Trovò[1]

[1]Department of Radiation Oncology, ASUIUD, Udine, Italy;
[2]Medial Physics, ASUIUD, Udine, Italy;
[3]Department of Radiology, ASUIUD, Udine, Italy;
[4]Department of Radiation Oncology, ASUIUD, Udine, Italy;
[5]Medical Physics, ASUIUD, Udine, Italy

Background/Aim: Magnetic resonance imaging (MRI)-guided stereotactic body radiation therapy (SBRT) has been established as a safe and effective treatment for prostate cancer. The goal of prostate SBRT is to treat the entire prostate and proximal seminal vesicles, while limiting radiation dose to the adjacent critical structures, including the bladder, rectum, and membranous urethra. Since the prostate apex is commonly involved with cancer, under-dosing this region would likely increase the risk of recurrence. MRI imaging better defines the prostate and reduces the overall target volume compared to Computed Tomography (CT) imaging. In addition, the prostatic-rectal and prostatic-bladder interfaces are better defined by MRI than by CT imaging. Furthermore, the more accurate delineation of the prostatic apex allows for dose reduction to the genitourinary diaphragm (GUD). A phase-II study of SBRT for localized prostate cancer at low-/intermediate- risk (according to NCCN score) and risk of lymph node involvement <17% (Roach Index) was carried out between November 2015 and July 2017. In this report, the preliminary results in terms of acute toxicity are documented. *Materials and Methods:* This is a prospective analysis of 30 patients treated with SBRT using volumetric modulated arc therapy (VMAT) technique. The plans were created by the Eclipse™ Treatment Planning System (ver. 10, Varian Medical Systems). Dose distributions were calculated using a 6-MV beam and the AAA dose calculation algorithm. The SBRT-VMAT plans were set up with two full arc arrangements. The prescription dose was 36.25 Gy, administered in 5 fractions; assuming α/β 1.5 Gy, it corresponded to a biologically effective dose (BED) to the prostate equal to 211.5 Gy. The gross tumor volume (GTV) (prostate with the 1/3 proximal seminal vesicles) was delineated using the MRI T2-weighted (T2w) and FLAIR images, co-registered with planning-CT images. Our local rigid registration method employed the 3 intraprostatic gold fiducial markers (GFM) as landmarks. The GTV was delineated also on CT-images and compared to MR-based GTV, by using the DICE metric. All patients were contoured under the supervision of the same physician (AM). For the planning, an isotropic margin of 6 mm around the MR-based GTV is added to obtain the planning tumor volume (PTV). To study the potential association to the bladder trigone on long-term urinary function, the bladder trigone was MR-based contoured too. An indwelling catheter was inserted to aid in the delineation of the urethra. The request for prescription dose was (V100%)>95% of the PTV. According to our internal protocol, minimum dose (98%) to PTV > 97%, and maximum dose (2%) <110% of the prescribed dose were recommended. The rectal dose- volume goals were V50% <50%, V80% <20%, V90 <10%, V100% <5%. The bladder dose-limits were V50% <40%, V92.4% <12.7%, and V100% <10%. Concerning the urethra and the trigone, the constraints for the maximum dose (Dmax) were Dmax<39.9 Gy and Dmax<38.9 Gy, respectively. The image-guided radiotherapy protocol was based on 3 intraprostatic fiducial markers, with daily online checks by cone beam computed tomography. The acute toxicity gastrointestinal (GI) and genitourinary (GU) were recorded using the Radiation Therapy Oncology Group (RTOG)/European Organization for Research and Treatment of Cancer scale. Additional data are collected by means of International Prostate Symptom Score (I-PSS) and International Index of Erectile Function (IIEF-5) questionnaires. *Results:* Between November 2015 and July 2017, 30 patients were enrolled in this prospective study; the median follow-up duration was 6 months (range, 3-18 months). The median age was 74 years (range=60-81). The mean target registration error was 0.05±0.02 mm (SD). The CT-contoured prostate resulted on average 35% larger that the true gland (MR-based volume) with a mean DICE coefficient of 0.79 (range=0.61-0.90), such that posterior portions were always missed and anterior normal tissue always included. The requests for coverage of the PTV were accomplished for all the VMAT plans; dose constraints for each organ at risk

were largely fulfilled. Acute GU and GE toxicity of grade 2 were observed in 26% and 10% patients respectively. The patients presented with urinary obstructive symptoms before radiation treatment had a slight increase in the severity of their symptoms, with the complete recovery at 3 months from the end of the radiotherapy. *Conclusion:* The present study showed an important reduction in volume of MR-guided prostate, in agreement with literature data. These reductions are primarily due to reduced variation at the superior and inferior extent of the prostate, and translate into reductions in delivered dose to the rectum. This improved soft tissue visualization on MRI has also been shown to reduce inter-observer variation in prostate contouring. The dosimetric data of these first 30 patients are favorable for both target coverage and organs at risk dose limits, indicating that SBRT-VMAT planning in conjunction with MRI-based prostate is safe for localized prostate cancer patients at low- or intermediate-risk. Our preliminary moderate acute toxicity results were consistent with these dosimetric data. Finally, despite these encouraging results, longer follow-up periods are necessary to confirm them.

35

PRIMARY RENAL CELL CARCINOMA (RCC): FOCUS ON STEREOTACTIC BODY RADIOTHERAPY (SBRT)

Marco Andrea Signor[1], Lucrezia Grillone[2], Alessandro Magli[1], Giuseppe Parisi[1], Roberto Bortolus[3], Mauro Urpis[1], Marco Trovò[1] and Rossano Girometti[4]

[1]Department of Radiation Oncology, ASUIUD, Mortegliano, Udine, Italy;
[2]Medical Department, University of Udine, Udine, Italy;
[3]Department of Radiation Oncology, CRO Aviano, Italy;
[4]Institute of Radiology, University of Udine, Udine, Italy

Background/Aim: Poor-surgical candidates with primary renal cell carcinoma (RCC) have limited treatment options. In this difficult cohort, stereotactic body radiotherapy (SBRT) is an emerging, potentially curative, treatment approach that delivers very high doses of radiation in 1-5 outpatient sessions. Historically considered radio-resistant, both pre-clinical and clinical data now support the sensitivity of RCC to high-dose per fraction radiotherapy, as used in SBRT. Moreover, in contrast to radiofrequency ablation and cryotherapy, SBRT is capable of treating both larger tumors and those adjacent to collecting vessels and ureteric ducts. Additionally, this novel technique is non-invasive and delivered whilst the patient is fully awake. To focus on SBRT for the treatment of primary renal cell carcinoma, local control, survival, and toxicity outcomes were assessed in a multi-institutional setting. Finally, outcomes between single and multi-fraction SBRT were compared. *Materials and Methods:* A systematic search on PubMed was performed using structured search terms, for studies between 1995 and 2017. The following structured search terms were employed: kidney neoplasms [MeSH] AND radiotherapy [Title] OR radiosurgery [Title] OR stereotactic [Title] OR radiation [Title] NOT (metastases [Title] OR metastasis [Title]) NOT brain [Title]. Then, the citations in relevant publications and abstracts in the major North American and European radiotherapy journals were selected. For data extraction, all the papers were scrutinized for the following information: study design (retrospective, prospective); number of patients; follow-up; total dose; dose per fraction, clinical outcomes and toxicity. *Results:* In total, 14 clinical studies were selected and 215 patients treated for primary RCC were identified. Relevant clinical information concerning tumor characteristics, treatment techniques, duration of patient follow-up, treatment-related toxicities are reported in Table I. Eight studies were retrospective and 6 were prospective. Nomiya *et al*. (1) reported the use of a heavy carbon-ion particle accelerator; Kaplan *et al*. (2) and Ponksy and Vricella (3) used a robotic arm-held linear accelerator system; all the other studies used conventional gantry-operated linear accelerators. There were: no size restrictions; no excluded tumors based on proximity to collecting vessels or renal vasculature; no reports of pathological confirmation of tumor response through post-treatment biopsy. Techniques and dose fractionation schedules varied widely. The most commonly employed fractionation schedule was 40 Gy delivered over five fractions. Siva *et al*. performed a radiosurgical approach: 26 Gy in a single fraction to targets <5 cm (4). The median or mean follow-up ranged between 9 and 57.5 months. Local control was reported in 12/14 studies, ranging from 84% to 100%. The weighted 2-year local control rate was estimated at 93.1%. Overall survival was inconsistently reported in these series. The most common reported toxicities were fatigue and nausea, followed by radiation dermatitis and enteritis. Rates of severe toxicity (grade >3) were very low, although in one study a 19% rate was recorded whilst Nomiya *et al*. (1) reported one late grade 4 skin toxicity. The weighted rate of severe toxicity was 3.8%, and the weighted rate of minor toxicity (grade 1-2) was 21.4%. One study noted a baseline neutrophil: lymphocyte ratio that may be predictive of immune-mediated response and warrants further investigation. We also analyzed one systematic review and one individual patient data meta-analysis. *Discussion:* SBRT can be performed using conventional gantry-operated linear accelerators having the advantage of being readily accessible in most radiotherapy departments. Moreover, SBRT is non-invasive and delivered in outpatient sessions without anaesthesia or premedication. Additionally, it is capable of treating both larger tumors and those adjacent to collecting vessels and ureteric ducts. Herein, SBRT appeared to be

Table I. *Studies assessing SBRT in RCC*.

Author, year of publication	Patients	Study design	Follow-up (median or mean)	Dose × fractions	Local control (%)	Estimated 2-years local control	Overall survival (median)	Toxicity
Qian *et al*. 2003 (6)	20	Retrospective	12	8 Gy × 5	93	86	Not reported	Not reported
Beitler *et al*. 2004 (7)	9	Retrospective	26.7	8 Gy × 5, 7 Gy × 6	100	100	4/9 patients alive	33% G1-G2, Nil G3 +
Wersäll *et al*. 2005 (8)	8	Retrospective	37	8 Gy × 5, 10 Gy × 4, 15 Gy × 3	100	100	58 months	20% G1-G2, 19% G3, Nil G4
Gilson *et al*. 2006 (9)	33	Retrospective	17 Median	8 Gy × 5	94	92	Not reported	Not reported
Svedman *et al*. 2006 (10)	5	Prospective phase II	52	8 Gy × 4, 10 Gy × 4, 15 Gy × 2, 15 Gy × 3	80	91	32 months	89% G1-G2, 4% G3
Teh *et al*. 2007 (11)	2	Retrospective	9	24-48 Gy × 3-6	100	100	Not reported	Not reported
Svedman *et al*. 2008 (12)	7	Retrospective	39	10 Gy × 3 or 10 Gy × 4	86	91	Not reported	58% G1-G2, Nil
Nomiya *et al*. 2008 (1)	10	Retrospective	57.5 Median	4.5 Gy × 16	100	100	5-years OS 74%	10% G4
Kaplan *et al*. 2010 (2)	12	Prospective phase I	Not reported	Max 13 Gy × 3	84	Not reported	Not reported	Nil
Ponsky and Vricella, 2012 (3)	20	Prospective phase I	Not reported	Max 16 Gy × 3	Not reported	Not reported	Not reported	Nil
Ellis *et al*. 2012 (13)	20	Prospective phase I	2-41 months	DE total dose: 4-24 Gy, 6-32 Gy, 4-40 Gy, and 6-48 Gy	SD or PR in 94%	Not reported	Not reported	10% G1 fatigue
Pham *et al*. 2014 (14)	20	Prospective phase I	Not reported	42 Gy × 3 to targets >5 cm, 26 Gy × 1 to targets <5 cm	Not reported	Not reported	Not reported	60% G2
Chang *et al*. 2016 (15)	16	retrospective	19 months (range=7-30)	30-40 Gy × 5	100	Not reported	Not reported	6.3% G2; 25% G4
Siva *et al*. 2017 (4)	33	Prospective phase I	24 months	42 Gy × 3 to targets >5 cm, 26 Gy × 1 to targets <5 cm	100	100	Not reported	78% G1-G2; 3% G3

DE, Dose escalation; SD, stable disease; PR, partial response.

tolerable and was associated with excellent local cancer control in inoperable cohorts, at 2 years and early survival. Post-treatment renal impairment was acceptably low. On the other hand, only 6 studies were prospective phase I trials. The mean number of treated patients was 15; the total was 215. Biopsies were not obtained in every patient. Some of these patients were referred for SBRT because they were very frail and would not have been able to tolerate a biopsy. Although the non-biopsied tumors were noted to have increased in size over time on serial imaging, it is possible that some of them were not malignant. The follow-up period was short at this stage and there may not have been enough time to document local failures or all potential late toxicities. RCC has been shown to have slow growth in active surveillance studies and literature data have shown local failures after 30 months of follow-up (5). Furthermore, late toxicities, such as declining renal function, might worsen over time. Therefore, with longer follow-up more cases of local failures and higher rates of late toxicities may be found. Also, the small sample size limited the ability to draw conclusions from these results. Finally, as with all retrospective studies, potentially not all toxicity data were obtained. We aim to address the above limitations by carrying out a prospective multicentre trial. *Conclusion:* SBRT for both small and large primary RCC was

associated with encouraging local cancer control at 2 years and early survival in inoperable cohorts. Post-treatment renal impairment is acceptably low. Ten groups used conventional gantry-operated linear accelerators. The most commonly employed fractionation schedule was 40 Gy delivered over five fractions; however, outcomes were similar between single and multifraction regimens. Prospective multicenter validation is essential to confirm the efficacy and safety of this non-invasive, nephron-sparing, ablative technique and provide further information to help refine patient selection and develop better biomarkers of response.

1 Nomiya T, Tsuji H, Hirasawa N, Kato H, Kamada T, Mizoe J, Kishi H, Kamura K, Wada H, Nemoto K and Tsujii H: Carbon ion radiation therapy for primary renal cell carcinoma: Initial clinical experience. Int J Radiat Oncol Biol Phys *72*: 828-833, 2008.

2 Kaplan ID, Redrosa I, Martin C, Collins C and Wagner A: Results of a phase I dose escalation study of stereotactic radiosurgery for primary renal tumors. Int J Radiat Oncol Biol Phys *78*: S191, 2010.

3 Ponsky L and Vricella G: Radiosurgery for renal tumors. In: Robotic radiosurgery treating prostate cancer and related genitourinary applications. Berlin, Springer-Verlag, pp. 179-184, 2012.

4 Siva S, Pham D, Kron T, Bressel M, Lam J, Tan TH, Chesson B, Shaw M, Chander S, Gill S, Brook NR, Lawrentschuk N, Murphy DG and Foroudi F: Stereotactic ablative body radiotherapy for inoperable primary kidney cancer: a prospective clinical trial. BJU Int *120*: 623-630, 2017.

5 Chawla SN, Crispen PL, Hanlon AL, Greenberg RE, Chen DY and Uzzo RG: The natural history of observed enhancing renal masses: Meta-analysis and review of the world literature. J Urol *175*: 425-431, 2006.

6 Qian G, Lowry J, Silverman P, Grosman I, Makara D and Lederman G: Stereotactic extra-cranial radiosurgery for renal cell carcinoma. Int J Radiat Oncol Biol Phys *57*: S283, 2003.

7 Beitler JJ, Makara D, Silverman P and Lederman G: Definitive, high-dose-perfraction, conformal, stereotactic external radiation for renal cell carcinoma. Am J Clin Oncol *27*: 646-648, 2004.

8 Wersall PJ, Blomgren H, Lax I, Kälkner KM, Linder C, Lundell G, Nilsson B, Nilsson S, Näslund I, Pisa P and Svedman C: Extracranial stereotactic radiotherapy for primary and metastatic renal cell carcinoma. Radiother Oncol *77*: 88-95, 2005.

9 Gilson B, Lederman G, Qian G, Fastaia M and Cangiane L: 2249: Hypo-fractionated Stereotactic Extra-Cranial Radiosurgery (HFSR) for Primary and Metastatic Renal Cell Carcinoma. Int J Radiat Oncol Biol Phys *66*: S349, 2006.

10 Svedman C, Sandstrom P, Pisa P, Blomgren H, Lax I, Kälkner KM, Nilsson S and Wersäll P: A prospective Phase II trial of using extracranial stereotactic radiotherapy in primary and metastatic renal cell carcinoma. Acta Oncol *45*: 870-875, 2006.

11 Teh B, Bloch C, Galli-Guevara M, Doh L, Richardson S, Chiang S, Yeh P, Gonzalez M, Lunn W, Marco R, Jac J, Paulino A, Lu H, Butler E and Amato R: The treatment of primary and metastatic renal cell carcinoma (RCC) with image-guided stereotactic body radiation therapy (SBRT). Biomed Imaging Interv J *3*: e6, 2007.

12 Svedman C, Karlsson K, Rutkowska E, Sandström P, Blomgren H, Lax I and Wersäll P: Stereotactic body radiotherapy of primary and metastatic renal lesions for patients with only one functioning kidney. Acta Oncol *47*: 1578-1583, 2008.

13 Ellis RJ, Patel RB, Kunos C, Zhang Y, Brindle J, Kudithipudi V, Kaminsky DA and Ponsly L: Stereotactic radiosurgery for renal cancer: Phase I safety and toxicity. Int J Radiat Oncol Biol Phys *84*: S119, 2012.

14 Pham D, Thompson A, Kron T, Foroudi F, Kolsky MS, Devereux T, Lim A, Siva S: Stereotactic ablative body radiation therapy for primary kidney cancer: a 3-dimensional conformal technique associated with low rates of early toxicity. Int J Radiat Oncol Biol Phys *90*: 1061-1068, 2014.

15 Chang JH, Cheung P, Erler D, Sonier M, Korol R and Chu W: Stereotactic ablative body radiotherapy for primary renal cell carcinoma in non-surgical candidates: Initial clinical experience. Clin Oncol *28*: 109-114, 2016.

36

ACTIVE SURVEILLANCE IN PROSTATE CANCER PATIENTS: PREDICTING THE CHANCE OF CONTINUING AS AFTER RE-BIOPSY

Nicola Nicolai[1], Maria Francesca Alvisi[2], Tiziana Rancati[2], Barbara Avuzzi[3], Fabio Badenchini[2], Mario Catanzaro[1], Maurizio Colecchia[4], Teresa Di Florio[2], Tiziana Magnani[2], Cristina Marenghi[2], Simona Massa[4], Sara Morlino[3], Barbara Noris Chiorda[3], Biagio Paolini[4], Silvia Stagni[1], Antonio Tesone1, Tullio Torelli[1], Sergio Villa[3], Nadia Zaffaroni[5], Roberto Salvioni[1] and Riccardo Valdagni[6]

[1]Division of Urology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[2]Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[3]Division of Radiation Oncology 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[4]Division of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[5]Division of Experimental Oncology and Molecular Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[6]Division of Oncology And Hemato-oncology, Università degli Studi di Milano, Milan, Italy

Background/Aim: Prostate biopsy findings at diagnosis and follow-up are essential criteria in active surveillance (AS). In a previous work (1) upgrading (UPG) and upsizing (UPS) at 1-year re-biopsy were shown to be independent outcomes, and they were associated with different predictors. In this context, a combined model was also proposed to predict the probability of dropping out of AS, starting from the separate probabilities of UPG and UPS. The aim of the present work was to validate these models on an independent population, and also to evaluate the probability of not developing UPG at the first re-biopsy, thus continuing AS. *Materials and Methods:* Patients enrolled in AS between 2005 and 2011 were considered for model development, while patients enrolled from 2011 to 2017 were included in the validation dataset. Model for UPG included: age as continuous variable, prostate-specific antigen (PSA) density as continuous variable, and more than 60 cc of prostate volume. Area under the curve (AUC) of the model on the original population after bootstrapping was 0.60. Model for UPS considered: age as continuous variable, more than 5% of maximum percent of core length containing cancer core and more than 2 positive cores at diagnosis, AUC after bootstrapping was 0.63. Using the two separate models for UPG and UPS, the new combined model (OUT) for PCa reclassification after 1 year AS was defined as p(OUT)=1–{[1–p(UPG)] ×(1–p(UPS)]}, with AUC equal to 0.63. Performance of the three models on the independent population was evaluated through AUC and calibration (calibration slope and R2 for calibration fit). Logistic model for not-developing UPG at 1 year (*i.e.* a model predicting the chance of continuing AS after re-biopsy) was fitted using all available AS patients and a nomogram estimating the likelihood of continuing AS was developed. *Results:* A total of 433 prostate cancer patients with 1 year re-biopsy were included in the validation set. At 1 year re-biopsy UPG was registered in 43 patients, UPS was found in 29 patients, and 38 patients had both UPG and UPS. Median age at enrolment

	DEVELOPMENT (n=318)			VALIDATION (n=433)		
Upgrading	**OR**	**p**	**AUC**	**OR**	**p**	**AUC**
Age (continuous)	1.06	0.04		1.09	0.0	
Prostate volume >60 cc	0.2	0.03	0.60	0.4	0.04	0.72
PSA density (continuous)	1.02	0.3		1.05	0.01	
Upsizing						
Age (continuous)	0.97	0.29		1.0	0.88	
>5% core involvement	2.9	0.04	0.63	1.3	0.35	0.66
>1 positive cores	1.6	0.29		3.0	0.0	
OUT			0.63			0.69

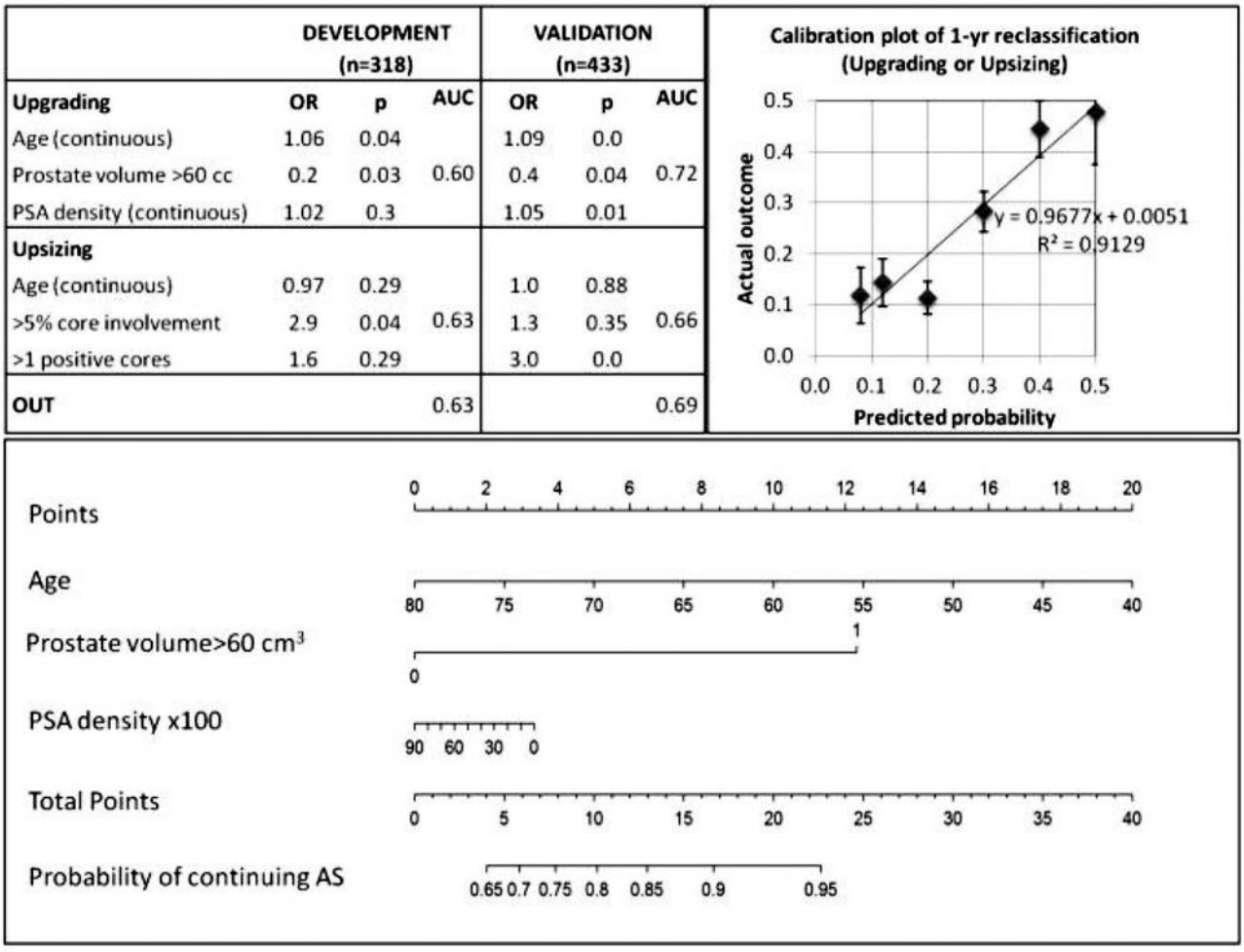


Figure 1. *Multivariate logistic regression models for upgrading, upsizing and 1 year reclassification. Calibration plot and nomogram for 1 year reclassification (upgrading or upsizing).*

in AS was 64.4 years (range=42-79) for the validation set, and 66 years (range=43-79) for developing set; median PSA density was 0.11 ng/ml/cc (range=0.1-0.43) *vs*. 0.12 ng/ml/cc (range=0.02-0.52) for validation and developing set, respectively; median prostate volume was 48 cc (range=10-53) *vs*. 45 cc (13-155). In the validation cohort, 40.4% of patients had more than one positive core at diagnosis (30.8% in the developing cohort) and 60.5% of patients had more than 5% of cancer in the positive cores at diagnosis (50.9% in the developing cohort). Predictors for UPG and UPS were mainly confirmed in the validation cohort (Figure 1), with odds ratios (OR) very similar to the development model. Discrimination was confirmed: AUCs are reported in the Figure 1 and calibration was excellent. Specifically, calibration slope and R^2 fit for the validation of UPG model were 0.83 and 0.94, respectively, while calibration slope and R2 fit for UPS model validation were 1.01 and 0.99, respectively. Calibration plot of the combined model is presented in Figure 1. Probability of continuing AS after re-biopsy (*i.e*. of not-developing UPG) was evaluated on 751 patients and resulted to be associated with age (younger patients have higher probability to continue AS after re-biopsy), prostate volume (patients with large prostate volumes have higher probability to continue AS) and PSA density (patients with lower PSA density have higher probability to keep on with AS). Figure 1 shows the nomogram that can be used at enrolment to estimate the individual patient probability of continuing AS after 1-year re-biopsy. *Conclusion:* UPG and UPS at re-biopsy were associated with different disease features at diagnosis. Prostate cancer UPG and UPS in AS patients should be considered independent events and their management implies different strategies. Specifically, age, prostate volume, and PSA density play a key role in the decision to continue AS, *i.e*. in not developing UPG. From a practical perspective, a prognostic nomogram was developed in order to estimate, at the entrance in AS, the likelihood of continuing the observational strategy after the first re-biopsy.

1 Nicolai N, Alvisi MF, Rancati T, Salvioni R, Stagni S, Marenghi C, Magnani T, Bellardita L, Colecchia M, Morlino S, Avuzzi B, Zaffaroni N and Valdagni R: Different predictors of upgrading and upsizing at 1-year repeat biopsy in men with low-risk prostate cancer undergoing active surveillance in prospective trials. Eur Urology *12(6)*: 153-154, 2013.

37

DOES THE PRESENCE OF THE PRIMARY TUMOR MODIFY THE CLINICAL OUTCOME IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER PATIENTS SUBMITTED TO RADIUM-223 THERAPY?

Vincenzo Serretta[1], Cristina Scalici Gesolfo[2], Cristina Scalici Gesolfo[2], Cristina Scalici Gesolfo[1], Nicola Borsellino[3], Francesco Verderame[4], Giuseppe Cicero[5], Alessandra Morabito[2], Vincenzo Tripoli[2], Maria Licari[2] and Chiara Sanfilippo[6]

[1]Section of Urology, Department of Surgical, Oncological and Stomatological Sciences, University of Palermo, Palermo, Italy; [2]Nuclear Medicine Unit, University of Palermo, Palermo, Italy; [3]Department of Oncology, Ospedale Buccheri La Ferla Fatebenefratelli, Palermo, Italy; [4]Department of Oncology, Ospedali Riuniti Villa Sofia- Cervello, Palermo, Italy; [5]Section of Medical Oncology, Department of Surgical, Oncological and Stomatological Sciences, University of Palermo, Palermo, Italy; [6]Statistics, GSTU Foundation, Palermo, Italy

Background/Aim: Radium-223 (^{223}Ra) improves survival in patients with metastatic castration-resistant prostate cancer (mCRPC). Although anti-androgen hormonal therapy is maintained, the treatments for CRPC are usually not given in patients undergoing ^{223}Ra. The primary prostate tumor could progress during ^{223}Ra treatment, particularly if hematological toxicity, patient compliance, general status, and other factors might limit the early start of further therapy. The aim of our study was to evaluate the clinical impact of the presence or absence of primary tumor in terms of progression, death, and treatment withdrawal in patients with mCRPC undergoing ^{223}Ra therapy. *Materials and Methods:* The clinical files of mCRPC symptomatic patients treated with ^{223}Ra between January 2016 and July 2017 were reviewed. All patients provided written informed consent. In all patients luteinizing hormone-releasing hormone analogues therapy was maintained. Technetium-99m bone scan and total-body computed tomography (CT) scan were obtained within one month of the planned start of the treatment. The ^{223}Ra treatment schedule consisted in the administration of 55 kBq/kg every 4 weeks for up to six injections. No other anticancer therapy was given during ^{223}Ra treatment. Patients were stratified according to the presence or absence of the primary prostate tumor. ^{223}Ra treatment was discontinued at patient's request, on occurrence of CTCAE grade 3 or 4 neutropenia, anemia or thrombocytopenia lasting longer than 14 days, or due to visceral progression or a dose delay (>4 weeks). Hematological toxicity was monitored with different intervals according to the number of metastases. Clinical outcomes in terms of progression, death, and treatment withdrawal due to toxicity were analyzed according to the presence/absence of the primary tumor. *Results:* The clinical records files of 44 consecutive patients were reviewed.

Median age was 76 years and median body mass index 27.2. The Gleason grade of the prostate tumor was 7, 8, and 9-10, in 11 (25%), 13(29.5%), and 13 (29.5%) patients, respectively. Sixteen (36.4%) patients were previously submitted to radical prostatectomy and 5 (11.3%) to prostatic radiotherapy, while in 28 (63.6%) the primary prostate tumor did not receive any local treatment. All patients had bone metastases, the number of lesions was less than 6 in 9 (20.4%), between 6 and 20 in 10 (22.7%), and more than 20 in 24 (54.5%) patients. Twenty-six (59.1%) patients had previously received systemic chemotherapy. ^{223}Ra regimen was suspended in 17 patients (41%): for toxicity in 9 (20.4%), for progression in 7 (15.9%), and for other causes in 1 (2.3%). Fourteen of these 17 patients (77.7%) were not submitted to prostatectomy (2/14 patients previously treated previous radiotherapy). Out of 12 (27.3%) patients showing progression, 9 (75%) patients were not submitted to prostatectomy (1/9 submitted to previous radiotherapy). Five patients died, 4 of them due to their prostate. Although no statistical analysis was performed due to the small patients' number, our results suggest the relevant prognostic role of the presence/absence of the primary tumor in terms of treatment completion and progression. *Discussion and Conclusion:* During ^{223}Ra treatment, in absence of other concomitant anticancer therapies different than androgen deprivation, 78% of the treatment discontinuations and 75% of the clinical progressions were recorded among patients without prostatectomy. In our preliminary experience, the presence of the primary prostate tumor plays a detrimental role in terms of treatment completion and clinical response in ^{223}Ra treatment.

GSTU Foundation, Palermo, Italy for the laboratory kits supply and the statistical support.

38
DOES THE NEUTROPHIL-TO-LYMPHOCYTE RATIO PLAY A PROGNOSTIC ROLE IN UNSELECTED NON–MUSCLE-INVASIVE BLADDER CANCER?

Vincenzo Serretta[1], Giorgio Ventura[1], Giulio Bevilacqua[1], Sandro Billeci[1], Cristina Scalici Gesolfo[1], Marco Vella[1] and Chiara Sanfilippo[2]

[1]Section of Urology, Department of Surgical, Oncological and Stomatological Sciences, University of Palermo, Palermo, Italy; [2]Statistics, GSTU Foundation, Palermo, Italy

Background/Aim: Several recent studies report neutrophil-to-lymphocyte ratio (NLR) as a useful biomarker of systemic inflammatory response in several tumor types. A higher preoperative NLR has been associated with poor prognosis and pathologic upstaging in patients with muscle invasive bladder cancer (MIBC) undergoing cystectomy. Up to date, the predictive value of NLR in non-muscle-invasive bladder cancer (NMIBC) has been rarely studied with uncertain results. D'Andrea and colleagues (1) recently found an independent association of NLR with unfavorable clinical outcome in selected patients with high-risk NMIBC, identifying patients failing intravesical immunotherapy. The aim of our study was to examine whether NLR could predict pathologic upstaging and recurrence in unselected patients undergoing transurethral resection (TUR) for primary NMIBC. *Materials and Methods:* The medical records of 162 consecutive patients submitted to TUR for primary NMIBC between January 2013 and December 2015 were reviewed. Informed consent and ethical committee approval was obtained. Patients with other malignancies or with known autoimmune or inflammatory diseases or clinical evidence of advanced bladder cancer were excluded. Numeric values were compared by Wilcoxon-Mann-Whitney test. Chi-square test was used for the comparison of the non-numeric values. A NLR cut-off value of 3 was adopted, according to recent literature (1). A p-value <0.05 was considered statistically significant (Software R version 3.4.2). *Results:* The study cohort comprised 142 (87.7%) men and 20 women with a median age of 70 (23-90) years. Fifty four (33.3%) patients were active smokers, 73 (45.1%) former smokers, and 35 (21.6%) never smokers, with a median number of 20 cigarettes per day and a median smoking period of 25 years. A pathological diagnosis of NMIBC in 130 (80.2%) and of MIBC in 32 (19.8%) patients was obtained. Particularly, high-grade tumors were found in 76 (46.9%) patients. Among NMIBC, 30 T1 (23%), 3 Tis (1.9%), and 42 (32.3%) high-grade tumors were diagnosed. Tumors were multiple in 131 patients (80.9%). Tumor size was <2 cm, between 2 and 5 cm, and more than 5 cm in 81 (50%), 77 (47.5%), and 4 (2.5%) patients, respectively. The median NLR was 2.7 (range=0.2-42.1). At a median follow-up of 25 months (range: 3-48), 54 (39.9%) patients recurred. Mean time to recurrence was 12.9 months. No correlation was found between NLR (cut-off of 3) and age (p=0.85), gender (p=0.38), smoking status (p=0.50), G-grade (p=0.24), tumor size (p=0.77), or the adoption of adjuvant intravesical therapy (p=0.48). Moreover, no correlation was detected between NLR and recurrence (p=0.17). However, a statistically significant association was detected between NLR and multiplicity (single *vs.* multiple) (p=0.018), and T-stage (NMIBC *vs.* MIBC) (p<0.005). *Discussion and Conclusion:* A recent study (2) suggested an independent prognostic value of NLR in advanced bladder cancer and in high-risk NMIBC. In our experience in consecutive patients undergoing TUR for a clinical diagnosis of NMIBC we found a statistically significant association of NLR with multiplicity and with T-stage was found, both factors enhancing host immune

response. However, no relation between NLR and patients' outcome in terms of recurrence was detected. In conclusion, although related with tumor multiplicity and T-stage, NLR has no predictive value for recurrence in unselected NMIBC treated in common clinical practice.

We wish to thank the GSTU Foundation for the statistical support.

1 D'Andrea D, Moschini M, Gust K, Abufaraj M, Ozsoy M, Mathieu R, Soria F, Briganti A, Roupret M, Karakiewicz PI and Shariat SF: Prognostic role of neutrophil-to-lymphocyte ratio in primary non–muscle-invasive bladder cancer. Clin Genitourin Cancer *15(5)*: e755-e764, 2017.

2 Kang M, Balpukov UJ, Jeong CW, Kwak C, Kim HH and Ku JH: Can the preoperative neutrophil-to-lymphocyte ratio significantly predict the conditional survival probability in muscle-invasive bladder cancer patients undergoing radical cystectomy? Clin Genitourin Cancer *15(3)*: e411-e420, 2017.

39

PREDICTORS OF A CLINICALLY SIGNIFICATIVE PROSTATE CARCINOMA IN PATIENTS WHO UNDERWENT TO RADICAL PROSTATECTOMY BUT WERE AFFECTED BY A CANCER SUITABLE FOR ACTIVE SURVEILLANCE

Carmelo Agostino Di Franco, Giovanni Giliberto, Daniele Porru, Tiziano Cebrelli and Bruno Rovereto

Department of Urology, University Hospital IRCCS Policlinico S. Matteo, Pavia, Italy

Background/Aim: Active surveillance (AS) represents a therapeutic alternative to an immediate radical treatment in patients affected by localized prostate cancer, with favorable prognosis and long life expectancy. Sometimes, discrepancy between biopsy and prostatectomy specimen, in terms of Gleason Score and pathological stage, risks addressing a low-risk patient to a radical treatment and its related effects. The aim of this work was to evaluate the correlation between biopsy and surgical specimen after radical prostatectomy, in patients affected by low-risk prostate cancer suitable for AS, and moreover, to identify predictive factors of clinically significant disease. *Materials and Methods:* This is a retrospective, non-randomized, study. A cohort of 461 consecutive patients who underwent to radical prostatectomy between 2010 and 2017 in a single centre were evaluated. Data about age, preoperative prostate-specific antigen (PSA), number of bioptic cores, number of positive bioptic cores, percentage of positive biopsy cores, biopsy and pathological Gleason Score, clinic and pathological stage, prostate volume at the operative specimen, PSA density, and positive surgical margins were recorded for each patient. Prostatic volume was calculated with ellipsoid formula. Then, 135 patients suitable for AS were selected based on the European Association of Urology (EAU) guidelines 2017. The upstaging and the upgrading to clinical significant disease after radical prostatectomy was defined as "reclassification of the disease", while the upstaging ≥ pT3a and/or the upgrading ≥ Gleason Score 4+3 was defined as "unfavorable disease". All data were collected in Excel database. To identify predictive factors of clinically significant disease we used univariate and multivariate analysis. *Results:* In a cohort of 461 patients, overall upgrading and uspstaging rate was 60.3% and 39.9%, respectively. Both upstaging and upgrading was observed in 36% of patients, whereas in 24.3% of cases we had only upgrading to Gleason Score >7. Multivariate analysis on 461 patients showed that PSA density and percentage of positive biopsy cores correlated with upstaging and upgrading risk, whereas the age correlated only with upgrading. In 135 patients suitable for AS, upgrading and upstaging rate was 38.5% and 29.6%, respectively. Both upgrading and upstaging was reported in 23.7% of patients, only upgrading in 14.8%, while 55.6% of patients had no reclassification after radical prostatectomy. Gleason Score was 4+3 in 11.1% patients of the 135 suitable for AS. Multivariate analysis in "AS cohort" showed that age and PSA density correlated with upstaging risk, whereas upgrading risk is associated only to age. *Conclusion:* In patients suitable for AS, on the basis of parameters suggested by EAU Guidelines 2017, around 40-50% of patients are indeed affected by a clinically significant prostate cancer. Higher age and higher PSA density were identified as predictive factors of clinically significant disease. There are certain limitations of this study: retrospective design, different pathologist, prostatectomy performed in open retropubic, laparoscopy and robot-assisted way. We suggest, that in the presence of factors suggesting a clinically significant disease, other diagnostic studies (*e.g.* multiparametric RMN) should be performed before starting an AS program.

40

ENDOSCOPIC INTRAVESICAL FIBRIN GLUE APPLICATION IN THE TREATMENT OF REFRACTORY HAEMORRHAGIC RADIATION CYSTITIS

Pierluigi Bove[1], Valerio Iacovelli[1], Chiara Cipriani[1], Maria Cristina Tirindelli[2], Gerardo Paolo Flammia[3], Luca Cindolo[4], Angelo Salvatore Ferraro[5], Daniele Bianchi[1], Matteo Ferro[6], William Arcese[7], Gianluca Ingrosso[8], Giuseppe Vespasiani[1] and Enrico Finazzi Agrò[1]

[1]Department of Experimental Medicine and Surgery, Urology Unit, Tor Vergata University of Rome, Rome, Italy;

[2]Hematology and Stem Cell Transplant Transfusion Medicine and Cellular Therapy, Campus Bio-Medico University Hospital, Rome, Italy;
[3]Department of Urology, Campus Bio-Medico University Hospital, Rome, Italy;
[4]Department of Urology, ASL Abruzzo2, Vasto, Italy;
[5]Blood Bank and Immunohematology, Tor Vergata University of Rome, Rome, Italy;
[6]Department of Urology, European Institute of Oncology, Milan, Italy;
[7]Hematology and Stem Cell Transplant Unit, Tor Vergata University of Rome, Rome, Italy;
[8]Diagnostic Imaging, Molecular Imaging, Interventional Radiology and Radiotherapy Unit, Tor Vergata University of Rome, Rome, Italy

Background/Aim: Hemorrhagic radiation cystitis (HRC) is a complication of radiation therapy to pelvic tumors for which, several treatment options are described (1, 2). However, a multitude of these are anecdotal and presented in case reports or very small case series and the paucity of high quality evidence in the form of randomized control trials does not allow to develop a standard of treatment. We have previously demonstrated the effectiveness of the endoscopic intravesical fibrin glue (FG) application for treating hemorrhagic cystitis after allogeneic stem-cell transplantation (3). Herein, on the base of our experience, we have evaluated the use of endoscopic intravesical FG application in a single cohort of refractory HRC patients. *Patients and Methods:* The data from 20 HRC patients treated with fibrin glue at our institution between May 2012 and May 2015 were reviewed retrospectively. All patients with grade ≥2 HRC (macroscopic hematuria), received endoscopic intravesical FG application after failure of conventional therapy. FG was obtained from virus-inactivated fresh frozen human plasma (Octaplas, Vienna, Austria) and produced using Vivostat System (Vivolution, Alleroed, Denmark), an automatic method for processing and applying FG starting from either whole blood or fresh frozen plasma. For each application, 12 ml of FG were prepared. Patient demographics, types of pelvic malignancy and radiotherapy, total radiation dose, onset and severity of hematuria, and prior intravesical management were evaluated. Clinical improvement was defined as (1) clinical response, disappearance of dysuria, urgency, and frequency; analgesic agent discontinuation; and Foley catheter removal with persistence of hematuria grade <2; (2) complete response, clinical response and absence of hematuria; or (3) no response, no clinical response and persistence of hematuria. *Results:* Twenty patients (8 females and 12 males, median age 69±7.50 years) received an endoscopic application of 12 ml of FG intravesically. HRC was due to prior pelvic radiation therapy for prostate cancer (n=7, 35%), bladder cancer (n=6, 30%), and gynecological malignancies (n=7, 35%). The median radiation dose was 60±2.50 Gy. The median time from radiation therapy to HRC onset was 3±1.90 years. The median duration of hematuria was 3.5±2.50 months. All patients had failed conventional therapy with hyperhydration, catheterization, continuous bladder irrigation and transurethral endoscopic clot evacuation and hemostasis. Four patients (20%) underwent multiple transfusions. Two patients were previously treated with an unsuccessful hypogastric artery embolization and trans-urethral endoscopic clot evacuation and hemostasis. Of the 20 patients, a complete response was obtained in 16 patients (80%) and a clinical response in 4 patients (20%). Four patients were treated twice. For the entire cohort, the median follow-up was 26.2±9.78 months. Treatment was well tolerated in all the patients. No major adverse events were reported. Minor adverse events included bladder spasms in 6 patients. No urinary tract infections were reported. *Discussion and Conclusion:* The results of this pilot study suggest that the endoscopic application of FG should be considered a safe and simple therapeutic tool for the management of refractory HRC developing in frail patients. In particular, FG therapy is a feasible, effective, repeatable, and affordable procedure for treating grade ≥2 HRC and should be applied early from the onset of HRC.

1 Marks LB, Carroll PR, Dugan TC and Anscher MS: The response of the urinary bladder, urethra, and ureter to radiation and chemotherapy. Int J Radiat Oncol Biol Phys *31(5)*: 1257-1280, 1995.
2 Linder BJ and Boorjian SA: Management of Emergency Bleeding, Recalcitrant Clots, and Hemorrhagic Cystitis. AUA Updatate Series 2014.
3 Tirindelli MC, Flammia GP, Bove P, Cerretti R, Cudillo L, De Angelis G, Picardi A, Annibali O, Nobile C, Cerchiara E, Dentamaro T, De Fabritiis P, Lanti A, Ferraro AS, Sergi F, Di Piazza F, Avvisati G, Arcese W and Rome Transplant Network: Fibrin glue therapy for severe hemorrhagic cystitis after allogeneic hematopoietic stem cell transplantation. Biol Blood Marrow Transplant *20(10)*: 1612-1617, 2014.

41
URINARY UNDIVERSION: FEASIBLE SURGERY WITH LOW COMPLICATIONS TO IMPROVE QUALITY OF LIFE OR RENAL FUNCTION

Giovanni Muto[1], Federico Germinale[2], Gianluca Muto[3], Marisa Kurti[2], Devis Collura[1] and Alessandro Giacobbe[1]

[1]Division of Urology, Humanitas Gradenigo, Turin, Italy;
[2]Division of Urology, Campus Bio-Medico, Rome, Italy;
[3]Division of Urology, A.O.U. Careggi, Florence, Italy

Aim: To assess early and late surgical complications as well as quality of life in patients treated with urinary undiversion. *Materials and Methods:* A retrospective analysis of our

multicenter prospective maintained database was performed. All procedures were performed by a single surgeon (G.M.) from 1994 to 2017. Median follow-up was 166 months (range=8-276). Complications were assessed by the Clavien-Dindo classification with a time point of 30 days for early and late complications. Quality of life before and after surgery was compared with Mann-Whitney *U*-test. *Results:* At total of 44 patients (29 men and 15 women) with a median age of 62 (interquartile range=44-72) were identified. Indications for urinary undiversion were: urinary fistula (n=10, 22.7%), cancer recurrences (n=7, 15.9%), urinary incontinence (n=6, 13.6%), hydronephrosis with Chronic Kidney Disease (n=4 9%), recurrent urinary tracts infections (n=5, 11.3%), missing adaptation to the stoma (n=10, 22.7%), stomal infection (n=1, 2.2%) and parastomal hernia (n=1, 2.2%). Overall, 27 (61.3%) patients had neobladder and were treated with incontinent urinary undiversion and eteretopic continent urinary undiversion in 23 (52.2%) and 4 (9%) cases, respectively. Eight (18.1%) patients had incontinent urinary diversion and were treated with neobladder (n=5, 11.3%) and eterotopic continent undiversion (n=3, 6.8%). Five (11.3%) patients had ureterosigmoidostomy and were treated with eterotopic continent undiversion (n=2, 4.5%) and incontinent urinary undiversion (n=3, 6.8%). One (2.2%) patient with ureterocutaneostomy was treated with eterotopic continent urinary undiversion, while one (2.2%) with eterotopic continent urinary diversion was treated with incontinent urinary undiversion. Finally, the urinary diversion was relocated in 2 (4.5%) patients. In many of these cases it was possible to use the same intestinal segment of the previous urinary diversion in order to perform the urinary undiversion without any intestinal resection. At total of 9 (20.4%) complications occurred postoperatively and were classified as follows. Early complications Clavien I (fever >38.5˚C) and Clavien IIIA (wound dehiscence) were observed in 3 (6.8%) and 2 (4.5%) patients, respectively. Regarding late complications, 4 (9%) patients developed a stricture of the ureteroileal anastomosis, requiring surgical reparation and were therefore classified as Clavien IIIB. A significant rise in quality of life in patients undergone urinary undiversion ($p<0.05$) was found. *Conclusion:* Despite the surgical complexity of urinary undiversion, postoperative complications are relatively low compared to other major urological surgeries such as radical cystectomy. It is possible to perform this procedure in selected patients in order to increase quality of life and renal function.

42

ACTIVE SURVEILLANE IN A HIGH-VOLUME CENTRE: ONCOLOGICAL OUTCOMES AND MANAGEMENT CHANGES OF A 12 YEARS EXPERIENCE

Michele Catellani, Stefano Luzzago, Andrea Conti, Francesco Alessandro Mistretta, Andrea Russo, Ettore Di Trapani, Roberto Bianchi, Gabriele Cozzi, Matteo Ferro, Gennaro Musi, Deliu Victor Matei and Ottavio De Cobelli

Division of Urology, IEO European Institute of Oncology, Milan, Italy

Background/Aim: Active surveillance (AS) represents a viable option for favorable-risk prostate cancer (PCa) patients, reducing the risk of overtreatment. A 12-year experience with long-term follow-up of a single high-volume center AS protocol is reported, analyzing changes in clinical practice during time and oncological results. *Materials and Methods:* From April 2005 to April 2017, 389 PCa patients were enrolled in AS protocol at our hospital. Men with low-risk PCa were included, according to the Prostate Cancer Research International: Active Surveillance criteria, and followed prospectively on AS. From 2012, other criteria were included, such as the use of multiparametric MRI of the prostate (mpMRI), a third positive biopsy core, and a single positive 3+4 Gleason score (GS) core. Follow-up consisted of regular PSA tests, digital rectal examinations, repeated mpMRIs (140 men underwent more than one mpMRI) and biopsies. Kaplan-Meier analyses quantified progression-free survival (PFS) in patients submitted/or not to mpMRI at the AS begin. Cox- regression analyses tested independent predictors of any cause discontinuation and biopsy-progression (Bp) (*i.e.* upgrading and/or volume progression) during AS. Moreover, logistic regression analyses were used to predict clinically significant PCa (csPCa), *i.e.* GS >4+3 and/or extraprostatic extension and/or pN+, at pathological evaluation. *Results:* Median time of persistence in AS was 47 months (range=23-58). Overall PFS rates at 1, 3, 5, and 10 years were 91%, 73%, 52%, and 29%, respectively. Patients submitted to confirmatory mpMRI showed a significantly higher PFS and a lower Bp at 3 (85% and 90% *vs.* 75% and 80%) and 5 years (70% and 85% *vs.* 40% and 65%), respectively (all $p<0.05$). Overall, 140 (36%) men were switched to active treatment during AS, with a median time to progression of 21 months. Sixty-seven (48%), 31 (22%), and 33 (24%) patients discontinued AS due to Bp, prostate imaging reporting and data system score 5, and patient choice, respectively. Overall, 119 (85%) men were treated with robot assisted radical prostatectomy (RARP) at our centre and 32 (23%) of them showed a csPCa. Nine (6.4%) patients experienced biochemical recurrence and 7 (5%) underwent adjuvant or salvage RT. No patients died because of PCa. At multivariable Cox-regression analyses, a higher number of positive cores [odds ratio (OR)=1.420; 95% confidence interval (CI)=1.091-1.849; $p=0.009$] at diagnostic biopsy and a confirmatory negative mpMRI (OR=0.510; 95%

CI=0.311-0.839; *p*=0.008) were independent predictors of progression to active treatment during AS. Moreover, only confirmatory negative mpMRI was associated to Bp over time (OR=0.480; 95% CI=0.232-0.993; *p*=0.048). No clinical parameter was found to predict cSPCa at final histology.
Conclusion: Long-term follow-up of a single institution AS program shows similar oncological results of those previously described by large European and American cohorts. However, the inclusion of mpMRI at the beginning of the protocol seems to confer a better PFS and a longer stay in AS.

43
ROSAI-DORFMAN DISEASE: A RARE CASE OF TESTICULAR INVOLVEMENT

Valeria Lami, Lorenzo Ruggera, Alex Anh Ly Nguyen, Fabio Vianello and Filiberto Zattoni

Department of Surgery, Oncology, and Gastroenterology - Urology Clinic, Urology Clinic University of Padua, Padua, Italy

Background: The RDD, first described as clinic-pathological disorder in 1969 by Drs. Rosai and Dorfman, is also known as "sinus histiocytosis with massive lymphadenopathy". It is an idiopathic nonmalignant histiocytosis, typically presenting with fever, leukocytosis, and non painful cervical lymphadenopathy, commonly affecting childhood. Extra-nodal involvement is described in up to 25% of cases: skin, soft tissue, upper respiratory tract and bone. Rarer manifestations are in genitourinary system, with an intra-scrotal involvement in less than 1%. Multifocal and extra-nodal forms have been described in older patients with underlying immunological disorder. RDD pathogenesis is still unknown: the reactive nature of involved cells and the presence of auto-immune antibodies in the active disease suggest an infective and immune dysregulatory process. Possible etiologies are linked to human herpesvirus, parvovirus B19, and Epstein–Barr virus. Coexistence with hematologic disorders has been also described. Differential diagnosis is with malignant or non-malignant causes of lymphadenopathy, such as other histiocytic disorders or Hodgkin and non-Hodgkin lymphoma. Most patients affected by RDD are asymptomatic and do not need for therapy. For symptomatic patients, surgery is indicated for excision of single or primary masses, whenever feasible, achieving prolonged results. For patients requiring systemic therapy, steroids represent nowadays the gold-standard. In refractory disease, different types of chemotherapy have been used (vinca alkaloids, alkylating agents, 6-mercaptopurine, methotrexate or the anti-CD20 antibody, rituximab), obtaining variable response rates. Histology typically highlights emperipolesis, a phenomenon in which histiocytes phagocytize whole lymphocytes or

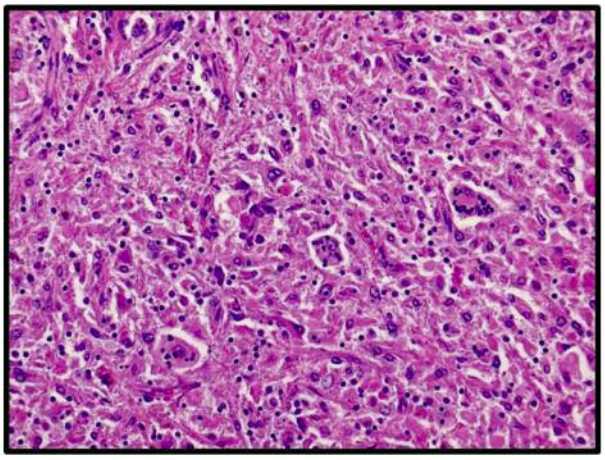


Figure 1. *Representative histopathological images of Rosai-Dorfaman disease: histiocytes with emperipolesis.*

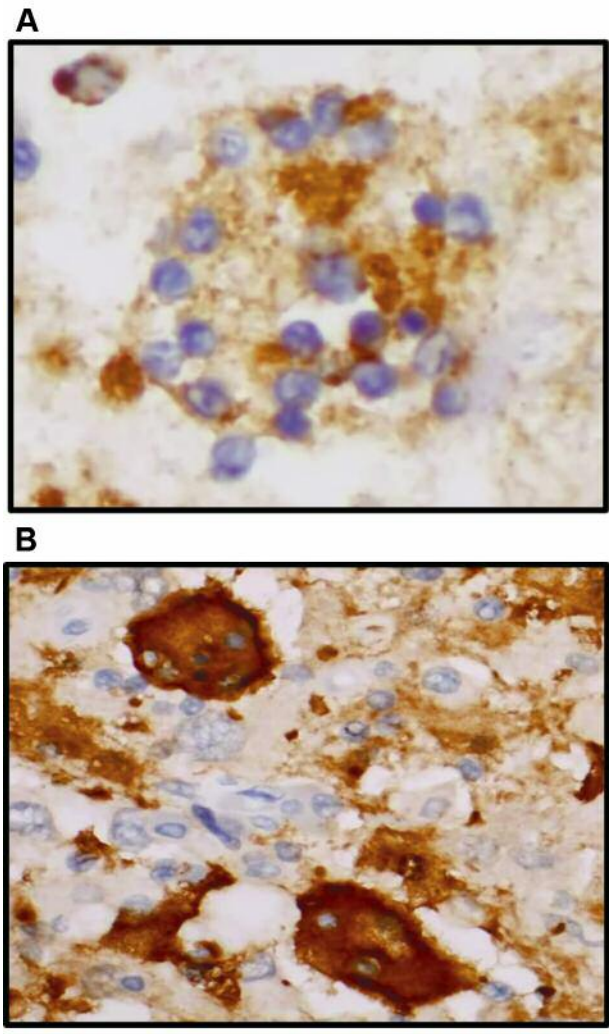


Figure 2. *A. Histiocytes with emperipolesis immunoreactive for CD68. B. Histiocytes with emperipolesis immunoreactive for S-100.*

plasma cells. These histiocytes are characterized by large pale eosinophilic cytoplasm, positivity for immunohistochemical stains S-100 and CD68 and negativity for CD1a. Herein, a case of testicular RDD in an otherwise healthy adult patient is described. *Case Report:* A 52-year-old male came to our attention for right testicular enlargement without fever or other clinical manifestations. Patient was otherwise healthy, with a previous right hydrocelectomy 30 years ago, and a history of couple infertility. Clinical examination revealed a large painless hard wood right testis; the left one was regular and inguinal lymph nodes were bilaterally not palpable. Color Doppler ultrasound showed a 35 mm right testicular lump with vascularization; serum blood count, β-human chorionic gonadotropin (β-HCG), and α-fetoprotein were normal. Patient underwent right orchiectomy; at macroscopic examination testis and epididymis were totally occupied by a yellowish 5-cm lesion with hemorrhagic areas. The specimen weighed 110 g, comprising 8 cm of spermatic cord. Testis was fully inhabited by histiocytic elements with lymphocytes often inside their pale eosinophil cytoplasm, suggesting emperipolesis phenomenon (Figure 1). Plasma cells were also present whereas no albugineal involvement was detected. Immunohistochemistry showed S-100 and CD68 positive staining and CD1a negativity, suggesting for Rosai-Dorfman disease (RDD) (Figure 2). Post-operative course was regular and patient was discharge in post-operative day one. *Discussion:* As previously described, RDD rarely affected the testis. Since its first characterization in 1969, a gonadal involvement has been described in literature in only 9 males, with patient age ranging from 41 to 72 yrs (1-4). Another case has been retrospectively identified analyzing a 1966 case report of a 4-year old boy with systemic classical disease and bilateral testicular "histiocytosis" (5). In most of these cases, testis was not the only affected site, often was associated with hematological disorders or other disease and there was no available follow-up. The largest urological series was reported by Wang in 2014, with 3 testicular and 3 renal cases of RDD (6). Gonadal involvement was unilateral in each case; patient's co-morbidity or other site manifestations were not fully declared and prominent emperipolesis was not described in all specimens. To our knowledge, the last case of Rosai-Dorfman disease localized in the testis has been detected by Torres in 2015 (7) in an asymptomatic 49-year old man affected by a single testicular nodule without any comorbidity; even in this case any kind of follow-up was declared. This is the 10th case of testicular RDD in an otherwise healthy adult patient.

1 De Guzman R, Montpetit VJA, Barr JR, Bishop DR, Jung RC and Bach RK: Sinus histiocytosis with massive lymphadenopathy: A case with multiple organ involvement and progressive multifocal leukoencephalopathy. Advances in lymphology, proceedings of VIII International Congress of Lymphology, Montreal, pp. 602-609, 1981.

2 Lossos I. S, Okon E, Bogomolski-Yahalom V, Ron N and Polliack A: Sinus histiocytosis with massive lymphadenopaty (Rosai-Dorfman disease): report of a patient with isolated renotesticular involvement after cure of non-Hodgkin's lymphoma. Ann Hematol *74*: 41-44, 1997.

3 Fernandopulle SM, Hwang JS, Kuick CH, Lui J, Tan PH, Siow WY and Wong M: Rosai-Dorfman disease of the testis: an unusual entity that mimics testicular malignancy. J Clin Pathol *59*: 325-327, 2006.

4 Del Gobbo A, Moltrasio F, Young RH and Rosai J: Involvement of the testis and related structures by Rosai-Dorfman disease: report of 2 new cases and review of literature. Am J Surg Pathol *37*: 1871-1875, 2013.

5 Azoury FJ and Reed RJ: Histiocytosis. Report of an unusual case. N. Engl J Med *274*: 928-930, 1996.

6 Wang CC, Al-Hussain TO, Serrano-Olmo J and Epstein JI: Rosai-Dorfman disease of the genito-urinary tract: analysis of six cases from the testis and kidney. Histopathology *65*: 908-916, 2014.

7 Rodrìguez Torres C, Riazuelo Fantova G, Escartín Martínez I, Castillo Escudero JJ and del Agua Arias C: Rosai-Dorfman disease with atypical intrascrotal involvement. Int J Urol *22*: 794-796, 2015.

44

OPTIMIZING THE PATH OF CARE FOR PATIENTS WITH PROSTATE CANCER: WORKING IN A NETWORK

Tiziana Magnani[1], Giancarlo Albo[2], Barbara Avuzzi[3], Lara Bellardita[1], Alessandra Casale[4], Mario Catanzaro[5], Annamaria Cerrotta[6], Maurizio Colecchia[7], Letizia De Luca[1], Teresa Di Florio[1], Simona Donegani[1], Paola Dordoni[1], Carlo Fallai[6], Paolo Grassi[8], Fabrizio Longo[2], Alberto Macchi[5], Cristina Marenghi[1], Julia Menichetti[1], Antonella Messina[4], Sara Morlino[3], Barbara Noris Chiorda[3], Biagio Paolini[7], Giuseppe Procopio[8], Silvia Stagni[5], Antonio Tesone[5], Tullio Torelli[5], Marta Vaiani[4], Elena Verzoni[8], Sergio Villa[3], Nadia Zaffaroni[9], Nicola Nicolai[5], Roberto Salvioni[5], Emanuele Montanari[2], Patrizia Monti[10] and Riccardo Valdagni[3]

[1]Prostate Cancer Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[2]Division of Urology, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy;
[3]Division of Radiotherapy 1, Prostate Cancer Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[4]MRI Unit, Prostate Cancer Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;

[5]Division of Urology, Prostate Cancer Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[6]Division of Radiotherapy 2, Prostate Cancer Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[7]Division of Pathology, Prostate Cancer Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[8]Division of Medical Oncology - GU Tumors, Prostate Cancer Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[9]Division of Molecular Pharmacology, Prostate Cancer Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[10]Direzione Sanitaria, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Background/Aim: According to the status of disease, multiple therapies and observational strategies are available for prostate cancer patients, including surgery, external radiotherapy, brachytherapy, hormonal therapy, chemotherapy, and radionuclide metabolic therapy, as well as observational programs such as active surveillance and watchful waiting. The path of care for this malignancy is rather complex, involving several health care professionals, and it requires a multidisciplinary approach at specific time points of the disease trajectory. When the health settings cannot provide prostate cancer patients with all the consultations and procedures required for a proper disease management, efforts should be made to implement the path of care, in order to address all patient needs through the collaboration among institutions. This is also in line with Valdagni *et al*. (1, 2), who stressed the importance of formalizing networks to meet all requirements of a Prostate Cancer Unit. *Materials and Methods:* Although multidisciplinary clinics (weekly multidisciplinary first consultations and twice a week observational program follow-up) and activities (weekly tumor boards) for prostate cancer patients had been running on a regular basis since 2004, the Prostate Cancer Unit at Fondazione IRCCS Istituto Nazionale dei Tumori, Milan (INT PCU), was only formalized in 2009, and updated with respect to staff and activities in 2013. In 2014, also with the help of external auditors, bottlenecks and areas with room for improvement were identified (3). Besides organizational and administrative problems, the auditors stressed the lack of robot-assisted surgery and of emergency department (ER). In addition, the uro-oncologists attending the PCU had limited experience with functional and andrologic urology. The Division of Urology at Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico (Policlinico) of Milan, hosting the Specialty in Urology of Milan University, was a referring center for robot-assisted surgery, with extensive experience in urology and andrology. Policlinico had no radiotherapy or brachytherapy unit as well as no experience in the multidisciplinary management of prostate cancer patients and no significant caseload of patients on active surveillance or watchful waiting. In February 2017, INT PCU and with INT become an academic center as Policlinico, and Policlinico formalized an agreement aimed to join efforts, share common diagnostics and therapeutic guidelines to implement the path of care for prostate cancer patients. The collaboration was meant to offer prostate cancer patients referring to both centers a complete path of care, to optimize human and technological resources and meet the standards of a PCU as described in Valdagni *et al*. (1) and Valdagni *et al*. (2). INT PCU and Policlinico identified a scientific coordinator and a project manager in each center to supervise the collaboration and check activities and work flows, respectively. Scientific coordinators and project managers agreed on a provisional caseload for every single procedure in each center, which was included in the agreement and was evaluated every 3 months. Moreover, a detailed description of the work flow, the activities, the specialists in charge, and both contact and patient information was prepared and shared among INT PCU, Policlinico clinical and admin team. In detail, INT PCU patients could be referred to Policlinico for functional urologic consultations and procedures, robot-assisted surgery, andrologic consultations, semen cryopreservation, and ER admission. Policlinico patients could be referred to INT PCU for radiotherapy, brachytherapy, observational programs (active surveillance and watchful waiting) and chemotherapy. In addition, Policlinico urologists could attend the INT PCU tumor boards and start working in a MDT setting. On the other hand, INT PCU urologists could assist to robotic radical prostatectomies performed at Policlinico. The agreement refers to the possibility of starting a second phase, focused on clinical, experimental, and translational research projects as well as fund raising and educational activities. *Results:* Between February 2017 and October 2017, Policlinico referred 17 patients to INT PCU. Nine patients were evaluated by INT PCU radiation oncologists for radiotherapy, 6 patients were discussed in INT PCU tumor board, 1 patient was evaluated by INT PCU medical oncologists. Prostate Specific Membrane Antigen Positron Emission Tomography scan was prescribed to 1 patient, and it was performed in one of the few centers working in this field in Italy, which has had a strong collaboration with INT PCU. PCU INT referred to Policlinico 14 patients. Seven patients were evaluated for urinary symptoms, 2 patients requested the consultation by urologists expert in sexual therapy, 1 patient was interested in robotic surgery, 1 patient referred to Policlinico ER, 1 patient on active surveillance required biopsy in narcosis and 1 patient had macro-hematuria after radiotherapy. Patients referred to INT PCU and Policlinico, and participation of Policlinico urologists at INT PCU tumor boards were recorded by INT PCU project manager, who checked on the

data every month as regards caseload and update of patient charts with external consultations. Although both centers paid much attention to detailing work flows and responsibilities and to sharing information with the staff, a few problems occurred. Particularly, patients of both INT PCU and Policlinico referred to the centers without an appointment or documentation for 4 times. One patient, who referred to ER with post-biopsy complications, was seen by clinicians not informed of the formalized collaboration. These inconveniences could be explained by the little promotion that was intentionally acted by INT and Policlinico directors, by the inadequate knowledge of protocols and procedures run by the centers, by the working habits in non-formalized networks, and by the insufficient knowledge of the group members. However, solutions were found and were implemented in order to overcome these barriers. The scientific coordinators spread news of the formalized collaboration with colleagues of other specialties; the project managers organized meetings with clinicians and the administrative staff. Meetings will be scheduled over the forthcoming months to present single activities and protocols. *Conclusion:* The collaboration proved to be helpful for both INT PCU and Policlinico 1) to complete the path of care for each institution, 2) to improve efficacy and efficiency of diagnostic and therapeutic procedures, 3) to make therapies accessible, 4) to optimize the use of resources, and 5) to promote cross-talk between groups. Patients were happy to have appointments organized and a referral center in touch with one's clinicians. However, it is important to organize meetings to share thoughts, experience and guidelines between the groups. At the same time, it is fundamental to improve data collection of the cases from each center, to monitor the collaboration and identify potential weaknesses and criticisms that might hamper this synergy. In addition, other areas of interest could be explored and excellences of both centers further appreciated.

Acknowledgements to Fondazione I. Monzino for supporting the activities and the projects of INT Prostate Cancer Programme.

1 Valdagni R, Albers P, Bangma C, Drudge-Coates L, Magnani T, Moynihan C, Parker C, Redmond K, Sternberg CN, Denis L and Costa A: The requirements of a specialist Prostate Cancer Unit: a discussion paper from the European School of Oncology. Eur J Cancer *47*: 1-7, 2011.

2 Valdagni, Van Poppel H, Aitchison M, Albers P, Berthold D, Bossi A, Brausi M, Denis L, Drudge-Coates L, De Santis M, Feick G, Harrison C, Haustermans K, Hollywood D, Hoyer M, Hummel H, Mason M, Mirone V, Müller SC, Parker C, Saghatchian M, Sternberg CN, Tombal B, van Muilekom E, Watson M, Wesselmann S, Wiegel T, Magnani T and Costa A: Prostate Cancer Unit Initiative in Europe: A position paper by the European School of Oncology. Crit Rev Haematol Oncol *95*: 133-143, 2015.

3 Voigt W, Hoellthaler J, Magnani T, Corrao V and Valdagni R: 'Act on oncology' as a new comprehensive approach to assess prostate cancer centres - method description and results of a pilot study. PLoS One *9*: e106743, 2014.

45

IMPROVING INDIVIDUALIZING TREATMENT AND SURVEILLANCE OF NON-MUSCLE INVASIVE BLADDER CANCER: A CONDITIONAL SURVIVAL ANALYSIS

David D'Andrea[1], Francesco Soria[1], Mohammad Abufaraj[1], Beat Foerster[1], Shoji Kimura[1], Andrea Mari[2], Andrea Haitel[3], Paolo Gontero[4] and Shahrokh Shariat[1]

[1]Department of Urology, Medical University of Vienna, Vienna, Austria;
[2]Department of Urology, University of Florence, Careggi Hospital, Florence, Italy;
[3]Department of Pathology, Medical University of Vienna, Vienna, Austria;
[4]Department of Urology, University of Turin, Turin, Italy

Aim: Individualization of treatment and surveillance of non-muscle invasive bladder cancer (NMIBC) need further improvements in order to reduce invasive investigations in patients unlikely to recur, and to improve the selection of patients with the highest risk for progression, for early radical cystectomy (RC). *Materials and Methods:* Data of patients with NMIBC at two tertiary care centers (Vienna, Austria and Turin, Italy) were retrospectively analyzed. The patients were stratified according to tumor stage and grade, and the risk of progression to muscle invasive bladder cancer (MIBC) with conditional survival probabilities was assessed. Two methods were applied for the analysis: Kaplan-Meier weights and landmark approach with 2000 bootstrap replicates. *Results:* Patients with pure or concomitant carcinoma *in situ* as well as those lost to follow-up were excluded. A total of 340 patients with primary NMIBC were eligible for the analysis. Overall, 153 (45%) pTaLG, 56 (16.5%) pTaHG, 7 (2%) pT1LG, and 124 (36.5%) pT1HG were identified. Within a median follow-up of 20.8 months (interquartile range=10.5-32), 24 patients progressed to MIBC. Twenty (83%) patients were pT1HG and had a significant higher risk of progression to MIBC if a recurrence occurred at 3 months ($p<0.001$). The risk of progression for patients with pT1HG, who experienced a recurrence at one year, was not statistically different from those with other stages. Limitations are inherent to the retrospective design and the small sample size. *Conclusion:* Our analysis corroborates the evidence that patients with pT1HG need more personal attention and should be counselled for early RC if intravesical therapy fails.

46

FORMALIZED PROSTATE CANCER UNIT: WHAT DOES IT ADD TO MULTIDISCIPLINARY MANAGEMENT OF PROSTATE CANCER PATIENTS? THE EXPERIENCE OF FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI, MILAN

Tiziana Magnani[1], Alessandra Alessi[2], Barbara Avuzzi[3], Augusta Balzarini[4], Nice Bedini[3], Lara Bellardita[1], Claudia Borreani[5], Mauro Carrara[6], Alessandra Casale[7], Mario Catanzaro[8], Annamaria Cerrotta[9], Maurizio Colecchia[10], Flavio Crippa[2], Letizia De Luca[1], Teresa Di Florio[1], Simona Donegani[1], Paola Dordoni[1], Carlo Fallai[9], Tommaso Giandini[6], Paolo Grassi[11], Rodolfo Lanocita[12], Mauro Maccauro[2], Alberto Macchi[8], Cristina Marenghi[1], Cinzia Martini[4], Julia Menichetti[1], Antonella Messina[7], Sara Morlino[3], Barbara Noris Chiorda[3], Biagio Paolini[10], Emanuele Pignoli[6], Giuseppe Procopio[11], Carla Ripamonti[13], Ettore Seregni[2], Carlo Spreafico[12], Silvia Stagni[8], Antonio Tesone[8], Tullio Torelli[8], Marta Vaiani[7], Elena Verzoni[11], Sergio Villa[3], Ernesto Zecca[4], Roberto Salvioni[8], Nicola Nicolai[8], Patrizia Monti[14] and Riccardo Valdagni[3]

[1]Prostate Cancer Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[2]Division of Nuclear Medicine, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[3]Division of Radiotherapy 1, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy;
[4]Division of Palliative Care And Rehabilitation Programs, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[5]Division of Clinical Psychology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[6]Division of Medical Physics, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[7]MRI Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[8]Division of Urology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[9]Division of Radiotherapy 2, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[10]Division of Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[11]Division of Medical Oncology - GU Tumors, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[12]Division of Diagnostic And Interventional Radiology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[13]Supportive Care Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[14]Direzione Sanitaria, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Background/Aim: It is commonly accepted that oncologic patients benefit from a multidisciplinary management that involves all the professionals participating in the path of care and facilitates timely access to therapy, rehab programs and counseling delivered by experienced experts. Multidisciplinary management implements simultaneous care and shifting from a disease-focused to a patient-centered approach in accordance with the policy statement of the European Partnership for Action Against Cancer (EPAAC) (1). This is most true for prostate cancer patients for whom, according to the state of disease, multiple therapies and observational strategies are available and several health care professionals have a role in the disease trajectory. This work describes the experience of Fondazione IRCCS Istituto Nazionale dei Tumori (INT), Milan (Italy), which formalized the multidisciplinary management of prostate cancer patients running since 2004 in a Prostate Cancer Unit (PCU) and how the PCU affected assistance and care. *Materials and Methods:* The organization of multidisciplinary activities organized before (from March 2004, when the Prostate Cancer Program (PCP) was launched, to December 2013, when INT PCU, formalized in 2009, was updated) and after the PCU second formalization (from December 2013 until now) were analyzed. INT PCP redirected translational, preclinical, and clinical research according to disease-focused shared strategies. In 2004, a multidisciplinary working group focused on writing diagnostic and therapeutic guidelines for evidence-based clinical decisions was established. In 2005, INT PCP started the weekly multidisciplinary clinics for newly referred patients, the weekly follow-up clinics for patients on active surveillance and watchful waiting and the weekly tumor boards. Specialists participating in the PCP were urologists, radiation oncologists, medical oncologists, and uropathologists. Experts in imaging were involved in particular cases, also in consideration of the personal commitment to PCP and the disease. Psychologists, participating as consultants, were supported by a grant from a private donor. In 2009, INT PCU was first formalized, identifying the Chair, the Vice Chair, the clinicians, and the researchers involved in the PCP research and clinical activities. In 2013 and then in 2017, the document was updated in line with Valdagni's *et al*. reports on PCUs (2, 3) and in partial response to issues raised by the 2013 external audit (4), with a specific focus on clinical activities, personnel participating, responsibilities and work flows. In details: (i) PCU Chair, Vice Chair, and project manager were nominated. (ii) An agreement was reached between PCU Chair and the Heads of the specialties, concerning the dedication to the PU activities and the time to dedicate (for all the clinicians involved in the path of care). (iii) Clinicians were divided in core team, including specialties that have to attend the PCU activities on a routine basis and non-core team, consisted of specialties involved in

specific steps of the disease trajectory; considering that the core team may mutually agree on documented exception to the rule, to optimize resources pathologists participated in selected cases. (iv) PCU clinics were described with respect to organization, clinicians' participation, and responsibilities. (v) Interdisciplinary collaboration was described in details, including information about the involvement of the non-core team members in the PCU activities. *Results:* The formalization and update of INT PCU allowed naming the clinicians participating in the PCU upon agreement between the PCU Chair and the directors of the specialties, specifying also the amount of time to be dedicated to the pathology and the PCP activities. Moreover, professionals such as experts in imaging, in nuclear medicine, rehab programs, support, and palliative care were involved, in line with the growing importance of emerging techniques, drugs and procedures. Core and non-core teams were distinguished in order to limit the participation in the PCU activities, thus optimizing effort and resources. In addition, formalization identified the activities and the responsibilities of administrative staff; it described multidisciplinary activities with respect to organization-, participation-, documentation- and communication-related issues, and rationalized the access to clinical case discussion sessions by identifying categories of patients that need to be evaluated multidisciplinarily. Furthermore, formalization facilitated the decisions on reports exiting from multidisciplinary clinics, as well as, the clinical case discussions assessing the participation of multiple professionals. Finally, the importance of periodically reassessing PCU with respect to personnel, activities, and organization, paying particular attention to emerging techniques and procedures and bottlenecks, was appreciated, as well as the importance of having an agreement on evidence-based clinical decisions, coordination of treatments, procedures, professionals and communication within the team and with the patients. Our experience of multidisciplinary approach and PCU activities, however, suggests that there are the following points that need improvement. (i) Although the PCU is formalized, the organizational model is functional, thus determining tasks, roles, and responsibilities, but with limited capacity of Chair and Vice Chair to act on professionals who report on a divisional structure model. (ii) Time for active participation in the PCU should be protected, with the possibility of reassessing it based on unmet needs that may come up from the clinical routine. (iii) Solutions should be found to allow the participation of multiple PCU professionals in the clinical case discussions, making them lively sessions also for educational purposes. *Conclusion:* The formalization of INT PCU proved helpful 1) to improve the efficacy and efficiency of the multidisciplinary organizational model, 2) to optimize resources and procedures, 3) to facilitate interprofessional collaboration and synergy. However, efforts should be made by Admin as well as experts in organization, management, and human resources to overcome the limitation of functional organization. Solutions to boost motivation and permit the participation of professionals in the clinical case discussions as often as possible should also be found. Activities and participation should be checked on a routine basis to identify bottlenecks and criticisms that might hinder the multidisciplinary synergy.

Acknowledgements to Fondazione I. Monzino for supporting the activities and the projects of INT Prostate Cancer Programme.

1 European Partnership Action Against Cancer consensus group: Policy statement on multidisciplinary cancer care. Eur J Cancer *50*: 475-80, 2014.

2 Valdagni R, Albers P, Bangma C, Drudge-Coates L, Magnani T, Moynihan C, Parker C, Redmond K, Sternberg CN, Denis L and Costa A: The requirements of a specialist Prostate Cancer Unit: a discussion paper from the European School of Oncology. Eur J Cancer *47*: 1-7, 2011.

3 Valdagni R, Van Poppel H, Aitchison M, Albers P, Berthold D, Bossi A, Brausi M, Denis L, Drudge-Coates L, De Santis M, Feick G, Harrison C, Haustermans K, Hollywood D, Hoyer M, Hummel H, Mason M, Mirone V, Müller SC, Parker C, Saghatchian M, Sternberg CN, Tombal B, van Muilekom E, Watson M, Wesselmann S, Wiegel T, Magnani T and Costa A: Prostate cancer unit initiative in Europe: a position paper by the European School of Oncology. Crit Rev Haematol Oncol *95*: 133-143, 2015.

4 Voigt W, Hoellthaler J, Magnani T, Corrao V and Valdagni R: 'Act on oncology' as a new comprehensive approach to assess prostate cancer centres - method description and results of a pilot study. PLoS One *9*: e106743, 2014.

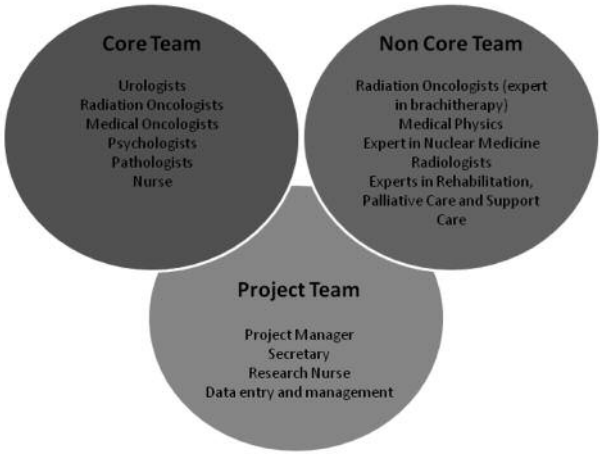


Figure 1. *Prostate Cancer Unit personnel.*

47

ACCURATE PREDICTION OF PROGRESSION TO MUSCLE INVASIVE DISEASE IN PATIENTS WITH T1G3 BLADDER CANCER: A CLINICAL DECISION-MAKING TOOL

David D'Andrea[1], Mohammad Abufaraj[1], Franceso Soria[1], Martin Susani[2], Robin Ristl[3], Beat Foerster[1], Shoji Kimura[1], Andrea Mari[1], Alberto Briganti[4], Pierre Karakiewicz[5], Kilian Gust[1], Morgan Roupret[6] and Shahrokh Shariat[1]

[1]Department of Urology, Medical University of Vienna, Vienna, Austria;
[2]Department of Pathology, Medical University of Vienna, Vienna, Austria;
[3]Center for Medical Statistics, Informatics and Intelligent Systems (CEMSIIS), Medical University of Vienna, Vienna, Austria;
[4]Department of Urology, Urological Research Institute, Vita-Salute University, San Raffaele Scientific Institute, Milan, Italy;
[5]Department of Urology, University of Montreal, Montreal, Canada;
[6]Academic Department of Urology of La Pitié-Salpétrière, Assistance-Publique Hôpitaux de Paris and Faculté De Médecine Pierre et Marie Curie, University Paris VI, Paris, France

Aim: To improve current prognostic models for the selection of patients with T1G3 urinary bladder cancer (UBC), who are more likely to fail intravesical therapy and progress to muscle invasive bladder cancer (MIBC). *Materials and Methods:* A retrospective analysis of 1,289 patients with pT1G3 UBC, treated with transurethral resection of bladder tumor (TURB) and adjuvant intravesical bacillus Calmette-Guérin (BCG) was performed. Random split sample data and competing-risk regression were used to identify the independent impact of lymphovascular invasion (LVI) and (variant histology) VH on progression to MIBC. A nomogram was developed for predicting patient-specific probability of disease progression at 2 and 5 years after TURB. Decision curve analysis (DCA) was performed to evaluate the clinical benefit associated with the use of our nomograms. *Results:* In the development cohort, within a median follow-up of 51.6 months [interquartile range (IQR)=19.3-92.5] disease progression occurred in 89 patients (13.8%). A total of 84 (13%) patients were found to have VH and 57 (8.8%) had LVI at TURB. Both factors were independently associated with disease progression on multivariable competing risk analysis [hazard ratio (HR)=4.4, 95% confidence interval (CI)=2.8-6.9, p=<0.001 and HR=3.5, 95% CI=2.1-5.8, p<0.001, respectively]. DCA showed superior net benefits for the nomogram within a threshold probability of progression between 5-55%. Limitations are inherent to the retrospective design. *Conclusion:* We demonstrated the clinical value of the integration of LVI and VH in a prognostic model for the prediction of MIBC. Indeed, our tool provides superior individualized risk estimation of progression facilitating decision-making regarding early RC.

48

COMPARATIVE EFFECTIVENESS OF RADIOTHERAPY AND RADICAL CYSTECTOMY IN UNFIT PATIENTS WITH RESECTABLE URINARY BLADDER CANCER

David D'Andrea[1], Francesco Soria[1], Judith Stangl-Kremser[1], Mohammad Abufaraj[1], Beat Foerster[1], Andrea Mari[2], Andrea Haitel[3], Gregor Goldner[4] and Shahrokh Shariat[1]

[1]Department of Urology, Medical University of Vienna, Vienna, Austria;
[2]Department of Urology, University of Florence, Careggi Hospital, Florence, Italy;
[3]Department of Pathology, Medical University of Vienna, Vienna, Austria;
[4]Department of Radiotherapy, Medical University of Vienna, Vienna, Austria

Background/Aim: Radical cystectomy (RC) is associated with high morbidity and mortality rates. Moreover, patients who are candidates for this intervention are generally older and morbid. This often biases treatment selection towards non-invasive therapies like radiotherapy (RT). Aim of this study was to investigate cancer-specific (CSS) and overall survival (OS) in a group of patients considered unfit for surgery or trimodal therapy and compared it to a matched cohort of patients treated with RC. *Materials and Methods:* Within our institutional database (1988-2016), 97 and 453 patients treated with RT and RC, respectively, were identified. Multiple imputation was used to handle missing data. Patients with metastatic (cN+ or cM+) as well as non-resectable tumors (≥cT4) and those who received any form of chemotherapy were excluded. Patients treated with RT were matched 1:1 with those treated with RC using propensity scores, adjusted for age, gender, stage, Charlson comorbidity index, body mass index, and ASA score. *Results:* Two perfectly matched groups consisting of 47 patients each were identified. Median age was 77 [interquartile range (IQR)=72.5-82.5] years and 76 (IQR=71-81) years in the RT and RC group, respectively. Median age-adjusted Charlson score was 7 in both groups. During a median follow-up of 10.3 [95% confidence interval (CI)=4.9-38] months 19 (40.4%) and 39 (83%) patients in the RT and RC group have died, respectively. There was no difference in overall survival

(OS) [hazard ratio (HR)=0.9, 95% CI=0.5-1.6, p=0.69] or CSS (HR=0.9, 95% CI=0.4-1.8, p=0.75) between the two groups. *Conclusion:* Despite the old age and the morbidity of the patient population, treatment with RT or RC showed similar survival rates. Further studies should emphasize on quality of life, complications, and the need for further treatments during the follow-up.

49

MULTIPARAMETRIC MAGNETIC-RESONANCE TO CONFIRM ELIGIBILITY TO AN ACTIVE SURVEILLANCE PROGRAM FOR LOW-RISK PROSTATE CANCER: INTERMEDIATE TIME RESULTS OF A THIRD REFERRAL HIGH VOLUME CENTER PROTOCOL

Stefano Luzzago[1], Michele Catellani[1], Andrea Russo[1], Francesco Alessandro Mistretta[1], Ettore Di Trapani[1], Roberto Bianchi[1], Gabriele Cozzi[1], Eleonora Ancona[2], Paola Pricolo[2], Giuseppe Petralia[2], Giuseppe Renne[3], Gennaro Musi[1], Deliu Victor Matei[1] and Ottavio De Cobelli[1]

[1]Division of Urology, European Institute of Oncology - IEO, Milan, Italy; [2]Division of Radiology, European Institute of Oncology - IEO, Milan, Italy; [3]Division of Pathology, European Institute of Oncology - IEO, Milan, Italy

Background/Aim: Active surveillance (AS) represents a viable option for patients with low-risk prostate cancer (PCa). However, a significant number of patients discontinue AS protocols at the 1-year biopsy due to PCa re-classification. The role of confirmatory multiparametric magnetic resonance imaging (mpMRI) in reducing disease misclassification, when performed at the time of patient enrollment, was evaluated in this work. *Materials and Methods:* From 2012 to 2016, 383 patients with low-risk PCa were evaluated. All patients met PRIAS criteria and underwent a confirmatory 1.5-T mpMRI. AS was proposed to patients with PI-RADS score ≤3 and no extraprostatic extension (EPE) at mpMRI, whereas patients with PI-RADS score ≥4 and/or EPE were submitted to radical prostatectomy (RP). Clinically significant-PCa (csPCa) was defined as Gleason score >6 or non-organ-confined disease at RP. Kaplan-Meier analyses quantified progression-free survival (PFS) over time in patients enrolled in our AS program. Logistic regression analyses tested the association between confirmatory mpMRI and csPCa at RP. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for mpMRI, in patients submitted to immediate RP. *Results:* Overall, 133 patients were included in AS program. Median time of persistence in AS protocol was 24 months [interquartile range (IQR)=13-38]. PFS rate was 99%, 90%, and 86% at 1, 2 and 3 years, respectively. Overall, 13 (9.7%) patients were submitted to active treatment during follow-up; five (38.4%) due to PI-RADS 4/5 at repeated mpMRI, 1 (7.8%) for GS upgrading, 3 (23%) for >3 positive cores, 3 (23%) for rising PSA, and 1 (7.8%) because of patient preference. Eleven (84.6%) patients underwent RP and csPCa was detected in 6 of them (54.5%). On the other hand, 250 patients were submitted to immediate RP. Overall, 21 (8.4%), 65 (26%), 77 (30.8%) and 87 (34.8%) patients had a PI-RADS score ≤2, 3, 4 and 5, respectively. EPE score 1 rate was 27%. Pathological examination revealed 134 (53.6%) csPCa. At multivariable analysis, high Prostate Imaging Reporting and Data System (PI-RADS) score increased the probability of having a csPCa (PIRADS 3 odd ratio (OR)=1.2, p=0.26; PI-RADS 4 OR=5.1, p=0.02; PI-RADS 5 OR=6.7; p=0.009). Moreover, age (OR=0.96, p=0.03) and EPE score (OR=11.8, p<0.001) represented independent predictors of csPCa. Overall, confirmatory mpMRI, with regard to csPCa, showed sensibility, specificity, PPV and NPV of 85%, 55%, 68% and 76%, respectively. *Conclusion:* Confirmatory mpMRI at the time of AS enrollment improves selection of patients suitable for AS, reducing the misclassification rate of aggressive disease. We suggest performing confirmatory targeted biopsies in patients with PI-RADS score 3 and 4 lesions, based on the PPV and the NPV of confirmatory mpMRI with regard to csPCa.

50

LOW-RISK PROSTATE CANCER IN THE CONTEMPORARY MAGNETIC-RESONANCE ERA: ARE WE EXCLUDING TOO MUCH PATIENTS SUITABLE FOR ACTIVE SURVEILLANCE?

Stefano Luzzago[1], Michele Catellani[1], Ettore Di Trapani[1], Francesco Alessandro Mistretta[1], Maurizio Delor[1], Antonio Brescia[1], Giovanni Cordima[1], Antonio Cioffi[1], Andrea Russo[1], Giuseppe Petralia[2], Matteo Ferro[1], Gennaro Musi[1], Deliu Victor Matei[1] and Ottavio De Cobelli[1]

[1]Division of Urology, European Institute of Oncology - IEO, Milan, Italy; [2]Division of Radiology, European Institute of Oncology – IEO, Milan, Italy

Background/Aim: Currently used active surveillance (AS) criteria incorrectly exclude some patients eligible for AS and misclassify some who harbor clinically significant prostate cancer (csPCa). Multiparametric magnetic resonance imaging (mpMRI) has emerged as a novel tool that reduces disease misclassification. We analyzed mpMRI results in a cohort of patients unsuitable for AS and submitted to radical

prostatectomy (RP) at our center. *Materials and Methods:* We reviewed our PCa dataset and selected patients submitted to RP between 2012 and 2017. All patients were not eligible for AS because they did not fulfill one or more Prostate Cancer Research International Active Surveillance (PRIAS) criteria. Overall, 567 men underwent a 1.5-T mpMRI before RP. CsPCa was defined as Gleason score (GS)≥6 and/or extra-prostatic disease at RP. Prostate findings at mpMRI were considered positive for csPCa if Prostate Imaging Reporting and Data System (PI-RADS) score≥4 and negative if ≤3. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for mpMRI, in patients not eligible for AS because they did not fulfill 1, 2, 3 and 4 of PRIAS criteria. Prostate-specific antigen (PSA) density was not available for each patient and was not used in our analysis. *Results:* Overall, 344 (60.6%) patients were excluded from AS because of not meeting only one (1-out patients) PRIAS criterion; 44 (12.7%), 12 (3.5%), 65 (19%), 104 (30%), 82 (24%) and 37 (10.8%) due to PSA>10 ng/ml, cT>2a, GS 3+4, 3, 4 or 5 positive cores, respectively. At pathological evaluation, 123 (35.7%) patients had a non-csPCa, of whom 71 (58%) had also a negative mpMRI. Overall, sensitivity, specificity, PPV and NPV of mpMRI in 1-out patients with regard to csPCa were 84%, 52%, 76% and 65%, respectively. After excluding patients with GS 3+4 and 4 or 5 positive cores, the NPV of mpMRI significantly increased to 72%. Moreover, 183 (32.3%) patients did not respect two (2-out patients) criteria (12 possible combinations. Prostate specimens revealed 37 (20.2%) non-csPCa, of whom 16 (43.3%) had also a negative imaging. Overall, the PPV and NPV of mpMRI in 2-out patients were 86.5% and 60%, respectively. After excluding any single combination that includes GS 3+4 or 4/5 positive cores, only 32 patients and 13 non-csPCa were available for final analysis. In this setting, the NPV of mpMRI reached 89%. Thirty-five (6.2%) patients were 3-out patients (10 possible combinations). Of them, only 3 (8.5%) had a non-csPCa and everyone showed a PIRADS 3 lesion at mpMRI. No one of the 5 (0.9%) 4-out patients (3 possible combinations) had a non-csPCa. *Conclusion:* A significant number of patients with non-csPCa are considered not suitable for AS when PRIAS criteria are used. A negative mpMRI can help identify most of these patients, avoiding possible side effects related to active treatment. However, the NPV of mpMRI in 1-out and 2-out cohorts suggests the need to perform a confirmatory biopsy before choosing management strategy.

51
DE NOVO METASTATIC PROSTATE CANCER: EVALUATION OF THE CONCORDANCE BETWEEN CHAARTED AND LATITUDE PROGNOSTIC CLASSIFICATIONS

Claudia Mosillo[1], Chiara Ciccarese[2], Emanuela Fantinel[2], Davide Bimbatti[2], Alberto Della Volta[2], Lisa Stefani[2], Giampaolo Tortora[2] and Roberto Iacovelli[2]

[1]Department of Radiological, Oncological, and Pathological Sciences, "Sapienza" University of Rome, Rome, Italy; [2]Department of Medical Oncology, Azienda Ospedaliera Universitaria Integrata (AOUI) Verona, Verona, Italy

Background/Aim: In Europe, about 4% of prostate cancer (PC) patients have metastatic disease at the time of diagnosis (1). A prognostic stratification of these patients still lacks. Recently, CHAARTED and LATITUDE trials demonstrated improved outcomes with the addition of docetaxel and abiraterone acetate to androgen deprivation therapy (ADT) in metastatic hormone sensitive PC (mHSPC) with high-volume (HV) and high-risk (HR) disease, respectively (2,3). The aim of the present study was to evaluate how many patients with HR disease according to the LATITUDE trial can also be considered as HV based on the CHAARTED study, and *vice versa*, in the subset of *de novo* metastatic PC. *Patients and Methods:* A retrospective analysis was performed on patients with *de novo* metastatic PC referring to our Institution between January 2007 and September 2017. Clinical and pathological features were recorded (Table I). Patients were divided according to the CHAARTED and LATITUDE prognostic groups in three categories: 1) HV/HR, 2) low-volume (LV)/ low-risk (LR), and 3) HV or HR (HV/LR and LV/HR). The PASW software (Predictive Analytics SoftWare; v 21; IBM SPSS) was used for the statistical analysis. Survivals were estimated by the Kaplan-Meier method. Comparisons of survival across groups using the log-rank test Cox proportional-hazard models, stratified according to the baseline characteristics, were used to estimate hazard ratios for overall survival. *Results:* We identified 126 *de novo* metastatic PC patients, with a median age of 72.0 years [interquartile range (IQR)=64.6-78.4], 73.8% of Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0-1 (n=93), and the remaining 26.2% of ECOG PS ≥2 (n=33). Tumours were mainly of high Gleason Score (GS ≥ 8 in 69.8% of cases). The most frequent metastatic sites were: bone (88.9%), lymph node (68.3%), lung (16.7%), and liver (5.6%). The median value of prostate-specific antigen (PSA) at the time of diagnosis was 89.0 ng/ml. Data available allowed to stratify all patients (n=126) according to the CHAARTED classification (LV n=30; HV n=96), while 106 out of 126 patients were evaluated for the LATITUDE score (LR n=33; HR n=73). Therefore, the final study population included 106 patients analysed for both prognostic risk groups: 69 patients (65.1%) were HV/HR, 23 patients (21.7%) were LV/LR, and 14 patients (13.2%) fulfilled the criteria of only one of the two classification systems (HV or HR: 10 patients HV/LR and 4 patients LV/HR) (Table II). After a median follow-up of 35.6 months 69 deaths occurred. The median overall survival (mOS)

of the entire population was 32.6 months (95% CI=24.8-40.3). In accordance with the CHAARTED classification, HV patients had a mOS of 28.2 months (95% CI=21.0-5.4) compared with 60.9 months (95% CI=27.1-94.7) of LV patients, with a statistically significant difference (p=0.008). Similarly, mOS significantly differed between the two prognostic groups based on LATITUDE criteria, with mOS of 28.2 months in HR patients (95% CI=22.8-33.6) compared to 40.6 months (95% CI=24.7-56.4) in LR patients (p=0.022). Concerning the three categories previously identified, a statistically significant difference in OS was observed between HR/HV group and LR/LV population (p=0.005), with a mOS of 26.3 months (95% CI=20.0-32.7) and 72.6 months (95% CI=25.5-119.6), respectively. Analogously, mOS was significantly longer in LV/LR patients compared to HV or HR (mOS of HV/LR and LV/HR was 35.1 months; 95% CI=31.4-38.8) patients (p=0.003). No difference in OS was observed when HV/HR patients were compared with HV or HR patients (p=0.7). *Conclusion:* To date, chemotherapy with docetaxel or hormonal therapy with abiraterone acetate represent two possible therapeutic options for mHSPC (2,3). However, a direct comparison between these two strategies still lacks. Therefore, patient stratification is important in guiding clinicians to an adequate treatment selection. The present analysis showed the absence of a complete concordance between CHAARTED and LATITUDE prognostic stratification systems in the cohort of *de novo* metastatic PC patients. In particular, 13.2% of patients met only one of the two prognostic classifications (HV/LR and LV/HR). We can speculate that patients with HV/LR could be treated with chemotherapy plus ADT, while LV/HR patients could receive abiraterone acetate plus ADT. When the concordance between CHAARTED and LATITUDE systems was observed (in about 86.8% of cases), two opposite clinical disease patterns could be delineated: patients with very good prognosis (LV/LR group) and patients with poor prognosis (HV/HR group). The prognosis of patients belonging to only one of the two risk classifications did not differ from the HV/HR group prognosis. Significantly better outcome was observed in LV/LR group, which could benefit from ADT alone. Conversely, the prognostic stratification systems of the LATITUDE and CHAARTED trials did not help to better delineate the subgroup of HV/HR and HV or HR (HV/LR and LV/HR) disease, which represent the majority of de novo metastatic PC. Further clinical and or molecular prognostic factors supporting the choice of a specific therapy for HV/HR disease are warranted.

1 Buzzoni C, Auvinen A, Roobol MJ, Carlsson S, Moss SM, Puliti D, de Koning HJ, Bangma CH, Denis LJ, Kwiatkowski M, Lujan M, Nelen V, Paez A, Randazzo M, Rebillard X, Tammela TL, Villers A, Hugosson J, Schröder FH and Zappa M: Metastatic prostate cancer incidence and prostate-specific antigen testing: new insights from the European Randomized Study of Screening for Prostate Cancer. Eur Urol *68(5)*: 885-890, 2015.

2 Sweeney CJ, Chen YH, Carducci M, Liu G, Jarrard DF, Eisenberger M, Wong YN, Hahn N, Kohli M, Cooney MM, Dreicer R, Vogelzang NJ, Picus J, Shevrin D, Hussain M, Garcia JA and DiPaola RS: Chemohormonal therapy in metastatic hormone-sensitive prostate cancer. N Engl J Med *373(8)*: 737-746, 2015.

3 Fizazi K, Tran N, Fein L, Matsubara N, Rodriguez-Antolin A, Alekseev BY, Özgüroğlu M, Ye D, Feyerabend S, Protheroe A, De Porre P, Kheoh T, Park YC, Todd MB, Chi KN and LATITUDE Investigators: Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer. N Engl J Med *377(4)*: 352-360, 2017.

Table I. *Baseline patient characteristics.*

Characteristics	Patients N=126
Median age (years)	72
Gleason Score ≥ 8 (%)	69.8%
Median PSA (ng/dl)	89.0
ECOG Performance Status (%)	
0-1	73.8
≥2	26.2
Site of metastases (%)	
Bone	88.9
Nodes	68.3
Lung	16.7
Liver	5.6
CHAARTED Classifications (%)	
High-volume (HV)	76.2
Low-volume (LV)	23.8
LATITUDE Classifications (%)	
High-risk (HG)	68.9
Low-risk (LR)	31.1

Table II. *Patients classification according to CHAARTED and LATITUDE risk groups.*

	High volume	Low volume
High-risk	69 (65.1%)	4 (3.7%)
Low-risk	10 (9.3%)	23 (21.7%)

52

MULTI-PARAMETRIC MAGNETIC RESONANCE OF THE PROSTATE SECOND OPINION MAY REDUCE THE NUMBER OF UNNECESSARY BIOPSIES: A SINGLE CENTER EXPERIENCE

Stefano Luzzago[1], Michele Catellani[1], Francesco Alessandro Mistretta[1], Andrea Conti[1], Raffaele Bianco[1], Alessandro Serino[1], Andrea Russo[1], Ettore Di Trapani[1], Matteo Ferro[1], Sarah Alessi[2], Giuseppe Petralia[2], Gennaro Musi[1], Deliu Victor Matei[1] and Ottavio De Cobelli[1]

[1]Division of Urology, IEO European Institute of Oncology, Milan, Italy; [2]Division of Radiology, IEO European Institute of Oncology, Milan, Italy

Background/Aim: Multiparametric magnetic resonance (mpMRI) is a useful tool for detection of prostate cancer (PCa). Previous studies confirmed the existence of a steep learning curve in its interpretation. We systematically reviewed mpMRI performed at other centers to decide on the best clinical management for each patient. *Materials and Methods:* From 2016 to 2017, 267 patients were submitted to mpMRI at other centers. Images obtained were than reviewed by 2 expert radiologists (G.P. and S.A.) with 7 and 5-years experience, respectively. Number, size, location, and grading [Prostate Imaging Reporting and Data System (PI-RADS) score v.2] of mpMRI lesions before and after exam review were recorded. The rate of clinical strategy changes was assessed after a second read according to PI-RADS score. *Results:* Overall, 222 (83%), 29 (11%) and 16 (6%) exams were performed for detection, active surveillance (AS) and before radical prostatectomy (RP), respectively. Reported Index Lesion (IL) PI-RADS score was ≤2 in 39 (14.5%), 3 in 84 (31.4%), 4 in 101 (37.8%) and 5 in 16 (6.2%) patients. Surprisingly, in 27 (10.1%) IL, a PI-RADS score was not assigned. Initial clinical management was: to perform a targeted biopsy (195 patients, 73%) or a systematic random biopsy (8 patients, 3%), to continue AS (29 patients, 10.8%), to submit patients to RP (16 patients, 6%) or "only follow-up" (19 patients, 7.1%). Overall, reviewed IL PI-RADS score was ≤2 in 126 (47%), 3 in 38 (14%), 4 in 60 (22.5%) and 5 in 14 (5.5%) patients, respectively. Twenty-nine (10.8%) exams were considered inadequate due to the presence of suboptimal images, and mpMRI repetition was indicated. Overall, mpMRI re-read did not change IL PI-RADS score in 89 (41.4%) cases, although in 19 (8.9%) and 107 (49.7%) PI-RADS were increased or decreased, respectively. Moreover, our radiologist confirmed the presence of 50% (27/55) of the second-lesions seen at other hospitals. Definitely, clinical management changed in 113 (47.5%) patients. Overall, 93 (52.8%) targeted and 61 (33.1%) total biopsies were skipped by mpMRI second look. Seventeen (60%) of the 29 unreadable mpMRI were repeated at our center. The IL PI-RADS score discordance rate was 59%. Moreover, 54.5% and 45.5% of targeted and total biopsies in these patients were thus skipped. Fifty-two (62.5%) of 83 recommended targeted biopsies were performed at our hospital and a clinically-significant PCa was found in 77% of them. Moreover, 8 (20%) 2 (7%) and 1 (1.5%) of men needed active treatment during later months in the "systematic random biopsy", "AS", and "only follow-up" groups, respectively. *Conclusion:* A second mpMRI opinion may change clinical management in about 45% of patients. Roughly 55% of targeted and 33% of total biopsies, as well as related side effects and costs can be spared. Therefore, mpMRI-revision should be taken into account before taking clinical decisions.

53
URETERORENOSCOPIC THULIUM LASER TREATMENT OF UPPER URINARY TRACT CARCINOMA: A MULTI-INSTITUTIONAL ANALYSIS OF SURGICAL AND ONCOLOGICAL OUTCOMES

Francesco Alessandro Mistretta[1], Gennaro Musi[1], Andrea Russo[1], Michele Catellani[1], Andrea Conti[1], Giovanni Cordima[1], Ettore Di Trapani1, Danilo Bottero[1], Matteo Ferro[1], Deliu Victor Matei[1], Luca Carmignani[2] and Ottavio De Cobelli[1]

[1]Division of Urology, IEO European Institute of Oncology, Milan, Italy; [2]Division of Urology, IRCCS Policlinico San Donato, Milan, Italy

Aim: The aim of the study was to evaluate the efficacy and safety of ureteroscopic thulium laser treatment of upper urinary tract carcinoma (UTUC). *Materials and Methods:* Forty-two patients underwent conservative thulium laser treatment for UTUC at two referral institutions. All patients underwent preliminary biopsy and then laser vaporization. Laser fibers of 272 μm and 365 μm were used with a flexible and semirigid scope, respectively. Ablation was performed at power levels of 10-20 W. *Results:* Mean age of patients at surgery was 68 years (standard deviation=10.7). Mean tumour size was 14.3 mm (range=2-30). Preliminary biopsy revealed the presence of low-grade disease in 29 (69.1%) patients, high-grade in 4 (9.5%) and one (2.4%) carcinoma *in situ*, while it was not conclusive in 8 (19%) cases. Final stage was pTa and pTis in 41 (97.6%) and 1 (2.4%) patients, respectively. Sixteen patients (38%) experienced Clavien-Dindo grade I complication, 47.6% (n=20) a grade II and 2.4% (n=1) a grade III. Five (12%) patients underwent a second-look procedure due to residual disease. Eight (19%) patients experienced clinical recurrence. The median estimated recurrence-free survival was 44 months (standard error=3.68). Four patients (9.5%) underwent a nephroureterectomy. The final pathological stage was pTis, pT3 high grade, pTa low grade and pT0.

Median follow-up was 26.3 (range=2-54 months) months, and no progression or upstaging of disease occurred. *Conclusion:* Thulium laser management of UTUC was described as a safe and effective conservative treatment, with optimal vaporization and haemostatic control in the absence of major complications.

54
POSTOPERATIVE HYPOFRACTIONATED RADIOTHERAPY IN PROSTATE CANCER

Francesco Tramacere[1], Stefano Arcangeli[2], Roberta Castagna[1], Maria Chiara De Luca[1], Cristina De Tommaso[1], Maria Carmen Francavilla[1], Antonietta Pignatelli[1] and Maurizio Portaluri[1]

[1]Radiotherapy Dept, "Antonio Perrino " Hospital ASL Brindisi, Brindisi, Italy; [2]U.O.C. Radiotherapy, Azienda Ospedaliera S. Camillo-Forlanini Circonvallazione Gianicolense, Rome, Italy

Aim: To retrospectively investigate outcomes, acute and late complications following postoperative hypofractionated 3D-conformal radiotherapy (HCRT) in patients who underwent radical prostatectomy with adverse pathological features or early biochemical failure. *Materials and Methods:* Overall, 69 consecutive patients were treated. The median age was 69 years (range=51-77). All patients underwent radical prostatectomy. Surgical pathological specimens showed pT2 in 31% (R1 81%), pT3a in 41% (R1 57%, Close 7%), pT3b in 26% (R1 72%), respectively. HCRT was administered to the prostatic fossa by means of a LINAC 6-15 MV, 7 fields, to a total dose of 62.5 Gy in 25 fractions (2.5 Gy/fraction) in 5 consecutive weeks. Androgen deprivation therapy (ADT) was administrated in 20%. All the patients were evaluated for urinary and rectal late complications according to CTCAE 4.0 and the Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer scale. *Results:* Median follow-up was 53 months (range=34-72 months). Five-year overall survival (OS) and biochemical disease-free survival (bDFS) were 95% and 68%, respectively. Two patients died from non-cancer and non-treatment related causes and one patient died of disease. Median prostate-specific antigen at last follow-up was 0.08 ng/ml (range=0-13). Genitourinary (GU) and gastrointestinal (GI) acute toxicity ≥ grade 2 (G2) was reported in 12% and 5% of patients, respectively. Twelve % of patients experienced GU late toxicity ≥G2 (1 patient developed a G4 urinary fistula), while GI late toxicity ≥G2 occurred in 5%. Urinary incontinence ≥G2 was recorded in 19%. *Conclusion:* The present findings showed that HRT, either in the adjuvant or salvage setting, resulted in acceptable rates of acute and late toxicity with good tumor control while reducing overall treatment time. Confirmatory results from ongoing prospective trials are awaited.

55
USE OF CURATIVE CONCOMITANT CHEMORADIOTHERAPY (CCRT) IN PATIENTS WITH BLADDER CANCER: A MONO-ISTITUTIONAL EXPERIENCE

Chiara Reverberi[1], Luca Marinelli[1], Manuela Giuliani[1], Sara De Matteis[1], Paolo Bonome[1], Serena Macrini[2], Anna Maria Aschelter[2], Vitaliana De Sanctis[1], Mattia Falchetto Osti[1] and Maurizio Valeriani[1]

[1]Radiation Oncology, S. Andrea Hospital, Sapienza University of Rome, Rome, Italy; [2]Oncology, S. Andrea Hospital, Sapienza University of Rome, Rome, Italy

Aim: To evaluate outcomes and toxicities of curative concurrent chemoradiotherapy (CCRT) in patients with muscle-invasive bladder cancer (MIBC). *Patients and Methods:* Sixteen patients with high-grade transitional cell MIBC (T2-4, N0) were treated with CCRT after extensive TURB from 2008 to 2017 in our institution. Thirteen patients were male (81%) and 3 female (19%). Median age at diagnosis was 74 years (range=60-89). All patients received curative RT on the pelvis with a total dose of 45 Gy in 25 fractions, and a RT boost on the bladder for a dose of 22-26 Gy in 11-13 fractions, with concomitant platinum-based chemotherapy (carboplatin AUC 2 weekly in 5 cases and cisplatin 40 mg/m^2 weekly in 11 cases). Five patients (31%) received neoadjuvant chemotherapy, before CCRT. Toxicities were evaluated with the Radiation Therapy Oncology Group scale. *Results:* Median follow-up was 26.5 months (range=1-73). The median overall survival (OS) was 29 months, with 3-year OS 45.8%. Nine patients (56.2%) were deceased (5 from disease and 4 for causes not related to disease) and 7 (43.8%) are alive. The median disease-specific survival (DSS) was not reached, 3-year DSS was 68.9%. The median disease-free survival (DFS) and local relapse-free survival (LRFS) were both 58 months, 3-year DFS was 72.0% and 3-year LRFS was 77.8%. Four patients (25%) relapsed in the bladder. Nine patients (56.2%) presented Grade 1-2 acute genitourinary (GU) toxicity and 4 (25%) acute grade 3 GU toxicity. Nine patients (56.2%) presented Grade 1-2 acute GU toxicity and 4 (25%) acute grade 3 GU toxicity. Eight patients (50%) presented grade 1-2 gastrointestinal (GI) toxicity. Late grade 1-2 GU and GI toxicity were observed in 6 (37.5%) and 1 (6.2%) cases, respectively. No grade 3 late toxicity was observed. *Conclusion:* Despite the small size of the study population, it was confirmed that CCRT is an effective treatment option in terms of survival and local control with an acceptable rate of acute and late toxicities.

57

LOW-RISK PROSTATE CANCER PATIENTS TREATED WITH HYPOFRACTIONATED RADIATION THERAPY: LONG TERM OUTCOMES, TOXICITY AND SEXUAL FUNCTION

Luca Marinelli, Chiara Reverberi, Mattia Falchetto Osti, Vitaliana De Sanctis, Lidia Tronnolone, Manuela Giuliani and Maurizio Valeriani

Radiation Oncology, S. Andrea Hospital, Sapienza University of Rome, Rome, Italy

Aim: To assess efficacy and toxicity rates in low-risk prostate cancer patients scheduled for image-guided hypofractionated radiotherapy (HFRT). *Patients and Methods:* Ninety low-risk prostate cancer patients [Gleason score ≤6, prostate-specific antigen (PSA)≤10 ng/ml, clinical stage T1/T2a-b N0 M0 assessed with multi-parametric contrast-enhanced MRI] were treated with HFRT from March 2007 to February 2017. Clinical target volume (CTV) encompassed prostate with proximal seminal vescicles, and adding 5 mm margin in all directions from CTV to create planning target volume (PTV). Treatment schedule was delivered with image-guided RT 3D-conformal RT, for a total dose of 60 Gy in 20 fractions (5 fractions/week) to PTV, daily cone beam computed tomography was performed. Acute and late toxicities were evaluated according to Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer scoring scale. *Results:* Ranging from 8 to 129, median follow up reached 66 months. The actuarial 8-year overall survival (OS) was 97.3% (median not reached). Eight-year biochemical relapse free survival (BRFS) was 98.9%, with no clinical local recurrence. Median PSA at diagnosis was 3.25 ng/ml (range=1.71-9.98) and at the last follow-up was 0.39 ng/ml (range=0.02-2.11). Acute mild to moderate toxicities were: grade 1-2 gastrointestinal (GI) toxicity occurred in 14 patients (15.5%), grade 1-2 genitourinary (GU) toxicity in 35 cases (38.9%), meanwhile grade 3 GU toxicity occurred in only 2 patients (2.2%). Sexual function was scored as: absence (A), presence of erection but insufficient (I) or sufficient (S) for intercourse. Before RT, 4.4 % had A, 44.4% had I and 51.1% had S. After RT, 36.7% of patients presented A, 45.6% I, and 17.8% S (chi square p=0.011). Patients under 70 years presented A in 16.7% of cases, I in 60%, and S in 23.3%. In patients over 70 years, 46.7% presented A, 38.3% I and 15.0% S (chi square p=0.021). *Conclusion:* HFRT is a safe and well-tolerated treatment option in low-risk prostate cancer. Despite that overall sexual function significantly worsened, age might be a predictive factor to maintain any form of sexual function after therapy.

59

CISPLATIN AND GEMCITABINE NEOADJUVANT CHEMOTHERAPY IN MUSCLE-INVASIVE BLADDER CANCER: A SINGLE INSTITUTE EXPERIENCE

Elena Verri[1], Roberta Mascia[2], Maria Cossu Rocca[2], Gaetano Aurilio[2], Daniela Cullurà2, Gennaro Musi[3], Gabriele Cozzi[3], Ettore Di Trapani[3], Andrea Russo[3], Ottavio De Cobelli[3] and Franco Nolè[2]

[1]Medical Oncology Division of Urogenital and Head & Neck Tumors, European Institute of Oncology, Milan, Italy; [2]Medical Oncology Division of Urogenital and Head & Neck Tumors, European Institute of Oncology, Milan, Italy; [3]Urology Division, European Institute of Oncology, Milan, Italy

Background/Aim: Bladder cancer is the second most common malignancy of the genitourinary tract and the cornerstone therapy for the muscle-infiltrating stages is the radical cystectomy and extended pelvic lymph node dissection. However, nearly half of patients develop metastatic disease within two years due to the presence of early micro-metastases. Neoadjuvant chemotherapy is known to determine 5-10% improvement in 5-year cancer-specific survival compared to surgery alone. Randomized trials demonstrated that the 5-year cancer-specific survival is 90% for responders (<ypT2) in contrast to 30-40% for not responders. Early eradication of micro-metastases, primary tumor downstaging, and a better toxicity profile are the advantages of neoadjuvant compared with adjuvant chemotherapy. Recent data suggest a trend of an increasing use of this therapeutic option also thanks to the development of novel highly effective preoperative regimens which can be administered safely such as cisplatin-based schedules (*i.e.* MVAC, dose dense MVAC, CG) (1-6). Moreover, complete response to neoadjuvant chemotherapies is a strong predictor of better overall survival, but actually there are no other defined predictive biomarkers. The aim of the present single centre observational study was to determine the effectiveness and safety of cisplatin and gemcitabine regimen before cystectomy. *Patients and Methods:* Patients with a clinical stage T2-4 and N0-1 M0 bladder carcinoma, Eastern Cooperative Oncology Group (ECOG) performance status 0-1, and an adequate bone marrow and renal function were enrolled. Smoking habit and comorbidities by ACE-27 system were also evaluated (Table I). Disease clinical assessment was performed by a thorax and abdomen computed tomography scan for every patient and a Fludeoxyglucose-positron emission tomography (FDG-PET) scan for 16 patients. The patients received neoadjuvant chemotherapy with gemcitabine 1,000 mg/m^2, on days 1 and 8, plus cisplatin 70 mg/m^2, on day 1 every 21 days for 3-4 cycles and then, underwent

Table I. *Patient features (n=55).*

Median age (years)	62.2
≥70	25%
<70	75%
Gender	
Men	90%
Women	10%
Smoking habit	
Smokers, ex-smokers	44%
Non -smokers	56%
ECOG Performance status	
≥1	0%
<1	100%
Previous TCC	
Yes	20%
No	80%
Histology	
TCC	91%
Mixed	9%
Clinical stage at diagnosis	
cT2	84%
cT3	8%
cT4	8%
N0	86%
N+	14%
Nephrostomy	
Yes	18%
No	82%
N/L Ratio pre-chemotherapy	
≥3	35%
<3	49%
N/L Ratio post-chemotherapy	
≥3	40%
<3	60%

TCC, Transitional cell cancer; N/L, neutrophil to lymphocyte.

Table II. *Grade 3 (G3) and grade 4 (G4) adverse events.*

G3 or G4	n	%
Leukopenia	1	1.82
Neutropenia	2	3.64
Anemia	5	9.09
Thrombocytopenia	1	1.82
Nausea	3	5.45
Vomit	2	3.64
Total	14	25.46

radical cystectomy and extended pelvic lymphadenectomy with or without bladder reconstruction. Primary endpoint was the complete and near complete response rate (pT0-pTis-pT1), secondary endpoints were one-year disease free survival (DFS), overall survival (OS) and safety. The Kaplan-Meier survival analysis with the log-rank test has been used to evaluate the differences in time to recurrence and survival between different groups of patients. A p-value <0.05 was considered statistically significant. *Results:* From March 2011 to March 2017 55 patients were prospectively evaluated at our institution. Their median age was 62.2 years (range=41-82; 25% were more than 70 years old. Eight patients (14%) had clinical lymph node involvement at the time of diagnosis. A total of 44 patients (80%) received 4 cycles and 9 (16%) received 3 cycles of chemotherapy. Overall 51 patients were able to undergo surgery and thus, were evaluable for pathologic response. Half of the 51 patients obtained a successful response: 14 (29%) had complete response (pT0) and 10 patients (21%) a near complete response (pT1-pTis) (Figure 1). When compared to the stage at diagnosis, pathologic complete response was seen in 30% of the patients defined as clinical T2 or T3 *versus* no pathologic complete response in T4 stages (Figure 2). Thirteen patients (26%) had lymph node disease after surgery: 20% of these patients were node-negative at the time of the diagnosis. Patients with clinical node positive became node-negative after neoadjuvant chemotherapy and surgery in 40% of cases (Figure 3). Median follow-up was 14 months. One-year OS was 88% and one-year DFS was 85% (Figures 4 and 5). The used regimen was well-tolerated. Only 2 patients suspended chemotherapy due to severe adverse events (G3-G4) after 2 cycles, but underwent radical cystectomy (Table II) anyway. There was no grade 3/4 renal toxicity, febrile neutropenia, or death. *Conclusion:* The present analysis confirmed the efficacy and the safety of cisplatin and gemcitabine regimen when used in the neoadjuvant setting, since high rates of pathologic complete and near complete response without severe adverse events were observed. Patients with node-positive disease at diagnosis, who had fairly good response rates, were also included in the study, resulting in a better outcome after combined regimens of chemotherapy and surgery. Further studies for the identification of other clinical and/or molecular factors to predict in advance chemotherapy responder patients would be of great importance.

1 Advanced Bladder Cancer Meta-analysis Collaboration: Neoadjuvant chemotherapy in invasive bladder cancer: A systematic review and metaanalysis. Lancet *361*: 1927-1934, 2003.

2 Advanced Bladder Cancer (ABC) Metaanalysis Collaboration: Neoadjuvant chemotherapy in invasive bladder cancer: Update of a systematic review and meta-analysis of individual patient data advanced bladder cancer (ABC) meta-analysis collaboration. Eur Urol *48*: 202-205; discussion 205-206, 2005.

3 Pal SK, Ruel NH, Wilson TG and Yuh BE: Retrospective analysis of clinical outcomes with neoadjuvant cisplatin-

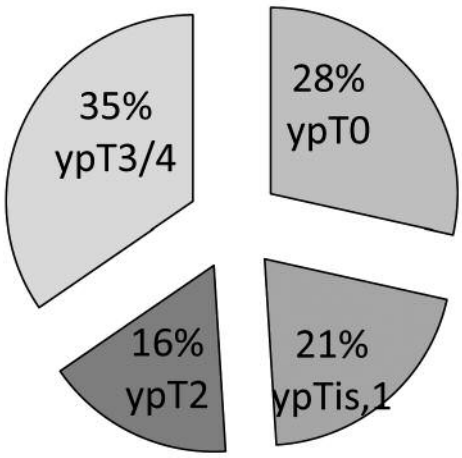


Figure 1. *Pathological stage after neoadjuvant chemotherapy. yp, Post-treatment stage.*

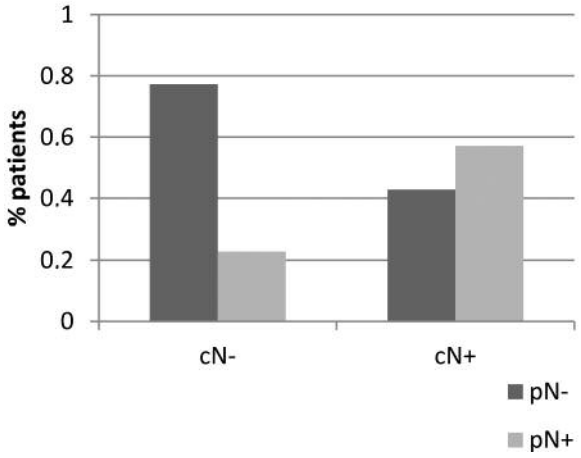


Figure 3. *Relationship between pathological lymph node status and clinical lymph node status. C, Clinical stage.*

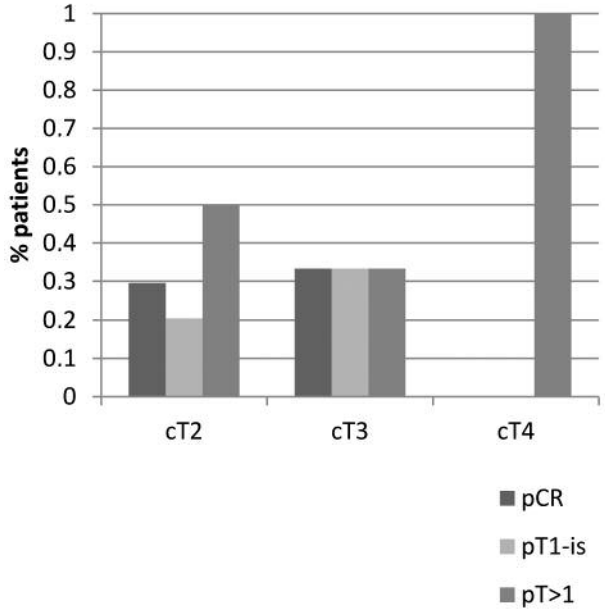


Figure 2. *Relative frequencies of pathological response per stage. CR, Complete response.*

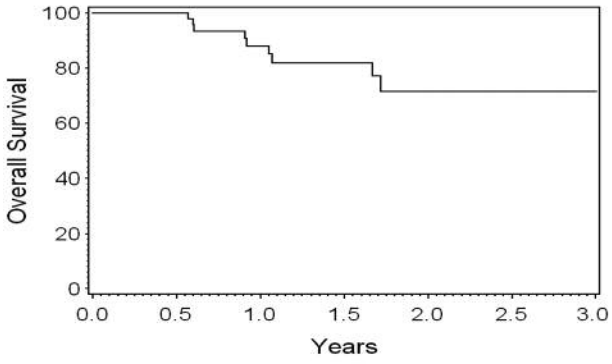


Figure 4. *Overall survival.*

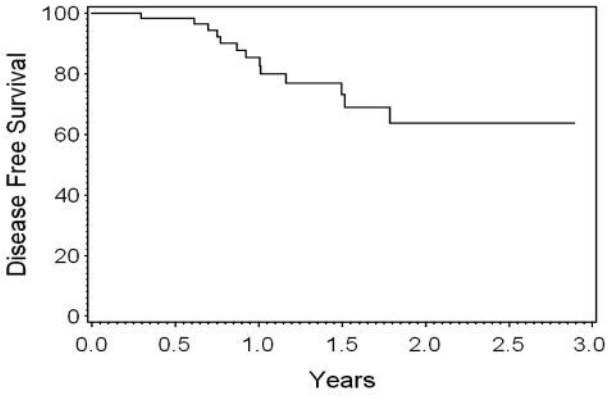


Figure 5. *Disease-free survival.*

basedregimens formuscle- invasive bladder cancer. Clin Genitourin Cancer *10*: 246-250, 2012.

4 Witjes JA, Comperat E, Cowan NC, De Santis M, Gakis G, Lebret T, Ribal MJ, Van der Heijden AG, Sherif A and European Association of Urology: EAU guidelines on muscle-invasive and metastatic bladder cancer: Summary of the 2013 guidelines. Eur Urol *65*: 778-792, 2014.

5 Zargar H, Espiritu PN, Fairey AS Mertens LS, Dinney CP, Mir MC, Krabbe LM, Cookson MS, Jacobsen NE, Gandhi NM, Griffin J, Montgomery JS, Vasdev N, Yu EY, Youssef D, Xylinas E, Campain NJ, Kassouf W, Dall'Era MA, Seah JA, Ercole CE, Horenblas S, Sridhar SS, McGrath JS, Aning J, Shariat SF, Wright JL, Thorpe AC, Morgan TM, Holzbeierlein JM, Bivalacqua TJ, North S, Barocas DA, Lotan Y, Garcia JA, Stephenson AJ, Shah JB, van Rhijn BW, Daneshmand S, Spiess PE and Black PC: Multicenter assessment of neoadjuvant chemotherapy for muscle-invasive bladder cancer. Eur Urol *67*: 241-249, 2015.

6 Yin M, Joshi M, Meijer RP, Glantz M, Holder S, Harvey HA, Kaag M, Fransen van de Putte EE, Horenblas S and Drabick JJ: Neoadjuvant chemotherapy for muscle-invasive bladder cancer: A systematic review and two-step meta-analysis. Oncologist *21(6)*: 708-715, 2016.

60
NEUTROPHIL TO LYMPHOCYTE RATIO AS A PREDICTIVE FACTOR OF CISPLATIN BASED NEOADJUVANT CHEMOTHERAPY IN MUSCLE-INVASIVE BLADDER CANCER

Roberta Mascia[1], Elena Verri[2], Maria Cossu Rocca[2], Gaetano Aurilio[2], Daniela Cullurà[2], Gennaro Musi[3], Gabriele Cozzi[3], Andrea Russo[3], Ottavio De Cobelli[3] and Franco Nolè[2]

[1]Medical Oncology Division of Urogenital and Head & Neck Tumors, European Institute of Oncology, Milan, Italy; [2]Medical Oncology Division of Urogenital and Head & Neck Tumors, European Institute of Oncology, Milan, Italy; [3]Urology Division, European Institute of Oncology, Milan, Italy

Background/Aim: Systemic inflammation plays an important role in cancer development and progression, and has been especially implicated in bladder cancer. Neutrophil to lymphocyte ratio (NLR) is an established measure of the systemic inflammatory response used in several studies and reflects a higher count as compared to the lymphocyte count in response to stress such as infection and inflammation. NLR is easily calculated from a complete blood count and high values have been retrospectively shown to be associated with decreased overall survival across the spectrum of solid tumors and also specifically in bladder cancer. Nowadays, there are no validated markers of response to neoadjuvant chemotherapy for muscle invasive bladder cancer; NLR is an attractive and easily accessible laboratory marker but further prospective validation is yet required. The aim of the present single-center observational study was to determine the relationship between complete and near complete pathologic response and pre-chemotherapy NLR value in patients treated with neoadjuvant chemotherapy such as cisplatin and gemcitabine regimen, administered every three weeks for 3-4 cycles before cystectomy. *Patients and Methods:* From March 2011 to March 2017 we collected retrospective data from 55 consecutive patients with muscle invasive bladder carcinoma who received neoadjuvant chemotherapy with cisplatin 70 mg/m^2 on day 1 and gemcitabine 1000 mg/m^2 on days 1 and 8 for 3-4 cycles and then underwent radical cystectomy and pelvic lymphadenectomy, for whom the clinical and pathological stage were available. Patients with cT2-4 N0- 1M0 were selected for this analysis. Other inclusion criteria were a good Eastern Cooperative Oncology Group (ECOG) performance status (0-1) and a proper renal function; smoking habit and comorbidities by ACE-27 system were also evaluated (Table I). Primary endpoint was the complete and near complete response rate (pT0-pTis-pT1) and the relationship between complete pathologic response

Table I. *Patients sample features (n=55).*

Median age (years)	62.2
≥70	25%
<70	75%
Gender	
Men	90%
Women	10%
Smoking habit	
Smokers, ex-smokers	44%
Non -smokers	56%
ECOG Performance Status	
≥1	0%
<1	100%
Previous TCC	
Yes	20%
No	80%
Histology	
TCC	91%
Mixed	9%
Clinical stage at diagnosis	
cT2	84%
cT3	8%
cT4	8%
N0	86%
N+	14%
Nephrostomy	
Yes	18%
No	82%
N/L Ratio pre-chemotherapy	
≥3	35%
<3	49%
N/L Ratio post-chemotherapy	
≥3	40%
<3	60%

TCC, Transitional cell cancer; N/L, neutrophile to lymphocyte; c, clinical stage.

Table II. *NLR Median and interquartile range before and after chemotherapy divided for pathological stage and lymph node stage.*

	N		Median NLR	Lower Quartile	Upper Quartile
All	49	Baseline	2.50	1.10	8.50
	55	Post	2.20	0.66	11.28
	49	Change post-pre	–0.11	–7.00	7.18
Response					
PR	27	Baseline	2.48	2.1	3.42
		Post	2.15	1.76	3.39
		Change post-pre	–0.17	–1.08	0.46
SD	23	Baseline	2.43	2.11	3.50
		Post	2.29	1.46	4.49
		Change post-pre	0.21	–0.95	2.51
PD	5	Baseline	2.94	2.59	5.08
		Post	2.90	2.50	5.10
		Change post-pre	–0.15	–2.63	1.63
pN					
N–	37	Baseline	2.42	2.03	3.42
		Post	2.15	1.68	4.49
		Change post-pre	–0.11	–0.67	0.46
N+	14	Baseline	3.15	2.49	3.60
		Post	2.49	1.77	4.98
		Change post-pre	0.52	–0.705	1.90
pT					
0	15	Baseline	2.42	1.92	3.5
		Post	1.77	1.46	4.3
		Change post-pre	–0.24	–0.95	0.27
>0	36	Baseline	2.68	2.11	3.47
		Post	2.39	1.805	5.04
		Change post-pre	0.10	–0.35	2.51

NLR, Neutrophil to lymphocyte ratio; SD, stable disease; PD, progressive disease; PR, partial response; pT, pathological stage; pN, pathological lymph-node status.

and pre-chemotherapy NLR value; secondary endpoints were one-year disease free survival (DFS), the overall survival (OS) and safety. NLR ratio has been evaluated in association to clinical endpoints and it has been calculated from a blood count before chemotherapy and before radical cystectomy. The change of NLR value before and at the end of the entire chemotherapy period was also considered. A p-value <0.05 was considered statistically significant. *Results:* Overall, 51 patients were able to undergo surgery and were thus evaluable for pathologic response; 14 (29%) had complete response (pT0) and 10 patients (21%) had a near complete response (pT1-pTis) (Figure 1). When compared to the stage at the diagnosis, pathologic complete response was seen in 30% of the patients defined as clinical T2 or T3 *versus* no pathologic complete response in T4 stages (Figure 2). In 13 patients (26%) was found lymph node disease after chemotherapy (pN1-2). NLR cut-off has been determined based on NLR median values after chemotherapy. NLR values were higher either before or after chemotherapy in patients who had a disease progression after chemotherapy, in patients with lymph node disease at diagnosis and in those who did not reach a pathologic complete response even if differences were not statistically significant (Tables II and III). At a median follow-up of 14 months, one-year OS was 88% and one-year DFS was 85% (Figures 3 and 4). *Conclusion:* The present analysis suggests an increasing NLR trend in non-responders and in locally advanced disease. We also found higher

Table III. *Patients relative frequencies with NLR values >2.2 divided for response to chemotherapy.*

		PR	SD	PD	Total
Total	n	27	23	5	55
	%	49.09	41.82	9.09	100
NLR post ≤2.2	n	15	11	1	27
	%	55.56	47.83	20	
NLR post >2.2	n	12	12	4	28
	%	44.44	52.17	80	

NLR, Neutrophil to lymphocyte ratio; SD, stable disease; PD, progressive disease; PR, partial response.

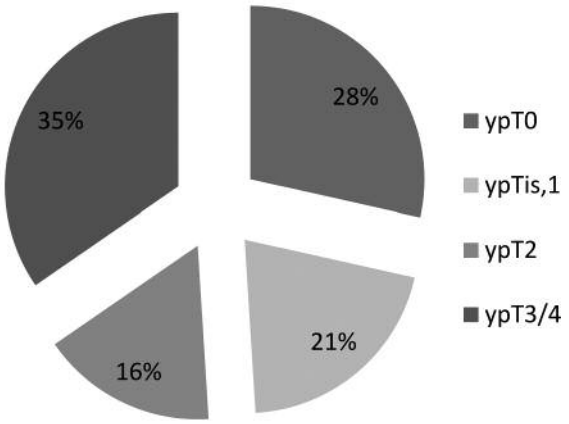


Figure 1. *Pathological stage after neoadjuvant chemotherapy. yp, Stage after treatment.*

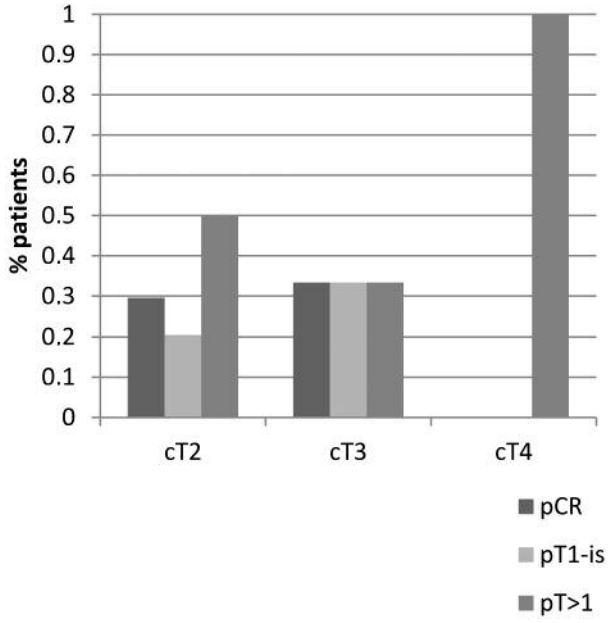


Figure 2. *Relative frequencies of pathological response per stage.*

absolute values before and after chemotherapy in patients who had a disease progression. The possible correlation between high basal NLR values and positive lymph node disease at diagnosis has been already investigated in other clinical studies including ovarian cancer, colorectal cancer, larynx cancer and bladder cancer but no definitive conclusion was drawn (1-5). Despite the small and heterogeneous patient cohort, the trend was clear and it supports further investigations in this direction. NLR is an easy accessible and low-cost marker and its future validation may reveal a broad spectrum of potential applications in clinical practice.

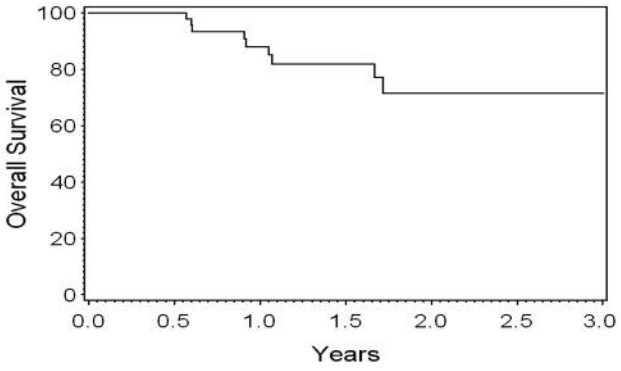


Figure 3. *Overall survival.*

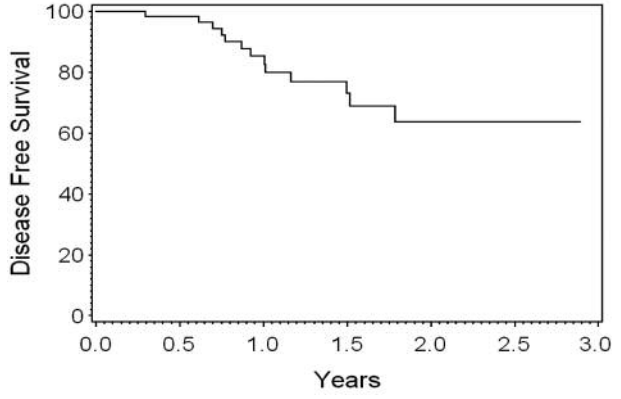


Figure 4. *Disease free survival.*

1 Templeton AJ, McNamara MG, Seruga B, Vera-Badillo FE, Aneja P, Ocana A, Leibowitz-Amit R, Sonpavde G, Knox JJ, Tran B, Tannock IF and Amir E: Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: A systematic review and meta-analysis. J Natl Cancer Inst 106: dju 124, 2014.

2 Luo Y, She DL, Xiong H and Fu SJ and Yang L: Pretreatment neutrophil to lymphocyte ratio as a prognostic predictor of urologic tumors: a systematic review and meta-analysis. Medicine *94*: e1670, 2015.

3 Gunduz S, Mutlu H, Tural D, Yıldız Ö, Uysal M, Coskun HS and Bozcuk H: Platelet to lymphocyte ratio as a new prognostic for patients with metastatic renal cell cancer. Asia Pac J Clin Oncol *11*: 288-292, 2015.

4 Malietzis G, Giacometti M, Kennedy RH, Athanasiou T, Aziz O and Jenkins JT: The emerging role of neutrophil to lymphocyte ratio in determining colorectal cancer treatment outcomes: A systematic review and meta-analysis. Ann Surg Oncol *21*: 3938-3946, 2014.

5 Thavaramara T, Phaloprakarn C, Tangjitgamol S and Manusirivithaya S: Role of neutrophil to lymphocyte ratio as a prognostic indicator for epithelial ovarian cancer. J Med Assoc Thai *94*: 871-877, 2011.

61
GRANULOSA CELL-TUMOR OF THE TESTIS: A CASE REPORT OF A VERY RARE TUMOR AND REVISION OF THE LITERATURE

Emanuela Trenti[1], Salvatore Mario Palermo[1], Tamara Tischler[1], Carolina D' Elia[1], Evi Comploj[1], Christian Ladurner[1], Dorian Huqi[1], Esther Hanspeter[2] and Armin Pycha[1]

[1]Division of Urology, Central Hospital of Bolzano, Bolzano, Italy;
[2]Division of Pathology, Central Hospital of Bolzano, Bolzano, Italy

Background/Aim: Granulosa cell tumors (GCT) of the testis belong to the sex-cord stromal tumors and represent 4-5% of all testicular tumors. They were described for the first time in 1952 and they can be classified into two categories, the juvenile type and the adult type. Although the juvenile-type represents only 1-4% of pre-pubertal testicular tumors, it is the most common testis neoplasm in the first 6 months of life. The adult type is instead extremely rare and occurs at any age after puberty with only a limited number of reported cases to date: after a review of the literature we have found only 51 published cases, mostly isolated as case reports. Unlike the juvenile type, which is typically benign, 20-25% of the adult type has been reported to be malignant with a metastatic potential even after 10 years: the retroperitoneal lymph nodes are the most common metastatic regions but liver, lung and bone metastases have been also described. Gynecomastia, erectile dysfunction and decreased libido may be present in 20- 25% of the cases, due to hormonal or chromosomal abnormalities. Because of his low incidence and the lack of data, the prognosis is not really known and consequently it's almost difficult to decide what surgery to perform and if a radical treatment is really needed. We present a case of a patient with an adult type of GCT of the testis, treated with testis sparing surgery. *Case Report:* We describe a case of a 32-year-old patient, who was admitted to our department with suspicion of tumor in the left testis. The ultrasonography showed a 15 mm hypo-echoic, vascularised lesion in the upper pole of the left testis. The patient had no history of cryptorchidism and his past medical history was not significant, including only a spontaneous pneumothorax, when he was 18 years old. The patient denied decreased libido or erectile dysfunction in the months before. Alpha- fetoprotein (alfa-FP), human chorionic gonadotropin (HCG) and lactate dehydrogenase (LDH) were normal. During the operation a frozen section was requested as usual in our department, before performing a radical treatment. The lesion was small, intra-parenchymal, and simple to remove, without infiltration of the surrounding tissue. The pathologist suspected a GCT and the surgeon decided to perform a testis sparing surgery while waiting for the definitive histology. *Results:* The postoperative course was uneventful and the patient was released from the hospital the day after the operation, without complications. The definitive histology confirmed the previous report of adult-type GCT; the lesion measured 1.5 cm and showed to be not infiltrating. There was no evidence of angio-invasion or necrosis. The tumor was composed of clusters of cells with scanty cytoplasm in a predominantly micro-follicular pattern; very few mitoses could be identified. The immunohisto-chemical study showed positivity for calretinin, inhibin, CD-99, and beta-catenin while chromogranin, cytokeratin, and melan-A were negative. Computed tomography showed absence of lymph node enlargement or distant metastases. The patient underwent regular follow-up without any other surgery: an ultrasound of the testicles was performed every 3 months; 6 months after surgery an abdominal ultrasound and a chest X-ray were performed, and after one year the patient is well and shows no signs of residual disease on ultrasound and computed tomography. *Conclusion:* The adult-type GCT is a rare entity, which can be malignant in 20-25% of the cases. A testis-sparing surgery could be offered in selected cases by small, intra- parenchymal lesions, if frozen sections are suspicious for a GCT, waiting for the definitive histological diagnosis: by angio-invasion, necrosis, infiltrating margins, severe nuclear atypia or elevated mitotic count a delayed radical orchiectomy should be performed although no cut-off for the tumor size is offered in the guidelines.

62
ORGAN-SPARING SURGERY IN TESTICULAR SEX CORD-STROMAL TUMORS: RESULTS OF A LITTLE SERIES

Emanuela Trenti[1], Salvatore Mario Palermo[1], Carolina D' Elia[1], Evi Comploj[1], Christian Ladurner[1], Dorian Huqi[1], Tamara Tischler[1], Esther Hanspeter[2] and Armin Pycha[1]

[1]Division of Urology, Central Hospital of Bolzano, Bolzano, Italy;
[2]Division of Pathology, Central Hospital of Bolzano, Bolzano, Italy

Background/Aim: Testicular sex-cord stromal tumors (TSCST) arise from nongerminal cell lines of the male testis and represent 3-5% of all testicular tumors: the most common subtype is represented from Leydig cell tumors

(75-80%) but this group of tumors includes also Sertoli and Granulosa cell tumors, mixed and undifferentiated tumors, thecomas, and fibromas. They can occur at any age with a range from 12 to 76 years. The most common clinical presentation is a palpable testicular mass. Gynecomastia, erectile dysfunction, or decreased libido are reported in one third of patients. The great majority of these tumors show a good clinical outcome but a malignant behavior has been reported in about 10% of all cases. Because of their low incidence and the lack of data from prospective studies, their management remains controversial: the guidelines recommend an organ-sparing procedure in every small ultrasound-detected, non-palpable intraparenchymal lesion to obtain a histological diagnosis and, in case of malignancy, to perform a delayed orchiectomy; however, a cut-off value of tumor size is not defined. The potential malignancy and the difficulty to individuate the unfavourable cases can be an element for urologists to perform a radical surgery and the testis-sparing surgery (TSS) can remain only an option. We present a small series of 11 consecutive patients with TSCST, with the intent to evaluate the possibility to standardize the surgical treatment. *Materials and Methods:* Between 2005 and 2016, a TSCST was diagnosed in 11 patients at our department. The age ranged from 14 to 83 years. The blood screening with alpha-fetoprotein (alfa-FP), human chorionic gonadotropin (HCG) and lactate dehydrogenase (LDH) was assessed preoperative in all patients. All patients underwent inguinal access to the testis. During the operation, frozen sections were request before to choose the definitive surgical strategy and a TSS was performed always in case of TSCST, waiting for the definitive histology, before to perform a radical orchidectomy. A thoracic and abdominal computed tomography was performed after the surgery. The follow-up was scheduled according to the European Association of Urology guide-lines for testicular tumors. *Results:* All lesions were intraparenchymal and detected in ultrasound. No patient presented gynecomastia. Alpha-FP, HCG and LDH were negative in all patients. The intra-operative histology showed a TSCST in 10 patients, who were treated with TSS. Orchiectomy was performed in one patient, because the tissue section suspected a seminoma but the definitive histology showed a TSCST. The tumor-size ranged from 7 to 40 mm. There was no evidence of angioinvasion, margin infiltration or necrosis in the definitive histology. The mitosis-index was low in all patients (<1%). All postoperative courses were uneventful and the patients were discharged one day after the operation without complications. The computed tomography showed absence of lymph node enlargement or distant metastases in all patients. Follow-up ranged from 10 to 108 months (mean 43.8 months), every 6 months for 5 years and then every year. All patients were free from disease and alive except one, who died after 108 months, due to other reasons. *Conclusion:* Our small prospective series confirm that a TSS could be safely performed in case of TSCST by frozen sections, when the tumor size is smaller than 4 cm and the lesion is easy to resect, leaving sufficient testicular parenchyma, with a very low-risk to perform a delayed radical surgery. In presence of one or more pathologic risk factors in the definitive histology a radical surgery should always be considered. Although there is a good prognosis of these tumors, we remark the need of a regular follow-up.

64

KIDNEY SPARING SURGERY *VS.* RADICAL NEPHROURETERECTOMY FOR UPPER TRACT UROTHELIAL CARCINOMA IN PATIENTS WITH *VS.* WITHOUT RENAL FAILURE: A MULTICENTER STUDY

Alberto Abrate[1], Francesco Sessa[2], Arcangelo Sebastianelli[2], Cristina Scalici Gesolfo[1], Mirko Preto[3], Alberto Olivero[4], Virginia Varca[5], Andrea Benelli[5], Carlo Pavone[1], Vincenzo Serretta[1], Marco Vella[1], Eugenio Brunocilla[6], Sergio Serni[2], Carlo Trombetta[7], Carlo Terrone[4], Andrea Gregori[5], Andrea Lissiani[7], Paolo Gontero[3], Riccardo Schiavina[6], Mauro Gacci[2] and Alchiede Simonato[1]

[1]Department of Surgical, Oncological and Stomatological Sciences, Section of Urology, University of Palermo, Palermo, Italy;
[2]Department of Urology, AOU Careggi, University of Florence, Florence, Italy;
[3]Division of Urology, Department of Surgical Science, A.O.U. Città Della Salute E Della Scienza di Torino - Presidio Molinette, University of Turin, Turin, Italy;
[4]Department of Urology, IRCCS AOU San Martino, University of Genoa, Genoa, Italy;
[5]Department of Urology, ASST Rhodense, G. Salvini Hospital, Milan, Italy;
[6]Department of Urology, University of Bologna, St. Orsola-Malpighi Hospital, Bologna, Italy;
[7]Department of Urology, University of Trieste, Trieste, Italy

Background/Aim: Radical nephroureterectomy (RNU) with bladder cuff removal represents the standard of care for the treatment of upper tract urothelial carcinoma (UTUC). However, due to the morbidity associated with chronic renal failure, particularly in patients with impaired renal function and consequent increased risk of non-cancer related death, kidney-sparing surgery (KSS) has been proposed as an alternative to RNU, in selected cases. Aim of our study was to evaluate the overall (OS) and cancer

specific survival (CSS) of patients electively treated with KSS or RNU for UTUC, and determine whether normal or high serum creatinine levels could influence the assessed outcomes. *Patients and Methods:* Data from patients treated with RNU or KSS for UTUC in 5 European tertiary referral centers from January 2003 were collected and analyzed. All patients were diagnosed using computed tomography (CT) urography or with RMN urography (MRU), and preoperative ureteroscopy with biopsy was performed in respect of imaging diagnostic uncertainty. Patients with history of other malignancies, metastatic disease, radical cystectomy or renal pelvis cancer were excluded. Patients were treated with RNU or KSS (segmental ureterectomy) according to surgeon preference and followed-up every 3 months the first year after surgery, every 4 months the second year, every 6 months from the third to the fifth year, then annually. A subgroup analysis has been carried out stratifying patients with "normal" (≤1.2 mg/dl) or "high" (>1.2 mg/dl) serum creatinine levels before surgery. Baseline characteristics were compared using the t-test for continuous variables and chi-squared for categorical variables. The same analysis was performed at the end of the follow-up period. Unadjusted overall survival and cancer-specific survival curves were compared by using Kaplan–Meier method for all-causes mortality and cumulative incidence for cancer-specific mortality. *Results:* Overall, 433 patients were eligible for the analysis, 339 treated with RNU and 94 with KSS. Pre-operative characteristics were similar between the two groups, except for multifocality (RNU: 16.8% *vs*. KSS: 8.5%, $p<0.05$) and serum creatinine (RNU: 1.3 mg/dl *vs*. KSS: 1.1 mg/dl, $p=0.03$). A total of 102 (23.6%) patients had normal creatinine values (mean±SD: 0.89±0.16 mg/dl): 78 (76.5%) treated with RNU and 24 (23.5%) treated with KSS. Overall 331 (76.4%) patients had high creatinine values (mean±SD: 1.51±0.58 mg/dl): 261 (78.8%) treated with RNU and 70 (21.2%) treated with KSS. The median follow-up was 89 months (range=3-116). In the subgroup of patients with normal creatinine values, no significant differences have been observed for both OS and CSS in patients treated with RNU or KSS. Indeed, 5-year OS was 75% *vs*. 77% ($p=0.665$) and 5-year CSS 90% *vs*. 95% ($p=0.441$) in patients treated with RNU or KSS, respectively. Conversely, in the subgroup with high creatinine values, patients treated with KSS *vs*. RNU showed better 5-year OS (81% *vs*. 67%, $p=0.002$) and better 5-year CSS (92% *vs*. 80%, $p=0.038$), both statistically significant different between the two groups. *Conclusion:* In our experience the greatest part of patients with UTUC showed elevated (>1.2 mg/dl) creatinine levels. Moreover, patients with high serum creatinine could benefit the most from KSS, since there is a significant advantage over RNU in OS and CSS.

65

TERMINO-TERMINAL URETERAL ANASTOMOSIS *VS.* SEGMENTAL RESECTION OF DISTAL PELVIC URETER WITH BLADDER CUFF REMOVAL AND URETERAL REIMPLANTATION FOR UROTHELIAL CARCINOMA OF THE URETER: RESULTS OF A MULTICENTER STUDY

Alberto Abrate[1], Francesco Sessa[2], Arcangelo Sebastianelli[2], Cristina Scalici Gesolfo[1], Mirko Preto[3], Alberto Olivero[4], Virginia Varca[5], Andrea Benelli[5], Carlo Pavone[1], Vincenzo Serretta[1], Marco Vella[1], Eugenio Brunocilla[6], Sergio Serni[2], Carlo Trombetta[7], Carlo Terrone[4], Andrea Gregori[5], Andrea Lissiani[7], Paolo Gontero[3], Riccardo Schiavina[6], Mauro Gacci[2] and Alchiede Simonato[1]

[1]Department of Surgical, Oncological and Stomatological Sciences, Section of Urology, University of Palermo, Palermo, Italy; [2]Department of Urology, AOU Careggi, University of Florence, Florence, Italy; [3]Division of Urology, Department of Surgical Science, A.O.U. Città Della Salute E Della Scienza di Torino - Presidio Molinette, University of Turin, Turin, Italy; [4]Department of Urology, IRCCS AOU San Martino, University of Genoa, Genoa, Italy; [5]Department of Urology, ASST Rhodense, G. Salvini Hospital, Milan, Italy; [6]Department of Urology, University of Bologna, St. Orsola-Malpighi Hospital, Bologna, Italy; [7]Department of Urology, University of Trieste, Trieste, Italy

Background/Aim: Kidney-sparing surgery (KSS) has been proposed as an alternative to radical nephroureterectomy (RNU) for upper tract urothelial carcinoma (UTUC). However, segmental resection of the iliac and lumbar ureter seems to be associated with greater failure than for the distal pelvic ureter. The aim of the present study was to evaluate the overall (OS) and cancer-specific survival (CSS) of patients with ureteral UTUC electively treated with segmental resection and termino-terminal anastomosis of the iliac or lumbar ureter (TT) *vs*. segmental resection of distal pelvic ureter with bladder cuff removal and ureteral reimplantation (RR). Moreover, as secondary endpoint, we evaluated the impact on renal function of TT *vs*. RR. *Patients and Methods:* Data from patients treated with KSS for UTUC in five European tertiary referral centers from January 2003 to December 2013 were collected and analyzed. All patients were diagnosed using computed tomography (CT) urography or magnetic resonance urography (MRU): preoperative ureteroscopy with biopsy was performed when imaging diagnostic uncertainty was reported. Patients with history of other malignancies, metastatic disease, radical cystectomy or previous transitional cell carcinoma of the upper

and or lower urinary tract were excluded. Patients were treated with TT or RR according to tumor location and followed-up every 3 months the first year after surgery, every 4 months the second year, every 6 months from the third to the fifth year, then annually. Baseline characteristics were compared using the *t*-tests for continuous variables and chi-squared for categorical variables. The same analysis was performed at the end of the follow-up period. Un-adjusted overall survival and cancer-specific survival curves were compared by using Kaplan–Meier method for all-causes mortality and cumulative incidence for cancer-specific mortality. For the aforementioned outcomes, in the adjusted analysis, multivariate Cox regression adjusted for age, gender, smoking status, biopsy, tumor localization, hydronephrosis, pre-operative creatinine, history of bladder carcinoma and multifocality tumor pathological stage/grade, lymphadenectomy, number of lymph nodes surgically excised, necrosis, positive surgical margin, lymphovascular invasion, concurrent bladder carcinoma, and tumor *in situ* was used. Multivariate linear regression model was used to compare RNU and KSS for postoperative creatinine (at 3 months). *Results:* Overall, 85 patients were eligible for the analysis, 62 treated with TT and 23 with RR. Pre-operative characteristics were comparable between the two groups. The median follow-up was 89 months (range=24-116). Patients treated with TT showed similar 5-year OS and 5-year CSS as compared to those treated with RR (87% *vs.* 69%, p=0.148 and 93% *vs.* 92%, p=0.953, respectively). Moreover, at the adjusted analysis, no statistically significant postoperative differences were observed in delta creatinine among patients underwent TT and RR, and the only significant determinant for postoperative creatinine variation was preoperative creatinine level. *Conclusion:* Patients treated with TT and RR showed comparable 5-year OS and 5-year CSS. Moreover, the only determinant on postoperative creatinine variation is preoperative creatinine level, irrespective of the surgical technique.

66
KIDNEY SPARING SURGERY FOR UPPER TRACT UROTHELIAL CARCINOMA: LONG TERM RESULTS OF A MULTICENTER STUDY IN COMPARISON WITH RADICAL NEPHROURETERECTOMY

Francesco Sessa[1], Arcangelo Sebastianelli[1], Alberto Abrate[2], Cristina Scalici Gesolfo[2], Mirko Preto[3], Alberto Olivero[4], Virginia Varca[5], Andrea Benelli[5], Carlo Pavone[2], Vincenzo Serretta[2], Marco Vella[2], Eugenio Brunocilla[6], Sergio Serni[1], Carlo Trombetta[7], Carlo Terrone[4], Andrea Gregori[5], Andrea Lissiani[7], Paolo Gontero[3], Riccardo Schiavina[6], Alchiede Simonato[2] and Mauro Gacci[1]

[1]Department of Urology, AOU Careggi, University of Florence, Florence, Italy;
[2]Department of Surgical, Oncological and Stomatological Sciences, Section of Urology, University of Palermo, Palermo, Italy;
[3]Division of Urology, Department of Surgical Science, A.O.U. Città Della Salute E Della Scienza di Torino - Presidio Molinette, University of Turin, Turin, Italy;
[4]Department of Urology, IRCCS AOU San Martino, University of Genoa, Genoa, Italy;
[5]Department of Urology, ASST Rhodense, G. Salvini Hospital, Milan, Italy;
[6]Department of Urology, University of Bologna, St. Orsola-Malpighi Hospital, Bologna, Italy;
[7]Department of Urology, University of Trieste, Trieste, Italy

Background/Aim: Radical nephroureterectomy (RNU) with bladder cuff removal represents the gold standard for the treatment of upper tract urothelial carcinoma (UTUC). However, kidney-sparing surgery (KSS) has been proposed in selected cases as an alternative to RNU to overcome the morbidity associated with chronic renal failure and the consequently increased risk of non-cancer related death. Aim of our study was to compare cancer-specific survival (CSS), overall survival (OS) and the postoperative creatinine variations in patients electively treated with KSS or RNU for UTUC. *Patients and Methods:* Data from patients treated with RNU or KSS for UTUC collected in five European tertiary referral centers from January 2003 to December 2013 were evaluated. All patients were diagnosed by using computed tomography (CT) urography or RMN urography (MRU). Preoperative ureteroscopy with biopsy was performed when imaging diagnostic uncertainty was reported. Patients with history of other malignancies, metastatic disease, "or previous transitional cell carcinoma of the upper and or lower urinary tract" were excluded. Patients were treated with RNU or KSS (segmental ureterectomy) according to patients' conditions (tumor characteristics and comorbidities) and surgeon preference and were followed-up every 3 months the first year after surgery, every 4 months the second year, every 6 months from the third to the fifth year, then annually. Baseline characteristics and follow-up variables were compared using the *t*-tests for continuous variables and chi-squared for categorical variables. Unadjusted cancer-specific survival and overall survival curves were compared by using Kaplan–Meier method for all-causes mortality and cumulative incidence for cancer-specific mortality. For the aforementioned outcomes, in the adjusted analysis, multivariate Cox regression adjusted for age, gender, smoking status, biopsy, tumor localization, hydronephrosis, preoperative creatinine, history of bladder carcinoma and multifocality tumor pathological stage/grade, lymphadene-

ctomy, number of lymph nodes surgically excised, necrosis, positive surgical margin, lymph vascular invasion, concurrent bladder carcinoma, and tumor *in situ* was used. Multivariate linear regression model was used to compare RNU and KSS for postoperative creatinine. *Results:* Overall, 433 patients were analyzed, 339 treated with RNU and 94 with KSS. Pre-operative characteristics were comparable between the two groups, apart from multifocality (RNU: 16.8% *vs*. KSS: 8.5%, $p<0.05$) and serum creatinine (RNU: 1.3 mg/dl *vs*. KSS: 1.1 mg/dl, $p=0.03$). The median follow-up was 89 months (range=12-120). At multivariable Cox regression model, patients treated with KSS showed better 5-year CSS and 5-year OS as compared to those treated with RNU (92% *vs*. 81%, $p=0.026$ and 80% *vs*. 69%, $p=0.003$, respectively). However, in the adjusted analysis, no statistically significant differences in terms of CSS and OS between the two groups were found, and the only two significant determinants on both CSS and OS were age at time of diagnosis and pathological stage (≥pT3). At multivariable linear regression model, patients treated with KSS had lower but not statistically significant postoperative creatinine serum level compared to those treated with RNU [-0.24 mg/dl; 95% confidence interval (CI)=-0.66 mg/dl 0.18 mg/dl; $p=0.26$]. *Conclusion:* In selected cases, KSS seems to be a safe and effective surgical option for the treatment of UTUC compared to RCN, providing better CSS and OS outcomes, with concomitant sparing of renal function. Age at time of diagnosis and pathological stage are the main determinants for both OS and CSS. Further studies are needed to better understand the strengths and limits of this investigational procedure.

67

EFFICACY AND SAFETY OF SUNITINIB AND EVEROLIMUS AS FRONTLINE TREATMENT FOR NON-CC-RCC: A POOLED-ANALYSIS FROM RANDOMIZED TRIALS

Carlo Messina[1], Marco Messina[2], Carlo Cattrini[1], Luigi Cerbone[1], Giuseppe Mastrocinque[3], Elisa Zanardi[1] and Pietro Spatafora[4]

[1]Academic Unit of Medical Oncology, San Martino Polyclinic Hospital, Institute for Cancer Research and Treatment, Genoa, Italy; [2]Medical Oncology, Hospital S. Raffaele G. Giglio, Cefalu, Italy; [3]Department of Urology, OUC Urologia, Ospedali Riuniti di Padova Sud, Euganea, Italy; [4]Department of Urology, Minimally Invasive and Robotic Surgery, and Kidney Transplantation, University of Florence AOUC- Careggi Hospital, Florence, Italy

Background/Aim: Non-clear renal cell carcinoma (non-ccRCCs) account for about 25% of all RCC and represent a heterogeneous group of neoplasms, including papillary (10-15%), chromophobe (5-10%), oncocytic (3-7%), collecting duct (Bellini's duct, <1%), and unclassified tumours (< 5%), which are generally associated with a poorer outcome in metastatic setting. Previous studies have reported that these tumours show more aggressive behaviour and worse prognosis compared with ccRCCs; however, another report have reported no difference in clinical outcome after adjusting for poor clinic-pathological features such as stage and tumor grading. An optimal treatment for patients with metastatic non-ccRCC has not been established yet. Most of the pivotal trials that led to the approval of targeted therapies in metastatic ccRCC, excluded patients with non-ccRCC histology; hence, available data are mainly based on expanded access programs and single-arm phase II trials. The optimum treatment for patients with metastatic non-ccRCC has not been established yet; therefore, sunitinib and everolimus still represent two feasible options as frontline therapy, given the results reported from single-arm trials and expanded access studies. Hence, we provided a pooled analysis from prospective randomized trials to evaluate the benefit and risks of these therapies for patients with metastatic non-ccRCC. *Materials and Methods:* The study design was a quantitative synthesis of randomized trials aiming to evaluate the efficacy and safety of sunitinib *versus* everolimus as frontline treatment for metastatic non-ccRCC. A literature search using PubMed, Embase was carried out with no date restriction up to June 2017. The search strategy included the keywords "renal cell carcinoma", "non-clear-renal cell carcinoma", "papillary RCC", "chromophobe RCC", "oncocytic RCC", "renal collecting duct tumor", "sunitinib", and "everolimus". A computerized search of the abstracts reported in the ASCO and ESMO libraries was performed in order to identify other relevant data. Specific keywords for each database and free text terms were combined with Boolean operators. Two reviewers screened all full-text articles and abstracts independently. A third author (CC) reviewed the search results to apply the eligibility criteria to both sets of search outcomes and acted as an arbiter in case of disagreement between the two reviewers. Finally, a cross-check of references from review articles and relevant studies on the same topic was performed to confirm retrieval of all possible pertinent trials. Eligible studies had to fulfill the following criteria: randomized prospective trial comparing the efficacy of sunitninb and everolimus as first-line therapy in patients with metastatic non-ccRCC. Studies excluded: non-randomized prospective trials, subgroup analysis data deriving from randomized prospective trials carried out on metastatic ccRCC population. No language restriction was applied. Data were pooled using RevMan 5.3 software. *Results:* The literature search identified

29 potential titles and abstracts of whom only 2, recruiting a total of 176 metastatic-non ccRCC patients (sunitinib: 84, everolimus: 92), fulfilled our eligible criteria and were included in the pooled analysis. Disease progression occurred in 68 (81%) of the 84 sunitinib-treated patients and in 77 (83.7%) of the 92 patients who received everolimus. No statistically significant difference in terms of pooled PFS results between the two arms was observed (OR=0.83, 95% CI=0.38-1.78), although significant heterogeneity between the two studies was observed (I2=71%). A total of 40 deaths occurred in 84 patients (47.6%) treated with sunitinib and 53 in the 92 patients (57.6%) who received everolimus. The pooled OR was 0.67 (95% CI=0.37-1.21), indicating a trend towards a lower probability of death among patients with metastatic non-ccRCC who received sunitinib compared with those who received everolimus. No significant heterogeneity between the two studies was observed (I^2=0%). Moreover, sunitinib was associated with more Grade 3-4 adverse events (HR=3.06, 95% CI=1.60-5.84), compared to everolimus. *Conclusion:* This pooled analysis suggests slightly better outcomes for sunitinib *versus* everolimus in terms of PFS and OS, even if no statistically significant differences were observed. However, treatment with sunitinib was associated with more relevant G3-G4 AEs. Given the rarity and large heterogeneity of RCC subtypes, differences in outcomes, and response to targeted therapies, we believe that patients with metastatic non-ccRCC should be encouraged to be enrolled in clinical trials. An individual participant data meta-analysis is warranted to better assess the impact of RCC subtype heterogeneity on outcome after treatment with sunitinib and everolimus.

68

WHAT IS BEHIND INTRAOPERATIVE FOCAL MARGINS DURING ROBOT-ASSISTED RADICAL PROSTATECTOMY: THE EXPERIENCE OF A HIGH VOLUME THIRD REFERRAL CENTER

Francesco Alessandro Mistretta[1], Ettore Di Trapani[1], Roberto Bianchi[1], Andrea Conti[1], Andrea Russo[1], Stefano Luzzago[1], Gabriele Cozzi[1], Maurizio Delor[1], Alessandro Serino[1], Matteo Ferro[1], Gennaro Musi[1], Deliu Victor Matei[1], Giuseppe Renne[2] and Ottavio De Cobelli[1]

[1]Division of Urology, European Institute of Oncology - IEO, Milan, Italy; [2]Division of Pathology, European Institute of Oncology – IEO, Milan, Italy

Background/Aim: The aim of the study was to assess the rate of intraoperative focal positive margins (IFPM) during robot-assisted prostatectomy (RARP) and to determine potential predictors of biochemical relapse (BCR) in case of IFPM. *Materials and Methods:* From January 2014 to April 2017, a total of 1,788 consecutive patients were subjected to RARP for prostate cancer, 98% underwent a preliminary mpMRI. Tissue sections from all patients were received to determine possible positive surgical margins (PSMs), and focal margins were assessed if <1mm. All data were prospectively collected in a customized database and retrospectively analysed. Univariable analysis (UVA) was used to identify potential predictors of BCR in case of IPFM. *Results:* Out of all patients subjected to mpMRI and RARP, in 195 (11.1%) a PSM was determined, and among them in 53 (27.2%) IPFM was assessed. Preoperative median prostate-specific antigen (PSA) was 8.98 ng/ml [interquartile range (IQR)=5.91-13.18]. Gleason Score (GS) was 3+3 in 20 patients (37.7%), 3+4 in 13 (24.5%), 4+3 in 8 (15.1%) and >4+4 in 12 (22.7%) patients. Clinical stage was T1 in 21 (39.6%) patients, T2 in 24 (45.3%) and T3 in 8 (15.1%). Index lesion (PI-RADS) was <3 in 9 (17%) patients, 4 in 14 (26.4%) and 5 in 30 (56.6%). Nerve-sparing was executed in 46 (86.8%) patients, 78.3% bilateral and 21.7% monolateral. All IPFM were selectively resected in 22 (41.5%) of patients and the bundle resection resulted negative for PCa in 17 (77.3% out of 22). At final pathology, all margins were confirmed as positive and 37 (69.8%) confirmed as focal. After a median follow-up of 22 months (range=15-27), a BCR occurred in 5 (9.4%) patients. At UVA, cT3 and GS 7 were significant predictors for BCR (p<0.01). Preoperative PSA did not correlate with BCR in presence of IPFM. Moreover, selective resection of the bundle appeared to be protective against BCR (p=0.004). *Conclusion:* Our results demonstrated that the introduction of the mpMRI in the preoperative workout and intraoperative histological analysis had lowered the rate of definitive PSMs if compared with data present in literature. In our series IPFMs represented more than a quarter of PSMs and were described as not free from BCR even in a short-term follow-up. Although, worse preoperative oncological outcomes correlated with BCR, selective resection in case of IPFM was described preventive of biochemical relapse.

69

OLIGOMETASTATIC PROSTATE CANCER: THE IMPORTANCE OF A MULTIDISCIPLINARY APPROACH IN A HIGH VOLUME ROBOTIC CENTER

Andrea Conti, Michele Catellani, Maurizio Delor, Stefano Luzzago, Francesco Alessandro Mistretta, Alessandro Serino, Roberto Bianchi, Gabriele Cozzi, Andrea Russo, Ettore Di Trapani, Matteo Ferro, Gennaro Musi, Deliu Victor Matei and Ottavio De Cobelli

Division of Urology, European Institute of Oncology - IEO, Milan, Italy

Background/Aim: Oligometastatic prostate cancer (OmPCa) is now being diagnosed more frequently thanks to the improvements in diagnostic modalities. Retrospective studies suggest that primary treatment, such as open radical prostatectomy and local or metastasis-directed radiotherapy (RT), can be performed in the metastatic setting with minimal risk of toxic effects. Our study aimed at assessing peri-operative oncologic and functional outcomes of robot assisted radical prostatectomy (RARP) in oligometastatic disease. *Materials and Methods:* We prospectively collected and retrospectively analyzed data on patients affected by OpCa. Oligometastatic disease was defined as the presence of ≤5 bone lesions whit or without suspicious pelvic or retroperitoneal nodal involvement at preoperative imaging. Perioperative surgical outcomes, clinical progression, castration-resistance status (CRPCa) and cancer-specific mortality were evaluated. *Results:* From January 2010 to December 2016, 34 patients with OmPCa underwent RARP with extended lymph nodes (LN) dissection. Median age at surgery was 66 years (range=58-68) with a median BMI of 26 (range=24.8-27.75). Thirteen (38%), 14 (42%), and 7 (20%) patients presented LN, bone or both site of metastases at diagnosis, respectively. Three (9%) patients started androgen deprivation therapy (ADT) before surgery. Median operative time, blood loss, and length of stay were 240 min (range=197-285), 200 ml (range=100-300), and 2.5 days (range=2-5), respectively. No hematic transfusions were performed. In 11 cases a monolateral nerve sparing procedure was performed. Catheter was removed in 5 post-operative day in 27 (79,4%) patients. Overall, 1 and 2 Clavien-Dindo grade II and III complication were recorded, respectively. Five patients (6%) were readmitted to hospital because of a symptomatic lymphocele and were treated with percutaneous drainage. Median number of LN removed was 17.5 (range=11.25-26.75). At pathological evaluation 7 (20.5%), 5 (14.5%), and 22 (65%) ISUP grade group 3, 4, and 5 were found, respectively. Twenty-eight (82%) and 14 (40%) patients had LN invasion and positive surgical margins, respectively. Adjuvant ADT was administered to 29 (85%) patients after surgery and 17 (50%) underwent adjuvant RT. Median follow-up time was 29 months (range=19.75-48.5). At 1-year evaluation, 82% of patients were continent (0-1 pads), 15% have mild incontinence (2-3 pads), and only 3% developed complete incontinence (>4 pads). Potency was not analyzed due to the high rate of ADT. Overall, 18 (53%) patients developed clinical progression with a median time of 19 months (range=12.75-33). Five (15%) patients developed CRPCa with a median time of 37 months (range=18-57) No patients died because of PCa. *Conclusion:* RARP is a safe and efficacious procedure with good functional outcome for OmPCa. A multimodal approach represents a feasible treatment in selected men and provides acceptable oncologic outcomes.

70

"GIVE ME FIVE" ULTRA HYPOFRACTIONATED RADIOTHERAPY (RT) FOR LOCALIZED PROSTATE CANCER (PCA): SAFETY WITHOUT LOSING EFFICACY

Giulia Marvaso[1], Giulia Riva[2], Delia Ciardo[1], Sara Gandini[3], Cristiana Fodor[1], Dario Zerini[1], Stefania Comi[4], Federica Cattani[4], Ottavio De Cobelli[5], Roberto Orecchia[6] and Barbara A. Jereczek-Fossa[7]

[1]Radiotherapy, European Institute of Oncology, Milan, Italy;
[2]Radiotherapy, European Institute of Oncology Milan, Italy;
[3]Division of Epidemiology and Biostatistics, European Institute of Oncology, Milan, Italy;
[4]Medical Physics Unit, European Institute of Oncology, Milan, Italy;
[5]Department of Urology, European Institute of Oncology, Milan, Italy;
[6]Scientific Direction, European Institute of Oncology, Milan, Italy;
[7]Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy

Background/Aim: Ultra-hypofractionated radiotherapy (RT) is given over a shorter time with larger doses per treatment in patients with localized prostate cancer (PCa). The use of hypofractionation is supported both from the radiobiological point of view (the low a/b-ratio in PCa and dose escalation) and from the rising number of clinical evidences. The aim of this study was to review our data regarding oncological outcomes (biochemical progression-free survival and progression-free survival), acute and long-term toxicities in patients treated with a short course of RT (ultra-hypofractionation). *Patients and Methods:* A series of 194 patients with clinically localized PCa treated primarily with ultra-hypofractionated RT using image-guided intensity-modulated radiation therapy (IG-IMRT), in our Institute from 2012 to 2015, were included in this analysis. Patients according to NCCN risk group classification were low-risk 65 (33.5 %), intermediate-risk 101 (52.1%), and high-risk 25 (14.4%). Androgen deprivation therapy (ADT) was given to 81 patients (41.7 %). A total of 169 patients (87%) received a dose of 35 Gy in 5 fractions, while for 25 patients (13%) the dose level was 32.25 Gy. The median duration of the treatment was 10 days [interquartile range (IQR)=9-12]. Biochemical relapse free survival (b-PFS) was defined as a rise of prostate-specific antigen (PSA) >2 ng/ml above nadir. b-PFS as well as clinical progression free survival, freedom from gastrointestinal (GI) toxicity and from genitourinary (GU) toxicity curves were calculated by the Kaplan-Meier method. Log-rank test and multivariate Cox models were used to investigate the role of RT dose and heterogeneity in NCCN risk groups adjusting for prognostic factors. Data on acute-

and late-term toxicities were collected according to RTOG/EORTC grading system. *Results:* With a median follow-up of 30 months (2.5 years), there were 17 patients who experienced PSA failure (9%). The 3-year biochemical free survival rate was 87% for all patients, rates stratified for the NCCN risk were: 94%, 82% and 66% for low-, median-, and high-risk groups, respectively. Log-rank tests indicated that biochemical progression was significantly greater for patients with initial PSA (iPSA) >7 ng/ml (p=0.04), high- and intermediate- risk groups (p=0.002), low total dose (p=0.02) and Gleason score (GS) ≥7 (p=0.04). No significant association was found with T stage or ADT. In multivariate analyses total dose (p=0.03) and risk groups (p=0.03) remained significantly associated with recurrence. Acute and late GI and GU toxicity were acceptable. *Conclusion:* The toxicity of ultra-hypofractionated IG-IMRT in a large clinical cohort of PCa patients were tolerable and confirmed that this treatment is safe and offers excellent tumor control. Moreover, the hypofractionated RT allows to deliver the whole RT over 10 days with a sensible impact in patients' quality of life and potential overall health system and social benefits.

71

IN-BORE MAGNETIC RESONANCE (MPMRI)-GUIDED BIOPSIES REPRESENT THE FUTURE OF PROSTATE CANCER DIAGNOSIS? A SINGLE CENTER EXPERIENCE AND IMPLICATIONS FOR FOCAL THERAPY

Stefano Luzzago[1], Michele Catellani[1], Francesco Alessandro Mistretta[1], Andrea Conti[1], Giuseppe Petralia[2], Andrea Russo[1], Ettore Di Trapani[1], Maurizio Delor[1], Antonio Brescia[1], Gennaro Musi[1], Deliu Victor Matei[1] and Ottavio De Cobelli[1]

[1]Division of Urology, IEO European Institute of Oncology, Milan, Italy; [2]Division of Radiology, IEO European Institute of Oncology, Milan, Italy

Background/Aim: Target biopsies have emerged as a useful tool for prostate cancer (PCa) detection. In-bore magnetic resonance (mpMRI)-guided technique represents an innovative method to better achieve an accurate evaluation of mpMRI index lesion (IL). We reported a single center experience and analyzed clinical management according to biopsies results. *Patients and Methods:* From 2015 to 2017, 334 patients were submitted to mpMRI-guided biopsies. All procedures were performed by two expert mpMRI radiologists (G.P. and S.A.) with seven and five years' experience, respectively. All biopsy procedures were performed on a 1.5T MR scanner (Magnetom Avanto, Siemens Healthineers, Erlangen, Germany) using a commercially available transrectal biopsy device (DynaTRIM, Invivo, Gainesville, FL, USA). After calibration of the biopsy device the first sample was obtained using the coordinates provided by the device software to guide the needle along a trajectory to the IL lesion. The trajectory of subsequent samples was manually adjusted to improve localization to the target. Logistic regression analyses tested independent predictors of PCa and clinically significant PCa (csPCa: GSO7) detection at biopsies. Moreover, for patients treated at our center, we analyzed the concordance rate between biopsy and pathological Gleason score (GS). Logistic regression analyses were used to find independent predictors of GS discordance. *Results:* Two-hundred-fifty (75%) and 84 (25%) biopsies were performed for PCa detection and during Active Surveillance (AS), respectively. Reported IL PI-RADS score was highly suspicious of cancer (*i.e.* PI-RADS>4) in 209 (62.5%) men. Overall, 138 (41.5%) and 33 (10%) patients had >1 lesion and more than one lesion highly suspicious for PCa at mpMRI, respectively. Median (IQR) number of cores performed was 4 (3-6). Overall, 187 (56%) and 112 (33.5%) biopsies were positive for PCa and for csPCa, respectively. At multivariable (MVA) analyses, PSA-density (OR=1.3; p=0.048), total number of cores taken (OR=2.1; p=0.002), cT stage (cT2 *vs.* cT1; OR=4.7; p=0.07), high IL PI- RADS score (OR=5.2; p<0.001) and previous negative biopsies (OR=0.8; p=0.05) were independent predictors of cancer findings. Moreover, age (OR=1.08; p=0.01), total cores taken (OR=1.5; p=0.04) and high IL PI-RADS (OR=2.9; p<0.01) were predictors of a csPCa disease. Active management and AS were then recommended in 155 (46.4%) and 38 (11%) cases. Seventy-three (47%) patients were submitted to radical prostatectomy (RP) at our institution. Interestingly, in 33 (45%) patients a GS change was observed between biopsy and RP-specimen. These figures resulted in 24 (33%) risk-group changes (75% of them from low to intermediate-risk D'Amico group). At MVA logistic regression analyses, a high number of lesions (OR=2.3; p=0.02) and high secondary lesion PI-RADS score (OR=1.2; p=0.05) at mpMRI were independent predictors of GS variation. Finally, the number of lesions (OR=1.1; p=0.05) and the IL PI-RADS score (OR=4.4; p=0.03) were associated with D'Amico risk group changes. *Conclusion:* In bore mpMRI-guided biopsies represent an accurate method to study the IL aggressiveness. However, clinical parameters and mpMRI findings should be taken into account before deciding clinical management of these patients.

72

STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR BONE OLIGOMETASTATIC CASTRATION-SENSITIVE RECURRENT PROSTATE CANCER (MCSPC): SERIES OF 55 PATIENTS

Giuseppe Fanetti[1], Giulia Marvaso[1], Annaisabel Rese[2], Sabrina Vigorito[3], Floriana Pansini[3], Federica Cattani[3], Dario Zerini[1], Rosalinda Ricotti[1], Cristiana Fodor[1], Ottavio De Cobelli[4], Roberto Orecchia[5] and Barbara A. Jereczek-Fossa[6]

[1]Radiotherapy, European Institute of Oncology, Milan, Italy; [2]Department of Radiation Oncology, A.O.U. Federico II, Naples, Italy; [3]Medical Physics Unit, European Institute of Oncology, Milan, Italy; [4]Urology Department, European Institute of Oncology, Milan, Italy; [5]Scientific Directorate, European Institute of Oncology, Milan, Italy; [6]Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy

Background/Aim: To evaluate outcome in patients treated with SBRT with or without androgen deprivation therapy (ADT) on bone oligorecurrences (BM) from mCPSC after primary treatment (RT or surgery). *Materials and Methods:* We retrospectively collected data of patients treated on BM from mCPSC with SBRT between 03/2012 and 11/2016. Inclusion criteria were: <3 lesions at time of SBRT detected with positron emission tomography/computer tomography (PET/CT), magnetic resonance imaging (MRI) and CT, hormone-naïve disease at first extra-regional localization, no evidence of local recurrence. PSA was measured every 3 months after SBRT. Biochemical response was evaluated with PSA level variation (ΔPSA) between pre-SBRT and post-SBRT: biochemical response (BCR) as ΔPSA lower than -20%, progression (BCP) for ΔPSA>+20% and stability (BCS) –20%<ΔPSA<+20%. Imaging was performed in case of BCP. Biochemical and clinical progression- free survival (PFS) as well as in field recurrence curves were elaborated with log-rank test. *Results:* Fifty-five patients were treated on 77 BM. Median age, initial PSA (iPSA) and pre-SBRT PSA score were 72 years, 9.12 ng/ml and 3.5 ng/ml, respectively. Initial NCCN class risk was low, intermediate and high in 2, 12 and 41 patients, respectively. Median dose was 24 Gy/3 fractions. All patients received Image Guided RT. In 30 (55%) patients, ADT was added to SBRT. Median follow-up was 17.6 months. No acute or late toxicity was reported. BCR, BCS and BCP were observed in 38 (69%), 5 (9%) and 12 (22%), respectively. Clinical progression was observed in 30 (55%) patients after a median time of 7.24 months. In-field progression occurred in 8 (15%) patients. One-year biochemical, clinical and in-field PFS (b-, c-, and if-PFS) rates were 52%, 55% and 89%, respectively. b-PFS was significantly lower in patients treated with SBRT alone (p=0.0246). On the contrary, c-PFS was similar. In those patients, ADT was started after a median time of 4.5 months (range=2.3-34.5). At the time of analysis 14 (25%) patients were alive with no evident disease, 36 (65%) alive with disease, 3 (5%) patients deceased of disease and 2 (5%) deceased of other causes. *Conclusion:* SBRT is safe and allows high local control rate (85%). One out of two patients is free of biochemical progression at one year after SBRT. Addition of ADT to SBRT improved b-PFS but not c-PFS. Further investigation is warranted to identify patients that could benefit most from this treatment modality and the optimal combination with androgen deprivation or other systemic treatments.

73
DOSE TEAM: A NEW SETTING OF MULTIDISCIPLINARY WORKING TO EXPLORE AND PROMOTE

Lidia Strigari[1], Luca Bertini[2], Vicente Bruzzaniti[1], Antonino Guerrisi[3], Sara Ungania[2] and Stefano Canitanio[2]

[1]Division of Medical Physics, IRCCS Istituto Nazionale Tumori Regina Elena, Rome, Italy; [2]Division of Radiology, IRCCS Istituto Nazionale Tumori Regina Elena, Rome, Italy; [3]Division of Radiology, Istituto Santa Maria E San Gallicano, Rome, Italy

Multidisciplinary teams (MDTs) are an alliance of all medical and health care professionals involved in the path of care for a specific tumor and are internationally considered as the best setting to approach and manage oncologic patients. As a result, MDT meetings are integral to the delivery of optimal cancer care, with professionals participating in ways that may differ according to the cancer site and the state of the disease. However, besides the well acknowledged role in oncologic care, it is high time the scientific community should evaluate a new declination of MDTs: the Dose Team (1). The Dose Team is a multiprofessional setting that should be implemented in every health care setting (oncologic and non-oncologic) in which a radiologist, a radiation oncologist, a physician expert in nuclear medicine, an interventional radiologist, a medical physicist and a radiological technician (Figure 1) collaborate to optimize the radiologic and radiotherapeutic procedures and techniques of the clinical path whenever ionizing radiation is delivered to patients and the performance of the radiologic and radiotherapeutic equipment (2). The importance of the Dose Team derives from the need to pay attention to crucial aspects of radiology and radiation oncology, namely the increased use of imaging in all aspects of high-quality cancer care, from diagnosis through treatment and follow-up, the radiological protection of both patients and personnel working in imaging facilities, the demand for hyper-specialization in oncologic imaging

and, as the consequence, the importance of improving sub-specialization potentially ensuring care in the dose delivery in all settings and in all diseases (2-4).

The Dose Team is shown in (Figure 2):

- Identifying the quality levels of the images as per the different phases of the procedure, monitoring doses delivered to patients in the commissioning phase and at each change in techniques, materials and procedures;
- Organizing the radiology rooms with respect to the evaluation of technical and logistic requirements necessary for the procedure and the radioprotection of professionals and patients;
- Collaborating with the companies supplying the technological equipment in the commissioning and set up phases;
- Monitoring doses delivered to patients during the procedure;
- Exploring and analyzing procedure steps;
- Introducing changes aimed to optimize procedures and techniques and to adapt technique to individual patient;
- Organizing educational events and refresh courses for personnel working in the Radiological Area on radioprotection-related issues and new procedures and techniques;
- Checking on patient information sheets and informed consents.

In addition, the Dose Team should be involved in educational and teaching programs of radiologists, radiation oncologists, medical physicists, nuclear medicine physicians, radiologic and radiation oncologic technologists, nurses working in imaging facilities on core aspects of radiology, dosimetry and radioprotection. A Teach the Teacher approach should be implemented to deliver information, know-how and expertise to other health care settings where the Dose Team is not implemented (2-4).

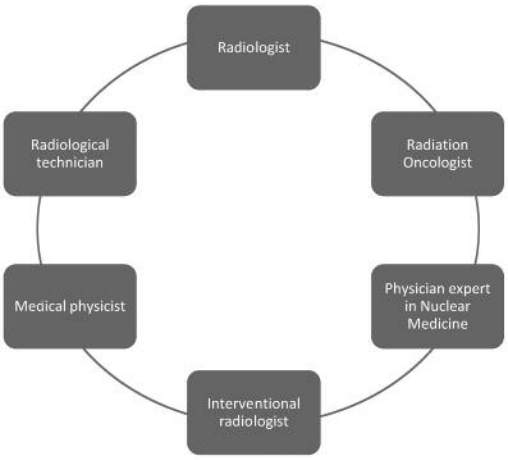


Figure 1. *Professionals participating in the Dose Team.*

The Dose Team should have a leader identified in the Radiological Areas, meet on a regular basis (frequency depending on the case load of the Imaging and Radiotherapy Department), receive the agenda of the meeting beforehand, write minutes of the meeting and, in case any change should be introduced or any decision taken on a specific point, produce a report. It is very important that the Dose Team should benefit from administrative support in the organization of meetings and circulation of documents. The Dose Team should illustrate the state of the art, the results of study on dosimetric and image quality, as well as the mandatory technical improvements to stakeholders including the strategic directors of the Institutes/Hospitals (2-4).

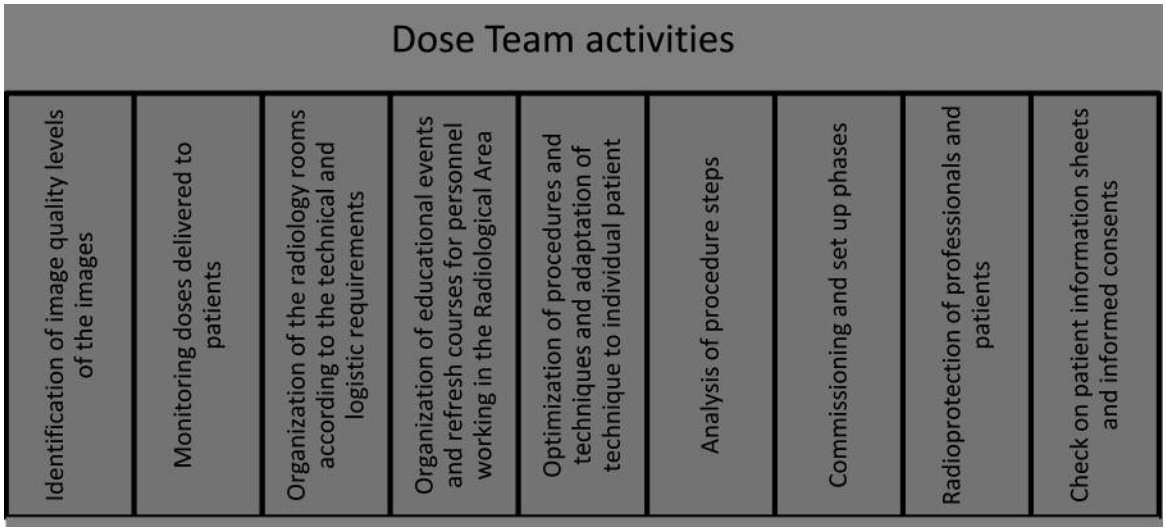


Figure 2. *Dose Team activities.*

Considering the novelty of the Dose Team in the health care settings, professional societies should promote their establishment and formalization, facilitate the exchange of experience between the Dose Teams, monitor their activity and periodically assess their results. In parallel, besides this top down approach, it is important to present this new multidisciplinary and multiprofessional setting in scientific meetings and happenings to raise awareness in the oncologic community.

1 European Partnership Action Against Cancer Consensus Group: Policy statement on multidisciplinary cancer care. Eur J Cancer *50*: 475-480, 2014.
2 Gruppo di Studio per l'Assicurazione di Qualità in Radiologia Interventistica, Istituto Superiore di Sanità: Indicazioni operative per l'ottimizzazione della radioprotezione nelle procedure di radiologia interventistica. Rapporti ISTISAN 15/41 IISN 2384-8939.
3 Schlemmer HP, Bittencourt LK, D'Anastasi M, Domingues R, Khong PL, Lockhat Z, Muellner A, Reiser MF, Schilsky RL and Hricak H: Global challenges for cancer imaging. J Global Oncol, 2017. doi: 10.1200/JGO.17.00036.
4 Balasubramaniam R, Subesinghe M and Smith JT: The proliferation of multidisciplinary team meetings (MDTMs): how can radiology departments continue to support them all? Eur Radiol *25*: 3679-3684, 2015.

74
SAFETY AND EFFICACY OF ABIRATERONE IN ELDERLY PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER: MULTICENTRIC REAL-LIFE EXPERIENCE

Zuzana Sirotovà[1], Giulia Courthod[2], Alfredo Tartarone[3], Orazio Caffo[4], Francesca Maines[4], Veronica Prati[5], Maurizio Bertuccelli[6], Alessandra Mosca[7], Giuseppe Fornarini[8], Pamela Guglielmini[9], Franco Morelli[10], Erica Palesandro[11], Cinzia Ortega[12], Stefania Miraglia[13], Valentina Perrone[14], Gianmauro Numico[9], Giacomo Allegrini[15], Michele Aieta[3] and Marina Schena[1]

[1]Oncology and Oncohematology, Regional Hospital Parini Aosta, Aosta, Italy; [2]Oncology, Regional Hospital Parini Aosta, Aosta, Italy; [3]Oncology, IRCCS Referall Cancer Center of Basilicata, Rionero In Vulture, Potenza, Italy; [4]Oncology, Santa Chiara Hospital, Trento, Italy; [5]Oncology, ASLCN2 Alba-Bra, Alba, Italy; [6]Oncology, General Hospital Livorno, Livorno, Italy; [7]Oncology, Maggiore Della Carita University Hospital, Novara, Italy; [8]Oncology, San Martino Hospital Genova, Genoa, Italy; [9]Oncology, SS Antonio E Biagio General Hospital, Alessandria, Italy; [10]Oncology, IRCCS Casa Sollievo Della Sofferenza, San Giovanni Rotondo, Foggia, Italy; [11]Oncology, IRCCS Candiolo, Candiolo, Turin, Italy; [12]Oncology, ASLCN2 Alba-Bra, Bra, Italy; [13]Oncology, Hospital Martini, Turin, Italy; [14]Oncology, Maggiore Della Carita University Hospital Novara, Novara, Italy; [15]Medical Oncology, General Hospital Livorno, Livorno, Italy

Background/Aim: Metastatic castration resistant prostate cancer (mCRPC) is diagnosed mainly in elderly patients that are usually frail and affected by different comorbidities that can negatively influence the outcome of any mCRPC treatment. Until a decade ago the only treatment option for mCRPC was chemotherapy. Since the elderly patients usually experienced more toxic effects of chemotherapy compared with those reported by the younger ones, they often had to discontinue the treatment due to toxicity or, in many cases, they received only the best supportive care. Abiraterone acetate (AA) is a selective androgen biosynthesis inhibitor that showed the efficacy in either chemotherapy-naive patients or those pre-treated with docetaxel. Its oral administration and good tolerability make it a manageable treatment option for elderly mCRPC patients. *Patients and Methods:* In this retrospective study, data from 252 mCRPC patients treated with AA in 13 Italian Centers since April 2013 were collected. Patient age was >75 years (median=79, range=75-90) and 48% of patients were octagerians. One third of the patients (32%) had oligometastatic disease while 68% presented with more than 5 lesions, and nearly 50% had involvement of two or more metastatic sites (Table I). There was equal distribution of patients with exclusively bony metastases between pre and post-docetaxel patients. In post-docetaxel group there were 9% of patients with liver metastases while in pre-docetaxel group it was only 2%. There was no significant difference in Gleason score between pre and post-docetaxel patients. Post-docetaxel patients had higher baseline PSA and EGOG PS and lower hemoglobin levels. Nearly all the patients showed comorbidities (Table II), the most frequent being hypertension (58%), cardiac comorbidities (30%), and diabetes type II (17%). All the patients took one or more medications for their comorbidities. Before they started the AA treatment all the patients underwent EKG and cardiac ecography with cardiological counselling when necessary. We considered duration of the AA treatment, overall response rate (ORR), 50% PSA decline, time to progression (TTP), overall survival (OS) and the observed toxicities. All patients signed informed consent for data collection. *Results:* A total of 252 patients, 147 pre-treated with docetaxel and 105 chemo naive, were included.

Table I. *Clinical characteristics of the patients*.

	All (n=252)	Pre-CT (n=105)	Post-CT (n=147)
Gleason score			
<7	30 (11.9%)	17 (16.1%)	13 (8.8%)
7	81 (32.1%)	28 (26.6%)	53 (36%)
>7	111 (44%)	48 (45.7%)	63 (42.8%)
NA	30 (11.9%)	12 (11.4%)	18 (12.4%)
ECOG			
0-1	177 (70.2%)	73 (69.5%)	104 (70.7%)
2	75 (29.8%)	35 (30.5%)	40 (29.3%)
Metastatic lesions			
<5	82 (32.5%)	44 (42%)	38 (25.9%)
>5	166 (65.8%)	58 (55.2%)	108 (73.5%)
Metastatic sites			
Only bone	105 (41.6%)	47 (44.8%)	58 (39.5%)
Only nodes	25 (9.9%)	14 (13.3%)	11 (7.5%)
HBG level			
>12	166 (65.8%)	75 (71.4%)	91 (61.9%)
<12	77 (30.5%)	25 (23.8%)	52 (35.4%)

CT, Chemotherapy treatment; ECOG, Eastern Cooperative Oncology Group; HBG.

Table II. *Comorbidities*.

Comorbidities	All	Pre-CT	Post-CT
Hypertension	58%	53%	61%
Cardiac	30%	25%	32%
Vascular	18%	16%	19%
Diabetes	17%	14%	19%
Renal	14%	13%	14%
Gastrointestinal	10%	9%	11%

CT, Chemotherapy treatment.

Table III. *Response rate*.

Best response	All (n=216)	Pre-CT (n=99)	Post-CT (n=117)
ORR (CR+PR)	67 (31%)	35 (35.4%)	32 (27.4%)
Disease control (CR+PR+SD)	155 (71.8%)	65 (65.7%)	90 (77%)

CT, Chemotherapy treatment; ORR, overall response rate.

Table IV. *Toxicities*.

Toxicities	All patients G1-G2	All patients >G3	Pre-CT G1-G2	Pre-CT >G3	Post-CT G1-G2	Post-CT >G3
Anemia	78 (30.9%)	1 (0.4%)	15 (14.2%)	0	63 (42.8%)	1 (0.7%)
Fatigue	93 (36.9%)	5 (2%)	24 (22.8%)	1 (0.9%)	69 (46.9%)	4 (2.7%)
Dyspnea	17 (6.7%)	0	4 (3.8%)	0	13 (8.8%)	0
Hypertension	27 (10.7%)	1 (0.4%)	15 (14.2%)	0	13 (8.8%)	1 (0.7%)
Cardiac failure	7 (2.7%)	2 (0.8%)	1 (0.9%)	1 (0.9%)	6 (4%)	1 (0.7%)
Hepatic tox	21 (8.3%)	4 (1.6%)	5 (4.7%)	2 (2%)	16 (10.8%)	2 (1.4%)
Edema	22 (8.7%)	0	7 (6.6%)	0	15 (10.2%)	0

CT, Chemotherapy treatment.

Median duration of hormonal treatment before castration resistance was 47 months (range=7-152 months). In post-chemotherapy treatment (post-CT) group the median number of docetaxel cycles was 6 (range=1-23 cycles). Median duration of treatment with AA was 8.6 months in post-CT and 11.5 in CT naive patients. ORR was 35.3% in pre-docetaxel and 27.4% in post-docetaxel group (Table III). PSA reduction (50%) was observed in 64 (65%) and 51 (46%) patients, the in pre- and post-docetaxel group, respectively. Median TTP was 8.6 in post-docetaxel and 11.9 in CT naive patients. mOS was 13.8 months in post-CT group, while for CT naive patients data were not mature. AA was well tolerated. Only 8 (3.2%) patients discontinued treatment due to toxicity, while in 4 (1.6%) temporary dose reductions were performed. In one patient the treatment was interrupted after four months and with PSA in complete response because of accidental death. The most frequent G3 toxicities were hypertension and liver toxicity in 4 patients (1.6%) and 5 patients (2%), respectively (Table IV). We observed WHO grade 3 hyperglycemia in 3 patients (1.2%), however it did not occur in patients previously scheduled for diabetes. We reported less than 1% of WHO grade 3 cardiac failure. After progressing on AA, 85 patients (34%) received at least one additional treatment. 40 patients (15.9%) are still on treatment. *Discussion and Conclusion:* Optimising therapy of mCRPC in elderly patients is mandatory as nowadays the median age of men is increasing and many comorbidities can be controlled and cured. However, these patients remain frail showing lower tolerance for side effects of a variety of treatments. Recently some other treatment options for

mCRPC became available like enzalutamide and alpharadin. These drugs as well as AA are of great interest because of their favourable safety profile and efficacy in prolonging overall survival. Recently published data from randomised studies STAMPEDE and LATITUDE suggest that AA is able to increase survival also when given in earlier stages of prostate cancer, either in castration sensitive high-risk non-metastatic or in metastatic castration sensitive high burden disease, respectively. As some of these findings could be brought soon into the clinical practice, it is supposed that the number of elderly patients eligible for AA treatment could increase. Consequently, it is mandatory to choose drugs with good safety profile that will ensure compliance to treatment, which, in case of AA, is usually of long duration. As suggested by our data, in elderly patients, good tolerability of AA leads to excellent compliance to treatment. We reported outcome of AA treatment in 252 elderly mCRPC patients, in 13 Italian centers. Even if almost all the patients reported numerous comorbidities and 30% of them had PS ECOG 2, nearly all of the patients were able to complete the treatment with AA without its premature withdrawal due to toxicity. Only few patients required a temporary dose reduction. According to our experience we can affirm that AA is well-tolerated and efficient treatment also in elderly patients.

75
THE INTRODUCTION OF A SURGICAL CHECKLIST FOR THE TRANSURETHRAL RESECTION OF THE BLADDER IMPROVES RECURRENCE-FREE SURVIVAL IN NON-MUSCLE INVASIVE BLADDER CANCER PATIENTS

Francesco Soria[1], David D'Andrea[1], Mirko Preto[2], Kilian M. Gust[1], Alberto Briganti[3], Shahrokh F. Shariat[1] and Paolo Gontero[2]

[1]Department of Urology and Comprehensive Cancer Center, Medical University of Vienna, Vienna General Hospital, Turin, Italy;
[2]Division of Urology, AOU Città Della Salute E Della Scienza Di Torino, Presidio Molinette, Turin, Italy;
[3]Department of Urology, Urological Research Institute, Vita-Salute University, San Raffaele Scientific Institute, Milan, Italy

Background/Aim: More than half of patients with non-muscle invasive bladder cancer (NMIBC) will experience an intravesical recurrence, requiring additional treatment and its resulting morbidity, decreasing quality of life and increasing healthcare costs. The quality of surgical resection is essential in the management of bladder cancer (BC) patients and may have a significant impact on the risk of intravesical recurrence. To standardize the procedure and to improve surgical outcomes, the introduction of a surgical checklist (SC) has been proposed. Moreover, the SC improves operative reporting, which can be considered a proxy of surgical quality. However, studies reporting the impact of a SC on oncological outcomes are lacking. The aim of our study was to evaluate the impact of the introduction of a SC on recurrence-free survival (RFS) of NMIBC patients undergoing TURBT. *Materials and Methods:* An eight-item SC was progressively implemented into clinical practice at two tertiary referral centers. We reviewed the reports of TURBTs performed before and during the SC implementation. Patients undergoing TURBTs between January 2012 and January 2017 were enrolled in this retrospective study. The number of reported items was collected from surgical reports. A multivariable logistic regression was performed to assess the impact of operative report on the presence of detrusor muscle in pathologic specimen. A multivariable Cox regression model was built to assess the impact of operative reports on RFS rate. *Results:* Overall, 547 patients were included in the study and 266 of them (49%) underwent TURBT after the SC implementation. Median follow-up for patients alive at last follow-up was 20 months c (IQR)=10-31]. Median age at TURBT was 72 years (IQR=63-78) and 459 (84%) patients were male. Most of the patients had NMIBC (91%) and high-grade disease (58%). Detrusor muscle in TURBT specimen was detected in 60% of the cases. The implementation of the SC increased the number of reported items from 5 to 6 (median values). On logistic multivariable regression analysis, the number of reported items was not significantly associated with the presence of detrusor muscle in the surgical specimen [hazard ratio (HR)=1.01, 95% confidence interval (CI)=0.75-1.35, p=0.9). On multivariable Cox regression analysis, the number of reported items was independently associated with a significant improvement of RFS [odds ratio (OR)=0.78, 95% CI=0.61-0.99, p=0.04]. *Conclusion:* TURBT is essential in the management of BC patients. We demonstrated that the implementation of a SC into clinical practice increases the quality of operative report thereby potentially improving individualized risk-stratification and care resulting in lower disease recurrence-rate. Therefore, the introduction of a SC should be recommended in order to enhance oncological outcomes by improving surgical standardization and operative reporting.

76
THE IMPACT OF SURGICAL EXPERIENCE ON THE PRESENCE OF MUSCLE DURING TRANSURETHRAL RESECTION OF THE BLADDER

Francesco Soria[1], David D'Andrea[1], Mirko Preto[2], Kilian M. Gust[1], Alberto Briganti[3], Shahrokh F. Shariat[1] and Paolo Gontero[2]

[1]Department of Urology and Comprehensive Cancer Center, Medical University of Vienna, Vienna, Austria; [2]Division of Urology, AOU Città Della Salute E Della Scienza di Torino, Presidio Molinette, Turin, Italy; [3]Department of Urology, Urological Research Institute, Vita-Salute University, San Raffaele Scientific Institute, Milan, Italy

Background/Aim: Transurethral resection of the bladder (TURBT) is essential in the management of non-muscle invasive bladder cancer (NMIBC) as its quality is associated with the burden of care and oncological outcome. The presence of detrusor muscle (DM) in surgical specimen is a quality of care indicator that predicts staging accuracy and early recurrence. TURBT is a routine procedure that is performed early during the training by residents and young consultants. However, it is well known that standardization, with a systematic and detailed approach are necessary for a high-quality resection. Only few studies evaluated the impact of surgical experience on outcomes of TURBT, without definitive results. Therefore, the aim of our study was to evaluate the impact of surgical experience on the presence of muscle in the specimen during TURBT for bladder cancer. *Materials and Methods:* Data from patients who underwent TURBT at two tertiary referral centers between 2012 and 2017 were retrospectively assessed. Primary surgeons were divided into three groups based on their surgical experience: residents, young consultants and experienced consultants. A multivariable logistic regression was performed in order to assess the impact of surgical experience on the presence of detrusor muscle in pathologic specimen. Moreover, we evaluated the clinical relevance of our findings by restricting the analyses to T1 patients. A multivariable Cox regression model was built in order to assess the impact of surgical experience on recurrence-free survival (RFS) rate. *Results:* Overall, 496 patients with complete clinical, pathologic and follow-up data were enrolled in the study. Median follow-up for patients alive at last follow-up was 20 months [interquartile range (IQR)=10-31]. Median age at TURBT was 72 years (IQR=63-78) and 417 (84%) patients were male. DM was in surgical specimen was present in 306 (64%) patients. Considering surgeon experience, DM was present in 144 (59%), 65 (67%), and 97 (70%) of TURBT surgical specimens performed by experienced consultants, young consultants, and residents, respectively. At multivariable logistic regression analysis, that accounts for the effect of standard preoperative factors, surgeon's experience (residents *vs.* experienced consultants) was independently associated with the presence of DM [odds ratio (OR)=2.06, 95% confidence interval (CI)=1.16-3.67 p=0.01]. This difference remained significant even when the analyses were restricted to T1 (for the first TURBT) patients (OR=3.64, 95% CI=1.10-12.09 p=0.035). At multivariable Cox regression analyses, surgeon's experience was not a predictor of recurrence- and progression-free survival. *Conclusion:* Surgeon experience was inversely associated with the presence of DM in the specimen. Hypothesis explaining this finding include attention to detail that is likely to be higher in younger urologists as well as adherence to guidelines with a systematic approach to performing TURBT.

77

PERCUTANEOUS IMAGE-GUIDED THERMAL RADIOFREQUENCY ABLATION FOR CT1A-B RENAL MASSES: LONG-TERM FOLLOW-UP EXPERIENCE OF A TERTIARY REFERRED CENTER

Francesco Alessandro Mistretta[1], Ettore Di Trapani[1], Andrea Russo[1], Roberto Bianchi[1], Andrea Conti[1], Stefano Luzzago[1], Fabrizio Verwij[1], Gennaro Musi[1], Deliu Victor Matei[1], Giuseppe Renne[2], Franco Orsi[3] and Ottavio De Cobelli[1]

[1]Division of Urology, IEO European Institute of Oncology, Milan, Italy; [2]Division of Pathology, IEO European Institute of Oncology, Milan, Italy; [3]Division of Interventional Radiology, IEO European Institute of Oncology, Milan, Italy

Aim: To assess the technical safety and oncologic efficacy of percutaneous image-guided thermal radiofrequency ablation (TRFA) for cT1a-b renal masses, evaluating the possible preoperative predictors of persistence/relapse. *Materials and Methods:* From January 2008 to June 2015 a total of 155 consecutive patients were subjected to image-guided percutaneous TRFA. All patients received a preliminary intraoperative biopsy. All data were prospectively collected in a customized database and retrospectively analyzed. Primary outcomes investigated included technical success, complications, treatment response, oncologic outcome, and overall survival. Univariable (UVA) and multivariable (MVA) analysis were used to identify predictors of persistency/ relapse of the disease. *Results:* Median age was 66 [interquartile range (IQR)=60.5-75] years. 11 (7.1%) patients had a solitary kidney. Median tumour diameter was 27.5 mm (range=7-60), with a median number of 1 mass treated per procedure (range=1-7). Eighty-one (52.2%) patients had a right kidney lesion, 68 (43.9%) had a left kidney lesion and 6 (3.9%) a bilateral lesion. Overall, the median PADUA score was 7 (IQR=7-10); 56.2% and 43.8% of the population had an endophytic and an exophytic lesion, respectively. All patients were subjected to a CT-scan control at first postoperative day. Persistence of disease was described in 13 (8.4%) patients. Out of them, 11

(7.1%) patients experienced a second TRFA that was successful, the remaining 2 decided for an active surveillance protocol. Five (3.3%) patients were subjected to a second (or multiple) TRAF due to multiple locations of renal masses. Eight (5.2%) patients experienced a local recurrence, 1 (0.6%) patient presented distant recurrence in the contralateral adrenal gland. All these patients were subjected to a second TRAF that was successful. Median follow-up was 72.5 months (range=28-117). No progressions were described, while two patients died due to kidney cancer unrelated causes. According to Society of Interventional Radiology (SIR) complication scale, 7 (4.5%) patients experienced an A grade complication, 7 (4.5%) a C grade, 3 (1.9%) a D grade complication. At MVA an endophytic lesion was the only predictor of relapse, while PADUA score failed to predict outcome. *Conclusion:* CT-guided percutaneous thermal radiofrequency ablation was described as an oncologically safe and reliable procedure, with a low rate of complications. The presence of an endophytic lesion was the only predictor of relapse/ persistency of the disease.

78
EVALUATION OF PI-RADS SCORE ≤3 LESIONS AT MULTIPARAMETRIC MRI. IMPLICATION FOR CLINICAL MANAGEMENT AND PROSTATE CANCER DIAGNOSIS

Ettore Di Trapani, Michele Catellani, Andrea Russo, Andrea Conti, Francesco Alessandro Mistretta, Matteo Ferro, Raffaele Bianco, Antonello Cioffi, Gennaro Musi, Giuseppe Renne, Deliu Victor Matei and Ottavio De Cobelli

Division of Urology, IEO European Institute of Oncology, Milan, Italy

Background/Aim: Multi parametric magnetic resonance imaging (mpMRI) of the prostate has been used in the diagnosing and staging of prostate cancer (PCa). While lesions with PI-RADS score ≥4 are predictive of clinically significant disease, PI-RADS score ≤3 lesions are equivocal. We aimed at evaluating the clinical and pathological implications of PCa patients who had a PI-RADS ≤3 lesions at mpMRI. *Materials and Methods:* We included 588 patients with a PI-RADS score ≤3 lesion at mpMRI who underwent prostate biopsy for a suspected PCa at a single referral tertiary Centre between June 2011 and December 2015. All patients underwent 1.5 Tesla mpMRI with an eight-channel phased-array coil and images were reviewed by a highly experienced dedicated radiologist, using PI-RADS version 2. Uni- (UVA) and multi variable (MVA) logistic regression analyses assessed the predictors of PCa, AS criteria and clinically significant PCa at final pathology. *Results:* Median age at biopsy was 63 years [interquartile range (IQR)=57-68]. Overall, 232 (39.5%) and 356 (60.5%) patients had a PI-RADS score 2 or 3 lesions, respectively. Prostate cancer was diagnosed in 412 patients (70.1%), out of these 261 (36.6%) were eligible for active surveillance (AS) according to PRIAS criteria. Of the 268 (45.6%) patients that underwent RARP, 114 (42.5%) had a clinically significant disease. Overall, 165 (61.6%), 97 (36.2%), and 6 (2.3%) had a Gleason score ≤6, 7, and 8≥, respectively. Out of these, 232 (86.5%) and 36 (13.5%) had a pT2 and a pT3 disease, respectively. On an outpatient setting: clinical stage, PSA and prostate volume (all $p<0.02$) significantly predicted PCa at MVA ($p=0.4$). A PI-RADS ≤3 lesion in patients with a previous negative biopsy efficiently predicted PCa suitable for active surveillance (AS) according to PRIAS criteria ($p=0.004$) when compared to other confounders. In biopsy naïve patients, the higher prostate volume and the absence of a second lesion at MRI significantly predicted patient's fitness for AS (all $p<0.05$). Moreover, in patients who underwent surgery, the biopsy Gleason score ($p<0.01$) but not the PI-RADS predicted a clinically significant PCa at final pathology. *Conclusion:* Despite the non-negligible number of patients with a PI-RADS ≤3 lesion shown to have a PCa, mpMRI was not a predictor of PCa. On the other hand, PI-RADS ≤3 lesions in PCa patients predicted the suitability for AS. Accordingly, in patients that underwent RARP, PI-RADS ≤3 lesions did not predict a clinically significant PCa at final pathology.

79
POSITIVE SURGICAL MARGINS AFTER ROBOT-ASSISTED RADICAL PROSTATECTOMY IN THE MULTIPARAMETRIC MRI ERA: THE EXPERIENCE OF A HIGH VOLUME THIRD REFERRAL CENTRE

Francesco Alessandro Mistretta[1], Ettore Di Trapani[1], Andrea Russo[1], Michele Catellani[1], Alessandro Serino[1], Andrea Conti[1], Matteo Ferro[1], Gennaro Musi[1], Deliu Victor Matei[1], Giuseppe Renne[1], Giuseppe Petralia[2] and Ottavio De Cobelli[1]

[1]Division of Urology, IEO European Institute of Oncology, Milan, Italy; [2]Division of Radiology, IEO European Institute of Oncology, Milan, Italy

Background/Aim: The aim of the study was to assess the rate of concordance of positive surgical margins (PSM) after robot-assisted prostatectomy (RARP) with multi parametric MRI (mpMRI) and to determine potential predictors of PSM in case of discordance with mpMRI. *Materials and Methods:* From January 2014 to April 2017, a total of 1788 consecutive patients were subjected to RARP for prostate cancer, 98% underwent a preliminary mpMRI. Possible PSMs were determined in frozen sections from all patients. All data were

prospectively collected in a customized database and retrospectively analyzed. The primary outcome investigated was the concordance between PSMs and the location of primary lesions detected with mpMRI. Univariable (UVA) and multivariable (MVA) analyses were used to identify potential predictors of PSM in case of discordance with mpMRI. *Results:* Out of all patients subjected to mpMRI and RARP, PSM was determined in 187 (10.67%), and among them, mpMRI primary lesion location and PSM were discordant in 56 (3.2%) (with a 76.8% of PI-RADS 4 or 5 as index lesion). Out of these 56, 20 patients had an intraoperative PSM (35.7%), described as focal (<1 mm of extension) in 17 patients. Moreover, in 23 (41.1%) patients a multifocal mpMRI significant disease was detected (secondary lesion > PI-RADS 3), and among them, PSM was discordant with both primary and secondary lesions detected by mpMRI in 11 (19.6%; 5.9% of total) patients. Fifty-three (94.6%) patients were subjected to nerve- sparing, 14 (25%) monolaterally, 39 (69.9%) bilaterally. At definitive histology, Gleason Score (GS) was 3+3 in 6 patients (10.7%), 3+4 in 25 (44.6%), 4+3 in 14 (25%) and > 4+4 in 11 (19.7) patients. In 22 patients the GS was assessed in the specimens of PSMs, and was 3+3 in 12 patients, 3+4 and 4+3 in 7 and 2 patients respectively, and 4+4 in the remaining 1. Twenty-three patients (41.1%) resulted in pT2, 25 (44.6%) in pT3a and 8 (14.3%) in pT3b. The distribution of PSMs was found divided in 14.8% anterior and 85.2% posterolateral. Among the latter, 21 (42%) margins were apical and 17 (34%) basal. At MVA, low and intermediate GS (low: 6; intermediate: 7) were significantly associated with discordance between index lesion and PSMs (all $p<0.05$). *Conclusion:* Our results demonstrated that the introduction of the mpMRI in the preoperative workout had reduced the rate of PSMs. However, in a small number of patients subjected to nerve-sparing, discordance between the site of PSM and MRI lesions still exists. This issue has been described in particular for preoperative pathological low-/intermediate- risk patients due to a more aggressive nerve-sparing procedure performed distant from the mpMRI index lesion.

81
WIDESPREAD USE OF PROTOCOL-BASED ACTIVE SURVEILLANCE IN PROSTATE CANCER: THE SIURO PRIAS ITA EXPERIENCE

Fabio Badenchini[1], Maria Francesca Alvisi[1], Michele Battaglia[2], Bollito Enrico[3], Marco Borghesi[4], Giacomo Cicchetti[5], Piergiuseppe Colombo[6], Maurizio Colecchia[7], Giuseppe Cusumano[8], Luigi Da Pozzo[9], Pasquale Di Tonno[2], Davide Diazzi[10], Michelangelo Fiorentino[11], Ezio Frego[12], Michele Gallucci[8], Angela Giliberti[2], Giorgio Guazzoni[13], Rodolfo Hurle[13], Tommaso Jaeger[14], Alberto Lapini[14], Giuseppe Martorana[4], Rodolfo Montironi[15], Giorgio Napodano[16], Biagio Paolini[17], Luisa Pasini[18], Carlo Patriarca[19], Maria Rosa Raspollini[20], Marco Roscigno[9], Roberto Sanseverino[21], Steno Sentinelli[22], Marco Tanello[12], Andrea Turci[5], Tiziana Rancati[1], Tiziana Magnani[1], Giario Conti[23] and Riccardo Valdagni[24]

[1]Prostate Programme, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[2]Division of Urology, Policlinico, Bari, Italy;
[3]Division of Pathology, Azienda Ospedaliero-Universitaria San Luigi Gonzaga, Orbassano, Turin, Italy;
[4]Division of Urology, Policlinico S. Orsola Malpighi, Bologna, Italy;
[5]Division of Urology, Ospedale M. Bufalini, Cesena, Italy;
[6]Division of Phatology, Istituto Clinico Humanitas, Rozzano, Italy;
[7]Division of Genito-Urinary Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[8]Division of Urology, Istituto Regina Elena, Rome, Italy;
[9]Division of Urology, Ospedale Giovanni XXIII, Bergamo, Italy;
[10]Division of Urology, Policlinico S. Orsola Malpighi, Bologna, Italy;
[11]Division of Pathologist, Policlinico S. Orsola Malpighi, Bologna, Italy;
[12]Division of Urology, Ospedale Civile, Desenzano, Italy;
[13]Division of Urologist, Istituto Clinico Humanitas, Rozzano, Italy;
[14]Division of Urology, Azienda Ospedaliera Universitaria Carreggi, Florence, Italy;
[15]Division of Pathology, Ospedali Riuniti Torrette, Ancona, Italy;
[16]Division of Urology, Ospedale Umberto I, Nocera Inferiore, Italy;
[17]Division Genito-Urinary Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[18]Division of Urology, Istitttuto Clinico Humanitas, Rozzano, Italy;
[19]Division of Pathology, Ospedale S.Anna, Como, Italy;
[20]Division of Pathology, Azienda Ospedaliera Universitaria Carreggi, Florence, Italy;
[21]Division of Pathology, Ospedale Umberto I, Nocera Inferiore, Italy;
[22]Division of Pathology, Istituto Regina Elena, Rome, Italy;
[23]Division of Urology, Ospedale S. Anna, Como, Italy;
[24]Division of Oncology and Hemato-oncology, Università degli Studi di Milano, Milan, Italy

Background/Aim: Active Surveillance (AS) is proposed to patients with localized prostate cancer as an alternative to radical treatment strategies (namely surgery, external

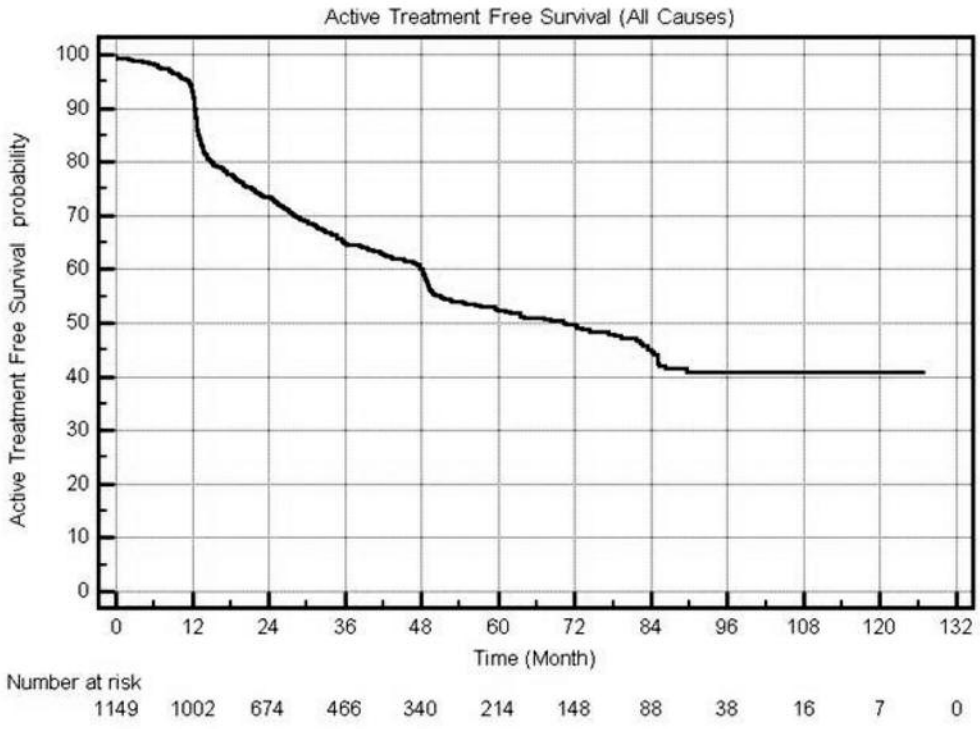


Figure 1. *Kaplan-Meier curve of active treatment-free survival for all causes.*

radiotherapy and brachytherapy). Although AS is now among the therapeutic and observational options accepted by all national and international guidelines, it should be carried out according to well defined and shared protocols clearly establishing inclusion, exclusion and discontinuation criteria and follow-up management. We report the 8-year experience with the SIUrO PRIAS ITA working group, composed of 11 centers participating in the Prostate Cancer Research International: Active Surveillance (PRIAS) protocol under the auspices of the Italian Society for Urologic Oncology (Società Italiana di Urologia Oncologica-SIUrO), coordinated by the PCU at Fondazione IRCCS Institute Nazionale dei Tumori, Milan (INT PCU). *Patients and Methods:* The SIUrO PRIAS ITA working group was established in December 2009 and composed of 11 centers participating in PRIAS under the auspices of SIUrO and coordinated by INT PCU staff (3 figures: Principal Investigator, Clinical Trial Coordinator and Data Manager). New centers joined over time. Each center had to identify one or more delegates with whom the coordinator center could communicate and to whom patient's requests could be addressed. As PRIAS is an observational protocol, before starting enrolment, centers had to check with their local Ethical Committees the need to gather formal approval. In addition to PRIAS criteria for inclusion, exclusion, discontinuation and follow-up management, SIUrO PRIAS ITA introduced mandatory pathological review of diagnostic biopsies by a pool of qualified pathologists, experts in genito-urinary tumors, to grant high quality of diagnostic data. Furthermore, besides basic data mandatory for PRIAS (PSA, biopsy, digital rectal examination), SIUrO PRIAS ITA collected extensive clinical, socio-demographical and diagnostic information plus data on urinary symptoms, erectile dysfunction and patient health-related quality of life through 3 patient-reported outcomes (IPSS, IIEF and FACT-P). Inclusion of new patients was centralized to the coordinator center, where new patient documens were checked and included in the PRIAS central database. The patient then returned to the participating center with follow-up calendar. Follow-up was the responsibility of participating centers who, while visiting patients, registered PSA, digital rectal examination, and biopsy data if performed. If discontinuation was necessary, the coordinator center had to be informed with respect to the reason for AS discontinuation and therapy chosen by patients. Coordinator center collaborated with PRIAS coordinator, Erasmus Medical Center in Rotterdam, to check on registered data and compliance of follow-up. Coordinator center was also contacted by participating centers when dealing with complex cases, especially during follow-up. *Results:* A total of 1,149 patients from 11 centers were enrolled in PRIAS by SIUrO PRIAS ITA working group. Average rate of enrolment was ≈2 patients/week. Median age at inclusion was 66 years (range=42-81). Median time in AS was 29.54 months (range=0-126.21). Eleven patients asked to be followed up by a SIUrO

PRIAS ITA near home centre after inclusion. Seven hundred two patients are still on AS. Kaplan-Meier actuarial curve of patients on AS is presented in Figure 1. Seven years after prostate cancer diagnosis, 40% of patients are still on AS. This result is in line with previous reports on AS. *Conclusion:* SIURO PRIAS ITA working group contributed significantly to PRIAS enrolment (1,149 patients out of 5,318 total PRIAS patients, 21.6%). The multi-centric organization of the group presented many advantages for the study but also required some attention, such as compliance in follow-up schedule. Centralized enrolment helped define patients with suitable inclusion criteria and patients requiring histological revisions and register extensive clinical, socio-demographical and diagnostic information plus data on urinary symptoms, erectile dysfunction and patient health-related quality of life. The auspices of SIUrO as multidisciplinary scientific society plus the multicentre setting and synergy favored the promotion of the AS concept in Italy and, at the same time, allowed the involvement of medium/small hospital centers that were supported in the management of AS follow-up scheme, thus keeping a high standard of protocol adherence and of clinical care.

Acknowledgements to Fondazione I. Monzino for supporting the activities and the projects of INT Prostate Cancer Program.

82
IMMUNO-PET: A NEW TOOL FOR PROSTATE CANCER IMAGING

Sara Morlino[1], Barbara Frigerio[2], Elena Luison[3], Flavio Crippa[4], Alessandra Alessi[4], Marta Mira[4], Anna Bogni[4], Carlo Chiesa[4], Barbara Avuzzi[5], Barbara Noris Chiorda[5], Michela Dispinzieri[5], Sergio Villa[5], Riccardo Valdagni[6] and Mariangela Figini[2]

[1]Radiotherapy Unit 1, IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[2]Biomarkers Unit, DRAST Department, IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[3]Molecular Therapies Unit, Department of Experimental Oncology and Molecular Medicine, IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[4]Department of Nuclear Medicine, IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[5]Radiotherapy Unit 1, IRCCS Istituto Nazionale dei Tumori, Milan, Italy;
[6]Department of Oncology and Hemato-oncology, Università degli Studi, Milan, Italy

Background/Aim: Prostate cancer (PCa) is the second leading cause of cancer-related death in Western men. Positron emission tomography/computed tomography (PET/CT) with emerging radiopharmaceuticals promises accurate staging of disease and detection of metastatic lesions. Prostate-specific membrane antigen (PSMA) is a well-characterized imaging biomarker of PCa. PSMA expression is directly related to androgen independence, metastasis and progression rendering this tumor associate antigen (TAA) a good target for the development of new radiopharmaceuticals for PET. A major unmet medical need is a highly specific and sensitive molecular imaging agent or method for staging and monitoring patients with PCa. We have previously demonstrated that using a single-chain variable fragment (scFv) radiolabeled with ^{123}I, we can have very good tumor localization (Figure 1A) that disappear with an excess of cold antibody (Figure 1B) indicating its high specificity (1). The aim of this study was to demonstrate *in vivo* whether ^{124}I-scFvD2B could be useful also for immunoPET compared to classical metabolic tracers in the same animal model. *Materials and Methods:* Radio /Metabolic tracers ^{18}F-FDG, ^{18}F-FLT, 11C-choline have been used in comparison with the immunoPET performed using a scFv directed against PSMA (^{124}I- scFvD2B). ^{18}F-FDG was prepared according to the well known Hamacher method (2) whereas ^{18}F-FLT and ^{11}C-choline were prepared as previously described. Quality controls of the tracers were performed according to European Pharmacopoea. Radioiodination of scFvD2B with ^{124}I was performed with iodogen-coated tube (Pierce, Rockford, IL) and ^{124}I-scFvD2B was purified on PD10 column. The immunoreactivity was assayed on PSMA positive and PSMA negative cells. The experiments were performed in mice bearing in one flank PSMA-positive and in the controlateral flank PSMA-negative tumors (PC3-PIP and PC3 cells, respectively). The same mice bearing tumours used for microPET were analyzed for ex vivo biodistribution of ^{124}I-scFvD2B. Animals were bleed and sacrificed to allow tissue of interest collection. Blood and organ samples were then wet-weighed and counted in a gamma counter with internal standard to correct the decay. Measurements were expressed as percentage of injected dose per gram of tissue (%ID/g) and as tissue/tumour to blood ratio (T/B). *Results:* The imaging profiles ^{18}F-FDG, ^{18}F-FLT and 11C-choline were compared with ^{124}I-scFvD2B in nude mice to determine the optimal radionuclide for PET imaging of prostate tumor. Using ^{18}F-FDG a diffuse background was evident in all the body of mice due to a poor contrast resolution of ^{18}F-FDG (Figure 2); same results were obtained with ^{18}F- FLT. Using the ^{11}C-choline as tracer we observed an intense uptake in the kidneys (Figure 3) which, as in humans, could hamper the evaluation of the tracer distribution in the abdomen. ImmunoPET showed the best tumour to blood ratio between 15 and 24 hours after ^{124}I-scFvD2B injection. During this range of time a specific uptake on PSMA-positive tumor was evident and confirmed by the *ex vivo* biodistribution data. The use of immunoPET tracer ^{124}I-scFvD2B was able to localize significantly better only in

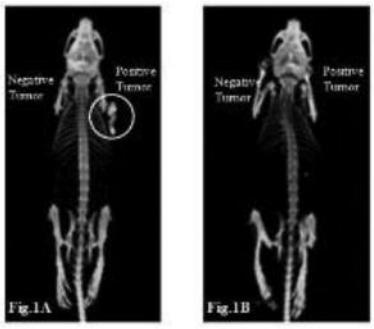


Figure 1. *Representative SPET/CT images after intravenous administration of ^{123}I-scFvD2B.*

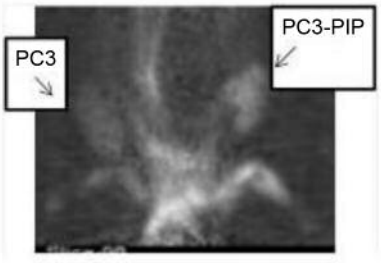


Figure 2. *MicroPET imaging data after intravenous injection of ^{18}F-FDG demonstrated uptake in PSMA positive and negative tumors (PC3-PIP and PC3 cells).*

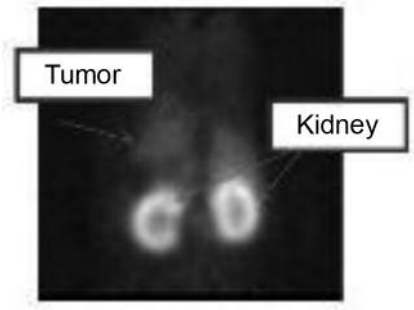


Figure 3. *MicroPET imaging data after intravenous injection of the ^{11}C-choline is not able to detect tumors and shows an intense kidney uptake.*

the PSMA-expressing tumour (Figure 4) and the biodistribution study for ^{124}I- scFvD2B performed on the same animals confirmed the imaging. The PSMA-expressing tumours yield a median of target/background ratio around 30-40%. *Conclusion:* At the optimal time point defined between 15 h and 24 h, ^{124}I-scFvD2B was able to localize significantly better in the PSMA expressing tumours yielding a significantly better target/background ratio compared to

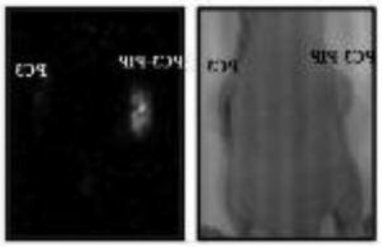


Figure 4. *MicroPET imaging data after intravenous injection of ^{123}I-scFvD2B.*

metabolic tracers used. The results demonstrate that PSMA ligand PET/CT could be superior to other modalities for the diagnosis of recurrent PCa.

1 Frigerio B, Frassen G, Luison L, Satta A, Seregni E, Colombatti M, Fracasso G, Valdagni R, Mezzenzanica D, Boerman O, Canevari S and Figini M: Full preclinical validation of the ^{123}I-labeled anti-PSMA antibody fragment ScFvD2B for prostate cancer imaging. Oncotarget *8*: 10919-10930, 2017.

2 Pascali C, Bogni A, Fugazza L, Cucchi C, Crispu O, Laera L, Iwata R, Maiocchi G, Crippa F and Bombardieri E: Simple preparation and purification of ethanol-free solutions of 3'-deoxy-3'-[^{18}F]fluorothymidine by means of disposable solid-phase extraction cartridges. Nucl Med Biol *39*: 540-550, 2012.

83
IMPACT OF MULTI-PARAMETRIC MRI IN PROSTATE CANCER STRATIFICATION AND PROPOSAL OF A NEW RISK CLASSIFICATION

Ettore Di Trapani, Michele Catellani, Andrea Russo, Gabriele Cozzi, Roberto Bianchi, Maurizio Delor, Andrea Conti, Raffaele Bianco, Francesco Alessandro Mistretta, Danilo Bottero, Gennaro Musi and Ottavio De Cobelli

Division of Urology, European Institute of Oncology - IEO, Milan, Italy

Background/Aim: Lately multi parametric magnetic resonance imaging (mpMRI) of the prostate is used in the diagnosis and staging of prostate cancer (PCa). We aimed at evaluating the risk of lymph node invasion (LNI) of patients with PCa with respect of mpMRI data such as PI-RADS and ECE score. *Materials and Methods:* We included 301 patients who underwent mp MRI and RARP with lymph node dissection for PCa at a single referral tertiary centre between 2012 and 2013. All patients underwent 1.5 Tesla mpMRI with an eight-

Variables	Significance	Odds ratio	95% Confidence interval	
			Lower	Upper
IEO risk groups				
Low	0.1			
Intermediate	0.40	0.34	0.03	4.18
High	0.05	5.23	1.02	26.83
D'Amico risk class				
Low	0.03			
Intermediate	0.20	6.20	0.368	104.53
High	0.04	21.03	1.19	369.78
Age	<0.001	0.91	0.87	0.96
Prostate volume (ml)	0.75	0.99	0.96	1.03
Number of positive cores	0.19	1.12	0.95	1.32

Figure 1. *Multivariable analysis predicting lymph node invasion.*

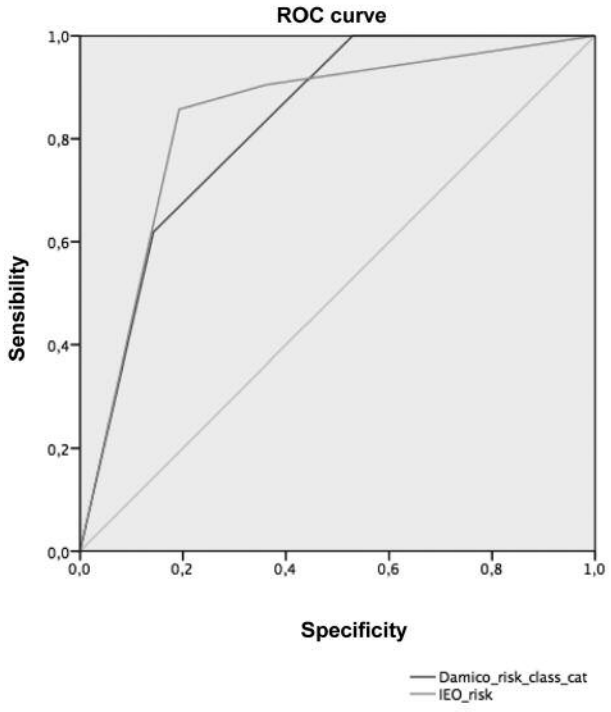


Figure 2. *ROC curve comparing accuracy of the two predicting tools.*

channel phased-array coil and images were reviewed by a highly experienced dedicated radiologist, using PIRADS version 2. Uni- (UVA) and multi variable (MVA) logistic regression analyses assessed the predictors of LNI. Three different groups of risk (low-, intermediate-, and high- risk) were set. A ROC curve analysis assessed the accuracy of our model compared to the D'Amico risk classification. *Results:* Median age at biopsy was 64 years [interquartile range (IQR)=58.3-68.4]. Overall 182 (60,5%) patients had a pT2 disease at final pathology, 42 (14%) had a PI-RADS <3 lesion at MRI, 71 (23,6%) had a PI-RADS 4 and 188 (62.5%) had a PI-RADS 5 lesion. Roughly the 60% (188 patients) of our cohort had an ECE score >3. Globally, 168 (55.8%), 102 (33.9%) and 31 (10.3%) had a Gleason 6, or >8 respectively, and 21 (7%) patients had positive nodes at final pathology. At MVA high-risk group of our and the D'Amico classification were significantly associated with LNI, while older age was linked with a lower rate of LNI (Figure 1). The ROC curve analysis showed better accuracy (84%) compared to the D'Amico risk classification (82%) (Figure 2). *Conclusion:* We demonstrated the use of MpMRI to better stratify PCa patients compared to the standard clinical tools. We propose the use of our classification identifying three groups predicting LNI risk.

84

MULTI-DISCIPLINARY MANAGEMENT OF PROSTATE CANCER PATIENTS AT FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI: AN UPDATE

Fabio Badenchini[1], Tiziana Magnani[1], Alessandra Alessi[2], Barbara Avuzzi[3], Augusta Balzarini[4], Nice Bedini[3], Lara Bellardita[1], Claudia Borreani[5], Mauro Carrara[6], Alessandra Casale[7], Mario Catanzaro[8], Annamaria Cerrotta[9], Maurizio Colecchia[10], Flavio Crippa[2], Letizia De Luca[1], Teresa Di Florio[1], Simona Donegani[1], Paola Dordoni[1], Carlo Fallai[9], Tommaso Giandini[11], Paolo Grassi[12], Rodolfo Lanocita[13], Marco Maccauro[2], Alberto Macchi[8], Cristina Marenghi[1], Cinzia Martini[4], Julia Menichetti[1], Antonella Messina[7], Sara Morlino[3], Barbara Noris Chiorda[3], Biagio Paolini[14], Emanuele Pignoli[11], Giuseppe Procopio[12], Carla Ripamonti[15], Ettore Seregni[12], Carlo Spreafico[13], Stagni Silvia[8], Antonio Tesone[8], Tullio Torelli[8], Marta Vaiani[7], Elena Verzoni[12], Sergio Villa[3], Ernesto Zecca[4], Roberto Salvioni[8], Nicola Nicolai[8], Patrizia Monti[16] and Riccardo Valdagni[3]

[1]Prostate Programme, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Milan, Italy;
[2]Division of Nuclear Medicine, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy;
[3]Division of Radiotherapy 1, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy;
[4]Division of Palliative Care And Rehabilitation Programs, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy;

[5]Division of Clinical, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy;
[6]Division of Medica Physics, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy;
[7]MRI Unit, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy;
[8]Division of Urology, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy;
[9]Division of Radiotherapy 2, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy;
[10]Division of Pathologist, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy;
[11]Division of Medical Physics, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy;
[12]Division of Medical Oncology, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy;
[13]Division of Diagnostic and Interventional Radiology, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy;
[14]Division of Pathology, Fondazione IRCCS, Istituto Nazionale Dei Tumori, Milan, Italy;
[15]Supportive Care Unit, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy;
[16]Direzione Sanitaria, Fondazione IRCCS, Istituto Nazionale Dei Tumori, Milan, Italy

After the launch of the Prostate Cancer Programme in September 2004, the clinical management of prostate cancer (PCa) patients at Fondazione IRCCS Istituto Nazionale dei Tumori (INT), in Milan, became multidisciplinary, and multidisciplinary consultations and clinical case discussions were organized on a weekly routine basis. From the start it was clear that the model needed to be adaptable to meet new clinical and organizational needs. Magnani *et al*. (1) referred to the 2004-2011 experience. This abstract describes the initial multidisciplinary consultations and the clinical case discussions in terms of numbers, organization and access and the changes introduced in 2012-2017. From March 2005 to October 2017 an average of 350 multidisciplinary consultations per year were performed on a weekly basis. An urologist, a radiation oncologist and a psychologist were seeing 8 patients with a PCa diagnosis in any state of disease who refer to INT for the first time. Medical oncologists are also involved in advanced or metastatic PCa. From March 2005 to October 2017, an average of 340 clinical case discussions per year was performed on a weekly basis. At least one representative for urology, radiation oncology, medical oncology, the research nurse and the project manager participated mandatorily, while other professionals (for example imaging specialists, uropathologists, palliative care specialists) were called in on particular cases. Prostate Cancer Unit (PCU) was formalized in 2009 and updated in 2013. In February 2017 the collaboration between INT PCU and Urology Division at Policlinico, Milan, was made official to implement the PCa path of care of both institutes, also in line with Valdagni's *et al*. papers on PCU (2, 3). Magnani *et al*. reported on INT multidisciplinary activities from March 2005 to March 2011 (1). Since 2012, an increase in very low-/low-risk class patients (61.5% *vs*. 51%) and a decrease in high-risk (13% *vs*. 26%) and metastatic (1.5% *vs*. 5%) patients were observed, compared to the period 2005-2011. The percentage of intermediate-risk patients was maintained (26% *vs*. 24%). 9.5% of the patients had already received a PCa treatment before visit. The following changes were introduced in the organizational model: (i) Due to the lack of resources (psychologists are supported by a grant from a private donor) the individual counselling meeting with the psychologist after the first multidisciplinary consultation was interrupted in 2014. Patients who seemed to potentially benefit from psychological support were invited to meet the psychologist in the afternoon or schedule an appointment. (ii) Selection of cases for clinical case discussions: In the 2005-2011 period, all cases examined in the multidisciplinary clinic were discussed in the weekly tumour board to evaluate adherence to guidelines, check on the quality of the decisions formulated in the clinic, to tailor therapeutic or observational strategies and to facilitate the interdisciplinary collaboration and education. After carefully analyzing the data on the clinical case discussions and the changes applied to the decisions taken in the clinic, in 2014 we chose not to discuss all the cases examined in the first multidisciplinary consultations. Since 2014 clinical case discussions were mainly focused on patients who, after the multidisciplinary consultations, had to complete staging before therapeutic and observational options could be proposed and patients on active surveillance or watchful waiting with borderline situations with respect to institutional protocols. (iii) Since 2015 a research nurse has participated in the clinical case discussions, thus enabling the selection of patients to be included in clinical trials. In addition, the nurse became the contact person between clinicians and patients and follows up after the discussion to schedule appointments, to plan future steps and to inform patients and clinicians. (iv) The formalization of the PCU identified and named the specialists involved in the PCa path of care divided in core and non-core team, described the PCa dedicated activities and the participation in the PCU multidisciplinary activities. As regards the clinical case discussions, professionals of the non-core team needed on a particular case were receiving a request from the PCU Secretary and upon their confirmation the case was scheduled. (v) Since the formalization of INT PCU-Policlinico collaboration, urologists from Policlinico participate in the clinical case discussions presenting their cases. *Conclusion:* Multidisciplinary approach has proven successful to address PCa complexity. A flexible organizational model is necessary to meet new scenarios

(both clinical and organizational). Monitoring is mandatory to detect bottle necks and criticisms.

1 Magnani T1, Valdagni R, Salvioni R, Villa S, Bellardita L, Donegani S, Nicolai N, Procopio G, Bedini N, Rancati T and Zaffaroni N: The 6-year attendance of a multidisciplinary prostate cancer clinic in Italy: incidence of management changes. BJU Int *110*: 998-1003, 2012.
2 Valdagni R1, Albers P, Bangma C, Drudge-Coates L, Magnani T, Moynihan C, Parker C, Redmond K, Sternberg CN, Denis L and Costa A: The requirements of a specialist Prostate Cancer Unit: a discussion paper from the European School of Oncology. Eur J Cancer *47*: 1-7, 2011.
3 Valdagni R, Van Poppel H, Aitchison M, Albers P, Berthold D, Bossi A, Brausi M, Denis L, Drudge-Coates L, De Santis M, Feick G, Harrison C, Haustermans K, Hollywood D, Hoyer M, Hummel H, Mason M, Mirone V, Müller SC, Parker C, Saghatchian M, Sternberg CN, Tombal B, van Muilekom E, Watson M, Wesselmann S, Wiegel T, Magnani T and Costa A: Prostate Cancer Unit Initiative in Europe: A position paper by the European School of Oncology. Crit Rev Haematol Oncol *95*: 133-143, 2015.

85

PREDICTIVE VALUE OF G8 SCREENING TOOL IN ELDERLY POPULATION UNDERGOING RADICAL CYSTECTOMY: PRELIMINARY EVALUATION

Riccardo Boschian, Nicola Pavan, Enrica Verzotti, Tommaso Silvestri, Fabio Traunero, Giovanni Liguori and Carlo Trombetta

Department of Urology, ASUITS - University of Trieste, Trieste, Italy

Background/Aim: Although malignant tumours can occur in people of all ages, cancer disproportionately affects those aged 65 years and older, and the number of elderly patients with cancer will increase substantially in the coming decades as a result of increasing life expectancy and population ageing. The guidelines of the National Comprehensive Cancer Network, the International Society of Geriatric Oncology, and the European Organisation for Research and Treatment of Cancer recommend that all patients with cancer age 70 years old undergo some form of geriatric assessment. In geriatric practice, the G8 screening tool represents a valid instrument for the identification of functional decline in oncological elderly patients. Recently it has demonstrated good predictive value in surgery to identify fragile patient candidates for oncological abdominal surgery. Our study has the objective to define if G8 score is a good tool to identify the risk of post-operative complications in elderly patients (≥70 years) undergoing radical cystectomy (RC). *Patients and Methods:* From January 2012 to August 2017, we recruited 56 patients 70 years old or older at the surgical time, undergone RC. Median age was 76 years (SD=4.37), 41 patients were male (73.2%) and 15 patients female (26.8%). Median BMI was 25.73 (SD=4.03). 8 patients (14.3%) were affected by type 2 diabetes mellitus, 32 (57.1%) suffered hypertension and 18 (32.1%) had stage III or higher chronic kidney disease. The G8 screening questionnaire was performed to all patients preoperatively, and fragile patients were identified with a score ≤14. We registered intra operative complications, post-operative complications and their gravity using Clavien Dindo scale, estimated glomerular filtration rate (eGFR) and its variation postoperatively, length of hospital stay after surgery and readmission rate within 30 days. We compared the clinicopathological data between the frail (G8 score <=14) and not frail (G8 score >14) group. Statistical analysis was made by computing software SPSS. *Results:* Median preoperative G8 score was 13.65 (SD=2.3). Patients were divided in fragile (N=35, 62.5%) and not fragile (N=21, 37.5%). Intra-operative complications were registered in 1 patients (2.8%) with G8 score ≤14 and 0 pt (0%) with G8>14 (p=0.625). Post-operative complications occurred in 24 patients (68.5%) with G8 score ≤14 and 8 patients (38.09%) with G8>14 (p=0.025), 12 and none of them had a Clavien Score ≥3 respectively (p=0.015). Postoperative eGFR was 61.45 (SD=29.2) in G8≤14 group and 57.66 (SD=25.84) in G8>14 group (p=0.62) and median variation between pre- and postoperative eGFR was 7.8 (SD=27.43) and 8.0 (SD=26.01) for each group (p=0.97). Median hospital stay was 25.45 days (SD=11.01) for fragile patients and 24.23 days (SD=11.32) for patients not fragile (p=0.69). Five patients (14.28%) with G8 score≤14 were readmitted within 30 days of discharge, and for 6 patients (28.57%) with G8 score>14 was necessary to be hospitalized (p=0.298). No significant difference was registered for overall mortality (p=0.23) and cancer related mortality (p=0.53) between the two groups. *Conclusion:* Our study demonstrated that the G8 screening tool represents a good predictive instrument for RC morbidity, identifying fragile patients at risk of post-operative complications and their severity. However, it doesn't demonstrate good affability in identification of patients at risk of intraoperative complications and within 30 days of operation with necessity of hospital readmission. Considering these results, it is possible to perform safely and efficiently this screening test for frailty in older patients qualified for RC. This instrument may offer physicians additional information that can be used in the postoperative optimization of the treatment of the high-risk group of patients. However further analyses are necessary to confirm the data obtained from this preliminary study.

86

BLADDER CANCER IN VERY ELDERLY PATIENTS: CLINICAL OUTCOMES AND SURVIVAL IN A RETROSPECTIVE ANALYSIS

Enrica Verzotti, Giacomo Di Cosmo, Nicola Pavan, Tommaso Silvestri, Giovanni Liguori and Carlo Trombetta

Department of Urology, ASUITS - University of Trieste, Trieste, Italy

Background/Aim: Non-muscle invasive urothelial bladder cancer (NMIBC) represents a common neoplasm in patients older than 75 years old. The management of this pathology in very elderly patients needs a careful evaluation of outcomes and the real benefits of the treatment in terms of quality of life, overall survival and oncological outcomes especially considering that among these patients there's a high prevalence of complications and comorbidities. Our aim was then to analyze retrospectively the population of patients older than 85 years old treated at our department for bladder tumors and try to assess which category of patients had real benefit from surgical or medical treatment. Primary outcome measures were the evaluation of overall survival (OS) and recurrence related to clinico-pathological features. Secondary outcome measures were the evaluation of any relation between treatments and OS. *Patients and Methods:* We looked retrospectively at 118 patients aged 85 years old or more who underwent transurethral resection (TURBT) for bladder tumor (BT) in our hospital between 2001 and 2015. We registered pre-operative clinical-pathological features and clinical outcomes. Statistical analysis was performed by SPSS. *Results:* A total of 47 females (39.8%) and 71 males (60.2%) with a mean age of 88.13 (SD +/- 3.17) and mean ASA score 2.55 (+/- 0.5) were included in this study; 91 patients deceased (77.1%) and 27 (22.9%) are alive. Median time-to-death was 13.5 months (IQR 2-34) and median disease-free survival (DFS) was 8 months (IQR=0-24). At diagnosis, 28 patients already had advanced disease (23.72%). 4 patients underwent radical cystectomy (RC), 2 had partial cystectomy, 1 had radiotherapy for palliation and 110 had no further radical treatments (93.22%). Histological type was urothelial in 99 patients (83.89%), squamous in 9 patients (7.62%) and undifferentiated in 10 cases (8.47%). Overall, 92 patients had no intravesical therapy (77.96%); 19 had BCG (16.1%) and 7 had MMC (5.93%). Among these patients, only one was over 90 years and received MMC; 25 patients were younger than 90 and most of them received BCG (72%). 79 patients had low grade (LG) disease (66.94%), 38 had high grade (HG) disease (32.20%) and 1 patient had CIS (0.84%). Among patients with high grade disease 7 survived (18.4%) and 31 deceased (81.6%); among those with low grade disease 20 survived (25.3%) and 59 deceased (74.7%). Among patients who received an intravesical treatment 33.33% survived; among those who did not received any kind of intravesical treatment 19.57% survived. Total recurrence rate was 38.14%. *Conclusion:* Bladder cancer is a well-known disease with a high rate of morbidity and mortality. In our series, HG grade disease, was not associated with higher mortality rate (p=0.157) nor with recurrence rate (p=0.452). Tumor size and histological type seemed to be related to recurrence (p=0.001 and p=0.009 respectively). Intravesical treatment did not seem to improve OS (p=0.06). Age over 90 years old was associated with less prescription of intravesical treatment (p=0.003). Men seemed to have higher risk of recurrence (p=0.006). In the whole population recurrence did to not affect overall survival (p=0.72) suggesting that in most of cases an invasive treatment or an intravesical therapy were not able to improve overall survival. This has to be considered especially for those patients who have high grade disease and that usually are sent to bladder instillations or multiple transurethral resections. Our study seems to demonstrate that clinical-pathological features of bladder tumour do not affect overall survival in very elderly patients. Moreover, age seems to be a factor influencing the lower rate of prescription of more invasive treatments without affecting overall survival. Especially in those patients at higher risk of complications, a careful evaluation between risks and complications related to the treatment is mandatory.

87

METASTATIC MALIGNANT MELANOMA OF THE BLADDER: AN EXTREMELY RARE CONDITION

Giacomo Di Cosmo[1], Tommaso Silvestri[1], Enrica Verzotti[1], Lorenzo Zandona[2], Rossana Bussani[2], Giovanni Liguori[1] and Carlo Trombetta[1]

[1]Department of Urology, ASUITS - University of Trieste, Trieste, Italy; [2]Department of Pathology ASUITS - University of Trieste, Trieste Italy

Background/Aim: Metastatic malignant melanoma of the bladder is an extremely rare condition with only 25 confirmed clinical cases. In this article we discuss the best management for correct differential diagnosis by presenting an unusual clinical case that required a multidisciplinary approach. *Case Report:* We report a case of a 79-year-old man who had lower urinary tract symptoms and after flexible cystoscopy was found positive for metastatic malignant melanoma of the bladder. We performed a literature search that presented 25 confirmed clinical case reports, most of which were asymptomatic. *Results:* A 79-year-old man came to our attention for emptying and voiding LUTs with the evidence of severe flow obstruction. His medical history described a

malignant melanoma on the right arm diagnosed five years ago, for which he underwent wide local excision and sentinel lymph node biopsy. The histological examination of the excision revealed that the melanoma was ulcerated and infiltrating the reticular derma, with no intratumoral flogistic reaction and moderate perilesional reaction and high mitotic index (five mitosis per mm^2). Clark's level was IV, TNM 2009 was pT3b with surgical borders free from disease (7.46 mm from the deepest border 5.55 mm from the lateral one). Sentinel lymph node biopsy was negative for metastasis. He was regularly followed up and stayed asymptomatic until nowadays when an ultrasonography imaging of the entire abdomen revealed a 25 mm large hyperechogenic lesion on the left liver lobe strongly suspected for secondarism. A transurethral flexible cystoscopy was performed, which revealed a 1 cm hyperemic and elevated area on the bladder neck (3h) on which biopsy was performed. The histology of two samples of bladder mucosa revealed a poorly differentiated neoplasm [immunophenotype: CK 7-; p 63-; CD 45 (LCA)-; S100++; MELAN A++]. The histopathology was therefore consistent with a melanoma metastasis (Figure 1, Figure 2). A total-Body CT-Scan was then performed showing some nodular lesions, among which the largest one sized about 12 mm, on the upper right lung field with other millimetric lesions in other fields. Moreover, at the CT-Scan multiple and spread hypodense lesions were noticed on the liver, the largest one measuring about 38 mm, strongly suggesting metastasis. Finally, scintigraphy was performed and indicated multiple areas suspicious for metastatic bone lesions in most of the ribs in both hemithorax, in all the rachis metamers, on the basin and on the femur head. A diagnosis of stage IV malignant metastatic melanoma was made. The genetic examination revealed a BRAF mutation (V600K). Based on this evidence, treatment with Dabrefenib 150 mg x2/day and Trametinib 2 mg x1/day was indicated. Due to multiple metastatic localizations and the general condition of the patient, no TUR was indicated. Three months since the treatment beginning, the patient showed up a polydistrectual progression of the disease leading to a second line treatment with Dacarbazine. *Discussion and Conclusion:* In this review of the literature we examined, among other works, the autopsy series performed by Das Gupta and Brasfield (125 patients with metastatic melanoma) (1), who found that 18% of patients had metastases to the bladder. The evidence of bladder metastatic malignant melanoma is an exceptionally rare finding and most of the literature reviews performed on this subject suggested less than ten cases in the whole English literature. Malignant melanoma most common sites of metastasis are regional lymph nodes, lungs, liver and brain. For bladder metastasis, when symptomatic, in most of cases, gross hematuria was found. Recently a wider review (2) included 24 known cases of malignant melanoma metastasis in the urinary bladder and, among them, sixteen had hematuria as the main symptom. Most of these patients (sixteen) had synchronous metastases. Documentable urinary obstruction was present in only one reported case although in 1964 a case of a 69 years old man who presented urinary retention as main symptom was reported (3, 4). Moreover, it has also been reported a case of a 75-year-old man who presented bladder metastasis of melanoma with LUTs associated to hematuria and 12 cm large hypogastric mass treated by partial cystectomy. In summary, we could state that even if it is an exceptionally rare finding, metastatic malignant melanoma of the bladder has to be suspected in all patients with clinical history of melanoma presenting hematuria, dysuria or hypogastric disease. Lonely LUTs appear to be an extremely rare finding with only two cases including this as main symptom. Cystoscopy appears to be the most useful diagnostic exam thanks to the direct visualization of the bladder mucosa. The biopsy of the suspicious lesion with morphological examination of the tissue sample and immunohistochemical assessment, are mandatory.

1 Das Gupta T and Brasfield R: Metastatic melanoma. A clinicopathological study. Cancer *17*: 1323-1339, 1964.
2 Meunier R, Pareek G and Amin A: Metastasis of malignant melanoma to urinary bladder: A case report and review of the literature. Case Rep Pathol *2015*: 173870, 2015.
3 Maeda T, Uchida Y, Kouda T, Matsui H, Kawahara Y, Sato T and Nakajima F: Metastatic Malignant melanoma of the urinary bladder presenting with hematuria: a case report. Hinyokika Kiyo *54*: 787-790, 2008.
4 Weston PA and Smith BJ: Metastatic melanoma in the bladder and urethra. Br J Surg *51*: 78-79, 1964.

88

MODERATE HYPOFRACTIONATED POST-PROSTATECTOMY VOLUMETRIC ARC THERAPY WITH IMAGE GUIDANCE (VMAT-IGRT): FEASIBILITY AND ACUTE TOXICITY

Elisa Villa[1], Micaela Motta[1], Andrea Ravasio[1], Raffaella Gualano[1], Sofia Cirelli[2], Giorgia Marai[2] and Vittorio Vavassori[1]

[1]Radiation Oncology Unit, Humanitas Gavazzeni, Bergamo, Bergamo, Italy; [2]Statistic Unit, Humanitas Gavazzeni, Bergamo, Italy

Background/Aim: Moderate hypofractionation may have a role in a post-prostatectomy setting, allowing reduction of treatment time and improving local control, but the risk of toxicity may be increased. The aim of this analysis was to evaluate acute toxicity in patients with prostate cancer (PC) who underwent radical prostatectomy and treated with hypofractionated regimen and volumetric modulated arc

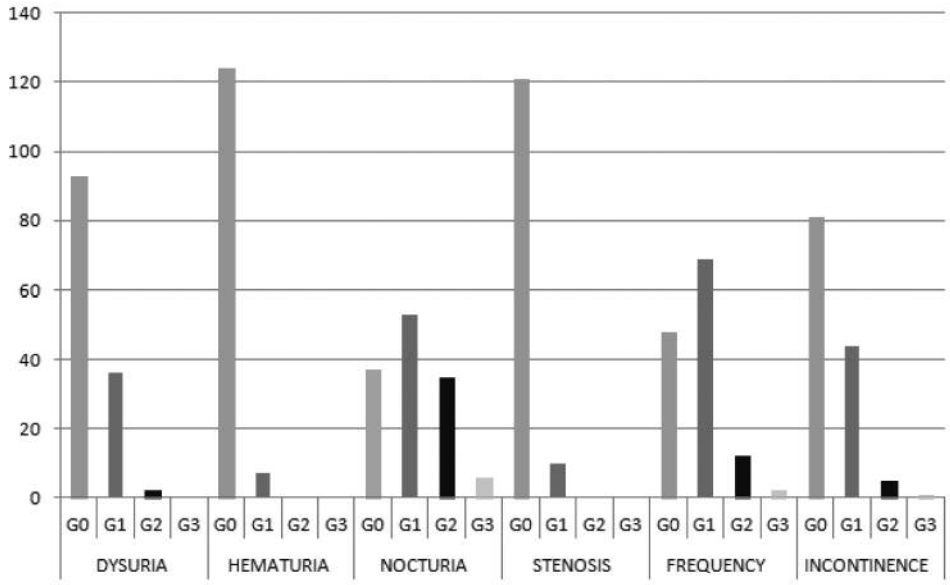


Figure 1. *Acute genitourinary toxicity.*

therapy (VMAT). *Materials and Methods:* From March 2011 to September 2017, 131 patients who underwent radical prostatectomy, received hypofractionated radiotherapy; 89 were treated in an adjuvant setting, because of the presence of at least one histopathological risk factor (Gleason score >7, positive surgical margins, seminal vesicle invasion, extracapsular invasion) and 39 with salvage intent at biochemical relapse (PSA>0.2 ng/ml), or in 3 cases for a clinical relapse. The median age was 67 years old, all the patients had an ECOG performance status of 0 to 2. Seventy-five patients were treated only on prostate bed whereas 56 were treated also on lymph node areas. Eighty-six patients underwent hormonal treatment. Patients were treated with VMAT (RapidArc) and Simultaneous Integrated Boost (SIB) in 30 fractions for a total dose of 66 or 67.5 Gy to the tumor bed (2.2-2.25 Gy/fraction), and 54 Gy to the lymph node volume (1.8 Gy/fraction), respectively. Genitourinary and gastrointestinal toxicities were scored according to CTCAE version 3.0. Urinary symptoms were evaluated also with IPSS questionnaire at baseline and at the end of radiotherapy in 113 patients. *Results:* All the patients completed the planned treatment. Acute gastrointestinal and rectal toxicity was mild with G2 as a maximum grade in 9 patients (6.9%), and none G3. The maximum acute genitourinary toxicity was G3 in 7 patients (5.3%), of whom 5 patients were treated in adjuvant and 2 in salvage setting. G2 acute genitourinary toxicity was observed in 40 patients (30.5%). Analyzing each G3 symptom, we recorded urinary frequency in 2 patients (1.5%), urinary incontinence in 1 patient (0.7%) and nocturia in 6 patients (4.6%) (Figure 1). Maximum grade of dysuria and spasm was G2 in 2 patients (1.5%). No hematuria or stenosis greater than G1 were observed. We also evaluated IPSS score pre- and post-RT in 113 patients and calculated Δ (delta). Mean variation was Δ=6 points (range=[-10]-[+18]). In 18 patients we didn't record any variation between baseline and the end of treatment; 36 patients had an improvement of IPSS score (7 with Δ>5 points - 6.2%) while 59 had an IPSS deterioration (10 with Δ>5 points- 8.8%). *Conclusion:* According to our results, moderate postoperative hypofractionated RT (2.2-2.25 Gy/fraction) seems to be feasible and safe, with a good acute toxicity profile, without unacceptable detrimental effects. Longer follow-up is needed to assess late toxicity and clinical outcomes.

90
STEROTACTIC BODY RADIATION THERAPY FOR LOW AND INTERMEDIATE RISK PROSTATE CANCER: 3 FRACTIONS HYPOFRACTIONATED SCHEDULE

Alessia Farneti[1], Valeria Landoni[2], Maria Grazia Petrongari[3], Biancamaria Saracino[3], Adriana Faiella[3], Giuseppe Iaccarino[2], Antonella Soriani[2], Marilia Ferriero[4], Michele Gallucci[4] and Giuseppe Sanguineti[3]

[1]Department of Radiotherapy Oncology, National Cancer Institute Regina Elena IFO, Rome, Italy; [2]Laboratory of Medical Physics, IFO, Istituto Nazionale Tumori Regina Elena, Rome, Italy;

[3]Department of Radiotherapy Oncology, IFO,
Istituto Nazionale Tumori Regina Elena, Rome, Italy;
[4]Urology, IFO, Istituto Nazionale Tumori
Regina Elena, Rome, Italy

Background/Aim: Due to the low value of alfa/beta of prostate cancer (PCa), hypofractionation has shown to be related with a higher rate of local control; furthermore the increase in delivery capability allows a better sparing of organs at risk. Many studies have been published reporting results from experiences of sterotactic body radiation therapy (SBRT) in low-risk prostate cancer and the 5 fractions schedule has shown to be reasonably safe (1-3). Our aim was to investigate the possibility of an ablative treatment escalating the dose to the prostate while respecting the tolerance of normal surrounding tissue. *Materials and Methods:* Since November 2015, 10 patients have been enrolled in a phase I-II feasibility trial. All patients had low (n=9) or intermediate risk (n=1) PCa, Gleason score (GLS) 6, (3+3; n=9) GLS 7, (3+4; n=1), median PSA 6.28 ng/ml (range=4.52-13.6 ng/ml), median age 75 years (range=69-83 years), median IPSS at accrual was 7 (range=2-13 IPSS). Each patient was asked to fill out questionnaires focusing on quality of life (EORTC QLQ C-30, FACT), urinary incontinence (ICIQ-ST), erectile dysfunction (IIEF-5) and general satisfaction (FACIT-TS-G). Toxicity was graded according to the CTCAE v4.0 scale. Two patients were administered hormonal therapy to reduce the prostate gland volume to about less than 80 ml to fulfill protocol inclusion criteria. Radiotherapy schedule consisted of 40 Gy in 3 fractions administered every other day. All patients underwent a diagnostic multi parametric pelvic magnetic resonance imaging (MRI). Afterwards, patients were specifically prepared with gold fiducials (Visicoils) inserted in the prostate gland and with a gel spacer to delocate rectum. A simulation CT and MRI were acquired with the patient immobilized with either prostep or a personalized immobilization system for Cyberknife (CK) and with urethral catheter. Rectal and bladder filling were controlled also at each treatment. Six patients received a LINAC based treatment while 4 were treated with CK. Accordingly to the treatment machine, treatment plans were generated either by Eclipse TPS by using a VMAT technique with 10 MV FFF photons or Multiplan by using 6 MV FFF photons technique. At the linac, patients underwent a CBCT imaging before and after the delivery of each arc, while at Cyberknife the imaging frame consisted of the acquisition of 1 image per minute. Pretreatment dosimetric verification was performed for each patient. *Results:* Median clinical target volume, *i.e.* prostate gland, (CTV) was 74.6 ml (range=48.2-92) while median planning target volume (PTV) was 115.8 ml (range=78.7-140). Mean dose to 90% of the PTV was 34.4 Gy, 30 Gy were warranted to the border of the target. Doses to 1 ml of organs at risk were kept below 28.4 Gy for rectum, 37.8 Gy for bladder and 21.6 Gy for trigone. Prudently no more than 29.4 Gy were given to 0.1 ml of urethra. In any case maximum doses were below 44 Gy, 110% of the prescription dose. Median follow-up was 6.63 months (range=3-24). One patient showed acute GU grade 2 toxicity and 1 patient showed acute GI grade 2 toxicity. No late toxicity was reported till now. At 6 months median IPSS was 3 (range=1-7), global quality of life was satisfactory for all patients even though a slight decline in sexual performance was reported by 3 patients. *Conclusion:* The proposed schedule of SBRT for PCa administered in 3 fractions seems to be promising in terms of overall satisfaction maintaining a favorable acute toxicity profile. Nevertheless, a longer follow-up is needed to assess the late toxicity and the biochemical disease control. Furthermore, also the difference in treatment delivery due to different technology used may be worth of future investigation.

1 Loblaw A, Cheung P, D'Alimonte L, Deabreu A, Mamedov A, Zhang L, Tang C, Quon H, Jain S, Pang G and Nam R: Prostate stereotactic ablative body radiotherapy using a standard linear accelerator: Toxicity, biochemical, and pathological outcomes Radiother Oncol *107*: 153-158, 2013.
2 Boike TP, TP, Lotan Y, Cho LC, Brindle J, DeRose P, Xie XJ, Yan J, Foster R, Pistenmaa D, Perkins A, Cooley S and Timmerman R: Phase I dose-escalation study of stereotactic body radiation therapy for low- and intermediate-risk prostate cancer. J Clin Oncol *29*: 2020-2026, 2011.
3 Katz A and Kang J: Stereotactic body radiotherapy with or without external beam radiation as treatment for organ confined high-risk prostate carcinoma: A six-year study. Radiat Oncol *9*: 1, 2014.

91

ROBOTIC RADICAL CYSTECTOMY IS ASSOCIATED WITH SHORTER LENGTH OF STAY AND LESS BLOOD LOSS THAN OPEN RADICAL CYSTECTOMY: RESULTS FROM A LARGE MULTICENTER RETROSPECTIVE COHORT

Francesco Soria[1], Marco Moschini[2], Romain Mathieu[3], Killian M. Gust[1], Giuseppe Simone[4], Anoop Meraney[5], Suprita Krishna[6], Morgan Rouprêt[7], Matthew Perry[8], Edward Rowe[9], Guillaume Ploussard[10], Stephen A. Boorjian[11], Peter Wiklund[12], Prasanna Sooriakumaran[13] and Shahrokh F. Shariat[1]

[1]Department of Urology and Comprehensive Cancer Center, Medical University of Vienna, Vienna, Austria;
[2]Department of Urology, Urological Research Institute, San Raffaele Scientific Institute, Milan, Italy;

[3]Department of Urology, Rennes University Hospital, Rennes, France;
[4]Department of Urology, "Regina Elena" National Cancer Institute, Rome, Italy;
[5]Division of Urology, Hartford Healthcare Medical Group, Hartford, CT, U.S.A.;
[6]Department of Urology, University of Minnesota, Minneapolis, MN, U.S.A.;
[7]Department of Urology, Pitié-Salpêtrière Academic Hospital, Department of Urology, Assistance Publique-Hôpitaux De Paris, Pierre and Marie Curie Medical School, Paris 6 University, Paris, France;
[8]Department of Urology, St George's Hospital, London, U.K.;
[9]Department of Urology, Bristol Urological Institute, North Bristol NHS Trust, Southmead Hospital, Bristol, U.K.;
[10]Department of Urology, Saint-Louis Hospital, APHP, Paris 7 University, Paris, France;
[11]Department of Urology, Mayo Clinic, 200 First Street Southwest, Rochester, MN, U.S.A.;
[12]Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden;
[13]Department of Uro-oncology, University College London Hospital NHS Foundation Trust, London, U.K.

Background/Aim: Utilization of robotic assisted radical cystectomy (RARC) is rapidly increasing. However, to date, open radical cystectomy (ORC) preceded by neoadjuvant chemotherapy, still represents the standard of treatment for muscle-invasive and high-risk non-muscle invasive bladder cancer. A partially criticized randomized trial reported no difference in perioperative morbidity but did not assess long term complications. On the other hand, retrospective investigations reported better perioperative outcomes for RARC. However, the lack of a control group in many of these reports, the relatively short follow-up and the relatively small number of patients included (especially for the robotic arm), limited the conclusions. Since the results from large prospective trials are still lacking, the effectiveness of RARC *vs*. ORC in terms of perioperative outcomes is still a matter of debate. Therefore, the aim of our study was to evaluate the morbidity, including perioperative quality indicators as well as 30 and 90-days complications, of RARC *vs*. ORC in a large multicenter retrospective cohort of patients. *Materials and Methods:* Patients who underwent radical cystectomy at 10 referral centers were included. Only patients with complete data about perioperative outcomes were retained for the analyses. Outcomes collected included blood loss, operative time and time to discharge complications, readmission, reoperation and mortality rates at 30 and 90 days. First, multiple imputation was performed to handle missing data for preoperative variables. Second, to account for selection bias, differences in baseline characteristics were controlled for with inverse probability of treatment weighting (IPTW) analysis. IPTW-multivariable-adjusted regression and logistic analyses were performed to evaluate the impact of RARC and ORC on perioperative outcomes. *Results:* Overall, 1,552 patients (1,197 RARC and 355 ORC) patients with complete data regarding perioperative outcomes were enrolled in the study. After IPTW-adjusted analysis, no difference between groups in terms of preoperative characteristics such as age, gender, body mass index (BMI), ASA score and clinical stage were observed. Overall, 664 and 413 patients experienced at least one complication at 30 and 90 days from surgery, respectively. In multivariable regression analyses that adjusted for the effects of preoperative characteristics, year of surgery and type of urinary diversion, RARC was associated with reduced blood loss ($p<0.001$), shorter length of stay ($p=0.02$) and increased operation time ($p<0.001$). On multivariable logistic analyses that adjusted for the same variables, RARC was not associated with 30-days ($p=0.06$) and 90-days ($p=0.5$) complications rates. Conversely, RARC was associated with an increased readmission rates, both at 30 ($p=0.001$) and 90 days ($p<0.001$). Similar results were obtained when the analyses were adjusted for the effects of pathologic characteristics. *Conclusion:* We found no difference in 30- and 90-days complications. We confirmed that RARC is associated with less blood loss and shorter length of stay compared to ORC. On the other hand, ORC is associated with shorter operative time and less readmissions.

92

PROSPECTIVE EVALUATION OF EARLY COMPLICATION RATE IN PATIENTS SUBMITTED TO RADICAL CYSTECTOMY AND URINARY DIVERSION

Tommaso Prayer Galetti, Valeria Lami, Alex Anh Ly Nguyen, Francesco Cattaneo and Filiberto Zattoni

Department of Surgery, Oncology, and Gastroenterology - Urology Clinic, University of Padua, Urology Clinic, University of Padua, Padua, Italy

Background/Aim: Radical cystectomy is a complex procedure with high-risk of perioperative complications and readmission rates. The aim of our study was to evaluate 30 and 90 days complication rate using prospectively a standardize methodology and comparing medical, nurse and administrative records. *Patients and Methods:* We analyzed prospectively collected records of 145 consecutive patients who underwent radical cystectomy at our Institution from January 2015 to June 2017. All patients were treated following a standardized protocol. Complications were classified

according to Clavien-Dindo and related to previous medical history, ASA score, Age Adjusted Charlson Comorbidity Index (ACCI), operating surgeon, blood loss, operative time, transfusions rate, type of urinary diversion, pre- operative and 3-days post-operative blood count and creatinine levels, postoperative patients' mobilization time, nasogastric tube removal, free diet restarting. Furthermore, complications were analyzed comparing medical and nurse records during hospital stay and at 30 and 90 days following patients' discharge. *Results:* Our population had 4.18 male:female ratio with a 69.25 years mean age (median 71±10.41), and a 26.51 mean body mass index (BMI) (median 26.30±3.64). Median ASA score was 2 in 87 patients (60%) while the other 40% were ASA score 3 or more. Median ACCI was 6, with 82.76% of patients having ACCI >4 and 33.8% of patients ACCI >6. In our population of patients undergoing cystectomy, 102 received a Wallace external urinary diversion (70.34%), 29 (20%) an orthotopic ileal bladder (VIP: Vescica Ileale Padovana) and 12 an ureterocutaneus diversion (8.27%). Two patients (1.37%) did not receive urinary diversion because radical cystectomy was associated to bilateral nephroureterectomy. Mean operative time was 349.75 min and mean blood loss 802.96 ml. Mean patients' hospital stay was 18.54 days (median 16±8.88) with 18.04 days in patients undergoing Wallace urinary diversion and 20.89 days in those undergoing VIP orthotopic ileal bladder. Among patients submitted to VIP diversion, those living within 60 Km from the hospital had a mean recovery length of 19.31 days while those living further had a longer (22.78 days) hospital stay. Re-admission rate was 5.5% and 2.76% at 30 and 90-day after patients' discharge. Relevant complications were observed in 56 patients (38.62%) during post operatory hospital time. 29 complications were Clavien-Dindo 1-2 (51.78%) while 27 (48.2%) were Clavien 3-4. No Clavien-Dindo complication 5 was observed. Clavien-Dindo complications 3-4 did not relate to preoperative characteristics, ASA score and ACCI or operatory parameters such as surgeon, operative time, blood loss, and transfusion rate. Relevant complications were observed to be related to ileus resection for urinary diversion. Post-operatory ileum was observed in 16 patients (11%), requiring surgery in 62.5% of cases. All patients with mechanical ileum were previously submitted to Wallace or VIP diversion and 60% had a previous abdominal surgery. Wound complications were observed in 11 patients (7.58%) and were associated to ACCI with 60% of patients having ACCI >6. No difference in complication rates was observed stratifying patients by urinary diversion type. Length of operative time was not associated with increased risk of intestinal or wound complication. A significant difference in patients' mobilization was observed between medical and nurse records (mean 3.73 days±2.62 *vs.* 4.6±2.77; p=0.006). Among patients re-admitted at 30 and 90 days we verified respectively a 37.5% and 50% rate of Clavien-Dindo 3-4 complications. Noteworthy all patients readmitted at 90 days had a preoperative ACCI >6. *Conclusion:* In our high median ACCI population of patients submitted to radical cystectomy and urinary diversion early Clavien-Dindo 3-4 complications did not relate to preoperative or operative parameters. In this population intestinal resection was the main reason of postoperative Clavien-Dindo 3-4 complications, while preoperative ACCI >6 was related to wound problems. Operative time did not correlate to wound complication probably because of a routine use of antibiotic recall after 4 hours of surgery. At our institution distance between patients' residence and hospital influenced hospitalization length. Our prospective analysis reports a mismatching between medical and nurse records, calling for a higher degree of interaction between healthcare providers. A longer hospitalization time may reduce, in high-risk patients, hospital 30-90-day readmissions and Clavien-Dindo 3-5 complication rate. Fragile Patients with Age Adjusted Charlson Comorbidity Index (ACCI) >6 are at risk for 90-days hospital readmission.

93

DISCREPANCY IN TRANSRECTAL ULTRASOUND GUIDED PROSTATE BIOPSY: A PROSPECTIVE CLINICAL TRIAL

Simone Morselli, Arcangelo Sebastianelli, Ferdinando Daniele Vitelli, Riccardo Fantechi, Gianmartin Cito, Andrea Mari, Graziano Vignolini, Andrea Minervini, Alberto Lapini, Mauro Gacci, Marco Carini and Sergio Serni

Department of Urology, Careggi University Hospital, Florence, Italy

Background/Aim: At present time, prostate cancer (PCa) is the second most diagnosed cancer in men. The mortality associated with the disease is low, thus PCa is sometimes considered overtreated, with both surgery and radiation therapy. Literature suggests that almost half cases may be managed with deferred treatment, as it would not impact life expectancy of patients, because treatment may change their Quality of Life (QoL). As low risk-PCa may be managed conservatively, high- and intermediate-risk disease requires an active treatment. For these reasons, correct staging and accurate biopsy are fundamental. *Materials and Methods:* Patients that were candidates to random Trans Rectal Ultrasound (TRUS) guided prostate biopsy at our center from May 2016 were selected. Exclusion criteria were age >71 years, prostate-specific antigen (PSA) level <3 ng/ml or >20 ng/ml and previous diagnosis of PCa. Prior negative biopsies were admitted in the study. A further selection was made among the PCa positive biopsy, based on the treatment offered. Definitive histopathological analysis from patients submitted to radical prostatectomy and previous

biopsy were evaluated. In these patients, age, core numbers, discrepancy rate, PSA level, PSA density, familiar history of PCa, presence of high-grade prostate intraepithelial neoplasia (HG-PIN) and digital rectal examination (DRE) were evaluated. Pearson's Chi-square and Student's *t*-test were used for statistical analysis. *Results:* A total of 227 patients were enrolled. Mean age was 62.6 years [standard deviation (SD)=6.3], median biopsy cores number was 14 [interquartile range (IQR)=14-16], mean prostate-specific antigen (PSA) level was 7.3 ng/ml (SD=3.6). A familiar history of PCa was found in 45 patients (19.8%), median prostate volume was 36 ml (IQR=21-48). PCa positive biopsies were 95 (41.9%) and 71 patients accepted radical prostatectomy (31.3% of the total, 74.7% of positive biopsies), the others begun active surveillance protocol or underwent radiation therapy. Bioptic histopathological evaluation found a Gleason Score (GS) 3+3 in 36 (37.9%), GS 3+4 in 35 (36.8%), GS 4+3 in 11 (11.6%), GS 4+4 in 9 (9.5%), GS 4+5 in 3 (3.2%) and GS 5+4 in 1 (1.1%). PCa detection was not related to bioptic core number at statistical analysis. At definitive pathological examination, a discrepancy between bioptic cores and complete prostate analysis was found in 31 patients (43.6%), with an upgrading of D'Amico Risk Class in 16 (22.5%). Results are shown in Table I. However, none of the factors analyzed was correlated with the discrepancy. High PSA value and positive DRE were associated with a higher PCa diagnosis at Student's *t*-test and Pearson's Chi Square analysis ($p<0.05$). Our results were in line with literature for the incidence on PCa on prostate biopsy and even for the rate of histological discrepancy (1). Pokorny *et al*. found a 14,7% of under staging with Magnetic Resonance Imaging (MRI) guided prostatic biopsies, and a 24% of under staged diseases with TRUS only guided biopsies, so not even the help of MRI may avoid this problem, as some significant PCa may be missed with MRI (1). Gandaglia *et al*. has also recently raised the awareness on proposing active surveillance or non-radical treatment to PCa, since contemporary PCa patients seem to have more aggressive cancer characteristics compared to patients included in previous trials (2). If this trend is confirmed, the current PCa treatment approach should be reconsidered (2). *Conclusion:* PSA and DRE are associated with PCa detection at biopsy; however, prostate biopsy alone may underestimate the disease stage and lead to inappropriate patient treatment. Further studies are needed to increase the diagnostic accuracy of prostate biopsy, since recent evidence raised its importance for a correct approach to PCa.

1 Pokorny MR, de Rooij M, Duncan E, Schröder FH, Parkinson R, Barentsz JO and Thompson LC: Prospective study of diagnostic accuracy comparing prostate cancer detection by transrectal ultrasound–guided biopsy *versus* magnetic resonance (MR) imaging with subsequent MR-guided biopsy in men without previous prostate biopsies. Eur Urol *66(1)*: 22-29, 2014.

2 Gandaglia G, Tilki D, Zaffuto E, Fossati N, Pompe RS, Dell'Oglio P, Graefen M, Montorsi F and Briganti A: Are the results of the prostate testing for cancer and treatment trial applicable to contemporary prostate cancer patients treated with radical prostatectomy? Results from two high-volume European institutions. Eur Urol Focus *197(4)*: (Suppl)e984, 2017.

Table I. *Discrepancy rate in D'Amico risk class in prostate cancer positive patients who underwent radical prostatectomy (n=71).*

	Similarity (n=40)	Discrepancy (n=31)	*p*-Value
PCa family history, n (%)			
Absent	33 (82.5%)	25 (80.6%)	0.548
Present	7 (17.5%)	6 (19.4%)	
DRE, n (%)			
Negative	8 (20.0%)	5 (16.1%)	0.418
Suspect	18 (45.0%)	17 (54.9%)	
Positive	14 (35.0%)	9 (29.0%)	
PIN-HG at biopsy, n (%)			
Absent	38 (95.0%)	30 (96.8 %)	0.914
Present	2 (5.0%)	1 (3.2%)	
PSA density ng/ml/cc (mean, SD)	0.32 (0.18)	0.41 (0.29)	0.126
PSA level ng/ml (mean, SD)	7.87 (4.25)	7.79 (3.39)	0.244
Core number (median, IQR)	14 (14-14)	14 (14-16)	0.424

PCa, Prostate cancer; DRE, digito rectal examination; PIN-HG, prostatic intraepithelial neoplasia – high-grade; PSA, prostate-specific antigen.

94
HYPOFRACTIONATED STEREOTACTIC RADIOTHERAPY WITH CYBERKNIFE® SYSTEM IN LOCALIZED PROSTATE CANCER: A MONOISTITUTIONAL EXPERIENCE

Valetina Borzillo[1], Rossella Di Franco[1], Giuseppe Totaro[1], Gianluca Ametrano[1], Fabrizio Cammarota[1], Giuseppe Quarto[2], Domenico Sorrentino[2], Sisto Perdonà[2] and Paolo Muto[1]

[1]Division of Radiotherapy, Istituto Nazionale Tumori-IRCCS- Fondazione G. Pascale, Naples, Italy; [2]Division of Urology Oncology Surgery, Istituto Nazionale Tumori- IRCCS- Fondazione G. Pascale, Naples, Italy

Background/Aim: Hypofractionated Stereotactic radiotherapy (HySRT), that delivers higher dose on the target tissue in small number (≤5) of fractions with low dose to adjacent organs- at-risk, is increasingly used in the treatment of localized prostate cancer (LPC), given the favorable

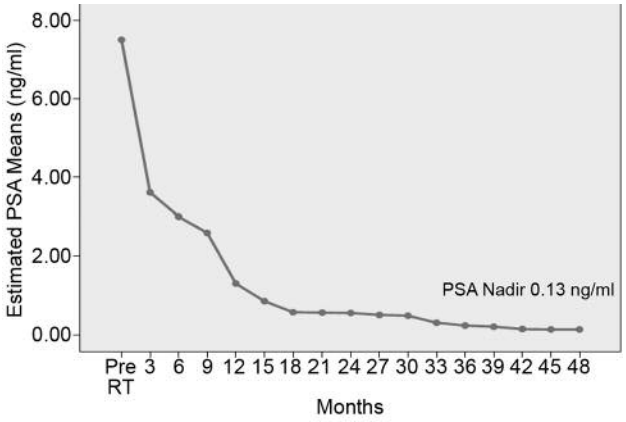


Figure 1. *The course of PSA means during follow-up.*

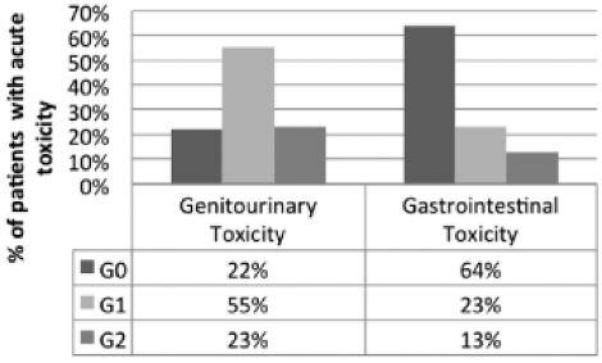


Figure 2. *Acute toxicity.*

Table I. *Patient and tumor characteristics (N=102).*

Characteristics		
	years	(range)
Median age	72	(46-88)
	n	(%)
Tumor staging		
T1	37	(36.3%)
T2	65	(67.7%)
Gleason score		
>7	24	(23.5%)
<7	78	(76.5%)
RT Site		
Prostate only	40	(39.2%)
Prostate and seminal vesicles	62	(60.8%)
Hormonal therapy		
No	76	(74.5%)
Yes	26	(25.5%)
PSA at diagnosis		
Mean	8.2 ng/ml	
Median	7.4 ng/ml	
PSA at diagnosis		
<10 ng/ml	78	(76.5%)
>10 ng/ml	24	(23.5%)
PSA pre-RT		
Mean	6.8 ng/ml	
Median	6.48 ng/ml	
PSA pre-RT		
<10 ng/ml	83	(81.4%)
>10 ng/ml	19	(18.6%)
Dose		
35 Gy	67	(65.7%)
36,25 Gy	35	(34.3%)

RT, Radiotherapy; PSA, prostate-specific antigen.

radiobiological profile of prostate cancer (PCa) at high radiation doses (1, 2, 3). In this study we reported our initial experience with HySRT using CyberKnife® System (CK) in the treatment of LPC. *Patients and Methods:* From February 2013 to October 2017, 123 patients with LPC, median age 72 years, were treated with CK-HySRT. Ten days before the HySRT, all patients were submitted to the eco-guided implants of 4 gold intraprostatic fiducial markers to allow CK to track, detect and correct target movements during the radiotherapy session. All patients underwent a simul-CT and MRI, and contouring was performed on image fusion. All patients were treated with CK HySRT in 5 fractions of 7-7.25 Gy/fraction for a total dose of 35-36,25 Gy. Acute and late gastrointestinal (GI) and genitourinary (GU) toxicity was evaluated using RTOG scale, biochemical control using mean decrease of PSA level during follow-up. In this study, we have analyzed the results in the 102 patients with almost 3 months of follow-up. *Results:* Overall, 102/123 patients that had almost 3 months of follow-up and were analyzed. Patients and tumor characteristics are shown in Table I. Median follow-up was 17 months. Three patients died of non-related cancer causes. Gastrointestinal acute toxicity was 23% and 13% for G1 and G2 (perineal pain and rectal tenesmus), respectively (Figure 2). Genitourinary acute toxicity was 55% for G1 (dysuria) and 23% for G2 (urgency and nocturia) (Figure 2). G2 Genitourinary late toxicity was 4% (Figure 4) and G2 Gastrointestinal late toxicity (Figure 3) was 3%. All patients responded with decreased levels of PSA (Figure 1). The PSA drop between the start of the therapy and 21 months of follow-up, was significant with $p<0.01$ ($p=0.00001$). *Conclusion:* HySRT is an effective and safe treatment option for patients with LPC. The results of multiple prospective trials have shown biochemical control rates of 90%-100% for low-risk and 84%-100% for intermediate-risk PCa, and the

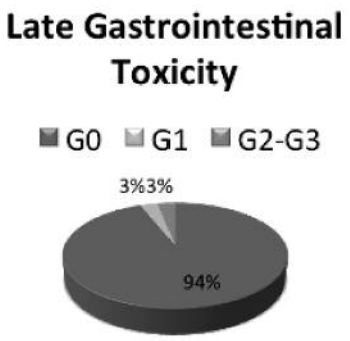


Figure 3. *Late gastrointestinal toxicity.*

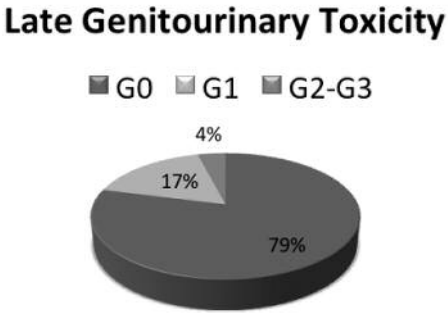


Figure 4. *Late genitourinary toxicity.*

average incidence of grade G3, GI or GU toxicity ranges between 0.17%-0.28% and 0.61%-1.61% for acute and late effects, respectively. In our experience CK-HySRT seems to be safe and reliable in the treatment of LPC. No severe toxicities were reported and the patients were very compliant. Careful patient selection is critical to achieve maximum effectiveness by CK HySRT. More patients and longer follow-up are necessary in order to evaluate the real advantage of HySRT with respect to standard fractionation in terms of overall survival, biochemical free survival and late toxicity.

1. Katz AJ, Santoro M, Diblasio F and Ashley R: Stereotactic body radiotherapy for localized prostate cancer: disease control and quality of life at 6 years. Radiat Oncol *8*: 118, 2013.
2 Kishan AU and King CR: Stereotactic Body Radiotherapy for Low- and Intermediate-Risk Prostate Cancer. Semin Radiat Oncol *27*: 268-278, 2017.
3 De Bari B, Arcangeli S, Ciardo D, Mazzola R, Alongi F, Russi EG, Santoni R, Magrini SM and Jereczek-Fossa BA; on the behalf of the Italian Association of Radiation Oncology (AIRO): Extreme hypofractionation for early prostate cancer: Biology meets technology. Cancer Treat Rev *50*: 48-60, 2016.

95

SURGICAL OUTCOMES AND PERIOPERATIVE MORBIDITY OF CLAMP *VS*. OFF-CLAMP LAPAROSCOPIC PARTIAL NEPHRECTOMY

Roberto Sanseverino, Olivier Intilla, Giovanni Molisso, Tommaso Realfonso and Giorgio Napodano

Department of Urology, Umberto I Hospital - ASL Salerno, Nocera Inferiore, Salerno, Italy

Background/Aim: Nephron sparing surgery (NSS) is now reference standard for many T1 renal tumors. To reduce renal damage, several techniques have been proposed; cold ischemia, artery clamping, selective artery clamping, zero ischemia. We retrospectively compared perioperative results of clamp *vs*. no clamp procedure in patients affected by T1 renal cancer. *Materials and Methods:* From the database of our institution we reviewed patients affected by single, clinical T1 tumor who underwent a laparoscopic partial nephrectomy (LPN). A transperitoneal approach was performed in all patients. In Clamp LPN group renal artery was clamped using laparoscopic Bull dog. In off-clamp group, a controlled hypotension, to carefully lower the mean arterial pressure (MAP) while

Table I. *Baseline characteristics.*

	Clamp group	Off-clamp group	*p*-Value
Patients			
n	59	67	
Age			
years	59.8±13.6	58.4±12.4	0.57
BMI	28.5±4.6	27.8±5.3	0.56
cTumor size			
mm	40.5±11.7	42.7±15.4	0.41
pTumor size			
mm	44.7±16.4	41.3±16.0	0.40
ASA score (%)			
I	6.1	5.9	0.56
II	39.4	47.1	
III	51.5	45.1	
IV	3.0	1.9	
Renal (%)			
Low	17.0	20.3	
Medium	57.6	72.5	
High	25.4	7.2	

BMI, Body mass index; ASA, American Society of Anesthesiologists.

Table II. *Operative outcomes*.

	Clamp group	Off-clamp group	*p*-Value
Operative time min	214.5±56.6	147.6±54.7	0.001
Resection time min	6.9± 2.9	8.5±4.6	0.46
Suture time min	16.3±7.3	9.6±6.4	0.006
Blood loss min	747.4±706.3	357.1±340.4	0.001
Hb drop gr/dl	2.3±1.7	2.1±1.1	0.51
Transfusion (n)			
0	33	58	0.002
1	13	3	
2	5	5	
3	8	0	
Hospitalization Days	10.2	7.4	0.03

Table III. *Histological outcomes*.

	Clamp group	Off-clamp group	*p*-Value
Type			
RCC	38	34	
Chromophobe	1	5	
Papillary	6	12	
Unclassifiable	1	1	
Oncocytoma	6	9	
AML	3	3	
Benign	4	3	
Stage			
T1a	26 (56.5)	25 (48.1)	0.87
T1b	15 (32.6)	20 (38.5)	
T2	1 (2.2)	2 (3.8)	
T3a	4 (8.7)	5 (9.6)	
Positive surgical margins	1 (1.7%)	0	

RCC, Renal cell carcinoma; AML, angiomyolipoma.

Table IV. *Perioperative complications*.

	Clamp group	Off-clamp group
Hemorrhage	2 (3.4%)	0
Diaphragmatic lesion	2 (3.4%)	1 (1.5%)
Urine leakage	3 (5.1%)	2 (3.0%)
Pneumothorax	1 (1.7%)	0
Fever	2 (3.4%)	5 (7.5%)

maintaining excellent systemic perfusion, was maintained at approximately 60 mmHg. To induce hypotension, the dose of inhalational isoflurane was increased. The renal lesion was excised using cold Endoshears. Parenchyma was repaired with Vicryl™ sutures arrested with absorbable clips and Hem-O-lok™ . In clamp group bull dog was removed while in the off –clamp group blood pressure was restored to preoperative levels. Biologic hemostatic agents and Surgicel™ were applied to the resection bed when appropriated. *Results:* We identified 59 patients in the clamp group and 67 in off-clamp group; baseline characteristics of the two groups are described in Table I. Patients of the off-clamp group presented significant less operative time, blood loss and transfusion rate than the clamp group. Hospitalization and suture time were also shorter for off-clamp group (Table II). No significant differences were observed in terms of histological evaluation (Table III). Postoperative complications were rare (Table IV). *Conclusion:* Clamp and off-clamp laparoscopic partial nephrectomy are equally safe and reproducible techniques in terms of perioperative outcomes and complications. However, the appropriate procedure should be selected taking into account tumor complexity, patient comorbidity and surgeon experience.

96
TRANSPERINEAL MRI-TARGETED PROSTATE BIOPSY UNDER LOCAL ANAESTHESIA: DOES TARGETED SAMPLING INFLUENCE PROCEDURAL FEASIBILITY?

Alessandro Marquis[1], Stefano Tappero[1], Daniele D'agate[1], Giancarlo Marra[1], Marco Agnello[1], Marco Oderda[1], Marco Falcone[1], Marco Allasia[1], Andrea Zitella[1], Riccardo Faletti[2], Laura Bergamasco[2], Luca Molinaro[3] and Paolo Gontero[1]

[1]Department of Urology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy; [2]Department of Radiology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy; [3]Department of Pathology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy

Background/Aim: To date, MRI targeted prostate biopsies (TBx) are vastly performed for the diagnosis of prostate cancer (PCa). Many authors still suggest the carrying-out of a systematic sampling (SC) after the targeted cores (TC). The

leading aim of our study was the evaluation of the morbidity of TBx under local anaesthesia (LA) using a transperineal freehand approach (TPF), in particular focusing on the impact of TC added to the SC in the TPFTBx. *Materials and Methods:* From September 2016 to July 2017, two cohorts of men were enlisted in a prospective single centre study: the first one underwent LA TPFTBx (TC, 4 cores per target + SC) using Esaote fusion platform and the other one TPFSBx (12 SC only). Clinical and pathological data, complications, procedural timings, VAS pain scale, IPSS and IIEF-5 were collected before, during and at 40 days from the procedure. Men >80 years, with PSA>20ng/ml or with previous PCa diagnosis were excluded. Continuous and categorical variables were compared using Mann-Whitney and Fisher or Chi square test respectively. *Results:* The study included 137 and 110 patients respectively undergone TBx and SBx. TBx showed a clinically significant (CS) PCa detection rate of 55.5%. Between the two groups, the only significant baseline differences were recorded about the number of specimens taken (TBx 15.1±2.4; SBx 12.1±0.3; $p<0.01$) and the number of Bx naïve patients (TBx 46.7%; SBx 81.8%; $p<0.01$). Overall, no significant differences were present in: A) periprocedural pain (TBx VAS 5.1±2.5; SBx VAS 4.9±2.2; $p=0.45$), with previous biopsy status not influencing peri-procedural pain ($p=0.58$); B) periprocedural complications (urinary retention, TBx n=2, SBx n=1, $p>0.99$; vasovagal reaction TBx n=4, SBx n=3, $p>0.99$); C) post-procedural complications (hematuria TBx 73.8%, SBx 76.6%, $p=0.73$, lasting 9.1±8.9 days for TBx and 9.0±8.2 days for SBx, $p=0.9$; hematospermia, TBx 52.8%, SBx 57.5%, $p=0.56$, lasting 19.5±13.3 days for TBx and 21.4±13.4 days for SBx, $p=0.3$). No cases of major complications (Clavien ≥3), infections or sepsis were recorded. IIEF-5 and IPSS did not significantly vary from pre to post-procedural assessment and amongst the two groups (ΔIPSS $p=0.32$; ΔIIEF-5 $p=0.28$). Longer timings were required to perform TBx (18.7±6.2 *vs*. SBx 11.2±3, $p<0.01$) due to MRI and TRUS imaging overlap (6.5±3.9min) and TC sampling (3.4±2.3 min per target). *Conclusion:* TPFTBx performed in ambulatory setting under LA provides a remarkable CSPCa detection rate and moreover is safe and well-tolerable. Adding TC to SC does not influence patient pain neither peri- and post-procedural complication rate, only increases the duration of the biopsy.

97
PRIMARY TRANSRECTAL RANDOM PROSTATE BIOPSY: IS STILL ACTUAL?

Giorgio Napodano[1], Antonio Campitelli[1], Tommaso Realfonso[1], Giovanni Molisso[1], Olivier Intilla[1], Maria Addesso[2] and Roberto Sanseverino[1]

[1]Department of Urology, Umberto I Hospital - ASL Salerno, Nocera Inferiore,, Salerno, Italy; [2]Department of Pathology, Umberto I Hospital - ASL Salerno, Salerno, Italy

Background/Aim: Random prostate biopsy is still the gold standard procedure to detect prostate cancer. Multiparametric MRI has been introduced to guide target prostate biopsy to improve detection of clinically significant prostate cancer. Today it is debated whether primary biopsy should be performed with random or target approach. We evaluated outcomes of patients who had undergone first transrectal random prostate biopsy. We also evaluated predictive factors of prostate cancer diagnosis. *Materials and Methods:* Patients suspicious of prostate cancer based on prostate-specific antigen (PSA), digital rectal examination (DRE), ultrasound findings underwent a TRUS guided transrectal biopsy. Procedures were performed under local anesthesia or intravenous sedation as indicated. Clinical and pathological data were prospectively collected from May 2010 to September 2017 in our database. We calculated cancer detection rate and we identified predictive factors of cancer. Statistical analysis was performed using Chi square test, Mann Whitney, logistic regression test, as appropriate (SPSS 19). *Results:* Data on 1974 patients were available. Patient characteristics are reported in Table I. Indications for biopsy are reported in Table II. Prostate cancer has been diagnosed in 46.4% of the patients (Table III). There is an increasing trend in cancer detection rate per year (Table IV). Positive patients presented ≥3 positive cores or Gleason ≥3+4 in 78.5% and 86.7%, respectively. At multivariate analysis, age, PSA, DRE, prostate volume, number of cores, and year of biopsy are predictive of cancer diagnosis (Table V). *Conclusion:* Random transrectal prostate biopsy identified cancer in 46% of all patients. In the last three years, cancer detection rate is more than half of the patients. More than three quarters of patients presented a clinically significant cancer. Age, PSA, positive DRE, prostate volume and number of cores are correlated with the presence of cancer.

Table I. *Patient characteristics*.

Age (years)	66.3
BMI (n)	27.4±8.4
PSA (ng/ml)	14.9±39.8
Prostate volume (ml)	60.8±3.3
PSA density	0.28±0.79
Core number (n)	12.7±2.8
Positive DRE (%)	37.9

BMI, Body mass index; PSA, prostate-specific antigen; DRE, digital rectal examination.

Table II. *Indication for biopsy.*

	%
PSA	70.7
PSA+DRE	27.3
PSA+TRUS	0.2
DRE	1.7
TRUS	0.1

PSA, Prostate-specific antigen; DRE, digital rectal examination; TRUS, transrectal ultrasound.

Table III. *Prostate biopsy results.*

Result	%
BPH	40.0
ASAP	4.3
HGPIN	9.3
Cancer	46.4

BPH; Benign prostatic hyperplasia; ASAP, atypical small acinar proliferation; HGPIN; high-grade prostatic intraepithelial neoplasia.

Table IV. *Cancer detection rate per year.*

Year	Patients (n)	Cancer detection rate (%)
2010	176	39.2
2011	266	41.7
2012	303	37.6
2013	309	46.9
2014	239	50.9
2015	307	53.1
2016	205	54.2
2017	169	49.1

Table V. *Multivariate analysis for cancer detection rate.*

Variable	*p*-Value	OR	95% CI
Age	0.002	1.034	1.012-1.056
BMI	0.13	1.019	0.994-1.044
+DRE	<0.001	0.293	0.212-0.407
PSA	<0.001	0.939	0.909-0.971
Prostate volume	<0.001	0.986	0.977-0.994
Core number	<0.001	0.874	0.816-0.937
Year of biopsy	<0.001	1.101	1.055-1.149

OR, Odds ratio; CI, confidence interval; BMI, body mass index; DRE, digital rectal examination; PSA, prostate-specific antigen.

99

COMPLICATIONS AFTER RANDOM TRUS GUIDED TRANSRECTAL PROSTATE BIOPSY

Giorgio Napodano[1], Antonio Campitelli[1], Tommaso Realfonso[1], Olivier Intilla[1], Giovanni Molisso[1], Maria Addesso[2] and Roberto Sanseverino[1]

[1]Department of Urology, Umberto I Hospital - ASL Salerno, Nocera Inferiore, Salerno, Italy; [2]Department of Pathology, Umberto I Hospital - ASL Salerno, Nocera Inferiore, Salerno, Italy

Background/Aim: Prostate biospy is the gold standard procedure to diagnose prostate cancer. The technique is usually performed under transrectal ultrasound (TRUS) guidance with transrectal or transperineal approach. Every year more than 1 million procedures are realized in Europe. Complication rate is quite low; however, fearsome infectious complications are increasing. We have retrospectively evaluated complication rate in our database and analyzed predictive factor of complications. *Materials and Methods:* Databases of our institution were evaluated regarding complications of patients who had undergone transrectal random prostate biopsy for suspicion of prostate cancer. Complications were classified as bleeding more than 3 days after biopsy (hematuria, hematospermia, rectal bleeding), infection defined as fever more than 38˚C, acute urinary retention (AUR). Hospitalization due to complication has also been recorded. We correlated every complication with age, prostate volume, prostate-specific antigen (PSA), PSA density, body mass index, number of cores, cancer detection, diabetes mellitus, previous urinary or genital infection, chronic obstructive pulmonary disease (COPD), previous urological surgery, previous or concomitant tumor. Statistical analysis was performed using Chi-square test, Mann Whitney, logistic regression test, as appropriate (SPSS 19). *Results:* Data on 2,106 patients were collected. Patient characteristics are reported in Table I. Complications occurred in 6.4% of the patients (Table II). Multivariate analysis revealed correlation only for infection with previous history of urinary or genital infection [$p<0.001$, odds ratio (OR)=0.012, 95% confidence interval (CI)=0.001-0.162] (Table III). A minority of patients (15/2,106, 0.7%) required hospitalization because of complications (11 for infection, 2 for hematuria, 1 for rectal bleeding, 1 for AUR). However, 11.2% (15/134) of patients with complications needed hospital admission. Previous urinary or genital infection was the only factor associated with hospitalization ($p<0.001$). *Conclusion:* Transrectal random prostate biopsy is a common and safe procedure. Complications rate is generally low (6.4%); hematospermia is more frequent complication (4.7%). Hospitalization is rarely needed (0.7%). However fearsome and life-threatening infectious complications are main causes of hospital admission.

Table I. *Patient characteristics*.

Patients (n)	2,106
Age (years)	69.4±8.0
BMI	27.3±8.2
Positive DRE (%)	37.2
PSA (ng/ml)	14.6±39.0
Prostate volume (cc)	59.7±30.7
PSA density	0.28±0.79
Cores (n)	12.6±3.2
PCa (%)	46.8
Diabetes (%)	12.2
COPD (%)	3.4
UTI (%)	2.0
Urological surgery (%)	3.7
Urological tumors (%)	3.4
Other tumors (%)	2.9
Neurological disease (%)	2.5
Any concomitant disease (%)	23.7

BMI, Body mass index; DRE, digital rectal examination; PSA, prostate-specific antigen; Pca, prostate cancer; COPD, chronic obstructive pulmonary disease; UTI, urinary tract infection.

Table II. *Complications of prostate biopsy.*

	%
Infection	2.1
Hematuria	2.2
Hematospermia	19.8
Rectal bleeding	0.2
Acute urinary retention	0.9
Hospitalization	0.7
Overall complications	24.7

100
CLAMPLESS LAPAROSCOPIC PARTIAL NEPHRECTOMY (LPN): PRELIMINARY EXPERIENCE

Roberto Sanseverino[1], Olivier Intilla[1], Giovanni Molisso[1], Tommaso Realfonso[1], Maria Addesso[2] and Giorgio Napodano[1]

[1]Department of Urology, Umberto I Hospital - ASL Salerno, Nocera Inferiore, Salerno, Italy; [2]Department of Pathology, Umberto I Hospital - ASL Salerno, Nocera Inferiore, Salerno, Italy

Background/Aim: Nephron-sparing surgery is the current reference standard for many T1 renal tumors. Although hilar clamping creates a bloodless operative field, it necessarily imposes kidney ischemic injury. "Zero ischemia" partial nephrectomy allows to eliminate ischemia during nephron sparing surgery. We report our experience of "zero ischemia" laparoscopic partial nephrectomy realized by controlled hypotension. *Materials and Methods:* Patients with a single, T1 stage tumor were candidates for "zero ischemia" laparoscopic partial nephrectomy. High-risk patients with severe, preexisting, cardiopulmonary, cerebrovascular, or hepatorenal dysfunction were not eligible. The preoperative work-up comprised medical history, physical examination, routine laboratory tests and computed tomography (CT) scan or magnetic resonance imaging (MRI). A transperitoneal approach was performed in all patients; four or five laparoscopic ports were inserted. The hilar vessels were prepared in the event that bulldog clamping

Table III. *Multivariate analysis of complications. Statistically significant differences are shown in bold.*

	Infection	Hematuria	Hematospermia	Rectal bleeding	AUR	Hospitalization
Age	0.11	0.49	0.26	0.16	0.41	0.47
BMI	0.67	0.67	0.97	0.84	0.89	0.59
PSA	0.32	0.84	0.19	0.36	0.24	0.93
Prostate volume	0.09	0.85	0.86	0.54	0.98	0.09
PSA density	0.28	0.95	0.50	0.32	0.31	0.90
Diabetes	0.88	0.99	0.46	0.99	0.98	0.98
COPD	0.78	0.99	0.64	0.98	0.99	0.36
Infections	**0.001**	0.97	0.98	0.98	0.99	**0.001**
						0.005
						0.000-0.125
Previous urological surgery	0.31	0.98	0.69	0.97	0.99	0.09
Urological tumors	0.99	0.62	0.75	0.45	0.97	0.98
Other tumors	0.11	0.97	0.83	0.97	0.98	0.99
Neurological disease	0.99	0.98	0.29	0.96	0.98	0.08
Any concomitant disease	0.28	0.98	0.76	0.98	0.98	0.98
Core number	0.23	0.82	0.79	0.43	0.11	0.86
PCa	0.38	0.83	0.31	0.96	0.86	0.15

AUR, Acute urinary retention; BMI, body mass index; PSA, prostate-specific antigen; COPD, chronic obstructive pulmonary disease; PCa, prostate cancer.

might subsequently be needed. Intraoperative monitoring included electrocardiogram, central venous pressure (CVP), electroencephalographic bispectral (BIS) index (BIS monitor™), NICOM (non invasive cardiac output monitoring), urinary Foley catheter. A controlled hypotension to carefully lower the mean arterial pressure (MAP), while maintaining excellent systemic perfusion, was maintained at approximately 60 mmHg. To induce hypotension, the doses of inhalational isoflurane were increased. The renal lesion was excised using cold Endoshears. Upon completion of tumor excision, blood pressure was restored to preoperative levels. Parenchyma was repaired with Vicryl™ sutures arrested with absorbable clips and Hem-O-lok™. Biologic hemostatic agents and Surgicel™ were applied to the resection bed. *Results:* Eighty-five patients affected by renal tumor underwent zero ischemia LPN. Mean age and mean body mass index (BMI) were 58.2 (±12.2) years and 27.8 (±5.3), respectively. American Society of Anesthesiologists (ASA) score was 1, 2 and 3 in 5, 47 and 48 patients, respectively. Charlson comorbidity index was 3.2±1.6. Renal score was low (4-6) in 20.5%, moderate (7-9) in 71,8% and high (10-12) in 7,75 or the patients. Mean tumor size was 42.9 mm (±15.4 mm). Operative time, blood loss, and ΔHb were 148.7 min (±54.9), 374.2 ml (±365.5), and 2.1 gr/dl (±1.2), respectively. Hilar vessels were isolated in 44.2% of the patients. In all cases the procedure was performed without clamping. Resection, first and second suture times were 7.9 (±3.9), 9.6 (±6.4) and 7.3 (±3.2) minutes, respectively. Hospital stay was 6.5 (±5.6) days. Postoperative complications were: 5 fever (Clavien I), 1 fever (Clavien II), 3 urine leakage managed conservatively (Clavien IIIa). Histological evaluation revealed benign lesion in 4 patients, Oncocytoma in 10 patients, AML in 4 patients, complex cyst in 1 patients, Papillary RCC in 14 patients, Cromophobe RCC in 5 patients, clear cell RCC in 47 patients [pT1a (31 patients), pT1b (25 patients), T2 (2 patients), T3a (7 patients)]. Preoperative and postoperative serum creatinine was 0.8±0.24 mg/dl and 0.9±0.22 mg/dl, respectively (Δ0.05±0.08; Δ% -6.2); preoperative and postoperative glomerular filtration rate (GFR) was 96.43±33.03 ml/min and 88.03±26.35 ml/min, respectively (Δ-8.41±12.97 Δ% -8.7). *Conclusion:* Zero ischemia LPN represents a safe and reproducible technique that allows sparing renal parenchyma and preserving renal function. However, long-term results are needed.

101
STEREOTACTIC BODY RADIATION THERAPY IN THE MANAGEMENT OF OLIGOMETASTATIC KIDNEY CANCER: NEW CHANCE OF CURE?

Ciro Franzese, Lucia Di Brina, Giuseppe Roberto D'Agostino, Pierina Navarria, Pietro Mancosu, Stefano Tomatis and Marta Scorsetti

Department of Radiotherapy and Radiosurgery, Humanitas Clinical and Research Hospital, Milan, Italy

Background/Aim: Rate of kidney cancer increases by 1.7% annually. Renal cell carcinoma (RCC) is the most common kidney cancer, and can metastasize. Our aim is to analyze patients treated with Stereotactic Body Radiation Therapy (SBRT) on extracranial metastases from kidney cancer. *Materials and Methods:* From 2004 to 2016, 64 patients and 81 lesions were treated with SBRT. Patients were candidate to SBRT if maximum 3 distant metastases were diagnosed. Tumour response was classified according to European Organization for Research and Treatment of Cancer Response Evaluation Criteria in Solid Tumours (EORTC-RECIST) criteria version 1.16. *Results:* The majority of the patients were affected by RCC, in particular clear cell type (75%). Thirty-nine metastases were located in the lungs and 25 (30.5%) were represented by lymph nodes. Less common were bone (8.5%), liver (6.1%) and adrenal gland (6.1%) metastases. Median follow-up was 16.7 months (range=3.5-157.1). Rates of local control at 12 and 18 months were 88.2% and 88.2%, respectively. Systemic treatment before SBRT [hazard ratio (HR)=0.24, 95% confidence interval (CI)=0.06-0.98; p=0.048) had an impact on LC. Overall survival at 1, 2, and 5 years were 100%, 98% and 86%. *Conclusion:* Oligometastatic patients from kidney cancer benefit from SBRT as an effective and safe treatment. A multimodal approach including SBRT and systemic therapy prolongs control of disease and improve quality of life.

102
CONUT SCORE AS A PREDICTIVE BIOMARKER OF RECURRENCE IN PATIENTS WITH MUSCLE-INVASIVE BLADDER CANCER

Francesco Claps, Nicola Pavan, Matteo Boltri, Fabio Traunero, Giovanni Liguori and Carlo Trombetta

Urology Clinic, ASUITs - University of Trieste, Department of Medical, Surgical and Health Science, Trieste, Italy

Aim: The aim of the study was to investigate the ability of the Controlling Nutritional Status (CONUT) score to predict the correlation between malnutrition and recurrence outcome in patients affected by muscle-invasive bladder cancer (MIBC) treated with radical cystectomy (RC). *Materials and Methods:* We retrospectively evaluated the available data from 127 patients who underwent RC for MIBC at our Institute. Preoperative Controlling Nutritional Status (CONUT) score was calculated based on the serum albumin concentration, lymphocyte count and total cholesterol concentration. Patients were classified into two groups: those with high CONUT score and those with low

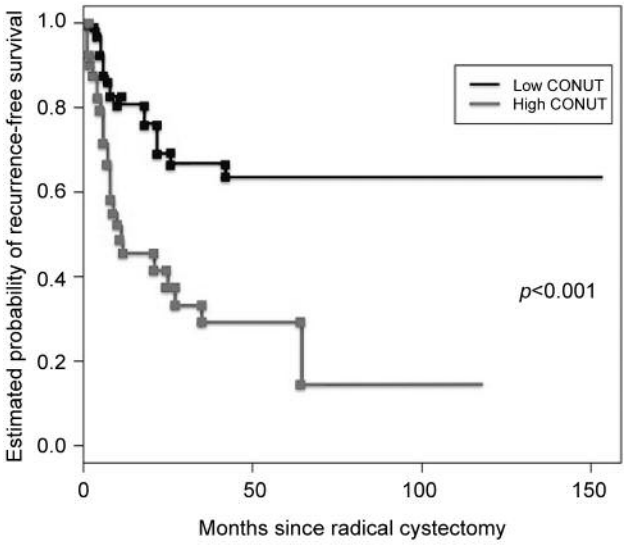


Figure 1. *Recurrence-free survival rate.*

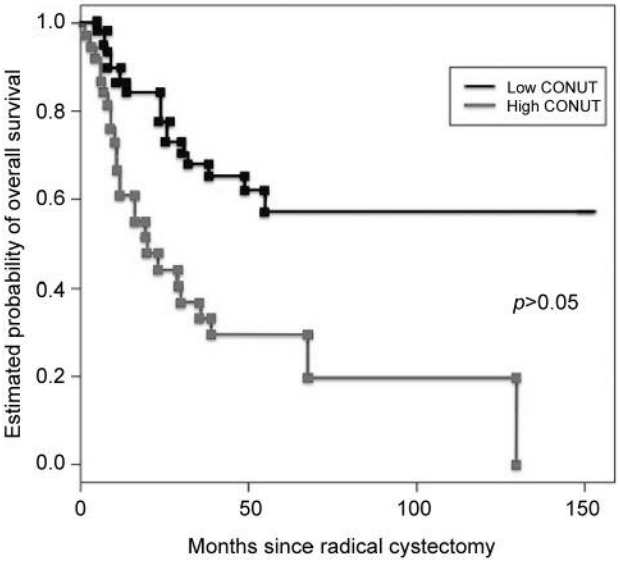


Figure 2. *Overall survival rate.*

CONUT score. Univariate and multivariate analyses were performed. Recurrence - free Survival (RFS) and Overall Survival (OS) rates were calculated and compared between the two groups (Figures 1 and 2). *Results:* Cut-off value to discriminate between high and low Controlling Nutritional Status (CONUT) score was determined calculating the ROC curve: the area under the curve was 0.715 with an optimal cut-off of 3 points. 42 (33.1%) patients had high CONUT score. Distribution of data in low and high CONUT groups as mean age at surgery (71.4±9.5 *vs.* 73.8±7.6, p=0,16), sex (male 46 *vs.* 21 and female 39 *vs.* 21, p=0.70), mean hospitalization time (24.2±10.9 *vs.* 21.2±6.7, p=0.11), tumor site and presence of multifocal disease (p=0.56), pT stage (p=0.80), pN stage (p=0.77), presence of high-grade disease (75 *vs.* 35, p=0.22) lymphovascular invasion (LVI) (34 *vs.* 18, p=0.85), use of adjuvant chemotherapy (23 *vs.* 7, p=0.17), mean body mass index (BMI) (25.4±4.1 *vs.* 25.7±4.6, p=0.79) and urinary diversion (ureterocutaneostomy, ileal conduit and orthotopic neobladder) were not statistically different between two groups (p>0.05). Only mean fibrinogen, as acute inflammatory index, was statistically greater in the high CONUT score group (370±103.2 *vs.* 437.7±144, p=0.03). OS and RFS rates were calculated with a mean follow-up of 30.5±35.7 months in low CONUT group and 24.2±28.8 in high CONUT group (p=0.34). Totally, 54 (42.5%) patients were alive: 44 (81.5%) with low score and 10 (18.5%) with high score (p=0.002). Forty-four (34.6%) had a recurrence disease: 19 (43.2%) in the low score group and 25 (56.8%) in the high score group (p<0.001). Results of the multivariate analysis, after adjustment for pT stage, pN stage, tumor grading, LVI and fibrinogen level, revealed that preoperative CONUT score was an independent predictor of RFS [hazard ratio (HR)=3.11, range=1.69-5.71; p<0.001]. *Conclusion:* Preoperative determination of CONUT score can be used as a biomarker to predict outcomes in patients affected by MIBC undergoing RC. Considering a cut-off of 3 points a high preoperative CONUT score is predictive of recurrence disease. A limitation of this study was the lack of information about the causes of death and so about the Cancer Specific Survival. Further investigations should be necessary to confirm the good potential of this tool.

103
STEREOTACTIC BODY RADIATION THERAPY AS LOCAL TREATMENT FOR OLIGOMETASTASES FROM PROSTATE CANCER: EFFICACY AND IMPACT ON SYSTEMIC TREATMENT

Ciro Franzese, Lucia Di Brina, Giuseppe Roberto D'Agostino, Pietro Mancosu, Stefano Tomatis and Marta Scorsetti

Department of Radiology and Radiosurgery, Humanitas Clinical and Research Hospital, Milan, Italy

Background/Aim: Oligometastatic state from Prostate cancer (PCa) is not a rare event. In this setting, local treatments could impact on disease control, survival of patients and

management of systemic treatments. Stereotactic Body Radiation Therapy (SBRT) is considered a non-invasive and well tolerated local approach. The aim of this report is to evaluate the outcome and change in systemic approach of oligometastatic PCa patients treated with SBRT. *Materials and Methods:* From 2009 to 2016, 65 patients were treated with SBRT on 90 metastases. Patients with the evidence of 1 to 3 treated metastases were included. The Clinical Target Volume included the macroscopic disease and microscopic extension based on the computed tomography (CT) images eventually registered with ^{11}C-choline-positron emission tomography (PET) scan imaging. The treatment was executed with the RapidArc version of volumetric modulated arc therapy and was erogated with a median dose of 42 Gy (range=18-60 Gy) in 2-8 fractions. Clinical outcome was evaluated every 3 months, with prostate-specific antigen (PSA) determination and, in the majority of patients, with post-treatment ^{11}C-choline-PET. Local control (LC), biochemical progression-free survival (BPFS) and time to initiation of new systemic therapy were evaluated. *Results:* Median time from detection of metastases to SBRT was 1.85 months (range=0-58.5). Patients were more commonly treated on abdominal or pelvic lymph nodes (50 patients, 78.1%); two (3.1%) patients were treated on lymph node and bone metastases while 10 (15.6%) patients only on bone lesions. Lung metastases were treated in 2 (3.1%) patients. Forty-one (64.1%) patients were treated on 1 single metastases while 20 (31.2%) and 3 (4.7%) patients on 2 and 3 metastases, respectively. Thirty-seven (57.81%) patients were free from systemic therapy when treated with SBRT. Thirty-seven (57.8%) patients were castration-sensitive while 28 (42.2%) patients were castration-resistant. Median follow-up time was 15.2 months (range 6-101.4 months). Best radiologic response after SBRT was classified as Complete Response in 41 (64.1%) patients, partial response in 10 (15.6%) patients and stable disease in 2 (3.1%) patients. Median value of nadir PSA reached after SBRT in the whole group was 1.64 ng/ml (range=0-45.05). Median nadir value of PSA in patients without progression after RT was 0.39 ng/ml (range=0.01-5.8 ng/ml). LC at 6-, 12- and 18- months was 94%, 88% and 84% respectively. Median time to local relapse was 14.1 months (range=2.5-101.4). Forty-three patients had biochemical relapse during follow-up with a median time of 7.1 months (range=1.1-42.7). Rates of BPFS at 6, 12, and 18 months were 73%, 41%, and 28%, respectively. Median time from radiotherapy to the onset of new systemic treatment was 10.1 months (range 1.6-47.1). *Conclusion:* SBRT is an effective approach for the treatment of metastases from PCa, giving the possibility to delay the onset of systemic treatments. The low value of PFS rates implies the need of randomized prospective trials to select the patients who will benefit the most from this local approach.

104

INCIDENTAL PROSTATE CANCER AT THE TIME OF RADICAL CYSTECTOMY: PREDICTIVE FACTORS AND SURVIVAL OUTCOMES

Francesco Claps[1], Nicola Pavan[1], Paolo Umari[2], Michele Rizzo[1], Rossana Bussani[3], Fabio Barbone[4], Giovanni Liguori[1] and Carlo Trombetta[1]

[1]Urology Clinic, ASUITs - University of Trieste, Department of Medical, Surgical and Health Science, Trieste, Italy;
[2]Department of Urology, University of Piemonte Orientale "Amedeo Avogadro", Novara, Italy;
[3]Department of Pathology, ASUITs - University of Trieste, Department of Medical, Surgical and Health Science, Trieste, Italy;
[4]IRCCS "Burlo Garofalo", University of Trieste, Department of Medical, Surgical And Health Science, Trieste, Italy

Background/Aim: To analyze the incidence, preoperative findings, histopathological features and prognosis in patients with prostate cancer incidentally detected (iPCa) at cystoprostatectomy (RCP) for muscle invasive bladder cancer (MIBC). *Materials and Methods:* We retrospectively reviewed the available data of patients who underwent cystoprostatectomy for MIBC at our Institute between January 2002 and March 2015. Data regarding patient history, preoperative digital rectal examination (DRE), and total serum prostate-specific antigen (PSA) level were collected from the chart review. Patients with a history of previous prostate cancer were excluded. The prostate gland specimen was step-sectioned at 3-mm intervals and our pathologist studied all amount of sections. The apex was embedded as a shave margin to assess the urethra in cross section or radically sectioned in cone-like. Incidental prostate cancer was considered clinically significant (csiPCa) if the tumor had Gleason Score 7 or greater, in case of extracapsular extension, seminal vesicle invasion, positive surgical margins (R) or lymph node metastasis. Univariate and multivariate analyses were performed. Recurrence-free Survival (RFS) and overall survival (OS) rates were calculated. PSA recurrence (rPSA) was defined as two subsequent rises >0.2 ng/ml. *Results:* During the study period 198 patients underwent cystoprostatectomy at our Institute. 21 patients were excluded from the study because of history of previous prostatic disease. The median age was 69 years (range=42-89). Of 177 patients 80 (45.2%) had an incidental prostate cancer and 27 (33.8%) of them met criteria for clinically significant prostate disease. Prostatic involvement by urothelial carcinoma (PUC) was identified in 36 (20.3%) of the prostates. PSA exceeded the threshold only in 16 (9%) cases, 9 (56.3%) with incidental prostate cancer and 6 (66.7%) were clinically significant (p=0.04). In 46 patients with suspicious digital

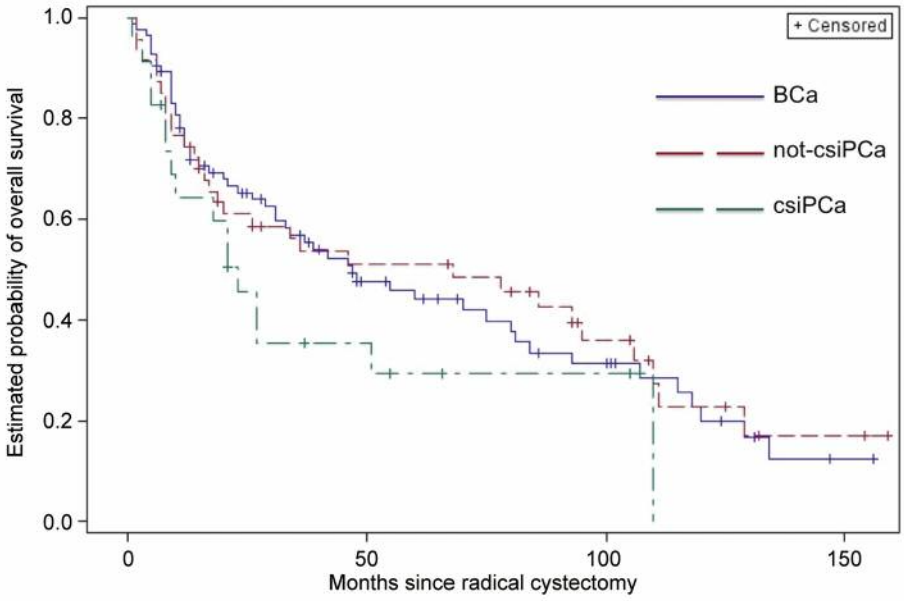


Figure 1. *Overall survival rate*.

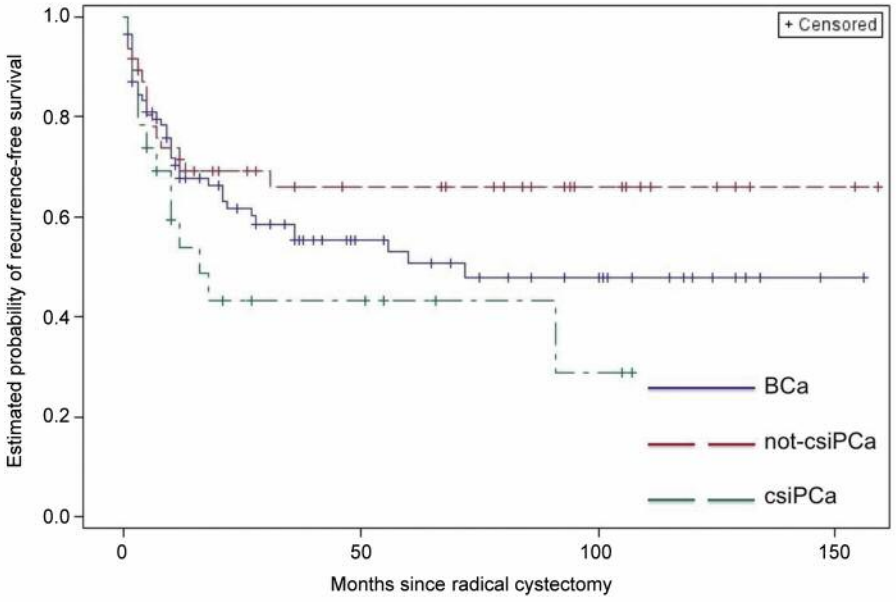


Figure 2. *Recurrence-free survival rate*.

rectal examination, 12 (26.1%) were free of prostate disease, 34 (73.9%) had an incidental finding of prostatic tumor (p<0.0001). Digital rectal examination was positive in more than 50% of patients that had a prostatic involvement by urothelial carcinoma (p<0.0001) and in 50% of patients with involvement of the prostatic apex (p=0.07). 4 patients had PSA recurrence during the median follow-up of 28 months (range=1-159): these, preoperatively, had a median PSA of 4.6 ng/ml (p=0.0112) and digital rectal examination in each of them was always suspicious (p=0.0257). After adjusting for age, pT stage, and pN stage, the 5-year and 10-year RFS and OS rates were not influenced by incidental prostate cancer, whatever was its clinical significance (p=0.1147, p=0.2895, respectively) (Figures 1 and 2). *Conclusion:* Incidental prostate

cancer is quite common in our study group. Preoperatively PSA value had poor accuracy to identify prostate cancer although it maintains its reliability for significant disease while preoperative digital rectal examination showed some benefits for predicting a neoplastic presence in the prostate. The prognosis of these patients is dramatically influenced by muscle invasive bladder cancer stage and the incidental findings of prostatic disease were not influencing the survival outcomes.

105

VALUE OF SECOND-LOOK URETERORENOSCOPY AFTER ENDOSCOPIC TREATMENT IN UPPER TRACT UROTHELIAL CARCINOMA

David D'Andrea[1], David D'Andrea[2], Beat Foerster[1], Tim Muilwijk[3], Evanguelos Xylinas[4], Thoma Seisen[5], Leonardo Monteiro[6], Marco Bandini[7], Donald Schweitzer[8], Mohammad Abufaraj[1], Marco Bianchi[7], Uzoma Anele[9], Kees Hendricksen[8], Francesco Soria[1], Steven Joniau[3], Morgan Roupret[5], Alberto Briganti[7], Riccardo Autorino[9], Wassim Kassouf[6], Hubert John[10], Bas W.G. Van Rhijn[8], Pierre Colin[11] and Shahrokh F. Shariat[1]

[1]Department of Urology, Medical University of Vienna, Vienna, Austria;
[2]Department of Urology, Medical University of Vienna, Vienna, Austria;
[3]Department of Urology, University Hospitals Leuven, Leuven, Belgium;
[4]Department of Urology, Cochin Hospital, Assistance-Publique Hôpitaux de Paris, Paris Descartes University, Paris, France;
[5]Department of Urology, Pitié-Salpétrière, Assistance-Publique Hôpitaux de Paris And Faculté de Médecine Pierre et Marie Curie, University Paris VI, Paris, France;
[6]Department of Urology, McGill University Health Center, Montreal, Canada;
[7]Department of Urology, Urological Research Institute, Vita-Salute University, San Raffaele Scientific Institute, Milan, Italy;
[8]Department of Urology, The Netherlands Cancer Institute-Antoni Van Leeuwenhoek Hospital, Amsterdam, the Netherlands;
[9]Division of Urology, Virginia Commonwealth University, Richmond, VA, U.S.A.;
[10]Department of Urology, Kantonsspital Winterthur, Winterthur, Switzerland;
[11]Department of Urology, Hôpital Privé de La Louvière, Générale de Santé, Lille, France

Background/Aim: Endoscopic kidney-sparing surgery (KSS) for therapy of upper tract urothelial carcinoma (UTUC) has been suggested to be safe and effective when performed according to the pretreatment risk stratification of the European Association of Urology (EUA) guidelines. Aim of our study was to investigate the rate of residual disease, to evaluate predictors of management change and assess an adequate timeframe for early re-ureterorenoscopy (reURS). *Materials and Methods:* A multicenter retrospective study that included 214 patients who underwent endoscopic KSS and early reURS within the first three months for localized UTUC between 2000 and 2017 was conducted. We performed logistic regression and Cox proportional hazard regression analyses to investigate predictors of recurrence, progression (management change to radical nephroureterectomy) and cancer-specific survival (CSS). *Results:* Overall, 125 (58.4%) patients experienced recurrence and 13 (6.1%) died to UTUC during a median follow-up of 22.1 months. Seventy-nine patients (36.9%) had recurrence or residual disease within early reURS. Forty-two of them underwent third-look URS and 28 (66.7%) showed repeated recurrence. Among the 135 (63.1%) patients who had no recurrence on reURS, only 10 (11.6%) had a recurrence within third-look URS and 46 (34.1%) during the whole follow-up. Tumor size >1 cm [odds ratio (OR)=5.7, p=0.009] and female gender (OR=2.6, p=0.046) were independently associated with residual/recurrent disease in reURS, while biopsy grade, cytology and multifocal disease were not. In multivariable Cox regression models, reURS recurrence was the strongest prognostic factor for recurrence-free [hazard ratio (HR)=11.4, p<0.001] and progression- free survival (HR=63.0, p<0.001). In addition, early reURS ≤8 weeks after first URS treatment was an independent protective factor for progression-free survival (HR=0.52, p=0.039), while tumor size and female gender did not retain significance. In univariable Cox regression analyses, management change to radical treatment was associated with CSS (HR=3.45, p=0.044). Multivariable analyses for CSS could not be performed due to the low number of events (cancer mortality). *Conclusion:* Residual or early-recurrent disease within reURS seems to be the strongest prognostic factor for recurrence and progression in patients undergoing ureteroscopic KSS. Furthermore, our results show that second-look URS performed within 8 weeks following first endoscopic laser ablation could improve prognosis. This suggests that reURS should be performed within 2 months or earlier to ensure adequate patient selection for KSS and improvement of oncologic outcomes.

106

TRANSPERINEAL MRI-TARGETED PROSTATE BIOPSY IN AMBULATORY SETTING: IS THE SYSTEMATIC SAMPLING ACTUALLY ESSENTIAL?

Stefano Tappero[1], Alessandro Marquis[1], Daniele D'Agate[1], Giancarlo Marra[1], Marco Agnello[1], Marco Oderda[1], Marco Falcone[1], Marco Allasia[1], Andrea Zitella[1], Riccardo Faletti[2], Laura Bergamasco[2], Luca Molinaro[3] and Paolo Gontero[1]

[1]Department of Urology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy;
[2]Department of Radiology, San Giovanni Battista Hospital, città Della Salute e della Scienza and University of Turin, Turin, Italy;
[3]Department of Pathology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy

Background/Aim: Nowadays, MRI-targeted free-hand transperineal prostate biopsies (TPF TBx) are widely used in prostate cancer (PCa) diagnosis. Prevailing international guidelines recommend to perform a randomized systematic sampling (SC) together with targeted cores (TC). We need to know if SC, added to TC, increase clinically significant (CS) PCa diagnosis or just the detection of non CS (nCS) ones, compared to the lone TC, under local anaesthesia (LA) in ambulatory setting, using the transperineal route. So we assessed the oncological and functional impact of adding SC to TC in LA TPFTBx. *Materials and Methods:* From September 2016 to July 2017 a prospective cohort of men underwent LA TPFTBx (4 cores per target (TC) + SC), at a single referral centre. Esaote Navisuite 5.0 platform was used to carry out the whole procedure. Before, during and 40 days after the procedure, we collected the clinical and pathological data, with a particular care for complications, procedural timings, pain visual analogue scale (VAS), International Index of Erectile Function (IIEF-5) and International Prostate Symptom Score (IPSS). CS PCa was defined according to the START Criteria. Men >80 years, with prostate-specific antigen (PSA) >20 ng/ml or with previous PCa diagnosis were excluded. MRI and pathology were reviewed by dedicated radiologist, using PiradsV2 scale, and pathologist respectively, both blinded to clinical information. Continuous and categorical variables were compared using Mann-Whitney and Fisher or chi-squared test respectively. *Results:* We enlisted 137 TPFTBx. Table I shows the baseline features. Mean number of cores taken was 15.1±2.4. Overall, CSPCa detection rate was 55.5% (n=76 men with CS PCa). Detection rate was 18.5%, 34.2% and 77.3% for PI-RADS 3, 4 and 5 respectively. TC alone diagnosed n=60 CS PCa, but would have missed n=16 CS PCa (21.1%) which resulted positive on SC only. Overall, no nCS PCa were found. Peri-procedural pain was acceptable (VAS 5.1±2.5). Peri-procedural complications included urinary retention in n=2 cases and vasovagal reaction in n=4, whereas main postprocedural complications were hematuria in 73.8% (lasting 9.1±8.9 days) and hematospermia in 52.8% (lasting 19.5±13.3 days). No cases of major complications (Clavien ≥3), infections or sepsis were recorded. IIEF-5 and IPSS were unchanged by the procedure. Overall procedural time was 18.7±6.2 min (MRI and TRUS imaging overlap 6.5±3.9 min; TC sampling 3.4±2.3 min per target). *Conclusion:* LA TPFTBx, performed in ambulatory setting, provides a considerable CS PCa detection rate and is highly tolerable and safe. To avoid CS PCa underdiagnosis, still SC must be carried-out along with TC.

Table I. *Pre-biopsy patient features.*

	n (%)/mean±SD TPFTBx
N	137
Age	69.5±6.8
Family history of PCa	16 (11.7)
BMI	25.9±3.5
ASA classification	
1	75 (54.7)
2	53 (38.7)
3	9 (6.6)
Smokers	
Never-smokers	49 (35.8)
Active-smokers	20 (14.6)
Ex-smokers	68 (49.6)
Diabetes	14 (10.2)
Previous prostatitis	26 (19)
Previous prostate biopsy	
0	64 (46.7)
1	45 (32.8)
≥2	28 (20.4)
PSA level	8.7±6.9
PSA (ng/ml)	7.7±4.0
Suspicious DRE	54 (39.4)
Prostate volume (cc)	51.8±26.1
mpMRI lesion volume (cc)	0.58±0.84
IPSS	8.9±6.2
IIEF-5	13.6±8.7
Pre-procedural anxiety (VAS)	3.8±3.4
Previous prostate surgery	
No	122 (89.1)
Adenomectomy	4 (2.9)
TURP	11 (8)

SD, Standard deviation; TPFTBx, transperineal free-hand targeted biopsy; PCa, prostate cancer; ASA, American score of anesthesiologists; BMI, body mass index; DRE, digital rectal examination; mpMRI, multi-parametric magnetic resonance imaging; IPSS, international prostatic symptoms score; IIEF-5, international index of erectile function; VAS, visual analogue; TURP, trans-urethral resection of the prostate.

107

TRANSPERINEAL MRI-TARGETED VERSUS SYSTEMATIC PROSTATE BIOPSY UNDER LOCAL ANAESTHESIA: INITIAL FUNCTIONAL AND ONCOLOGICAL OUTCOMES

Stefano Tappero[1], Alessandro Marquis[1], Daniele D'Agate[1], Giancarlo Marra[1], Marco Agnello[1], Marco Oderda[1], Marco Falcone[1], Andrea Zitella[1], Riccardo Faletti[2], Laura Bergamasco[2], Luca Molinaro[3] and Paolo Gontero[1]

[1]Department of Urology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy;
[2]Department of Radiology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy;
[3]Department of Pathology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy

Background/Aim: MRI-targeted biopsies (TBx) are widely used for the prostate cancer diagnosis (PCa). Our aim was to compare the clinically significant prostate cancer (CSPCa) detection rate of the MRI-targeted and the standard systematic (SBx) prostate biopsies performed in ambulatory setting, under local anaesthesia (LA) with a transperineal freehand approach. *Materials and Methods:* From September 2016 to July 2017 two prospective cohorts of men underwent LA TPFTBx (4 cores per target (TC) + SBx without the core of the area already sampled by TC, if applicable) *versus* LA TPFSBx (12 cores) respectively, at a single referral centre. Before, during and 40 days after the procedure, we collected the clinical and pathological data, with a particular care for complications, procedural timings, VAS pain scale, IIEF-5 and IPSS. We excluded men >80 years, with PSA >20 ng/ml or with previous PCa diagnosis. MRI and pathology were reviewed by dedicated radiologist, using PiradsV2 scale, and pathologist respectively, both blinded to clinical information. Continuous and categorical variables were compared using Mann-Whitney and Fisher or χ^2 test respectively. *Results:* 137 (TBx) and 110 (SBx) men have been included. No baseline differences were recorded except for the number of cores taken (TBx 15.1±2.4; SBx 12.1±0.3; $p<0.01$) and of Bx naïve men (TBx 46.7%; SBx 81.8%; $p<0.01$, Table I). CSPCa detection was 55.5% for TBx and 41.8% for SBx overall ($p=0.045$) and 67% for TBx *versus* 42% for SBx in Bx naïve men ($p<0.001$). No significant differences among the 2 groups were present in peri-procedural pain ($p=0.45$), peri-procedural complications (urinary retention n=3, $p>0.99$; vasovagal reaction n=7, $p>0.99$) and in postoperative complications (hematuria 75.7%, $p=0.73$, lasting 9.02±8.6 days, $p=0.9$; hematospermia, 55.7%, $p=0.56$, lasting 20.8±13.1 days, $p=0.3$). No cases of Clavien ≥3 complications, infections or sepsis were recorded. IIEF-5 and IPSS did not significantly vary from pre to post-procedural assessment and among the two groups (ΔIPSS $p=0.32$; ΔIIEF-5 $p=0.28$). Longer timings were required to perform TBx (18.7±6.2 *vs*. SBx 11.2±3, $p<0.01$). *Conclusion:* Both in the group of naïve patients only and the overall scheduled patients, LA TPFTBx shows a higher detection accuracy compared to LA TPFSBx. No significant differences among these two techniques were recorded regarding morbidity and tolerability; merely, TPFTBx has a longer duration.

Table I. *Demographic and clinical characteristics of the patients.*

	n (%)/mean±SD			
Characteristics	Overall	TPFTBx	TPFSBx	*p*-Value
N	247	137	110	
Age	67.6±7.3	69.5±6.8	67.6±7.9	0.97
Family History of PCa	33 (13.3)	16 (11.7)	17 (15.5)	0.49
ASA Classification				0.65
1	129 (52.2)	75 (54.7)	54 (49.1)	
2	100 (40.5)	53 (38.7)	47 (42.7)	
3	17 (5.7)	9 (6.6)	8 (8.2)	
Charlson Comorbidity Index	2.8±1.2	2.8±1.1	2.8±1.4	0.88
BMI	25.9±3.7	25.9±3.5	25.8±4.1	0.84
Smokers				0.24
Never-smokers	92 (37.2)	49 (35.8)	43 (39.1)	
Active-smokers	43 (17.4)	20 (14.6)	23 (20.9)	
Ex-smokers	112 (45.3)	68 (49.6)	44 (40)	
Diabetes	28 (11.3)	14 (10.2)	14 (12.7)	0.67
Previous prostatitis	43 (17.4)	26 (19)	17 (15.5)	0.57
Previous prostate biopsy				<0.001
0	154 (62.3)	64 (46.7)	90 (81.8)	
1	60 (24.3)	45 (32.8)	15 (13.6)	
≥2	33 (13.4)	28 (20.4)	5 (4.5)	
PSA (ng/ml)	7.4±4.3	7.7±4.0	6.8±3.9	0.09
Suspicious DRE	100 (40.5)	54 (39.4)	46 (41.8)	0.80
IPSS	9.7±6.9	8.9±6.2	10.7±7.7	0.11
IIEF-5	12.9±8.8	13.6±8.7	12.0±8.8	0.15
n Cores taken	13.7±2.3	15.1±2.4	12.1±0.3	<0.001
Pre-procedural anxiety (VAS)	3.9±3.3	3.8±3.4	4.1±3.2	0.52
Previous prostate surgery				0.90
No	218 (88.3)	122 (89.1)	96 (87.3)	
Adenomectomy	8 (3.2)	4 (2.9)	4 (3.6)	
TURP	21 (8.5)	11 (8)	10 (9.1)	

SD, Standard deviation; TPFTBx, transperineal free-hand targeted biopsy; TPFSBx, transperineal free-hand standard systematic biopsy; PCa, prostate cancer; ASA, American score of anesthesiologists; BMI, body mass index; PSA, prostate-specific antigen; DRE, digital rectal examination; IPSS, international prostatic symptoms score; IIEF-5, international index of erectile function; VAS, visual analogue; TURP, trans-urethral resection of the prostate.

108
CURRENT TECHNIQUES TO OPTIMIZE EARLY RETURN OF URINARY CONTINENCE FOLLOWING RADICAL RETROPUBIC PROSTATECTOMY

Vincenzo Maria Altieri[1], Mario Sodano[1], Rocca Lisanti[1], Nicola Pesenti[1], Alberto Vismara[1], Giovannalberto Pini[2] and Emanuele Micheli[1]

[1]Division of Urology, Humanitas Gavazzeni, Bergamo, Italy;
[2]Division of Urology, San Raffaele Turro, Milan, Italy

Background/Aim: A variety of different surgical techniques are thought to impact on urinary continence (UC) recovery in patients undergoing open retropubic radical prostatectomy (RRP) for prostate cancer. Although RRP has been the most commonly used surgical technique for patients with localized prostate cancer for decades, urinary incontinence has remained one of the most important causes for concern among patients who seek surgical treatment for prostate cancer. In this study, we discuss the intraoperative techniques to improve outcomes for early return of urinary continence and we evaluate the continence rate at different time points. *Materials and Methods:* This retrospective study enrolled 95 patients with localized prostate cancer who underwent RRP. Continence was evaluated using International Consultation on Incontinence Questionnaire Short Form (ICIQ-SF) at 1, 3, 6, 12, 24, and 36 months postoperatively. In our surgical procedure, the urethrovesical anastomosis was made using six single sutures and we fixed the urethral stump laterally to the medial portion of levator ani muscle. Also, we perform in our surgical technique maximal sparing of the membranous urethral length and of the bladder neck. *Results:* The mean post-perative ICIQ-SF score was 9.5 at 1 month, 8.3 at 3 months, 8.9 at 6 months, 4.8 at 12 months, 3.9 at 24 months and 3.7 at 36 months. The degree of post-perative incontinence showed an important decrease at 12 months compared with the early postoperative results. *Conclusion:* Our procedure suggest that minimizing damage to the urinary sphincters, maximal sparing of urethral length, creating a secure vesicourethral anastomosis, and providing lateral ani muscle support to the anastomosis can avoid retraction and deviations of the urethra and improve early UC recovery post RRP.

109
HIGH-PRECISION SALVAGE RE-IRRADIATION FOR ISOLATED LOCAL RECURRENCE OF PROSTATE CANCER: A MONO-INSTITUTIONAL SERIES OF 64 PATIENTS

Damaris Patricia Rojas[1,2], Barbara Alicja Jereczek-Fossa[1,2], Dario Zerini[2], Cristiana Fodor[2], Anna Viola[1,2], Giuseppe Fanetti[1,2], Stefania Volpe[1,2], Giulia Marvaso[2], Rosa Luraschi[3], Alessia Bazani[3], Elena Rondi[3], Federica Cattani[3], Andrea Vavassori[2], Cristina Garibaldi[4], Sarah Alessi[5], Paola Pricolo[5], Giuseppe Petralia[5], Ottavio De Cobelli[6], Gennaro Musi[6] and Roberto Orecchia[7]

[1]Department of Oncology And Hemato-oncology, University of Milan, Milan, Italy;
[2]Division of Radiation Oncology, European Institute of Oncology, Milan, Italy;
[3]Division of Medical Physics, European Institute of Oncology, Milan, Italy;
[4]Radiation Research Unit, European Institute of Oncology, Milan, Italy;
[5]Division of Radiology, European Institute of Oncology, Milan, Italy;
[6]Division of Urology, European Institute of Oncology, Milan, Italy;
[7]Department of Medical Imaging and Radiation Sciences, European Institute of Oncology, Milan, Italy

Aim: To evaluate high-precision external beam re-irradiation (re-EBRT) for local relapse of prostate cancer (PCa) after radiotherapy. *Materials and Methods:* This retrospective study included data of patients with biochemical failure and evidence of isolated local recurrence of PCa after radical/salvage EBRT or brachytherapy that received image-guided (IG) re-EBRT between 11/2009 and 11/2016. Biopsy was not mandatory if all elements were univocal (Prostate Specific Antigen evolution, choline-positron emission tomography and magnetic resonance imaging). Re-EBRT was delivered with image guided - intensity modulated radiation therapy (IG-IMRT) and/or stereotactic technology (Rapid Arc®, VERO® and CyberKnife®). Acute and chronic toxicity was registered by a radiation oncologist according to the RTOG/European Organization for Research and Treatment of Cancer Guideline during re-EBRT, and subsequently every 6 -12 months after the end of re-EBRT. Serum PSA levels was tested every 3 months until any biochemical or clinical progression. Biologically effective dose (BED) of re-EBRT was calculated using an alpha/beta value of 1.5 Gy. *Results:* The data of 64 patients were analyzed, median age at re-EBRT was 73.2 years (range=52.6-90.5). The median initial PSA level was 11.4 ng/ml (range=0.5-228.5). Initial Gleason score was 7 (range=2-9). Median pre re-EBRT PSA was 3.99 ng/ml (range=0.37-21). In patients under ADT median pre re-EBRT PSA was 3.5 ng/ml (range=0.2-51.83). Biopsy of the radiologically documented recurrent lesion was performed in 28 patients (45%) and was positive for PCa in 23 cases (82%). In case of negative biopsy, the indication to re-EBRT was reviewed and confirmed by the multidisciplinary team based on the available clinical and radiological data of a single

patient. Re-EBRT was performed for intraprostatic recurrence and for post-prostatectomy bed recurrence in 45 (70%) and 19 (30%) cases, respectively. Extreme hypofractionation was employed in the majority of patients. Median dose was 30 Gy (range: 20-30 Gy) given in 5 fractions (range=2-10) (BED 150 Gy). Concomitant ADT was prescribed in 16 patients (25%) and included luteinizing hormone-releasing hormone agonist (LHRHa), antiandrogens and combined androgen blockade (CAB) in 8, 4 and 4 patients, respectively. One acute G≥3 genitourinary (GU) event (transitory macroscopic hematuria) and 1 late G≥3 GU (permanent reduction in bladder capacity) event were observed. No patient experienced G≥ 3 bowel toxicity. At the median follow-up of 26.1 months from re-irradiation (range=3.1-82.4) tumor progression was observed in 41 patients (64%). In all these cases, clinical progression followed biochemical progression. Eighteen patients (28%) experienced local relapse. Median time-to-progression was 14 months. The 2-year actuarial local control, biochemical and clinical relapse free survival rates were 75%, 40% and 53%, respectively. Overall survival and prostate cancer specific survival rates at 2 years were 92% and 95%, respectively. BED >130 Gy was correlated with higher tumor control rates when compared to <130 Gy (tumor progression was observed in 28 out of 30 of patients (93 %) treated with a total BED under 130 Gy, and in 13 out of 34 patients (38 %) treated with a total BED dose ≥130 Gy). At the last follow-up, 30 patients (47%) showed no evidence of disease, 28 patients (44%) were alive with biochemical or clinical disease and 1 was lost for follow-up. 5 patients died: 3 of disease progression, 1 for another type of tumor and 1 for unknown cause. *Conclusion:* High-precision salvage re-EBRT for isolated local PCa recurrence is a safe, feasible and noninvasive treatment offering satisfactory tumor control if BED of >130 Gy is administered, without significant acute and late complications. Further investigation is warranted to define the optimal patient selection and establish the optimal dose and volume parameters for this particular clinical scenario.

110
OPEN *VERSUS* ROBOT-ASSISTED SALVAGE RADICAL PROSTATECTOMY: FUNCTIONAL OUTCOMES AND COMPLICATIONS OF A MULTICENTRE STUDY

Giancarlo Marra[1], Marco Oderda[1], Paolo Alessio[1], Anna Palazzetti[1], Francesca Pisano[1], Antonino Battaglia[1], Stefania Munegato[1], Bruno Frea[1], Paolo Gontero[1], Fernando Munoz[2], Claudia Filippini[3], Estefania Linares[4], Rafael Sanchez Salas[4], Sanchia Goonewardene[5], Prokar Dasgupta[5], Declan Cahill[5], Ben Challacombe[5], Rick Popert[5], David Gillatt[6], Raj Persad[6], Juan Palou[7], Steven Joniau[8], Salvatore Smelzo[9], Thierry Piechaud[9], Alexandre De La Taille[10], Morgan Roupret[11], Simone Albisinni[12], Roland Van Velthoven[12], Alessandro Morlacco[13], Sharma Vidit[13], Giorgio Gandaglia[14], Alexander Mottrie[14], Joseph Smith[15], Shreyas Joshi[15], Gabriel Fiscus[15], Andre Berger[16], Monish Aron[16], Henk Van Der Poel[17], Derya Tilki[18], Declan Murphy[19], Nathan Lawrentschuk[19], John Davis[20], Gordon Leung[20] and Robert Jeffrey Karnes[13]

[1]Department of Urology, San Giovanni Battista Hospital, Città della Salute e della Scienza, University of Turin, Turin, Italy;
[2]Department of Radiotherapy, Parini Hospital, Aosta, Italy;
[3]Department of Statistics, University of Turin, Turin, Italy;
[4]Department of Urology, Institut Mutualiste Montsouris, Paris, France;
[5]Department of Urology, Urology Centre, Guy's Hospital, London, U.K.;
[6]Department of Urology, North Bristol NHS Foundation Trust, Bristol, U.K.;
[7]Department of Urology, Fundaciò Puigvert, Barcelona, Spain;
[8]Department of Urology, Leuven University Hospitals, Leuven, Belgium;
[9]Department of Urology, Clinique Saint Augustin, Bordeaux, France;
[10]Department of Urology, CHU Mondor, Créteil, France;
[11]Department of Urology, Pitié Salpétrière Hospital University Paris 6, Paris, France;
[12]Department of Urology, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium;
[13]Department of Urology, Mayo Clinic, Rochester, MN, U.S.A.;
[14]Department of Urology, OLV Hospital, Aalst, Belgium;
[15]Department of Urology, Vanderbilt University, Medical Center North, Nashville, TN, U.S.A.;
[16]Department of Urology, USC Norris Comprehensive Cancer Center and Hospital, University of South California, Los Angeles, CA, U.S.A.;
[17]Department of Urology, Netherlands Cancer Institute, Amsterdam, the Netherlands;
[18]Department of Urology, Martini Klinik, Hamburg, Germany;
[19]Department of Urology, Peter MacCallum Cancer Centre, Melbourne, Australia;
[20]Department of Urology, Division of Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX, U.S.A.

Background/Aim: Salvage radical prostatectomy (sRP) has always been associated to high morbidity and low quality functional outcomes. The purpose of this study was to determine and compare functional outcomes of a wide contemporary series of robotic (RsRP) *vs*. open (OsRP) sRP.

Materials and Methods: In a retrospective collection between 2000 and 2016, 615 men underwent sRP at 18 Tertiary referral centers. Complications were collected according to the Clavien-Dindo score. Erectile function (EF), evaluated with IIEF questionnaire before and according to the type of therapy needed to obtain erections after sRP, and urinary continence (Con), determined with the number of pads/day used, were assessed before sRP, at 6 and/or 12 months. Men with insufficient data or a follow-up <6 months were excluded. Continuous variables were compared with Wilcoxon-Mann-Whitney; categorical variables with Chi-square or Fisher's exact tests; analysis of variance for repeated measures was used to determine Con trends. *Results:* Three hundred ninety-five men (186 OsRP and 209 RsRP) who underwent sRP after primary active treatments were included. At baseline, the only significant differences amongst the two groups were Gleason Score (slightly higher in RsRP, p=0.0159), the CCI (higher in RsRP (2.17±2.4 *vs*. OsRP 0.85±1.32; p<0.01)) and the lymph-node template used (more extended for OsRP (p<0.01)). Previous mono or bilateral (19.75% *vs*. 8.33%) nerve sparing surgery was higher in the RsRP group (p=0.01). OsRP had shorter operating time (213.6 *vs*. 227.9 min; p<0.01), longer hospital stay (HS) (5.6, IQ=3-7, *vs*. 2.9, IQ=1-4 days, p<0.01) and higher mean blood loss (BL) (714.9 *vs*. 221.74 ml; p<0.01). However, no differences in post-operative transfusions were present (4.61% of men receiving ≥1 unit; p=0.09). No significant differences were present in men experiencing at least 1 complication (34.9%, p=0.66) or 1 major (Clavien ≥3) complication (10.1%, p=0.16). The only significant differences amongst the two groups in terms of complications were acute renal failure (OsRP 2.96 *vs*. 0%, p=0.04) and anastomotic strictures (OsRP 17.7% *vs*. 7.7%, p=0.01). Rectal injury was rare (2.96% of OsRP *vs*. 0.5% of RsRP; p=0.055). EF was similar in the two groups at 6 months (p=0.076) but was then higher in RsRP at 1 year (52.5% having no erections *vs*. 69.8% in OsRP, p=0.03). Con was higher for RsRP both at 6 (22.3% *vs*. 38.1% in OsRP having severe inCon using ≥3 pads/day, p=0.02) and 12 months (severe inCon 19.8% *vs*. 34.2% in OsRP, p=0.04). *Conclusion:* sRP involves acceptable functional outcomes and complication rates if performed in tertiary referral centers. Compared to OsRP, RsRP yields shorter HS, lower BL and may improve EF and Con recovery. However, complication rates remain comparable amongst the two groups.

111
RADICAL PROSTATECTOMY IN A SALVAGE SETTING: RESULTS OF A CONTEMPORARY MULTICENTRE SERIES OF 395 CASES

Giancarlo Marra[1], Paolo Alessio[1], Marco Oderda[1], Anna Palazzetti[1], Francesca Pisano[1], Antonino Battaglia[1], Stefania Munegato[1], Bruno Frea[1], Paolo Gontero[1], Fernando Munoz[2], Claudia Filippini[3], Estefania Linares[4], Rafael Sanchez Salas[4], Sanchia Goonewardene[5], Prokar Dasgupta[5], Declan Cahill[5], Ben Challacombe[5], Rick Popert[5], David Gillatt[6], Raj Persad[6], Juan Palou[7], Steven Joniau[8], Salvatore Smelzo[9], Thierry Piechaud[9], Alexandre De La Taille[10], Morgan Roupret[11], Simone Albisinni[12], Roland Van Velthoven[12], Alessandro Morlacco[13], Sharma Vidit[13], Giorgio Gandaglia[14], Alexander Mottrie[14], Joseph Smith[15], Shreyas Joshi[15], Gabriel Fiscus[15], Andre Berger[16], Monish Aron[16], Henk Van Der Poel[17], Derya Tilki[18], Declan Murphy[19], Nathan Lawrentschuk[19], John Davis[20], Gordon Leung[20] and Robert Jeffrey Karnes[13]

[1]Department of Urology, San Giovanni Battista Hospital, Città della Salute e della Scienza, University of Turin, Turin, Italy;
[2]Department of Radiotherapy, Parini Hospital, Aosta, Italy;
[3]Department of Statistics, University of Turin, Turin, Italy;
[4]Department of Urology, Institut Mutualiste Montsouris, Paris, France;
[5]Department of Urology, Urology Centre, Guy's Hospital, London, U.K.;
[6]Department of Urology, North Bristol NHS Foundation Trust, Bristol, U.K.;
[7]Department of Urology, Fundaciò Puigvert, Barcelona, Spain;
[8]Department of Urology, Leuven University Hospitals, Leuven, Belgium;
[9]Department of Urology, Clinique Saint Augustin, Bordeaux, France;
[10]Department of Urology, CHU Mondor, Créteil, France;
[11]Department of Urology, Pitié Salpétrière Hospital University Paris 6, Paris, France;
[12]Department of Urology, Institut Jules Bordet, Université Libre De Bruxelles, Brussels, Belgium;
[13]Department of Urology, Mayo Clinic, Rochester, MN, U.S.A.;
[14]Department of Urology, OLV Hospital, Aalst, Belgium;
[15]Department of Urology, Vanderbilt University, Medical Center North, Nashville, TN, U.S.A.;
[16]Department of Urology, USC Norris Comprehensive Cancer Center and Hospital, University of South California, Los Angeles, CA, U.S.A.;
[17]Department of Urology, Netherlands Cancer Institute, Amsterdam, the Netherlands;
[18]Department of Urology, Martini Klinik, Hamburg, Germany;
[19]Department of Urology, Peter MacCallum Cancer Centre, Melbourne, Australia;
[20]Department of Urology, Division of Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX, U.S.A.

Background/Aim: Men with biochemical recurrence (BCR) after primary treatment benefit from salvage radical prostatectomy (sRP) as a valid curative choice. However, present evidence rests on series of patients operated more than 50 years ago. In this study, oncological outcomes of a wide contemporary series of sRP are examined. *Materials and Methods:* From 2000 to 2016, in a multicenter study of 18 tertiary referral centers, 615 patients with BCR underwent sRP. We retrospectively collected pre-, intra- and post- procedural clinical and pathological data. Information about erectile function (EF) and urinary continence (Con) was detected before sRP, at 6 and/or at 12 months. No men with a follow-up <6 months or unavailable data were included. Wilcoxon-Mann-Whitney test was used to compare continuous variables; chi-squared or Fisher's exact tests to assess categorical ones. *Results:* The study included 395 men. As primary treatments, 66.8% of patients underwent radiotherapy, 3.5% cryotherapy, 3% HIFU, 22.3% brachytherapy and 3.3% other primary treatments. Mean prostate-specific antigen (PSA) and age pre-sRP were 6.36 [interquartile range (IQR)=2.5-7.3] ng/ml and 66.3 (IQR=61.8-70.5) years, respectively. No extra-nodal metastasis were present, n=143 (37.1%) men were on HT whereas n=15 (3.8%) had castration resistant prostate cancer (CRPC). Mean ASA score was 2.17±0.78. A super-extended lymphadenectomy, including retroperitoneal nodes, was performed in 1.74% (n=6) whilst 14.1% (n=44) underwent a nerve sparing procedure. Mean operating time was 221.159 (range=IQR=150-250) min, with a mean blood loss of 439.979 ml (150-500). Final pathology revealed that n=152 (43.43%) patients had a GS ≥8, whereas n=215 (54.7%) had local extra-prostatic extension (T stage ≥3) and n=62 (18.73%) had positive nodes. Positivity on surgical margins was reported in n=165 men (50.9%). At least one major (Clavien ≥3) complication occurred in n=40 patients (10.1%). One year later, only 8.1% had spontaneous or PDE-5 erections and 25.9% were gravely incontinent (≥3 pads/day). At a median follow-up of 3 (IQR=1.7-4.9) years, 150 (48.39%) men had BCR and n=81 (20.47%) had CRPC. Five-year overall and cancer specific survival were 95.02% and 96.2% respectively. *Conclusion:* Oncological outcomes have a promising improvement in short- to medium-term with sRP. However, rates of BCR and positive surgical margins persist relatively high; the same occurs to major complications and severe incontinence rates. The preservation of the erectile function is low. The results of our study need large long-term prospective series of sRP to be confirmed.

112

USEFULNESS OF PRE-SALVAGE RADICAL PROSTATECTOMY PROSTATE BIOPSIES: DO THEY RIGHTLY PREDICT THE FINAL HISTOLOGY?

Giancarlo Marra[1], Paolo Alessio[1], Marco Oderda[1], Anna Palazzetti[1], Francesca Pisano[1], Antonino Battaglia[1], Stefania Munegato[1], Alessandro Marquis[1], Stefano Tappero[1], Bruno Frea[1], Paolo Gontero[1], Fernando Munoz[2], Claudia Filippini[3], Estefania Linares[4], Rafael Sanchez Salas[4], Sanchia Goonewardene[5], Prokar Dasgupta[5], Declan Cahill[5], Ben Challacombe[5], Rick Popert[5], David Gillatt[6], Raj Persad[6], Juan Palou[7], Steven Joniau[8], Salvatore Smelzo[9], Thierry Piechaud[9], Alexandre De La Taille[10], Morgan Roupret[11], Simone Albisinni[12], Roland Van Velthoven[12], Alessandro Morlacco[13], Sharma Vidit[13], Giorgio Gandaglia[14], Alexander Mottrie[14], Joseph Smith[15], Shreyas Joshi[15], Gabriel Fiscus[15], Andre Berger[16], Monish Aron[16], Henk Van Der Poel[17], Derya Tilki[18], Declan Murphy[19], Nathan Lawrentschuk[19], John Davis[20], Gordon Leung[20] and Robert Jeffrey Karnes[13]

[1]Department of Urology, San Giovanni Battista Hospital, Città della Salute e della Scienza, University of Turin, Turin, Italy;
[2]Department of Radiotherapy, Parini Hospital, Aosta, Italy;
[3]Department of Statistics, University of Turin, Turin, Italy;
[4]Department of Urology, Institut Mutualiste Montsouris, Paris, France;
[5]Department of Urology, Urology Centre, Guy's Hospital, London, U.K.;
[6]Department of Urology, North Bristol NHS Foundation Trust, Bristol, U.K.;
[7]Department of Urology, Fundaciò Puigvert, Barcelona, Spain;
[8]Department of Urology, Leuven University Hospitals, Leuven, Belgium;
[9]Department of Urology, Clinique Saint Augustin, Bordeaux, France;
[10]Department of Urology, CHU Mondor, Créteil, France;
[11]Department of Urology, Pitié Salpétrière Hospital University Paris 6, Paris, France;
[12]Department of Urology, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium;
[13]Department of Urology, Mayo Clinic, Rochester, MN, U.S.A.;
[14]Department of Urology, OLV Hospital, Aalst, Belgium;
[15]Department of Urology, Vanderbilt University, Medical Center North, Nashville, TN, U.S.A.;
[16]Department of Urology, USC Norris Comprehensive Cancer Center and Hospital, University of South California, Los Angeles, CA, U.S.A.;
[17]Department of Urology, Netherlands Cancer Institute, Amsterdam, the Netherlands;
[18]Department of Urology, Martini Klinik, Hamburg, Germany;
[19]Department of Urology, Peter MacCallum Cancer Centre, Melbourne, Australia;

[20]Department of Urology, Division of Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX, U.S.A.

Background/Aim: In case of prostate cancer biochemical recurrence (BCR), the choice to undergo salvage radical prostatectomy (sRP) is based on the positivity of a prostate biopsy (Bx). Nowadays, not many results about confirmatory pre-sRP biopsy (cBx) in large cohorts have been reported even if a cBx Gleason Score (GS) ≤7 is one of the EAU Guidelines Criteria for the indication to sRP. Our aim was to evaluate pre-sRP prostate Bx detection rate, establish the GS concordance (Conc) of cBx and first diagnostic biopsy (fBx, before PCa first line treatment) with the final sRP specimen GS, and analyse the GS Conc between the fBx and cBx GS. *Materials and Methods:* Between 2000 and 2016, 615 patients underwent sRP after BCR at 18 tertiary referral centers were scheduled. Baseline information included age, PSA, TNM, imaging and previous treatments. We excluded men without these data collected and also those ones undergone sRP without cBx or fBx. FBx, cBx and sRP GS sums were categorised in ≤6, 7, 8, 9 and 10. Cohen's Kappa coefficient was used for Conc to consider inter-rater agreement. Detection rate, Conc, upgrading (UpGr, first procedure GS score lower than the following procedure GS) and downgrading (DownGr, defined *vice versa*) were reported as number of events and percentages. *Results:* The study included 400 patients, all having negative imaging for extra-nodal metastasis. Mean age was 65.8±7.9 year, initial and pre-sRP PSA were 15.3 and 6.34 ng/ml respectively. On the sRP sample pathological stage was pT2 in 44.6%, pT3 in 53.9%. 5 sRP were not evaluable due to radiation injury or had no tumour (pT0). 26 men did not undergo biopsy before sRP. CBx detection rate was 90.9% (n=340) with the remaining 9.1% (n=34) having no PCa diagnosis due to radiation injury or absence of tumour being detected; of these n=4 (11.4%) revealed pT0 although only one had subsequent BCR. Conc, UpGr and DownGr between cBx and sRP specimen were 63.7% (n=202), 23% (n=73) and 13.3% (n=42); agreement was fair (k=0.487). Conc, UpGr and DownGr between fBx and cBx were 36.3%(n=102, 58.7% (n=165) and 5% (n=14); agreement was poor (k=0.126). Conc, UpGr and DownGr between fBx and sRP specimen were 32.8% (n=97), 63.2% (n=187) and 4% (n=12) respectively, also with poor agreement (k=0.076). *Conclusion:* Pre-sRP prostate biopsy plays a necessary role in confirmation of PCa recurrence after primary non-surgical treatment in case of BCR, although in a considerable portion of cases a higher GS at the final histology of the sRP specimen was detected. The lone original diagnostic biopsy cannot be used to plan treatment in case of PCa recurrence because in more than half of the cases an upgrading is recorded.

113

AN INTERNATIONAL SURVEY ABOUT FOCAL THERAPY FOR PROSTATE CANCER FROM THE YOUNG ACADEMIC UROLOGISTS (YAU): THE OPINION OF 484 PHYSICIANS

Marra Giancarlo[1], Guillaume Ploussard[2], Piet Ost[3], Pieter J.L. De Visschere[3], Prasanna Sooriakumaran[4], Alberto Briganti[5], Giorgio Gandaglia[5], Derya Tilki[6], Christian I. Surcel[7], Igor Tsaur[8], Roderick Van Den Bergh[9], Alexander Kretschmer[10], Hendrik Borgmann[11], Paolo Gontero[1], Hashim Ahmed[12] and Massimo Valerio[13]

[1]Department of Urology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy;
[2]Department of Urology, Saint Jean Languedoc Hospital, Toulouse, France;
[3]Department of Urology and Radiology, Ghent University, Ghent, Belgium;
[4]Department of Urology, University College London Hospital, London, U.K.;
[5]Department of Urology, Vita and Salute University and San Raffaele Hospital, Milan, Italy;
[6]Department of Urology, Martini Klinik, Hamburg, Germany;
[7]Department of Urology, Fundeni Clinical Institute, Bucharest, Romania;
[8]Department of Urology, University of Mainz, Mainz, Germany;
[9]Department of Urology, University of Utrecht, Utrecht, the Netherlands;
[10]Department of Urology, Ludwig-Maximilians-University of Munich, Munich, Germany;
[11]Department of Urology, University Hospital of Mainz, Mainz, Germany;
[12]Department of Surgery And Cancer, Imperial College London, London, U.K.;
[13]Department of Urology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

Background/Aim: Currently, Focal Therapy (FT) for the treatment of localised Prostate Cancer (PCa) is not widely exploited in the common clinical practice. This finds its reason in several concerns that limit the enthusiasm related to the encouraging medium-term oncological and functional outcomes: how to deal with multifocality, and furthermore with low-risk cancer which is better served with active surveillance. Long term data will be needed to clarify these doubts, and until that moment International Guidelines will limit its use to clinical trials only. We want to assess the current opinion about this topic among the wide European general urological community. *Materials and Methods:* A 25-item (12 on baseline demographics, 9 on FT and 4 clinical

cases) anonymised English language questionnaire was created according to the Cherries checklist, and distributed to single urologists through the SurveyMonkey® platform using a web-link from November/2016 to October/2017. After a pilot validation amongst 40 urologists, the survey was sent through the mailing list of the EAU as well as to European national urology societies consenting to participate (6/15 countries). Twitter was also used to disseminate the survey during 2017's EAU Annual Congress. *Results:* Four hundred eighty-four replies from 51 countries have been recorded (88.4% of responders were from European countries). Four hundred thirty-nine responders (91.3%) were urologists; 324 (67.8%) work in academic and/or tertiary centers and 302 (63.5%) declared PCa as their main field of expertise. 22 (4.6%) had never heard about FT. Two hundred-seventeen (44.8%) stated FT would represent a step forward in PCa management if demonstrated effective; 23 (5.2%) abstained and 167 (37.7%) were ensure. 252 (57%) would suggest FT to a patient. Three hundred forty-four responders (78.0%) agreed that FT would become a standard option after improvements in patient selection (n=66) or when its effectiveness was proven (n=78), or both (n=199). The most used definition of FT was treatment of all significant (life-threatening) cancer foci whilst leaving untreated the rest of the gland (43.8%, n=190). 144 (33.0%) considered FT as an alternative to radical prostatectomy or radiotherapy, 121 (27.8%) as an alternative to AS, 33 (7.6%) as a salvage treatment for radiation failure, 138 (31.7%) for clinical trials only. Three hundred sixteen physicians (71.5%), almost three-quarters, had access to FT to treat PCa either in their own centre (n=141) or in their region (n=175). *Conclusion:* The Survey has been a useful tool for the evaluation of the entire urological community's opinion about the role of FT in the PCa treatment. Many general urologists hope, for the very future, in a consistent improvement of patient selection and demonstration of the effectiveness of this technique, aiming to make it become a standard therapeutic procedure.

114
COMPARISON OF MRI-BASED AND STANDARD PATHWAY FOR PROSTATE CANCER DIAGNOSIS: THREE YEARS RESULT OF A PROSPECTIVE RANDOMIZED STUDY

Francesco Porpiglia[1], Matteo Manfredi[1], Fabrizio Mele[1], Stefano De Luca[1], Riccardo Bertolo[1], Diletta Garrou[1], Daniele Amparore[1], Enrico Checcucci[1], Sabrina De Cillis[1], Agostino De Pascale[2], Dario Gned[2], Filippo Russo[3], Stefano Cirillo[4], Enrico Bollito[5] and Cristian Fiori[1]

[1]Department of Urology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy;
[2]Department of Radiology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy;
[3]Department of Radiology, IRCC, Candiolo-Turin, Italy;
[4]Department of Radiology, Mauriziano Hospital, Turin, Italy;
[5]Department of Pathology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy

To compare the standard diagnostic pathway for PCa diagnosis with a new one based on MRI and fusion biopsy, 432 biopsy-naïve patients were randomized into: arm A (MRI-based) and arm B (standard). The patients were biopsied as follows: arm A with PIRADS>3 mp-MRI, fusion biopsy; arm A with negative mp-MRI and arm B: 12 samples transrectal TRUS-guided biopsy. The results of the study are shown in Table I.

115
THE ROLE OF OPERATOR IN THE DETECTION RATE OF MRI/TRUS FUSION TRANSRECTAL PROSTATE BIOPSY

Francesco Porpiglia[1], Matteo Manfredi[1], Fabrizio Mele[1], Stefano De Luca[1], Riccardo Bertolo[1], Diletta Garrou[1], Daniele Amparore[1], Enrico Checcucci[1], Sabrina De Cillis[1],

Table I. *Results of the study at 3 years follow-up.*

	Biopsy approach	Patients	Samples mean (SD)	PCa (%)	CS/total PC n/N (%)	Total cancer core length, mm, median (IQR)	Complications (%)
Arm A							
pos MRI	FB	168	5.7 (2.2)	113 (67.3)	105/113 (92.9)	17 (11-32)	5 (2.9)
neg MRI	SB	48	12 (0)	10 (20.8)	1/10 (10.0)	3 (2-3)	4 (8.3)
Arm B	SB	216	12 (0)	66 (30.5)	35/66 (53.0)	6 (2-21)	25 (11.5)
p-Value							
FB *vs.* SB (arm B)		NA	<0.001	<0.001	<0.001	<0.001	0.0014

SD, Standard deviation; PCa, prostate cancer; CS, clinically significant; IQR, interquartile range; MRI, magnetic resonance imaging; pos, positive; neg, negative; FB, fusion biopsy; SB, systematic biopsy; NA, not applicable.

Agostino De Pascale[2], Dario Gned[2], Filippo Russo[3], Stefano Cirillo[4], Enrico Bollito[5], Daniele Tota[5] and Cristian Fiori[1]

[1]Department of Urology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy;
[2]Department of Radiology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy;
[3]Department of Radiology, IRCC, Candiolo-Turin, Turin, Italy;
[4]Department of Radiology, Mauriziano Hospital, Turin, Italy;
[5]Department of Pathology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy

Background/Aim: The MRI/TRUS software fusion-guided transrectal prostate biopsy (fusion biopsy, FB) has become an established diagnostic tool for improved detection of prostate cancer in the last few years. In most Divisions with an established FB program only few urologists are trained in performing this procedure. Of note, the knowledge of the learning curve characteristics could contribute to efficient training and to maintenance of institutional biopsy quality. The aim of this study was to evaluated potential differences in FB detection rate between expert consultants, senior residents and young residents. *Materials and Methods:* In 05/2014 the Biojet® (D&K Technologies) software for FB was introduced in our Division. The minimum MRI requirements were multiparametric registration including T2w, DCE and DWI, a magnetic field strength of at least 1.5 T and a written report by the radiologist defining the accurate position of the suspected lesion in the prostate according to the PI-RADS scoring system. Despite Biojet® system allows both trans-rectal and trans-perineal approach, for the purpose of this study we included in our analysis only trans-rectal FB, and only the index lesions were analysed. The operators experience was defined as follows: consultants had performed at least 10 years of trans-rectal systematic prostate biopsies, whilst senior residents at least two years; young residents started their experience in biopsies with FB after performing at least 15 procedures supported by an experienced operator. Populations and pathological characteristics were recorded. Detection rates for each group (consultants, senior and young residents) were separately evaluated according to PI-RADS (PI-RADS 3 *vs*. PI-RADS 4-5 lesions), and to the number of previous biopsies (first *vs*. repeated biopsy). The operative time and the complication rate were then recorded for each group. *Results:* Overall, 508 transrectal FB were performed. Stratified population and pathological characteristics and detection rates are reported in Table I. Of note, no differences were found in detection rate and operative time between the

Table I. *Stratified population and pathological characteristics.*

	Consultant (267 patients)	Senior Resident (159 patients)	Young Resident (82 patients)	*p*-Value
Age, years; mean (SD)	65 (8.07)	65 (7.41)	67 (7.21)	0.06
PSA, ng/ml; mean (SD)	8.35 (6.03)	8.25 (4.82)	8.59 (7.27)	0.71
Prostate volume, cc; mean (SD)	44.59 (8.22)	49.33 (2.85)	48.05 (3.69)	0.41
Positive DRE, number (%)	43 (16.10)	12 (7.54)	16 (19.5)	0.11
Operative time, min; mean (SD)	14.6 (4.61)	15.96 (3.25)	15.74 (6.56)	0.78
First FB biopsy detection rate				
PIRADS 3	10/26 (38.46)	2/17 (11.76)	4/15 (26.66)	0.12
PIRADS 4-5	61/82 (74.39)	45/66 (68.18)	21/30 (70)	0.74
Repeated biopsy detection rate				
PIRADS 3	8/55 (14.54)	6/27 (22.22)	2/8 (25.0)	0.70
PIRADS 4-5	60/104 (57.69)	31/49 (63.26)	17/29 (58.62)	0.30
Gleason score, number (%)				
6	23 (16.54)	14 (16.66)	4 (9)	0.65
3+4	68 (48.92)	32 (38.09)	17 (38.63)	0.45
4+3	29 (20.86)	22 (26.19)	14 (31.81)	0.75
>8	19 (13.66)	16 (19.04)	9 (20.45)	0.85
Positive cores, number (%)	415 (97.41)	245 (96.07)	142 (98.61)	0.91
Total cancer core length, mm; mean (SD)	20 (17.64)	19 (15.32)	19 (14.93)	0.75
Complication, number (%)				
Hematuria	105 (39.32)	61 (38.36)	54 (65.85)	<0.0001
Febrile urinary tract infection	8 (2.99)	16 (10.06)	0 (0)	0.0001
Hospitalization	0 (0)	7 (4.40)	0 (0)	0.0001

groups. Conversely, complication rate seemed lower in the consultant group (Table I). *Conclusion:* Our results showed that the detection rate of FB seemed high from the beginning of the learning curve. Residents had higher complication rates compared to consultants. The preliminary study supports the adoption of FB into urological practice, thanks to its reproducibility and efficacy, independently to the operator experience.

116

MULTI-MODAL FIBER SPECTROSCOPY FOR UROTHELIAL CANCER DIAGNOSIS

Mauro Gacci[1], Simone Morselli[1], Arcangelo Sebastianelli[1], Riccardo Fantechi[1], Suresh Anand[2], Enrico Baria[2], Riccardo Cicchi[2], Francesco Saverio Pavone[3] and Sergio Serni[1]

[1]Department of Urology, Careggi University Hospital, Florence, Italy;
[2]European Laboratory for Non-Linear Spectroscopy, Sesto Fiorentino, Florence, Italy;
[3]Department of Physics, University of Florence, Florence, Italy

Background/Aim: Bladder cancer is a relevant malignancy in Italy, with 26000 new cases in 2016, and represents the fourth tumour for incidence in men, while is less frequent in women. It is usually related to smoking exposure or to working exposure to carcinogenic agents. The current gold standard for diagnosis is white-light cystoscopy, followed by tissue biopsy and pathological examination. However, such process is invasive, time-consuming and prone to sampling errors. In addition, urothelial carcinoma *in situ* (CIS) is plane and may be misdiagnosed because it may appear as an erythematous urothelium due to inflammation as in cystitis, thus requiring additional diagnostic strategies to improve accuracy of tissue sampling. In this framework, optical spectroscopy techniques may provide fast, label-free and non-invasive alternatives to standard histopathology. The aim of this study is to evaluate the application of combined auto-fluorescence, diffuse reflectance and Raman spectroscopy for discriminating normal bladder tissues from urothelial tumours at different stages. *Materials and Methods:* We prospectively collected fresh biopsies of urothelial tumour and healthy bladder from 65 patients undergoing Transurethral Resection of Bladder Tumours (TURBT). Fluorescence, reflectance, and Raman spectra were recorded within 30 minutes from surgical resection. For these measurements, we used four light sources – three laser diodes (378 and 445 nm for fluorescence, 785 nm for Raman) and a tungsten halogen lamp (for diffuse reflectance) – coupled into a fiber probe. The process required less than 2 minutes for each sample. Then, the recorded data were analysed using both ratiometric approach and Principal Component Analysis (PCA) for obtaining a classification algorithm based on the spectral information provided by the three techniques. *Results:* Normal and tumour bladder tissues were successfully discriminated based on the observed spectral differences, as confirmed by the subsequent histopathological examination. Fluorescence and reflectance spectra allowed discrimination between healthy and diseased tissues through ratiometric scoring. For 378-nm-excited spectra, the average ratio between fluorescence emitted at 510 nm and 600 nm (F510/600) was 57% higher for normal tissues than for tumour ones. A 19% difference was found when calculating the average F520/580 for 445-nm-excited spectra. PCA analysis provided 83% specificity and 80% sensitivity when applied to 378-nm excited spectra, 83% and 76% for 445-nm excited spectra, 75% and 75% for diffuse reflectance spectra. Moreover, Raman spectroscopy appears to be a promising tool for classifying tumour stages *via* PCA. *Conclusion:* These results are promising, as they may improve the diagnostic accuracy of bladder tumour, especially in the cases of CIS, or in second look TURBT to grant a better disease-free status. In fact, a 2002 study made by Brausi *et al.* found that a relevant part of the early recurrence at 3 months in bladder tumours can be subsequent to a residual tumour or to a cancer present, but not visible at white light cystoscopy at TURBT time (1). In this frame this technique can obtain a relevant role to improve the quality of the endoscopic resections. However, all the analysis was made *in vitro*, not *in vivo* so all these techniques are not yet available for clinical purposes and still need to be validated in clinical trials both for diagnostic accuracy and in a second time to prove if they may reduce the recurrence rate. In this study, we presented a spectroscopic system based on a fiber probe for multimodal spectroscopy combining fluorescence, Raman, and diffuse reflectance spectroscopy. Our findings indicate that the presented strategy provides a rapid discriminating capability comparable to gold standard histology. This approach could be implemented for *in vivo* detection of bladder tumour.

1 Brausi M, Collette L, Kurth K, van der Meijden AP, Oosterlinck W, Witjes JA, Newling D, Bouffioux C and Sylvester RJ: EORTC Genito-Urinary Tract Cancer Collaborative Group. Variability in the recurrence rate at first follow-up cystoscopy after TUR in stage Ta T1 transitional cell carcinoma of the bladder: a combined analysis of seven EORTC studies. Eur Urol *(5)*: 523-531, 2002.

117

EVALUATION OF SAFETY AND FEASIBILITY OF ROBOTIC ASSISTED PARTIAL NEPHRECTOMY FOR RENAL MASSES ≥4 CM BASED ON THE COMPARISON OF TRIFECTA AND PENTAFECTA RATE

Roberto Castellucci[1], Giulia Primiceri[2], Michele Marchioni[2], Pietro Castellan[1], Carlo D'orta[2], Luca Cindolo[3] and Luigi Schips[1]

[1]Department of Urology, "SS. Annunziata" Hospital, Chieti, Italy; [2]Department of Urology, "G. D'Annunzio" University - "SS. Annunziata" Hospital, Chieti, Italy

Background/Aim: Robotic Assisted Partial Nephrectomy (RAPN) is preferred to radical nephrectomy in patients with renal masses (RM) less than 4 cm. The aim of this study is to evaluate the safety and feasibility of RAPN based on the comparison of Trifecta and Pentafecta for RM ≥4 cm. *Materials and Methods:* Entire cohort was divided in 2 groups: RM <4 cm (range=0.8-3.9) and ≥ 4 cm (range=4-7.4) cm. We relied on univariable and multivariable logistic regression models adjusting for possible confounders namely: age, gender, BMI, preoperative renal function, preoperative hemoglobin, tumor complexity assessed according PADUA score, WIT, estimated blood loss, pathological surgical margin status and histological sub-type. *Results:* Out of 123 patients, 85 had RM <4 and 38 RM ≥4 cm. In preoperative demographic characteristics were not significant differences except for tumor complexity (p=0.02). About perioperative outcomes, median EBL was 166.3 ml and 287.4 ml for RM <4 cm and ≥4 cm respectively (p<0.01). The median OT was 105.9 min (<4 cm) and 133.4 min (≥4 cm). WIT was ≤25 min in 100% and 73.7% of patients with RM <4 cm and ≥4 cm respectively (p<0.01). The rate of achievement of Trifecta for RM <4 cm and ≥4 cm was 72.9% and 44.7% respectively (p<0.01) and Pentafecta was 23.5% and 10.5% respectively (p=0.08). Significant predictive factor for Trifecta was tumor diameter (OR=0.30, 95% CI=0.14-0.67, p<0.01) and postoperative Hb (OR=1.76, 95% CI=1.29-2.39, p<0.01). While for Pentafecta significant predictive factor was age only (OR=0.96, 95% CI=0.93-0.99, p=0.01). *Conclusion:* RPN could be considered safe and feasible with good postoperative outcomes even for patients with RM ≥4 cm.

118
PROSTATE CANCER AND EARLY BIOCHEMICAL RECURRENCE: WHICH IS THE ROLE OF GALLIUM-68-PROSTATE SPECIFIC MEMBRANE ANTIGEN POSITRON EMISSION TOMOGRAPHY?

Francesco Porpiglia[1], Cristian Fiori[1], Stefano De Luca[1], Matteo Manfredi[1], Enrico Checcucci[1], Giorgio Alleva[1], Diletta Garrou[1], Daniele Amparore[1] and Enrico Bollito[2]

[1]Department of Urology, AOU San Luigi Gonzaga Orbassano– Turin, Turin, Italy; [2]Department of Pathology, AOU San Luigi Gonzaga Orbassano– Turin, Turin, Italy

Background/Aim: Biochemical recurrence (BCR) in prostate cancer (PCa) patient presents a therapeutic challenge. Data support early intervention with salvage radiation therapy after radical prostatectomy (RP) and argues against prolonged monitoring of detectable post-RP PSA levels. Gallium-68-prostate specific membrane antigen positron emission tomography (^{68}Ga-PSMA PET) has been shown to detect sites of disease recurrence at serum PSA levels that are lower than those levels detected by conventional imaging. We investigated the role of PSMA-PET in PCa early BCR. *Materials and Methods:* We enrolled patients treated with Radical Prostatectomy (RP) undergone to ^{68}Ga-PSMA PET for BCR (PSA >0.2 ng/ml). Adjuvant radiotherapy (RDT) and/or anti-androgen therapy (HT) were not considered exclusion criteria. PSA value and positive site (prostatic lodge, lymph nodes, bone lesions, other lesions) were collected. *Results:* Thirty patients with a median age of 71 years [interquartile range (IQR)=63-76] and Gleason score 7 (IQR=7-7.75) were analyzed. Four (13.3%) patients had positive margins, 4 pT2c, 16 pT3a, 10 pT3b stages. RDT were performed in 13 patients (2 adjuvants, 11 salvages RDT); HT post RP in 3 patients. Median PSA before ^{68}Ga-PSMA PET was 0.66 ng/ml (IQR=0.184-3.84). ^{68}Ga-PSMA PET was positive in 24 patients (80%), radiological local and distant recurrence were discovered in 16.6 (median PSA=0.73 ng/ml, IQR=0.48-0.92) and 83.4% (median PSA=0.881 ng/ml, IQR=0.40-1.22), respectively. Positive lymph nodes were present in 12 patients (50%). The site of distant metastases were: bone, bronchialpulmonary apparatus, esophagus and abdominal wall (in the site of trocar placement during robot assisted RP 4 years before) in 3, 3, 1 and 1 patients (33.4%), respectively. ^{68}Ga-PSMA PET was negative in 6 cases (median PSA=0.493 ng/ml, IQR=0.46-0.86). Histological confirmation of PCa metastasis was available in 2 patients (internal iliac lymph node and abdominal wall). *Conclusion:* Our results support the use of ^{68}Ga-PSMA for PCa restaging after RP +/- adjuvant or salvage RDT at PSA values <1 ng/ml. However, considering the limited number of similar studies in this setting of patients, there is still a considerable scope for further research in this field.

119
STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR OLIGOMETASTATIC TRANSITIONAL CELL CARCINOMA: SINGLE INSITUTION SERIES OF 11 PATIENTS/19 LESIONS

Matteo Augugliaro[1], Giulia Marvaso[1], Dario Zerini[1], Giulia Riva[1], Elena Rondi[2], Sabrina Vigorito[2], Stefania Comi[2], Ottavio De Cobelli[3], Roberto Orecchia[4] and Barbara Alicja Jereczek-Fossa[1]

[1]Division of Radiotherapy, European Institute of Oncology, Milan, Italy;
[2]Unit of Medical Physics, European Institute of Oncology, Milan, Italy;
[3]Division of Urology, European Institute of Oncology, Milan, Italy;
[4]Scientific Direction, European Institute of Oncology, Milan, Italy

Aim: The aim of our study was to retrospectively report on the image guided stereotactic body radiotherapy (SBRT) in the oligo-recurrent bladder cancer. Eleven patients treated for low-volume metastatic transitional cell urinary bladder carcinoma (TCC) were reviewed. The primary endpoint was to evaluate the safety and efficacy of SBRT, proposed as an alternative to systemic treatment in unfit patients and/or to defer the start of a second line chemotherapy. *Materials and Methods:* Inclusion criteria for our retrospective study were as follows: adult oligometastatic TCC patients with lymph node or bone recurrence that underwent SBRT but not other local/systemic therapy. Previous radiotherapy, systemic therapy or surgery on the primary tumor were allowed. The median treatment dose was 25 Gy (range=20-30) given over a median of 5 fractions (range=3-15). Toxicity and tumor response were evaluated. Progression free-survival was also evaluated. All cases were discussed in a multidisciplinary urologic board. *Results:* Eleven patients with a total of 19 lesions were treated with CyberKnife or Vero System-SBRT between 2012 and 2016. Median age at SBRT was 67.9 years (range=50-80) and Karnofsky performance status (KPS) was 90 (range=70-90). Mean interval between TCC diagnosis and the first SBRT fraction was 2.9 years. Median follow-up was 20.4 months (range=2.4-30). Radiological response evaluated at the first imaging assessment was complete response, partial response, local progression and not evaluable 11, 1, 6 and 1 lesions, respectively. The radiological progression of disease was registered in 7 patients at the median of 8.2 months (range=2.3-18.5) from SBRT; in 5 cases it was out-field and in-field progression, while in 2 patients only out-field progression was observed. At the time of analysis (June 2017), 3 patients are alive with no evidence of disease (median of 20.9 months from SBRT), 1 alive with evidence of disease, 6 died of cancer related disease and 1 was lost to follow-up. No severe acute and late toxicity were observed. *Conclusion:* SBRT on lymph node or bone oligo-recurrence from TCC offers a good in-field tumor control with very low toxicity profile. One out of 3 patients was free of disease at 20 months. Further studies are needed to establish a role of SBRT in the oligometastatic recurrent bladder cancer. In literature there are no consistent data about the oligometastatic setting of TCC. SBRT offers a good in-field tumor control with a very low toxicity profile.

120

MPMRI PREDICTIVE VALUE IN THE DIFFERENT PROSTATE AREAS IN DETECTING PROSTATE CANCER

Lorenzo Montesi, Luca Leone, Matteo Cevenini, Lucio Dell'Atti, Michele Pucci and Andrea B. Galosi

Urological Clinic, Politecnical University of Marche Region, Ancona, Italy

Background/Aim: The aim of this study was to determine the predictive value of suspicious areas at multiparametric magnetic resonance imaging (mpMRI) considering the different prostatic regions. *Materials and Methods:* Between May 2015 and March 2017 110 patients were analyzed. Of these patients, 58 were naïve of a prostate biopsy, 26 were undergoing a first negative prostate biopsy, but have a persistent suspicious of prostate cancer (PCa), 9 had a history of PIN or ASAP, 17 were in active surveillance. The mpMRIs were performed in different centers. Twenty-seven quadruple prostate maps were used to locate the neoplasms. Five macroareas were considered: Apex, mid, base, transitional zone (1a, 3a, 5a, 7a, 9a, 11a) and anterior zone (2a, 4a, 6a, 8a, 10a, 12a, 13as, 14as, 15as). For each suspicious area a PIRADSv2 value was assessed. We made fusion "cognitive" biopsy on each patient in a single center. In case of negative mpMRI a prostate mapping was performed. *Results:* Mean age of the patients was 63.91 years, mean prostate volume was 46.75 ml, and mean number of specimens was 14.74. In 10 cases the mpMRI was not used. A total of 128 suspected lesions was found in Base areas: 32, Medium: 36, Apex: 19, Transition: 35, Anterior: 6. From the analysis of results, the following zonal features emerged: Anterior (Specificity: 98.9%; Sensitivity: 83.3%; PPV: 83.3%; NPV: 99%; Accuracy: 98%); Apex (Specificity: 89.5%; Sensitivity: 47.8%; PPV: 57.9%; NPV: 85%; Accuracy: 80%); Mid (Specificity: 71.4%; Sensitivity: 63.7%; PPV: 38.8%; NPV: 87.3%; Accuracy: 70%); Base (Specificity: 70%; Sensitivity: 42.1%; PPV: 25%; NPV: 83.6%; Accuracy: 64.5%); Transition (Specificity: 68.2%; Sensitivity: 63.6%; PPV: 20%; NPV: 93.8%; Accuracy: 67.7%). There was no correlation between the Gleason score and the PIRADS found in mpRMI in the same region. In total, 33 PIRADS 3 sites were evaluated and 11 areas (33%) were positive for prostate cancer (GG1: 5, GG2: 3, GG3: 1, GG4: 2). In the other cases, however, the areas classified with PIRADS 3 showed a negative tumor response, creating doubts regarding the real utility of classifying suspected lesions with this statement. *Conclusion:* The predictive value of mpRMI changes according to the prostate region was examined. The transition zone was burdened by a large number of false positives, but by a fairly negative predictive value. The front and apical regions had an excellent positive predictive value and discrete negative

predictive value. The median and base regions had uncertain results. This result could guide the operator in choosing the number of withdrawals to be made in biopsy, in active surveillance, and in the ability to discriminate against any false positive. In the transition area we found the major false positives of our cases. In contrast, the suspected areas identified in the front area appeared to have more specific tumor characteristics. As far as the peripheral prostate region is concerned, it was noticed that the apex region showed more specific tumor characteristics, while mid and base regions showed less specificity.

121

VALIDATION STUDY ABOUT THE ROLE OF 3D PRINTED VIRTUAL MODELS FOR ROBOT-ASSISTED-RADICAL-PROSTATECTOMY AND PARTIAL-NEPHRECTOMY

Francesco Porpiglia[1], Riccardo Bertolo[1], Matteo Manfredi[1], Fabrizio Mele[1], Daniele Amparore[1], Enrico Checcucci[1], Diletta Garrou[1], Giovanni Cattaneo[1], Dario Gned[2], Federica Solitro[2], Enrico Bollito[3], Daniele Tota[3] and Critian Fiori[1]

[1]Department of Urology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy; [2]Department of Radiology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy; [3]Department of Pathology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy

In the present study 18 patients were enrolled who underwent live surgery during an urological meeting (8 robot-assisted radical prostatectomy and 10 partial nephrectomy) to test the face and content validity of 3D virtual rendered printed models created from mp-magnetic resonance imaging and contrast-enhanced computed tomography to be used before surgery. A total of 144 urologists answered a questionnaire about their opinion expressed in Likert scale regarding the benefit of the models. A score >8/10 was obtained in all the items. The values obtained for each question permitted to achieve the model validation. In our experience, 3D printing model technology was perceived as a useful tool for surgical planning, physician training, and patient counseling.

122

MULTI-PARAMETRIC-MAGNETIC RESONANCE/ULTRASOUND FUSION PROSTATE BIOPSY: CAN THE NUMBER AND SPATIAL DISTRIBUTION OF CORES PLAY A ROLE IN THE INDEX TUMOR DETECTION AND CHARACTERIZATION?

Francesco Porpiglia[1], Stefano De Luca[1], Matteo Manfredi[1], Fabrizio Mele[1], Riccardo Bertolo[1], Diletta Garrou[1], Daniele Amparore[1], Enrico Checcucci[1], Dario Gned[2], Agostino De Pascale[2], Enrico Bollito[3] and Cristian Fiori[1]

[1]Department of Urology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy; [2]Department of Radiology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy; [3]Department of Pathology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy

To evaluate the minimum cores number for a better index tumor detection during a prostate fusion biopsy, 327 patients with a previous negative biopsy were submitted to 4 or 6 cores target biopsy, depending on the diameter of each index lesion, ≤8 or >8mm. 50.7% of patients were diagnosed with prostate cancer. Positive cores and a prevalence of Gleason pattern ≥4 were observed mostly in the central zone of the lesion. Taking two cores in the central zone is recommended.

123

EVALUATION OF THE IMPACT OF MINIMALLY-INVASIVE PARTIAL NEPHRECTOMY ON RENAL VOLUME AND RENAL FUNCTION: A PROSPECTIVE STUDY

Francesco Porpiglia[1], Riccardo Bertolo[1], Daniele Amparore[1], Matteo Manfredi[1], Fabrizio Mele[1], Diletta Garrou[1], Enrico Checcucci[1], Stefano De Luca[1], Andrea Veltri[2], Enrico Bollito[3], Daniele Tota[3] and Cristian Fiori[1]

[1]Department of Urology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy; [2]Department of Radiology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy; [3]Department of Pathology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy

We prospectively enrolled 51 consecutive patients who underwent partial nephrectomy for a renal mass, to evaluate renal function by renal scintigraphy and of kidney volume by CT-scan elaboration, prior and after surgery. In multivariate analysis, when the model was tested on the variable "effective renal plasma flow (ERPF) drop", none of the variables was significant; conversely, when it was tested on the "volume drop", ischemia time was found to be a significant predictor (p=0.009).

124

FEASIBILITY OF PROSTATE MRI-TRUS FUSION SOFTWARE-BASED TARGETED BIOPSY IN AN OUTPATIENT SETTING: OUR RESULTS

Francesco Porpiglia[1], Cristian Fiori[1], Fabrizio Mele[1], Matteo Manfredi[1], Roberta Aimar[1], Daniele Amparore[1], Enrico Checcucci[1], Diletta Garrou[1], Daniele Tota[2] and Enrico Bollito[2]

[1]Department of Urology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy; [2]Department of Pathology, AOU San Luigi Gonzaga Orbassano – Turin, Turin, Italy

Background/Aim: MRI-TRUS fusion software-based targeted biopsy (fusion biopsy, FB) is a recently introduced technique that is acquiring an increasingly role in the diagnosis of prostate cancer (PCa). MRI-TRUS software-based registration is probably the most reproducible targeted biopsy strategy, combining the accessibility of TRUS with the diagnostic accuracy of multiparametric prostate MRI (mp-MRI) and the guidance of a fusion software. Some systems allow making FB using a transperineal approach, but usually the operating room under sedation or spinal anesthesia is required to perform the procedure. This is in discord with the idea of mini-invasive procedure, prolonging the biopsy time and increasing costs. The aim of the study was to present the experience of our tertiary center in which we perform FB in an outpatient setting under local anesthesia. *Materials and Methods:* In this prospective study we enrolled patients with suspicion of PCa and the presence of one or more lesion of interest (LOI) on MRI (09/2015–03/2017). The MRI study consisted of T2-weighted, DWI and DCE imaging. All lesions were classified according to PIRADS v.1 system. All patients were subjected to FB using the Biojet® system (D&K Technologies), sampling at least 3 cores for LOI. Transrectal (TR) approach was used for LOIs in the peripheral zone while transperineal (TP) approach for LOIs in the transition, central or anterior zone. We performed FB under TR approach with local anesthesia by injection of 2% lidocaine (6-8 ml) at the angle between the seminal vesicle and prostate base, identified in the longitudinal TRUS scan. We performed FB under TP approach with 1 ml of 2% lidocaine into the perineal subcutaneous tissue at the point suggested by Biojet® software to perform the sampling, and then 3-4 ml of 2% lidocaine through a 18G spinal needle along the route up to periapical site. Pain was assessed using an 11-point visual analog scale (VAS) from 0 (no discomfort) to 10 (the most severe pain). *Results:* Overall, 290 patients were enrolled; 24.6% patients were biopsied under TP approach, 75.4% under TR approach. In 12.6% of cases, a standard biopsy was added to target one, due to first biopsy or active surveillance protocol. Mean operative time for TR and TP approach was 21.6 (+3.6) and 20.9 (+5.2) minutes, respectively. No intraoperative complications occurred, and no intravenous sedation was required. VAS score was 1.32 (+0.85) and 1.93 (+1.35) for TR and TP approach, respectively (not statistically significant). Of the examined patients, 8.8% referred a mild post-operative pain controlled with paracetamol 1g. *Conclusion:* Local anesthesia during FB procedures showed a good efficacy on intra- and post-operative pain control.

126

VALIDATION OF PRE-TREATMENT RISK STRATIFICATION PARAMETERS ACCORDING TO EAU GUIDELINES ON UPPER TRACT UROTHELIAL CARCINOMA (UTUC)

Francesco Soria[1], Beat Foerster[1], Surena F. Matin[2], Thomas Seisen[3], Evanguelos Xylinas[4], Shoji Kimura[5], Leonardo L. Monteiro[6], Mounsif Azizi[7], Marco Bandini[8], Timothy Clinton[9], Kees Hendricksen[10], Ja H. Ku[11], Markus Grabbert[12], Anna K. Czech[13], Romain Mathieu[14], Tim Muilwijk[15], Uzoma Anele[16], Firas Petros[2], Laura-Maria Krabbe[9], Morgan Rouprêt[17], Alberto Briganti[8], Axel Heidenreich[12], Armin Pycha[18], Riccardo Autorino[19], Shin Egawa[5], Philippe E. Spiess[20], Steven Joniau[15], Wassim Kassouf[21] and Shahrokh F. Shariat[1]

[1]Department of Urology And Comprehensive Cancer Center, Medical University of Vienna, Austria; [2]Department of Urology, MD Anderson Cancer Center, Houston, TX, U.S.A.; [3]Department of Urology, Pitié-Salpétrière, Assistance-Publique Hôpitaux de Paris And Faculté de Médecine Pierre et Marie Curie, University Paris VI, Paris, France; [4]Department of Urology, Cochin Hospital, Assistance-Publique Hôpitaux de Paris, Paris Descartes University, Paris, France; [5]Department of Urology, Jikei University School of Medicine, Tokyo, Japan; [6]Department of Urology, McGill University Health Center, Montreal, Canada; [7]Department of Genitourinary Oncology, Moffitt Cancer Center, Tampa, FL, U.S.A.; [8]Department of Urology, Urological Research Institute, Vita-Salute University, San Raffaele Scientific Institute, Milan, Italy; [9]Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX, U.S.A.; [10]Department of Urology, The Netherlands Cancer Institute-Antoni Van Leeuwenhoek Hospital, Amsterdam, the Netherlands; [11]Department of Urology, Seoul National University Hospital, Seoul, Republic of Korea;

[12]Department of Urology, Uro-Oncology, Robot Assisted and Reconstructive Urologic Surgery, University Hospital Cologne, Cologne, Germany;
[13]Department of Urology, Jagiellonian University, Krakow, Poland;
[14]Department of Urology, University of Rennes, Rennes, France;
[15]Department of Urology, University Hospitals Leuven, Leuven, Belgium;
[16]Division of Urology, Virginia Commonwealth University, Richmond, VA, U.S.A.;
[17]Department of Urology, Pitié-Salpétrière, Assistance-Publique Hôpitaux de Paris And Faculté de Médecine Pierre et Marie Curie, University Paris VI, Paris, France;
[18]Department of Urology, Central Hospital of Bolzano, Bolzano, Italy;
[19]Department of Urology, Virginia Commonwealth University, Richmond, VA, U.S.A.;
[20]Department of Genitourinary Oncology, Moffitt Cancer Center, Tampa, FL, U.S.A.;
[21]Department of Surgery (Division of Urology), McGill University Health Center, Montreal, Canada

Background/Aim: The European Association of Urology (EAU) Guidelines recently renewed the criteria for pre-treatment risk stratification as exclusion criteria for kidney-sparing surgery (KSS). The aim of the present study was to evaluate the additive value of each factor including the whole model for identifying advanced pathologic stage after RNU. *Materials and Methods:* We conducted a multi-institutional retrospective study that included 406 patients who underwent ureterorenoscopy with biopsy followed by radical nephroureterectomy (RNU) for non-metastatic UTUC between 2000 and 2017. Patients who received preoperative chemotherapy were excluded. We performed logistic regression analyses with area under the curve receiver operating characteristics (AUC-ROC) to compare the different factors in predicting ≥pT2 pathologic stage. Furthermore, we conducted decision curve analysis to assess the clinical net benefit and net reduction. *Results:* Overall, 146 (35.6%) patients had a high-grade biopsy, 94 (23.2%) high-grade cytology, 39 (9.6%) invasive disease in computed tomography urography (CTU), 201 (49.5%) tumor size >2 cm, 112 (27.6%) preoperative hydronephrosis, 18 (4.4%) previous cystectomy and 80 (19.7%) multifocal disease. The final RNU pathology revealed 173 (42.6%) patients with ≥pT2 disease. In a preoperative multivariable model, biopsy high-grade [odds ratio (OR)=4.44, $p<0.001$], CTU invasion (OR=4.19, $p<0.001$), tumor size >2 cm (OR=1.75, $p=0.013$) and high-grade cytology (OR=1.72, $p=0.039$) were independently associated with muscle-invasive pathologic stage. On the other hand, preoperative hydronephrosis, previous cystectomy and multifocality were not. The addition of these three factors improved the model's accuracy from 74 to 75% and the negative predictive value (NPV) from 89 to 90%. Decision curve analyses showed a maximum clinical net benefit of 0.19 at the threshold probability of 0.25 for the model with biopsy grade, cytology, CTU invasion and tumor size >2 cm. Preoperative hydronephrosis, previous cystectomy and multifocality did not convey any clinical net benefit nor net reduction to this model. *Conclusion:* High-grade ureteroscopic biopsy and cytology, CTU invasion and tumor size >2cm seem to be the best factors to identify patients who harbor muscle-invasive disease within a box model. The additive value of preoperative hydronephrosis, previous cystectomy and tumor multifocality could be limited. Further biomarkers are needed to best identify the patients who could most likely benefit from endoscopic KSS.

127
CAN ROBOT-ASSISTED LAPAROSCOPIC PROSTATECTOMY BE RECOMMENDED TO OBESE PATIENTS? OUR EXPERIENCE

Ambra Rizzoli[1], Jamil Ghahhari[1], Piergustavo De Francesco[1], Giulia Primiceri[1], Michele Marchioni[1], Pietro Castellan[2], Luca Cindolo[2] and Luigi Schips[1]

[1]Department of Urology, Robotic Unit, "SS Annunziata" Hospital, G. D'Annunzio University, Chieti, Italy;
[2]Department of Urology, "SS. Annunziata Hospital" Chieti, Italy

Background/Aim: With the increase of obesity in our country in the last years, a significant proportion of robot-assisted laparoscopic prostatectomy (RALP) candidates have an elevated body mass index. The aim of the present study was to analyze the possible effect of BMI on RALP oncological and functional outcomes and postoperative complications to determinate if this surgical procedure can be recommended in obese patients. *Materials and Methods:* We consecutively collected data about patients who underwent RALP in our center between March 2013 and December 2016. A single expert surgeon performed all the surgeries following the Patel's technique, with da Vinci Si System. Patients were divided into three groups based on their preoperative BMI: group 1 normal weight, <25 kg/m^2 (n=71); group 2 overweight, ≥25 and ≤30 kg/m^2 (n=88); group 3 obese, >30 (n=73). Preoperative, perioperative and postoperative data as long term oncological and functional outcomes were compared between the three groups, using multiple linear regressions and multiple logistic regression, based on the results of bivariate analysis. *Results:* Two hundred and twenty two RALP were performed (Table I). There were no significant differences in demographic data among the three groups, except for anti-platelet therapy

Table I. *Demographics of patients who underwent robot-assisted laparoscopic prostatectomy.*

		Group 1 (n=71)	Group 2 (n=88)	Group 3 (n=73)	Total (n=222)	*p*-Value
Demographics						
Age	Mean (SD)	66. (5.4)	66.1 (5.7)	66 (5.8)	65.9 (5.7)	0.91
Prostate weight	Mean (SD)	57.6 (30)	56.6 (22)	60 (23)	58.8 (25)	0.75
PSA	Mean (SD)	9.1 (4)	8.4 (3.6)	9.4 (4.2)	8.9 (4)	0.74
Console time	Mean (SD)	119 (41.2)	124.4 (47)	137.3 (41.1)	123.6 (43.3)	0.53
Anti-platelet therapy	N (%)	6 (8.5)	16 (18.9)	20 (31.8)	42 (19)	0.03
Abdominal surgery	N (%)	26 (36.6)	44 (50)	29 (46)	99 (44.6)	0.48
Peri- and post-operative						
Hb delta	Mean (SD)	2.5 (1.5)	2.15 (1.2)	2.2 (1.4)	2.3 (1.3)	0.24
Blood loss	Mean (SD)	161.7 (139)	163.7 (117)	189.8 (177)	170.2 (143)	0.45
Hospital stay	Mean (SD)	4.8 (4.1)	3.8 (1.4)	4.2 (2.6)	4.2 (2.9)	0.07
Dreinage days	Mean (SD)	3.7 (3.9)	2.74 (1.2)	3.1 (2.5)	3.1 (2.7)	0.07
Days of catheterization	Mean (SD)	10.8 (3.7)	10.1 (0.8)	10.9 (3.3)	10.5 (2.8)	0.13
Complications	N (%)	8 (11.2)	3 (3.1)	6 (9.5)	17 (7.7)	0.14
Follow-up (FU)						
Last FU continence	N (%)	27 (38)	30 (34.9)	22 (34.9)	79 (35.6)	0.48
Continence recovery time (days)	Mean (DS)	55 (50.8)	41.7 (35.5)	33 (23)	42.5 (43)	0.27
Last FU erectile function	N (%)	24 (33.8)	25 (28.4)	26 (41.3)	75 (33.8)	0.26
Spontaneouserection	N (%)	14 (19.7)	26 (29.6)	18 (28.6)	58 (26.1)	0.29
Oncological outcomes						
Positive margins	N (%)	20 (28.2)	30 (34,9)	21 (33.3)	71 (32)	0.7
Extracapsular extension	N (%)	20 (28.2)	28 (31.8)	19 (30.2)	67 (30.2)	0.88

PSA, Prostate-specific antigen; SD, standard deviation.

assumption. Mean patient age was 65.92±5.72 years. Mean PSA was 8.89±3.9 ng/ml. The median operative time was longer in group 3, even if it is not statistically significant. A statistical trend toward significance has been demonstrated in the length in drainage and hospital stay (p=0.07), resulting in a increase in Group 1. There were no significant differences in median estimated blood loss, mean prostate volume, positive surgical margin rate and time to continence without pads. BMI had also no significant effects on overall complications rate. *Conclusion:* Our results showed that obese patients can also be safely considered as candidates for robotic assisted laparoscopic radical prostatectomy with no significant increase in blood loss, complications, length of hospital stay and time to continence without pads. RALP is a safe and effective procedure in patients with elevated BMI.

129
COMBINED POSITIVITY FOR P63 AND ERG IN INTRADUCTAL CARCINOMA OF THE PROSTATE

Alessio Tognarelli[1], Tommaso Di Vico[1], Jacopo Durante[1], Chiara Polito[1], Iacopo Meneghetti[1], Lorenzo Tesi[1], Ramona Baldesi[1], Pinuccia Faviana[2] and Riccardo Bartoletti[1]

[1]Urology Unit, Department of Translational Medicine and New Technologies, University of Pisa, Pisa, Italy; [2]Anatomia e istologia patologica 3, Dipartimento di Patologia Chirurgica, Medica, Molecolare e dell'Area Critica, Pisa, Italy

Background/Aim: The term "intraductal carcinoma of the prostate" (IDC-P) was introduced almost 40 years ago and describes an expansive proliferation of malignant prostatic secretory epithelial cells within prostate ducts and acini, associated with at least partially preserved basal cell layer and significant architectural and cytological atypia. The presence of IDC-P in a pathological specimen is frequently associated with large tumour volume, advanced stage, high Gleason score, increased recurrence risk and poor prognosis, regardless of treatment status. ERG is a highly specific prostate cancer marker which is activated in more than 50% of prostate cancer cases, generally through a gene fusion with the androgen-responsive promoter of transmembrane protease serine 2.P63 protein has been regarded as a basal cell immunohistochemical marker. P63 is expressed in the proliferative layer of cells near the basement membrane where it likely prevents basal cells from differentiating and thereby helps to maintain their basal cell status. Immunohistochemical expression of both p63 and ERG

protein is frequently found in patients with aggressive prostate cancer, despite the fact of expression of each independent marker in about 5% of patients with benign disease. The aim of the present study was to evaluate the potential impact of combined ERG and p63 expression in patients with aggressive high-risk prostate cancer. *Materials and Methods:* Pathological specimens from 69 patients who had previously undergone both radical retropubic prostatectomy and robotic assisted laparoscopic prostatectomy with bladder neck sparing (BNP) approach for medium-/high- risk prostate cancer between 2011 and 2015 have been selected to evaluate the prevalence of IDC-P. The criteria proposed by Guo and Epstein have been used for pathological analysis; according to these Authors, IDC-P is defined as malignant epithelial cells filling large acini and prostatic ducts, with preservation of basal cells forming either solid or dense cribriform patterns or loose cribriform or micropapillary patterns with either marked nuclear atypia (nuclear size 6× normal or larger) or comedonecrosis. Immunohistochemical staining for p63 and ERG was used to confirm retention of the basal layer and explore their potential role in diagnosis and in the long term disease prognosis. The mean age at time of prostatectomy was 67±6.9 years; tumor stage was pT2aN0 in 1 case, pT2aN1 in 1 case, pT2bN0 in 1 case, pT2cN0 in 16 cases, pT2cN1 in 3 cases, pT3aN0 in 19 cases, pT3aN1 in 3 cases, pT3bN0 in 7 cases, pT3bN1 in 18 cases. Gleason score was 6 in 7 cases, 7 in 43 cases, 8 in 11 cases, 9 in 8 cases. Positive surgical margins (PSM) were found in the 85.6% specimens. Mean follow-up was 4.6±1.6 years. All 69 patients received conformational adjuvant radiotherapy. Biochemical progression-free survival curve was constructed according to the Kaplan-Meier method. *Results:* IDC-P was found in 31 out 69 cases (44.9%), in whom the pathological diagnosis was immunohistochemically confirmed by the combined positivity for p63 and ERG expression. Biochemical recurrence was found in 51.6% in the IDC-P group and 36.8% in the other group respectively. No significant differences in cancer related survival were found between the two groups. *Conclusion:* The presence of intraductal carcinoma of the prostate should be evaluated and documented correctly in both radical prostatectomy and needle prostate biopsy and the clinical implications thereof should be taken into consideration during treatment and follow-up of prostate cancer. On prostatectomy histological sections, p63 and ERG immune stains combines the high sensitivity of p63 and the high specificity of ERG and may be potentially useful in the work-up of prostate biopsies for the early identification of IDC-P and high-risk prostate cancer patients, above all in cases where the total amount of prostatic tissue is insufficient for a correct final pathological diagnosis.

130

SALVAGE RADIOTHERAPY FOR RECURRENT PROSTATE CANCER AFTER PROSTATECTOMY: FROM THE INVISIBLE TO THE VISIBLE CONCEPT

Maria Alessia Zerella[1], Giulia Marvaso[1], Olga Oneta[1], Simona Arculeo[1], Stefano Durante[1], Dario Zerini[1], Stefania Comi[2], Alessia Bazani[2], Federica Cattani[2], Roberto Orecchia[3] and Barbara Alicja Jereczek Fossa[1]

[1]Division of Radiotherapy, European Institute of Oncology, Milan, Italy; [2]Unità di Fisica Medica, European Institute of Oncology Milan, Italy; [3]Direzione Scientifica, European Institute of Oncology Milan, Italy

Background/Aim: Standard salvage radiotherapy (SRT) for biochemical post-prostatectomy recurrence of prostate cancer (PCa) includes prostatic bed +/- pelvis (1). Thanks to advances in imaging, such as ^{11}C-choline positron emission tomography/computed tomography (^{11}C-choline PET/CT) and multiparametric magnetic resonance imaging (MRI), it is possible to identify the macroscopic local recurrence (2). This has led to greater interest in SRT delivered only on the macroscopic/radiological relapse with hypofractionated schedules in highly selected patients with the potential in sparing the toxicity of a salvage treatment that involves a bigger volume (3, 4). The aim of this study is to retrospectively review our data on the feasibility, the prostate-specific antigen (PSA) response and toxicity of hypofractionated SRT for isolated relapse in the prostatic bed from PCa after prostatectomy in RT- naïve patients treated in our Institution. *Materials and Methods:* Inclusion criteria were as follows: RT-naïve patients (no previous adjuvant pelvic RT); biochemical recurrence according to EAU guidelines and followed by clinically evident local recurrence assessed with MRI or/and ^{11}C-choline PET/TC (Figure 1); N0, M0, informed consent (Table I). SRT was performed using Vero® System, a 6-MV C-band linac with a fast MLC mounted on an O-ring gantry. No fiducials markers were implanted in prostate bed before treatment but contouring may be facilitated by MRI or ^{11}C-choline PET/TC fusion techniques and Cone-beam CT (CBCT) was performed before every Vero system session to verify matching of CBCT images to reference planning CT. Static Step-and-Shoot Intensity Modulated Radiation Therapy (IMRT) with seven coplanar fields of 6-MV photons or Dynamic Wave Arc (DWA) technique were used for treatment planning (Figure 2). Biochemical response will be evaluated with PSA test every 3 months after treatment: biochemical response (BCR) as a reduction of PSA value >10% with respect to pre-SRT PSA value, progression (BCP) as a PSA increase >10%, and stability (BCS) as a PSA stabilization between 10% and -10%

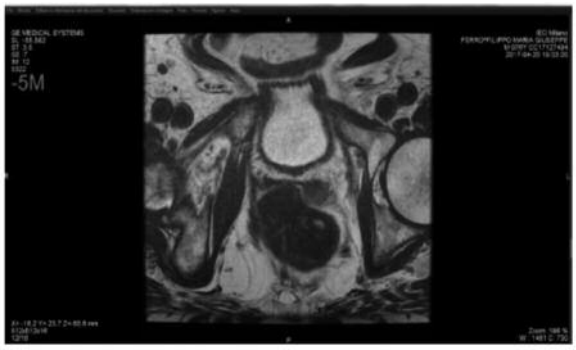


Figure 1. *MRI image showing macroscopic disease recurrence in left prostatic bed (diameter: 17 mm).*

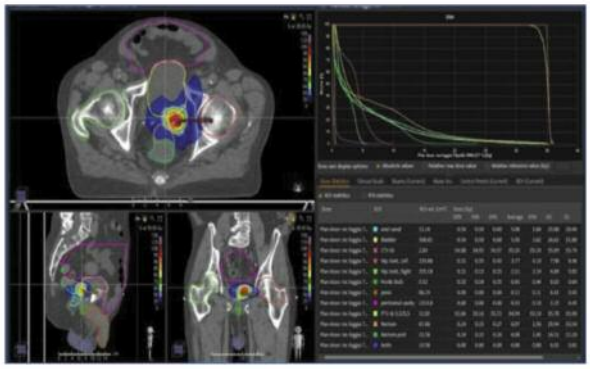


Figure 2. *Treatment planning with DVH of hypofractionated salvage radiotherapy delivered.*

Table I. *Inclusion and exclusion criteria used in the study.*

Inclusion criteria	RT-naïve patients (surgery as primary treatment and no previous adjuvant/pelvic RT)
	isolated radiologically evident recurrence in the prostatic bed from PCa after prostatectomy
	no evidence of extra-regional localization (N0, M0)
	Written informed consent signed
Exclusion criteria	Nodal involvement or distant metastasis (cN1 cM1)
	Previous pelvic RT
	Non-conformity to dose constraints at the treatment planning
	Mental diseases that cannot ensure a valid informed consent

RT, Radiotherapy; PCa, prostate cancer.

(5). Clinical follow-up will be performed at 6 and 12 months after treatment and every 12 months afterward in order to assess genito-urinary (GU) and gastrointestinal (GI) toxicity (RTOG-EORTC). *Results:* We retrospectively analyzed 19 patients treated between 8/2013 and 6/2017 for clinically visible PCa recurrence in the prostatic bed with hypofractionated Intensity Modulated Radiation Therapy (IMRT) schedules. Median interval between diagnosis of PCa and SRT was 76 months (range=3-166) and median PSA at clinical progression was 1.3 ng/ml (range=0.14-9.61). Four patients received concomitant hormonal therapy (HT) and SRT. No GI or GU acute toxicity > G2 was reported. At 3 months PSA evaluation BCR was observed in 17 of 19 patients (89.5%), BCS in 1 of 19 patients (5.2%) and BCP in 1 of 19 patients (5.2%). At median follow-up of 6 months BCR was confirmed in 12 patients (63.2%); BCP occurred in 7 patients (36.8%) after a median time of 12 months (range=6-24) from the SRT; clinical progression followed BCP in 5 cases (71.5%), after a median time of 18 months (range=8-30) from the SRT and was detected by radiological imaging; no late GI or GU toxicity was reported at all. *Conclusion:* To the best of our knowledge this is the first study on isolated macroscopic PCa recurrence in prostatic bed in RT naive patients treated with salvage extremely hypofractionated RT. On the basis of available data, extremely hypofractionated salvage IMRT is feasible and safe for isolated macroscopic recurrence in the prostatic bed, with a low acute toxicity profile. Moreover the PSA response was excellent: progression was registered only in 7 patients (36.8%), and 5 of these 7 patients were classified as unfavorable intermediate, high or very high-risk PCa at first diagnosis, confirming need for strict patient selection. In accordance with our results, a better stratification of patients is needed in order to perform an optimal management in this setting, and achieve the best possible outcome and develop a real personalized medicine. Further studies are necessary to compare hypofractionated SRT with standard SRT on the whole prostatic bed and with systemic therapy, but the growing interest for fusion MRI/Choline PET imaging, low toxicity profile of our treatment and good results we obtained in terms of local control and toxicity are a first step in this direction.

1 Cornford P, Bellmunt J, Bolla M, Briers E, Santis MD, Gross T and Mottet N: EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part II: Treatment of Relapsing, Metastatic,

and Castration-Resistant Prostate Cancer. Eur Urol *71(4)*: 630-642, 2017.
2 Hernandez D, Salas D, Giménez D, Buitrago P, Esquena S, Palou J, de la Torre P, Pernas J, Gich I, Gómez de Segura G, Craven-Bartle J and Sancho G: Pelvic MRI findings in relapsed prostate cancer after radical prostatectomy. Radiat Oncol *10*: 262, 2015.
3 Brenner DJ, Martinez AA, Edmundson GK, Mitchell C, Thames HD and Armour EP: Direct evidence that prostate tumors show high sensitivity to fractionation (low alpha/beta ratio), similar to late-responding normal tissue. Int J Radiat Oncol Biol Phys *52(1)*: 6-13, 2002.
4 Detti B, Bonomo P, Masi L, Doro R, Cipressi S, Iermano C, Bonucci I, Franceschini D, Di Brina L, Baki M, Simontacchi G, Meattini G, Carini M, Serni S, Nicita G and Livi L: CyberKnife stereotactic radiotherapy for isolated recurrence in the prostatic bed. World J Urol *34*: 311-317, 2016.
5 Jereczek-Fossa BA, Beltramo G and Fariselli L: Robotic image-guided stereotactic radiotherapy, for isolated recurrent primary, lymph node or metastatic prostate cancer. Int J Radiat Oncol Biol Phys *82*: 889-897, 2012.

131

ANGIOMYOLIPOMA OF THE RENAL SINUS: CASE REPORT AND REVIEW OF THE LITERATURE

Lucio Dell'Atti, Simone Scarcella, Matteo Cevenini, Lorenzo Montesi and Andrea Benedetto Galosi

Institute of Urology, University Hospital "Ospedali Riuniti", Ancona, Italy

Background/Aim: Angiomyolipoma (AML) is a well-known type of tumor; its name is derived from three components: blood vessels, smooth muscle, and fat. It is an uncommon tumor that though benign in most cases can present difficult management decisions. An AML that originates from the renal sinus rather than the renal parenchyma is extremely rare and is therefore difficult to differentiate from other fat containing masses, such as lipomatosis, lipoma, and liposarcoma (1). Only 14 cases of AML involving or originating in the renal sinus have been previously reported in literature (2). We present a rare case of a partially exophytic AML of the renal sinus in a 56 a year-old woman with a relatively rapidly growing. *Case Report:* A 56-year-old woman visited a hospital in April 2016 for diagnostic evaluation of a right kidney mass renal tumor that had been detected during a routine medical checkup. Neither she nor anyone in her family had a history of tuberous sclerosis (TS). Computed tomography (CT) showed a 4.2×3.4×4.6 cm mass originating from the right renal sinus. The mass was mainly composed of fat with some contrast enhancement, and was subsequently diagnosed as an AML of the renal sinus. In May 2017, she was referred to our department for follow-up of the mass. CT revealed a 6.4×5.1×6.2 cm mass originating from the right renal sinus and that appeared to extend into the perinephric soft tissues (Figure 1). Considering the rapid growth of the first lesion and that the mass was significantly pushing aside the duodenum, though the patient had no symptoms associated with the enlarged tumor, a surgical resection of the mass was performed. Surgery was performed using an intra-operative ultrasonography to identify intrarenal lesions margins and renal masses were removed without need of vascular clamping and renal warm ischemia. The patient was discharged after 4 days without post-operative complications. The definitive histopathological examination confirmed the radiologic diagnosis of renal angiomyolipoma At six months CT scan follow-up, no local or metastatic recurrence was documented, preserving a renal function unchanged. *Discussion and Conclusion:* AML has an incidence of 0.1-0.22% in the general population, and is four times more frequent in women than in men (1). The lesions may present as sporadic cases or in association with TS. TS is an autosomal dominant neurocutaneous disorder that may affect several organs, *e.g.* brain, skin, eyes, heart, kidney and lungs. Since patients are usually asymptomatic, the diagnosis of AML is often incidental; this happens with lesions with a diameter of less than 4 cm. Lesions greater than 4 cm in diameter are often symptomatic and manifest with a clinical picture characterized by lumbar pain, anaemia and hematuria (2). Retroperitoneal hemorrhage and/or bleeding into the renal collecting system are the major complications of AML; both conditions may put the patient's life at risk. The therapeutic strategy varies from case to case: selective embolization of the renal artery and surgical removal of the lesion are the pillars of AML management (1,

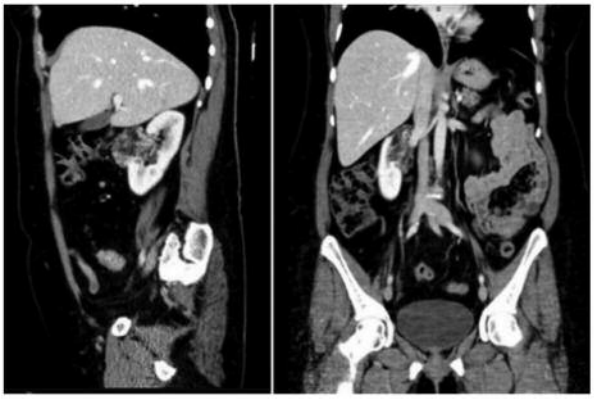


Figure 1. *Computed tomography scan shows an angiomyolipoma originating from the right renal sinus.*

2). Alternatively, it is possible to follow the clinical course, with periodic surveillance of the lesions. Nephrectomy or nephron sparing surgery can be opted for in more severe cases such as case aforementioned. Only one report showed that MRI-guided percutaneous aspiration biopsy appears to be a useful diagnostic procedure when there is concern about the nature and malignant potential of fatty renal sinus masses that have an unusual appearance (2). The remaining 13 cases were diagnosed by open surgery, usually a nephrectomy. The first cases of AML involving renal sinus reported in literature were in 1972 by Cass and Ireland (3) The authors described 2 patients with renal angiomyolipoma that presented as renal pelvic masses. However, all 14 cases were treated with nephrectomy and all were shown microscopically to involve the kidney parenchyma, suggesting that these masses were not of a true renal sinus origin. If at all possible, a preoperative diagnosis of AML is desirable so as to avoid open exploration, as the proximity of the tumor to the vascular pedicle confers a risk of nephrectomy even in cases when only a biopsy is planned (1, 2). On ultrasound (US), AMLs are almost always hyperechoic compared to renal parenchyma due to the presence of macroscopic fat. However, renal cell carcinoma also appears hyperechoic on US in approximately one third of cases. CT and MRI, with their ability to detect small quantities of fat, can reliably diagnose the usual parenchymal AML, but their ability to definitively diagnose renal sinus AMLs has not been established (2). The diagnosis of AML originating in the renal sinus, although exceedingly rare, should be considered when imaging studies demonstrate a fat-containing renal sinus mass with characteristics of an AML (3). Various imaging and interventional radiographic techniques now available may allow surgery to be avoided in some of these cases (1, 2). Percutaneous aspiration biopsy appears to be a useful diagnostic procedure when there is concern about the nature and malignant potential of fatty renal sinus masses that have an unusual appearance, and can allow a definitive diagnosis. In conclusion, we describe a rare case of partially exophytic AML in the renal sinus treated with an enucleation of the renal mass. However, the management of AMLs is complex and challenging, especially for cases originating from the renal sinus and those without TS, and is therefore difficult to differentiate from other fat containing masses, such as lipomatosis, lipoma, and liposarcoma.

1 Shirotake S, Yoshimura I, Kosaka T and Matsuzaki S: A case of angiomyolipoma of the renal sinus. Clin Exp Nephrol *15*: 953-956, 2011.

2 Flum AS, Hamoui N, Said MA, Yang XJ, Casalino DD, McGuire BB, Perry KT and Nadler RB: Update on the Diagnosis and Management of Renal Angiomyolipoma. J Urol *195*: 834-846, 2016.

3 Cass AS and Ireland GW: Angiomyolipoma of the kidney. Report of 2 cases presenting as pelvic masses. Br J Urol *44*: 129-132, 1972.

132

PATTERNS AND PREDICTORS OF RESECTION TECHNIQUES DURING PARTIAL NEPHRECTOMY FOR T1 RENAL MASSES: RESULTS OF A MULTI-CENTRE PROSPECTIVE COHORT STUDY FROM THE SURFACE-INTERMEDIATE-BASE (SIB) MARGIN SCORE INTERNATIONAL CONSORTIUM (IDEAL PHASE 2B)

Riccardo Campi[1], Alexander Kutikov[2], Brian Lane[3], Ottavio De Cobelli[4], Francesco Sanguedolce[5], Georgios Hatzichristodoulou[6], Andrea Mari[7], Alessandro Antonelli[8], Oscar Rodriguez-Faba[9], Johan Langenhuijsen[10], Tobias Klatte[11], Marco Roscigno[12], Bulent Akdogan[13], Nihat Karakoyunlu[14], Martin Marszalek[15], Umberto Capitanio[16], Alessandro Volpe[17], Sabine Brookman-May[18], Robert Uzzo[2], Marco Carini[19], Alberto Lapini[19] and Andrea Minervini[19]

[1]Department of Urology, University of Florence, Careggi Hospital, Florence, Italy;
[2]Division of Urologic Oncology, Fox Chase Cancer Center, Philadelphia, PA, U.S.A.;
[3]Department of Urology, Spectrum Health Medical Group, Grand Rapids, MI, U.S.A.;
[4]Department of Urology, European Institute of Oncology (IEO), Milan, Italy;
[5]Department of Urology, Southmead Hospital-North Bristol NHS Trust, Bristol, U.K.;
[6]Department of Urology, Technical University of Munich, University Hospital Klinikum Rechts der Isar, Munich, Germany;
[7]Department of Urology, Department of Urology, University of Florence, Careggi Hospital, Florence, Italy;
[8]Department of Urology, University of Brescia, Brescia, Italy;
[9]Uro-oncology Unit, Fundacio Puigvert, Barcelona, Spain;
[10]Laparoscopy, Robotics And Endourology, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands;
[11]Department of Urology, Medical University of Vienna, Vienna, Austria;
[12]Department of Urology, AO Papa Giovanni XXIII, Bergamo, Italy;
[13]Department of Urology, Hacettepe University, School of Medicine, Ankara, Turkey;
[14]Department of Urology, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey;

[15]Department of Urology And Andrology, Donauspital, Vienna, Austria;
[16]Department of Urology, University Vita-Salute San Raffaele, Scientific Institute Hospital San Raffaele, Milan, Italy;
[17]Department of Urology, University of Eastern Piedmont, Maggiore Della Carità Hospital, Novara, Italy;
[18]Department of Urology, Janssen Research & Development, Global Clinical Operations Germany; Ludwig-Maximilians-University, Munich, Germany;
[19]Department of Urology, Department of Urology, University of Florence, Florence, Italy

Background/Aim: To date, EAU Guidelines do not provide specific recommendation on resection techniques (RT) for tumor excision during partial nephrectomy (PN). To fill this unmet clinical need, we created in 2014 the SIB Margin score International Consortium designing a prospective multi-stage project (SIB project) following the IDEAL model. The aim of the study is to assess patterns and predictors of RTs in a cohort of patients undergoing PN for localized renal tumors (IDEAL Phase 2b). *Materials and Methods:* Consecutive patients with cT1-2 N0 M0 renal tumors treated with NSS from September 2014 to March 2015 were included. SIB score assignment is shown in

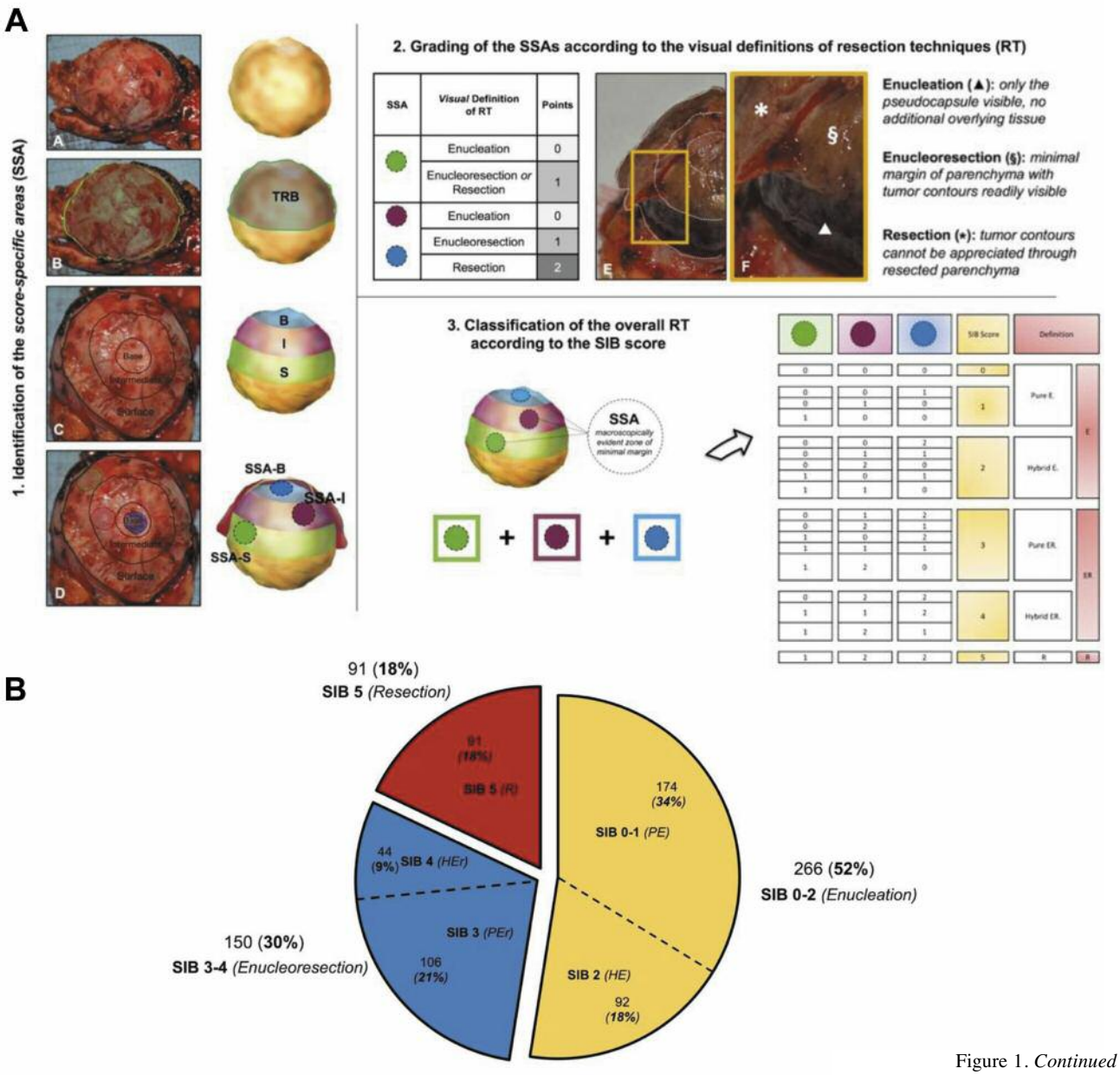


Figure 1. *Continued*

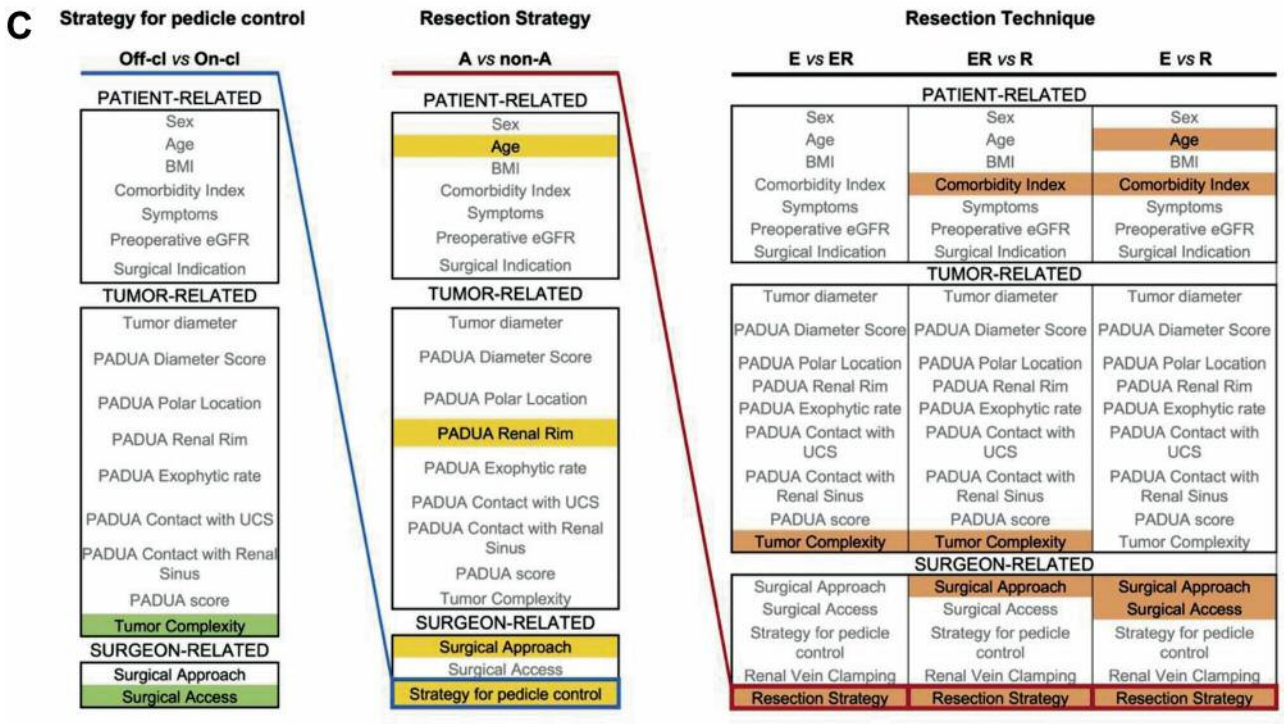


Figure 1. *Principles of surface-intermediate-base (SIB) score assignment (A). SIB score assignment in our cohort (B). Overview of multivariable analysis assessing predictors of resection technique, resection strategy and strategy for renal pedicle clamping in our cohort (C).*

Figure 1A. Multivariable models explored the predictors of RTs, resection strategy (RS) and strategy for renal pedicle control (SRPC). *Results:* Overall, 507 patients were included. SIB score assignment in the entire cohort is shown in Figure 1B while descriptive statistics in Table I. At multivariable analysis, patient age, CCI≥2, high tumor complexity, surgical approach, RS and surgical access were significantly associated with RT (Table II). Increasing patient age, medial renal rim, clampless strategy for renal pedicle control, open and laparoscopic were independent significant predictors of anatomic *vs*. non-anatomic RS. Finally, high or intermediate tumor complexity, retroperitoneal surgical access and laparoscopic surgical approach were significantly predictor of a clampless *vs*. on-clamp strategy (Figure 1C). *Conclusion:* Our study showed for the first time that RT did vary across surgeons worldwide and that specific factors were significant predictors of RT, RS and SRPC during PN. IDEAL Phase 3-4 studies are needed to validate our results and to assess potential associations between RTs and PN outcomes.

Table I. *Patient-, tumor-, and surgery-related factors in the overall cohort and stratified by SIB score.*

		Resection Technique according to the SIB Margin Score			
		Enucleation (SIB 0-2) (n=266)	Enucleoresection (SIB 3-4) (n=150)	Resection (SIB 5) (n = 91)	Overall (n=507)
Patient-related					
Sex (n, %)	Male	182 (68.4)	97 (64.7)	55 (60.4)	334 (65.9)
	Female	84 (31.6)	53 (35.3)	36 (39.6)	173 (34.1)
Age (years) (mean, SD)		62 (12.0)	61 (13.0)	57 (13.0)	61 (13.0)
Body mass Index (BMI) (median, IQR)		26.4 (24.2 – 29.7)	27.0 (24.1-30.9)	26.3 (24.2-29.3)	26.7 (24.2-29.8)
Charlson Comorbidity Index (CCI) (n, %)	>1	90 (33.8)	40 (26.7)	51 (56.0)	181 (35.7)
	0-1	176 (66.2)	110 (73.3)	40 (44.0)	326 (64.3)
Preoperative eGFR (ml/min/1,73m2, CKD-EPI 2009) (median, IQR)		86 (69-96)	85 (67-96)	89 (63-100)	87 (70-97)
Tumor-related					
Tumor diameter at preoperative imaging (mm) (median, IQR)		30 (25-42)	35 (26-45)	30 (20-42)	30 (25-43)
PADUA score (median, IQR)		8 (7-9)	9 (7-10)	8 (6-9)	8 (7-9)
Tumor Complexity (PADUA) (n, %)	Low (PADUA 6-7)	114 (42.9)	42 (28.0)	43 (47.3)	199 (39.3)
	Intermediate (PADUA 8-9)	95 (35.7)	63 (42.0)	33 (36.3)	191 (37.7)
	High (PADUA 10-13)	57 (21.4)	45 (30.0)	15 (16.4)	117 (23.0)
Surgeon-related					
Surgical Approach (n, %)	Open	68 (25.6)	51 (34.0)	29 (31.9)	148 (29.2)
	Laparoscopic	44 (16.5)	19 (12.7)	6 (6.6)	69 (13.6)
	Robotic	154 (57.9)	80 (53.3)	56 (61.5)	290 (57.2)
Surgical Access (n, %)	Retroperitoneal	80 (30.1)	31 (20,7)	14 (15.4)	125 (24.7)
	Transperitoneal	186 (69.9)	119 (79.3)	77 (84.6)	382 (75.3)
Resection Strategy (n, %)	Anatomic	207 (77.8)	56 (37.3)	14 (15.4)	277 (54.6)
	Non-anatomic	59 (22.2)	94 (62.7)	77 (84.6)	230 (45.4)
Strategy for renal pedicle control (n, %)	Clampless	88 (33.1)	22 (14.7)	12 (13.3)	122 (24.1)
	On-clamp	178 (66.9)	128 (85.3)	79 (86.7)	385 (75.9)

Table II. *Multivariable analysis assessing predictors of resection technique in our cohort.*

		Enucleation (SIB 0-2) vs Enucleoresection (SIB 3-4)			Enucleoresection (SIB 3-4) vs Resection (SIB 5)			Enucleation (SIB 0-2) vs Resection (SIB 5)		
Covariates		OR	95%CI	p	OR	95%CI	p	OR	95%CI	p
Patient-related										
Age (10-y fold)		1.00	0.84 -1.22	0.9	1.36	1.08 - 1.70	0.08	1.37	1.09 – 1.73	0.007
Comorbidity Burden	High (Charlson Comorbidity Index [CCI]) ≥ 2	1.04	0.60 – 1.80	0.9	0.24	0.13 – 0.49	<0.001	0.25	0.13 – 0.47	<0.001
	Low (CCI 0-1) (ref)	-	-	-	-	-	-	-	-	-
Tumor-related										
Tumor Complexity	High (PADUA score ≥10)	0.54	0.29 – 1.01	0.05	3.06	1.34 – 6.98	0.008	1.65	0.71 – 3.86	0.25
	Intermediate (PADUA score 8-9)	0.72	0.41 – 1.24	0.24	1.58	0.80 – 3.10	0.19	1.13	0.57 – 2.22	0.72
	Low (PADUA score 6-7) (ref)	-	-	-	-	-	-	-	-	-
Surgeon-related										
Strategy for renal pedicle control	Clampless	1.48	0.80 – 2.72	0.21	0.99	0.41 – 2.37	0.98	1.47	0.64 – 3.37	0.37
	On-clamp (ref)	-	-	-	-	-	-	-	-	-
Surgical approach	Open	0.84	0.49 – 1.46	0.54	1.40	0.71 – 2.74	0.33	1.17	0.59 – 2.36	0.65
	Laparoscopic	1.23	0.55 – 2.76	0.62	3.3	1.02 – 10.43	0.04	4.00	1.26 – 12.70	0.02
	Robotic (ref)	-	-	-	-	-	-	-	-	-
Resection strategy	Anatomic	5.33	3.30 – 8.60	<0.001	3.40	1.70 – 6.90	<0.001	18.10	9.10 – 36.04	<0.001
	Non-anatomic (ref)	-	-	-	-	-	-	-	-	-
Surgical access	Retroperitoneal	1.70	0.93 – 3.13	0.09	1.31	0.59 – 2.94	0.5	2.24	1.01 – 5.12	0.05
	Transperitoneal (ref)	-	-	-	-	-	-	-	-	-

133

ROBOT-ASSITED PARTIAL NEPHRECTOMY WITH ENUCLEATIVE RESECTION STRATEGY FOR HIGHLY COMPLEX RENAL MASSES: RESULTS FROM A HIGH-VOLUME REFERRAL CANCER CENTRE

Riccardo Campi, Andrea Mari, Francesco Sessa, Davide Vanacore, Simone Sforza, Giovanni Tasso, Fabrizio Di Maida, Giulia Bencini, Simone Morselli, Alberto Lapini, Marco Carini and Andrea Minervini

Department of Urology, University of Florence, AOU Careggi, Florence, Italy

Background/Aim: Tumor excision (TE) is a fundamental step during partial nephrectomy (PN), yet underreported in previous studies. We introduced the concepts of resection strategy (RS, the surgeon's preoperative intent) and resection technique (RT, the actual surgical result) to describe the complexity of TE during PN in a standardized way across published series. In a video we describe in detail the technique of robot-assisted partial nephrectomy (RAPN) performed with a pure enucleative RS for the treatment of highly complex renal masses. *Materials and Methods:* From 2010, >1,000 RAPN were performed with pure enucleative RS at our Institution for the treatment of localized renal masses. After institutional review board approval, data were prospectively collected into our kidney cancer institutional database and retrospectively reviewed to select patients with highly complex renal masses, defined as a) cT1b/T2; b) hilar and c) completely endophytic tumors. Demographic, perioperative and pathologic data were collected. RAPN was performed with a pure enucleative RS aiming to develop the anatomic dissection plane between the tumor pseudocapsule and the surrounding healthy parenchyma. *Results:* Overall, 115 patients with highly complex renal masses were included in the study. Median PADUA Score was 9 (IQR=7-11). Among the 99 (86.1%) tumors with clinical diameter ≥4 cm, 28 (28.3%) had a PADUA score ≥10 and 71 (71.7%) a PADUA Score <10, of which 20 (28.2%) 6-7 and 51 (71.8%) 8-9. Completely endophytic cT1a renal masses were 6 (5.2 %); half of these (50%) had a PADUA Score ≥10. There were 10 (8.7%) hilar renal masses, all with a PADUA Score ≥10. Mean WIT and operative time were 17.3 and 160 minutes, respectively. Mean length of hospitalization was 5 days. Postoperative complications were recorded in 9.6% of patients, of which 5.2%, 3.5% and 0.9% Clavien grade 1, 2 and 3, respectively. No Clavien grade 4 complications were reported. Surgical margins were negative in all but one patient. *Conclusion:* Taking advantage of the key anatomic

features of the tumor-parenchymal interface, namely the architecture of the kidney parenchyma and intrarenal vasculature, the presence of a distinct fibrous pseudocapsule in the majority of renal tumors and the histological modifications at the tumor-parenchyma interface, enucleative RAPN technique maximizes the preservation of vascularized kidney while ensuring oncological efficacy. This is of particular importance in case of highly complex renal masses, especially cT1b tumors. We have shown that enucleative RAPN is safe and achieves optimal perioperative outcomes. We believe the enucleative RS represents a key approach for highly complex renal tumors with optimal cancer control and potential maximal preservation of vascularized healthy renal tissue.

134

PSEUDOCAPSULE INFILTRATION, POSITIVE SURGICAL MARGINS AND LOCAL RECURRENCE AFTER ENUCLEATIVE ROBOT-ASSISTED \PARTIAL NEPHRECTOMY (RAPN) FOR RENAL CELL CARCINOMA (RCC): RESULTS AT A MEDIAN FOLLOW-UP OF 56 MONTHS

Riccardo Campi[1], Fabrizio Di Maida[1], Andrea Mari[1], Giulia Bencini[1], Ilaria Montagnani[2], Simone Morselli[1], Alessandro Pili[1], Agostino Tuccio[1], Alberto Lapini[1], Maria Rosaria Raspollini[2], Marco Carini[1] and Andrea Minervini[1]

[1]Department of Urology, University of Florence, AOU Careggi, Florence, Italy; [2]Department of Pathology, University of Florence, AOU Careggi, Florence, Italy

Background/Aim: The prognostic role of psecudocapsule (PC) infiltration and positive surgical margins for local recurrence after enucleative RAPN for RCC is still unknown. In this study we report a detailed histopathological analysis of the tumor-parenchymal interface after enucleative RAPN, validating the recently proposed i-Cap (invasion of pseudocapsule) scoring system, and assessing its prognostic value for local recurrence at mid-long term follow-up. *Materials and Methods:* Data from patients undergoing enucleative RAPN at our centre by expert robotic surgeons were prospectively collected from January 2011 to December 2013. A dedicated uropathologist classified the degree of PC infiltration according to our previously reported scheme (PC-, PCK+, PCK++) and retrospectively re-coded it according to the i- Cap scoring system (Figure 1). Patients with benign tumors and follow-up <48 months were excluded from the analyses. *Results:* One hundred twenty-five patients were included. PC was absent in 3 (2.4%) cases. Histopathological data according to histotypes and i-Cap score system are shown in Figure 1B and 2A, respectively. At multivariable analysis, tumor histotype was the only independent predictor of i-Cap score (Figure 2B). Positive surgical margins were recorded in 3 (2.4%) patients. At a median follow-up of 56 months (interquartile range=52-65), 3 cases of local recurrence were detected, all distant from the tumor enucleation bed. *Conclusion:* In our series, tumor histology and pT stage were the strongest predictors of PC invasion after enucleative RAPN. However, neither PC invasion nor positive margins were associated with local recurrence within the enucleation bed, confirming the oncologic safety of this technique. Further studies are needed to validate our results assessing the prognostic role of PC invasion for different resection techniques.

135

IMPACT OF SURGICAL POSITIVE MARGINS ON DISEASE PROGRESSION AFTER RADICAL PROSTATECTOMY IN PT2-PT3 STAGE

Tommaso Di Vico, Alessio Tognarelli, Jacopo Durante, Chiara Polito, Iacopo Meneghetti, Lorenzo Tesi and Ramona Baldesi

Urology Unit, Department of Translational Medicine and New Technologies, University of Pisa, Pisa, Italy

Background/Aim: Bladder neck preservation (BNP) during radical prostatectomy is considered as a method to gain an earlier recovery of urinary continence, despite the concern over a possible increase of positive surgical margins (PSM). PSM is defined as "tumor that extends to the surface of the prostate wherein the surgeon has cut across the tissue plane". For the prostate, lacking a true histological capsule, the definition can be unclear. To define surgical margins (SM) status the entire surgical specimens have been inked and fixed. A positive margin has been identified as "cancer cells extending to the inked surface of the specimen". In a recent systematic review, the overall PSM rates ranged between 7-36%. Positive surgical margins in T2-3 high-risk prostate cancer patients after radical prostatectomy have been defined as able to impact cancer biochemical progression in more than 80% of patients. Different molecular markers such as Myc, p63, ERG and Hif1alfa have been estimated to have a potential role in the tumor progression definition. The amplification of the proto-oncogene MYC occurs in more than 50% of advanced tumors and has been linked with poorer prognosis in several studies. ERG protein expression is a highly specific prostate cancer marker which is activated in more than 50% of prostate cancer cases. P63 protein has been regarded as a basal cell immunohistochemical marker. Up-regulation of HIF-1α has been shown to promote prostate adenocarcinoma (PCa) progression, the mechanism is still

A

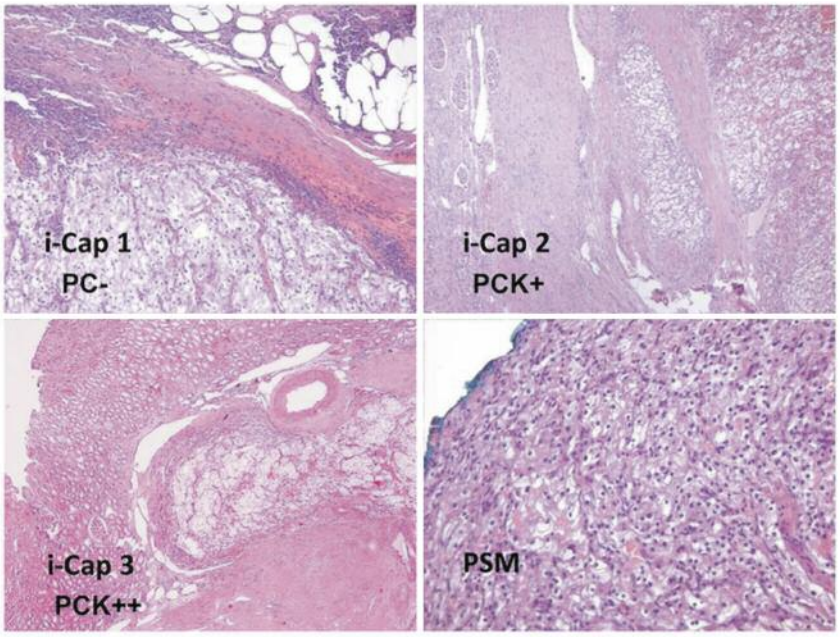
		i-Cap 1 (n=48)	i-Cap 2 (n=49)	i-Cap 3 (n=24)	Total (n=121)	*p*-Value
Tumor Complexity (PADUA) (n, %)	Low (PADUA 6-7)	32 (66.7)	35 (71.4)	16 (66.7)	83 (68.6)	0.2
	Intermediate (PADUA 8-9)	12 (25.0)	5 (10.2)	6 (25.0)	23 (19.0)	
	High (PADUA 10-13)	4 (8.3)	9 (18.4)	2 (8.3)	15 (12.4)	
Pathological diameter (cm), median (IQR)		2.6 (1.9-3.8)	3.0 (2.2-3.7)	3.3 (2.5-4.8)	3.0 (2.0-3.7)	0.2
Histotype (n, %)	ccRCC	28 (58.3)	36 (73.5)	11 (45.8)	75 (62.0)	**0.006**
	pRCC	5 (10.4)	6 (12.2)	8 (33.3)	19 (15.7)	
	chRCC	7 (14.6)	6 (12.2)	5 (20.8)	18 (14.9)	
	LMP	8 (16.7)	1 (2.0)	0 (0.0)	9 (7.4)	
ISUP nucleolar grading (simplified) (n, %)	1-2	33 (80.5)	35 (81.4)	11 (57.9)	79 (76.7)	0.1
	3-4	8 (19.5)	8 (18.6)	8 (42.1)	24 (23.3)	
pT staging (n, %)	pT1a	39 (81.3)	39 (79.6)	8 (66.7)	86 (71.1)	**0.001**
	pT1b	9 (18.8)	10 (20.4)	2 (25.0)	21 (17.4)	
	pT3	0 (0.0)	0 (0.0)	14 (8.3)	14 (11.6)	
Mean healthy renal margin (HRM) beyond PC thickness (µm), median (IQR)		582 (250-1206)	499 (256-936)	735 (220-1332)	576 (243-1031)	0.6
Mean PC thickness (µm), median (IQR)		303 (171-454)	275 (143-464)	197 (113-369)	275 (140-454)	0.3
Surgical margins (n, %)	Negative	48 (100-0)	49 (100.0)	21 (87.5)	118 (97.5)	**0.002**
	Positive	0 (0.0)	0 (0.0)	3 (12.5)	3 (2.5)	
Local recurrence (n, %)	No	46 (95.8)	49 (100.0)	23 (95.8)	118 (97.5)	0.4
	Yes	2 (4.2)	0 (0.0)	1 (4.2)	3 (2.5)	

B

		i-Cap 2 vs i-Cap 1			i-Cap 3 vs i-Cap 1			i-Cap 3 vs i-Cap 2		
Covariates		**OR**	**95%CI**	*p*-Value	**OR**	**95%CI**	*p*-Value	**OR**	**95%CI**	*p*-Value
Mean PC thickness		1.00	0.99-1.00	0.36	1.00	0.99-1.00	0.98	0.99	0.99-1.00	0.50
Mean HRM thickness		1.00	0.99-1.00	0.27	1.00	0.99-1.00	0.75	1.00	0.99-1.00	0.66
Grading	1-2	0.75	0.24-2.42	0.64	1.34	0.35-5.11	0.66	1.78	.46-6.82	0.39
	3-4 (ref)	-	-	-	-	-	-	-	-	-
Tumor Complexity	PADUA score ≥10	1.41	0.36-5.46	0.63	0.33	0.03-3.64	0.37	0.24	0.02-2.35	0.22
	PADUA score 8-9	0.31	0.08-1.17	0.08	0.11	0.26-4.63	0.90	3.60	0.72-17.92	0.12
	PADUA score 6-7 (ref)	-	-	-	-	-	-	-	-	-
Histotype	LMP	0.008	0.001-0.75	**0.03**	0.003	0.001-0.01	**<0.001**	0.05	0.009-0.06	**0.003**
	chRCC	1.08	0.28-4.13	0.91	1.89	0.39-8.99	0.42	2.05	0.42-1.00	0.38
	pRCC	0.86	0.22-3.35	0.83	3.9	1.02-16.71	**0.05**	4.55	1.08-19.14	**0.04**
	ccRCC (ref)	-	-	-	-	-	-	-	-	-

Figure 1. *Tumor related features, margin status and oncologic outcomes among tumors with different pattern of pseudocapsule invasion (A). Multivariable multinomial logistic regression analysis assessing predictors of pseudocapsule invasion in our cohort (B). I-Cap 1, No invasion; I-Cap 2, partial invasion; I-Cap 3, complete invasion.*

A



- PC intact and without evidence of neoplastic infiltration (PC- ; i-Cap 1);
- PC has either a focal absence or <100% infiltration into the PC but not into the normal parenchyma (PCK + ; i-Cap 2);
- Any degree of carcinoma infiltration completely through the PC and into the normal parenchyma (PCK ++; i-Cap 3).

B

		LMP (n=10)	ccRCC (n=75)	pRCC (n=19)	chRCC (n=18)	Total (n=122)	*p*-Value
Tumor Complexity (PADUA) (n, %)	Low (PADUA 6-7)	6 (60.0)	50 (66.7)	13 (68.4)	14 (77.8)	83 (68.0)	0.571
	Intermediate (PADUA 8-9)	4 (40.0)	15 (20.0)	3 (15.8)	2 (11.1)	24 (19.7)	
	High (PADUA 10-13)	0 (0.0)	10 (13.3)	3 (15.8)	2 (11.1)	15 (12.3)	
i-Cap score (n,%)	i-Cap 1	8 (88.9)	28 (37.3)	5 (26.3)	7 (38.9)	48 (39.7)	**0.006**
	i-Cap 2	1 (11.1)	36 (48.0)	6 (31.6)	6 (33.3)	49 (40.5)	
	i-Cap 3	0 (0.0)	11 (14.7)	8 (42.1)	5 (27.8)	24(19.8)	
Pathological diameter (cm), median (IQR)		2.0 (1.7-3.7)	3.0 (2.2-3.8)	3.0 (2.0-4.5)	2.9 (2.2-3.1)	3.0 (2.0-3.7)	0.463
ISUP nucleolar grading (simplified) (n, %)	1-2	10 (100.0)	59 (78.7)	11 (57.9)	0 (0.0)	80 (76.9)	**0.030**
	3-4	0 (0.0)	16 (21.3)	8 (42.1)	0 (0.0)	24 (23.1)	
pT staging (n, %)	pT1a	9 (90.0)	57 (76.0)	10 (52.6)	11 (61.1)	87 (71.3)	**0.002**
	pT1b	1 (10.0)	15 (20.0)	2 (10.5)	3 (16.7)	21 (17.2)	
	pT3	0 (0.0)	3 (4.0)	7 (36.8)	4 (22.2)	14 (11.5)	
Mean healthy renal margin (HRM) beyond PC thickness (μm), median (IQR)		414 (317-696)	499 (225-1024)	299 (231-814)	1181 (499-1764)	571 (237-1031)	0.520
Mean PC thickness (μm), median (IQR)		534 (409--597)	312 (226-468)	183 (118-275)	99 (57-143)	276 (140-457)	**<0.001**
Surgical margins (n, %)	Negative	10 (100.0)	74 (98.7)	17 (89.5)	18 (100.0)	119 (97.5)	0.100
	Positive	0 (0.0)	1 (1.3)	2 (10.5)	0 (0.0)	3 (2.5)	
Local recurrence (n, %)	No	10 (100.0)	73 (97.3)	18 (94.7)	18 (100.0)	119 (97.5)	0.719
	Yes	0 (0.0)	2 (2.7)	1 (5.3)	0 (0.0)	3 (2.5)	

Figure 2. *Classification of pseudocapsule invasion in our study (A). Tumor-related features, margin status and oncologic outcomes among different tumor histotypes in our cohort (B). LMP, Low malignant potential; ccRCC, clear cell renal cell carcinoma; chRCC, chromophobe renal cell carcinoma; pRCC, papillary renal cell carcinoma.*

unclear. Objective of the study was to evaluate the long term clinical outcome of patients presenting high-risk pT2-T3 prostate tumors and PSM, with a median follow-up after the surgery over 4 years. *Materials and Methods:* Fifty-five patients with PSM in T2-T3 high-risk prostate cancer undergone to both retropubic and robotic assisted laparoscopic prostatectomy performed with bladder neck sparing (BNP) technique in our centre in the period 2010-2016 were retrospectively evaluated with a telephone re-call and investigated regarding adjunctive adjuvant treatments, biochemical recurrence time and cancer related survival. All patients received conformational radiotherapy after the surgery. Median follow-up time was 49.3 months. P63, ERG, MYC and HIF1α were immunohistochemically investigated to define the potential tumor aggressiveness identification. The pathological TNM stage was T2bN0 in 1 case, T2cN0 in 13 cases, T2cN1 in 2 cases, T3aN0 in 18 cases, T3aN1 in 2 cases, T3bN0 in 9 cases and T3bN1 in 10 cases. The Gleason Score was 3+4 in 21 patients (38.2%), 4+3 in 16 patients (29.1%), 4+4 in 9 patients (16,4%), 4+5 in 7 patients (12.7%) and 5+4 in 2 (3.6%) patients. The mean age was 67.4 years. *Results:* Biochemical disease recurrence (defined as total PSA ≥ 0.20 ng/ml) was documented in 26 patients (47.3%) after a median time of 12 months (range=2-51 months). No significant indications were obtained from immunohistochemical investigations regarding the disease progression and prognosis. Further hormonal deprivation was provided with peripheral antiandrogens (bicalutamide) or LHRH analogues (leuprorelin or triptorelin) or both on 13 out 26 patients (50%) due the presence of significant clinical symptoms such as bone pain and/or urinary symptoms. 10 out 13 of these patients had biochemical recurrence within 12 months from the surgery. Cancer related survival was 100% for the entire study population. *Conclusion:* PSM in high-risk T2-T3 prostate cancer patients have limited significance in terms of biochemical and clinical progression at a median 4 years follow-up despite adjunctive treatments are required in the case of early biochemical recurrence within 1 year after the surgery. Molecular analysis with P63, ERG, Myc and Hif1 alfa did not provide significant indication regarding the cancer progression and the disease progression. Adjunctive adjuvant treatments were required just in 24% of cases.

136
UTILITY OF CHEST X-RAY IN FOLLOW-UP OF PT1 RENAL CELL CARCINOMA

Enrica Verzotti[1], Giacomo Di Cosmo[2], Stefano Bucci[1], Alexandre Mottrie[3], Andrea Minervini[4] and Carlo Trombetta[1]

[1]Department of Urology, ASUITS - University of Trieste, Trieste, Italy;
[2]Department of Urology, University of Novara, Novara, Italy;
[3]Department of Urology, Onze-Lieve-Vrouw Hospital, Aalst, Belgium;
[4]Department of Urology, University Hospital Careggi, Florence, Italy

Background/Aim: According to the European Association of Urology (EAU), American Urological Association (AUA), National Comprehensive Cancer Network (NCCN) and Canadian Urological Association (CUA) guidelines all patients surgically treated for Renal Cell Cancer should routinely undergo chest-imaging examinations for recurrences detection. Surveillance schemes that are based on low level evidence and the benefits of chest examination in all Renal Cell Cancer patients are not clearly confirmed. European Guideline suggests the use of computed tomography of the chest for oncological follow-up purposes even in all low-risk patients however many urologists prefer to base follow-up on chest x-ray according to American Urological Association (AUA), National Comprehensive Cancer Network (NCCN) and Canadian Urological Association (CUA) guidelines. Finally, the potential exposure of the patients to the risks connected to unnecessary ionizing radiations is an important factor to consider. *Materials and Methods:* We retrospectively reviewed the pathological reports from all patients who underwent radical or partial nephrectomy between January 2003 and September 2015 in two European University Urological Departments. All pT1 Renal Cell Cancers were included in our examination. All patients with less than six months follow-up were excluded from the study. Demographics, pathological data (TNM, Fuhrman Grade, presences of intra-tumoural necrosis state of margin and lymphovascular invasion) and postoperative follow-up data (imaging, laboratory and clinical data) were recorded and analysed. In particular we collected data from chest imaging performed every 6 months during the first postoperative year, according to oncological the Renal Cell Cancer follow-up protocol of both Departments. *Results:* Two hundred thirty-four pT1 Renal Cell Cancer patients were included in our study, of these: 175 were Clear Cell Renal Cell Cancer, 44 Papillary Renal Cell Cancer and 15 Chromophobe Renal Cell Cancer. Median follow-up was 56 months. Nineteen (8%) patients developed recurrences. Three (1.3%) patients developed chest recurrences, one patient was clear cell Renal Cell Cancer pT1a, Fuhrman 2, chest recurrence was diagnosed by computed tomography of the chest performed for symptoms 93 months after surgery, this patient had a negative chest x-ray 6 month before computed tomography. The other 2 patients with chest recurrences were both clear cell Renal Cell Cancer pT1b, Fuhrman 3. No chest recurrences were detected at 1-year follow-up. No patients with pT1 papillary Renal Cell Cancer had chest recurrences.

No chromophobe pT1 Renal Cell Cancer recurred. Mean of 5.6 chest x-ray was used for every patient. *Discussion:* In our series, follow-up based on chest x-ray required more than 1,300 exams to permit diagnosis of recurrences in 2 patients, both cases presented Fuhrman 3 and cannot be considered low-risk. Only one low-risk patient had chest recurrence. Given the low incidence of chest recurrences, this series is not sufficient to identify a class of patients who do not require chest follow-up. However, in contrast with the American Urological Association (AUA), National Comprehensive Cancer Network (NCCN) and Canadian Urological Association (CUA) guidelines suggest that one year's chest-x-ray is unnecessary for the oncological follow-up of pT1 renal cell cancer. *Conclusion:* According to our data current guidelines for RCC surveillance potentially expose a considerable number of patients to unnecessary chest examinations. We all have to remember that chest follow-up expose patient with long survival expectancies to the risk of radio-induced tumours, produce emotional stress and represent a cost for the society. Chest follow-up schedule should be tailored on more prognostic groups in order to avoid the possible side effect of unnecessary exams. The limit of this study is that it was conducted retrospectively, it is necessary to conduct new prospective studies to confirm this data.

137

NON-CLEAR CELL RENAL CELL CARCINOMA: A META-ANALYSIS OF CLINICAL TRIALS COMPARING VEGFR-TKIS *VERSUS* MTORI

Chiara Ciccarese[1], Roberto Iacovelli[1], Matteo Brunelli[2], Francesco Massari[3], Claudia Mosillo[4], Davide Bimbatti[1], Emanuela Fantinel[1], Vincenzo De Marco[5], Antonio Benito Porcaro[5], Guido Martignoni[2], Walter Artibani[5] and Giampaolo Tortora[1]

[1]Department of Medical Oncology, Azienda Ospedaliera Universitaria (AOUI) Verona, University of Verona, Verona, Italy; [2]Department of Pathology and Diagnostic, Azienda Ospedaliera Universitaria (AOUI) Verona, University of Verona, Verona, Italy; [3]Department of Medical Oncology, S. Orsola-Malpighi Hospital, Bologna, Italy; [4]Department of Radiological, Oncological and Pathological Sciences, University Sapienza of Rome, Rome, Italy; [5]Urologic Clinic, Azienda Ospedaliera Universitaria (AOUI) Verona, University of Verona, Verona, Italy

Background/Aim: Non-clear cell renal cell carcinoma (nccRCC) is a heterogeneous group of tumors that are different in terms of morphology, genetic profile, clinical behavior and prognosis. The ideal treatment algorithm for nccRCC is still unknown and derived mainly from evidence available for clear cell RCC, being therefore represented by VEGFR-tyrosine kinase inhibitors (TKis) and mammalian target of rapamycin inhibitors (mTORis). We aimed to compare the efficacy of VEGFR- TKis and mTORi for the treatment of nccRCC patients. We performed a systematic review and meta-analysis of the available evidence in order to investigate the antitumor efficacy of VEGFR-TKis compared to mTORi for the treatment of nccRCC patients. *Materials and Methods:* Searching the MEDLINE/PubMed, Cochrane Library and ASCO Meeting abstracts prospective studies were identified. Data extraction was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The measured outcomes were progression-free survival (PFS), overall survival (OS), and overall response rate (ORR). OS and PFS were evaluated in the experimental over the control arm based on the hazard ratios (HR) and relative 95% confidence intervals (CIs) set out in selected studies. Study quality was assessed using the Jadad 5-item scale. *Results:* Four randomized controlled trials were selected for final analysis, based on their adequate quality and relevance for inclusion in the meta-analysis. The RECORD3, ASPEN, and ESPN trials compared the mTORi everolimus to the TKi sunitinib for first-line treatment of RCC patients. The phase 3 INTORSECT study compared the mTORi temsirolimus *versus* the TKi sorafenib for second-line treatment of metastatic ccRCC and nccRCC, reporting a *post hoc* analysis of the nccRCC subgroup. A total of 332 patients were available for the analysis: 164 patients were treated with VEGFR-TKis (sunitinib or sorafenib), while 168 patients received a mTORi (everolimus or temsirolimus). The most common non–clear cell histologies were papillary (147 out of 242 patients) and chromophobe (40 out of 242 cases). Treatment with TKi significantly reduced the risk of progression compared to mTORi (fixed-effect; HR=0.71; 95% CI=0.60-0.84; $p<0.0001$). This difference remained significant when sunitinib was compared to everolimus in first-line setting (fixed-effect; HR=0.67; 95% CI=0.56-0.80; $p<0.00001$). No significant heterogeneity was observed in the PFS analysis of both the entire population ($Chi^2=4.18$, $p=0.24$; $I^2=28\%$) and the subgroup treated in first-line therapy ($Chi^2=0.26$, $p=0.88$; $I^2=0\%$) In 332 patients evaluable for OS, no significant difference was found between TKi and mTORi (HR=0.86; 95% CI=0.67-1.12; $p=0.27$). No significant heterogeneity was observed in the analysis for OS ($Chi^2=1.19$, $p=0.76$; $I^2=0\%$). Similar results, confirming the lack of a survival benefit, were obtained when the analysis was restricted to the first-line setting (ASPEN, ESPN, and RECORD-3 studies): sunitinib treatment did not significantly prolong the OS compared to everolimus (HR=0.93; 95% CI=0.69-1.26; $p=0.64$). Data about the ORR were available in two (ASPEN and ESPN) out of four studies, with a total of

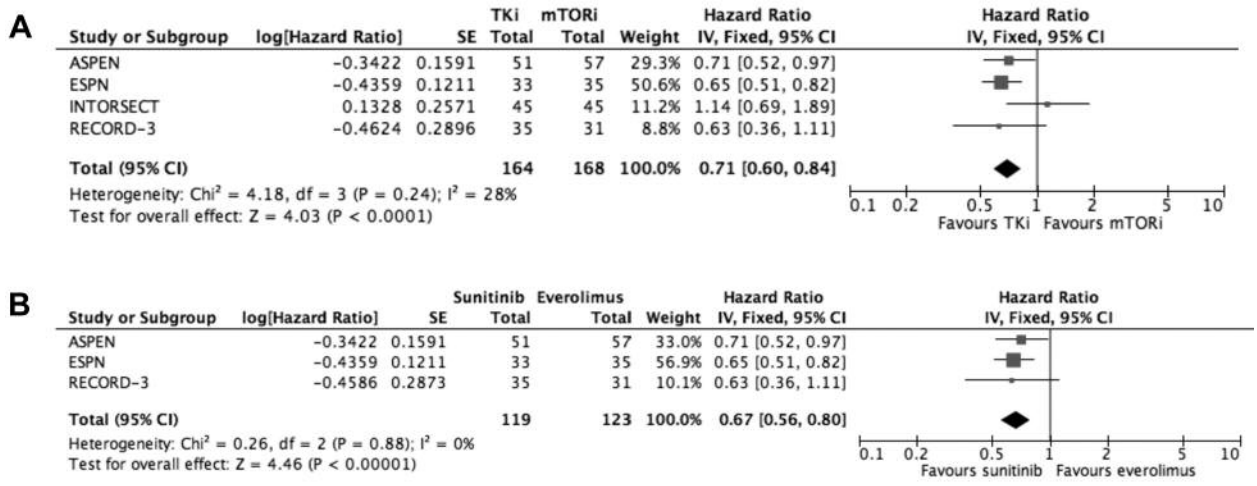


Figure 1. *Progression-free survival (PFS) in patients treated with TKis compared to mTORi. Overall population (A). First-line therapy (B). TKis, Tyrosine kinase inhibitors; mTORis, mTOR inhibitors; SE, standard error; CI, confidence interval.*

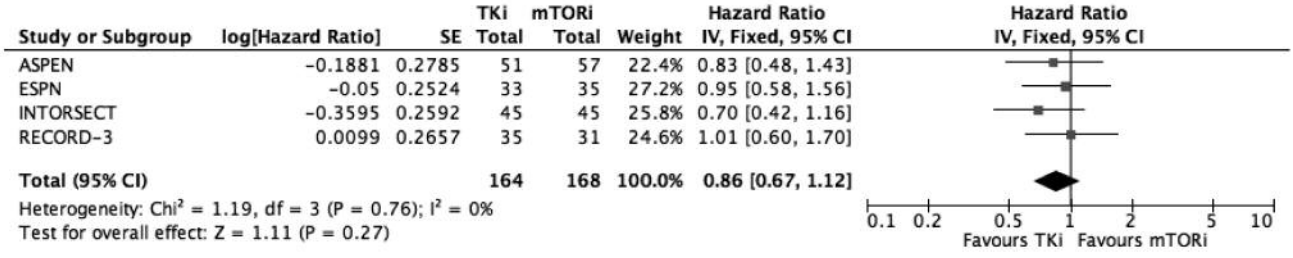


Figure 2. *Overall survival in patients treated with tyrosine kinase inhibitors (TKis) compared to mTOR-inhibitors (mTORis). SE, Standard error; CI, confidence interval.*

Table I. *Selected studies for final analysis.*

Trial name	First author	Year	Trial design						Jadad score
			Phase of study	Experimental arm			Control arm		
				Drug	Patients (n)	Age	Drug	Patients (n)	Age	
ASPEN	Armstrong *et al.*	2016	2	EVEROLIMUS	57	64	SUNITINIB	51	59	3
ESPN	Tannir *et al.*	2016	2	EVEROLIMUS	35	58	SUNITINIB	33	60	2
RECORD-3	Motzer *et al.*	2014	2	EVEROLIMUS	31	62	SUNITNIB	35	62	3
INTORSECT	Hutson *et al.*	2014	3	TEMSIROLIMUS	ccRCC 214 nccRCC 45	60	SORAFENIB	ccRCC 208 nccRCC 45	61	3

ccRCC, Clear cell renal cell carcinoma; nccRCC, non-clear cell renal cell carcinoma.

176 evaluable patients. TKis therapy did not improve the ORR when compared to mTORi (RR=2.21; 95% CI=0.87-5.60; p=0.09), even if treatment with sunitinib doubled the probability of achieving a tumor response. *Conclusion:* Treatment with TKis confers a PFS benefit compared to mTORi for the treatment of nccRCC, significantly reducing the risk of progression by 29%. This PFS advantage increases even more (reaching the 33%) when sunitinib was compared

to everolimus as first-line therapy, therefore supporting the standard treatment paradigm broadly used for ccRCC patients. The lack of a significant OS benefit, together with the relatively modest efficacy of available targeted therapies, reinforces the need of future histological-based, molecular-driven therapeutic paradigm.

138
RED BLOOD CELL DISTRIBUTION WIDTH: A NEW POSSIBLE LABORATORY PARAMETER IN THE MANAGEMENT OF PROSTATE CANCER

Jacopo Durante[1], Damiano Bracchitta[1], Alessio Tognarelli[1], Tommaso Di Vico[1], Chiara Polito[1], Iacopo Meneghetti[1], Lorenzo Tesi[1], Ramona Baldesi[1] and Roberto Ponchietti[2]

[1]Urology Unit, Department of Translational Medicine and New Technologies, University of Pisa, Pisa, Italy; [2]Department of Medicine, Surgery and Neuroscience, University of Siena, Siena, Italy

Background/Aim: The RDW (Red blood cell Distribution Width) is a simple parameter of the standard complete blood count, which evaluates the variation in cellular volume of the erythrocyte population. Several studies published in recent years have correlated RDW to patients' outcomes in cardiovascular disease and sepsis. More recently, we have also tried to evaluate this parameter in the field of malignant neoplastic diseases (thyroid, colon and pancreas). Scientific literature seems to be oriented, both in cardiovascular and infectious diseases, to relate higher values of RDW with a worse outcome or with more advanced stages of illness. The aim of this study is to evaluate RDW in patients with prostatic disease as a possible useful parameter for the diagnosis and follow-up of prostate carcinoma. *Materials and Methods:* The study considered 178 patients divided into four groups depending on histological diagnosis obtained with prostate biopsy: 23 patients with benign prostatic hyperplasia (BPH), 9 with granulomatous flogosis, 28 with Prostatic Intraepithelial Neoplasia - PIN (only high grade PINs were inserted in the study) and 97 with prostate adenocarcinoma. A fifth group included 21 patients who underwent a surgical or radiotherapy prostate cancer treatment and then developed a biochemical disease recurrence (BCR - defined as total PSA ≥0.20 ng/ml). In patients with glandular atrophy, PIN and granulomatous prostatitis, the closest complete blood count to the biopsy (within a period of 3 months before or after the biopsy) was evaluated. In patients with prostate cancer (confirmed on specimen after radical prostatectomy) the pre- operative complete blood count was considered. In patients with BCR, the first post-diagnosis blood count was evaluated, but always prior to a new therapeutic treatment. Patients affected by anemia and other hematological diseases were excluded from the study. For each patient, blood count parameters (white blood cells, red blood cells, hemoglobin, hematocrit, MCV and RDW), glycaemia, albumin, triglycerides, total cholesterol, HDL and LDL, and PSA were evaluated. Patients with glandular atrophy were defined as "healthy patients" and considered as the control group. Binary associations were then performed between the different categories in which the patients of the study were classified. Since RDW depends on patient's nutritional status, age and age-related illnesses, it was necessary to obtain as uniform as possible groups. Particularly for age, we encountered some objective difficulties in obtaining a homogeneous sample in patients with prostatitis, glandular atrophy, HGPIN, adenocarcinoma and BCR. *Results:* Regarding the difference between the adenocarcinoma group and the BPH group, the value of RDW is higher in malignant disease and is statistically significant (p=0.001). A statistical significance was also found between the BCR group and the atrophy group (p=0.001), with higher levels of RDW in the former. Significantly higher RDW values were also found in prostatitis than atrophy (p=0.001), where there is also a higher value of leukocytes concentration (p=0.017). Unfortunately, however, the specificity of the RDW does not seem particularly elevated. We could not demonstrate a significant difference in RDW between the prostatitis group and the adenocarcinoma group. There was no difference even between adenocarcinomas group and the BCR group. *Conclusion:* In the investigated sample, RDW seems to correlate with neoplastic disease and inflammatory prostatic conditions. BPH, on the other hand, is associated with inferior RDW values. The highest RDW values were observed in patients with biochemical recurrence. In addition, the RDW seems to correlate with phlogosis and neoplastic proliferation more significantly than other blood count parameter. The lack of a statistical significant difference between cancer and biochemical disease recurrence groups may be related to the fact that at the time of the blood sample, both patients with cancer and patients with biochemical disease recurrence had to be considered ill. If the RDW value in patients undergone to radical prostatectomy had been considered at least 120 days (average life of a red blood cell) after the surgery, a significant difference could have been observed.

140
ATYPICAL ADENOMATOUS HYPERPLASIA (AAH) OF THE PROSTATE IN A CASE REPORT WITH PREVIUOS DIAGNOSIS OF ATYPICAL SMALL ACINAR PROLIFERATION (ASAP): A REVIEW OF THE LITERATURE

Giovanni Luca Giliberto[1], Nicolò Fiorello[1], Alessandra Viglio[2], Carlo Marchetti[1], Andrea Ringressi[1], Cesare Regina[1] and Bruno Rovereto[1]

[1]Division of Urology San Matteo Hospital Pavia, IRCCS Foundation Polyclinic San Matteo Hospital Pavia, Pavia, Italy;
[2]Division of Pathology San Matteo Hospital Pavia, IRCCS Foundation Polyclinic San Matteo Hospital Pavia, Pavia, Italy

Background/Aim: Atypical adenomatous hyperplasia (AAH) is a rare finding on prostate biopsy, often considered as a benign small glandular lesion of the transition zone that simulates acinar adenocarcinoma. In the last years, the sampling of the transition zone has increased with ultrasound-guided multiple segmental prostate biopsies, and pathologists have become more experienced to detect AAH and to avoid misinterpretation as prostate adenocarcinoma (1). This is a case report of a patient diagnosed with AAH and a review of the literature concerning AAH. The differences of AAH with low-grade adenocarcinoma or precancerous lesions like prostatic intraepithelial neoplasia (PIN) or atypical small acinar proliferation (ASAP) are highlighted. It was not possible to make sure of diagnosis so the patient repeated the prostate biopsy after 6 months, with new dosage of PSA. Before the second biopsy the presentation clinical and the dosage of PSA were stable (4.1 ng/ml). The second biopsy showed. *Case Report:* A 61 year-old male man performed periodic checks of prostate-specific antigen (PSA) with elevated level of 4.02 ng/ml and ratio (PSA free/PSA total) 18%. He did not present with symptoms of urinary obstruction. Digital rectal examination revealed a large prostate (estimated volume doubled) without nodules suggestive of malignancy. Some needle biopsies were performed. The first biopsy showed glandular atypia on lateral right and intermediate left side. The specimens showed lymphogranulocyte inflammation with lymphoid aggregates; in one of these, there was a glandular microaggregate with nuclear atypia, and negative immunoreaction for anti-cytokeratin 34betaE12. It was not possible to make sure of diagnosis so the patient repeated the prostate biopsy after 6 months, with new dosage of PSA. Before the second biopsy the presentation clinical and the dosage of PSA were stable (4.1 ng/ml). The second biopsy showed lymphocyte inflammation and evidence of ASAP on the left apex, and negative immunoreaction for anti-cytokeratin 34betaE12. European and American guidelines suggest repeating prostate biopsy within 6 months. Before the third biopsy the presentation clinical and the dosage of PSA were stable (3.8 ng/ml). The third biopsy (12 specimens) was negative for atypical or cancerous lesions. Two months after the last biopsy, the patient performed an abdominal nuclear magnetic resonance (NMR) that was negative for neoplasms, and it showed homogeneity of prostatic parenchyma. After 6 months from the last biopsy the patient performed a saturation biopsy with 32 specimens. The clinical features and the dosage of PSA were stable (4.12 ng/ml, ratio=17%). The specimens showed evidence of AAH on left lateral side, with slight positive for alphamethylacyl-coenzyme A-racemase (AMACR) and patchy immuno-staining high-molecular-weight cytokeratin 34betaE12. *Discussion:* AAH is a pseudoneoplastic lesion that can mimic the prostate adenocarcinoma (2). AAH is usually an incidental finding in transurethral resection of prostate (TURP) or found in the transition zone in a prostate biopsy (3). The present study reported that AAH was found on left lateral side, with

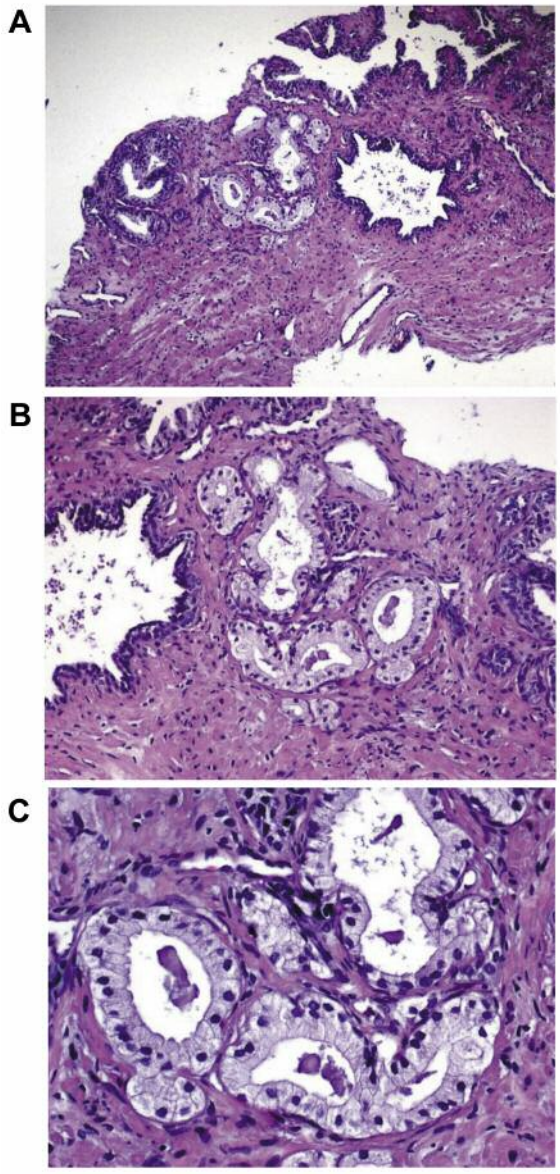


Figure 1. *Microarea (with progressive zoom) of atypical adenomatous hyperplasia (AAH). Hematoxylin and eosin stain.*

glandular atypia (suspicious for malignancy) in the first biopsy on lateral right and intermediate left side, and with ASAP in the second biopsy on the left apex. The specimens were examined always in the same laboratory. In the existing literature, AAH is a rare finding reaching only 2% of TURP specimens and <1% of core biopsy specimens (4). Typically, glands are lined by cuboidal and short columnar cells. The glands are densely packed and don't show evidence of fusion. The luminal borders are usually serrated and irregular. The lumens of glands/acini are often empty but can contain corpora amylacea and crystalloids in 24% of biopsies (Figure 1) (5). AAH is frequently multifocal, and in 84% of cases has been associated with nodular hyperplasia. It can be difficult to distinguish AAH from low-grade prostatic adenocarcinoma because both can be observed in the transition zone and can show intraluminal crystalloids and mitotic figures. The crucial feature of all AAH cases is a fragmented basal cell layer, which can be demonstrated by patchy immunostaining for high-molecular-weight cytokeratin 34betaE12 or p63 (6). Today, there is no available evidence indicating the progression of AAH into prostatic intraepithelial neoplasia (PIN) (7). A similar histological pattern can be the partial atrophy. It may seem a cancerous lesion because AMACR is found in 69.1% of cancers. AMACR is found by staining with cytokeratin 34betaE12/p63, but can be negative in 31.4% of cancers. Typcally it is found on the peripheral side of the gland and goes into differential diagnosis with AAH (8). *Conclusion:* AAH is a rare histological finding on prostate biopsies. Despite the fact that there are some typical findings of immunohistochemistry to distinguish an ASAP/PIN, a low grade adenocarcinoma, and a partial atrophy from AAH, only an experienced pathologist is able to make a diagnosis. The indications to repeat biopsy are: rising and/or persistently elevated PSA; suspicious digital rectal examination; ASAP or extensive high-grade PIN; parenchymal inhomogeneity (mostly PIRADS 4-5 lesions) at multiparametric magnetic resonance. European Guidelines do not specify the AAH follow-up care pathway; however, some studies say the patients continue the controls like in benign lesions (once a year). Our team, considering the previous diagnosis of ASAP, although there is no evidence of progression into cancerous lesion either of correlation between ASAP and AAH, has decided to continue follow-up with a dosage of PSA every 4 or 6 months and to perform another NMR. Prostatic biopsy will be performed if the dosage of PSA shows a significant increase (also evaluating PSA velocity, PSA Ratio, PSA density) or parenchymal inhomogeneity at NMR.

1 Montironi R, Mazzucchelli R, Lopez-Beltran A, Cheng L and Scarpelli M: Mechanisms of disease: high-grade prostatic intraepithelial neoplasia and other proposed preneoplastic lesions in the prostate. Nat Clin Pract Urol *4*: 321-332, 2007.

2 Rekhi B, Jaswal TS and Arora B: Premalignant lesions of prostate and their association with nodular hyperplasia and carcinoma prostate. Indian J Cancer *41*: 60-65, 2004

3 Stamatiou K, Alevizos A, Natzar M, Mihas C, Mariolis A, Michalodimitrakis E and Sofras F: Associations among benign prostate hypertrophy, atypical adenomatous hyperplasia and latent carcinoma of the prostate. Asian J Androl *9*: 229-233, 2007.

4 Postma R, Schröder FH and van der Kwast TH: Atrophy in prostate needle biopsy cores and its relationship to prostate cancer incidence in screened men. Urology *65*: 745-749, 2005.

5 Kwak JT, Hewitt SM, Sinha S and Bhargava R: Multimodal microscopy for automated histologic analysis of prostate cancer. BMC Cancer, vol. 11, article 62, 2011.

6 Lopez-Beltran A, Qian J, Montironi R, Luque RJ and Bostwick DG: Atypical adenomatous hyperplasia (adenosis) of the prostate: DNA ploidy analysis and immuno-phenotype. Int J Surg Pathol *13*: 167-173, 2005.

7 Anim JT, Ebrahim BH and Sathar SA: Benign disorders of the prostate: A histopathological study. Ann Saudi Med *18*: 22-27, 1998.

8 Bostwick DG and Qian J: Atipical adenomatous hyperplasia of the prostate. Am J Surg Pathol *19*: 506-518, 1995.

141

MAGNETIC RESONANCE IMAGING AND ULTRASOUND FUSION BIOPSY IN FOLLOW-UP OF PATIENTS IN ACTIVE SURVEILLANCE PROTOCOL

Marco Roscigno[1], Maria Nicolai[1], Giovanni La Croce[1], Giovanna Perugini[2], Gianfranco Deiana[1], Michele Manica[1], Giulia Querques[2], Daniela Chinaglia[3], Sandro Sironi[2] and Luigi Filippo Da Pozzo[1]

[1]Urology, ASST Papa Giovanni XXIII, Bergamo, Italy; [2]Radiology, ASST Papa Giovanni XXIII, Bergamo, Italy; [3]Pathology, ASST Papa Giovanni XXIII, Bergamo, Italy

Background/Aim: To evaluate the role of Magnetic Resonance Imaging (MRI) and Ultrasound Fusion Target Biopsy in follow-up of patients (patients) undergoing Active Surveillance (AS) protocol for prostate cancer (PCa). *Materials and Methods:* We retrospectively evaluated 96 patients undergoing confirmatory or follow-up biopsy according to PRIAS protocol, from June 2016 to September 2017. All patients were submitted to mpMRI on a 3T magnet with a 32-channel surface coil, using triplanar high-resolution T2-w, axial DWI (b values 25, 500, 1000, 2000 s/mm^2), and 3D T1-w dynamic contrast-enhanced sequences after injection of paramagnetic contrast agent. Patients with negative (-) mpMRI subsequently underwent systematic random biopsy. Patients with positive (+) mpMRI (PI-RADS-

V2 score ≥3) underwent trans rectal free hand targeted fusion prostate biopsies (3 cores) + systematic random biopsies (12-16 cores), performed with Esaote Virtual Navigator System. The primary objective of the study was detection of clinically significant (cs) Pca (Gleason score ≥3+4). Descriptive statistics and chi-square test were used to calculate differences between proportions. Receiver Operating Characteristics (ROC) curve was used to show the predictive accuracy of target *vs*. systematic biopsies on csPCa detection, according to PIRADS score. *Results:* 37 patients had mpMRI (–); out of 56 patients with mpMRI (+), 12 (22%) had PI-RADS 3, 27 (48%) PI-RADS 4, and 17 (30%) PI-RADS 5 lesions. At target + random sextant biopsy, PCa was diagnosed in 47 patients (84%), while significant disease was found in 30 patients (54%). Targeted biopsies detected 41/47 (87%) PCa and 28/30 (93%) csPCa. In 4/30 (13%) patients csPCa was detected only in targeted biopsies, while in 2/30 (7%) cases csPca was discovered by sextant biopsies only. Overall detection rate of significant PCa was 35%, 58%, and 79% respectively for PIRADS 3, 4 and 5, respectively (p<0.001). Target biopsies detected significant Pca in 14%, 50%, and 79% in case of PIRADS 3,4 and 5 respectively (p<0.001). Predictive accuracy for csPCa (ROC curve analysis) was 57% for random biopsies and 75% for target biopsies. In the mpMRI (–) group, PCA was detected at random biopsies in 17/37 (46%), but only 2/37 (5%) patients had csPCa. *Conclusion:* mpMRI and Ultrasound Fusion Biopsy allows accurate detection of csPCa in patients undergoing AS. The majority of csPCa could be detected by target biopsies. Moreover, mpMRI (–) has an extremely high NPV, with only 5% of patients with csPCa at random biopsy.

144
EXTENDED PELVIC LYMPH NODE DISSECTION (EPLND) DURING ROBOT-ASSISTED LAPAROSCOPIC PROSTATECTOMY: SINGLE-SURGEON LEARNING CURVE AND COMPARISON WITH RESULTS OF LND DURING OPEN RADICAL PROSTATECTOMY

Marco Roscigno[1], Maria Nicolai[1], Richard Naspro[1], Michele Manica[1], Federico Pellucchi[1], Lorenzo Rocchini[1], Diego Angiolilli[1], Daniela Chinaglia[2], Giovanni La Croce[1] and Luigi Filippo Da Pozzo[1]

[1]Urology, ASST Papa Giovanni XXIII, Bergamo, Italy; [2]Pathology, ASST Papa Giovanni XXIII, Bergamo, Italy

Background/Aim: We aim to evaluate the single-surgeon learning-curve of robot-assisted ePLND, and compare results with those of the open radica prostatectomy (ORP) performed in the same period. *Materials and Methods:* From October 2014 to June 2017 we prospectively collect 266 patients with intermediate-/high- risk prostate cancer (PCa), treated by ORP + ePLND (165 patients) or RALP + ePLND (101 patients). All patients were treated by a single surgeon with >500 ORP experience. Overall surgical time and ePLND time were recorded as well as the number of nodes (LN) removed, of positive nodes (LN+), pT stage and Gleason sum (GS). For analysis of complication, assessed within a 90 days period, Clavien-Dindo scoring was used. Chi-square and ANOVA test were used to examine the differences in categorical and continuous variables, respectively. Bivariate (Pearson) correlation analysis assessed the relationship between the number of LN removed, surgical time and ePLND time. *Results:* No differences in preoperative features were found between the ORP and RALP groups, with exception for age (66 *vs*. 64; p=0.017). In the RALP group, overall surgical time and ePLND time significantly decreased with the increase of surgical procedures (all p<0.001). Median overall surgical time changed from 285 min in the first 25 cases to 197 min in the last 25. Median eLND time ranged from 49 min to 40 min. However, the number of LN removed did not increased during cases, with a median count of 25 LNs. Comparing ORP and RALP group, the number of LNs removed was 23 and 27, respectively (p=0.025). However, LN+ rate did not differ between the two groups (16% *vs*. 11%; p=0.216). Complication rate did not differ between ORP and RALP group, (Clavien grade I-II: 19.2% *vs*. 20.6%; Clavien grade IIIa-b: 3.6% *vs*. 3%); the incidence of symptomatic lymphoceles was 3% (5/165) in ORP and 1% (1/101) in RALP. *Conclusion:* ePLND during RALP allows removal of a number of LNs that is similar to ORP, with no significantly different LN+ detection rate. Overall complication rates are comparable to ORP group and incidence of symptomatic lymphoceles is very low. Even though the number of LNs removed seem to be not related to the number of procedures performed, learning curve is characterised by progressive reduction of overall surgical and eLND time during our first 100 cases.

145
ULTRASOUND/MRI FUSION PROSTATE BIOPSIES WITH ESAOTE VIRTUAL NAVIGATOR SYSTEM: A MULTI-CENTRIC ITALIAN EXPERIENCE

Marco Roscigno[1], Giovanni La Croce[1], Federico Deho'[2], Armando Stabile[2], Angelo Naselli[3], Giancarlo Marra[4], Paolo Gontero[4], Francesco Montorsi[2] and Luigi Filippo Da Pozzo[1]

[1]Urology, Papa Giovanni XXIII, Bergamo, Italy; [2]Urology, San Raffaele Hospital, Vita Salute San Raffaele University, Milan, Italy; [3]Urology, San Giuseppe Hospital, Milan, Italy; [4]Urology, Molinette hospital, Universita' degli Studi di Torino, Turin, Italy

Background/Aim: Multiparametric magnetic resonance imaging (mpMRI) allows identification of clinical significant suspicious areas. Targeted prostate biopsies by ultrasound fusion biopsy are associated with higher rate of clinically significant prostate cancer (csPCa) detection. The aim of our study was to evaluate our initial casisitic with the Esaote Virtual Navigator System and free hand biopsy technique. *Materials and Methods:* Data were retrospectively collected from 4 tertiary care Italian centers. From 2016 to 2017 we collected 237 patients submitted to trans rectal or transperineal free hand fusion prostate biopsies performed with Esaote Virtual Navigator System by expert biopsy surgeon. Patients with mpMRI PIRADS-V2 score ≥3 underwent targeted biopsy (3 cores) + systemic random biopsies (12 to 16 cores). Descriptive statistic was used to describe population features. Overall PCa and cs PCa (Gleason score ≥3+4) detection was calculated. Correlation between the detection of a histopathological clinical significant PCa and the PIRADS-score classification was assessed by univariate logistic regression analyses. Finally Receiver Operating Characteristics (ROC) curve was used to show the predictive accuracy of target *vs*. systematic biopsies on csPCa detection, according to PIRADS score. *Results:* Median age was 67 years [interquartile range (IQR)=47-80]. Median PSA value was 6 ng/ml (IQR=1.2-47). Overall, mpMRI detected 34 (14%) PIRADS 5, 133 (56%) PIRADS 4, 70 (29%) PIRADS 3 lesions, respectively. At targeted + random sextant biopsy, PCa was diagnosed in 159 patients (67%), while significant disease was found in 118 patients (50%). Targeted biopsies detected 127 (53%) PCa and 94 (40%) clinically significant PCa. In 23 patients clinically significant PCa was detected in targeted biopsies only, while in 14 cases clinically significant Pca was discovered by sextant biopsies only. Detection rate of significant PCa was 74%, 59%, and 21% respectively for PIRADS 5, 4 and 3. Targeted biopsies detected significant Pca in 74%, 42%, 14% in case of PIRADS 5, 4 and 3 respectively. At univariate analysis higher PIRADS-score was associated with detection of clinical PCa [odds ratio (OR)=1.77; confidence interval (CI)=1.07-2.27; $p<0.001$]. Specifically, PIRADS 5 was associated with higher risk of clinically significant PCa than 4 and 3: OR=4.51; CI=2.01-10.11; OR=2.62; CI=1.23-3.31; OR=0.27; CI=0.14-0.51, respectively; all $p<0.001$). The ROC curve showed an AUC of 71% for target biopsies and of 56% for systemic biopsies ($p<0.001$) in identifying clinically significant PCa. *Conclusion:* In this initial experience with Esaote Virtual Navigator System, results indicate a high PCa detection rate by target biopsies, that are more accurate than random biopsies in detecting clinically-significant PCa.

Authors Index*

(Figures indicate abstract number. *Missing abstracts were withdrawn.)