

# ABSTRACTS OF THE 35th ANNUAL MEETING OF THE ITALIAN SOCIETY OF URO-ONCOLOGY (SIUrO)

25-27 September 2025, Naples, Italy

Hotel Royal Continental, Via Partenope, 38

Honorary Chair: Sergio Bracarda, Rolando M. D'Angelillo

Italian Society of Uro-Oncology



This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.  
©2025 The Author(s). Anticancer Research is published by the International Institute of Anticancer Research.



**Italian Society of Uro-Oncology (SIUrO)**

*President:* Sergio Bracarda, Terni, Italy

*Board*

PRESIDENT: Sergio Bracarda  
VICE PRESIDENT: Rolando M. D'Angelillo  
SECRETARY GENERAL & TREASURER: Giario N. Conti  
PAST PRESIDENT: Alberto Lapini

*Advisors*

Stefano Arcangeli	Paolo Castellucci
Elena Bertelli	Rodolfo Hurlé
Nicolò Borsellino	Roberta Lucianò
Orazio Caffo	Giovanni Pappagallo
	Marco Roscigno

*Young SIUrO*

COORDINATOR: Luca Eolo Trodella  
VICE-COORDINATOR: Andrea Conti

*Advisors*

Matteo Bauckneht	Alessia Cimadamore
Michele Catellani	Stefano Luzzago
Chiara Ciccarese	Maria Brigida Maiorano
	Luca Nicosia

*Scientific Secretariat*

Società Italiana di Uro-Oncologia (SIUrO)  
Via Jacopo Barozzi 2 - 40126 Bologna, Italy  
Tel: +390513549497  
e-mail: [segreteria@siuro.it](mailto:segreteria@siuro.it) - web: [www.siuro.it](http://www.siuro.it)

*Organizing Secretariat*

MI&T  
Centro Direzionale Bolomnia, Via Guelfa 5 - 40138 Bologna, Italy  
Tel: +39 051220427 - Fax: +39 0510822077  
e-mail: [segreteria@mitcongressi.it](mailto:segreteria@mitcongressi.it)  
[www.mitcongressi.it](http://www.mitcongressi.it)

*Referees of Abstracts*

ARCANGELI STEFANO  
BOLLITO ENRICO  
BORSELLINO NICOLÒ  
BRACARDA SERGIO  
BRUNI ALESSIO  
CAFFO ORAZIO  
CASTELLUCCI PAOLO  
CECCARELLI ROBERTA  
COLLOCA GIUSEPPE  
CONTI ANDREA

CONTI GIARIO N  
D'ANGELILLO ROLANDO M  
HURLE RODOLFO  
LAPINI ALBERTO  
LUCIANÒ ROBERTA  
MANCON STEFANO  
PAPPAGALLO GIOVANNI  
ROSCIGNO MARCO  
TRODELLA LUCA E

**1  
PROSTATE CANCER AND HOMOLOGOUS  
RECOMBINATION REPAIR (HRR) GENES  
MUTATIONS: AN OBSERVATIONAL MONOCENTRIC  
STUDY ON CLINICAL AND HISTOPATHOLOGICAL  
FEATURES AND THEIR ASSOCIATION  
WITH ONCOLOGICAL OUTCOMES**

Gennaro Alberico<sup>1</sup>, Elisabetta Coppola<sup>2</sup>,  
Giovanni Luca Scaglione<sup>3</sup>, Florinda Feroce<sup>4</sup>,  
Cristin Roma<sup>5</sup>, Gelsomina Iovane<sup>2</sup>, Marilena Di Napoli<sup>2</sup>,  
Lorenzo Lobianco<sup>2</sup>, Carmela Pisano<sup>2</sup>,  
Sabrina Chiara Cecere<sup>2</sup>, Rosa Tambaro<sup>2</sup>, Anna Passarelli<sup>2</sup>,  
Jole Ventriglia<sup>2</sup>, Gabriele Calvanese<sup>6</sup>, Erika Perri<sup>7</sup>,  
Maria Rosaria Lamia<sup>8</sup>, Debora D'Ausilio<sup>2</sup>, Sisto Perdonà<sup>9</sup>,  
Sandro Pignata<sup>2</sup> and Sabrina Rossetti<sup>2</sup>

<sup>1</sup>Department of Oncology, San Luca  
Hospital, Salerno, Italy;

<sup>2</sup>Experimental Uro-Gynecological Oncology Unit,  
National Cancer Institute IRCCS "Fondazione  
G. Pascale", Naples, Italy;

<sup>3</sup>Bioinformatics Unit, IDI-IRCCS, Rome, Italy;

<sup>4</sup>Pathological and Cytopathological Anatomy Unit,  
National Cancer Institute IRCCS "Fondazione  
G. Pascale", Naples, Italy;

<sup>5</sup>Cellular Biology and Biotherapies Unit, National Cancer  
Institute IRCCS "Fondazione G. Pascale", Naples, Italy;

<sup>6</sup>Department of Hematology and Oncology,  
University of Milan, Milan, Italy;

<sup>7</sup>Department of Precision Medicine, University of  
Campania "Luigi Vanvitelli", Medical  
Oncology, Naples, Italy;

<sup>8</sup>Department of Clinical Medicine and Surgery,  
University of Naples Federico II, Naples, Italy;

<sup>9</sup>Urology Unit, National Cancer Institute IRCCS  
"Fondazione G. Pascale", Naples, Italy

*Background/Aim:* Metastatic hormone-sensitive prostate cancer (mHSPC) is a heterogeneous disease, and the prognostic implications of mutations in homologous

Table I. *Clinical and histopathological features of metastatic hormone-sensitive prostate cancer (mHSPC) patients with homologous recombination repair gene mutations (n=45).*

Median age (range), years	70 (64-74)
Median PSA (range), ng/ml	31 (13.0-102.2)
Site of metastasis, n (%)	
Bones	23 (51.1%)
Lymph nodes	15 (33.3%)
Lung	6 (13.3%)
Pelvis	1 (2.2%)
Perirectal fat	1 (2.2%)
Kidney	1 (2.2%)
Solid presacral tissue	1 (2.2%)
Gleason score	
Gleason 6	1 (2.2%)
Gleason 7	11 (24.5%)
Gleason 8	7 (15.6%)
Gleason 9	15 (33.3%)
Gleason 10	10 (22.2%)
Missing	1 (2.2%)
Histology	
Adenocarcinoma	24 (53.4%)
Acinar	18 (40.0%)
Intraductal	1 (2.2%)
Acinar/Neuroendocrine	1 (2.2%)
Neuroendocrine	1 (2.2%)
Stage at diagnosis, n (%)	
M0	18 (40.0%)
M1 High Volume*	18 (40.0%)
M1 Low Volume*	8 (17.8%)
Missing	1 (2.2%)

\*According to CHAARTED criteria (1).

recombination repair (HRR) genes, particularly BRCA1 and BRCA2, remain unclear. This study investigated the clinical outcomes of mHSPC patients with HRR gene mutations and their potential association with clinical outcomes. *Patients and Methods:* This monocentric, retrospective study was conducted at the National Cancer Institute of Naples. Clinical and histopathological data were collected from 45 mHSPC patients who underwent HRR gene mutation testing between 2019 and 2023. Mutation status was assessed using primary or metastatic tumor samples, circulating tumor DNA (ctDNA), and germline DNA. Prognostic outcomes, including progression-free survival (PFS) and overall survival (OS), were evaluated descriptively without statistical testing. *Results:* Out of 400 screened patients, 45 (11%) had at least one HRR mutation. BRCA2 was the most commonly altered gene (51.1%), followed by ATM (17.8%)

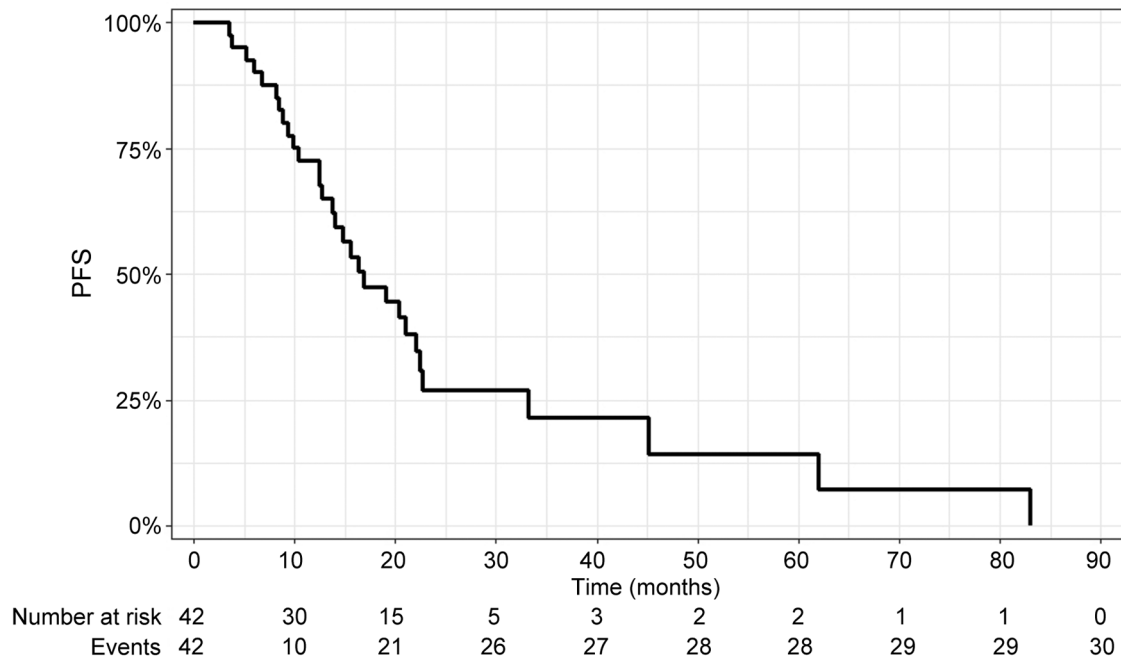


Figure 1. Kaplan-Meier curve of progression-free survival (PFS).

Table II. Median progression-free survival (PFS) and overall survival (OS) according to BRCA2 domains.

BRCA2 Functional Domains	Median PFS (95%CI)	PFS (events)	Median OS (95%CI)	OS (events)
DBD (n=5)	15.6 (15.8, NA)	4/5	NA (20.1, NA)	1/5
Exon 11 (n=3)	12.7 (5.91, NA)	3/3	64.9 (38.9, NA)	2/3
RAD51-BD (n=4)	15.7 (8.48, NA)	3/4	-	0/4
Other mutations (n=8)	33.2 (9.9, NA)	5/8	NA	1/8
BRCA2 functional domains (DBD, exon11 and RAD51-BD)	14.0 (12.7, NA)	10/11	64.9 (38.9, NA)	3/11
Other mutations	33.2 (9.9, NA)	5/8	NA	1/8

BRCA: Breast cancer gene; DBD: DNA binding domain; RAD51-BD: RAD51 binding domain; NA: not available.

and *BRCA1* (13.3%). Other rare HRR mutations were found in 12 patients (26.7%). The median age was 70 years (range=64-74 years). HRR mutations were associated with poorly differentiated prostate cancer, with 32 patients (71.1%) having a Gleason score  $\geq 8$ , including 10 (22.2%) with a Gleason score of 10. At diagnosis, 26 patients (57.8%) had metastatic disease, and 18 (40%) had high-volume disease. The most common metastasis sites were the bones and lymph nodes, with only six patients (13.3%) having visceral metastasis (Table I). As shown in Figure 1, of the 42 patients who received treatment, 30 (71.4%) experienced

progression or death, resulting in a median PFS of 16.8 months (95%CI=13.7-22.7 months). Descriptive analyses suggested that mutations in functional domains of *BRCA2*, including the DNA-binding domain (DBD), exon 11, and RAD51-BD, were associated with worse PFS and OS outcomes, compared to patients with mutations in non-functional regions of *BRCA2* (Table II). Figure 2A and B depict the distribution of mutations in *BRCA1* and *BRCA2* genes, respectively. Seven mutations were found in known *BRCA1* domains, while 27 mutations were identified in *BRCA2*. Of these, 16 samples carried 17 distinct mutations



Figure 2. Distribution of mutations in BRCA1 (A) and BRCA2 (B) genes.

in BRCA2, while 6 samples carried 7 different mutations in BRCA1. **Conclusion:** Despite the study's small sample size and monocentric design, the findings suggest that HRR mutations are associated with a more aggressive prostate cancer phenotype and may be associated with a poorer prognosis compared to epidemiologic data. Mutations in the functional domains of BRCA2 appear to correlate with unfavourable clinical outcomes. However, further research with larger cohorts and prospective studies is needed to confirm these findings and establish predictive biomarkers for treatment decisions in HRR-mutated mHSPC patients.

1 Kyriakopoulos CE, Chen YH, Carducci MA, Liu G, Jarrard DF, Hahn NM, Shevrin DH, Dreicer R, Hussain M, Eisenberger

M, Kohli M, Plimack ER, Vogelzang NJ, Picus J, Cooney MM, Garcia JA, DiPaola RS, Sweeney CJ: Chemohormonal therapy in metastatic hormone-sensitive prostate cancer: long-term survival analysis of the randomized phase III E3805 CHARTED Trial. J Clin Oncol 36(11): 1080-1087, 2018. DOI: 10.1200/JCO.2017.75.3657

## 2 RETROSPECTIVE OBSERVATIONAL REAL-LIFE STUDY ON METASTATIC RENAL CELL CARCINOMA TREATED IN FIRST LINE WITH PEMBROLIZUMAB PLUS AXITINIB: A PROJECT OF THE CAMPANIA ONCOLOGY NETWORK

Marilena Di Napoli<sup>1</sup>, Elisabetta Coppola<sup>1</sup>, Carmine D’Aniello<sup>2</sup>, Sarah Scagliarini<sup>3</sup>, Carlo Buonerba<sup>4</sup>, Andrea Muto<sup>5</sup>, Luigi Formisano<sup>6</sup>, Francesco Sabbatino<sup>7</sup>, Davide Bosso<sup>8</sup>, Lorenzo Lobianco<sup>1</sup>, Sabrina Rossetti<sup>1</sup>, Carmela Pisano<sup>1</sup>, Sabrina Chiara Cecere<sup>1</sup>, Rosa Tambaro<sup>1</sup>, Anna Passarelli<sup>1</sup>, Jole Ventriglia<sup>1</sup>, Gabriele Calvanese<sup>9</sup>, Giuseppina Canciello<sup>1</sup>, Roberto Contieri<sup>10</sup>, Giuseppe Quarto<sup>10</sup>, Francesco Fiore<sup>11</sup>, Florinda Feroce<sup>12</sup> and Sandro Pignata<sup>1</sup>

<sup>1</sup>Experimental Clinical Uro-Gynecological Oncology Unit, National Cancer Institute IRCCS “Fondazione G. Pascale”, Naples, Italy;

<sup>2</sup>Medical Oncology, AORN dei Colli-Monaldi, Naples, Italy;

<sup>3</sup>Medical Oncology, AORN “A. Cardarelli”, Naples, Italy;

<sup>4</sup>Medical Oncology, “Andrea Tortora” Hospital, Pagani, Italy;

<sup>5</sup>Medical Oncology, “San Giuseppe Moscati” Hospital, Avellino, Italy;

<sup>6</sup>Department of Medicine and Surgery, Federico II University Hospital, Naples, Italy;

<sup>7</sup>Department of Oncology, “San Giovanni di Dio and Ruggi d’Aragona” University Hospital, Salerno, Italy;

<sup>8</sup>Medical Oncology, Ospedale del Mare, Naples, Italy;

<sup>9</sup>Department of Oncology and Onco-Hematology, University of Milan, Milan, Italy;

<sup>10</sup>Urology Unit, National Cancer Institute IRCCS “Fondazione G. Pascale”, Naples, Italy;

<sup>11</sup>Interventional Radiology Unit, National Cancer Institute IRCCS “Fondazione G. Pascale”, Naples, Italy;

<sup>12</sup>Pathological and Cytopathological Anatomy Unit, National Cancer Institute IRCCS “Fondazione G. Pascale”, Naples, Italy

**Background/Aim:** Several combination therapies are used as first-line treatments for metastatic renal cell carcinoma (mRCC). However, outcomes and toxicity profiles observed in clinical trials may differ from those in routine practice due to differences between trial populations and the broader patient population. Oncology Networks are key in

Table I. *Baseline cohort demographics and disease characteristics.*

	Overall (N=117)
Median age (range), years	59 [34.0, 88.0]
Male, n (%)	84 (71.8%)
Female, n (%)	33 (28.2%)
IMDC risk group, n (%)	
Favorable	23 (19.6%)
Intermediate	55 (47.0%)
Poor	21 (18.0%)
Unknown	18 (15.4%)
Comorbidities	
Hypertension	50 (42.7%)
Cardiovascular disease	22 (18.8%)
Metabolic disease	17 (14.5%)
Diabetes	16 (13.7%)
Lung disease	4 (3.4%)
Hepatitis	3 (2.5%)
Autoimmune disease	3 (2.5%)
CKD	2 (1.7%)
Previous nephrectomy, n (%)	53 (45.3%)
Histology	
Clear cell	102 (87.2%)
Papillary	6 (5.1%)
Sarcomatoid features	4 (3.4%)
Chromophobe	1 (0.8%)
Mixed	1 (0.8%)
Unknown	3 (2.5%)
Metastatic disease, n (%)	
Recurrence	38 (32.5%)
<i>De novo</i>	79 (67.5%)
Site of metastasis in <i>de novo</i> patients, n (%)	
Brain	43 (36.8%)
Lung	41 (35.0%)
Bones	36 (30.8%)
Lymph nodes	34 (29.1%)
Adrenals	8 (6.8%)
Liver	7 (6.0%)
Pancreas	4 (3.4%)
Peritoneal carcinosis	3 (2.6%)
Spleen	2 (1.9%)
Rectum	2 (1.7%)
Time from diagnosis to treatment <1 year n (%)	77 (65.8%)
BMI, median (range), kg/m <sup>2</sup>	25.25 [18.75, 38.74]
ECOG performance status	
0	36 (30.8%)
1	56 (47.9%)
2	6 (5.1%)
3	1 (0.8%)
Unknown	18 (15.4%)

IMDC: International mRCC Database Consortium. Favorable risk corresponds to an International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) score of 0, intermediate risk to a score of 1 or 2, and poor risk to a score of 3 to 6. IMDC risk score is determined by the total number of the following six risk factors: Karnofsky performance-status score of less than 80 (on a scale from 0 to 100, with lower scores indicating greater disability), a time from initial diagnosis to randomization of less than 1 year, a hemoglobin level below the lower limit of the normal range, a corrected serum calcium level above the upper limit of the normal range, an absolute neutrophil count above the upper limit of the normal range, and platelet count above the upper limit of the normal range); CKD: chronic kidney disease; BMI: Body Mass Index; ECOG: Eastern Cooperative Oncology Group.

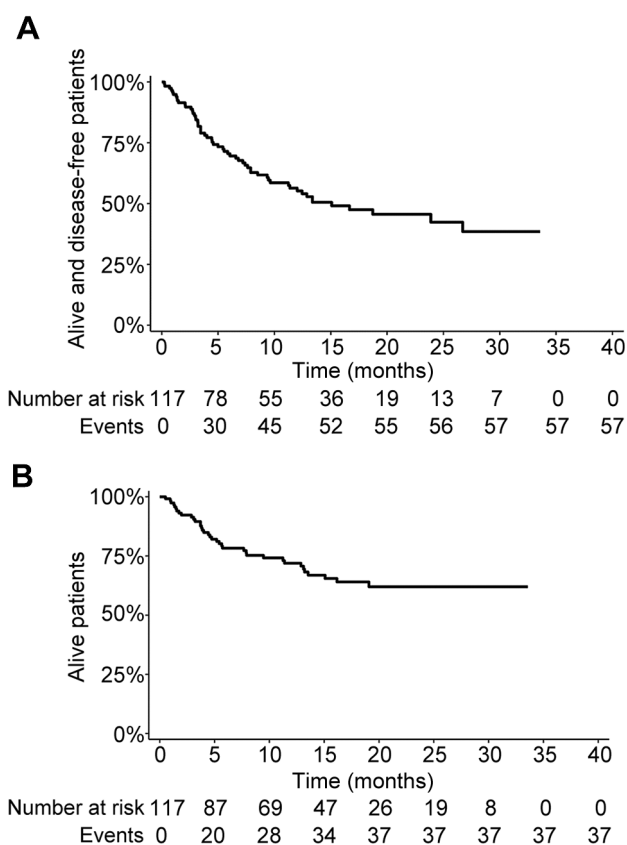


Figure 1. Progression-free survival (A) and overall survival (B) in the overall population.

generating real-world data (RWD) and supporting clinical decision-making through real-world evidence (RWE). We retrospectively analyzed mRCC patients treated with first-line Pembrolizumab plus Axitinib within the Campania Oncology Network (ROC). *Patients and Methods:* This

multicentre retrospective study included untreated mRCC patients receiving Pembrolizumab plus Axitinib at eight ROC centers. Primary endpoints were progression-free survival (PFS) and overall survival (OS), while secondary endpoints were objective response rate (ORR) and safety. *Results:* From January 2021 to November 2023, 117 mRCC patients were treated with Pembrolizumab plus Axitinib at eight ROC centers. International Metastatic RCC Database Consortium (IMDC) risk was favorable in 19.6%, intermediate/poor in 65%, and unknown in 15.4%. Median age at diagnosis was 59 years, and 53.8% had ECOG Performance Status (PS-ECOG)  $\geq 1$ . Clear cell histology was the most common (87.2%), and main metastatic sites included the brain (36%), lungs (35%), bones (30%), and lymph nodes (29%) (Table I). After a median follow-up of 12.8 months, median PFS was 15.1 months, ORR was 27.3%, and median OS was not reached (Figure 1A and B). Subgroup analysis showed relevant response benefits in non-clear cell RCC, with an ORR of 41.7% (Table II). In the overall population, PD and adverse events (AEs) were responsible for 49% and 6% of treatment discontinuations, respectively. Most adverse events (AEs) were G1-2, including diarrhea (23.9%), asthenia (18%), hypothyroidism (12.8%), and hypertension (9.4%). In our study, G1-2 toxicity was significantly more frequent in females (57.6%) than males (35.7%) ( $p=0.05$ ). *Conclusion:* Our study supports the applicability of Pembrolizumab plus Axitinib in a real-world setting. As no frontline regimen has proven superior, RWD comparisons may help personalize treatment strategies in clinical practice.

Table II. Best tumor responses in overall and histology-based subgroups.

	Overall (n=117)	Clear cell histology (n=102)	Non-clear cell histology (n=12)
ORR, % (95%CI)	27.3% (19.3-35.4%)	26.5% (17.9-35.0%)	41.7% (13.8-69.5%)
DCR, % (95%CI)	79.5% (72.2-86.8%)	78.4% (70.4-86.4%)	83.3% (62.1-100%)
CR, n (%)	2 (1.8%)	2 (1.9%)	
PR, n (%)	30 (25.6%)	25 (24.5%)	5 (41.7%)
SD, n (%)	61 (52.1%)	53 (52.0%)	5 (41.7%)
PD, n (%)	24 (20.5%)	22 (21.6%)	2 (16.7%)

ORR: Overall response rate; DCR: disease control rate; CR: complete response; PR: partial response; SD: stable disease; PD: progressive disease. Three patients had unclassifiable histological subtype.

### 3 **STEREOTACTIC BODY RADIATION THERAPY (SBRT) AS A METASTASIS DIRECTED THERAPY (MDT) IN OLIGOMETASTATIC PROSTATE CANCER**

Enrico Raggi<sup>1</sup>, Carlo Furlan<sup>1</sup>, Anna Chiara Camilletti<sup>1</sup>,  
Filippo De Renzi<sup>1</sup>, Margherita Crespi<sup>2</sup>,  
Giovanni Liguori<sup>3</sup> and Alessandro Magli<sup>4</sup>

<sup>1</sup>UOC Radiation Oncology, AULSS1 Dolomiti  
Belluno, Belluno, Italy;

<sup>2</sup>UOC Medical Physics, AULSS1 Dolomiti, Belluno, Italy;

<sup>3</sup>Urology Clinic, Cattinara Hospital, Trieste, Italy;

<sup>4</sup>Radiation Oncology Unit, Trieste Hospital, Trieste, Italy

*Background/Aim:* Stereotactic body radiation therapy (SBRT) is an emerging metastasis directed therapy (MDT) in oligometastatic prostate cancer. *Patients and Methods:* This retrospective analysis is focused on a patient population consisting of 14 patients: eight patients had metachronous oligometastatic prostate cancer, whilst six patients had synchronous oligometastatic prostate cancer. Median age of the whole population was 72 years (range=58-87 years). Among the metachronous group, six patients had previously undergone prostatectomy and two patients had received radiotherapy to the prostate gland. In the synchronous group all six patients received SBRT to the prostate [42 Gray (Gy) in 7 fractions, 6 Gy/fraction] as treatment for the primary tumor. For the metachronous group, SBRT was delivered without concurrent androgen deprivation therapy (ADT) to postpone its initiation upon future relapse. In contrast, all synchronous patients received ADT together with SBRT. SBRT to the metastatic sites was administered with volumetric modulated arc radiotherapy (VMAT) and image-guided radiotherapy (IGRT), including daily cone-beam computed tomography (CBCT). *Results:* Eight patients had lymph node metastases only, while six patients had bone metastases only. Median prostate specific antigen (PSA) levels before SBRT were 0.38 ng/ml (range=0.25-1.05

ng/ml) in the metachronous group and 37 ng/ml (range=11-150 ng/ml) in the synchronous group. Median radiation dose to the metastatic sites was 30 Gy (range=25-35 Gy); median radiation dose/fraction was 10 Gy (range=5-10 Gy); and median number of fractions was 3 (3-5). Six patients out of 14 recurred after MDT with SBRT with a median time to progression of 12 months (range=6-31 months). Median follow up was 12 months (range=6-31 months). SBRT had a favorable toxicity profile with no grade 3-5 toxicity according to Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. *Conclusion:* SBRT to the metastatic sites in oligometastatic prostate cancer patients is well tolerated and effective in prolonging disease control. In metachronous cases, it may delay the initiation of ADT, while in synchronous cases already receiving ADT, it may postpone the need for second-line therapies.

### 4 **STEREOTACTIC BODY RADIATION THERAPY (SBRT) AS A LOCAL RESCUE THERAPY IN AN ELDERLY PATIENT POPULATION WITH LOCALLY RECURRENT PROSTATE CANCER AFTER RADIOTHERAPY: FEASIBILITY AND TOXICITY**

Enrico Raggi<sup>1</sup>, Carlo Furlan<sup>1</sup>,  
Margherita Crespi<sup>2</sup> and Alessandro Magli<sup>3</sup>

<sup>1</sup>AULSS 1 Dolomiti, UOC Radiation Oncology,  
San Martino Hospital, Belluno, Italy;

<sup>2</sup>AULSS 1 Dolomiti, Health Physics Unit,  
San Martino Hospital, Belluno, Italy;

<sup>3</sup>ASUGI, Radiation Oncology Unit,  
Maggiore Hospital, Trieste, Italy

*Background/Aim:* A subgroup of patients previously treated with radiotherapy will relapse only locally with no evidence of extraprostatic disease. In these patients, local therapies may be an alternative to androgen deprivation therapy. We report the outcomes of a small cohort of

patients who underwent stereotactic body radiation therapy (SBRT) as reirradiation for local intraprostatic recurrence following previous radiotherapy. *Patients and Methods:* We analyzed retrospectively a cohort of six patients with isolated prostatic relapse after previous radiotherapy to the prostate gland. Median age was 78 years (range=74-85 years). median Karnofsky Performance Status was 90 (range=80-100). The median total radiation dose for the first course of radiotherapy was 76 Gray (Gy) (range=70-76 Gy) with a median dose/fraction of 1.8 Gy (range=1.8-2.5 Gy). For reirradiation, all patients received SBRT to a total dose of 30 Gy in 5 fractions every other day (6 Gy/fraction). Four patients underwent whole prostate SBRT, while two patients were treated with focal SBRT. The median time between the first course of radiotherapy and reirradiation was 124 months (range=42-171 months). The median follow-up from reirradiation was 10 months (range=7-31 months). Acute and late genito-urinary (GU) and gastrointestinal (GI) toxicities were evaluated using Common Terminology Criteria for Adverse Events (CTCAE) Version 5. Reirradiation with SBRT was performed by volumetric-modulated arc therapy (VMAT), with daily image guidance *via* cone beam computed tomography. *Results:* The median GU and GI toxicities before reirradiation were 0 (range=0-2) and 0 (range=0-1), respectively. The median acute GU and GI toxicities after reirradiation were 0 (range=0-2) and 0 (range=0-1), respectively. Similarly, median late GU and GI toxicities after reirradiation were 0 (range=0-1) for both. The use of VMAT and daily set-up verification by cone beam computed tomography ensured adherence to organ-at-risk dose constraints in all cases. *Conclusion:* In this small cohort of patients, reirradiation with SBRT was feasible and well tolerated, with no significant toxicities. High-technology irradiation techniques and the emerging use of tissue spacers that increase the distance between the prostate and rectal wall can pave the way to dose escalation. Larger prospective clinical trials are strongly warranted to validate these findings and support the development of standardized treatment guidelines for prostate reirradiation.

7

**THE EXOGENOUS EXPRESSION OF P53 SUPPRESSES HIF1 ALPHA AND DEACTIVATES VEGF RECEPTOR IN A MECHANISM INVOLVING MDM2 IN KIDNEY CANCER CELLS**

Lucio Dell'Atti<sup>1</sup>, Maria Elena Meo<sup>2</sup>, Carmelo Ippolito<sup>3</sup> and Gianluca Aguiari<sup>4</sup>

<sup>1</sup>Urology Clinic, Azienda Ospedaliero-Universitaria delle Marche, Ancona, Italy;

<sup>2</sup>Department of Neuroscience and Rehabilitation, University of Ferrara, Ferrara, Italy;

<sup>3</sup>Urology Division, Arcispedale S. Anna, Ferrara, Italy;

<sup>4</sup>Department of Neuroscience and Rehabilitation, University of Ferrara, Ferrara, Italy

*Background/Aim:* Multidrug therapy has been approved for the treatment of metastatic renal carcinoma (mRCC), including inhibitors of mTOR (mammalian target of rapamycin) and different tyrosine kinase inhibitors (TKIs). Recently, the treatment of metastatic clear cell renal cell carcinoma (ccRCC) has been changed with the introduction of immune checkpoint inhibitors (ICIs) targeting PD-1, PD-L1, and CTLA-4, which are either used alone or in combination with TKIs. Here, we report that exogenous expression of p53 dramatically reduces hypoxia-inducible factor 1 $\alpha$  (HIF1 $\alpha$ ) protein levels as well as the activation of the vascular endothelial growth factor receptor (VEGFR) leading to the inhibition of the angiogenic pathway. Moreover, treatment with the compound RG7112, an inhibitor of the murine double minute 2 (MDM2) protein, reverses this effect by restoring HIF1 $\alpha$  expression and VEGFR activation. *Materials and Methods:* 4/5 and HEK293 control kidney cells as well as Caki-1, Caki-2, and KJ29 ccRCC cells were cultured in DMEM/F12 supplemented with 10% fetal bovine serum. As a control, cells were transfected with an irrelevant plasmid encoding the jellyfish protein Aequorin (Aeq). After transfection, cells were treated for 24 h with the MDM2 inhibitor RG7112 (5  $\mu$ M) or in presence of the

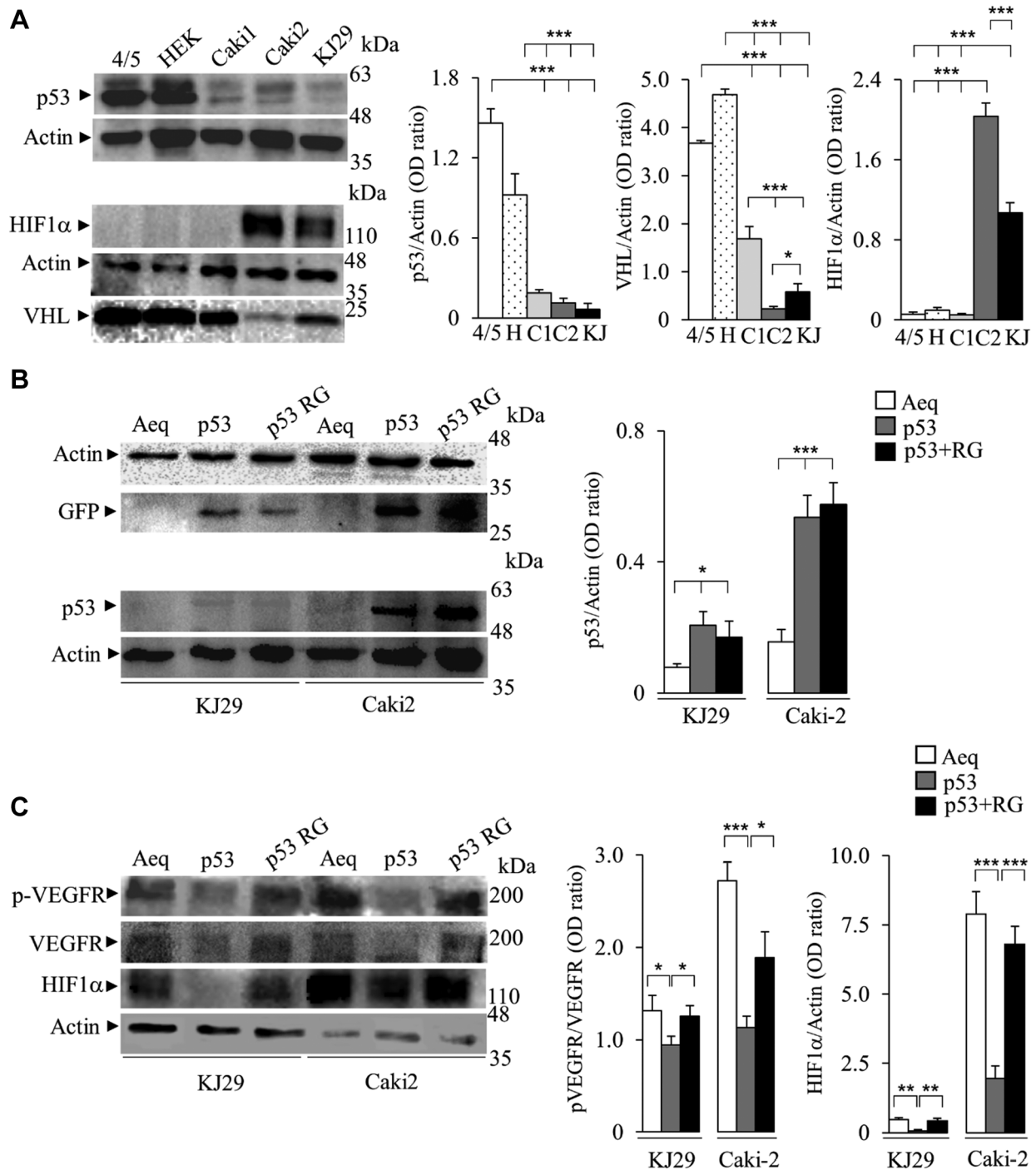


Figure 1. Analysis of p53 and angiogenesis-related protein expression in normal kidney and in clear cell renal cell carcinoma cells. (A) The presence of p53, VHL and HIF1α was evaluated in 4/5 and HEK293 (H) control cells as well as in Caki-1 (C1), Caki-2 (C2) and KJ29 (KJ) ccRCC cells in basal conditions of culture. The levels of GFP and p53 (B) as well as pVEGFR, VEGFR and HIF1α (C) were analyzed in KJ29 and Caki-2 cells transfected with a plasmid expressing wild type p53 fused with GFP (p53-GFP) and with an irrelevant plasmid (Aeq). After transfection, cells were cultured for 24h in presence/absence of 5 μM RG7112 (RG). Values are expressed as mean±standard deviation calculated from three independent experiments; \*p<0.05, \*\*p<0.01 and \*\*\*p<0.001.

vehicle (DMSO). Cell lysates were obtained using a buffer solution containing 1% triton-X 100 and a cocktail of protease and phosphatase inhibitors. Western blotting was used to analyze the expression and activation levels of p53, HIF1 $\alpha$ , and VEGFR using specific antibodies. *Results:* Western blot analysis under basal conditions showed that the expression of p53 was lower in Caki-1, Caki-2, and KJ29 ccRCC cells than in 4/5 and HEK293 control cells (Figure 1A). In particular, the expression of p53 in KJ29 tumor cells was markedly lower compared to the other ccRCC cells. Moreover, the von Hippel Lindau (VHL) protein, an inhibitor of HIF transcription factors, was strongly expressed in control and Caki-1 cells but was decreased or absent in KJ29 and Caki-2, respectively (Figure 1A). Accordingly, Caki-2 and KJ29 VHL-down-regulated cells expressed high levels of HIF1 $\alpha$ , whereas this protein in control and Caki-1 cells was not detected. Based on this, Caki-2 and KJ29 cells were selected to investigate the impact of exogenous p53 expression on the angiogenic pathway. Transfection with the p53-GFP construct led to visible GFP expression in Caki-2 and KJ29 cells, confirming successful transfection (Figure 1B). Interestingly, the transfection of ccRCC cells with the p53-GFP vector significantly increased the levels of wild type p53, especially in Caki-2 cells. Moreover, treatment with the MDM2 inhibitor RG7112 did not affect the expression of p53 in both ccRCC cell lines (Figure 1B). Notably, the increased levels of p53 in ccRCC transfected cells caused a dramatic reduction in HIF1 $\alpha$  expression and inhibited VEGFR activation. However, co-treatment with RG7112 in p53-GFP transfected ccRCC cells reversed this effect, restoring HIF1 $\alpha$  expression and VEGFR activity (Figure 1C). *Conclusion:* Although p53 mutations are rarely found in ccRCC, p53 could have an important anticancer role in kidney carcinoma. In fact, we have previously demonstrated that p53 is subject to autophagic degradation in ccRCC cells. Moreover, the inhibition of autophagy by silencing the ATG7 gene increases the levels of p53, inhibits cell growth, and induces apoptosis. We have observed that kidney cancer cells express reduced levels of p53 compared with control kidney cell lines,

suggesting that ccRCC cells down-regulate this tumor suppressor protein likely through the activation of autophagy. The increased expression of p53 suppresses HIF1 $\alpha$  expression and consequently the activation of VEGFR, indicating that p53 inhibits the angiogenic pathway in ccRCC cells. Some studies have suggested that MDM2 might lead to HIF1 $\alpha$  degradation *via* the proteasome pathway involving p53. In our study, MDM2 inhibition by RG7112 reversed the anti-angiogenic effects of p53, restoring HIF1 $\alpha$  and VEGFR activity. These findings support a model in which p53 and MDM2 collaborate to regulate HIF1 $\alpha$  stability and VEGFR activity in ccRCC. In conclusion, the expression of wild type p53 suppresses angiogenesis leading to HIF1 $\alpha$  down-regulation and VEGFR deactivation through a mechanism involving the MDM2-proteasome system. Therapeutic strategies that enhance wild-type p53 expression or function may offer a promising approach to inhibit tumor progression and improve treatment outcomes in mRCC patients.

## 8 MACHINE LEARNING FOR RECURRENCE STRATIFICATION IN NMIBC: A CLINICAL OVERVIEW

Dalila Incognito<sup>1</sup>, Vincenzo Ficarra<sup>2</sup>,  
Giuliana Ciappina<sup>3</sup>, Leonardo Tonelli<sup>4</sup>,  
Claudia Gelsomino<sup>1</sup>, Mariacarmela Cavaleri<sup>1</sup>,  
Antonio Picone<sup>5</sup> and Massimiliano Berretta<sup>5,6</sup>

<sup>1</sup>Medical Oncology Unit, Department of Human Pathology "G. Barresi", School of Specialization In Medical Oncology, University of Messina, Messina, Italy;

<sup>2</sup>Section of Urology, Department of Human and Pediatric Pathology Gaetano Barresi, University of Messina, Messina, Italy;

<sup>3</sup>Department of Medical Sciences of Experimental Medicina, University of Ferrara, Ferrara, Italy;

<sup>4</sup>Candiolo Cancer Institute, FPO – IRCCS, Turin, Italy;

<sup>5</sup>Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy;

<sup>6</sup>Division of Medical Oncology, AOU “G. Martino” Hospital, University of Messina, Messina, Italy

**Background/Aim:** Non-muscle-invasive bladder cancer (NMIBC), which accounts for ~75% of urothelial carcinomas, has high recurrence and progression risk. Its management often involves invasive surveillance, affecting patients’ quality of life and healthcare resources (1). Conventional tools such as EORTC and CUETO scores show limited accuracy, underestimating recurrence in low-grade and overestimating it in high-risk cases, leading to suboptimal decisions (2). Machine learning (ML) approaches that integrate clinical, imaging, pathological, and genomic data may improve recurrence prediction and patient stratification (3). This review evaluates ML-based models for recurrence risk assessment in NMIBC and their role in guiding individualized clinical decisions (1). **Materials and Methods:** A narrative review was conducted (Jan 2022-Mar 2024) using PubMed to identify studies on ML applications in NMIBC. Search terms included “artificial intelligence”, “bladder cancer”, “NMIBC”, and “recurrence

prediction”. Eligible publications included original articles, reviews, and retrospective/prospective clinical studies on ML for diagnosis, stratification, recurrence prediction, or treatment planning. Editorials, case reports, abstracts, and non-urological papers were excluded. ML methods, input types, and clinical endpoints were extracted. **Results:** Convolutional neural network (CNNs) applied to cystoscopy achieved high diagnostic accuracy (>90% sensitivity/specificity) for flat lesions and high-grade tumors. Blue-light cystoscopy further improved detection. Retrospective studies reported CNNs outperforming expert evaluation in selected cases (1). Supervised ML models (*e.g.*, logistic regression, support vector machines (SVMs), random forests) trained on multimodal data (clinical, imaging, pathological, genomic) outperformed traditional scores, with area under the receiver operating characteristic curve (AUCs) from 0.80 to 0.90 (2). Combining radiomics from magnetic resonance imaging (MRI) and positron emission tomography-computed tomography (PET-CT) with genomics improved risk stratification and identification of high-risk patients (2). However, most models remain

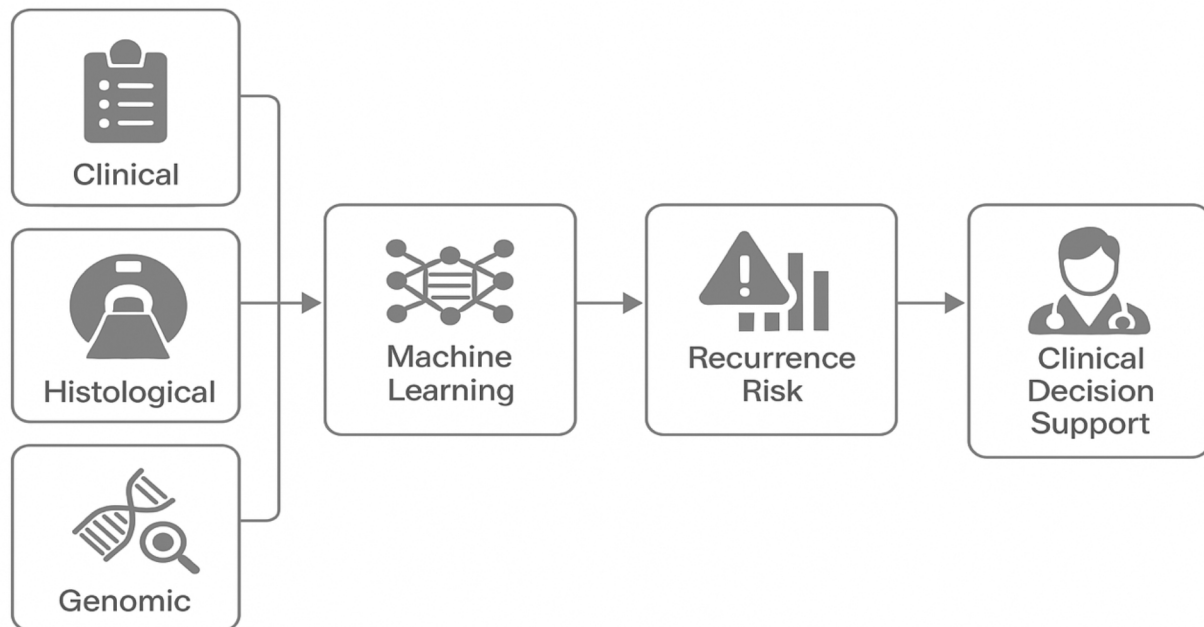


Figure 1. Machine learning-based workflow for recurrence risk in non-muscle-invasive bladder cancer.

retrospective and lack prospective validation (3). *Conclusion:* NMIBC management is challenging due to biological heterogeneity. Conventional tools often exclude key biomarkers and imaging data (2). ML integrates multimodal inputs, offering better stratification than traditional scores (2, 3). CNNs on cystoscopy and MRI showed high accuracy, occasionally exceeding human assessment (1). ML combined with urinary biomarkers and digital pathology may identify high-risk patients and reduce overtreatment in low-risk cases (2, 3). However, clinical application is limited by data heterogeneity, model interpretability, and lack of prospective validation (3). A conceptual overview of the clinical workflow supported by ML-based predictive models is presented in Figure 1. In conclusion, ML models represent a promising tool to improve recurrence risk assessment in NMIBC. By integrating clinical, imaging, pathological, and genomic data, these approaches support tailored decisions. However, prospective validation, methodological harmonization, and integration into clinical workflows are needed.

1 Laurie MA, Zhou SR, Islam MT, Shkolyar E, Xing L, Liao JC: Bladder cancer and artificial intelligence: emerging applications. *Urol Clin North Am* 51(1): 63-75, 2024. DOI: 10.1016/j.ucl.2023.07.002

2 Shalata AT, Shehata M, Van Bogaert E, Ali KM, Alksas A, Mahmoud A, El-Gendy EM, Mohamed MA, Giridharan GA, Contractor S, El-Baz A: Predicting recurrence of non-muscle-invasive bladder cancer: current techniques and future trends. *Cancers (Basel)* 14(20): 5019, 2022. DOI: 10.3390/cancers14205019

3 Ma J, Vaishnani DK, Lin R, Lyu J, Ni B, Zhang Y, Hu M, Chen G: Artificial intelligence in bladder cancer: current trends and future possibilities. *Chin Med J (Engl)* 135(7): 881-882, 2022. DOI:10.1097/CM9.0000000000001830

Dalila Incognito<sup>1</sup>, Vincenzo Ficarra<sup>2</sup>, Giuliana Ciappina<sup>3</sup>, Roberta Foti<sup>4</sup>, Antonio Bottari<sup>5</sup> Antonio Picone<sup>6</sup> and Massimiliano Berretta<sup>6</sup>

<sup>1</sup>Medical Oncology Unit, Department of Human Pathology “G. Barresi”, School of Specialization in Medical Oncology, University of Messina, Messina, Italy;

<sup>2</sup>Section of Urology, Department of Human and Pediatric Pathology Gaetano Barresi, University of Messina, Messina, Italy;

<sup>3</sup>Department of Medical Sciences, Selection of Experimental Medicine, University of Ferrara, Ferrara, Italy;

<sup>4</sup>Division of Rheumatology, A.O.U. “Policlinico-San Marco”, Catania, Italy;

<sup>5</sup>Section of Radiological Sciences, Department of Biomedical Sciences and Morphological and Functional Imaging, University of Messina, Policlinico “G. Martino”, Messina, Italy;

<sup>6</sup>Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

*Background/Aim:* The treatment landscape of advanced renal cell carcinoma (aRCC) has markedly evolved through the integration of immune checkpoint inhibitors (ICIs) and tyrosine kinase inhibitors (TKIs). These agents, used either sequentially or in combination, have improved outcomes. However, their use in patients with pre-existing autoimmune diseases (AIDs) remains challenging due to the risk of immune-related adverse events (irAEs), often leading to exclusion from pivotal trials (1). The combination of ICIs and TKIs may amplify both therapeutic effects and toxicity, requiring refined management strategies (2, 3). This work aimed to critically review recent evidence on toxicity profiles and clinical management of ICI-TKI regimens in aRCC with AIDs. *Materials and Methods:* A focused review of the literature was performed using PubMed to identify studies on ICI-TKI combinations in renal cell carcinoma. Three peer-reviewed articles were selected based on relevance, including a narrative review (1), a clinical review on irAE management (2), and a systematic review and meta-analysis

## 9

### MANAGING TOXICITY OF ICI-TKI THERAPY IN RENAL CELL CARCINOMA WITH AUTOIMMUNE CONDITIONS

on treatment toxicity (3). Data on toxicity incidence, immune-related events, and management strategies were extracted. *Results:* Combinations such as pembrolizumab–lenvatinib and nivolumab–cabozantinib are approved first-line therapies for aRCC (2). Grade  $\geq 3$  treatment-related toxicities are observed in over 50% of patients receiving ICI-TKI regimens, with discontinuation rates approaching 16% (3). VEGFR-TKI-related toxicities (*e.g.*, hypertension, hypothyroidism) frequently overlap with ICI-induced irAEs (*e.g.*, colitis, pneumonitis), complicating attribution and management (2). Despite this, current data suggest that toxicities do not exhibit synergistic escalation but require structured, multidisciplinary interventions (2, 3). High-dose corticosteroids are employed in up to 29% of patients (2). *Conclusion:* The administration of ICI-TKI combinations in patients with autoimmune comorbidities remains a debated area, balancing oncologic benefit against immune-mediated risk. Current evidence, albeit derived primarily from retrospective analyses and heterogeneous cohorts, supports cautious implementation of these regimens with rigorous toxicity monitoring (2, 3). Coordination with rheumatologists and pre-therapy risk stratification may enhance safety. However, the lack of standardized guidelines and underrepresentation of AID patients in clinical trials limit definitive conclusions (1, 2). In conclusion, targeted therapy combinations incorporating ICIs and TKIs are potentially viable in aRCC patients with autoimmune conditions, provided that risk is carefully assessed and managed. While emerging data highlight the feasibility of treatment under close surveillance, the absence of prospective, controlled studies weakens the strength of current recommendations. Future efforts must prioritize the inclusion of AID populations in clinical trials and the development of validated algorithms for immune toxicity prediction and mitigation.

1 Atkins MB, Clark JI, Quinn DI: Immune checkpoint inhibitors in advanced renal cell carcinoma: experience to date and future directions. *Ann Oncol* 28(7): 1484-1494, 2017. DOI: 10.1093/annonc/mdx151

2 Leucht K, Ali N, Foller S, Grimm MO: Management of

immune-related adverse events from immune-checkpoint inhibitors in advanced or metastatic renal cell carcinoma. *Cancers (Basel)* 14(18): 4369, 2022. DOI: 10.3390/cancers14184369

3 O'Reilly D, O'Leary CL, Reilly A, Teo MY, O'Kane G, Hendriks L, Bennett K, Naidoo J: Toxicity of immune checkpoint inhibitors and tyrosine kinase inhibitor combinations in solid tumours: a systematic review and meta-analysis. *Front Oncol* 14: 1380453, 2024. DOI: 10.3389/fonc.2024.1380453

## 12

### **PRE-TREATMENT BLADDER ULTRASOUND SCANNING IN PROSTATE CANCER PATIENTS UNDERGOING PELVIC RADIOTHERAPY: A SIMPLE AND EFFECTIVE PROCEDURE IN REDUCING THE NUMBER OF DAILY CBCT SCANS**

Luigi De Cicco<sup>1</sup>, Francesco Moretti<sup>2</sup>, Linda Torresan<sup>1</sup>, Elena Petazzi<sup>1</sup>, Rossella Margherita Mancuso<sup>1</sup>, Andrea Maucieri<sup>1</sup>, Alessandra Cocchi<sup>1</sup>, Angelo Giovanni Lanceni<sup>1</sup>, Sandra Buttignol<sup>1</sup>, Antonio Starace<sup>1</sup>, Elisa Della Bosca<sup>1</sup>, Luca Marzoli<sup>2</sup>, Rita Lorusso<sup>2</sup>, Annalisa Pepe<sup>2</sup>, Paolo Imperiale<sup>2</sup>, Lorenzo Bianchi<sup>2</sup> and Barbara Bortolato<sup>1</sup>

<sup>1</sup>Asst Valle Olona, Division of Radiotherapy, Busto Arsizio (VA), Italy;

<sup>2</sup>Asst Valle Olona, Division of Medical Physics, Busto Arsizio (VA), Italy

*Background/Aim:* In the radiation treatment of patients with localized prostate cancer, daily pre-treatment cone-beam CT (CBCT) is a commonly used method to verify the correct positioning of the target and the condition of the pelvic organs at risk. The position of the prostate gland or prostatic lodge, in the case of operated patients, is conditioned by the variations in volume of the bladder and rectum. Furthermore, the increased bladder volume allows for a reduction in the dose to the bladder and the likelihood of

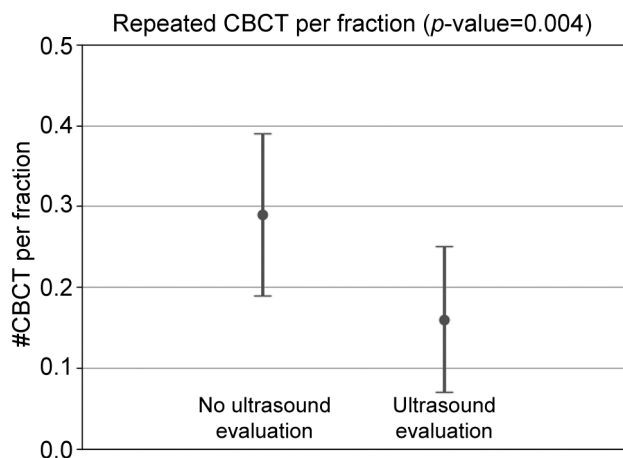


Figure 1. Means of exceeding cone-beam-CT (CBCT) per treatment fraction with their standard deviations in the two groups: without or with preliminary ultrasound evaluation ( $p=0.004$ ).

consequent bladder toxicity (1). Many patients have difficulty understanding their bladder filling status, which often leads to inadequate bladder filling observed during daily CBCT. As a result, treatment may be delayed, the procedure interrupted, and the patient asked to drink more fluids before a subsequent attempt. Since October 2024, at our center, we have introduced a pre-treatment bladder ultrasound assessment for prostate cancer patients undergoing pelvic radiotherapy, specifically for treatments delivered on one of our three linear accelerators. Using a hand-held ultrasound scanner (Cerbero 4,0 – ATL s.r.l., Milan, Italy) bladder volume was evaluated prior to each treatment session and compared to the planned volume from the simulation CT. This check was performed daily outside the treatment room, before starting the treatment with CBCT. We investigated whether the new method reduced the number of daily CBCTs required, by pre-screening bladder volume with ultrasound before proceeding to treatment. *Patients and Methods:* Data from 96 non-metastatic prostate cancer patients treated from October 2024 to March 2025 with adjuvant or radical pelvic radiotherapy were analyzed. We calculated the number of CBCTs daily repeated for any reason (*e.g.*, inadequate bladder or rectum preparation, target missing or other) for the two groups of patients, with

or without a preliminary bladder ultrasound scan. *Results:* Figure 1 shows the mean number of additional CBCTs per treatment fraction with its standard deviation, in the two groups. We recorded a significant decrease ( $p=0.004$ ) in the number of CBCTs in the ultrasound-guided group. The mean number of repeated CBCTs per fraction decreased from 0.29 in the control group to 0.16 in the ultrasound group. *Conclusion:* In our retrospective series, the use of a low-cost, ultrasound-based bladder scanner for preliminary assessment prior to daily pelvic radiotherapy improved the concordance between bladder filling on treatment-day CBCT and the planned volume on simulation CT, in line with findings reported in the literature (2). This has allowed to reduce the number of CBCTs per patient, with possible clinical, organizational and cost effects.

- 1 Grün A, Kawgan-Kagan M, Kaul D, Badakhshi H, Stromberger C, Budach V, Böhmer D: Impact of bladder volume on acute genitourinary toxicity in intensity modulated radiotherapy for localized and locally advanced prostate cancer. *Strahlenther Onkol* 195: 517-525, 2019. DOI: 10.1007/s00066-018-1398-8
- 2 Nathoo D, Loblaw A, Davidson M, Musunuru HB, Khojaste A, Ravi A: A feasibility study on the role of ultrasound imaging of bladder volume as a method to improve concordance of bladder filling status on treatment with simulation. *J Med Imaging Radiat Sci* 49(3): 277-285, 2018. DOI: 10.1016/j.jmir.2018.04.031

## 15 DETRIMENTAL EFFECT OF DELAYED OR INCOMPLETE BACILLUS CALMETTE-GUÉRIN PROTOCOLS ADMINISTRATION AFTER TRANS-URETHRAL TUMOR RESECTION IN PATIENTS WITH NON MUSCLE-INVASIVE BLADDER CANCER: A SYSTEMATIC REVIEW

Ettore Di Trapani<sup>1</sup>, Arturo Lo Giudice<sup>2</sup>, Elio Mazzone<sup>3</sup>, Gabriele Sorce<sup>2</sup>, Stefano Luzzago<sup>1</sup>, Francesco Alessandro Mistretta<sup>1</sup>, Giovanni La Croce<sup>4</sup>, Mattia Luca Piccinelli<sup>1</sup>,

Dario Di Trapani<sup>3</sup>, Marco Moschini<sup>5</sup>, Paolo Dell'Oglio<sup>3</sup>, Antonio Galfano<sup>3</sup>, Francesco Montorsi<sup>5</sup>, Alberto Briganti<sup>5</sup>, Ottavio de Cobelli<sup>1</sup> and Gennaro Musi<sup>1</sup>

<sup>1</sup>European Institute of Oncology,  
Urologic Surgery, Milan, Italy;

<sup>2</sup>Gaetano Martino University Hospital,  
Urology, Messina, Italy;

<sup>3</sup>ASST Grande Ospedale Metropolitano  
Niguarda, Urology, Milan, Italy;

<sup>4</sup>ASST Papa Giovanni XXIII, Urology, Bergamo, Italy;

<sup>5</sup>IRCCS San Raffaele Scientific Institute,  
Urology, Milan, Italy

*Background/Aim:* Bacillus Calmette-Guérin (BCG) immunotherapy remains the standard treatment for high-risk non-muscle-invasive bladder cancer (NMIBC). While the European Association of Urology (EAU) guidelines recommend initiating BCG treatment no later than 4-6 weeks following transurethral resection of bladder tumors (TURBT), delays in BCG administration are not uncommon due to factors such as pathological assessment timelines, patient-related issues, healthcare system limitations, and drug shortages. This systematic review aimed to evaluate the impact of delayed BCG therapy on oncological outcomes, trying to establish the best treatment option for these patients. *Materials and Methods:* A comprehensive literature search was conducted across multiple databases (PubMed, Scopus, Web of Science) for studies published from January 2010 to the present. After screening 241 publications, relevant prospective and retrospective studies, systematic reviews, and meta-analyses were included. We retrieved 12 manuscripts evaluating different BCG schedule or doses. Only two papers specifically referred to the delay in the treatment of high-risk NMIBC. *Results:* The findings highlight that the delays in initiating BCG therapy beyond six weeks are associated with worse recurrence-free survival (RFS), progression-free survival (PFS), and cancer-specific survival (CSS) rates. However, evidence on the progression to MIBC or metastatic disease remains inconclusive, with only a few

studies suggesting a potential impact. Despite these delays, even reduced dose or shortened BCG regimens appear to offer some level of protection against disease progression. *Conclusion:* This review emphasizes the importance of adhering to standard BCG treatment schedules to minimize the risk of recurrence and suggests that, in cases of unavoidable delay, strict endoscopic follow-up is crucial and an optimal treatment in case of cancer relapse must be offered. Further prospective studies are needed to conclusively determine the long-term effects of delayed therapy.

## 16

### UPPER TRACT UROTHELIAL CARCINOMA AND LYNCH SYNDROME: EPIDEMIOLOGY, CLINICAL ASPECTS AND TREATMENTS

*Elena Lievore*, Francesco Alessandro Mistretta, Stefano Luzzago, Mattia Luca Piccinelli, Chiara Vaccaro, Luca Sarchi, Giovanni Cordima, Antonio Brescia, Francesco Caimi, Giuseppe Cicala, Antonio Cimmino, Ottavio de Cobelli and Gennaro Musi

European Institute of Oncology, Urologic Surgery, Milan, Italy

*Background/Aim:* To compare clinical and tumor characteristics, treatments and oncological outcomes in patients with newly diagnosed upper tract urothelial carcinoma (UTUC) with Lynch syndrome (LS) *versus* those with sporadic UTUC. *Patients and Methods:* This retrospective single-center study included 18 patients with LS UTUC and 336 with sporadic UTUC who underwent surgical treatment between 2001 and 2024. First, EAPC illustrated temporal trends in LS UTUC diagnoses and the prevalence of patients meeting the Bethesda guidelines and Amsterdam II criteria over time. Second, the Wilcoxon test and chi-square tests were used to assess differences in medians and proportions, respectively, for clinical/tumor characteristics and treatment patterns over time. Third, Kaplan-Meier plots were used to

compare oncological outcomes across five different endpoints: 1) bladder recurrence; 2) grade progression; 3) stage progression; 4) nodal recurrence; 5) metastatic progression. *Results:* Overall, 5.1% of patients had LS UTUC, with the percentage increasing over time (0% in 2001 vs. 15% in 2024). Additionally, 48 (14%) and 117 (34%) met the Bethesda guidelines and modified Amsterdam II criteria, respectively. Compared to sporadic UTUC, LS UTUC patients were younger (62 vs. 70 years;  $p=0.01$ ), more frequently female (44% vs. 29%;  $p=0.2$ ), and more frequently non-smokers (50% vs. 27%;  $p=0.09$ ). Furthermore, LS UTUC patients less frequently had bladder cancer before UTUC diagnosis (28% vs. 40%;  $p=0.2$ ) but more frequently had bilateral disease (23% vs. 1%;  $p=0.002$ ). Despite similar rates of initial conservative management between the two groups (URS: 72% vs. 68.5%;  $p=0.8$ ), LS UTUC patients more frequently underwent repeated URS (45.7% vs. 14.3%;  $p=0.03$ ), ureterectomies (16.5% vs. 2%;  $p=0.02$ ), and RNU (89% vs. 65%;  $p=0.003$ ). Notably, over time, eight (44.5%) LS UTUC patients were treated for bilateral disease. Although LS UTUC patients had lower 5-year grade progression-free survival rates (67% vs. 88%;  $p=0.05$ ), no significant differences were observed for other oncological outcomes between LS UTUC and sporadic UTUC. *Conclusion:* LS UTUC accounts for 5.1% of all newly discovered UTUCs, with an increasing trend over years. Certain peculiar characteristics of LS UTUC patients and tumors could be utilized in daily practice for distinguishing them from sporadic UTUC. A correct and personalized management of LS UTUC tumors could ensure excellent oncological outcomes, comparable to those of sporadic UTUC.

17

**STAGING OF PATIENTS WITH NEWLY DIAGNOSED UNFAVORABLE INTERMEDIATE- OR HIGH-RISK PROSTATE CANCER: THE ALL-IN-ONE WHOLE BODY MAGNETIC RESONANCE IMAGING PROTOCOL**

Stefano Luzzago, Francesco Alessandro Mistretta, Mattia Luca Piccinelli, Chiara Vaccaro, Elena Lievore,

Ettore Di Trapani, Matteo Fontana, Sara Nardini, Daniele Stroppa, Elena Scanferla, Ester Zino, Ottavio de Cobelli and Gennaro Musi

European Institute of Oncology, Urologic Surgery, Milan, Italy

*Background/Aim:* Current international guidelines recommend bone scintigraphy (BS) and abdominopelvic computed tomography (CT), alongside PET-PSMA, as primary staging modalities for unfavorable intermediate and high-risk prostate cancer (PCa) patients. A potential one-step staging approach has been proposed using multiparametric magnetic resonance imaging (mpMRI) combined with whole-body MRI (WB-MRI) to assess nodal and metastatic disease status in a single session. *Materials and Methods:* This multicentric, prospective, interventional study compares the accuracy of All-in-One MRI staging *versus* the standard BS and CT pathways for unfavorable intermediate and high-risk PCa patients. All patients undergo BS, CT, and WB-MRI within a six-week period, with radiologists blinded to findings from other imaging tests. The primary outcome measures are per-patient sensitivity, specificity, and accuracy of WB-MRI *versus* BS+CT for detecting nodal and distant metastases. Secondary outcomes include changes in disease management, rates of equivocal findings, cost analysis, radiation exposure, patient compliance and preferences, side effects, and interobserver variability. Treatment decisions are made by a multidisciplinary team (MDT) based on WB-MRI findings. Non-metastatic patients' staging accuracy is evaluated against final pathology and PSA values during follow-up, while metastatic patients' accuracy is assessed based on changes in metastatic appearance post-treatment. The study commenced on 01/12/2022 and aims to recruit patients over 36 months, with a minimum one-year follow-up for all participants. With 137 patients enrolled as of February 2025, the study targets 350 patients to achieve 80% statistical power. *Results:* Preliminary analysis showed a 1.4% refusal rate for WB-MRI due to claustrophobia among enrolled

patients. Among the remaining 135 patients, 28.5% exhibited discordant staging results between WB-MRI and BS+CT. Specifically, WB-MRI resulted in upstaging for 20% and downstaging for 8.2% of patients compared to BS+CT. Upstaging with WB-MRI led to changes from cN0M0 to cN1M0 in 14% of cases and to cN0/1M1a or cN0/1M1b in 5.2% and 3.7% of cases, respectively. Downstaging occurred in 4.4% of cases from cN0M1b to cN0M0. MDT decisions resulted in changes to disease management for 16.3% of patients. For surgically treated patients, WB-MRI demonstrated higher sensitivity (68% vs. 40%), specificity (94% vs. 89%), positive predictive value (78% vs. 56%), and negative predictive value (90% vs. 82%) for detecting lymph node metastases compared to CT. **Conclusion:** Systemic staging with All-in-One WB-MRI in unfavorable intermediate and high-risk PCa patients resulted in significant changes in disease stage (28.5%) and subsequent treatment decisions (16%) compared to BS+CT. These preliminary findings warrant further validation upon completion of the study.

## 18 ROBOT-ASSISTED VS OPEN INGUINAL LYMPH NODE DISSECTION: A COMPARATIVE ANALYSIS ON PERI- AND POSTOPERATIVE OUTCOMES

Chiara Vaccaro<sup>1</sup>, Francesco Alessandro Mistretta<sup>1</sup>, Stefano Luzzago<sup>1</sup>, Mattia Luca Piccinelli<sup>1</sup>, Elena Lievore<sup>1</sup>, Ettore Di Trapani<sup>1</sup>, Matteo Fontana<sup>1</sup>, Sara Nardini<sup>1</sup>, Daniele Stroppa<sup>1</sup>, Elena Scanferla<sup>1</sup>, Ester Zino<sup>1</sup>, Sara Coppola<sup>2</sup>, Elisabetta Pennacchioli<sup>2</sup>, Ottavio de Cobelli<sup>1</sup> and Gennaro Musi<sup>1</sup>

<sup>1</sup>Urologic Surgery, European Institute of Oncology, Milan, Italy;

<sup>2</sup>Melanoma and Sarcoma Surgery, European Institute of Oncology, Milan, Italy

**Background/Aim:** Inguinal lymph node dissection is a surgical procedure, which is performed for malignancies

with several different histologies (*i.e.*, urological, gynecological or cutaneous). However, it is often associated with multiple and/or severe comorbidities. With the advent of minimally invasive surgery, comparative data between the open and robotic approaches remain limited. This study aimed to evaluate and compare perioperative and postoperative outcomes in patients undergoing open (OIL) *versus* robotic inguinal lymphadenectomy (RAIL). **Patients and Methods:** We retrospectively analyzed data from patients harboring different tumor histologies (namely penile carcinoma and skin or appendages tumors), who underwent inguinal lymphadenectomy at a single center between 2012 and 2024. Patient demographic characteristics, perioperative, and postoperative data were recorded. Perioperative and postoperative variables consisted of operative time (OT), estimated blood loss (EBL), days of use of nonsteroidal anti-inflammatory drugs (NSAIDs) and opiates, length of stay (LOS), groin drain indwelling days, and intraoperative and postoperative groin complications (classified as: early if occurred within seven days or late if within 90 days). Descriptive statistics depicted differences between OIL and RAIL. Multivariable logistic regression models tested for differences in operative time, EBL, LOS, and overall complications. All models were adjusted for age, BMI, sex, CCI, and lymph node yield. **Results:** Out of 163 patients, 129 (79%) were treated with OIL and 34 (21%) with RAIL. Patient characteristics were similar between the two groups in terms of demographic and histological features. RAIL group had significantly lower median EBL (129 ml vs. 363 ml in OIL;  $p<0.001$ ). Conversely, OIL group had lower median operative time (157 min vs. 264 min in RAIL;  $p<0.001$ ). Lower rates of complicated skin lesion (7 vs. 2.9%) and lymphedema (12 vs. 0%) were reported after RAIL, but higher rates of seroma (19 vs. 38%) and fever (5.4 vs. 15%) were reported in this group. No differences in terms of use of NSAIDs and opiates, LOS, drain indwelling days, intraoperative and early postoperative complication rates were recorded between the two groups. In MLRM analyses, RAIL was associated with higher operative time (OR=1.68;  $p<0.01$ ) and lower

EBL (OR=0.49;  $p<0.01$ ), and no significant differences have been reported in terms of complications. *Conclusion:* Robotic approach might lead to lower median blood loss and fewer severe postoperative groin complications compared to the open technique. However, RAIL does not seem to be associated with reduced need for NSAIDs or opioids, LOS and drain indwelling duration, or the rate of non-severe complications.

19

**PATIENT SELECTION FOR THERMAL ABLATION OF SMALL RENAL MASSES: GUIDELINES COMPARISON ACCORDING TO PERIOPERATIVE AND RECURRENCE OUTCOMES**

Mattia Luca Piccinelli, Francesco Alessandro Mistretta, Stefano Luzzago, Chiara Vaccaro, Elena Lievore, Luca Sarchi, Giovanni Cordima, Antonio Brescia, Francesco Caimi, Giuseppe Cicala, Antonio Cimmino, Ottavio de Cobelli and Gennaro Musi

European Institute of Oncology, Urologic Surgery, Milan, Italy

*Background/Aim:* Marked heterogeneity in percutaneous thermal ablation (PTA) patient selection criteria exists according to different international guidelines for small renal masses (SRM). We aimed to compare PTA patient selection criteria across eight international guidelines according to perioperative and oncological outcomes. *Materials and Methods:* Overall, 538 patients (cT1a-b cN0 cM0) were treated with PTA (2008-2022). The outcomes of interest were trifecta status and recurrence-free survival (RFS). Failure to achieve trifecta was defined as the presence of any of the following: partial SRM ablation, a postoperative complication classified as Clavien–Dindo  $\geq 3$ , or a  $\geq 30\%$  decline in postoperative estimated glomerular filtration rate. Kaplan-Meier analyses tested 5-year RFS rates. Logistic and Cox regression models predicting trifecta and overall recurrence, respectively, were stratified

according to each guideline selection criteria. *Results:* Overall, 473 (88%) vs. 340 (63%) vs. 313 (58%) vs. 203 (38%) satisfied NCCN vs. ASCO/SIR/CIRSE/ESMO vs. AUA vs. CUA vs. EAU selection criteria for PTA, respectively. In univariable logistic regression models ASCO/SIR/CIRSE/ESMO [odds ratio (OR)=4.3] and AUA (OR=2.9) selection criteria emerged as predictors of trifecta achievement. In the overall population, the 5-year RFS rate was 80%. In Cox regression models, AUA [hazard ratio (HR)=0.5.  $p<0.001$ ] selection criteria emerged as a protective factor for overall recurrence. Limitations included the retrospective and monocentric nature of the study. *Conclusion:* We demonstrated high variability in PTA patient selection across international guidelines. ASCO/SIR/CIRSE/ESMO and AUA selection criteria showed similar ability to select patients with higher trifecta achievement rates. AUA-selected patients reported an association with lower overall recurrence rates. High-quality evidence is essential to strengthen clinical practice guidelines recommendations for PTA patient selection.

20

**MULTI-PARAMETRIC MAGNETIC RESONANCE IMAGING AND APPARENT DIFFUSION COEFFICIENT TO OPTIMALLY SELECT PROSTATE CANCER PATIENTS SUITABLE FOR ACTIVE SURVEILLANCE**

Francesco Alessandro Mistretta, Stefano Luzzago, Mattia Luca Piccinelli, Chiara Vaccaro, Elena Lievore, Ettore Di Trapani, Matteo Fontana, Sara Nardini, Daniele Stroppa, Elena Scanferla, Ester Zino, Ottavio de Cobelli and Gennaro Musi

European Institute of Oncology, Urologic Surgery, Milan, Italy

*Aim:* To evaluate the potential of multiparametric prostate magnetic resonance imaging (mpMRI) and apparent diffusion coefficient (ADC) values to predict unfavorable disease (UFD) and biochemical recurrence

(BCR) or prostatic specific antigen (PSA) persistence in potential active surveillance (AS) candidates undergoing surgery. *Patients and Methods:* We retrospectively selected 689 patients with Grade Group 1 (GG1) or GG2 prostate cancer (PCa) in the peripheral zone operated between 2012 and 2015. The outcomes of interest were UFD (GG  $\geq 3$  and/or pT  $\geq 3a$  and/or pN1), and BCR or PSA persistence. Logistic regression models assessed predictors including age, PSA density, GG at biopsy and percentage of positive cores (Model 1). Additional models incorporated Prostate Imaging Reporting and Data System (PI-RADS) category, extraprostatic extension (EPE) score, and ADC values *Results:* A total of 366 patients (53.1%) had UFD with 127 experiencing BCR or PSA persistence; 180 patients (26%) experienced BCR or PSA persistence and of these 127 had UFD. A significant difference in median ADC values was observed, with lower values in patients with UFD and BCR/PSA persistence (878 vs. 964  $\mu\text{m}^2/\text{s}$  and 873 vs. 933  $\mu\text{m}^2/\text{s}$ , respectively;  $p < 0.001$ ); a 100-unit ADC decrease was associated to a 27% higher risk of UFD and a 18% increased risk of BCR. A nomogram was developed to calculate the individual probability of UFD and BCR based on the final model, incorporating ADC, clinical, biopsy, and mpMRI data. *Conclusion:* The integration of ADC values into a nomogram with clinical, biopsy and mpMRI findings improved patient selection for AS.

## 21

### **THERMAL ABLATION FOR LOCAL TUMOUR RECURRENCE AFTER PREVIOUS PARTIAL NEPHRECTOMY: PERIOPERATIVE AND ONCOLOGICAL OUTCOMES**

Chiara Vaccaro, Francesco Alessandro Mistretta, Stefano Luzzago, Mattia Luca Piccinelli, Elena Lievore, Ettore Di Trapani, Matteo Fontana, Sara Nardini, Daniele Stroppa, Elena Scanferla, Ester Zino, Ottavio de Cobelli and Gennaro Musi

European Institute of Oncology, Urologic Surgery, Milan, Italy

*Background/Aim:* Percutaneous thermal ablation (PTA) has emerged as an alternative to salvage radical nephrectomy (RN) for the treatment of renal cell carcinoma (RCC) local recurrence. We report perioperative and oncological outcomes of patients treated with PTA for RCC local recurrence. *Patients and Methods:* We retrospectively analyzed 27 patients with on-site recurrence, who received either radiofrequency (RF) [8 (29.6%)] or microwaves (MW) [19 (70.4%)], in a high-volume Center from 2008-2022. Primary endpoints were perioperative outcomes, complications and readmission rates. Secondary endpoints were on-site and out-site tumor recurrence. Last, we collected renal function outcomes after PTA. *Results:* Median [interquartile range (IQR)] treatment time was 75 (63-106) minutes and median length of stay (LOS) was 3 days. Intraoperative complications occurred in one (3.7%) patient (urinary leakage that did not require additional treatments), while postoperative in 2 (7.4%) patients (one urinary leakage requiring ureteral double J stent placement). Three patients (11%) received incomplete ablation. Of those, local control was achieved after 1 adjunctive MW session in one patient and after RN in 2 patients. Overall, 4 (16%) patients developed on-site recurrence after a median follow-up of 30 (23-43) months: in three subsequent PTA achieved local control, while no other local treatments were performed in one for bone metastases. Moreover, 6 (24%) patients developed out-site recurrence after a median follow-up of 16 (10-23) months. Last, median creatinine drop at one month and at one year after surgery was -0.03 (-0.11-0.01) and -0.11 (-0.20-0.05), while median eGFR drop was 2 (0-7.65) and 9.5 (5-13.45). *Conclusion:* PTA is a safe and feasible approach for the management of on-site recurrences after partial nephrectomy. Low perioperative complication rates and optimal local cancer control were achieved in most patients, where 3 cm tumor diameter cut-off remains the optimal size, with no significant impairment of residual renal function.

22

**A NOVEL MULTI-PARAMETRIC MAGNETIC RESONANCE IMAGING RISK TOOL FOR PREDICTION OF 5-YEAR CLINICAL RECURRENCE AFTER RADICAL PROSTATECTOMY FOR PROSTATE CANCER**

Stefano Luzzago, Francesco Alessandro Mistretta, Mattia Luca Piccinelli, Chiara Vaccaro, Elena Lievore, Luca Sarchi, Giovanni Cordima, Antonio Brescia, Francesco Caimi, Giuseppe Cicala, Antonio Cimmino, Ottavio de Cobelli and Gennaro Musi

European Institute of Oncology, Urologic Surgery, Milan, Italy

*Background/Aim:* The adoption of magnetic resonance imaging (MRI)-based risk tools for prediction of prostate cancer (PCa) prognosis is still scarce, due to lack of data on disease progression and cancer-specific mortality. The aim of the study was to evaluate the potential of the recently developed PIPEN risk tool in predicting the risk of 5-year clinical recurrence after radical prostatectomy (RP). *Patients and Methods:* In this retrospective single-center analysis of 1,459 patients with PCa who underwent multiparametric prostate MRI (mpMRI) before RP (2012-2015), the outcome of interest was 5-year clinical recurrence, defined as imaging evidence of PCa recurrence (either: local recurrence, N1 or M1a, M1b or M1c) after surgery. Kaplan–Meier plots estimated survival probabilities. Separate multivariable Cox regression models were fitted with all variables included in the PIPEN, EAU, UCSF CAPRA, Cambridge Prognostic Groups, MSKCC and Partin risk classifications. Models were refitted after considering PIPEN, EAU, UCSF CAPRA and Cambridge Prognostic Groups risk groups. C-index of the models before and after 10-fold cross-validation were calculated. Receiver Operating Characteristic (ROC) curves depicted the Area Under the Curve (AUC). *Results:* Median [interquartile range (IQR)] follow-up time was 60 (32-74) months. Overall, 146 (10%) patients developed clinical recurrence. In separate multivariable Cox regression models predicting clinical

recurrence over time and fitted with all single variables, the PIPEN risk model achieved greater accuracy (C-index: 0.83), compared to EAU (C-index: 0.81), UCSF CAPRA (C-index: 0.78), Cambridge Prognostic Groups (C-index: 0.80), MSKCC (C-index: 0.79) and Partin (C-index: 0.79) risk calculators. The PIPEN model achieved even greater accuracy (C-index: 0.81), relative to EAU (C-index: 0.76), UCSF CAPRA (C-index: 0.74) and Cambridge Prognostic Groups (C-index: 0.77), also when multivariable Cox models were re-fitted with models considering risk groups. A progressive shift from PIPEN very low to PIPEN very high-risk category was associated with increasing number of sites (1 vs. 2 vs. 3 vs. 4) and worse location of tumor recurrences (local recurrence vs. N1 vs. M1a vs. M1b vs. M1c). *Conclusion:* The PIPEN score provided greater accuracy, compared to the other commonly used risk calculators, for predicting clinical recurrence after RP. Moreover, higher PIPEN risk groups were associated with increasing number of sites and worse location of tumor recurrence.

23

**TARGETING THE AR-ADAR2-PD-L1 AXIS TO OPTIMIZE BCG THERAPY IN PAPILLARY BLADDER CARCINOMA**

Gabriele Ricciardi<sup>1,2</sup>, Valeria Zuccalà<sup>3</sup>, Vincenzo Fiorentino<sup>3</sup>, Mariagiovanna Ballato<sup>1</sup>, Walter Giuseppe Giordano<sup>1</sup>, Emanuela Germanà<sup>1</sup>, Guido Fadda<sup>3</sup>, Giuseppe Giuffrè<sup>3</sup> and Maurizio Martini<sup>3</sup>

<sup>1</sup>Department of Biomedical, Dental, Morphological and Functional Imaging Sciences, University of Messina, Messina, Italy;

<sup>2</sup>Istituto Clinico Polispecialistico C.O.T. Cure Ortopediche Traumatologiche s.p.a., Messina, Italy;

<sup>3</sup>Department of Human Pathology in Adult and Developmental Age, University of Messina, Messina, Italy

*Background/Aim:* Bacillus Calmette-Guérin (BCG) immunotherapy is the standard of care for non-muscle-

invasive papillary bladder carcinoma, but clinical response is highly variable. Identifying molecular and immune features associated with therapeutic efficacy could improve patient stratification. This study evaluated the relationship between tumor markers, immune profiles and microenvironment in patients treated with BCG. *Patients and Methods:* A cohort of 80 patients with papillary bladder carcinoma, treated with BCG, was retrospectively analyzed. Among them, 57 patients had T1 tumors and 23 had Ta tumors. The expression of androgen receptor (AR), Adenosine Deaminase Acting on RNA 2 (ADAR2), and Programmed Death-Ligand 1 (PD-L1), as well as the CD4/CD8 tumor-infiltrating lymphocyte (TIL) ratio, was assessed by immunohistochemistry. miR-200a-3p and interferon-gamma (IFN- $\gamma$ ) levels were evaluated by real-time PCR. Results were correlated with clinicopathological features and recurrence-free survival (RFS). *Results:* High AR expression was significantly associated with reduced ADAR2, elevated PD-L1, a higher CD4/CD8 ratio, and multifocal tumors ( $p < 0.001$ ), regardless of tumor stage. These features correlated with significantly shorter RFS ( $p < 0.0001$  in T1 and  $p = 0.0003$  in Ta). Combined analysis of AR, ADAR2, and PD-L1 expression improved the predictive value for recurrence. Furthermore, tumors with low AR and high ADAR2 expression showed significantly higher miR-200a-3p and IFN- $\gamma$  levels ( $p < 0.0009$  and  $p < 0.0003$ , respectively). *Conclusion:* AR expression modulates PD-L1 expression and TILs through ADAR2, miR-200a-3p, and IFN- $\gamma$ , influencing BCG response in papillary bladder carcinoma. These findings suggest that AR and ADAR2 may serve as potential predictive biomarkers and therapeutic targets for optimizing treatment strategies.

## 24

### **PAPILLARY FEATURES IN ADULT WILMS' TUMOR: A RARE THERAPEUTIC OPPORTUNITY**

Stefano Travaglini, Adelaide Mazzocca,  
Silvia Del Monaco, Silvia Villani, Giovanni Belletti,  
Rebecca Chiariotti, Rosedwige Marchitelli,

Francesco Savino, Mariapaola Masiello,  
Rachele Piccinini, Giada Pinterpe and Rossana Berardi

Marche Polytechnic University, Azienda Ospedaliero-  
Universitaria delle Marche, Ancona, Italy

*Background/Aim:* Wilms' tumor (WT) is a rare renal cancer diagnosed predominantly in children, with an adult incidence of approximately 0.2 per millions per year (1). Around 10%-20% of cases are associated with genetic syndromes or congenital anomalies (2-3). Clinically, the disease typically presents with a painless abdominal mass in 75-95% of cases, although hypertension, hematuria, and abdominal pain may also occur (4). Diagnosis involves physical examination, blood tests, and imaging, including abdominal ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) (5). Treatment is multimodal, involving surgery, chemotherapy (CTx), and radiotherapy. We present the exceptionally rare and complex therapeutic pathway of an adult patient diagnosed with Wilms' tumor, managed at our center over several years. *Case Report:* The patient, a man born in 1985, was referred to our Center in 2017 for an adult-onset recurrence of WT, initially diagnosed and treated during childhood. Notably, in 1997, the patient had undergone resection of a retroperitoneal nephroblastoma (or WT), followed by adjuvant CTx with Adriamycin and Ifosfamide. Twenty years later, recurrent episodes of hematuria led to imaging that revealed a large retroperitoneal mass originating from the right kidney with intrahepatic extension. Renal biopsy confirmed the diagnosis of an epithelial variant of nephroblastoma, consistent with the tumor subtype diagnosed in 1997. Neoadjuvant CTx was administered according to the AIEOP-TW-2003 protocol with Vincristine, Doxorubicin, and Actinomycin D. Subsequently, the patient underwent right nephrectomy, and histological analysis confirmed the epithelial variant of nephroblastoma without anaplasia. Adjuvant therapy continued with the AIEOP-TW-2003 protocol until March 2018, along with radiotherapy to the nephrectomy bed (May-July 2017). Follow-up with

abdominal MRI and thoracic CT was started and continued until disease relapse in September 2019, with bone involvement at the D7 vertebral body. At that time, the patient underwent CTx (Vincristine, Irinotecan, and Topotecan, plus Bevacizumab) and received radiotherapy from D6 to D8. In February 2021, due to skeletal, lymph nodal, and pulmonary progression, the patient received second line CTx with Vincristine, Irinotecan, and Everolimus, which continued until December 2021. This choice was based on biomolecular analysis, showing overexpression of the mTOR pathway. The metastatic lesion at D7 was surgically removed, and histological examination revealed an epithelial neoplasm with a papillary pattern, compatible with renal cell carcinoma (RCC). These uncommon findings suggest the rare co-existence of nephroblastoma and RCC. In January 2022, following multidisciplinary discussion with national referral centers, treatment with Pembrolizumab plus Axitinib - an immunotherapy (IO) and tyrosine kinase inhibitor (TKI) combination - was initiated in accordance with RCC guidelines. The best response achieved at four months was a complete lung response and partial responses in lymph nodes and bone lesions. The patient reached progression-free survival (PFS) of 14 months, until March 2023. Due to bone progression, fourth line therapy with Cabozantinib was started and continued until April 2024, when pulmonary progression occurred. At that point, Everolimus was reintroduced and continued until November 2024. A subsequent CT scan revealed new pleural, pulmonary, and hepatic lesions; treatment was switched to Sunitinib at a personalized dosage, which the patient continued until his death in February 2025. *Conclusion:* Given the rarity of WT in adults, the identification of a papillary RCC component was an exceptional and clinically relevant finding. In a patient with no standard therapeutic options, it enabled a personalized approach with IO-TKI therapy, leading to symptom improvement and prolonged disease control. The case highlights the value of tailored treatments and the essential role of multidisciplinary, shared management with national referral centers.

- 1 Modi S, Tiang KW, Inglis P, Collins S: Adult Wilms' tumour: case report and review of literature. *J Kidney Cancer VHL* 23(2): 1-7, 2016. DOI: 10.15586/jkcvhl.2016.52
- 2 Scott RH, Stiller CA, Walker L, Rahman N: Syndromes and constitutional chromosomal abnormalities associated with Wilms tumour. *J Med Genet* 43(9): 705-715, 2006. DOI: 10.1136/jmg.2006.041723
- 3 Narod SA, Hawkins MM, Robertson CM, Stiller CA: Congenital anomalies and childhood cancer in Great Britain. *Am J Hum Genet* 60(3): 474-485, 1997.
- 4 Xu S, Sun N, Zhang WP, Song HC, Huang CR: Management of Wilms tumor with intravenous thrombus in children: a single center experience. *World J Pediatr* 15(5): 476-482, 2019. DOI: 10.1007/s12519-019-00272-0
- 5 Servaes S, Khanna G, Naranjo A, Geller JI, Ehrlich PF, Gow KW, Perlman EJ, Dome JS, Gratias E, Mullen EA: Comparison of diagnostic performance of CT and MRI for abdominal staging of pediatric renal tumors: a report from the Children's Oncology Group. *Pediatr Radiol* 45(2): 166-172, 2015. DOI: 10.1007/s00247-014-3138-2

## 25

### **DIAGNOSTIC VALUE OF BLADDER EPICHECK TEST AND XPERT BC MONITOR IN FOLLOW-UP OF NON-MUSCLE INVASIVE BLADDER CANCER: UN UPDATE**

Emanuela Trenti<sup>1</sup>, Carolina D'Elia<sup>1</sup>, Margherita Palermo<sup>1</sup>, Bianca Barioglio<sup>2</sup>, Christine Mian<sup>2</sup>, Christine Schwienbacher<sup>2</sup>, Giovanni Mazzucato<sup>1</sup>, Salvatore M. Palermo<sup>1</sup> and Armin Pycha<sup>1</sup>

<sup>1</sup>Department of Urology, Provincial Hospital of Bolzano, Bolzano, Italy;

<sup>2</sup>Sigmund Freud Private University, Medical School, Vienna, Austria;

<sup>3</sup>Department of Pathology, Provincial Hospital of Bolzano, Bolzano, Italy

*Background/Aim:* The surveillance of patients diagnosed with non-muscle invasive bladder cancer (NMIBC) relies

on cystoscopy and urinary cytology. Cystoscopy is an invasive procedure that can cause complications, anxiety, and significant discomfort for the patient. Its sensitivity is high for papillary lesions but not for flat lesions, and it requires experience and is operator dependent. Urinary cytology is commonly used in addition to cystoscopy, especially to detect flat lesions that cannot be recognized during cystoscopy. It has a high sensitivity for high-grade (HG) tumors and a low sensitivity for low-grade (LG) tumors. The limitations of cytology and cystoscopy have led to decades of research for urinary markers for the early diagnosis of bladder cancer (BC). At the Hospital of Bozen two urinary markers based on real-time polymerase chain reaction (PCR) are routinely analyzed: the Bladder EpiCheck Test, based on DNA methylation alterations associated with BC, and the Xpert BC Monitor test, which measures the levels of five target mRNAs. The aim of this study is to confirm the diagnostic accuracy of these two urinary markers and to compare them with each other and with urinary cytology in the same cohort of patients undergoing follow-up for NMIBC. *Patients and Methods:* In this prospective study, 975 patients undergoing follow-up for NMIBC (757 male and 218 female patients) were enrolled with a mean age of 76.5, for a total of 4011 samples. During their follow-up patients were tested with urinary cytology and cystoscopy, Bladder EpiCheck, and Xpert BC Monitor. Suspicious lesions found during cystoscopy were biopsied or removed transurethrally, and the samples were reported according to the TNM classification of bladder cancer. *Results:* A total of 451 samples were excluded due to invalid values, 146 in the Xpert BC Monitor test (3.7%) and 229 (5.7%) in the Bladder EpiCheck test. Cytology was non-diagnostic in 88 cases (2.1%). Of the remaining 3560 samples, 266 showed NMIBC recurrence, specifically 182 low-grade (LG) NMIBC and 84 high-grade (HG) NMIBC. The other 3294 cases were negative on cystoscopy and/or histology. The overall sensitivity of cytology was found to be 19.9%. Based on tumor grade, it was 6.5% for LG tumors and 51.1% for HG tumors, with a specificity of 98.9%, a positive predictive value (PPV) of 60.2%, and a negative predictive value

(NPV) of 93.8%, respectively, with an accuracy of 93%. The Bladder EpiCheck test showed an overall sensitivity of 64.6%. The specificity was 84.8%, with a PPV of 25.6% and an NPV of 96.7%, respectively. The Xpert BC Monitor test showed an overall sensitivity of 74.4%. The specificity was 88.1%, with a PPV of 33.7% and an NPV of 97.7%, respectively. Running both tests and considering a result positive if either test was positive, Bladder EpiCheck and Xpert BC Monitor together identified 81.9% of tumors, 76.3% of LG tumors, and 94% of HG tumors. The specificity of the two tests combined was 78.2%, with a PPV of 23.3% and an NPV of 98.1%. *Conclusion:* Xpert BC Monitor and Bladder EpiCheck achieved excellent results in terms of sensitivity, significantly higher than that of cytology in both tumor groups, LG and HG, especially when used together. Together, the two tests identified 94% of HG tumors. Their specificity is high, but it does not reach the one of cytology. The negative predictive value (NPV) was comparable between the two tests and higher than that of cytology, especially when used together (98.1%).

## 26

### EVALUATION OF THE M371 TEST UNDER REAL LIFE CONDITIONS FOR THE DIAGNOSIS OF TESTICULAR GERM CELL CANCER

Carolina D'Elia<sup>1</sup>, Emanuela Trenti<sup>1</sup>,  
Salvatore Mario Palermo<sup>1</sup>, Christine Mian<sup>2</sup>,  
Christine Schwienbacher<sup>2</sup>, Margherita Palermo<sup>1</sup>,  
Silvia Clauser<sup>1</sup> and Armin Pycha<sup>1,3</sup>

<sup>1</sup>Department of Urology, Provincial Hospital of Bolzano, Bolzano, Italy;

<sup>2</sup>Department of Pathology, Provincial Hospital of Bolzano, Bolzano, Italy;

<sup>3</sup>Sigmund Freud Private University, Medical School, Vienna, Austria

*Background/Aim:* Testicular germ cell cancer (GCT) is the tumor most frequently diagnosed in men between 15 and

50 years. The cure rate is very high, and the 5-year survival exceeds 90% for clinical stage (CS) I and II and is above 80% for CS III. Currently, the gold standard for the management of GCT is represented by execution of computed tomography (CT) or magnetic resonance (MR) and by measurement of the serum tumor markers alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (b-HCG) and lactate dehydrogenase (LDH). However, due to their low sensitivity, the utility of tumor markers is limited. In previous studies, miRNA-371a-3p was found to be a promising biomarker in the diagnosis of GCT with a better performance than the conventional markers. The aim of this study was to evaluate the M371-Test under real life conditions, comparing it with the classical markers AFP, b-HCG and LDH, using the Rotor-Gene Q (Qiagen) Thermocycler platform. *Materials and Methods:* Seventy M371 tests were performed (median age 37 years) and were included in this prospective study. All patients presented with suspicion of testicular cancer. Results of M371, AFP, b-HCG, LDH were compared with the histology, considered as gold standard. Two samples have been excluded from our analysis due to non-diagnostic indeterminate M371. Cut-off of M371 was set at >5 RQ to calculate sensitivity, specificity, and predictive values. *Results:* In the patients with suspicion of TC, the M371-Test showed a sensitivity of 95%, AFP of 20%, LDH of 40.5% and b-HCG of 45.2%. Specificity of the markers was 89.8% for M371, 96.3% for both AFP and LDH and 100% for b-HCG (Table I). In addition, positive predictive value (PPV) was 92.7% for M371, 88.9% for AFP, 94.4% for LDH and 100% for b-HCG. M371 showed a negative predictive value (NPV) of 92.3%, and AFP, LDH and b-HCG respectively 44.8%, 51% and 54% (Table I). Stratifying the performance of M371 according to the tumor histotype, M371 shows a sensitivity of 100% in non seminomatous tumors and 87% in seminomas. *Conclusion:* Even under real life conditions and using a different thermocycler, the M371 test maintains a very good performance, significantly higher than conventional markers in terms of sensitivity and NPV and should, therefore, be considered in the management of patients with GCT.

Table I. Sensitivity, specificity, PPV and NPV of the markers.

	AFP	LDH	Beta	miRNA
Sensitivity	20.93%	41.86%	46.51%	90.70%
Specificity	96.30%	96.30%	100.00%	88.89%
PPV	90.00%	94.74%	100.00%	92.86%
NPV	43.33%	50.98%	54.00%	85.71%

PPV: Positive predictive value; NPV: negative predictive value.

## 29

### BOOST TO DOMINANT INTRAPROSTATIC LESION: A PRECISION APPROACH IN LOCALIZED PROSTATE CANCER

Rocco Luca Emanuele Liardo<sup>1</sup>, Roberto Milazzotto<sup>1</sup>, Grazia Acquaviva<sup>1</sup>, Madalina La Rocca<sup>2</sup>, Maria Chiara Lo Greco<sup>1</sup> and Corrado Spatola<sup>1</sup>

<sup>1</sup>Unit of Radiation Oncology, University Hospital Policlinico "G. Rodolico - San Marco", Catania, Italy;

<sup>2</sup>Unit of Radiation Oncology and Nuclear Medicine, Ospedale Civile di Sondrio, Sondrio, Italy

*Background/Aim:* The addition of a focal boost to dominant intraprostatic lesion (DIL) is an emerging strategy to potentially improve tumor control in patients with organ confined prostate cancer. The aim of this case series was to evaluate the safety, feasibility and acute toxicity of moderately hypofractionated external beam radiotherapy followed by focal boost on DIL. *Patients and Methods:* Ten patients with newly diagnosed organ-confined prostate cancer, with clinical stage T1-T2c adenocarcinoma, prostate volume ≤90 ml, Gleason Score (GS) ≤7 and prostate-specific antigen (PSA) level <20 ng/ml were included in this case series. The presence of only one DIL on mpMRI, classified as PIRADS >3, confirmed on targeted ultrasound-fusion biopsy, was mandatory for inclusion in this series. Two separate nodules were allowed, only if contiguous and in the same lobe. All patients underwent CT simulation and image fusion with mpRM for boost volume identification. PET PSMA fusion was optional. Radiotherapy was

administered with volumetric modulated arc radiotherapy techniques. The dose planned to prostate was 60 Gy/20 fr. with a sequential focal boost of 9 Gy/3 fr. to DIL. Genitourinary (GU) and gastrointestinal (GI) toxicity was reported using the Common Terminology Criteria for Adverse Events (CTCAE). To evaluate urinary symptoms, the International Prostatic Symptoms Score (IPSS) questionnaire was administered to all patients, before, at the end and six months after the end of radiotherapy. Every result, in terms of toxicity and dosimetry, were compared with a group of patients with the same characteristics treated in the same period, at the same dose to prostate, but without focal boost. *Results:* From June 2023 to June 2024, a total of 10 men underwent hypofractionated radical radiotherapy to prostate with sequential focal boost to DIL (60 Gy/20 fr and 9 Gy/3 fr to DIL, respectively). All patients completed radiation treatment. Median patient age was 71.8 years (range=67-78 years). Median initial PSA was 13.1 ng/ml (range=7-25 ng/ml). At baseline, International Prostate Symptom Score was mild for 7 patients and moderate for 3. The majority of treated DILs were in the peripheral zone (80%). Two patients had Gleason Score 6 (3+3), four 7 (3+4) and four 7 (4+3). In seven patients, androgen-deprivation therapy was administered in accordance with current clinical practice. All the radiotherapy plans met the predetermined target coverage objectives. All rectal and bladder dose constrains was respected. At a median follow-up of 12 months (range=8-20 months), no acute GU or GI toxicity of grade 2 or more was observed. Only one patient had a single episode of rectal bleeding eight months after the end of radiotherapy. No significant differences in acute toxicity were found when compared to patients who did not receive boosting. *Conclusion:* Our preliminary results show that approaching prostate cancer with hypo-moderate fractionation followed by external beam focal Boost to dominant intraprostatic lesion in patients with localized prostate cancer is safe and effective. Preliminary data collected suggest that this treatment is not associated with increased acute morbidity. Longer follow up is needed to evaluate tumor control and late toxicity.

31

### EXPERIENCE WITH <sup>177</sup>LUTETIUM-PSMA-617 IN A PATIENT WITH PROGRESSIVE ADVANCED PROSTATE CANCER AND SUBSTANTIAL TOXICITY REDUCTION COMPARED TO PREVIOUS TREATMENT

Olga Gordeeva<sup>1</sup>, Špela Emeršič<sup>2</sup>,  
Yury Gordeev<sup>1</sup> and Boštjan Šeruga<sup>1</sup>

<sup>1</sup>Division of Medical Oncology, Institute of Oncology Ljubljana, Ljubljana, Slovenia;

<sup>2</sup>Department of Nuclear Medicine Institute of Oncology Ljubljana, Ljubljana, Slovenia

*Background/Aim:* Management of patients with metastatic castration resistant prostate cancer (mCRPC) remains a significant challenge. Recently, the theranostic approach with <sup>68</sup>Ga-PSMA-11 and <sup>177</sup>Lu-PSMA-617 has been introduced. <sup>177</sup>Lu-PSMA-617 is a radioligand therapy that delivers beta particle radiation to the prostate-specific membrane antigen (PSMA)-expressing cells and the surrounding microenvironment. PSMA is highly expressed in mCRPC (1). We present the first case of radioligand therapy at our Institution. This case report highlights the importance of the availability of theranostic treatment in patients with mCRPC and severe toxicity induced by the previous cancer treatment. *Patients and Methods:* In December 2024, a 76-year-old patient with CRPC underwent the PET/CT with <sup>68</sup>Ga-PSMA-11 (Figure 1). Patient's medical history began in a 2002 when he was postoperatively treated with chemo-radiotherapy for his squamous cell carcinoma of the right tonsil (stage pT1N2b). In 2015, he was diagnosed with a prostate adenocarcinoma (iPSA 14 ng/ml, Gleason Score 7). He underwent radical prostatectomy with pelvic lymphadenectomy (pT3aN0M0). In October 2020, a biochemical recurrence was detected and the patient received salvage radiotherapy along with initiation of androgen deprivation therapy with LHRH agonist. After 26 months, in January 2023, disease progression was confirmed by the choline-based PET/CT, which revealed

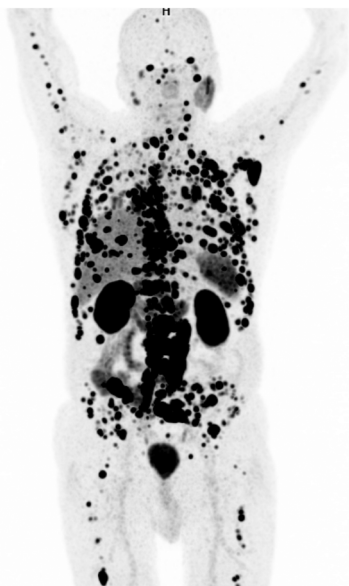


Figure 1. PET/CT ( $^{68}\text{Ga}$ -PSMA-11) before treatment: High PSMA expression in bone lesions and abdominal lymph nodes. PSMA: Prostate-specific membrane antigen.

lymph node metastases in the retroperitoneal and iliac regions. The PSA level also increased, confirming both biochemical and radiological progression and the transition to the mCRPC. Hormonal therapy with enzalutamide was started and a temporary stabilization of the disease was achieved. After 8 months, the treatment was changed to the abiraterone acetate due to the memory deterioration and hallucinations. In May 2024, further progression of disease was noted in the retroperitoneal lymph nodes, accompanied by the increasing PSA levels. Second-line systemic treatment with docetaxel was initiated, however, progressive disease was eventually observed after several months. Molecular and genetic testing did not identify any clinically relevant genetic alterations. In December 2024, further progression was observed in the bones, lymph nodes and lungs, as confirmed by CT, bone scintigraphy and PET/CT with  $^{68}\text{Ga}$ -PSMA-11. Our patient was not a candidate for cabazitaxel due to the comorbidities and previous treatment-related complications. He had arterial hypertension, depression, toxic polyneuropathy as a result of docetaxel toxicity and

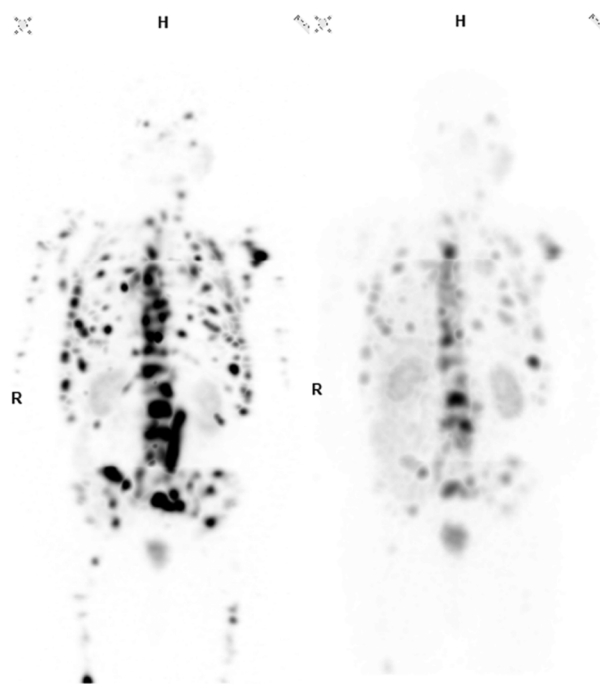


Figure 2. SPECT scans after cycles 1 and 2 of  $^{177}\text{Lu}$ -PSMA-617. SPECT: Single photon emission computed tomography.

late treatment-induced cranial nerve damage involving the third branch of the right trigeminal nerve after treatment of his cancer of the right tonsil.  $^{68}\text{Ga}$ -PSMA-11 PET/CT revealed no PSMA-negative lesions and no significant lytic bone destruction. Performance status was reported as 2, and laboratory tests were unremarkable. **Results:** The patient has received two applications of  $^{177}\text{Lu}$ -PSMA-617 to date. Reported side-effects included dry mouth, dry eye syndrome and nausea, which were managed with metoclopramide and artificial tears. The PSA level decreased substantially (from 896 ng/ml to 450 ng/ml after cycle 2), which has a favorable prognostic value for response to  $^{177}\text{Lu}$ -PSMA-617 therapy (2). Single photon emission computed tomography (SPECT) scans performed 24 hours after each  $^{177}\text{Lu}$ -PSMA-617 application showed significantly reduced radiopharmaceutical uptake in the left para-aortic lymph nodes and in the majority of bone metastases (Figure 2). A clinical benefit was observed, with the patient reporting the absence of pain and

demonstrating increased physical activity. *Conclusion:* This case demonstrates the clinical benefit of implementing <sup>177</sup>Lu-PSMA-617 radioligand therapy in a real-world setting. The patient, with heavily pre-treated mCRPC and significant comorbidities, tolerated the treatment well and showed an early biochemical, radiological and clinical response. Our experience demonstrates the PSMA-targeted radioligand therapy as a valuable option in the management of advanced mCRPC, particularly in patients with limited tolerance to conventional therapies.

1 Sartor O, de Bono J, Chi KN, Fizazi K, Herrmann K, Rahbar K, Tagawa ST, VISION Investigators: Lutetium-177-PSMA-617 for metastatic castration-resistant prostate cancer. *N Engl J Med* 385(12): 1091-1103, 2021. DOI: 10.1056/NEJMoa2107322

2 Armstrong AJ, Sartor O, de Bono J, Chi K, Fizazi K, Krause BJ, Herrmann K, Rahbar K, Tagawa ST, Saad F, Beer TM, Wu J, Mirante O, Morris MJ: Association of declining prostate-specific antigen levels with clinical outcomes in patients with metastatic castration-resistant prostate cancer receiving [<sup>177</sup>Lu]Lu-PSMA-617 in the Phase 3 VISION Trial. *Eur Urol* 85(5): 566-574, 2024. DOI: 10.1016/j.eururo.2024.08.021

**32**  
**IMPACT OF THE USE OF <sup>18</sup>F-PSMA PET/CT IN MEN WITH BIOCHEMICALLY RECURRENT PROSTATE CANCER AFTER PRIMARY TREATMENT ON A MULTI-DISCIPLINARY TREATMENT APPROACH**

Giorgio Caracciolo<sup>1</sup>, Sara Peri<sup>1</sup>, Suela Vukcaj<sup>2</sup>, Irene Gotuzzo<sup>3</sup>, Daniele Cignoli<sup>4</sup>, Michele Catellani<sup>4</sup>, Giovanni La Croce<sup>4</sup>, Paolo Barzaghi<sup>4</sup>, Maurizio Giovanni Agostino Portaluri<sup>2</sup>, Paola Anna Erba<sup>3</sup>, Luigi Filippo Da Pozzo<sup>1</sup> and Marco Roscigno<sup>1</sup>

<sup>1</sup>Department of Urology, ASST Papa Giovanni XXIII, University of Milan-Bicocca, Milan, Italy;

<sup>2</sup>Department of Radiation Oncology, ASST Papa Giovanni

XXIII, University of Milan-Bicocca, Milan, Italy;

<sup>3</sup>Department of Nuclear Medicine, ASST Papa Giovanni XXIII, University of Milan-Bicocca, Milan, Italy;

<sup>4</sup>Department of Urology, ASST Papa Giovanni XXIII, University of Milan-Bicocca, Milan, Italy

*Aim:* To evaluate the diagnostic role and clinical impact of <sup>18</sup>F-PSMA-1007 PET/CT in the restaging of patients with biochemical recurrence (BCR) after radical prostatectomy for prostate cancer (PCa). *Patients and Methods:* We retrospectively reviewed data of 184 patients with BCR after primary treatment for PCa who underwent prostate-specific membrane antigen (PSMA) PET/CT scans from September 2019 to March 2024 at our Institution. Therapeutic indications were modified by a multi-disciplinary team to develop a personalized treatment plan based on the number and localization of the disease highlighted by PET/CT scan. The impact of PET/CT on treatment was investigated by comparing the treatment based on PET/CT results with the standard planned treatment (salvage prostatic bed radiotherapy +/-ADT). BCR-free survival after “PET/CT-guided” treatment was evaluated by Kaplan Meier analysis and multivariate Cox analysis. *Results:* Median PSA level was 0.49 ng/ml. Out of 184 patients, PSMA PET/CT was negative in 40 patients (21.7%), while in 144 patients (78.3%), suspicious uptake sites for disease were identified: in the prostatic bed (9.8%), in lymph nodes (19.6%), and in bone or metastatic sites in other areas (48.9%). For statistical purposes, negative PET/CT results and those positive only in the prostatic bed (31.5%) were combined into a single category (Local Disease) as they did not change the therapeutic approach. The treatment plan changed in 60% of patients based on PET/CT findings according to MDT decisions. After a median follow-up of 24 months, 55% of patients experienced BCR. BCR-free survival was significantly higher in patients with Local Disease compared to those with extrapelvic nodal involvement (35 vs. 11 months) and those with bone metastases (35 vs. 19 months). However, no difference was observed between patients with Local Disease and those with pelvic nodal involvement only (35

vs. 29 months). Progression-free survival was significantly higher in patients with Local Disease compared to those with pelvic nodal involvement (41 vs. 34 months), with extrapelvic nodal involvement (41 vs. 22 months) and those with bone metastases (41 vs. 20 months). At multivariable Cox analysis, PET/CT positivity in extrapelvic nodes and bone sites emerged as an independent negative prognostic factor of BCR free survival. Instead, pelvic nodes, extrapelvic nodes and bone metastases were predictors of impaired progression-free survival. *Conclusion:* Our study confirmed the high positivity rate of PSMA PET/CT (78.3%) in patients with BCR after radical prostatectomy, which translates into a change in therapeutic choice in about approximately 60% of cases, guided by the PET/CT results. PET/CT positivity in extrapelvic nodes or bones represents a negative prognostic factor for BCR-free survival and progression-free survival after the “PET-guided” treatment.

### 35

#### **THE ACCURACY OF PSMA-PET/CT IN THE PREOPERATIVE STAGING OF INTERMEDIATE-UNFAVOURABLE AND HIGH-RISK PROSTATE CANCER PATIENTS**

Aurora Bagatin<sup>1</sup>, Graziella Zaffora<sup>1</sup>, Suela Vukcaj<sup>2</sup>, Irene Gotuzzo<sup>2</sup>, Daniele Cignoli<sup>1</sup>, Michele Catellani<sup>1</sup>, Giovanni La Croce<sup>1</sup>, Paolo Barzaghi<sup>1</sup>, Maurizio Giovanni Agostino Portalupi<sup>2</sup>, Paola Anna Erba<sup>3</sup>, Luigi Filippo Da Pozzo<sup>1</sup> and Marco Roscigno<sup>1</sup>

<sup>1</sup>Department of Urology, ASST Papa Giovanni XXIII, University of Milan-Bicocca, Milan, Italy;

<sup>2</sup>Department of Radiation Oncology, ASST Papa Giovanni XXIII, University of Milan-Bicocca, Milan, Italy;

<sup>3</sup>Department of Nuclear Medicine, ASST Papa Giovanni XXIII, University of Milan-Bicocca, Milan, Italy

*Aim:* To evaluate the impact of <sup>18</sup>F- prostate-specific membrane antigen (PSMA)-1007 PET/CT on preoperative staging and subsequent clinical management in a

population of intermediate-unfavorable or high-risk prostate cancer (PCa) patients. *Patients and Methods:* We retrospectively evaluated 226 patients who underwent primary staging with PSMA-PET/CT imaging from March 2022 to October 2024. Therapeutic indications were adjusted by a multidisciplinary team to create a personalized treatment plan based on PET/CT scan findings. The impact of the PET/CT on treatment was investigated by comparing the treatment decisions based on PET/CT results with the standard planned treatment. Multivariable logistic regression analyses (MVA) assessed predictors of PET positivity and change in management. Histological data from 130 patients who underwent RARP were collected and compared with PSMA-PET/CT results to assess its diagnostic accuracy. MVA was used to create three models predicting the probability of positive nodes at histology: a basic model including only clinical variables (age, PSA, ISUP grade and cT stage), a PET/CT model including only CT findings, and a full model including both the previous ones. The predictive accuracy (PA) of each model was quantified using the Area Under the Curve (AUC). *Results:* Median PSA was 7.54 ng/ml. Clinical stage was T1c, T2, T3-4 in 74, 81 and 46 patients. ISUP Grade Group (GG) 2, 3, 4 and 5 were detected in 33, 69, 85 and 39 patients. PET positivity, was observed in 102/226 (45%): pelvic nodes only in 19 patients, while extrapelvic nodes or bone metastases in 83 patients. PSMA-PET/CT changed treatment decisions in 59 patients (26%). MVA identified PSA as the only significant predictor of PSMA-PET/CT positivity, while PSA, ISUP grade group and PET positivity are predictors of treatment modifications. Evaluating histological results in the RARP subgroup, lymph node invasion (LNI) was found in 22 patients (17%), whilst was absent in 108 patients (83%). Overall, histopathology and PET imaging were concordant in 85% of cases and discordant in 15%. Among PET-negative cases, LNI was found in 9% patients (10/109). Conversely, among PET positive cases, LNI was absent at histology in 43% of patients (9/21). Finally, ROC curve analysis showed predicted probabilities of LNI at histology of 74%, 80% and 90% for PSMA-PET/CT, clinical parameters and

the two combined respectively. *Conclusion:* PSMA-PET/CT changed disease staging in up to 45% of patients and influenced the treatment choice in 25% of cases, even though oncological outcomes are yet to be evaluated. PSMA-PET/CT has high specificity, with 9% of PET-negative patients which may still show LNI at histology. Predictive accuracy should be further increased integrating PET/CT findings into a comprehensive evaluation of clinicopathological parameters.

### 37

#### **COMPARISON BETWEEN MICRO-ULTRASOUND AND MULTIPARAMETRIC MRI-TARGETED BIOPSY. A SINGLE INSTITUTIONAL EXPERIENCE**

Giuliana Martello, Daniele Cignoli, Marco Guido Negri, Paolo Barzaghi, Michele Catellani, Giovanni La Croce, Stefano Corti, Antonino Sacca', Luigi Filippo Da Pozzo and Marco Roscigno

Department of Urology, ASST Papa Giovanni XXIII, University of Milan-Bicocca, Milan, Italy

*Aim:* This study aimed to analyze our initial experience with the Exact-VU™ system and compare the diagnostic accuracy of micro-ultrasound (microUS) and multiparametric MRI (mpMRI) in detecting clinically significant prostate cancer (csPCa). *Patients and Methods:* From January 2024 to March 2025, 287 consecutive patients, previously submitted to mpMRI for elevated PSA or abnormal DRE findings, underwent prostate biopsy using the ExactVu™ 29 MHz microUS system. Prostate imaging was performed by two urologists experienced in conventional ultrasound and fusion biopsy, but initially naïve to micro-US. Both urologists completed standardized online training and were supported by a product specialist. Before biopsy, the prostate was evaluated using an EV 29 L MHz side-fire transducer (Exact Imaging, Markham, Canada), with suspicious lesions recorded in real-time using the PRI-MUS protocol. The operator performing microUS was blinded to

mpMRI results. mpMRI images were uploaded by another operator before microUS scanning and were not available until micro-US scanning was completed. Lesions detected by micro-US were targeted with 3 samples, while MRI-targeted biopsies (3 samples) were performed using the Fusion-Vu device on the Exact-Vu system. No additional targeted samples were taken when micro-US and mpMRI lesions were identified at the same location. All patients subsequently received systematic biopsy in regions without suspicious lesions on micro-US and mpMRI. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of microUS for csPCa were calculated using the pathology results from any biopsy sample. The predictive accuracy (PA) of both micro-US and mpMRI for csPCa detection was quantified using the Area Under the Curve (AUC). Clinically significant cancer (csPCa) was defined as Gleason pattern >3 tissue (Gleason Sum  $\geq 7$ , Grade Group  $\geq 2$ ). *Results:* csPCa was detected in 46% (132/287) of patients. The detection rate of csPCa for PRIMUS 2, 3, 4, and 5 was 34%, 43%, 74%, and 93%, respectively ( $p < 0.001$ ). The detection rate for PI-RADS 2, 3, 4, and 5 was 26%, 38%, 49%, and 74%, respectively ( $p = 0.006$ ). Sensitivity, specificity, PPV, and NPV for csPCa detection were 61%, 65%, 60%, and 69% with PRI-MUS  $\geq 3$ , and 89%, 58%, 51%, and 75% with PI-RADS  $\geq 3$ , respectively. ROC analyses showed similar predictive accuracy for PRI-MUS and PI-RADS (AUC=0.67 and 0.66, respectively;). The csPCa detection rate for negative MRI and microUS was 18% (7/38 pts), while for positive MRI and microUS it was 62% (64/103 pts). *Conclusion:* In our population, micro-US showed comparable predictive accuracy in the detection of csPCa. Moreover, the combination of both techniques may increase detection of csPCa and help stratifying PI-RADS lesions at higher risk of csPCa detection.

### 39

#### **THE ASSOCIATION BETWEEN PROSTATE HEALTH INDEX DENSITY AND GLEASON SCORE UPGRADING PATIENTS WITH PROSTATE CANCER**

Francesco Pellegrino<sup>1</sup>, Marco Tozzi<sup>1</sup>, Giuseppe Fallara<sup>1</sup>,  
Francesco Chierigo<sup>1</sup>, Martina Maggi<sup>1</sup>,  
Letizia Maria Ippolita Jannello<sup>1</sup>, Andrea Triggiani<sup>1</sup>,  
Vincenzo Martorello<sup>1</sup>, Clara Marzorati<sup>1</sup>, Savino Doronzo<sup>1</sup>,  
Federico Lesma<sup>1</sup>, Emanuela Santangelo<sup>1</sup>,  
Oliviero Guglielmo<sup>1</sup>, Mattia Sangalli<sup>1</sup>,  
Tiziana Gemma Gerace<sup>1</sup>, Barbara Mangiarotti<sup>1</sup>,  
Emanuele Itri<sup>1</sup>, Stefano Paparella<sup>1</sup>, Rosa Sirica<sup>2</sup>,  
Carmela Polito<sup>2</sup>, Mariano Fiorenza<sup>2</sup>, Evelina La Civita<sup>2</sup>,  
Paolo Bernardini<sup>1</sup>, Alberto Del Nero<sup>1</sup>, Roberto Bianchi<sup>1</sup>,  
Daniela Terracciano<sup>2</sup> and Matteo Ferro<sup>1</sup>

<sup>1</sup>Urology Division, ASST Santi Paolo and Carlo,  
Milan, Italy;

<sup>2</sup>Department of Translational Medical Sciences,  
University of Naples Federico II, Naples, Italy

**Background/Aim:** Gleason Score (GS) undergrading at biopsy has important implications for patient management, potentially leading to suboptimal or inappropriate treatment decisions. Several biomarkers – such as prostate-specific antigen (PSA), PSA density (PSAD), the Prostate Health Index (PHI), and PHI density (PHID) – are commonly used to identify patients at risk for clinically significant prostate cancer (csPCa) at the time of biopsy. However, limited evidence is available regarding the ability of these markers to predict upgrading from biopsy to the final histopathological findings after radical prostatectomy (RP). This study aimed to evaluate the association between these markers and the risk of upgrading. **Patients and Methods:** We analyzed a cohort of 126 patients who underwent RP after targeted prostate biopsy. We excluded patients with biopsy ISUP (bISUP) grade 5. The outcome of the study was GS upgrading from biopsy to final pathology after RP. To evaluate the association between biomarkers – including PSA, PSAD, PHI, and PHID – and the risk of upgrading, we performed multivariable logistic regression analyses (MVA) adjusted for clinical stage, PIRADS score, and bISUP. For each model, we calculated the Area Under the Curve (AUC) to assess predictive accuracy. The DeLong test was used to compare

the performance of the models. Additionally, the LOESS smoothing function was applied to graphically illustrate the relationship between PHID and the probability of upgrading by PI-RADS score. **Results:** Median PSA, PSAD, PHI, and PHID were 6.20 ng/ml (IQR=4.72-8.03), 0.15 (IQR=0.10-0.24), 58 (IQR=44-73), and 1.40 (IQR=0.80-2.62), respectively. Overall, 52 (41%), 26 (21%), 17 (13%), and 31 (25%) patients had a biopsy ISUP (bISUP) grade of 1, 2, 3, and 4-5, respectively. At final pathology, 19 (15%), 10 (7.9%), 16 (13%), and 81 (64%) had an ISUP grade of 1, 2, 3, and 4-5, respectively. In total, 74 (59%) patients experienced upgrading at RP. In MVA, only PHI [odds ratio (OR)=1.01; 95% confidence interval (CI)=1.01-1.03] and PHID (OR=1.53; 95% CI=1.09-2.27) were significantly associated with upgrading. The model including PHID showed a higher AUC (0.83 vs. <0.81) and demonstrated superior accuracy compared to other models based on the DeLong test ( $p<0.05$ ). As shown by the LOESS function, the risk of upgrading steadily increases (from 20% to 90%) with increasing PHID values. In patients with PIRADS  $\leq 3$ , the risk of upgrading was approximately 40% for PHID values  $<2.5$  but rose sharply for PHID values  $>2.5$ . **Conclusion:** PHID appears to be a valuable biomarker for predicting GS upgrading in patients with PCa. Its integration into clinical practice and prediction tools may enhance patient risk stratification and aid in selecting the most appropriate treatment approach. Further prospective studies are necessary to validate and confirm these data.

#### 40 DEVELOPMENT AND PHASE-1 VALIDATION OF PREVES-HOR: AN ADT-SPECIFIC PATIENT-REPORTED OUTCOME MEASURE FOR PROSTATE-CANCER QUALITY OF LIFE

Carlo Buonerba<sup>1</sup>, Raffaele Baio<sup>2</sup>,  
Francesco Grillone<sup>3</sup>, Francesco Passaro<sup>4</sup>,  
Antonella Ferraioli<sup>5</sup>, Eleonora Monteleone<sup>4</sup>,  
Sabrina Rossetti<sup>6</sup>, Francesco Prata<sup>7,8</sup>, Oriana Strianese<sup>5</sup>,  
Concetta Ingenito<sup>5</sup>, Francesco Maiorino<sup>9</sup>,

Rocco Papalia<sup>7,8</sup>, Raffaella Francesca Leo<sup>5</sup>,  
Alfredo Tartarone<sup>10</sup>, Giovanni Bozza<sup>11</sup>, Matteo Ferro<sup>12</sup>,  
Pierluigi Bove<sup>13</sup>, Aniello Donnarumma<sup>14</sup>, Felice Crocetto<sup>15</sup>,  
Sisto Perdonà<sup>16</sup>, Vittorio Riccio<sup>17</sup>, Franco Morelli<sup>18</sup>,  
Antonio Aliberti<sup>19</sup>, Francesca Cappuccio<sup>5</sup>,  
Vittorino Montanaro<sup>20</sup>, Giacomo Metta<sup>21</sup>,  
Luca Scafuri<sup>1,5</sup> and Giuseppe Di Lorenzo<sup>1,5</sup>

<sup>1</sup>O.R.A. ETS - Oncology Research Assistance  
Association, Salerno, Italy;

<sup>2</sup>Department of Urology, Umberto I Hospital,  
Nocera Inferiore, Salerno, Italy;

<sup>3</sup>Medical Oncology Unit, "Mater-Domini"  
University Hospital, Catanzaro, Italy;

<sup>4</sup>Department of Urology, National Cancer Institute  
IRCCS "Fondazione G. Pascale", Naples, Italy;

<sup>5</sup>Oncology Unit, "Andrea Tortora" Hospital,  
ASL Salerno, Salerno, Italy;

<sup>6</sup>Department of Urology & Gynecology, National Cancer  
Institute IRCCS "Fondazione G. Pascale", Naples, Italy;

<sup>7</sup>Department of Urology, Campus Bio-Medico  
University Hospital Foundation, Rome, Italy;

<sup>8</sup>Research Unit of Urology, Campus Bio-Medico  
University Hospital Foundation, Rome, Italy;

<sup>9</sup>Director, Robotic and Minimally Invasive Urology Unit,  
Tor Vergata University Hospital, Rome, Italy;

<sup>10</sup>Division of Medical Oncology, Department of Onco-  
Hematology, IRCCS-CROB, Rionero in Vulture, Italy;

<sup>11</sup>Division of Medical Oncology, Department of Onco-  
Hematology, IRCCS-CROB, Rionero in Vulture, Italy;

<sup>12</sup>Division of Urology, European Institute  
of Oncology IRCCS, Milan, Italy;

<sup>13</sup>Department of Experimental Medicine,  
University of Rome Tor Vergata, Rome, Italy;

<sup>14</sup>Hematology Unit, "A. Tortora" Hospital -  
Pagani, ASL Salerno, Italy;

<sup>15</sup>Urology Unit, Department of Neurosciences,  
Reproductive Sciences and Odontostomatology,  
University of Naples "Federico II," Naples, Italy;

<sup>16</sup>Urology Department, National Cancer Institute IRCCS  
"Fondazione G. Pascale", Naples, Italy;

<sup>17</sup>Santa Maria della Pietà Hospital, Naples, Italy;

<sup>18</sup>Oncology Unit, Casa Sollievo della Sofferenza,  
San Giovanni Rotondo, Italy;

<sup>19</sup>Urology Unit, "Fucito" Hospital, Salerno, Italy;

<sup>20</sup>Urology Unit, San Leonardo Hospital,  
Castellammare di Stabia, Naples, Italy;

<sup>21</sup>Medical Director, Azienda Ospedaliera  
Sant'Anna and San Sebastiano di Caserta, Naples, Italy

*Background/Aim:* Androgen-deprivation therapy (ADT) is pivotal in prostate-cancer management yet provokes physical, emotional, cognitive, sexual and body-image sequelae that the established patient-reported-outcome (PRO) instruments under-represent (1-3). PREVES-HOR, a 29-item questionnaire anchored to patient-perceived distress, was developed to quantify this ADT-specific burden. In this study, we report on its Phase-1 psychometric validation. *Patients and Methods:* PREVES-PEARL is a multicenter, cross-sectional survey. Between February 2025 and March 2025, 145 Italian-speaking men (median age 75 years) receiving continuous ADT for  $\geq 30$  days completed PREVES-HOR plus comparator scales for fatigue (REST), anxiety-depression (HEAL-BDLC), well-being (WHO-5) and sleep quality (PEACE). Internal consistency was estimated with Cronbach's  $\alpha$  and McDonald's  $\omega$ . Dimensionality was explored by exploratory factor analysis (polychoric matrix, principal-axis factoring, oblimin rotation, Horn parallel analysis). Convergent validity was assessed with Spearman correlations between PREVES-HOR (total and domain scores) and the comparator scales. *Results:* PREVES-HOR exhibited excellent reliability ( $\alpha=0.95$ ;  $\omega=0.97$ ; domain  $\alpha=0.80-0.95$ ). Six factors - physical fatigue and pain, emotional well-being, mental clarity, quality-of-life/stress, sexual health and body image - explained 79% of total variance, while a dominant general-distress factor accounted for  $\sim 50\%$  of the total variance. Twenty-five of 29 items satisfied communality  $\geq 0.40$  and cross-loading  $< 0.30$ . The total PREVES-HOR score correlated strongly with fatigue (REST  $\rho=0.69$ ) and anxiety-depression (HEAL-BDLC  $\rho=0.78$ ) and inversely with well-being (WHO-

5  $\rho=-0.49$ ) and sleep quality (PEACE  $\rho=-0.37$ ) (all  $p<0.001$ ), confirming convergent but non-redundant validity. *Conclusion:* Phase-1 data demonstrate that PREVES-HOR possesses robust internal consistency, a stable six-factor structure and meaningful convergence with related constructs, indicating that it captures clinically important ADT-related distress overlooked by broader tools such as EPIC or FACT-P. The forced-choice, no-skip design prevented missing data but may inflate reliability; responsiveness, test-retest stability, minimally important difference and cross-cultural adaptation will be addressed in a planned 1000-patient Phase-2/3 program. Pending confirmation, PREVES-HOR could complement existing PROs to individualize supportive care and evaluate interventions aimed at mitigating the burden of ADT.

1 Wei JT, Dunn RL, Litwin MS, Sandler HM, Sanda MG: Development and validation of the expanded prostate cancer index composite (EPIC) for comprehensive assessment of health-related quality of life in men with prostate cancer. *Urology* 56: 899-905, 2000. DOI: 10.1016/s0090-4295(00)00858-x

2 Dun YJ, Liu HX, Yu LP, Li Q, Zhang XW, Tang X, Qin C-P, Xu TL: Development and initial validation of the novel scale for assessing quality of life of prostate-cancer patients receiving androgen-deprivation therapy. *Chin Med J (Engl)* 130: 2082-2087, 2017. DOI: 10.4103/0366-6999.213416.

3 Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JCM, Stein Kaasa S, Marianne Klee M, Osoba D, Razavi D, Rofe PB, Schraub S, Sneeuw K, Sullivan M, Takeda F: The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 85: 365-376, 1993. DOI: 10.1093/jnci/85.5.365

#### 41

### **EFFICACY OF INTRAVESICAL BCG IN PATIENTS AGED OVER 75 YEARS WITH HIGH-RISK NON-MUSCLE-INVASIVE BLADDER CANCER**

Marco Tozzi<sup>1</sup>, Francesco Pellegrino<sup>1</sup>, Giuseppe Fallara<sup>1</sup>, Francesco Chierigo<sup>1</sup>, Martina Maggi<sup>1</sup>, Letizia Maria Ippolita Jannello<sup>1</sup>, Andrea Triggiani<sup>1</sup>, Vincenzo Martorello<sup>1</sup>, Savino Doronzo<sup>1</sup>, Federico Lesma<sup>1</sup>, Clara Marzorati<sup>1</sup>, Emanuela Santangelo<sup>1</sup>, Roberto Bianchi<sup>1</sup>, Giuseppe Lucarelli<sup>2</sup>, Fabrizio Verweij<sup>3</sup>, Marco Racioppi<sup>4</sup>, Andrea Conti<sup>5</sup>, Giovanni Liquori<sup>6</sup>, Emanuele Montanari<sup>7</sup>, Alessandro Antonelli<sup>8</sup>, Fabrizio Dal Moro<sup>9</sup>, Giuseppe Carrieri<sup>10</sup>, Luigi Cormio<sup>10</sup>, Carlo Terrone<sup>11</sup>, Francesco Porpiglia<sup>12</sup>, Roberto Contieri<sup>13</sup> and Matteo Ferro<sup>1</sup>

<sup>1</sup>ASST Santi Paolo and Carlo, Urology Division, Milan, Italy;

<sup>2</sup>Department of Precision and Regenerative Medicine and Ionian Area, Urology, Andrology and Kidney Transplantation Unit,

University of Bari "Aldo Moro", Bari, Italy;

<sup>3</sup>ASST Urology, Viale Concordia, Cremona, Italy;

<sup>4</sup>IRCCS University Hospital "Fondazione Gemelli", Rome, Italy;

<sup>5</sup>IRCCS Galeazzi Hospital, Milan, Italy;

<sup>6</sup>Giuliano Isontina University Health Authority (ASU GI), Trieste, Italy;

<sup>7</sup>Department of Urology, IRCCS Ca' Granda Foundation – Ospedale Maggiore Policlinico, Milan, Italy;

<sup>8</sup>Department of Urology, University of Verona, Verona, Italy;

<sup>9</sup>Urology Clinic, Department of Surgery, Oncology and Gastroenterology, University of Padua, Padua, Italy;

<sup>10</sup>Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy;

<sup>11</sup>Department of Surgical and Diagnostic Integrated Sciences (DISC), University of Genoa, Policlinico San Martino Hospital, Genoa, Italy;

<sup>12</sup>Department of Urology, San Luigi Gonzaga Hospital, University of Turin, Orbassano, Turin, Italy;

<sup>13</sup>National Cancer Institute of Naples – IRCCS "Fondazione G. Pascale", Naples, Italy

*Background/Aim:* Bladder cancer (BCa) primarily affects the elderly, and its incidence is expected to rise further with the aging population. Intravesical Bacillus Calmette-

Guérin (BCG) remains the treatment of choice for patients with high-risk non-muscle-invasive bladder cancer (NMIBC). However, the optimal management of BCa in elderly patients remains uncertain and is still a subject of debate. This study aimed to evaluate the efficacy of BCG immunotherapy in elderly patients with high-risk NMIBC. *Patients and Methods:* We analyzed 344 patients diagnosed with high-risk NMIBC between 2014 and 2023 and who received either BCG therapy or no intravesical treatment. The study outcomes were cancer recurrence and progression, defined as an increase in tumor stage and/or grade. Multivariate Cox models were used to assess the association between age, number of BCG installations and oncological outcomes. The analyses were adjusted for the 2004 WHO risk classification (high vs. very high risk). We then examined whether the effect of BCG varied with patient age using interaction analyses. Finally, we plotted the hazard ratios (HR) from our models against age, to evaluate how the effect of BCG changed across the age spectrum. *Results:* Among 344 patients, the median age was 74 years [interquartile range (IQR)=69-80]. Overall, 24 (7.0%), 229 (67%), and 91 (26%) patients had Carcinoma *in situ* (CIS), T1, and Ta tumors, respectively. According to the 2004 WHO risk classification, 135 (39%) patients were very high risk. Overall, 287 (83%) received intravesical BCG, with a median number of instillations of 6.0 (IQR=5.0-9.0). At a median follow-up of 18 months (IQR=11-29) among patients without recurrence, 139 patients (40%) experienced recurrence, while 60 patients (17%) experienced progression. Multivariate analysis demonstrated that a higher number of BCG instillations was significantly associated with a reduced risk of both recurrence (HR=0.93; 95% CI=0.90-0.97) and progression (HR=0.92; 95% CI=0.87-0.97). Increasing age was independently associated with a higher risk of progression (HR=1.03; 95% CI=1.00-1.06) and recurrence (HR=1.02; 95% CI=1.01-1.04). Interaction analysis revealed a significant negative interaction between age and the number of BCG instillations ( $p<0.05$ ), suggesting a reduced therapeutic effect of BCG in older patients.

Graphical representation of HRs across age showed that the protective effect of BCG (HR<1) was evident in patients <75 years, whereas in those >75 years, the HR exceeded 1 for both recurrence and progression, suggesting a diminished benefit of BCG therapy in this age group. *Conclusion:* BCG remains a key therapeutic option in NMIBC, even in elderly patients. However, its efficacy appears reduced in individuals aged over 75. These findings suggest that age should be considered when tailoring treatment strategies and follow-up protocols in high-risk NMIBC patients.

## 42

### THE KEY VALUE OF PROSTATE HEALTH INDEX (PHI) FOR THE PREDICTION OF ADVERSE PATHOLOGICAL FEATURES IN PROSTATE CANCER PATIENTS UNDERGOING RADICAL PROSTATECTOMY

Clara Marzorati<sup>1</sup>, Francesco Pellegrino<sup>1</sup>, Giuseppe Fallara<sup>1</sup>, Francesco Chierigo<sup>1</sup>, Martina Maggi<sup>1</sup>, Letizia Maria Ippolita Jannello<sup>1</sup>, Marco Tozzi<sup>1</sup>, Andrea Triggiani<sup>1</sup>, Savino Doronzo<sup>1</sup>, Vincenzo Martorello<sup>1</sup>, Federico Lesma<sup>1</sup>, Emanuela Santangelo<sup>1</sup>, Oliviero Guglielmo<sup>1</sup>, Angelica Grasso<sup>1</sup>, Matteo Giulio Spinelli<sup>1</sup>, Igor Piacentini<sup>1</sup>, Nicola Macchione<sup>1</sup>, Paolo Dell'Orto<sup>1</sup>, Rosa Sirica<sup>2</sup>, Carmela Polito<sup>2</sup>, Mariano Fiorenza<sup>2</sup>, Evelina La Civita<sup>2</sup>, Roberto Bianchi<sup>1</sup>, Daniela Terracciano<sup>2</sup> and Matteo Ferro<sup>1</sup>

<sup>1</sup>ASST Santi Paolo and Carlo, Urology Division, Milan, Italy;

<sup>2</sup>Department of Translational Medical Sciences, University of Naples Federico II, Naples, Italy

*Background/Aim:* The Prostate Health Index (PHI) has shown its utility in clinical practice in identifying patients at high risk of prostate cancer (PCa) who may require a biopsy. However, its role in identifying PCa patients at higher risk of adverse pathology at the time of radical

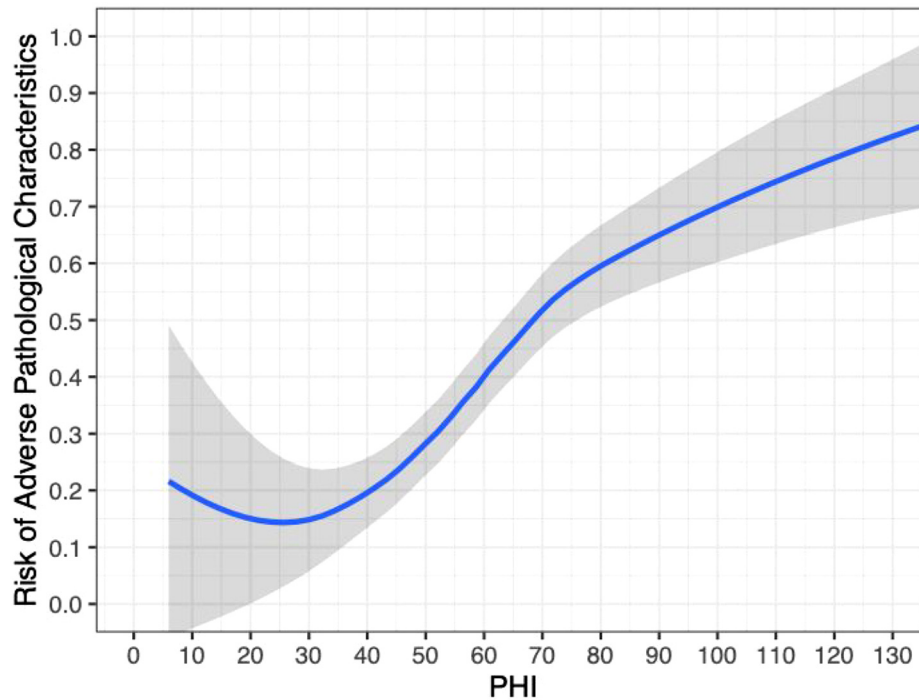


Figure 1. LOESS curve showing the rising risk of adverse pathology with increasing PHI values, notably above 40.

prostatectomy (RP) remains unclear. This study aimed to assess whether PHI or PHI density (PHID) is associated with adverse pathological features in patients undergoing RP. *Patients and Methods:* We analyzed a cohort of 126 patients who underwent RP following a targeted biopsy, with PHI measurement at the time of prostate biopsy. The primary outcome of the study was the presence of adverse pathological features at RP, defined as pT3-4 and/or pN1 disease. We evaluated the association of PHI, PHID, PSA, or PSA density (PSAD) with the outcome using four multivariable models adjusted for key clinical variables, including clinical stage, PI-RADS score, and ISUP grade group (ISUP G) at biopsy. The area under the curve (AUC) was calculated for each model, and model accuracies were compared using the DeLong test. Finally, we illustrated the association between PHI and adverse pathological features using the LOESS function. *Results:* Median values for PSA, PSAD, PHI, and PHID were 6.20 ng/ml [interquartile range (IQR)=4.72-8.03], 0.15 ng/ml/cm<sup>3</sup> (IQR=0.10-0.24), 58 (IQR=44-73), and 1.40 (IQR=0.80-

2.62), respectively. Overall, 15 patients had a suspicious digital rectal examination. The distribution of PI-RADS scores was 4% for PI-RADS 1, 17% for PI-RADS 3, and 79% for PI-RADS 4-5. Regarding biopsy results, 52 (41%), 26 (21%), 17 (13%), 31 (25%) had ISUPG 1, 2, 3, and 4-5. At RP, 47 patients (37%) presented with adverse pathological features, with 43 showing pT $\geq$ 3 disease and 5 having pN1 involvement. Overall, 19 (15%), 10 (7.9%), 16 (13%), 81 (63%) patients had ISUP 1, 2, 3, 4-5 at final pathology. Only the multivariate logistic models including PHI [odds ratio (OR)=1.04; 95% confidence interval (CI)=1.02-1.06] and PSA (OR=1.37; 95% CI=1.09-1.75) were significantly associated with adverse pathology. The model including PHI demonstrated the highest discriminative ability, with an AUC of 0.88 compared to  $\leq$ 0.83 for the other models and outperformed them in accuracy according to the DeLong test ( $p < 0.05$ ). As shown by the LOESS function (Figure 1), the risk of adverse features was approximately 20% for PHI values  $< 40$  but increased sharply for PHI values  $> 40$ . *Conclusion:* PHI is

associated with an increased risk of adverse pathological features in PCa patients undergoing radical prostatectomy. Using a cutoff value of 40, PHI may serve as a useful tool for stratifying patients prior to surgery. Future studies should explore the integration of PHI into nomograms for predicting adverse pathological outcomes at RP.

### 43

#### **STEREOTACTIC BODY RADIATION THERAPY FOR THE RE-IRRADIATION OF LOCAL RELAPSE OF PROSTATE CANCER: RESULTS IN TERMS OF OUTCOMES AND TOXICITY**

Raffaella Lucchini<sup>1</sup>, Marco Badalamenti<sup>2</sup>,  
Luciana Di Cristina<sup>1</sup>, Lorenzo Lo Faro<sup>1</sup>,  
Marta Scorsetti<sup>1,2</sup> and Ciro Franzese<sup>1,2</sup>

<sup>1</sup>Humanitas Clinical and Research  
Center –IRCCS, Milan, Italy;

<sup>2</sup>Department of Biomedical Sciences,  
Humanitas University, Milan, Italy

*Aim:* To conduct a retrospective assessment of toxicity and clinical outcomes associated with re-irradiation (re-RT) in patients experiencing macroscopic local recurrence of prostate cancer (PCa) who previously received definitive or postoperative radiotherapy (RT). *Patients and Methods:* In our institution, 36 patients with local relapse following prior definitive or postoperative RT were treated with Stereotactic Body Radiotherapy (SBRT). The prescribed dose ranged from 25 to 30 Gy delivered in 5 fractions. Gastrointestinal (GI) and genitourinary (GU) side effects were documented according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. The primary endpoints included biochemical relapse-free survival (BRFS) and distant metastasis-free survival (DMFS), evaluated through Kaplan-Meier survival analysis. Both univariate and multivariate Cox regression were used to explore the relationship between clinical variables and survival outcomes. *Results:* Out of the total, 26 patients had

previously undergone definitive RT, while 10 had received postoperative RT. At the time of re-RT, the median prostate-specific antigen (PSA) level was 2.57 ng/ml (range=0.23-13.10). Local relapse was identified via choline-PSMA PET or MRI in 18, 17, and 1 patient, respectively. The median clinical target volume (CTV) was 17.8 cc (range=1-93.1). In 39% of cases, the target was the visible macroscopic recurrence, whereas in 61%, the entire prostate or prostate bed was targeted. The median follow-up duration was 28.2 months. No late adverse effects >G2 were observed. Only one patient experienced grade 2 GI toxicity, while 8 patients experienced GU side effects (6 with grade 1 and 2 with grade 2). The median BRFS was 19 months, with 1-year and 2-year BRFS rates of 63.5% (95% CI=42.5-78.6) and 37.0% (95% CI=17.5-56.8), respectively. Univariate analysis revealed that PSA level at the time of re-RT was a significant predictor of BRFS (HR=1.43, 95% CI=1.19-1.73;  $p=0.000$ ). The 1- and 2-year DMFS rates were 88.0% (95% CI=66.8-96.0) and 72.4% (95% CI=48.1-86.8). The median DMFS was 19.6 months for patients treated targeting the relapsing nodule, whereas it was not reached for those treated on the entire prostate or surgical bed. In univariate analysis, irradiation of the macroscopic recurrence versus whole gland/bed (HR=5.91, 95% CI=1.35-25.80;  $p=0.018$ ) and higher PSA at re-RT (HR=1.20, 95% CI=1.01-1.41;  $p=0.030$ ) were associated with worse outcomes. Multivariate analysis confirmed that treating only the macroscopic recurrence was an independent predictor of better prognosis (HR=4.48, 95% CI=1.09-18.37;  $p=0.037$ ). *Conclusion:* Re-RT in patients previously treated with definitive or postoperative RT appears to be a safe approach, with encouraging toxicity profiles and promising biochemical control results.

### 44

#### **METACHRONOUS OLIGOMETASTATIC HORMONE-SENSITIVE PROSTATE CANCER TREATED WITH STEREOTACTIC BODY RADIATION THERAPY: EVALUATION OF THE OUTCOME AND PREDICTIVE FACTORS OF LONG-TERM DISEASE CONTROL**

Luciana Di Cristina, Raffaella Lucchini, Lorenzo Lo Faro, Marco Badalamenti, Marta Scorsetti and Ciro Franzese

Radiotherapy and Radiosurgery Department,  
Humanitas Research Hospital, Rozzano, Italy

*Aim:* To evaluate clinical outcomes and impact of radiation therapy on systemic therapy in metachronous oligometastatic hormone-sensitive prostate cancer (PCa) patients receiving Stereotactic Body Radiation Therapy (SBRT). *Patients and Methods:* This retrospective study included patients treated with SBRT for a maximum of 5 oligometastases. Only patients naïve to systemic therapy were included in the study. End-points of the study were progression-free survival (PFS), systemic-therapy free survival (STFS), local control (LC) and overall survival (OS). *Results:* We included a total of 69 PCa patients treated with 97 SBRT courses for 121 oligometastases. Among these, 90 (74%) were nodal metastases and 31 (26%) were bone lesions. Median time to metastases (disease free interval, DFI) was 32.4 months (range=3-148). Patients received a median radiation dose of 40 Gy in 1 to 6 fractions, with a median BED10 of 79 Gy (range=37-105). The median total tumor volume was 1.9 cc (range=0.1-233.4). With a median follow-up of 39.8 months, median PFS was 12.6 months, with 1- and 2-year rates of 59.8%, and 35.6%, respectively. PFS was significantly lower in patients with DFI  $\leq$ 24 months ( $p=0.002$ ), with 1- and 2-years rates of 42.2%, and 21.8% for DFI  $\leq$ 24 months, and 69.5% and 43.0% for DFI  $>$ 24 months. Also, ISUP group was a significant predictor of PFS ( $p=0.022$ ), with 1- and 2-year PFS rates of 63.6% and 38.6% for Grade Group 1-3, and 40% and 20% for Grade Group 4-5. Considering the combination of DFI and ISUP group as predictive factors, median PFS was 19.5 months for patients with no risk factors, 11.7 months for patients with either Grade group 4-5 or DFI  $\leq$ 24 months, and 3.9 months for patients with both ISUP 4-5 and DFI  $\leq$ 24 months. Twenty-one patients received multiple SBRT courses for subsequent oligometastatic disease after first treatment. The median time to systemic therapy activation

was 26.3 months, with 1-, and 2-years STFS rates of 78.2%, and 54.2% respectively. The median LC was not reached, with 1- and 2-year rates of 89% and 83%, respectively. All patients were alive at time of analysis. *Conclusion:* The study highlights the importance of DFI, ISUP Grade group, and their combination to predict treatment outcomes in patients with oligometastatic hormone-sensitive PCa. These findings underline the importance of selecting patients who could benefit from SBRT, offering long-term disease control and potentially delaying the need for systemic therapy.

#### 45

#### **CLINICAL PREDICTORS OF BCG-RELATED TOXICITY IN PATIENTS WITH NMIBC: IMPACT OF AGE AND SMOKING**

Giuseppe Fallara<sup>1</sup>, Marco Tozzi<sup>1</sup>, Francesco Pellegrino<sup>1</sup>, Francesco Chierigo<sup>1</sup>, Martina Maggi<sup>1</sup>, Letizia Maria Ippolita Jannello<sup>1</sup>, Andrea Triggiani<sup>1</sup>, Federico Lesma<sup>1</sup>, Savino Doronzo<sup>1</sup>, Clara Marzorati<sup>1</sup>, Vincenzo Martorello<sup>1</sup>, Emanuela Santangelo<sup>1</sup>, Oliviero Guglielmo<sup>1</sup>, Mattia Sangalli<sup>1</sup>, Roberto Bianchi<sup>1</sup>, Giuseppe Lucarelli<sup>2</sup>, Fabrizio Verweij<sup>3</sup>, Marco Racioppi<sup>4</sup>, Andrea Conti<sup>5</sup>, Giovanni Liquori<sup>6</sup>, Emanuele Montanari<sup>7</sup>, Alessandro Antonelli<sup>8</sup>, Fabrizio Dal Moro<sup>9</sup>, Giuseppe Carrieri<sup>10</sup>, Luigi Cormio<sup>10</sup>, Carlo Terrone<sup>11</sup>, Francesco Porpiglia<sup>12</sup>, Roberto Contieri<sup>13</sup> and Matteo Ferro<sup>1</sup>

<sup>1</sup>ASST Santi Paolo and Carlo, Urology Division, Milan, Italy;

<sup>2</sup>Department of Precision and Regenerative Medicine and Ionian Area, Urology, Andrology and Kidney Transplantation Unit, University of Bari "Aldo Moro", Bari, Italy;

<sup>3</sup>ASST Urology Cremona, Cremona, Italy;

<sup>4</sup>IRCCS University Hospital

"Fondazione Gemelli", Rome, Italy;

<sup>5</sup>IRCCS Galeazzi Hospital, Milan, Italy;

<sup>6</sup>Giuliano Isontina University Health Authority (ASU GI), Trieste, Italy;

<sup>7</sup>Department of Urology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy;

<sup>8</sup>University of Verona, Department of Urology, Verona, Italy;

<sup>9</sup>Urology Clinic, Department of Surgery, Oncology and Gastroenterology, University of Padua, Padua, Italy;

<sup>10</sup>Department of Urology and Renal Transplantation, University of Foggia, Foggia, Italy;

<sup>11</sup>Department of Surgical and Diagnostic Integrated Sciences (DISC), University of Genoa, Policlinico San Martino Hospital, Genoa, Italy;

<sup>12</sup>Department of Urology, San Luigi Gonzaga Hospital, University of Turin, Orbassano, Turin, Italy;

<sup>13</sup>National Cancer Institute of Naples – IRCCS “Fondazione G. Pascale”, Naples, Italy

*Background/Aim:* Intravesical Bacillus Calmette-Guérin (BCG) is the treatment of choice for patients with intermediate and high-risk non-muscle-invasive bladder cancer (NMIBC). However, its use is often limited by a high incidence of adverse events (AE). This study aimed to evaluate the incidence of BCG-related AE in patients with NMIBC and to identify clinical predictors of treatment intolerance. *Patients and Methods:* We retrospectively analyzed 329 patients treated with BCG for NMIBC between 2014 and 2023. Clinical, demographic, and pathological features were compared between patients who experience AEs and those who did not. Two multivariate logistic regression models (MVA) were performed to identify independent predictors of AEs and treatment discontinuation due to toxicity. Variables included in the models were age, comorbidity burden (Charlson Comorbidity Index - CCI), sex, smoking status (active vs. no), and tumor characteristics. *Results:* A total of 156 patients (47.4%) developed at least one BCG-related AE, with 112 (72%) of them discontinued treatment before completing the planned schedule due to toxicity. The most commonly reported AEs were cystitis (83%), fever (9%), epididymis/orchitis (3.8%), and

hematuria (3.2%). Median age and CCI among patients who experienced AEs were 75 years [interquartile range (IQR)=69-80] and 6.00 (IQR=5.00-7.00), compared to 72 years (IQR=64-79) and 6.00 (IQR=4.00-7.00), respectively, among those who did not. In the AE group vs. non-AE group, 140 (81%) vs. 119 (76%) were male, and 42 (24%) vs. 52 (33%) were active smokers. The distribution of tumor stage was similar: carcinoma in situ (Tcis) (6.4% vs. 3.8%), Ta (29% vs. 28%), and T1 (65% vs. 69%). However, multifocal tumors were more frequent in the AE group (48% vs. 29%) ( $p<0.05$ ). In the AE group vs. non-AE group, 165 (95%) vs. 97 (62%) patients had recurrent tumors ( $p<0.05$ ). At MVA, increasing age was significantly associated with both the occurrence of AE [odds ratio (OR)=1.06; 95% confidence interval (CI)=1.03-1.10] and treatment discontinuation (OR=1.04; 95% CI=1.01-1.08). Active smoking was significantly associated with a higher likelihood of AE (OR=1.81; 95% CI=1.03-3.21), but not with treatment interruption. Interestingly, patients with multifocal disease or previous recurrences showed a lower risk of both toxicity and early discontinuation ( $p<0.005$ ). *Conclusion:* Almost half of patients receiving BCG therapy for NMIBC experience AEs, and a substantial proportion discontinue treatment prematurely due to toxicity. Advanced age is a strong predictor of both adverse events and BCG intolerance, while active smoking appears to increase the risk of developing BCG-related toxicity. These findings highlight the importance of careful patient selection and close monitoring, especially in elderly and smoking individuals.

#### 46

#### SERUM FATTY ACID-BINDING PROTEIN 4 AS A POTENTIAL NONINVASIVE BIOMARKER FOR CLEAR CELL RENAL CELL CARCINOMA

Roberto Bianchi<sup>1</sup>, Marco Tozzi<sup>1</sup>, Giuseppe Fallara<sup>1</sup>, Francesco Pellegrino<sup>1</sup>, Letizia Maria Ippolita Jannello<sup>1</sup>, Martina Maggi<sup>1</sup>, Andrea Triggiani<sup>1</sup>, Vincenzo Martorello<sup>1</sup>, Clara Marzorati<sup>1</sup>, Federico Lesma<sup>1</sup>, Savino Doronzo<sup>1</sup>,

Emanuela Santangelo<sup>1</sup>, Oliviero Guglielmo<sup>1</sup>,  
Angelica Grasso<sup>1</sup>, Mattia Sangalli<sup>1</sup>, Igor Piacentini<sup>1</sup>,  
Paolo Bernardini<sup>1</sup>, Paolo Dell'Orto<sup>1</sup>, Rosa Sirica<sup>2</sup>,  
Carmela Polito<sup>2</sup>, Mariano Fiorenza<sup>2</sup>,  
Evelina La Civita<sup>2</sup>, Giuseppe Lucarelli<sup>3</sup>,  
Daniela Terracciano<sup>2</sup> and Matteo Ferro<sup>1</sup>

<sup>1</sup>ASST Santi Paolo and Carlo, Urology  
Division, Milan, Italy;

<sup>2</sup>Department of Translational Medical Sciences,  
University of Naples Federico II, Naples, Italy;

<sup>3</sup>Department of Precision and Regenerative Medicine  
and Ionian Area, Urology, Andrology and Kidney  
Transplantation Unit, University of Bari  
"Aldo Moro", Bari, Italy

**Background/Aim:** Fatty Acid-Binding Protein 4 (FABP4), a lipid chaperone secreted by adipocytes, has emerged as a potential biomarker in several cancers, including breast, colon, and ovarian cancer. However, limited evidence exists regarding its possible role in clear cell renal cell carcinoma (ccRCC). In this study, we assessed circulating FABP4 levels in patients with ccRCC to explore its potential relevance. **Patients and Methods:** We analyzed a cohort of 35 patients with ccRCC who underwent radical nephrectomy and 23 healthy donors (HD) who underwent surgery for living kidney donation at the Department of Urology at the University of Naples "Federico II" and the Department of Andrology and Kidney Transplantation Unit of the University of Bari "Aldo Moro" between January 2022 and December 2024. Serum samples were collected from all participants and analyzed using ELISA. Serum FABP4 levels were compared between groups using the Mann-Whitney test. Furthermore, to evaluate whether conditions other than cancer could influence serum FABP4 concentrations, we compared FABP4 levels based on body mass index (BMI  $\leq 25$  vs. BMI  $> 25$ ), presence of type 2 diabetes (yes vs. no), and hypertension (yes vs. no), also using the Mann-Whitney test. **Results:** Overall, 74% of the ccRCC patients and 52% of the HD were men. Median age was  $63 \pm 11$  and  $55 \pm 10$  years among ccRCC patients and HD, respectively. Median BMI was

$27 \pm 4$  and  $25 \pm 3$  Kg/m<sup>2</sup> among ccRCC patients and HD, respectively. Overall, 6 (17%) and 26 (74%) ccRCC patients had diabetes mellitus and hypertension, while no HD had these comorbidities. Overall, 7 (20%) ccRCC patients had  $\geq pT2$  tumor. The Fuhrman grade was G1, G2, G3, and G4 in 7 (20%), 13 (37%), 10 (29%), and 5 (1%) ccRCC patients. Median serum FABP4 levels were significantly higher in ccRCC patients compared to HD [18,680 pg/ml, interquartile range (IQR)=24,930-13,388 vs. 14,090 pg/ml IQR=18,733-11,288;  $p=0.0292$ ]. No statistically significant differences were found between patients with BMI  $\leq 25$  and those with BMI  $> 25$  ( $p=0.54$ ), subjects with hypertension vs. those without hypertension ( $p=0.62$ ) and subjects with T2D and those without T2D ( $p=0.99$ ). **Conclusion:** Serum FABP4 levels are significantly elevated in ccRCC patients compared to healthy donors. These findings suggest that serum FABP4 may serve as a promising noninvasive biomarker for the early identification of patients with ccRCC. Further studies are warranted to assess its diagnostic accuracy and potential utility in clinical practice.

47

#### **MALE PERINEAL URETHRAL CARCINOMA: A SINGLE-CENTER EXPERIENCE**

Enzo Palminteri<sup>1</sup>, Stefano Toso<sup>2</sup>, Francesco Chierigo<sup>3</sup>,  
Niccolo' Lenci<sup>4</sup> and Vincenzo Cangemi<sup>5</sup>

<sup>1</sup>Urethral Surgery Center, Humanitas, Turin, Italy;

<sup>2</sup>C.U.R.E. Group, Urology, Hesperia  
Hospital, Modena, Italy;

<sup>3</sup>ASST Santi Paolo and Carlo,  
San Paolo Hospital, Milan, Italy;

<sup>4</sup>Humanitas, Humanitas Cellini, Turin, Italy;

<sup>5</sup>University of Florence, Urology, Careggi University  
Hospital, University of Florence, Florence, Italy

**Background/Aim:** Urethral carcinoma is a rare and aggressive disease whose treatment depends on tumor stage and site (1). In this study we report our single-center

experience in 2024 about the surgical management of perineal urethral masses, consisting of mass removal and perineal urethrostomy. *Patients and Methods:* For this study, we recruited only patients who underwent perineal urethral mass removal and urethrostomy with diagnosis of urethral carcinoma. All of them had a history of previous urethral surgery or urethral dilatations and/or a diagnosis of lichen sclerosus. The form of presentation of the disease was similar in all of them, demonstrating the presence of a perineal abscess with local pain and severe fever some weeks or months before surgery (2). Surgery starts with an inverted U-shaped perineal incision under the previous urethrostomy. Then, once urethral mass is identified and its borders delimited, we begin to isolate it from the adjacent structures. Once isolation is completed, mass and bulbar urethral tract involved are removed. Biopsies of corpora cavernosa and urethral stumps are taken. Subsequently, a perineal re-urethrostomy at the level of the proximal urethra is performed. *Results:* Four patients in total were treated at our center by this procedure between May and September 2024. Median age was 58 years old. Three patients were diagnosed with squamous cell carcinoma. One of them underwent bilateral inguinal lymphadenectomy. The fourth case resulted in adenocarcinoma, in which disease focally involved also proximal stump and corpora cavernosa samples. Moreover, in this case, pathological left inguinal lymph nodes were found at subsequent needle biopsy. After discussion at multidisciplinary committee, urethrectomy combined with prostatectomy and regional lymphadenectomy was proposed (1, 3) but patient refused. A chemoradiotherapy treatment was accepted. At 6 months, no recurrent lesions were found on MRI in all patients and physical examination revealed a regular aspect of urethrostomy and surgical wound. No other abscess and fever episodes were reported. *Conclusion:* Early diagnosis and surgical treatment of urethral cancer can have an impact on prognosis (1, 4, 5). Otherwise, surgery can be helpful to reduce the risk of potentially fatal non-oncological complications such as sepsis, because of the frequent development of local post-cancer abscess (2).

- 1 EAU Guidelines Primary Urethral Carcinoma. Available at: <https://uroweb.org/guidelines/primary-urethral-carcinoma> [Last accessed on June 29, 2025]
- 2 Mizusawa H, Hara H, Mimura Y, Kato H: Primary male urethral squamous cell carcinoma presenting with a genital abscess. *IJU Case Rep* 2(4): 225-228, 2019. DOI: 10.1002/iju5.12090
- 3 Wang M, Yang M, Wu P, Deng S, Wang J, Chen J, Wang J, Liu M: Transperineal-incision urethrectomy combined with laparoscopic prostatectomy for a male patient with squamous cell carcinoma involving distal plus proximal urethra and untypical symptoms-a case report. *Transl Androl Urol* 10(2): 976-982, 2021. DOI: 10.21037/tau-20-984
- 4 Koh Y, Ujike T, Fujita K, Uemura M, Kiuchi H, Imamura R, Miyagawa Y, Nonomura N: A case of urethral carcinoma in situ resected by urethrectomy of anterior urethra. *Hinyokika Kyo* 65(8): 337-340, 2019. DOI: 10.14989/Acta UrolJap\_65\_8\_337
- 5 Poblador AF, Palacios MH, Vegas MR, Medina AA, Mayayo ES, Barreras SG, Conejo GF, Patrón RR, Constatino VC, González AS, Revilla JB: Male perineal carcinoma: experience in 4 cases and literature review. *Case Rep Urol* 2022: 4466602, 2022. DOI: 10.1155/2022/4466602

#### 48

#### **5-FRACTION PROSTATE SBRT WITH MRI-BASED DIL SIMULTANEOUS BOOST, FIDUCIALS TRACKING AND RECTAL SPACING: ACUTE TOXICITY AND DOSIMETRY RESULTS OF A PROSPECTIVE OBSERVATIONAL STUDY**

Federico Colombo<sup>1</sup>, Marco Galaverni<sup>1</sup>,  
 Claudia Grondelli<sup>1</sup>, Francesco Salaroli<sup>1</sup>,  
 Donatello Gasparro<sup>2</sup>, Francesco Ziglioli<sup>3</sup>,  
 Carmelinda Manna<sup>4</sup>, Giulio Negrini<sup>5</sup>,  
 Livia Ruffini<sup>6</sup>, Umberto Maestroni<sup>3</sup>,  
 Nunziata D'Abbiero<sup>1</sup> and Nicola Simoni<sup>1</sup>

<sup>1</sup>Radiation Oncology Unit, AOU Parma, Parma, Italy;

<sup>2</sup>Oncology Unit, AOU Parma, Parma, Italy;

<sup>3</sup>Urology Unit, AOU Parma, Parma, Italy;

<sup>4</sup>Unit of Radiological Sciences, AOU Parma, Parma, Italy;

<sup>5</sup>Radiology Unit, AOU Parma, Parma, Italy;

<sup>6</sup>Nuclear Medicine Unit, AOU Parma, Parma, Italy

**Background/Aim:** Dose escalation to the dominant intraprostatic lesion (DIL) is a promising approach to increase the therapeutic ratio of stereotactic body radiotherapy (SBRT) in prostate cancer. The aim of the study was to report acute toxicity and dosimetry results of prostate SBRT with a simultaneous integrated boost (SIB) to the DIL (SBRT-SIB<sub>DIL</sub>). **Patients and Methods:** Patients with histologically confirmed localized prostate adenocarcinoma and gland volume ≤90 cc were included in this prospective observational study. DIL was defined using multiparametric magnetic resonance imaging (mmMRI) T2-weighted, diffusion and perfusion images. SBRT prescription dose was 36.25 Gy in 5 fractions to the

Planning Target Volume (PTV) with a SIB to the DIL up to 45 Gy. Genitourinary (GU) and gastrointestinal (GI) toxicity, as well as planning dosimetry data, were analyzed. **Results:** From June 2022 to August 2024, a total of 41 men treated with prostate SBRT-SIB<sub>DIL</sub> at our Institution were enrolled. Median patient age was 76 years (interquartile range=73-78). D'Amico/NCCN class risk was defined as low-, intermediate-, and high- risk in 7 (17.1%), 29 (70.7%), and 5 (12.2%) patients, respectively. Thirty-two (72.7%) DILs were in the peripheral zone and 3 (7.3%) patients had 2 DILs. SBRT was delivered with volumetric modulated arc radiotherapy (VMAT), fiducial markers tracking was used for all patients, while rectal spacer insertion was optional and placed in 24 (58.5%) patients. Androgen deprivation therapy (ADT) was administered in 14 (34.1%) cases. At a median estimated follow up of 13.7 months (95% confidence interval: 11.5-18.2), no G≥3 acute toxicity was observed, with a cumulative acute G2

Table I. Cumulative CTCAE acute genitourinary (GU) and gastrointestinal (GI) toxicity (n=41).

Cumulative toxicity	GU toxicity			GI toxicity		
	Grade 1+	Grade 2+	Grade 3+	Grade 1+	Grade 2+	Grade 3+
	56.1%	24.4%	0%	19.5%	14.6%	0%

CTCAE: Common Terminology Criteria for Adverse Events.

Table II. Dominant intraprostatic lesion (DIL) and organ at risk (OAR) treatment plan dosimetric parameters.

Target/OAR structure	Parameter	Goal	Median	Minimum	Maximum
PTV DIL	Volume		7.7 cc	1.8 cc	31.8 cc
	Dmax		43.3 Gy	40.6 Gy	49.7 Gy
	D50%		41.5 Gy	40.1 Gy	46.7 Gy
Rectum	V40Gy	<1 cc	0.00 cc	0.00 cc	0.07 cc
	V38Gy		0.01 cc	0.00 cc	0.50 cc
	V36Gy	<1 cc (optimal) <2 cc (mandatory)	0.35 cc	0.00 cc	2.61 cc
Bladder	V24Gy	<50%	10.4%	0.0%	32.9%
	V40Gy	<2 cc	0.0 cc	0.0 cc	1.5 cc
	V37Gy	<5 cc (optimal) <10 cc (mandatory)	4.7 cc	0.0 cc	15.4 cc
Urethra	V18.1Gy	<40%	15.8%	2.7%	46.7%
	Dmax	<42 Gy	40.4 Gy	36.7 Gy	43.8 Gy

OAR: Organ at risk; PTV: planning target volume; DIL: dominant intraprostatic lesion; cc: cubic centimeters; Gy: gray.

GU and GI toxicity rate of 24.4% and 14.6%, respectively (Table I). A summary of DIL dosimetric parameters and organ at risk (OAR) constraints is outlined in Table II. Rectal dosimetric parameters were significantly improved by the use of rectal spacer (spacer vs. no spacer rectal V38Gy 0.0 cc vs. 0.2 cc,  $p<0.001$ ; V36Gy 0.0 cc vs. 1.7 cc,  $p<0.001$ ; V24Gy 5.9% vs. 15.3%,  $p<0.001$ ); however, this did not translate into a significant difference in G2 rectal toxicity (spacer vs no spacer 4.9% vs. 9.8%,  $p=0.175$ ). All patients experienced biochemical response. Patient-reported QoL metrics at last follow-up were not significantly different from pre-SBRT baseline. *Conclusion:* Prostate SBRT with a focal DIL boost up to 45 Gy is associated with favorable GU and GI toxicity. Rectal spacer significantly improves dosimetric parameters, without a corresponding significant reduction in acute rectal toxicity.

#### 49

#### **RADICAL PROSTATE RADIOTHERAPY WITH OR WITHOUT INTRAPROSTATIC FIDUCIALS: PRELIMINARY EFFICACY DATA**

Luigi De Cicco<sup>1</sup>, Francesco Moretti<sup>2</sup>,  
Angelo Giovanni Lanceni<sup>1</sup>, Andrea Maucieri<sup>1</sup>,  
Alessandra Cocchi<sup>1</sup>, Rita Lorusso<sup>2</sup>, Luca Marzoli<sup>2</sup>,  
Lorenzo Bianchi<sup>2</sup> and Barbara Bortolato<sup>1</sup>

<sup>1</sup>Asst Valle Olona, Division of Radiotherapy,  
Busto Arsizio (VA), Italy;

<sup>2</sup>Asst Valle Olona, Medical Physics,  
Busto Arsizio (VA), Italy

*Background/Aim:* In radical external beam radiotherapy of localized prostate cancer patients, image-guided radiotherapy (IGRT) is essential for the correct daily repositioning of the target. One of the most used patients' repositioning techniques in IGRT is the on-board cone-beam computed tomography (CBCT). The use of intraprostatic fiducial markers (FMs), in addition to daily CBCT, is currently a matter of clinical debate, particularly in

long-course conventional or moderately hypofractionated treatments compared to extremely hypofractionated regimens. According to our previous study, intraprostatic FMs appear to aid in the identification and correction of rotational errors during daily CBCT imaging (1). Furthermore, the use of FMs reduced the time to treatment initiation, which is critical for minimizing the risk of intrafractional organ motion (1). Herein, we aimed to retrospectively analyze a case series of localized prostate cancer patients treated with IGRT with daily CBCT. Prostate-specific antigen (PSA) levels at the last follow-up were compared between patients with and without intraprostatic FMs. *Patients and Methods:* Outcome data were analyzed from the follow-up of 82 consecutive patients with non-metastatic prostate cancer treated with volumetric modulated arc therapy (VMAT) radiotherapy (RT) technique, between November 2021 and January 2024, on the prostate alone or the prostate plus seminal vesicles. Twenty-five patients had received FMs transperineal implantation, while 57 did not. During the follow-up only one biochemical relapse of the disease, defined as  $PSA > \text{"PSA nadir post-RT} + 2 \text{ ng/ml"}$ , was recorded. Due to the limited follow-up duration, we compared the PSA levels at the last follow-up between the two groups as a potential early indicator of treatment efficacy. *Results:* Patient characteristics are in Table I. Median follow-up time was 18.7 months for no FMs group and 29.7 for FMs one. Despite a lower proportion of patients in clinical Stage I (according to AJCC Prognostic Groups) in the FMs group, this cohort achieved a significantly lower mean PSA after radiotherapy compared to the group without FMs. Figure 1 shows the mean PSA values with their standard deviations after radiotherapy in prostate cancer patients in the two groups. The FM group achieved a mean PSA of 0.28 ng/ml, while the non-FM group had a mean PSA of 0.59 ng/ml. This represents a significantly lower mean value in the FM group ( $p=0.04$ ). *Conclusion:* There is evidence in the literature indicating that the nadir PSA level after RT is an independent predictor of disease-free survival (DFS) in patients with localized prostate cancer. A PSA nadir of 0.5 ng/ml or less has been associated

with a 5-year DFS rate of 93%, compared to a DFS rate of 26% in patients with a PSA nadir between 0.6 and 1 ng/ml (2). In our series, post-RT PSA levels at the last follow-up were significantly lower in patients treated with IGRT using CBCT and the implantation of intraprostatic FMs (Figure 1). This may indicate better disease control. According to our experience, transperineal implantation of prostatic FMs in patients with localized prostate cancer is safe (3) and, if confirmed, could ensure greater disease control.

Table I. Patient characteristics.

	No FMs group n (%)	FMs group N (%)
Total n	57	25
Median age at RT time (years)	76	78
AJCC prognostic groups		
Stage I	12 (21.1%)	2 (8%)
Stage IIA-C	45 (78.9%)	22 (88%)
Stage IIIA	0	1 (4%)
Stage ≥IIIB	0	0
Total dose/dose per fraction		
70/2.5 Gy	45 (79%)	9 (36%)
60/3 Gy	11 (19.3%)	14 (56%)
36.25/7.25	1 (1.7%)	0

FMs: Fiducial markers; RT: radiotherapy; AJCC: The American Joint Committee on Cancer.

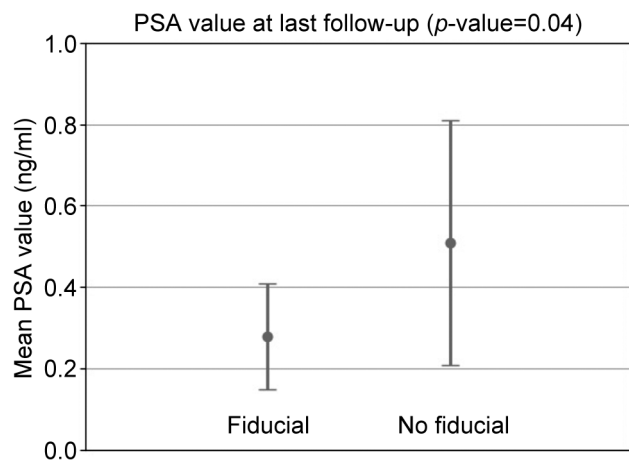


Figure 1. Mean PSA values with their standard deviations after radiotherapy in prostate cancer patients in the fiducial group and no fiducial one. The patients treated with implanted fiducials achieve a lower PSA value with a smaller standard ( $p=0.04$ ).

1 De Cicco L, Marzoli L, Lorusso R, Mancuso RM, Petazzi E, Lanceni AG, Della Bosca E, Buttignol S, Starace A, Verusio C, Bortolato B: CBCT-based prostate IGRT with and without implanted markers: assessment of geometric corrections and time for completion. *Anticancer Res* 43(1): 405-408, 2023. DOI: 10.21873/anticancer.16175  
 2 Critz FA, Levinson AK, Williams WH, Holladay DA, Holladay CT: The PSA nadir that indicates potential cure after radiotherapy for prostate cancer. *Urology* 49(3): 322-326, 1997. DOI: 10.1016/S0090-4295(96)00666-8  
 3 De Cicco L, Bracelli S: Fiducial markers implantation for prostate image-guided radiotherapy: a report on the transperineal approach. *Radiol Med* 124(2): 132-135, 2019. DOI: 10.1007/s11547-018-0949-5

## 50

### HOW CAN PET-CT IMPROVE THE STAGING OF MIBC COMPARED TO CONVENTIONAL METHODS? RETROSPECTIVE ANALYSIS ON VARIANT HISTOLOGY

Francesco Pio Bizzarri<sup>1</sup>, Fabrizio Bellavia<sup>2</sup>, Adam Nelson<sup>3</sup>, Alexander Colquhoun<sup>3</sup>, Pierluigi Russo<sup>2</sup>, Francesco Rossi<sup>2</sup>, Lorenzo D'Amico<sup>2</sup>, Marco Campetella<sup>4</sup>, Maria Chiara Sighinolfi<sup>2</sup>, Bernardo Cesare Maria Rocco<sup>2</sup>, Salvatore Marco Recupero<sup>4</sup>, Emilio Sacco<sup>1</sup> and Niyati Lobo<sup>3</sup>

<sup>1</sup>Catholic University of the Sacred Heart, Gemelli Isola Tiberina Hospital, Rome, Italy;  
<sup>2</sup>Catholic University of the Sacred Heart, Agostino Gemelli University Hospital, Rome, Italy;  
<sup>3</sup>University of Cambridge, Addenbrooke's Hospital, Cambridge, U.K.;  
<sup>4</sup>Gemelli Isola Tiberina Hospital, Rome, Italy

**Background/Aim:** Lymph node (LN) involvement is a key factor in determining the prognosis for bladder cancer patients (1). Accurate staging is essential to identify appropriate and timely therapeutic strategies. To enhance

the precision of LN detection, 18-fluorodeoxyglucose positron emission tomography/computerized tomography (18F-FDG PET-CT) has been increasingly adopted as an alternative to traditional methods like CT or magnetic resonance imaging (MRI) (2). Molecular imaging of muscle-invasive bladder cancer (MIBC) is focused on assessing its locoregional and distant metastases in variant histologies (3). Herein, we aimed to analyze the correlation between findings from the preoperative PET-CT and observations from the pathological examination. *Patients and Methods:* A retrospective study was conducted from 2018 to 2024. Patients who underwent radical cystectomy at our department whose histological variants were not purely urothelial were selected. We also collected information related to PET-CT and conventional imaging, including MRI and CT urography. *Results:* We identified 39 patients (24 males, 15 females) who underwent radical cystectomy at our institution. All patients routinely underwent PET-CT, CT scan, and MRI. The mean time between PET-CT and cystectomy was 26.8 days (SD=39). Preoperatively, PET-CT agreed with CT scan in 74.4% of cases ( $p=0.021$ ) and with MRI in 79% ( $p=0.039$ ) in lymph nodes findings. In all cases, the discrepancy was on nodal size and identification with PET-CT. After analyzing a mean of 16 lymph nodes per cystectomy and performing logistic regression, we observed a statistically significant association between N stage and PET-CT (95% CI=0.2-0.86), and PET-CT was concordant with the histopathology in 82% of cases with a specificity of 76%. *Conclusion:* In patients with muscle-invasive bladder cancer with histological variants, the role of PET-CT seems to be unquestionable, considering its ability to detect lymph node metastases. However, there does not seem to be a significant discrepancy with traditional methods which, although less accurate, are able to identify a large part of the extra vesical disease.

1 Guo L, Zhang L, Wang J, Zhang X, Zhu Z: Pelvic lymph node dissection during cystectomy for patients with bladder carcinoma with variant histology: does histologic type matter? *Front Oncol* 10: 545921, 2020. DOI: 10.3389/fonc.2020.545921

2 Fu M, Klose C, Sparks A, Whalen M: Impact of variant histology on occult nodal metastasis after neoadjuvant chemotherapy for muscle-invasive bladder cancer: a review of the national cancer database. *Clin Genitourin Cancer* 20(2): e135-e139, 2022. DOI: 10.1016/j.clgc.2021.11.011

3 Guo CC, Lee S, Lee JG, Chen H, Zaleski M, Choi W, McConkey DJ, Wei P, Czerniak B: Molecular profile of bladder cancer progression to clinically aggressive subtypes. *Nat Rev Urol* 21(7): 391-405, 2024. DOI: 10.1038/s41585-023-00847-7

## 51

### A MARKERLESS AUGMENTED REALITY PLATFORM FOR COGNITIVE SUPPORT IN ROBOTIC LYMPHADENECTOMY

Laura Cruciani<sup>1</sup>, Eleonora Pollini<sup>1</sup>, Matteo Fontana<sup>2</sup>, Gennaro Musi<sup>2</sup> and Elena De Momi<sup>1</sup>

<sup>1</sup>Department of Electronics, Information and Bioengineering, Politecnico di Milano, Milan, Italy;

<sup>2</sup>Department of Urology, European Institute of Oncology, IRCCS, Milan, Italy

*Background/Aim:* Robotic-assisted minimally invasive surgery (RAMIS) has significantly improved the accuracy and safety of oncologic procedures. However, it still poses challenges when navigating anatomical structures with poor visibility. This is particularly evident during pelvic lymph node dissection (PLND), where lymphatic tissue is embedded in fat and lacks reliable landmarks making surgeons reliant on experience and increasing the risk of omission. Fiducial-based navigation, electromagnetic tracking, and augmented reality (AR) with external markers have limitations such as invasiveness and occlusion. Markerless AR offers a non-intrusive alternative but often relies on rigid models or manual setup. We propose a markerless AR platform that provides visual guidance during robotic lymphadenectomy, by overlaying a deformable aligned 3D model of the common iliac artery

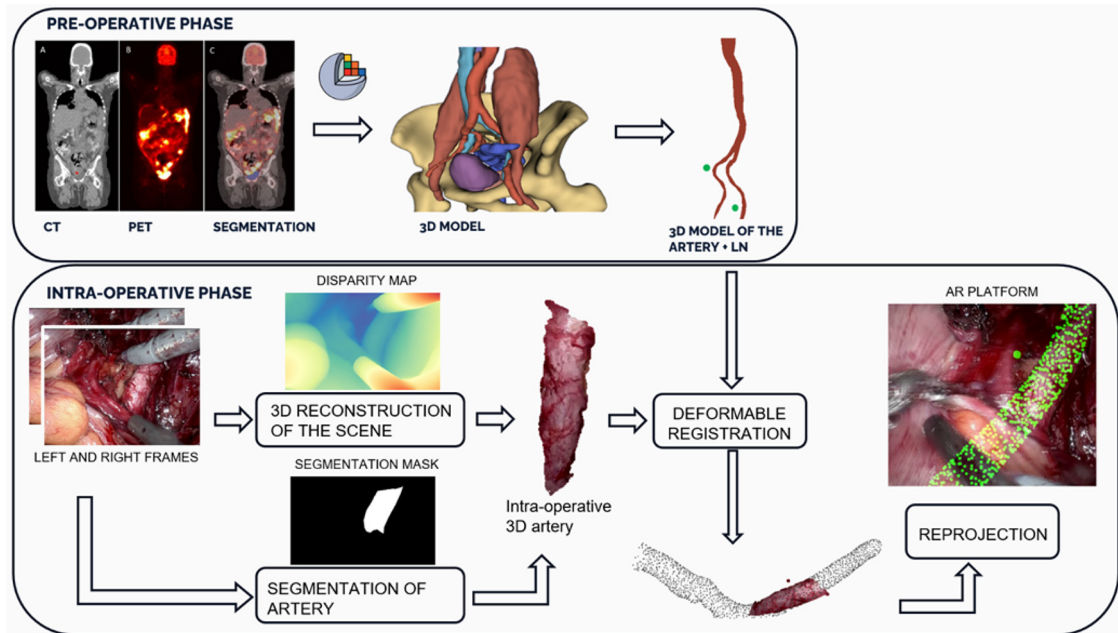


Figure 1. Workflow of the markerless augmented reality platform. Given rectified stereo image pairs  $(I_l, I_r)$  coming from a stereo laparoscope and a pre-operative 3D model of the common iliac artery  $P_{pre}$  our goal is to generate a dense 3D reconstruction of the intraoperative field, register the pre-operative model onto it, and project the aligned anatomy back into the laparoscopic video for real-time guidance.

onto the laparoscopic feed, without altering the surgical workflow. This works as a key landmark to contextualize the surgical field. *Materials and Methods:* Figure 1 illustrates the pipeline. Stereo laparoscopic images are used to reconstruct the intra-operative anatomy as a 3D point cloud. Disparity between the two views is estimated via a deep learning model (HSMNet) (1) and converted to depth using stereo calibration:

$$Z(u, v) = \frac{fB}{d(u, v)}$$

where  $f$  is the focal length,  $B$  is the known baseline, and  $d(u, v)$  is the disparity value at pixel location  $(u, v)$ . We isolate the common iliac artery using a U-Net trained from scratch on 593 manually annotated frames from 10 robot-assisted prostatectomies. The resulting binary mask selects relevant 3D points from the reconstruction. To align the pre-operative model  $P_{pre}$  with the intra-operative 3D anatomy  $P_{intra}$ , we employ a two-step strategy accounting

for rigid positioning and deformation. First, a rigid transformation is estimated to roughly align the models. This step is based on extracting distinctive geometric features from both point clouds and identifying anatomical correspondences. Next, we apply a deformable refinement step. This stage uses a data-driven model based on multi-scale multi-layer perceptions (MLPs) (2) to predict local shape adjustments. *Results:* Stereo reconstruction was quantitatively assessed on the SERV-CT (3) dataset, which provides ground-truth 3D points for validation. Letting  $p_i$  be ground-truth points and  $\hat{p}_i$  the corresponding predicted points, we computed the mean absolute error (MAE) and root mean squared error (RMSE) as:

$$MAE = \frac{1}{N} \sum_{i=1}^N |\hat{p}_i - p_i|$$

$$RMSE = \sqrt{\frac{1}{N} \sum_{i=1}^N |\hat{p}_i - p_i|^2}$$

Our method yielded an MAE of  $2.65 \pm 1.64$  mm and an RMSE of  $5.47 \pm 1.46$  mm. The segmentation model was evaluated on a private dataset comprising 118 annotated frames. Let  $A$  and  $B$  be the predicted segmentation and the ground truth. We used the Dice coefficient and Intersection-over-Union (IoU):

$$\text{Dice} = \frac{2(|A \cap B|)}{(|A| + |B|)}$$

$$\text{IOU} = \frac{|A \cap B|}{|A \cup B|}$$

The network achieved a Dice score of 78.5% and an IoU of 60.8%. To assess the registration module, we generated a synthetic dataset from CT-derived 3D artery models, introducing elastic deformations and visibility loss to simulate intra-operative conditions. Accuracy was measured as RMSE between registered  $p_r$  and target ground truth points  $p_t$ :

$$\text{RMSE} = \sqrt{\frac{1}{N} \sum_{i=1}^N |p_r - p_t|^2}$$

After rigid alignment and deformable refinement, the registration achieved a median RMSE of 7.58 mm.

*Conclusion:* We presented a markerless augmented reality framework for intra-operative guidance in robotic pelvic lymphadenectomy by combining stereo 3D reconstruction, artery segmentation, and deformable registration to align a pre-operative model with the intra-operative surgical scene. Unlike prior approaches relying on fiducial markers or manual annotation, our method operates autonomously and does not require any changes to the surgical workflow. Current limitations include reliance on synthetic deformation models for evaluation, absence of *in vivo* ground-truth registration data, and lack of user studies. Overall, this work contributes toward robust, context-aware surgical navigation in robotic oncology, enabling intra-operative support while maintaining full surgeon control.

- 1 Yang G, Manela J, Happold M, Ramanan D: Hierarchical deep stereo matching on high-resolution images. *In: Proceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition*, pp. 5515-5524, 2019. DOI: 10.1109/CVPR.2019.00566
- 2 Li Y and Harada T: Non-rigid point cloud registration with neural deformation pyramid. *In: Advances in Neural Information Processing Systems*, Vol. 35, pp. 27757-27768, 2022.
- 3 Edwards PE, Psychogyios D, Speidel S, Maier-Hein L, Stoyanov D: Serv-CT: A disparity dataset from cone-beam CT. *Med Image Anal* 76: 102302, 2022. DOI: 10.1016/j.media.2021.102302

### Authors Index\*

(Figures indicate abstract number. \*Missing abstracts were withdrawn.)

Alberico G, 1	Incognito D, 8, 9
Bagatin A, 35	Liardo, RLE, 29
Bellavia F, 50	Lievore E, 16
Bianchi R, 46	Lucchini R, 43
Buonerba C, 40	Luzzago S, 17, 22
Cangemi V, 47	Martello G, 37
Caracciolo G, 32	Marzorati C, 42
Colombo F, 48	Mistretta FA, 20
Cruciani L, 51	Pellegrino F, 39
D'Elia C, 26	Piccinelli ML, 19
De Cicco L, 12, 49	Raggi E, 3, 4
Dell'Atti L, 7	Ricciardi G, 23
Di Cristina L, 44	Tozzi M, 41
Di Napoli M, 2	Travaglini S, 24
Di Trapani E, 15	Trenti E, 25
Fallara G, 45	Vaccaro C, 18, 21
Gordeeva O, 31	