ABSTRACTS OF THE 25th ANNUAL MEETING OF THE ITALIAN SOCIETY OF URO-ONCOLOGY (SIUrO)

21-23 June, 2015, Rome, Italy
Università Cattolica del Sacro Cuore, Facoltà di Medicina e Chirurgia “A. Gemelli”

Honorary Chair: Gigliola Sica
Abstracts of the 25th Annual Meeting of the Italian Society of Uro-Oncology (SIUrO), 21-23 June, 2015, Rome, Italy

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Via Dante 17 – 40126 Bologna  
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Introduction and Objectives: The intravesical administration of hyaluronic acid and chondroitin sulphate solution (HA-CS) has been proven active in patients affected by interstitial cystitis (1). The gene expression of fibronectin (FN) in bladder washings has recently been correlated with local toxicity of adjuvant intravesical therapy (2). The aim of the study was to investigate the genetic evidence of the healing or protective action that HA-CS could carry out also in patients suffering from topical toxicity induced by intravesical adjuvant therapy given for non-muscle invasive bladder cancer. Materials and Methods: The study included 50 patients submitted to adjuvant intravesical therapy with mitomycin, epirubicin or bacillus Calmette–Guérin (BCG). Ten age-matched healthy patients were enrolled as control group. Before, during and after intravesical therapy, bladder washing samples were collected to investigate the gene expression of FN. In 9 more patients the samples were collected also immediately before and a week after the instillation of HA-CS. Topical toxicity was classified into 3 grades: 0-1, light (no medical therapy); 2, moderate (medical therapy); 3, severe (instillation postponed). Bladder washing samples were analyzed by isolation of cellular RNA using a miRNeasy Mini Kit (Qiagen®). RT-PCR was performed in order to analyze FN gene expression. Changes in the FN content were calculated using the ΔΔCt method after normalization with endogenous reference 18s rRNA and calibrating Ct value for each RNA obtained for triplicate reactions. Statistical analysis was performed to correlate the FN gene expression to tumor characteristics, treatment, topical toxicity and intravesical administration of HA-CS. Results: FN median value before the adjuvant treatment was 1.1-fold, with higher levels in patients with multiple tumors (median FN=1.5; mean=3.9; p=0.0003). Twenty patients (34%) showed grade 2-3 toxicity. Compared to controls (FN=1), FN increased during therapy a median of 4-fold (range=0.2-45.2; mean=7.5) in presence of grade 2-3 toxicity, remaining stable in asymptomatic patients (median FN=0.6; range=0.1-3.2), with a statistically significant difference (p=0.0005). In 9 patients, one week after single instillation of HA-CS, the median FN gene expression decreased from 3.2 to 0.33 with concomitant symptomatic relief. Discussion and Conclusion: Fibronectin is a fundamental element for the repair of urothelial damage. FN gene is probably activated by the need of fibronectin for healing process and down-regulated by the integrity of bladder urothelium. In our preliminary experience FN gene expression in bladder washings resulted strictly related to local toxicity induced by intravesical therapy. It increases after transurethral resection (TUR) of multiple tumors due to the greater urothelial damage. It increases also during intravesical therapy reaching the highest levels in case of severe toxicity due to the extensive urothelial damage. A single instillation of intravesical hyaluronic acid and chondroitin sulphate solution induces a rapid reduction of FN gene expression levels, particularly when high levels are present. The FN gene down-regulation induced in patients with toxicity is due to intravesical therapy and might represent an objective and measurable indicator of the healing activity of intravesical instillation of HA-CS.


2 COMPARISON OF OPEN AND LAPAROSCOPIC RADICAL NEPHRECTOMY IN RENAL TUMORS WITH SIZE ≥10 CM

Lucio Dell’ Atti and Carmelo Ippolito

Division of Urology, University Hospital “S. Anna”, Ferrara, Italy

Introduction: Laparoscopic radical nephrectomy (LRN) is considered standard of care for T1 renal tumors not amenable to nephron-sparing surgery. The role of LRN in the management of very large renal masses has yet to be determined. Few recent publications showed that LRN could also be performed for large renal tumors. Indications are now expanding to include patients with T2 or T3 tumors. Ritchie and colleagues (1) emphasized that patients within T2 stage
were operated with LRN safely, although there are more challenging procedures. We reported our experience managing renal masses ≥10 cm with transperitoneal LRN and compared this technique versus open radical nephrectomy (ORN) in terms of duration of hospitalization, complications, operative and perioperative outcomes. Materials and Methods: A retrospective analysis was performed in 114 patients (ORN=65; LRN n=49) that underwent surgery for kidney tumors from 2007 until 2012. Patients with T1 and T4 tumors (tm) were excluded from the study. The transperitoneal approach was preferred in all patients who underwent LRN. Patients' age, tumor size, preoperative surgical risk score, duration of hospitalization, complications and hospitalizations' costs were recorded. The complications (cp) in both groups were specified with the Modified Clavien System in five grades. Chi square test was used to assess differences in the response between the two groups and the Fisher's test, if necessary. All \( p \)-values less than 0.05 were considered statistically significant. Results: The mean age was found 56.34±14.54 years in the ORN group (G) and 57.18±13.41 years in the LRN G \( (p=0.247) \). Tumor size was calculated 9.52±2.36 (7-16) cm in the ORN G and 9.72±1.73 (7-15) cm in the LRN G \( (p=0.495) \). In the ORN G, T2 tm were found in 51 (78.4%) patients and T3 tm in 14 (21.5%) patients. In the LRN G, T2 tm were identified in 37 (75.5%) patients and T3 tm in 12 (24.5%) patients \( (p=0.362) \). There was no significant difference between the two groups in terms of mean age, American Society of Anesthesiologists (ASA) score, mean tumor size and tumor stages. After an early post-operative period pain necessitating analgesics was observed in all patients (100%) of both groups (Grade 1 cp). Blood transfusion was required in 19 patients (29.2%) in the ORN G and 11 (22.4%) patients in the LRN G \( (p=0.560) \). Grade 3 cp was not observed in either group. Grade 4 cp occurred in 4 (6.1%) patients (acute tubular necrosis (2), the need for dialysis, pulmonary embolism, atrial fibrillation) in the ORN G and in 1 (2%) patient (atrial fibrillation) in the LRN G. Grade 5 cp did not occur in either group. The mean hospital stay was 4.95±1.85 days in the ORN G and 3.10±1.67 days in the LRN G \( (p<0.001) \). The mean follow-up period was calculated 39 months for the ORN G and 32 months for the LRN G. Local recurrence occurred in 2 (3%) patients in the ORN G. Two patients in ORN G and 2 patients in LRN G died during the follow-up period. Discussion and Conclusion: The most controversial topic in literature concerns the risk of local recurrence in patients with T2 or T3 tm that underwent LRN, although the incidence of disease recurrence seems to be more prominent in patients with high-grade tm (2). Therefore, LRN can be safe in terms of duration of hospitalization, complications, operative and perioperative outcomes by experienced laparoscopists for very large renal masses (≥10 cm). In our study blood transfusion and complication rates are higher for ORN in pT2/T3 patients and unrelated to tumor and total specimen size.


3 SIGNIFICANCE OF INCIDENTAL PROSTATE CANCER AFTER RADICAL CYSTOPROSTATECTOMY FOR INVASIVE BLADDER UROTHELIAL CARCINOMA: OUR EXPERIENCE

Lucio Dell'Att i, Gianni Ughi, Gaetano Capparelli and Carmelo Ippolito
Division of Urology, University Hospital “S. Anna”, Ferrara, Italy

Introduction/Aim: In this study we retrospectively reviewed data of patients with incidental prostate carcinoma (PCa) that underwent radical cystoprostatectomy (RCP) for invasive bladder cancer. Our aim was to analyze their features with regard to incidence, pathologic characteristics, clinical significance and implications for management. Materials and Methods: The clinical data and pathological features of 64 patients who underwent standard RCP for bladder cancer at our institution from January 2006 to May 2013 were retrospectively reviewed. The preoperative assessment included digital rectal examination (DRE), prostate-specific antigen (PSA), chest radiographies, while computed tomography (CT) urography and/or magnetic resonance imaging (MRI) were used for clinical staging. Patients with an abnormal result of DRE or PSA, suspicious of PCa and finally confirmed by prostate biopsy before the surgery, were excluded from the study. Clinically significant PCa was defined as a tumor with a Gleason 4 or 5 pattern, stage ≥pT3, lymph node involvement, positive surgical margin or multifocality of three or more lesions. Postoperative follow-up was scheduled at 3-month intervals after the surgery, then every 3 months the first year, every 6 months the second and third year, and annually thereafter. A biochemical recurrence was defined as a second confirmatory level of serum PSA of >0.2 ng/ml. Chi-square analysis (or Fisher’s exact test for nonparametric variables) was used to analyze categoric variables and \( t \)-test to analyze continuous variables. A \( p \)<0.05 was considered to indicate statistical significance.
Results: Primary tumors were transitional cell carcinoma (TCC) of the bladder in 62 patients (96.9%), sarcoma and adenocarcinoma of the bladder in the remaining two patients (3.1%), respectively. Carcinoma in situ and non-invasive high-grade urothelial papillary carcinoma were seen in 6 (9.7%) and 2 (3.3%) patients, respectively. In 20 (32.3%), 18 (29%) and 13 (20.9%) patients, urothelial carcinoma had invaded the subepithelial connective tissue, muscularis propria and perivesical tissue, respectively. Stage pT4 (direct extension to the prostate) was seen in 5 patients (7.8%). Eleven out of 64 patients (17.2%) that underwent RCP had incidentally diagnosed PCa. The mean age was 73.3±7.2 years and 74.9±6.9 years for patients with incidental PCa and without incidental cancer, respectively (p=0.255). A preoperative median PSA in 11 cases with incidental PCa was 2.79±1.94 ng/ml and in 53 patients without incidental cancer was 2.19±1.88 ng/ml, which showed no significant difference (p=0.144). Two patients were found to have apex involvement of PCa. Three cases (3/11, 27.3%) were diagnosed as significant PCa, while 8 cases (8/11, 72.7%) were clinically insignificant. The positive surgical margin of PCa was detected in 1 patient with significant disease. The prostate apex involvement was present in 1 patient of significant PCa group. There was no statistical difference in pathological staging and the pelvic lymph node involvement of the bladder cancer between the two groups. Follow-up data were available for all 64 patients who underwent RCP. Median follow-up period was 47.8±29.2 (range=4-79). All 11 patients with incidental PCa had undetectable serum PSA levels after 3 months after RCP. During the follow-up, biochemical recurrence occurred in 1 patient (9%), treated with androgen deprivation therapy.

Discussion and Conclusion: In the present study, in line with published studies (1, 2), incidental PCa does not impact on the prognosis of bladder cancer patients undergoing RCP. However, it is important to identify patients with high-risk PCa prospectively, so that they can be offered adjuvant treatment with view to longer-term risk reduction. Preoperative prostate assessment in those going for RCP may influence not only the decision but also the technique used. Prostatic apical sparing for better continence or prostate capsule preserving for erectile function in neobladder formation should be considered only in carefully selected patients.

4 CLINICAL AND PATHOLOGICAL FEATURES OF A PRIMARY SARCOMATOID CARCINOMA OF THE PROSTATE: CASE REPORT

Lucio Dell’ Atti, Gianni Ughi,
Carmelo Ippolito and Gian Rosario Russo
Division of Urology, University Hospital “S. Anna”,
Ferrara, Italy

Introduction: Sarcomatoid carcinoma of the prostate (SCP) is a very rare and highly aggressive neoplasm responsible for <1% of primary prostate malignancies in adults (1). Until now, less than 100 cases have been reported in the literature. It is generally associated with a poor prognosis. Clinically, the patient presents urinary tract obstruction, symptoms of frequency, urgency and nocturia. Materials and Methods: We report a case of a 73 year old man who presented at the emergency room with haematuria, urinary frequency, nocturia, urgency and a sense of incomplete emptying. He had no history of urinary tract infection, urinary lithiasis or other genitourinary pathology. The digital rectal examination (DRE) revealed a palpable, painful and tumescent prostatic mass. Blood analysis indicated leucocytosis (14.20×10^3 cells/μl) and neutrophilia (72.6×10^3 cells/μl). The prostatic specific antigen (PSA) level was 0.8 ng/ml and urine cultures were negative. Transrectal ultrasound revealed a large mass, apparently arising from the prostate and superiorly infiltrating into urinary bladder, filling its lumen incompletely. An abdomino-pelvic magnetic resonance imaging (MRI) was provided; it showed an abnormal heterogeneous signal intensity mass lesion in the pelvis showing peripheral post-contrast enhancement with central necrotic component measuring 72×55×66 cm in antero-posterior, transverse and cranio-caudal dimensions (Figure 1). Computed chest and brain tomography, as well as bone scan, were negative for metastatic disease.

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Results: A transurethral bladder resection (TURB) and a prostate trasrectal biopsy were performed. Microscopically, the TURB specimens showed a malignant lesion made of epithelial and stromal components. The stromal component consisted of bizarre cells with pleomorphic, hyperchromatic nuclei and abnormal mitotic figures. The patient underwent radical cystoprostatectomy and ileal conduit derivation with pelvic lymphadenectomy. The final histopathological diagnosis was SCP with infiltration of the prostate capsule and bladder without infiltration of the rectum. The patient did not show relapse 12 months after surgical intervention. Discussion and Conclusion: The rarity of adult prostate sarcoma is a major obstacle in clinical research and contemporary data are scarce (2). SCP is often suspected before surgery, especially when the patients present with lower urinary tract obstruction, a markedly enlarged prostate and a normal PSA value. In contrast to prostate adenocarcinoma, the PSA level in SCP is generally not elevated, fact that could be explained by the non-epithelial origin of sarcoma. For most patients, the initial diagnosis can be preoperatively established using image-guided needle biopsy, which can be helpful in selecting treatment. Our case study confirmed that surgery with curative intent offers the best chance of survival in patients presenting with non-metastatic disease. Neoadjuvant or adjuvant chemotherapy and radiotherapy for SCP have been much less effective in adults than in children. Adult prostate sarcoma might be more resistant to chemotherapy and the value of radiotherapy in these cases is debatable. However, in the case described, it should be performed in case of tumor recurrence. Additional collaborative large-scale studies are necessary for appropriate management of this dire entity.


5 EVALUATION OF TWO DIFFERENT TYPES OF CARBON DIOXIDE INSUFFLATORS DURING LAPAROSCOPIC RADICAL PROSTATECTOMY: IMPLICATIONS IN RESPIRATORY MANAGEMENT

Sergio Lacquinti, Francesco Varvello, Enrico Conti, Jacopo Antolini and Giuseppe Fasolis
Division of Urology, San Lazzaro Hospital, Alba, Cuneo, Italy

Aim: We retrospectively compared two different carbon dioxide insufflators, Thermoflator (standard gas flow rate) and Airseal IFS (continuous bidirectional gas flow, lower flow rate), during laparoscopic radical prostatectomy and extended pelvic lymphadenectomy (t-LRP) in order to detect any differences in the anesthetic respiratory management. Materials and Methods: Seventy-seven consecutive patients underwent t-LRP. The last 38 patients, treated using Thermoflator (group A), have been compared with the first 39 patients treated using Airseal (group B). Mean intrabdominal pressure was maintained at 12 mmHg in all patients. Baseline tidal, minute ventilation and positive end expiratory pressure (PEEP) were set at 8 ml/Kg, 10 breaths/minute and 5 cm H2O respectively in both groups. End-tidal (et) CO2 and arterial blood gas analysis were monitored during surgery. Changes of the baseline mechanical ventilator parameters have been made in the case of etCO2 greater than 40 mmHg. Results: Mean intraoperative etCO2 was 38.21 mmHg in group A and 39.28 mmHg in group B. Baseline mechanical ventilator parameters had to be modified in 21/38 group A patients and in 5/39 group B patients (p<0.01). These changes allowed to maintain the etCO2 within 40 mmHg in all patients of both groups. Discussion: Laparoscopic urological interventions have always been demanding procedures. The duration of general anaesthesia should be taken in account for planning. AirSeal insufflator could be a useful device in order to reduce anaesthesiology implications. Conclusion: In our experience, the AirSeal system simplified the anesthetic respiratory management and potentially limited pulmonary damage.

8 CAN THE INTRAOPERATIVE AND POSTOPERATIVE OUTCOMES OF RADICAL PROSTATECTOMY BE INFLUENCED BY THE PROSTATE BIOPSY?

Lucio Dell' Atti, Carmelo Ippolito, Gaetano Capparelli and Gian Rosario Russo
Division of Urology, University Hospital “S. Anna”, Ferrara, Italy

Introduction: Prostate cancer is diagnosed through a prostate biopsy. Traditionally, urologists recommend an interval of >4-6 weeks after transrectal prostate biopsy before radical prostatectomy (RP) to allow time for resolution of biopsy-induced inflammation (1), which might eliminate the surgical planes of dissection. In the study of Ikonen et al. (2), assessing endorectal magnetic resonance imaging (MRI) after prostate biopsy, 77% of patients had visible haemorrhage after biopsy. The effects diminish after 21 days.
with an obvious decrease in the amount of blood by 28 days. The aim of our study was to evaluate whether the interval from prostate biopsy to RP affects immediate operative outcomes. 

**Materials and Methods:** The study population of 473 patients undergoing open RP from March 2007 to April 2013 was retrospectively reviewed. The patients were divided into three groups according to the time interval between biopsy and RP: Group 1 (G1), ≤4 weeks; Group 2 (G2), >4 weeks and ≤6 weeks; Group 3 (G3), >6 weeks. We excluded patients who received neoadjuvant androgen ablation therapy and salvage RP. Using a series of univariate and multivariate logistic regression analyses, we evaluated whether the interval between biopsy and RP was a significant independent predictor of operative duration (OD), estimated blood loss (EBL), positive surgical margin (PSM), hospital stay (HS) and complications after RP. These parameters were analysed using a Fisher’s exact test and chi-square analysis to determine statistically significant differences between the groups. 

**Results:** A total of 116 patients (24.5%) were in G1, 179 (37.9%) in G2 and 178 (37.6%) in G3. No significant difference was noted between the groups when comparing age, preoperative PSA level, prostate volume, body mass index (BMI), biopsy number, clinical stage and Gleason grade. Using univariate analysis, the mean OD time (223.4±78.5 min) was found longer (p<0.002) and EBL (652.11±321.07 ml) was found greater (p<0.001) in G2. An increasing EBL was associated with an elevated BMI in all groups (p<0.001). Longer OD times were associated with an elevated BMI (p<0.001) and Gleason grade (p=0.003). Also, positive surgical margins were associated with pathologic stage (p=0.006), PSA level (p<0.002), Gleason grade (p=0.003) and extracapsular extension (p<0.002). Finally, urinary continence and erectile function were associated with patient age (p=0.001 and p<0.003, respectively). Both univariate and multivariate analyses, however, failed to show that the interval from biopsy to surgery had any significant relations with OD time, EBL, PSM, HS, postoperative urinary continence and sexual potency. 

**Discussion and Conclusion:** Transrectal prostate biopsy can cause inflammatory reactions, bleeding and haematoma around the prostate (2). A fair number of studies have been carried out on surgical outcomes compared according to the interval from prostate biopsy to surgery. The outcome and complications had no relation to the interval between biopsy and surgery; however, intraoperative blood loss showed significant differences (3). Nonetheless, our results suggest that the interval from biopsy to surgery had no significant correlations with OD, EBL, PSM, urinary continence and potency. In this study, long-term postoperative outcomes, such as the rates of biochemical recurrence and overall survival, were excluded. In this respect, further studies are recommended with a prospective experimental design and in a larger subject group.

**References:**


**11 DOMINANT INTRAPROSTATIC LESION OF INTERMEDIATE RISK PATIENTS IRRADIATED WITH EXTRA BOOST USING IMRT-SIB-IGRT BY TOMOTHERAPY**

**Elisabetta Garibaldi**, Elena Delmastro

**1Radiotherapy Unit, Candiolo Cancer Center - IRCCS, Candiolo, Turin, Italy; 2Neuroscience Department University of Turin, Human Physiology Unit of Neuroscience Department University of Turin, Turin, Italy; 3Medical Physics Unit, Candiolo Cancer Center - IRCCS, Candiolo, Turin, Italy; 4Oncology Unit, Candiolo Cancer Center - IRCCS, Candiolo, Turin, Italy

**Introduction:** Local recurrence in prostate cancer most frequently occurs within or close to the primary tumor, often at the level of one or more macroscopic lesions defined as dominant intra-prostatic lesions (DIL). Multiparametric magnetic resonance imaging (MRI) (with T2 weighted diffusion weighted imaging (DWI) and dynamic contrast-enhanced (DCE) sequences) is the golden standard to detect and to guide DIL contouring. In prostate cancer, irradiation of DIL with a boost dose is a widespread but still experimental protocol. In our Centre, we have performed a phase II randomized dose escalation study on DIL identified by functional MRI. The aim of this abstract is to present our experience of DIL irradiation up to an equivalent dose (EQD2) of 93.2 Gy with Helical Tomotherapy focusing on the technical and clinical feasibility of the procedure, early and intermediate toxicities examinations reported during the follow-up and oncologic outcome. 

**Materials and Methods:** Between March 2011 and June 2014, 12 stage II patients with intermediate-risk prostate cancer were enrolled in our protocol of DIL dose escalation by Tomotherapy. All
patients were submitted to a multiparametric MRI (including T2 weighted, DCE and DWI series) in order to evaluate and visualize DIL. The prescribed doses were 75.2 Gy in 32 fractions of 2.35 Gy per day (EQD$_2$=80.5 Gy, considering the $\alpha/\beta$ ratio between 1 and 4) on prostate gland; between 67.2 Gy and 75.2 Gy in 32 fractions of 2.1 or 2.35 Gy (EQD$_2$ between 70 and 80.5 Gy) on seminal vesicle; 83.2 Gy in 32 fractions of 2.6 per die (EQD$_2$=93.2 Gy) on DIL; 54.4 Gy in 32 fractions of 1.7 Gy per die (EQD$_2$=51.2 Gy) on pelvic volume. \textit{Results:} With an average follow-up of 18 months (range=4-45), the acute gastrointestinal (GI) toxicity $\geq$ G2 was 8.3% (1/12 patients) and the acute genitourinary (GU) toxicity $\geq$ G2 was 16.6% (2/12 patients). No rectal acute toxicity $\geq$ G2, neither overall severe acute toxicity $\geq$ G3, was observed. Late toxicity was evaluable in 8 patients: in these patients no late toxicity $\geq$ G2 was observed. At last follow-up, the biochemical disease-free survival was 100%. \textit{Conclusion:} The irradiation of whole prostate and seminal vesicles up to an EQD2 of 80.5 Gy and of DIL up to 93.2 Gy was clinically feasible and safe without acute severe toxicity, although -with a short follow-up- a severe late toxicity is currently absent. However, in order to evaluate late toxicity and definitive outcome, a longer follow-up is needed.

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\textbf{Figure 1.} \textit{In color wash isodoses on different PTVs: in red the DIL-PTV (prescribed dose 83.2 Gy), in yellow the prostate-PTV (prescribed dose 75.2 Gy) and in light blue the VS-PTV (prescribed dose 67.2 Gy).}

\section*{UROTHELIAL CARCINOMA OF THE PROSTATIC URETHRA: LONG-TERM FOLLOW-UP STUDY}

Savino Mauro Di Stasi$^1$, Francesco Celestino$^2$, Cristian Verri$^1$ and Francesco De Carlo$^1$

$^1$Department of Experimental Medicine and Surgery, Tor Vergata University, Rome, Italy; $^2$Operative Unit of Urologic Oncology, Policlinico Casilino, Rome, Italy

\textit{Introduction/Aim:} The involvement of the prostatic urethra in high risk non-muscle invasive bladder cancer (NMIBC) varies between 10 to 40%. Treatment strategies and expected outcomes of this disease are not well defined. In a retrospective study, we looked at the long-term outcomes in patients with urothelial carcinoma of the prostatic urethra (UCPU) concomitant with high risk NMIBC.

\textit{Materials and Methods:} From January 1998 to December 2010, 39 patients with high risk NMIBC and concomitant UCPU were recruited. After the initial transurethral resection of all visible tumors upon endoscopy, and random cold-cup biopsies of the bladder and prostatic urethra, all patients underwent restaging transurethral resection of the bladder and prostatic urethra 4-6 weeks later. Patients with non-muscle invasive UCPU (n=33) underwent adjuvant intravesical bacillus Calmette-Guerin (BCG) therapy, while patients with prostatic stromal or ductal invasion (n=6) underwent neoadjuvant platinum-based systemic chemotherapy and radical cystectomy. Patients with non-muscle invasive UCPU were followed up with cystoscopy and urinary cytology every 3 months. A yearly computed tomography (CT) scan was performed in all patients. The primary endpoint was disease-free interval; secondary endpoints were recurrence rate, progression rate, time to progression, as well as overall and disease-specific survival rates. \textit{Results:} Median follow-up was 96 months (interquartile range (IQR)=73-122). The median disease-free interval was 15 months (IQR=12-14) and 9 months (IQR=7-11) for UCPU and NMIBC, respectively; recurrence rate was 30% for UCPU and 38% for NMIBC; progression rate was 10.2% (4 patients) for UCPU and 17.9% (7 patients) for NMIBC; time to progression was 12 months (IQR=10-14) for UCPU and 9 (IQR=8-10) for NMIBC; overall and disease-specific survival rates for UCPU were 87.2% and 92.4%, respectively. The disease free-interval in patients with prostatic stromal or ductal invasion was 8 months (IQR=7-9). Progression to metastatic disease in patients with prostatic stromal or ductal invasion was observed in 3/6 patients (50%). During the follow-up an upper urinary tract urothelial carcinoma was diagnosed in 6/39 patients (15.4%). \textit{Conclusion:} Trans-urethral resection and adjuvant intravesical BCG therapy are effective treatments for UCPU. Radical cystectomy should be reserved as primary treatment in patients with stromal or ductal involvement. Strict follow-up of UCPU patients with concomitant NMIBC is mandatory to detect metachronous upper urinary tract tumors.
13 MINIMAL SUBCOSTAL MUSCLE-SPARING EXTRAPERITONEAL OPEN ACCESS FOR RENAL AND UPPER URINARY TRACT OPEN SURGERY

Savino Mauro Di Stasi, Cristian Verri, Francesco Celestino and Francesco De Carlo

Department of Experimental Medicine and Surgery, Tor Vergata University, Rome, Italy

Introduction: Classical open renal and upper urinary tract surgery has been the standard approach accompanied by larger and more traumatic incisions with significant post-surgical pain, longer hospitalization time and an unpredictable complication rate when compared to minimally invasive procedures, such as laparoscopic and robotic-assisted techniques. The minimal incision is a surgical technique practiced with minimal scarring and less blood loss, pain and recovery time. Feasibility and outcomes of minimal subcostal muscle-sparing extraperitoneal open access for renal and upper urinary tract open surgery were evaluated. Patients and Methods: Between January 2006 up to December 2013, the minimal subcostal muscle-sparing extraperitoneal approach was performed in 104 patients who underwent partial nephrectomies for renal cancer (n=43), pyeloplasty (n=29), pyelolithotomy (n=9) and nephrectomies for renal cancer (n=9). The procedure consisted of a standard flank position and a 8x2 cm subcostal lateral and semi-oblique incision starting at the lower edge of the intercostal space between the tenth and the eleventh ribs. The external oblique, internal oblique and transversus abdominis muscles were dissected parallel to the course of their fibers and the retroperitoneal fat and peritoneum, bluntly pushed anteriorly, are exposed. Then Gerota's fascia is dissected off the renal surface and access to the hilum of the kidney, the renal pelvis, the ureteropelvic junction and the lumbar ureter is easily achieved. Operative time, blood loss, transfusion rate, complication rates assessed according to Clavien grading system and hospital stay were evaluated. Moreover, visual analog pain scale (VAS) scores were collected for each patient. Results: All 104 procedures were accomplished successfully. The mean operative time was of 103 minutes (range=89-148) with nephrectomies and partial nephrectomies that were more time consuming (range=122-148) if compared with the other surgical procedures (range=89-102). The mean blood loss was 205 ml (range=180-462) with a transfusion rate of 7.6% (8 patients). All patients requiring blood transfusion underwent nephrectomies or partial nephrectomies (3 and 5 patients, respectively). The overall complication rate was 16.3% (17 patients), 7 patients with grade I and 10 patients with grade II of Clavien score. The mean hospital stay was 4 days (range=3-7). Visual analog pain scale scores were 5.1, 4.7 and 4.3 on the day of operation, postoperative day 1 and postoperative day 2, respectively. Conclusion: The minimal subcostal muscle-sparing extraperitoneal open access is an effective technique for the surgical management of the kidney and upper urinary tract with a painful minimal scarring and shorter hospitalization and operative times. Quickness and feasibility of the procedure, combined with the potential improvement of cost-benefit ratio, encourages further studies in order to consider this technique as an alternative for the most common surgical procedure performed on kidney and upper urinary tract.

15 GENITOURINARY TOXICITY IN MODERATE HYPOFRACTIONATION PROSTATE CANCER WITH VOLUMETRIC MODULATED ARC THERAPY

Sergio Persino, Rosario Mazzola, Francesco Ricchetti, Niccolò Giag Levra, Alba Fiorentino, Stefania Naccarato, Gianluisa Sicignano, Ruggero Ruggieri, Stefano Cavalleri and Filippo Alongi

1Division of Radiation Oncology, Sacro Cuore Don Calabria Hospital, Negrar Verona, Negrar, Verona, Italy; 2Urology, Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy

Aim: To report genitourinary (GU) toxicity profile in prostate patients treated with simultaneous integrated boost (SIB) with volumetric modulated arc therapy (VMAT) in a radical moderate hypofractionated regimen. Patients and Methods: A total of 60 patients were analyzed. The population was stratified into low 42% (25/60), intermediate 27% (16/60) and high-risk 31% (19/60) groups. Target volumes, expanded to define the planning volumes (PTVs), were clinical target volume (CTV) 1: prostate; CTV2: CTV1 + seminal vesicles; CTV3: CTV2 + pelvic nodes. Low-risk patients received 73.5 Gy to PTV1; intermediate-risk 73.5 Gy to PTV1 and 66 Gy to PTV2; high-risk 73.5 Gy to PTV1, 66 Gy to PTV2 and 54 Gy to PTV3. All treatments were performed in 30 fractions. The median follow-up was 24 months (range=12-30). According to common terminology criteria for adverse events (CTCAE) v4.0, acute and late toxicity were prospectively collected and retrospectively evaluated. Results: Acute GU toxicity was recorded as follows: G0 in 26% (16/60), G1 in 32% (19/60), G2 in 42% (25/60). No case of acute toxicity ≥ G3 was registered. During treatment, median week onset of GU toxicity was 3th (range=2th-5th). Late GU toxicity was recorded as follows: G0 in 33% (20/60), G1 in 50% (30/60), G2 in 17% (10/60). No case of toxicity ≥ G3 was registered. Using logistic regression analysis, significant correlations between GU toxicity and the volume of bladder irradiation V50 Gy > 45% (p<0.03)
and V60 Gy > 35% (p<0.001) were found. A planning bladder volume < 250 cc is related to G2 acute toxicity. Conclusion: The current moderate hypofractionation schedule was shown to be safe, with acceptable GU moderate toxicity and without severe effects. Longer follow-up is needed to assess clinical outcomes.

16 TREATMENT VOLUMES CHANGING IN DEFINITIVE PROSTATE CANCER WITH VOLUMETRIC MODULATED RADIATION THERAPY AFTER 18F-CHOLINE PET/TC

Niccolò Giaj Levra, Rosario Mazzola, Francesco Ricchetti, Sergio Fersino, Alba Fiorentino, Veronica Malfatti, Sara Tadayyon, Ruggero Ruggieri, Matteo Salgarello and Filippo Alongi

Division of Radiation Oncology, Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy

Introduction/Aim: The role of 18F-choline positron emission tomography/computed tomography (Cho-PET/CT) in diagnosis and staging before definitive radiotherapy (RT) in localized prostate cancer (PC) patients is not well standardized. The aim of the current analysis is to evaluate the impact of Cho-PET/CT in decision making strategy of patients with localized PC eligible to definitive RT. Patients and Methods: From January 2011 to August 2014, sixty patients with biopsy proven prostate adenocarcinoma, with no prior treatment on primary tumor and staged with Cho-PET/CT before RT were prospectively enrolled. Median age was 73 years (60-81 years); Gleason score was 6 in 32 patients (54%), 7 in 14 patients (23%) and ≥8 in 14 patients (23%); median prostate-specific antigen (PSA) value at diagnosis was 6.79 ng/ml (2.3-143 ng/ml). All patients were treated with Volumetric Modulated Arc Therapy (Varian RapidArc®) with simultaneous integrated boost (SIB) in 28 fractions (moderate hypofractionation) as follows: for low risk prostate planning target volume (PTV) only, for intermediate risk prostate and seminal vesicles PTVs and for high risk prostate, seminal vesicles and pelvic lymph nodes. Androgen deprivation therapy (ADT) was prescribed according to National Comprehensive Cancer Network (NCCN) risk classification. Cho-PET findings were used to define the stage according to the detection of primary tumor (T), pelvic lymph nodes (N) and distant metastases (M). Therapeutic strategy based on the Cho-PET/CT evaluation was compared to the strategy that would have been proposed in case of PET not available and/or not strictly indicated according to international and national PC guidelines. Results: Cho-PET was positive in 57 cases (95%): T in 45 (79% of all positive cases); T in combination with N in 8 (14%); and M (bone) in combination with T or N or both in 4 (7%). After the Cho-PET, patients were stratified according to NCCN risk classification as follows: 26 (43%) low risk, 10 (16%) intermediate risk and 24 (41%) high risk. Cho-PET shifted treatment indication in 13 cases (21%). The changes regarding radiation treatment volumes were as follows: 6 intermediate risk patients (10%) shifted to high risk and consequently were irradiated on prostate, seminal vesicles and pelvic nodes PTVs; in 7 high risk patients (11%) the Cho-PET showed bone and/or N uptake and, consequently, a SIB on PET positive sites was prescribed. No upstaging of low risk patients to a higher risk was observed. Conclusion: Our results have shown that Cho-PET seems to be a promising diagnostic tool in patients that are candidates for radical RT and support the decision making in treatment planning, in particular in intermediate-high risk. Although a SIB on Cho-PET positive sites is still under investigation, it could be a viable option to intensify local radiation treatment in this setting.

17 RECTAL TOXICITY IN MODERATE HYPOFRACTIONATION PROSTATE CANCER WITH VOLUMETRIC MODULATED ARC THERAPY

Francesco Ricchetti1, Sergio Fersino1, Rosario Mazzola1, Niccolò Giaj Levra1, Alba Fiorentino1, Stefania Naccarato1, Gianluisa Sicignano1, Ruggero Ruggieri1, Stefano Cavalleri2 and Filippo Alongi1

1Division of Radiation Oncology, Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy; 2Urology, Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy

Purpose: To report rectal toxicity profile in prostate patients treated with simultaneous integrated boost (SIB) with volumetric modulated arc therapy (VMAT) in a radical moderate hypofractionated regime. Patients and Methods: A total of 60 patients were analyzed. The population was stratified into low 42% (25/60), intermediate 27% (16/60) and high-risk 31% (19/60) groups. Target volumes, expanded to define the planning volumes (PTV), were clinical target volume (CTV) 1: prostate; CTV2: CTV1 + seminal vesicles; CTV3: CTV2 + pelvic nodes. Low-risk patients received 73.5 Gy to PTV1; intermediate-risk 73.5 Gy to PTV1 and 66 Gy to PTV2; high-risk 73.5 Gy to PTV1, 66 Gy to PTV2 and 54Gy to PTV3. All treatments were performed in 30 fractions. The median follow-up was 24 months (range=12-30). According to common terminology criteria for adverse events (CTCAE) v4.0, acute and late toxicity were prospectively collected and
18 VISCERAL FAT TISSUE ACTIVITY DOES NOT CORRELATE TO HIGH GRADE PROSTATE CANCER RISK AT BIOPSY
Salvatore Scurria1, Simone Siracusano1, Ninfa Giacalone1, Antonina Graziella Cangemi2, Stefano Caruso3, Rosalinda Allegro3, Antonio Russo2, Renzo Colombo4 and Vincenzo Serretta1

1Section of Urology, Department of Surgical, Oncological and Stomatological Sciences, Azienda Ospedaliera Universitaria Policlinico "Paolo Giaccone", Palermo, Italy; 2Section of Medical Oncology, Department of Surgical, Oncological and Stomatological Sciences, Azienda Ospedaliera Universitaria Policlinico "Paolo Giaccone", Palermo, Italy; 3Statistics, Gruppo Studi Tumori Urologici (GSTU) Foundation, Palermo, Italy; 4Department of Urology, San Raffaele Scientific Institute, Milan, Italy

Introduction/Aim: High-grade prostate cancer (PCa) has been reported in association with metabolic syndrome (MS). In a previous study we found no significant correlation between body mass index (BMI) and prevalence of high Gleason score at biopsy (1). BMI could be not an accurate marker of the endocrine activity of visceral adipose tissue responsible of high plasmatic levels of adipokines promoting PCa aggressiveness. We estimated visceral adiposity dysfunction by the visceral adiposity index (VAI) considering waist circumference (WC), BMI, triglycerides (TG) and high density lipoproteins (HDL) plasma levels of each patient (2). The aim was to correlate VAI values with PCa detection rate and Gleason patterns 4 and 5 at biopsy. Patients and Methods: Patients who underwent prostate biopsy for suspicious digital rectal examination and/or elevated PSA levels were enrolled. After informed consent, a transrectal prostate biopsy, 12 cores at least (24 in case of re-biopsy), was performed. VAI was expressed as: WC/[39.68 + (1.88 × BMI)] × TG/1.03 ∗ 1.31/HDL, assuming VAI=1 in healthy, non obese men with TG and HDL levels within normal limits. PCa detection at biopsy, Gleason score patterns, VAI and BMI were statistically analyzed using the Mann Whitney U-test.

Results: Ninety-five patients were entered with a median age of 67 years (range=47-79). The median BMI was 27 kg/m² (range=17.4-40) and the median VAI was 4.47 (range=1.3-15.6). Median PSA was 7.9 ng/ml (range=0.47-53). A prostate nodule was palpable in 27 (28.4%) patients. Ten patients (10.5%) had a previous negative biopsy. A prostate cancer was diagnosed in 43 (45.2%) patients, Gleason patterns 4 and 5 were detected in 18 (41.8%) patients. Median BMI and VAI were 27.4 Kg/m² and 26.3 Kg/m² (p=0.53) and 4.25 and 4.66 (p=0.28) in patients with positive and negative biopsy, respectively. Median BMI and VAI resulted 27.7 Kg/m² and 27.3 Kg/m² and 4.78 and 3.98 in patients with and without Gleason patterns 4 or 5, respectively. No statistically significant difference was highlighted for VAI (p=0.37) or BMI (p=0.85). Discussion and Conclusion: The identification of patients harboring an aggressive PCa remains an important goal. To date the relation between MS and PCa remains contradictory. Moreover, an accurate marker of MS has not yet been determined (3). VAI might be a more accurate marker than BMI in indicating the activity of visceral fat. In spite of VAI adoption, our analysis does not reveal any statistically significant correlation between VAI, PCa detection rate and incidence of Gleason patterns 4 or 5 at biopsy. Diet, race and other environmental and genetic factors, playing a promoting or protective role in PCa, should be also considered in further studies.

The statistical support of the GSTU Foundation is acknowledged.

DETECTION OF DNA MUTATIONS IN URINE OF PATIENTS WITH PROSTATE CANCER BY NGS TECHNOLOGY

Gianluca Aguiari1, Alessandra Mangolini2, Federico Pagliotto1, Giovanni Lanza3, Massimo Negrini2 and Lucio Dell’atti4
1Department of Biomedical and Specialty Surgical Sciences, University of Ferrara, Ferrara, Italy; 2Department of Morphology, Surgery and Experimental Medicine, Section of Oncology, Pathology and Experimental Biology, University of Ferrara, Ferrara, Italy; 3Department of Morphology, Surgery and Experimental Medicine, Section of Pathological Anatomy, University of Ferrara, Ferrara, Italy; 4Department of Urology, University Hospital “St. Anna”, Ferrara, Italy

Introduction: Prostatic carcinoma (PCa) is the most common cancer in males. Approximately 16% of patients develop the disease with about 3-4% of deaths (1). PCa diagnosis is based on the detection of serum prostate-specific antigen (PSA), which is the only serum biomarker for the diagnosis of prostatic carcinoma. However, at low levels, PSA is inaccurate, resulting in a high negative biopsy rate (2). Currently, no specific standard protocols to identify low-form high-risk patients are available. Therefore, direct DNA analysis from urine may represent a non-invasive test to detect gene mutations associated with poor prognosis (3). Materials and Methods: Cell-free DNA from urine samples and nuclear DNA from paraffin-embedded tumor tissues, derived from PCa patients, was extracted by using specific DNA isolation kits. Cell-free urine DNA, as well as DNA extracted from prostatic cancer tissue, was quantified by DNA isolation kits. Cell-free DNA from urine samples and nuclear DNA derived from urine and prostatic carcinoma tissue of the same patient, respectively, as well as from urine of normal subjects, was sequenced for gene mutations by next-generation sequencing (NGS). Specific panels containing exon sequences of genes involved in cancer development and progression were used. NGS analysis of DNA isolated from urine of PCa patients was able to identify germinal and somatic mutations in different genes including MET oncogene, mTOR kinase and KDR gene that codifies for the VEGFR-2 tyrosine kinase receptor. Interestingly, an inactivating stop mutation in the SMAD4 tumor suppressor gene, which was mutated in advanced cancers, including prostatic carcinoma, was detected. These mutations were also detected in the paired prostate cancer tissues but not found in urine DNA from normal samples. Discussion: NGS analysis is an innovative and powerful approach to detect gene mutations also starting from low amounts of DNA. Therefore, this analysis is suitable for the research of DNA mutations in biological fluids like urine. Mutated genes, discovered thanks to this approach, could lead to the identification of high-risk patients who should be subjected to pharmacological therapy. Consistently, some of identified gene mutations were already found in prostatic cancer tissues suggesting their important role in this disease. The linkage between DNA mutations and patient outcome could lead to the identification of low and high risk patients, detecting new prognostic markers for the PCa. Conclusion: These data indicate how this novel approach is able to detect gene mutations related to disease analysing DNA directly from urine of PCa patients. The analysis of DNA mutations in PCa patients could lead to the detection of new molecules able to correct altered signals associated with the disease, thus improving the pharmacological therapy.


NBI CYSTOSCOPY INCREASES THE DETECTION RATE OF CARCINOMA IN SITU: RUA’S EXPERIENCE

Luca Albanesi, Barbara Cristina Gentile, Gabriella Mirabile, Paola Tariciotti, Gabriella Mirabile, Francesco Pisanti, Giorgio Rizzo, Giorgio Vincenti and Roberto Giulianelli
Division of Urology, Nuova Villa Claudia, Rome, Italy

Background/Aim: Narrow banding imaging (NBI) was developed with the goal of enhancing the definition of small

Discussion:
lesions of the bladder that might be missed during white light (WL) endoscopy. The aim of this study was to evaluate the capacity of NBI to increase the detection rate of lesions not visible with WL cystoscopy and show whether visibility of carcinoma in situ (CIS) can be increased. 

**Design, Setting and Participants:** From June 2010 to April 2012, 797 patients underwent WL plus NBI cystoscopy and subsequently bipolar transurethral resection of bladder tumor (TURBt). In the 797 patients, we identified a total of 1,571 suspected lesions of which 496 (50.6%) were single lesions and 1,075 (49.3%), instead, multiple lesions. The use of cystoscopy with WL has allowed the identification of 1,337 lesions. With the subsequent use of NBI light, we discovered 234 lesions not otherwise visible with WL. During cystoscopy, the topography and characterization of lesions by WL and NBI were recorded. All the removed tissue was sent separately for histological evaluation. The logistic regression model was used in order to identify the relationships between the structural variables and the ability of the new technique to detect the disease, the indices of sensitivity and specificity of the test to compare the two techniques, the test of hypothesis Z for the difference in percentages and the index of relative risk.

**Results and Limitations:** In our experience, the use of NBI significantly increases the ability of WL cystoscopy in identifying lesions \((p<0.05)\) Using NBI during cystoscopy, we recorded 234 suspicious lesions not visible to WL, 127 (12.1%) of those after TURBt resulted in bladder neoplasms. Concerning these lesions, NBI+WL, 15 were CIS, 12 were primate lesions and 3 were recurrences. The characteristics are summarized in the Table. The use of NBI cystoscopy is useful in the identification of CIS lesions. Comparing sensitivity, specificity, positive predictive value, negative predictive value of NBI vs. WLI cystoscopy regarding the CIS lesions, we noted that sensitivity and NPV were the only statistically significant values (100%, 95% CI, \(p<0.005\) and 80.62%, 95% CI, 100%, 95% CI, \(p<0.005\) and 78.35%, respectively). 

**Conclusion:** Bladder cancer remains an important and hard to treat pathology in modern urology as it is considered the most expensive tumour with regard either cost per patient per year or lifetime cost per patient. Despite the high-rate of false positives (35.75%), the overall capacity of NBI cystoscopy to increase the predictive power to identify suspicious bladder lesions significantly increases compared to the use of WL cystoscopy alone. In our experience, the use of NBI cystoscopy -compared to WL cystoscopy- was particularly useful in the identification of CIS lesions showing a sensitivity and a NPV of 100% vs. 80.62% and 100% vs. 78.35% \((p<0.05)\). We can conclude that the combination of WL and NBI cystoscopy before TURBt is an economic and better diagnostic approach for bladder tumours and, in particular, carcinoma in situ.

### Table. (Abstract 20).

<table>
<thead>
<tr>
<th>Lesions (127) NBI + oncol</th>
<th>Primitive</th>
<th>Recurrences</th>
<th>Unifocal</th>
<th>Multifocal</th>
<th>&lt;3 cm</th>
<th>&gt;3 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>pTa (%)</td>
<td>39 (56.52)</td>
<td>30 (43.48)</td>
<td>41 (59.42)</td>
<td>28 (40.58)</td>
<td>53(75.8)</td>
<td>16 (23.19)</td>
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<tr>
<td>pT1 (%)</td>
<td>12 (52.17)</td>
<td>11 (47.83)</td>
<td>22 (95.65)</td>
<td>1 (4.35)</td>
<td>23 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>pCIS (%)</td>
<td>12 (80.0)</td>
<td>3 (20.0)</td>
<td>9 (60.0)</td>
<td>6 (40.0)</td>
<td>12 (80.0)</td>
<td>3 (20.0)</td>
</tr>
<tr>
<td>pT2 (%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>PUNMPL (%)</td>
<td>14 (70)</td>
<td>6 (30)</td>
<td>14 (70)</td>
<td>6 (30)</td>
<td>20 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>LG (%)</td>
<td>25 (45.45)</td>
<td>30 (54.55)</td>
<td>35 (63.64)</td>
<td>20 (36.36)</td>
<td>44 (80)</td>
<td>11 (20)</td>
</tr>
<tr>
<td>HG (%)</td>
<td>39 (73.58)</td>
<td>14 (26.42)</td>
<td>38 (71.70)</td>
<td>15 (28.30)</td>
<td>45 (84.91)</td>
<td>8 (15.09)</td>
</tr>
</tbody>
</table>

22

**IMPACT OF [11C]CHOLINE PET/CT IN THE CLINICAL MANAGEMENT AND RADIATION TREATMENT PLANNING OF RECURRENT PROSTATE CANCER FOLLOWING EBRT**

Giancarlo Beltramo, Achille Bergantin, Anna Stefania Martinotti, Francesco Ria, Marta Invernizzi, Alessandro Vai and Livia Corinna Bianchi

Cyberknife Unit, Centro Diagnostico Italiano, Milan, Italy

**Purpose:** Prostate pathology studies suggest, in many cases, that a dominant cancer focus exists within the gland and may be a driver of the aggressiveness of the cancer and the epicenter of recurrence following radiotherapy treatment. Advances in positron emission tomography (PET) show promise in identifying prostate gross tumor volumes (GTVs) and advances in precision radiotherapy. We studied the role of integrated [11C]choline PET/CT to improve radiation treatment planning for cyberknife stereotactic hypofractionated radiotherapy (SBRT) in patients with recurrent prostate cancer following external beam radiation therapy (EBRT).

**Patients and Methods:** From December 2012 through June 2014, a cohort of 14 from 59 patients previously treated with salvage stereotactic Cyberknife
Radiosurgery for locally-recurrent prostate cancer following external beam radiotherapy were referred to our Department for second salvage Cyberknife SBRT. Primary radiotherapy doses ranged from 74 to 79.2 Gy (median=76) followed by a SBRT treatment with doses that ranged between 30-35 Gy delivered in 5 consecutive fractions on the whole prostate gland. The mean age of patient population at the time of Cyberknife re-treatment was 76 years (range=64-84) with a median pre-reirradiation PSA of 4.46 ng/ml (range=1.23-13.04). To reconstruct clinical target volume (CTV) and organ at risk, computed tomography (CT) scan and magnetic resonance imaging (MRI) with T1-T2 sequences were performed and [11C]choline PET/CT images were fuse for prostate GTVs definition. Three patients received 3 fractions of 10 Gy (total dose 30 Gy), 11 patients received 3 fractions of 12 Gy DFT: 36 Gy delivered to the PET positive uptake prostate node with a median volume of 14.3 cc (range=5.75-65.04). Results: The Cyberknife treatment was well tolerated without any radiation therapy oncology group (RTOG) grade 3 acute or late toxicity. With a median follow-up of 11 months (range=3-22) we observed the following results: no in field recurrence, resulting in a local control of 100%. In 3 patients, respectively at 11, 13 at 21 months, we recorded in field recurrence, resulting in a local control of 100%. In 3 patients, respectively at 11, 13 at 21 months, we recorded biochemical recurrence with a new PET positive uptake prostate node outside the irradiated field requiring a third Cyberknife salvage treatment. Conclusion: In clinical practice, advances in modern imaging show promise for improved detection and characterization of prostate cancer at the different stage of its management, including diagnosis, staging treatment planning and follow-up. Although our results are very encouraging with no in-field clinical progression and low toxicity profile, this approach cannot be considered as the standard of care. Prospective trials are needed to better define the role of differential prostate treatment on imaging defined GTVs.

28 CYBERKNIFE STEREOTACTIC RADIOTHERAPY FOR ISOLATED RECURRENCE IN THE PROSTATIC BED

Giulio Francolini1, Beatrice Detti1, Pierluigi Bonomo1, Irene Giacomelli1, Sabrina Cappelli1, Linda Poggesi1, Davide Franceschini1, Muhammed Baki1, Marco Carini2, Giulio Nicita2, Sergio Serni2, Valentina Baldazzi1, Lucia Di Brina1, Anna Mancuso1, Eleonora Monteleone1, Giulio Alberto Carta1, Cristina Muntoni1, Cinzia Ciabatti1 and Lorenzo Livi1

1Radiotherapy Unit, Azienda Ospedaliera Universitaria Careggi, University of Florence, Florence, Italy; 2Urology Unit, Azienda Ospedaliera Universitaria Careggi, University of Florence, Florence, Italy

Background: We report a preliminary clinical experience in stereotactic body radiation therapy (SBRT) delivered using Cyberknife for isolated nodal metastases from prostate cancer. Patients and Methods: Between November 2011 and December 2013, 30 patients (39 lesions) were treated with Cyberknife stereotactic treatment (SRT) for recurrent prostate cancer with isolated nodal metastases. Prescribed doses and schedules of fractionation varied according to site of disease ranging from 24 Gy in 1 fraction to 36 Gy in 3 fractions. Most commonly used schedules were 30 Gy in 3 fractions and 36 in Gy in 3 fractions on alternating days. Biochemical response, acute and late toxicity were analyzed. Results: At a median follow-up of 12 months (range=2-24.9), reduction of PSA ≥50% was observed in 18 cases, reduction <50% was observed in 7, while PSA was stable in 1 case and increased in 8 cases. At the time of analysis, among the 30 patients treated, 2 were dead from systemic disease; 12 patients experienced a relapse of disease in other sites and were treated with hormonal therapy (HT) and salvage chemotherapy. Sixteen patients were still free of disease. In 24 cases, imaging evaluation, three months after treatment, was available. No in field recurrence was detected, CR was detected in three cases, PR in 14 and SD in 8 patients. The treatment with Cyberknife was well tolerated: one patient experienced G2 acute genitourinary toxicity. Late toxicity was evaluated in patients with more than 3 months of follow-up and only one complained G1 proctitis. We did not observe any acute or late severe toxicity (≥G3). Conclusion: Our experience shows that SRT with Cyberknife for isolated nodal relapse from prostate cancer is a safe treatment with promising results in terms of efficacy.

27 CYBERKNIFE STEREOTACTIC RADIOTHERAPY FOR ISOLATED NODAL RECURRENCE OF PROSTATE CANCER

Linda Poggesi1, Beatrice Detti1, Pierluigi Bonomo1, Irene Giacomelli1, Sabrina Cappelli1, Davide Franceschini1, Muhammed Baki1, Marco Carini2, Giulio Nicita2, Sergio Serni2, Valentina Baldazzi1, Lucia Di Brina1, Anna Mancuso1, Eleonora Monteleone1, Giulio Alberto Carta1, Cristina Muntoni1, Cinzia Ciabatti1 and Lorenzo Livi1

1Radiotherapy Unit, Azienda Ospedaliera Universitaria Careggi, University of Florence, Florence, Italy; 2Urology Unit, Azienda Ospedaliera Universitaria Careggi, University of Florence, Florence, Italy

Background: We report a preliminary clinical experience in stereotactic body radiation therapy (SBRT) delivered using Cyberknife for isolated nodal metastases from prostate cancer. Patients and Methods: Between November 2011 and December 2013, 30 patients (39 lesions) were treated with Cyberknife stereotactic treatment (SRT) for recurrent prostate cancer with isolated nodal metastases. Prescribed doses and schedules of fractionation varied according to site of disease ranging from 24 Gy in 1 fraction to 36 Gy in 3 fractions. Most commonly used schedules were 30 Gy in 3 fractions and 36 in Gy in 3 fractions on alternating days. Biochemical response, acute and late toxicity were analyzed. Results: At a median follow-up of 12 months (range=2-24.9), reduction of PSA ≥50% was observed in 18 cases, reduction <50% was observed in 7, while PSA was stable in 1 case and increased in 8 cases. At the time of analysis, among the 30 patients treated, 2 were dead from systemic disease; 12 patients experienced a relapse of disease in other sites and were treated with hormonal therapy (HT) and salvage chemotherapy. Sixteen patients were still free of disease. In 24 cases, imaging evaluation, three months after treatment, was available. No in field recurrence was detected, CR was detected in three cases, PR in 14 and SD in 8 patients. The treatment with Cyberknife was well tolerated: one patient experienced G2 acute genitourinary toxicity. Late toxicity was evaluated in patients with more than 3 months of follow-up and only one complained G1 proctitis. We did not observe any acute or late severe toxicity (≥G3). Conclusion: Our experience shows that SRT with Cyberknife for isolated nodal relapse from prostate cancer is a safe treatment with promising results in terms of efficacy.
Between November 2011 and November 2013, 16 patients were treated with SBRT for a macroscopic isolated recurrence of prostate cancer in the prostatic bed. All patients were initially treated with radical prostatectomy and half of them also received radiotherapy. Two schedules of SBRT were used, 30 Gy in 5 fractions in previously irradiated patients, 35 Gy in 5 fractions in radiotherapy naïve patients. Results: At a median follow-up of 10 months (range=2-21 mo), a significant biochemical response was found in all but one patient. At imaging evaluation, no local progression was noted, 10 patients showed partial response, while 4 showed stable disease. At the moment of analysis, all 16 patients were alive. Seven of them experienced distant relapse, while nine maintained biochemical control with no further therapy. Median time to relapse was 9.3 months (range=3-15.2). The treatment was well-tolerated: one patient experienced G2 acute genitourinary and gastrointestinal toxicity. Conclusion: Our experience shows that SBRT with Cyberknife is a safe and well-tolerated treatment for isolated nodal relapse.

29 CYBERKNIFE STEREOTACTIC TREATMENT FOR LOW AND INTERMEDIATE RISK PROSTATE CANCER. PRELIMINARY DATA ABOUT TOXICITY, SINGLE INSTITUTION EXPERIENCE

Anna Mancuso1, Beatrice Detti1, Pierluigi Bonomo1, Irene Giacomelli1, Sabrina Cappelli1, Linda Poggesi1, Davide Franceschini1, Muhammed Baki1, Marco Carini2, Giulio Nicita2, Sergio Serni2, Valentina Baldazzi1, Lucia Di Brina1, Anna Mancuso1, Eleonora Monteleone1, Giulio Alberto Carta1, Cristina Muntoni1, Cinzia Ciabatti1 and Lorenzo Livi1

1Radiotherapy Unit, Azienda Ospedaliera Universitaria Careggi, University of Florence, Florence, Italy; 2Urology Unit, Azienda Ospedaliera Universitaria Careggi, University of Florence, Florence, Italy

Background: Cyberknife stereotactic treatment (SRT) is an emerging treatment for early stage prostate cancer. We present a single institution experience, reporting toxicities and outcomes. Materials and Methods: Between October 2012 and January 2014, 32 patients were treated with SRT for early stage organ confined prostate cancer. Prescribed dose was 35-36.25 Gy in five fractions. Kaplan Meier biochemical progression-free survival and toxicity outcomes were assessed. Results: At a mean follow up of 10.1 months (range=2-36.8), reduction of PSA ≥50% was observed in 22 cases, reduction <50% was observed in 6, while PSA was stable in 4 cases. Four patients experienced G2 acute genitourinary toxicity and in two cases we recorded G3 acute GU toxicity. Five patients experienced G2 acute proctitis. At the last follow-up visit, all patients were still alive. Twenty-nine remained free of disease at last follow-up appointment, while 3 developed a biochemical recurrence. Conclusion: Our experience confirms the efficacy and safety of SRT with Cyberknife for localized prostate cancer.

30 FEASIBILITY AND SAFETY OF ABIRATERONE ACETATE IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER AFTER DOCETAXEL-BASED CHEMOTHERAPY: A SINGLE CENTER EXPERIENCE

Muhammed Baki1, Beatrice Detti1, Pierluigi Bonomo1, Irene Giacomelli1, Sabrina Cappelli1, Linda Poggesi1, Davide Franceschini1, Marco Carini2, Giulio Nicita2, Sergio Serni2, Valentina Baldazzi1, Lucia Di Brina1, Anna Mancuso1, Eleonora Monteleone1, Giulio Alberto Carta1, Cristina Muntoni1, Cinzia Ciabatti1 and Lorenzo Livi1

1Radiotherapy Unit, Azienda Ospedaliera Universitaria Careggi, University of Florence, Florence, Italy; 2Urology Unit, Azienda Ospedaliera Universitaria Careggi, University of Florence, Florence, Italy

Background/Aim: Treatment of castration-resistant prostate cancer (mCRPC) remains an area of unmet medical need. Abiraterone acetate (AA) is a selective androgen biosynthesis inhibitor, both gonadal and extra-gonadal, that in combination with low-dose prednisolone improved overall survival (OS) in a randomized trial in mCRPC progressing after docetaxel. The aim of this retrospective study was to evaluate the feasibility and safety profile of AA used in a group of patients after failure of primary metastatic line with docetaxel. Patients and Methods: Twenty patients with metastatic castration resistant prostate cancer were enrolled in this study at AOU Careggi/Florence, from 2013, all previously treated with docetaxel chemotherapy. The median age at diagnosis was 65, while the median age at the moment of therapy with abiraterone acetate was 72; the majority of them (45%) graded as low-risk group based on the Gleason score. All patients were concomitantly in hormonal therapy with degarelix (LHRH antagonist) at the start of therapy with abiraterone acetate. Bone metastasis was found in only 12 (60%) patients prior to therapy with AA. Results: After a median follow-up of 6.8 months (range=2.5-14), 14 patients developed progressive disease (70%) demonstrated with either biochemical relapse or bone metastasis; only one case developed visceral metastasis. The mean time occurrence of progression was 6.07 months (range=2.5-14). Treatment with abiraterone was well tolerated in all patients; no grade 3 or 4...
toxicities have been recorded; none of the patients interrupted therapy with abiraterone due to drug related toxicities. Only one (5%) patient has shown elevated liver enzymes (GOT= 58 IU/l). Conclusion: Our experience shows that AA is a feasible and well-tolerated therapy for patients with mCRPC following docetaxel, hence providing an important treatment option for elderly patients that may not tolerate alternative therapies with greater toxicity.

31
MINIMAL RECTAL TOXICITY USING STEREOTACTIC BODY RADIOTHERAPY FOR PROSTATE CANCER PATIENTS SUBMITTED TO GEL SPACER INJECTION (SPACEOAR) BETWEEN PROSTATE AND RECTUM
Niccolo’ Giaj Levrà1, Riccardo Ballario2, Sergio Fersino1, Alba Fiorentino1, Francesco Ricchetti1, Rosario Mazzola1, Stefano Cavalleri2 and Filippo Alongi1

Introduction/Aim: Thanks to technological improvements and the recent radiobiological data, “extreme hypofractionated radiotherapy (RT)” by means of stereotactic body RT techniques (SBRT) has been introduced in the last years as a potential treatment option for “selected” prostate cancer patients. The end-point of the present report is to assess feasibility and rectal preliminary tolerability of SBRT in prostate cancer patients with gel spacer injection (SPACEOARTM). Materials and Methods: Between November 2013 and November 2014, 10 patients were “selected” and recruited in a treatment protocol of SBRT with radical intent using a gel spacer injection (SPACEOARTM) between prostate and rectum. Inclusion criteria were PSA ≤20 ng/ml, histologically proven prostate adenocarcinoma, T1-T2 stage, no distant metastases, no previous surgery other than transurethral resection of the prostate (TURP), International Prognostic Scoring System (IPSS) 0-7. The schedule was 35 Gy in 5 days. SBRT was delivered with RapidArc VMAT, with 10MV FFF photons. Toxicity assessment was performed according to CTCAE v4.0 scale. Expanded prostate cancer index composite (EPIC) questionnaires assessed Quality-of-Life. Neoadjuvant/concomitant hormonal-therapy was prescribed according to risk classification. SpaceOAR™ gel was implanted by the urologist with rectal ultra sound guide and with transperineal needle injection to increase the separation space between the prostate and the anterior rectal wall. Magnetic resonance imaging (MRI) was performed 7-10 days after injection; MRI(T2)/CT image fusion was used to define the gel spacer placement during treatment planning. Regarding the distance between posterior part of prostate and anterior rectal wall after gel injection, a measure of spacer dimension was performed in each CT/MRI slide of each patient, in axial and sagittal view. Results: After the gel injection, a median distance of 1.25 cm (0.50-1.63) in axial view and 1.26 cm (0.53-1.67) were found in the population of study. Only in 2 out of 10 cases, a distance inferior than 1 cm was measured. All patients finished the treatment with a minimum follow-up (FUP) of 60 days after the end of the treatment. Acute rectal toxicity was recorded as follows: 2 patients experienced rectal G1 toxicity (tenesmus), one patient complain G2 rectal pain needing drugs. In 7 cases no rectal toxicity was documented within 3 months. Conclusion: Spacer Gel was able to increase the minimum distance between rectum and prostate of more than 1 cm in 8/10 cases and no rectal toxicity (any grade) was found in 7/10 cases. Although more mature results are needed, early findings suggest that SBRT with RapidArc and flattening filter free (FFF) beams for prostate cancer in 5 fractions with SpaceOAR™ gel injection is feasible and well tolerated in rectal acute setting. Longer follow-up is needed for assessment of late rectal toxicity and outcome.

32
INHIBITION OF XPO1-DEPENDENT NUCLEAR EXPORT SENSITIZES PROSTATE CANCER CELLS TO CYTOTOXIC AGENTS
Giovanni Luca Gravina1,2, Andrea Mancini1, Simona Delle Monache3, Yoseph Landesman4, Dilara Mccauley4, Michael Kauffman4, Sharon Shacham4 and Claudio Festuccia1

Background/Aim: CRM1/XPO1 is the major nuclear export receptor in the cell, which controls the nuclear-cytoplasmic localization of many proteins and RNAs. This is also a promising drug target as the transport receptor is over-expressed in many cancers where some of its cargos are misregulated and mislocalized to the cytoplasm. Nuclear-
cytoplasmic trafficking of proteins is also a significant factor in the development of drug resistance. Selective inhibitors of nuclear export (SINE) bind to XPO1 to irreversibly inhibit its ability to export proteins. Here we investigated the effects of SINE compounds in prostate cancer cell models in combination with docetaxel and cisplatin. Materials and Methods: Two SINE compounds (KPT-251 and KPT-330) having different: (i) potency with broad-spectrum, (ii) tumor-selective cytotoxicity in vitro and in vivo, (iii) tolerability and (iv) pharmacokinetic profiles have been tested in two models of aggressive prostate cancer cells (22rv1 and PC3) in vitro and in vivo in association with docetaxel and cisplatin. Results and Conclusion: XPO1 is over-expressed in prostate cancer relative to normal or hyperplastic tissue. Increased XPO1 expression, mostly in the nuclear compartment, was associated with increased Gleason score and bone metastases. SINE compounds inhibited proliferation and promoted apoptosis of tumor cells but did not reduce the viability of immortalized non-transformed prostate epithelial cells. Nuclei from SINE treated cells showed short-term accumulation of XPO1, survivin and cyclin D1followed by degradation of these proteins leading to cell cycle arrest and apoptosis. Combination treatment of SINE compounds increased the cytotoxicity of cisplatin and docetaxel in vitro by synergistic/additive manner through the inhibition of DNA damage repair. Oral administration of KPT-251 and KPT-330 reduced tumor cell proliferation and angiogenesis and induced apoptosis in PC3 and 22rv1 xenograft-bearing nude mice resulting in synergy with cisplatin and additive effects with docetaxel. Our results provide conclusive evidence to support global therapy for advanced/castration resistant prostate cancers with SINE alone and in combination with chemotherapy and warrants continued clinical research and drug development for metastatic prostate cancer.

33 REDUCED DOSE ABIRATERONE ACETATE WITH CONCOMITANT LOW DOSE PREDNISONE IN THE TREATMENT OF ≥85 YEARS AGED PATIENTS WITH ADVANCED CASTRATE-RESISTANT PROSTATE CANCER

Giandomenico Roveriolo1, Edoardo Francini2, Anna Ida Fiaschi1, Letizia Laera1, Salvatora Tindara Miano1 and Roberto Petrioli1

1Oncology Unit, Medical Oncology, University of Siena, Siena, Italy; 2Medical Oncology Unit, Policlinico Umberto I Hospital, University of Rome, Rome, Italy; 3Pharmacology Unit, Department of Medicine, Surgery and Neurosciences, Siena, Italy

Aim: The aim of this study was to evaluate the activity and safety of reduced dose abiraterone acetate (AA) in ≥85 years aged patients with advanced castrate resistant prostate cancer (CRPC). Patients and Methods: Patients received 750 mg of oral AA as three 250 mg tablets once daily, with concomitant oral prednisone at 5 mg daily. The primary endpoint was prostate-specific antigen (PSA) response. Patient monitoring and laboratory tests were performed every two weeks. Results: Twenty-six patients were enrolled; of these, 12 patients had been previously exposed to chemotherapy with weekly docetaxel. Median age was 88 years (range=85-93). PSA response was observed in 18 (69.2%) subjects, median time to PSA progression was 6.4 months (95% confidence interval (CI)=2.8 to 8.8) and median overall survival was 14.3 months (95% CI=7.2 to 18.3). The treatment was well tolerated and adverse events related to mineralocorticoid excess were of grade 1-2 in all of the patients. Conclusion: Reduced dose of AA combined with very low dose of prednisone seems to be an effective and well-tolerated treatment option for very elderly patients with advanced CRPC.

37 LYMPHADENECTOMY EXTENSION FOR PROSTATE CANCER PREDICTS PN+ STATUS

Domenico Gabriele1, Giovanni Muto2, Paolo Gontero3, Donato Randone4, Maria Teresa Carchedi4, Chiara Fiorito5, Arianna Gillo6, Ilaria Stura1 and Pietro Gabriele7

1Neuroscience Department, Human Physiology Section, University of Torino, Turin, Italy; 2Urology Division, San Giovanni Bosco Hospital, Turin, Italy; 3Urology Division, Molinette Hospital, University of Torino, Turin, Italy; 4Urology Division, Gradenigo Hospital, Turin, Italy; 5Urology Division, Molinette Hospital, Turin, Italy; 6Urology Division, Regional Hospital, Aosta, Italy; 7Radiation Oncology Division, FPO-IRCCS Cancer Center, Candriolo, Italy

Aim: To study the association between the lymphadenectomy extension for prostate cancer and the finding of positive nodes at the post-prostatectomy pathologic examination. Patients and Methods: We selected 2,291 patients eligible for the study from our database of 3,538 radical prostatectomy cases, collected in the EUREKA-1 multicentric retrospective study on prostate cancer, part of the CHIC European project (grant agreement number 600841). The number of lymph nodes resected was available for all patients and this factor was evaluated as a continuous, as well as categorical variable, splitting the patients into three
categories according to the inclusiveness of the pelvic lymphadenectomy, i.e. less than 10 nodes versus 10-23 nodes versus 24+ nodes resected. The end-point was post-surgical pathologic nodal status (pN). Data were analysed with Logit regression models, initially in a univariate analysis and, thereafter, in a multivariate analysis too, including in the algorithm as covariates the pre-surgical risk factors initial prostate-specific antigen (PSA), biopptic Gleason Score and clinical staging. Results: The number of nodes resected during the lymphadenectomy procedure is associated with the risk of positive nodes at the pathologic exam both in univariate (p<0.001) and multivariate analysis (p=0.01) (Table I).

<table>
<thead>
<tr>
<th>Odds Ratio</th>
<th>Std. Err.</th>
<th>Z</th>
<th>p</th>
<th>95% Confidence interval (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td># nodes cropped</td>
<td>1.031</td>
<td>0.012</td>
<td>2.56</td>
<td>0.010</td>
</tr>
<tr>
<td>Initial PSA</td>
<td>1.037</td>
<td>0.007</td>
<td>5.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cT1</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>Reference</td>
</tr>
<tr>
<td>cT2</td>
<td>3.15</td>
<td>0.73</td>
<td>4.91</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cT3</td>
<td>5.15</td>
<td>1.63</td>
<td>3.18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GS 6</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>Reference</td>
</tr>
<tr>
<td>GS 7</td>
<td>2.84</td>
<td>0.76</td>
<td>3.90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GS 8-10</td>
<td>5.58</td>
<td>1.66</td>
<td>5.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Constant</td>
<td>0.006</td>
<td>0.002</td>
<td>16.64</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

In particular, it is possible to divide patients into 3 statistically different risk classes according to the lymphadenectomy extension (1-9 vs. 10-23 vs. 24+ lymph nodes cropped) with pN+ risk of 2.9 %, 7.6 % and 12.1 %, respectively (Table II and Figure 1).

Table II. Multiple comparisons through logistic regression between 1-9, 10-23 and 24+ nodes resected.

<table>
<thead>
<tr>
<th>Odds Ratio</th>
<th>Std. Err.</th>
<th>Z</th>
<th>p</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-23 versus 1-9</td>
<td>2.73</td>
<td>0.61</td>
<td>4.47</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24+ versus 1-9</td>
<td>4.58</td>
<td>1.31</td>
<td>3.52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24+ versus 10-23</td>
<td>1.68</td>
<td>0.40</td>
<td>2.19</td>
<td>0.029</td>
</tr>
</tbody>
</table>

Discussion and Conclusion: The extension of the pelvic lymphadenectomy, quantified in this study by the number of lymph nodes resected during the surgical procedure, is an independent predictive factor of nodal involvement at the pathology examination. Because of the huge (up to four-fold) difference in pN+ incidence between low sample and high sample lymphadenectomies, we advise to avoid and not to consider accurate a removal of less than 10 nodes; we evaluate as standard a procedure removing between 10 and 23 lymph nodes and we deem optimal a lymphadenectomy sampling 24 or more nodes.

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PERINEURAL AND VASCULAR INVASION IN PROSTATE CANCER: A PREDICTIVE ABILITY EVALUATION

Domenico Gabriele1, Enrico Bollito2, Francesco Porpiglia3, Carlo Terrone4, Giuseppe Arena5, Fabio Venzano5, Scipio Annoscia6, Luca Bellei6, Maurizio Moroni7 and Caterina Guiot1

1Neuroscience Department, Human Physiology Section, University of Torino, Turin, Italy;
2Pathology Division, San Luigi Hospital, Orbassano, Turin, Italy;
3Urology Division, San Luigi Hospital, University of Torino, Turin, Italy;
4Urology Division, Maggiore Hospital, University of Novara, Novara, Italy;
5Urology Division, Santa Croce Hospital, Cuneo, Italy;
6Urology Division, ASL TO4, Ivrea-Cirié, Turin, Italy;
7Urology Division, Maria Vittoria Hospital, Turin, Italy
Aim: To study the association between perineural infiltration and vascular invasion at post-prostatectomy pathologic examination and the incidence of biochemical and clinical relapse. Patients and Methods: We selected patients eligible for the study from our database of 3,538 radical prostatectomy cases, collected in the EUREKA-1 multicentric retrospective study on prostate cancer, part of the CHIC European project (grant agreement number 600841). Information regarding perineural infiltration (PNI) was available in 3,078 patients and in 2,269 cases for vascular invasion (VI). Perineural infiltration was defined as a cancer spread along the neural sheath and contiguous perineural lymphatic vessels, while vascular invasion was defined as a penetration of cancer cells inside blood vessels, with or without distinct neoplastic embola. All histologic analyses were performed on the post-prostatectomy pathologic samples. The end-points evaluated were biochemical recurrence (BCR), pN status, prostate surgical bed recurrence and lymph node or bone metastasis clinical progression during follow-up. Data were analysed with the Cox proportional hazard regression model for BCR or with logistic regression for clinical progression, initially in a univariate analysis and, thereafter, in a multivariate analysis too, including in the algorithm as covariates the main risk factors initial prostate-specific antigen (PSA), pathologic Gleason Score and pathologic staging. Results: PNI and VI are both associated to a higher risk of BCR in univariate analysis (p<0.001). Perineural diffusion holds a statistical significance even in multivariate analysis (p=0.017, Table I); besides, vascular invasion is associated to perineural infiltration, higher pathologic Gleason score and the kick-off of an adjuvant androgen depriving therapy (p<0.001).

Table I. Multivariate Cox regression, end-point BCR, independent variables initial PSA, pathologic Gleason score, pathologic staging, PNI and VI.

<table>
<thead>
<tr>
<th></th>
<th>Haz. Ratio</th>
<th>Std. Err.</th>
<th>z</th>
<th>p</th>
<th>95% Confidence interval (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA</td>
<td>1.023</td>
<td>0.004</td>
<td>5.43</td>
<td>&lt;0.001</td>
<td>1.015 1.032</td>
</tr>
<tr>
<td>GS ≤6</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Ref.</td>
</tr>
<tr>
<td>GS 7</td>
<td>1.57</td>
<td>0.21</td>
<td>3.42</td>
<td>0.001</td>
<td>1.21 2.04</td>
</tr>
<tr>
<td>GS ≥8</td>
<td>3.20</td>
<td>0.51</td>
<td>7.28</td>
<td>&lt;0.001</td>
<td>2.34 4.38</td>
</tr>
<tr>
<td>pT3/4</td>
<td>1.83</td>
<td>0.22</td>
<td>5.04</td>
<td>&lt;0.001</td>
<td>1.45 2.32</td>
</tr>
<tr>
<td>PNI</td>
<td>1.33</td>
<td>0.16</td>
<td>2.39</td>
<td>0.017</td>
<td>1.05 1.69</td>
</tr>
<tr>
<td>VI</td>
<td>1.22</td>
<td>0.17</td>
<td>1.44</td>
<td>0.15</td>
<td>0.93 1.61</td>
</tr>
</tbody>
</table>

In multivariate investigations, PNI is associated to an increased risk of surgical bed recurrence (p=0.04, see Table II) and nodal progression (almost significant p of 0.09), while vascular invasion is related to pN positive status (p=0.001, Table III) and bone metastasis risk (p=0.011, Table IV).

Table II. Logistic regression, end-point surgical bed recurrence, independent variables initial PSA, pathologic GS, pathologic staging, PNI and VI.

<table>
<thead>
<tr>
<th></th>
<th>Haz. Ratio</th>
<th>Std. Err.</th>
<th>z</th>
<th>p</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPSA</td>
<td>1.009</td>
<td>0.022</td>
<td>0.40</td>
<td>0.69</td>
<td>0.966 1.053</td>
</tr>
<tr>
<td>GS ≤6</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Ref.</td>
</tr>
<tr>
<td>GS 7</td>
<td>1.12</td>
<td>0.54</td>
<td>0.24</td>
<td>0.81</td>
<td>0.44 2.86</td>
</tr>
<tr>
<td>GS ≥8</td>
<td>1.16</td>
<td>0.80</td>
<td>0.21</td>
<td>0.83</td>
<td>0.30 4.51</td>
</tr>
<tr>
<td>pT3/4</td>
<td>0.68</td>
<td>0.35</td>
<td>-0.75</td>
<td>0.45</td>
<td>0.25 1.86</td>
</tr>
<tr>
<td>PNI</td>
<td>2.97</td>
<td>1.57</td>
<td>2.06</td>
<td>0.04</td>
<td>1.05 8.36</td>
</tr>
<tr>
<td>VI</td>
<td>2.18</td>
<td>1.23</td>
<td>1.31</td>
<td>0.19</td>
<td>0.69 6.58</td>
</tr>
<tr>
<td>Constant</td>
<td>0.005</td>
<td>0.002</td>
<td>-10.26</td>
<td>&lt;0.001</td>
<td>0.002 0.013</td>
</tr>
</tbody>
</table>

Table III. Logistic regression, end-point pN+ status, independent variables initial PSA, pathologic GS, pathologic staging, PNI and VI.

<table>
<thead>
<tr>
<th></th>
<th>Haz. Ratio</th>
<th>Std. Err.</th>
<th>z</th>
<th>p</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPSA</td>
<td>1.034</td>
<td>0.009</td>
<td>3.77</td>
<td>&lt;0.001</td>
<td>1.016 1.053</td>
</tr>
<tr>
<td>GS ≤6</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Ref.</td>
</tr>
<tr>
<td>GS 7</td>
<td>4.13</td>
<td>2.57</td>
<td>2.28</td>
<td>0.022</td>
<td>1.22 13.95</td>
</tr>
<tr>
<td>GS ≥8</td>
<td>13.56</td>
<td>8.52</td>
<td>4.15</td>
<td>&lt;0.001</td>
<td>3.96 46.47</td>
</tr>
<tr>
<td>pT3/4</td>
<td>7.32</td>
<td>2.66</td>
<td>5.48</td>
<td>&lt;0.001</td>
<td>3.59 14.91</td>
</tr>
<tr>
<td>PNI</td>
<td>0.61</td>
<td>0.19</td>
<td>-1.63</td>
<td>0.104</td>
<td>0.33 1.11</td>
</tr>
<tr>
<td>VI</td>
<td>2.44</td>
<td>0.69</td>
<td>3.18</td>
<td>0.001</td>
<td>1.41 4.23</td>
</tr>
<tr>
<td>Constant</td>
<td>0.003</td>
<td>0.002</td>
<td>-9.69</td>
<td>&lt;0.001</td>
<td>0.0008 0.0009</td>
</tr>
</tbody>
</table>

Table IV. Logistic regression, end-point bone metastasis, independent variables initial PSA, pathologic GS, pathologic staging, PNI and VI.

<table>
<thead>
<tr>
<th></th>
<th>Haz. Ratio</th>
<th>Std. Err.</th>
<th>z</th>
<th>p</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPSA</td>
<td>1.023</td>
<td>0.011</td>
<td>2.05</td>
<td>0.04</td>
<td>1.0009 1.045</td>
</tr>
<tr>
<td>GS ≤6</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Ref.</td>
</tr>
<tr>
<td>GS 7</td>
<td>3.70</td>
<td>2.86</td>
<td>1.69</td>
<td>0.09</td>
<td>0.81 16.81</td>
</tr>
<tr>
<td>GS ≥8</td>
<td>9.30</td>
<td>7.42</td>
<td>2.80</td>
<td>0.005</td>
<td>1.95 44.37</td>
</tr>
<tr>
<td>pT3/4</td>
<td>2.78</td>
<td>1.29</td>
<td>2.21</td>
<td>0.027</td>
<td>1.12 6.88</td>
</tr>
<tr>
<td>PNI</td>
<td>1.93</td>
<td>1.01</td>
<td>1.26</td>
<td>0.207</td>
<td>0.69 5.40</td>
</tr>
<tr>
<td>VI</td>
<td>2.65</td>
<td>1.02</td>
<td>2.54</td>
<td>0.011</td>
<td>1.25 5.62</td>
</tr>
<tr>
<td>Constant</td>
<td>0.001</td>
<td>0.0008</td>
<td>-8.75</td>
<td>&lt;0.001</td>
<td>0.0002 0.005</td>
</tr>
</tbody>
</table>

Abstracts of the 25th Annual Meeting of the Italian Society of Uro-Oncology (SIUrO), 21-23 June, 2015, Rome, Italy

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These findings are confirmed by frequency tables showing an increased risk of local recurrence of 1.8% versus 0.9% (p=0.042) and of nodal progression of 2.8% versus 0.7% (p<0.001) respectively for PNI, and a ratio of pN+ of 24.5% versus 3.4% (p<0.001) and of bone metastases of 8.3% versus 1.0% (p<0.001), respectively, for vascular invasion. Conclusion: PNI and VI provide additional useful information beyond major risk factors to predict biochemical and clinical recurrence risks in prostate cancer. In particular, perineural involvement identifies quite indolent patients at risk for prostate surgical bed recurrence and nodal progression, while vascular invasion correctly marks patients at severe risk of positive nodes at lymphadenectomy and of distant metastatic spread to bones.

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KPT-8752, A POTENT ORALLY BIO-AVAILABLE P21-ACTIVATED KINASE 4 (PAK-4) ALLOSTERIC MODULATOR (PAM), IS ABLE TO SUPPRESS TUMOR CELL GROWTH AND INVASIVENESS OF ADVANCED PROSTATE CANCER CELLS IN VITRO AND IN VIVO

Giovanni Luca Gravina1, Andrea Mancini1, Luca Ventura2, Patrizia Sanità1, Erkan Baloglu1, William Senapedis3, Dilara Me Cauley3, Sharon Shacham3 and Claudio Festuccia1

1Department of Biotechnological and Applied Clinical Sciences, Laboratory of Radiobiology, University of L’aquila, L’Aquila, Italy;
2Pathology Department, San Salvatore Hospital, City, Italy;
3Drug Development, Karyopharm Therapeutics, Inc., Newton, MA, U.S.A.

Introduction: In the initial stages, prostate cancer (PrCa) is typically androgen-dependent with hormone- and chemo-resistance developing over time. Progression to castration resistance is a major problem in the treatment of advanced PrCa and is likely driven by activation of several molecular pathways. P21-activated kinase 4 (PAK4) is a serine/threonine kinase involved in the regulation of cytoskeletal reorganization, cell proliferation, gene transcription, oncogenic transformation and cellular invasion. PAK4 is overexpressed in a variety of human tumors. It has been demonstrated that stable knock-down of PAK4 in PC3 and DU145 prostate cancer cells inhibited tumor formation in nude mice. Materials and Methods: Immunohistochemical evaluation for PAK4 and p-PAK4 expression and in vitro and in vivo tests for the evaluation of PAK4 antagonism were used associating PAK4 inhibitors with standard chemotherapy. Results: We showed that PAK4 was cytoplasmic and expressed in normal, hyperplastic and neoplastic prostate tissues. Normal and hyperplastic sections presented 1+/2+ without 3+ staining in the totality of fields, whereas in neoplastic tissues 2+/3+ staining was evident in >60% cases. Prostate cancer with low histological grade (Gleason ≤7) presented about 50% of cases with 2+/3+ staining intensity, whereas more than 80% of 2+/3+ cases were present in high and less differentiated PrCa (Gleason grade >7), as well as in lymph-node and bone metastases. Phospho-PAK4 staining was lower and in some of the cases was nuclear. Therefore, PAK4 is a potential therapeutic target for aggressive/advanced PrCa. We tested the effects of novel PAK4 allosteric modulators (PAMs; KPT-7189, KPT-7349 and KPT-8752) in vitro in 4 models of advanced prostate cancer derived from a Gleason 9 primary tumor (22rv1), bone (PC3), brain (DU145) and lymph node metastases (NCI-H660). All 4 models have low, intermediate and high neuroendocrine phenotypes. PAMs suppressed cell proliferation and induced cell death in these cells in vitro with half maximal inhibitory concentration (IC50) values ranging from 25 to 120 nM. Western blotting analyses showed that these compounds reduced (i) phosphorylation of PAK4, (ii) expression of cyclin D1 and (iii) activity of epidermal growth factor receptor (EGFR). Using KPT-8752, the IC50 values for inhibition of cell proliferation for each cell line were 120, 50, 75 and 25 nM in 22rv1, PC3, DU145 and NCI-H660, respectively. Cell killing occurred at 75-100 nM of KPT-8752 after 48 hours of treatment in PrCa cell lines. We evaluated the efficacy of KPT-8752 in vivo by using oral administration at 20, 60 and 100 mg/kg/day. KPT-8752 inhibited tumor growth of PC3, DU145 and 22rv1 in a dose-dependent manner with tumor weights reduced by 25%, 42% and 63% in PC3; 32%, 54% and 80% in DU145 and 17%, 28% and 47% in 22rv1. In addition, KPT-8752 increased the sensitivity of cisplatin (CDDP) in PC3 and 22rv1 xenografts. Conclusion: Taken together, these results suggest that inhibition of PAK4 activity, by PAMsasa mono-therapy or in combination, can be used as a novel therapeutic strategy for the treatment of aggressive/advanced PrCa of diverse etiologies.

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HYPOFRACTIONATED VS. CONVENTIONALLY FRACTIONATED 3DCRT FOR HIGH-RISK PROSTATE CANCER: UPDATED RESULTS OF A RANDOMIZED TRIAL

Carolina Giordano1, Anna Maria Ferraro1, Biancamaria Saracino1, Maria Grazia Petrongari1, Giorgio Arcangeli1, Valeria Landoni2, Stefano Arcangeli3, Lidia Strigari2, Sara Gomellini4, Fabio Arcidiacono1 and Giuseppe Sanguineti1

1Department of Radiation Oncology, Regina Elena National Cancer Institute, Rome, Italy;
Aim: To update results of a trial comparing conventionally fractionated (80 Gy/40 fractions (fxs)/8 wks)(CF) vs. hypofractionated (62 Gy/20 fxs/5 wks) (HYPO) three-dimensional conformal radiotherapy (3DCRT) for high-risk prostate cancer. The study aimed at comparing morbidity, while the two schedules were assumed to be isoeffective on tumor control for an α/ß ratio of 1.5 Gy and disregarding the time factor (1, 2).

Materials and Methods: This randomized phase III trial was run at a single Institution from 2002 to 2005 and included 9-month androgen deprivation therapy in both arms. The target consisted in both the prostate and seminal vesicles. Freedom from biochemical failure (FFBF) (Phoenix), freedom from distant metastases (FFDM) and prostate cancer-specific survival (PCSS) are reported after a median follow-up of 96.5 months (6.2-130.8) for living patients. Results: One hundred and sixty-eight patients were accrued. The two arms are slightly unbalanced in favor of CF with respect to initial prostate-specific antigen (iPSA) level; Mann Whitney U-test p=0.17. Overall, the 8-year FFBF is 74.2±3.8%, 66.0±5.9% for CF and 82.0±4.7% for HYPO, p=0.058. At multivariate analysis, treatment arm (CF vs. HYPO, hazard ratio (HR)=0.40, 95% confidence interval (CI)=0.20-0.79, p=0.009), Gleason score (GLS)(cont, p=0.001) and iPSA (cont, p<0.001) were independently correlated to biochemical failure. Only 20 patients developed distant metastases for an actuarial rate for FFDM of 88.1±2.6% at 8 years. Patients treated with HYPO had a slightly higher rate of distant control at 8 years, 91.6±3.3% vs. 84.9±4.0%, but neither at univariate or multivariate analyses the difference reached statistical significance (p=0.321 and p=0.199, respectively). Of note, the HR of distant failure is 0.55 (95%CI=0.22 to 1.36) in favor of HYPO over CF. Both iPSA and GLS were highly correlated to FFDM, p=0.004 and p<0.001, respectively. Out of 42 observed deaths, only 10 were due to prostate cancer-related causes. Overall, PCSS at 8 years is 92.8±2.2%. Eight-year PCSS is 89.0±3.7% and 96.7±2.3% for CF and HYPO, respectively, HR=0.24, 95%CI=0.05-1.12, p=0.07. At multivariate analysis, only GLS (p=0.037) reached statistical significance, while a trend was confirmed for the treatment arm (HR=0.23, 95%CI=0.05-1.10, p=0.068). Discussion and Conclusion: Despite the limited sample size and the lack of radiobiological expectations on tumor control, HYPO resulted in a statistically higher biochemical control over CF that tends to lead to a lower likelihood of both distant disease and prostate-cancer death.
a multifunctional device combining one-step sealing and the functionality of a Maryland dissector, auttraumatic grasper and cold scissors.

43 PLEOMORPHIC HYALINIZING ANGIOECTATIC TUMOR (PHAT) OF RENAL PARENCHYMA. FIRST CASE REPORTED IN LITERATURE

Vincenzo Serretta1, Cristina Scalici Gesolfo1, Salvatore Scurria1, Ninfa Giacalone1, Giovanna Scaduto1, Francesco D’amato1, Elisabetta Barresi2 and Vito Franco2

1Section of Urology, Department of Surgical, Oncological and Stomatological Sciences, Azienda Ospedaliera Universitaria Policlinico "Paolo Giaccone", Palermo, Italy; 2Section of Pathology, Department of Sciences For Health Promotion and Maternal and Child “G. D’Alessandro”, Azienda Ospedaliera Universitaria Policlinico "Paolo Giaccone", Palermo, Italy

Introduction: The pleomorphic hyalinizing angiectatic tumor (PHAT) is a rare non-metastatic tumor of soft tissue identified in 1996 (1). In adults, it generally occurs in the subcutaneous tissue of the lower limbs, although reported also in chest wall, buttock and arms. In the literature, only one case of PHAT has been described in the kidney at the level of the hilum but not involving renal pelvis or parenchyma (2). The clinical behavior of PHAT is characterized by a slow growth and a rate of local recurrences higher than 50%. Metastasis has not been reported. Case Report: A 61-year-old Caucasian obese female with a medical history of hypertension and hypercholesterolemia was admitted at the Emergency Unit for recurring gross hematuria since one year, becoming more frequent and severe in the last 3 months. Due to the severe anemia (hemoglobin of 7.7g/dl), the patient was transfused. Computed tomography (CT) scan revealed a parenchymal lesion of 4 cm in diameter of the lower pole of the right kidney. The lesion was only partially capsulated, mixed with a well evident cystic component, in strict contact with the lower calyx suspicious for infiltration. At cystoscopy, a clot emerging from the right ureteral meatus was evident. Urine cytology was negative and no imaging was indicative of a transitional upper urinary tract tumor. After written informed consent, a right nephrectomy was performed and the patient was discharged on the 4th day. The histological exam revealed a partially capsulated lesion (3.7 cm in diameter) with a pseudo-cystic structure, including hemosiderin depositions, compressing but not invading the dilated lower calyx. The lesion was characterized by hyalinized clusters of thin-walled ectatic blood vessels within a stroma composed of sheets and fascicles of spindled and pleomorphic atypical cells with intranuclear inclusions. At immunohistochemical analysis, AE1/AE3, EMA, CD31, S100, desmin, actin of smooth muscle, HMB45, ALK resulted negative. The lesion was classified as a PHAT. The patient is maintained in follow-up. Discussion: PHAT is a low-grade mesenchymal neoplasm of uncertain lineage described in soft tissue and characterized by diffusely infiltrative borders, although some do have well-circumscribed margins. The immunohistochemistry of S-100 protein, actin, desmin, cytokeratin, CD-31, factor VIII antigens or epithelial membrane antigen are negative. To date approximately 22 cases of PHAT and 40 cases of its precursor, "early PHAT", have been described in the world literature. At least 3 cases of PHAT were reported to progress to high-grade myxofibrosarcoma (1). A case of PHAT arising in the hilum of the kidney, clinically mimicking an infiltrating tumor of the renal pelvis, has been described in 2012 (2). Our case is the second described in retro-peritoneum and the first of the renal parenchyma. In our patient, a partial nephrectomy was not carried out due to the absence of well-defined margins and apparent involvement of the lower calyx, although not confirmed by the pathological exam. If a partial nephrectomy is performed, a strict follow-up should be considered due to the high percentage of local recurrence characterizing the clinical behavior of PHAT (3).


44 RES529, A DUAL TORC1/TORC2 INHIBITOR, POTENTIATES THE IN VITRO AND IN VIVO EFFICACY OF HORMONE MANIPULATIONS IN THE 22RV1 PROSTATE CANCER CELL MODEL

Giovanni Luca Gravina1,2, Francesco Marampon1, Alessandro Colapietro1, Luca Scarsella1, Ana Jitariuc1, Patrizia Sanità1, David Sherris2 and Claudio Festuccia1

1Department of Applied Clinical Sciences and Biotechnologies, University of L’Aquila, L’Aquila, Italy; 2Department of Biotechnological and Applied Clinical Sciences, Division of Radiotherapy, University of L’Aquila, L’Aquila, Italy.

3Drug Development, RestorGenex, Buffalo Grove, IL, U.S.A.
Background: Carcinoma of the prostate (CaP) is an increasing healthcare problem. Given the poor outcome of patients with castration-resistant prostate cancer (CRPC), new strategies are needed to improve the current therapeutic regimens, slow down the insurgence of hormone refractory disease and/or develop novel treatments. Emerging evidence demonstrates a key role for the PI3K-AKT-mTOR signaling axis in the development and maintenance of CRPC. This pathway, which is deregulated in the majority of advanced prostate cancers, serves as a critical nexus for the integration of growth signals with downstream cellular processes, such as protein synthesis, proliferation, survival, metabolism and differentiation, thus providing mechanisms for cancer cells to overcome the stress associated with androgen deprivation. In addition, aberrant function of mTOR has been shown to present in the proliferation of cancer stem cells (CSCs) or tumor initiating cells. Aim: To investigate the role of TORC1 and TORC2 in the proliferation and apoptosis induced by hormone manipulation in androgen sensitive or castration resistant prostate cancer models. In addition we intended to evaluate the possible potentiating effects of the dual TORC1/TORC2 inhibitor, RES529.

Results: Here, we demonstrated that siRNA for raptor (TORC1 silencing) had no significant change in the growth of 22rv1 cells, whereas the siRNA for rictor (TORC2 silencing) induced a marked inhibition of cell proliferation. TORC1 silencing increased the expression of AR and Ser473 Akt, whereas TORC2 marked reduced them. This suggests that TORC2 is a promising target for prostate cancer; therefore, RES-529, a dual TORC1/TORC2 inhibitor, was tested in comparison with RAD001 in experiments of combination with androgen deprivation and AR inhibition both in vitro and in vivo. In vivo we tested the combination effects of 5α-reductase (finasteride or dutasteride), CYP17 (abiraterone) and AR (bicalutamide) inhibitors. We observed that RES-529 was able to synergize with hormone manipulations in 22rv1 cells. In chronic in vitro experiments, RES-529 seems to prevent the insurgence of CRPC disease. Lower effects were showed by a rapamycin analog (RAD001), a specific TORC1 inhibitor. The importance of TORC2 in this phenomenon was also demonstrated by using metformin, a well-known adenosine monophosphate-activated protein kinase (AMPK) inhibitor that phosphorylates TORC2, thereby blocking its nuclear translocation. Metformin administration reduces TORC2 phosphorylation status increasing the effects of RAD001. Conclusion: Our results provide a rationale for combination treatment with conventional hormone therapy and mTOR inhibitors, including TORC1/TORC2 dissociative compounds like RES-529. This may be a promising therapeutic approach for the treatment of both hormone-sensitive and CR diseases.

EVALUATION OF A CORRELATION BETWEEN PSA END AND BIOCHEMICAL FAILURE IN PROSTATE CANCER AFTER RADIOTHERAPY

Filippo De Renzi, Tiziana Iannone and Alessandro Testolin
Department of Radiation Oncology, Osp. S.Martino Belluno, Italy

Background/Aim: A study of D’Amico (Lancet Oncology 2012 Feb, 13(2) 189-95) assessed whether prostate-specific antigen (PSA) nadir or PSA end concentrations of more than 0.5 ng/ml were surrogates for prostate cancer-specific mortality. We investigated the possible correlation between PSA end values exceeding 0.5 ng/ml and biochemical failure. Patients and Methods: We evaluated 24 patients treated with radiotherapy between June 2008 and March 2009. We used Phoenix criteria to evaluate biochemical failure in localised or locally advanced prostate cancer. Low risk patients were 8/24 (33%), intermediate risk 10/24 (42%), high risk 6/24 (25%). Total dose to prostate was 76 Gy (1.9 Gy/fr) in three-dimensional conformal radiotherapy (3D CRT). Androgen suppression therapy was used in 19/24 (79%). Median age 73 (61-79) years. Median follow-up 65 (50-67) months. Median PSA end 0.22 (0.05-3.06) ng/ml. Results: Among all the patients, only 2/24 (8%) had a biochemical failure and were treated with hormonal therapy. These 2 patients were of intermediate risk and initially treated with a six-month androgen suppression therapy. In one case biochemical failure was associated to PET/CT local relapse. These two patients had respectively 0.49 and 0.23 ng/ml PSA end. Discussion and Conclusion: Early observation does not confirm a possible correlation between PSA end values exceeding 0.5 ng/ml and biochemical failure. Data increasing of the study could conduct to other results about biochemical failure, evaluating Kaplan Meier analysis and Cox regression. Differences on age or androgen suppression therapy should be assessed. For further development of the study, univariate and multivariate logistic regression analysis is needed.

UNSCHEDULED PRESENTATIONS OF UROLOGICAL CANCER OUTPATIENTS IN AN ONCOLOGY CLINIC: A SINGLE INSTITUTION RETROSPECTIVE STUDY

Caterina Fontanella1, Paola Ermacora1, Claudia Andreetta1, Karim Rihawi1, Giuseppe Aprile1, Alessandro Magli2, Gianpiero Fasola1 and Cosimo Stanislaos Pio Sacco1

1Department of Clinical Oncology, University Hospital of Udine, Udine, Italy;
Background/Aim: The AIRTUM registry documented approximately 80,000 new urogenital tumors diagnosed in 2014 in Italy (1). Moreover, the availability of new therapeutic strategies makes the treatment process more complex and considerably increases the risk of toxicities and complications. As a result, more cancer outpatients may ask for unplanned visits in oncology clinic (2). Accordingly, a large retrospective study showed that prostate cancer is the fourth most common tumor in patients admitted to Emergency departments in the United States (3). Our study aims to describe the magnitude of unscheduled visit of urological cancer patients and to identify risk factors for repeated unplanned presentations and hospitalization.

Patients and Methods: From October 1st 2006 to September 30th 2008, 1,431 cancer patients accessed to our acute oncology clinic and 2,811 unplanned consultations were reviewed over this 2-year period. We focused our analysis on 113 subjects with a diagnosis of urological cancer (205 total unplanned consultations). Baseline demographic data (age, gender and Karnofsky performance status (KPS)) and clinical variables (primary cancer site, type of chemotherapy regimen and treatment setting) were all recorded together with reasons for presentation, laboratory values and outcome of the visit. Cross-tables, χ² test and logistic regression were used to evaluate the relation of potential predictors for the two outcome events: repeated presentations and hospitalization. The study was approved by the Investigational Review Board.

Results: Among our 113 consecutive patients, 32 (28.3%) were diagnosed with prostate cancer, 48 (42.5%) with renal cell cancer, 19 (16.8%) with bladder cancer, 9 (7.9%) with testicular cancer and 5 (4.4%) with other transitional cell cancers. Overall, 60 patients (53.1%) received chemotherapy and 17 (15.0%) received endocrine treatment during the 90 days before the unplanned consultation. The median KPS, at the time of the unscheduled presentation, was 70% and the median age was 69.1 years (range=25.5 to 87.7). More than 85% of patients were male (98 men versus 15 women). Pain (38.5%), fatigue (20.5%), hematological disorders, such as anemia, neutropenia or thrombocytopenia (16.6%), dyspnea (11.7%), cachexia (11.2%) and fever (9.3%) were frequently reported; 50.2% of patients had more than 1 reason for the unplanned visit (Table I). In this cohort, 47 patients (41.6%) had repeated unplanned presentations and 14 consultations (6.8%) led to hospital admission. According to univariate analysis, pain (p=0.009), dyspnea (p<0.001), pleural effusion/ascites (p<0.001), cachexia (p<0.001), neurological disorders (p=0.036) and multiple reasons for unscheduled visit (p<0.001) were signs/symptoms related to higher risk of hospitalization (Table II).

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentages (%)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>38.5</td>
<td>79</td>
</tr>
<tr>
<td>Fatigue</td>
<td>20.5</td>
<td>42</td>
</tr>
<tr>
<td>Hematological disorders</td>
<td>16.6</td>
<td>34</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>11.7</td>
<td>24</td>
</tr>
<tr>
<td>Cachexia</td>
<td>11.2</td>
<td>23</td>
</tr>
<tr>
<td>Fever</td>
<td>9.3</td>
<td>19</td>
</tr>
<tr>
<td>Urinary tract disorders</td>
<td>8.3</td>
<td>17</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>7.3</td>
<td>15</td>
</tr>
<tr>
<td>Neurological disorders</td>
<td>7.3</td>
<td>15</td>
</tr>
<tr>
<td>Pleural effusion/Ascites</td>
<td>6.3</td>
<td>13</td>
</tr>
<tr>
<td>Mucositis</td>
<td>5.4</td>
<td>11</td>
</tr>
<tr>
<td>Thromboembolic events</td>
<td>5.4</td>
<td>11</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.9</td>
<td>10</td>
</tr>
<tr>
<td>Skin reaction</td>
<td>4.4</td>
<td>9</td>
</tr>
<tr>
<td>Single reason for visit</td>
<td>50.2</td>
<td>103</td>
</tr>
<tr>
<td>Multiple reasons for visit</td>
<td>49.8</td>
<td>102</td>
</tr>
</tbody>
</table>

*47 patients (41.6%) had repeated unplanned presentations.

<table>
<thead>
<tr>
<th>Factors</th>
<th>p-Value for univariable analysis</th>
<th>p-Value for multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>0.009*</td>
<td>0.524</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0.144</td>
<td></td>
</tr>
<tr>
<td>Hematological disorders</td>
<td>0.212</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Cachexia</td>
<td>&lt;0.001*</td>
<td>0.016*</td>
</tr>
<tr>
<td>Fever</td>
<td>0.421</td>
<td></td>
</tr>
<tr>
<td>Urinary tract disorders</td>
<td>0.872</td>
<td></td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>0.300</td>
<td></td>
</tr>
<tr>
<td>Neurological disorders</td>
<td>0.036*</td>
<td>0.602</td>
</tr>
<tr>
<td>Pleural effusion/Ascites</td>
<td>&lt;0.001*</td>
<td>0.429</td>
</tr>
<tr>
<td>Mucositis</td>
<td>0.764</td>
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<tr>
<td>Thromboembolic events</td>
<td>0.760</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0.380</td>
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</tr>
<tr>
<td>Skin reaction</td>
<td>0.603</td>
<td></td>
</tr>
<tr>
<td>Age &gt;70 years</td>
<td>0.163</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy within 90 days</td>
<td>0.226</td>
<td></td>
</tr>
<tr>
<td>Abnormal laboratory tests</td>
<td>0.067</td>
<td></td>
</tr>
<tr>
<td>Multiple reasons for visit</td>
<td>&lt;0.001*</td>
<td>0.996</td>
</tr>
</tbody>
</table>

*Statistically significant factors.
In multivariate analysis, only dyspnea ($p<0.001$) and cachexia ($p=0.016$) were significant predictors of hospitalization (Table II). Similarly, pain ($p=0.048$), hematological disorders ($p<0.001$), cachexia ($p=0.037$), chemotherapy administered within 90 days ($p<0.001$) and multiple complaints ($p=0.003$) were signs/symptoms related with repeated unscheduled consultations (Table III). In multivariate analysis, only cachexia ($p=0.003$) and chemotherapy administered within 90 days ($p=0.048$) were significant predictors of multiple unscheduled visits (Table III).

Table III. Demographic and clinical factors potentially related with repeated unscheduled presentations to our acute oncology clinic.

<table>
<thead>
<tr>
<th>Factors</th>
<th>$p$-Value for univariable analysis</th>
<th>$p$-Value for multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>0.048*</td>
<td>0.997</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0.094</td>
<td>-</td>
</tr>
<tr>
<td>Hematological disorders</td>
<td>$&lt;0.001*$</td>
<td>0.121</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>0.422</td>
<td>-</td>
</tr>
<tr>
<td>Cachexia</td>
<td>0.037*</td>
<td>0.003*</td>
</tr>
<tr>
<td>Fever</td>
<td>0.275</td>
<td>-</td>
</tr>
<tr>
<td>Urinary tract disorders</td>
<td>0.060</td>
<td>-</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>0.294</td>
<td>-</td>
</tr>
<tr>
<td>Neurological disorders</td>
<td>0.634</td>
<td>-</td>
</tr>
<tr>
<td>Pleural effusion/Ascites</td>
<td>0.266</td>
<td>-</td>
</tr>
<tr>
<td>Mucositis</td>
<td>0.090</td>
<td>-</td>
</tr>
<tr>
<td>Thromboembolic events</td>
<td>0.092</td>
<td>-</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0.123</td>
<td>-</td>
</tr>
<tr>
<td>Skin reaction</td>
<td>0.421</td>
<td>-</td>
</tr>
<tr>
<td>Age &gt;70 years</td>
<td>0.105</td>
<td>-</td>
</tr>
<tr>
<td>Chemotherapy within 90 days</td>
<td>$&lt;0.001*$</td>
<td>0.048*</td>
</tr>
<tr>
<td>Abnormal laboratory tests</td>
<td>0.966</td>
<td>-</td>
</tr>
<tr>
<td>Multiple reasons for visit</td>
<td>0.003*</td>
<td>0.996</td>
</tr>
</tbody>
</table>

*Statistically significant factors.

Conclusion: Urogenital cancer outpatients may frequently ask for unplanned care, with pain still being the most frequent reason. The optimal management of these unscheduled presentations is becoming crucial in order to improve quality of oncology services, as well as patients quality of life. A more correct approach would also reduce both interferences with the ordinary work and inappropriate hospital admissions. An updated analysis on a longer period is ongoing and will be available soon.


48 IMAGE-GUIDED ROBOTIC RADIOSURGERY TREATMENT AS SALVAGE THERAPY FOR LOCALLY RECURRENT PROSTATE CANCER

Giancarlo Beltramo¹, Victor Matei², Giovanni Longo³, Maria Cristina Locatelli⁴, Achille Bergantin¹, Anna Stefania Martinotti¹, Francesco Ria¹, Marta Invernizzi¹, Alessandro Vai⁵, Livia Corinna Bianchi¹, Matteo Maggioni³ and Guido Dormia³

¹Cyberknife Center, Centro Diagnostico Italiano, Milan, Italy;
²Division of Urology, European Institute of Oncology, Milan, Italy;
³Division of Urology, San Carlo Borromeo Hospital, Milan, Italy;
⁴Division of Oncology, San Carlo Borromeo Hospital, Milan, Italy

Aim: Despite improvements in external beam irradiation for prostate cancer, a significant number of patients develop locally recurrent disease. Salvage local therapy may well induce a prolonged biochemical remission and, possibly, even cure. We evaluate the feasibility of re-irradiation with Cyberknife (CK) for intra-prostatic recurrence after external beam radiotherapy (EBRT). Materials and Methods: Between September 2007 and August 2013, 59 patients with a median age of 72 years (range=56-89) diagnosed with biopsy-confirmed locally-recurrent prostate cancer after EBRT and with absence of severe chronic urinary and rectal late toxicity were referred to our Radiotherapy Department for salvage treatment with CK stereotactic radiosurgery. The initial stage, according the National Comprehensive Cancer Network 2008, was defined as low, intermediate and high in 14, 12 and 33 patients, respectively. The EBRT median dose was 76 Gy (range=70-80 Gy) with a median interval between EBRT and diagnosis of recurrent prostate cancer of 84 months (range=18-220). The median pre-re-irradiation prostate-specific antigen (PSA) was 5.23 ng/ml (range=1.47-23.22). The planning treatment volume (PTV) included the prostate gland expanded by 3 mm in all directions except posteriorly, where 2 mm were added. For the first 29 patients, we prescribed 5 fractions of 6 Gy for a total dose of 30 cGy. For the following 30 patients, our CK stereotactic radiosurgery protocol provided a prescribed
PTV dose of 35 Gy given in 5 daily fractions. Results: After a median follow-up of 41 months (range=13-84), 3 patients developed severe urinary acute and late Radiation Therapy Oncology Group (RTOG) toxicity (grade 3). The actuarial PSA relapse-free survival rate was 84.2% (confidence interval (CI)=75.0%-93%) at the first year and 56% (CI: 34.0%-86%) at the second year, respectively. Conclusion: CyberKnife-based SRT is a feasible approach for locally recurrent prostate cancer offering excellent in-field tumor control and low toxicity profile. Further experience and longer follow-up are needed to evaluate the role of CK in the treatment of local recurrences and to identify patients most likely to benefit from it.

49 STEREOTACTIC BODY RADIOTHERAPY FOR PROSTATE CANCER
Giancarlo Beltramo1, Giovanni Longo2, Cristina Locatelli3, Achille Bergantin3, Anna Stefania Martinotti1, Francesco Ria1, Marta Invernizzi1, Alessandro Vai1, Livia Corinna Bianchi1, Matteo Magnioni2 and Guido Dormia2

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

Background/Aim: There now is convincing evidence that biochemical control is improved with higher cumulative doses of radiation to the prostate. Hypofractionated radiation therapy for prostate cancer has become of increasing interest with the recognition of a potential improvement in therapeutic ratio. We evaluate the clinical outcome of a cohort of localized prostate cancer patients (pts) treated with Cyberknife stereotactic body radiation therapy. Materials and Methods: Between July 2007 and October 2013, a retrospective analysis was carried out on 162 consecutive patients with a median age of 74 (range=52-86) years and clinically localized prostate cancer that underwent Cyberknife stereotactic radiosurgery at our Institution. The majority of patients, 85 (52%), were low risk, 44 pts (27%) were intermediate risk and 33 pts (20%) were high risk using the National Comprehensive Cancer Network (NCCN) criteria. Pre-treatment prostate-specific antigens (PSAs) ranged from 1.75 to 51.13 ng.ml (median=7.8). Among the entire study cohort, 17 of 33 high risk patients received androgen deprivation therapy (ADT); ADT was not administered to any low – intermediate risk patients. A prescribed dose of 38 Gy in four fractions was delivered to the PTV, which was defined as the prostate (plus seminal vesicles in high risk patients). Real-time intrafractional motion tracking was used. Results: Acute urinary symptoms (frequency, disuria, urgency, hesitancy and nicturia) were common to 46% of patients experiencing grade I-II Radiation Therapy Oncology Group (RTOG) acute urinary toxicity. No patients experienced RTOG grade 3 acute urinary toxicity, while 5 patients (3%) experienced RTOG grade 3 late urinary toxicity, as consequences of repeated urological instrumentation, including cystoscopy and urethral dilatation. No RTOG grade 3 acute and late rectal toxicity was observed. The actuarial median follow-up is 41 months (range=12-87). The five-year actuarial PSA relapse-free survival rate is 96.1% (confidence interval (CI)=94.3%-97.9%) with 100% for low risk, 90.1% for intermediate and 83% for high. One patient died from bone metastases, 13 patients died from unrelated causes. Conclusion: Cyberknife SBRT produces excellent biochemical control rates at up to 5 years with mild toxicity and minimal impact on quality of life. Median PSA levels compare favourably with other radiation modalities and strongly suggest durability of our results.

50 ROBOTIC IMAGE-GUIDED STEREOTACTIC RADIOTHERAPY FOR ISOLATED LYMPH NODE PROSTATE METASTASES
Giancarlo Beltramo1, Victor Matei2, Giovanni Longo3, Maria Cristina Locatelli2, Achille Bergantin1, Anna Stefania Martinotti1, Francesco Ria1, Marta Invernizzi1, Alessandro Vai1, Livia Corinna Bianchi1, Matteo Magnioni3 and Guido Dormia3

1Cyberknife Center, Centro Diagnostico Italiano, Milan, Italy;
2Division of Urology, European Institute of Oncology, Milan, Italy;
3Division of Oncology, San Carlo Borromeo Hospital, Milan, Italy

Objective: Patients with metastasized prostate cancer after primary treatment are generally considered palliative and androgen deprivation is considered the current standard therapy. Oligometastatic patients often have a long survival time and non-invasive low-toxicity approaches could be of great value to this large patients population. We investigated the role of salvage stereotactic radiotherapy for patients with limited prostate cancer metastases to defer the initiation of palliative androgen deprivation therapy (ADT). Materials and Methods: Between March 2009 and March 2013, a cohort of
30 patients with up to 3 synchronous lymph node prostate metastases staged with $^{[11C]}$-choline positron emission tomography (47 lesions with a median volume of 12.92 cc, range=0.39-111.67), following biochemical recurrence after local curative treatment, were treated with Cyberknife stereotactic body radiotherapy in our Center. The mean age of the patient population at the time of Cyberknife treatment was 68 years (range=55-84). Cyberknife prescription doses were 3,000-3,600 cGy delivered in 3 consecutive fractions of 1,000-1,200 cGy. The dose was prescribed to the mean 80% isodose line by use on a non isocentric Cyberknife treatment technique. In 14 lesions (37%), Cyberknife Stereotactic Radiotherapy Treatment (SBRT) was performed as re-irradiation (the recurrent lesion was situated in the previously irradiated volume). Clinical progression was defined as the detection of local progression or distant disease at reassessment. In case of an oligometastatic recurrence outside the previous stereotactic body irradiated field, a re-treatment was performed. ADT was initiated if more than 3 metastases were detected during follow-up, even when patients were still asymptomatic. Toxicity was scored using the Common Terminology Criteria for Adverse Events. Results: The Cyberknife treatment was well tolerated without any acute or late toxicity at all. There were no in field recurrence resulting in a local control of 100%. Eleven and 3 patients, respectively, required a second and third salvage treatment for metacronous metastatic disease. The median time to clinical progression was 14 months (range=3-54). After a median follow-up of 33 months (range=13-73), 16 patients started with ADT because of polymetastatic disease resulting in an ADT-free survival (FS) of 80% at 1 year and 65% at 2 years. The median time of ADT was deferred to 26 months (range=4-56). Conclusion: Recent evidence of the potential toxic nature of ADT suggests that effective local therapy might reduce the burden of systemic therapies usually given to patients with metastatic prostate cancer. Cyberknife salvage hypofractionation stereotactic body radiotherapy is a safe and effective treatment option in patients with lymph node prostate metastases and could defer initiation of palliative ADT.

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RENAL CELL CARCINOMA
METASTASIS TO THE BLADDER

Matteo Maggioni1, Fabio Masserini2, Guido Dormia1, Valentina Bertolfini3, Giovanni Longo1, Maria Cristina Locatelli4 and Giancarlo Beltramo5

1Division of Urology, San Carlo Borromeo Milano, Milan, Italy;
2Division of Gynecology, University of Milan (Mangiagalli), Milan, Italy;
3Division of Antomopathology, San Carlo Borromeo Milano, Milan, Italy;
4Division of Oncology, San Carlo Borromeo Milano, Milan, Italy;
5Division of Radiotherapy, Centro Diagnostico Italiano Milano, Milan, Italy

Background: Metastases from distant primary tumors represent less than 2% of all bladder neoplasms. Gastric carcinoma, melanoma and carcinoma of the breast and colon are the most common sources of secondary vesical cancers. Renal cell carcinoma, on the other hand, spreads uncommonly to the bladder, with fewer than 50 cases reported in medical literature. Metastases may be synchronous or metachronous and may be discovered even years after the diagnosis of the primary renal tumor. Materials and Methods: We present the case of a 82-year-old man who underwent radical prostatectomy in 2007 (prostate cancer G3 GS 7, pT3b N0 cM0) and radical right nephrectomy in 2009 (kidney cancer G3 pT2 N0 cM0) and was, subsequently, treated with 150 mg bicalutamide since 2011 for disease recurrence. The patient presented himself at our Institution in July 2014 complaining of hematuria.

Figure 1.

Figure 2.
Abdominal ultrasound showed significant left hydronephrosis caused by a solid lesion involving the left hemitrigonal wall and papilla. Subsequent positron emission tomography (PET) scanning showed no evidence of secondary lesions. Results: The patient underwent transurethral resection of the left hemitrigonal lesion and placement of double-J (DJ) stent (anatomical pathology report: infiltrating vesical carcinoma of renal origin). The patient’s immunohistochemical profile was as follows: CK7, CK20, p63, PSA negative, Cd10, Vimentin positive (Fig 1-2). After a 5-month follow-up, the patient had no recurrence of hydronephrosis and hematuria and his overall health condition was deemed to be good. Conclusion: Due to the rarity of these tumors, their management is not standardized. Transurethral resection and partial cystectomy have been described. Genitourinary metastases are generally thought of as harbingers of poor prognosis; however, long-term survival is occasionally reported.

52 MRI EVALUATION OF PROSTATE VOLUME SHRINKAGE AFTER NEOADJUVANT HORMONE THERAPY IN PROSTATE CANCER PATIENTS TREATED WITH DEFINITIVE HYPOFRACTIONATED RADIOTHERAPY

Rocco Luca Emanuele Liardo, Roberta Bevilacqua, Alessandra Tocco, Giuseppe Privitera and Corrado Spatola
Division of Diagnostic Radiology and Radiation Oncology, AOU "Policlinico - Vittorio Emanuele", Catania, Italy

Aim: The aim of this study was to evaluate, by means of magnetic resonance imaging (MRI), the amount of prostate volume shrinkage in patients with intermediate risk prostate cancer who underwent neoadjuvant hormone therapy (NHT) before definitive treatment with radical radiotherapy. We hypothesize that target volume reduction can permit a better treatment optimization when an hypofractionated radiotherapy (HRT) is planned. Materials and Methods: Twelve patients with histologically proven adenocarcinoma of the prostate (intermediate risk), with prostate volume >50 cc, were selected to be treated with NHT, with bicalutamide 150 mg/day. The patients' median age was 73 years (range=68-76). All patients underwent clinical assessment and cardiological examination before starting NHT. We proceeded as follows: (i) execution of MRI 1 (baseline), computed tomography (CT) simulation and HRT treatment plan 1; (ii) starting of NHT, planned for six months; (iii) execution of MRI 2, CT simulation and HRT treatment plan 2; (iv) radiation treatment. Prostate volume evaluation was performed by means of MRI of the lower abdomen and pelvis, with and without contrast agent, using three-dimensional fast spoiled gradient-echo (3D-FSPGR) sequences and evaluated by the same team. Radiation treatment was performed with 3D conformal technique and started after six months of NHT. The total dose administered was 72.5 Gy by means of a mild hypofractionation regimen, 2.5 Gy/day, 29 fractions. Hormone therapy was maintained during HRT and stopped at the end of treatment. Another MRI scan was made after 6 months from the end of HRT (MRI 3) to evaluate the possible further prostate downsizing. Results: MRI 2, compared with the baseline MRI 1, showed a prostate shrinkage between 12% and 24% from the initial volume. The HRT treatment plan simulation 2, unlike the first plan, showed a reduction in dose delivered to the rectum (between 8-10%) and bladder (between 13-19%). All patients completed both NHT and HRT. Radiation therapy was well tolerated with no events of acute G3 or higher toxicities (according to Common Terminology Criteria for Adverse Events (CTCAE), v4.03). Nine patients developed a moderate gynecomastia. MRI 3 showed a further slight prostate volume reduction, variable between 5% and 11%. Conclusion: The results demonstrate the effectiveness of NHT in prostate volume shrinkage. Downsizing achieved help to perform 3D conformal radiotherapy, especially when a hypofractionation regimen is planned, with a low toxicity profile.

53 IMAGE-GUIDED HYPOFRACTIONATED RADIOTHERAPY FOR LOCALIZED PROSTATE CANCER WITH 42 GY IN 7 FRACTIONS: RADIOBIOLOGY AND PRELIMINARY CLINICAL RESULTS OF A PHASE-II STUDY

Alessandro Magli1, Tino Ceschia1, Francesca Titone1, Miriam Isola2, Vittorio Vavassori3, Maria Rosa Malisan4 and Sandro Fongione1
1Department of Radiation Oncology, University Hospital Udine, Department of Radiation Oncology, University Hospital Udine, Udine, Italy; 2Department of Biological Sciences, University of Udine, Department of Biological Sciences, University of Udine, Udine, Italy; 3Department of Radiation Oncology, Cliniche Gavazzeni of Bergamo, Department of Radiation Oncology, Cliniche Gavazzeni of Bergamo, Bergamo, Italy; 4Department of Medical Physics, University Hospital Udine, Department of Medical Physics, University Hospital Udine, Udine, Italy

Introduction: The evolution of radiation technology, which integrates 3-dimensional anatomy, conformal dose coverage and image guidance combined with a better understanding of prostate cancer radiobiology and fraction sensitivity of the tumor relative to nearby normal tissue, has led to hypofractionated radiation therapy schedules. Clinical data now exist from several studies, including randomized trials using various moderately hypofractionated regimens, with dose-per-fraction ranging from 2.5 Gy per fraction for 70 Gy
and 3.1 Gy per fraction for 62 Gy (1, 2) up to, more recently, extreme hypofractionation schemes of 7.25 Gy per fraction for 36.25 Gy or 10 Gy for 5 fraction (3) using stereotactic body radiation therapy (SBRT) approaches. Hypofractionation for prostate cancer, and in particular SBRT, results in a means of radiobiological dose escalation and potentially represents a therapeutic gain. It also affords a more economical course of definitive radiation therapy, improves patient access to care and enhances patient convenience. 

**Aim:** We have performed a phase II study concerning hypofractionated radiotherapy (HRT) with a dose of 42 Gy in 7 fractions, in patients with localized prostate cancer at low/intermediate risk (according to National Comprehensive Cancer Network (NCCN) score) and risk of lymph node involvement <17% (Roach Index) in order to evaluate the feasibility and acute toxicity. 

**Materials and Methods:** Since 2012, 40 patients at low/intermediate risk for localized prostate cancer have been planned for HRT (Table I). Fraction size is 6 Gy for 7 fractions scheduled to be delivered twice a week for a total dose of 42 Gy. Treatment has been delivered with a VMAT technique, with 2 arcs using 6MV photons from a Varian 2300 iX linac. Planning was performed with Eclipse 10.0 TPS with the AAA algorithm by 3 different planners. Dose prescription is the average dose to PTV with the request V95%≥95%. The dose-volume histogram (DVH) constraints for organs at risk (OARs) have been derived from literature and local experience. Constraints for acute urinary toxicity have been recently introduced after the paper of Carillo et al. (4). To reduce the organ motion, patients have been premedicated before treatment with butylscopolamine. The protocol is based on 3 image-guided radiation therapy (IGRT) intraprostatic fiducial markers, with daily online checks by cone beam computed tomography (CBCT). The acute and late toxicity is recorded using the Radiation Therapy Oncology Group and the European Organization for Research and Treatment of Cancer (RTOG/EORTC) scale. Additional data are collected by means of International Prostate Symptom Score (II-PSS) and International Index of Erectile Function (IIEF-5) questionnaires.

**Results:** Thirty-two patients have been followed for three months or more. Urinary toxicities were most common. At 3 month, 12% of patients reported grades 1 urinary toxicities (RTOG/EORTC scale). At 6 months no patients reported grade 1 urinary toxicities. At 18 months, one patient reported grade 1 proctitis and grade 1 rectal bleeding, which resolved without intervention. Thirteen patients have been followed for 12 months or more. Biochemical response was rapid the first 12 months of follow-up: mean pre-treatment and 12-month post-treatment values were 3.75 ng/ml and 0.7 ng/ml, respectively. The results of organ motion intrafraction (OMI) movement are shown in Figure 1. By implementing principals of manipulation and premedication of the patient we have a control of OMI ≤2 mm in 98% of treatment sessions. 

**Conclusion:** Intrafraction motion of the prostate is minimal when patients follow the special diet and are premedicated before treatment with butylscopolamine. The proposed scheme is estimated more effective to high-dose conventional regimens. The absence of acute toxicity seems to confirm the validity of the adopted normal tissue complication probability (NTCP) model and could be predictive of late toxicity. At this early follow-up point, prostate HRT results in favorable toxicity and biochemical outcomes and appears to support the strategy of hypofractionation in the management of localized prostate cancer. Further follow-up is necessary to validate these early, promising results.

<table>
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<tr>
<th>Characteristic</th>
<th>RT alone (n=22)</th>
<th>RT plus ADT (n=18)</th>
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<tr>
<td>Age (range)</td>
<td>70 (56-80)</td>
<td>71 (57-78)</td>
</tr>
<tr>
<td>Pretreatment PSA level</td>
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<td>7.3 ng/ml</td>
</tr>
<tr>
<td>Gleason Score</td>
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<td></td>
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<tr>
<td>6</td>
<td>18 (82%)</td>
<td>4 (22%)</td>
</tr>
<tr>
<td>3+4</td>
<td>4 (18%)</td>
<td>11 (61%)</td>
</tr>
<tr>
<td>4+3</td>
<td>0</td>
<td>3 (17%)</td>
</tr>
<tr>
<td>T stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>16 (73%)</td>
<td>13 (72%)</td>
</tr>
<tr>
<td>T2a-b</td>
<td>6 (27%)</td>
<td>3 (17%)</td>
</tr>
<tr>
<td>T2c</td>
<td>0</td>
<td>2 (11%)</td>
</tr>
</tbody>
</table>

**Table I. Patients and treatment characteristics.**

ADT androgen deprivation therapy; PSA prostate-specific antigen; RT radiation therapy.

**Figure 1. Organ motion intrafraction (OMI) movement (mm).**
CRYOTHERAPY IN RENAL CELL CANCER: EVALUATION OF CONTRAST-ENHANCED ULTRASONOGRAPHY (CEUS)

Salvatore Siracusano¹, Michele Bertolotto², Francesca Cacciato³, Matilde Cazzagon⁴, Stefano Ciciliato¹, Laura Toffoli¹, Francesco Visalli¹, Tommaso Silvestri¹ and Fulvio Stacul²

¹Departments of Urology and ²Radiology, Trieste University, Trieste, Italy

Aim: To evaluate the diagnostic accuracy of contrast enhanced ultrasound (CEUS) in the early detection of residual tumour after cryoablation (1-3). Materials and Methods: Twenty-six patients with 31 renal tumors (20 men, 6 women) with a mean age of 69 years (range=52-81) underwent percutaneous cryoablation between August 2011 and July 2013. All tumors were treated with computed tomography (CT) guidance. Patients underwent CEUS before, within 1 day (early follow-up CEUS), 1 month and 3 months after the ablation. In patients with persistent lesion vascularity at early follow-up CEUS, the test was repeated 1 week and 1 month after the treatment. Reference standard was magnetic resonance imaging (MRI)/CT performed every 6 months after cryoablation for the first 2 years and then yearly. Results: The mean tumor size was 19.7 mm (range=6-37). One patient was lost to follow-up. Twenty-five patients with 30 renal tumors were followed up for at least 6 months and all underwent CEUS. MRI was performed in 21 patients, CT in 4 patients who had contraindications to MR scanning. The mean follow-up period was 15 months (range=6-24). Early CEUS follow-up displayed a completely avascular lesion in 24/30 renal lesions. Minimum to mild perilesional enhancement was present in 4 cases, which disappeared progressively during the follow-up. One type IV cystic tumor had 2 intralesional vegetations (1 and 2 cm, respectively), which were still vascularized early after cryoablation and during the follow-up and were categorized as residual tumor. Severe comorbidities precluded from repeated cryoablation. Two lesions were vascularized in the early CEUS follow-up, while the CEUS investigation repeated 1 week and 1 month after the treatment documented progressive devascularization of the mass. Discussion: CEUS is an effective alternative to CT and MRI for the early diagnosis of residual tumor after renal percutaneous cryoablation. Conclusion: CEUS offers good outcomes in early diagnosis of residual renal tumor after cryoablative treatment. Care should be taken, however, in interpreting persistent vascularity in the early CEUS follow-up as residual tumor. Repeated CEUS investigations allow to differentiate between a late devascularization of a successfully ablated tumor and persistent disease.

LONG-TERM FOLLOW-UP AFTER NEOBLADDER WITH PROSTATIC CAPSULE AND SEMINAL-SPARING CYSTECTOMY (PCSSC) FOR BLADDER CANCER

Salvatore Siracusano¹, Renzo Colombo², Stefano Ciciliato¹, Francesco Visalli¹, Laura Toffoli¹, Maurizio Brausi¹ and Renato Talamini¹

¹Department of Urology, Trieste University, Trieste, Italy; ²Department of Urology, S. Raffaele Milano University, Milan, Italy; ³Department of Urology, Carpi Hospital, Capri, Italy

Background/Aim: Prostatic capsule and seminal-sparing cystectomy (PCSSC) has been reported to improve functional results due to low risk to damage autonomic nerves and the sphincter area (1-3). The aim of the study was to evaluate long-term oncological and functional outcomes after PCSSC in selected patients who underwent cystectomy for bladder cancer. Patients and Methods: We evaluated 56 patients that underwent orthotopic neobladder with PCSSC from 2000 to 2013. Follow-up visits included a physical examination, urinary cytology, blood test, prostate-specific
antigen (PSA) measurement, abdominal and pelvic computed tomography (CT). Functional results were obtained during the visit using a symptom checklist for urinary incontinence and the International Index for Erectile Function (IIEF) questionnaire. Patients were considered continent when they used no pads and potent when erectile function permitted sexual activity. Univariate and multivariate analysis were performed to assess clinical and pathological characteristics as predictors for recurrence of disease and cause specific mortality by using Cox proportional model (Hazard ratios (HR) and 95% confidence interval (CI)). Results: The mean age of patients was 57.3±9.9 years. The pathological findings were pT0 in 16 (28.6%) cases, pT1 in 14 (25.0%) patients, pT2 in 12 (15.0%) patients, pT3 in 6 (14.3%) patients and carcinoma in situ (CIS) in 10 (14.3%) of patients. After a median follow-up of 65.8 months (range=8.2-168.4), 12 patients (21.4%) showed a recurrence of disease. In particular, three patients (5.3%) developed a local recurrence, 6 patients (10.7%) showed an upper urinary-tract recurrence, while in 5 (8.9%) cases a widespread metastases was diagnosed. At last follow-up, 7/56 patients (12.5%) died for cancer-specific disease. At multivariate analysis, CIS was an independent predictor of recurrence of disease and cause specific mortality as predictors for recurrence of disease and cause specific mortality. The percentage of day-time and night-time continence was of 84.9% and 63.0%, respectively, while potency was preserved in 75.0% of patients. Discussion: It is evident that in patients affected by CIS, the PCSSC should not be carried out due to the high recurrence of disease. Conclusion: A careful and strict preoperative selection of patients is needed to perform a safe PCSSC in accordance with the principles of cancer control.


56 HRQOL IN 112 MEN AND 33 WOMEN UNDERGOING ILEAL CONDUIT: EVALUATION IN LONG-TERM SURVIVORS
Salvatore Siracusano¹, Stefano Ciciliato¹, Renato Talamin³, Laura Toffoli¹, Francesco Visalli¹, Emanuele Belgrano¹, Mauro Niero³, Cristina Lonardi², Maria Angela Cerruto³, Ciro Imbimbo⁴, Marco Racioppi⁵, Massimo Iafrate⁶, Carolina D'elia³, Giovanni Cacciamani³, Davide De Marchi³, Pierfrancesco Bassi³, Paolo Verze⁴ and Walter Artibani³

Introduction: Patients undergoing urinary radical cystectomy (RC) and urinary diversion for bladder cancer had some early and late complications and experience substantial limitations in health-related quality of life (HRQoL). There are just a few studies that have evaluated the levels of discomfort in long-term survivors (1-3). In the present study, we used the validated Italian version of QLQ-BLM30 and QLQ-C30 from European Organisation for Research and Treatment of Cancer (EORTC) to assess bladder cancer-specific HRQoL in men and women with ileal conduit (IC) after RC and with long term follow-up. Patients and Methods: From June 2007 to September 2013, a total of 145 consecutive patients with bladder cancer (112 male and 33 female), who underwent RC with IC from five urological academic centres, were included in this study. All patients had no evidence of tumor recurrence and were actively followed up. Clinical and pathological data, as well as clinical outcomes, were retrospectively analyzed. Quality of life was analyzed using Italian versions of the EORTC BLM30 and QLQ-C30 questionnaires. Mean values with standard deviations (±SD) were computed for all items. The Wilcoxon rank test was used to verify differences by sex in the long-term follow-up. Statistical significance was achieved if p-value was ≤0.05 (two-sides). Results: The median age of men was 72 years (range=49-95) and 71 years (range=52-86) in women undergoing IC. The median of follow-up was 34 months (range=49-95) in 112 men and 40 months (range=6-153) in the 33 women with IC. Our data showed that women with IC had greater problems than men in cognitive functioning (higher score means a better functionality) (77.3±27.9 and 87.8±18.6, respectively; p=0.04) as well in future perspective (lower score means a low level of symptomatology/problems) (42.4±34.4 and 21.9±24.6, respectively; p=0.001). In contrast, men, undergoing IC, had more problems in sexual functioning than women (23.3±24.5 and 7.0±20.3, respectively; p=0.001). Discussion: Our study, based on long-term follow-up in women and men undergoing RC with IC, showed a better cognitive functioning and a more optimistic vision of the future in men than in women and a worse sexual function in men in comparison with women. Conclusion: RC and IC have a different impact in men and in women in relation to HRQoL in long-term.
HRQOL in 48 Women Undergoing Ileal Orthotopic Neobladder and Ileal Conduit: Evaluation in Long-Term Survivors

Salvatore Siracusano¹, Stefano Ciciliato¹, Renato Talamini¹, Laura Toffoli¹, Francesco Visalli¹, Emanuele Belgrano¹, Mauro Niero², Cristina Lonardi², Maria Angela Cerruto³, Ciro Imbimbo⁴, Marco Racioppi⁵, Massimo Iafrate⁶, Carolina Delia³, Giovanni Cacciamani³, Davide De Marchi³, Pierfrancesco Bassi³, Paolo Verze⁴ and Walter Artibani³

¹Department of Urology, Trieste University, Trieste, Italy; ²TeSIS Department, Verona University, Verona, Italy; ³Department of Urology, Verona University, Verona, Italy; ⁴Department of Urology, Federico II Naples University, Naples, Italy; ⁵Department of Urology, Cattolica Sacro Cuore Rome University, Rome, Italy; ⁶Department of Urology, Padua University, Padua, Italy

Introduction: Women undergoing urinary radical cystectomy (RC) and urinary diversion for bladder cancer have some early and late complications and experience substantial limitations in health-related quality of life (HRQoL). At present, there are sparse studies that have evaluated the levels of discomfort in long-term survivors (1-3). In the present study, we used the validated Italian version of QLQ-BLM30 and QLQ-C30 from European Organisation for Research and Treatment of Cancer (EORTC) to assess bladder cancer-specific HRQoL between patients with bladder cancer undergoing ileal orthotopic neobladder (IONB) and ileal conduit (IC) after RC and with long term follow-up. Patients and Methods: From June 2007 to September 2013, we evaluated 48 females with bladder cancer in five urological academic centres. In this study, we retrospectively analyzed the HRQoL in 33 women undergoing IC and in 15 females with IONB; all patients had no evidence of tumor recurrence and were actively followed up. Questionnaire results were analyzed in order to evaluate the HRQoL in women undergoing IONB and IC. Mean values with standard deviations (±SD) were computed for all items. The Wilcoxon two sample test was used to verify differences.

Results: The median age of patients with IONB was 56 years (range=44-81) and 71 years in those with IC (range=52-86). The median of follow-up was 39 months (range=16-120) in those with an IONB and 40 months (range=6-153) in the 33 remaining women with IC. Our data showed that patients with IC had a better physical functioning (higher score means a better functionality) in comparison to those with IONB (75.4±24.0 and 58.2±20.8, respectively; p=0.008) as well in social functioning (80.3±23.7 and 60.0±23.4, respectively; p=0.01). In addition women with IC had fewer symptoms (lower score means a low level of symptomatology/problems), such as nausea and vomiting in comparison with those with IONB (2.5±7.4 and 12.2±16.0, respectively; p=0.008) and also had lower financial difficulties (10.1±17.6 and 31.1±36.7, respectively; p=0.04).

Conclusion: Our study, based on long-term follow-up, showed a better physical and social functioning, less symptoms, such as nausea and vomiting, and reduced financial difficulties patients with IC in comparison with patients undergoing IONB.

Discussion: Patients with IONB have a negative impact on HRQoL in comparison with patients with IC.
Introduction: Nephroureterectomy (NU) is considered the gold standard treatment for invasive and non-metastatic upper tract urothelial carcinoma (UTUC) (1-3). We evaluated the role of age as an independent predictive risk factor of recurrence-free survival (RFS) and cancer-specific survival (CSS) in patients with UTUC who underwent NU or segmental ureterectomy (SU). Patients and Methods: We evaluated 412 patients with UTUC from 2001 to 2013 from 5 urological academic centers. Three hundred and twenty-four (79%) patients underwent NU, while 88/412 (21%) were treated by SU. Clinical and pathological characteristics were analyzed with reference to age (≥70 vs. >70 years), gender (male vs. female), type of surgery (NU vs. SU), pTNM-stage (pT0-pT2 vs. pT3), grading (G0-G2 vs. G3) and synchronous bladder cancer (Yes vs. No). Univariate and multivariate analysis were performed to assess clinical and pathological characteristics as predictors for RFS and CSS by using Cox proportional model (Hazard ratios (HR) and 95% confidence interval (CI)). Results: No significant differences were found between the two types of surgery with reference to male gender (73.5% (38/524) vs. 78.4% (69/88), respectively), mean age (71.4±9.3 vs. 69.6±9.0 years, respectively), mean follow-up (35.4±28.7 vs. 31.9±31.7 months, respectively) and number of recurrences (44.4% (144/324) vs. 44.3% (39/88), respectively). By contrast, we found a higher percentage of mortality in the NU group 28.1% (91/324) vs. SU group 11.4% (10/88) (p=0.001) and in the percentage of cause-specific mortality (14.8% vs. 4.6%, respectively, for NU and SU; p=0.01). At univariate and multivariate analysis, age, pTNM-stage and synchronous bladder cancer were significant predictor risk factors for RFS. The risk for recurrence was as follows: age >70 vs. ≤70 years: 1.49 (95%CI=1.10-2.03), p=0.01; for pT3 vs. pT0-pT2: 1.60 (95%CI=1.18-2.18), p=0.003; and for synchronous bladder cancer yes vs. no: 1.94 (95%CI=1.35-2.79), p=0.003. For CSS at univariate analysis, age, type of surgery, pTNM-stage, grading and synchronous bladder cancer were statistically significant and only 3 of them remained statistically significant at multivariate analysis. The risk for CSS (HR) was: for age >70 vs. ≤70 years: 2.07 (95%CI=1.14-3.77), p=0.02; for pT3 vs. pT0-pT2: 3.13 (95%CI=1.68-5.84), p=0.003; for grading G3 vs. G0-G2: 9.72 (95%CI=2.87-32.95), p=0.003. At 3 years, the probability of RFS was 91% and 81% for ≤70 years vs. >70, respectively. Discussion: NU with bladder cuff removal remains the gold-standard treatment for UTUC but the identification of predictive risk factors remains uncertain yet. Tumor stage and grading are used as predictors of prognosis, while age seems to be associated with a more aggressive kind of UTUC. Conclusion: Age could be an independent predictive factor for RFS and CSS in patients with UTUC.
Δ + of 16.02% compared to lesions located on the bottom (p<0.05) and a Δ of +17.652% compared to lesions located on the both areas (p<0.05). In the 526 lesions (33.46%) highlighted as oncologically significant, only after repeat NBI-TURBT, 509 lesions (32.3%) were lesions that persisted after WL-TURBT (incidence exposed=0.484), while the remaining 17 lesions (1.08%) were lesions that were negative after WL-TURBT; instead, they were oncologically positive (incidence not exposed=0.032). Thanks to the use of repeat NBI-TURBT, we have detected a greater number of LG lesions compared to the ones identified after WL-TURBT: pT1LG identified on the margins of resection (+1.36, p<0.05) and on the bed (+8.77, p<0.05) and pTaLG identified on the bed (+3.43, p>0.05). Conclusion: The use of NBI (repeat NBI-TURBT) offers a clear advantage in identifying persistent lesions after WL-TURBT.

62 CAPACITY OF THE NBI CYSTOSCOPY TO INCREASE THE PREDICTIVE POWER TO IDENTIFY SUSPICIOUS BLADDER LESIONS COMPARED TO THE USE OF THE CYSTOSCOPY IN WHITE LIGHT
Luca Albanesi, Barbara Cristina Gentile, Gabriella Mirabile, Paola Tariciotti, Francesco Pisanti, Giorgio Rizzo, Giorgio Vincenti and Roberto Giuliani
Division of Urology, Nuova Villa Claudia, Rome, Italy

Introduction: Narrow banding imaging (NBI) was developed with the goal of enhancing the definition of small lesions of the bladder that might be missed during white light (WL) endoscopy. The aim of this study was to evaluate, in the same patient before WL transurethral resection of bladder tumour (TURBT), the probability to increase our ability to detect bladder cancer comparing the predictive power NBI visible lesions cystoscopy versus white light visible lesions cystoscopy. Patients and Methods: From June 2010 to April 2012, 797 consecutive patients, 423 male and 374 female, affected by suspected bladder cancer lesions, on the basis of the European Association of Urology (EAU) guidelines 2010, were subjected to WL plus NBI cystoscopy and, subsequently, to WL bipolar Gyrus PlasmaKinetic™ (PK) TURBT. The average of the follow-up was at 24 (range=16-38) months. The mean age was 67.7 years (range=46-88). All patients underwent preoperative white light cystoscopy; topography and characterization of neoplasms and/or suspicious lesions followed by a similar evaluation using NBI. Subsequently, all the patients underwent WL resection (WLTURBT) of the previously identified lesions. All the removed tissue was sent separately for histological evaluation after mapping the areas of resection on a topographic sheet. The follow-up was carried out according to the EAU guidelines on non-muscle invasive bladder tumors. Results: A total of 797 patients were enrolled in this study. In our experience, we observed an overall suspicious bladder lesions detection rate equal to 1,571 bladder lesions. Overall, we identified 234 patients (14.8%) with visible lesions only at NBI light. After the WLTURBT, we observed 1,051 (66.85%) neoplastic lesions of the bladder; among them, 521 (33.14%) were negative. We observed 127 (12.1%) bladder neoplasms in 99 patients (19.8%, p<0.05) with negative WL and positive NBI cystoscopy. The use of WL and NBI cystoscopy allowed us to have a sensibility of 80.66% and of 97.85% with a positive predictive value (PPV) of 68.49% and of 63.74%, respectively. Regarding the accuracy, we observed a rate of 63.74% and of 62.86%, respectively. Staging (carcinoma in situ (CIS), p<0.05), grading (low-grade (LG), p<0.05), focality (unifocal, p<0.05) and dimensions (<3 cm, p<0.05) were statistically significant as well. Statistical Analysis: In carrying out this work, we used the logistic regression model in order to identify the relationships between the structural variables and the ability of the new technique to detect the disease. In order to compare the two diagnostic techniques, we used the indices of sensitivity and specificity of the test; instead, to verify the significance of the results, we used the test of hypothesis Z for the difference in percentages. Finally, we used the index of relative risk. Conclusion: This is the first work in the literature where, in the same patient, the overall capacity of the NBI cystoscopy to increase the predictive power to identify suspicious bladder lesions, compared to the use of the cystoscopy in white light alone, was assessed. After NBI cystoscopy, we observed an overall increased suspicious bladder lesions detection rate by 24.34% (194 patients) and a bladder tumor NBI positive detection rate by 12.1% (99 patients). Overall, the false positive detection rate was 35.75% (285 patients). The combination of white light and NBI cystoscopy and, subsequently, bipolar TURBT seems to offer a better diagnostic and therapeutic approach to bladder tumors, especially in CIS lesions, LG lesions, primitive, unifocals and <3 cm lesions. The high rate of false positives could depend on artefacts produced during white light endoscopy.

63 HOW LONG SHOULD THE FOLLOW-UP BE EXTENDED AFTER SURGERY FOR RENAL CANCER? RETROSPECTIVE ANALYSIS OF A COHORT OF PATIENTS WITH MORE THAN 10 YEARS OF FOLLOW-UP
Alessandro Antonelli, Mario Sodano, Maria Furlan, Giacomo Galvagni, Francesca Carobbio, Alberto Cozzoli, Tiziano Zanotelli and Claudio Simeone
Division of Urology, Spedali Civili di Brescia, Brescia, Italy
**Introduction and Objectives:** There is no agreement in literature on the duration of follow-up after surgery for renal cell carcinoma (RCC). The present study analyzes the oncological outcome in a large cohort of patients followed for at least 10 years. Materials and Methods: A retrospective consultation of a database that stores the data of more than 2,300 consecutive patients submitted to surgery for RCC at a tertiary academic institution, from 1983 to 2013, was used. All patients underwent a tailored follow-up protocol extended for an indefinite period of time. For the present study, the records of patients with M0 RCC, followed for a minimum of 10 years during which no progression of the disease was detected, were retrieved. The rate and features of progression and survival were analyzed. Results: In this study, 554 patients (231 female, 323 male, medium age 59.3±11.6 years) with a M0 RCC, followed for a median follow-up time of 15.1 years (range=11.2-18.1), submitted to partial (131 cases) or radical nephrectomy (423 cases) were included; the mean tumor diameter was 5.1 cm (range=3.0-6.5); the pathological stage was 1 in 386 cases (70.3%), 2 in 53 (9.7%), 3 in 104 (18.9%) and 4 in 6 (1.1%); the grading was 1 in 85 (16.1%), 2 in 301 (56.9%), 3 in 113 (21.4%) and 4 in 30 (5.7%); histology was consistent with clear cell RCC cell in 477 cases (86.1%), papillary in 40 (7.2%), chromophobe in 27 (4.9%), other in 9 (1.6%). The cancer-specific survival was 98.2% and 96.0% at 15 and 20 years, respectively. A progression was observed in 29 patients (5.2%) after a median time of 161 months (range=132-172) from surgery. The sites of progression were: the contralateral kidney in 10 cases (1.8%), lung in 5 (0.9%), bone in 1 (0.2%), liver in 1 (0.2%), some other atypical sites in 5 (0.9%), multiple sites in 4 (0.7%), a local relapse in 3 cases (0.6%). Through a logistic regression analysis, it was found that the pathological stage was the only independent factor related to progression. Conclusion: The risk of progression after surgery for RCC after ten years of negative follow-up is around 5%, related to pathological stage, while the most frequent sites involved are the contralateral kidney and the lung.

**Aim:** To evaluate the prognostic role of venous tumor thrombus consistency (VTCC) in patients with renal cell carcinoma. Materials and Methods: A retrospective evaluation of the data of patients with renal cancer and a tumor thrombosis submitted to surgery from 2000 to 2013 was performed. Histological slides were revised by two uropathologists, blinded of the clinical outcome, to assess VTCC classified as solid (sVTCC) or friable (fVTCC). The statistical correlation between VTCC and other adverse features was assessed. Then, the predictive ability of an integrated prognostic model, generated by Cox regression and random survival forests, was evaluated, with and without the inclusion of VTCC, by integrated Brier score, dynamic receiver operating characteristic (ROC) curves, integrated discrimination improvement index and category-less net reclassification index. Results: The data of 147 patients were analyzed: 79 with a sVTCC and 68 with a fVTCC, followed for a median period of 40.5 months. VTCC was assessed with a high interobserver agreement (145/147 cases). The presence of a fVTCC was associated with some adverse prognostic factors (symptoms, lymph nodal and distant metastasis, larger tumor diameter, higher cephalad thrombosis level, necrosis, microvascular invasion) and to a worse cancer-specific and overall survival at univariate analysis. However, VTCC was not predictive of survival and did not improve the performance of a multivariable model that included a set of informative predictors. Conclusion: Even if VTCC is associated with some other adverse prognostic factors, its independent prognostic role is not evident.

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**THE QUALITY OF LIFE OF MEN BEFORE, DURING AND AFTER ACTIVE SURVEILLANCE**

Claudia Repetto1, Silvia Villa1, Nice Bedini2, Davide Biasoni3, Massimo Maffezzini3, Cristina Marenghi1, Sara Morlino3, Tiziana Rancati3, Tullio Torelli3, Sergio Villa2, Roberto Salvioni2, Tiziana Magnani1, Riccardo Valdagni1,2 and Lara Bellardita12

1Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Departments of 2Radiation Oncology 1 and 3Urology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

*equally contributed to the manuscript

**Introduction:** An important issue addressed by the scientific community is the investigation of the health-related quality of life (HRQoL) in patients with localized prostate cancer (PCa) who opted for active surveillance (AS). The level of HRQoL during AS sometimes was called into question; however,
several studies highlighted that most of patients on AS did not experience a decrease of psychological well-being (1). The goal of the present study was to monitor HRQoL over time for those patients who, after being enrolled in AS for either clinical or personal reasons, switched to an active treatment.

Patients and Methods: Forty-three patients who discontinued the AS protocols were enrolled in the present study. All of them received by regular mail or e-mail (according to individual preferences) the questionnaire assessing HRQoL together with forms collecting clinical information about treatment, drugs and tests run after exiting AS. Furthermore, they previously had accepted to participate in an ancillary HRQoL study and, thus, they had undergone an initial assessment of HRQoL at enrollment in AS and after a 10-months period from diagnostic biopsy, about 2 months before the first re-biopsy. Therefore, data on HRQoL were collected at three time points. HRQoL was measured by the Functional Assessment of Cancer Therapy scale - Prostate Version (FACT-P). In order to detect changes over time, Friedman non-parametric tests were conducted for each of the FACT-P subscales: functional well-being (FWB), emotional well-being (EWB), prostate cancer symptoms (PCS), physical well-being (PWB), social well-being (SWB).

Results: The mean age of the study population was 71±6.58 years (range=57-81). Table I illustrates descriptive normalized scores for FACT-P at the enrolment (T0), after 10 months from the diagnostic biopsy (T1) and after the discontinuation of the AS protocol (T2).

The results showed that:
– Prostate cancer symptoms (PCS) decreased in T2 with respect to T0 and T1 (F2,84=4.74; p=0.011);
– Physical well-being (PWB) changed over time, and in particular it was lower after AS discontinuation compared to T0 and T1 (F2,84=5.14; p=0.08);
– Social well-being (SWB) was lower in T2 compared to T0 but not to T1 (F2,82=3.41; p=0.038).

FWB and EWB did not show any change over time.

Discussion and Conclusion: The present study illustrates how the different dimensions of HRQoL change over time considering three time points very important for patients who chose AS and then discontinued the observational approach switching to an active treatment: the enrolment in AS protocol, the period preceding the first biopsy and after the discontinuation of the AS protocol. According to the present findings, changes have been detected with respect to the physical and social well-being and the treatment symptoms, which appear affected after exiting AS compared to the previous time points. This result makes sense if we take into consideration that all patients in T2 had already undergone an active treatment and possibly they bear the related side effects. In conclusion, the present study suggests that, in PCa, patients who opted for AS and then switched to an active treatment, the critical point, potentially harmful for at least some dimensions of HRQoL, is the period after the discontinuation of the AS protocol. This result suggests that these patients may need clinical and psychological support to overcome physical impairments and social issues in order to help them find a new and integrated psychophysical balance. Acknowledgements to Foundations I. Monzino.

1 Van Den Bergh et al., Curr Opin Urol, 2012.

67 CAN DAILY INTAKE OF ASPIRIN AND/OR STATINS INFLUENCE THE BEHAVIOR OF NON-MUSCLE-INVASIVE BLADDER CANCER? A RETROSPECTIVE STUDY ON A LARGE COHORT OF PATIENTS UNDERGOING TRANSURETHRAL BLADDER RESECTION

Antonio Luigi Pastore, Giovanni Palleschi, Andrea Fuschì, Andrea Ripoli, Luigi Silvestri, Antonino Leto, Samer Al Rawashdah and Antonio Carbone

Department of Medico-Surgical Sciences and Biotechnologies, Urology Unit, Sapienza University of Rome, Faculty of Pharmacy and Medicine, Latina, Italy
**Aim:** This study aimed to evaluate the behavior of non-muscle-invasive bladder cancer (NMIBC) in patients submitted to transurethral bladder resection (TURB) comparing subjects in chronic therapy with aspirin, statins or both drugs to untreated ones. **Patients and Methods:** This retrospective study was conducted on 574 patients diagnosed with NMIBC who underwent TURB between March 2008 and April 2013. The study population was divided into two main groups: treated (aspirin and/or statins) and untreated. The treated group was further divided into three therapeutic subgroups: Group A (100 mg of aspirin, daily for at least two years); Group B (20 mg or more of statins, daily for at least two years); and Group C (100 mg of aspirin and 20 mg of statins together). The mean follow-up of patients was 45.06 months. **Results:** No significant differences were observed among the different groups at baseline. On multivariate analysis, statin treatment, smokers and high-stage disease (T1) achieved the level of independent risk factor for the occurrence of a recurrence. When patients were stratified according to the different treatment, patients treated with statins (Group B) presented an higher rate of failure (56/91 patients; 61.5%) when compared to Group A (42/98 patients; 42.9%), Group C (56/98; 57.1%) and (133/287 patients; 46.3%). This difference corresponds to a significant difference in recurrence failure-free survival (p=0.01; Figure 1). **Conclusion:** Our results suggest that long-term treatment with aspirin in patients with NMIBC might play a role in reducing the risk of tumor recurrence. In contrast, in our investigation data from statins and combination treatment groups showed increased recurrence rates. A long-term randomized prospective study could definitively assess the possible role of this widely used drug in NMIBC.

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**68 ARE EARLY CONTINENCE RECOVERY AND ONCOLOGICAL OUTCOMES BIASED BY THE USE OF DIFFERENT DEVICES IN PROSTATIC APEX DISSECTION DURING LAPAROSCOPIC RADICAL PROSTATECTOMY?**
Background/Aim: Prostate cancer treatment has considerably evolved over the last decade, with new surgical devices that can achieve better oncologic and functional outcomes. Although monopolar scissors (MS) are still widely used, radiofrequency (RF) and ultrasound scalpels (US) have been introduced for use during laparoscopic radical prostatectomy (LRP). Despite the widespread use of these scalpels in LRP, there are only a few studies comparing the impact of these devices on oncologic and functional outcomes. Here, we aimed to compare the effect of MS, RF and US on urinary continence recovery and positive margins in patients undergoing extraperitoneal LRP (ELRP). Patients and Methods: In total, 150 men were prospectively enrolled during the period between September 2009 and April 2013. The patients were randomly assigned to one of 3 groups according to the use of MS, RF or US and underwent ELRP. The postoperative evaluation of continence was performed for all patients. Results: No differences in operative times, blood loss or apical margin positivity were observed between the groups. Moreover, differences were not observed among the patient groups during functional outcome evaluations (International Consultation on Incontinence self-administered Questionnaire scores) at 1, 3 and 6 months after surgery. The use of RF or US or the use of cold-blade scissors yielded similar results with respect to operative time, blood loss and postoperative hospital stays; shorter catheterization times were found in the patients in the RF group. Discussion: The purpose of the current study was to analyse the effects of different devices, used during similar surgical procedures, on the recovery of continence after surgery and positive surgical margins after ELRP. The results of the present study showed that the use of RF, US and MS were similar with respect to operative time, blood loss and postoperative hospital stay; however, a shorter catheterization time was observed in the patients for whom RF was used. Blood loss during the apex approach, using these different devices, was minimal compared with the open approach and transfusions were rarely needed. In addition, in our case series, continence recovery was achieved by 71.7% of patients within 3 months of surgery and this value reached 94.7% within 6 months. Conclusion: This study represents the first evaluation of continence recovery following LRP performed using different devices for prostatic apex dissection. The oncologic, functional and operative outcomes were similar among the patients undergoing LRP with the different devices, thus confirming their efficacy and safety.

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PURE INTRACORPOREAL LAPAROSCOPIC RADICAL CYSTECTOMY WITH ORTHOTOPIC "U"-SHAPE ILEAL NEOBLADDER
Antonio Luigi Pastore, Giovanni Palleschi, Andrea Ripoli, Luigi Silvestri, Andrea Fuschi, Antonino Leto, Vincenzo Petrozza and Antonio Carbone

1Department of Medico-Surgical Sciences and Biotechnologies, Urology Unit, Sapienza University of Rome, Faculty of Pharmacy and Medicine, Latina, Italy; 2Department of Medico-Surgical Sciences and Biotechnologies, Pathology Unit, Sapienza University of Rome, Faculty of Pharmacy and Medicine, Latina, Italy; 3Department of Medico-Surgical Sciences and Biotechnologies, Pathology Unit, Sapienza University of Rome, Faculty of Pharmacy and Medicine, Latina, Italy

Background/Aim: Radical cystectomy with pelvic lymph node dissection represents the standard treatment for muscle-invasive and high-risk non-muscle-invasive bladder cancers. The aim of this study was to report our case series of 30 patients undergoing totally laparoscopic radical cystectomy (LRC) with reconstruction of an intracorporeal orthotopic ileal neobladder. Intra- and perioperative results, as well as the functional and oncological outcomes 9 months after operation are reported. Patients and Methods: Between October 2010 and December 2012, 30 male patients underwent LRC with a pure laparoscopic orthotopic ileal "U"-shaped neobladder diversion (Figure 1). The men had a median age of 67 years, a median body mass index of 22.3 and a mean American Society of Anesthesiologists (ASA) score of 2.2; they represented various clinical stages of disease. Results: None of the patients required conversion to open surgery and no perioperative mortalities were reported. The median operating time was 365 min and the median blood loss was 290 ml, with a transfusion rate of 26.6%. All surgical margins were negative; 8 patients with non-organ-confined disease or positive lymph nodes received adjuvant chemotherapy. Early complications (within 30 days) occurred in 7 patients, while late complications occurred in 6 patients. The mean hospital stay was 9 days. At 9 months after surgery, the daytime continence rate was 83.3% and the nighttime continence rate was 73.3%. Conclusion: Pure LRC with intracorporeal orthotopic ileal neobladder reconstruction may represent a viable alternative to open radical cystectomy with a significant reduction in patient morbidity. Future, large, randomized controlled trials with extensive follow-up are needed to confirm our encouraging results.
IMPACT ON POST-OPERATIVE SURVIVAL OF THE STATUS OF DISTAL URETERAL MARGIN. IS IT NECESSARY TO ACHIEVE A NEGATIVE MARGIN AT THE TIME OF RADICAL CYSTECTOMY?

Marco Moschini1,2, Stefano Luzzago1, Giorgio Gandaglia1, Vito Cucchiara1, Marco Bianchi1, Andrea Salonia1, R. Jeffrey Karnes2, Rocco Damiano3, Shahrokh Shariat4, Alberto Briganti1, Francesco Montorsi1, Renzo Colombo1

1Department of Oncology and Urology, Irccs Ospedale San Raffaele, Università Vita-Salute San Raffaele, Milan, Italy; 2Department of Urology, Mayo Clinic, Rochester, MN, U.S.A.; 3Department of Urology, Magna Graecia University of Catanzaro, Catanzaro, Italy; 4Department of Urology, Comprehensive Cancer Center, Medical University of Vienna, Vienna General Hospital, Vienna, Austria

Background: Despite several studies, the adequate management of positive distal ureter margin at the time of radical cystectomy (RC) remains controversial. Particularly, it is not clear whether the achievement of negative distal ureter margin at the intra-operative frozen sections impact on both post-operative cancer specific (CSS) and overall survival (OS). Materials and Methods: Overall, 1,517 consecutive patients treated with RC for bladder cancer (BCa) at a single center between January 1990 and August 2013 were considered. Complete clinical, pathological and follow-up data were available for all patients. Intraoperative frozen section (IFS) results of the distal ureteral margin were recorded in details. Specifically, pathological result of first section, number of section and pathological result of the last section. Patients were divided in 3 categories: negative at IFS, positive at IFS and converted to a negative final margin and positive at IFS not converted to negative at final pathology. Overall mortality (OM), cancer-specific mortality (CSM) and recurrence-free survival (RFS) were analyzed by Kaplan-Meyer estimation. Univariable (UVA) and multivariable (MVA) Cox regression analyses were used to test the impact of positive distal ureteral margin on overall (OM) and cancer-specific (CSM) mortality, after adjusting for age, gender, positive soft tissue surgical margin (STSM), lymph node invasion (LNI) and pathological stage. Results: Mean patient age was 67 years. At IFS, 444 patients (29%) experienced at least one positive margin. Of these, a negative margin at final pathology could be achieved in 254 (57%), while in 190 (43%) a positive ureteral margin was found at final pathology. The mean follow-up was 95 months (median=102). At UVA Cox regression analyses, patients,
where a negative ureteral margin was not achieved after an initially positive IFS, experienced a higher risk of disease recurrence (hazard ratio (HR)=1.53, confidence interval (CI)=1.07-2.17, p=0.02). CSM (HR=1.70, CI=1.18-2.41, p=0.004) and OM (HR=1.64; CI=1.19-2.26 p=0.002). At MVA, patients not converted to negative ureteral margin (HR=1.52, p=0.04), age (HR=1.04, p=0.002), pT3-pT4 (HR=2.47, p=0.001) were associated with a detrimental effect on CSM; however, gender, LNI and positive STSM did not (all p>0.1). Conclusion: Patients with positive ureteral margin at IFS during RC, where a negative margin was not achieved, are at higher risk of dying of BCa. Further studies are needed to reconsider this parameter in survival analyses.

71 IMPACT OF THE SITE OF RECURRENCE AFTER RADICAL CYSTECTOMY ON SURVIVAL: DIFFERENT SITES FOR DIFFERENT OUTCOMES

Marco Moschini, Stefano Luzzago, Giorgio Gandaglia, Vito Cucchiara, Marco Bianchi, Walter Cazzaniga, Andrea Salonia, Alberto Briganti, Francesco Montorsi and Renzo Colombo

Department of Oncology and Urology, Ircos Ospedale San Raffaele, Università Vita-Salute San Raffaele, Milan, Italy

Objectives: The recurrence of urothelial cancer after radical cystectomy (RC) for bladder cancer (BCa) associates with a reduced survival during follow-up. However, data about different patterns of recurrence is limited in the literature and the impact of the site of the first recurrence on cancer-specific mortality (CSM) still remains to be defined. Patients and Methods: The study included 1,250 consecutive BCa patients treated with RC at a single tertiary care institution between January 1990 and August 2013; all with recurrence information available. Complete clinical, pathological and follow-up data were available for all the patients. Moreover, status, timing, as well as site of first recurrence, were available for all patients. Kaplan-Meier curves assessed the time to recurrence and time to survival after first recurrence. Logistic regression analyses were performed in order to assess characteristics related to dead within 3 months and beyond 12 months after first recurrence. Results: With a mean follow-up of 106 months (median=88), recurrences were recorded for 416 patients (33.2%). Of these, 11 patients experienced brain recurrence (2.6%), 63 liver recurrence (15.1%), 61 nodes recurrence (14.7%), 66 bone recurrence (15.9%), 30 pelvic recurrence (7.2%), 19 peritoneal recurrence (4.6%), 81 lung recurrence (19.5%), 16 ureter recurrence (3.8%), 17 urethral recurrence (4.1%) and 52 (12.5%) patients have unknown site of recurrence. The mean survival after recurrence was 10 months (median, interquartile range (IQR)). Specifically, brain recurrence has a CSM at 3, 6 and 12 months of 45, 36 and 9%, liver of 74, 53 and 32%, lung of 70, 59 and 34%, bone 82, 51 and 23%, pelvic of 78, 33 and 12%, nodal of 93, 76 and 48%, peritoneal 47%, 27% and 9%, ureteral 92, 83, 72% and urethral 100, 91 and 51%. Patients with peritoneal or brain recurrence had the highest rate of death within 3 months after recurrence (p=0.02 and 0.04, respectively vs. other recurrences). Conversely, patients with nodal and ureteral recurrence had the highest chance of surviving for 12 or more months (p=0.01 and 0.004, respectively vs. other recurrences). Conclusion: Based on the results of our monocentric series, BCa-specific mortality times vary according to the site of first disease recurrence after RC. This information might be helpful to physicians in order to adopt different therapeutic and palliative strategies for patients according to the site of recurrence.

72 VIDEOURODYNAMIC EVALUATION OF INTRACORPOREALY RECONSTRUCTED ORTHOTOPIC U-SHAPED ILEAL NEOBLADERS

Giovanni Pallechi1, Antonio Luigi Pastore1, Andrea Fuschi1, Andrea Ripoli1, Luigi Silvestri1, Antonino Leto1, Samer Al Rawashdah2 and Antonio Carbone1

1Department of Medico-Surgical Sciences and Biotechnologies, Urology Unit, Sapienza University of Rome, Faculty of Pharmacy and Medicine, Latina, Italy; 2Department of Medico-Surgical Sciences and Biotechnologies, Pathology Unit, Sapienza University of Rome, Faculty of Pharmacy and Medicine, Latina, Italy

Objective: To study the functional outcomes of 30 patients who had previously undergone laparoscopic radical cystectomy (LRC) with intracorporeal orthotopic ileal neobladder reconstruction using videourodynamic (VUDM) assessment 180 days post-operatively. Patients and Methods: Between November 2010 and December 2013, 30 male patients had undergone LRC with bilateral standard pelvic lymphadenectomy and pure laparoscopic orthotopic ileal U-shaped neobladder diversion. The demographic data were: median age, 67 years (range=62-79); body mass index (BMI), 22.3 (range=16-26.1); and mean American Society of Anaesthesiologists (ASA) score, 2.2 (range=1-3). Functional outcomes were assessed performing a standard VUDM study combined with perineal floor electromyography 180 days post-operatively. Results: Videourodynamic evaluations showed good functional outcomes of the reservoirs. Mean maximal neobladder capacity was 287 ml (range=210-335). Residual peristaltic activity was observed in all the individuals evaluated; however, only 9/30 (30%) individuals displayed severe peristaltic activity. Six of these nine
Individuals experienced urinary leakage during these contractions. Mean post-void residual volume was 44 ml (range=0-105), and peak flow rate was 13.9 ml/s (range=9.7-29.2). The Valsalva manoeuvre was positive in 5/30 (17%) subjects. Bladder morphology assessed during contrast cystography showed the desired U-shape in all cases (Figure 1). Ureteral reflux was observed in 7/30 (23.3%) of individuals. Conclusion: Based on VUDM, our study shows that U-shaped ileal neobladders achieved by a totally laparoscopic approach obtained good functional outcomes. These findings support the evidence that a minimally invasive approach does not impose technical limitations that negatively impact the surgical results.

Impact and Reliability of CN+ in Bladder Cancer Population That Underwent Radical Cystectomy

Marco Moschini1,2, Sia Daneshmand3, Stefano Luzzago1, Giorgio Gandaglia1, Gus Miranda3, Brian Hu3, Nazareno Suardi1, Andrea Salonia1, R. Jeffrey Karnes2, Rocco Damiano4, Shahrokh Shariat5, Alberto Briganti1, Francesco Montorsi1 and Renzo Colombo1

1Department of Oncology and Urology, Ircs Ospedale San Raffaele, Università Vita-Salute San Raffaele, Milan, Italy; 2Department of Urology, Mayo Clinic, Rochester, MN, U.S.A.; 3USC Institute of Urology, USC/Norris Comprehensive Cancer Center, Los Angeles, CA, U.S.A.; 4Department of Urology, Magna Graecia University of Catanzaro, Catanzaro, Italy; 5Department of Urology, Comprehensive Cancer Center, Medical University of Vienna, Vienna General Hospital, Vienna, Austria

Introduction and Objectives: The literature about the impact and the reliability of clinical N+ in the context of radical cystectomy (RC) due to bladder cancer is scarce. Under this light, we presented the first work trying to assess concordance between clinical and pathological N status and to calculate how these parameter could impact on survival. Patients and Methods: Overall, 3,966 consecutive radical cystectomy (RC) patients at three centers (Milan-HSR, Mayo Clinic, and USC) between January 1980 and December 2013 were identified. Clinical N+ are defined according to European guidelines as pelvic nodes >8 mm or abdominal nodes >10 mm in maximum short-axis diameter detected by computed tomography (CT) or magnetic resonance imaging (MRI). Independent-sample t-test and chi-square test were used for...
comparison of means and proportions, respectively. Kaplan-Meyer estimates were used to assess cancer-specific mortality (CSM) and overall mortality (OM) after RC. Univariable (UVA) Cox regression analyses were performed for prediction of CSM and OM for all available variables. Results: Mean age at RC was 67 years. Considering clinical N status, 413 (10.4%) patients were considered clinical N+. The mean number of nodes removed and the number of positive nodes were 31 vs. 28 (p=0.2) and 1.15 vs. 5.5 for patients cN- and cN+ (p<0.001), respectively. Overall, 129 patients with clinical N+ did not experience lymph node invasion (LNI) while 725 patients were found with pathological node metastases although not detected at preoperative imaging. Sensitivity, in the detection of pN+, was 24% and specificity 90%. Although the low sensitivity, patients with clinical N+ were more likely to experienced LNI, worst pathological stage and positive surgical margin (all p<0.001); nevertheless, patients with cN+ experienced higher neoadjuvant chemotherapy rate (31.4% vs. 5.5%, p<0.001) in comparison to patients with cN-. With a mean follow-up time of 126 months (interquartile range=122-130), the 5- and 10-year CSM were 79% and 70% vs. 65% and 65% vs. 37% and 32% vs. 32% and 32% for patients that were cN0pN0 vs. cN+ pN0 vs. cN0pN+ vs. cN+pN+, respectively (p<0.001, Figure 1). Considering the LNI population, at univariable analyses, patients who experienced clinical N+ status were more likely to succumb to bladder cancer (hazard ratio (HR)=1.29, confidence interval (CI)=1.05-1.59; p=0.02). Conclusion: Our study confirms the low sensibility of N staging in a large population; however, cN+ is strongly related to several predictors of adverse outcomes and to a worst survival when considering only the LNI population.

Figure 1. (Abstract 73).
completed the prescribed radiotherapy, without major interruption due to acute toxicity. The evaluable patients were 86. Six patients were lost at follow-up. With an average follow-up of 27.6 months (range=19-48), the severe (≥G3) acute toxicity was the following: genito-urinary 5.8% (5 patients), gastro-intestinal 1.2% (1 patient). The severe late toxicity (≥G3) was: genito-urinary 1.2% (1 patient), gastro-intestinal 4.6% (4 patients). At last follow-up, 25 patients are still receiving ADT. Eight percent of patients (7) had a progression disease in nodes or bone sites. One patient died due to progression disease. The biochemical disease-free survival was 92%. Conclusion: Pelvic radiotherapy was well-tolerated considering delivered doses and irradiated volumes with a limited severe acute and late toxicity and a good disease control. Currently, the clinical result is very good considering the stage of patients included in the study; however, further follow-up is necessary to evaluate biochemical disease-free survival and late toxicity. This paper was supported by the grant 5%1000 (2008-2009) of the Financial Ministry of the Italian Republic.

TOWARDS THE MULTIDISCIPLINARY MANAGEMENT OF PROSTATE CANCER PATIENTS: THE PERSTEP PROJECT EXPERIENCE


1Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milano, Italy; 2Medical Oncology, Azienda Ospedaliera Giovanni XXIII, Bergamo, Italy; 3Medical Oncology, Ospedale Di Bolzano, Bolzano, Italy; 4Medical Oncology, Azienda Ospedaliero Universitaria Careggi, Firenze, Italy; 5Medical Oncology, Azienda Ospedaliera Treviglio E Caravaggio, Treviglio, Italy; 6Medical Oncology, Università Cattolica Del Sacro Cuore, Policlinico Universitario A. Gemelli, Rome, Italy; 7Urology, Università Cattolica Del Sacro Cuore, Policlinico Universitario A. Gemelli, Rome, Italy; 8Medical Oncology, IRCCS Istituto Oncologico Veneto, Padova, Italy; 9Urology, Azienda Ospedaliera " Ospedali Riuniti Marche Nord", Fano, Italy; 10Prostate Cancer Unit, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milano, Italy; 11Urology, Azienda USL 1, Sanremo, Italy; 12Clinic Scientific Director’s office, Istituto Clinico Humanitas Gavazzeni, Bergamo, Italy; 13Radiotherapy, CRO-Istituto Nazionale Tumori, Aviano, Italy; 14Medical Oncology, Ospedale San Donato, Arezzo, Italy; 15Medical Oncology, Ospedale Bellaria, Bologna, Italy; 16Urology, Ospedale Bellaria, Bologna, Italy; 17Radiotherapy, Azienda Ospedaliera " Ospedali Riuniti Marche Nord", Fano, Italy; 18Medical Oncology, Ospedale Santa Chiara, Trento, Italy; 19Radiotherapy, Ospedale Sant’Anna, Como, Italy; 20Radiotherapy, Azienda Ospedaliera Giovanni XXIII, Bergamo, Italy; 21Medical Oncology, Istituto Clinico Humanitas Gavazzeni, Bergamo, Italy; 22Medical Oncology, Ospedale Civile, Desenzano, Italy; 23Radiotherapy, IRCCS Istituto Oncologico Veneto, Padua, Italy; 24Radiotherapy, Istituto Clinico Humanitas, Rozzano, Italy; 25Urology, Azienda Ospedaliera Giovanni XXIII, Bergamo, Italy; 26Medical Oncology, Ospedale Civile, Desenzano, Italy; 27Radiotherapy, Policlinico Vittorio Emanuele, Catania, Italy; 28Urology, Ospedale Santa Chiara, Trento, Italy; 29Medical Oncology, Istituto Nazionale Tumori, Milan, Italy;
The multidisciplinary management is acknowledged as the best approach towards cancer patients. The experience and knowledge of multiple specialists have also become fundamental in the care of prostate cancer (PC) patients who, depending on the state, can be addressed to surgery, radiotherapy, brachytherapy, hormonal therapy, chemotherapy, active surveillance and watchful waiting. The interaction of urologists, radiation oncologists, medical oncologists, pathologists, psychologists, imaging specialists, as well as physiotherapists, geriatricians and nurses, enables to put the patients at the center of the path of care, offer them objective, not contradictory information on one’s options, reduce the number of consultations and favour individualized proposals. On this assumption, the Italian Society for Urologic Oncology (SIUrO) and the Board of Medical Oncology Directors (CIPOMO) decided to support PerSTEP, an educational project aimed to promote the cultural and organizational switch to multidisciplinarity and multiprofessionality in Italy. Started with a phase 1 in 2012, a phase 2 was opened in June 2013 following the requests to participate received from 23 centers (Table I).

Table I. Centers participating in PerSTEP.

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<thead>
<tr>
<th>City</th>
<th>Hospital</th>
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<tr>
<td>Arezzo</td>
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<td>Aviano</td>
<td>CRO-IRCCS Istituto Nazionale Tumori</td>
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<td>Bergamo</td>
<td>Istituto Humanitas</td>
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<td>Candiolo</td>
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<td>Catania</td>
<td>Policlinico Vittorio Emanuele</td>
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<td>Como</td>
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<td>Cosenza</td>
<td>Ospedale Ospedaliero Mariano Santo</td>
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<td>Desenzano</td>
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<td>Fano</td>
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<td>Firenze</td>
<td>Azienda Ospedaliera Universitaria Careggi</td>
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<td>Milano</td>
<td>Fondazione IRCCS Istituto Nazionale dei Tumori</td>
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<tr>
<td>Napoli</td>
<td>Istituto Nazionale Tumori</td>
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<tr>
<td>Padova</td>
<td>Clinica Urologica, Università - IRCCS Istituto Oncologico Veneto</td>
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<tr>
<td>Ravenna</td>
<td>Ospedale Civile Santa Maria delle Croci</td>
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<tr>
<td>Roma</td>
<td>Università Cattolica del Sacro Cuore, Policlinico Universitario A. Gemelli</td>
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<td>Rozzano</td>
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<td>Sanremo</td>
<td>Azienda USL 1</td>
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<td>Trento</td>
<td>Ospedale Santa Chiara</td>
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<td>Treviglio</td>
<td>Azienda Ospedaliera Treviglio e Caravaggio</td>
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Summary of the activities accomplished within PerSTEP: 1. Collection of information on the centers’ organizational models and personnel involved in the care of PC patients; 2.
Meetings with the centers; 3. Communication through newsletter and press releases.

The collection of information enabled to have a detailed picture of the working models applied by the centers, which pointed to a rather multivariate situation. In fact, some centers were already organized according to formalized multidisciplinary models, others enjoyed good collaboration and relations among specialists, others worked in monodisciplinary setting and requested specialist consultations occasionally. The multifaceted scenario was stimulus to the centers already organized multidisciplinarily to improve their organizational models and to the centers working in a monodisciplinary setting to start the reorganizational process. The meetings with the centers allowed to share information and experiences of the individual centers, as well as published in the literature and trace minimal requirements to favour the switch to multidisciplinarity: 1. involvement of the Directors (general, scientific, administrative, depending on the center) to have the support in the organizational process, 2. involvement of the Directors of the specialties involved in the path of care to have the support in the organizational process and in the team building, 3. identification of a team leader within the multidisciplinary team, 4. adoption of evidence-based guidelines and elaboration of paths of care, 5. evaluation of the possible multidisciplinary activities to be implemented (i.e. multidisciplinary clinics, case discussions/tumor boards) and the different modalities (i.e. for multidisciplinary clinics synchronic vs. in sequence interaction; for case discussions: vis à vis virtual meetings), based on the personnel available and the time that can dedicate to the tasks, 6. activation of case discussions/tumor boards as starting point of the reorganization process.

The meetings were also the occasion to share problems encountered by the centers, such as: 1. resistance towards the multidisciplinary management of patients, 2. not univocal interpretation of guidelines, 3. no formalized collaboration to overcome the unavailability of a particular specialty, 4. unavailability of contractual time to attend multidisciplinary activities.

The communication plan enabled to promote sensibilization actions on the importance of the multidisciplinary approach and include new centers.

Last updated December 2014, PerSTEP produced marvelous results, such as: 1. good interaction among centers, 2. formalization and update of 6 PC Units, 3. constitution of 7 new multidisciplinary teams, 4. activation of 10 tumor boards.

Further effort is, nevertheless, needed to support the cultural and organizational change towards a multidisciplinary and multiprofessional management of PC patients.

A special thank to SANOFI for supporting the communication plan.

### 76 RALP CAN REDUCE THE RATE OF POSITIVE SURGICAL MARGIN: COMPARISON WITH OPEN PROSTATECTOMY IN A MEDIUM VOLUME CENTER

**Alessandro Antonelli, Mario Sodano, Irene Mittino, Maria Furlan, Angelo Peroni and Claudio Simeone**

Division of Urology, Spedali Civili Di Brescia, Brescia, Italy

**Aim:** To analyze the risk of positive margins (PSM) after radical prostatectomy in patients undergoing robotic surgery (robotic assisted laparoscopic prostatectomy (RALP)) compared with those undergoing open surgery (open retropubic prostatectomy (ORP)).

**Materials and Methods:** Consultation of an institutional database that, since 2008, stores the data of 661 patients submitted to prostatectomy. The patients who had neoadjuvant hormonal therapy (66 patients) or without complete information about margin status (19) were excluded. A univariable and multivariable logistic regression was performed to evaluate the factors related to PSM. **Results:** Five hundred and seventy-six patients were included in the study, 285 OP and 291 RALP. The characteristics of the patients are described in Table I. The PSM overall rate was 28.1% (162/414 patients (pts)); 20.6% in pT2 cases, 51.8% in >pT2; PSM rate for OP vs. RALP was 31.9% vs. 24.4 % (p=0.044). The factors that showed a correlation with the a PSM were: stage pT3a (relative risk (RR)=4.149, p=0.001); Gleason score ≥7 (RR=2.863, p=0.001); volume of cancer as percentage of prostate volume (RR=1.031, p=0.001); surgical approach (RALP vs. OP, RR=0.688, p=0.045); nerve sparing procedure (RR=0.641, p=0.019). At multivariable analysis, maintained a significant correlation with the risk of PSM the presence of extra capsular tumor (RR=2.979, p=0.001); Gleason score ≥7 (RR=1.662, p=0.026); volume of cancer (RR=1.019, p=0.008) and surgical technique (RALP vs. OP, RR=0.647, p=0.039). **Conclusion:** The RALP is emerging on the OP, thanks to a proven advantage in the post-operative course and the possible benefits on the recovery of continence and erectile functions. The oncological outcome of the two techniques is considered as equivalent, although some studies suggest a lower PSM rate for RALP. This study evaluates a medium case-load institution and compares an initial experience of RALP, performed by surgeons without previous experience of prostatectomy, with a series of OP performed by experienced surgeons. Our analysis shows that the risk of PSM is lower for RALP, also adjusting the data for local staging, tumor volume and the final Gleason score that proved to be independent predictive factors for PSM. In conclusion, RALP allows a lower rate of PSM compared to OP, also in an initial experience and with naive surgeons.
A NEW PROPOSAL FOR T1 HIGH-GRADE BLADDER CANCER MICRO-STAGING DEFINITION

Rodolfo Hurle1, Carlo Patriarca2, Luisa Pasini1, Pier Giuseppe Colombo3, Luigi Castaldo1, Marco Moschini4, Lucia Ferrari2, Massimo Maffezzini5, Maurizio Colecchia6, Tiziana Magnani7, Massimo Freschi8, Paolo Capogrosso4, Giario Conti9 and Renzo Colombo4

Departments of 1Urology and 3Pathology, Istituto Clinico Humanitas, Rozzano, Milan, Italy; Departments of 2Pathology and 4Urology, Ospedale Sant’Anna, Como, Italy; Departments of 6Urology and 8Pathology, Ospedale San Raffaele, Milan, Italy; Departments of 4Urology and 9Pathology, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy; 7Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy

Introduction and Objectives: The oncological outcome of T1, high-grade urothelial bladder carcinoma cannot yet be adequately estimated and its management in routine practice remains controversial. Histological T1 sub-staging has been advocated as a potential prognostic factor for many years. However, it is only rarely reported by pathologists and the related clinical impact is still under debate. The absence of a well standardized reporting method, the consistent interobserver variability and the absence of a definitive clinical validation configure some of major limiting factors to the spreading of T1 sub-staging in routine practice. This study was aimed to assess both feasibility and prognostic reliability of a novel procedure (ROL) for the assessment of the T1 sub-staging. In addition, the prognostic impact of this method was compared to that of other sub-staging methods already proposed and clinically tested. Materials and Methods: The ROL sub-staging was defined as ROL 1: <1 power field (PF) (20x) corresponding to 1mm/field diameter of lamina propria thickness invasion and as ROL 2: >1 PF (20x) or multifocality sizing more than 1mm/field diameter of lamina propria invasion. Multiple slides of a series of consecutive patients with T1, high-grade (according to the 2004-WHO classification system) urothelial bladder carcinoma at initial transurethral resection (TUR) were revisited by uropathologists of four different centers for both staging confirmation and sub-staging assessment. Both feasibility and prognostic reliability of the ROL method were compared to those of T1a/T1b,c subdivision (tumor front not passing through the muscularis mucosae vs. tumor front over the muscularis mucosae) and T1m/T1e subdivision (<1 high-power field (HPF) 40x corresponding to 0.5 mm/field diameter of invasion thickness vs. >1 HPF 40x or multifocality), according to Orsola/Angulo and to van Rhijn methods, respectively. Progression-free survival (PFS) and recurrence-free survival (RFS) were analyzed by Kaplan-Meyer estimation. Univariable Cox regression analyses were used to test the risk factors associated with a detrimental effect on survival. Results: A total of 318 T1 patients, including 250 patients who received a second transurethreal resection of the bladder (TURB), were confirmed as T1, high-grade and entered the study. Mean age was 71 years and overall 40 patients were female. At a mean follow-up of 45 months, 116 patients (36.5%) experienced a recurrence, 36 (11.3%) experienced a progression and 52 eventually underwent radical cystectomy. The ROL method was feasible in 99.7% of cases compared to 72.3% for Orsola and 99.7% van Rhijn, respectively. Recurrence-free survival rate was 74% and 26% acc. to T1a and T1b/c, 41% and 59 acc. to T1m and T1e and 53.4% and 46.6% acc. to ROL 1 and ROL 2 method, respectively (all p=0.2). Progression-free rate survival at 3-year follow-up was 94% and 76% for T1a and T1b/c (p=0.04), 91% and 92% for T1m and T1e (p=0.2) and 95% and 90% for ROL 1 and ROL 2 (p=0.04), respectively. Conclusion: According to the results of this retrospective study, the new threshold of sub-staging (ROL 1/2) of pT1, high-grade bladder cancer was documented to be feasible in all cases, easy to report and highly reproducible due to its objective standardized definition. In addition, the ROL sub-staging resulted as a reliable predictor of oncologic outcomes also when compared to other sub-staging systems. These results may have a consistent impact in clinical practice and deserve to be confirmed in prospective multicentric investigations.

THE IMPACT OF PROSTATE VOLUME ON GENITOURINARY TOXICITY USING A MODERATE HYPOFRACTIONATION WITH VOLUMETRIC MODULATED ARC THERAPY FOR DEFINITIVE PROSTATE CANCER

Filippo Alongi1, Rosario Mazzola1, Sergio Fersino1, Alba Fiorentino1, Francesco Ricchetti1, Niccolò Giaj Levra1, Ruggero Ruggieri1, Gioacchino Di Paola2, Maurizio Nicodemo3, Stefania Gori3 and Stefano Cavalleri4

1Radiation Oncology, Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy; 2Statistic Faculty, University of Palermo, Palermo, Italy; 3Medical Oncology, Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy; 4Urology, Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy

Aim: To analyze clinico-dosimetric predictors of genitourinary (GU) toxicity in a cohort of prostate cancer patients treated with moderate hypofractionation and

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Introduction and Objectives: Active surveillance (AS) represents a viable option for patients with low-risk prostate cancer (PCa). However, a significant number of patients exit AS protocols at the 1-year biopsy due to biopsy reclassification and, more importantly, up to 30% of them harbor misclassified aggressive disease. We aimed at defining a more detailed biopsy scheme in order to increase the accuracy of currently used AS criteria. Patients and Methods: The study included 414 consecutive patients submitted to radical prostatectomy (RP) who could have been considered eligible for AS according to the Prostate Cancer Research International Active Surveillance (PRIAS) criteria (cT1T2a; prostate-specific antigen (PSA)<10 ng/ml; PSA density <0.2; Gleason score <7; <3 positive cores). We analyzed the results of histological evaluation at RP. Patients with pathological T3a and T3b and N1, as well as those with pathological Gleason score 8 or higher, were considered as harboring unfavorable disease. Patients were stratified according to the number of cores taken at biopsy and the most informative cutoff methodology was used in order to identify the number of cores, which better stratify patients according to the rate of unfavorable PCa characteristics at final pathology. Finally, multivariable logistic regression analyses addressed the association between total number of cores and the presence of unfavorable disease at final pathology. Covariates consisted of age and prostate volume. Results: Of 414 patients with AS characteristics, 36 (8.7%) showed unfavorable disease at RP, as defined by pT3a, pT3b, pN1 and/or Gleason score 8-10. Specifically, 24 (5.8%) had extracapsular extension, 7 (1.7%) had seminal vesicles invasion, 9 (2.2%) had pathological Gleason 8 and 8 (1.9%) had lymph node invasion. When patients were stratified according to the number of cores taken at biopsy, 14 cores emerged as the most informative cutoff in reducing the rate of misclassification. Patients who

**79 A MINIMUM OF 14 CORES SHOULD BE TAKEN AT BIOPSY BEFORE PLANNING ACTIVE SURVEILLANCE FOR PATIENTS WITH LOW-RISK PROSTATE CANCER**

**Vincenzo Scattoni**, Nazareno Suardi, Nicola Fossati, Giorgio Gandaglia, Marco Bianchi, Alessandro Nini, Andrea Salonia, Massimo Freschi, Francesco Montorsil and Alberto Briganti

Division of Oncology/Unit of Urology; URI, IRCCS Ospedale San Raffaele, Milan, Italy

**Abstracts of the 25th Annual Meeting of the Italian Society of Uro-Oncology (SIUrO), 21-23 June, 2015, Rome, Italy**

**Introduction and Objectives:** Active surveillance (AS) represents a viable option for patients with low-risk prostate cancer (PCa). However, a significant number of patients exit AS protocols at the 1-year biopsy due to biopsy reclassification and, more importantly, up to 30% of them harbor misclassified aggressive disease. We aimed at defining a more detailed biopsy scheme in order to increase the accuracy of currently used AS criteria. **Patients and Methods:** The study included 414 consecutive patients submitted to radical prostatectomy (RP) who could have been considered eligible for AS according to the Prostate Cancer Research International Active Surveillance (PRIAS) criteria (cT1T2a; prostate-specific antigen (PSA)<10 ng/ml; PSA density <0.2; Gleason score <7; <3 positive cores). We analyzed the results of histological evaluation at RP. Patients with pathological T3a and T3b and N1, as well as those with pathological Gleason score 8 or higher, were considered as harboring unfavorable disease. Patients were stratified according to the number of cores taken at biopsy and the most informative cutoff methodology was used in order to identify the number of cores, which better stratify patients according to the rate of unfavorable PCa characteristics at final pathology. Finally, multivariable logistic regression analyses addressed the association between total number of cores and the presence of unfavorable disease at final pathology. Covariates consisted of age and prostate volume. **Results:** Of 414 patients with AS characteristics, 36 (8.7%) showed unfavorable disease at RP, as defined by pT3a, pT3b, pN1 and/or Gleason score 8-10. Specifically, 24 (5.8%) had extracapsular extension, 7 (1.7%) had seminal vesicles invasion, 9 (2.2%) had pathological Gleason 8 and 8 (1.9%) had lymph node invasion. When patients were stratified according to the number of cores taken at biopsy, 14 cores emerged as the most informative cutoff in reducing the rate of misclassification. Patients who
had 14 or more cores taken at biopsy had a misclassification rate of 4.9% vs. 13.2% in patients with less than 14 cores \( (p=0.002) \). At multivariable logistic regression analyses, after adjusting for age and prostate volume, the number of cores at biopsy emerged as independent predictor of unfavorable disease (odds ratio \((OR)=0.92\); \( p=0.04 \)). Interestingly, prostate volume did not represent an independent predictor of misclassification \( (p=0.3) \). \textbf{Conclusion:} Roughly, 10% of patients eligible for AS harbor aggressive disease and are at significant risk of progression. The adoption of a standardized scheme of prostatic biopsy with 14 cores reduces significantly the rate of patients with aggressive disease. When AS is considered as an option, a minimum of 14 cores should be taken at biopsy in order to reduce the risk of misclassification. A confirmatory biopsy should be considered if less than 14 cores were taken at initial, diagnostic biopsy.

\section*{80 DOES SURGICAL APPROACH IMPACT ON THE RISK OF POSITIVE SURGICAL MARGIN AT RADICAL PROSTATECTOMY IN PATIENTS WITH CLINICALLY LOCALIZED PROSTATE CANCER? A SINGLE INSTITUTION ANALYSIS}

\textbf{Vincenzo Scattoni}\textsuperscript{1}, Nazareno Suardi\textsuperscript{1}, Nicola Fossati\textsuperscript{1}, Giorgio Gandaglia\textsuperscript{1}, Andrea Gallina\textsuperscript{1}, Andrea Salonia\textsuperscript{1}, Massimo Freschi\textsuperscript{2}, Francesco Montorsi\textsuperscript{1} and Alberto Briganti\textsuperscript{1}

\textsuperscript{1}Division of Oncology/Unit of Urology; URI, IRCCS Ospedale San Raffaele, Milan, Italy; \textsuperscript{2}Pathology, IRCCS Ospedale San Raffaele, Milan, Italy

\textbf{Introduction and Objectives:} Robotic-assisted radical prostatectomy (RARP) might improve the rate of positive surgical margins (PSM) as compared to the open approach (ORP). However, these results are based on multi-institutional series with great variability in terms of both surgical approaches and pathological examinations. We evaluated the rate of PSM at RARP and ORP performed at a single tertiary care center using standardized surgical technique and pathological examination. \textbf{Patients and Methods:} The study included 6,932 patients submitted to ORP (n=4995; 72.1\%) and RARP (n=1936; 27.9\%) between 1999 and 2014. Patients were stratified according to the D'Amico risk groups. A PSM was defined as the presence of tumor cells at the inked margin. We addressed the rate of PSM according to the surgical approach in the overall population, as well as in each risk group category. PSM rate was assessed among patients operated on by two expert surgeons (>200 cases performed) who routinely perform both RARP and ORP. Chi-square test was used to quantify the differences in the rate of PSM between RARP and ORP in the overall population and in each patient category, respectively. Multivariable (MVA) logistic regression analyses assessed the impact of the technique on the risk of PSM. Covariates consisted of risk group characteristics, nerve-sparing procedure, tumor and prostate volume. \textbf{Results:} Overall, 1,494 patients had one or more PSM with a PSM rate of 21\%. PSM were detected in 1,144 (22.9\%) and 309 (16.0\%) of ORP and RARP, respectively \( (p<0.001) \). PSM rate was 13.8, 22 and 27.5\% in low, intermediate and high-risk patients. When patients were stratified according to preoperative risk groups, RARP showed statistically significant lower rate of PSM in low \( (11.5\% \text{ vs. } 15.2\% \text{, } p=0.01) \), as well as in intermediate risk patients \( (18.9\% \text{ vs. } 23.3\% \text{, } p=0.01) \). The greatest benefit of RARP was seen in high-risk patients, where the rate of PSM was 19.5\% vs. 29.6\% for RARP vs. ORP \( (p<0.001) \). When the analyses were repeated in the population of patients operated on by two expert surgeons, RARP showed a significantly lower rate of PSM only in high-risk patients \( (19.3\% \text{ vs. } 26.7\% \text{, } p=0.04) \), while in low and intermediate risk patients no benefit was observed \( (p=0.14 \text{ and } p=0.17 \text{, respectively}) \). In MVA, RARP represented an independent predictor of lower PSM rate \( \text{vs. ORP (} \text{odds ratio (OR)}=0.79; \text{ } p<0.001) \). \textbf{Conclusion:} RARP leads to a significant reduction of PSM across all risk-groups patients. However, the benefit of RARP reaches its highest in patients with high-risk disease.

\section*{85 CONCORDANCE OF PROSTATE BIOPSIES WITH RADICAL PROSTATECTOMIES: A COMPARISON OF TRANSRECTAL, TRANSPERINEAL AND TRANSPERINEAL SECTOR-BASED TEMPLATE TECHNIQUES}

\textbf{Giancarlo Marra}\textsuperscript{1}, Chiara Fiorito\textsuperscript{1}, David Eldred-evans\textsuperscript{2}, Marco Oderda\textsuperscript{1}, Ben Challacombe\textsuperscript{2}, Mieke Van Hemelrijck\textsuperscript{3}, Christian Brown\textsuperscript{4}, Declan Cahill\textsuperscript{2}, Lorenzo Daniele\textsuperscript{5}, Bruno Frea\textsuperscript{1}, Paolo Gontero\textsuperscript{1}, Rick Popert\textsuperscript{2} and Gordon Muir\textsuperscript{4}

\textsuperscript{1}Department of Urology, San Giovanni Battista Hospital, Turin, Italy; \textsuperscript{2}Department of Urology, Guy's Hospital, London, U.K.; \textsuperscript{3}Division On Cancer Studies, King's College, London, U.K.; \textsuperscript{4}Department of Urology, King's College Hospital, London, U.K.; \textsuperscript{5}Department of Pathology, San Giovanni Battista Hospital, Turin, Italy

\textbf{Background/Aim:} Risk stratification is paramount in prostate cancer diagnosis and transrectal biopsy remains the current standard. Notwithstanding renewed interest in transperineal approaches, little evidence is available on the...
ability of template-based techniques in predicting the final histology of radical prostatectomy specimens. Our aim was to evaluate the accuracy of systematic transperineal sector mapping biopsy (TPSMB) in predicting pathological grade at radical prostatectomy (RP); to compare the concordance with subsequent radical prostatectomy specimens of the former with standard transrectal ultrasound-guided biopsies (TRUS) and transperineal freehand biopsy (TPF); to establish the clinical impact of discordance between biopsies and RP on subsequent surgical management.

**Patients and Methods:** This retrospective multi-institutional study included 305 patients from 2008 to 2013. All underwent RP following one of three different prostate biopsy techniques: TPSMB (Group 1, n=204), TRUS (Group 2, n=51) and TPF (Group 3, n=50). Exclusion criteria included previous hormonal treatment, previous TURP, previous radiotherapy or a time lapse longer than 6 months between the biopsy and RP. All mismatches between biopsies and RP were assessed for significance by three consultant urologists using the Delphi method. Percentages and Cohen’s Kappa coefficient were used to evaluate the concordance in the three Groups. **Results:** Concordance between biopsy result and RP specimen was highest in the TPSMB group (75.49%), followed by TPF (70%) and TRUS (64.70%). Cohen’s Kappa coefficient was 0.42, 0.34 and 0.68, respectively. Use of the Delphi method showed lower clinical impact of discordances for Group 1 (0.42), Group 2 (0.34) and Group 3 (0.68). **Conclusion:** TPSMB had the highest accuracy for predicting the predominant grade at radical prostatectomy and showed superior pathological concordance with RP specimen compared with standard TRUS and TPF biopsy techniques. TPSMB provides an effective approach for systematic prostate biopsy to evaluate overall prostate cancer and stratify patients to treatment modalities, including active surveillance.

**SIUrO-PRIAS-ITA PROJECT: FIVE YEAR EXPERIENCE ON ACTIVE SURVEILLANCE**

Fabio Badenchini1, Maria Francesca Alvisi1, Giario Conti2, Michele Gallucci3, Giuseppe Martorana4, Davide Diazi4, Roberto Sanseverino5, Giorgio Napodano5, Ezio Fregò6, Marco Tanello6, Giorgio Guazzoni7, Rodolfo Hurle7, Luisa Pasini8, Andrea Turci9, Giacomo Cicchetti9, Pasquale Ditonno9, Enrico Bollito10, Michelangelo Fiorentino12, Rodolfo Montironi13, Carlo Patriarca14, Maria Rosa Raspollini1, Steno Sentinelli1, Tiziana Rancati1, Tiziana Magnani1, Chris Bangma17 and Riccardo Valdagni18

1Prostate Cancer Programme, Fondazione IRCCS, National Institute of Tutors, Milan, Italy;
2Department of Surgery, Division of Urology, Ospedale Sant’Anna, Como, Italy;
3Division of Urology, Istituto Regina Elena, Rome, Italy;
4Division of Urology, Policlinico Sant’Orsola Malpighi, Bologna, Italy;
5Division of Urology, Ospedale Umberto I, Nocera Inferiore, Italy;
6Division of Urology, Ospedale Civile, Desenzano, Italy;
7Division of Urology, Istituto Clinico Humanitas, Rozzano, Italy;
8Division of Urology, Ospedale M. Bufalini, Cesena, Italy;
9Division of Urology, Policlinico di Bari, Bari, Italy;
10Department of Pathological Anatomy, Az. Ospedaliera Universitaria San Luigi Gonzaga, Orbassano, Italy;
11Department of Pathological Anatomy, Fondazione IRCCS, National Institute of Tutors, Milan, Italy;
12Department of Pathological Anatomy, Policlinico Sant’Orsola Malpighi, Bologna, Italy;
13Department of Pathological Anatomy, Ospedali Riuniti, Torrette di Ancona, Ancona, Italy;
14Department of Pathological Anatomy, Ospedale Sant’Anna, Como, Italy;
15Department of Pathological Anatomy, Azienda Ospedaliera Universitaria Careggi, Florence, Italy;
16Department of Pathological Anatomy, Istituto Regina Elena, Rome, Italy;
17Department of Urology, Erasmus University Medical Centre Rotterdam, Rotterdam, the Netherlands;
18Radiation Oncology 1, Prostate Cancer Programme, Fondazione IRCCS, National Institute of Tutors, Milan, Italy

**Introduction:** We here report on the 5-year experience on active surveillance (AS). The correlation between active treatment-free survival (ATFS) and patients’ characteristics at diagnosis is an important step when trying to predict disease reclassification after a short period in AS. Materials and Methods: In December 2009, the SIUrO-PRIAS-ITA working group started including patients in PRIAS (Prostate cancer Research International: Active Surveillance). Eligibility criteria are: prostate-specific antigen (PSA) at diagnosis (iPSA) ≤10ng/ml, Gleason score (GPS) ≤6, clinical stage T1c or T2a, PSA density≤0.2ng/ml/cc, maximum 2 positive cores. Patients drop out from AS due to upgrading (GPS>6) or upsizing (>2 positive cores) at re-biopsy or if PSA doubling time<3years. ATFS was evaluated using Kaplan-Meyer analysis. The relationship between ATFS and clinical risk factors at diagnosis was determined through the log-rank test and Cox proportional hazard model. **Results:** Between December 2009 and October 2014, 661 patients were included in PRIAS. Median age at inclusion was 65 years.
(range=41-81), median iPSA 5.4 ng/ml (range=0.5-10 ng/ml). One hundred and ninety-two out of 661 (29%) patients had two positive cores at diagnostic biopsy. Six hundred and nineteen out of 661 (93.6%) patients were classified as T1c at digital rectal exam (DRE). Four hundred and sixty-six out of 661 patients (71%) are still on AS with a median follow-up of 36 months (range=1-91 months), while 195/661 (29.5%) patients dropped out from AS due to disease reclassification/progression, 128 due to upgrading and/or upsizing at re-biopsy (82/195 at first re-biopsy, one year after inclusion) and 14 due to PSA doubling time. Median time in AS is 23 months (range=1-
91 months). Biopsy-driven ATFS was found to be correlated to PSA density ≤ 0.12 ng/ml/cc (p = 0.002, ATFS at 48 months 77% vs. 43%), prostate volume (p = 0.003, volume stratified in three groups: ≤ 40 cc, 40-60 cc, > 60 cc, ATFS at 48 months 63% vs. 75% vs. 86%, respectively), number of positive cores at diagnostic biopsy (p = 0.004, ATFS at 48 months 79% vs. 62%, 1 core vs. 2 cores, respectively), number of total cores at diagnostic biopsy (p = 0.01, ATFS at 48 months 71% vs. 77%, ≤ 12 vs. > 12 cores, respectively) and DRE (p = 0.09, ATFS at 48 months 70% vs. 64%, for T1c and T2a, respectively). Kaplan Meier curves are shown in Figure 1. Best fit multivariable Cox model for biopsy-driven ATFS resulted in a 3-variable model (overall p = 0.007) including DRE = T2a (risk factor, hazard ratio (HR) = 1.44), prostate volume > 50 cc (protective factor, HR = 0.64) and PSA density (continuous variable, risk factor, HR = 1.02).

Conclusion: Most of drop out events occurred after one year re-biopsy, which should probably be considered as a confirmatory biopsy. PSA density, DRE, number of positive, total cores at diagnostic biopsy and prostate volume correlated with biopsy-related ATFS. While the first four variables are disease-related, i.e. they indicate a disease state that is somehow at higher risk of reclassification after a short period in AS, the last one (prostate volume) is probably underlining a technical problem in correctly sampling a high volume prostate. Cox multivariable model confirmed the independent role of PSA density, DRE and prostate volume.

88 NATURAL HISTORY OF HGPIN AND ASAP: A 6-YEAR FOLLOW-UP OF 1012 PATIENTS

Maurizio Barale1, Marco Agnello1, Marco Oderda1, Simone Giona1, Francesca Pisano1, Giancarlo Marra1, Lorenzo Daniele2, Paola Dalmasso3, Nathalie Nicolaiew4, Alexandre De La Taille5, Bruno Frea1, Hendrik Van Poppel6, Steven Joniau6 and Paolo Gontero1

Departments of 1Urology, 2Pathology and 3Epidemiology, San Giovanni Battista Hospital, Turin, Italy; 4Faculty of Medicine, Université Paris-Est Créteil Val De Marne, Paris, France; 5Department of Urology, CHU Mondor, Créteil, Paris, France; 6Department of Urology, University Hospital Gasthuisberg, Leuven, Belgium

Introduction/Aim: A significant proportion of patients with high-grade prostatic intraepithelial neoplasia (HGPIN) and atypical small acinar proliferation (ASAP) is diagnosed with prostate cancer (PCa) at re-biopsy. However, long-term risk of developing PCa remains to be determined. We retrospectively evaluated the natural history and assessed the long-term cancer risk of these precancerous lesions in a large multicentric series. Materials and Methods: One thousand and twelve HGPIN and/or ASAP patients underwent prostate biopsy between 2001 and 2010. All were followed up with periodical urological visits and prostate-specific antigen (PSA) measurements. Eight
hundred and two patients (79.2%) received at least one re-
biopsy. All specimens underwent central pathological review.
Prostate cancer risk was assessed by retrospective evaluation of
follow-up re-biopsies and digital rectal exam (DRE) + PSA at
last follow-up. Results: Sixty-two percent of men remained
cancer-free in the mean observation period of 6 years. The
cumulative risk of PCa was 25% for monofocal HGPIN, 28%
for multifocal HGPIN, 36% for ASAP and 43% when ASAP
and HGPIN were contemporarily present at the first biopsy
(Figure 1). Fifty percent of PCa diagnosis occurred within 12
months, 80% within 3 years. In more than 91% of the cases,
cancer identified on re-biopsy was a low-grade cancer (Gleason
score ≤7). Age, PSA levels and number of biopsies at baseline
were not significant cancer predictors. Figure 1 shows the
Kaplan-Meier prostate cancer free curves. Conclusion: Findings
of ASAP and ASAP + HGPIN are strong risk factors for
developing PCa within the next year. More than 50% of patients
with precancerous lesions will remain free from a clinical
diagnosis of prostate cancer beyond 5 years.

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EFFICACY AND SAFETY OF A
NEW DEVICE FOR INTRA VESICAL
THERMOCHMOTHERAPY IN NON-GRADE
3 BCG RECURRENT NMIBC. A PHASE I-II STUDY
Francesco Soria1, Francesca Pisano1, Filippo Sogni2,
Massimiliano Di Marco3, Vincenzo Pagliarulo4,
Paola Milla5, Luigi Cattel6,
Bruno Fre3 and Paolo Gontero1
1Division of Urology, Azienda Ospedaliera Città della
Salute E Della Scienza Di Torino - Molinette, Turin, Italy;
2Division of Urology, Ospedale Maggiore della Carità,
Novara, Italy;
3Division of Urology, Casa di Cura Guarnieri, Rome, Italy;
4Division of Urology, Università degli Studi di Bari, Bari, Italy;
5Department of Pharmacology, Università degli Studi di
Torino, Turin, Italy

Introduction/Aim: Intravesical administration of mitomycin C
(MMC-C) with hyperthermia (HT) has proved an effective
second-line therapy in bacillus Calmette-Guerin (BCG) recurrent
non-muscle invasive bladder cancer (NMIBC). In the current
study we report, for the first time, the activity and safety of
Unithermia®, a novel device for MMC-C HT that employs
conductive heating, in a series of non-grade 3 NMIBC that failed
BCG. Patients and Methods: Patients with non-grade 3 NMIBC
recurring after at least a full induction course of BCG were
eligible for this phase I-II prospective single arm study. Six
weekly instillations of 40 mg of MMC-C HT with Unithermia®
for 45 minutes were scheduled following complete transurethral
resection (TUR). Adverse events were graded according to the
Common Terminology Criteria for Adverse Events (CTCAE) v6.

Follow-up consisted of urine cytology and cystoscopy at regular
intervals. Primary end points were treatment safety and response
rate (RR), the latter defined as the absence of any unfavorable
outcome at 12 months. Any grade 3 and/or muscle invasive
(T>1) recurrence was considered as progression. The Kaplan-
Meier estimation of the time to recurrence and progression,
cancer-specific survival (CSS) and overall survival (OS) at the
available follow-up were taken as secondary end points. Results:
Thirty-four eligible patients entered the study between January
2009 and April 2011. All but 4 patients completed the treatment
course. RR was documented in 20/34 (59%). Among the 14/34
(41%) non responders, 4 developed G3 disease, 1 developed
carcinoma in situ (CIS) and 1 progressed to muscle-invasive
bladder cancer, with an overall 18% progression rate at 1 year.
Five-year projected recurrence and progression rates were 46%
and 44%, respectively. Toxicity did not go beyond grade (G) 2
except in 5 cases (2 G3 systemic skin reaction and 3 G3 bladder
spasms). Kaplan-Meier estimation of time to recurrence and
progression are shown in Figures 1 and 2.
Discussion and Conclusion: Initial experience with MMC-HT with Unithermia® showed an interesting activity and safety profile in non-grade 3 NMIBC recurring after BCG suggesting a role as second-line therapy in this selected subgroup of NMIBC.

90 CLINICAL AND MOLECULAR EFFECTS OF DIETARY SUPPLEMENTS: A RANDOMISED DOUBLE-BLIND CONTROLLED PHASE I-II STUDY IN PATIENTS WITH ASAP AND/OR MULTIFOCAL HGPIN

Francesco Soria1, Giancarlo Marra1, Marco Oderda1, Andrea Zitella1, Francesca Baratta2, Paola Brusa2, Giovanna Chiorino3, Ilaria Gregnagnin3, Lorenzo Daniele4, Bruno Frea1 and Paolo Gontero1

1Division of Urology, Azienda Ospedaliera Città Della Salute E Della Scienza di Torino - Molinette, Turin, Italy; 2Department of Pharmacology, University of Turin, Turin, Italy; 3Cancer Genomics Laboratory, Fondazione Edo Tempia, Biella, Italy; 4Department of Pathology, AOU Città Della Salute E Della Scienza di Torino, Turin, Italy

Introduction/Aim: Controversy exists on dietary supplements’ ability to prevent prostate cancer (PCa). We assessed clinical and molecular activity of a combination of selenium (Se), lycopene and green tea catechins (GTC), administered at the maximum non-toxic dose, in men with atypical small acinar proliferation (ASAP) and/or multifocal high-grade prostatic intraepithelial neoplasia (HGPIN).

Patients and Methods: Randomized double blind controlled trial included 60 men with ASAP and/or multifocal HGPIN receiving daily lycopene 35mg, Se 55 μg and GTC 600mg or placebo for 6 months. Primary end-point was to evaluate differences of incidence of PCa in the two arms, at re-biopsy. Upon confirmation of plasma lycopene concentrations falling within 1.2-90 mcg/l and no side-effects during phase I (n=10), the study proceeded to phase II (n=50). Clinical and pathological characteristics were recorded including prostate-specific antigen (PSA), international prostate symptoms score (IPSS) and quality of life questionnaire - prostate module (PR25) questionnaires at baseline and end of treatment, when a minimum 12-core biopsy was scheduled. After unblinding of pathological results, 8 men (4 placebo and 4 active treatment, 2 with no evidence of disease and 2 with diagnosis of PCa within each arm, respectively) were selected and total RNA extracted from normal tissue areas. MicroRNA profiling was carried out with the Agilent platform. Raw data were processed using R statistical language, linear models for microarray analysis and 2-factor ANOVA. Hierarchical clustering on differentially expressed miRNAs was performed with the TMev software. Results: At 6 months, 53 men underwent re-biopsy and 24.5% (n=13) had PCa: 77% of them (n=10) were in the supplementation group, whereas 3 were in the placebo group (p=0.053). Table I reports clinico-pathological variables changes in the 2 arms before and after treatment. No significant variations in PSA, IPSS and PR25 questionnaires were observed. At a mean total follow-up of 37 months, 3 more PCa were found (all placebos). A consistent group of microRNAs, over-expressed in PCa and present in progression from HGPIN to metastasis, were up-regulated in the supplementation group only on re-biopsy. In the same group, some microRNA suppressing the proliferation, invasion and migration of PCa, as well as one underexpressed in PCa vs. non-cancer stroma were down-regulated. Thirty-one microRNAs were differently modulated on re-biopsy in patients who progressed, with a stronger effect in the supplementation group. Amongst them were oncosuppressors miR-203b-5p and miR-7-2-3p (down-regulated) and oncomiR miR-18a-3p (up-regulated). Discussion and Conclusion: High dose combination of lycopene, GTC and Se administered in men harbouring HGPIN and/or ASAP was associated with a higher incidence of PCa at re-biopsy and over-expression of microRNA implicated in PCa progression.

91 PRIAS VS. SAINT: COMPARING TWO ACTIVE SURVEILLANCE PROTOCOLS

Maria Francesca Alvisi1, Tiziana Rancati1, Fabio Badenchini1, Cristina Marenghi1, Maurizio Colecchia2, Roberto Salvioni3, Sergio Villa4, Massimo Maffeizzi5, Silvia Stagni6, Mario Catanzaro7, Tullio Torelli8, Nicola Nicolai9, Barbara Avuzzi9, Nice Bedini1, Sara Morlino4, Edoardo Tulli Baldwin1, Lara Bellardita1, Tiziana Magnani1 and Riccardo Valdagni9

1Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 2Pathological Anatomy, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 3Urology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 4Radiation Oncology 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 5Prostate Cancer Program and Radiation Oncology 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Introduction/Aim: At our institution, patients have been proposed active surveillance (AS) in the frame of two
different protocols: Sorveglianza Attiva Istituto Nazionale dei Tumori (SAINT), a mono-institutional cohort study and Prostate cancer Research International: Active Surveillance (PRIAS), an international trial coordinated by the Erasmus University Medical Center in Rotterdam. Outcomes of these two protocols were compared focusing on the association between survival in AS (i.e. freedom from disease reclassification/progression) and patients’ characteristics at diagnosis. Material and Methods: Eligibility criteria for SAINT were: histologically confirmed prostate cancer (PCa), no previous treatment, fit to radical treatments, initial prostate-specific antigen (PSA) ≤10 ng/ml, clinical stage ≤T2a (2002 TNM), Gleason pattern score (GPS) ≤3+3, positive biopsy cores ≤20%, maximum core length containing cancer ≤50%. PRIAS protocol differs from SAINT for 3 inclusion criteria: no more than two biopsy cores invaded with PCa (<10% positive cores in case of saturation biopsy), clinical stage T1c or T2 and PSA density <0.2 ng/ml/cc. Actuarial active treatment-free survival (ATFS) was assessed using Kaplan-Meier analysis. Correlation between ATFS and clinical risk factors was determined using the log-rank test and Cox proportional hazards model. Results: Six hundred and twenty-two patients were enrolled in AS, 401 (64.5%) in PRIAS (November 2007–October 2014) and 221 (35.5%) in SAINT (March 2005–October 2014). Mean age at inclusion was statistically different in the two populations: 64.4 years (range=41-78) in PRIAS and 66.3 years (range=50-79) in SAINT (t-test, p=0.0014), PSA distribution at diagnosis was also statistically different with mean values 5.3 ng/ml (PRIAS) vs. 6.9 ng/ml (SAINT) (p<0.001). Prostate volume was similar in the two populations: 52.5 cc for PRIAS patients and 47.9 cc for SAINT patients (mean values, p=0.36). PSA density distribution was largely different: mean values 0.11 ng/ml/cc vs. 0.17 ng/ml/cc (p<0.001). Proportions of T1c vs. T2a were similar in the two groups, while there was a significant difference in the number of positive core at diagnosis: 69.6% vs. 60.5% patients with 1 positive core in PRIAS and SAINT, respectively (Mann-Whitney, p=0.0005). Ninety-five out of 401 (23%) PRIAS patients and 82/219 (37%) SAINT patients dropped out from AS due to upgrading and/or upsizing at re-biopsy. Biopsy-driven ATFS (Figure 1) resulted to be lower in SAINT (p=0.002, hazard ratio (HR)=1.6). Stratifying for AS protocols, univariate model for ATFS resulted to be correlated to age >66 years in PRIAS, PSA density ≥12 ng/ml/cc and prostate volume <50cc for both protocols. Best fit multivariable model for biopsy-driven ATFS resulted in a three-variable model for PRIAS (overall p<0.0001, c-index=0.64), including age >66 years (p=0.002, HR=1.9), PSA density ≥0.12 ng/ml/cc (p=0.01, HR=1.8) and prostate volume ≥50cc (protective factor, p=0.21, HR=0.7). While for SAINT, only two variables were retained: PSA density ≥0.12 ng/ml/cc (p=0.31, HR=1.4) and prostate volume ≥50cc (protective factor, p=0.06, HR=0.6).
a unique Cox regression model, four variables are included: to be in SAINT vs. PRIAS (p = 0.03, HR = 1.49), age > 66 years (p = 0.003, HR = 1.4), prostate volume ≥ 50 cc (protective factor, p = 0.02, HR = 0.7) and PSA density ≥ 0.12 ng/ml/cc (p = 0.01, HR = 1.6). Conclusion: The two AS protocols differ in the time frame; most patients were enrolled with some inclusion criteria and partly in the follow-up schedule. For these reasons, the two populations are significantly different from the point of view of age, PSA, number of positive cores and PSA density distributions. Survival in AS is lower in SAINT and partly explained by the broader inclusion criteria. More loose criteria prompted a tighter follow-up schedule in SAINT (biopsy at 1 and 2 years and every 2 years afterwards) and this probably also explains part of the increased probability of detecting disease reclassification/progression in SAINT. Noteworthy, in both protocols high prostate volumes are indicated as “protective” factors, underlining the technical problem of adequately sampling a large volume prostate during random biopsy procedures.

**PROSTATE CANCER-RELATED ANXIETY: FROM ENROLMENT TO ONE YEAR AFTER THE FIRST RE-BIOPSY**

Silvia Villa¹, Claudia Repetto¹, Tiziana Rancati¹, Barbara Avuzzi², Mario Catanzaro³, Cristina Marenghi¹, Nicola Nicolai³, Silvia Stagni², Massimo Maffezzini³, Roberto Salvioni³, Tiziana Magnani¹, Riccardo Valdagni³ and Lara Bellardita¹

Introduction/Aim: “Living with untreated prostate cancer (PCa)” may cause distress in men on active surveillance (AS). We aimed to evaluate PCa-related anxiety from enrolment to one year after the first re-biopsy. Patients and Methods: Between 2007-2014, 207 patients progressively completed the Memorial Anxiety Scale for Prostate Cancer (MAX-PC), a self-report tool providing 4 indexes: PCa anxiety, prostate-specific antigen (PSA) anxiety, fear of recurrence, MAX-PC total score. Assessment was conducted at entrance in AS protocol (T0), 2 months before first re-biopsy from diagnostic one (T1), after re-biopsy (T2) and 1 year after re-biopsy (T3). On average, patients completed MAX-PC at T3 after 19 months from entrance. Cronbach’s α coefficients were calculated to estimate reliability. Descriptive analyses were performed. The Wilcoxon test was used to detect statistically significant changes over time. Changes with effect size (ES) ≥ 0.5 or ≤ –0.5 were considered as clinically relevant (1).

Results: Two hundred and seven patients completed the MAX-PC at T0. Mean age of sample at diagnosis was 64+7 years (range=42-79). Figure 1 shows results of descriptive analyses. The majority of patients had low scores in all the subscales and the MAX-PC total index.
(coefficients of skewness >0). Cronbach’s α values ranged from 0.76-0.93 and were similar to the reliability indexes of the original scale (2). The Wilcoxon test showed statistically significant reductions in MAX-PC total score (N=52, 61% of patients (pts), p=0.0006) and PCa anxiety subscale (N=49, 58% of pts, p=0.0012) between T1 and T2. These variations were found to be clinically meaningful (ES≥0.5) for 19% (N=16) and 22% (N=19) of patients, respectively. Statistically significant increases were found between T1 and T2 in MAX-PC total (N=24, 28% of pts, p=0.0006) and PCa anxiety (N=25, 29% of pts, p=0.0006) scores. These changes emerged as clinically meaningful (ES≤0.5) for 7% (N=6) and 9% (N=8) of patients, respectively. Conclusion: Our results showed PCa anxiety as favourably low over time for most of the men in our sample. A decrease in anxiety occurred after the first re-biopsy, which may highlight a potentially reassuring role of the medical examinations included in the AS monitoring scheme. Despite a small group of patients experienced an increase of PCa anxiety, scores mostly remained at the low or mid-range level. Our findings about PCa anxiety in AS are coherent with other studies (3). We found that the Italian version of the MAX-PC that we developed had good reliability. Further research is needed to confirm the validity in the Italian population of AS patients. In conclusion, we may argue that overall PCa-related anxiety seemed not to represent a major burden for our AS patients.

Acknowledgements to Foundation I. Monzino.

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3 Venderbos et al. (2014). Psycho-Oncology

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EPHRIN A2 ANTAGONISM REDUCES SURVIVAL OF PROSTATE CANCER CELLS AFTER CHEMOTHERAPIC TREATMENTS AND ANGIOGENESIS IN PROSTATE CANCER CELLS BOTH IN VITRO AND IN VIVO

Claudio Festuccia1, Giovanni Luca Gravina1, Andrea Mancini1, Simona Delle Monache1, Patrizia Sanità1, Massimiliano Tognolini2, Riccardo Castelli2 and Alessio Lodola2

1Department of Applied Clinical Sciences and Biotechnologies, University of L’Aquila, L’Aquila, Italy; 2Department of Pharmacological Sciences, University of Parma, Parma, Italy

Background/Aim: Prostate cancer cells are sensitive to chemotherapy but resistance has also been described. A series of molecules are involved in the resistance mechanisms, including chemokine receptors, c-Met and Ephrin (Eph) receptors. The increased expression of these molecules is associated to cancer stem cell phenotype and treatments targeting the transition of quiescent cancer stem cells to aggressive tumor initiating cells is very attractive.

Materials and Methods: UPR1331 is a novel EphA2 antagonist obtained from a medicinal chemistry optimization campaign performed around the 3β-hydroxy-∆5-cholenic acid nucleus. UPR1331 inhibits binding of ephrin-A1 to EphA2 with a competitive and reversible mechanism of action with a Ki of 1.4 microM as indicated by displacements studies performed with an ELISA assay. These data are confirmed by surface plasmon resonance (SPR) analysis showing that UPR1331 directly binds the extracellular domain of EphA2 with a single digit micromolar activity. UPR1331 dose-dependently inhibits EphA2 phosphorylation induced by ephrin-A1 in intact cells (PC3) and in vitro angiogenesis (human umbilical vein endothelial cells (HUVEC)) at low micromolar concentrations. Here we investigated the effects of a new class of EphrA2 antagonist in prostate cancer cell models in association with docetaxel and cisplatin.

Results and Conclusion: Ephrins and Ephrin receptors are increased in aggressive hormone-treated prostate cancer in respect to normal, hyperplastic or naïve tissues supporting the use of eprin receptor inhibitors/antagonist in advanced prostate cancer. Here we observed that UPR1331 was not able to reduce in vitro cell proliferation of PC3, 22rv1 and DU145 cells. This compound reduced cell adhesion, migration and invasion and promoted anoikis of tumor cells. When PC3 cells were cultured in suspension in the presence of B27, EGF and FGF (stem cell medium), the size and the number of prostate sphere (cancer stem cells) were reduced. UPR1331, in this culture conditions, sensitizes to cisplatin and docetaxel. However, oral administration of UPR1331 and KPT330 in PC3 xenograft-bearing models offers a global therapy for advanced/castration-resistant prostate cancers and warrants advanced clinical investigations.

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TREATMENT OF PENILE GLANS CARCINOMA IN SITU BY TOPICAL IMIQUIMOD

Tullio Torelli1, Mario Catanzaro1, Nicola Nicolai1, Maurizio Colecchia2, Davide Biasoni1, Luigi Piva1, Massimo Maffezzini1, Silvia Stagni1, Andrea Necchi3, Patrizia Giannatempo1, Daniele Raggi3 and Roberto Salvioni1

1Division of Urology, National Tumor Institute, Milan, Italy; Departments of 2Pathology and 3Medical Oncology, National Tumor Institute, Milan, Italy
**Introduction:** For non-invasive treatment of penile lesions like carcinoma *in situ* (CIS), topical agents like 5-fluorouracil (5-FU) or imiquimod 5% (IQ) are indicated (1). Imiquimod is a new immunomodulator with unclear mechanism of action. Its success is reported in case reports and small series but no large-scale long-term efficacy data are currently available. **Aim:** Seven patients with CIS were treated by IQ as first-line therapy in our center. A biopsy was performed before and after the treatment to analyze the pathological response (primary end point). Moreover, local toxicity and adverse effects were recorded (secondary end points). **Materials and Methods:** From 2010 to 2014, a retrospective review of all patients with penile CIS referred to our center was conducted. Seven patients, with small lesions (less than 3 cm), were treated by IQ with an application of a small dose on the lesion for 12 h every 48 h for at least three months. Five patients had viral features in their original biopsies; one patient had previous lichen and the last one had pagetoid CIS secondary to radiotherapy. Treatment response (primary end point) was assessed by clinical and photographic examination, 5% acetic acid test, and small series but no large-scale long-term efficacy data are currently available. **Conclusions:** Our study shows that therapy with imiquimod is effective to treat penile CIS with low incidence of local toxicity and adverse effects. Nevertheless, the lack of long-term efficacy data and the rarity of penile CIS render this approach unknown to many urologists.


**98 PRIMARY ANGIOSARCOMA OF THE ADRENAL GLAND**

Tullio Torelli1, Stefano Radaelli2, Biagio Paolini3, Mario Catanzaro1, Nicola Nicolai1, Davide Biasoni1, Luigi Piva1, Massimo Maffezzini1, Silvia Stagni1, Andrea Necchi4, Patrizia Gianmatempo4, Daniele Raggi4 and Roberto Salvioni1

1Division of Urology, National Tumor Institute, Milan, Italy;
2Melanoma and Sarcoma Unit, National Tumor Institute, Milan, Italy;
Departments of 3Pathology and 4Medical Oncology, National Tumor Institute, Milan, Italy

**Introduction:** Angiosarcomas are malignant tumors arising from the endothelial lining of blood vessels and are less than 1% of all soft tissue sarcomas. The overall survival is poor with 5-year overall survival rates of 30%. The adrenal gland is an uncommon site for angiosarcoma. To our knowledge, only 22 cases have been reported in the English literature and, among them, only 20 cases are available for review. **Case Report:** On 29 January 2014, a 55-year-old woman (U.E.) was admitted to the Urology Department of the National Tumour Institute in Milan (Italy) to investigate a right adrenal mass measuring 45×29 mm at abdomen computed tomography. The patient complained of significant weight loss and severe asthenia and dispnea. A fine needle biopsy revealed a primary epithelial angiosarcoma. The diagnosis was made after twenty days from biopsy owing to difficult
histological examinations. The patient died due to severe respiratory failure, due to lung metastases, on 23rd of February 2014. Discussion: Angiosarcomas are a very rare group of malignant tumors with poor prognosis. A patient may either be asymptomatic or suffer from weight loss, anorexia and chronic pain, as in our patient. No hormonal activity is found and there are no radiologic pathognomonic findings (1). Thus far, the diagnosis is supported by histopathology and immunohistochemistry, even if it is very difficult for extensive cystic changes with necrosis that make it difficult to identify a focus of primary adrenal angiosarcoma. Moreover, angiosarcoma is typically identified by a vasoformative pattern on histologic sections. However, most primary angiosarcomas are of epithelial type, as in our patient, with a solid epithelioid pattern rather than a vasoformative pattern. Therefore, immunohistochemical reactivity for epithelial markers may be useful but cytokeratin reactivity may occur also in non-epithelial tumors like sarcoma. Thus, when confronted with an epithelial adrenal tumor, pathologists are advised to include an endothelial marker in the spectrum of antibodies (2). Surgery is the only possible curative treatment known so far. If the tumor is confined to the adrenal gland, it is suggested not only removing it but also taking out the periadrenal fat tissue and pericaval and periaortic tissue. In the metastatic disease, cytotoxic chemotherapy is the treatment of choice with anthracyclines, ifosfamide and taxanes. Their dose-limiting toxicity does not allow to prolong these therapies for more than 6-7 months and, for these reasons, gemcitabine seems very promising. Also, in advanced disease, the sequential use of taxanes and gemcitabine could be more advisable than their combination (3). Conclusion: Adrenal angiosarcoma is a very rare and aggressive tumor with a 5-year survival not exceeding 30%. Thus, early diagnosis is mandatory but is very difficult because clinical symptoms are non-specific, endocrinological studies are not indicative and radiology workup may suggest only an indistinct malignancy. A definitive diagnosis is still based on histomorphological and immunohistochemical studies that are difficult and time-consuming procedures. Sometimes, diagnosis is often achieved when there is an advanced disease, with no therapeutic options, as in our patient.

patients, a synchronous Tis was diagnosed. The median EGF-R expression resulted 2.4-fold compared to controls (EGF-R=1). Four patients (15%) presented elevated levels of EGF-R after transurethral resection (TUR) and before adjuvant therapy with a median value of 4-fold. EGF-R expression increased during follow-up in 9 patients (34%) with a median of 4-fold (range=2.5-8); returning within limits in 3 of them after adjuvant therapy. Discussion: EGF-R is detected in the basal layer of normal urothelium. Its expression in NMI-BC is limited and increases in high grade and invasive tumors. EGF-R activation promotes tumor growth by blocking apoptosis and increasing cell proliferation, motility, adhesion and invasive capacity. The results obtained in NMI-BC on EGF-R as an independent predictor of progression are scarce and conflicting (1). Only few data have been obtained in NMIBC (2). Our study suggests the feasibility of EGF-R evaluation in bladder washings of patients affected by NMI-BC avoiding tissue biopsies. It was technically possible to evaluate its expression after TUR in more than 80% of our patients resulting up-regulated in 15% of them. EGF-R up-regulation might represent a marker of potential aggressiveness of the tumor, failure of the treatment and progression during follow-up.


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A SURGICAL TEMPLATE IN SALVAGE LYMPHADENECTOMY FOR PROSTATE CANCER NODAL RECURRENCE: DOES PELVIC INVOLVEMENT PREDICT RETROPERITONEAL POSITIVITY?
Guglielmo Melloni1, Marco Oderda1, Marco Falcone1, Stefania Munegato1, Hannes Van De Bosche2, Steven Deconinck2, Robert Jeffrey Karnes3, Fabio Zattoni3, Steven Joniau2 and Paolo Gontero1
1Department of Urology, University of Turin, Turin, Italy; 2Department of Urology, University Hospitals of The KULeuven, Leuven, Belgium; 3Department of Urology, Mayo Clinic, Rochester, MN, U.S.A.
Introduction: Salvage lymph node dissection (sLND) has been considered as an option for prostate cancer nodal recurrence management after primary treatment. However, a surgical template has not been identified yet. An extended template may be necessary for curative intents but at the cost of increased morbidity of the procedure. We found a surgical template for sLND by investigating if positivity to presacral and common iliac nodes predicts retroperitoneal involvement. Materials and Methods: A retrospective analysis of 26 men who underwent sLND after diagnosis of pelvic nodal recurrence at PET/CT scan. Previous treatments were radical prostatectomy (n=24), radiotherapy (n=1) or brachytherapy (n=1). Irrespective of PET results, all sLND included pelvic and retroperitoneal fields. Dissected nodes were included into 3 anatomical regions: A (internal iliac, obturatory, external iliac), B (presacral, common iliac), C (retroperitoneal). Statistical analysis included Chi square test on crosstabs. Regression analysis was also performed. Results: At sLND, pelvic nodes were positive in twenty men (76.9%): 15 (57.6%) in region A and 15 (57.6%) in region B. Ten (38.4%) had retroperitoneal involvement. The mean number of dissected and positive nodes was 19.1 and 3.1 in the pelvic region (10.1 and 1.9 in region A, 8.9 and 1.1 in region B) and 7.8 and 1.0 in the retroperitoneal region. Retroperitoneal involvement was associated with positivity in region A+B in 45% of cases. Negative predictive value (NPV) was 83.3%. The crosstabs of nodal positivity, stratified by anatomical regions, are shown in Table I. No pelvic region significantly predicted retroperitoneal involvement on multivariate analysis. The predictive ability did not improve with the number of dissected and positive nodes. Conclusion: Anatomical regions, predictive of retroperitoneal involvement during sLND, were not found, probably due to the low number of patients enrolled. The high NPV of pelvic regions suggests that a threshold can be identified to select patients who need retroperitoneal LND. Currently, an extended template, including pelvic and retroperitoneal regions, must be used, if having curative intents.

Introduction/Aim: Gleason score (GS) is a cornerstone amongst prognostic factors for clinical behavior and treatment response of prostate cancer (PCa) predicting the risk of biochemical recurrence (BCR) after radical prostatectomy (RP). A biopsy GS (bGS) upgraded at pathology (pGS) is a dangerously common finding, which may cause suboptimal surgical treatment, if believing to address a more indolent cancer than what actually is. Our aim was to evaluate the impact of GS upgrading and downgrading on BCR-free survival and surgical outcomes in a large cohort of high-risk PCa. Patients and Methods: A retrospective analysis of 7,310 men from the EMPaCT database who underwent RP between 1986 and 2014 and were stratified as high-risk PCa according to at least: prostate-specific antigen (PSA) ≥20 ng/ml, bGS ≥8, cT ≥3. Patients were subdivided according to the GS in: A) bGS ≥8 downgraded to pGS 6-7; B) bGS and pGS 6-7; C) bGS and pGS 8-10; D) bGS <8 upgraded to pGS 8-10. ANOVA and Chi-square tests were used for group comparisons. Kaplan-Meier curves were performed for BCR-free survival. Univariate and multivariate logistic regression analyses were used to test predictors of BCR.
Results: Baseline characteristics and surgical outcomes are shown in Table I. Overall, bGS 8-10 downgrading to pGS 6-7 occurred in 51.3% (n=1954) and bGS 6-7 upgrading to pGS 8-10 in 11.8% (n=416). Patients with pGS 8-10 had higher positive margins, N+ and BCR, irrespectively of GS upgrade. Upgraded GS yielded lower BCR-free survival (Figure 1) and were associated with BCR both at univariate (odds ratio (OR)=1.49 (range=1.21-1.83), \( p<0.001^{*} \)) and multivariate (OR=1.05 (range=0.83-1.33), \( p<0.04 \)) regression analyses. Conclusion: Downgrading to pGS 6-7 is a common event in high-risk PCa defined as bGS 8-10 and RP should be strongly considered in these men. Upgrade from bGS 6-7 to pGS 8-10 is a rare event and is associated with increased risk of BCR: these patients should be followed up with more carefulness.

Figure 1. (Abstract 104).

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METASTATIC PROPERTIES AND RESISTANCE TO DOCETAXEL ARE INHIBITED BY ANTAGONISM OF CXCR4 AND E-SELECTIN IN EXPERIMENTAL PROSTATE CANCERS MIMICKING A TUMOR WITH HIGH RISK TO DEVELOP METASTASES OR GROWING IN BONE MICROENVIRONMENT

Giovanni Luca Gravina, Alessandro Colapietro, Simona Delle Monache, Adriano Angelucci, Alessia Calgani, Patrizia Sanità, William E. Fogler, John L. Magnani and Claudio Festuccia

1Department of Applied Clinical Sciences and Biotechnologies, University of L'Aquila, L'Aquila, Italy; 2Drug Development, Glycomimetics, Inc., Gaithersburg, MD, U.S.A.
Background/Aim: Prostate cancer (PCa) patient morbidity can be attributed to bone metastases posing a significant clinical obstacle. Therefore, a better understanding of this phenomenon is imperative and might help to develop novel therapeutic strategies. PCa cells preferentially roll and adhere on bone marrow vascular endothelial cells, where abundant E-selectin and stromal cell-derived factor 1α (SDF-1α) are expressed, subsequently initiating a cascade of activation events that eventually lead to the development of metastases. This suggests that agents able to suppress this signaling pathway may be used as pharmacological treatments of bone metastatic disease. In addition it has been suggested that chemotherapy has scarce success when administered to patients with bone metastases since in this site the CXCR4 activation may determine protection vs. cell death. In this preliminary study, we investigate if the dual E-selectin/CXCR4 inhibitor (GMI1359) plays a role in the reduction of bone growth of PC3 cell line collaborating with docetaxel in the control of tumor burden and osteolysis. We compare GMI11359 with the sole E-selectin (GMI1271) and CXCR4 (plerixafor) inhibitory activity by using intratibial injection of PC3M-luciferase cells. Results: PCa cells with aggressive phenotype ability to determine visceral and bone metastases express high levels of CXCR4 and E-selectin ligands than normal or not aggressive/non-metastasizing PCa cell lines. In vitro, we demonstrated that bone microenvironment sustains CXCR4 and SDF1-α expression determining increased efficacy toward CXCR4 pharmacological inhibition. Additionally, SDF-1α induced tumor cell migration and invasion, as well as MMP-9, MMP-2 and uPA expression that were reduced by CXCR4 inhibition. In vivo, we demonstrated that the percentage of tibiae positive by X-ray and the size of osteolytic lesions were reduced by treatments mainly when we used plerixafor and GMI11359, whereas GMI11271 effects were not significant when compared to controls. The amounts and the size of bone metastases were significantly reduced when mice were treated with plerixafor, GMI1359 and GMI1271 in combination with docetaxel. The effects were more marked with plerixafor and GMI1359 when compared with GMI11271. The reduced intra-osseous growth of PC3M cells, as a result of treatments, correlated with decreased osteolysis and serum levels of both mTRAP and type I collagen fragments. Conclusion: Our report provides novel information on the potential activity of CXCR4 inhibitors as compounds able to increase/restore docetaxel sensitivity of metastatic bone lesions and supports a biological rationale for the use of these inhibitors in men at high risk to develop clinically evident bone lesions who have undergone taxane-based chemotherapy as first-line of therapy. However, further experiments are necessary to examine the effective role of CXCR4 and/or E-selectin in the metastatic process of PCa.

1Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy;
2Medical Oncology, Azienda Ospedaliera Giovanni XXIII, Bergamo, Italy;
3Medical Oncology, Ospedale Di Bolzano, Bolzano, Italy;
4Medical Oncology, Azienda Ospedaliero Universitaria Careggi, Firenze, Italy;
5Medical Oncology, Azienda Ospedaliera Trevisiglio E Caravaggio, Trevisiglio, Italy;
6Medical Oncology, Universitá Cattolica Del Sacro Cuore, Policlinico Universitario A. Gemelli, Rome, Italy;
7Urology, Universitá Cattolica Del Sacro Cuore, Policlinico Universitario A. Gemelli, Rome, Italy;
8Medical Oncology, IRCCS Istituto Oncologico Veneto, Padua, Italy;
9Urology, Azienda Ospedaliera " Ospedali Riuniti Marche Nord", Fano, Italy;
10Prostate Cancer Unit, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy;
Besides promoting the cultural and organizational switch to multidisciplinarity and multiprofessionality in Italy, the educational project PerSTEP supported by the Italian Society for Urologic Oncology (SIUrO) and the Board of Medical Oncology Directors (CIPOMO) wanted to make a picture of the multidisciplinary activities performed by the participating centers and start a discussion on the efficacy of the interdisciplinary collaboration in the management of prostate cancer patients. The 23 centers participating in PerSTEP were invited to collect and send the data of 3 months’ activity. Nineteen joined the call and gathered this information: - number of patients with genito-urinary cancers (total and split for cancer site) managed with a multidisciplinary approach (either in clinics or discussed in tumor boards); - number of patients to whom the Multidisciplinary Team changed the stage; - number of patients to whom the Multidisciplinary Team changed the therapeutic and observational options; - number of patients who had received partial or incorrect information in previous consultations; - number of patients who required psychological support. The patients with genito-urinary cancers managed with a multidisciplinary approach were 1,420. Prostate cancer patients were 920. Fourteen centers reported that the multidisciplinary evaluation was effective in a better definition of the stage of the patients. This happened in 80 cases (8.7%). Fifteen centers reported that the multidisciplinary approach led to changing the therapeutic and observational options that patients had received before. This happened in 153 cases (12.5%). Sixteen centers reported that patients had received partial or incorrect information in previous consultations. This happened in 197 cases (21.4%). Ten centers reported that patients asked for psychological support after the multidisciplinary evaluation. This happened in 86 cases (0.9%).
Despite the limitations of this data collection, PerSTEP centers wanted to determine if the interaction of urologists, radiation oncologists and medical oncologists, supported by other specialists, such as pathologists, psychologists and imaging specialists, could prove effective in the management of prostate cancer patients and confirm the theoretical assumption of the advantages of multidisciplinary working. Having said this, further data on the way the centers work are needed to make a more detailed picture and to support these preliminary interesting results. Last but not least, further effort will be necessary to promote the cultural and organizational change towards a multidisciplinary management of prostate cancer patients and overcome the barriers towards multiprofessional team working effectively for health professionals and patients.

A special thank to SANOFI for supporting the communication plan of PerSTEP.

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DOES CHOLINE PET/CT SCAN ACCURATELY DETECT NODAL RELAPSES OF PROSTATE CANCER AFTER BIOCHEMICAL RECURRENCE? RESULTS FROM A MULTI-INSTITUTIONAL STUDY

Marco Oderda1, Paolo Gontero1, Guglielmo Melloni1, Stefania Munegato1, Marco Falcone1, Hannes Van Den Bosche2, Steven Deconinck2, Fabio Zattoni3, Robert Jeffrey Karnes3 and Steven Joniau4

1Department of Urology, San Giovanni Battista Hospital, Turin, Italy;
2Department of Urology, University Hospitals of The KU Leuven, Leuven, Belgium;
3Department of Urology, Mayo Clinic, Rochester, MN, U.S.A.;
4Department of Urology, University Hospitals of The KU Leuven, Leuven, Belgium

Introduction and Objectives: 11C-choline positron emission tomography (PET)/computed tomography (CT) scan has a sensitivity ranging between 38% and 98% in staging procedures for prostate cancer (PCa) biochemical recurrence (BCR) after initial radical treatment with curative intent. Only a few reports have focused on the correlation between PET/CT scan and clinical lymph node (LN) relapse at pathological examination in men who underwent pelvic and/or retroperitoneal LN dissection. Our aim was to assess PET scan accuracy for the detection of LN relapses after BCR.

Materials and Methods: This retrospective multi/institutional study included 102 patients with BCR of PCa after radical treatment; all men underwent choline PET/CT staging and subsequent salvage lymphadenectomy. A comparison of PET/CT to histological findings was performed and analyzed in terms of sensitivity, specificity and accuracy, stratifying into three main anatomical regions (Region A: internal iliac, obturator and external iliac; region B: presacral and common iliac; region C: retroperitoneal, including the mesenteric level up to the renal vessels). Results: Mean age and PSA at BCR was 65 years (range=47-81) and 3.1 (range=0.2-47.7), respectively. First-line treatment was radical prostatectomy (n=97), radiotherapy (n=3) and brachytherapy (n=2). Overall sensitivity, specificity and accuracy of PET/CT were 71.7%, 67.1% and 69.4%, respectively (Table I). When stratified by anatomical region, sensitivity was very high (90.9%) for pelvic region A, at the cost of low specificity (43.5%); on the contrary, retroperitoneal region C had high specificity (89.5%) but low sensitivity (54.2%). At regression analyses, PET/CT accuracy improved at the increase of the total number of dissected nodes. Mean dissected node numbers were 12.3±8.1, 8.7±5.7 and 9.7±10.6 for region A, B and C, respectively. Conclusion: Detection of LN relapses by PET/CT imaging is limited by a high false positive rate in the iliac-obturatory region and, more alarmingly, a high false negative rate in the retroperitoneal regions. PET accuracy increases with the number of lymphadenectomy dissected nodes. An extended and predefined template should be followed in this procedure.

Table I. (Abstract 110).

<table>
<thead>
<tr>
<th></th>
<th>Pelvic region (A)</th>
<th>Pelvic region (B)</th>
<th>Retroperitoneal region (C)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>90.9% (60/66)</td>
<td>54.2% (26/48)</td>
<td>54.2% (13/24)</td>
<td>71.7% (99/138)</td>
</tr>
<tr>
<td>Specificity</td>
<td>43.5% (10/23)</td>
<td>71.4% (20/28)</td>
<td>89.5% (17/19)</td>
<td>67.1% (47/70)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>82.2% (60/73)</td>
<td>76.5% (26/34)</td>
<td>86.7% (13/15)</td>
<td>81.1% (99/128)</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>62.5% (10/16)</td>
<td>47.6% (20/42)</td>
<td>60.7% (17/28)</td>
<td>54.6% (47/86)</td>
</tr>
<tr>
<td>Area under the curve (AUC)</td>
<td>67.2%</td>
<td>62.8%</td>
<td>71.8%</td>
<td>69.4%</td>
</tr>
<tr>
<td>Odds ratio (OR)</td>
<td>7.69 (2.37-24.94), p&lt;0.001</td>
<td>2.95 (1.09-8.01), p=0.003</td>
<td>10.04 (1.89-53.40), p=0.007</td>
<td>5.18 (2.78-9.65)</td>
</tr>
</tbody>
</table>

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URINARY AND ERECTILE FUNCTION IN PROSTATE CANCER PATIENTS: RADICAL RADIOTHERAPY VS. ACTIVE SURVEILLANCE

Maria Francesca Alvisi1, Tiziana Rancati1, Fabio Badenchini2, Claudio Fiorino3, Cesare Cozzarini4, Federica Paolorini5, Vittorio Vavassori5, Giuseppe Girelli6, Claudio Degli Esposti7, Barbara Avuzzi8, Nice Bedini8, Sara Morlino8, Sergio Villa8, Mario Catanzaro9, Massimo Maffezzini9, Nicola Nicolai9, Silvia Stagni9, Tullio Torelli9, Roberto Salvioni9, Cristina Marengi9, Edoardo Tulli Baldoin1, Silvia Villa1, Lara Bellardita1, Tiziana Magnani1 and Riccardo Valdagni10

1Prostate Program, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 2Prostate Program and Radiotherapy, Fondazione IRCCS Istituto Nazionale dei Tumori and San Raffaele Scientific Institute, Milan, Italy; 3Medical Physics, San Raffaele Scientific Institute, Milan, Italy; 4Radiotherapy, San Raffaele Scientific Institute, Milan, Italy; 5Radiotherapy, Gavazzeni - Humanitas, Bergamo, Italy; 6Radiotherapy, Ospedale ASL9, Ivrea, Italy; 7Radiotherapy, Ospedale Bellaria, Bologna, Italy; 8Radiation Oncology 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 9Urology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 10Prostate Program and Radiation Oncology 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Aim: International prostate symptoms score (IPSS) and International index of erectile function (IIEF-5) were assessed in prostate cancer (PCa) patients. We here compare IPSS and IIEF-5 in active surveillance (AS) vs. radical radiotherapy (RT).

Materials and Methods: Questionnaires filled in at 4 follow-up times: T0=enrollment in AS/RT; T1=10 months after diagnosis (fairly corresponding to 3 months from RT end); T2=12 months from diagnosis/6 months from RT and T3=24 months from diagnosis/18 months from RT. RT population also had measurement at RT end. In the RT population, the subset of patients without androgen deprivation (AD) was selected for IIEF-5 analysis. IPSS was divided into 3 classes: 0-7 (mild symptoms), 8-19 (moderate symptoms), 20-35 (severe symptoms). IIEF-5 was separated into 3 levels: 22-25 (no erectile dysfunction (ED)), 12-21 (mild/moderate ED), 0-11 (severe ED). Significant changes in IPSS over time were defined as > 6 (moderate worsening) and > 10 (severe worsening) increase. Z-test for proportions was used to investigate statistically significant differences in % of patients with moderate to severe worsening in the two cohorts (AS vs. RT). Significant decline in IIEF-5 was defined as severe ED in patients with IIEF-5 >11 at T0.

Results: Cohorts: 247 patients (AS), 494 patients (RT-IPSS),

Figure 1. a, b. Mean of variation in IPSS relative to baseline during the follow up period for AS patients (a) and RT patients (b). c, d. IIEF mean scores for AS and RT patients, grouped by IIEF at T0 for age <70 years old (c) and age>= 70 years old (d).
202 patients (RT-no AD). Median age: 64 (AS) vs. 72 (RT) years. IPSS significantly greater in high prostate volumes (>65cc, \( p=0.007 \)). IIEF-5 declines with age (continuous, \( p=0.001 \)). When considering IPSS changes coupled to baseline class stratification (no symptoms vs. mild vs. severe; Figure 1a-b), a different behavior is highlighted for AS vs. RT in no and mild symptoms class: AS patients show a slight worsening with time (aging?), while RT patients show a marked worsening at RT end, which is then recovered till AS levels are reached. Notably, patients with severe symptoms at baseline display partial resolution of their symptoms in both cohorts. This is probably due to prescription of drugs for benign prostatic hyperplasia in AS cohort and to AD in RT patients. Moderate IPSS worsening was reported in 2% vs. 14% patients at T1, (AS patients). Moderate IPSS worsening was reported in 2% of patients with severe symptoms at baseline. Worsening in RT seems here entirely due to RT (younger patients reported just a small decline. Older patients: effect of ageing were more evident in AS with substantial decline over time. RT patients showed combined effect of ageing+RT with worsening and no recover. Ageing effect was less evident in patients with mild baseline ED: here, a decline at time of rebiopsy (in AS) was observed, but then initial levels recovered. Worsening in RT seems here entirely due to RT (younger patients exhibiting greater decline). Significant decline in IIEF, defined as severe ED in patients with IIEF-5 >11 at T0, was always significantly higher in RT, about 13% vs. 40% (\( p<0.05 \)). Conclusion: IPSS showed a significant worsening in RT at short follow-up (acute phase of radioinduced toxicity). Due to the timing of onset of late urinary toxicity, these results (limited to 18 months follow-up) cannot be considered conclusive for this endpoint. Greater worsening of ED in RT is shown, especially when younger patients are considered. For older patients, the effect of ageing sums up with dose, especially for initially potent patients. Comparison between AS and RT allows evaluation of confounding factors (ageing, psychological aspects) when studying ED after RT, thus allowing a more confident estimation of the role of RT in the onset of this kind of morbidity.

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THIRTY YEARS OF RADICAL PROSTATECTOMIES AT A SINGLE TERTIARY CARE REFERRAL CENTER

Vincenzo Scattoni\(^1\), Paolo Dell’oglio\(^1\), Nicola Fossati\(^1\), Giorgio Gandaglia\(^1\), Alessandro Nini\(^1\), Nazareno Suadri\(^1\), Andrea Salonia\(^1\), Massimo Freschi\(^1\), Patrizio Rigatti\(^2\), Francesco Montorsi\(^1\) and Alberto Briganti\(^1\)

\(^1\)Division of Oncology/Unit of Urology; URI, IRCCS Ospedale San Raffaele, Milan, Italy;  
\(^2\)Department of Urology, Istituto Auxologico Italiano, Milan, Italy

Introduction and Objectives: After the introduction of screening programs for early prostate cancer (PCa) detection, the incidence of organ confined PCa has steadily increased. Moreover, several alternative treatments have been introduced for the management of PCa in latest years. However, only few studies have shown the changing clinical characteristics of patients submitted to radical prostatectomy (RP) over a long period of time. We hypothesized that the clinical characteristics of patients submitted to RP for clinically localized PCa has changed over the last 30 years. Materials and Methods: We evaluated 8,580 PCa patients treated with RP in the last 30 years (1985-2014) at a single center. Patients were divided into decades according to the year of surgery. ANOVA test and Chi-square analysis of proportions were used in order to analyze the differences of clinical and pathological characteristics according to the date of surgery for continuous and categorical variables, respectively. The trend test was used to test the statistical significance of trends in proportions over time. Results: Mean age was 65 years. Overall, 2,643 (30.8%), 3,835 (44.7%) and 2,102 (24.5%) patients had low, intermediate and high-risk disease. Mean age was 66.8 and 64.1 years in the 1st and 6th decile (\( p<0.001 \)). The proportion of low risk patients was 10.7% in the first vs. 24.5% in the last decile, respectively (\( p<0.001 \)). There was a significant trend towards higher rates of low risk patients submitted to RP up to 2008 (39.7%) and, thereafter, the trend was toward lower rates. The proportion of intermediate-risk patients was 41.5% in the first vs. 49.5% in the last decile, with no significant variations among time. The proportion of high-risk patients was 47.8% in the first vs. 26% in the last decile. After an initial sharp decrease in the rate of high-risk patients submitted to RP, a constant trend towards higher rates was observed after 2008. Lymph node invasion was 17.2% in the first vs. 13.9% in the last decile, respectively. Finally, pathologically assessed tumor volume (TV) decreased significantly over time from 2000 to 2008 with a significant trend towards higher TV in the last 6 years. Conclusion: Our 30-year data show a trend towards less aggressive and less advanced disease between 1985 and 2008 in patients submitted to RP. However, in the last 6 years, a trend towards more aggressive disease is observed in surgical candidates. These figures might be related to the recent introduction of conservative management strategies.

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IMPACT OF STAGE MIGRATION AND PRACTICE CHANGES ON HIGH-RISK PROSTATE CANCER: RESULTS FROM PATIENTS TREATED WITH RADICAL PROSTATECTOMY AT A SINGLE CENTER OVER THE LAST TWO DECADES
Nicola Fossati, Umberto Capitanio, Giorgio Gandaglia, Marco Bianchi, Nazareno Suardi, Andrea Salonia, Massimo Freschi, Francesco Montorsi, Alberto Briganti and Vincenzo Scattoni

Division of Oncology/Unit of Urology; URI, IRCCS Ospedale San Raffaele, Milan, Italy

Introduction and Objectives: Phenotype of prostate cancer (PCA) at diagnosis has changed through the years due to prostate specific antigen (PSA) screening and changes in Gleason grading. The objective of this study was to determine whether tumor characteristics have changed over time in the high-risk population and whether this has resulted in a change in oncological outcomes. Materials and Methods: We evaluated 1,033 high-risk patients, defined as the presence of at least one of the following risk factors: prostate-specific antigen (PSA) >20 ng/ml and/or clinical stage ≥T3 and/or biopsy Gleason score ≥8. Patients were treated with radical prostatectomy and extended pelvic lymph node dissection at a single center between 1990 and 2013. Year-per-year trends of clinical and pathologic characteristics were examined. Multivariable Cox regression analysis was used to test the relationship between year of surgery and oncologic outcomes that consisted of biochemical recurrence (defined as PSA value ≥0.2 ng/ml) and distant metastasis. Covariates were age at surgery, PSA, pathologic Gleason score and specimen confined disease. Results: The total number of prostatectomies performed yearly on high-risk patients increased over the course of the study, from 5 procedures in 1990 to more than 100 procedures in 2013. We observed a decrease over time in the proportion of high-risk patients with a preoperative PSA level >20 ng/ml (odds ratio (OR)=0.64; p<0.001) or clinical stage ≥T3 (OR=0.90; p=0.07). An opposite trend was seen for biopsy Gleason score ≥8 (OR=1.65; p<0.001). We observed a considerable increase in the median number of lymph nodes removed (coefficient=2.01; p<0.001) that was associated with an increased rate of lymph node invasion (OR=1.12; p=0.08). At multivariable Cox regression analysis, year of surgery was associated with a reduced risk of biochemical recurrence (hazard ratio (HR)=0.96; p=0.01) and distant metastasis (HR=0.91; p=0.042). Conclusion: Improvements in diagnostic strategies over the last two decades have led to an increased diagnosis of localized and less extensive high-grade PCAs. However, the rates of higher Gleason grade increased and this was likely due to refinements in Gleason attribution. Radical prostatectomy combined with anatomically extended pelvic lymph node dissection has shown an improvement in cancer control over time. The changes in phenotype of high-risk PCAs, as well as the improved outcomes of surgery, need to be considered for the optimal management of contemporary high-risk patients.

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IMPACT OF PRE-TREATMENT PSA LEVEL ON CANCER CONTROL AFTER EARLY SALVAGE RADIATION THERAPY POST RADICAL PROSTATECTOMY: NEED FOR PATIENT STRATIFICATION ACCORDING TO PROSTATE CANCER FEATURES

Nicola Fossati1, Jeffrey Karnes2, Cesare Cozzarini3, Claudio Fiorino3, Steven Joniau4, Wolfgang Hinkelbein5, Karin Haustermans6, Bertrand Tombal7, Shahrokhi F. Shariat8, Gregor Goldner9, Francesco Montorsi3, Hein Van Poppel4, Thomas Wiegel10, Alberto Briganti1 and Vincenzo Scattoni1

1Division of Oncology/Unit of Urology; URI, IRCCS Ospedale San Raffaele, Milan, Italy; 2Department of Urology, Mayo Clinic, Rochester, MN, U.S.A.; 3Department of Radiotherapy, IRCCS Ospedale San Raffaele, Milan, Italy; 4Department of Urology, University Hospitals Leuven, Leuven, Belgium; 5Department of Radiation Oncology, Charité Universitätsmedizin, Campus Benjamin Franklin, Berlin, Germany; 6Department of Radiotherapy, University Hospitals Leuven, Leuven, Belgium; 7Department of Urology, Université Catholique de Louvain, Brussels, Belgium; 8Department of Urology, Medical University of Vienna, Vienna General Hospital, Vienna, Austria; 9Department of Radiation Oncology, Medical University of Vienna, Vienna, Austria; 10Department of Radiation Oncology, University Hospital Ulm, Ulm, Germany

Introduction and Objectives: Early salvage radiotherapy (eSRT) represents an option for biochemical recurrence (BCR) after radical prostatectomy (RP). However, the optimal prostate-specific antigen (PSA) level for eSRT initiation is still unclear. We hypothesized that the association between PSA at eSRT and cancer control is not linear and that it is significantly associated with prostate cancer features at RP. Materials and Methods: We evaluated a multi-institutional cohort of 716 node-negative patients with early undetectable postoperative PSA (<0.1 ng/ml) who experienced BCR after RP. All patients received eSRT, defined as local radiation to prostate and seminal vesicle bed, delivered at PSA ≤0.5 ng/ml. BCR after eSRT was defined as two consecutive PSA values ≥0.2 ng/ml. Multivariable Cox regression analyses tested the association between pre-eSRT PSA level and BCR. Covariates consisted of pathologic stage, pathologic Gleason score and surgical margin status. Locally weighted scatter plot smoothing (lowess) methods were used to explore the relation...
between pre-eSRT PSA level and BCR-free survival rate at 5 years after eSRT according to cancer characteristics at RP.

Results: Median follow-up after eSRT was 47 months. The 5-year BCR-free survival rate was 81%. At multivariable analysis, pre-eSRT PSA level was associated with BCR after eSRT (hazard ratio (HR)=4.89; \(p<0.0001\)). Moreover, pathologic stage ≥pT3b (HR=2.07; \(p=0.007\)), pathologic Gleason score ≥8 (HR=2.69; \(p=0.0002\)) and negative surgical margins (HR=2.50; \(p<0.0001\)) were associated with BCR and were identified as risk factors. Overall, using lowess methods, we observed a decrease of 5-year BCR-free survival rate from 87% to 75% for pre-eSRT PSA level ranging from 0.1 ng/ml to 0.5 ng/ml. Overall, the 5-year BCR risk increased by 3% per 0.1 ng/ml of PSA level. However, when patients were stratified according to the number of risk factors (≤1 vs. ≥2), the effect of increasing PSA at eSRT on cancer control was higher in men with more aggressive disease. Specifically, patients with ≥2 pathologic risk factors showed a 5-year increased risk of BCR equal to 10% per 0.1 ng/ml of PSA level vs. 1.5% in patients with a single risk factor (\(p<0.001\)).

Conclusion: Cancer control after eSRT depends on pretreatment PSA level. This effect is highest in men with, at least, two of the following features: pT3b/pT4 disease, pathologic Gleason score ≥8 and negative surgical margins. In these patients, eSRT should be administered at the very first sign of PSA increase in order to maximize cancer control.

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ROBOT-ASSISTED LAPAROSCOPIC VESICULECTOMY FOR LARGE SEMINAL VESICLE CYSTOADENOMA: A CASE REPORT AND REVIEW OF THE LITERATURE

Riccardo Campi1, Maria Rosaria Raspollini2, Agostino Tuccio1, Andrea Mari1, Jacopo Frizzi1, Giampaolo Siena1, Sergio Serni1, Marco Carini1, Alberto Lapini1 and Andrea Minervini1

1Department of Urology, Careggi Hospital, University of Florence, Florence, Italy;
2Department of Pathology, Cargo Hospital, University of Florence, Florence, Italy

Figure 1. (Abstract 115).
Case Report: A 47-year-old patient was referred to our centre for gross hematuria, mild dysuria and other lower urinary tract symptoms (LUTS). Past medical history was unremarkable and no co-morbidities were present. Digital rectal examination (DRE) revealed, cranially to the prostate, a tense-elastic mass with undefined upper and lateral boundaries. Prostate-specific antigen (PSA) level was 1.7 ng/ml. Physical examination and laboratory tests were otherwise normal. Trans-abdominal ultrasound showed no lesions or abnormalities in the upper urinary tract; high-resolution trans-rectal ultrasound (TRUS) confirmed the presence of a multi-septed, solid-cystic pelvic mass occupying the retrovesicle space. An office cystoscopy showed no lesions within the bladder. Pelvic magnetic resonance imaging (MRI) confirmed the presence of a retrovesicle, 6.0×4.5 cm in size.

Table I. Strategies for diagnosis and types of surgical approach for seminal vesicle cystoadenoma according to the published series. TRUS, transrectal ultrasound; CT, computed tomography; MRI, magnetic resonance imaging; CYS, cystoscopy; FNA, fine needle aspiration; Abd US, abdominal ultrasound, RALV, robot-assisted laparoscopic vesiculectomy.

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient’s age (years)</th>
<th>Tumor size (greatest diameter) (cm)</th>
<th>Diagnostic strategy</th>
<th>Surgical procedure</th>
<th>Perioperative complication Y=present, N=absent</th>
<th>Local recurrence Y=present, N=absent (years after surgery)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soule et al. Proc Staff Meet Mayo Clin., 1951.</td>
<td>47</td>
<td>14</td>
<td></td>
<td>Open (Conservative)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Damjanov et al. J Urol., 1974.</td>
<td>52</td>
<td>5.5</td>
<td>Autopsy</td>
<td>Open (Cysto-prostatovesiculectomy)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Lundhus et al. Scand J Urol Nephrol., 1984.</td>
<td>39</td>
<td>7.4</td>
<td></td>
<td>Open (Conservative)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Mazur et al. Am Jour of Surg Path 1987.</td>
<td>49</td>
<td>7</td>
<td></td>
<td>Open (Conservative)</td>
<td>N</td>
<td>Y (2)</td>
</tr>
<tr>
<td>Raghuvmeer et al. Indian J Pathol Microbiol., 1989.</td>
<td>63</td>
<td>3</td>
<td></td>
<td>Open (Conservative)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Mazzucchelli et al. J Urol., 1992.</td>
<td>50</td>
<td>12</td>
<td></td>
<td>Open (Conservative)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Ranschaert et al. J Belge Radiol., 1992.</td>
<td>49</td>
<td>15</td>
<td></td>
<td>Open (Conservative)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Lagalla et al. Abdom Imaging 1993.</td>
<td>49</td>
<td>3</td>
<td>CT, MRI, FNA - Cytology, Biopsy</td>
<td>Open (Conservative)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Santos et al Pathology., 2001.</td>
<td>49</td>
<td>7</td>
<td></td>
<td>Open (Conservative)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Gil et al International Braz J Urol., 2003.</td>
<td>49</td>
<td>7</td>
<td>Abd US, CT, MRI</td>
<td>Open (Conservative, retrovesicle approach)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Lee et al. Intern Jour of Urol., 2006.</td>
<td>46</td>
<td>7.5</td>
<td>CT, MRI, Explorative Laparotomy CT, MRI, Abd US, Biopsy</td>
<td>Open (Conservative)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Lorber et al Eur Urol., 2011.</td>
<td>52</td>
<td>14</td>
<td></td>
<td>Open (Conservative, transvesicle)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Kural et al. Journ of Endourol., 2011.</td>
<td>48</td>
<td>6</td>
<td>TRUS, Biopsy</td>
<td>RALV</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Ploumidis et al. Intern Jour of Surg Case Reports 2012.</td>
<td>45</td>
<td>17.2</td>
<td>TRUS, CT, MRI, CYS, FNA-Cytology, Intra-operative Biopsy</td>
<td>RALV</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Arora et al. Urology 2013.</td>
<td>23</td>
<td>5</td>
<td>TRUS, MRI</td>
<td>Open (Conservative)</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Zhu et al. Asian Journ of Andrology 2013.</td>
<td>31</td>
<td>5</td>
<td>CT, MRI</td>
<td>LV</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Zhang et al. Urology 2013.</td>
<td>32</td>
<td>5</td>
<td></td>
<td>LV</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Zhang et al. Urology 2013.</td>
<td>64</td>
<td>4.5</td>
<td></td>
<td>LV</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Zhang et al. Urology 2013.</td>
<td>50</td>
<td>3.8</td>
<td></td>
<td>LV</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>
cm well-defined pseudo-nodular mass, arising from the right seminal vesicle (SV) and vas deferens (VD) (Figure 1).

TRUS-guided prostatic and SVs biopsies showed no neoplastic proliferation in all the samples from both the prostate and the mass. The patient was then scheduled for robot-assisted laparoscopic vesiculectomy (RALV). After a transversal incision of the peritoneum at the level of the Douglas pouch, a voluminous mass, firmly adherent to the surrounding tissues, was found. The plane between the mass, the rectum and the bladder was carefully developed until the tumor was completely released from the surrounding adhesions. The left VD and SV were preserved during the dissection. The neuro-vascular bundles (NVBs) were approached bilaterally in an athermal, traction-free manner in
order to preserve continence and potency. The specimen was then removed intact through the camera port by using a retrieval bag. Accurate hemostatic control was achieved and a tube drain was positioned. Console time and estimated blood loss were, respectively, 120 minutes and 50 cc; no intraoperative complications were recorded. The postoperative course was uneventful and the patient was discharged on the fourth postoperative day with normal blood tests and spontaneous voiding. A two-year follow-up showed no evidence of disease recurrence. At present, the patient is free of symptoms with full preservation of continence and potency. Histopathological examination revealed a 7.0×4.5×4.5 cm cystic SV cystoadenoma (Figure 2).

No significant cytologic atypia, mitotic activity or necrosis were present. The proliferation index was <1%. Review of the Literature: A systematic review of the English-language literature was performed using the Medline, Embase and Web of Science databases up to December 2014. Twenty case reports have been published in literature on SV cystoadenoma (Table I).

Median patient age and median tumor diameter were 49 years (inter-quartile range (IQR)=42–51) and 7.0 cm (IQR 5.0–12.0), respectively. No perioperative complications were reported in all the published series. Local recurrence occurred in 2 cases (10%) after 2 and 3 years, respectively. The differential use of diagnostic investigations and surgical approaches for SV cystoadenoma in the published series is shown in Figure 3. Discussion and Conclusion: Primary tumors of SVs are very rare and the differential diagnosis must be based on a multimodality approach. Most cases of SV cystoadenoma were managed with open surgery through transvesicle/retrovesicle approaches or radical cysto-prostate-vesiculectomy. To date, minimally-invasive seminal vesiculectomy (MISV) is increasingly used for the treatment of beginning diseases of SVs achieving optimal oncologic and functional results. Therefore, they could be considered the new gold standard for the treatment of such rare diseases.

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CURRENT STRATEGIES FOR DIAGNOSIS AND TREATMENT OF BENIGN TUMORS OF SEMINAL VESICLES: A SYSTEMATIC REVIEW OF THE LITERATURE
Riccardo Campi, Agostino Tuccio, Giampaolo Siena, Andrea Mari, Gianni Vittori, Michele Lanciotti, Andrea Coci, Riccardo Fantechi, Andrea Chindemi, Tommaso Jaeger, Sergio Serni, Marco Carini, Alberto Lapini and Andrea Minervini
Department of Urology, Careggi Hospital, University of Florence, Florence, Italy

Introduction/Aim: Benign tumors (BT) of seminal vesicles (SV) are very rare. Diagnosis could be challenging and often requires the histopathological analysis after surgical excision. The best surgical treatment is still matter of discussion. The aim of this review is to analyze the current strategies for diagnosis and treatment of such tumors. Materials and Methods: A systematic review of English literature was performed using the Medline, Embase and Web of Science databases up to October 2014. Use of diagnostic investigations, options of surgical management, perioperative complications rate and oncologic outcomes were analyzed for each tumor histotype. Results: Fifty-eight case reports have been published in literature on BTs of SVs (Table I). Of these, 5 were excluded from the analysis due to lack of data. Cystoadenoma was found in 20 cases (38%), leiomyoma in 10 (19%), schwannoma in 8 (15%), mixed epithelial-stromal tumor in 5 (9%), phyllodes tumor in 4 (8%) and other BTs in 6 (11%) (Figure 1). Median patient age and median tumor diameter were 50 years (range=23–79) and 5.0 cm (range=2.0–29.0),
Table I. Overview of the 53 published series on benign tumors of seminal vesicles included in the analysis.

<table>
<thead>
<tr>
<th>Histopathological definition (according to the study)</th>
<th>Number of studies n (%)</th>
<th>Patients’ age (years), median (range)</th>
<th>Tumor size (greatest diameter) (cm), median (range)</th>
<th>Number of studies with a precise definition of the diagnostic strategy n (%)</th>
<th>Number of studies with a precise definition of the therapeutic strategy n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystoadenoma</td>
<td>20 (38)</td>
<td>49 (23-64)</td>
<td>7.0 (3.0-17.2)</td>
<td>10 (50)</td>
<td>19 (95)</td>
</tr>
<tr>
<td>Mixed epithelial - stromal tumors (MEST) - low grade</td>
<td>5 (9)</td>
<td>61 (37-70)</td>
<td>6.5 (2.5-29.0)</td>
<td>4 (80)</td>
<td>5 (100)</td>
</tr>
<tr>
<td>Leiomyoma</td>
<td>10 (19)</td>
<td>61 (37-74)</td>
<td>5.0 (2.0-14.5)</td>
<td>7 (70)</td>
<td>9 (90)</td>
</tr>
<tr>
<td>Phyllodes Tumor</td>
<td>4 (8)</td>
<td>43 (39-59)</td>
<td>7.6 (5.5-14.5)</td>
<td>3 (75)</td>
<td>4 (100)</td>
</tr>
<tr>
<td>Schwannoma (Neurilemmoma)</td>
<td>8 (15)</td>
<td>45 (31-79)</td>
<td>3.0 (2.2-7.0)</td>
<td>5 (63)</td>
<td>8 (100)</td>
</tr>
<tr>
<td>Others (mammary-type myofibroblastoma, paraganglioma, cystomyoma, low-grade adnexal tumour of Wollfian origin, solitary fibrous tumor)</td>
<td>6 (11)</td>
<td>55 (29-79)</td>
<td>5.8 (2.0-14.0)</td>
<td>5 (83)</td>
<td>6 (100)</td>
</tr>
<tr>
<td>All tumors</td>
<td>53 (100)</td>
<td>50 (23-79)</td>
<td>5.5 (2.0-29.0)</td>
<td>34 (64)</td>
<td>51 (96)</td>
</tr>
</tbody>
</table>

Figure 2. (Abstract 116).
**Table II. Use of diagnostic investigations in the published literature on benign tumors of seminal vesicles.**

<table>
<thead>
<tr>
<th>Histopathological Definition (according to the study)</th>
<th>Ultrasound (TRUS +/- Abd US), n (%)</th>
<th>CT n (%)</th>
<th>MRI n (%)</th>
<th>Tumor biopsy n (%)</th>
<th>Intraoperative biopsies n (%)</th>
<th>Exploratory laparotomy n (%)</th>
<th>Other strategies (Cystoscopy, FNA - Cystology, IV Urography, etc.), n (%)</th>
<th>Autopsy n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cistoadenoma</td>
<td>6 (60)</td>
<td>6 (60)</td>
<td>7 (70)</td>
<td>4 (40)</td>
<td>1 (10)</td>
<td>1 (10)</td>
<td>2 (20)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Mixed epithelial - stromal tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(MEST) low-grade</td>
<td>1 (25)</td>
<td>4 (100)</td>
<td>2 (50)</td>
<td>3 (75)</td>
<td>0 (0)</td>
<td>1 (25)</td>
<td>1 (25)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Leiomyoma</td>
<td>3 (43)</td>
<td>4 (57)</td>
<td>4 (57)</td>
<td>2 (29)</td>
<td>0 (0)</td>
<td>1 (15)</td>
<td>0 (0)</td>
<td>1 (15)</td>
</tr>
<tr>
<td>Phylloides tumors</td>
<td>2 (67)</td>
<td>2 (67)</td>
<td>2 (67)</td>
<td>1 (33)</td>
<td>0 (0)</td>
<td>1 (33)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Schwannoma (neurilemmoma)</td>
<td>5 (100)</td>
<td>4 (80)</td>
<td>3 (60)</td>
<td>4 (80)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Others (mammary-type myofibroblastoma, paraganglioma, cystomyoma, low-grade adnexal tumour of Wolffian origin, solitary fibrous tumor)</td>
<td>2 (40)</td>
<td>3 (60)</td>
<td>2 (40)</td>
<td>3 (60)</td>
<td>0 (0)</td>
<td>1 (20)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>All tumors</td>
<td>19 (56)</td>
<td>23 (68)</td>
<td>20 (59)</td>
<td>17 (50)</td>
<td>1 (3)</td>
<td>5 (15)</td>
<td>3 (9)</td>
<td>2 (6)</td>
</tr>
</tbody>
</table>

Numbers and percentages are referred to those studies where a precise definition of the diagnostic work-up was clearly stated (see Table I). TRUS, transrectal ultrasound; CT, computed tomography; MRI, magnetic resonance imaging; CYS, cystoscopy; FNA, fine needle aspiration; Abd US, abdominal ultrasound.
Table III. Use of different surgical treatments in the published literature on benign tumors of seminal vesicles. Numbers and percentages are referred to those studies where a precise definition of the surgical technique was clearly stated (see Table I).

<table>
<thead>
<tr>
<th>Histopathological definition (according to the study)</th>
<th>Open - Conservative tumorectomy (with different approaches) n (%)</th>
<th>Open - Cysto-vesiculectomy n (%)</th>
<th>Laparoscopic vesiculectomy (LV) n (%)</th>
<th>Robot-assisted laparoscopic vesiculectomy (RALV) n (%)</th>
<th>Perioperative complications (Y=any complication reported; N=no complications reported)</th>
<th>Local recurrence n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cistoadenoma</td>
<td>11 (58)</td>
<td>1 (5)</td>
<td>5 (26)</td>
<td>2 (11)</td>
<td>N</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Mixed epithelial - stromal tumors (MEST) low grade</td>
<td>2 (40)</td>
<td>2 (40)</td>
<td>1 (20)</td>
<td>0 (0)</td>
<td>N</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Leiomyoma</td>
<td>5 (55)</td>
<td>1 (11)</td>
<td>3 (33)</td>
<td>0 (0)</td>
<td>N</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Phylloides tumors</td>
<td>2 (50)</td>
<td>0 (0)</td>
<td>2 (50)</td>
<td>0 (0)</td>
<td>N</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Schwannoma (neurilemmoma)</td>
<td>2 (25)</td>
<td>1 (13)</td>
<td>5 (63)</td>
<td>0 (0)</td>
<td>N</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Others (mammary-type myofibroblastoma, paraganglioma, cystomyoma, low-grade adnexal tumour of Wolffian origin, solitary fibrous tumor)</td>
<td>4 (67)</td>
<td>1 (17)</td>
<td>1 (17)</td>
<td>0 (0)</td>
<td>N</td>
<td>1 (17)</td>
</tr>
<tr>
<td>All tumors</td>
<td>26 (51)</td>
<td>6 (12)</td>
<td>17 (33)</td>
<td>2 (4)</td>
<td>N</td>
<td>3 (6)</td>
</tr>
</tbody>
</table>

Figure 4. (Abstract 116).
respectively. In 34 papers (64%), the diagnostic work-up was accurately described (Table II, Figure 2). In these studies, ultrasound (US) was used in 19 cases (56%), CT scan in 23 (68%), endorectal MRI in 20 (59%), preoperative biopsy in 17 (50%) and intraoperative biopsy in 1 case (3%). Explorative laparotomy was carried out in 5 cases (15%), while cystoscopy and other modalities in 3 (9%); finally, 2 cases (6%) were found at the time of autopsy. In 51 studies (96%), the surgical technique was well defined (Table III, Figure 3). An open approach was used in most cases, with conservative tumorectomy in 26 cases (51%) and radical cysto-prostato-vesiculectomy in 6 (12%). Laparoscopic and robotic seminal vesiculectomy (SVe) were performed in 17 (33%) and 2 (4%) cases, respectively. Differential use of diagnostic modalities and surgical techniques for each tumor histotype is presented in Figures 4 and 5, respectively. No perioperative complications were reported in the published series. Local recurrence occurred in 3 cases (6%). Nonetheless, the period of follow-up was highly variable among the studies.

Discussion and Conclusion:
The first priority during the diagnostic assessment of a SVs neoplasm is to rule out primary or secondary malignancies. The overall preoperative evaluation is critical to choose the most appropriate surgical treatment. MRI and preoperative biopsy are fundamental in the diagnostic work-up in order to define the anatomic relationships of the tumor and characterize its nature. MRI accurately defines the anatomic relationships of the tumor, while biopsy the characterization of its nature and, consequently, the more appropriate surgical strategy. SVe is the recommended treatment for solid masses that are benign on biopsy, if symptomatic. Although most cases in the literature were managed with open surgery, nowadays, laparoscopic or robotic SVe should be considered the gold standard treatment since they combine a minimally-invasive approach with excellent oncologic outcomes. Nonetheless, the overall grade of recommendation is currently low as the evidence is still based on case reports and sporadic case series.

117
LARGE PELVIC GOSSYPIBOMA DIAGNOSED AT THE TIME OF RADICAL PROSTATECTOMY 30 YEARS AFTER INGUINAL HERNIOPLASTY
Giampaolo Siena, Riccardo Campi, Andrea Mari, Andrea Minervini, Marco Carini, Alberto Lapini and Sergio Serni
Department of Urology, Careggi Hospital, University of Florence, Florence, Italy

Case Report: A 71-year-old man was referred to our centre for obstructive lower urinary tract symptoms (LUTS) and history of a vague, chronic discomfort in the right groin and testis since many years. Prostate-specific antigen (PSA) level was 12 ng/dl. The diagnostic work up revealed a Gleason score 4+4=8 adenocarcinoma of the prostate. No bone metastases were
present. At the preoperative computed tomography (CT) scan, there was no evidence of pathologic pelvic lymph nodes on the left side of the pelvis, while a 3.0×5.0 cm solid mass of unknown nature was found close to the right iliac vessels (Figure 1).

The central area was dishomogeneous as due to necrotic tissue; in turn, the peripheral, hypodense crown contained several hyperdense spots. The densitometric aspect of the prostate was highly irregular. The patient was then scheduled for open radical prostatectomy and extended pelvic lymph node dissection (ePLND). During the right lymph node dissection, a solid mass, firmly adherent to the right iliac vessels, was carefully isolated and removed intact. The intraoperative examination revealed a retained surgical sponge with a peripheral fibrous pseudocapsule resulting from an inflammatory foreign-body reaction, known in literature as gossypiboma or textiloma (Figure 2) (1).

Indeed, the patient underwent emergency surgery for incarcerated inguinal hernia 30 years before. Discussion and Conclusion: Although more infrequent with standardized surgical counting (2), gossypibomas can still be either asymptomatic occasional findings or, if not promptly diagnosed, life threatening causes of intestinal obstruction and acute abdomen. Moreover, they can simulate intra-abdominal gastrointestinal stromal tumors making the differential diagnosis challenging. The problem of retained surgical items affects both open and minimally invasive surgery (3). Prevention is a key aspect to ensure the maximal safety of surgical patients.


Figure 2. (Abstract 117).

118 CURRENT STATUS OF SIMPLE ENucleATION IN THE SCENARIO OF NEPHRON-SPARING SURGERY: A SYSTEMATIC REVIEW OF THE LITERATURE

Riccardo Campi, Gianni Vittori, Andrea Mari, Giampaolo Siena, Tommaso Jaeger, Agostino Tuccio, Mauro Gacci, Sergio Serni, Alberto Lapini, Marco Carini and Andrea Minervini
Department of Urology, Careggi Hospital, University of Florence, Florence, Italy
Introduction/Aim: Nephron-sparing surgery (NSS) is the gold standard treatment for localized renal tumors. At present, NSS can be performed either as standard partial nephrectomy (PN) defined as the excision of the tumor and of an additional margin of healthy peritumor renal parenchyma or as simple enucleation (SE)/enucleative partial nephrectomy. The aim of this review is to critically analyze the current status of SE in NSS.

Materials and Methods: A systematic review of the literature was performed using the Medline, Embase, Web of Science and Cochrane Library databases up to September 2014. Papers were rated through the International Consultation on Urological Diseases (ICUD) Levels of Evidence (LE) scale. The final GR was given following the ICUD rules for developing and grading guideline recommendations.

Results: Thirty-four studies have been published in literature on SE (Table I). Three were reviews of case series, while 31 original papers. Of these, 3 (10%) were good quality prospective cohort studies (LE 3), 20 (64%) good quality case series (LE 3) and 8 (26%) expert opinions (LE 4). The great majority of the evidence highlighted the positive value of SE; the overall GR is B. A synthesis of the evidence is presented. SE can be performed with open, laparoscopic and robotic approaches for T1a-T1b tumors (LE3; Grade C), both as elective treatment and for relative/absolute indications to NSS (LE3; Grade B). High Fuhrman grade might be a contraindication, even if no final recommendations can be stated. A possible advantage of SE was reported for tumors with unfavorable nephrometric scores (LE4; Grade C). Warm ischemia time (WIT) and perioperative complications are similar between SE and standard PN (LE3; Grade C), as well as local recurrence-free survival and cancer-specific survival (CSS) for T1a-T1b tumors (LE2-3; Grade B). SE is at least non-inferior to standard PN regarding the risk of positive SMs (LE3; Grade C). Most studies found no difference in progression-free survival between patients with and without neoplastic penetration of the pseudocapsule at long-term follow-up after SE. No comparative data on mid- and long-term functional outcomes have been reported to date. Discussion and Conclusion: The evidence in literature highlights the oncologic safety of SE. Some studies have shown a lower incidence of positive SMs for SE compared to standard PN. However, there is a substantial lack of standardized reporting in literature. Some studies do not even use the term “enucleation”; therefore, they could not be included in the analysis, losing a great body of evidence. Prospective studies are warranted to test the efficacy of SE for tumors with adverse nephrometric scores and to compare the results with standard PN. To date, the GR for SE is rather high. Nonetheless, the LE is still not optimal. Defining surgical standards in NSS is warranted to achieve a more appropriate analysis of literature and a clearer comparison of different techniques.

119 DOES HEXAMINOLEVULINATE DETECT CHROMOSOMAL ABERRATIONS IN THE FALSE-POSITIVE BLADDER BIOPSIES?

David D’andrea1, Valerio Olivieri2, Christine Mian3, Emanuela Trenti1, Salvatore Mario Palermo1, Evi Comploj1 and Armin Pycha1

1Urology, Central Hospital of Bolzano, Bolzano, Italy; 2Department of Urology, Sapienza University of Rome, Rome, Italy; 3Biology, Central Hospital of Bolzano, Bolzano, Italy

Abstracts of the 25th Annual Meeting of the Italian Society of Uro-Oncology (SIUrO), 21-23 June, 2015, Rome, Italy
**Introduction:** With the introduction of photosensitizing drugs allowing photodynamic diagnostic (PDD) for the bladder cancer, diagnosis has become more accurate. The main limitation of the procedure is the false-positive detection rate, which ranges from 12% to 60%. The onset of multifocal transitional cell carcinoma has been described as a panurothelial disease as it evolves because of genetic defects that are present also in histological negative urothelial tissue. **Objective:** We analyzed chromosomal patterns of false-positive lesions in the PDD and compared them with the findings of random biopsies with the intent to observe if hexaminolevulinate detects chromosomal aberrations in histological healthy tissue.  

**Patients and Methods:** Included in the study were 18 patient, 16 men and 2 women, with a mean age of 70.5 (range=47-83) years. All had false-positive PDD confirmed in the histology. A random sample was taken from all patients. The chromosomal patterns of all samples were analyzed with fluorescence in situ hybridization (FISH).  

**Results:** From January 2012 until November 2014, a total of 266 bladder biopsies were performed in 30 patients with a positive PDD finding. Eighteen patients had false-positive biopsies in a total of 40 biopsies. In these patients, a total of 25 random biopsies were also performed. Seven out of 18 patients showed chromosomal aberration in 10 (25%) of the false-positive biopsies. All 10 biopsies showed aneusomy of the Locus 9p21 (p16), 6 (13%) aneusomy of chromosome 3 and 5 biopsies (12,5%) aneusomy of chromosome 7 and chromosome 17. In 4 patients, the FISH of the control random biopsy was positive. One had an aneusomy of Locus 9p21 (p16), the other three had aneusomy also for chromosomes 3, 7 and 17. **Conclusion:** In our trial, over a third of the patients with a false-positive PDD finding already express chromosomal aberrations in these lesions.

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**120 SIMPLE ENUCLEATION FOR THE TREATMENT OF HIGHLY COMPLEX RENAL TUMORS: PERIOPERATIVE, FUNCTIONAL AND ONCOLOGICAL RESULTS**

Gianni Vittori, Andrea Mari, Riccardo Campi, Jacopo Frizzi, Tommaso Jaeger, Andrea Chindemi, Riccardo Fantechi, Andrea Cocci, Mauro Gacci, Alberto Lapini, Sergio Serni, Marco Carini and Andrea Minervini

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

**Aim:** To assess perioperative, functional and oncological results of simple enucleation (SE) in patients with highly complex renal tumors (PADUA score 10-13).  

**Materials and Methods:** Data of 510 patients treated with SE for renal cell carcinoma (RCC) between July 2006 and August 2013 in our Department were gathered in a prospectively maintained database. Of these, 96 had highly complex renal tumors (PADUA 10-13, Figure 1A) and were selected for this study, including 76 treated open and 20 with robotic SE (endoscopic robotic-assisted simple enucleation (ERASE)). Conventional perioperative variables were collected and compared between open and robotic approach with univariate analysis. Survival status and functional data were gathered at follow-up. The probability of survival was estimated by the Kaplan-Meier method.  

**Results:** Mean (range) clinical tumor diameter was 4.8 cm (interquartile range (IQR)=3-10). PADUA score was 10, 11, 12 and 13 in 57.3%, 29.2%, 11.5% and 2.1% of tumors, respectively. Overall, 19.8% of...
patients had stage ≥3 chronic kidney disease (CKD) and 17.7% an imperative/relative indication. Clamping of renal pedicle was used for almost all patients (99%) with a mean warm ischemia time (WIT) of 19.2±5.7 minutes. Mean operative time was 126 minutes, mean estimated blood loss (EBL) 200 cc and median length of stay (LOS) 6 days (IQR=5-7). Percentage of patients with postoperative complications was 26.1% (2.1% Clavien 1, 14.6% Clavien 2, 8.3% Clavien 3, 1% Clavien 4). Benign tumors accounted for 12.5% of patients. Positive surgical margin (PSM) rate was 3.6% (3/84). The trifecta outcome was accomplished in 56.2% of patients. The mean±SD (range) follow-up was 54±26 (14-96) months. The 5-year cancer-specific survival (CSS), recurrence-free survival (RFS) and overall survival (OS) rates resulted 96.1%, 90.8% and 88.0%, respectively. Preoperative, 3rd postoperative day, one month postoperative and follow-up median (IQR) estimated glomerular filtration rate (eGFR) was 79 (64-97), 68 (51-82), 76 (56-88) and 66 (50-81) ml/min/1.73 m², respectively (Figure 1B).

**Discussion and Conclusion:** The optimal oncological and functional results of SE suggest that ERASE is particularly appropriate to treat highly complex renal masses, minimizing the loss of healthy renal volume and widening the indications of NSS according to the latest European Association of Urology (EAU) guidelines.

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**122**

**ASAP AND HGPIN PREDICTIVE VALUE OF PROSTATE CANCER DIAGNOSIS: CAN WE IMPROVE IT?**

Marco Agnello¹, Maurizio Barale¹, Marco Oderda¹, Simone Giona¹, Giancarlo Marra¹, Lorenzo Daniele², Donatella Pacchioni², Luisa Delsedime², Paola Dalmasso³, Nathalie Nicolaiew⁴, Alexandre De La Taille⁵, Bruno Frea¹, Hendrik Van Poppel⁶, Steven Joniau⁷ and Paolo Gontero¹

Departments of ¹Urology, ²Pathology, and ³Epidemiology, San Giovanni Battista Hospital, Turin, Italy; ⁴Faculty of Medicine, Université Paris-Est Créteil Val De Marne, Paris, France; ⁵Department of Urology, CHU Mondor, Créteil Val De Marne, Paris, France; ⁶Department of Urology, University Hospital Gasthuisberg, Leuven, Belgium

**Introduction and Objectives:** Operator-dependency and lack of standardized diagnostic criteria may affect ability of high grade prostatic intraepithelial neoplasia (HGPIN) and atypical small acinar proliferation (ASAP) to predict prostate cancer (PCa). We assessed the long-term predictive ability of...
PCa diagnosis of a cohort of ASAP and HGPIN undergoing pathological review and recategorization according to standardized criteria. **Patients and Methods:** Five hundred and eighty-one patients underwent prostate biopsy between 2001 and 2010, with an initial diagnosis of HGPIN and/or ASAP, in the absence of PCa. Three uro-pathologists blindly reviewed the slides of these precancerous lesions using standardized criteria and stratifying ASAP into high, moderate or low suspicion for malignancy. Results were compared with the long-term risk of developing PCa. **Results:** The level of concordance between initial diagnosis and after pathological review was high for monofocal HGPIN (70.2%) and ASAP (86.9%); 3 cases with initial diagnosis of ASAP (1%) were converted into PCa. The cumulative risk of developing tumor was 56.5% for ASAP reclassified as “highly suspicious for malignancy”, 40% for “intermediate suspicious” ASAP, 22% for “low suspicious” ASAP and multifocal HGPIN. Seventeen percent of monofocal HGPIN and 26.7% of ASAP and/or HGPIN patients at initial diagnosis developed PCa. The mean observation period was 6 years. Half of all cancers occurred within 12 months and 80% within 3 years. In “high-suspicious” ASAP, more than 45% of tumors were already detected within 3-6 months (Figure 1). Neither the number of nucleoli nor the extent of the ASAP focus on the pathologic review appeared to be significant cancer predictors. Conclusion: High level of concordance between initial diagnosis and diagnosis after the review confirms the validity of the diagnostic criteria already existent for HGPIN and ASAP. However, adoption of ASAP stratification into three subgroups would better define the risk of developing PCa in these patients.

123 MULTIDIMENSIONAL GERIATRIC EVALUATION AT INITIAL TREATMENT IN UROLOGICAL NEOPLASMS: A MULTICENTER PROSPECTIVE STUDY


1Division of Radiotherapy, Niguarda Hospital, Milan, Italy; 2Division of Radiotherapy, National Cancer Institute, Milan, Italy; 3Division of Urology, National Cancer Institute, Milan, Italy; 4Division of Urology, "Università Degli Studi", Milan, Italy; 5Division of Urology, Niguarda Hospital, Milan, Italy; 6Division of Radiotherapy, S.Gerardo Hospital, Monza, Italy; 7Division of Radiotherapy, Humanitas Clinical Institute, Rozzano, Italy; 8Division of Urology, San Donato Hospital - San Donato Milanese, Milan, Italy; 9Division of Oncology, San Carlo Hospital, Milan, Italy; 10Geriatric Oncology, Don Gnocchi Foundation - Palazzolo Institute, Milan, Italy; 11Mario Negri Institute for Pharmacological Research, Milan, Italy

**Introduction:** Multidimensional geriatric evaluation (MGE) is a method that allows, through an interdisciplinary approach, the detection of physical changes, psychosocial and functional disability in elderly patients, and is helpful in the identification of “vulnerable” patients. MGE considers the patient, and not only his/her disease, and is used in elderly patients with neoplastic diseases in order to elaborate a therapeutic program that also takes into account the patients' functional ability, health conditions and quality of life. **Patients and Methods:** From November 2012 to November 2014, a MGE was offered to all patients older than 70 years who were operated or treated with radical radiotherapy at the main Departments of Urology and Radiotherapy of Milan, Italy. These patients were recruited within a study supported by the Italian Ministry of Health designed to examine the geriatric care required by patients with prostate, bladder and renal cancer after the initial treatment. The MGE was carried out by 2 trained evaluators and the results were supervised by a Geriatrician in order to stratify patients into fit, frail and vulnerable categories according to the Balducci’s definition (CROH 46:211, 2003). **Results:** A MGE could be carried out in 455 patients. Only 30 refused to be examined. A prostatic cancer was observed in 295 patients, while 119 had bladder cancer and 40 a kidney tumor. Patients with prostatic carcinoma had an average age of 75 years (range=70-91); patients with bladder cancer (9 female and 49 male) had a mean age of 78 years (range=70-93); patients with kidney cancer (6 women, 6 men) had a mean age of 75 years (range=70-87). All bladder and kidney cancers were treated with surgery. The distribution of fit, frail and vulnerable patients in these tumor types was the following:

<table>
<thead>
<tr>
<th>Patients</th>
<th>Bladder</th>
<th>Kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fit</strong></td>
<td>21 (21%)</td>
<td>7 (22%)</td>
</tr>
<tr>
<td><strong>Vulnerable</strong></td>
<td>45 (44%)</td>
<td>13 (41%)</td>
</tr>
<tr>
<td><strong>Frail</strong></td>
<td>36 (35%)</td>
<td>12 (37%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>102</td>
<td>32</td>
</tr>
</tbody>
</table>
In 258 patients with prostatic cancer, the distribution of fit, vulnerable and frail patients between surgery and radiotherapy is shown as follows:

<table>
<thead>
<tr>
<th>Patients</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fit</td>
<td>135 (53%)</td>
</tr>
<tr>
<td>Vulnerable</td>
<td>91 (35%)</td>
</tr>
<tr>
<td>Frail</td>
<td>31 (12%)</td>
</tr>
</tbody>
</table>

One hundred and twenty-two out of 258 patients (47%) receiving radical treatment (radiotherapy and/or surgery) were frail or vulnerable. The majority of frail patients with prostatic cancer received radiotherapy (87%) but a minority was also treated with surgery (30%). Vulnerable and fit patients were more frequently treated with radiotherapy (80%). Conclusion: Among patients with kidney and bladder cancer, surgical candidates were mostly vulnerable and, to a lesser extent, frail patients. The majority of vulnerable and frail patients with prostate cancer were treated with radiotherapy but a minority of frail patients received surgery. Being this study addressed to determine the care needs during the follow-up, the MGE was performed when patients had already primary treatment; however, in future studies, it should be conducted before treatment to allow a decision on the treatment choice to be taken also considering the weight of the age-associated conditions.

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**TESTICULAR ADRENOGENITAL TUMOUR**

Tommaso Pray-galetti¹, Marina Gardiman², Alessandro Morlacco³ and Michele Colicchia³

¹Urology, Azienda Ospedaliera Padova, Padua, Italy; ²Pathology, Azienda Ospedaliera Padova, Padua, Italy; ³Urology, Padova University, Padua, Italy

Introduction/Aim: A growing number of Klinefelter syndrome patients are submitted to diagnostic and therapeutic procedures for male infertility. At our Institution, we recently observed an incidental adrenogenital tumor in a Klinefelter syndrome patient. Our aim is to present this unusual tumour’s features. Patient and Methods: A 36-year-old Caucasian man presented at our Clinic with infertility. The patient’s partner evaluation was uneventful. Sperm count disclosed an azoospermia. Testosterone was 9.16 ng/ml, luteinizing hormone (LH) 10.4 U/l and prolactin (PRL) 7.1 U/l. Ultrasound study showed a right testis of 1.6 cc and a left one of 3 cc with a dishomogeneous upper pole structure. Both testes were hyperechoic at ultrasound. Doppler study was bilaterally negative for varicocele. The patient’s kariotype was 46XX short Y. The patient underwent a bilateral biopsy for parenchymal harvesting prior to in vitro fertilization. As an incidental finding at the upper pole of the left testicle, close to the epididimous, a nodular lesion of 1.8 cm in diameter was found. The nodule was completely resected preserving the remaining testis. Results: The patient had a regular post operatory recovery and was discharged within 24 hours from surgery. At pathology, the resected nodule was composed of multiple brown/black nodules rich in large eosinophilic cells arranged in anastomosing nests separated by a prominent fibrous stroma. The cytoplasm contained brown-yellow pigment and the nuclei were atypical in a spotty manner but without mitotic activity. Preserved seminiferous tubules were present within the nodules. Immunohistochemical stains were positive for synaptophysin, alpha-inhibin and CD56. At 6 months, the patient’s follow-up is regular at physical examination and ultrasound. Discussion and Conclusion: We report the first case, to our knowledge, of a testicular adrenogenital tumor in a Klinefeter patient. Surgical enucleation of this tumor can be performed successfully by this procedure of choice, which is recommended for patients with this type of tumor since, such an approach, maximizes future fertility potential.

**125**

**CAN THE USE OF LIGHT NBI IMPROVE OUR ABILITY TO IDENTIFY PERSISTENT LESIONS AFTER WL TURBT IN THE FOLLOW-UP OF NON-MUSCLE INVASIVE TUMORS? RUA’S EXPERIENCE**

Roberto Giulianelli, Barbara Cristina Gentile, Luca Albanesi, Gabriella Mirabile, Paola Tariciotti, Giorgio Rizzo and Francesco Pisanti

Urology, Clinic Villa Claudia, Rome, Italy

Introduction/Aim: The treatment for non-muscle invasive bladder cancer is endoscopic resection of the tumor. The significant risk of residual tumor after initial transurethral resection of the bladder (TURB) of Ta, T1 lesions has been demonstrated. Reported recurrence after TURBT is about 30% to 70%. Tumor recurrence can be attributed to a combination of missed tumors, incomplete resection, reimplantation of tumor cells after resection and de novo tumor occurrence in high-risk urothelium. The aim of this study was to evaluate if use of light narrow band imaging (NBI) (repeat NBI-assisted TURBT), during the follow-up, allows a statistically significant advantage to identify undetected residual tumors following white light (WL)-TURBT. Patients and Methods: From June 2010 to April 2012, 797 patients (423 male and 374 female) affected by primitive, recurrent or suspicious bladder lesions, underwent WL plus NBI cystoscopy and following WL-TURBT.
bipolar Gyrus PlasmaKinetic™ (PK). Of those, 512 presented a oncological bladder lesion and 444 patients, in according with European Association of Urology (EAU) guidelines, were submitted to a 12-month follow-up. After performed WL TURBT, 6 risk factors were assessed: tumor size (cm), number of tumors, recurrence rate within one year, staging (T), grading (G) and the presence of carcinoma in situ (CIS). Then, based on mentioned factors and using the European Organisation for Research and Treatment of Cancer (EORTC) scoring system, the total score for recurrence for each patient was calculated separately. According to the total score, patients were divided into 4 recurrence risk groups. Patients with total recurrence score 0 were classified to group I, 1-4 points to group II, 5-9 to group III and 10-17 to group IV risk of recurrence. Every three months, we performed a WL-TURBT and a repeat NBI-assisted TURBT on any suspected lesion (or scar), on our relative margins and buttom. We calculated the time to first recurrence (disease-free time) as months to detect recurrence on WL-TURBT or repeat NBI-assisted TURBT after the diagnosis of bladder cancer. The follow-up period had to be at least year. Statistically, we performed Kaplan-Meier survival analysis, as well as univariate and multivariate Cox proportional hazard regression analyses. Results: Following WL-TURBT, we observed that one hundred and six patients (23.8%) developed recurrent bladder tumor in 12 months of follow-up. After repeat NBI-assisted TURBT we observed residual disease in 338 patients (76.12%), of those 129 (29.05%) on margins, 79 (17.7%) on buttom and 137 (30.8%) margins plus buttom. Regarding to stratification in the EORTC risk recurrent group, we observed, on the margins, 27.1%, 42.6% and 30.2%, on the buttom 15.2%, 52.7% and 31.9% and margins plus buttom 27.7%, 42.3% and 29.9% for II, III and IV groups, respectively. The intermediate risk groups presented a high-risk to have a persistent disease following repeat NBI-assisted TURBT than low- and high-risk groups. Regarding to distribution in pT and grading, see Table I. In 338 bladder persistent disease following repeat NBI-assisted TURBT, the overall time to recurrence was 6.11 months, while it was found 7.3 and 3.8 months on the margins and buttom, respectively. In the statistical evaluation, primitive, multifocal and < 3 cm lesions were the significant predict indicators to persistent disease following repeat NBI-assisted TURBT. Conclusion: Repeat NBI-assisted TURBT offers a statistically significant advantage in identifying undetected residual tumors following WL-TURBT.

Table I. (Abstract 125).

<table>
<thead>
<tr>
<th></th>
<th>WLTURBT</th>
<th>NBI Margins</th>
<th>NBI Buttom</th>
<th>NBI Margins+ Buttom</th>
<th>Total NBI score</th>
</tr>
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<tbody>
<tr>
<td>Punmpl</td>
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<td>23</td>
<td>3</td>
<td>23</td>
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<td></td>
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<td>29.48717949</td>
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</tr>
<tr>
<td>pTaLG</td>
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<td>pCISHG</td>
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</table>

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CHALLENGES IN CONCOMITANT LYMPHOMA AND KIDNEY NEOPLASM TREATMENT

Tommaso Prayer-Galetti 1, Alessandro Morlacco 2, Michele Colicchia 3 and Renato Zambello 3

1Urology, Azienda Ospedaliera Padova, Padua, Italy; 2Urology, Padova University, Padua, Italy; 3Hemato-Oncology, Padova University, Padua, Italy

Introduction/Aim: More and more frequently patients present at Urology and Oncology Departments with two different contemporary tumors. We herein present the difficult clinical management of a patient who presented at our Institution with a small kidney solid mass and a lymphoplasmocytoid lymphoma (LL). Case Presentation: On June 2011, a 61-year-old Caucasian man presented to the Oncology Department of our Institution with an histologically proved LL and a back bone collapse. During the diagnostic workup, a small solid lesion (2.2 cm in diameter) was incidentally identified at ultrasound in the
The patient underwent treatment with Leukeran and Deltacorten. Given the prominence of the hematologic neoplasm, the renal lesion was submitted to an active surveillance program. On July 2009, the right renal lesion was stable (2.2 cm) but LL progressed and, therefore, a second-line Rituximab-Endoxan-Dexametason treatment was undertaken. On march 2011, a pleural effusion was detected and a Rituximab-Bendamustine treatment was started. At the 6-month follow-up, a computed tomography (CT) scan showed the disappearance of the pleural effusion but a slight increase of the right kidney tumor size (3.0 cm). Given the 3.0 cm nodule size and the concomitant LL clinical evolution, the active surveillance program of the kidney solid lesion was confirmed. On September 2012, a new LL progression was documented and a Bendamustine treatment was started with a good clinical response for 3 months. At a 6-month follow-up, a CT scan showed an increase in size of the kidney tumor up to 4.3 cm. The patient was considered eligible for a cryotherapy but as a LL progression was noted a Velcade-Desametazon regimen was started. On May 2014, LL’s clinical response with stable disease was achieved and the patient was considered eligible for cryotherapy. On June 2014, a pre-operative CT scan showed a kidney tumor progression with marked increase in size (5.5 cm) and renal vein involvement (V1); therefore, the patient was no more considered eligible for cryotherapy and an open surgery was planned. On July 2014, preoperative workup disclosed a severe anemia with LL progression and open surgical procedure was cancelled. Shortly, at CT scan, multiple pulmonary metastases were documented and the patient entered a palliative care program; he died 6 months later. Discussion: The contemporary treatment of 2 different neoplasms may be challenging. Our case report highlights the use of a more aggressive treatment of a small renal lesion (3 cm) that may be appropriate when a concomitant oncological treatment, that could alter the usual biological behaviour of small solid renal masses, is ongoing.

**127 COMPLEMENTARY VALUE OF CONTRAST-ENHANCED ULTRASOUND (CEUS) AFTER CONTRAST-ENHANCED COMPUTED TOMOGRAPHY (CECT) IN EVALUATION OF INDETERMINATE SMALL HYPOVASCULAR RENAL MASSES**

Giovanni Christian Rocca1, Massimo Tilli2, Massimiliano Bernabei1, Sergio Dall’ara2, Chiara Ballista1, Gamanji Stela2, Giorgio Benea2 and Maurizio Simone1

1Division of Urology, AOI/AUSL Ferrara, Ferrara, Italy; 2Department of Diagnostic and Interventional Radiology, AOI/AUSL Ferrara, Ferrara, Italy

**Aim:** To assess the value of contrast-enhanced ultrasonography (CEUS) in the characterization of indeterminate small renal masses (SRM) seen on contrast-enhanced computed tomography (CT) (CECT) and its promising role in diagnostic algorithm. **Materials and Methods:** From January 2011 to September 2014, 66 consecutive patients (age range=45-86 years; 38 men, 28 women) with SRM (<4 cm) underwent renal surgery, after preoperative CECT for lesion characterization and treatment planning. Thirty-five patients with hypervascular lesions at CECT were submitted to surgery with no additional imaging examination. CECT findings demonstrated indeterminate characteristics of SRM in 31 patients, with pseudo-enhancement or unclear endolesional vascularization. These patients underwent CEUS to evaluate real-time lesional wash-in in order to better define their further management (surgery or follow-up). **Results:** Twenty-three out of 31 patients showed contrast enhancement wash-in into the lesion and, therefore, underwent surgery. Pathologic findings confirmed malignancy in 19 patients (3 clear cell carcinoma, 14 papillary renal cell carcinoma, 2 cromophobe) and benign lesions in 4 patients (2 oncocytoma, 2 angiomylipoma, 1 hemorrhagic cysts). Nine lesions with no clear enhancement at CEUS are currently under follow-up (CEUS and magnetic resonance imaging (MRI)) with no evidence of modified pattern (median follow-up=15 months) representing complicated cysts Bosniak II. **Conclusion:** CEUS can be a useful tool to determine real-time enhancement in SRM, especially for tumors with indeterminate pattern at CECT. Contrast-enhanced ultrasonography is very sensitive in detecting slight tumor blood flow, facilitating the evaluation of tumor perfusion by analyzing tumor vascular enhancement patterns. The promising role of CEUS should be considered in newer diagnostic algorithms of SRM management, also as problem-solving in indeterminate findings at CECT or MRI.

**128 ASSESSMENT OF LOCAL PROSTATE CANCER RECURRENT AFTER PROSTATECTOMY USING MULTI-PARAMETRIC MAGNETIC RESONANCE WITHOUT ENDORECTAL COIL:**

Preliminary Experience

Giovanni Christian Rocca1, Massimo Tilli2, Chiara Ballista1, Martina Gatti2, Massimiliano Bernabei1, Giorgio Benea2 and Maurizio Simone1

1Division of Urology, AOI/AUSL Ferrara, Lagosanto, Italy; 2Department of Diagnostic and Interventional Radiology, AOI/AUSL Ferrara, Lagosanto, Italy;
**Introduction and Objectives:** Clinical suspicion of prostate cancer (PC) recurrence after radical prostatectomy (RP) is based on biochemical relapse. An imaging modality is strongly desirable to identify and correctly localize local PC recurrence, also in order to guide possible target locoregional therapy and to reduce procedure-related complications and toxicity. The aim of this preliminary study is to evaluate clinical practice value of multiparametric magnetic resonance imaging (Mp-MRI) in the detection of local recurrence after RP.

**Materials and Methods:** Thirty-two consecutive patients with biochemical failure after RP underwent mp-MRI with a 1.5-T magnet with phased array coil. Prostate-specific antigen (PSA) levels ranged from 0.15 to 5.86 ng/ml. Two radiologists, blinded to clinical data, reviewed MRI scans together and quantified likelihood of tumor recurrence on a 1 to 5 confidence scale, considering each MRI parameter (T2-weighted (T2-w), diffusion-weighted imaging (DWI) and dynamic contrast-enhanced (DCE)). A MRI cutoff threshold (at least grade 3) was adopted to define positive MRI results. Standard of reference for MRI results were considered $^{11}$C-Chol positron emission tomography (PET) positivity, positive biopsy findings in prostatectomy bed and reduction of PSA values after radiotherapy. 

**Results:** Twenty-four out of 32 patients presented nodules with highly suspicion of recurrence at MRI images (3 with grade 5, 16 with grade 4 and 9 with grade 3 of confidence). Diameter of suspected local recurrences detected varied from 0.5 to 2 cm. In comparison to reference standards, we obtained values of sensibility and specificity, respectively of 85% and 90%.

Positive and negative predictive values in detecting locoregional relapse were, respectively, 94.5% and 75%. Among different MRI parameters, DCE appears to have higher specificity (95%) in detecting tumor recurrence. 

**Conclusion:** Mp-MRI can be a promising tool in the management of suspected recurrence in patients with biochemical failure after RP. Detection and localization of local recurrence could also improve the targeting of salvage radiotherapy or other locoregional ablative techniques, also reducing complications.

**Background/Aim:** The use of fiducial markers (FM) as surrogate of prostate position in image-guided radiation therapy (IGRT) modality requires a stable markers’ position within the gland. Several factors can affect their stability as there may be spontaneous marker migration soon after implantation or prostate volume reduction or deformation during the radiotherapy course. The aim of this study was to assess the true marker migration, if it occurs, during the full course of prostate radiotherapy.

**Materials and Methods:** The analysis was performed on 55 low-risk cT1-2 prostate cancer patients, treated with IGRT between June 2009 and May 2014. Three markers were implanted at the base (A), middle (B) and apex (C) of the gland (gold markers in 40 patients and carbon steel markers in 15 patients). All patients underwent computed tomography (CT sim) 1-mm thickness within 10 days after implantation; a daily cone beam computed tomography (CBCT) was used to correct prostate organ motion by checking markers’ position before each treatment session. Retrospectively, CT sim and CBCTs acquired at 1st, 10th, 20th, 30th and 39th fraction were used to record FM coordinates (x,y,z). The distances between markers (FMD) as AB, BC, CA were measured in mm as:

$$d_{xy} = \sqrt{(x_1 - x_2)^2 + (y_1 - y_2)^2 + (z_1 - z_2)^2}$$

FMDs variations before and during the full course of radiotherapy were then calculated as the differences between CBCTs and CTs data. 

**Discussion and Conclusion:** The average absolute variation in FMD was 8.96 mm. Ninety-four percent of recorded variations were 3 mm or less, while 80% were ≤ 2 mm or less. A simultaneous progressive reduction of FMDs (negative values in mm) was seen in 77% of patients and it was related to the shrinking of the prostate volume during the treatment (Figure 1). Three main trends of the FMDs variation were observed: i) constant reduction of FMDs due to the prostate volume reduction during the whole treatment (Figure 2a); ii) initial increase of the FMDs due to the large post-implantation edema (Figure 2b); iii) multiple peaks of the FMDs due to the prostate organ motion. No correlation was found between FMDs variations and initial prostate volume. Smaller variations were recorded in patients with a gap between markers implantation and CT sim acquisition ≥ 10 days and in patients with a gap between CT sim and the start of the radiotherapy ≥ 22 days. 

Discussion and Conclusion: The results obtained in our patient population indicate small variations in the relative position of the markers (1.20±0.67 mm), in accordance with the literature data (1–3). The obtained values could be related to the uncertainties of our IGRT system (also marker length=3 mm) rather than to the markers’ migration.
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IMAGE-GUIDED (IGRT) HYPOFRACTIONATED RADIOTHERAPY IN LOW-RISK PROSTATE CANCER PATIENTS: RESULTS AND TOXICITY

Maurizio Valeriani, Paolo Bonome, Mattia Falchetto Osti, Vitaliana De Sanctis, Stefano Bracci, Fabiana Bellafiore and Riccardo Maurizi Enrici

Radiotherapy Department, S. Andrea Hospital, University "La Sapienza" of Rome, Rome, Italy

Introduction/Aim: Hypofractionation presents crescent interest on the treatment of prostate cancer. We have evaluated the acute toxicity in patients with low-risk prostate cancer treated with hypofractionated image-guided radiation therapy (IGRT) treated in our institution. Patients and Methods: Between March 2007 and January 2015, we have treated 75 patients with low-risk prostate cancer (T1-T2, Gleason score ≤6 and prostate-specific antigen (PSA) ≤10 ng/ml). The median age was 71 (range=58–82) years. All patients underwent prostate biopsy. All patients performed a simulation computed tomography (CT) scan with 2.5 mm slice thickness to execute 3D conformal planning. Patients were immobilized in supine position with a footlocker. All patients were treated with a total dose of 60 Gy on prostate and the first 1.5 cm of seminal vesicles; 3 Gy per fraction 5 times a week and for a total time of 4 weeks. Margin from clinical target volume (CTV) to planning target volume (PTV) was 5 mm in all directions.

Figure 1. FMD mean variations (mm) distribution a) absolute values; b) values with the sign.

Figure 2. Trend of the recorded FMDs variation at CT sim (tc) and at day 1,10,20,30 and 39 during RT: a) constant reduction of FMDs; b) FMDs initial increase and following decrease; c) FMD variability during RT.
The external beam radiation therapy was performed with IGRT, with daily cone-beam TC. Follow-up evaluations were performed at 3, 6, 9 and 12 months after treatment and every 6 months thereafter. Acute side effects were evaluated according to the Radiation Therapy Oncology Group/the European Organization for Research and Treatment of Cancer (RTOG/EORTC) late morbidity scoring scale. Results: Median follow-up was 35 months (range=3-82). The acute toxicities during the treatment were: grade 1-2 gastrointestinal (GI) toxicity in 16% of patients, grade 1-2 genitourinary (GU) toxicity in 44% of patients; grade 3 GU toxicity in 4% patient. Late toxicities were grade 1-2 GI in 4% of patient, grade 1-2 GU in 14% of patients. The median PSA before the start of radiotherapy was 6 (range=1.74-9.43) and at the last follow-up was 0.63 ng/ml (range=0-3.05 ng/ml). Discussion and Conclusion: This study showed that hypofractionated radiation therapy was well-tolerated with a low-grade of toxicity but needs longer follow-up to determine local control.

131 HYPOFRACTIONATED RADIOTHERAPY IN INTERMEDIATE PROSTATE CANCER

Maurizio Valeriani, Paolo Bonome, Stefano Bracci, Vitaliana De Sanctis, Mattia Falchotto Osti, Linda Agolli, Teresa Falco and Riccardo Maurizi Enrici

Radiotherapy Department, "S. Andrea Hospital, University "La Sapienza" of Rome, Rome, Italy

Aim: To evaluate the tolerance and the clinical efficacy of hypofractionated radiotherapy in patients affected by intermediate-risk prostate cancer. Patients and Methods: Between March 2007 and January 2015, 146 patients with intermediate-risk prostate cancer were treated with 3-dimension conformal hypofractionated radiotherapy. Intermediate risk was defined as clinical stage T1–T2, a pre-radiotherapy prostate-specific antigen (PSA) between 10 and 20 ng/ml and Gleason score equal to <7 or clinical stage T1–T2, pre-radiotherapy PSA between ≤20 ng/ml and Gleason score equal to 7. A total dose of 43.8 Gy was delivered to seminal vesicles and 54.75 Gy to the prostate; 3.65 Gy per fraction, three times a week for a total of 5 weeks. All patients underwent neoadjuvant, concomitant and adjuvant hormonal therapy (OT) for a total duration of 9 months. Acute and late toxicities were evaluated according to Radiation Therapy Oncology Group (RTOG) scale. The nadir PSA after radiotherapy plus 2 ng/ml was used for defining biochemical relapse (Phoenix criteria). Results: Median follow-up was 45 months (range=4-84). Seven patients (4.7%) developed biochemical failure. Six patients (4%) died from causes different from prostate cancer without biochemical failure, while 2 patients (1.3%) died due to disease progression. Acute toxicities (within 3 months from the end of RT) were as follows: Grade 1 genitourinary (GU) toxicities were 41.2%, while 12% presented Grade 2 toxicities; Grade 1 gastrointestinal (GI) toxicities were 11.6%, Grade 2 GI toxicities were 13.8%. Late GU and GI toxicities ≥ Grade 2 recorded at the last follow-up were 3.8% and 5.6%, respectively. No patient developed grade 4 toxicity. The 3-year biochemical progression-free survival (BFS) and 5-year BFS were 95.4% and 93%, respectively. Discussion and Conclusion: The hypofractionated schedule used is well tolerated with a low rate of acute and late grade ≥ 2 GI and GU toxicities. Hypofractionation is useful to obtain high-rate tumor control also, if longer follow-up is needed.

132 IMAGE-GUIDED INTENSITY MODULATED HYPOFRACTIONATED RADIOTHERAPY IN HIGH-RISK PROSTATE CANCER PATIENTS: TOXICITY AND PRELIMINARY RESULTS

Maurizio Valeriani, Paolo Bonome, Mattia Falchotto Osti, Vitaliana De Sanctis, Stefano Bracci, Linda Agolli and Riccardo Maurizi Enrici

Radiotherapy Department, "S. Andrea Hospital, University "La Sapienza" of Rome, Rome, Italy

Aim: To evaluate efficacy and toxicity of hypofractionated intensity-modulated simultaneous integrated boost (IMR-T-SIB) and image-guided radiotherapy (IGRT) in the treatment of high-risk prostate cancer patients. Patients and Methods: Ninety-five patients with high-risk prostate cancer were analysed. An IMRT treatment was planned delivering 68.75 Gy to the prostate, 55 Gy to the seminal vesicles and positive nodes and 45 Gy to the pelvis in 25 fractions, 4 or 5 fraction per week. Cone-Beam CT was performed every day. All patients were submitted to hormonal therapy. Results: The median follow-up was 36 months. Acute grade 1-2 gastrointestinal (GI) toxicity rates were 13.4%. Grade 1-2 and grade 3 genitourinary (GU) toxicity rates were 22% and 1.2%, respectively. Grade 1 and 2 GI late toxicity rates were 1.2%. No grade ≥3 toxicity was recorded. Grade 1 GU late toxicity rate was 2.4%. No grade ≥2 toxicity was recorded. No significant difference was calculated in terms of acute and late toxicity between patients treated 4 or 5 times weekly. The actuarial 4-year overall survival and freedom from biochemical failure were 96.6% and 90.3%, respectively. Conclusion: The present study demonstrated that hypofractionated IGRT-IMRT-SIB in patients with high-risk prostate cancer is efficient with acceptable toxicity profile. Outcome, in terms of survival, is promising; however, longer follow-up is needed.
MVCT AND INTRAPROSTATIC MARKERS MAKE FEASIBLE THE TREATMENT OF PATIENTS WITH BILATERAL HIP PROSTHESIS

Massimo Cardinali1, Giovanna Mantello1, Francesco Fenu1, Sara Costantini1, Melissa Scricciolo1, Vito Lacetera2, Giovanni Muzzonigro2, Andrea Benedetto Galosi3, Marco Valentì4 and Stefania Maggi4

Departments of 1Radiotherapy and Oncology and 4Physics, Azienda Ospedaliero-Universitaria Ospedali Riuniti Ancona, Ancona, Italy; 2Division of Urology, Azienda Ospedaliero-Universitaria Ospedali Riuniti Ancona, Ancona, Italy; 3Division of Urology, Ospedale Augusto Murri, Fermo, Italy

Background/Aim: Traditionally treatment through hip prosthesis is not advised due to the inability to accurately calculate the dose. In fact high atomic number of metallic prosthesis create artifacts in the kilovoltage computed tomography image (KVCT sim) due to large attenuation coefficient in the diagnostic X-ray range. As these artifacts may hinder anatomic structure delineation, physicians have to draw bigger margins in order to be sure to include the target and, at the same time, provide erroneous density information used for dose calculation. Differently, by using higher energy tomotherapy, the megavoltage computed tomography (MVCT) does not suffer strong artifacts from the prosthesis and provide sufficient (even if not excellent) (1-2) soft-tissue contrast to help delineate the prostate, bladder and rectum, thus making treatment technically possible. In addition, intraprostatic marker implantation, as surrogate of prostate position, can further help in patient set up and organ motion correction. In the current study, we would like to show the feasibility to treat a patient with prostate cancer and bilateral hip replacement who would, otherwise, not be treatable with a standard approach. Patient and Methods: A 75-year-old low-risk prostate cancer patient with bilateral hip replacement was addressed for radiotherapy to our Department after refusal of treatment from another Institution. A first KVCT sim was acquired to highlight the expected artifacts (Figure 1a) and was used as reference for planning MVCT acquisition. Three gold markers were placed in the prostate (left base, apex and right mid-gland) under ultrasound guidance by the referring Urologist. MVCT scans of the pelvic region (Figure 1b) was acquired (volumetric acquisition, pitch 1, 2 mm reconstruction) as for standard KVCT sim, with the patient in the treatment position, 10 days after implantation, when markers’ stability was achieved. The patient was asked to keep a full bladder and an empty rectum in order to reduce inter-fraction organ filling variability. The physician contoured the prostate without seminal vesicles as clinical target volume (CTV) and the rectum, bladder, femoral heads as the organs at risk (OARs); a 5 mm margin was added to define planning target volume (PTV) (Figure 2). The plan was optimized according to our constraints for organs at risk and regarding PTV coverage; PTV 70: 7000 cGy, 2.5 Gy fraction; rectum: V50<=50, V60<=35, V65<=25, V70 <=20, bladder: V65<=50%. The patient underwent helical tomotherapy (HT) treatment in 28 fractions for a cumulative dose of 70 Gy. Daily marker match was performed between daily MVCT and planning MVCT in order to correct the prostate position. Results: No artifacts were found both in planning MVCT and in daily MVCT with sufficient soft-tissue contrast to help delineate the target and the OARs.
The visibility of the markers was good enough to help online prostate position correction. Good tolerance during treatment and in the 4 months after the end of the radiotherapy was recorded. Discussion and Conclusion: For our prostate patients with bilateral prostheses, treatment with conventional conformal techniques provides unacceptable plans; however, uncertainties in CTV delineation and dose calculation errors in KVCT-based treatment plans can be substantially reduced by using the MVCT and intraprostatic markers implantation that can help in on-line prostate position correction. Our experience confirmed the role of MVCT, together with intra-prostatic implanted markers, in offering a safe external beam treatment to the patients who, otherwise, would not have been able to be treated.


MULTI-VARIABLE MODELS OF ACUTE URINARY TOXICITY: FINAL RESULTS OF A LARGE PROSPECTIVE STUDY

Federica Palorini1, Tiziana Rancati2, Cesare Cozzarini3, Andrea Botti4, Viviana Carillo1, Valeria Casanova Borca3, Claudio Degli Esposti6, Pierfrancesco Franco7, Elisabetta Garibaldi8, Giuseppe Girelli9, Cinzia Iotti10, Angelo Maggio11, Marcella Palombarini12, Alessandro Pierelli13, Emanuele Pignoli14, Vittorio Vavassori15, Sergio Vii16, Riccardo Valdagni17 and Claudio Fiorino1

Departments of Medical Physics and Radiotherapy, San Raffaele Scientific Institute, Milan, Italy; Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy; Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Departments of Medical Physics and Radiotherapy, Arcispedale Santa Maria Nuova, Reggio Emilia, Italy; Departments of Medical Physics and Radiotherapy, Ospedale ASL9, Ivrea, Italy; Departments of Radiotherapy and Medical Physics, Ospedale Bellaria, Bologna, Italy; Department of Radiotherapy, Ospedale Regionale U.Parini-AUSL, Valle D’Aosta, Aosta, Italy; Departments of Radiotherapy and Medical Physics, IRCCS-Candiolo, Candiolo, Italy; Departments of Medical Physics and Radiotherapy, Cliniche Gavazzeni-Humanitas, Bergamo, Italy; Departments of Medical Physics and Radiation Oncology 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Prostate Cancer Program and Department of Radiation Oncology 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Aim: To assess clinical and dosimetric factors affecting acute urinary toxicities on a large cohort of patients treated with external beam radical radiotherapy (RT) for prostate cancer.

Patients and Methods: The final dataset of the DUE01 trial, a prospective multicentre study, was considered. It included 539 patients treated with conventionally (74-80 Gy at 1.8-2 Gy/fr) or moderately hypofractionated radiotherapy (RT) (65-75.2 Gy at 2.2-2.7 Gy/fr) in 5 fractions per week. Relevant clinical factors were collected for each patient: T stage, concomitant morbidities and drugs, use of hormonal therapy (HT), previous surgery, smoking, alcohol, age and body mass index (BMI). Urinary symptoms were self-reported by each patient through the International Prostate Symptom Score (IPSS) before and after RT; based on previous results, absolute (cm²) weekly dose-surface histograms (DSHw) were chosen as dosimetric descriptors.

Two endpoints were here considered: i) the onset of moderate-severe urinary toxicities at RT end (IPSSend ≥15) for the subgroup of patients with none/mild symptoms before RT (IPSSbefore ≤15); ii) a worsening of urinary symptoms after RT described by an IPSS increase of at least 10 points after RT (ΔIPSS ≥ 10).

Odds ratio Occurrences
(OR) (OCC)

(1) Endpoint: IPSSend ≥15 (AUC=0.70)

| Constraint: IPSSbefore ≤15 | IPSSbefore | 1.17 | 92% |
| HT | 0.63 | 79% |
| Hypertensives | 2.12 | 78% |
| T stage | 1.81 | 64% |
| DSHw at 12.5 Gy (continuous variable) | 1.02 | 57% |
| Smoke | 1.38 | 51% |

(2) Endpoint: ΔIPSS ≥ 10 (AUC=0.66)

| HT | 0.49 | 72% |
| DSHw at 8 Gy | 1.01 | 46% |
| Hypertensives (continuous variable) | 1.72 | 40% |
| Age | 0.95 | 28% |
| BMI | 0.95 | 24% |
after RT (ΔIPSS≥10). A multivariate logistic regression (MVR) was then performed on both endpoints. The choice of relevant factors to be included was carried out through an in silico methodology combining a bootstrap resampling, a backward feature selection based on minimization of residuals and a basket and network analysis of bootstrapped models. The features with the greatest percentage of occurrences (OCC) in the bootstrapped models were included in the MVR. A dedicated software for data mining (KNIME) was used.

Results: IPSS scores before and after RT were available for 429 patients. Ninety-seven out of 385 patients (25%) with none/mild symptoms before RT showed IPSSend ≥15, while ΔIPSS≥10 was found in 85/429 (20%) patients. Results of MVR are reported in Table I: models with six (area under the curve (AUC)=0.70) and five variables (AUC=0.66) were considered for the IPSSend ≥15 (1) and ΔIPSS ≥10 (2) endpoints, respectively. The most robustly predictive clinical variables were: IPSS score before RT (odds ratio (OR)=1.17, occurrences (OCC)=92%) for toxicity endpoint (1) and HT (OR=0.63, OCC=79% and OR=0.49, OCC=72%) and the use of hypertensives (OR=2.12, OCC=78% and OR=1.72, OCC=40%) present in both endpoints as protective and risk factor, respectively. A dosimetric variable was also recovered as a risk factor for both toxicity endpoints: weekly dose-surface-histogram (DSHw) at 12.5 Gy (OR=1.02, continuous variable, OCC=57%) and DSHw at 8 Gy (OR=1.01, continuous variable OCC=46%) for IPSSend ≥15 and ΔIPSS ≥10, respectively. Figure 1 (A and B) shows occurrences of all variables for the two endpoints. Conclusion: Correlations between clinical/dosimetric parameters and the onset or worsening of urinary symptoms were studied. Two definitions of acute toxicity were considered: the onset of moderate-severe urinary toxicities (IPSSend ≥15) and a worsening of urinary symptoms after RT (ΔIPSS ≥10). The role of pre-treatment for urinary symptoms was confirmed as a risk factor. The medium-high weekly doses and the use of hypertensives were found as risk predictors, while HT was a protective factor for both toxicity endpoints.

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ARE EORTC RISK TABLES USEFUL IN EVALUATING THE RESULTS OF PATIENTS WITH NON-MUSCLE INVASIVE BLADDER CANCER SUBMITTED TO WL TURBT? RUA’S EXPERIENCE

Luca Albanesi, Barbara Cristina Gentile, Gabriella Mirabile, Francesco Pisanti, Paola Tariciotti, Giorgio Rizzo, Giorgio Vincenti and Roberto Giulianelli

Division of Urology, Nuova Villa Claudia, Rome, Italy

Background/Aim: The European Organisation for Research and Treatment of Cancer (EORTC) risk tables are a new nomogram constructed by EORTC to predict the probability of recurrence and progression in patients treated for non-muscle invasive bladder cancer. The scoring system used in this nomogram is based on the six clinical and pathological factors, such as number of tumors, tumor size, recurrence rate within one year, T category, grade and the presence of carcinoma in situ (CIS). The aim of the study was to assess the EORTC risk tables usefulness in daily urological practice.

Patients and Methods: Four hundred forty-four patients, aged 43 to 86, treated for non-muscle invasive bladder cancer with white light (WL) bipolar transurethral resection of bladder tumor (TURBT) were analyzed. After performed WL TURBT, 6 risk factors were assessed and, based on mentioned factors and using the EORTC scoring system, the total score for recurrence and progression for each patient was calculated separately. According to the total score, patients were divided into 4 recurrence risk groups. Patients with total recurrence score 0 were classified to group I, 1-4 points to group II, 5-9 to group III and 10-17 to group IV risk of recurrence. During follow-up, according to the European Association of Urology (EAU) guidelines for non muscle invasive bladder cancer, a WL TURBT on suspected lesions or scars was carried out. Adjuvant therapy were done in according to EAU guidelines.

Results: One
hundred six patients (23.8%) developed recurrent bladder tumor in 12 months of follow-up. Statistical analysis showed a relationship between the occurrence of recurrence after one year and recurrence risk groups. The risk of bladder tumor recurrence was statistically higher in the intermediate-risk group. The recurrence rate was 0%, 28.6%, 44.7% and 17.4% in I, II, III and IV recurrence risk group, respectively. Regarding the staging and grading, we observed a recurrence rate in the PUNMPL group of 3.48%, in pTaLG of 6.55%, in pTaHG of 9.42%, in pT1LG of 1.02 %, in pT1HG of 6.96% and in pCISHG dell’1.84%. If we evaluate the progression, as an increasing recurrence in staging and grading of the primary lesion but always non-muscle invasive, in the analyzed group -within one year- occurred in 52 patients (11.7%). The risk of bladder tumor progression was statistically higher in the intermediate-risk group. The recurrence rate was 0%, 19.2%, 55.7% and 25.0% in I, II, III and IV progression risk group, respectively. Stratifying these data for staging (pT) and grading, we observed a progression in the 1.9% of PUNMPL, in the 53.8% of the pTaLG, in the 36.5% of the pTaHG, in the 1.92 % of the pT1LG and in the 7.6% of the pCISHG. Instead, if we consider the progression as the transition to a stage pT2 or more, we observed it in 3 patients (0.67%), two in the II and one in the other III risk group, both of them in the pTaHG group. Conclusion: EORTC risk tables are useful in predicting the possibility of recurrence and progression in patients with non-muscle invasive bladder cancer using EORTC nomograms as it is possible to separately estimate the risk of recurrence and progression for patients treated with TUR for primary or recurrent non-muscle invasive bladder cancer.

CAN LIGHT NBI IMPROVE OUR ABILITY TO IDENTIFY DISEASE PROGRESSION IN THE FOLLOW-UP OF NON-MUSCLE INVASIVE TUMORS? RUA'S EXPERIENCE

Luca Albanesi, Barbara Cristina Gentile, Gabriella Mirabile, Francesco Pisanto, Paola Tariciotti, Giorgio Rizzo, Giorgio Vincentii and Roberto Giulianelli

Division of Urology, Nuova Villa Claudia, Rome, Italy

Background/Aim: Although non-muscle invasive bladder cancer (NMIBC) is usually not life-threatening in the early stage, more than half of these tumors will relapse and approximately 10% to 20% of them will develop into muscle-invasive bladder tumors. The aim of this study was to evaluate if the use of light narrow band imaging (NBI) (repeat NBI-assisted transurethral resection of bladder tumour (TURBT)), during the follow-up, can lead advantage to identify undetected residual tumors following white light (WL)-TURBT. Patieats and Methods:

From June 2010 to April 2012, 797 patients, 423 male and 374 female, affected by primitive, recurrent or suspicious bladder lesions, underwent WL plus NBI cystoscopy and subsequent WL-TURBT with bipolar Gyrus PlasmaKinetic™ (PK). Of those, 512 presented oncological bladder lesions and 444 patients, in accordance with EAU guidelines, were submitted to a 12-month follow-up. After performing WL-TURBT, 6 risk factors were assessed: tumor size (cm), number of tumors, recurrence rate within one year, staging (T), grading (G) and carcinoma in situ (CIS). Then, based on mentioned factors and using the European Organisation for Research and Treatment of Cancer (EORTC) scoring system, the total score for recurrence for each patient was calculated separately. According to the total score, patients were divided into 4 recurrence risk groups. Patients with total recurrence score 0 were classified to group I, 2-6 points to group II, 7-13 to group III, and 14-23 to group IV risk of recurrence. Every three months, we performed a WL-TURBT and a repeat NBI-assisted TURBT on any suspected lesion (or scar), on our relative margins and buttom and collected all data. We calculated the time to first progression to decide to perform WL cystoscopy or repeat NBI-assisted TURBT after the diagnosis of bladder cancer. The follow-up period had to be at least a year. Statistically, we performed Kaplan-Meier survival analysis, as well as univariate and multivariate Cox proportional hazard regression analyses. Results: Following WL-TURBT, we observed that three (0.67%) patients had progression to muscle invasion bladder lesions and after repeat NBI-assisted TURBT eleven patients (2.48%) developed progression to pT2 bladder tumor in 12 months of follow-up. Of those, all lesions were localized in the buttom. Concerning the stratification, in the EORTC risk progression group, we observed that 41.6% and 58.3% were II, and IV groups, respectively. The high-risk groups presented an elevated risk to present a persistent progression disease following repeat NBI-assisted TURBT than low- and intermediate-risk groups. Stratifying these data for staging (pT) and grading, we observed a progression to pT2 in 16.6% pTaLG and pTaHG in 58.3% pT1HG and in 8.3 pCISHG, respectively. If we evaluate the progression, as an increasing recurrence in staging and grading of the primary lesion but always non-muscle invasive, in the analyzed group -within one year- this occurred in 265 patients (59.6%). The risk of bladder tumor progression was statistically more frequent in the intermediate-risk group. The recurrence rate was 0%, 18.8%,45.6% and 35.4% in the I, II, III and IV progression risk groups, respectively. In multivariate analysis, focality (p<0.05) was a significant predictor to progression than status (p=0.35 ) and dimensions (p=0.43). The overall time to progression following repeat NBI-assisted TURBT in patients with progression to pT2 -than only upgrading staging and grading- was 3.7 months; on buttom and margins times were 3.29 and 6.41, respectively. Conclusion: Repeat NBI-assisted TURBT allows a statistically significant
advantage in identifying progression of undetected residual tumors after WL-TURBT. Focality was a significant predictor to progression.

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CAN LIGHT NBI IMPROVE OUR ABILITY TO IDENTIFY LESIONS AFTER TURB WITH WHITE LIGHT OF NON-MUSCLE INVASIVE TUMORS? RUA’S EXPERIENCE
Luca Albanesi, Barbara Cristina Gentile, Gabriella Mirabile, Francesco Pisanti, Paola Tariciotti, Giorgio Rizzo, Giorgio Vincenti and Roberto Giuliani
Division of Urology, Nuova Villa Claudia, Rome, Italy

Background/Aim: The treatment for non-muscle invasive bladder cancer is endoscopic resection of the tumor. The significant risk of residual tumor after initial TURB of Ta, T1 lesions has been demonstrated. Reported recurrence after transurethral resection of bladder tumour (TURBT) is about 30% to 70%. Tumor recurrence can be attributed to a combination of missed tumors, incomplete resection, reimplantation of tumor cells after resection and de novo tumor occurrence in high-risk urothelium. The aim of this study was to evaluate if use of light narrow band imaging (NBI) (repeat NBI-assisted TURBT), during the follow-up, allows a statistically significant advantage to identify undetected residual tumors following white light (WL)-TURBT.

Materials and Methods: From June 2010 to April 2012, 797 patients, 423 male and 374 female, affected by primitive, recurrent or suspicious bladder lesions, underwent WL plus NBI cystoscopy and subsequent WL-TURBT with bipolar Gyrus PlasmaKinetic™ (PK). Of those, 512 presented oncological bladder lesions and 444 patients, according to the European Association of Urology (EAU) guidelines, were submitted to a 12-month follow-up. After performing WL-TURBT, 6 risk factors were assessed: tumor size (cm), number of tumors, recurrence rate within one year, staging (T), grading (G) and the presence of carcinoma in situ (CIS). Then, based on mentioned factors and using the European Organisation for Research and Treatment of Cancer (EORTC) scoring system, the total score for recurrence for each patient was calculated separately. According to the total score, patients were divided into 4 recurrence risk groups. Patients with total recurrence score 0 were classified to group I, 1-4 points to group II, 5-9 to group III and 10-17 to group IV risk of recurrence. Every three months, we performed a WL-TURBT and a repeat NBI-assisted TURBT on any suspected lesion (or scar), on our relative margins and buttom. We calculated the time to first recurrence (disease-free time) as months to detect recurrence on WL TURBt or repeat NBI-assisted TURBT after the diagnosis of bladder cancer. The follow-up period had to be at least a year. Statistically, we performed Kaplan-Meier survival analysis and also univariate and multivariate Cox proportional hazard regression analyses. Results: Following WL-TURBT, we observed that one hundred six patients (23.8%) developed recurrent bladder tumor in 12 months of follow-up. After repeat NBI-assisted TURBT we observed residual disease in 338 patients (76.12%), of those 129 (29.05%) on margins, 79 (17.7%) on buttom and 137 (30.8%) on margins plus buttom. Regarding the stratification in the EORTC risk recurrent group, we observed on the margins, 27.1%, 42.6% and 30.2%, on the buttom 15.2%, 52.7% and 31.9% and margins plus buttom 27.7%, 42.3% and 29.9% for II,III and IV groups, respectively. The intermediate risk groups presented a high risk to have a persistent disease following repeat NBI-assisted TURBT than low- and high-risk groups. The distribution in pT and grading is given in Table I. In 338 bladder persistent cases, following repeat NBI-assisted TURBT, the overall time to recurrence was

Table I. (Abstract 137).

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Introduction: Repeat NBI-assisted TURBT offers a statistically significant advantage in identifying undetected residual tumors following WL-TURBT.

Conclusion: Repeat NBI-assisted TURBT offers a statistically significant advantage in identifying undetected residual tumors following WL-TURBT.

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LAPAROSCOPIC PARTIAL NEPHRECTOMY AFTER PREVIOUS IPSILATERAL RENAL PROCEDURES

Mauro Seveso, Luigi Castaldo, Rodolfo Hurle, Gianluigi Taverna, Massimo Lazzeri, Luisa Pasini, Nicolò Maria Buffi, Giovanni Lughazzani, Paolo Casale, Silvia Zandegiacomo De Zorzi, Alessio Benetti and Giorgio Ferruccio Guazzoni

Department of Urology, Istituto Clinico Humanitas, Rozzano, Milan, Italy

Introduction: Previous ipsilateral renal surgery has been considered a relative contraindication for subsequent laparoscopic partial nephrectomy because of the likelihood of dense postoperative adhesions and distorted tissue planes, which could render hilar control and renal mobilization more difficult. We report the perioperative outcomes for 18 patients treated with laparoscopic partial nephrectomy (LPN) after previous ipsilateral renal surgery. Materials and Methods: Of the 251 patients undergoing LPN for a renal mass from March 2005 to March 2014 at our institution, 18% had undergone previous ipsilateral open and percutaneous renal procedures. They were informed about the details of the laparoscopic procedure and an informed consent was obtained that included the possibility of an emergency laparotomy. The LPN registry and patients’ charts were analyzed to obtain the demographic data, preoperative surgical history, operative details and postoperative outcomes. Surgical techniques: All procedures performed were carried out through a 3-port transperitoneal approach with an access obtained through the most geographically distant quadrant to minimize the risk of inadvertent intra-abdominal injury and a meticulous lysis of any abdominal adhesions. The LPN technique included hilar dissection, mobilization of the kidney, tumor excision performed off-clamp, tumor bed meticulously examined for residual tumor and, in case of bleeding, controlled via bipolar diathermy. Results: Mean age of the patients was 57.6 years (range=41-78). Fourteen had a previous history of percutaneous surgery (percutaneous nephrolithotomy (PCNL) in 9 and renal biopsy in 5) and 4 had a previous history of open renal surgery (pyelolithotomy in 2, partial nephrectomy in 1 and pyeloplasty in 1). The mean interval from previous surgery was 5.3 years. The procedure was successful in all patients. No open conversions were needed and no kidneys were lost. The mean tumor size was 2.1 cm (range=1-4.5) and the estimated blood loss was 145 ml. The mean operative time was 183 minutes (range=122-241) and the hospital stay was 3.1 days (range=2-7). Metastatic disease did not develop in any patient during follow-up. In one patient, a recurrent renal mass needed a laparoscopic nephrectomy. Discussion: Laparoscopic partial nephrectomy, after previous ipsilateral surgery, is feasible. It is not associated with a significant increase in operative time and complication rate compared with patients with no prior ipsilateral renal surgery. However, it can be technically challenging and adequate previous experience with LPN is necessary.

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SENSITIVITY, SPECIFICITY, PPV/NPV OF MRI "TARGET" WITH TARGETED "FUSION BIOPSY"

Franco Bertolotto, Matteo Raggio, Francesco Germinale, Paolo Puppo

Division of Urology, Division of Urology ASL1 Imperia, Sanremo, Italy

Objectives: Prostate biopsy (Bx) has for 3 decades been performed in a systematic but blind fashion using 2D ultrasound (US). We have described the initial clinical evaluation of a 3D Bx tracking and targeting device (Urostation Koelis). Our main objective was to test accuracy of the magnetic resonance imaging (MRI) target (sensitivity (Sens), specificity (Spec), positive predictive value (PPV), negative predictive value (NPV)), incidence of the phase contrast angiography (Pca) outside the target, Gleason score in the target areas and extra target and detection rate fusion biopsy. Patients and Methods: This study involved 82 consecutive patients who underwent MRI and fusion biopsy between May 2013 and September 2014 (16 months) (28/5/13-20/9/14). In these pts MRI indicated 1 or 2 target 1.5 T endorectal coil --> T2 --> diffusion-weighted imaging (DWI), dynamic contrast-enhanced (DCE) (any prostate imaging-reporting and data system (PI-RAD) score >0). We performed fusion biopsy with 20 samples (10/lobe) plus 2 or 3-targeted biopsy. Average time: 32.5' (20-45'). Overall age population: 45-54 years: 6 (7.4%), 55-64 years: 32 (39%), 65-74 years: 37 (45.1%), 75-85 years: 7 (8.5%), <74 years: (91.46%) 75/82 patients > 74 years: (8.54%) 7/82 patients. Overall prostate-specific antigen (PSA) population: 0-5 ng/ml: 29 (35.5%), 5-10 ng/ml: 40 (48.7%), 10-20 ng/ml: 9 (10.9%), >20 ng/ml: 4
DOES NEGATIVE MRI (ABSENCE OF ANY TARGET) ACTUALLY MEAN NO (SIGNIFICANT) TUMOR AT BIOPSY?
Franco Bertolotto, Matteo Raggio, Francesco Germinale and Paolo Puppo
Division of Urology, ASL1 Imperia, Sanremo, Italy

Objectives: Prostate biopsy (Bx) has -for 3 decades- been performed in a systematic but blind fashion using 2D ultrasound (US). We have described the initial clinical evaluation of a fusion biopsy (Urostation Koelis). Our main objective was to clinically test the absence of target in magnetic resonance imaging (MRI).

Patients and Methods: This study involved 125 consecutive patients (pts) who underwent multiparametric MRI (mp MRI) (1.5 T endorectal coil → T2−→ diffusion-weighted imaging (DWI), dynamic contrast-enhanced (DCE) (any prostate imaging-reporting and data system (PI-RAD) score >0) and "fusion" biopsy between May 2013 and September 2014 (28/5/13-20/9/14).

Average age 63.7 years (range=50-74). No history of prostate cancer (PCa), no previous biopsy. The selection was carried out clinically, considering mostly age and excluding prostate-specific antigen (PSA) over 20. We performed fusion biopsy with 20 samples (10/lobe) Average time: 27.5' (20-35'). Age population: 45-54 years: 3 pts (7%), 55-64 years: 17 pts (40%), 65-74 years: 23 pts (53%), total: 43 pts < 74 years: (100%). PSA distribution: 0-5 ng/ml:7 pts (16%), 5-10 ng/ml: 30 pts (70%), 10-20 ng/ml: 6 pts (14%), PSA >20 ng/ml 0 pts. PSA <10 ng/ml: 86% (37 pts), PSA 10-20 ng/ml: 14% (6 pts). We have evaluated two populations: Group 1 (any age, any PSA) (43 pts had no MRI suspected area submitted to a random fusion biopsy) and Group 2 (PSA <10 ng/ml) (37 pts had no MRI suspected area submitted to a random fusion biopsy).

Results: Group 1: Fusion biopsy mapping was negative in 31 out of 43 cases (72%). Cap was present in 12 out of 43 cases (false-negative ratio 28%). In 10 pts, the Gleason score was 6 (83%), in only 2 pts was >6 (aggressive cancers). Group 2: In a population for PSA lower than 10 ng/ml, stereotactic mapping was negative in 26 out of 37 cases (70%). It was positive in 11 out of 37 cases (false-negative ratio 30%). In 10 pts, Gleason score was 6 (91%), in only 1 was >6 (9%). Conclusion: Negative MRI (in our hands) has a negative predictive value around 70%. If we consider only aggressive tumors (Gleason >6) the negative predictive value is around 85 %. For PSA <10, the negative predictive value is 91 %. The clinical risk of missing an aggressive cancer, not undergoing the biopsy in negative MRI pts with PSA <10, is 9%.
Aim: The aim of the present analysis was to assess the predictors of impotence 1 year after radical radiotherapy for prostate cancer in a cohort or patients who were potent before radiotherapy and who did not receive hormonal therapy. Materials and Methods: Within a multicentric prospective study (DUE01 trial), the International Index of Erectile Function (IIEF) was used. Absence of impotence (both before and after radiotherapy (RT)) was defined as a score in the first 5 questions of IIEF greater than 11 (IIEF1-5>11). Ninety-one potent patients (IIEF1-5 >11 before RT) and not submitted to hormonal therapy were available. At the time of this analysis, the information on potency, one year after treatment, was obtainable for 50/91 patients. Prospectively collected individual data were available for all patients and included: pre-radiotherapy IIEF1-5 (IIEF1-5_pre), age, body mass index, diabetes, use of anti-hypertensives, use of anti-coagulants, use of anti-aggregants, use of finasteride/dutasteride, use of drugs for the treatment of erectile dysfunction, previous surgery, smoke (y/n), alcohol (y/n), T stage (T1 vs. T2), prostate-specific antigen (PSA), Gleason score (GS) (<≥8), pelvic-node/seminal vesicle irradiation. The following dosimetry/technical parameters were considered: prostatic planning target volume (PTV), penile bulb volume, total dose, daily dose, mean dose (Dmean) and dose at 1% (D1%) to the penile bulb. As different fractionation schemes were permitted, Dmean and D1% were also corrected into 2Gy-equivalent doses using linear-quadratic model and an alpha/beta=3Gy and named EQD2_mean/ EQD2_1%, respectively. For each patient, the penile bulb was contoured on the planning computed tomography (CT) by each radiation oncologist responsible for the single participating Institute, following the written study guidelines and after having participated into a dummy run exercise. Predictors of 1-year impotency were assessed through uni- and multi-variable backward logistic regression: best cut-off values discriminating between potent and impotent patients were assessed by receiver operating characteristic (ROC) analyses. Results: After one year, 24/50 patients (pts) (48%) were impotent. Mean and median values of IIEF1-5 declined from 20.3/21 (before radiotherapy) to 12.7/14 (Wilcoxon test, p<0.0001). The only variables associated to impotence were basal IIEF1-5 (continuous variable, odds ratio (OR)=0.76, p=0.002) and EQD2_1% >74.2Gy (dichotomic variable, OR=6.7, p=0.012). The area under the curve (AUC) of this two-variable model was 0.83 (95% confidence interval (CI)=0.70-0.92). The figure shows the 1-year risk of impotence vs. IIEF1-5_pre for patients with EQD2_D1% above or below the 74.2 Gy cut-off. Experimental rates of impotence, as a function of IIEF1-5_pre, are also reported (Figure 1b). Conclusion: The 1-year risk of impotency after high-dose radiotherapy in potent men depends on EQD2_1% to penile bulb and on the basal potency score. Our results clearly support the idea that the sparing of the penile bulb may lead to a relevant increase of potency preservation in the subgroup of patients with none or very mild potency problems before radiotherapy, corresponding to an IIEF1-5 value >15-20; on the other hand, the impact of bulb sparing on patients with lower IIEF1-5 score seems to be questionable. The growing fraction of young patients and the possible reduction of the use of androgen deprivation consequent to the delivery of higher doses may translate in the future in a relevant increase of “fully potent” patients that could largely benefit from the sparing of the penile bulb. The use of a planning MRI for the definition of the prostatic apex may be strongly suggested for these patients. Among the limits of our work, the most important ones are the relatively low number of patients and the current unavailability of the full dose-volume histogram (DVH) information.

Figure 1. (Abstract 141).

142 DETECTION RATE OF STEREOTACTIC PROSTATE MAPPING WITH NEEDLE TRACKING AND VIRTUAL SIMULATOR
Franco Bertolotto, Matteo Raggio, Francesco Germinale and Paolo Puppo
Division of Urology, Division of Urology ASL1 Imperia, Sanremo, Italy
Aim: Given the limitations of prostate-specific antigen (PSA) and standard biopsies for detecting prostate cancer, we evaluated the cancer detection rate of transrectal ultrasound 3D biopsy with tracking of samples (stereotactic and fusion biopsy - Urostation Koelis).

Materials and Methods: We performed a total of 153 prostate biopsies with needle tracking and virtual simulator between 28/05/13 and 20/09/14. No history of prostate cancer (PCa), no previous biopsy, prostate volume: 80% patients (pts) <60 cc. Increasing PSA (at least 2 examinations) or suspected digital rectal exam (DRE).

We performed fusion biopsy with 20 samples (10/lobe).

Average time 27.5' (range=15-40'). Average age of population: 70.26 years (range=46-83): 45-54 years: 5 (3.3%); 55-64 years: 21 (13.7%); 65-74 years: 80 (52.3%); 75-85 years: 47 (30.7%). <74 years: 106 pts (69.3%) and 30 pts with >=75 years not fit for radical treatment.

Overall PSA distribution: 0-5 ng/ml 39 (25.5%); 5-10 ng/ml 47 pts (30.7%) >=75 years not fit for radical treatment. 75-85 years: 47 (30.7%). <74 years: 106 pts (69.3%) and 30 pts with >=75 years not fit for radical treatment.

PSA between 10-20 ng/ml. The detection rate was 7.2%. PSA < 10 ng/ml: 123 pts (80.4%) and 30 pts with 10 ng/ml: 67%.

Group I (any age, any PSA) naive: 153 pts, II˚ group (< 74 years): 106 pts, III˚ group: Group I: 72%, Group II: <74 years: 65%, PSA 0-5 ng/ml: 67%.

Patients were evaluated in three groups: I˚ group (any age, any PSA) (153 pts): PCa 108/153 pts (70.6%); Neg 45 pts (29.4%). Gleason score was >6: 78 (72%), <=6: 30 (28%).

Group II (< 74 years) (106 pts): PCa 69 pts (65%); Negative 37/106 (35%). Gleason score was >6: 46 (66.7%), <=6: 23 (33.3%).


Negative 3/19 pts (16%); >20 ng/ml (11 pts): Positive: 10/11 (91%), [Gleason score >6: 9/11 (90%), Gleason score=6: 1/11 (10%)]. Negative: 1/1 (10%).

Finally, PSA 0-10 ng/ml (123 pts): Positive: 82/123 [(Gleason score >6: 55/82 (67%), Gleason score=6: 27/82 (33%), negative: 41. Summarizing detection rate in any group: Group I: 72%, Group II: <74 years: 65%, PSA 0-10 ng/ml: 67%.

Conclusion: There is reasonable evidence in our data that stereotactic mapping offers better performances in detecting prostate cancers than conventional mapping. A double-blind protocol could give even more evident results; however it is not so easy to be performed and the differences between the two procedures are intuitive. Therefore, stereotactic mapping should become the first choice in the naive pts. It has to be demonstrated that, combining stereotactic mapping and MRI, fusion detection rate will consistently improve.

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BASAL STATUS AND DOSE TO THE PENILE BULB PREDICT IMPOTENCE ONE YEAR AFTER RADIOTHERAPY FOR PROSTATE CANCER

Cesare Cozzarini1, Fabio Badenchini1, Federica Palorini2, Barbara Avuzzi3, Claudio Degli Esposti4, Giuseppe Girelli5, Vittorio Vavassori6, Riccardo Valdagni7, Tiziana Rancati8 and Claudio Fiorino2

Departments of 1Radiotherapy and 2Medical Physics, San Raffaele Scientific Institute, Milan, Italy; 3Department of Radiation Oncology 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 4Department of Radiotherapy, Ospedale Bellaria, Bologna, Italy; 5Department of Radiation Oncology, Ospedale ASL9, Ivrea, Italy; 6Department of Radiation Therapy, Cliniche Gavazzeni-Humanitas, Bergamo, Italy; 7Prostate Cancer Program and Department of Radiation Oncology 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 8Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Aim: The aim of the present analysis was to assess the predictors of impotence 1 year after radical radiotherapy for prostate cancer in a cohort of patients who were potent before radiotherapy and who did not receive hormonal therapy.

Materials and Methods: Within a multicentric prospective study (DUE01 trial), the International Index of Erectile Function (IIEF) was used. Absence of impotence (both before and after radiotherapy (RT)) was defined as a score in the first 5 questions of IIEF greater than 11 (IIEF1-5 >11). Ninety-one potent patients (IIEF1-5 >11 before RT) and not submitted to hormonal therapy were available. At the time of this analysis, the information on potency, one year after treatment, was obtainable for 50/91 patients. Prospectively collected individual data were available for all patients and included: pre-radiotherapy IIEF1-5 (IIEF1-5_pre), age, body mass index, diabetes, use of anti-hypertensives, use of anti-coagulants, use of anti-aggregants, use of finasteride/dutasteride, use of drugs for the treatment of erectile dysfunction, previous surgery, smoke (y/n), alcohol (y/n), T stage (T1 vs. T2), prostate-specific antigen (PSA), Gleason score (GS) (<=8), pelvic-node/seminal vesicle irradiation. The following dosimetry/technical parameters were considered: prostatic planning target volume (PTV), penile bulb volume, total dose, daily dose, mean dose (Dmean) and dose at 1% (D1%) to the penile bulb. As different fractionation schemes were permitted, Dmean and D1% were also corrected into 2Gy-equivalent doses using linear-quadratic model and an alpha/beta=3Gy and named EQD2_mean/ EQD2_1% respectively. For each patient, the penile bulb was contoured on the planning computed
tomography (CT) by each radiation oncologist responsible for the single participating Institute, following the written study guidelines and after having participated into a dummy run exercise. Predictors of 1-year impotency were assessed through uni- and multi-variable backward logistic regression: best cut-off values discriminating between potent and impotent patients were assessed by receiver operating characteristic (ROC) analyses. Results: After one year, 24/50 patients (pts) (48%) were impotent. Mean and median values of IIEF1-5 declined from 20.3/21 (before radiotherapy) to 12.7/14 (Wilcoxon test, p<0.0001). The only variables associated to impotence were basal IIEF1-5 (continuous variable, odds ratio (OR)=0.76, p=0.002) and EQD2_1%>74.2Gy (dichotomic variable, OR=6.7, p=0.012). The area under the curve (AUC) of this two-variable model was 0.83 (95% confidence interval (CI)=0.70-0.92). Figure 1 shows the 1-year risk of impotence vs. IIEF1-5_pre for patients with EQD2_D1% above or below the 74.2Gy cut-off. Experimental rates of impotence, as a function of IIEF1-5_pre, are also reported.

Figure 1.

Conclusion: The 1-year risk of impotency after high-dose radiotherapy in potent men depends on EQD2_1% to penile bulb and on the basal potency score. Our results clearly support the idea that the sparing of the penile bulb may lead to a relevant increase of potency preservation in the subgroup of patients with none or very mild potency problems before radiotherapy, corresponding to an IIEF1-5 value >15-20; on the other hand, the impact of bulb sparing on patients with lower IIEF1-5 score seems to be questionable. The growing fraction of young patients and the possible reduction of the use of androgen deprivation consequent to the delivery of higher doses may translate in the future in a relevant increase of “fully potent” patients that could largely benefit from the sparing of the penile bulb. The use of an MRI for the definition of the prostatic apex may be strongly suggested for these patients. Among the limits of our work, the most important ones are the relatively low number of patients and the current unavailability of the full dose-volume histogram (DVH) information.

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MUCIN POOR VARIANT OF MUCINOUS TUBULAR AND SPINDLE CELL RENAL CELL CARCINOMA. A CASE REPORT

Luca Ventura1, Giovanni Luca Gravina2, Claudio Festuccia3, Luigi Zugaro4 and Cinzia Mercurio1

Divisions of 1Pathology and 2Radiology, San Salvatore Hospital, L’Aquila, L’Aquila, Italy; 3Division of Radiotherapy, Department of Biotechnological and Applied Clinical Sciences, University of L’Aquila, L’Aquila, Italy; 4Department of Biotechnological and Applied Clinical Sciences, University of L’Aquila, L’Aquila, Italy

Background: Mucinous tubular and spindle cell (MTSC) is a rare, low-grade subtype of renal cell carcinoma (RCC) firstly described in 2001 and recently recognized as a distinct entity also in the Vancouver classification of renal neoplasia (1). Patients exhibit an age range of 32-79 years (mean=53) with female predominance (male to female ratio=1:4) and a relatively good prognosis. We report a case of MTSC RCC, mucin poor variant, incidentally discovered in a female patient with cholelithiasis. Patient and Methods: A 67-year-old woman went to our observation after a control abdominal ultrasonography performed for gallstones. She underwent total body computed tomography scanning displaying a solid, expansile growth in the mid-lower portion of the left kidney with bosselated margins. A left radical nephrectomy with homolateral adrenalectomy was then performed and the specimen, fixed in 10% buffered formalin, was submitted to histopathology examination. Results: The kidney measured 105×60×55 mm. On cut sections, a well-circumscribed mesorenal solid neoplasm was present showing greyish color and measuring 48×45×40 mm. Histological examination showed a chord-like or tubular proliferation of low cuboidal cells and diffuse spindle cells areas within scant myxoid stroma. Neoplastic cells showed eosinophilic, focally vacuolated cytoplasm and low-grade nuclei. Limited amounts of stromal mucin were evident only after Alcian blue staining. Nuclear atypia, mitotic figures, desmoplasia and infiltrative growth were absent. Neoplastic cells were diffusely immunoreactive for vimentin, cytokeratin 7, EMA, racemase and RCC marker; they were negative for HMB-45, CD10, cytokeratin 8-18 and CD117. These features allowed the diagnosis of MTSC RCC, mucin poor variant. Discussion and Conclusion: MTSC RCC is a rare neoplasm and the diagnosis can be difficult due to its great morphologic heterogeneity.
Between the histologic variations described, the mucin poor variant shows a predominance of tubular and spindle cell components and only minimal mucinous background (1, 2). Helpful clues in recognizing these variants are bland cytologic features and adjacent tubular and spindle cell components (2). Despite the different histologic variants, MTSC almost always has a benign behavior with occasional recurrences but very rare distant metastasis or death from disease.

The histogenesis of MTSC carcinoma continues to be debatable. The classically proposed origin from the distal nephron is disproved by recent studies. The frequent immunohistochemical positivity for racemase would indicate a proximal convoluted tubule differentiation (3). The immunophenotype of MTSCs is nearly identical to papillary RCC (positive for CK7 and racemase, negative for CD10 and RCC marker), leading some to speculate that they may be a variant of papillary RCC, although genetic studies on the characteristic molecular aberrations seen in papillary RCC yielded discordant results. The positivity for RCC marker observed in the present case and described in 7% of the tumors, as well as the significant overlap of other markers in papillary and MTSC (3), do not allow firm conclusions about the histogenesis of these neoplasms.


**145 TYPE I GNRRH RECEPTOR MEDIATES THE ANTITUMOR EFFECT OF DAUNORUBICIN-GNRRH-III BIOCONJUGATES ON AGGRESSIVE CASTRATION-RESISTANT DU145 AND PC3 PROSTATE CANCER CELL LINES**

Marina Montagnani Marelli¹, Marilena Manea², Roberta M. Moretti¹, Monica Marzagalli¹, Andrea Mancini³, Giovanni Luca Gravina³, Claudio Festuccia³ and Patrizia Limonta¹

¹Department of Pharmacological and Biomolecular Sciences, University of Milan, Milan, Italy; ²Department of Chemistry, University of Konstanz, Konstanz, Germany; ³Department of Applied Clinical Sciences and Biotechnologies, University of L’Aquila, L’Aquila, Italy

**Background:** Prostate cancer is usually androgen-dependent in its early stage; the standard therapy is represented by androgen deprivation through chemical castration with gonadotropin-releasing hormone (GnRH) analogues (eventually in combination with antiandrogens). After an initial excellent response, the tumor progresses to a more aggressive phase (castration-resistant prostate cancer (CRPC)); in this case, the classical treatment is represented by chemotherapy (i.e., docetaxel), that can only improve the median survival time by few months. GnRH receptors (GnRH-R) are expressed at pituitary level; however, they are also expressed in many tumors, such as CRPC, where they mediate the antitumor effects of GnRH analogs. Based on these observations, these receptors are considered an effective molecular target for cytotoxic-GnRH peptide-based bioconjugates. GnRH-III, a GnRH isoform isolated from sea lamprey, has an insignificant luteinizing hormone (LH) and follicle-stimulating hormone (FSH)-releasing potency in mammals but it has a strong antitumor activity on tumor cells expressing GnRH-R.

**Materials and Methods:** On the basis of these observations, we performed experiments to evaluate the antitumor activity of two daunorubicine-GnRH-III bioconjugates on two CRPC cell lines (DU145 and PC3) and to identify the GnRH-R isoform that mediate these effects. MTT assay was performed to have indication on the cytostatic effects of the compounds. In addition, caspase activities were tested to verify apoptotic effects. PC3 and DU145 cells were also xenografted in CD1 nu/nu male mice to verify the effective antitumor effects of compounds. Results: First, taking advantage of the autofluorescence properties of daunorubicine, we assessed the internalization of both bioconjugates into cells by fluorescence microscopy. We then evaluated the vitality of the treated cells by MTT assay: both bioconjugates exerted a significant dose-dependent cytostatic effect. They also increased the cleavage of caspase-3, indicating the activation of the apoptosis process. We demonstrated that these effects are mediated by the classical (type I) GnRH-R since the co-treatment of the cells with the specific GnRH-R antagonist Antide and the silencing of type I GnRH-R (by means of the siRNA technique) completely abrogated the antitumor activity of these compounds. In vivo, we observed that the bioconjugates showed better antitumor activity when compared to daunorubicin alone determining a sensitive increase in time to progression (TTP) parameter used as preclinical marker of efficacy. Conclusion: Taken together, these results indicate that daunorubicin-GnRH-III bioconjugates exert a significant and
specific antitumor effect on CRPC cells both in vitro and in vivo. GnRH-III can be considered as an effective targeting moiety to deliver chemotherapeutic agents directly to tumor cells expressing GnRH-R (specifically, CRPC cells), thus avoiding undesired side-effects. Moreover, these results support the notion that it is the type I GnRH-R that mediates the biological effects of the different GnRH isoforms, including GnRH-III.

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FOLLOW-UP OF PROSTATE CANCER AFTER TREATMENT WITH CURATIVE INTENT: A SYSTEMATIC REVIEW OF LITERATURE

Remigio Pernetti1, Fabiano Palmieri1, Salvatore Voce1 and Maurizio Leoni2

U.O. 1Di Urologia and 2Di Oncologia, Ospedale Di Ravenna Santa Maria Delle Croci, Ravenna, Italy

Patients who receive curative therapy are followed up to diagnose a relapse or a complication. Curative treatment is defined as radical prostatectomy (RP) or radiotherapy (external beam radiotherapy or low- or high-dose brachytherapy) or any combination thereof. The prostate-specific antigen (PSA) level and, eventually, digital rectal examination (DRE) are the only tests that need to be carried out routinely. The measurement of PSA is basic for the follow-up. The reduction of the PSA varies depending on the treatment performed and the level at which to define treatment failure differs between RP cases and radiation-treated cases. However, PSA recurrence nearly always precedes clinical recurrence after either treatment, in some cases by many years. Thus, it is recommended that the finding of a single, elevated, serum PSA level should be reconfirmed before starting second-line therapy based solely on PSA elevation. After 6 weeks postoperatively, the PSA should be undetectable. A persistently elevated PSA level in patients is generally thought to be due to residual cancer, either micrometastases or residual disease in the pelvis. Most of the literature considers, following RP, that recurrent cancer can be defined by two consecutive PSA values of 0.2 ng/ml or more. However, other authors have argued for an even higher cut-off PSA level of 0.4 ng/ml as a better definition of patients with a high-risk for clinical progression. A rapidly increasing PSA level (high PSA velocity, short PSA doubling time (PSADT)) indicates distant metastases, while a later and slowly increasing concentration of PSA is most likely to indicate local disease recurrence. Only in patients with undifferentiated tumors, both local treatment failure and distant metastases have been shown to occur with undetectable PSA levels. The PSA level falls slowly after radiotherapy compared with RP. The optimal cut-off value for a favourable PSA nadir after radiotherapy is somewhat controversial. Achieving a PSA nadir of less than 0.5 ng/ml seems to be associated with a favorable outcome. The interval before reaching the nadir PSA may be very long and can sometimes take up to 3 years or more. At the 2006 RTOG-ASTRO Consensus conference, a new definition of radiation failure was proposed: a rise of 2 ng/ml above the post-treatment PSA-nadir (lowest value). It applies to patients treated with or without hormonal therapy. DRE is, with PSA measurement, first-line examination in follow-up after radiotherapy or RP. Its importance is even more evident from the cases of undifferentiated tumors where a local disease recurrence after curative treatment is possible without a concomitant rise in PSA level. However, in cases with favorable pathology, PSA measurement may well be the only test. Imaging techniques like transrectal ultrasonography (TRUS), bone scintigraphy, computed tomography (CT), magnetic resonance imaging (MRI), 11C-choline positron emission tomography (PET)/CT have no place in routine follow-up of localized prostate cancer (PCa). They are only justified in individuals with biochemical failure or in patients with symptoms for whom the findings will affect the treatment decision. Biopsy of the prostate bed and urethrovesical anastomosis are only indicated if the finding of a local recurrence affects the treatment decision. When to follow-up? There are different patterns of timing follow-up. All agree in thinking to follow-up more closely during the first years after treatment when the risk of failure is highest. These should be performed at 3, 6 and 12 months after treatment, then every 6 months until 3 years and, then, annually. How long to perform the follow-up? The follow-up should be executed for at least 10 years.

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PATIENTS WITH OLIGOMETASTATIC PROSTATE CANCER: RADIOTHERAPY MAY BE A TERAPEUTIC OPTION?

Fabiana Bellafiore, Maurizio Valeriani, Teresa Falco, Mattia Falchietto Osti and Riccardo Maurizi Enrici

Radiotherapy Department, S. Andrea Hospital, University "La Sapienza" of Rome, Rome, Italy

Aim: To analyze, retrospectively, local control and overall survival in patients with oligometastatic (≤5 lesions) prostate cancer (PCa) with high dose external beam radiotherapy (EBRT) used both on primitive tumor and metastatic sites (MTS).

Materials and Methods: From January 2010 to December 2014, 14 patients with oligometastatic PCa were treated. Mean age at diagnosis was 70 years (range=56-79), Gleason score (GS)=8 (range=6 - 9) and the prostate-specific antigen (PSA) median value was 27.8 (range=5.47-68.5). Seven
Background/Aim: Prostate cancer (PCa) patients are generally stratified in high-, intermediate- and low-risk categories. Categorization is mainly done on the basis of serum prostate-specific antigen (PSA) measurement, Gleason score and trans-rectal ultrasound (TRUS). When the disease in not organ-confined, risk group and therapy significantly change, thus imaging methods are of crucial importance. Non-invasive imaging includes contrast enhanced computed tomography (CT) and magnetic resonance (MR), diffusion MR TRUS and positron emission tomography (PET) with $^{18}$F choline ($^{18}$F CH). CT and MR, however, are not enough sensitive nor specific to become reliable standard methods to detect nodes and to guide surgical or radiation therapy. The role of $^{18}$F CH and its relationship with other imaging methods, such as contrast enhanced MR and diffusion weighted MR (DWI), are not exhaustively studied at the moment. The aim of our work is to study the impact of MR and $^{18}$F CH PET on the final assessment of risk group and the consequent treatment planning in patients with newly diagnosed prostate cancer (PCa). Materials and Methods: Fifty patients, assigned to low- or intermediate-risk class on the basis of Gleason score, PSA level and TRUS, were submitted to $^{18}$F CH PET and pelvic MR, including contrast enhanced NMR and DWI. After the eventual restaging on the basis of MR/radioisotope imaging, the patients were treated with radiation therapy and androgen ablation lasting 3 years. Radiation therapy was performed with 54.75 to 60 Gy on prostate in low- and intermediate-risk patients; 68.75 Gy on prostate and 45 Gy on pelvis in high-risk patients. When evidence occurred of the invasion of seminal vesicles or lymph nodes, 55 to 68.75 Gy were delivered on seminal vesicles and an adjunctive boost of 55 Gy was given on each invaded node. Six months after the end of androgen ablation, PSA and imaging exams were repeated. Though semi-quantitative parameters were measured on PET and diffusion MRI, the positivity was decided visually on the basis of agreement between two well experienced radiologists or, respectively, two nuclear medicine physicians. Results: On the basis of PET and MRI, 24 patients (48%) passed from the initial low- or intermediate-risk category to the high-risk category and were consequently treated. In 17 patients, re-categorization was due to the finding of extra-capsular invasion of PCa, mainly demonstrated by MRI; in 7 patients the re-categorization was due to discovery of pelvic or iliocaval lymph node invasion, mainly due to $^{18}$F CH PET. In the case of re-categorization due to extra-capsular invasion, both PET and MRI were positive but the morphological evidence of this invasion was clearly evident with MR, whereas it was not so clear with PET due to its suboptimal spatial resolution. Conversely, several pelvic nodes were suspicious, though not clearly positive at MRI: the only conclusive evidence of the invasion was given by the uptake of 18F CH in some of the suspicious nodes. Of course, the adjunctive boost can be delivered to patients presented a single metastatic localization and the other 7 two or more metastatic localizations. In total, 26 lesions were treated. The metastatic sites were bone and lymphonodes (LN). The EBRT on the primitive tumor was delivered following this schedule: Twelve patients with intensity modulated radiotherapy-simultaneous integrated boost (IMRT-SIB) in 25 fractions to the pelvis, seminal vesicle (VVSS) and prostate; the total dose was, respectively, 45, 55 and 68.75 Gy; 1 patient received 45 Gy to VVSS and 60 Gy to prostate in daily fraction of 3 Gy, 1 patient received 56 Gy to VVSS and 74 Gy to prostate in daily fraction of 2 Gy. Metastases were treated as follows: 6 MTS (4 bones and 2 LN) were treated with stereotactic body RT (SBRT) in 1 or 4 fractions; the total dose varied from 14 to 32 Gy; 20 MTS (13 bones and 7 LN) were treated with 3D conformal RT (3D-CRT) with a daily fraction of 1.8 or 2.2 Gy in 20 or 25 fractions; the total dose varied from 40 to 55 Gy. All patients received, concomitantly to the radiation treatment, hormonal therapy (ADT). Results: Median follow-up was 22 months (range=2-48). After a median follow-up of 10.5 months (range=3-30), 4 patients had a progression of 1.8 or 2.2 Gy in 20 or 25 fractions; the total dose varied from 14 to 32 Gy; 20 MTS (13 bones and 7 LN) were treated with SBRT in 1 or 4 fractions; the total dose varied from 14 to 32 Gy; 20 MTS (13 bones and 7 LN) were treated with 3D conformal RT (3D-CRT) with a daily fraction of 1.8 or 2.2 Gy in 20 or 25 fractions; the total dose varied from 40 to 55 Gy. 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few, not to several nodes per patient. Six months after the end of therapy, PSA, MRI and PET were negative in all the patients. We are waiting for the results at the 5-year follow-up. Conclusion: \(^{18}\)F CH PET is useful for N staging, whereas MRI is more effective in detecting the local stage in PCa.

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ROLE OF RMDWI AND DCE IN THE LOCAL STAGING OF PROSTATE CANCER AND ADVANTAGES OF FUSION IMAGING FOR RADIATION TREATMENT PLANNING

Paolo Bonome\(^1\), Maurizio Valeriani\(^1\), Giuseppe Argento\(^2\), Vitaliana De Sanctis\(^3\), Mattia Falchetto Osti\(^3\), Stefano Bracci\(^3\), Lara Cristiano\(^4\), Alessandra Berrettoni\(^4\), Giulia Fioroni\(^4\) and Riccardo Maurizi Enrici\(^1\)

\(^1\)Radiotherapy Department, S. Andrea Hospital, University "La Sapienza" of Rome, Rome, Italy;
\(^2\)Radiology Department, S. Andrea Hospital, University "La Sapienza" of Rome, Rome, Italy;
\(^3\)Radiography, S. Andrea Hospital, University "La Sapienza" of Rome, Rome, Italy;
\(^4\)Radiology, S. Andrea Hospital, University "La Sapienza" of Rome, Rome, Italy

Aim: To evaluate the usefulness of multiparametric magnetic resonance imaging (MRI) for a better locoregional staging and the radiation treatment planning in prostate cancer. Materials and Methods: Between 2008 and 2014, 150 patients with histologically-proven prostate cancer underwent, before radiation treatment, a multiparametric MRI consisting of T2-weighted turbo spin-echo (T2 TSE) sequences, diffusion weighted imaging (DWI)/apparent diffusion coefficient (ADC) and dynamic contrast-enhanced (DCE), for staging purpose. MRI were also registered with the computed tomography (CT) simulation for a better delineation of the target and organs at risks (OAR). Results: All patients presented alterations in the T2 sequences. DWI/ADC and DCE confirmed the lesions evidenced to T2 sequences in 129 and 106 patients, respectively. DWI/ADC was able to find more alterations than T2 sequences in 9/21 cases without perfect correspondence. DCE was capable to find more alterations than T2 sequences in 5/44 cases without perfect correspondence. DCE was capable to find more alterations than T2 sequences in 5/44 cases without perfect correspondence. In 94/150 patients, MRI staging modify risk class prevalently from low intermediate to high-risk. In all cases, MRI helps to better delineate volumes contouring CT simulation alone. Conclusion: We confirm that multiparametric MRI (T2-weighted, DWI and DCE sequences) is able to overcome the limitations of conventional MRI sequences. The accuracy in the staging of disease helps us to “tailor” the treatment protocol based of risk class.

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SEQUENCING NEW AGENTS AFTER DOCETAXEL IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

Francesca Maines\(^1\), Orazio Caffo\(^1\), Antonello Vecchia\(^1\), Giampaolo Tortora\(^2\), Enzo Galligioni\(^1\) and Emilio Bria\(^2\)

\(^1\)Medical Oncology, S. Chiara Hospital, Trento, Italy;
\(^2\)Medical Oncology, Azienda Ospedaliera Universitaria Integrata, University of Verona, Verona, Italy

Background/Aim: Two new hormonal agents (NHAs), abiraterone and enzalutamide, and one chemotherapeutic agent, cabazitaxel (CABA), improved overall survival (OS) in patients with metastatic castration-resistant prostate cancer (mCRPC) who progress after docetaxel. Although several analyses of patient cohorts receiving a sequence of two different NHAs after docetaxel have been published, no definite conclusions can be drawn regarding the best treatment sequence. The aim of this pooled-analysis was to evaluate the clinical outcomes of mCRPC patients receiving third-line new agents (NAs) after having previously received docetaxel and another NA. All published studies reporting monthly OS rates of mCRPC patients treated with one of the six possible two-NA sequences have been analyzed. Materials and Methods: The treatments were merged into three groups: one NHA followed by another, one NHA followed by CABA and CABA followed by one NHA. The cumulative monthly OS rates in each group were determined using a weighted-average approach. Results: Ten retrospective studies, including 735 patients who received NHA/NHA (320), NHA/CABA (249) or CABA/NHA (166), were evaluated. The 12-month OS rates were 26.1%, 60.5% and 78.3%, respectively. There were no statistically significant differences in terms of known prognostic factors. Conclusion: Despite the retrospective nature of the studies and potential selection biases, our data seem to confirm the potential cumulative survival benefit of using the NAs sequentially after docetaxel. There was no clear superiority of any one of the three strategies; however, a CABA-based sequence seemed to offer a possible OS advantage.

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INTRA VESICAL THERMOCHEMOTHERAPY WITH MYTOMICIN C AS A TREATMENT FOR HIGH- AND INTERMEDIATE-RISK NON-MUSCLE INVASIVE BLADDER CANCER: NINE YEAR SINGLE CENTRE EXPERIENCE ON ACTIVITY, TOLERABILITY AND TECHNICAL ASPECTS

Giorgio Canepa\(^1\), Fabio Campodonico\(^1\), Giacomo Capponi\(^1\), Paolo Pasquini\(^1\), Tiziana Calcagno\(^1\), Giuseppe Conzi\(^1\), Stefania Tamagno\(^1\) and Matteo Puntoni\(^2\)

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**Introduction:** The recurrence control of intermediate- and high-risk non-muscle invasive bladder cancer (NMIBC) after transurethral resection is limited despite the type and the schedule of adjuvant treatments adopted. We report our long-term experience on a treatment combing intravesical hyperthermia with mitomycin C (HT-MMC) delivered with a dedicated device.

**Materials and Methods:** From August 2004 to November 2013, 107 patients were included for adjuvant HT-MMC. The majority of patients were at high-risk, including G3 (36%) and carcinoma in situ (CIS) (15%). The planned schedule was composed by an inductive cycle (four weekly treatments) and a maintenance cycle (nine treatments administered along 9 months). All patients were followed with cytology and cystoscopy every 3 months and bladder biopsies, when required, for a median follow-up of 40.8 months. First aims were the recurrence-free survival (RCF) and disease progression for stage and grade (PFS), the secondary aims were the tolerability and adherence to the proposed schedule of treatment.

**Results:** A total of 107 patients completed the schedule with a median of 13 treatments. Mean age was 79 years (range=40-84); 75% were male. The RFS at 1, 2 and 5 years was 89.6%, 79.2% and 68.3%, respectively. The PFS at 1, 2 and 5 years was 98%, 96.2% and 83.7%, respectively. Progression to muscle invasive disease were found in 15 patients who underwent radical cystectomy. The median temperature recorded on each treatment was 42.1°C. The safety profile showed mainly grade 1 and 2 side effects. Thirty-one patients had allergy to each treatment was 42.1°C. The safety profile showed mainly grade 1 and 2 side effects. Thirty-one patients had allergy to MMC, including 8 patients G2. Twenty-three allergic patients were converted on hyperthermia with epirubicin (EPI). Ten patients complained of grade 3 side-effects, including 1 patient with bladder spasms/pain during treatment, 3 patients with dysuria and 6 patients with urgency after treatment.

**Conclusion:** HT-MMC/HT-EPI has shown to be an affective treatment for intermediate- and high-risk NMIBC with a low RFS, especially in the first two years. The PFS was low considering the percentage of high-risk patients. Tolerability was good withouth relevant systemic side-effects and most patients demonstrated a complete adherence to the proposed schedule of treatment.

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**153 TESTICULAR CANCER: CLINICAL FEATURES IN A RETROSPECTIVE SURVEY ANALYSIS OF A SINGLE INSTITUTION OF SARDINIA**

Roberta Mascia¹, Daniele Parnanzini², Silvia Cugudda¹, Maria Teresa Ionta¹, Francesco Atzori¹ and Antonello De Lisa²

**1SC Urologia, EO Ospedale Galliera, Genoa, Italy; ²Scientific Direction and Biostatistics, EO Ospedale Galliera, Genoa, Italy**

**1Medical Oncology Department, Policlinico di Monserrato, Monserrato, Italy; ²Urology Clinic, Ss. Trinità Hospital, Cagliari, Italy**

**Background:** Primary testicular cancer (TC) is the most common solid malignant tumor in men between the ages of 20 and 35 years in Italy. This cancer, the most frequent malignancy among young men, has an unusual age distribution with one peak in incidence in young adults (aged 20-39) and a second peak in over 60. In Italy, the annual incidence is about 11% among men younger than 50 years. For unknown reasons, the incidence of TC increased during the last century. TC has one of the highest cure rates of all cancers with an average five-year survival rate of 95%. Even for the relatively few cases of advanced disease, chemotherapy offers a cure rate of at least 80%.

**Patients and Methods:** We retrospectively queried all patients (pts) diagnosed with TC in our Institution in the time-frame 1998-2014. Clinical features and outcome parameters were the primary endpoints. A total of 64 patients with TC were identified. Median age was 33 years (interquartile range (IQR)=19-71), 37 (57%) seminomas, 19 (29.65%) embryonal carcinoma, 3 teratomas (4.6%), 1 teratocarcinoma (1.5%), 1 Leydig cell tumor (1.5%), 1 (1.5%) mixed form carcinoma; in 38 (59.3%) pts, the primary tumor was localized in the right testicle, whereas in 23 (35.9%) pts, in the left; in one case (1.5%) the primary tumor was mediastinical and 1 (1.5%) was retroperitoneal. According to the American Joint Committee on Cancer (AJCC) tumor stage classification, 40 (62.5%) pts presented initially with stage I disease, 10 (15.6%) pts with stage II, 10 (15.6%) pts with stage III, 4 (6.2%) pts with stage IV. Eighteen (28%) patients had metastatic sites, 9 abdominal lymph nodes, 1 upper diaphragmatic lymph node, 5 lungs and 1 liver; Five (6.2%) pts with stage I disease received 3 cycles of adjuvant PEB (Cisplatin-Etoposide-Bleomycin), 2 (3.1%) pts with seminoma received one single dose of carboplatin AUC 7.35 (54.6%) pts received first-line chemotherapy of which 32 pts were treated with PEB for 3-4 cycles, 1 with PVB (Cisplatin-Vinblastine-Bleomycin), 2 with carboplatin AUC 7. **Results:** The overall response rate (RR) was 91.3%. In more details, clinical complete remission was achieved in 24 (68.5%) pts, partial response in 8 (22.8%) pts, 1 (2.8%) pt died due to toxicity related to the treatment (neutropenic sepsis) and 1 (2.8%) pt showed disease progression under treatment; Six pts received second-line chemotherapy, 3 ICE (ifosfamide, carboplatin, etoposide), 2 TIP (paclitaxel, ifosfamide, cisplatinum), 1 PEI (cisplatin, etoposide, ifosfamide). After a median follow-up of 63 month (IQR=12-204), 60 pts (93.7%) were alive and disease-free, 3 (4.6%) died due to disease progression. All the patients with stage I and II disease did not relapse. The patients who died were 2 (20%) on stage III and 2 (50%) on stage IV. **Conclusion:** Testicular
cancer is increasing in incidence in many countries; however, mortality rates remain low and most men are cured. Our study confirms the excellent prognosis among all tumor stages with an extremely low rate of disease progression and death, which are limited to advanced stages.

154 PROSTATE CANCER AND PREDICTIVE MODELS: COULD AN ONTOLOGY DEVELOPMENT HELP CLINICIANS IN CLINICAL CHOICES?

Anna Rita Alitto, Roberto Gatta, Andrea Damiani, Francesco Catucci, Bruno Fionda, Marco Vernaleone, Vincenzo Frascino, Gian Carlo Mattiucci, Vincenzo Valentini and Giovanna Mantini

Radiation Oncology Department, Gemelli-ART, Catholic University of The Sacred Heart, Rome, Italy

Background/Aim: Classical clinical trials are normally built enrolling homogeneous clinical cases as this reduces the amount of enrolled patients and the cardinality of the dataset. This approach underestimates the information stored into Departmental Databases (which has much more biometric measures) and forces to design and build Decision Support System on a cluster of patients, an approach that does not seize the complexity of the clinical cases faced in the daily clinical practice. A way to deal with this limitation can be the exploitation of all the data available in Departmental Databases, adopting a “large database” approach: in this new approach data heterogeneity is an added value that better allows to move toward the paradigm of Personalized Medicine (PM). While the growing computational complexity, induced by a large number of biometric measures, can be faced by modern models from the discipline of Computer Science, the problem of ambiguities and misunderstandings about the meaning of the terms needs an explicit specification by a formal ontology, which has to be created and shared. The use of a shared ontology is the key to preserve from misunderstanding and enrich a large database with the contribution of many centres. Our aim is to build a prostate cancer ontology able to represent a list of the main concepts involved in this semantic domain and how those concepts are related, by a graph. Materials and Methods: The variables to be collected were organized in three levels: "Registry", which includes the patients' general epidemiological information (e.g., age, gender, etc.); "Procedures", which relates to information regarding patients' disease, treatment and related toxicities, as well as outcomes’ evaluation; the last, "Research", which includes clinical, genomic, imaging and Quality of Life information for advanced research projects. This ontology describes each concept with a unique reference, preferably correlated to a published coding system (e.g. NCI Thesaurus, CTCAE, etc.). We decided to adopt a trade-off between the formal explication of the ontology and the effective usability of it: even if a formal ontology is a powerful tool to allow automatic inference and represents, in a not-ambiguous way, a semantic, it is hard to be handled and properly validated. The so-built ontology, even not formal, is designed to be easily formalized by one of the available languages for this purpose (i.e. RDFS, OWL, etc.). Results: More than 200 variables related with prostate cancer were selected. The three data storing levels were used to classify all the variables to allow queries depending on the different types of analysis (e.g., epidemiological, treatment, toxicities, outcomes). Many concepts can be shared with other ontologies, for example related to other cancer sites (CTCAE, TNM, etc.), while others are prostate specific (PSA, etc.). Conclusion: Computer Science and Knowledge Engineering allows us to share concepts in a not ambiguous way by the use of ontologies and related languages. This is crucial for moving toward the development of heterogeneous large databases to support PM. The creation of an ontology allows the development of a standardized and organized dataset and improve the clearness of the meaning of the involved concepts. The so-created datasets are not ambiguous, mapped on most common international standards and suitable to create predictive models, which complement existing consensus or guidelines.

155 MODERN TECHNOLOGY IN RADIOTHERAPY TO PERSONALIZE PROSTATE CANCER TREATMENT: IGRT INTERNAL SCHEDULE

Anna Rita Alitto, Nicola Dinapoli, Francesco Catucci, Bruno Fionda, Marco Vernaleone, Gian Carlo Mattiucci, Vincenzo Frascino, Mario Balducci, Vincenzo Valentini and Giovanna Mantini

Radiation Oncology Department, Gemelli-ART, Catholic University of The Sacred Heart, Rome, Italy

Aim: To analyze whether an internal schedule of image-guided radiotherapy (IGRT), applied on prostate cancer patients treated with simultaneous integrated boost (SIB) through the rapid arc technique and long-term (>1 year) androgen deprivation therapy (ADT), could help to personalise treatment. Materials and Methods: Prostate cancer patients, with high- and intermediate-risk features, were enrolled in a prospective study. The clinical target volumes (CTVs) were irradiated by SIB-IMRT; for patients, subdued to prostate only radiotherapy (RT) (PORT), the CTVs include: prostate (CTV1, total dose of 80 Gy) and seminal vesicles (SVs) (CTV2, total dose of 72 Gy) in forty fractions. For patients who underwent whole pelvis RT (WPRT), CTVs were: CTV1 prostate and seminal vesicles (CTV1, total dose 6750 cGy/270 cGy fx) and pelvic lymph...
nodes (CTV2, total dose 4500 cGy/180 cGy fx). During the CTV delineation procedure, each patient was planned twice: the first time using a standard CTV to planning target volume (PTV) enlargement with common margins. During the first week of therapy, patients underwent 5 daily cone beam computed tomography (CT) (CBCT) scans before delivery. CBCTs were registered with the simulation CT and a new CTV-IGRT-based contour was defined from all the positions of the prostate and SVs; finally, an individualized IGRT-based PTV was obtained through adding 3 mm of margins in all directions. The sizes of PTVs in both phases of the treatment were compared. We used the Mann Whitney test/Wilcoxon rank-sum test with continuity correction for statistical analysis. Results: A total of 1,253 CBCT were executed on 123 included patients with a median of 10 CT scans (range=0-27) for each patient. Ninety-eight patients were planned to receive a total dose of 80 Gy on CTV1 (prostate) (mean dose=79.5 range=56-80; only three patients did not receive prescribed dose for other reasons) delivered in 40 fractions; CTV2 received a total dose of 72 Gy fractionated into 1.8 Gy/die. Median overall treatment time was 58 days (range=32-127). Fifteen high-risk patients - CTV1 - (prostate and base or whole seminal vesicles, depending on the stage) received a total dose of 67.5 Gy fractionated into 2.7 Gy/die and CTV2 (pelvic lymph nodes) received a total dose of 45 Gy fractionated into 1.8 Gy/die. Median follow-up time was 20.4 months (IC=16.8-24.1). Only one patient was dead at last observation for other causes. Mean PTV1 (prostate) was 139.94 cm³; the difference between PTV1 and PTV1r was statistically significant \( p=0.000882 \). Mean PTV2 (seminal vesicles) was 192.22 cm³. The difference between PTV2 and PTV2r was statistically significant \( p=0.000723 \). Mean PTV3 (pelvic lymph nodes) was 326 cm³. Mean PTV3 replanning (PTV3r) was 245 cm³. The difference between PTV3 and PTV3r was also statistically significant \( p=0.002122 \). Toxicity was in accord with the literature and, in some cases, lower. Conclusion: IGRT is a method that may reduce irradiated volume and organs at risk whilst maintaining high delivered treatment doses and personalizing treatment plans.

**156 CURRENT GUIDELINES’ APPLICATION IN NEPHRON SPARING SURGERY: SINGLE CENTER EXPERIENCE USING TUMOR ENUCLEORESECTION**

Andrea Benedetto Galosi¹, Giulia Sbrollini¹, Giacomo Tucci¹, Asim Ettamimi¹, Guevar Maselli¹, Gaetano Donatelli¹, Rodolfo Montironi² and Marco Cordari¹

¹Division of Urology, "Augusto Murri" Hospital - Fermo, Fermo, Italy; ²Institute of Pathological Anatomy and Histopathology, United Hospitals, Polytechnic University of Marche Region, United Hospitals, Ancona, Italy

**Introduction:** In the last decade, surgical treatment of renal cancer has turned toward a more conservative surgery: sparing kidney unit how much is possible (preferring nephron sparing surgery if technically feasible) and to spaying renal parenchyma how much is possible adopting simple enucleation over traditional partial nephrectomy (PN), as suggested by a recent study (J Urol 2011;185:1604-10). However, surgical and functional outcomes are difficult to evaluate since several biases occur: surgical approach (open, pure laparoscopic or robot-assisted), ischemia time, tumor location and characteristics, patient comorbidity and surgeon’s expertise and skills. Aim: To evaluate surgical complications, functional and oncological outcome in a consecutive series of patients submitted to open enucleoresection as nephron-sparing surgery. Materials and Methods: From 09/2011 to 01/2015, we evaluated 97 consecutive renal neoplasms for surgical treatment: 51 scheduled for PN and 46 for radical nephrectomy. The mean age was of 65.6 years (range=32-91). The mean tumor diameter was of 4.06 cm (min 1-max 10). 23, 21 and 7 patients were grouped according to RENAL classification in the low, moderate and high nephrometry class, respectively. According to renal function (estimated glomerular filtration rate (eGFR) based on chronic kidney disease (CKD) classification in five categories), 27, 11, 11, 2, 1 patients (pts) were in the category (ctg) 1, 2, 3, 4 and 5, respectively. Multiple neoplasms in the same kidney were observed in 2 pts (3.9%) with 2 and 5 lesions, respectively. Nephron sparing surgery was performed using the enucleoresection technique: enucleation in medullary tumor segment close the renal sinus was used, resection in the cortical tumor segment was performed detaching a thin rim of healthy tissue around the tumor (1-4 mm). All cases were completed by open flank incision and retroperitoneal approach. Warm ischemia was used only if bleeding blurred the surgical field. Early declamping was done as soon as possible to identify bleeding vessels. A 4/0 PDS suture was used for hemostasis and collecting system repair in the deep surgical bed, while a 3/0 Monocryl suture was used for cortical parenchymal hemostasis. We recorded intra or post-operating bleeding; ultrasound was done in all case before discharge and renal function (eGFR) was checked. Follow-up data were prospectively recorded. Results: In our experience, PN was proposed and performed successfully in 48 of 97 patients (49.4%). Total nephrectomy was performed in 46 of 97 cases (50.6%): 4/46 (8%) in lesions less than 4 cm and 42/46 (92%) in lesions >4 cm. Partial nephrectomy was technically feasible in 48 of 51 patients initially scheduled for

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conservative surgery. Three out of 51 cases were converted to total nephrectomy: 1 for incomplete tumor resection and 2 for bleeding and incomplete vascular control. PN was technically feasible also in 19 pts with T1b(13) and T2(6). Perioperative complications: mean intraoperative blood loss was 280 ml (range=0-1,000). Five out of 45 pts (10.4%) required blood transfusion. Saline flushing from the ureteral catheter was used in 25 cases (52%) to identify eventual urine leaks and repaired intraoperatively. Any ancillary maneuver was performed, if necessary, such as stent placement or drain placement. Pancreatitis developed in a man who underwent right kidney surgery. Any fistula in the urinary collecting system, delayed bleeding or artery-venous fistula has not been observed yet. Digital parenchymal compression without any artery clamping was enough to complete surgery in 32 of 48 cases (60%). Warm ischemia was used in 16 of 48 cases (30.8%): 2 with segmentary artery clamping. The mean ischemia time was 16 minutes (< 10' in 4, 10'-20' in 7, 20'-30' in 5; range=5'-28'). Decline in renal function insufficiency (+ 1 degree) was observed in 10 pts (19.2%), in particular in T1b disease. Positive margin was observed in 2/47 (4.2%), excluding 1 case 1 case of positive margin that was observed in a man who underwent cytoreductive partial nephrectomy with impaired renal function. The overall positive margin rate was 6.2% (3/48). No death was recorded (overall survival and cancer specific survival was 100%) also in relation to short follow-up. One local recurrence with distant metastasis was observed in 1 case with pT1b R0 disease after 16 months (1/48, 2%) after surgery; he underwent metastasectomy and nephrectomy and has been considered disease-free. Conclusion: Considering the current therapeutic standards suggested by the latest guidelines, PN has been proposed to half of our population and proven technically feasible (also in selected T1-T2 disease; 23%, 13/55). Indicators of quality of the oncologic surgery: our data are interesting and remarkable but with a limited number of cases. Warm ischemia was used in 1/3 of cases and the time was found to be short (16 min). The oncological outcomes are comparable to international results, while the perioperative complications seem to be limited if compared to those in literature.

EVALUATION OF PROSTATIC CAPSULAR INVASION WITH PREOPERATIVE MP-MRI: CAN WE PREDICT THE INFORMATION OF PATHOLOGICAL ANALYSIS?

Francesco Porpiglia1, Matteo Manfredi1, Fabrizio Mele1, Filippo Russo2, Daniele Regge2, Mauro Papotti3, Enrico Bolli3, Daniele Amparore1, Giovanni Cattaneo1, Roberta Aima1, Riccardo Bertolo1, Nicoletta Serra1, Stefano De Luca1, Susanna Grande1 and Cristian Fiori1

Departments of 1Urology and 3Pathology, San Luigi Hospital, University of Turin, Orbassano, Turin, Italy; 2Department of Radiology, Candido Cancer Institute, Turin, Italy

Background/Aim: Prostate multiparametric magnetic resonance imaging (mp-MRI) provides precise identification of focal areas and local staging of prostate cancer (PCa). Particularly, mp-MRI is able to demonstrate extracapsular extension and seminal vesicle invasion, which have significant implications for patient management. However, surgeons would like to have information about prostatic capsular invasion (PCI) to chose the most appropriate surgical technique for each patient during radical prostatectomy (RP): standard, partial or minimal nerve sparing. In pathologic setting, Wheeler et al. proposed a detailed classification of levels of PCI that provides valuable prognostic information. The aim of our study was to evaluate the ability of mp-MRI in identifying PCI by comparing its results with those obtained with pathological analysis. Patients and Methods: The study included 350 consecutive patients with PCa who underwent preoperative MRI before RP. Patients underwent MRI performing a conventional study with T1-w, T2-w and diffusion sequences acquired after administration of contrast medium. MRI was performed in three reference centers with the same characteristics of equipment and experience of radiologists. Both for MRI and pathological analysis, the location and extent of each cancer was identified and detailed tumor maps were prepared for each case. The level of PCI for each lesion was defined as Level 0 (L0): tumor confined to prostatic stroma within the boundary of normal prostatic acini; L1: confined to stroma, but outside the boundary of normal prostatic acini, L2: confined to the prostate in a layer more fibrous than muscular (capsule); L3F: outside the prostate to a depth of less than one high-power field on no more than two separate sections; L3E: any tumor more than L3F, as reported by Wheeler. The level of PCI on mp-MRI was defined as L0 or L1 (taken together): tumor to more than 10 mm from the capsule without signs of alteration of that; L2: little margin of contact with the capsule (less than 15 mm) or when prostate margin is redundant or retracted; L3F: any mild irregularities of the fibrous capsule to outward extension; L3E: asymmetry of the neurovascular bundles and obliteration of recto-prostatic angle, direct evidence of abnormal tissue in the periprostatic adipose tissue, generally associated with disruption of the fibrous capsule. Results: The pathological report revealed: 93 pT2a-b; 161 pT2c; 58 pT3a and 38 pT3b stage prostate cancer, the overall number of tumor lesions was 639. Mp-MRI correctly identified 201/226 (88.9%), 165/182 (90.6%), 71/78 (91.0%) and 26/29 (89.7%) lesions classified by pathological analysis as L0-1, L2, L3F and L3E, respectively. Cohen's kappa coefficient was 0.909. Conclusion: MRI was able to correctly identify a significant number of tumor lesions and the level of PCI was predicted with almost
perfect agreement with pathological analysis. On the basis of these results, we think that mp-MRI is a basic piece in the mosaic of the RP’s tailoring.

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IS THE FUSION BIOPSY HELPFUL IN DETECTING CLINICALLY SIGNIFICANT PROSTATE CANCER? OUR INITIAL EXPERIENCE

Francesco Porpiglia1, Matteo Manfredi1, Marco Cosso1, Fabrizio Mele1, Enrico Bollito2, Mauro Papotti2, Nicoletta Serra1, Giulia Ottaviano1, Tomas Moretti1, Andrea Velti3, Agostino De Pascale3, Filippo Russo4, Stefano Cirillo5 and Cristian Fiori1

Departments of 1Urology, 2Pathology and 3Radiology, San Luigi Hospital, University of Turin, Orbassano, Turin, Italy; 4Department of Radiology, Candiolo Cancer Institute, Turin, Italy
5Department of Radiology, Mauriziano Hospital, Turin, Italy

Background/Aim: Diagnosis and accurate staging and grading of prostate cancer (PCa) are essential for “tailoring” the best treatment for each patient. Multiparametric magnetic resonance imaging (mp-MRI)/transrectal ultrasound (TRUS) fusion biopsy (FB) has shown encouraging results for detecting clinically significant PCa. The aim of our study was to report the initial results about FB in routine clinical practice. Materials and Methods: Patients with suspicion for prostate cancer and any abnormalities on 1.5 Tesla mp-MRI were enrolled in this prospective study from May 2014. Mp-MRI/TRUS FB, using a rigid system (Geoscan BioJet®), were performed in all patients and 12 systematic biopsies were added in patients undergoing first prostate mapping. Imaging data and pathological findings of targeted and systematic biopsies were analyzed. Lesions suspicious for PCa on mp-MRI were classified according to Prostate Imaging-Reporting and Data System (PIRADS). All biopsy adverse effects were recorded. Results: Seventy-three patients were enrolled in this study. Median age was 63.5 years (range=43-79) and mean PSA was 8.2±4.5 ng/ml. 62.2% of patients underwent transrectal, while 37.8% transperineal FB. Of the men, 53.4% previously underwent TRUS-guided random biopsies, which were negative; thus, only in 34 patients (46.3%) systematic biopsies were added. The overall detection rate for PCa was 49.3% (36/73) and 89% of biopsy-proven prostate cancer were clinically significant according to Epstein criteria. Biopsy Gleason score (GS) was as follows: 4 (11.1%) GS 6, 18 (50%) GS 7 (3+4), 12 (33.3%) GS 7 (4+3), 1 (2.8%) GS 8, 1 (2.8%) GS 9. Concerning FB only, the overall tumor detection rate was 48% (35/73), while the detection rate for the lesions classified as PIRADS ≥3 on mp-MRI was 73.3% (33/45). In patients who underwent first prostate biopsy, only one (2.9%) was diagnosed only with systematic biopsies and not with FB. Finally, 10 patients with PCa diagnosis (27.8%) underwent radical prostatectomy; all of them diagnosed with FB. In this subgroup of patients, we recorded a concordance between biopsy and pathologic GS of 100%. Regarding adverse effects, we registered 10 cases (13.7%) of mild hematuria that did not require treatment and one (1.4%, a patient who underwent transrectal FB and systematic transperineal mapping) case of septic febrile urinary tract infection (UTI) who necessitated hospital admission. Conclusion: Regarding our preliminary results, mp-MRI/TRUS FB, both transrectal and transperineal, provide high detection of clinically significant prostate cancers with a reasonable adverse effect rate. Moreover, it seems to improve risk stratification by obtaining biopsies that are really representative of pathologic Gleason score.

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IS THE PREOPERATIVE MULTIPARAMETRIC MRI IN PATIENTS WITH LOCALIZED PROSTATE CANCER HELPFUL TO CHOOSE THE BEST THERAPEUTIC APPROACH?

Francesco Porpiglia1, Fabrizio Mele1, Matteo Manfredi1, Massimiliano Poggio1, Enrico Bollito2, Mauro Papotti2, Ivano Morra1, Riccardo Bertolol1, Francesca Ragni1, Andrea Di Stasio1, Filippo Russo1, Daniele Regge1 and Cristian Fiori1

Departments of 1Urology and 2Pathology, San Luigi Hospital, University of Turin, Orbassano, Turin, Italy; 3Department of Radiology, Candiolo Cancer Institute, Turin, Italy

Background/Aim: Nowadays, prostate cancer (PCa) is mostly diagnosed in the localized stage. This has led to the development of minimally invasive surgical approaches, able to obtain the best results in terms of the “trifecta”: oncological radicality, sexual potency and urinary continence conservation. Robotic-assisted radical prostatectomy (RARP) is one of the most important actors in this scenario. The prostatic multiparametric magnetic resonance imaging (mp-MRI) has grown rapidly and is increasingly used in clinical practice for the PCa staging and, on the basis of its findings, surgeon can use a “tailored” surgical technique. The aim of this study was to evaluate if this “MRI-tailored” approach can modify oncologic and functional outcomes after RARP. Materials and Methods: We retrospectively reviewed our prospectively maintained database of RARP and extracted data of patients (pts) treated from January 2011 to September 2014. The patients were divided into two groups: group A (350 pts who underwent preoperative mp-MRI) and group B (190 pts who did not). In group A, the mp-MRI consisted of a T1, T2-weighed study and diffusion images were acquired after administration of contrast medium. mp-MRIs were performed in three reference centers with the same
characteristics of equipment and experience of radiologists. In this group, mp-MRI information was used for tailoring of the surgical technique (i.e., intra/inter/extrafascial prostatectomy) for each patient. In group B, mp-MRI was not performed for reasons that were independent of prostate disease (i.e., claustrophobia, implanted metallic devices, cardiac pacemakers) and surgical technique was based on clinical and biopsy findings. The two groups were compared regarding preoperative, intra-operative (type of nerve-sparing approach (extra-, inter- or intra- fascial)) and pathological data. The primary endpoint was the comparison of the trifecta defined as: positive surgical margin rate (PSMr), urinary continence at catheter removal and one month after RARP, sexual potency at one month after nerve-sparing RARP. 

Results: The two groups were comparable in terms of preoperative, intraoperative and pathological characteristics. The PSMr was 14% for group A and 22.1% for group B (p=0.022). Urinary continence at catheter removal was 68.0% (238/350) in group A and 58.9% (121/190) in group B (p=0.055), while at one month, it was 82.8% (290/350) and 77.9% (148/190), respectively (p=0.20). Sexual potency at one month amounted to 30.6% in group A and 27.9% in group B (p=0.95).

Conclusion: The results showed a favorable trend toward a reduction of PSMr and a faster recovery of urinary continence and sexual potency. Oncologically, we obtained the confirmation that mp-MRI is essential in the planning of radical prostatectomy. The statistical significance of the functional results is probably reduced by the small sample size.

160 MANAGEMENT OF RENAL PEDICLE DURING LAPAROSCOPIC PARTIAL NEPHRECTOMY: CAN THE TYPE OF CLAMPING INFLUENCE THE FUNCTIONAL OUTCOME AT RENAL SCANNING? 

Francesco Porpiglia, Riccardo Bertolo, Daniele Amparore, Giulia Ottaviano and Cristian Fiori

Department of Urology, San Luigi Hospital, University of Turin, Orbassano, Turin, Italy

Background/Aim: Minimization of warm ischaemia time (WIT) during laparoscopic partial nephrectomy (LPN), when looking for the highest achievement rate of trifecta, has increased the importance of alternative techniques to global ischemia for management of renal artery. The aim of the study was to compare the outcomes of LPN with clamping of renal artery, selective clamping of a branch of renal artery and without renal artery clamping. Patients and Methods: From January 2013 to July 2014, 119 patients with renal mass suitable for LPN were prospectively enrolled in the present study. Patients were divided into 3 Groups according to management of renal artery: Group A, clamping of renal artery; Group B, selective clamping of an extra-renal branch of renal artery if identified during dissection of renal artery; Group C, no clamping of renal artery. Indications to clampless were given till September 2013. Since October 2013, all patients underwent clamping of renal artery; when identification of an extra-renal branch of renal artery was possible, selective clamping was performed. Demographic and perioperative data were collected and analyzed. Functional outcomes were evaluated by estimated glomerular filtration rate (eGFR) (modification of diet in renal disease (MDRD) formula) and renal scanning (RS), at baseline and at 3rd month postoperatively. The percentage of loss of renal function evaluated by RS parameters was calculated. Statistical analysis was performed in order to assess any differences among the Groups. All p-values <0.05 were considered significant. Results: 42, 45 and 32 patients were enrolled in the study (Group A, B and C, respectively). Groups were comparable in demographic and preoperative data. No differences were found in intraoperative data excluding WIT. WIT was 20±7.9 and 21.7±9.3 in Group A and B, respectively (p>0.05). Neither eGFR nor percentage of loss of renal function according to RS parameters were significantly different among the Groups. At multivariate analysis, no independent factors neither of higher WIT nor of higher loss of renal function were found. No difference in complications* and positive surgical margins' rate were found; accordingly, no differences were found in trifecta achievement’s rate among the Groups. Conclusion: After more than 250 LPNs were performed, no differences were evident when comparing clamping of renal artery, selective clamping of one of its branch and no clamping at all. Results should be confirmed by a larger sample size.

161 MICRORNA EXPRESSION PROFILES IN HIGH-GRADE PROSTATIC INTRAEPITHELIAL NEOPLASIA (HGPIN): RE-DEFINING THE PROSTATE CANCER PRECURSOR LESION ACCORDING TO THE GENETIC SIGNATURE

Fabio Campodonico1, Silvia Viaggi2, Domenico Coviello3, Alfredo Ferro4, Alessandro Lagana5, Alfredo Pulvirenti5, Rosalba Giugno4, Irena Marie2, Roberto Bandelloni7 and Massimo Maffezzini8

1Urology Unit, EO Ospedali Galliera, Genoa, Italy; 2Human Genetics Unit, EO Ospedali Galliera, DISTAV University of Genova, Genoa, Italy; 3Human Genetics Unit, EO Ospedali Galliera, Genoa, Italy; Departments of 4Clinical and Molecular Biomedicine and 5Mathematics and Computer Science, University of Catania, Catania, Italy; 6Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, U.S.A.; 7Pathology Unit, EO Ospedali Galliera, Genoa, Italy; 8Urology Unit, National Cancer Institute, Milan, Italy.
Background/Aim: The heterogeneous behavior of prostate cancer (PCa) depends on molecular and genetic profiles of cancer cells. In the last decade, a growing number of publications indicated micro-RNAs (miRNAs), short noncoding nucleic acids regulating gene expression, as potential biomarkers of cancer development/progression. In this study, we analyzed miRNA expression in normal prostate tissue, high-grade - prostatic intraepithelial neoplasia (HGPIN) from patients with HGPIN alone and HGPIN from patients including PCa on biopic specimens. The aim was to individuate a subset of miRNAs being useful in defining clinical relevance of HGPIN. Patients and Methods: We retrospectively studied 50 patients who underwent prostate biopsy for elevated serum prostate-specific antigen (PSA) or abnormal digital rectal examination. MiRNAs were extracted from 25 HGPIN biopic samples from patients with HGPIN alone, from 25 HGPIN biopic samples from patients who developed PCa and from 50 biopic samples, from the same patients, including normal prostate tissue. Results: The miRNA expression analysis showed a subset of miRNAs differentially expressed in the different groups of samples. The HGPIN lesion did not express the same subsets of miRNAs in patients with HGPIN alone compared with patients diagnosed with PCa. The heat map of miRNA that was differentially expressed in the different group of biopsies showed a quite homogeneous distribution within the group of HGPIN alone and within the group of PCa-associated HGPIN; control samples showed some variability. Conclusion: The differential expression of miRNAs in HGPIN alone and HGPIN associated to PCa showed that the two lesions are genetically heterogeneous despite the same histological and immunohistochemical pathology report. The validation of this finding would be helpful in distinguishing between HGPIN non-progressing (or progressing to a low-risk PCa) from HGPIN evolving to an aggressive Pca and may be relevant in planning diagnostic strategies for early cancer detection in patients at risk.

162 PROSTATE BIOPSY: PATHOLOGICAL PATTERNS IN MEN WITH PROSTATE CANCER GENE 3 (PCA3) SCORE FLUCTUATIONS
Stefano De Luca1, Roberto Passera2, Enrico Bollito3, Susanna Cappia4, Daniele Amparore1, Giovanni Cattaneo1, Matteo Manfredi1, Fabrizio Mele1, Riccardo Bertolo1 and Francesco Porpiglia1
Departments of 1Urology, 2Pathology and 4Molecular Biology and Cancer Research, San Luigi Hospital, University of Turin, Orbassano, Turin, Italy; 3Department of Nuclear Medicine, San Giovanni Battista Hospital, University of Turin, Turin, Italy

Background/Aim: As several years have passed from first prostate cancer gene 3 (PCA3) diagnostics, the number of patients having ≥2 PCA3 scores is increasing. Being a genetic marker, it would be expected to have a stable score on repeated measures over time. Very few data in literature reported a 20-30% fluctuation in repeated measures of PCA3 score, but covering only a limited 3-4 week time period. The aim of this study was to evaluate prostate biopsy (Bx) pathological patterns in men with upgraded and downgraded risk class in PCA3 score on time course and with elevated serum prostate-specific antigen (PSA) and/or positive digital rectal examination (DRE), undergoing a repeat biopsy (re-Bx). Patients and Methods: Between October 2008 and June 2014, a series of 437 men underwent at least two PCA3 score assessments in the same laboratory. Of the 437 men, 329 (75.3%) maintained their PCA3 score risk category: 189 of them had PCA3 score ≤35, while 140 had PCA3 score >35. Only the remaining 108 patients (24.7%), who changed their PCA3 score risk class (upgraded/downgraded), were enrolled in this survey. Comparison of PCA3 score either in patients with negative re-Bx (normal parenchyma, benign prostatic hyperplasia (BPH), chronic prostatitis, high-grade prostate intraepithelial neoplasia (HG-PIN), atypical small acinar prostate (ASAP)) or positive re-Bx was performed. Results: The upgrading and downgrading rates for PCA3 score were 71.3% (77 pts) and 28.7% (31 pts), respectively. Among the 77 upgrading patients, the median PCA3 score upgrade was 24 (4-69), while among the 31 downgrading ones, the median PCA3 score downgrade was -17 (-2/-55). Twenty-four patients out of 29 (82.7%) patients with prostate cancer (PCa) upgraded their PCA3 score. No association was found among the PCA3 score cross-up/cross-down and age≥65 years (p=0.975), family history for PCa (p=0.796), DRE (p=0.179), use of 5-alpha-reductase inhibitors (p=0.793) and BPH/prostatitis/HG-PIN/ASAP diagnosis (p=0.428). Conclusion: PCA3 score can be considered a stable over time marker in most cases; notably, up to 20% patients have a clinically notable risk class change. The rate of PCa was quite higher in PCA3 score upgraded patients, even if no robust cut-off for PCA3 score fluctuations was identified.

163 PROSTATE CANCER GENE 3 SCORE, PROSTATE HEALTH INDEX AND PERCENTAGE-FREE PROSTATE-SPECIFIC ANTIGEN: WHICH IS THE BEST IN DIFFERENTIATING HISTOLOGICAL INFLAMMATION FROM PROSTATE CANCER AND OTHER NON NEOPLASTIC ALTERATIONS OF THE PROSTATE AT INITIAL BIOPSY?
Stefano De Luca1, Roberto Passera2, Enrico Bollito3, Simonia Vattrano4, Antonino Sottile5, Daniele Amparore1, Giovanni Cattaneo1, Giulia Ottaviano1, Enrico Checucci4, Riccardo Bertolo1 and Francesco Porpiglia1
Background/Aim: Acute and chronic histological inflammation is commonly found (35% to 100% of prostate biopsies) among asymptomatic men biopsied for elevated prostate-specific antigen (PSA). The aim of this study was to determine if this prospective study, 274 patients, undergoing negative digital rectal examination.

Patients and Methods: In this prospective study, 274 patients, undergoing PCA3, PHI and %fPSA assessments before initial biopsy, were enrolled. Among them, 31 patients (11.3%) had a history of chronic prostatitis. Exclusion criteria were: patients with acute bacterial prostatitis in the three months before biopsy, men with previous diagnosis of atypical small acinar proliferation (ASAP) or patients being treated with dutasteride/finasteride. Three multivariate logistic regression models were used to test PCA3, PHI and %fPSA as risk factors for prostatitis vs. BCA, vs. BPH and vs. HG-PIN. All the analyses were performed for the whole patient cohort and for the ‘gray zone’ of PSA (4-10 ng/ml) cohort (188 individuals). Results: The median PCA3 score was significantly different between men with a negative vs. those with positive biopsy (25 vs. 47, p<0.001), as for PHI (37.1 vs. 52, p<0.001) and %fPSA (14% vs. 12%, p=0.001). All the three biomarkers were determinants in the diagnosis of prostatitis vs. PCa (Odds Ratio (OR)=0.97 for PCA3, 0.96 for PHI and 0.94 for %fPSA). Unit increase of PHI was the only risk factor for prostatitis vs. BPH (OR=1.06) and unit increase of PCA3 score for prostatitis vs. HG-PIN (OR=0.98). In the ‘gray zone’ PSA cohort, the determinants for prostatitis vs. PCa were PCA3 score, PHI and %fPSA (OR=0.96, 0.94 and 0.92, respectively), PCA3 score and PHI for prostatitis vs. BPH (OR=0.96 and 1.08, respectively) and PCA3 score for prostatitis vs. HG-PIN (OR=0.97). Comparing men with acute inflammatory pattern (31 patients) vs. those with a chronic one (97 patients), there was no difference in median PCA3 score (20 vs. 21, p=0.985) or %fPSA (12% vs. 12%, p=0.385); conversely, there was for PHI (44 vs. 34.7, p=0.002). In patients with PCa associated with histological evidence of prostatitis, the inflammatory pattern (chronic prostatitis in the majority of cases) did not influence biomarker results. Conclusion: The clinical benefit of using PCA3 and PHI score to estimate prostatitis vs. PCa was comparable; even %fPSA had a good diagnostic performance, being a faster and cheaper marker. PHI was the only determinant for prostatitis vs. BPH, while PCA3 can determine between prostatitis vs. HG-PIN.


164 PERIPROSTATIC PHLEBOLITHS: A POTENTIAL PITFALL FOR WIDER RESECTIONS DURING RADICAL PROSTATECTOMY
Luca Ventura1, Giovanni Luca Gravina2, Claudio Festuccia3, Massimo Menichini4 and Cinzia Mercurio1

Divisions of 1Pathology and 4Nuclear Medicine, San Salvatore Hospital, L’Aquila, Italy; 2Division of Radiotherapy, Department of Biotechnological and Applied Clinical Sciences, University of L’Aquila, L’Aquila, Italy; 3Department of Biotechnological and Applied Clinical Sciences, University of L’Aquila, L’Aquila, Italy

Background/Aim: Phleboliths are areas of calcification in a vein representing the end product of thrombosis. They are frequently seen within the pelvis, in the veins around bladder, prostate, uterus and rectum (1). Sometimes they may be difficult to differentiate from distal ureteral stones on radiographs (2) but pelvic phleboliths are generally considered of no clinical significance (1). For this reason, they are actually neglected in radiology and histopathology reports and, to the best of our knowledge, their presence in prostatectomy specimens has never been described in the literature. During the last year, we observed periprostatic phleboliths in 4 radical prostatectomies submitted to histopathological examination. The aim of this study is to determine the main features of periprostatic phleboliths and evaluate their role as a mimetic of extraprostatic extension and as a potential pitfall for wider resections. Patients and Methods: After routine histopathological examination of radical prostatectomy specimens, the incidental presence of phleboliths was noted in 4 cases. According to international protocols, the prostate was serially sectioned and entirely

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submitted to histology, with at least a section of each sample stained with hematoxylin-eosin and microscopically observed. The age of the patients, tumor extension (pT), site of extraprostatic extension, margin status, site of positive margins and location of phleboliths were recorded. An abdomino-pelvic computed tomography scanning was available for one patient: no mention of phleboliths appeared in the report; however, retrospective evaluation of the scans allowed to identify multiple bilateral periprostatic calcifications. Results: The age range of the patients was 55-65 years (mean=60.75, median=60). Two cases were in pT2c category, whereas the other two were classified as pT3a. One out of four patients had positive margins (R1) in the prostatic apex region. Phleboliths, with the classic concentric calcification pattern, were observed outside the lateral aspects of the gland in 3 cases, in the periapical region in 1 case and near the prostatic base in 3 cases. In all cases, the phleboliths were surrounded by abundant normal periprostatic tissues and located far from intra- or extraprostatic neoplastic tissue. In each prostate specimen, different stages of periprostatic venous thrombosis were also evident. Discussion and Conclusion: Our findings suggest that phleboliths are a common finding in periprostatic tissues as they may be frequently identified during histopathological examination of radical prostatectomies. The most frequent locations of the phleboliths are outside the posterolateral regions of the prostate, where the neurovascular bundles adhere to the gland. Tactile evaluation is often used during nerve-sparing surgery, relying on cancer tissue firmness identified by palpation (3). Phleboliths may simulate extraprostatic extension of prostate carcinoma and, therefore, be responsible of unnecessary wider resections to achieve negative margins. Pre-operative recognition of phleboliths can be of help in distinguishing them from extraprostatic cancer and limit the entity of resection to guarantee safe margins. Further investigation on wider series is needed to understand the real entity of the problem. We are planning a retrospective evaluation of prostatectomy specimens in order to document the frequency of this finding and its role in surgical resection policy.

they improved the AUC by 8.4%-8.9% (pT3) and 9.3-9.4% (pGS≥7). In decision curve analysis for pT3 and pGS≥7, a net clinical benefit was observed. **Conclusion:** Both PHI and %p2PSA could play an interesting role to predict significant disease, improving predictive accuracy of RP pathological outcomes.

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**ROBOTIC-ASSISTED EXTENDED PELVIC LYMPHADENECTOMY FOR HIGH-RISK PROSTATE CANCER: WHICH IS THE ROLE OF MP-MRI?**

Francesco Porpiglia1, Matteo Manfredi1, Massimiliano Poggio1, Filippo Russo2, Andrea Veltri3, Agostino De Pascale3, Enrico Bollito4, Mauro Papotti4, Stefano De Luca1, Fabrizio Mele1, Riccardo Bertolo1, Andrea Di Stasio1, Danilla Garrou5, Enrico Checcucci1, Ivan Morra1 and Cristian Fiori1

Departments of 1Urology, 3Radiology and 4Pathology, San Luigi Hospital, University of Turin, Orbassano, Turin, Italy; 2Department of Radiology, Candiolo Cancer Institute, Turin, Italy; 5Department of Urology, Maggiore Della Carità Hospital, University of Eastern Piedmont, Novara, Italy

**Background/Aim:** Extended pelvic lymph node dissection (eLND) plays a key role in intermediate to high-risk patients with prostate cancer (PCa) representing the most accurate staging procedure for detection of lymph nodes’ invasion (LNI). However, there is no consensus on the indication to perform eLND. Unfortunately, standard imaging has a very limited ability to predict LNI (about 70% of metastatic lymph nodes are <8mm). In order to overcome this problem it is possible to rely on nomograms based on clinical data, pre-operative biochemical markers and biopsy findings. Prostate multiparametric magnetic resonance imaging (mp-MRI) has grown rapidly and is increasingly used in clinical practice for PCa. Although this exam is not able to directly identify LNI faithfully, it provides important information about the local staging and tumor aggressiveness. This type of information could be used to improve nomograms currently employed to indicate the eLND. The aim of this study was to assess and compare the performance of a preoperative risk assessment tool with or without additional information of mp-MRI in a population of men treated with radical prostatectomy. **Patients and Methods:** From January 2012 to September 2014, we performed eLND in 113 patients who were subjected to mp-MRI prior to robotic-assisted radical prostatectomy. mp-MRI scans (consisted of a T1, T2-weighted study and diffusion images acquired after administration of contrast medium) were performed in three reference centers with the same characteristics of equipment and experience of radiologists. Indications for eLND were defined according to nomogram proposed by Briganti et al. and based on pre-treatment prostate-specific antigen (PSA), clinical stage, biopic Gleason score and percentage of positive cores. Irrespective of Briganti nomogram results, eLND was performed in cases of: (i) evidence of extraprostatic disease (extracapsular extension or seminal vesicle invasion) and/or (ii) high aggressiveness disease (prevalence of Gleason pattern 4) revealed by mp-MRI. We retrospectively divided our patients into two groups evaluating whether, adding MRI data, could be possible to better select patients to submit to eLND: group A, 52 patients with LNI risk> 5%; Group B, 61 patients with both LNI risks (< or >5%) and mp-MRI criteria. The total lymph node yield, the frequency of lymph node metastases and the complication rate were compared retrospectively. Statistical analyses were performed by using Chi-square test; p-values <0.05 were considered statistically significant. **Results:** The median patient age was 64 years (interquartile range (IQR)=59-68). The median preoperative PSA level was 7.47 ng/ml (IQR=5.54-11.5). Mean number of lymph nodes retrieved was 25.02±8.45/patient (median:=25; IQR=19-30). The two groups were comparable in terms of preoperative, intraoperative and pathological characteristics. No difference in terms of complication rate was recorded. Thirteen patients (11.5%) had lymph node metastasis, 5 (9.6%) and 8 (13.1%) in group A and B, respectively (p=0.77). Median positive lymph nodes was 1 (IQR=1-5) with no difference in the two subgroups. **Conclusion:** Our preliminary results suggest that mp-MRI information can help the surgeon to identify the best candidates for eLND. Further studies with larger sample size are required to confirm our data.

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**RELATIONSHIP BETWEEN ENZALUTAMIDE ACTIVITY AND PREVIOUS ANTIANDROGEN WITHDRAWAL SYNDROME (AWS) IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (MCRPC)**

Daniele Alesini1, Michele Sisani2, Amelia Altavilla2, Giuseppe Procopio3, Alketa Hamzaj2, Francesco Grilone4, Francesco Massari5, Francesca Marroccholo2, Alberto Zaniboni6, Rodolfo Mattioli7, Sebastiano Buti8, Michele Battaglia9, Orazio Caffo10, Verena De Angelis11 and Sergio Bracarda2

1Oncologia Medica B, Policlinico Umberto I, Rome, Italy; 2Dipartimento di Oncologia Medica, Ospedale San Donato, Arezzo, Italy; 3Oncologia Medica, Fondazione IRCCS, Istituto Nazionale dei Tumori, Milan, Italy; 4Oncologia Medica, Fondazione Tommaso Campanella, Catanzaro, Italy;

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Antiandrogen withdrawal syndrome (AWS) is defined as a decline in prostate-specific antigen (PSA) after withdrawal of an antiandrogen (AA) during maximum androgen blockade, and it has been described in less than 20% of castration-resistant prostate cancer (CRPC) patients. The most likely mechanism of action for AWS is a switch of an AA from antagonistic to agonistic activity. The second generation AA Enzalutamide (ENZ) has recently been approved for CRPC patients after docetaxel failure. We analyzed possible relationship between a previous AWS and response to ENZ. Patients and Methods: We retrospectively analyzed data of all consecutive metastatic castration-resistant prostate cancer (mCRPC) patients treated with ENZ at 10 Italian centers within the compassionate use program. AWS was defined as PSA response after 6-8 weeks from an AA withdrawal. ENZ activity was evaluated by duration of response, calculated as the time (in months) from initial response to documented tumor progression or death from any cause. A t-test was used for statistical analysis. Results: At present, only 40 of 133 patients analyzed were evaluable for both AWS and ENZ activity. Median age was 73.5 years and median Gleason Score was 8. A favorable AWS was present in 6 patients (15%, median duration of AWS response=8.5 months); not present in 34. Patients with favorable AWS had a lower Gleason score (8 vs. 7, p=0.033), a trend in longer duration of response to ENZ (7.0 vs. 4.0 months, p=0.466) and were older than patients with no AWS (76.0 vs. 73.5 years, p=0.651). Conclusion: This case series represents the first report of a correlation between AWS and response to ENZ in mCRPC patients. Data suggest a correlation between the presence of AWS and duration of response to ENZ. These data failed to reach a statistical significance, probably due to the limited number of analyzed patients.
duration (TD). Patients and Methods: Data from all consecutive patients (pts) treated in 24 Italian centers with sunitinib on schedule 2/1 were analyzed according to the following groups: Group A, pts moved to schedule 2/1 because of treatment-related toxicities during initial therapy using schedule 4/2; Group B, pts treated ab initio with schedule 2/1 mainly because of poorer clinical conditions. The characteristics of the 249 consecutive pts treated from Nov 2005 to Aug 2013 were analyzed. Number of pts in Group A was 208, in Group B was 41. Their baseline characteristics were, respectively: median age 62 and 61 years; 94.7% and 87.8% of pts had a clear cell histology. Pts in group B had poorer characteristics compared to group A in terms of performance status, Memorial Sloan Kettering (MSKCC) risk and central nervous system (CNS) involvement. Efficacy: In Group A, the median TD was 28.2 months (m) (with a median of 4.3 on the initial schedule 4/2 and 19.7 on the following schedule 2/1); median PFS was 30.2m (95% confidence interval (CI)=23.2-47.1). In Group B, median TD was 7.8m and median PFS was 10.6m (95% CI, 7.7-23.0). Safety: In Group A, maximum toxicity grade (≥3) was significantly reduced on schedule 2/1 compared with the initial schedule 4/2 (8% vs. 46%, p<0.001). Specific toxicities, such as fatigue and hypertension were also reduced (respectively, 0% vs. 10%, p<0.001 and 2% vs. 9%, p=0.007). The maximum toxicity grade (≥3) was significantly reduced also in pts of group A who did not reduce the dose of sunitinib (n=108) moving to schedule 2/1 from the initial schedule 4/2 (7% vs. 41%, respectively). Conclusion: Patients who moved to a modified schedule 2/1 because of treatment-related toxicities during initial therapy using classical schedule 4/2 seem to have an improved safety profile with a reduction of overall grade 3-4 toxicities and of specific toxicities, such as fatigue and hypertension. The improved safety profile was also maintained in the subgroup of pts who did not reduce the dose of sunitinib. A potential improvement of PFS, to be confirmed in a prospective trial, has been demonstrated. The results observed in group B should be analyzed taking into account the poorer characteristics of pts.

USE OF TARGET THERAPIES IN PATIENTS WITH METASTATIC KIDNEY CANCER RECEIVING DIALYSIS: A CASE REPORT

Roberto Murialdo, Lucia Tixi, Roberta Gonella and Alberto Ballestrero

Department of Internal Medicine, A.O.U IRCCS S. Martino-IST, University of Genoa, Genoa, Italy

Little is known about the activity and tolerance of targeted therapies (TT) in patients receiving hemo- or peritoneal dialysis. Data regarding the efficacy and tolerability of sunitinib in patients with renal impairment are limited. The following report describes the case of a non-clear-cell histology that represents a rare subtype on which there is very little information on this setting. A 64-year-old man underwent left nephrectomy in March 2005 for papillary renal cell cancer (pRCC) pt3 G2 Nx M0. In August 2008, peritoneal dialysis was started because of renal failure due to evolution of pre-existing polycystic kidney syndrome and to previous renal surgery. In September 2009, a computed tomography (CT) scan revealed mediastinal and lomboaortic lymphadenopathy. The patient underwent mediastinoscopy in October 2009 with diagnosis of lymph node metastases of papillary renal cell carcinoma (RCC). Therapy with sunitinib, 37.5 mg/day for 4 weeks for every 6 weeks, was, therefore, initiated in January 2011. During the first cycle, the patient experienced a grade 2 hypertension, which was well controlled with medical therapy. The second cycle started in February 2011 with an increased dose of sunitinib to 50 mg/die. The patient unfortunately experienced grade 2 fatigue and stomatitis and developed a subclinical hypothyroidism requiring thyroxine supplementation. Dose reduction to 37.5 mg/day was required on the third cycle and the patient had a good tolerance. CT scan performed in April 2011 revealed a stable disease and, therefore, the patient continued therapy. Fourth cycle started in May 2011 with a sunitinib dose of 37.5 mg/day but the patient suffered grade 2 fatigue and mucositis and lack of appetite. He had a progressive performance status deterioration and fever at the end of June. In July 2011, the patient was admitted to the Nephrology Unit with diagnosis of sepsis, quickly evolving in Adult Respiratory Distress Syndrome (ARDS) and leading the patient to death. The main concerns regarding treatment in patients requiring dialysis are toxicity and efficacy, primarily in the era of available targeted therapies. The efficacy of sunitinib in patients with impaired renal function seemed not to be inferior when compared to the response to treatment in patients with normal renal function. Unfortunately, it is a fact that this is a setting of frail patients that represent a challenge for the clinician.
A 54-year-old man underwent right nephrectomy in May 2012 for a renal cell carcinoma (RCC). The pathological stage was T2 N0 M0 and no chemotherapy was initiated. In September 2012, a whole-body computed tomography (CT) scan revealed multiple lung lesions and oral administration of sunitinib 50 mg at standard dose was prescribed. After 8 cycles of sunitinib, the patient had a partial response with reduction in number and volume of lung lesions. Sunitinib was well tolerated with only one occurrence of skin toxicity for which the dose is lowered to 37.5 mg from September 2013. In May 2014, after two years of treatment with sunitinib, a whole-body CT scan revealed lung and lymph node progression. Based on the available evidence and, especially, based on characteristics of our patient (good PS, no excessive toxicity with TKI and a PFS of 20 months), a second-line treatment with axitinib (5 mg for twice a day) was decided. After only 4 cycles of axitinib, the patient had a partial response of the lung lesions and lymph node previously described. The drug is currently well tolerated by the patient. Conclusion: This case report, being only an example of importance in the absence of evidence in order to support unequivocally the superiority of second-line strategy, carefully evaluates the available data, the mechanism of action of each strategy and the characteristics of the patient to optimize the treatment outcomes.

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FORTH-LINE RESCUE THERAPY WITH AXITINIB IN RECURRENT RCC WITH MULTIPLE METASTASES: A CASE REPORT

Domenico Gattuso and Elena Petrelli
Oncologia Medica, San Filippo Neri Hospital, Rome, Italy

Background: Renal cell carcinoma (RCC) is the most common type of kidney cancer in adults. It accounts for approximately 3% of adult malignancies and 90-95% of neoplasms arising from the kidney. At the moment, several biological agents are used for the treatment of metastatic renal cell carcinoma (mRCC). Herein, we describe the case of a woman who has been treated with Afitinib (Inlyta®) for mRCC after multiple recurrences and multiple lines of therapy. At the time of writing, the patient is still receiving treatment and is showing a persistent objective response, prolonged duration of life expectancy and improved quality of life. Case Report: In July 2007, patient F.C. (female, 52-year-old) underwent left radical nephrectomy for kidney cancer; final histological diagnosis was clear-cell carcinoma, infiltrating the renal parenchyma, the renal capsule and the adipose capsule without passing it; extremely necrotic and hemorrhagic neoplasm; pT3a, G1. After surgery, she received radiation therapy to the left renal loggia (total dose 45 Gy). In February 2008, she underwent visceral lysis of adhesions and untwisting of volvulus. In June 2008, abdomen ultrasound showed a nodule in the middle third of right kidney, measuring about 2 cm, confirmed by a computed tomography (CT) scan, along with enlarged right paracaval lymph nodes. A biopsy of this nodule was performed: negative for neoplastic cells; instead, it described a framework of intense chronic pyelonephritis, associated with areas of fibrous sclerosis. In May 2009, a parenchymal nodule in the upper lobe of the right lung, already appeared in January, had a slight enlargement (9.2 mm vs. 8 mm); a solid mass of 13 mm in the right mediastinum, paratracheal, just above the azygos vein, was also documented, then found to be referable to partial volume phenomena on a subsequent control (CT scan of 7.7.2009). It also showed a slight increase in size of the process in the middle third of right kidney (3.2 vs. 2.2 cm on CT scan in January 2009). In October 2009, a full-body CT scan did not show significant changes in lesions, while the CT of 2.3.2010 documented a minimal increase in size of the right pulmonary nodule (below 20%) and an increase in volume of the mass in the right kidney, measuring about 4 cm. In April 2010, a new biopsy of the right kidney was performed according to which the patient underwent surgical enucleoresection of the newly formed renal mass (histological examination indicated clear-cell carcinoma, G2). In July 2010, she underwent pulmonary metastasectomy (histological examination confirmed pulmonary localization of RCC) but a new lesion in the right adrenal gland, with radiologic and scintigraphic characteristics of pheochromocytoma, was detected. In December 2010, an amputation of the right big toe was performed for metastatic RCC. Furthermore, a full-body CT scan documented the appearance of newly formed tissue in the left renal loggia, expression of local recurrence of the disease. For this reason, in January 2011, the patient has undertaken therapy with sunitinib (Sutent®), initially at a dose of 50 mg, then reduced to 37.5 mg for toxicity. In April 2011, a full-body CT scan showed a partial response (PR) both of the lung and of the left local recurrence, partially necrotic, but a new suspicious lesion in the left frontal area (4 mm) appeared. In May 2011, after magnetic resonance imaging (MRI) confirmation of the brain metastasis, the patient underwent radiosurgery on the brain (total dose 48 Gy). In July 2011, a CT scan showed a stable disease (SD) but it detected a new lesion in the left pterigional region and a significant increase of the brain metastasis. Therefore, in August 2011, a stereotactic treatment of this second brain...
lesion was performed. The re-evaluation in October 2011 (full-body CT scan and brain MRI) noted: substantial stability of visceral lesions, except for the appearance of a small (8 mm) nodular lesion in the lower lobe of the left lung; reduction of the left frontal lesion (5 mm) with modest peri-lesional edema; left peritrigonal lesion (14 mm) with peri-lesional edema. The patient continued treatment with sunitinib for seven complete cycles; the 8th cycle, started on 23.11.2011, was suspended for hematologic toxicity (anemia G3 and neutropenia G2). In December 2011, a CT scan revealed the presence of new micro-nodules in the lower lobe of the right lung and in the upper lobe of the left lung, while the left frontal lesion in the brain was significantly reduced. In January 2012, the patient was hospitalized for severe anemia (Hb: 7.7 g/dl) and she underwent video capsule enteroscopy, which showed metastases of the small intestine (completely removed). From 16.3.2012 to 14.11.2012 the patient was administered second-line chemotherapy with everolimus (Afinitor®), obtaining an initial SD, but progressive disease (PD) after 6 cycles. From 7.3.2013 to 18.10.2013, she was given a third-line chemotherapy with sorafenib (Nexavar®) for three cycles, maintaining a SD. Since the end of October 2013, the patient began therapy with axitinib (Inlyta®), after the permission of our Health Management Company with off-label procedure, gaining a significant partial response (PR) after only two cycles. She continued this treatment for 12 cycles (last started in February 2015). Clinical-instrumental re-evaluations, practiced every 2 months, showed a persistent objective response, prolonged duration of life expectancy and improved quality of life. Discussion: In the last years, new agents targeting vascular endothelial growth factor (VEGF) and its receptors and mammalian target of rapamycin (mTOR) have significantly changed our approach to advanced and metastatic RCC. In second-line treatment, evidence that TKIs are active after cytokines has been demonstrated with sorafenib, pazopanib and recently axitinib (1-3). Sunitinib also has activity in this setting. However, since VEGF-targeted therapy is now the first-line standard of care, the number of patients treated with cytokines is decreasing. After first-line treatment with VEGF-targeted therapy, both axitinib and everolimus are active (3, 4). Both drugs have shown significantly improved progression-free survival (PFS) over placebo (everolimus) or sorafenib (axitinib) but not overall survival (OS). Based on recent phase III trials (5), sorafenib can be used as an option. Beyond second-line treatment, enrolment into clinical trials is recommended where possible. However, some recent trials have been reported, helping to define two different scenarios: in patients already treated with two TKIs (or a TKI and bevacizumab), everolimus is recommended; in patients previously treated with VEGF-targeted therapy and mTOR inhibitor, sorafenib has shown activity (6). Another TKI or rechallenge with the same TKI is considered as an option. Based on the case reported, axitinib should be considered as well. The choice of the most appropriate agent is based not only on tumor histology, prognostic factors, patient comorbidities and preferences but also on the efficacy and safety profile of the individual agents. For this reason, the addition of new drugs to the panel of options for the treatment of mRCC has made the choice of the most appropriate targeted agent very difficult.


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LONG-TERM SURVIVAL OF A PATIENT WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER TREATED WITH A SEQUENCE OF NEW CHEMOTHERAPY AND HORMONAL AGENTS
Donatello Gasparro1, S. Tarasconi2, A. Gilli1 and Carmine Pinto1

1Medical Oncology Unit, University Hospital of Parma, Parma, Italy;
2Emergency Department, University Hospital of Parma, Parma, Italy

In the last few years, the development of new agents has significantly improved prognosis of patients with metastatic castration-resistant prostate cancer (mCRPC). We describe a case of a 69 year-old patient (D.S) who underwent transurethral resection of the prostate (TURP) on May 2006 for urinary retention, with histological diagnosis of adenocarcinoma G4 (Gleason score 8; 4+4). Prostate-specific
antigen (PSA) levels was 3,666 ng/ml. He was treated with androgen deprivation therapy (ADT; bicalutamide and triptoreline pamoate) till December 2008, when he came to our attention for disease progression (prostate and right obturator and external iliac lymph-nodes). PSA level was 71.9 ng/ml and the patient was asymptomatic; thus, we proposed active surveillance but he refused this option and asked for active treatment. In January 2009, we started treatment with ethinylestradiol and steroid but after two weeks we stopped it for the onset of deep venous thrombosis. In September 2009, disease progression occurred, PSA level was 98.2 ng/ml and a computed tomography (CT) scan revealed onset of bone metastases and an increase of number and size of lymph node metastases. Therefore, the patient was enrolled in the “VENICE” study and received 10 cycles of Taxotere + Aflibercept/placebo (until April 2010) and three cycles of Aflibercept/placebo (until July 2010). He experienced febrile neutropenia G4, fatigue G3, stomatitis G3 and thrombocytopenia G1. Toxicity required a dose reduction starting from the sixth cycle. A CT and bone scan, performed after eight and thirteen cycles, showed stable disease. PSA level gradually decreased until May 2010 (0.5 ng/ml). From June 2010 till April 2011, PSA values gradually increased but CT and bone scans showed stable disease. In May 2011, a CT scan showed local disease progression and PSA level was 75.1 ng/ml. The patient was enrolled in another clinical study and began treatment with cabazitaxel plus prednisone, obtaining a rapid biochemical response (PSA: 19 ng/ml after the first cycle). The treatment was continued till October 2011, with complete biochemical response (PSA: 1.6 ng/ml) and radiological disease stability. In June 2012, for new biochemical progression (PSA: 63.3 ng/ml), we chose to begin treatment with abiraterone acetate, continued till June 2013, obtaining complete biochemical response (PSA: 0.2 ng/ml) and radiological disease stability. The therapy was interrupted for the onset of neurological, not treatment-related disorders (familial Alzheimer disease). This case suggests that a sequential treatment with new chemotherapy and hormonal agents may determine prolonged disease control and induce long-term survival in patients with mCRPC.

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LONG-TERM RESPONSE TO SUNITINIB, EVEROLIMUS AND AXITINIB SEQUENTIALLY USED IN A YOUNG WOMEN WITH MRCC. A CASE REPORT

Elena Massa, Francesco Atzori, Francesca Notari, Marco Puzzoni, Grazia Pusole, Alessio Cubeddu, Alessandra Dessi, Maria Teresa Ionta and Mario Scartozzi
UOC Oncologia Medica, AOU Cagliari, Policlinico Universitario, Monserrato, Italy

Seven targeted agents (sorafenib, sunitinib, temsirolimus, bevacizumab (plus interferon), everolimus axitinib and pazopanib) have been approved for the treatment of patients with metastatic renal cell carcinoma (mRCC). As disease progression is inevitable, most patients will receive several lines of treatment. There appears to be no absolute crossresistance between tyrosine kinase inhibitors (TKIs) acting on the vascular endothelial growth factor-receptor (VEGF(R)) pathway and there have been numerous reports of two TKIs being successfully used in sequence. We report the case of a 28-year-old woman with good performance status and a medical history significant for kidney stones who visited our hospital in October 2005 complained of back pain. She underwent a ultrasonography that showed a left renal mass. Computed tomography (CT) scan ruled the presence of metastatic disease. She underwent radical nephrectomy in November 2005. The pathology report confirmed the presence of clear-cell RCC and included the following parameters: pT3a, N0, G2, M0, Ki-67 <20% and Fuhrman Grade 2. She received adjuvant chemotherapy (Velsna at 0.4mg/Kg q21) for 6 cycles. From April 2005, she started follow-up, always negative for recurrent disease since October 2009 when a TC scan showed a pelvic recurrence (ovaries bilaterally, subcutaneous tissue, pancreas). First-line treatment for the recurrence was started with sunitinib at a dose of 50 mg/day, on a four-week-on-two-week-off schedule. During treatment, the patient developed hypothyroidism requiring hormone replacement therapy; she also had grade 2 hypertension, requiring antihypertensive therapy, and anemia G1. After 17 months of sunitinib, disease recurred at the site of nephrectomy and the ovarian metastases progressed. In May 2011, she received second-line treatment for the recurrence with everolimus, 10 mg daily, which was well tolerated, except for grade 2 hypertension that required a reduction of the dosage of everolimus to 5 mg daily for only 2 weeks and a modification of the antihypertensive therapy. Disease remained stable for seventeen months. In October 2012, following bleeding of pelvic disease (metastasis of right ovary), the patient underwent surgery (salpingo-oophorectomy of right ovary; she refused bilateral salpingo-oophorectomy) and removal of two subcutaneous metastases of the abdominal wall. A CT scan performed after surgery showed the persistence of subcutaneous metastasis of the abdominal wall, a progression of disease in the left ovary and the occurrence of new metastasis in pelvic lymph node. The patient still had good performance status of 1. From March 2013, in off-label regimen, she received axitinib as third-line therapy for the recurrence of disease. During treatment, the patient had grade 2 hypertension, diarrhea grade 2 and anemia grade 2. In February 2015, the patient is continuing therapy and CT scan performed every 4 month (last in January 2015) confirmed stable disease (22 months). In conclusion, this case report suggests that the use of three TKIs in sequence (sunitinib, everolimus and axitinib) may be an effective treatment option.
This suggests that there is no absolute crossresistance between TKIs that target VEGFR and, thus, they should be considered as individual drugs and not as a single class. However, the optimum sequence of TKIs remains to be determined.

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TOO MUCH OF A GOOD THING.
RESPONSE TO SUNITINIB IN A POOR PERFORMANCE STATUS SARCOMATOID RENAL CANCER PATIENT: A CASE REPORT
Giacomo Bregni, Alessandro Pastorino and Giuseppe Fornarini

Oncologia Medica 1, IRCCS AOU San Martino –IST, Genoa, Italy

In the renal cell carcinoma (RCC) subset, any histologic subtype can be associated with sarcomatoid changes (1). Sarcomatoid dedifferentiation is found in 5 to 8% of all RCCs and it is linked to poor prognosis and low response to systemic treatment (2-4). Sunitinib has showed some results in the clear-cell RCC (ccRCC) with sarcomatoid features but response is still hard to come by (3). The relevant benefit brought by sunitinib therapy in the metastatic renal cell carcinoma (mRCC) setting is greatly diminished in the sarcomatoid-variant subset (5). A correlation between good performance status and radiological response was recently shown in sarcomatoid ccRCC (2). Here, we discuss the case of a poor performance status patient responding to sunitinib treatment with a bowel perforation. G.P. is a 70-year-old Italian patient seeking medical attention in August 2014 due to fever, malaise and weight loss. He underwent nephrectomy in the same month with a diagnosis of sarcomatoid renal carcinoma pT3a pN2 G4 cMx. A computed tomography (CT) scan, performed in November, showed bone, lymph node and soft tissues metastases; therefore, he started first-line treatment with sunitinib. At the end of January, clinical response was reported through measurement of superficial lymph nodes. After a few days, the patient first reported acute abdominal pain. He was accepted in a surgery ward where he was diagnosed with bowel perforation and operated on. The histological examination described a wide perforation surrounded by clear-cell renal cancer infiltration with large necrotic areas. Given the aforementioned clinically evident response, the timing suggests that the perforation was determined by necrosis and mass reduction of the neoplastic infiltration. The reported case shows the anecdotal evidence that sarcomatoid RCC of clear-cell origin can respond to sunitinib treatment even in poor performance status patients.


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RENAL CELL CARCINOMA WITH COLON METASTASIS: AN INFREQUENT SITE FOR METASTASIS
Francesca Andreozzi

Oncologia Medica, AORN COLLI Presidio Monaldi, Naples, Italy

Clinical Case: We present a case of a 41-year-old woman with a tumor detected during her annual health examination. One year before, she had undergone left nephrectomy for renal cell carcinoma (RCC). Computed tomography (CT) and colonoscopy revealed a mass on the splenic flexure. Biopsy reported a clear cell tumor. A left hemicolectomy was performed. Post-operative histological examination revealed that the tumor was a metastatic renal cell carcinoma (mRCC) of the clear-cell type. There was no evidence of tumor activity and the patient was being followed up. One year later, a new CT scan detected enlargement of retrocruural lymph nodes. As her disease was considered advanced, sunitinib at 50 mg once daily on the 4/2 schedule (four weeks on - two weeks off treatment cycle) was commenced. At the time of this report, 4 months after the commencement of sunitinib, there is radiologic evidence of stable disease and the patient feels well and is tolerating treatment with no significant toxicity.

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RECHALLENGE OF TKI THERAPY IN RCC AFTER COMPLETE REMISSION (CR): A CASE REPORT OF STOP AND GO THERAPY
Vittorio Ferrari1, D. Nonnis 1, F. Consoli1, F. Valcamonico1, G. Arcangeli1, L. Ferrari 1, A. Scalvini 1 and Alfredo Berruti 2

1U.O. Oncologia Medica, Spedali Civili di Brescia, Brescia, Italy;
2Oncologia Medica, Università degli Studi di Brescia, Brescia, Italy

Targeted agents have substantially improved patients’ outcomes in renal cell carcinoma (RCC), with median overall survival of more than 2 years observed with sunitinib. Rare patients obtain a complete response after TKI systemic therapy only in RCC as vascular endothelial growth factor (VEGF) inhibitors interrupt tumor growth increases. In the era of cytokine-based therapy, patients achieving complete response (CR) with interleukin-2 were able to maintain CR for a long period of time, without additional treatment. The choice to stop treatment with a TKI after CR may be an acceptable option. However, with TKI, it remains a matter of debate whether patients who achieve CR should continue or stop treatment. Here, we describe our case of stop and go therapy after CR. In 11/1990, a male patient underwent radical nephrectomy for a renal clear-cell carcinoma (T2N0M0) and then he was followed up. In 11/2006, he had continuous cough, without fever, and a total-body computed tomography (CT) scan showed a relapse with multiple lung lesions and mediastinal nodes. Hystological report of broncoscopic biopsy was relapse of RCC. In the same month, the patient was enrolled in the Sunitinib EAP at the dose of 50 mg/day 4/6 weels. On March 2007, a CT scan showed a partial response on each site and the patient’s adverse events, associated with targeted agents, were hypertension G1, fatigue G1, mucositis G1/2, dyspepsia G1/2, pyrosis and subclinical hypothyroidism; however, all symptoms could be effectively managed with standard medical treatments. After 13 cycles atstandard dose, we observed leukopenia and thrombocytopenia G2; we, thus, decreased the dose therapy at 37.5 mg die 4/6 weeks, and the patient continued for 26 cicles (the total sunitinib cycles were 39 and the cumulative dose was 45.500 mg). On 01/2012, a CT scan showed no evidence of tumour. The patient had G1 adverse events throughout the period of therapy and he wished to discontinue therapy, which, on February 2012, was suspended after several conversations and meetings. We planned a tight follow-up with instrumental revaluation every three months. On May 2014, a CT scan was suspicious for relapse disease in the liver and lung. On July 2014, the CT showed increase of liver lesions in number and size. In agreement with the patient, it was decided to resume sunitinib therapy at a dose of 50 mg according to standard schedule. After 3 months of therapy, the new CT scan evaluation showed a RP>50% further and the response improved after 6 months. In our experience, stopping treatment with aTKI after CR maybe an acceptable option. Cessation of VEGF-targeted therapy could be suggested in patients with long-term SD or toxicity; further research is also needed to identify factors to aid selection of patients who would be at less risk of recurrence after discontinuation of treatment.

177 C-MET: A POSSIBLE PREDICTIVE ROLE FOR RESPONSE TO FIRST-LINE TREATMENT IN METASTATIC RENAL CELL CARCINOMA

María Pagano1, Nuria Maria Asensio1, Giulio Rossi2, Roberta Gnoni1 and Corrado Boni1

1Oncology Unit, Department of Oncology and Advanced Technologies, Azienda Ospedaliera S. Maria Nuova/IRCCS, Reggio Emilia, Italy;
2Section of Pathologic Anatomy, Azienda Ospedaliero-Universitaria Policlinico of Modena, Modena, Italy

Background/Aim: Metastatic renal cell carcinoma (mRCC) is a fatal urological cancer with a 5-year survival rate of more or less 10%. During the last decade, 7 different molecules have been approved for the treatment of mRCC: vascular endothelial growth factor receptor-tyrosine kinase inhibitor (sorafenib, sunitinib, pazopanib and axitinib); monoclonal antibody anti-vascular endothelial growth factor (bevacizumab in combination with interferon) and two mammalian targets of rapamycin inhibitors (mTORi): temsirolimus and everolimus. In mRCC, the choice of the therapeutic approach is defined by histology, the risk class to which they belong according to the criteria Memorial Sloan-Kettering Cancer Center (MSKCC) and previous therapies performed. In patients with favorable or intermediate-risk, in first-line, sunitinib, bevacizumab in combination with interferon (IFN)alpha-2a and pazopanib are recommended treatments, while in patients with high-risk, temsirolimus is the choice of treatment. With the advent of targeted therapies, the recognition of predictive response factors that identify the patient population that could really benefit from a treatment rather than another, is critical, especially with noticeable improvement in the benefit / harm ratio and optimization of available resources. No predictive biological factors have been identified to date. Despite improvements in terms of progression-free survival (PFS) and overall survival (OS), acquired resistance to targeted therapies during treatment is common. Among possible mechanisms of resistance, an important role seems to be given by c-Met. The receptor tyrosine kinase, c-Met is involved in cell growth/differentiation, neovascularization and tissue repair in normal tissue, but also has been identified as a proto-oncogene. Dysregulation of c-Met and its ligand, hepatocyte growth factor (HGF), have been implicated in tumor development, invasion and angiogenesis for a range of malignancies. In the present study, we evaluated c-Met as predictor of response analyzing the association between c-Met immunohistochemical expression on mRCC paraffin tissue and response to first-line treatment with targeted therapies. Secondary end points included: correlation between c-Met state and histology, OS and time.

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to progression (TTP). Patients and Methods: We retrospectively analyzed the data from 40 patients from our center with mRCC, treated in first-line consecutively with targeted therapies. Patients with mRCC different histologies and measurable disease were included. The first-line treatment choice was decided according to risk category by Motzer. Standard dose reductions were applied in case of toxicity. The expression of c-Met was assessed by the use of two antibodies, by Invitrogen and Ventana, as well as Roche, on paraffin tissue. The use of two different antibodies for the same analysis was important for fortifying immunohistochemical data. C-met state was analyzed in patients treated in first-line with tirosin kinase or mTOR inhibitors and was correlated with treatment response. In every patient, immunostaining intensity was rated considering: 0 as negative, 1+ as weak, 2+ as moderate and 3+ as strong. Percentage of tumor cells positive for the antibody was also analyzed. Only lesions showing positive immunohistochemistry with intensity at least moderate (2+) and with more than 10% of neoplastic cells into adequate sub-cellular localization and cytoplasmic membrane were considered as positive (Figures 1 and 2). Data were collected regarding disease, the treatment performed, toxicity, response to treatment, disease progression and survival. Results: No correlation between c-Met expression and response to treatment was found regardless the different metabolic pathway inhibition (Invitrogen: stratified CMH=0.002, p-value=0.965; Roche: stratified CMH=0.313, p-value=0.576). Similarly, no association between c-Met expression and histology subtype was observed (Invitrogen: stratified CMH=0.455, p-value=0.500; Roche: stratified CMH=0.235, p-value=0.628). Finally, in the OS and TTP analysis, c-Met expression seemed to be of prognostic value. In fact, when c-Met expression was positive, the OS and TTP curves were significantly lower suggesting a worse prognosis for this population. An exception was observed for TTP with Invitrogen’s antibody for which confidence interval included the unit hazard ratio (HR). Discussion and Conclusion: In mRCC, therapeutic approach is defined by histology, the risk class according to the criteria MSKCC and prior therapies performed. In the target therapy era, it is critical to identify in advance a patient population that could benefit from a drug over another, with obvious improvement of the benefit / harm, also in terms of optimization of available resources. To date, no predictive biological factors have been identified and all the available information derives from small prospective studies or retrospective series. In 2013, Gibney et al. analyzed c-Met expression in 317 patients with histological diagnosis of RCC with different stages of disease. They concluded that c-Met expression was related with more aggressive disease and with worse survival. These data suggested the negative prognostic role of c-Met expression. In our series, higher c-Met expression was observed in more advanced disease stages and in more undifferentiated degrees affecting negatively on survival. Data were comparable with both laboratory methods used to valuate c-Met expression (Invitrogen and Ventana / Roche). In conclusion, our data confirm the already available information in literature: a higher c-Met state is observed in more advanced disease and in more undifferentiated degree with a negative relation on survival (OS and TTP). These data suggest a prognostic negative role of c-Met expression. In our series, C-Met state was not of predictive value. Therefore, until today, in mRCC patients, first-line therapy choice is still supported by clinical factors and not by molecular character elements.

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A NEW METHOD OF ANAL ANALGESIA FOR TRANSRECTAL PROSTATE BIOPSY IN PATIENTS WITH ANO-RECTAL ABNORMALITIES

Vittorino Montanaro1, Antonio Di Girolamo2, Antonio Pistone2, Armando Calogero3, Ali Akbar Jamshidi3, Luigi Pelosio1 and Vincenzo Altieri4
1Urology Unit, Kidney Transplantation Department, University of Naples "Federico II, Naples, Italy;
2Urology Department, University of Naples "Federico II Naples, Italy;
3General Surgery, University of Naples "Federico II Naples, Italy;
4Urology Unit, University of Salerno, Urology Department, Salerno, Italy

Aim: To evaluate the effectiveness of a new anal anesthesia, combined with the standard periprostatic infiltration for transrectal prostate biopsy, in order to obtain the best analgesic effect in patients with anal disorders. Patients and Methods: From January 2014 to January 2015, 35 consecutive patients with ano-rectal morbidity were selected (13 stenosis, 16 hypertonic sphincter, 6 anal fissure) to undergo a transrectal prostate biopsy. This new aesthetic technique provides an infiltration of total 10 ml of lidocaine in the anal submucosa at the four cardinal points; a one-minute finger massage of the orifice completes the procedure. According to different cases, a relaxation of the spincter hypertone, or rather a mechanical dilatation of the anal orifice, is sufficient to obtain a painless penetration of the probe. A standard periprostatic anaesthesia is then provided. Every step of the procedure was registered on a visual analogue scale (VAS). At the moment of discussion of the biopsy results, a questionnaire was given about analgesic satisfaction and possible alterations of the alveus. Results: Pain during the anesthetic infiltration was significant (VAS 4.5), mainly with the first injection, with gradual reduction with the following ones (VAS-I a 7.4 vs. VAS-I b 4.7, VAS-Ic 3.6 vs. VAS-Id 3.5). Pain during the probe injection was negligible (VAS 0.8). Pain registered during the periprostatic injection was 1.89. The control of the pain was 0.43 during the sampling. The anal anaesthesiological technique caused vagal manifestation in 3.5% and anal bleeding (however, auto-limiting) in 11.4%. Only in two cases it was not possible to complete the anaesthesiological anal procedure: in the first one because of a severe anal stenosis and in the second case because of the patient's decision to interrupt the procedure. The percentage of general complications, related to the procedure, did not differ from the average ones. Moreover, data from the questionnaire show a global satisfaction of 90% and an acceptance to eventually repeat the procedure with analogous methods of 80.7% (growing up to 100% in a subgroup subjected to a previous prostatic biopsy in other centers). Discussion: Ano-rectal abnormalities, more frequently summarized in the anal stenosis and in the sphincter hypertone, are responsible of the amplification of algogenic stimulus and result in reduction of the patient's compliance for the bioptic procedure. This often makes necessary postponing the biopsy in order to obtain the suitable preparation of the anal orifice, or rather the recourse to a delayed hospitalization linked to general or spinal anesthesia. All the above can obviously cause an increase in time and cost and sometimes the abortion of the biopsy by the patient. On the other hand, such a procedure was proven to be easy to perform and easily reproducible. Results of VAS show its effectiveness during either the introduction of the probe or during the sampling itself. Conclusion: The perianal anesthesia technique for infiltration should be considered an effective analgesic aid for patients with ano-rectal comorbidities.


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PARTIAL NEPHRECTOMY FOR BILATERAL RENAL CANCER: CASE REPORT

Roberto Sanseverino1, Oliver Intilla1, Umberto Di Mauro1, Giovanni Molisso1, Tommaso Realfonso1, Carmine Papa2 and Giorgio Napodano1

1Department of Urology, Umberto I Hospital – ASL Salerno, Nocera Inferiore, Salerno, Italy;
2Department of Anaesthesiology, Umberto I Hospital – ASL Salerno, Salerno, Italy

Introduction: We report a case of a patient affected by bilateral renal cancer who underwent a two-stage laparoscopic partial nephrectomy. Patient and Methods: A 65-year-old male presented bilateral renal tumours: a right mesorenal (42 mm) and a left hilar (38mm) lesions. Renal score of tumours was 8p and 9p, respectively. Renography revealed a glomerular filtration rate (GFR) 77 ml/min (right 40 ml/min; left 37 ml/min). The patient underwent two surgical procedures. In the first, a right transperitoneal approach was performed; the tumour is identified. The renal artery was clamped with bull dog. The tumour was excised. Renorraphy was performed with Vicryl™ sutures and secured with Hem-O-lock clips. The artery was unclamped. A Floseal™ was applied on the resected renal surface. In the second procedure, a left transperitoneal approach was performed; the tumour is identified. The renal artery was clamped with bull dog. The tumour was excised. Renorraphy was performed with Vicryl™ sutures and secured with absorbable clips. The
artery was unclamped. A Floseal™ was applied on the resected renal surface. Results: Warm ischemia time of both procedures was 20 and 23 minutes, respectively. No postoperative complications occurred. Histological evaluation revealed renal cell carcinoma (RCC) (pT1b and pT1a). Conclusion: Bilateral laparoscopic partial nephrectomy is a feasible and reproducible procedure that allows a good oncological control of bilateral synchronous renal cancer.

180 CLAMPLESS LAPAROSCOPIC PARTIAL NEPHRECTOMY FOR HILAR TUMOR

Roberto Sanseverino¹, Oliver Intilla¹, Umberto Di Mauro¹, Giovanni Molisso¹, Tommaso Realfonso¹, Giuseppe Lubrano² and Giorgio Napodano¹

Departments of ¹Urology and ²Anaesthesiology, Umberto I Hospital, ASL Salerno, Nocera Inferiore, Salerno, Italy

Introduction: Nephron sparing surgery is now reference standard for many T1 renal tumors. Although hilar clamping creates bloodless operative field, it necessarily imposes kidney ischemic injury. “Zero ischemia” partial nephrectomy allows to eliminate ischemia during nephron sparing surgery. It is possible to realize a clampless laparoscopic partial nephrectomy (LPN) also for the treatment of hilar tumors. Patient and Methods: A 65-year-old male presented at our Institution with hilar tumor of the left kidney (55 mm). Renal score was 11h and C index was 1.2. A transperitoneal approach was performed and hilar vessels are prepared in event that bulldog clamping may subsequently be needed. Intraoperative monitoring includes 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, is maintained at approximately 60 mmHg. To induce hypotension, the doses of inhalational isoflurane are increased. The renal lesion is excised using Ligasure™. Calyceal suture was performed with Vicryl™ sutures arrested with absorbable clips and Hem-O-lok™. Hemopatch and Floseal were applied to resection bed. Results: Body mass index (BMI), American Society of Anaesthesiologists' (ASA) score and tumor size were 26, II and 55mm, respectively. Operative time, blood loss, Δhemoglobin (Hb) were 185 min, 400 ml, 2.8 gr/dl, respectively. No transfusion was required. The procedure was performed without clamping. Hospital stay was 6 days. No postoperative complications occurred. Histological evaluation revealed renal cell carcinoma (RCC) pT1b, Furhman 2 with negative surgical margins. Conclusion: Clamping laparoscopic partial nephrectomy represents a safe and reproducible technique that allows sparing renal parenchyma and the preservation of renal function, also in a challenging case as a hilar tumor.

181 PHOTODYNAMIC DIAGNOSIS OF NON-MUSCLE INVASIVE BLADDER CANCER: PRELIMINARY EXPERIENCE

Giorgio Napodano¹, Antonio Campitelli¹, Tommaso Realfonso¹, Umberto Di Mauro¹, Maria Addesso² and Roberto Sanseverino¹

Departments of ¹Urology and ²Pathology, Umberto I Hospital, ASL Salerno, Nocera Inferiore, Salerno, Italy

Introduction: Bladder cancer (BC) is the most common tumour of the urinary tract. White light cystoscopy (WLC) is the standard investigation for the diagnosis of bladder tumors. Recent studies suggest that using exogenous fluorescence (photodynamic diagnosis (PDD)) can improve the diagnostic sensitivity and specificity of cystoscopy, as well as the radicality of transurethral tumor resection (TURB). We report our preliminary experience with PPD, comparing hexaminolevulinate fluorescence cystoscopy with white light cystoscopy for detecting papillary and flat lesions in patients with bladder cancer. Patients and Methods: Patients (pts) with known or suspected bladder cancer underwent bladder instillation with hexaminolevulinate (Hexvix) (85 mg) for 1 h. Cystoscopy was then performed using standard white light followed by blue light cystoscopy (PDD). Lesions or suspicious areas identified under the two illumination systems were mapped and biopsied for histological examination (cold biopsy or TURB). Results: A total of 53 pts (average age=66.9±10.7 years) with primitive known or suspected bladder cancer underwent combined cystoscopy (WL + PPD). At WLC cystoscopy, 11 (20.7%) pts had no lesions, 22 (41.5%) had single and 20 (37.8%) had multiple tumours, respectively. Histological evaluation of WL lesions revealed: inflammation (4 pts), hyperplasia (1 pt), dysplasia (3 pts), TaG1 (16 pts), T1G1 (2 pts), T1G2 (1 pt), T1G3 (9 pts), T1G3 + CIS (2 pts), carcinoma in situ (CIS) (1 pt), T2G3 (4 pts). PDD cystoscopy revealed 24 suspected areas in 19 pts (35.8%): inflammation (9 pts), hyperplasia (2 pts), dysplasia (2 pts), TaG1 (5 pts), T1G3 (1 pt), CIS (3 pts), T2G3 (2 pts). False-negative rate of WL and false-positive rate of PDD were 22.7% and 13.6%, respectively (Tables 1 and II). After PDD evaluation, prognosis changed in 9 out of 53 pts (17.0%) (Table III). Conclusion: Hexaminolevulinate fluorescence cystoscopy can be used in conjunction with white light cystoscopy to aid in the diagnosis of bladder cancer. In our preliminary
experience, Hexvix fluorescence cystoscopy detected at least 1 more tumor than white light cystoscopy in approximately a third of the patients. After histological evaluation, prognosis changed in 17% of patients. Whether this would translate to better outcomes in terms of recurrence and progression-free survival has yet to be determined.

Table I. False-positive and false-negative: per lesion analysis.

<table>
<thead>
<tr>
<th></th>
<th>WLC</th>
<th>PDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>False-positive</td>
<td>6.1% (4/66)</td>
<td>13.6% (9/66)</td>
</tr>
<tr>
<td>False-negative</td>
<td>22.7% (15/66)</td>
<td>-</td>
</tr>
<tr>
<td>New CIS</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

Table II. False-positive and false-negative: per patient analysis.

<table>
<thead>
<tr>
<th></th>
<th>WLC</th>
<th>PDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>False-positive</td>
<td>7.5% (4/53)</td>
<td>15.1% (8/53)</td>
</tr>
<tr>
<td>False-negative</td>
<td>1.9% (1/53)</td>
<td>-</td>
</tr>
<tr>
<td>New CIS</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

Table III. Reasons for changing prognosis after PDD.

<table>
<thead>
<tr>
<th>Patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>From single to multiple TCC</td>
</tr>
<tr>
<td>From &lt;3 to &gt;3 lesions</td>
</tr>
<tr>
<td>New diagnosis of T1HG</td>
</tr>
<tr>
<td>New CIS</td>
</tr>
<tr>
<td>Total pts</td>
</tr>
</tbody>
</table>


cancer. In our preliminary experience, PDD cystoscopy allowed to identify at least one more tumor than WLC in 31% of patients. After histological evaluation, prognosis changed in 21% of patients. Whether this would translate to better outcomes in terms of recurrence and progression-free survival remains to be determined.

Table I. *False-positive and false-negative: per lesion analysis.*

<table>
<thead>
<tr>
<th></th>
<th>WLC</th>
<th>PDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>False-positive</td>
<td>21.0% (8/38)</td>
<td>18.4% (7/38)</td>
</tr>
<tr>
<td>False-negative</td>
<td>36.8% (14/38)</td>
<td>-</td>
</tr>
<tr>
<td>New CIS</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

Table II. *False-positive and false-negative: per patient analysis.*

<table>
<thead>
<tr>
<th></th>
<th>WLC</th>
<th>PDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>False-positive</td>
<td>19.0% (8/42)</td>
<td>7.1% (3/42)</td>
</tr>
<tr>
<td>False-negative</td>
<td>19.0% (8/42)</td>
<td>-</td>
</tr>
<tr>
<td>New CIS</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

Table III. *Reasons for changing prognosis after PDD.*

<table>
<thead>
<tr>
<th>Reason</th>
<th>Patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>From single to multiple TCC</td>
<td>1</td>
</tr>
<tr>
<td>New diagnosis of Dysplasia</td>
<td>1</td>
</tr>
<tr>
<td>New diagnosis of T1HG</td>
<td>4</td>
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<tr>
<td>New CIS</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
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</tbody>
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