ABSTRACTS OF THE 30th ANNUAL MEETING OF THE ITALIAN SOCIETY OF URO-ONCOLOGY (SIUrO)

26 - 29 September 2020, Virtual Meeting

Honorary Chair: Cinzia Ortega, Francesco Porpiglia

Italian Society of Uro-Oncology

Italian Society of Uro-Oncology (SIUrO)

President: Alberto Lapini, Firenze, Italy

Board

PRESIDENT: Alberto Lapini
VICE PRESIDENT: Renzo Colombo
SECRETARY GENERAL & TREASURER: Giario N. Conti
PAST PRESIDENT: Riccardo Valdagni

Advisors

Sergio Bracarda
Orazio Caffo
Renzo Colombo
Rolando M. D'Angelillo
Luigi F. Da Pozzo
Andrea B. Galosi
Carlo Patriarca
Vittorio Vavassori
Alessandro Volpe
Nadia Zaffaroni

Elected Scientific Committee

Enrico Bollito, Vincenzo Altieri

Congress Scientific Committee

Cinzia Ortega
Francesco Porpiglia
Stefano Arcangeli
Roberto Bortolus
Alessio Bruni
Renzo Colombo
Stefano De Luca
Michelangelo Fiorentino
Andrea B. Galosi
Roberto Iacovelli
Barbara Jerekzec
Silvia Lucarini
Carmen Maccagnano
Carlo Patriarca
Sergio Serni
Marcello Tucci
Nadia Zaffaroni
Paolo A. Zucali

Scientific Secretariat

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

Organizing Secretariat

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

Referees of Abstracts

VINCENZO ALTIERI
ENRICO BOLLITO
ROBERTO BORTOLUS
ALESSIO BRUNI
ORAZIO CAFFO
ROBERTA CECCARELLI
FRANCESCO CECI
RENZO COLOMBO
ANDREA CONTI
ROLANDO MARIA D'ANGELILLO
STEFANO DE LUCA
ANDREA BENEDETTO GALOSI
ALBERTO LAPINI
SILVIA LUCARINI
CARMEN MACCAGNANO
CINZIA ORTEGA
GIOVANNI PAPPAGALLO
CARLO PATRIARCA
TOMMASO PRAYER GALETTI
MARCO ROSCIGNO
ROBERTO SALVIONI
VINCENZO SCATTONI
SERGIO SERNI
VINCENZO SERRETTA
VITTORIO VAVASSORI
NADIA ZAFFARONI

ANTICANCER RESEARCH *40*: 4571-4650 (2020)
doi:10.21873/anticanres.14463

1

POST-PUBERTAL TESTICULAR EPIDERMOID CYST: MAY TESTIS-SPARING SURGERY BE OFFERED?

Valerio Olivieri[1], Valentina Fortunati[2], Emanuele Corongiu[3], Flavio Forte[3], Silvia Ferrario[4], Gabriele Ruggiero[1] and Daniele Griffa[1]

[1]Division of Urology, Ivrea Hospital – ASL TO4, Ivrea, Italy;
[2]Division of Pathology, Hospital "Policlinico of Tor Vergata", Rome, Italy;
[3]Division of Urology, Hospital "Madre Giuseppina Vannini", Rome, Italy;
[4]Division of Radiotherapy, Ivrea Hospital – ASL TO4, Ivrea, Italy

Background: Testicular epidermoid cysts (TECs) are uncommon neoplasms (1, 2). They frequently occur in young people but may also be found in adults. Most TECs are incidentally discovered during self-examination. Serum markers and scrotal ultrasound represent the first step in characterizing the lesion. Computed tomography or magnetic resonance imaging add more information, ruling out metastatic spread. Diagnosis depends on histology. Considering these lesions as benign tumors, many authors suggest testis-sparing surgery such as partial orchiectomy or enucleation. However, the biological behavior of these neoplasms remains unknown (2). We report the case of an epidermoid cyst in an adult male which was treated by testis-sparing surgery. We also reviewed the literature. *Case Report:* A 21-year-old male presented to us for a firm mass in the left testis recently discovered on self-examination. Past anamnesis was uneventful and no familiality for testicular cancer was reported. On physical examination, the lesion presented as a painless non-tender mass at the upper pole. Serum markers were normal. Ultrasound findings revealed a 2 cm well-circumscribed mass with an echogenic rim. Vascularity within the lesion was ruled out on power-Doppler sonography. Total body contrast-enhanced MRI was negative for visceral and retroperitoneal lymph node metastases. Testicular biopsy with frozen section was offered. *Results:* Frozen section revealed a post-pubertal epidermoid cyst. On macroscopic evaluation the lesion presented as a 20 mm cyst. The wall was composed of amorphous material, well delimited by a fibrous epithelium (Figure 1). Teratomatous elements or dermal adnexal structures were not present. Association with intratubular germ cell neoplasm *in situ* (GCNIS) was also excluded on final analysis. No cellular atypia, necrosis or mitotic activity were revealed. *Discussion and Conclusion:* In young men presenting with a testicular mass, a high suspicion for malignant germ cell tumor must be maintained since epidermoid cysts are uncommon benign lesions and account for 1% (2). Approximately 300 cases have been reported in the literature. Caucasian males of pre-pubertal age are mostly affected as may adults. TECs occur rarely in the elderly. The peak of incidence is in those aged between 10 and 40 years old. Etiology is not completely understood (2) and it remains unclear whether these lesions may be classed as a variant of mature teratoma. Regarding the molecular pathways involved, isochromosome 12p and other over-representations of 12p are present in usual teratoma but not in epidermoid cyst; this may be a useful diagnostic tool for distinguishing TEC from teratoma (3). The two main forms of TEC which have been described are pre- and post-pubertal. Differentiating these forms represents a crucial step in planning surgical strategy. Pre-pubertal types do not show malignant features and are not related to GCNIS. Unfavorable prognostic factors are usually absent and no cases of spread have been reported to date in literature. For this reason, they have been named 'simple TEC'; in these cases, testis-sparing surgery represents the gold standard, while orchiectomy might result in overtreatment. Post-pubertal cysts may behave differently. Association with GCNIS has been reported in over 90% of patients; moreover, vascularity, cellular atypia, necrosis or coexisting additional lesions such as teratomatous element or granulomatous disease may be present as unfavorable prognostic factors. Differently from pre-pubertal forms, these cysts have been classed as 'complex TEC' and radical orchiectomy must be performed. Clinically, both types present as a firm, painless mass totally indistinguishable from malignant neoplasms. Serum markers are near always negative. Sonography may guide diagnosis since TECs appear as a well-circumscribed intratesticular 'onion-ring' mass; occasionally, an atypical presentation with a multilocular configuration has been described. MRI further reveals the lesion's features by showing a laminated high- and low-signal intensity corresponding to multiple layers of keratin debris; moreover, it helps in staging by ruling out the presence of metastases. The absence of vascularity on Doppler ultrasound also confirms the diagnosis; contrast-enhanced ultrasound may add more information. Diagnosis only depends on histology. Although orchiectomy represent the first-choice approach for post-pubertal TEC, testis-sparing surgery should be offered if unfavorable prognostic factors are absent. Unfortunately, data in literature are limited. In our case, the patient underwent serum marker analysis and abdominal MRI at 3 and 6 months, which were negative. Testicular ultrasound in our case excluded local recurrence. Consideration of microscopic features and prognostic factors are mandatory for surgical planning in order to prevent unnecessary orchiectomy.

1 Anhauser P, Kranz J, Stolle E, Hoflmayer D, Buscheck F, Muhlstadt S, Lock G and Djeckmann KP: Testicular epidermoid cysts: a reevaluation. BMC Urol *19(1)*: 52,

2019. PMID: 31185974. DOI: 10.1186/s12894-019-0477-1
2 Cakiroglu B, Sonmez NC, Sinanoglu O, Ates L, Aksov SH and Ozcan F: Testicular epidermoid cyst. Afr J Paediatr Surg *12(1)*: 89-90, 2015. PMID: 25659561. DOI: 10.4103/0189-6725.151002
3 Loberant N, Bhatt S, Messing and Dogra VS: Bilateral testicular epidermoid cysts. J Clin Imaging Sci *1*: 4, 2011. PMID: 21915385. DOI: 10.4103/2156-7514.73502

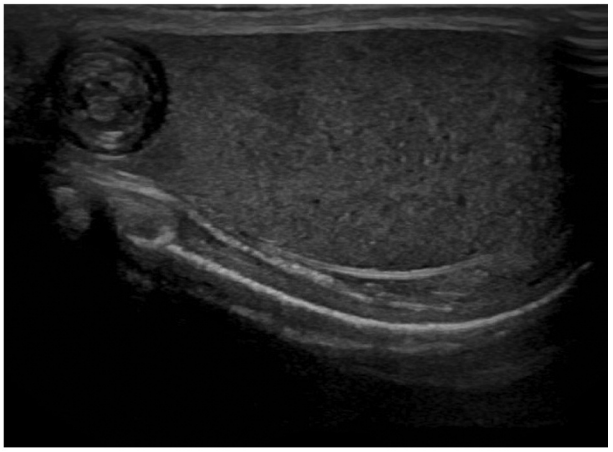

Figure 1. *Ultrasound findings of testicular epidermoid cyst.*

2

PRE-PUBERTAL INTRATESTICULAR KERATOCYST: CASE REPORT AND LITERATURE REVIEW

Valerio Olivieri[1], Valentina Fortunati[2], Emanuele Corongiu[3], Flavio Forte[3], Gabriele Ruggiero[1] and Daniele Griffa[1]

[1]Division of Urology, Ivrea Hospital – ASL TO4, Ivrea, Italy;
[2]Division of Pathology, Hospital "Policlinico of Tor Vergata", Rome, Italy;
[3]Division of Urology, Hospital "Madre Giuseppina Vannini", Rome, Italy

Background: Testicular epidermoid cysts (TECs), also known as keratocysts, are rare lesions accounting for 1% of all testicular masses. Most are incidentally discovered and radically treated. Clinically they present as a firm palpable mass, highly indistinguishable from other testicular cancer types. Scrotal sonography, contrast-enhanced ultrasound or magnetic resonance imaging (MRI) describe the lesion (1, 2) but diagnosis depends on histology. Although no cases of metastases have been reported to date in literature, the real issues of biological behavior and clinical management are unresolved (2, 3). We report the case of a young patient affected by testicular keratocyst who underwent surgical enucleation and review literature about histological features of pre-pubertal TEC and the feasibility and safety of this procedure. *Case Report:* A 16-year-old Caucasian male presented for a firm mass recently discovered on self-examination. Anamnesis was uneventful for genital infections or trauma, no familiality for testicular cancer was reported. The right testis presented a palpable painless mass in the middle of the testis, entirely covered by normal parenchyma. Inguinal and supraclavicular lymph nodes were negative as were serum markers. Scrotal sonography showed a well-circumscribed 2 cm mass within the right testis, with intervening septa and coexisting solid areas; intralesional calcifications were not detected. Intralesional vascularity was ruled out on Doppler ultrasound. MRI was negative for secondary lesions; furthermore, the examination did not reveal any intralesional contrast enhancement, suggesting a benign lesion. Testicular biopsy was offered. *Results:* Frozen section biopsy was suggestive of mature keratocyst and surgical enucleation was offered. Macroscopically, the lesion was a 20×22×25 mm mass highly indistinguishable from any malignant neoplasm and was totally covered by normal testicular parenchyma. On microscopic evaluation, the lesion was composed of horny material, well delimited by a cystic wall of squamous epithelium (Figure 1). No association with intratubular germ cell neoplasm was found nor cellular atypia or mitotic activity. Definitively, it was classed as pre-pubertal mature intratesticular epidermoid cyst. *Discussion and Conclusion:* TECs are benign tumors which arise from ectoderm, endoderm or mesoderm tissues. They account for around 1-2% of all testicular masses and typically present in mid-adulthood. Caucasians are more likely to be affected. The etiology is still debated (2, 3). Two main form of TECs have been described in literature: Pre-and post-pubertal. Pre-pubertal TECs have historically been considered benign lesions since no association with germ cell neoplasm *in situ* has been reported nor cases of metastatic spread. Histology often rules out unfavorable prognostic features such coexisting lesions or association with germ cell neoplasms. For this reason, they have been named "simple testicular epidermoid cyst". Clinically, they are highly indistinguishable from other types of testicular cancer, often presenting as a firm, painless palpable mass within the testis; the right testis seems to be more frequently involved than the left. Serum markers are always negative. Ultrasound may guide diagnosis since these lesions show typical radiographic features: a well-marginated intratesticular masses with a lamellar 'onion skin' or 'bull-eye' pattern and avascular center (1, 2) might always suggest testicular keratocyst. Contrast-enhanced ultrasound also provides with more information, ruling out intralesional vascularity. MRI better describes the tumor, rules out secondary or local infiltration,

and the absence of contrast enhancement further suggests a benign nature. Although these features can guide clinical orientation, diagnosis only depends on histology: differentiation from coexisting entities such as pure teratomas, germ cell tumors or granulomatous disease is mandatory in pre-pubertal forms. Uncommon features such as cellular atypia, mitotic activity, necrosis, hemorrhage and epithelial hyperplasia must be absent in these forms. Partial orchiectomy or testis-sparing excision with frozen section is becoming standard treatment (2); however, when the final pathology report describes a teratomatous lesion or malignant features, further radical orchiectomy is required. In our case, the patient underwent contrast-enhanced MRI at 6 and 12 months, which ruled out visceral and lymph node metastases. Ultrasound of the testis excluded local recurrence. The importance of accurate diagnosis is crucial for preventing unnecessary orchiectomy: testicular-sparing surgery should be offered.

1 Ashouri KB, Heiman JM and Kelly EF: Testicular epidermoid cyst: a rare case. Urol Ann *9(3)*: 296-298, 2017. PMID: 28794603. DOI: 10.4103/UA.UA_37_17

2 Cakiroglu B, Sonmez NC, Sinanoglu O, Ates L, Aksov SH and Ozcan F: Testicular epidermoid cyst. Afr J Paediatr Surg *12(1)*: 89-90, 2015. PMID: 25659561. DOI: 10.4103/0189-6725.151002

3 Dieckmann KP and Loy V: Epidermoid cyst of the testis: A review of clinical and histogenetic considerations. Br J Urol *73:* 436-441, 1994. PMID: 8199834. DOI: 10.1111/j.1464-410x.1994.tb07611.x

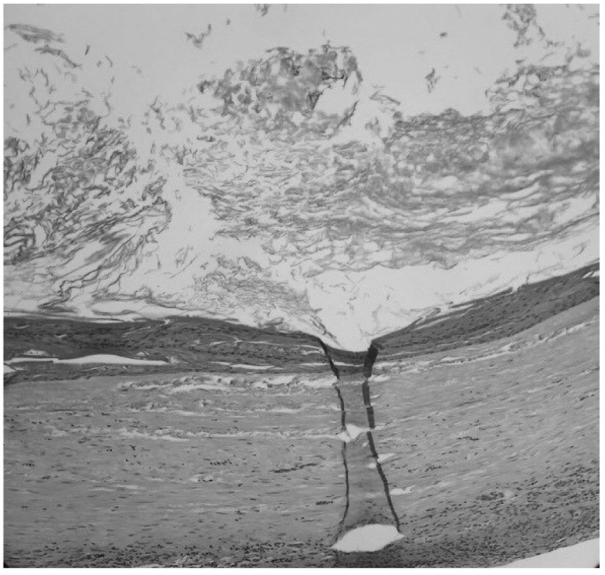

Figure 1. *Testicular keratocyst. Stratified squamous epithelium with adjacent keratin (original magnification, ×10).*

3

NON-UROTHELIAL BLADDER NEOPLASMS: SMALL-CELL NEUROENDOCRINE CANCER

Valerio Olivieri[1], Valentina Fortunati[2], Luca Bellei[1], Gianluca Del Vecchio[1], Massimo Massarelli[1], Massimo Ollino[1], Emanuele Corongiu[3], Flavio Forte[3] and Daniele Griffa[1]

[1]Division of Urology, Ivrea Hospital – ASL TO4, Ivrea, Italy;
[2]Division of Pathology, Hospital "Policlinico of Tor Vergata", Rome, Italy;
[3]Division of Urology, Hospital "Madre Giuseppina Vannini", Rome, Italy;

Background: Neuroendocrine tumors are uncommon neoplasms. Small-cell carcinoma of the bladder (SCCB) is a rare, poorly differentiated type of neuroendocrine tumor clinically characterized by gross hematuria. Patients are considered at highest-risk of progression. SCCB arises from cells of nervous and endocrine systems within the bladder. Data in literature are limited and the best therapeutic approach remains under discussion. Treatment may be multimodal. Prognosis is poor. Here we report the case of an elderly male affected by SCCB and review the literature. *Case Report:* An 85-year-old male presented to us for asymptomatic gross hematuria of recent onset. He was a former smoker, suffered from myocardial infarction and was on medication with acetylsalicylate; previous episodes of gross hematuria, asthenia and weight loss were ruled out on anamnesis. General and systemic examination were unremarkable. Blood examination revealed mild anemia (Hb 11 g/dl); White Blood Count, Reactive C-Protein and creatinine were normal. Bladder ultrasound revealed a 4 cm mass on the left bladder wall highly suspicious for neoplasm. Total body contrast-enhanced computed tomography confirmed the lesion, which appeared organ-confined; no signs of local infiltration, hydronephrosis or visceral-lymph nodes secondary lesions were described. Transurethral resection of the bladder was offered. *Results:* The pathology report revealed a high-grade T1G3 urothelial carcinoma (30% of specimen) associated with a small-cell neuroendocrine variant (70% of specimen); microscopic muscle involvement was excluded. In order to better characterize the neuroendocrine differentiation, immunohistochemistry was mandatory: cytokeratin AE1-3, synaptophysin and Ki-67 were used as molecular markers (Figure 1). The urothelial histotype was positive for cytokeratin but negative for synaptophysin, while the neuroendocrine variant was positive for both. The proliferative index using Ki-67 was 90%, suggesting an aggressive mixed bladder neoplasm. The patient was classed as at highest-risk. Radical cystectomy with extended lymph

node dissection was offered. *Discussion and Conclusion:* Non-urothelial bladder cancers are uncommon neoplasms and include neuroendocrine tumor, squamous cell carcinoma, adenocarcinoma, micropapillary, plasmocytoid and sarcoma. According to microscopic features, two forms of bladder neuroendocrine tumor have been described in literature: Small- and large-cell. SCCB is a very rare, poorly differentiated neuroendocrine tumor accounting for 0.5-1.0% of all bladder neoplasms (1) and characterized by a highly aggressive course. Patients affected are considered at highest-risk of metastatic spread and poor prognosis. Risk factors are not completely known. It has been suggested they may be similar to those for other bladder cancer types, including smoking, professional exposure or prolonged contact with aromatic amines. SCCB commonly arises from cells of the endocrine and nervous systems differently expressed within the human bladder; upper urinary tract, urethra and prostate may also be involved. Differently from common urothelial cancer, neuroendocrine lesions are histologically graded according to (Ki-67 index) rather than cellular polymorphism (2): when the urothelial histotype coexists, the WHO 2004 grading system (3) is used to classify the urothelial variant. On immunohistochemistry, SCCB is reactive for neuroendocrine markers such as synaptophysin, chromogranin and periodically for cytokeratin 7 and 20. The TNM system is currently used to staging these neoplasms. Clinical presentation is variable depending tumor location, staging and visceral-lymph node involvement. Treatment depends on several factors such as age, performance status, stadiation, stage, symptomatic hematuria. Radical cystectomy represents the gold standard; according to European Association of Urology guidelines, curative cystectomy is optional in patients older than 80 years but might be performed in cases of symptomatic hematuria as palliative intention whenever hemostatic resection is inconclusive. A multimodal treatment may be also offered combining surgery with chemotherapy regimens. The prognosis remains poor due to the high risk of metastasis; median overall survival is 1 to 5 years. In our case, the patient refused active treatment and best supportive care was offered.

1 Park S, Reuter V and Hansel E: Non-urothelial carcinomas of the bladder. Histopathology *74(1)*: 97-111, 2019. PMID: 30565306. DOI: 10.1111/his.13719

2 Oberg K and Castellano D: Current knowledge on diagnosis and staging of neuroendocrine tumors. Cancer Metastasis Rev *30*: 3-7, 2011. PMID: 21311954. DOI: 10.1007/s10555-011-9292-1

3 Montironi R and Lopez-Beltran A: The 2004 WHO classification of bladder tumors: a summary and commentary. Int J Surg Pathol *13(2)*: 143-153, 2005. PMID: 15864376. DOI: 10.1177/106689690501300203

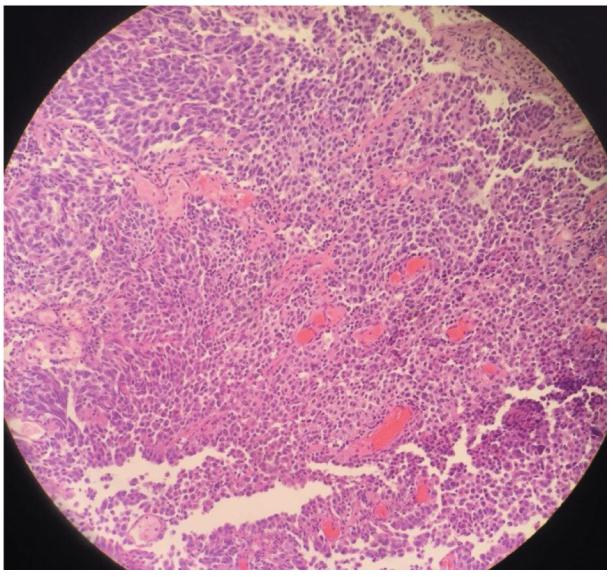

Figure 1. *Microscopic finding showing the small-cell carcinoma of the bladder (original magnification ×400).*

4
INHIBITION OF AUTOPHAGY REDUCES CELL PROLIFERATION AND MIGRATION BY P53 RESTORING IN ccRCC CELLS

Gianluca Aguiari[1], Simone Patergnani[2], Christian Rocca[3], Paolo Pinton[2], Andrea B. Galosi[4] and Lucio Dell'Atti[4]

[1]Department of Biomedical and Surgical Specialty Sciences, University of Ferrara, Ferrara, Italy;
[2]Department of Morphology, Surgery and Experimental Medicine, University of Ferrara, Ferrara, Italy;
[3]Division of Urology, University Hospital of Ferrara, Ferrara, Italy;
[4]Institute of Urology, University Hospital "Ospedali Riuniti", Ancona, Italy

Background: Clear-cell renal cell carcinoma (ccRCC) is one of the most frequent lethal urological tumors and accounts for about the 3-4% of all diagnosed human cancer (1). One-third of patients undergoing surgical resection will develop disease recurrence or distance metastases (mRCC), with overall survival at lower than 3 years. Mutations of some tumor-suppressor genes, including the cyclin-dependent kinase Inhibitor 2A (*CDKN2A)*, the tumor protein 53 (*TP53)*, and the phosphatase and tensin homolog *(PTEN)*, as well as the activation of different protein kinases, including the mammalian target of rapamycin (mTOR), contribute to cell growth and progression of kidney carcinoma. The activation

of mTOR leads to the synthesis of the mouse double minute 2 homolog (MDM2) protein ligase and induces the degradation of P53 by the proteasome machinery in KJ29 and Caki-2 kidney carcinoma cells (2). Down-regulation or mutation of *P53* may be associated with poor prognosis in renal cancer. Interestingly, P53-mutant proteins are able to activate autophagy that may drive cancer cells to grow, migrate and survive, contributing to disease progression. Here, we investigated the role autophagy might play in tumor progression and metastasis in kidney cancer. *Materials and Methods:* Analysis of autophagy was carried out in KJ29 and Caki-2 ccRCC cells by western blot using antibodies against the autophagic marker light chain 3 (LC3) protein. Autophagy was inhibited by specific short hairpin RNAs (shRNAs) silencing the autophagy related 7 (*ATG7)* gene. The expression of P53, E-cadherin, vimentin and P21 proteins was evaluated by immunoblot. Cell proliferation was analyzed by CellTiter assay (3), while cell migration was measured by groove re-colonizing assay in wild-type and *ATG7*-silenced ccRCC cells. For the analysis of cell migration, ccRCC cells were grown at confluence and detached by a sterile tip in order to produce a groove between the cells. The groove re-colonization was calculated by ImageJ software using a phase contrast microscope equipped with a CCD camera. The presence of P53 in autophagosomes was detected by immunofluorescence under fluorescence microscopy. Briefly, kidney carcinoma cells were co-transfected with a plasmid expressing wild type P53 linked to green fluorescent protein and a recombinant vector expressing sequences for miR501-5p (2). Next, cells were treated with an LC3 antibody conjugated with rhodamine and washed three times. Images were acquired by a CCD camera and processed by ImageJ program. Statistical analysis was carried out using ANOVA and *t*-test, as appropriate, with $p<0.05$ considered statistically significant. *Results:* ccRCC cells overexpressing *miR501-5p* showed an increased level of autophagy. This process affected the turnover of P53 in ccRCC cells by protein degradation into autophagosomes. The co-localization of P53-GFP with autophagic vesicles, especially in cells overexpressing the miR501-5p, indicated that some P53 is destroyed by the autophagic system. Silencing of *ATG7* gene significantly reduced autophagy and restored the P53 level in ccRCC cells. Moreover, the re-activation of P53 expression by autophagy inhibition strongly stimulated expression of cell-cycle inhibitor P21, which is positively regulated by tumor suppressor P53. As expected, the inhibition of autophagy by *ATG7* silencing reduced cell proliferation and migration in both KJ29 and Caki-2 cells. Reactivation of P53 by autophagy inhibition increased the expression of the epithelial marker E-cadherin and reduced the level of the mesenchymal protein vimentin in kidney carcinoma cells. These data indicate that autophagy may promote cell proliferation and migration in kidney cancer cells. *Discussion and Conclusion:* We described that the overexpression of *miR501-5p* correlates with poor prognosis in kidney cancer (2). Moreover, we found that the up-regulation of this miR may activate autophagy in ccRCC cells, suggesting that that this process may be associated with the progression of kidney carcinoma. The increase of autophagy causes inhibition of tumor suppressor P53. In fact, this protein is 'caught' and degraded by autophagosomal ingestion. On the other hand, the inhibition of autophagy leads to an increase in P53 expression and consequently to the synthesis of the cell-cycle inhibitor P21. Thereby the reduction of autophagy negatively affects cell proliferation, slowing growth of kidney carcinoma cells. Moreover, the epithelial to mesenchymal transition was inhibited through the up-regulation of E-cadherin and the reduction of mesenchymal marker vimentin in ccRCC cells with reduced autophagy. Taken together, these findings suggest that autophagy may affect cancer progression by the inactivation and degradation of P53, contributing to disease progression. In light of these observations, the inhibition of autophagy could open up new perspectives for the treatment of kidney carcinoma.

1 Capitanio U, Bensalah K, Bex A, Boorjian SA, Bray F, Coleman J, Gore JL, Sun M, Wood C and Russo P: Epidemiology of renal cell carcinoma. Eur Urol *75:* 74-74, 2019. PMID: 30243799. DOI: 10.1016/j.eururo.2018.08.036

2 Mangolini A, Bonon A, Volinia S, Lanza G, Gambari R, Pinton P, Russo GR, Del Senno L, Dell'Atti L and Aguiari G: Differential expression of microRNA501-5p affects the aggressiveness of clear cell renal carcinoma. FEBS Open Bio *4:* 952-965, 2014. PMID: 25426415. DOI: 10.1016/j.fob.2014.10.016

3 De Stephanis L, Mangolini A, Servello M, Harris PC, Dell'Atti L, Pinton P and Aguiari G: MicroRNA501-5p induces p53 proteasome degradation through the activation of the mTOR/MDM2 pathway in ADPKD cells. J Cell Physiol *233:* 6911-6924, 2018. PMID: 27278932. DOI: 10.1007/s10157-016-1289-1

5
EARLY COMPARISON BETWEEN ROBOT-ASSISTED RADICAL PROSTATECTOMY AND HEMI-GLAND CRYOABLATION IN ONCOLOGICAL AND FUNCTIONAL OUTCOMES

Giovanni Silecchia, Francesco Troiano, Oscar Selvaggio, Luigi Cormio and Giuseppe Carrieri

Division of Urology, University of Foggia, Foggia, Italy

Background/Aim: Cryo hemi-ablation (Cryo) is a minimally invasive procedure that preserves tissues around foci of

prostate cancer with consequent minor toxicity and blood loss (1). It has been raised as an alternative to robot-assisted radical prostatectomy (RARP) for the treatment of clinically localized prostate cancer in the setting of clinical trials. Nevertheless, there is a lack of high-quality evidence to recommend it as a first-line treatment choice. We aimed to compare the oncological and functional outcomes of the RARP and Cryo in patients with localized low- and intermediate-risk prostate cancer according to D'Amico score (2). *Patients and Methods:* We retrospectively enrolled in the study all consecutive patients who underwent RARP (n=80) between January 2017 to September 2018 and all patients who underwent Cryo (n=45) from February 2014 to September 2018 at the Division of Urology, Ospedali Riuniti of Foggia, Italy. Eligibility criteria were: prostate-specific antigen (PSA) <20 ng/ml, entry-staging biopsy with Gleason score <7 and no neoadjuvant hormonal therapy. Oncological outcome was defined as rates of biochemical disease-free (BCR-free) survival and biochemical failure in each group. In the RARP group, biochemical failure was defined as the presence of PSA greater than 0-4 ng/ml, while, in the group Cryo, it was defined as a rise of PSA >2 ng/ml from nadir, according to Phoenix criteria (3). The functional outcomes analyzed in this study were continence and sexual power, evaluated using ICIQ-SF and IIEF-5 respectively (4) (only the RARP-group received alprostadil for 4 weeks). Complications were scored using the Clavien-Dindo scale. The difference between the groups for qualitative and quantitative variables was made using the chi-square test and the Student *t*-test. Survival analysis was performed using Kaplan- Meier curves. *p*-Values <0.05 were considered statistically significant. *Results:* Median age was 65 (range=49-76) years for RARP and 75 (range=61-83) years for Cryo. Median follow-up was 11.4 months for RARP and 21.7 months for Cryo. The difference in BCR-free survival between the groups was not statistically significant (96.2% *vs*. 92% at 12 months, $p=0.535$). The analysis of IIEF-5 showed that RARP was significantly associated with lower potency rates at 3 months [6.59 (95%CI=4.94-8.24), *vs*. 12.29 (95%CI=14.77-9.81, $p=0.0002$)] but the difference became insignificant 6 months from the treatment. Conversely, the analysis of ICIQ-SF demonstrated that there was no difference in terms of continence between the two groups. Moreover, Cryo was associated with higher risk of further treatment (13% *vs*. 4%, $p=0,022$), but this group was followed-up for a longer period of time. Finally, no difference was observed between the groups in terms of complications (11.1% *vs*. 8.89% for RARP, $p=0.22$). *Discussion*: Radical prostatectomy is the gold standard of care for localized prostate cancer. Historically, cryotherapy treatment was indicated mainly as a salvage procedure for local recurrence following radiotherapy but more recently it has been used as a primary treatment for patients with localized prostate cancer (5). However, radical cryotherapy does not lack side-effects (6). This problem has led urologists to shift their attention to less and less destructive treatments such as RARP and focal/hemi-gland cryoablation. Our study had several limitations, including the small number of patients treated, non-randomized study and limited follow-up. *Conclusion:* In this study we demonstrated that hemi-gland cryoablation and RARP are comparable in terms of oncological outcomes at 12 months. The two treatments are similar in terms of continence and potency outcomes for the treatment of localized prostate cancer. However, further studies with a longer follow-up are needed to assess oncological outcomes.

1 Bahn D, de Castro Abreu AL, Gill IS, Hung AJ, Silverman P, Gross ME, Lieskovsky G and Ukimura O: Focal cryotherapy for clinically unilateral, low-intermediate risk prostate cancer in 73 men with a median follow-up of 3.7 years. Eur Urol *62*: 55-63, 2012. PMID: 22445223. DOI: 10.1016/j.eururo.2012.03.006

2 D'Amico AV, Moul J, Carroll PR, Sun L, Lubeck D and Chen MH: Cancer-specific mortality after surgery or radiation for patients with clinically localized prostate cancer managed during the prostate-specific antigen era. J Clin Oncol *21*: 2163-2172, 2003. PMID: 12775742. DOI: 10.1200/JCO.2003.01.075

3 Kongnyuy M, Lipsky MJ, Islam S, Robins DJ, Hager S, Halpern DM, Kosinski KE, Schiff JT, Corcoran AT, Wenske S and Katz AE: Predictors of biochemical recurrence after primary focal cryosurgery (hemiablation) for localized prostate cancer: A multi-institutional analytic comparison of Phoenix and Stuttgart criteria. Urol Oncol *35(8)*: 530.e15-530.e19, 2017. PMID: 28410986. DOI: 10.1016/j.urolonc.2017.03.016

4 Grabbert M, Buchner A, Butler-Ransohoff C, Kretschmer A, Stief CG and Bauer RM: Long-term functional outcome analysis in a large cohort of patients after radical prostatectomy. Neurourol Urodyn *37(7)*: 2263-2270, 2018. PMID: 29566265. DOI: 10.1002/nau.23557

5 de Castro Abreu AL, Bahn D, Leslie S, Shoji S, Silverman P, Desai MM, Gill IS and Ukimura O: Salvage focal and salvage total cryoablation for locally recurrent prostate cancer after primary radiation therapy. BJU Int *112*: 298-307, 2013. PMID: 23826840. DOI: 10.1111/bju.12151

6 Barqawi AB, Huebner E, Krughoff K and O'Donnell CI: Prospective outcome analysis of the safety and efficacy of partial and complete cryoablation in organ confined prostate cancer. Urology *112*: 126-131, 2018. PMID: 29126844. DOI: 10.1016/j.urology.2017.10.029

6

PARTIAL PROSTATE RE-IRRADIATION FOR ISOLATED LOCAL RECURRENCE OF PROSTATE CANCER: RESULTS FROM A MONO-INSTITUTIONAL SERIES

Fabio Matrone[1], Paola Chiovati[2], Filippo De Renzi[3], Giuseppe Fanetti[1], Alberto Revelant[1], Mauro Arcicasa[1] and Roberto Bortolus[1]

[1]Department of Radiation Oncology, National Cancer Institute, CRO-IRCCS, Aviano, Italy; [2]Medical Physics Unit, National Cancer Institute, CRO-IRCCS, Aviano, Italy; [3]Radiotherapy Unit, San Martino Hospital, Belluno, Italy

Background/Aim: The standard treatment for locally recurrent prostate cancer (PCa) has not yet been conclusively defined and remains an object of debate. At the present time, many different therapeutic options are available (1), including systemic therapy, *i.e.* androgen deprivation therapy, local salvage approaches with curative intent, such as salvage prostatectomy, re-irradiation [brachytherapy or external beam radiotherapy (EBRT)], cryotherapy and high-intensity focused ultrasound. However, there is no firm conclusion as to which is the most effective local therapy for locally recurrent PCa (2). The aim of the present study was to retrospectively evaluate partial prostate re-irradiation (PPR) given for isolated local relapse of PCa after primary radiotherapy in terms of feasibility, toxicity and efficacy. *Patients and Methods:* This retrospective study included patients with biochemical failure and evidence of isolated local recurrence of PCa after radical EBRT who received PPR. The diagnosis of local recurrence was based on biochemical failure confirmed by imaging studies. Advanced imaging studies were also used to exclude nodal and bone metastases. Biopsy was not mandatory if all diagnostic elements were univocal: prostate-specific antigen increase, choline positron-emission tomography (choline-PET/CT) or magnetic resonance imaging (MRI). Gross tumor volume (GTV) contouring was based on MRI/choline PET/CT co-registration. The clinical target volume (CTV) was defined as GTV; the planning target volume (PTV) was defined as the CTV plus a 3 mm margin (Figure 1). PPR was delivered with image guided-stereotactic body radiotherapy employing the RapidArc® (Varian Medical Systems, Palo Alto, CA, USA) system. All patients received a total dose of 35 Gy in seven daily fractions, a biologically effective dose of 151.7 Gy (for α/β 1.5 Gy) (Figure 2). Image-guided procedures were performed with cone beam CT before each fraction. No rectal spacer or fiducial markers were used. Gastrointestinal (GI) and genitourinary (GU) toxicities were registered according to the Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer Guideline (3) during PPR, and subsequently every 6 months after the end of radiotherapy. The serum PSA level was tested every 3 months until biochemical or clinical progression. *Results:* Between July 2012 and May 2019, 44 patients were treated with PPR. Previous EBRT included 3D-CRT in 28 patients and Intensity Modulated Radiation Therapy in 16. At the first EBRT, 26 patients were treated with conventional fractionation and 18 received moderate hypofractionation. The median interval between the first EBRT and PPR was 60 months. The median age at PPR was 76 years, and the median pre-PPR PSA level was 2.6 ng/ml. Concomitant androgen deprivation therapy with luteinizing hormone-releasing hormone agonist was used in 12 patients (Table I). All patients completed the planned treatment. The median post-PPR PSA level was 1.1 ng/ml. No acute grade 3 or more GU or GI nor late grade 3 or more GI events were observed. Two late grade 3 GU toxicities were registered (Table II). The median follow-up was 25.4 months (range=6-81.5 months). Tumor progression was observed in 18 patients (40.9%), with a median time to relapse of 18.1 months (range=7.6-53 months). In all cases, clinical progression was preceded by biochemical progression. Six

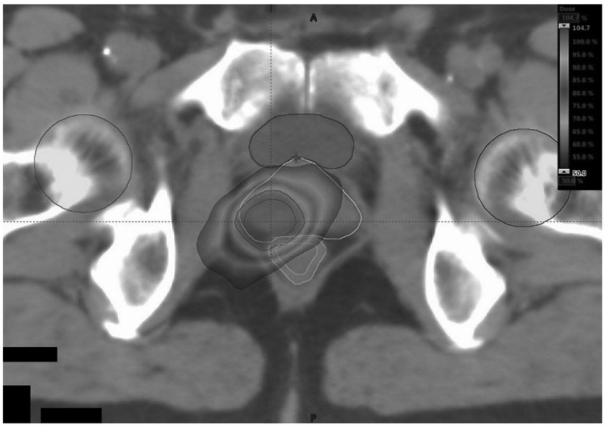

Figure 1. *Tumor volume contouring.*

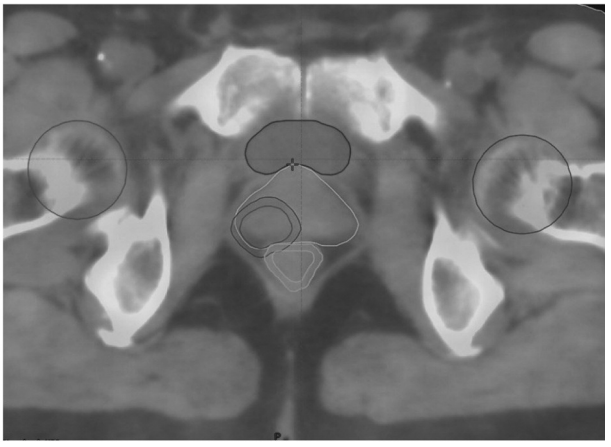

Figure 2. *Dose distribution.*

Table I. *Patient characteristics (N=44 patients).*

Characteristic	Value
Prior RT	
Age at diagnosis, years	
Median (range)	68 (51-81)
Initial PSA, ng/ml	
Median (range)	8.7 (2.6-46)
Initial Gleason score	
Median (range)	7a (6-9)
Prior RT modality	
3D	28 (64%)
IMRT	16 (36%)
BED, Gy	
Median (range)	177.3 (151.7-186.7)
Prophylactic pelvic irradiation	2 (4%)
Interval between first RT and PPR, months	
Median (range)	60 (16.9-615.5)
PPR	
Total	39 (89%)
Age at PPR, years	
Median (range)	76 (56-89)
Pre-PPR PSA, ng/ml	
Median (range)	2.6 (2-7.68)
Concomitant androgen deprivation, n (%)	
Yes	12 (27%)
No	32 (73%)
Duration, months	
Median (range)	4.2 (2.9-7.1)
Biopsy of the target lesion, n (%)	
Yes	5 (11%)
Positive	5
Gleason score	
Median (range)	6 (6-7a)
Diagnosis	
Histological/radiological, n	
Biopsy + PET + MRI	1
Biopsy + MRI	2
Biopsy + PET	2
PET/CT only	27
PET/CT+MRI	2
MRI only	10
Target lesion	
Left lobe	15
Right lobe	16
Apex	2
Seminal vesicle	2
Bilateral anteriorly	1
Bilateral posteriorly	8

RT: Radiotherapy; BED: biologically effective dose of first RT calculated for α/β 1.5 Gy.

Table II. *Acute and late toxicities. Genito-urinary (GU) and gastro-intestinal (GI) toxicities is presented for all patients.*

	Acute toxicity All patients		Late toxicity All patients	
Grade	GU	GI	GU	GI
0	30 (68%)	40 (92%)	28 (64%)	41 (93%)
1	10 (23%)	2 (4%)	8 (18%)	3 (7%)
2	4 (9%)	2 (4%)	6 (14%)	0
3	0	0	2 (4%)	0
Total patients	44	44	44	44

Table III. *Patterns of failure evaluated in the 44 patients.*

Outcome	All patients, n (%)
Biochemical relapse only	4 (22%)
Concomitant ADT	1
Clinical recurrence in-field	4 (22%)
Concomitant ADT	1
Clinical recurrence in-field and out of field	2 (11%)
Concomitant ADT	0
Clinical recurrence out of field	
Locoregional relapse with metastatic relapse	1 (6%)
Concomitant ADT	0
Locoregional relapse	6 (33%)
Concomitant ADT	1
Metastatic relapse	1 (6%)
Concomitant ADT	1
Total recurrences	18

ADT: Androgen-deprivation therapy.

patients (13.6%) experienced local relapse (Table III). Two-year local control, biochemical and clinical relapse-free survival rates were 92.7%, 57.9% and 67.5%, respectively. At the last follow-up, 43 patients were alive; 26 (59%) showed no evidence of disease, and 17 (38.6%) were alive with biochemical or clinical disease. Metastatic disease was reported in five patients, of whom two developed metastatic castration-resistant PCa. One patient with clinical recurrence died of other causes. No patient was lost to follow-up. At statistical analysis, the occurrence of relapse after PPR mildly correlated with the radiation dose delivered at the first treatment, as well as with the time interval between the first EBRT and PPR (p=0.06 and p=0.05, respectively). *Discussion and Conclusion:* Our study reports data from the largest patient population treated with PPR to date. Our study demonstrates that PPR is a feasible, safe and effective salvage treatment for isolated local PCa recurrence. Long-term prospective studies in larger populations are required in order to determine the optimal patient selection, radiation dose and treatment volume parameters.

1 Tetreault-Laflamme A and Crook J: Options for salvage of radiation failures for prostate cancer. Semin Radiat Oncol *27:* 67-78, 2017. PMID: 27986213. DOI: 10.1016/j.semradonc.2016.08.007

2 Cornford P, Bellmunt J, Bolla M, Briers E, De Santis M, Gross T, Henry AM, Joniau S, Lam TB, Mason MD, van der Poel HG, van der Kwast TH, Rouvière O, Wiegel T and Mottet N: EAU-ESTRO-SIOG Guidelines on prostate cancer. Part II: Treatment of relapsing, metastatic, and castration-resistant prostate cancer. Eur Urol *71:* 630-642, 2017. PMID: 27591931. DOI: 10.1016/j.eururo.2016.08.002

3 Cox JD, Stetz J and Pajak TF: Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys *31(5)*: 1341-1346, 1995. PMID: 7713792. DOI: 10.1016/0360-3016(95)00060-C

7
CIGARETTE SMOKING CESSATION AT PRIMARY DIAGNOSIS AND RECURRENCE OF NON-MUSCLE-INVASIVE BLADDER CANCER: RESULTS AT 3 YEARS OF A PROSPECTIVE STUDY

Vincenzo Serretta[1], Fabrizio Di Maida[1], Marco Vella[1], Nino Dispensa[1], Carlo Pavone[1], Loris Cacciatore[1], Davide Baiamonte[1] and Chiara Sanfilippo[2]

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

Background/Aim: Evidence that cessation of smoking at first diagnosis of non-muscle-invasive bladder cancer (NMIBC) reduces the risk of recurrence is lacking. The aim of our prospective study was to analyze the association between the change in patients' smoking habits after diagnosis and recurrence-free survival (RFS) at short- and medium-term follow-up. *Patients and Methods:* After transurethral resection of primary NMIBC, patients definitively stopping were classified as 'quitting' and those continuing or restarting to smoke as 'active smokers'. Smoking status was re-assessed 3-monthly for the first year and 6-monthly thereafter. Data on patient demographics, smoking status, tumor characteristics, treatments and follow-up were collected. Statistical analysis was performed using SPSS 15.0.1 and R3.4.2. software. *Results:* Out of 194 patients, 67 (34.5%) quit after their diagnosis, while 127 (65.5%) did not. The clinical and pathological characteristics were homogeneously distributed between the two groups (Table I). At a median follow-up of 38 months, 106 patients (54.6%) experienced recurrence, 33 (49.2%) from those who quit and 73 (60.3%) active smokers, with 3-year RFS of 42.3% and 50.7%, respectively (p=0.55). The median time to first recurrence was 9 and 11 months among active and quitting smokers, respectively. No statistically significant association between recurrence, pathological features of the primary tumor and patient smoking habit after diagnosis was detected. Similarly, no association was found between smoking habit and pathology of the recurrent tumor. At multivariate analysis, cigarette smoking cessation did not significantly reduce tumor recurrence. Results were not statistically influenced by the intensity (number of cigarettes per day) and duration (years) of smoking. Tumor multiplicity only was predictive of recurrence (p=0.003). *Discussion and Conclusion:* In our prospective study more than half of our patients recurred at 3 years. At multivariate analysis, cigarette smoking cessation did not significantly reduce tumor recurrence. However, the 8.4% reduction in those quitting suggests the need for larger studies with longer follow-up. Surprisingly, only 35% of smokers definitively quit when bladder cancer was diagnosed. Urologists should play a more active role in persuading patients to give up smoking at first diagnosis. *Acknowledgements*: We express our thanks to the GSTU Foundation, Palermo, Italy for editing and statistical support.

Table I. *Multivariate analysis*.

	HR	(95% CI)	p-Value
Age	1.006	(0.9816-1.020)	0.9508
T-category			
Tis	1		
Ta	0.7587	(0.3252-1.770)	0.523
T1	0.8926	(0.3907-2.039)	0.7875
Grade			
HG	1		
LG	0.9297	(0.6010-1.438)	0.7434
Multiplicity			
Multiple	1		
Single	0.4676	(0.3097-0.706)	0.003
Smoking cessation			
Yes	1		
No	0.7689	(0.5073-1.165)	0.2154
Years of exposure	0.9998	(0.9836-1.016)	0.9849
Cigarettes/day	1.009	(0.9867-1.032)	0.598

8
FLUCICLOVINE (ANTI-^{18}F-FACBC) PET/CT IN PATIENTS WITH PROSTATE CANCER: A PRELIMINARY CLINICAL EXPERIENCE

Michele Balma[1], Manuela Racca[2], Simona Cauda[2], Matteo Manfredi[2], Francesco Porpiglia[3], Stefano De Luca[3], Christian Fiori[3] and Paola Scapoli[4]

[1]Division of Nuclear Medicine, Candiolo Cancer Institute-FPO, IRCCS, Candiolo, Italy;

[2]Division of Nuclear Medicine, Candiolo Cancer Institute-FPO, IRCCS, Candiolo, Italy;
[3]Division of Urology, University of Turin, San Luigi Hospital, Orbassano, Italy;
[4]Division of Nuclear Medicine, Candiolo Cancer Institute-FPO, IRCCS, Candiolo, Italy

Background/Aim: Prostate cancer (PCa) is one of the leading causes of morbidity and death in the Western world, being the second most common type of cancer in men worldwide. In the past 10 years, positron-emission tomography/ computed tomography (PET/CT) has reached a pivotal role in the evaluation of patients with PCa, in particular in the setting of biochemical relapse following local therapy (*e.g.* surgery or radiotherapy). PET/CT performed with radiolabeled choline (taking part in phosphatidylcholine synthesis for cell membrane renewal) and ^{68}Ga-prostate-specific membrane antigen (targeting overexpression of this transmembrane protein) have both shown the ability to detect early recurrence of disease when conventional imaging is negative or inconclusive. A new tracer, *trans*-1-amino-3-^{18}F-fluorocyclobutanecarboxylic-acid (^{18}F-FACBC), also known as fluciclovine, has been shown to be promising in visualizing PCa [correlated to the up-regulated expression of amino acid transporter activity (LAT1) in prostate cancer cells]. It has been approved for detection of PCa in patients with an elevated PSA level following prior treatment. Few pooled data have been published about the role of ^{18}F-FACBC in patients with PCa. Our preliminary clinical experience aims to offer a little help in investigating the diagnostic performance of ^{18}F-FACBC in patients with recurrent PCa. This work is a retrospective analysis of 28 patients who were referred to our institution for ^{18}F-FACBC PET/CT. Data analysis was performed according to the principles of the declaration of Helsinki. Written informed consent was obtained from all patients. *Materials and Methods*: Twenty-eight ^{18}F-FACBC PET/CT scans from 28 patients with PCa in the setting of biochemical recurrence following local therapy were analyzed. Their age ranged from 56 to 83 years (mean age=70.5±7.8 years); Gleason score ranged from 6-9 (mean=7.5±0.8); PSA value ranged from 0.26-11 μg/l (mean=1.73±2.87 μg/l). Twenty-six patients had radical prostatectomy; of these, in 11 this was following radiotherapy and in five following androgen deprivation therapy. Only two patients received radical radiotherapy. Scans were performed by a Philips Gemini TF Scanner, combined with low-dose CT. The injected activity of ^{18}F-FACBC ranged from 261 to 370 MBq (mean=285.08±22.12 MBq). Early imaging was performed starting 4±1 min after injection from the midthighs, using 3 min per bed position for the pelvic region and the lower abdomen and 1.5 min per bed position for the rest of the body (from the upper abdomen to the cranial base). Lesions were considered abnormal when: i) Focal tracer uptake (axial size ≥1 cm) was ≥ than bone marrow accumulation; ii) focal tracer accumulation (axial size <1 cm) was greater than the blood pool uptake. Diagnosis of malignant lymph nodes on ^{18}F-FACBC PET/CT images was based on visual assessment; lymph nodes were considered benign when their axial size was not greater than 10 mm on CT scans and without abnormal ^{18}F-FACBC uptake. The interpretation of malignant or benign lesions usually depended on the anatomical localization and the presence/absence of ^{18}F-FACBC uptake (uptake was compared with the findings of correlative imaging). The analysis was performed by four physicians specialized in nuclear medicine, experts in PET/CT scans in the oncology field. The results were expressed as the mean±standard deviation for each variable. Comparison of data among various groups was performed with Student's unpaired *t*-test. A value of $p<0.05$ was considered statistically significant. To calculate correlation between PSA, PSA doubling time, SUVmax and number of metabolically active lesions, Spearman's rank correlation coefficient and simple linear regression for building the curves were used. In cases of non-Gaussian distribution, Mann–Whitney *U*-test was used. *Results:* In 13 positive ^{18}F-FACBC PET/CT scans (46.4%), a total of 18 metabolic active lesions were detected. In prostate and prostate bed, abnormal uptake was found in 10 cases (62.5%), with SUVmax ranging from 2.1 to 4.2 (mean=2.98±0.82). In local lymph nodes, eight lesions (44.4%) were found with an SUVmax of 1.8-7.5 (mean=3.75±2.75). No bone lesions were detected. The mean PSA level in patients with negative ^{18}F-FACBC PET/CT findings was 1.01±0.97 (0.3-2.4) μg/l, whereas in patients with positive ^{18}F-FACBC PET/CT findings, the mean PSA level was 2.58±4.15 (0.3-11.0) μg/l. The mean PSA level in patients with ^{18}F-FACBC PET/CT positive for prostate/prostate bed findings was 2.8±0.6 (2.1-4.2) μg/l, whereas the mean PSA level in patients with ^{18}F-FACBC PET/CT positive for lymph nodes findings was 4.1±2.3 (1.8-7.5) μg/l. There were no statistically significant differences in PSA values between patients with positive and negative findings ($p>0.5$, Mann–Whitney *U*-test). We did not find statistically significant differences even in PSA doubling time/velocity values between patients with positive and negative findings ($p>0.5$). We found an important difference in SUVmax values between patients with ^{18}F-FACBC PET/CT positive findings for prostate/prostate bed and patients with ^{18}F-FACBC PET/CT positive findings for lymph nodes (although not statistically significant; $p=0.12$). Our experience with ^{18}F-FACBC notes two important limitations of our study: A low sample size and a high heterogeneity of patients. Despite these limitations, there was a change in treatment management in some cases: Five patients with ^{18}F-FACBC PET/CT positive findings for lymph nodes underwent targeted radiotherapy treatment (*i.e.* tomotherapy). No patient experienced adverse reactions after tracer injection. *Discussion and Conclusion:* The synthetic

amino acid FACBC is an isoleucine analog and was developed for the assessment of the anabolic component of tumor metabolism. The cellular uptake of ^{18}F-FACBC is mediated by the large-neutral amino acid transport system and ^{18}F-FACBC is transported into cells but not incorporated into proteins. Because only a small amount of ^{18}F-FACBC is excreted into the urinary system and amino acid uptake is enhanced in malignancy, ^{18}F-FACBC may play a central role in patients with PCa. In the retrospective analysis of our clinical data, ^{18}F-FACBC PET/CT showed its potential for targeting active PCa. Our study was conducted on a very small and heterogeneous population; these are the most important limitations of our experience. However, our results seem promising and are in line with the data of the current literature. Although there were no statistically significant differences in the PSA values nor in PSA doubling time/velocity values between patients with positive and negative findings, we did find an important, although not statistically significant, difference in SUVmax values between patients with positive findings for the prostate/prostate bed and those with positive findings for lymph nodes. Perhaps the most important result of our study was the change in treatment management in five patients. Regarding the correlation between PSA levels and lesion detection, three patients were definitively positive when PSA was 0.8-0.9 μg/l, but we did not find any clear lesion at lower PSA levels, in particular less than 0.5 μg/l. In the literature, ^{18}F-FACBC uptake in a pelvic lymph node was reported in a patient previously treated with radical prostatectomy whose PSA level was as low as 0.03 μg/l. Our experience confirms that a regular distribution of ^{18}F-FACBC demonstrates an intense uptake in the pancreas and in the liver, and faint uptake in the bone marrow; these are good features for prostate cancer detection because these regions are usually free from disease in early stages. Urinary clearance seldom appears, although small urinary excretion was observed in some of our patients. From this preliminary clinical experience, we conclude that ^{18}F-FACBC PET/CT may play an important role in *in vivo* assessment of PCa, especially in patients with an elevated PSA level following prior treatment (*i.e.* biochemical recurrence). Furthermore, ^{18}F-FACBC PET/CT may have another central role in dose planning for targeted external beam radiation therapy. Further prospective studies are needed to increase our knowledge about ^{18}F-FACBC PET/CT in PCa and to compare this agent to other available radiotracers in this setting.

12
OUTCOMES AND PREDICTORS OF PAIN FROM A MULTICENTER STUDY OF 1,008 MEN UNDERGOING TRANSPERINEAL FREE-HAND mpMRI FUSION-TARGETED BIOPSY UNDER LOCAL ANESTHESIA

Alessandro Marquis[1], Junlong Zhuang[2], Giancarlo Marra[1], Mattia Beltrami[1], Xiaozhi Zhao[2], Giorgio Calleris[1], Yansheng Kan[2], Marco Oderda[1], Haifeng Huang[2], Riccardo Faleti[3], Qing Zhang[2], Luca Molinaro[4], Wei Wang[2], Laura Bergamasco[3], Hongqian Guo[2] and Paolo Gontero[1]

[1]Department of Urology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy;
[2]Department of Urology, Drum Tower Hospital, Medical School of Nanjing University, Nanjing University, Nanjing, P.R. China;
[3]Department of Radiology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy;
[4]Department of Pathology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy

Background: Peri-procedural pain is considered a major argument against the use of transperineal (TP) biopsy under local anesthesia (LA). Furthermore, in the context of multiparametric magnetic resonance imaging-TP fusion biopsies (TPFBx), patient movement due to procedural pain may be a potential source of inaccuracy, reducing clinically significant prostate cancer (csPCa) detection on target. *Patients and Methods:* From 2016 to 2019, we performed a multicenter prospective study in men undergoing TPFBx under LA. Primary outcome was to evaluate pain influence on csPCa target core detection. Pain scores in different procedural phases and factors associated with severe pain were also assessed. Pain scores were recorded using a numeric rating scale (NRS) at the time of: i) Transrectal ultrasound probe insertion; ii) LA; iii) prostate biopsy. Severe pain and pre-procedural anxiety were defined as NRS>6. csPCa was defined as: i) GS >6 or GS=6 having three or more positive cores or one core with >50% PCa involvement (D1); ii) GS ≥7(3+4) (D2). *Results:* A total of 1,008 men undergoing TPFBx under LA were included. Mean age and prostate volume were 66.7±7.4 and 50.9±27.1 cc, respectively. One target was present in 667 whilst 341 men had two or more target areas. The mean number of cores taken and procedural time were 15.3±1.4 and 15.9±4.9 min, respectively. The mean NRS pain scores were 3.9±2.1 for LA, 3.1±2.3 for biopsy; maximum mean experienced pain was 4.7±2.1. On multivariate analysis, age was a protective factor and severe anxiety a risk factor for both severe biopsy [age: odds ratio (OR)=0.96, 95% confidence interval (CI)=0.94-0.99; anxiety >6 OR=2.99, 95% CI=1.83-4.89] and severe maximum pain (age: OR=0.96, 95% CI=0.94-0.98; anxiety >6 OR=2.82, 95% CI=1.87-4.27). Procedural time was also associated with an increased risk

of experiencing maximum pain (OR=1.03, 95% CI=1.01-1.06). Severe biopsy pain was not associated with significantly lower csPCa detection on targeted cores defining csPCa according to both D1 (csPCa 29.4% *vs.* pain ≤6 35.6%, p=0.23) and D2 (csPCa 23.9% *vs.* pain ≤6 27.6%, p=0.47). *Conclusion:* TPFBx under LA was found to be tolerable, with highest pain scores being recorded during LA. Age and severe anxiety were associated with reduced and increased patient peri-procedural pain, respectively. Pain did not significantly influence csPCa target detection. Future studies are needed to confirm our findings.

13

SHORT-TERM NEO-ADJUVANT AND ADJUVANT CHEMO-HYPERTHERMIA IN INTERMEDIATE RISK NON MUSCLE INVASIVE BLADDER CANCER. PILOT STUDY ON FEASIBILITY AND TOLERABILITY

Vincenzo Serretta, Gabriele Tulone, Gaspare Maria Contino, Alessio Guarneri, Calogero Guzzardo, Paola Brunelli, Sonia Agiato, Carlo Pavone and Alchiede Simonato

Urology Unit, Department of Surgical, Oncological and Oral Sciences, University of Palermo, Palermo, Italy

Background/Aim: Intermediate risk non muscle invasive bladder cancer (IR-NMIBC) represents a therapeutic challenge, especially in the case of shortage of Bacillus Calmette Guerin or intolerance. Moreover, many patients show a low compliance to a maintenance regimen, often due to social and geographical difficulties. Hyperthermic intravesical chemotherapy (HIVEC) has been tested as adjuvant therapy in selected categories of patients with promising results. Yet the best administration schedule has not been standardized. Tolerance and security issues are still the object of debate, while efficacy needs to be confirmed by larger studies. A pilot study was carried out on the feasibility and tolerability of short-term perioperative HIVEC prior to transurethral resection of bladder tumor (TURBT) for IR-NMIBC. *Materials and Methods:* Patients affected by IR-NMIBC according to the guidelines of the European Association of Urology were recruited. Main exclusion criteria were urinary tract infection, tumor other than skin basal cell carcinoma, bladder capacity <150 ml, maximum diameter less than 3 cm, fewer than eight tumors, platelets <100,000/μI, coagulation disorders, anticoagulants or drugs inhibiting the coagulation system other than heparin and anti-aggregants, or intravesical mitomycin (MMC) in the last 12 months. MMC was administered at a 40 mg diluted in 40 ml of saline solution heated by the bladder-heating BRS device (Combat BRS)®. The target temperature was 43±1˚C, maintained for a dwell time of 60 min. The treatment schedule consisted of a single neoadjuvant instillation within 24 h before TUR followed by a single adjuvant instillation 14-21 days after TUR. Cystoscopy and cytology were scheduled every 3 months for the first year and 6-monthly thereafter. Toxicity was graded according to Common Terminology Criteria for Adverse Events version 3.0. *Results:* Eighteen cycles of HIVEC were evaluated in nine patients, eight men and one woman, median age of 74.4 years (range=66-87 years). Five patients were treated with antiplatelet drugs, one patient with heparin. The bladder tumor was recurrent in nine (100%) patients and multiple in seven (77.7%). The median number of tumors was 2 (range=1-5). The median diameter of the largest lesion was 10 mm (range=5-30 mm). The median temperature during neoadjuvant and adjuvant treatments was 43˚C (range=42.5-43.5˚C) and 43˚C (range=43-43.5˚C), respectively. One treatment was stopped early, after 45 min due to bladder spasms and pelvic discomfort. Adverse events were mild (grade 1) and self-limited, both during neoadjuvant and adjuvant treatments. Mild hematuria not requiring treatment interruption was detected in five (27.8%) treatments, three cases in the neoadjuvant setting. One patient suffered mild dysuria (grade 2) for up to 1 week after the treatment. No relevant hematuria was detected in patients receiving heparin or anti-aggregant drugs. In most patients, although asymptomatic, at TUR a vascularized area, mainly in the posterior bladder wall was detected and the tumors appeared edematous, and hypervascularized with hemorrhagic lesion; a partially necrotic area was evident in two patients. No perioperative complications were detected nor were unusual bleedings noted. At a median follow-up of 6 months (range=3-9 months) one patient experienced recurrence. *Conclusion:* Our experience, although preliminary, confirms the feasibility and the good tolerability of HIVEC with a single upfront instillation repeated in the adjuvant setting. Heparin or anti-aggregant drugs did not increase bleeding during the treatment or thereafter. Larger studies are needed to compare the efficacy of a short-term perioperative HIVEC treatment with the standard regimen of intravesical prophylaxis.

16

THE RELATIONSHIP BETWEEN PROSTATE CANCER ANXIETY AND MINDFULNESS ABILITY IN PATIENTS WITH PCa

Paola Dordoni[1], Letizia De Luca[1], Simona Donegani[1], Barbara Avuzzi[2], Melanie Claps[3], Tiziana Magnani[1], Cristina Marenghi[1], Barbara Noris Chiorda[2], Nicola Nicolai[4], Giuseppe Procopio[3], Antonio Tesone[4], Elena Verzoni[3] and Riccardo Valdagni[5]

[1]Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy;
[2]Division of Radiation Oncology 1, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy;
[3]Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy;
[4]Division of Urology, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy;
[5]Department of Oncology and Hemato-oncology, University of Milan, Radiation Oncology 1, Prostate Cancer Program, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Background/Aim: Anxiety related to prostate cancer (PCa) is one of the major psychological outcomes reported both before and after cancer treatment with the potential for affecting adherence to the treatment plan (1). However, patients reporting PCa anxiety may step back from their thoughts, reducing cognitive fusion with them, thus reducing anxiety related to cancer. This is mindfulness, which may serve patients as a healthful refuge in the present. Mindfulness refers to a particular way of paying attention, or a moment-to-moment awareness, by which the person remains non-judgmental and accepting of the different sensations, thoughts, and perceptions that cross their mind. The present study was pilot research which aimed to investigate PCa anxiety and mindfulness in men with PCa and examine their relationship. *Patients and Methods:* The study population included patients with PCa at Fondazione IRCCS Istituto Nazionale dei Tumori in Milan and was approved by the Ethical Committee. The research focused on patients who had received treatment (prostatectomy, or radiotherapy, or hormone therapy) or started active surveillance at least 1 year earlier (1). Patients were asked to fill in questionnaires. The Memorial Anxiety Scale for Prostate Cancer (MAX-PC) was used to explore patients' PCa-related anxiety (scores range from 0 to 3, with high scores indicating high anxiety levels); subscales were: i) PCa anxiety; ii) PSA anxiety; iii) fear of recurrence. The Mindfulness Awareness Attention Scale (MAAS) was used to explore men's awareness of their experience in the moment (scores range from 1 to 6, with high scores indicating high mindfulness). Descriptive analyses and correlation analyses were performed. *Results:* Between June 2018 and June 2019, 56 patients completed the questionnaire. Their mean (±SD) age was 65±10.1 (range=21-84) years. Table I shows descriptive analyses of each subscale of MAX-PC and MAAS. Findings suggest that men report low anxiety levels and good mindfulness. Table II shows the correlations between anxiety subscales and mindfulness. Results show a negative relation between PCa anxiety and mindfulness ($r=-0.333$, $p<0.05$). *Conclusion:* Our findings suggest that men who had received treatment (prostatectomy, or radiotherapy, or hormone therapy) or started active surveillance at least 1 year earlier had low anxiety levels and high mindfulness ability. After the decision-making phase, in which PCa anxiety is typically expressed, men may assume a "can do approach" when starting the active/observational treatment. In other words, thanks to their exposure to active/observational treatment, men may be much more in contact with their experience living in the present moment (*i.e.* mindfulness); as a consequence, the related mere exposure may contribute to reducing anxiety. Similar findings were observed by Korfage and colleagues (2) in longitudinal research on PCa: an improvement in mental health at 6-month follow-up after treatment was shown in both prostatectomy and radiotherapy groups. In conclusion, even if our results oppose previous findings on PCa anxiety, the present research recommends the assessment of anxiety and mindfulness in men with PCa and calls for particular attention at each treatment/observational phase.

Table I. *Descriptive analyses of anxiety subscales and mindfulness.*

	Score			
	Median	SD	Min.	Max.
Anxiety total score	1.12	0.61	0	2.5
PCa anxiety	0.94	0.72	0	2.4
PSA anxiety	1.15	0.96	0	3
Fear of recurrence	1.38	0.88	0	3
Mindfulness	4.86	0.74	2.7	5.8

Table II. *Correlations between anxiety subscales and mindfulness scores.*

	Mindfulness	Anxiety total score	PCa anxiety	PSA anxiety	Fear of recurrence
Mindfulness	-				
Anxiety total score	–0.24	-			
PCa anxiety	–0.33*	0.91**	-		
PSA anxiety	–0.13	0.85**	0.77**	-	
Fear of recurrence	0.00	0.57**	0.23	0.27*	-

*$p>0.05$; **$p>0.01$ ***$p>0.001$.

1 Watts S, Leydon G, Birch B, Prescott P, Lai L, Eardley S and Lewith: Depression and anxiety in prostate cancer: a systematic review and meta-analysis of prevalence rates. BMJ Open *4(3)*: e003901, 2014. PMID: 24625637. DOI: 10.1136/bmjopen-2013-003901

2 Korfage IJ, Essink-Bot ML, Janssens ACJW, Schröder FH and De Koning HJ: Anxiety and depression after prostate cancer diagnosis and treatment: 5-year follow-up. Br J Cancer *94(8)*: 1093-1098, 2006. PMID: 16622434. DOI: 10.1038/sj.bjc.6603057

17

IS SYSTEMATIC SAMPLING STILL NEEDED IN THE SETTING OF A TRANSPERINEAL mpMRI TARGETED BIOPSY UNDER LOCAL ANESTHESIA? ANALYSIS OF A MULTICENTER PROSPECTIVE COHORT OF 1,014 PATIENTS

Giorgio Calleris[1*], Giancarlo Marra[1*], Junlong Zhuang[2], Mattia Beltrami[1], Alessandro Marquis[1], Xiaozhi Zhao[2], Marco Oderda[1], Yansheng Kan[2], Alessandro Greco[1], Andrea Zitella[1], Haifeng Huang[2], Riccardo Faletti[3], Qing Zhang[2], Luca Molinaro[4], Wei Wang[2], Laura Bergamasco[3], Hongqian Guo[2] and Paolo Gontero[1]

[1]Department of Urology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy;
[2]Department of Urology, Drum Tower Hospital, Medical School of Nanjing University, Nanjing University, Nanjing, P.R. China;
[3]Department of Radiology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy;
[4]Department of Pathology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy

*These Authors contributed equally to this study.

Background/Aim: No definitive evidence on the added value and drawbacks of systematic prostate sampling, in addition to multiparametric magnetic resonance imaging (mpMRI) targeted cores, is available. We investigated this issue in a large multicenter prospective series of mpMRI targeted fusion transperineal biopsy (TPFBx) under local anesthesia (LA). *Materials and Methods:* At two tertiary referral institutions, 1,327 patients with a positive mpMRI undergoing TPFBx under LA from September 2016 to May 2019 were evaluated for inclusion. Men over 80 years old were excluded, as were those with prostate-specific antigen (PSA)>20 ng/ml or under active surveillance. The Esaote platform was employed for fusion of ultrasound and mpMRI, then systematic 12-core mapping was performed. The impact of performing systematic sampling after targeted biopsy on the following outcomes was evaluated: i) Clinically significant (cs) PCa detection [Definition 1 (D1): International Society of Uro-Pathology grade group (ISUP)>6 or >50% involvement of PCa in a single core or >2 cores; Definition 2 (D2): ISUP >6]; ii) concordance with radical prostatectomy (RP). We secondarily assessed: i) Peri-procedural pain (NRS) and its duration; ii) adverse events. *Results:* A total of 1,014 patients were included (mean age=66.8±7.4 years and mean PSA 8.1±4.1 ng/ml; n=1,424 mpMRI lesions). csPCa was diagnosed in 39.4% (D1). The detection rate by targeted plus mapping was significantly higher considering csPCa [4.6%, 95% confidence intervaI (CI)=3.5-6.1%, $p<0.001$] and non-csPCa (2.3%, 95% CI=1.5-3.4%, $p=0.04$) compared to targeted biopsy alone; every 22 procedures (95% CI=17-29) the targeted plus mapping approach identified a csPCa which would have been missed by target biopsy. The targeted plus mapping approach upgraded the targeted-only pathological ISUP score approximately once every 10 procedures (9%; 95% CI=7.4-10.9), also allowing an enhanced ISUP score agreement with the RP specimen (k=0.65 *vs*. k=0.40, $p<0.05$). Results of five out of six (84.1%) target biopsies were not substantially modified by considering random sampling. Hematuria and hematospermia were frequent and self-resolving (58.1% and 22.2% of men, lasting 9.6±7.2 and 18±11.9 days, respectively). No post-biopsy sepsis was registered, while fever occurred in 0.7%. Because of urinary retention, 1.7% of men underwent catheterization. *Conclusion:* TPFBx under LA demonstrated good diagnostic performance with few adverse events. Systematic prostate sampling in addition to targeted biopsy might not be mandatory in all patients, although being beneficial in terms of csPCa detection and grading concordance with RP.

We would like to thank Stefano Tappero and Daniele D'Agate.

18

ARE TRANSPERINEAL FREE-HAND mpMRI FUSION TARGETED PROSTATE BIOPSIES UNDER LOCAL ANESTHESIA ACCURATE AND FEASIBLE? OUTCOMES FROM A PROSPECTIVE MULTICENTER SERIES OF 1,014 CASES

Giorgio Calleris[1], Giancarlo Marra[1], Junlong Zhuang[2], Mattia Beltrami[1], Alessandro Marquis[1], Xiaozhi Zhao[2], Marco Oderda[1], Yansheng Kan[2], Alessandro Greco[1], Andrea Zitella[1], Haifeng Huang[2], Riccardo Faletti[3], Simone Cappuccelli[1], Qing Zhang[2], Luca Molinaro[4], Stefano Tappero[1], Daniele D'Agate[1], Wei Wang[2], Laura Bergamasco[3], Hongqian Guo[2] and Paolo Gontero[1]

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

Table I. *Multivariate analysis of predictors of clinically significant prostate cancer (csPCa) according to different csPCa definitions.*

	csPCa (Definition 1)				csPCa (ISUP >1)			
	Odds ratios	95% CI		*p*-Value	Odds ratios	95% CI		*p*-Value
Age, years	1.06	1.04	1.09	<0.0001	1.07	1.04	1.09	<0.0001
PCa familiality	1.6	0.89	2.88	0.11	1.55	0.86	2.79	0.14
Race (Asiatic)	0.66	0.59	0.75	<0.0001	0.64	0.56	0.72	<0.0001
Previous biopsy	0.36	0.22	0.58	<0.0001	0.41	0.25	0.66	0.0003
PSA density	2.794	598.0	13,063.0	<0.0001	749.0	181.97	3,085.44	<0.0001
DRE+	1.99	1.34	2.94	<0.0001	2.11	1.43	3.13	0.0002
RMN Center	1.29	0.78	2.13	0.323	1.49	0.9	2.45	0.12
Higher PIRADS	3.34	2.49	4.49	<0.0001	3.35	2.47	4.55	<0.0001
Anterior location	0.97	0.68	1.38	0.856	1.14	0.4	3.23	0.13
Lesion volume	0.92	0.77	1.1	0.367	0.89	0.73	1.08	0.25
Number of targets	-	-	-	-	0.89	0.67	1.19	0.42

PCa: Prostate cancer; PSA: prostate specific antigen; DRE+: positive digital rectal exam; PIRADS: prostate imaging reporting and data system.

[2]Department of Urology, Drum Tower Hospital, Medical School of Nanjing University, Nanjing University, Nanjing, P.R. China;
[3]Department of Radiology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy;
[4]Department of Pathology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy

Background/Aim: Accuracy and tolerability of multiparametric magnetic resonance imaging (mpMRI) targeted fusion transperineal biopsy (TPFBx) for prostate cancer (PCa) under local anesthesia (LA) have never been investigated in a large multicenter prospective study. Whether transperineal or transrectal biopsy is the better route is still an open question in times of growing antimicrobial resistance. *Materials and Methods:* From September 2016 to May 2019, at two high-volume referral centers, 1,327 men undergoing TPFBx (targeted and systematic cores) under LA with positive magnetic resonance imaging, performed because of elevated prostate specific antigen (PSA)/suspicious digital rectal exam (DRE), were prospectively screened. Exclusion criteria were: Age >80 years, known PCa or PSA>20 ng/ml. Primary outcomes were: i) Clinically significant (cs) PCa detection defined as: a) International Society of Uro-Pathology (ISUP)>6 or ISUP 6 with >50% PCa in a single core or >2 cores involved (D1); b) ISUP >6 (D2); ii) peri-procedural pain using numerical rating scale (NRS) and timings; iii) erectile (IIEF-5) and urinary (IPSS) function modifications; iv) adverse events. Factors associated with csPCa diagnosis were tested in a multivariable regression model. *Results:* A total of 1,014 patients were included (age 66.8±7.4 years, PSA of 8.1±4.1 ng/ml; n=1,424 mpMRI lesions). According to D1, csPCa was diagnosed in 39.4% (n=400) and no-csPCa in 4.4% (n=45), obtaining 46.2% csPCa for PI-RADS 4 and 73.9% for PI-RADS 5. The procedure was generally well-tolerated (mean pain: NRS 3.1±2.3), and duration was reasonable (15.9±4.9 min). No impact on erectile (p=0.45) or urinary (p=0.58) function was observed, along with low complication rate (Clavien grade 2 n=1, Clavien grade >2 n=0). No post-biopsy sepsis was recorded. Table I shows that on multivariable analysis, age, PSA density, DRE and PI-RADS were positively associated and Asiatic race and previous biopsy negatively associated with csPCa diagnosis (both definitions). Lesion area (whether anterior and/or apical) had no influence on csPCa detection rate. *Conclusion:* We achieved good csPCa detection using TPFBx under LA, also documenting short procedural duration, good patient tolerability and low complications, in an outpatient setting. Infectious risk was extremely low.

19
TRANSPERINEAL FREE-HAND mpMRI TARGETED PROSTATE BIOPSIES UNDER LOCAL ANESTHESIA: AN INITIAL CHARACTERIZATION OF LEARNING CURVES

Giorgio Calleris[1], Giancarlo Marra[1], Junlong Zhuang[2], Mattia Beltrami[1], Alessandro Marquis[1], Xiaozhi Zhao[2], Marco Oderda[1], Yansheng Kan[2], Alessandro Greco[1], Andrea Zitella[1], Alessandro Bisconti[1], Haifeng Huang[2], Riccardo Faletti[3], Qing Zhang[2], Luca Molinaro[4], Wei Wang[2], Marco Agnello[1], Maurizio Barale[1], Andrea Giordano[1], Daniele D'Agate[1], Stefano Tappero[1], Hongqian Guo[2] and Paolo Gontero[1]

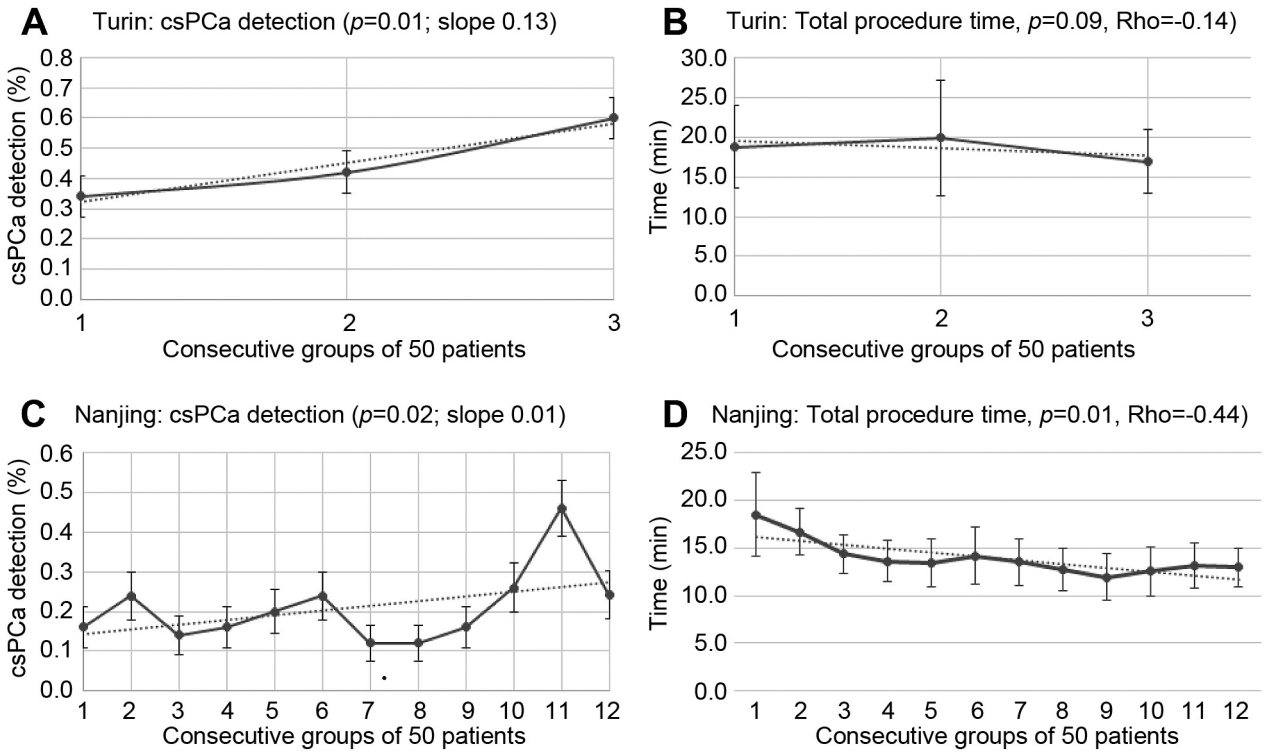

Figure 1. *Learning curves for rate of detection of clinically significant prostate cancer (csPCa) by free-hand transperineal multiparametric magnetic resonance imaging targeted fusion prostate biopsy and procedure duration at two centers in consecutive groups of patients. Data are means±standard error.*

[1]Department of Urology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy; [2]Department of Urology, Drum Tower Hospital, Medical School of Nanjing University, Nanjing University, Nanjing, P.R. China; [3]Department of Radiology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy; [4]Department of Pathology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy

Background/Aim: In the case of a positive magnetic resonance imaging (MRI), multiparametric (mp) MRI targeted fusion prostate biopsy (FBx) is the mainstay for prostate cancer (PCa) diagnosis. Transperineal FBx might lower infectious risk but the discussion on which is the better biopsy route is still an open question. The literature suggests the existence of a learning curve: Operator's experience might play an important role in achieving good results. *Patients and Methods:* We considered consecutive procedures performed from Sep 2016 to May 2019 by two surgeons in Turin (n=150) and two in Nanjing (n=600), drawing from a prospective cohort of transperineal free-hand FBx under local anesthesia (LA) at two high-volume referral centers. The operators, who were already experienced in transperineal biopsy, worked under the supervision of a specifically trained urologist. Learning curves were obtained using means and standard errors of consecutive groups of 50 patients (CPG-50s). Primary outcomes were: (a) Clinically significant PCa (csPCa) detection rate, defined for ISUP>6 or ISUP 6 with >50% PCa in a single core or >2 cores involved; (b) duration of the procedure, from LA to the end of the procedure, considering targeted and systematic biopsy. Chi-squared test for trends and Spearman's rank correlation coefficient were used to test detection and duration outcomes, respectively. We investigated factors associated with csPCa through a multi-variable regression model. *Results:* csPCa prevalence was 0.54 in Turin and 0.28 in Nanjing (considering targeted and systematic cores), likely because of population diversity. Performing a per-center analysis, CPG-50s were homogeneous for age, prostate specific antigen (PSA) or prostate imaging reporting and data system (PI-RADS) distribution (Table I). As shown in Figure 1A and C, in both centers, we noted a statistically significant

increase in detection rate on targeted cores. In Nanjing, the duration of the procedure consistently declined across CGP-50s (p=0.01, Figure 1D), the curve being steeper for the first 200 procedures (from a median of 17.8 to 13.4 min). Figure 1B shows a non-significant trend towards faster procedures with increasing experience in Turin (p=0.09). CPG-50, digital rectal exam (DRP), and PI-RADS score were significant predictors of csPCa (both centers) in a multivariable model. *Conclusion:* In referral institutions with adequate supervision, a good diagnostic performance for transperineal FBx was achieved from the beginning of the learning curve. With increasing expertise, we observed a mild but significant improvement in the detection rate and duration of the procedure. The identification of experience thresholds will require further research.

Table I. *Patient baseline characteristics per center, comparing groups of fifty consecutive patients.*

	Turin overall	*p*-Value*	Nanjing overall	*p*-Value*
Patients, n				
Total	150	-	600	-
CPG-50s, n				
Total	3	-	12	-
Age, years				
Median (range)	67 (62-72)	0.8	67 (62-72)	0.55
PSA, ng/ml				
Median (range)	6.4 (4.6-8.4)	0.2	7.9 (5.4-11.3)	0.11
PI-RADS, (%)				
3	19	0.052	48.6	0.11
4	61.9		40.1	
5	19.1		11.4	

CPG-50: Group of 50 consecutive patients; PSA: prostate specific antigen; PI-RADS: Prostate imaging reporting and data system; *Among CPG-50s, Kruskal–Wallis test for continuous variables and Pearson's chi-square for categorical variables.

20
INADEQUATE CONCERN REGARDING TOXICITY OF ANDROGEN-DEPRIVATION THERAPY IN COMMON CLINICAL PRACTICE: AN UPDATE OF A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY

Vincenzo Serretta[1], Simona Grutta[1], Sonia Agiato[1], Davide Baiamonte[1], Giuseppe Ferrera[2], Michele Ruoppolo[3], Alfredo Colombo[4], Emanuele Caldarera[5], Michele Barbera[6], Danilo Di Trapani[7], Nicolò Borsellino[8] and Sanfilippo Chiara[9]

[1]Department of Surgical, Oncological and Oral Sciences, Section of Urology, University of Palermo, Palermo, Italy;
[2]Radiotherapy Unit, ARNAS Civico Hospital, Palermo, Italy;
[3]Urology Unit, San Giovanni di Dio Hospital, Agrigento, Italy;
[4]Department of Oncology, Macchiarella Clinic, Palermo, Italy;
[5]Urology Unit, Paolo Borsellino Hospital, Marsala, Italy;
[6]Urology Unit, Giovanni Paolo II Hospital, Sciacca, Italy;
[7]Urology Unit, Buccheri La Ferla Fatebenefratelli Hospital, Palermo, Italy;
[8]Medical Oncology Unit, Buccheri La Ferla Fatebenefratelli Hospital, Palermo, Italy;
[9]Statistics, GSTU Foundation, Palermo, Italy

Background/Aim: The role of androgen deprivation therapy (ADT) in the treatment of locally advanced and metastatic prostate cancer is well established, with a main role played by gonadotropin-releasing hormone agonists or antagonists. The aim is to obtain castration with a plasma testosterone level lower than 50 ng/dl (although an optimal level would be less than 20 ng/dl). On the other hand, ADT causes several side-effects including metabolic, cardiovascular, disruption of bone homeostasis and sexual disorders. For this reason, it is necessary to determine patients' health status by minimal baseline clinical and laboratory examinations, not only at the beginning of ADT but also during follow-up, with particular awareness of testosterone levels and comorbidities. We prospectively investigated the management of patients submitted to first-line ADT in common clinical practice. An update of our previous results is herein presented. *Patients and Methods:* Patient characteristics and laboratory examinations at ADT start and during follow-up were recorded. All the investigations were performed at physician discretion according to their own everyday common clinical practice. Main exclusion criteria were: age >85 years, untreated localized prostate cancer and previous hormone therapy. The main end-point of our observational study was to evaluate the examinations required in common clinical practice by the specialists involved in the management of patients undergoing androgen deprivation at treatment start and during follow-up. Particularly attention has been given to the minimal investigations necessary to monitor the toxicity of the treatment. *Results:* From December 2017 to October 2019, 163 patients were included in this study, with a median age of 78 years. A total of 26 (15.9%) had a recurrence after radiotherapy or radical prostatectomy, 16 (9.8%) had a locally advanced tumor and 121 (74.2%) a metastatic tumor. ADT was prescribed by oncologists, urologists and radiotherapists in 19 (12%), 114 (70%) and 30 (18%) patients, respectively. Three patients were lost at baseline data collection. Luteinizing hormone-releasing hormone agonists and antagonists were given in 77 (48.1%) and 83 (52.9%) patients, respectively. Before the start of

ADT, testosterone and alkaline phosphatase (ALP) data were available in 74 (46.3%) and 88 (55%) patients, respectively. At 1 and 3 months, similar data were obtained: testosterone in 33% and in 51% respectively, ALP at 3 months in 45% of cases. Baseline prostate-specific antigen (PSA), creatinine, hemoglobin, performance status, body mass index and electrocardiogram with cardiological visit were obtained in 160 (100%), 122 (76.2%), 141 (88.1%), 151 (94.4%), 149 (93.1%) and 130 (81.2%) patients, respectively. At 3-month follow-up, PSA, creatinine, hemoglobin, performance status, body mass index and electrocardiogram with cardiological evaluation were collected in 133 (83.1%), 122 (76.2%), 141 (88.1%), 147 (91.8%), 101 (63.3%) and 87 (54.3%) patients, respectively. A further reduction in the conformity to monitoring testosterone and ADT toxicity was evident at 6 and 12 months. At 1 year, testosterone levels and cardiovascular status were obtained in fewer than 30% of the patients and bone health status was evaluated only sporadically. The toxicity occurring during the observation period was not recorded since the only aim of the study was to analyze if the investigations required to prevent and monitor the most common side effects were performed in common clinical practice. *Discussion and Conclusion:* In common clinical practice, most of the specialists involved in the management of first-line ADT for prostate cancer were well aware of their patients' health status at the start of treatment but were less than systematic in verifying testosterone levels during therapy; during follow-up, evaluation of ADT toxicity was omitted in several cases. An increase of specialists' awareness of ADT toxicities is needed.

We thank GSTU Foundation, Palermo, Italy for the editing and statistical support.

21

CAN LOCAL RADIOTHERAPY CONVERT METASTATIC CASTRATION-RESISTANT PROSTATE CANCER TO A CASTRATION-SENSITIVE DISEASE? A CASE REPORT

Sara Terrevazzi, Rita Marina Niespolo, Riccardo Ray Colciago, Stefano Lorenzo Villa, Pietro Pacifico and Stefano Arcangeli

Department of Radiation Oncology, San Gerardo Hospital Monza, Monza, Italy

Background: In metastatic prostate cancer, the standard of care when a castration-resistant status (*i.e.* rising prostate-specific antigen (PSA) under suppression of testosterone) arises is the intensification of systemic treatment, such as chemotherapy or next-generation hormonal therapy, assuming that the disease has spread systemically. Historically in this setting, radiotherapy (RT) has only been used with palliative intent. However, RT of primary tumor has recently been demonstrated to improve overall survival in men with low metastatic burden, according to the STAMPEDE trial (1, 2). *Case Report:* In June 2018, a 75-year-old man was diagnosed with adenocarcinoma of the prostate Gleason score 9 (5+4) with two metastatic lesions identified by conventional imaging, both confined to the pelvis. The initial PSA level was 25 ng/ml. The patient was started on androgen-deprivation therapy, and after 6 months the prostate-specific antigen had decreased to 4 ng/ml. Subsequently, the PSA level rose to 19 ng/ml, despite the testosterone remaining suppressed, and the patient became symptomatic at bone level. The restaging examinations showed progression within known sites of disease. In view of the oligometastatic status, we decided to treat both the pelvic bone metastases and the primary tumor before considering a change in the systemic therapy. The former were treated with a 8 Gy single fraction RT with palliative intent, while for the latter, a schedule of 55 Gy/20 fractions daily was applied using volumetric-modulated arc therapy with cone beam computed tomography. The treatment was well tolerated, with only grade 2 acute genitourinary toxicity. Symptoms from bone lesions rapidly disappeared. Six months later, the PSA level had dropped to 0.8 ng/ml, and the patient no longer had genitourinary symptoms. No evidence of disease progression was shown at post-RT imaging. *Conclusion:* Our findings shows that local RT may prevent the development of further metastases and overcome resistance to androgen-deprivation therapy, thus delaying the need for initiation of further systemic options and substantially improving quality of life.

1 Parker CC, James ND, Brawley CD, Clarke NW, Hoyle AP, Ali A, Ritchie AWS, Attard G, Chowdhury S, Cross W, Dearnaley DP, Gillessen S, Gilson C, Jones RJ, Langley RE, Malik ZI, Mason MD, Matheson D, Millman R, Russell JM, Thalmann GN, Amos CL, Alonzi R, Bahl A, Birtle A, Din O, Douis H, Eswar C, Gale J, Gannon MR, Jonnada S, Khaksar S, Lester JF, O'Sullivan JM, Parikh OA, Pedley ID, Pudney DM, Sheehan DJ, Srihari NN, Tran ATH, Parmar MKB, Sydes MR and Systemic Therapy for Advanced or Metastatic Prostate Cancer: Evaluation of Drug Efficacy (STAMPEDE) investigators: Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): A randomised controlled phase 3 trial. Lancet *392(10162)*: 2353-2366, 2018. PMID: 30355464. DOI: 10.1016/S0140-6736(18)32486-3

2 Choudhury A, Chen RC, Henry A, Mistry H, Mitin T, Pinkawa M and Spratt DE: STAMPEDE: Is radiation therapy to the primary a new standard of care in men with metastatic prostate cancer? Int J Radiat Oncol Biol Phys *104(1)*: 33-35, 2019. PMID: 30967237. DOI: 10.1016/j.ijrobp.2018.12.040

23
SURGICAL AND FUNCTIONAL OUTCOMES FOLLOWING TOTAL PENIS REPAIR WITH SPLIT-THICKNESS SKIN GRAFT

Elisa Berdondini, Federico Germinale, Lorenzo Tosco, Alessandro Giacobbe, Marisa Kurti and Giovanni Muto

Division of Urology, Humanitas Gradenigo Hospital, Turin, Italy

Aim: To report the outcomes of penile skin graft for total penis repair in our early experience. *Patients and Methods:* This was a retrospective study concerning patients affected by buried penis and distal penile urethral stricture due to lichen sclerosus from 2017 to 2019. All patients underwent subsequent urethral dilatation. The diagnosis was confirmed by hystological examination. *Results:* Three patients were included in the study. Median preoperative maximum flow rate (Qmax) was 7 ml/s (range=5-11ml/s). All patients referred preoperative poor quality of sexual life due to mucosal and skin lesions that caused pain and destruction of anatomicaI structures, and functional impairment. Their mean age was 65 years (range=60-68 years). All patients referred poor sexual function. During surgery, the penis was completely freed from scarred penile skin and de-gloved. A Johanson urethroplasty was made for 1-2 cm as necessary. A free split-thickness skin graft (STSG) was obtained from the supero-lateral thigh surface (about 9×7 cm). Once the graft was put in place, small incisions were made with the scalpel blade to obtain a tension-free graft and to permit fluid drainage. The graft was attached with quilted Vicryl 5/0 stiches. A compression bandage was left in place for 5 days. All three patients had a return to sexual activity without need for pharmacological support. Median postoperative Qmax was 22 ml/s (range=18-29 ml/s). *Conclusion:* The main principles of male genital reconstruction are the excision of all the diseased skin and coverage of the defect. STSG is easy to harvest and is free from hairs. STSG represents a promising solution for patients with buried penis due to lichen sclerosus, and provides a durable definitive repair.

24
OUR EXPERIENCE OF AN ENHANCED RECOVERY PROGRAM IN 30 PATIENTS UNDERGOING ROBOT-ASSISTED RADICAL CYSTECTOMY

Matteo Manfredi[1], Massimiliano Poggio[1], Ivano Morra[1], Daniele Amparore[1], Enrico Checcucci[1], Michele Sica[1], Diletta Garrou[1], Giovanni Cattaneo1, Enrico Bollito[2], Christian Fiori[1], Roberto M. Scarpa[3] and Francesco Porpiglia[1]

[1]Department of Urology, AOU San Luigi Gonzaga Orbassano, University of Turin, Turin, Italy;
[2]Department of Pathology, AOU San Luigi Gonzaga Orbassano, University of Turin, Turin, Italy;
[3]Campus Bio-medico University of Rome, Department of Urology, Rome, Italy

Background/Aim: Despite advances in surgical technique and perioperative care, robot-assisted radical cystectomy (RARC) is still associated with morbidity and prolonged hospital stay. Enhanced recovery after surgery (ERAS) protocols may improve a patient's postoperative course. Its intent is to improve the quality of care and reduce complications using treatments in all phases of perioperative care that could maintain preoperative organ function and reduce the stress response following surgery. ERAS protocols are based on preoperative counselling, optimization of nutrition, multimodal analgesia and anesthetic regimens, and early mobilization. The aim of the study was to present our preliminary experience of ERAS protocols after RARC. *Materials and Methods:* Data were prospectively collected on 30 patients undergoing RARC and urinary diversion (Bricker intervention, 18 patients; or Y neobladder, 12 patients) with ERAS protocol from 12/2016 to 03/2018. The ERAS protocol included: No oral bowel preparation, multimodal anesthesia (general plus epidural without opioids), removal of naso-gastric tube at the end of the surgery, oral clear fluids on the day of surgery, parenteral and enteral nutrition on postoperative day 1, early mobilization in postoperative day 2. We analyzed surgical variables, time to first bowel movement and to flatus, length of stay, complications (classified according to Clavien–Dindo), re-established oral intake and mobilization. For the aim of the study, "stable health status" was defined as no drain, free mobilization, normal oral intake and regular bowel function. *Results:* Demographic data are shown in Table I. The mean operative time was 280±24 min, mean blood loss was 489.7±52 ml. The drain was removed after 3.8±0.8 days. Time to flatus was 2.6±0.7 days, and time to return to normal bowel function was 4.8±1.2 days. Time to full oral intake and mobilization were 3.5±1 and 1.3+0.7 days, respectively. The median day on which patients were fit for discharge was day 8 (5-10). One patient did not complete fast track protocol for recurrent emesis. 4 complications with Clavien–Dindo grade >2 were recorded, and there were no differences between

Table I. *Demographic data for study patients.*

Demographic data	Mean±SD
Age at surgery, years	64.5±5
Body mass index, kg/m^2	25.8±2.4
Age-adjusted Charlson Comorbidity Index	3.2±2

SD: Standard deviation.

Bricker and neobladder groups for any of the variables considered ($p<0.05$). *Conclusion:* Our preliminary data showed that the ERAS protocol applied to RARC optimized postoperative patient care, with a fast return to bowel function without increasing complications. Further research is required to corroborate these encouraging findings.

25

PSYCHO-EMOTIONAL NEEDS OF PATIENTS WITH PROSTATE CANCER: A QUALITATIVE STUDY ON MEN UNDER ACTIVE SURVEILLANCE

Letizia De Luca[1], Paola Dordoni[1], Tiziana Magnani[1], Cristina Marenghi[1], Silvia Stagni[2], Sergio Villa[3] and Riccardo Valdagni[4]

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

Background/Aim: Prostate cancer (PCa) is the most common male cancer in industrialized countries, including Italy. The numbers of patients coping with the illness and its side-effects are high, and it is necessary to take into consideration men who need psychological support over time (1). The diagnosis of PCa and the consequent treatments can have a significant impact on a patient's psycho-emotional experience and on their quality of life (QoL) and literature confirmed that these aspects are particularly important for patients on active surveillance (AS). This strategy is available for those who are willing to accept an observational program and at the same time the risk of disease reclassification or progression in order to avoid the well-known complications associated with active treatments. Although patients under AS reported good QoL and did not appear to suffer from major negative psychological impacts (2), to the best of our knowledge there are no studies exploring the eventual specific psycho-emotional needs of this kind of patient, for example in managing anxiety, tolerating uncertainty, developing the capacity for mindfulness or paying attention to their lifestyle. This study presented the results of qualitative research precisely focused on this topic. *Patients and Methods:* An explorative qualitative study with focus groups was conducted; the use of group seems appropriate to investigate complex issues going beyond the sphere of behaviors and attitudes noted in individuals. Fourteen men with low-risk PCa enrolled in one of the PRIAS European Centers, with different ages and included in AS protocol up to a maximum of 1 year were involved. Focus groups comprised seven participants each; this small number was meant to create a secure and intimate place to talk with other unknown patients about personal experiences and eventually about sensitive topics. All the focus groups included two conductors and one observer, and all the discussions were recorded (prior to consent of all the participants) and transcribed. Following an ad hoc semi-structured track, eight areas indicated as being crucial in the literature were investigated: anxiety, positive and optimistic attitude, sexuality, patient engagement, healthcare and lifestyle, capacity for tolerating uncertainty, mindfulness, and attribution of meaning to life experience. A thematic analysis combined with an inductive approach was used, allowing the themes to flow from the data. *Results:* Patients with PCa under AS described their disease as a "challenge", an unexpected event that also brought aspects of opportunities with it. Characteristic low levels of anxiety were confirmed and no specific psycho-emotional needs emerged. In general, patients under AS reported good levels of psychological well-being. Therefore, it is not possible to talk about "needs", rather it is more appropriate to talk about "areas of interest" which patients under AS are particularly concerned with. These areas all have to do with the macro-dimension of the "dialogue": dialogue with experts, with the healthcare structure and with peers. Dialogue with experts: patients under AS underlined their interest in meeting regularly with health experts in order to receive information about lifestyle (nutrition, sexuality, sport, smoking, etc.) and to be updated on research on PCa. Dialogue with healthcare structure: patients underlined their interest in maintaining a relationship of trust with the healthcare structure; an empathic relationship with doctors seemed to play a central role in fostering the development of a positive and optimistic attitude towards the disease. Dialogue with peers: patients underlined their interest in having more moments dedicated to direct contact with peers (other AS patients) so as to be able to face common doubts or other important issues emerging during the focus group together. *Conclusion:* Findings of this study confirm that patients under AS show a good level of psychological well-being; they do not talk about "need", rather about "areas of interest" and they underline their willingness to regularly participate in specific informational programs. This kind of research may be extended to other groups of patients (for example, patients undergoing surgery, radiotherapy, drug therapy) and it might help healthcare professionals and healthcare organizations to design an experimental study in which an ad hoc intervention tailored to the needs of patients with PCa and aimed at promoting psychological well-being and QoL can be developed and evaluated.

1 McCaughan E, Prue G, McSorley O, Northouse L, Schafenacker A and Parahoo K: A randomized controlled trial of a self-management psychosocial intervention for men with prostate cancer and their partners: a study protocol. J Adv Nurs *69*: 2572-2583, 2013. PMID: 23528148. DOI: 10.1111/jan.12132

2 Bellardita L, Valdagni R, Van Den Bergh R, Randsdorp H, Repetto C, Venderbos L, Lane JA and Korfage IJ: How does active surveillance for prostate cancer affect quality of life? A systematic review. Eur Urol *67(4)*: 637-645, 2015. PMID: 25454617. DOI: 10.1016/j.eururo.2014.10.028

26
HYPERTHERMIC INTRAVESICAL CHEMOTHERAPY (HIVEC®) WITH ENDOVESICAL MMC IN PATIENTS WITH INTERMEDIATE- AND HIGH-RISK NMIBC NOT RESPONSIVE OR INTOLERANT TO BCG: OUR FIRST EXPERIENCE

Francesco Porpiglia[1], Massimiliano Poggio[1], Razvan G. Niculescu[1], Michele Sica[1], Matteo Manfredi[1], Enrico Checcucci[1], Daniele Amparore[1], Diletta Garrou[1], Enrico Bollito[2] and Christian Fiori[1]

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

Background/Aim: In patients with intermediate and high-risk non-muscle invasive bladder cancer (NMIBC), intravesical bacillus Calmette-Guérin (BCG) after trans urethral resection (TURB) reduces the risk of tumor recurrence. Despite adequate BCG treatment, a large proportion of patients experience recurrence. An alternative local therapy for patients who are non-responders to BCG or who who cannot tolerate it is high temperature intravesical instillation with mitomycin-C (MMC). Fluorescence cystoscopy with hexaminolevulinate (FC-HAL) compared to the standard cystoscopy improves detection of NMIBC and reduces recurrence rates. The aim of our study was to assess the effectiveness and safety of hyperthermic intravesical chemotherapy (HIVEC®) with MMC and of the follow-up with FC-HAL in BCG unfit patients with intermediate- and high-risk NMIBC. *Patients and Methods:* We prospectively enrolled patients with intermediate-and high-risk NMIBC who were planned to receive HIVEC® treatment with MMC at 43˚C between 12/2017 and 07/2019. The inclusion criteria were: Patients with recurrent high- or intermediate-risk NMIBC non responders or intolerant to BCG schedule; former tubercolosis (TBC) outcomes; Eastern Cooperative Oncology Group performance status (ECOG PS) 2-3. The HIVEC® treatment schedule consisted of weekly induction for 6 weeks and monthly maintenance for 6 months. All patients were followed up by FC-HAL and bladder mapping at the end of induction and with cystoscopy every 3 months in the first year. *Results:* A total of 29 patients were included. Table I lists the baseline characteristics of the patient cohort. 82.15% and 17.85% patients were high- and intermediate-risk NMIBC, respectively. Mean follow-up was 7.3±5.1 months. Eighteen out of 29 (62%) patients had BCG-unresponsive NMIBC; 11/29 (37.9%) patients had never been treated with BGC because of former TBC outcomes or ECOG PS of 2-3. Concerning HIVEC® treatment, 79.3% of patients completed the entire treatment (induction and maintenance), whilst the other 20.6% only completed the induction course. All patients underwent endoscopic evaluation after the entire treatment: 86.2% remained disease-free, whilst 10.3% had recurrent disease and 3.44% progression of disease. These four patients had carcinoma *in situ* before and after HIVEC®. All registered adverse events were Clavien grade I-II; 6.9% (2/29) of patients experienced bladder spasms during or after the treatment and transient hematuria. Of these, one drop out was registered. *Conclusion:* In our cohort, HIVEC® with MMC treatment seemed to be a feasible and effective option in BCG-unresponsive/intolerant patients with NMIBC.

Table I. *Baseline characteristics.*

Characteristic	
Mean age (±SD), years	67±11
Former smokers, n (%)	21 (72.4%)
Occupational exposure, n (%)	12 (41.3%)
Borderline or positive urinary cytology, n (%)	14 (48.2%)

27
NEW DIAGNOSTIC PATHWAY IN BIOPSY-NAÏVE MEN WITH SUSPECTED PROSTATE CANCER: THE ROLE OF BIPARAMETRIC PROSTATE MRI

Francesco Porpiglia[1], Stefano De Luca[1], Filippo Russo[2], Enrico Bollito[3], Matteo Manfredi[1], Daniele Amparore[1], Enrico Checcucci[1], Diletta Garrou[1], Razvan G. Niculescu[1] and Christian Fiori[1]

[1]Department of Urology, AOU San Luigi Gonzaga Orbassano, University of Turin, Turin, Italy; [2]Department Of Radiology, IRCC, Candiolo, Italy; [3]Department of Pathology, AOU San Luigi Gonzaga Orbassano, University of Turin, Turin, Italy

Background/Aim: Even if multiparametric magnetic resonance imaging (mpMRI) increases the detection of significant

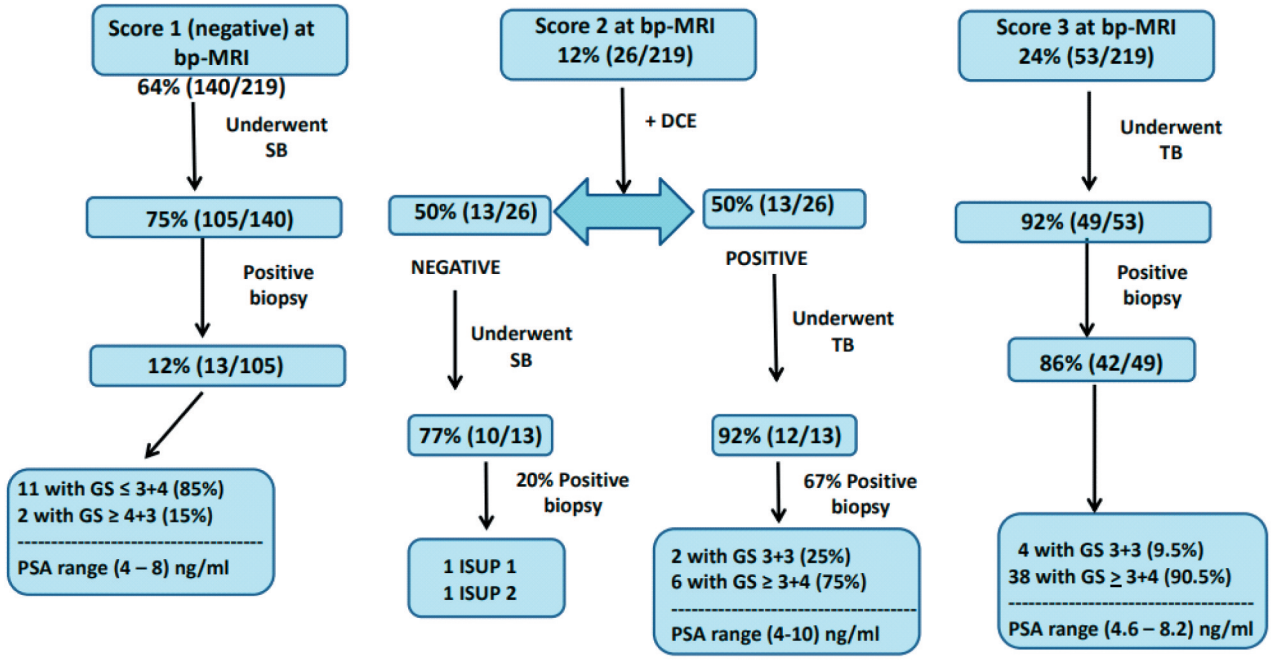

Figure 1. *Schema of the results for each arm off the study design.*

prostate cancer (PCa), allowing the execution of targeted biopsies, the added value of dynamic contrast enhancement (DCE) in combination with T2-weighted imaging and diffusion weighted imaging (DWI) is controversial. Moreover, their widespread use can be limited by cost, added time and risks related to contrast injection. For these reasons, biparametric MRI (bpMRI) is gaining importance as an alternative to mpMRI in selected patients. The aim of our study was to evaluate the detection rate of bpMRI for clinically significant PCa, defined as International Society of Urological Pathology grade 2 (ISUP) in biopsy-naïve men. *Patients and Methods:* We prospectively enrolled patients from 05/17 to 09/19. Inclusion criteria were: No prior biopsy, age <75 years, prostate-specific antigen level of 4-15 ng/ml and negative digital rectal examination. The bpMRI protocol included T2- and DWI sequences. All images of bpMRI were reviewed by an expert radiologist and the regions of interest were preliminarily evaluated on a 3-grade probability scale for PCa suspicion: Positive (score 1), uncertain (score 2) or negative (score 3). Each positive region of interest was ranked as 3-5 Prostate Imaging-Reporting and Data System (PIRADS) v.2 category. Those with a score of 1 (with or without DCE) underwent a 12-core transrectal standard biopsy or clinical follow-up. Those with a score of 2 underwent bpMRI with addition of DCE sequences. A targeted biopsy was performed in those with a score of 3 (with or without DCE). *Results:* The total number enrolled was 219. Mean prostate-specific antigen value was 6.1 (±2.2) ng/ml. Mean age was 64±7.0 years. Our results are shown in Figure 1. Patients with a score of 1 comprised 140 (75%) and 105 underwent standard biopsy; 12% (13/105) patients had PCa. Of those, 15% had GS ≥4+3. Of patients with a score of 2 with negative DCE (13/26, 50%), 77% underwent standard biopsy. In this group, one patient had non clinically significant and one had clinically significant PCa (ISUP 2). Moreover, of patients with a score of 2 with positive DCE (13/26, 50%), 92% underwent targeted biopsy. Of those, 16% and 50% had Gleason scores of 3+3 and ≥3+4, respectively. Finally, patients with a score of 3 who underwent targeted biopsy (49/53, 92%), 86% had PCa. In this group, 90.5% had Gleason score ≥3+4. *Conclusion:* In biopsy-naïve man with suspected PCa, bpMRI was feasible and had a good detection rate. In cases of negative bpMRI, the risk of missing clinically significant PCa was very low. Further research is required to corroborate these preliminary data.

28
TOXICITY PROFILE FOLLOWING POSTOPERATIVE RADIATION THERAPY FOR PROSTATE CANCER WITH MODERATE HYPOFRACTIONATION AND SIMULTANEOUS INTEGRATED BOOST (SIB)

Pietro Pacifico[1], Elisa Maria Bonetto[2], Rita Marina Niespolo[2], Elena De Ponti[3], Suela Vukcaj[2] and Stefano Arcangeli[1]

[1]University of Milan "Bicocca",
S. Gerardo Hospital, Italy, Monza, Italy;
[2]Division Of Radiation Oncology,
S. Gerardo Hospital, Milan, Italy;
[3]Medical Physics Department,
S. Gerardo Hospital, Milan, Italy

Background/Aim: Radiotherapy (RT) is being used with increased frequency in the management of prostate cancer following radical prostatectomy. However, there is some concern that its use in the form of a hypofractionated regimen may lead to tissue injury when carried out in the postoperative setting. We retrospectively reported on acute and late gastrointestinal (GI) and genitourinary (GU) toxicities in a series of patients who received a course of moderately hypofractionated RT post prostatectomy. *Patients and Methods:* Fifty patients with adverse pathological features or biochemical failure following radical prostatectomy were enrolled between 2013 and 2018. All patients were treated with volumetric modulated arc therapy (VMAT), and simultaneous integrated boost (SIB) in 28 fractions for a total dose of 66.64 Gy to the prostate bed and 53.2 Gy to the pelvic drainages, respectively. Androgen deprivation therapy was administered to 76% of patients. After completion of RT, follow-up was scheduled at 3 months and every 6-12 months thereafter. Acute and late toxicities were assessed using Common Terminology Criteria for Adverse Events v4. Biochemical disease-free survival (bDFS) at 2 years was also evaluated. Univariate analysis examining potential relationships between bladder/rectal dosimetric parameters and GU/GI toxicities was performed. *Results:* Median age was 70 (range=47-80) years. Median pre-treatment prostate-specific antigen level was 0.4 ng/ml. Thirty-seven (74%) patients had International Society of Urological Pathology (ISUP) grade ≥3, 35 (70%) had pT3 disease and 36 (72%) had positive margins. With a median follow-up of 22 months (range=5-57 months), none of the patients experienced grade 3 or more late GI or GU toxicities and no instances of grade 3 or more acute GI toxicities were recorded. Only one patient experienced grade 3 acute GU toxicity. Cumulative acute grade 2 GU and GI toxicity was 6% and for late grade 2 GU and GI toxicity was 8%. The median dose received by bladder and rectum was 44.52 (range=25.34-53.75) Gy and 44.68 (range=17.43-48.86) Gy, respectively. No statistically significant association was found between toxicities and rectal/bladder dosimetric values ($p>0.05$). bDFS at 2 years was 88%. No treatment interruptions >5 days occurred. *Conclusion:* Moderately hypofractionated RT for prostate cancer by means of VMAT and SIB technique resulted in an excellent toxicity profile when applied postoperatively. No dosimetric factor was found predictive of both acute and late toxicity. Long-term follow-up is needed to account for toxicities that might occur at later time points.

29

LATE BREAST CANCER METASTASIS TO THE BLADDER, 10 YEARS AFTER RADICAL MASTECTOMY AND HORMONOTHERAPY

Lorena Di Marco, Francesca Migliozzi, Matteo Boltri, Giovanni Liguori and Carlo Trombetta

Urology Department, University of Trieste, Trieste, Italy

Background: Breast cancer is the top cancer in women both in the developed and the developing world and represents the major cancer-specific cause of death in the female population. The common sites of metastases from breast cancer are lung, bone and liver while bladder is a rare metastatic destination. *Case Report:* A 79-year-old woman presented, with positive anamnesis for hypertension, hypothyroidism, heart stroke and radical right mastectomy with lymphadenectomy in 2009 for breast cancer (pT1c.N1a.G2), followed by hormonal therapy with Letrozole (from 2009 to 2014). After persistent macroscopic hematuria and lower urinary tract symptoms (LUTS) (dysuria, urge incontinence, nicturia), the patient underwent bladder mapping and contextual resection of hyperemic areas in the posterior-right wall of the bladder. Histopathological analysis was uncertain because the cancer was anaplastic and undifferentiated: it expressed different immunological markers including alpha-methylacyl-CoA racemase (AMACR) and cytokeratin 19 (CK19), common in urothelial cancer, but also estrogen receptors, while mammoglobin and gross cystic disease fluid protein 15 (GCDFP-15), typical of breast cancer, were absent. A thoracic and abdominal computed tomographic scan with urophases was performed; it was negative for tumors and hydronephrosis but showed an irregular thickening of the posterior bladder wall. This case was discussed in a multidisciplinary group of an oncologist, radiologist, urologist, radiotherapist and nuclear medicine physician. Different markers (CEA 3 =3.0 ng/ml, CA15-3=16.9 UI/ml) were all negative but a bone scan was positive for metastasis to femurs and pelvis; computed tomography of the pelvis was performed for a better morphological and numerical definition of those lesions. In the end, patient underwent anterior hemipelvectomy like therapy in both case of primary bladder cancer or metastatic breast carcinoma. Post-operative recovery was complicated by urinary infection treated with broad-spectrum antibiotics. Definitive histopathological examination confirmed diagnosis of anaplastic lobular breast cancer with ER (95% of sample), GATA3 and CK19 positivity, Ki67 expressed in 20%, and negativity for mammoglobin and p63 and progesteron receptors. There was massive involvement of the muscular bladder layer; cancer also invaded the uterus, vagina, ovaries and anterior pelvis with frequent neurotropism and some lymph nodes with micrometastases. *Conclusion:* Breast cancer metastasis

recurrence after 10 years is uncommon, especially if the first symptomatic localization is the bladder; secondary tumors of the urinary bladder are rare and most come from lung cancer, melanoma and lymphoma. Patients with a complex oncological history should be studied and discussed in multidisciplinary groups for a faster and wider analysis of the case because early detection of cancer greatly increases the chances for successful treatment. Bone scan is a valid diagnostic technique to complete bladder or breast cancer study and should be performed in those with suspected metastatic disease or in patients with positive anamnesis for both types of neoplasm, especially if presenting urge incontinence, macrohematuria and dysuria.

31
POST HIGH-INTENSITY FOCUSED ULTRASOUND (HIFU) RADIOTHERAPY WITH SALVAGE INTENT IN LOCALLY RELAPSED PROSTATE ADENOCARCINOMA: A MONO-INSTITUTIONAL ANALYSIS

Michele Rigo[1], Rosario Mazzola[1], Giuseppe Napoli[1], Niccolò Giaj-Levra[1], Vanessa Figlia[1], Luca Nicosia[1], Francesco Ricchetti[1], Francesco Cuccia[1], Carlo Bellorofonte[3] and Filippo Alongi[1,2]

[1]Advanced Radiation Oncology Department, IRCCS Sacro Cuore Don Calabria Hospital, Cancer Care Center, Negrar, Italy;
[2]Radiation Oncology Department, University of Brescia, Brescia, Italy;
[3]Columbus Clinic Center, Milan, Italy

Aim: The main objective of the present study was to evaluate tolerability, feasibility and biochemical control rates of salvage external beam radiotherapy (EBRT) in patients with local relapse from prostate cancer after high-intensity focused ultrasound (HIFU) as primary treatment. *Patients and Methods:* This was a retrospective analysis of 24 patients with histologically proven prostate adenocarcinoma treated with one or more HIFU sessions between 2007 and 2018. All patients presented biochemical failure after HIFU (defined according to the Stuttgard definition) and 11C choline positron-emission tomography (PET) or ^{68}Ga/^{18}F prostate-specific membrane antigen PET was performed for restaging and treatment planning in most cases (in one case only an ultrasound scan was performed and, in another case, pelvic magnetic resonance imaging and bone scintigraphy). The median interval between HIFU and EBRT was 39 months (range=3-136 months) and the median prostate-specific antigen (PSA) level before EBRT was 6.94 ng/ml (range=2.07-91 ng/ml). Salvage EBRT was performed with moderate hypofractionation schedule in 28 fractions (n=16) or with extreme hypofractionation schedule in 5 fractions (n=8) by means of image-guided volumetric modulation arc therapy. All patients were treated with EBRT to the residual prostate. In the cases of moderate hypofractionation, the median dose was 71.4 Gy (range=71.4-74.2 Gy) and seven patients concomitantly received pelvic lymph node EBRT (dose range=50.4-51.8 Gy). In the cases of extreme hypofractionation, the residual prostate was irradiated. with a median dose of 32.5 Gy (range=30-35 Gy). Five patients (21%) received concomitant/adjuvant androgen deprivation therapy. Primary endpoints were feasibility and toxicity associated to hypofractionated EBRT after HIFU failure. Genito-urinary and rectal and bowel toxicity were scored by common terminology criteria for adverse events version 4) scale. Biochemical response was assessed by ASTRO Phoenix criteria. *Results:* The median follow-up after EBRT was 28 months. The median PSA nadir was 0.26 ng/ml (range=0.01-12.05 ng/ml) and was obtained in a median of 17 months. In the cases of moderate hypofractionation, the median PSA nadir was 0.15 ng/ml (range=0.01-2.48 ng/ml) and occurred within a median time of 19 months (range=3-59 months). In the cases of extreme hypofractionation, the median PSA nadir was 0.64 ng/ml (range=0.12-12.05 ng/ml) and occurred within a median time of 8 months (range=3-27 months). No grade 3 or more acute or late toxicity after EBRT was observed. Only three patients presented grade 2 acute gastrointestinal toxicity (actinic proctitis), of whom one was treated with extreme hypofractionation. Twelve (50%) patients experienced acute grade 1 genito-urinary toxicities: 8/16 of men treated with moderate hypofractionation and 4/8 of men treated with extreme hypofractionation. At the time of follow-up, complete local control of disease was achieved in 23/24 patients (96%). *Conclusion:* Our data confirm the feasibility and low toxicity of salvage EBRT with both schedules of treatment after HIFU failure. The findings of low acute toxicity and good biochemical control rates are encouraging but a larger number of patients and a longer follow-up are needed to confirm these results.

32
^{68}Ga-PSMA PET-CT-GUIDED METASTASIS-DIRECTED STEREOTACTIC RADIOTHERAPY IN PATIENTS WITH PROSTATE CANCER: A MONO-ISTITUTIONAL PRELIMINARY EXPERIENCE

Michele Rigo[1], Rosario Mazzola[1], Giuseppe Napoli[1], Niccolò Giaj-Levra[1], Vanessa Figlia[1], Luca Nicosia[1], Francesco Ricchetti[1], Francesco Cuccia[1], Alessandro Bertaccini[3] and Filippo Alongi[1,2]

[1]Advanced Radiation Oncology Department, IRCCS Sacro Cuore Don Calabria Hospital, Cancer Care Center, Negrar, Italy;

[2]Radiation Oncology Department, University of Brescia, Brescia, Italy;
[3]Clinica Urologica, Università di Bologna Ospedale Sant'Orsola - Malpighi, Bologna, Italy

Aim: To investigate the efficacy and toxicity of ^{68}Ga-prostate-specific membrane antigen positron-emission tomography-computed tomography (PET-CT)-guided stereotactic radiotherapy (SBRT) in the treatment of oligometastatic recurrence of prostate cancer after primary treatment. *Patients and Methods:* Sixty-five patients with biochemical relapse of prostate cancer (44 castration-sensitive and 21 castration-resistant) were treated with volumetric-modulated arc therapy and image-guided SBRT to ≤5 metastatic sites detected by ^{68}Ga PSMA PET-CT. Androgen deprivation therapy was continued in patients with castration resistant disease. Biochemical control was evaluated with European Organization for Research and Treatment of Cancer and Phoenix definition. Toxicity was assessed according to Common Terminology Criteria for Adverse Events-criteria v. 4.03. *Results:* A total of 166 metastases in 65 patients were treated with SBRT. The involved sites were pelvic lymph or para-aortic nodes in 105, bone in 48, prostatic bed or seminal vesicles in 11, lung metastases in one and abdominal wall nodule in one. The median prostate-specific antigen (PSA) value prior to RT was 0.65 ng/ml (range=0.10-11.08 ng/ml), the median PSA-doubling time was 5.5 months (range=0.61-140) months and the median PSA post-RT was 0.63 ng/ml (range=0.01-13.55 ng/ml). A median dose of 35 Gy (range=18-70 Gy) was delivered in 2-10 fractions (the median BED2Gy was 144 Gy). At a median follow-up of 14 months (range=3-34 months) all patients were alive; 24 out of 65 patients (37%) were in remission and 41 were in progression (63%). In particular, 16 out of 21 with castration-resistant disease (76%) and 25 out of 44 with castration-sensitive disease (57%) were in progression. The actuarial 1-year local control, progression-free survival and cancer-specific survival rates were 92%, 38% and 100%. On receiver operating characteristics curve analysis, a PSA nadir <0.25 ng/ml was correlated with distant metastasis-free survival (DMFS). At the univariate analysis, DMFS was significantly longer for patients with PSA nadir <0.25 ng/ml (p<0.05). The median systemic treatment free survival was 19 months (range=13-24 months). No patient experienced grade 3 or more acute gastrointestinal or urinary toxicity. *Conclusion:* By providing optimal local control, low toxicity and promising progression-free survival, ^{68}Ga PSMA PET-CT-guided metastasis-directed SBRT may be considered a promising treatment strategy in patients with oligometastatic prostate cancer, with an acceptable toxicity profile and allowing systemic therapies burdened by side-effects to be postponed. In our analysis, reaching a PSA nadir <0.25 ng/ml was associated with improved DMFS and might serve as a surrogate endpoint for metastasis-directed SBRT.

33

MEDIUM-TERM ONCOLOGICAL RESULTS OF SALVAGE RADICAL PROSTATECTOMY: A LARGE MULTICENTER CONTEMPORARY SERIES

Giancarlo Marra[1], Paolo Gontero[1], Paolo Alessio[1], Giorgio Calleris[1], Marco Oderda[1], Fernando Munoz[2], Claudia Filippini[3], Estefania Linares[4], Rafael Sanchez-Salas[4], Sanchia Goonewardene[5], Prokar Dasgupta[5], Ben Challacombe[5], Rick Popert[5], Declan Cahill[6], David Gillatt[7], Raj Persad[7], Juan Palou[8], Steven Joniau[9], Thierry Piechaud[10], Alexandre De La Taille[11], Morgan Roupret[12], Simone Albisinni[13], Alessandro Morlacco[14], Giorgio Gandaglia[15], Alexander Mottrie[15], Joseph Smith[16], Andre Berger[17], Monish Aron[17], Andre Abreu[17], Inderbir S. Gill[17], Henk Van Der Poel[18], Derya Tilki[19], Declan Murphy[20], Nathan Lawrentschuk[20], John Davis[21] and Robert Jeffrey Karnes[14]

[1]Department of Urology, San Giovanni Battista Hospital, Città della Salute e della Scienza, University of Turin, Turin, Italy;
[2]Department of Radiotherapy, Pasini Hospital, Aosta, Italy;
[3]Department of Statistics, University of Turin, Turin, Italy;
[4]Department of Urology, Institut Mutualiste Montsouris, Paris, France;
[5]Department of Urology, Urology Centre, Guy's Hospital, London, U.K.;
[6]Department of Urology, Royal Marsden Hospital, London, U.K.;
[7]Department of Urology, Bristol NHS Foundation Trust, Bristol, U.K.;
[8]Department of Urology, Fundaciò Puigvert, Barcelona, Spain;
[9]Department of Urology, Leuven University Hospitals, Leuven, Belgium;
[10]Department of Urology, Clinique Saint Augustin, Bordeaux, France;
[11]Department of Urology, CHU Mondor, Créteil, France;
[12]Department of Urology, Pitié Salpétrière Hospital University Paris 6, Paris, France;
[13]Department of Urology, Institut Jules Bordet, Université Libre de Bruxelles, Bruxelles, Belgium;
[14]Department of Urology, Mayo Clinic, Rochester, MN, U.S.A.;
[15]Department of Urology, OLV Hospital, Aalst, Belgium;
[16]Department of Urology, Vanderbilt University, Medical Center North, Nashville, TN, U.S.A.;

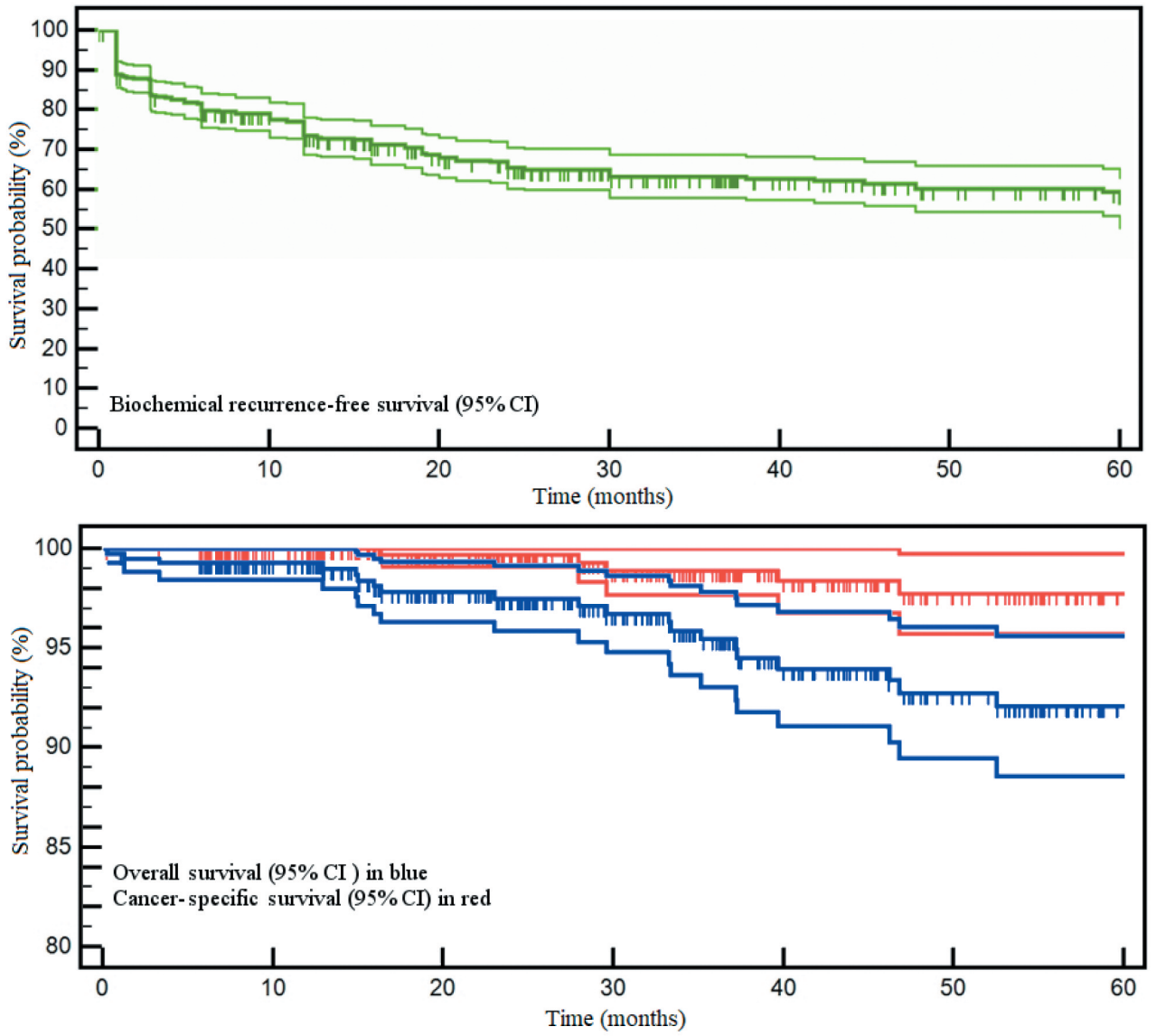

Figure 1. *Kaplan–Meier plots for biochemical recurrence-free survival (upper panel) and cancer-specific and overall survival (lower panel). CI: Confidence interval.*

[17]Department of Urology, USC Norris Comprehensive Cancer Center and Hospital, University of Southern California, CA, U.S.A.;
[18]Department of Urology, Netherlands Cancer Institute, Amsterdam, the Netherlands;
[19]Department of Urology, Martini Klinik, Hamburg, Germany;
[20]Department of Urology, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia;
[21]Division of Surgery, Department of Urology, The University of Texas MD Anderson Cancer Center, Houston, TX, U.S.A.

Background/Aim: Although salvage radical prostatectomy (sRP) has been associated in the past with discouraging continence results and frequent complications, contemporary robotic sRP series suggest improved, but still sub-optimal, outcomes. Thus, a substantial oncological benefit should be demonstrated to support this procedure. We evaluated sRP oncological results in a large contemporary multicenter cohort. *Patients and Methods:* Data of 629 sRP performed for recurrent prostate cancer (PCa) after local non-surgical treatment were retrospectively retrieved at 18 tertiary referral centers from 2000 to 2016. Patients with insufficient follow

up (<6 months), presenting castration-resistant cancer before sRP, undergoing laparoscopic sRP or missing data were excluded. A post-operative prostate-specific antigen (prostate-specific antigen) level>0.2 ng/ml was adopted to define biochemical recurrence (BCR). Predictors of positive surgical margins and BCR were assessed in a multivariable logistic regression model. *Results:* Primary treatment for the 414 included men had been radiotherapy (63.5%), brachytherapy (25.7%) or others (13.6%). At sRP, median PSA was 4.2 ng/ml; more than half of the patients had a biopsy Gleason score ≤7 (55.5%) and no extra-prostatic evidence of disease at imaging (93.3%). By contrast, definitive sRP histology demonstrated aggressive grade in 39.7% (Gleason ≥9; 27.6%). Extracapsular and nodal disease were present in 52.9% and 16%, respectively. Surgical margins were positive in almost one out of three men (29.7%). In Figure 1, Kaplan–Meier survival analysis is depicted. Five-year BCR-free, cancer-specific and overall survival were 56.7%, 97.7% and 92.1%, respectively. On multivariate analysis, non-radical resection (R1) was predicted by extra-prostatic disease (pT3a: odds ratio (OR)=2.9, 95% confidence intervaI (CI)=1.5-5.9; ≥pT3b: OR=2.4, 95% CI=1.3-4.4) and nodal involvement (pN1: OR 2.9, 95% CI=1.5-5.9). Similarly, BCR was associated with ≥T3b tumour (OR=2.4, 95% CI=1.3-4.1) and Gleason score (up to OR=7.2, 95% CI=1.9-27.1 for GS>8). *Conclusion:* Prostate cancer recurring after primary treatment is an aggressive disease associated with high rates of non-organ-confined and nodal disease. Nevertheless, in a contemporary series, sRP achieved interesting oncological control in the short to medium term. As expected, BCR was associated with locally advanced disease and higher Gleason score. Further research is warranted to confirm these finding in the long term.

34
IDENTIFYING THE BEST CANDIDATES FOR SALVAGE RADICAL PROSTATECTOMY: EAU GUIDELINES – COMPLIANT PATIENTS HAVE BETTER OUTCOMES

Giancarlo Marra[1], Paolo Gontero[1], Paolo Alessio[1], Giorgio Calleris[1], Marco Oderda[1], Fernando Munoz[2], Claudia Filippini[3], Estefania Linares[4], Rafael Sanchez-Salas[4], Sanchia Goonewardene[5], Prokar Dasgupta[5], Ben Challacombe[5], Rick Popert[5], Declan Cahill[6], David Gillatt[7], Raj Persad[7], Juan Palou[8], Steven Joniau[9], Thierry Piechaud[10], Alexandre De La Taille[11], Morgan Roupret[12], Simone Albisinni[13], Alessandro Morlacco[14], Giorgio Gandaglia[15], Alexander Mottrie[15], Joseph Smith[16], Andre Berger[17], Monish Aron[17], Andre Abreu[17], Inderbir S. Gill[17], Henk Van Der Poel[18], Derya Tilki[19], Declan Murphy[20], Nathan Lawrentschuk[20], John Davis[21] and Robert Jeffrey Karnes[14]

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

Background: Salvage radical prostatectomy (sRP) represents a curative and underused option in treating prostate cancer (PCa) recurrence; identifying the best candidates for salvage surgery is fundamental to enhancing oncological benefit, reducing adverse events. European Association of Urology (EAU) guidelines recommend considering sRP only for patients with a 10-year life-expectancy, pre-sRP prostate-

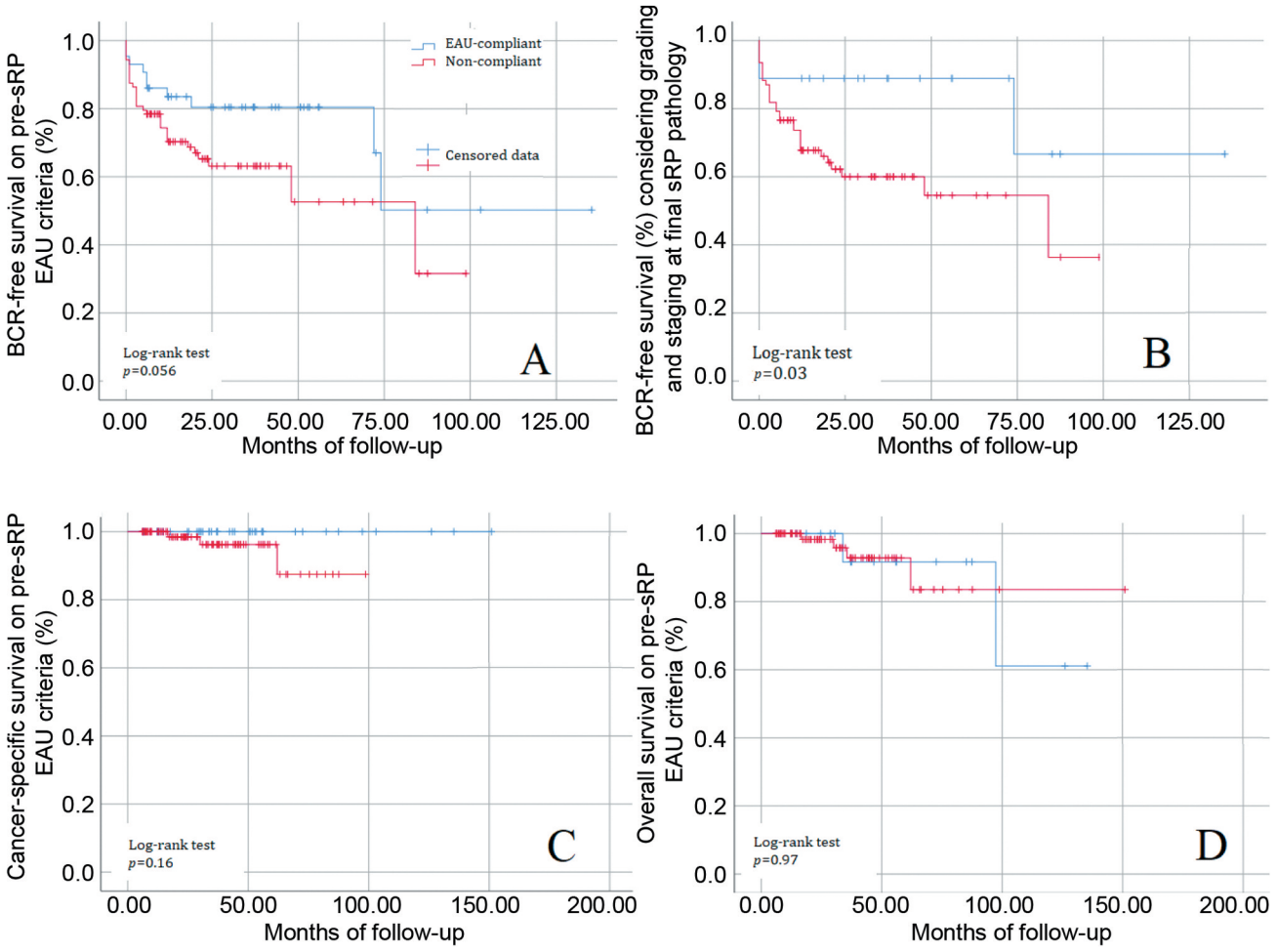

Figure 1. *Kaplan–Meier plots comparing European Association of Urology (EAU) guidelines compliant (EAU-c) patients in blue and non-EAU-c patients in red. A: Biochemical recurrence (BCR)-free survival (stratified according to EAU criteria using clinical, pre-surgical data); B: BCR-free survival (stratified according to EAU criteria using definitive pathology data); C: Cancer-specific survival; D: Overall survival.*

specific antigen <10 ng/ml, pre-sRP biopsy Gleason score ≤8, no evidence of nodal disease or distant metastasis, and previous clinically organ-confined (cT2) cancer. Materials and Methods: Searching a database of 629 sRP performed between 2000 and 2016 at 18 tertiary high-volume centers, 43 fully EAU-compliant (EAU-c) and 88 non-EAU-compliant (non-EAU-c) patients were identified. We excluded patients with insufficient follow-up (<6 months), presenting castration-resistant cancer before sRP, undergoing laparoscopic sRP or lacking data. A post-operative PSA >0.2 ng/ml was adopted to define biochemical recurrence (BCR). Pathological and medium-term oncological results were examined, comparing data by Mann–Whitney, Pearson chi-square and log-rank test as appropriate. *Results:* Table I shows pre- and post-sRP features. EAU-c and non-EAU-c patients had similar age at sRP and follow-up duration. EAU-compliant patients demonstrated significantly better International Society of Uro-Pathology grading group (ISUP), local staging (pT), nodal involvement (pN) and incidence of positive surgical margins at definitive histology. In Figure 1, Kaplan–Meier curves for BCR-free, overall and cancer-specific survival are depicted. For EAU-compliant patients 5-year BCR-free survival was 0.80±0.06 and was 0.52±0.08 for non-compliant patients. Furthermore, we noted that BCR-free survival was associated more strongly with sRP final histology than with pre-sRP biopsy and clinical staging. *Conclusion:* Well-selected patients show interesting oncological results after sRP. Around 80% of men completely adherent to EAU criteria were disease-free 5 years after sRP. On the grounds of a rigorous pre-treatment selection, this potentially curative salvage treatment should not be precluded a priori.

Table I. *Main population characteristics pre and post salvage radical prostatectomy (sRP).*

Characteristic		EAU-compliant (N=43)	Non-EAU compliant (N=88)	*p*-Value
Age, years	Median (IQR)	65 (60.5-67.5)	66 (62-70)	0.07
First treatment to sRP, months	Median (IQR)	44.7 (21.1-74.4)	63.4 (37.5-84.1)	**0.03**
Follow-up, months	Median (IQR)	37.1 (25.0-55.8)	30 (16.4-46.7)	0.75
PSA (pre-sRP)	Median (IQR)	4.9 (3.08-6.75)	6.1 (3.41-11)	**0.01**
cT stage, n (%)	cT1	32 (39.5%)	49 (60.5%)	**0.005**
	cT2	11 (39.3%)	17 (60.7%)	
	cT3 or more	0 (0%)	22 (100%)	
cN stage, n (%)	cN0	43 (35%)	80 (65%)	0.38
	cN+ or M1a	0 (0%)	8 (100%)	
ISUP (biopsy pre-sRP), n (%)	1	14 (63.6%)	8 (36.4%)	**0.001**
	2	14 (43.8%)	18 (56.2%)	
	3	15 (50%)	15 (50%)	
	4	0 (0%)	24 (100%)	
	5	0 (0%)	23 (100%)	
ASA score, n (%)	1	19 (33.9%)	37 (66.1%)	**0.001**
	2	24 (49%)	25 (51%)	
	3	0 (0%)	26 (100%)	
pT stage, n (%)	pT2	28 (48.3%)	30 (51.7%)	**0.001**
	pT3 or more	15 (20.5%)	58 (79.5%)	
pN stage, n (%)	N0	21 (28%)	54 (72%)	
	N1	2 (10%)	18 (90%)	**0.001**
	Nx	20 (55.6%)	16 (44.4%)	
ISUP on sRP, n (%)	1	8 (53.3%)	7 (46.7%)	
	2	17 (48.6%)	18 (51.4%)	
	3	14 (36.8%)	24 (63.2%)	
	4	2 (11.8%)	15 (88.2%)	**0.006**
	5	2 (7.7%)	24 (92.3%)	
Surgical margins, n (%)	Negative	33 (41.3%)	47 (58.7%)	**0.01**
	Positive	10 (19.6%)	41 (80.4%)	

EAU: European Association of Urology; IQR: inter-quartile range; sRP: salvage radical prostatectomy; PSA: prostate specific antigen; ISUP: International Society of Uro-Pathology grading group; ASA: American Society of Anesthesiology. Bold values show statistical significance.

35
SALVAGE PROSTATECTOMY FOR ORGAN-CONFINED CASTRATION-RESISTANT RECURRENT PROSTATE CANCER: RESULTS FROM A RETROSPECTIVE MULTICENTER SERIES

Giancarlo Marra[1], Giorgio Calleris[1], Paolo Alessio[1], Marco Oderda[1], Juan Palou[2], Steven Joniau[3], Thierry Piechaud[4], Salvatore Smelzo[4], Alessandro Morlacco[5], Sharma Vidit[5], Henk Van Der Poel[6], Robert Jeffrey Karnes[5] and Paolo Gontero[1]

[1]Department of Urology, San Giovanni Battista Hospital, Città della Salute e della Scienza, University of Turin, Turin, Italy;
[2]Department of Urology, Fundaciò Puigvert, Barcelona, Spain;
[3]Department of Urology, Leuven University Hospitals, Leuven, Belgium;
[4]Department of Urology, Clinique Saint Augustin, Bordeaux, France;
[5]Department of Urology, Mayo Clinic, Rochester, MN, U.S.A.;
[6]Department of Urology, Netherlands Cancer Institute, Amsterdam, the Netherlands

Background/Aim: Non-metastatic castration-resistant prostate cancer (CRPC) is an uncommon entity; novel anti-androgen therapies have recently proven effective in prolonging metastasis-free survival. Salvage radical prostatectomy (sRP) in this setting represents a substantially uncharted territory and no specific recommendations are present. Herein, we assessed the oncological and functional results of sRP in CRPC patients.
Patients and Methods: Drawn from a large retrospective sRP

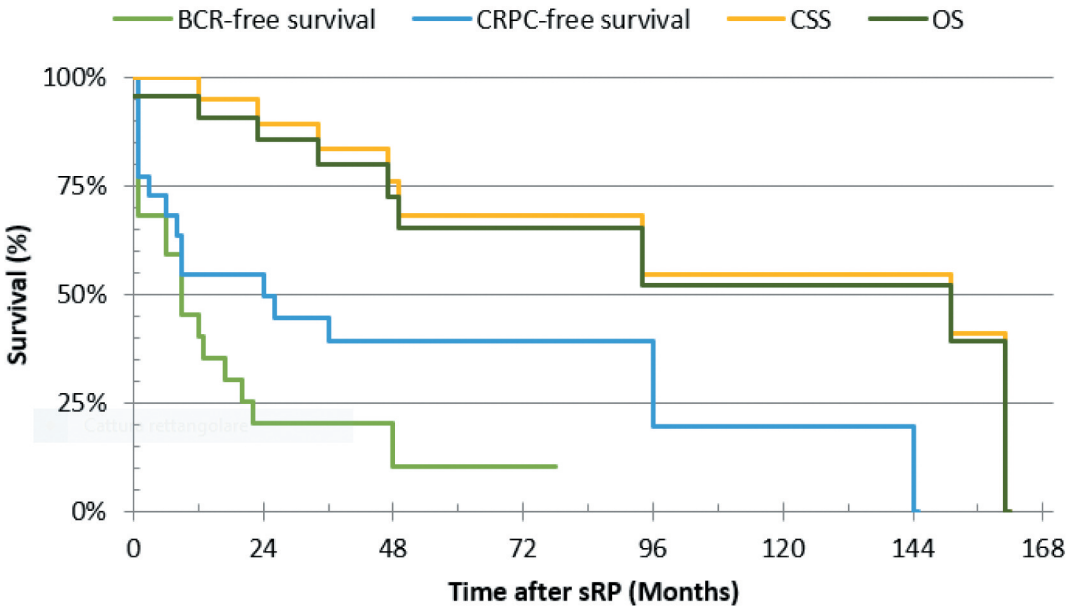

Figure 1. *Kaplan-Meier plots for biochemical recurrence (BCR)-free survival, castration-resistant prostate cancer (CRPC) free survival, cancer specific survival (CSS), and overall survival (OS). sRP: Salvage radical prostatectomy.*

database, 23 cases of radiorecurrent M0-CRPC patients, who underwent sRP between 2001 and 2014 at 6 high-volume centers, were included in the study. Baseline clinical and pathological characteristics, oncological outcomes and complications (graded using the Clavien-Dindo scale) were reviewed. We retrieved continence data pre-sRP, at 6 and/or at 12 months, evaluating the number of pads used per day. Exclusion criteria were insufficient data and a follow-up <12 months. *Results:* More than two-thirds of the patients (n=16) experienced at least 1 complication, while 10 of patients developed Clavien >2 events. Among the other patients, 2 cases of rectal fistula, 4 of anastomotic stricture, and 2 of urinary fistulae were recorded. Incontinence rate was around 40% (n=10) at last follow-up, including 3 severe cases. At sRP histology, low-grade organ-confined disease was uncommon (ISUP ≥4: 65.2%; ≥pT3b: 56.5%; pN1: 30.4%), PSA persistence was observed in 7 cases. Amongst the patients with complete PSA response, biochemical recurrence occurred in 68.7% (median=11 months, after sRP) and CRPC developed in 58.8% (median=31 months, after sRP). At a median follow-up of 48 months, 4 patients were disease-free, 8 died from PCa and 1 due to other causes. Figure 1 depicts Kaplan-Meier survival curves. *Conclusion:* When performing sRP in M0 CRPC settings, complications are common and continence rates are generally discouraging. Four patients in our series had no evidence of disease after sRP, while 11 experienced an ADT-free time window. The potential oncological benefit should be carefully balanced against treatment toxicity. In the era of new antiandrogen drugs, the role of sRP for M0 CRPC is uncertain and further evidence is needed.

36
RADIOTHERAPY WITH DOSE-ESCALATED SIMULTANEOUS INTEGRATED BOOST MRI-GUIDED IN LOCAL RECURRENCE AFTER PROSTATECTOMY FOR PROSTATE CANCER

Elisa Villa[1], Paolo Ghirardelli[1], Roberta Meroni[2], Andrea Ravasio[1], Alessandro Zanello[2], Federica Locatelli[3], Luca Trombetta[3], Paolo Salmoiraghi[3] and Vittorio Vavassori[1]

[1]Radiotherapy Unit, Humanitas Gavazzeni, Bergamo, Italy; [2]Department of Radiology, Humanitas Gavazzeni, Bergamo, Italy; [3]Physics Unit, Humanitas Gavazzeni, Bergamo, Italy

Background/Aim: The main treatment option for prostate cancer relapse after radical prostatectomy (RP) is salvage radiotherapy (SRT). Target volumes and delivery doses may be different when macroscopic recurrence occurs. Multiparametric magnetic resonance imaging (mpMRI) is a useful tool for detection of local relapse (LP), but also for contouring target volumes and treatment planning. Usefulness and the right time to perform mpMRI during follow-up after SRT are controversial. The study aims to evaluate clinical outcomes of SRT with simultaneous

integrated boost (SIB) dose escalated in patients with local recurrence after RP and usefulness of mpMRI during the follow-up. *Patients and Methods:* Between May 2015 and November 2017, 18 patients with macroscopic local recurrence after RP, referred to our Institute for SRT. In all patients local recurrence was detected by pre-RT pelvic mpMRI; mpMRI was then matched with computed tomography-simulation (CT-sim) for defining target volumes (Figure 1). Volumetric modulated arc therapy (VMAT) - image-guided radiation therapy (IGRT) technique, with daily cone beam computed tomography (CBCT), was used to deliver hypofractionated SRT (30 fractions with SIB): 60-67.5 Gy (2-2.25 Gy/fraction) to the prostatic bed and 69-72 Gy (2.3-2.4 Gy/fraction) to the macroscopic lesion; 7 patients were also treated on pelvic nodes (1.8 Gy/fraction). Concomitant androgen deprivation therapy (ADT) was prescribed in 8 patients. After RT, patients were evaluated with prostate-specific antigen (PSA) every 4-6 months, while mpMRI was performed at least once during follow-up, with variability in timing between 3 and 33 months. Toxicity was assessed using CTCAE v. 4.03 scale. *Results:* Median time from RP was 79 months (range=3-157), median pre-RT PSA level was 0.745 ng/ml (range=0.13-6.52). Median follow-up after SRT was 31 months (range=3-46) and median time to the first mpMRI post-RT was 9 months (range=3-33). At the first follow-up mpMRI, we recorded 11 complete radiologic responses (61.1%), 4 partial radiological responses (22.2%), and in 3 patients (16.7%) local lesion was unchanged. Five patients had a second mMRI imaging exam during follow-up (range=11-32 months): 3 patients were found to be disease-free and 2 patients (12 and 17 months after SRT) were found to have partial radiological response to the therapy (stable disease compared to the first control at 6 and 9 months, respectively) with minimum increase of PSA level. Two patients, with a stable radiological lesion at the first mpMRI but PSA level 0.01 ng/ml, refused a second radiological control. Biochemical progression-free survival was 100% at 1 year and 85% at 3 years. All patients but one had biochemical control of the disease (PSA nadir + 0.2 ng/ml). Biochemical failure (BF) occurred 22 months after RT, at the interruption of concomitant long term ADT (pre-RT: PSA=6.52 ng/ml, at BF: PSA=0.47 ng/ml), but local recurrence was not detectable at mpMRI 15 months post-RT, when PSA level was 0.22 ng/ml (PSA nadir). Restaging was performed at 30 months after RT (PSA=2.32 ng/ml), with ^{18}F-choline PET resulting negative. Acute toxicity (TOX) was mild: maximum genitourinary (GU) toxicity recorded was G2 in 8 and G1 in 7 patients. The main symptoms were nocturia, urinary frequency and urgency. Maximum gastrointestinal (GI) toxicity was G2 in 2 patients: 1 patient with fecal incontinence and 1 with diarrhea. In 8 patients we recorded G1 GI toxicity: main symptoms were diarrhea, tenesmus, and hematochezia (in 2 patients). Late GU toxicity was mild; only 1 patient had a stenosis G3 that required

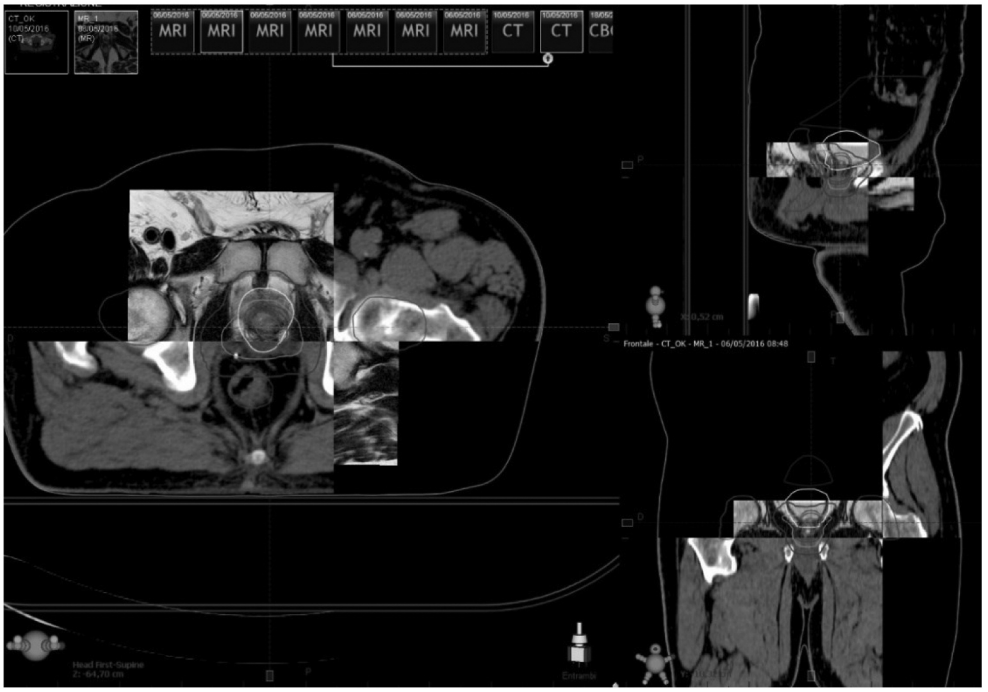

Figure 1. *Computed tomography-simulation (CT-sim)/ multiparametric magnetic resonance imaging (mpMRI) match for defining target volumes.*

urethrotomy. The main late GI toxicity was hematochezia; G2 in 1 patient treated with mesalazine, and G3 in 1 patient treated with APC cauterization. *Conclusion:* Dose escalated SRT with VMAT-IGRT (+/– ADT) for macroscopic LP after RP seems effective with good late toxicity profile. Pelvic mpMRI may be a useful tool not only for diagnosis, despite low PSA levels, but also for treatment planning and follow-up. The optimal time for performing mpMRI after SRT is yet to be defined: we suggest to wait until 6-12 months after the conclusion of RT before the first follow-up mMRI. Longer follow-up and larger series are warranted to confirm these findings.

38

STEREOTACTIC BODY RADIATION THERAPY IN THE MANAGEMENT OF OLIGOMETASTASES FROM BLADDER CANCER AND OTHER UROTHELIAL MALIGNANCIES

Ciro Franzese[1,2], Giulio Francolini[3], Luca Nicosia[4], Filippo Alongi[4,5], Lorenzo Livi[3,6] and Marta Scorsetti[1,2]

[1]Radiotherapy and Radiosurgery Department, Humanitas Cancer Center and Research Hospital, Milan, Italy;
[2]Department of Biomedical Sciences, Humanitas University, Milan, Italy;
[3]Radiation Oncology Unit, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy;
[4]Advanced Radiation Oncology Department, IRCCS Sacro Cuore Don Calabria Hospital, Cancer Care Center, Negrar, Italy;
[5]University of Brescia, Brescia, Italy;
[6]Departments of Biomedical, Experimental, and Clinical Sciences "Mario Serio", University of Florence, Florence, Italy

Background/Aim: Bladder cancer represents the most common type of urothelial carcinoma with poor prognosis in case of metastatic disease. Chemotherapy is the standard of care for metastatic setting; however, the median overall survival (OS) after chemotherapy is 12.5-15 months. In the present study we aimed to evaluate the role of stereotactic body radiation therapy (SBRT) in the management oligometastatic urothelial cancer. *Patients and Methods:* Data were collected from three Institutions to include patients diagnosed with bladder or other urothelial cancer, who developed synchronous or metachronous metastases (maximum 5 metastases). Concomitant systemic therapy was allowed. Patients were treated with Linac or robotic-arm SBRT. Tumour response was classified according to EORTC-RECIST criteria version 1.16. End points of the present study were the outcome in terms of local control of treated metastases (LC), out-field progression-free survival (dPFS), overall progression-free survival (PFS) and OS. *Results:* A total of 61 patients were treated on 82 lesions. Primary tumour was located in bladder in 50 (82%) patients, followed by kidney pelvis (7; 11.5%), and ureter (3; 4.9%). Most common sites of metastatic disease were lung (40.2%) and lymph nodes (35.4%). Twenty-nine patients (47.5%) received 1 to 3 lines of systemic therapy before RT and 14 (23%) patients had systemic therapy during SBRT. Median BED10 value was 78.7 Gy (range=37.5-151.2). Median follow-up was 17.2 months. Rates of LC at 1 and 2 years were 92% and 88.9%, respectively. Lines of systemic therapy before SBRT were predictive of LC (HR=2.62, p=0.034). PFS rates at 1 and 2 years were 47.9% and 38.1%, respectively. High number of metastases was negative predictive factor (HR=2.65, p=0.008). Median OS was 25.6 months; 1- and 2- year OS rates were 78.9% and 50.7%, respectively. Total delivered dose (HR=0.93, p=0.003) and BED10 (HR=0.97, p=0.006) were significantly correlated with OS. No adverse events >grade 2 were reported in this cohort. *Conclusion:* SBRT represents an effective and safe treatment in the oligometastatic setting from urothelial carcinoma. This local approach is potentially able to delay the onset of new systemic therapies with minimal impact on patient quality of life.

39

MAGNETIC RESONANCE IMAGING (MRI)-GUIDED ADAPTIVE STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR LOCALIZED PROSTATE CANCER: A MONO-INSTITUTIONAL INITIAL EXPERIENCE

Francesco Cuccia[1], Rosario Mazzola[1], Michele Rigo[1], Vanessa Figlia[1], Niccolò Giaj-Levra[1], Luca Nicosia[1], Francesco Ricchetti[1], Antonio De Simone[1], Stefania Naccarato[1], Gianluisa Sicignano[1], Ruggero Ruggieri[1] and Filippo Alongi[2]

[1]Advanced Radiation Oncology Department, IRCCS Sacro Cuore Don Calabria Hospital, Cancer Care Center, Negrar, Italy;
[2]Advanced Radiation Oncology Department, IRCCS Sacro Cuore Don Calabria Hospital, Cancer Care Center, University of Brescia, Brescia, Italy

Background/Aim: The recent introduction of MRI-guided linear accelerators (MRI-Linac) represents an important step forward for safe and high-precision radiotherapy. Unity Elekta is a unique MRI-Linac device that conjugates a 1.5 Tesla MRI unit with a 7 MV flattening-filter-free (FFF) accelerator mounted in a rotating gantry system. The possibility to use MRI-based on-board imaging enables the daily verification of real-time anatomy of the patient, allowing a daily treatment planning that represents the current highest level of adaptive radiotherapy. On 15th October 2019, we started our clinical activity at IRCCS Sacro Cuore Don Calabria Hospital with Unity Elekta MRI-

Linac aiming to propose a radiotherapy treatment option that provides better anatomical visualization of the prostate, seminal vesicles, and nearby healthy structures. This can be particularly helpful for prostate stereotactic body radiotherapy (SBRT), to reduce uncertainties and to take into account prostate motion, which may be modified by daily volume variations of both bladder and rectum. Moreover, MRI-Linac allows a daily plan re-optimization that may lead to a relevant reduction of normal tissue exposure. Herein, we report the data about the first 5 patients with low-intermediate risk prostate cancer treated with SBRT with Unity Elekta MRI-Linac. *Patients and Methods:* Five patients with prostate cancer were treated in the first month of clinical activity. The placement of a hydrogel spacer was proposed as optional to all patients and 2 out of 5 declined. All patients were educated at the use of a fleet enema 2 h before the planning CT and MRI-simulation; also, drinking 500 ml of water 30 min before the exam was required for a comfortable bladder filling. For all patients, we delineated prostate clinical target volume (CTV) as the entire gland plus the lower third of seminal vesicles with a margin of 5 mm in all directions except posteriorly, where a margin of 3 mm was applied. For intermediate-risk patients, we also delineated the remaining portion of seminal vesicles, applying the same margins. As organs at risk (OARs), we delineated penile bulb, femurs, bladder, and rectum; for the two latter OARs, we also delineated, as sub-structures, posterior bladder wall, and anterior rectal wall. Off-line treatment planning was performed using Monaco TPS 5.4 (Elekta AB, Stockholm, Sweden), to generate a patient-specific template on the simulation imaging, applicable for the on-line planning, if needed. The choice between the "adapt to shape" (ATS) or the "adapt to position" (ATP) workflow was based on the evaluation of daily MRI-imaging before each fraction. Furthermore, MRI-T2 weighted sequences were acquired during the intra-fraction interval, and after every daily session. For all patients, the prescription dose was 35 Gy in 5 fractions delivered in consecutive days by a 7MV (FFF) Linac. Toxicity and quality of life (QoL) assessment was performed at baseline and after treatment using Common Terminology Criteria for Adverse Events (CTCAE) v5.0, International Prostatic Symptoms Score (IPSS) index, EPIC-26, and EORTC-QLQ-C30 questionnaires. *Results:* Five patients were treated within the first month of using the Unity Elekta MRI-Linac for SBRT. The median age was 69 years (range=56-78); according to D'Amico classification, 1 patient was low risk, 3 were favorable intermediate-risk, and 1 was unfavorable intermediate risk. Median iPSA was 7.70 ng/ml (range=6.2-15.7); none of the patients received concurrent or adjuvant androgen deprivation therapy. Median prostate volume was 31 cm^3 (range=25-61.5), median baseline IPSS was 4 (range=0-9). Median time for single fraction was 57 min (range=25-124); ATP protocol was adopted in 15 sessions (60%) resulting in a median session time of 34 min (range=25-75), while for ATS workflow, performed in 10 cases (40%), the median session time was 55 min (range=41-124). All patients completed the treatment without any interruption. No G≥3 adverse event was observed; only 1 patient referred mild rectal tenesmus and urinary tract pain fully resolved with steroids. Post-treatment IPSS and QoL indices revealed no significant differences compared to baseline. We report one of the first series of patients treated with MRI-Linac for prostate SBRT. Compared to conventional linear accelerators, MRI-guided radiotherapy allows daily online adaptive radiotherapy by checking potential anatomical variations, target and OARs motion, and providing the possibility to daily generate treatment plans based on the real-time imaging assessment. One of the main concerns of MRI-Linac may be related to the time-consuming issue that can theoretically generate an impact in terms of the intra-fraction motion. Nevertheless, MRI-guided RT still allows a more accurate adaptation to daily anatomy, reducing doses to normal tissues. In our experience, we decided to adopt the ATS protocol only for cases not suitable for the ATP, which is usually faster and equally reliable. We reported excellent, though preliminary, outcomes in terms of toxicity with negligible adverse events reported. Furthermore, although the potentially longer treatment time may lead to patient discomfort, these time-consuming procedures are counter-balanced by a remarkable advantage in terms of reduction of acute toxicity and lower impact on the quality of life. This is also confirmed by the evaluation of our QoL questionnaires that reported no significant differences between baseline and post-treatment. *Conclusion:* Our very preliminary experience supports the use of MR-guided radiotherapy for the safe and feasible delivery of SBRT for low-intermediate risk prostate cancer. More mature data are warranted in order to evaluate the real impact of this technique regarding long-term tolerability and efficacy.

40
SKELETAL MUSCLE LOSS PREDICTS ONCOLOGICAL OUTCOMES IN T1HG PATIENTS TREATED WITH ADJUVANT INTRAVESICAL BCG: IMPLICATIONS FOR DECISION-MAKING

Maurizio Barale[1], Andrea Giordano[1], Giuseppe Pizzuto[1], Simone Mazzoli[1], Matteo Debellis[1], David D'Andrea[2], Shahrokh F. Shariat[2], Francesco Soria[1] and Paolo Gontero[1]

[1]Division of Urology, Department of Surgical Sciences, Torino School of Medicine, Turin, Italy;
[2]Department of Urology and Comprehensive Cancer Center, Medical University of Vienna, Vienna General Hospital, Vienna, Austria

Background/Aim: The optimal management of T1 high grade (HG) non-muscle invasive bladder cancer (NMIBC) remains a challenge, mainly due to its highly variable behavior. Despite

adequate treatment, a non-negligible subgroup of patients will experience progression to muscle-invasive disease, accounting for the 10-30% rate of cancer-specific mortality in T1HG bladder cancer. Identification of patients with T1HG NMIBC, who will not respond to conservative treatment (Bacillus Calmette-Guerin; BCG), is fundamental for the selection of patients for early radical cystectomy (eRC). A better selection in this population, could improve oncological outcomes without overtreating those patients who are likely to respond to intravesical immunotherapy. To date, current prognostic models for prediction of outcomes in patients with T1HG NMIBC are mainly based on standard clinico-pathologic features and suffer from limited predictive accuracy. Improving these models will pave the way towards a personalized treatment approach. Skeletal muscle loss (sarcopenia) has been shown to be able to predict survival outcomes in genitourinary cancers such as prostate, kidney, and urothelial neoplasms. However, this is not surprising since the majority of trials have been conducted in an advanced/metastatic setting, where sarcopenia is probably a reflection of the deterioration of patients' general clinical condition. To date, the role of sarcopenia in patients with NMIBC remains uninvestigated. Therefore, the aim of our study was to evaluate the ability of sarcopenia to predict recurrence-free (RFS) and progression-free survival (PFS) in T1HG NMIBC patients treated with adjuvant BCG. *Patients and Methods:* We retrospectively analyzed T1HG NMIBC patients treated with transurethral resection of the bladder (TURB) and adjuvant intravesical immunotherapy. Sarcopenia, identified from computed tomography scans performed within 2 months after TURB, was defined as a skeletal muscle index of <39 cm^2/m^2 for women and <55 cm^2/m^2 for men. To evaluate sarcopenic obesity, the body mass index-adjusted was used. Kaplan-Meier curves were built to evaluate differences in RFS and PFS according to the presence of sarcopenia. Univariable and multivariable models were used to assess the association between sarcopenia with oncological outcomes. C-index was calculated to evaluate the clinical impact of the models. *Results:* Overall, 100 patients met the inclusion criteria and were retained for the analyses. Sarcopenia was present in 65% of the patients. Within a median follow up of 29 months (IQR=19-39), disease recurrence and progression occurred in 37% and 18% of the patients, respectively. Three-year PFS rates were significantly worse in patients with sarcopenia (71%) compared to those without sarcopenia (93%) (p=0.02). On multivariable analyses that accounted for the effect of standard clinico-pathologic characteristics, sarcopenia was independently associated with PFS (p=0.005), while no association with RFS was observed. The Harrel C-index of a model for the prediction of PFS based on age, gender, body-mass index, smoking status, presence of concomitant carcinoma *in situ*, macroscopic appearance of the tumor, tumor size and focality was 0.82. By adding sarcopenia to this model, the c-index improved to 0.91. Limitations are inherent to the retrospective design of the study. *Conclusion:* Sarcopenia was present in 65% of patients with T1HG NMIBC treated with BCG. Sarcopenia was an independent predictor of progression to muscle-invasive disease. The addiction of sarcopenia to a model for the prediction of PFS significantly improved the accuracy of the model. Pending external validations, sarcopenia may be used in adjunct to current prognosticators for decision-making in T1HG patients.

41
EPIDERMOID CYST OF THE ADULT TESTIS. CASE REPORT AND LITERATURE REVIEW

Valerio Olivieri[1], Valentina Fortunati[2], Emanuele Corongiu[3], Flavio Forte[3], Gabriele Ruggiero[4], Danilo Abate[4], Nicoletta Serra[4] and Daniele Griffa[1,4]

[1]Division of Urology, Ivrea Hospital – ASL TO4, Ivrea, Italy;
[2]Division of Pathology, Hospital "Policlinico Tor Vergata", Rome, Italy;
[3]Division of Urology, Hospital "Madre Giuseppina Vannini", Rome, Italy;
[4]Division of Urology, Ciriè Hospital – ASL TO4, Ciriè, Italy

Background: Testicular epidermoid cysts (TEC) are rare benign tumors incidentally discovered during self-examination or scrotal ultrasound. Young patients are usually involved but adults may be affected too. Sonography and testicular magnetic resonance (MR) imaging helps in characterizing the lesion. Diagnosis depends on histology. The biological behaviour of these neoplasms in the adult testis still remains unknown leading to different surgical approaches. Herein, we report the case of TEC in an adult male undergone to testis-sparing surgery, and also review the literature. *Case Report:* A 40-year old Caucasian male presented to us for a mass in the left testis recently discovered on self-examination. His past anamnesis was uneventful. No familiarity for testicular cancer was reported. Inguinal and supraclavicular lymph nodes were negative on physical examination: serum levels of germ cell tumor markers were normal too. The testis presented with a painless mass at the upper pole. Scrotal sonography (US) revealed a 15-mm well-circumscribed mass, heterogeneous and characterized by an echogenic rim: contrast-enhanced MR ruled out intralesional vascularity. Testicular biopsy with frozen section was offered in order to avoid radical orchiectomy. *Results:* Frozen section analysis showed mature TEC. Testis-sparing surgery was offered. The final report revealed the following features. Macroscopically the lesion presented as a 1.5-cm cyst indistinguishable from malignant neoplasms. On microscopic evaluation, the cyst was lined by a fibrous membrane filled with layers of cornifying squamous epithelium composing the wall. Coexisting teratomatous

element were ruled out. Furthermore, atypical features such as association with germ cell tumor (GCT), necrosis, or high mitotic activity were also excluded. It was classed as post-pubertal mature TEC. *Discussion and Conclusion:* Epidermoid cysts are uncommon benign tumors accounting for around 1-2% of all testicular lesions (1). Incidence is higher in people between the ages of 10 and 40 years; Caucasian males are more frequently diagnosed with the disease and the right testis is affected more often than the left. Etiology is not completely understood (1, 2). Clinically, they present with a firm, painless palpable mass highly indistinguishable to all testicular neoplasms (2, 3). Serum markers are near always negative. US may help in diagnosis due to the typical heterogeneous "onion-ring" appearance of the mass. Contrast-enhanced ultrasound or MR may add more information such as the absence of vascularity and well-marginated borders. Total body contrast-enhanced CT is used for stadiation. Two forms of TEC have been described: pre- and post-pubertal. Pre-pubertal variant is considered as a benign tumor since it is not associated with GCT and no cases of metastatic spread have been reported to date in literature; moreover, unfavorable prognostic features are usually missing. Post-pubertal TEC are also known as "complex" TEC and may act differently from pre-pubertal ones (1). Ipsilateral or contralateral association with GCT has been described in literature as an unfavorable prognostic feature (2). Cellular atypia, high mitotic activity, necrosis or lymph-vascular invasion are rare but may be present in post-pubertal variant. Testis-sparing surgery may be offered, but radical orchiectomy becomes mandatory when unfavorable features coexist. Frozen section and histological diagnosis help to avoid unnecessary orchiectomy. In conclusion, epidermoid cysts of the testis are uncommon tumors commonly affecting young patients. Preoperative serum markers, radiology, and biopsy are important criteria for surgical planning: frozen section and microscopic features help to avoid unnecessary orchiectomy. Pre-pubertal and post-pubertal represent the main variants. Post-pubertal TEC usually act as benign neoplasms; however, biologic behaviour and clinical management is still controversial. Surgical enucleation may be offered as the first option but radical orchiectomy is mandatory whenever unfavorable features coexist.

1 Anheuser P, Kranz J, Stolle E, Höflmayer D, Büscheck F, Mühlstädt S, Lock G and Dieckmann KP: Testicular epidermoid cysts: a reevaluation. BMC Urol *19(1)*: 52, 2019. PMID: 31185974. DOI: 10.1186/s12894-019-0477-1

2 Çakıroğlu B, Sönmez NC, Sinanoğlu O, Ateş L, Aksoy SHand Özcan F: Testicular epidermoid cyst. Afr J Paediatr Surg *12(1)*: 89-90, 2015.PMID: 25659561. DOI: 10.4103/0189-6725.151002

3 Dieckmann KP and Loy V. Epidermoid cyst of the testis: A review of clinical and histogenetic considerations. Br J Urol *73:* 436-441, 1994. PMID: 8199834. DOI: 10.1111/j.1464-410x.1994.tb07611.x

42
METASTASIS-DIRECTED SBRT GUIDED BY ^{18}F-CHOLINE PET-CT *VERSUS* ^{68}Ga-PSMA PET-CT IN CASTRATION-SENSITIVE OLIGORECURRENT PROSTATE CANCER: A COMPARATIVE ANALYSIS

Rosario Mazzola[1], Giuseppe Napoli[1], Giulio Francolini[2], Luca Triggiani[3], Luca Nicosia[1], Vanessa Figlia[1], Niccolò Giaj-Levra[1], Francesco Ricchetti[1], Michele Rigo[1], Francesco Cuccia[1], Lorenzo Livi[2], Stefano Maria Magrini[3], Matteo Salgarello[4] and Filippo Alongi[1,5]

[1]Advanced Radiation Oncology Department, IRCCS Sacro Cuore Don Calabria Hospital, Cancer Care Center, Negrar, Italy;
[2]Department of Radiation Oncology, A.O.U. Careggi, University of Florence, Florence, Italy;
[3]Radiation Oncology Department, ASST Spedali Civili di Brescia - Brescia University, Brescia, Italy;
[4]Nuclear Medicine, IRCCS Sacro Cuore Don Calabria Hospital, Cancer Care Center, Negrar, Italy;
[5]University of Brescia, Brescia, Italy

Aim: The present analysis aimed to compare the impact of ^{18}F-choline and ^{68}Ga-prostatic specific membran antigen-11 positron emission tomography/computed tomography (^{68}Ga-PSMA PET-CT)-guided metastases-directed therapies (MDT) in a cohort of patients affected by castration sensitive oligorecurrent prostate cancer (PC). *Patients and Methods:* The present study is a retrospective multicenter analysis conducted at three Italian Academic Centers. Inclusion criteria for patients were: i) histologically confirmed diagnosis of prostate carcinoma, ii) patients affected by biochemical relapse after primary tumor treatment (radical prostatectomy or radical radiotherapy), iii) oligorecurrent PC, defined as the presence of 1-3 hypermetabolic lesions detected by means of ^{18}F-choline or ^{68}Ga-PSMA PET-CT, iv) ^{18}F-choline and ^{68}Ga-PSMA PET-CT performed in a single Nuclear Medicine division, patients treated with upfront SBRT without hormonal therapies, vi) SBRT delivered with a dose of at least 5 Gy per fraction to a biological effective dose (BED) of at least 80 Gy, using an α/β ratio of 2 Gy. In case of oligoprogression after MTD, a second-course of SBRT was generally proposed in cases with less than of ≤3 new lesions outside the previous irradiated field. In the remaining cases, androgen deprivation therapy (ADT) was administered. The primary endpoint was the distant progression-free survival (DPFS) after SBRT, defined as the interval between the end of SBRT and the detection of a new metastasis outside the field of irradiation. Secondary endpoints were: overall survival (OS), local control (LC) and ADT-free survival.

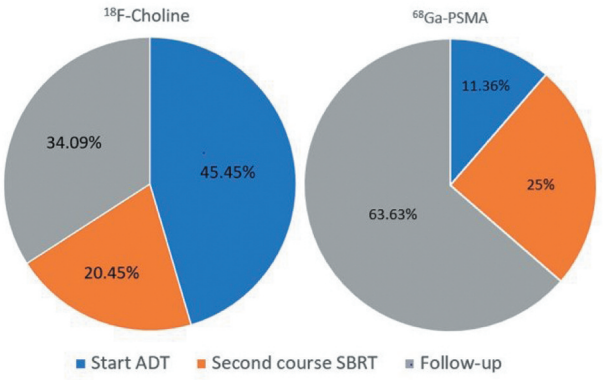

Figure 1. *Post-SBRT management depending on the SBRT response. In case of progression, a second course of SBRT was generally proposed if less than 3 new lesions were diagnosed outside the previous irradiated field. In the remaining cases, androgen deprivation therapy was administered.*

Results: A total of 118 lesions in 88 patients were analyzed. Forty-four (50%) patients underwent SBRT by means of ^{68}Ga-PSMA PET/CT whereas the remaining 50% by ^{18}F-choline PET/CT. The median follow-up was 25 months (range=5-87). For the entire population of study, OS and LC were 100%. In 48 patients (54.5%) a distant progression occurred. The DPFS was 22.8 months (range=14.4-28.8). Median PSA value before SBRT was 2.07 ng/ml in the choline PET cohort, and 0.6 ng/ml in the PSMA-PET arm. At the time of the analysis, disease-free survival was 63.6% compared to 34% in the ^{68}Ga-PSMA and choline PET group, respectively. No difference was observed regarding the DPFS between the two arms (p=0.06). The ADT administration rate was higher after PET-choline-guided SBRT (p=0.0003) due to the higher incidence of polymetastatic disease after a first-course of PET-choline SBRT, compared to ^{68}Ga-PSMA-guided SBRT, as shown in Figure 1. *Conclusion:* SBRT-guided by ^{68}Ga-PSMA PET allowed to obtain a higher rate of ADT-free patients compared to SBRT-guided by ^{18}F-choline PET, in the setting of oligorecurrent castration-sensitive PC. Randomized trials are strongly advocated.

43 ASSESSMENT OF mpMRI-BASED RADIOMICS TOOLS IN PCA FOR CANCER AGGRESSIVENESS PREDICTION, AIRC IG-13218

Matteo Pepa[1], Simone Giovanni Gugliandolo[1], Lars Johannes Isaksson[1,2], Giulia Marvaso[1], Sara Raimondi[3], Francesca Botta[4], Sara Gandini[3], Delia Ciardo[1], Stefania Volpe[1,5], Giulia Riva[1,5], Damaris Patricia Rojas[1], Dario Zerini[1], Paola Pricolo[6], Sarah Alessi[6], Giuseppe Petralia[6], Paul Summers[6], Alessandro Francesco Mistretta[7], Stefano Luzzago[7], Federica Cattani[4], Ottavio De Cobelli[1,5,7], Enrico Cassano[8], Marta Cremonesi[9], Massimo Bellomi[5,6], Roberto Orecchia[10] and Barbara Alicja Jereczek-Fossa[1,5]

[1]Division of Radiotherapy, IEO European Institute of Oncology IRCCS, Milan, Italy; [2]European School of Molecular Medicine, IFOM-IEO Campus, Milan, Italy; [3]Molecular and Pharmaco-Epidemiology Unit, Department of Experimental Oncology, IEO European Institute of Oncology IRCCS, Milan, Italy; [4]Medical Physics Unit, IEO European Institute of Oncology IRCCS, Milan, Italy; [5]Department of Oncology and Hemato-Oncology, Università degli Studi di Milano, Milan, Italy; [6]Division of Radiology, IEO European Institute of Oncology IRCCS, Milan, Italy; [7]Division of Urology, IEO European Institute of Oncology IRCCS, Milan, Italy; [8]Breast Imaging Division, IEO European Institute of Oncology IRCCS, Milan, Italy; [9]Radiation Research Unit, IEO European Institute of Oncology IRCCS, Milan, Italy; [10]Scientific Directorate, IEO European Institute of Oncology IRCCS, Milan, Italy

Background/Aim: Multi-parametric magnetic resonance imaging (mpMRI) of the prostate has greatly improved the detection, localization, and staging of prostatic disease, and consequently risk stratification. However, even with optimized scanning protocols and experienced radiologists, the diagnostic performance of mpMRI is still limited, while accuracy in the prediction of cancer extension by radiologists is widely ranging. A promising approach for quantitative analysis of mpMRI is represented by Radiomics, an emerging discipline that involves testing of the associations of a large number of quantitative imaging features with clinical characteristics. The purpose of this study was to extract a radiomic signature from axial T2-weighted (T2-W) multiparametric mpMRI able to predict oncological and radiological scores in prostate cancer (PCa). *Patients and Methods:* Give-me-five trial is a prospective phase II study designed for the treatment of PCa patients with ultra-hypofractionated radiotherapy scheduled in 5 fractions with 36.25 Gy delivered to the whole prostate and a concomitant boost of 37.5 Gy to the dominant intraprostatic lesion (DIL). All patients underwent a pre-treatment mpMRI for identifying the tumor and guiding radiotherapy treatment planning. T2-weighted (T2W) MRI sequences acquired with homogenous characteristics (0.59×0.59×3 mm^3 voxel size, 118ms Te, 3780 ms Tr) on a 1.5T MAGNETOM Avanto^{fit} scanner (Siemens Healthineers, Erlangen, Germany) were selected. The prostate, urethra, and DIL were identified and manually contoured on each image slice by two expert radiologists; then, were extracted as RT structure files using the Eclipse software, as part

Table I. *Predictive accuracy of radiomics signature*[1].

Outcome	Predictive features	*p*-Value	AUC (95% CI)[2]	Cross-validated AUC (95% CI)[2]
Gleason score 3+4/4+3	3D-GLCM_2-4 AutoCorrelation	0.004	0.80 (0.68-0.93)	0.75 (0.61-0.89)
	GLCM3_10-4 InverseVariance	0.01		
T stage cT2	ID_15 Percentile	0.004	0.81 (0.61-1.00)	0.74 (0.51-0.98)
ECE score 3/4	ID_80 Percentile	0.003	0.84 (0.69-0.99)	0.81 (0.65-0.97)
PIRADS score 4/5	3D-GLCM_12-7 ClusterProminence[3]	0.008	0.94 (0.86-1.00)	0.90 (0.79-1.00)
Risk class Intermediate	3D-GLCM_6-4 Correlation	0.02	0.86 (0.74-0.98)	0.82 (0.68-0.97)
	ID_60 Percentile	0.01		

AUC, Area under the receiving operator characteristic curve; CI, confidence interval; 3D-GLCM, three-dimensional gray-level co-occurrence matrix; GLRLM, gray level run length matrix; GOH, gradient orient histogram; ID, intensity direct ECE, extracapsular extension; PIRADS, Prostate Imaging – Reporting and Data System. [1]Obtained by unconditional logistic regression models with stepwise selection of the cluster representative radiomics features for each outcome. [2]95% CI obtained by the De Long method (1). [3]per 1,000 unit increase.

of the original trial. Of the 65 patients enrolled in the clinical trial, only those with regions of interest (ROI) and contours that did not generate parsing errors during the import process to IBEX -an open source software for the extraction of radiomic features (shape, first-order statistics and textural features)- were included in the radiomic analysis. We tested univariate and multivariate association of each radiomic feature with T-stage (cT1 *vs*. cT2), Gleason score (GS, 3+3 *vs*. 3+4/4+3), extracapsular extension (ECE, 1/2 *vs*. 3/4) score, Prostate Imaging – Reporting and Data System (PIRADS, 2/3 *vs*. 4/5) score and risk class (intermediate *vs*. low), and selected the feature with the lowest *p*-value in each cluster as representative. Statistical analysis was performed with the SAS/STAT® software. *Results:* Of the 65 prospectively enrolled patients, 49 T2W-MRI sequences fulfilled the inclusion criteria. Among the 1702 features extracted, 3 to 6 features with the highest predictive power were selected for each outcome. A logistic regression (machine learning) classifier was trained to predict clinical outcomes. Radiomic signature for prediction of high Gleason score included only three-dimensional grey level co-occurrence matrix (3D-GLCM) texture features. Radiomic signature for prediction of cT2 stage as well as for 3/4 ECE score included first-order statistics intensity features. A 3D-GLCM texture was the most predictive feature for 4/5 PIRADAS score, with excellent predictive accuracy. Finally, radiomic signature for prediction of intermediate risk class included both 3D-GLCM texture and first-order statistics intensity features, with good predictive accuracy. Overall, the multivariable radiomic signature predicted oncological and radiological scores with AUC ranging from 0.74 to 0.94 (Table I). *Discussion and Conclusion:* MRI-based radiomics in PCa for the prediction of tumour phenotype is a feasible and promising approach. It might lead to a semi-automated definition of tumour characteristics and thus reduce the intra/inter-operator variability in the radiologic image interpretation. A closer look at the relevant features showed that the most predictive ones are almost exclusively texture (particularly from the 3D-GLCM category) and intensity features, which tend to quantify properties related to homogeneity, symmetry and correlation within the region. Although a significant association was found between the selected features and all the mentioned clinical and radiological scores, further validations on larger cohorts are needed before applying these findings in the clinical practice.

1 DeLong ER, DeLong DM and Clarke-Pearson DL: Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics *44(3)*: 837-845, 1988. PMID: 3203132.

44
SHORT-TERM HIGH PRECISION RT FOR EARLY PCA WITH SIB TO THE DIL: QOL ASSESSMENT (AIRC IG 13218)

Giulia Marvaso[1], Simone Giovanni Gugliandolo[1], Federica Bellerba[3], Sara Gandini[3], Giulia Corrao[1,2], Stefania Volpe[1,2], Giulia Riva[1,2], Damaris Patricia Rojas[1], Dario Zerini[1], Matteo Pepa[1], Paola Pricolo[4],

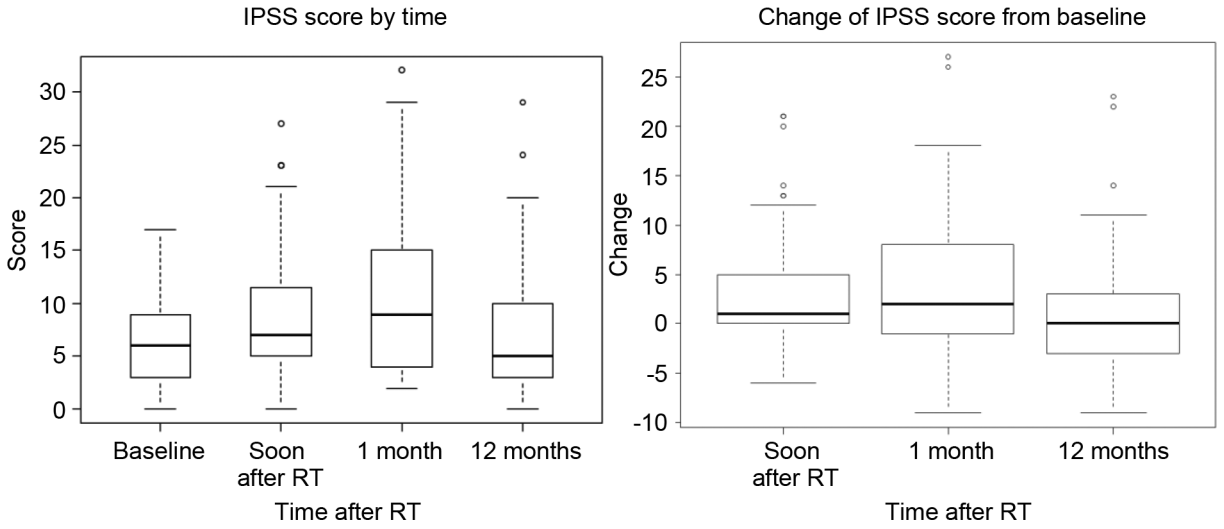

Figure 1. *International Prostate Symptom Score (IPSS) score by time and changes from baseline. The dots represent the outliers.*

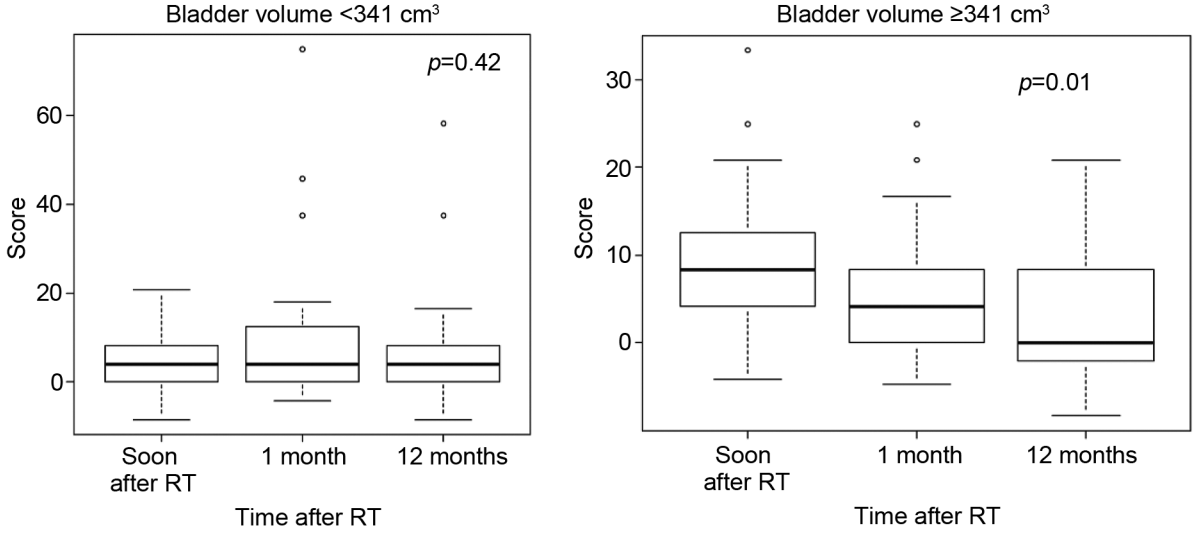

Figure 2. *Prostate Cancer Module (EORTC QLQ-PR25) – Change of urinary symptoms score from baseline. The dots represent the outliers.*

Sarah Alessi[4], Giuseppe Petralia[4], Federica Cattani[5], Ottavio De Cobelli[2,6], Roberto Orecchia[7] and Barbara Alicja Jereczek-Fossa[1,2]

[1]Division of Radiotherapy, IEO European Institute of Oncology IRCCS, Milan, Italy;
[2]Department of Oncology and Hemato-Oncology, Università degli Studi di Milano, Milan, Italy;
[3]Molecular and Pharmaco-Epidemiology Unit, Department of Experimental Oncology, IEO European Institute of Oncology IRCCS, Milan, Italy;
[4]Division of Radiology, IEO European Institute of Oncology IRCCS, Milan, Italy;
[5]Medical Physics Unit, IEO European Institute of Oncology IRCCS, Milan, Italy;
[6]Division of Urology, IEO European Institute of Oncology IRCCS, Milan, Italy;
[7]Scientific Directorate, IEO European Institute of Oncology IRCCS, Milan, Italy

Background/Aim: Curative-intent radiation therapy (RT) represents a well-established treatment option in the management of localized prostate cancer (PCa), with disease progression and cancer-specific death rates comparable to those of surgery. A recent body of evidence suggests that at least non-inferior outcomes would be achievable also with extremely

hypofractionated regimens. As part of the AIRC IG-13218, registered at ClinicalTrials.gov as NCT01913717, we analyzed data from 65 prospectively enrolled patients with low and intermediate risk prostate cancer treated with extremely hypofractionated radiotherapy (RT) to identify clinically meaningful information through the analysis of validated questionnaires testing gastrointestinal (GI) and genitourinary (GU) RT-related toxicity and their impact on quality of life (QoL). *Patients and Methods:* A prospective series of patients diagnosed with low- and intermediate- risk PCa were enrolled in this study and treated with RT between October 2014 and January 2018 at the IEO European Institute of Oncology IRCCS. The inclusion and exclusion criteria with RT treatment details and study design of this phase II prospective trial are described in the previously published protocol (1), registered at ClinicalTrials.gov as NCT01913717, and first results have already been reported (2). After the end of RT treatment, clinical assessment and prostate-specific antigen (PSA) measurements were performed every 3 months for at least 2 years. GI and GU toxicities were scored according to Radiation Therapy Oncology Group and European Organization for Research and Treatment of Cancer (RTOG/EORTC) scoring criteria. QoL of enrolled patients was assessed by the International Prostatic Symptoms Score (IPSS), Quality Life Questionnaire - Core 30 (QLQ-C30), QLQ for prostate specific (QLQ-PR25) and sexual activity by the International Index of Erectile Function (IIEF-5). Within-patient score changes of questionnaires were calculated at each time point from baseline: shortly after the end of RT, one month after RT, and 12 and 24 months after RT. *Results:* Overall, patient tolerance was assessed as satisfactory across all the considered time points, with no residual toxicity exceeding G2 at 6 months after the end of treatment, except for one patient who developed G3 GI symptoms. The most relevant deterioration in IPSS from baseline was reported after 1 month from the end of treatment, although a sizable recovery towards baseline value was assessed at 12 months. Boxplots reporting IPSS modification are shown in Figure 1. The QLQ-PR25 Urinary Symptoms score was also analyzed to evaluate the urinary function. A deterioration of GU symptoms from baseline was observed already after the end of RT and maintained at one month after, with a recovery towards baseline value at 12 months. Interestingly patients with a bladder volume under the median showed a worsening of symptoms after RT, whereas patients with a volume equal or greater than the median reported a significant decreasing trend of deterioration of symptoms with a median complete recovery at 12 months (Figure 2). The analysis of QLQ-C30 and IIEF-5 showed a non-statistically significant change of QoL from baseline. Only one patient out of the 65 patients died, though not for disease-related cause, leading to an OS of 98%. Biochemical progression-free survival (b-PFS) was of 97% at 2-years. Since 2014, only 2 patients experienced biochemical and clinical relapse. *Discussion and Conclusion:* The median follow-up is still too short to make our data about the oncological outcomes consistent, but the toxicity results and the relative assessed QoL appear to be encouraging. Our data showed that QoL of patients treated with extreme hypofractionation with a dose escalation to the DIL remains acceptable mainly because the related GI and GU toxicities were really low. In addition, although tumor outcomes are encouraging, longer follow up is warranted to confirm these findings. The increasing dose to the DIL does not compromise the RT toxicity and, at the same time, opens the question of the possibility of an even more escalate treatment.

1 Timon G, Ciardo D, Bazani A Garioni M, Maestri D, De Lorenzo D, Pansini F, Cambria R, Rondi E, Cattani F, Marvaso G, Zerini D, Vischioni B, Ciocca M, Russo S, Molinelli S, Golino F, Scroffi V, Rojas DP, Fodor C, Petralia G, Santoro L, De Cobelli O, Orecchia R and Jereczek-Fossa BA: Rationale and protocol of AIRC IG-13218, short-term radiotherapy for early prostate cancer with concomitant boost to the dominant lesion. Tumori *102(5)*: 536-540, 2016. PMID: 27514314. DOI: 10.5301/tj.5000547

2 Timon G, Ciardo D, Bazani A, Marvaso G, Riva G, Volpe S, Rojas DP, Renne G, Petralia G, Zerini D, Fodor C, Dicuonzo S, Maestri D, Pansini F, Cambria R, Cattani F, Golino F, Scroffi V, De Lorenzo D, De Cobelli O, Orecchia R and Jereczek-Fossa BA: Short-term high precision radiotherapy for early prostate cancer with concomitant boost to the dominant lesion: *ad interim* analysis and preliminary results of phase II trial AIRC-IG-13218. Br J Radiol *91(1089)*: 20160725, 2018. PMID: 29750539. DOI: 10.1259/bjr.20160725

45
CARBON-ION BOOST FOLLOWED BY PHOTON IMRT FOR PCA: DOSIMETRIC AND GEOMETRIC EVALUATIONS, AIRC-IG14300

Stefania Comi[1], Giulia Marvaso[2], Simone Giovanni Gugliandolo[2], Matteo Pepa[2], Stefania Russo[3], Barbara Vischioni[3], Francesca Valvo[3], Tommaso Giandini[4], Barbara Avuzzi[5], Riccardo Valdagni[5,6], Delia Ciardo[2], Barbara Alicja Jereczek-Fossa[1,6], Federica Cattani[1] and Roberto Orecchia[7]

[1]Medical Physics Unit, IEO European Institute of Oncology IRCCS, Milan, Italy;
[2]Division of Radiotherapy, IEO European Institute of Oncology IRCCS, Milan, Italy;
[3]Clinical Department, National Center for Oncological Hadrontherapy (CNAO), Pavia, Italy;
[4]Unit of Medical Physics, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;

Table I. *Dosimetric parameters of organs at risk (OAR).*

OAR	Constraint	1		2		3		4		5	
		CIRT + IMRT	IMRT-only	CIRT+ IMRT	IMRT-only	CIRT+ IMRT	IMRT-only	CIRT+ IMRT	IMRT-only	CIRT+ IMRT	IMRT-only
Rectum	$D_{0.03\ cm^3}$ (%)	98.5%	100.6%	100.2%	98.1%	98.5%	100.6%	97.5%	99.7%	100.0%	101.8%
	$V_{75\ Gy}$ (%)	0.8%	2.4%	0.6%	0.8%	5.3%	17.6%	0.1%	0.6%	0.2%	4.4%
	$V_{70\ Gy}$ (%)	3.4%	5.5%	2.8%	2.6%	16.7%	24.4%	0.5%	3.2%	0.6%	7.6%
	$V_{40\ Gy}$ (%)	40.0%	80.0%	25.7%	36.4%	21.0%	51.7%	21.0%	36.7%	20.3%	36.2%
Urinary bladder	$D_{0.03\ cm^3}$ (%)	98.8%	101.9%	101.3%	100.8%	99.4%	101.3%	101.8%	102.8%	101.3%	102.7%
	$V_{70\ Gy}$ (%)	1.8%	6.0%	5.5%	7.5%	9.0%	14.6%	10.6%	12.3%	4.4%	5.7%
	$V_{40\ Gy}$ (%)	36.0%	70.0%	31.5%	32.5%	37.0%	46.4%	47.5%	56.2%	33.0%	42.2%
Femoral heads	$V_{40\ Gy}$ (%)	1.8%	0.9%	4.1%	2.9%	6.5%	2.0%	3.5%	1.9%	4.0%	2.8%
Anal cavity	D_{mean} (Gy)	17.6	25.9	10.9	6.9	28.8	45.0	14.5	21.3	11.7	17.2
Penile bulb	$D_{0.03\ cm^3}$ (Gy)	48.9	55.4	17.0	10.7	55.0	63.4	38.0	30.0	5.8	7.9
	D_{mean} (Gy)	11.3	15.2	7.7	8.2	22.9	36.4	10.5	11.9	3.7	5.4

$D_{x\%}$, dose to x% of volume; $D_{0.03\ cm^3}$, dose to 0.03 cm^3 of volume; D_{mean}, mean dose; V_{xxGy}, volume receiving xx Gy.

[5]Department of Radiation Oncology 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [6]Department of Oncology and Hemato-Oncology, Università degli Studi di Milano, Milan, Italy; [7]Scientific Directorate, IEO European Institute of Oncology IRCCS, Milan, Italy

Aim: The aim of this study is to evaluate dosimetric uncertainties of a mixed beam approach for patients with high-risk prostate cancer (PCa). *Patients and Methods:* The treatment consists of a carbon ion radiotherapy (CIRT) boost followed by whole-pelvis intensity-modulated RT (IMRT). Dosimetric uncertainties were investigated both from a geometric perspective, by evaluating the entity of structures deformation, both from a dosimetric perspective, by comparing organs at risks (OARs) sparing between the actual CIRT+IMRT treatment and an conventional comparison treatment plan. As part of a prospective phase II study (AIRC IG-14300, "Carbon ions boost followed by pelvic photon intensity modulated radiotherapy for high-risk prostate cancer", registered at ClinicalTrials.gov as NCT02672449), high-risk non-metastatic PCa patients were treated with a CIRT boost receiving 16.6 Gy in 4 fractions followed by whole-pelvis IMRT of 50 Gy in 25 fractions (2 Gy/fraction), with following long-term androgen deprivation therapy. Deformable CT image registration (DIR) was performed and corresponding dose was used for plan sum. A comparative IMRT photon plan was obtained as whole-pelvis IMRT of 50Gy in 25 fractions followed by a sequential boost of 28Gy in 14 fractions (both 2 Gy/fraction). DIR performances were evaluated through structure-related validated parameters calculated using ImSimQA software (v4.1, Oncology Systems Limited, Shrewsbury, UK) and image characteristics validated parameters using Plastimatch (an open-source, BSD-style licensed software). *Results:* Until now, 5 out of ten 10 total enrolled patients have terminated the treatment, and thus are included in the present study. Dosimetric parameters were lower in CIRT+IMRT than IMRT-only plans for all organs at risks (OARs) considered, including rectum, urinary bladder, anal canal, and penile bulb. Conversely, the IMRT-only approach allows for lower dose to femoral heads, compared to the CIRT+IMRT approach (Table I). Regarding DIR evaluation, femoral heads resulted, as expected, the less deformed OAR. Penile bulb, bladder and anal canal showed intermediate deformation. Rectum was the most deformed OAR. *Conclusion:* Particle therapy allows reaching a better sparing of OARs, which is expected to reduce induced-toxicity, while increasing the efficacy due to the higher radio-biological effect of C-ions. However, a mixed beam approach could introduce DIR problems in case of multi-centric treatments with different operative protocols or, for instance, in image-guided adaptive radiation therapy. The future development of this prospective trial will lead to more mature data concerning the clinical impact of implementing DIR procedures in dose accumulation applications for high-risk PCa treatments.

46
IMPACT OF ADJUVANT RADIOTHERAPY IN NODE POSITIVE PROSTATE CANCER PATIENTS

Giulia Corrao[1,2], Marianna Montesano[1,2], Giulia Marvaso[2], Giovanni Carlo Mazzola[1,2], Jessica Franzetti[1,2], Cristiana Fodor[2], Dario Zerini[2], Ottavio De Cobelli[1,3], Sara Gandini[4], Simone Pietro De Angelis[4], Federica Cattani[5], Roberto Orecchia[6] and Barbara Alicja Jereczek-Fossa[1,2]

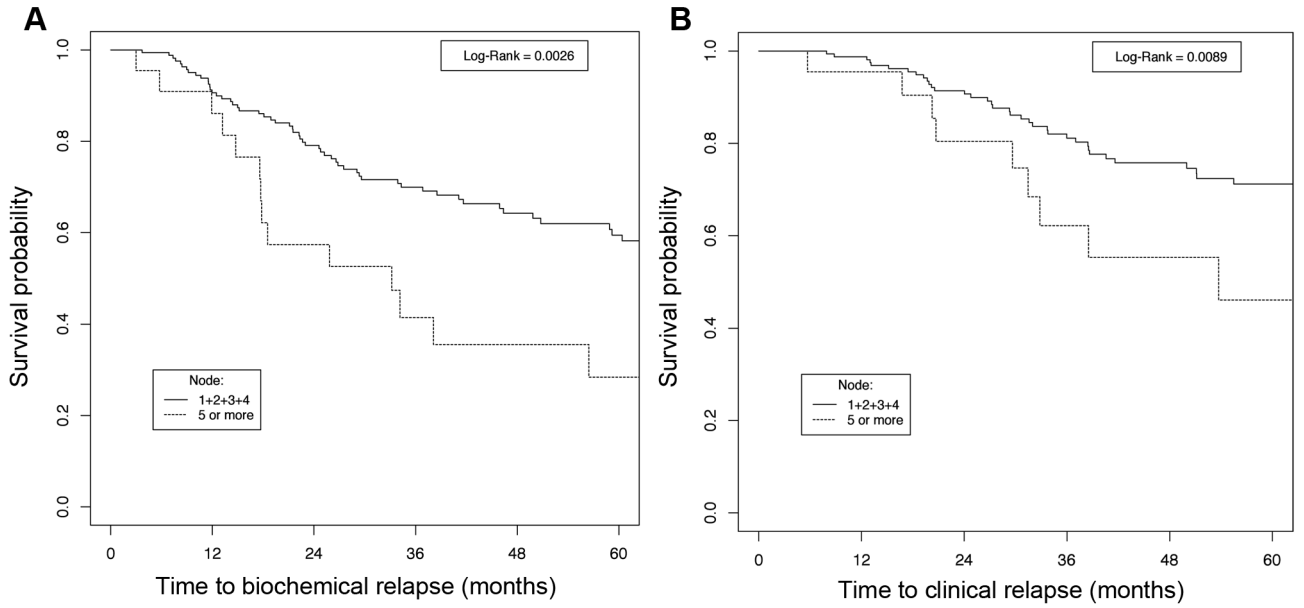

Figure 1. *Biochemical (A) and clinical (B) progression-free survival by number of positive lymph nodes.*

Table I. *Multivariable proportional hazard Cox models.*

Outcome	Parameter	Contrast	HR	95% CI		*p*-Value
Biochemical-PFS	Initial PSA		1.01	1.00	1.02	0.021
	Vascular invasion	no *vs.* yes	0.50	0.31	0.79	0.003
	Node	1+2+3+4 *vs.* 5 or more	0.47	0.27	0.83	0.010
Clinical-PFS	iSUP	1 *vs.* 3	0.34	0.13	0.88	0.046
		2 *vs.* 3	0.63	0.36	1.11	
	Node	1+2+3+4 *vs.* 5 or more	0.45	0.23	0.91	0.026
OS	Initial PSA		1.02	1.01	1.03	0.002
Metastasis-PFS	ISUP	6 *vs.* 8	0.33	0.11	0.94	0.047
		7 *vs.* 8	0.57	0.31	1.06	
	Node	1+2+3+4 *vs.* 5 or more	0.37	0.18	0.74	0.005

HR, Hazard ratio; PSA, prostate-specific antigen; CI, confidence interval; PFS, progression-free survival; OS, overall survival; ISUP, International Society of Urological Pathology.

[1]Department of Oncology and Hemato-Oncology, Università degli Studi di Milano, Milan, Italy;
[2]Division of Radiotherapy, IEO European Institute of Oncology IRCCS, Milan, Italy;
[3]Division of Urology, IEO European Institute of Oncology IRCCS, Milan, Italy;
[4]Molecular and Pharmaco-Epidemiology Unit, Department of Experimental Oncology, IEO European Institute of Oncology IRCCS, Milan, Italy;
[5]Medical Physics Unit, IEO European Institute of Oncology IRCCS, Milan, Italy;
[6]Scientific Directorate, IEO European Institute of Oncology IRCCS, Milan, Italy

Background/Aim: Large, prospective randomized studies have demonstrated that low volume-nodal prostate cancer (PCa) patients (one or two positive lymph nodes) have significantly higher survival rates compared to ones with higher volume-nodal disease, regardless of adjuvant treatment administrated. The management of this setting of patients is still under debate. The aim of this retrospective study was to assess the impact of adjuvant radiotherapy (aRT) in patients with pathological positive lymph nodes (pN1) in terms of overall survival (OS), biochemical (b), clinical (c) and distant metastasis (m) progression-free survival (PFS) and to correlate oncological outcomes with tumor characteristics. Urinary and rectal toxicities were also evaluated. *Patients and Methods:* Patients

with pN1 PCa, treated between 2008 and 2018 with radical prostatectomy (RP), extended pelvic lymph node dissection, aRT within 6 months from surgery and +/– androgen deprivation therapy (ADT), were included in this mono-institutional cohort. Log-rank tests and Cox proportional hazards were used to compare and identify independent prognostic factors of biochemical and clinical recurrence, with adjustment for relevant covariates. *Results:* One hundred eighty-seven patients were included in this study with a median follow-up of 49 months (range=3-172). At 5-years, we observed b-PFS, c-PFS, m-PFS and OS of 56%, 68%, 71% and 94%, respectively. To perform the analysis, patients were divided in two groups according to the most informative cut-off of positive nodes. A significant statistical impact was observed for patients who harbored 5 or more lymph-nodes (Figure 1). At univariate analysis, vascular invasion and number of positive nodes were significant predictors of b-PFS (all $p<0.005$). Multivariate analysis confirmed an increased risk of biochemical relapse for initial PSA value (iPSA) (HR=1.01, 95% CI=1.00-1.02; $p=0.021$), a reduced risk in patients without vascular invasion (HR=0.5, 95% CI=0.31-0.79; $p=0.003$) and number of lymph-nodes from 1 to 4 *vs*. 5 or more (HR=0.47, 95% CI=0.27-0.83; $p=0.010$) (Table I). Multivariate proportional Cox hazard models confirmed also significantly reduced risk of c-PFS and m-PFS for International Society of Urological Pathology (ISUP) grade <3 and lymph-nodes <5. OS was correlated only with the increase in iPSA value (HR=1.02, 95% CI=1.01-1.03; $p=0.002$). *Conclusion:* According to recent published studies, our data confirmed the excellent outcomes of pN1 PCa patients treated with adjuvant treatments. The significant beneficial effect of aRT on cancer-specific outcomes is supported by a low-grade of acute and chronic of toxicities. Moreover, we confirmed the key role represented by the number of positive nodes in predicting b-PFS, c-PFS, and m-PFS. These results support the need of perspective, randomized, larger cohort studies to individuate the patients who might benefit from aRT.

47

RADIOSA TRIAL: RADIOABLATION +/– HORMONOTHERAPY FOR PROSTATE CANCER OLIGORECURRENCES (AIRC IG-22159)

Matteo Augugliaro[1,2], Giulia Marvaso[1], Delia Ciardo[1*], Giulia Corrao[1,2], Sara Gandini[3], Matteo Pepa[1], Cristiana Fodor[1], Dario Zerini[1], Damaris Patricia Rojas[1], Giuseppina Bonizzi[4], Salvatore Pece[2,4], Federica Cattani[5], Ketti Mazzocco[2,6], Alessandro Francesco Mistretta[7], Gennaro Musi[7], Sara Alessi[8], Giuseppe Petralia[8], Gabriella Pravettoni[2,6], Ottavio De Cobelli[2,7], Pier Paolo Di Fiore[2,4], Giuseppe Viale[2,9], Roberto Orecchia[10] and Barbara Alicja Jereczek-Fossa[1,2]

*Affiliation at the time of study

[1]Division of Radiotherapy, IEO, European Institute of Oncology IRCCS, Milan, Italy;
[2]Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy;
[3]Molecular and Pharmaco-Epidemiology Unit, Department of Experimental Oncology, IEO, European Institute of Oncology IRCCS, Milan, Italy;
[4]Molecular Medicine Program, IEO, European Institute of Oncology IRCCS, Milan, Italy;
[5]Medical Physics Unit, IEO, European Institute of Oncology IRCCS, Milan, Italy;
[6]Applied Research Division for Cognitive and Psychological Science, IEO, European Institute of Oncology IRCCS, Milan, Italy;
[7]Division of Urology, IEO, European Institute of Oncology IRCCS, Milan, Italy;
[8]Division of Radiology, IEO, European Institute of Oncology IRCCS, Milan, Italy;
[9]Department of Pathology, IEO, European Institute of Oncology IRCCS, Milan, Italy;
[10]Scientific Directorate, IEO, European Institute of Oncology IRCCS, Milan, Italy

Background/Aim: Prostate cancer (PCa) is one of the most common malignancies in males. Recent advances in imaging techniques have led to an increased number of patients diagnosed with a low burden of disease, also known as oligometastatic state. In patients with high-volume, metastatic castration-sensitive PCa chemo-hormonal therapy is the standard of care, whereas additional chemotherapy has not been proven beneficial in oligometastatic patients. The role of systemic therapies for the management of oligometastatic PCa patients has been widely investigated; however, only few studies have explored the use of stereotatic body radiotherapy (SBRT) in such patients. SBRT could represent a feasible and safe treatment option for avoiding the toxicity induced by the androgen deprivation therapy (ADT). In order to select the best treatment and surveillance program, several biomarkers are used. The well-known limitations connected to the use of prostate-specific antigen (PSA) as a diagnostic and follow-up marker have paved the way to novel biological markers, including cell-free DNA, microRNA and blood-based parameters. However, a large amount of data is needed to obtain robust results. In this context, the main purposes of RADIOSA trial, which is prospectively registered at clinicaltrials.gov (NCT03940235, May 2019), are: i) to compare the efficacy, toxicity and quality of life (QoL) of SBRT with or without ADT for the treatment of oligorecurrent-castration-sensitive PCa (OCS-PCa), and ii) to develop biology- and imaging-based prognostic tools able to stratify OCS-PCa patients. *Patients and Methods:* RADIOSA is a prospective, double arm, randomized, phase II, monocentric clinical trial, which

is expected to recruit 160 OCS-PCa in 3 years. Inclusion criteria include: i) histologically proven initial diagnosis of adenocarcinoma of the prostate, ii) biochemical relapse of PCa following radical local prostate treatment (radical prostatectomy, primary radiotherapy or radical prostatectomy +/– prostate bed adjuvant/salvage radiotherapy) +/– ADT according to the European Association of Urology (EAU) guidelines 2016 or after any salvage therapy if biochemical progression is diagnosed in the context of castration sensitive PCa, iii) nodal relapse in the pelvis, extra-regional nodal relapse (M1a), bone metastases (M1b) on Ch-PET/CT or WBMRI with a maximum of 3 lesions, iv) serum testosterone level >50 ng/dl at the time of randomization (castration sensitive PCa), v) Eastern Cooperative Oncology Group (ECOG) performance status 0-1, vi) age ≥18 years, vii) no serious concomitant comorbidities or contraindication to SBRT and/or ADT, viii) no previous invasive cancer (within 3 years before the prostate cancer diagnosis) apart from non-melanoma skin malignancies, ix) ability to complete questionnaires about QoL, x) absence of mental diseases that cannot ensure valid informed consent, and xi) signed written informed consent. According to SBRT technique, high doses are delivered to small volumes in few fractions (≤5). In our framework, a schedule of 30 Gy in 3 fractions every other day (equivalent dose EQD2 = 98.6 Gy, considering α/β= 1.5 Gy), or equivalent regimens depending on disease site location are used. The primary endpoint is the evaluation of progression-free survival (PFS). Three tasks will be developed: i) randomized clinical study (3 years for accrual and 2 years for follow-up and data analysis); ii) imaging study, including imaging registration and Metastasis Reporting and Data System (MET-RADS) criteria; iii) pre-clinical study, development of a biobank of blood samples for the analysis of neutrophil-to-lymphocyte ratio and preparatory for a subsequent miRNA profiling. *Results:* Recruiting started in September 2019 and so far 10 patients, equally distributed in the two arms, have been enrolled in the trial. No acute toxicities were reported. *Discussion and Conclusion:* We aim to determine which arm is justified for testing in a subsequent Phase III trial. A decision-tree algorithm, based on prognosis, biological phenotype and imaging profile, will be developed. SBRT is expected to provide excellent PFS, local control, QoL and low toxicity. In the SBRT only arm, drug holiday due to ADT postponement will positively impact the QoL. A suitable number of blood samples will be collected to perform biological patient profiling. A tool for stratification of OCS-PCa patients will be developed according to the MET-RADS criteria. In the era of high-precision medicine and tailored treatments, this study will increase our knowledge of oligometastatic PCa and will accordingly define the highest effective therapy in terms of clinical outcome and cost-effectiveness.

48

SBRT FOR OLIGOMETASTATIC RENAL CELL CARCINOMA

Giulia Marvaso[1], Giulia Corrao[1,2], Olga Oneta[1,2], Giovanni Carlo Mazzola[1,2], Simone Giovanni Gugliandolo[1], Matteo Pepa[1], Agnese Cecconi[3], Sara Gandini[4], Gaia Piperno[1], Maria Cossu Rocca[5], Elena Verri[5], Gaetano Aurilio[5], Federica Corso[4], Daniela Cullurà[5], Elena Rondi[6], Sabrina Vigorito[6], Franco Nolè[5], Roberto Orecchia[7] and Barbara Alicja Jereczek-Fossa[1,2]

[1]Division of Radiotherapy, IEO European Institute of Oncology IRCCS, Milan, Italy;
[2]Department of Oncology and Hemato-Oncology, Università Degli Studi Di Milano, Milan, Italy;
[3]Division of Second Opinion, IEO European Institute of Oncology IRCCS, Milan, Italy;
[4]Molecular and Pharmaco-Epidemiology Unit, Department of Experimental Oncology, IEO European Institute of Oncology IRCCS, Milan, Italy;
[5]Medical Oncology Division Of Urogenital and Head and Neck Tumors, IEO European Institute of Oncology IRCCS, Milan, Italy;
[6]Medical Physics Unit, IEO European Institute of Oncology IRCCS, Milan, Italy;
[7]Scientific Directorate, IEO European Institute of Oncology IRCCS, Milan, Italy

Background/Aim: Renal cell carcinomas (RCCs) have traditionally been considered radioresistant, with a limited role for conventional fractionation as a local approach. However, since the appearance of stereotactic body radiation therapy (SBRT), radiotherapy (RT) has been increasingly employed in the management of metastatic RCC (mRCC). The aim of this study was to evaluate the role of SBRT for synchronous and metachronous oligo-metastatic RCC patients in terms of local control, delay of systemic treatment, overall survival and toxicity. *Patients and Methods:* Monocentric retrospective data collection from a single institution was performed. The inclusion criteria were as follows: (i) oligo-recurrent or oligo-progressive disease (less than 5) in mRCC patients after local surgery or during systemic therapy; (ii) surgery or other local therapies not feasible; and (iii) any contraindication to receive systemic therapy (such as comorbidities); (iv) all the histologies were included; (v) available signed informed consent form for treatment. Tumor response and toxicity were evaluated using the Response Evaluation Criteria in Solid Tumors and the Common Terminology Criteria for Adverse Events version 4.03, respectively. Progression-free survival (PFS) in-field and out-field and overall survival (OS) were calculated via the Kaplan-Meier method. The drug treatment-free interval

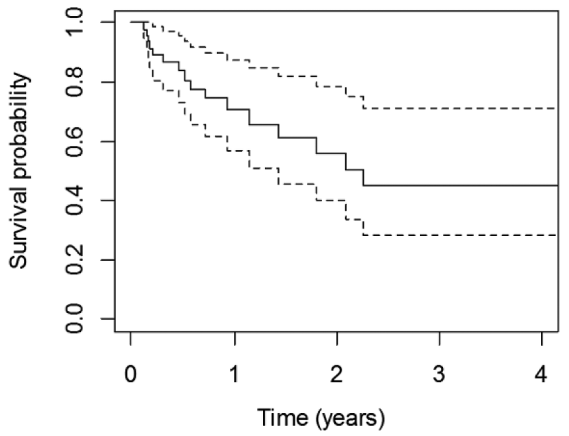

Figure 1. *Progression-free survival (PFS) in field.*

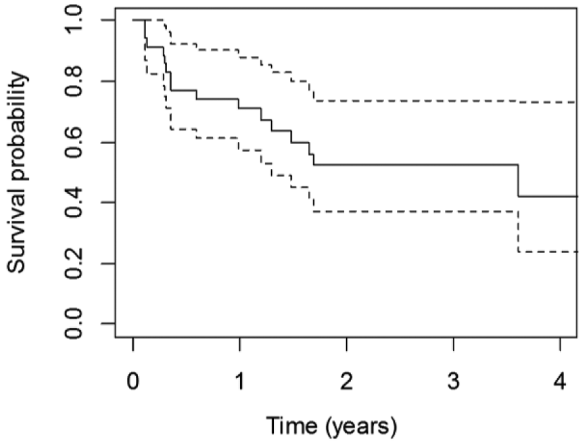

Figure 2. *The drug treatment-free interval.*

was calculated from the start of SBRT to the beginning of any systemic therapy. *Results:* From January 2012 to December 2018, 61 patients with extracranial and cranial metastatic RCC underwent SBRT on 83 lesions. The majority of patients (73.8%) were treated for one metastatic lesion. Lymph node, bone and brain metastases were included in the analysis. Median follow-up was 2.3 years (range=0-7.15). One- year PFS-in-field was 70% (Figure 1), and 2-year was 55%. One-year PFS-out-field was 40% and 1-year OS was 78%. Median RT dose was 25 Gy (range=10-52) in 5-10 fractions. Concomitant systemic therapy was used for only 11 patients, for the others 50 the drug treatment-free rate was of 70% and 50% at 1 year and 2 years respectively (Figure 2). No acute and late toxicities were reported. *Conclusion:* The pattern of failure was predominantly out of field, even if the population was negatively selected and the used RT dose could be considered palliative. So SBRT seems to be a feasible and safe approach in oligometastatic RCC patients, with an excellent PFS-in field, and well-tolerated as well. SBRT might play a role in the management of selected RCC patients allowing for a delay in the start of a systemic therapy.

49

HYPOFRACTIONATED VOLUMETRIC-MODULATED ARC THERAPY FOR RADICAL PROSTATE CANCER: EARLY RESULTS FROM A RETROSPECTIVE STUDY

Francesco Tramacere, Ester Sanfilippo, Vincenzo Cicalese, Rosa D'Agostino, Roberta Castagna, Chiara De Luca, Cristina De Tommaso, Maria Carmen Francavilla, Francesca Pati, Marcello Vinella and Maurizio Portaluri

Department of Radiotherapy, Ospedale "A. Perrino" ASL BR, Brindisi, Italy

Background/Aim: Moderately hypofractionated radiotherapy (2.4 to 4 Gy per fraction over 4-6 weeks) has been tested in randomized trials reporting similar efficacy and toxicity to conventionally fractionated radiotherapy. It is considered an alternative to the standard approach in recent guidelines (1). The aim of the study was to estimate survival, biochemical recurrence, and rectal and urinary tract toxicity when prostate and seminal vesicles receive moderate hypofractionated radiotherapy for prostate cancer. *Patients and Methods:* A total of 52 consecutive patients with prostate cancer were treated from 2015 to 2017. The median age was 75 years (range=58-82). According to the European Association of Urology guidelines, (1) prognostic classification, 29% of patients were low risk, 38% intermediate risk and 33% high risk. The patients were treated with total dose 62 Gy in 3.1 Gy per fraction (20 fractions) 4 fractions/weeks with arc therapy (Rapid Arc) with imagine guide radiotherapy (IGRT) Linac 6 MV. The median prostate-specific antigen (PSA) at the diagnosis was 8.7 ng/ml (range=3.9-94). Androgen deprivation therapy (ADT) was administrated in 92%. Median follow-up was 33 months, (range=20-45). All patients performed pre-treatment T2 magnetic resonance images (MRI) sequences and computed tomography (CT) scan on pelvic region. Failure was defined as a serum PSA level of nadir plus 2 ng/ml. All the patients were clinically evaluated for urinary and rectal late complications according to RTOG/EORTC (2) scale. *Results:* Three-year biochemical disease-free survival (bDFS) was 88% and overall survival (OS) was 94%. One patient died for other cause (intestinal infarction), and 2 patients for prostate

disease; 6% are alive with disease (AWD). Median PSA at last follow-up was 0.28 ng/ml, (range=0-4.6). For low risk patients bDFS was 100% (Table I). Acute genitourinary (GU) and gastrointestinal (GI) toxicities ≥ grade (G) 2 were both reported in 8% of patients. Late GU toxicity ≥G2 was reported in 9% (no patient with G3-4); at the follow-up no patient had urethral strictures. Late GI toxicity was found in 8% of patients, while 1 patient developed G4 GI severe complication (recto-urinary fistula). Urinary incontinence was 8% (only one severe). Evaluation of erectile dysfunction was impaired by the use of ADT. We also found 2 second tumors, in rectum and bladder. *Discussion and Conclusion:* Prostate cancer has been hypothesized to have a low α/β ratio based on several, but not all, retrospective analyses. A low α/β ratio, particularly a value of <3, suggests the use of hypofractionated radiotherapy (3). If the α/β ratio of prostate cancer was lower than that of the surrounding normal tissues, there would be a therapeutic gain by increasing the effects on the tumor relative to the surrounding normal tissues. Our findings show better biochemical control and rates of acute and late GI and GU toxicities, compared to our previous study, in which high-dose 3D conformal RT was used (equivalent doses to 62 Gy in 3.1 Gy) (4) (Table II). At the same time of follow-up the ≥G2 GU and GI toxicities were observed in 9% and 12%, respectively; the urinary strictures had appeared with a median of 10 months at the end of radiotherapy. Recovery from this toxicity, mainly consisting in rectal tenesmus or dysuria, occurred early. Interestingly, as already documented in the randomized trial by Pollack *et al*. (3) and in our series as well, baseline International Prostate Symptom Score (IPSS) was significantly associated with ≥2 GU late reactions suggesting a potential increased risk of toxicity in patients with pre-treatment compromised urinary function. The only severe complication, recto-urinary fistula, occurred in a patient who had previous surgery on the rectum, and the planning target volume (PTV) was 197 cm^3 while the median PTV was 142. Half of patients with GI toxicity were under anticoagulants for heart disease. The presence of acute toxicity had a significant influence on the long-term development of GU and GI late toxicity (5). In fact, among patients who had developed GU acute symptoms during treatment, the incidence of late toxicity was 33%, compared to 3.4% of all patients without acute toxicity. In conclusion in our data moderate hypofractionated regimen appeared a feasible option with similar toxicity to standard fractionated. Hypofractionated regimen is well-tolerated; however, more attention should be paid in patients under anticoagulants and antiplatelet agents, with large-volume PTV, and with pre-treatment-compromised urinary function. Long-term follow-up could render this result useful for internal quality control.

1 Mottet N, Bellmunt J, Briers E, Bolla M, Bourke L, Cornford P, De Santis M, Henry A, Joniau S, Lam T, Mason MD, Van den Poel H, Van den Kwast TH, Rouvière O and Wiegel T; members of the EAU – ESTRO – ESUR –SIOG Prostate Cancer Guidelines Panel: EAU – ESTRO – ESUR – SIOG Guidelines on Prostate Cancer. Available at: https://uroweb.org/guideline/prostate-cancer/

2 RTOG/EORTC Late Radiation Morbidity Scoring Schema. Available at: www.rtog.org

3 Pollack A, Walker G, Horwitz EM, Price R, Feigenberg S, Konski AA, Stoyanova R, Movsas B, Greenberg RE, Uzzo RG, Ma C and Buyyounouski MK: Randomized trial of hypofractionated external-beam radiotherapy for prostate cancer. J Clin Oncol *(31)*: 3860-3868, 2013. PMID: 24101042. DOI: 10.1200/JCO.2013.51.1972

4 Tramacere F, Arcangeli S, Pignatelli A, Castagna R and Portaluri M: Hypofractionated dose escalated 3D conformal radiotherapy for prostate cancer: Outcomes from a mono-institutional phase II study. Anticancer Res *35*: 3049-3054, 2015. PMID: 25964594.

5 Zelefsky MJ, Levin EJ, Hunt M, Yamada Y, Shippy AM, Jackson A and Amols HI: Incidence of late rectal and urinary toxicities after three-dimensional conformal radiotherapy and intensity-modulated radiotherapy for localized prostate cancer. Int J Radiat Oncol Biol Phys *70*: 1124-1129, 2008. PMID: 18313526. DOI: 10.1016/j.ijrobp.2007.11.044

Table I. *Status of life it based on prognostic risk*.

	NED	AWD	DOD	DOC
Low risk	100%	0	0	0
Intermediate risk	84%	14%	0	2%
High risk	74%	16%	5%	5%

NED, No evidence of disease; AWD, alive with disease; DOD, dead of disease; DOC, dead other cause.

Table II. *Acute and late toxicity.*

3DCRT			Rapid Arc		
Grade	GU	GI	Grade	GU	GI
G1	11%	2%	G1	21%	4%
G2	5%	10%	G2	9%	6%
G3	3%	1%	G3	0%	0%
G4	0	0	G4	0	2%
≥G2	9%	12%	≥G2	9%	8%

3DCRT, 3D Conformal radiotherapy; RapidArc, Arc therapy; GU, genitourinary toxicity; GI, gastrointestinal toxicity; G, grade of toxicity.

50

^{18}F-FLUCICLOVINE-PET/CT IN DETECTION OF RECURRENCE SITE IN PRIMARY TREATED PROSTATE CANCER PATIENTS: INITIAL CLINICAL EXPERIENCE

Valeria Pirro[1], Claudia Airaldi[2], Giovanni Brusasco[1], Baldassarre Osvaldo Elia[1], Alessandra Codegone[1], Maria Grazia Ruo Redda[2] and Riccardo Emanuele Pellerito[1]

[1]Nuclear Medicine Unit, Mauriziano Hospital, Turin, Italy; [2]Radiation Oncology Unit, Mauriziano Hospital, Turin, Italy

Background/Aim: Prostate cancer is the second common cancer in males in developed countries. Following primary radical treatment, biochemical relapse remains a common event, affecting about 20-40% of patients, despite advances in primary treatment and improved overall survival. By now, early detection of relapse site is a crucial point in the patient management and prognosis. In the last 10 years, positron emission tomography/computed tomography (PET/CT) had an increasing role in the evaluation of this patient population; ^{11}C and ^{18}F choline PET/CT has become a reference imaging modality in this setting, due to its ability in detecting the presence of early recurrence of disease when conventional imaging resulted negative or inconclusive. Nevertheless, it is well known that diagnostic accuracy of choline PET/CT is not completely satisfactory when PSA level is less than 1.0-1.5 ng/ml. The introduction of ^{68}Ga-PSMA (targeting overexpressed transmembrane prostate specific membrane antigen) has improved the detection rate, also in case of early recurrence of disease (PSA <0.5 ng/ml); however, despite it is a promising tracer, at present, it is still experimental. More recently, trans-1-amino-3-^{18}F-fluorocyclobutanecarboxylic-acid (^{18}F-FACBC), also named ^{18}F-fluciclovine, was introduced as a novel approved PET/CT tracer for restaging prostate cancer recurrent patients, showing attractive results. In our PET center, we started using this tracer in routinary practice since June 2019 in patients radically treated for prostate cancer presenting biochemical relapse and low PSA level. In this preliminary study we present our initial clinical experience with ^{18}F-fluciclovine PET/CT, aiming to determine the detection rate of biochemical recurrence at the patient and region level was our endpoint. *Patients and Methods:* This study included 16 consecutive patients with biochemical relapse after initial radical treatment (11 had radical prostatectomy±lymphadenectomy and 5 had radical radiotherapy) of prostate cancer (mean Gleason score±SD was 7.4±0.8 at diagnosis). All patients, with a mean age±SD of 70.6±11.1 years (range=57-88) and a mean PSA level±SD of 1.2±0.56 ng/ml (range=0.4-2.5), underwent ^{18}F-fluciclovine PET/CT in our PET centre at Mauriziano Hospital. None of patients was under hormonal treatment at the moment of the examination. ^{18}F-Fluciclovine PET/CT was performed by a Philips Ingenuity TF Scanner, according to the current UK Guidelines. PET scan started within 4 min from the intravenous injection of a fixed radiotracer activity (300 Mbq); imaging was performed form the midthighs (3 min/bed for pelvic district) to vertex (1.15 min/bed for the remaining districts). Imaging analysis was conducted by two experienced nuclear medicine physician on prostate cancer imaging. Findings were considered pathologic in accordance with the abovementioned Guidelines. In particular, lesions >1 cm were positive when tracer's uptake was greater than bone marrow background, while lesions <1 cm were positive when uptake was greater than blood pool background. Fluciclovine PET/CT findings were also compared with other imaging modalities (like mpMRI, Choline or PSMA PET/CT when available, or co-registered CT) in order to evaluate malignancy. The analysis was conducted per-patient and per-region (prostate or prostate bed; lymph nodes, bone or soft-tissue metastasis).

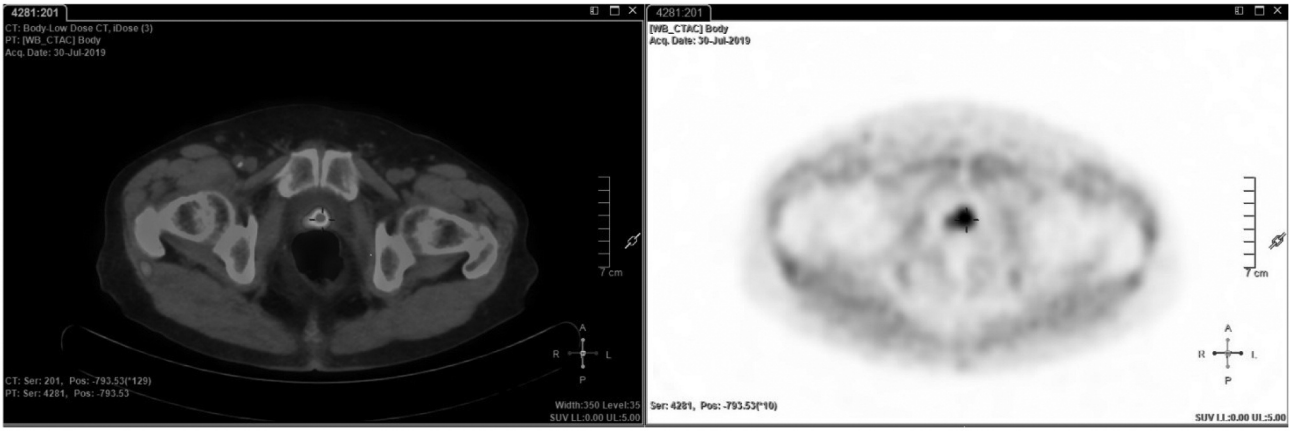

Figure 1. *Prostate cancer recurrence in prostate bed, fused and PET only transaxial view.*

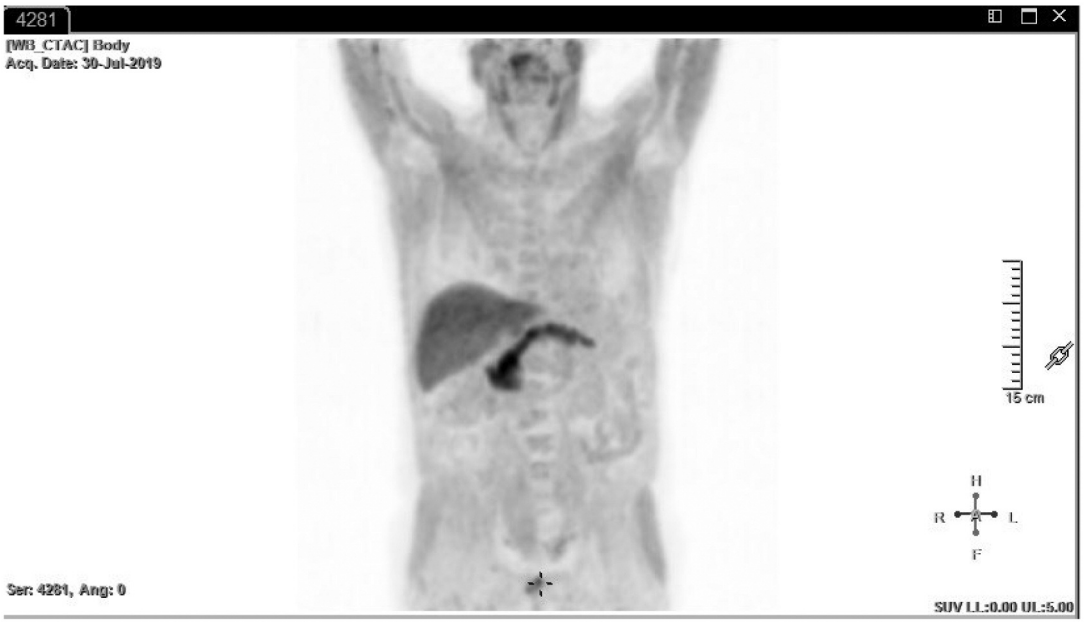

Figure 2. *Paravesical prostate cancer recurrence, fused and PET only transaxial views.*

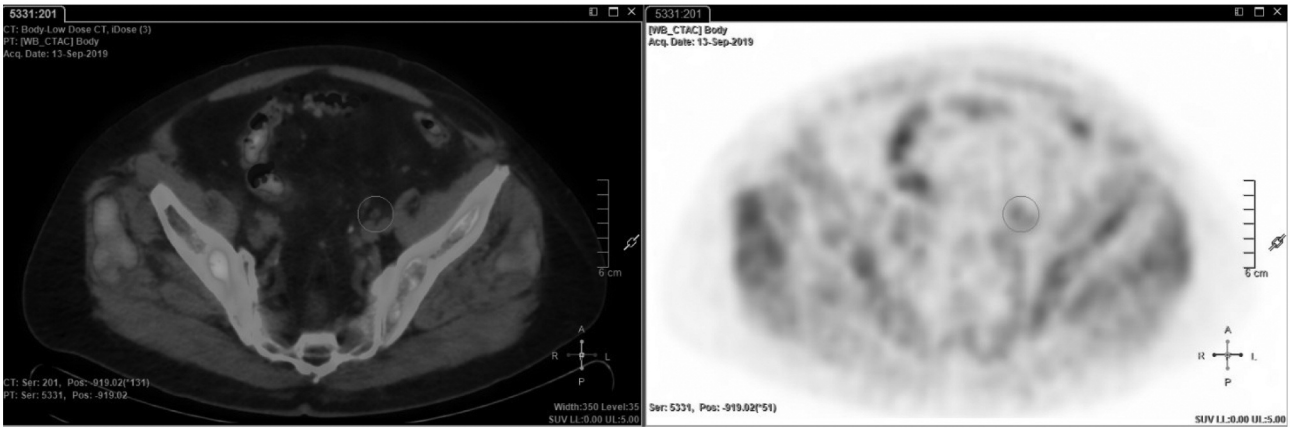

Figure 3. *External-iliac lymphnode localization of prostate cancer recurrence, fused and positron-emission tomography (PET) only transaxial view.*

Due to the small number of patients, the detection rate of disease relapse was determined. *Results:* No adverse reactions to ^{18}F-fluciclovine were noted. On a patient basis, PET/CT was positive in 12 patients and negative in 4. Eleven patients had only local relapse (Figure 1 and 2), 2 patients had only lymph-nodal localization (Figure 3) and 1 patient had both local and nodal relapse. On a lesion basis, ^{18}F-fluciclovine detected 18 lesions (4 prostate lesions in radiation-treated patients, 7 at the vescico-uretral anastomosis or prostate bed, 7 pelvic lymph nodes); no bone lesions were assessed. ^{68}Ga-PSMA-PET/CT was previously performed in 5 patients. In all these cases, ^{68}Ga-PSMA was negative but ^{18}F-fluciclovine identified pathologic uptake foci near to vescico-uretral anastomosis; these findings were subsequently confirmed by biopsy or pelvic MRI. *Conclusion:* Our preliminary results, according to current increasing literature, indicate that ^{18}F-Fluciclovine may be useful in the detection of prostate cancer recurrence, particularly in patients with low PSA levels. In recent clinical series, ^{18}F-fluciclovine detection rate seems to be better than ^{11}C or ^{18}F-choline one, either on a patient- and a lesion-based analysis and despite the PSA serum levels. The major advantage of this tracer is detection of curable localized

disease in close anatomical relation to the urinary bladder, due to the absence of urinary tracer excretion. Therefore, it is a promising diagnostic tool in the work-up of biochemically recurrent prostate cancer, given the high positivity rate as compared to the approved currently available imaging modalities. An impact of ^{18}F-Fluciclovine PET/CT in clinical management has been reported in about 60% of patients. Several studies are ongoing to assess efficacy in a larger series of prostate cancer patients. Further research is also needed to investigate whether higher detection rates and alteration of management could improve oncological outcomes.

51
SAFETY OF THE REDUCTION OF CTV-TO-PTV MARGINS IN PROSTATE CANCER RADIOTHERAPY: A DOSIMETRIC ANALYSIS

Vittorio Vavassori[1], Luca Trombetta[2], Elisa Villa[1], Paolo Ghirardelli[1], Giada Facoetti[3], Andrea Ravasio[1], Federica Locatelli[2], Alfredo Gambirasio[2] and Paolo Salmoiraghi[2]

[1]Radiotherapy Unit, Humanitas Gavazzeni, Bergamo, Italy; [2]Medical Physics Unit, Humanitas Gavazzeni, Bergamo, Italy; [3]Department of Engineering, Bergamo University, Dalmine, Italy

Aim: This study aimed to evaluate a practical path (patient preparation protocol and the setup imaging analysis to check both preparation and treatment setup) for radiotherapy treatment of localized prostate cancer, in order to reduce random and systematic geometrical errors and in an attempt to investigate the possibility of a safe decreasing of clinical target volume (CTV)-to-planning target volume (PTV) margins. A dosimetric evaluation on organs-at-risk sparing and CTV coverage is presented. *Patients and Methods:* In a total of 10 patients with localized prostate cancer, undergoing radical radiotherapy (3Gy/day per 20 fractions), we minimized random and systematic geometrical errors by: i) giving to patients strict instructions in terms of bladder filling (400 ml of water) and rectal evacuation before treatment to minimize inter- and intra-fraction motion and deformations of the target volume (prostate +/– seminal vesicles), and ii) performing cone beam computed tomography (CBCT) imaging on treatment couch for each fraction in order to check the anatomical results of the preparation described before and minimize set-up errors. Each patient was then treated using isotropic 8 mm CTV-to-PTV margins according to our clinical standards. Dose constraints for rectum wall and bladder wall organs at risk (OARs) suggested by the French genito-urinary group (GETUG) (1) were followed and respected during planning step. We reviewed all the CBCT set; OARs and CTV were re-contoured, and dose distributions were calculated to evaluate the dosimetric outcomes on the real daily patient anatomy. Then, the dose–volume histograms obtained from dose distributions (CBCT-DVHs) of OARs and CTV were extracted for each patient. The same procedure was also followed for a second hypothetical RT plan with isotropic 5 mm CTV-to-PTV margins. Finally, dosimetric comparison and analysis were made. For OARs, we analysed the differences between CBCT-DVHs in case of 8 mm and 5 mm; for the CTV, we analysed the differences between planned DVH and the CBCT-DVH for 5 mm margins. For OARs, we compared the percentage of total volume irradiated by the 37 Gy, 46 Gy and 60 Gy isodoses for rectal wall, and by the 41 Gy, 48 Gy and 60 Gy isodoses for bladder wall (1). Results are presented as mean±standard deviation. *Results:* For rectal wall, the percentage of total volume irradiated by the 37 Gy isodose was 33.6%±13.6 in case of 8 mm margins and 26.5%±13.3 for 5 mm margins, with a spared volume of

Table I. *Quantification of the dosimetric outcomes.*

	Rectal wall			Bladder wall		
	37 Gy (≤50%)	46 Gy (≤30%)	60 Gy (≤2%)	41 Gy (≤25%)	48 Gy (≤25%)	60 Gy (≤5%)
8 mm margins CBCT-DVH	33.6±13.6%	25.6±10.3%	8.0±4.1%	25.9±7.3%	21.8±7.3%	12.3±5.0%
5 mm margins CBCT-DVH	26.5±13.3%	18.7±9.1%	5.0±3.2%	20.9±8.0%	17.1±7.2%	8.3±5.3%
Δ (sparing)	7.1±5.5%	7.0±5.3%	3.0±2.0%	5.0±1.1%	4.8±1.2%	4.0±1.7%
	CTV 57 Gy (≥95%)					
5 mm margins planned DVH	100±0.0%					
5 mm margins CBCT-DVH	98.5±2.0%					
Δ (missing)	1.5±2.0%					

CBCT, Cone beam computed tomography; DVH, dose–volume histogram; CTV, clinical target volume.

7.1%±5.5 in the latter case; the 46 Gy isodose covered a percentage volume of 25.6%±10.3 in case of 8 mm margins and 18.7%±9.1 for 5 mm margins, with a spared volume of 7.0%±5.3; the 60 Gy isodose covered a percentage volume of 8.0%±4.1 in case of 8 mm margins and 5.0%±3.2 for 5 mm margins, with a spared volume of 3.0%±2.0. For bladder wall, the percentage of total volume irradiated by the 41 Gy isodose was 25.9%±8.2 in case of 8 mm margins and 20.9%±8.0 for 5 mm margins, with a spared volume of 5.0%±1.1 in the latter case; the 48 Gy isodose covered a percentage volume of 21.8%±7.3 in case of 8 mm margins and 17.1%±7.2 for 5 mm margins, with a spared volume of 4.8±1.2%; the 60 Gy isodose covered a percentage volume of 12.3%±5.0 in case of 8 mm margins and 8.3%±5.3 for 5 mm margins, with a spared volume of 4.0%±1.7. For CTV, the volume covered by the 95% isodose (57 Gy) was100%±0.0 in case of 5 mm margins for planned dose and 98.5%±2.0 for 5 mm margins for CBCT dose, with a missing volume of 1.5%±2.0 in the latter case. *Conclusion:* A quantification of the dosimetric outcomes is presented in Table I. Giving clear and written indications to the patients for bladder and rectal preparation as well as using CBCT daily as imaging for image-guided radiotherapy may reduce CTV-to-PTV margins from isotropic 8 mm to isotropic 5 mm, obtaining negligible target missing, with significant sparing of organs at risk.

1 Langrand-Escure J, de Crevoisier R, Llagostera C, Créhange G, Delaroche G, Lafond C, Bonin C, Bideault F, Sargos P, Belhomme S, Pasquier D, Latorzeff I, Supiot S and Hennequin C: Dose constraints for moderate hypofractionated radiotherapy for prostate cancer: The French genito-urinary group (GETUG) recommendations. Cancer Radiother *22*: 193-198, 2018. PMID: 29628205. DOI: 10.1016/j.canrad.2017.11.004

52
ACTIVE SURVEILLANCE OR RADICAL TREATMENT FOR LOW-RISK PROSTATE CANCER: UPDATED RESULTS OF THE START PROJECT*

Oscar Bertetto[1], Enrico Bollito[2], Giovannino Ciccone[3], Stefano De Luca[4] and Cooperative Group START

[1]Oncology Regional Network of Piedmont and Valle d'Aosta, AOU Città della Salute e della Scienza, Turin, Italy;
[2]Division of Pathology, AOU San Luigi Gonzaga Hospital Orbassano, Turin, Italy;
[3]Unit of Clinical Epidemiology, AOU Città della Salute e della Scienza, Turin, Italy;
[4]Division of Urology, AOU San Luigi Gonzaga Hospital Orbassano, Turin, Italy

Background/Aim: An active surveillance (AS) strategy is recommended as an appropriate management for men with newly diagnosed, low risk localized prostate cancer (PCa); however, its use, at least in the Oncology Regional Network of Piedmont and Valle d'Aosta (Northern Italy), was very limited, even after the implementation of a regional guideline on PCa (2009). The ongoing START project (Active Surveillance or Radical Treatment for newly diagnosed patients with a localized, low risk PCa) was launched in 2014 aiming to encourage the use of AS in the context of the Oncology Regional Network of Piedmont and Valle d'Aosta. The main objectives of the project are to: i) encourage the diffusion of AS at a regional level, in the context of a research project based on standardized criteria for patient selection and management; ii) supply standardized information about the benefits and risks of the available management options, including AS, to all newly diagnosed low-risk PCa patients in order to allow an informed choice; and iii) evaluate the clinical outcomes, quality of life (QoL), and costs associated to different management choices, at a population level. *Patients and Methods:* This is a comparative effectiveness research project. All newly diagnosed PCa patients fulfilling the low-risk definition, resident in Piedmont or in Valle D'Aosta, was invited to participate to this observational prospective study. All enrolled patients received full and clear information (both oral and written) about their prognosis, together with a balanced synthesis of the benefits and risks of the available management options (AS, surgery, or radiotherapy). For all the participants, independently from the management option chosen, baseline clinical, histological and psychological data, any treatment received and follow-up data (including clinical and QoL outcomes) were collected through electronic case report form (eCRF). Patients accepting AS were offered a structured follow-up program. Clinical, QoL, and cost outcomes were compared according to the different management options. To evaluate the association between clinical and socio-demographic characteristics of the patients and the selection of AS as a first-line management option we used multivariable logistic regression models, that included as covariates: age (60-69, ≥70 *vs.* <60), education (high, intermediate *vs.* low), marital status (yes *vs.* no), comorbidity Charlson index (1, 2 *vs.* 0), baseline level of PSA (>7 *vs.* ≤7 ng/ml), tumor stage (T2a *vs.* T1c), Gleason score (3+4 *vs.* 3+3), number of positive biopsy specimens (2 *vs.* 1), specialist that enrolled the patient (urologist *vs.* radiotherapist), implementation of multidisciplinary evaluation (yes *vs.* no), performance of multiparametric magnetic resonance imaging of the prostate at baseline (yes *vs.* no), execution of centralized histopathological review of the biopsy specimens (yes *vs.* no). Results are presented as odds ratio (ORs) with 95% confidence intervals (CI). The treatment-free survival (TFS) during the follow-up, for

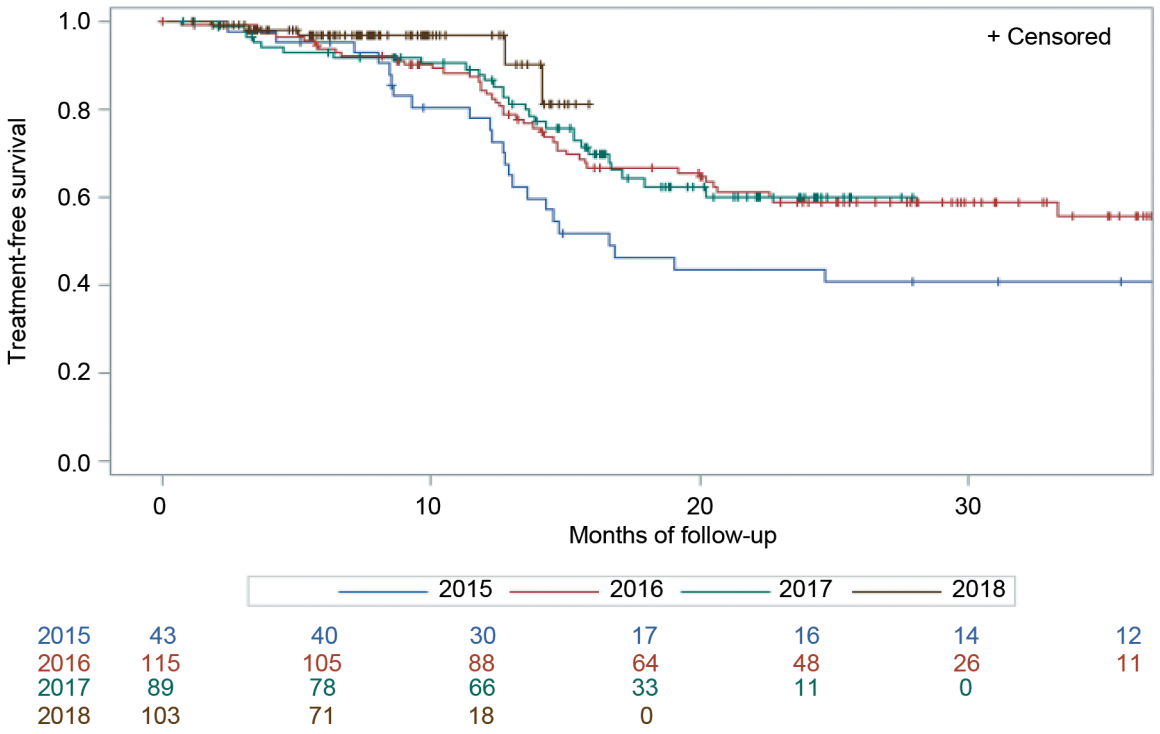

Figure 1. *Treatment-free survival for patients in active surveillance, by year of enrollment-START project.*

patients that selected AS as a first-line management option, was also evaluated using Kaplan Meyer method. Moreover, the level of anxiety and depression (with the Hospital Anxiety Depression Scale-HADS questionnaire) at baseline and after 6, 18 and 24 months of follow-up was compared between patients that chose AS or surgery as a first-line management option. *Results:* The START protocol has been designed by a multidisciplinary panel of specialists of the Regional Oncology Network, including urologists, radiotherapists, epidemiologists, pathologists, oncologists and patient representatives. Almost all the regional Hospital units of Urology, Radiotherapy and Pathology have been involved. A web-site has been implemented (www.start.epiclin.it) with both a public and a reserved area for data collection. From May 2015 to November 2019, 616 patients have been enrolled in the study. For the present analysis we included 503 patients who were enrolled until March 2019. The large majority of patients (80%) selected AS as a management option, 15% radical prostatectomy, and 5% radiotherapy. Despite the standardized research protocol, we observed heterogeneity among the participating centers of the Regional Network in the frequency of patients that chose AS as a management option. Factors that were positively associated with the selection of AS include: i) a multidisciplinary evaluation (OR=4.14, 95% CI=1.90-9.04, p=0.0004), ii) a Charlson index ≥2 (OR=2.46, 95% CI=1.16-

Table I. *Factors associated with the selection of active surveillance vs. Radical treatment as a first-line management option-START project.*

	Odds ratio	95% CI		*p*-Value
Age (years)				
60-69	1.212	0.592	2.480	0.5992
≥70	1.786	0.827	3.857	0.1397
Education				
Intermediate	0.854	0.477	1.529	0.5950
High	1.383	0.736	2.601	0.3137
Marital status (yes)	0.898	0.521	1.547	0.6978
Comorbidity				
Charlson index=1	1.063	0.601	1.879	0.8345
Charlson index≥2	2.461	1.158	5.231	0.0193
PSA >7 ng/ml	0.690	0.411	1.157	0.1590
Stage T2a	0.479	0.252	0.909	0.0243
Two positive biopsy specimens	0.540	0.327	0.893	0.0162
Gleason score 3+4	0.362	0.181	0.724	0.0041
Urology department	2.280	1.029	5.051	0.0423
Multidisciplinary evaluation	4.144	1.900	9.040	0.0004
Basal MR	1.098	0.661	1.826	0.7173
Histopathological review of biopsy	2.022	1.100	3.716	0.0234

CI, Confidence interval; PSA, prostate-specific antigen; MR, magnetic resonance.

5.23, p=0.02), and iii) a centralized histopathological review of biopsy tissue specimen (OR=2.02, 95% CI=1.10-3.72, p=0.02) (Table I). The selection of AS as a first-line treatment strategy was negatively associated with: i) the presence of 2 positive biopsy specimens (OR=0.54, 95% CI=0.33-0.89, p=0.02), ii) a more advanced tumor stage (OR=0.48, 95% CI=0.25-0.91, p=0.02), and iii) a Gleason score 3+4 (OR=0.36, 95% CI=0.18-0.72, p=0.004). Treatment-free survival (TFS) of patients that chose AS as first management option was 86% after 12 months and 58% after 24 months of follow-up (Figure 1). The results showed an increase of TFS for patients enrolled in more recent years (p=0.035). Preliminary results regarding the level of anxiety and depression at baseline and during follow-up do not show statistically significant differences between patients that chose AS or surgery as a management option. Recruitment in the START project is still ongoing; during the conference updated results will be presented. *Conclusion:* The results of the START project after about 4 years of enrollment are promising regarding the participation of the regional centres of the Oncology network as well as the large proportion of patients with low risk prostate cancer that accepted AS as a first-line management option. The initially low TFS seems to improve with increasing experience in AS management. A population-based research framework could represent a powerful and safe strategy to effectively implement AS in the National Health Service.

This work has received funding from Compagnia di San Paolo – Turin, and Rete Oncologica del Piemonte e Valle d'Aosta.

Table I. *Descriptive characteristics of the cohort of 26 patients underwent total glans resurfacing for localized penile cancer.*

Variables	n (%)
Follow-up*, months	38 (13-86)
Age*, years	65 (55-68)
BMI*	26 (24-28)
Smoking habit	10 (38.5)
Diabetes	5 (19.2)
Hypertension	9 (34.6)
History of LS	13 (50)
Symptoms requiring consultation	
Penile pain	9 (34.6)
Pruritus	9 (34.6)
Bleeding	8 (30.7)

LS, *Lichen sclerosus*. *Data presented as mean (IQR).

Table II. *Descriptive characteristics of the intra-/peri-operative outcomes of the cohort of 26 patients underwent total glans resurfacing for localized penile cancer.*

Variables	n (%)
Operative time*, min	135 (100-165)
Intraoperative complications	0 (0)
Hospital stay*, days	5 (2-6)
Blood loss*, cm^3	10 (0-50)
Urethral catheter removal*, days	7 (5-10)
Final histology	
CIS	11 (42.4)
T1	14 (53.8)
T2	1 (3.8)
Positive surgical margins	1 (3.8)

CIS, Carcinoma *in situ*. *Data presented as mean (IQR).

54
TOTAL GLANS RESURFACING FOR THE MANAGEMENT OF LOCALIZED PENILE CANCER: A RETROSPECTIVE COHORT ANALYSIS IN A TERTIARY REFERRAL NETWORK

Mirko Preto, Marco Falcone, Massimiliano Timpano, Omid Sedigh, Lorenzo Bertolino, Carlo Ceruti and Paolo Gontero

Division of Urology, A.O.U. Città della Salute e della Scienza di Torino - Molinette Hospital, Turin, Italy

Background/Aim: Penile cancer is a rare malignancy, representing 1% of male cancers worldwide. Strong evidences on organ preserving surgery are still lacking. Particularly, few data outline the effectiveness and safety of total glans resurfacing (TGS) in the management of localized penile cancer. The aim of our study is to report both surgical and oncological outcomes of TGS in a consecutive series of localized penile cancers. *Patients and Methods:* From 2004 to 2018 a consecutive series of 37 patients underwent a TGS

Table III. *Descriptive characteristics of the postoperative outcomes of the cohort of 26 patients underwent total glans resurfacing for localized penile cancer.*

Variables	n (%)
Overall postoperative complication	1 (3.8)
Genital wound infection	1 (3.8)
Graft total loss	0 (0)
Graft contracture	0 (0)
Donor site wound infection	0 (0)
Graft partial loss	4 (15.3)
Graft take*, ratio	95 (90-100)
Recurrence	3 (11.5)
Time for recurrence*, months	11 (9-14)
Salvage treatment for recurrence	
Wide local excision	1 (3.8)
Glansectomy	2 (5.5)
Inguinal staging lymphadenectomy	1 (3.8)
Regional nodal recurrence	0 (0)
Overall survival	26 (100)
One-year recurrence-free survival	24 (92.3)

*Data presented as mean (IQR).

in a tertiary referral network. Patients affected by lichen sclerosus were excluded from this study. Descriptive features and surgical outcomes were extrapolated from the clinical records. Medium-term oncological outcomes were assessed. Statistical analysis was conducted with Stata 12. *Results:* A total of 26 consecutive patients underwent a TGS for a localized penile cancer. Preoperative patient characteristics features are summarized in Table I. No intra-operative complications were reported. Median hospital stay was 5 days (Table II). Postoperative complications were minimal (3.8%). Overall, 96% of the patients had a complete graft take. Only 3 cases (11.5%) experienced a local recurrence and they were managed by a salvage organ sparing surgery at a median follow-up of 11 months (Table III). No regional nodal recurrence was reported. Final histology confirmed CIS in 42.4% and T1 in 53.8% of cases (Table II). The single patient who had a T2 cancer at final histopathology was managed by a glansectomy and a staging bilateral inguinal lymphadenectomy. Overall survival rate was 100% and 1-year recurrence-free survival was 92.3% (Table III). *Conclusion:* TGS was shown as an excellent option for organ preserving surgery in patients with a localized penile cancer. Surgical and oncological outcomes proved to be satisfactory.

Table I. *The non-validated questionnaire to assess patient-reported outcomes.*

1	Did the surgery improve your quality of life?	Yes	No
2	Are you satisfied with the aesthetic result of the glans?	Yes	No
3	Would you recommend the same procedure to someone else?	Yes	No
4	Would you consider undergoing the same procedure again?	Yes	No
5	Has the glans sensitivity been maintained after surgery?	Yes	No

Table II. *Descriptive characteristics of the cohort of 37 patients, who underwent total glans resurfacing for localized penile cancer.*

Variables	n (%)
Follow-up*, months	24 (13-77)
Age*, years	62 (55-68)
BMI*, value	27 (24-29)
Smoking habit	10 (27)
Diabetes	6 (16.2)
Hypertension	10 (27)
History of LS	16 (43.2)
Symptoms requiring consultation,	
Penile pain	12 (32.4)
Pruritus	14 (37.8)
Bleeding	11 (29.7)

LS, *Lichen sclerosus*. *Data presented as mean (IQR).

55
FUNCTIONAL AND PATIENT-REPORTED OUTCOMES AFTER TOTAL GLANS RESURFACING: RESULTS FROM A RETROSPECTIVE ANALYSIS IN A TERTIARY REFERRAL NETWORK

Mirko Preto, Marco Falcone, Massimiliano Timpano, Omid Sedigh, Lorenzo Bertolino, Carlo Ceruti and Paolo Gontero

Division of Urology, A.O.U. Città della Salute e della Scienza di Torino - Molinette Hospital, Turin, Italy

Background/Aim: Strong evidences on organ preserving surgery to address penile benign or malignant lesions are still lacking. Particularly, functional outcomes and patient-reported outcomes (PROs) have been rarely investigated. The aim of our study is to report functional outcomes and PROs of total glans resurfacing (TGR) in a consecutive series of patients with lichen sclerosus (LS) or localized penile cancer (PC). *Patients and Methods:* From 2004 to 2018 a consecutive series of patients underwent a TGS in a tertiary referral network. A retrospective analysis was conducted extrapolating data from the clinical records. Urinary and sexual outcomes were investigated through the International Index of Erectile Dysfunction (IIEF) and International Prostate Symptom Score (IPSS) validated questionnaires. PROs were extrapolated from a 5-item *ad hoc* created questionnaire (Table I) administered through a telephone interview at 1-year follow-up. Statistical analysis was conducted with Stata 12. *Results:* In the present study 37 consecutive patients were enrolled (Table II). Eleven patients showed a LS at the final histopathological examination, whereas a localized PC was detected in the rest of the patients. The validated questionnaires assessed that neither urinary nor sexual function deteriorated after surgery. An overall improvement of the quality of life was reported by 86.4% of patients. Glans sensitivity was fully maintained in 89.2% of cases. The majority (94.5%) of patients reported to be fully satisfied by the aesthetic appearance of the penis and would consider undergoing the same procedure again if necessary, while 91.9% of patients would recommend the same procedure to someone else (Table III). C*onclusion*; TGR ensured a satisfactory penile function and appearance. Thus, TGR represents an excellent surgical option for the management of selected benign or malignant penile lesions.

Table III. *Functional (sexual and urinary) and patient-reported outcomes after glans resurfacing.*

Variables	Preoperative Mean (IQR)	6-Months postoperative Mean (IQR)	12-Months postoperative Mean (IQR)
IIEF			
Erectile function	22 (17-25)	20 (15-23)	(17-24)
Orgasmic function	7 (7-8)	6 (6-7)	7 (6-8)
Sexual desire	8 (7-8)	7 (6-7)	7 (7-8)
Sexual satisfaction	11 (11-12)	11 (9-12)	11 (10-12)
Overall satisfaction	8 (7-8)	7 (6-7)	7 (7-8)
All domains	56 (50-62)	51 (44-56)	54 (47-60)
IPSS	10 (7-14)	13 (11-15)	12 (10-14)
PROs questionnaire, n (%)			n (%)
Overall improvement of the quality of life	-	-	32 (86.4)
Aesthetic glans satisfaction	-	-	35 (94.5)
Recommendation of surgery to someone else	-	-	34 (91.9)
Consider to undergo the same procedure again	-	-	35 (94.5)
Maintenance of glans sensitivity after surgery	-	-	33 (89.2)

IIEF, International Index of Erectile Dysfunction; IPSS, International Prostate Symptom Score; PROs, patients-reported outcomes.

56

EARLY ACUTE TOXICITIES IN STEREOTACTIC ABLATIVE RADIOTHERAPY FOR PROSTATE CANCER PATIENTS WITH SYNCHRONOUS OLIGOMETASTASES

Ivan Fazio[1], Gabriele Tulone[2], Davide Baiamonte[2], Nicolò Borsellino[3], Manuela Federico[1], Tiziana Bruno[1] and Vincenzo Serretta[2]

[1]Radiotherapy Unit, Macchiarella Clinic, Palermo, Italy; [2]Urology Unit, Department of Surgical, Oncological and Oral Sciences, University of Palermo, Palermo, Italy; [3]Oncology Unit, Buccheri La Ferla - Fatebenefratelli Hospital, Palermo, Italy

Background/Aim: Traditionally, radiotherapy in oligometastatic prostate cancer patients was reserved for palliative control of local or distant symptoms like pain, urinary discomforts, hematuria and others, mainly due to primary tumor or metastases unresponsive to systemic treatment. In recent years, growing evidence suggests that metastasis-directed therapy (MDT) and/or local therapy targeted to the primary tumor could improve the outcomes in oligometastatic patients, due to not only the treatment of the existing metastases but also to the inhibition of new metastatic growth. The development of new distant lesions seems to be influenced by compounds secreted by the primary tumor. Moreover, radiotherapy can be a valid strategy for elderly and/or frail patients unfit for systemic therapy due to concomitant pathologies. Nowadays radiotherapy might represent a treatment option both for the primary tumor and the metastatic sites. This option can be of particular interest in elderly patients unfit for or at risk of severe toxicity from systemic therapy. In our preliminary experience we investigated the feasibility and tolerability of stereotactic body radiotherapy (SBRT) in oligometastic elderly patients. The present study aimed to analyze the feasibility and early acute toxicity of simultaneous SBRT to primitive tumor and metastatic site in oligometastatic elderly prostate cancer frail patients. *Patients and Methods:* From April to October 2019, 6 prostate cancer patients with synchronous oligometastases and low volume burden disease at first diagnosis were enrolled. Two of them received a short course of androgen deprivation therapy. Four of them were considered unfit for hormonal therapy because of their severe comorbidities. Mean age was 82 years (range=76-90). PSA mean value was 33.5 ng/ml (range=2-87). Diagnosis was made in all patients by choline-positron emission tomography-computed tomography (PET/CT) and confirmed with whole-body magnetic resonance imaging (MRI) in 4 of them. Four patients had spinal metastases and 2 patients had pelvic bone metastases. The indication to the radiant treatment was given by a multidisciplinary team that included oncologists, radiotherapists, urologists and radiologists dedicated to prostate cancer. The patients underwent CT and nuclear magnetic resonance (NMR) simulation, permitting the accurate identification of the target volume in a reproducible position of the patient during the treatment session. Therefore, the target volume was contoured according to the Radiation Therapy Oncology Group (RTOG) guidelines and a margin of 2-4 mm was added in order to reduce the geographical missing. The

treatment plan was done through a treatment planning system (TPS) and the therapy was delivered with a linear accelerator and dynamic volumetric modulated arc therapy (VMAT). Before delivering each therapy session, the patients were subjected to a verification using cone beam computed tomography to avoid positioning errors. The fractionation schedule adopted were respectively 6 Gy/day for 5 days, for a total dose of 30 Gy on the site of the prostate tumor. A total dose of 30-37.5 Gy in 5 daily fractions was delivered to bone metastases. Toxicity was recorded according to the Common Terminology Criteria for Adverse Events (CTCAE) v 4.03. Each patient was visited at the beginning of each treatment session and then at 7 and 15 days after the end of the treatment. Patient compliance and acute toxicity were recorded. Side effects and toxicity were managed with the most appropriate supportive care. *Results:* Dose limits at organs at risk (OARs) have been respected: median bladder dose was 4.7 Gy (range=2.6-11.5); median dose to the rectum was 11.1 Gy (range=5.2-11.9); median value of femoral heads was 3 Gy (range=1-3.1). Therapy was well-tolerated by the patients, showing a good compliance to treatment in spite of their age and frailty due to comorbidities and limitations. No patient presented acute genitourinary and gastrointestinal grade 2-4 toxicities. Mild gastrointestinal and urinary toxicity required only temporary supportive care. *Conclusion:* SABR for oligometastatic prostate cancer elderly and frail patients with low volume burden disease was safe and well-tolerated. Further studies with a longer follow-up are warranted to evaluate chronic toxicity, local and systemic control.

Table I. *Characteristics of patients.*

		Number of patients
Basal-PSA	<10	18
	10-20	5
	>20	2
Gleason score	6 (3+3)	10
	7 (3+4)	10
	7 (4+3)	3
	8 (4+4)	1
	8 (3+5)	1
T-staging	1c	2
	2a	3
	2b	12
	2c	7
	3a	1
Risk group	Low	7
	Favorable intermediate	6
	Unfavorable intermediate	7
	High	5
Hormonal therapy	No	8
	Yes	17
Dose of radiotherapy	35 Gy	19
	64.5/72Gy	6
Number of fractions	5	19
	30	6
Target	Prostate	7
	Prostate+seminal vesicles	18

	Toxicity (RTOG Scale)		
	Intra-RT(%)	3 months (%)	6 months (%)
Genitourinary			
G0	64%	76%	92%
G1	32%	20%	4%
G2	4%	4%	4%
Rectal			
G0	96%	96%	96%
G1	4%	0%	0%
G2	0%	4%	4%

PSA, Prostate-specific antigen.

57
ACUTE TOXICITY IN HYPOFRACTIONATED/ STEREOTACTIC PROSTATE RADIOTHERAPY IN ELDERLY PATIENTS: USE OF IGRT WITH CLARITY-SYSTEM

Rossella Di Franco[1], Valentina Borzillo[1], Domingo Alberti[1], Gianluca Ametrano[1], Angela Petito[1], Gaetano Facchini[2], Sabrina Rossetti[2], Gelsomina Iovane[2], Sisto Perdonà[3], Giuseppe Quarto[3], Giovanni Grimaldi[3], Alessandro Izzo[3], Luigi Castaldo[3], Raffaele Muscariello[3] and Paolo Muto[1]

[1]Department of Radiation Oncology, Istituto Nazionale Tumori - IRCCS - Fondazione G. Pascale - Naples, Naples, Italy;
[2]Departmental Unit of Clinical and Experimental Uro-Andrologic Oncology, Istituto Nazionale Tumori - IRCCS - Fondazione G. Pascale – Naples, Naples, Italy;
[3]Uro-Gynecological Department, Istituto Nazionale Tumori - IRCCS - Fondazione G. Pascale – Naples, Naples, Italy

Background/Aim: Clarity is a system used for intrafraction prostate-motion management during radiotherapy treatment. It provides a real-time visualization of prostate with a trans-perineal ultrasound. The aim of this study was to evaluate the use of the Clarity image-guided radiotherapy (IGRT) in the correct alignment and intrafraction monitoring, as well as its impact on planning tumor volume margin and on urinary and rectal toxicity, in elderly patients not eligible for surgery. *Patients and Methods:* Twenty-fiev elderly prostate cancer patients (median age=75 years, range=75-90) were treated with volumetric radiotherapy and the Clarity IGRT,

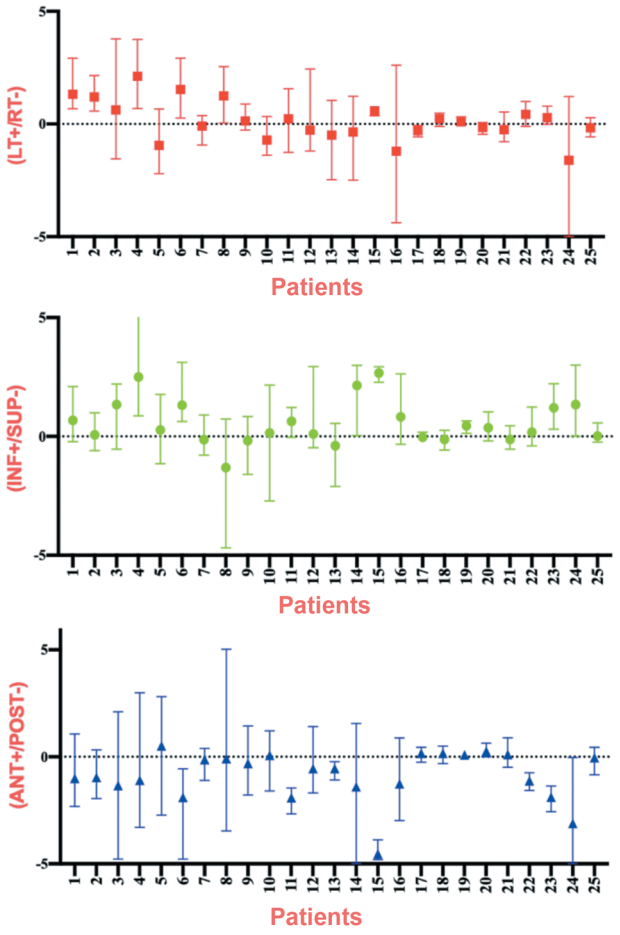

Figure 1. *Box-plot of misalignments in the three directions of the space. LT, Left; RT, right; INF, inferior; SUP, superior; ANT, anterior; POST, posterior.*

with 3 different schemes: i) 64.5/72Gy in 30 fractions on prostate and seminal vesicles (6 patients); ii) 35Gy in 5 fractions on prostate and seminal vesicles (12 patients); iii) 35Gy in 5 fractions on prostate (7 patients) (Table I). All patients underwent CT simulation with the Clarity ultrasound image guidance system. During every session ultrasound identification of the structures was performed; then these structures were overlapped with the structures obtained by CT simulation. In case of incongruity, a specific software calculated direction and entity of necessary shift to obtain a perfect match. This procedure allowed reduction of the margins of Planning Target Volume to 5 mm in all directions, and to 3 mm in posterior. For each patient the average of the misalignments in the three directions of the space we calculated and presented in box-plots (Figure 1). Moreover, acute urinary and rectal rates according to the RTOG scale were calculated. *Results:* All patients completed RT with mild to moderate toxicity. During radiation-treatment the genitourinary (GU) toxicity was 32% grade 1 (G1) and 4% G2. Rectal toxicity was 4% G1. At 3 months of follow-up, GU toxicity was 20% G1 and 4% G2. Rectal toxicity was 4% G2. At 6 months of follow-up, GU toxicity was 4% Grade 1 and 4% G2. Rectal toxicity was 4% Grade G2. Regarding misalignments, the Clarity system allowed movement control within the margins of the planning target volume. *Conclusion:* Radiotherapy with the Clarity ultrasound system in elderly patients, thanks to a perfect equivalence of position between simulation and RT session, allowed a reduction of PTV margins. Consequently, we can reduce the number of fractions and increase the total dose without increasing urinary and rectal toxicity. Mild toxicity and shorter duration of treatment resulted in greater patient compliance.

58
OLIGO-METASTATIC/OLIGO-RECURRENT PROSTATE CANCER: EXTENDED OR FOCUSED RADIOTHERAPY

Andrea Galla[1], Elisabetta Garibaldi[1], Ramona Parise[2], Amalia Di Dia[3], Gabriella Cattari[1], Gaetano Belli[1], Paola Scapoli[4], Antonia Salatino[1], Jacopo Di Muzio[2] and Marco Gatti[1]

[1]Radiation Oncology Unit, Candiolo Cancer Institute, Turin, Italy;
[2]University of Turin, Turin, Italy;
[3]Medical Physics Unit, Candiolo Cancer Institute, Turin, Italy;
[4]Nuclear Medicine Unit, Candiolo Cancer Institute, Turin, Italy

Background: Recent technology advances in diagnostic and radiotherapy (RT) field have allowed to detect and treat early oligo-metastasis/oligo-recurrences prostate cancer (OMPC) patients (pts). The aim of this study was to present our experience in RT of oligo-metastasis/oligo-recurrences prostate cancer pts focusing on local locoregional control, toxicity and time to recurrence. Materials and Methods: From October 2010 to December 2018, we treated 53 pts [mean age (min-max): 61 (45-77), Karnofsky Performance Scale: 80-100] with node and/or bone recurrences from prostate cancer. At diagnosis, the median Gleason Score was 7 and the median iPSA was 10.1 ng/ml. Of these 53 pts, 41 (77%) underwent primary treatment of radical prostatectomy and lymphadenectomy, while 11 (21%) received radiotherapy with radical intent and 1 (2%) only hormone therapy. Pts who received an adjuvant radiotherapy treatment (DFT 66 Gy/33 fr.) after surgery were 7 (13%) and 12 (22%) pts underwent salvage radiotherapy treatment (DFT 70 Gy/35 fr.), finally 15 (28%) pts also had hormone adjuvant therapy. At the time of biochemical

recurrence all pts received functional imaging (by ^{68}Ga-PSMA ligand/CT-PET in 21 pts, 18 choline/CT-PET in 32 pts and also multiparametric MRI in 6 pts). Pts were treated according to our internal protocol and they signed an informed consent form. The recurrence sites were nodal in 49 (pelvic in 27 pts, lumbar aortic in 22 pts), bone in 4 pts. For each pts number of metastases ranged between 1 and 5 (mean 2.5) for group 1 (extended RT) and between 1 and 2 lesions for group 2 (focused RT). Thirty-eight pts (group 1) were treated by IMRT-SIB-IGRT with tomotherapy on regional node with prophylactic doses (range=51-54 Gy – 1.7-1.8 Gy per fraction) and on positive nodes from 66 Gy (2.2 Gy per fraction) to 70.5 Gy, (2.35 Gy per fraction). Fifteen pts (group 2) were treated with targeted RT on lesions by Tomotherapy (11 pts) (doses: 24-35 Gy in 4-7 fractions) or SBRT LINAC-based (4 pts) (doses: 18-24 Gy in single fraction). *Results:* No GU/GI acute or late toxicity >G2 (RTOG scale) was observed in both groups. All constraints for normal tissues were respected according to QUANTEC. The mean follow-up was 51 months (range 10-91) in group 1 and 18.4 months (range=1-34) in the group 2. In group 1, 6 pts were dead from disease progression and 5 were lost to follow-up; local control (LC) and loco-regional control (LRC) were 94.9% and 75% respectively, and the average time to recurrence was 24 months (range 3-31); the site of recurrence was loco-regional in 8 pts, bone in 3 pts and both in 2 pts; 1 pts developed visceral and nodal metastases. In the group 2, LC was 100%, regional control was 68.2% and average time to recurrence was 6.7 months (range=1-13). The sites of recurrence in this group was loco regional (pelvic) in 7 pts; to date, 3 pts showed biochemical relapse. *Conclusion:* In the last few years, thanks to technological advances, new treatment perspectives have opened up in pts affected by oligo-metastases/oligo-recurrences prostate cancer. From our retrospective analysis it was shown that time to recurrence was better in the extended-RT group than in the focused RT, whereas similar results were obtained in terms of local control and treatment tolerance. These data suggest that focused RT do not always translate into good oncological results and that each case needs a multidisciplinary evaluation. The limitations of this study are the small sample size and the non-comparability of two treatment groups in terms of follow-up. In the future, studies are required to implement especially the follow-up times for focused RT.

60
SQUAMOUS VARIANT OF BLADDER CANCER AND COLON ADENOCARCINOMA WITH UNUSUAL PRESENTATION OF HEPATIC METASTASES: A CASE REPORT

Dante Di Domenico[1], Angela Luongo[2], Biagio Barone[3], Irene Stanislao[4], Nicola Gennarelli[2] and Domenico Prezioso[1]

[1]Department of Integrated Activity of General Surgery and Specialistic Surgery, of Kidney Transplant, Nephrology, Intensive, University of Naples Federico II, Naples, Italy; [2]Department of General and Endoscopic Surgery, University of Naples Federico II, Naples, Italy; [3]Department of Urology, University of Naples Federico II, Naples, Italy; [4]Department of Dentistry, University of Naples Federico II, Naples, Italy

Background: Primary squamous cell carcinoma of urinary bladder is a rare disease variant, accounting for less than 5% of all primary bladder cancers (1). The diagnosis of squamous cell carcinoma of bladder is based on criteria established by the World Health Organization classification system (2) and is a poorly differentiated tumor, that usually progresses rapidly and is characterized by a worse prognosis than the most frequently represented bladder carcinomas, the urothelial carcinoma (UC) (3). We report an unusual episode of a patient with squamous cell carcinoma of urinary bladder and contemporary adenocarcinoma of the descending colon asymptomatic, discovered in stages of staging and subsequently of hepatic metastases from colon adenocarcinoma. the patient underwent radical surgical therapy, ureterocutaneostomy and later chemotherapy for metastases. *Patients and Methods:* The case report we are talking about concerns a 74-year-old patient, female, who came to our attention for recurrent hematuria episodes, for several months (maybe eighteen), which have been treated with empirical antibiotic therapy (by general practitioner) without, however, further investigation with at least a radiological examination. After first stadiative investigations, the patient was diagnosed with a primary squamous bladder and a metachronous colon adenocarcinoma too, completely asymptomatic, so considered as an incidentaloma in the radiological diagnosis of staging. The complete diagnosis was obtained by ultrasound, cystoscopy, trans urethral bladder resection, colonoscopy with biopsy and PET/CT (by using fluoro-deoxyglucose as radiopharmaceutical). In 2017 the patient underwent transurethral resection of bladder cancer (TURBT) at our institution; the histological diagnosis elaborated was “Solid urothelial carcinoma (G3), with marked squamous differentiation infiltrating also the muscular tunic present”. Subsequently the patient was subjected to a stadiative PET/CT, which showed presence of a descending colon circular neoformation. The patient was then subjected to a colonoscopy (Figure 1), which confirmed the PET/CT (F-18 + FDG) suspected diagnosis, finding a circular lumen stenosing and ulcerated lesion, 40 cm away from the anal margin, and the lesion did not allow flexible endoscope further transit. Moreover, thanks to sub-optimal intestinal cleansing (Boston Score=3, as the other two traits of score were not assigned), it was possible to appreciate the

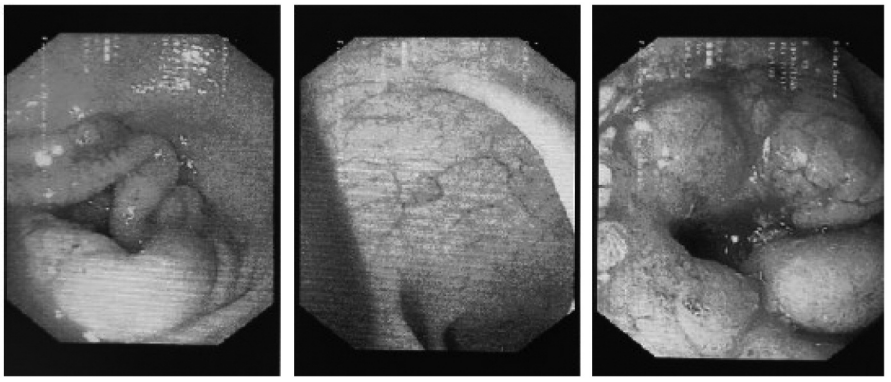

Figure 1. Colonoscopy.

presence of a pedunculated polyp (size: 8 mm), 10 cm away from the anal margin, despite the numerous and persistent diffuse intestinal musculature's spasms. During endoscopy, several biopsy samples were taken by the descending colon stenosing lesion, and the histological examination (in GB staining) revealed as outcome adenocarcinoma tissue. In January 2018 the patient underwent radical cystectomy with ureterocutaneostomy, partial colon resection with termino-terminal anastomosis, left lymphandenectomy and enlarged hysterectomy with partial vaginectomy. The histological report of the surgical specimen confirmed transurethral resection (TURBT) previous report: "solid urothelial carcinoma (G3) with marked squamous differentiation with muscular tunic infiltration". Colon resection showed the presence of adenocarcinoma, the surgical resection margin was negative. No infiltration of tumor cells was found in the uterus, in the excised appendages, in the anterior wall of the vagina and no involvement of the nearby nodes was detected. The patient performed both PET/CT (F-18 + FDG) and abdomen ultrasound six-month follow-ups. In February 2019, PET/CT (F-18 + FDG) detected, in the liver, altered glucose metabolism in some areas as VII (SUVmax 5.31), VIII (SUV max 11.5 *vs*. 3.91 previous PET control on 07/05/2018), III segment (SUVmax 11.6) and in VI segment (SUV max 6.92) (Figure 2). The remaining examined body areas were negative, within the method's limits. In March 2019, the patient underwent liver lesions' biopsy, shown by the PET/CT (F-18 FDG) last February, which confirmed the presence of liver metastases, of intestinal origin, with adenocarcinoma metastasis' characters. Since May 2019 She has undergone chemotherapy cycles, with Folfox protocol (5-fluoro-uracil, folinic acid, oxaliplatin), currently the patient is still receiving therapy (with poor performance status and poor compliance) and she is monitored with general follow-ups. *Results:* The patient after the surgical phase had a recovery without complications. The management of ureterocutaneostomy was home-based and

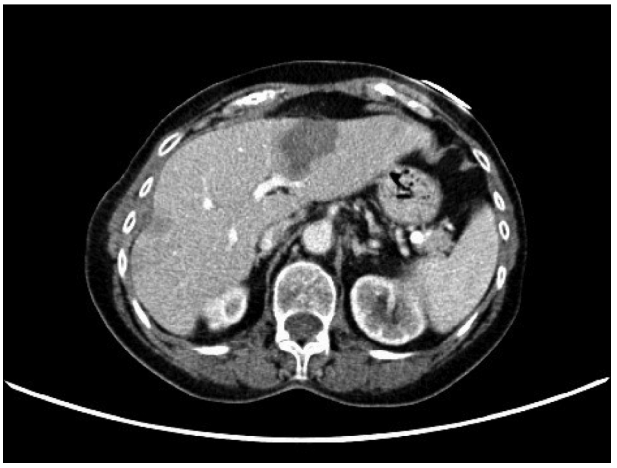

Figure 2. *February 2019, PET/CT (F-18 + FDG): Altered glucose metabolism in liver areas VII (SUVmax 5.31), VIII (SUVmax 11.5 vs. 3.91 previous PET control on 07/05/2018), III segment (SUVmax 11.6) and in VI segment (SUVmax 6.92).*

all tests were negative until the appearance of asymptomatic liver metastases. *Discussion and Conclusion:* The patient had a long disease-free duration after radical surgery. The presentation of hepatic metastases observed in our case was an event that emerged in the less-awaited follow-up compared to the possibility of local secondary or recurrence that we would have expected from the squamous cell carcinoma of urinary bladder.

1 Jagtap SV, Sarda SD, Demde RB, Huddedar AD and Jagtap SS: Primary squamous cell carcinoma of urinary bladder - a rare histological variant. J Clin Diagn Res *9(11)*: ED03-4, 2015. PMID: 26674660. DOI: 10.7860/JCDR/2015/14099.6746

2 Eble JN, Sauter G, Epstein J and Sesterhenn I: Pathology & genetics tumors of the urinary system and male genital

organs. WHO Classification of Tumours, 3rd Edition, Volume 7. IARC Press Lyon, France, 2004.
3 Tavora F and Epstein JI: Bladder cancer, pathological classification and staging. BJU Int *102(9 Pt B)*: 1216-1220, 2008. PMID: 19035884. DOI: 10.1111/j.1464-410X.2008.07962.x

62
DIAGNOSTIC RESULTS OF ^{18}F-CHOLINE PET/MRI FOR RECURRENT PROSTATE CANCER AFTER RADICAL PROSTATECTOMY

Tommaso Prayer Galetti[1], Carmelo Lacognata[2], Alessandro Morlacco[1], Alex Ahn Li Nguyen[1], Valeria Lami[1], Pietro Zucchetta[3], Filiberto Zattoni[1] and Giacomo Novara[1]

[1]Urology Clinic - Department of Surgery, Oncology, and Gastroenterology, University of Padua, Padua, Italy; [2]Radiology Unit - Department of Medicine DIMED, University of Padua, Padua, Italy; [3]Nuclear Medicine Unit, Department of Medicine DIMED, University of Padua, Padua, Italy

Background and Aim: The combination of high-resolution anatomical procedures (MRI) and nuclear functional imaging (PET with ^{18}F-choline) could improve the diagnosis and early detection of prostatic cancer recurrences after radical prostatectomy (RP) and allow a timely and targeted therapeutic approach. This study aimed to describe the results of PET-MRI in patients with biochemical recurrence after RP and identify potential predictors of PET/MRI positivity. *Patients and Methods:* During the period between September 2014 and May 2019, 31 patients with biochemical recurrence after radical prostatectomy and PSA lower than 1.0 ng/ml underwent PET/MRI. Complete data on the RP histopathology, timing of biochemical recurrence (BCR), PSA and its derivatives, and PET/MRI detailed results were collected. PET/MRI was performed with a Hybrid Siemens Biograph mMR administering 3 MBq/Kg of ^{18}F-Choline. All patients underwent subsequent radiotherapy with post diagnostic PET/MRI (post PET/MRI RT). We considered true-positive, patients with positive PET/MRI and PSA nadir lower than 0.1 ng/ml following RT performed after PET/MRI. *Results:* The median age at PET/MRI was 70 years (IQR=67-75) and the time between RP and PET/MRI was 56.5 (IQR=30-104) months, while BCR occurred at a median time of 50 (IQR=28-89) months after RP. The Gleason Score on the specimen after RP was 6 in 16.1% of patients, 7 in 48.4%, 8 in 16.1% and 9-10 in 19.4%. The 44.4% of patients had pT3a-b disease. Twenty-eight patients did not undergo radiation after RP while 3 underwent salvage RT; androgen deprivation therapy was used in 4 patients as salvage treatment. The median PSA at PET/MRI scan was 0.40 ng/ml (IQR=0.27-0.71) with a PSA-DT of 0.7 years (IQR=0.3-1.97). Overall, PET/MRI was positive in 25 patients (80.6%); of these, in 17 the PET/MRI positivity was in the anastomotic/prostate bed, 1 in the seminal vesicle bed, and non-local in 7 (pelvic lymph nodes). No significant differences between positive and negative PET/MRI imaging were seen for PSA-DT, PSA velocity, PSA slope and time-to-BCR, while PSA at PET/MRI approached statistical significance (0.5 *vs*. 0.27 ng/ml, p=0.06). No significant differences were seen analysing pT, pGS and pre-test treatments (all p>0.1). Diagnostic accuracy of PET/MRI was 55.1% compared to 51.7% for PET and 48.2% for MRI as a single imaging modality. PET/MRI positive predictive value was 83.3%. *Conclusion:* PET/MRI is a promising tool and can provide clinically useful data on local and nodal recurrence even at low levels of PSA; however, the definition of a precise PSA threshold requires larger series.

63
DOSE ESCALATED PELVIC RADIOTHERAPY FOR PROSTATE CANCER IN DEFINITIVE OR POSTOPERATIVE SETTING: A RETROSPECTIVE STUDY

Giulio Francolini[1], Lucia Pia Ciccone[1], Alessio Bruni[2], Anna Peruzzi[1], Marco Perna[1], Francesco Cuccia[3], Rosario Mazzola[4], Luca Triggiani[5], Simona Borghesi[6], Beatrice Detti[1], Isacco Desideri[1] and Lorenzo Livi[1]

[1]Division of Radiation Oncology, Radiation Oncology Unit AOU Careggi - University of Florence, Firenze, Italy; [2]Division of Radiotherapy, AOU Modena, Modena, Italy; [3]Radiation Oncology School, University of Palermo, Palermo, Italy; [4]Division of Radiation Oncology, Sacro Cuore Don Calabria Hospital, Negrar, Italy; [5]Division of Radiation Oncology, University and Spedali Civili Hospital, Brescia, Italy; [6]Division of Radiation Oncology, San Donato Hospital, Arezzo, Italy

Background and Aim: Whole-pelvis radiotherapy in prostate cancer is still a matter of debate, and several randomized trials failed to show improvement in clinical outcomes after this approach (1). The conventional approach in this setting is represented by a prophylactic dose of 45 Gy to the pelvic volume, which may be considered insufficient to eradicate regional nodal disease. However, adequate staging procedures (*e.g.* choline PET/CT) allows to detect nodal disease, and modern intensity modulated radiotherapy enables to deliver higher whole-pelvis radiotherapy doses (50-54 Gy) with acceptable toxicities (2). The use of a boost

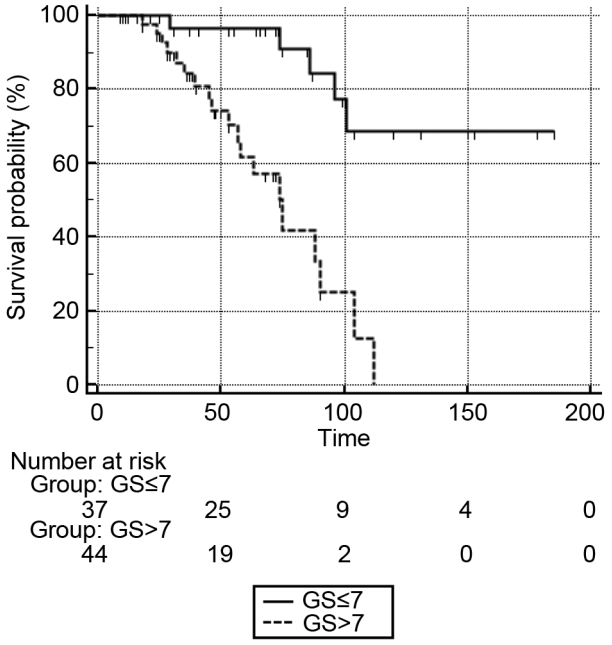

Figure 1. *RFS univariate analysis by GS.*

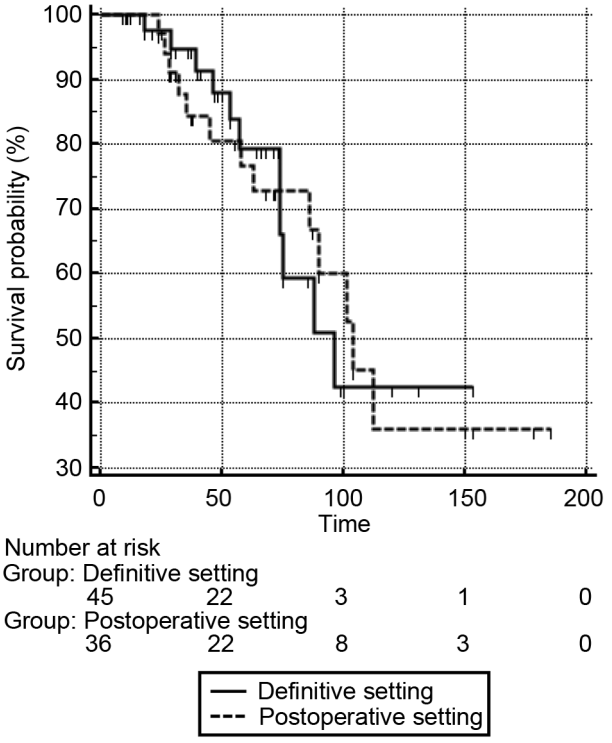

Figure 2. *RFS univariate analysis by primary treatment.*

on nodal disease is widely accepted, and contemplated in many prospective protocols, although literature regarding this approach is sparse and mostly based on limited number of treated patients (3). In the current multicentric series, data about patients treated with intensity modulated radiotherapy boost on pelvic nodal disease were reported in order to assess outcomes after this approach and provide evidence about its efficacy and feasibility. *Patients and Methods:* Clinical records about 81 patients consecutively treated in 5 different institutions since April 2004 to November 2018 were reviewed. All patients underwent postoperative or definitive treatment on prostate bed or prostate and whole pelvis. Patients included had pelvic nodal disease identified at staging evaluation with CT scan, MRI or choline PET/CT and received intensity modulated radiation therapy boost on macroscopic disease detected. Both simultaneous integrated and sequential techniques were allowed. Long course concomitant androgen deprivation therapy was prescribed in all patients. Data about treatment setting, baseline characteristics, survival and adverse events were retrospectively collected and reported. Kaplan-Meyer analysis were performed to explore the correlation between prognostic factors (Gleason score < *vs.* >7, definitive *vs.* postoperative setting, total dose administered to macroscopic nodal disease < *vs.* >60 Gy) and relapse-free survival. Gastrointestinal (GI) and genitourinary (GU) RT-related events were recorded according to Common Terminology Criteria for Adverse Events (CTCAE) score v.4.03. *Results:* Overall, 60 and 21 patients underwent postoperative and definitive treatment, respectively. After 68 months of median follow up, 24 patients (29.6%) experienced recurrence (5 local, 2 regional and 17 distant metastases, 22%, 8% and 70%, respectively). The estimated median relapse free survival time was 101 months (95%CI=86-112 months) in the analyzed population. At univariate analysis, Gleason score >7 was significantly related to relapse free survival (p<0.0001) (Figure 1), no correlation between relapse free survival and previous radical prostatectomy (p=0.94) (Figure 2) or radiation dose administered to nodal disease was found (p=0.25). Multivariate analysis confirmed Gleason score as an independent prognostic factor related to relapse-free survival. Toxicity was mild, with only 5 acute G>2 (2 GI and 3 GU, respectively) and 1 G2 late GU adverse events reported.*Conclusion:* Intensity modulated radiotherapy whole-pelvis radiotherapy with boost on macroscopic pelvic disease yielded optimal disease control with a favorable toxicity profile. Interestingly, only Gleason score significantly predicted clinical outcome, while previous radical surgery had no impact on relapse-free survival. Thus, despite the poor prognostic subset of these patients (high-risk localized prostate cancer or macroscopic pelvic nodal recurrence after radical prostatectomy), dose escalated pelvic intensity modulated radiotherapy with concomitant androgen

deprivation therapy allowed curative treatment in most of the population analyzed. Furthermore, 70% of relapsed patients had a distant metastasis only, underlining the importance of distant rather than local control of disease in this high-risk subset of patients. Considering the impact of radical prostatectomy on patients reported quality of life in terms of urinary continence and erectile dysfunction, role of surgery in patients with pelvic nodal disease should be thoroughly discussed with the patient. Potential further increase yielded by association with androgen receptor targeted agents should in this setting should be explored.

1 Lawton CA, DeSilvio M, Roach M, Uhl V, Kirsch R, Seider M, Rotman M, Jones C, Asbell S, Valicenti R, Hahn S and Thomas CR Jr.: An update of the phase III trial comparing whole pelvic to prostate only radiotherapy and neoadjuvant to adjuvant total androgen suppression: updated analysis of RTOG 94-13, with emphasis on unexpected hormone/radiation interactions. Int J Radiat Oncol Biol Phys *69*: 646-655, 2007. PMID: 17531401.

2 Alongi F, Fiorino C, Cozzarini C, Broggi S, Perna L, Cattaneo GM, Calandrino R and Di Muzio N: Intensity Modulated Radiotherapy significantly reduces acute toxicity of whole-pelvis irradiation in patients treated with post-operative adjuvant or salvage radiotherapy after radical prostatectomy. Radiother Oncol *93*: 207-212, 2009. PMID: 19766338. DOI: 10.1016/j.radonc.2009.08.042

3 Engels B, Soete G, Tournel K, Bral S, De Coninck P, Verellen D and Storme G: Helical tomotherapy with simultaneous integrated boost for high-risk and lymph node-positive prostate cancer: early report on acute and late toxicity. Technol Cancer Res Treat *8(5)*: 353-359, 2009. PMID: 19754211.

66
HOW TO PRESERVE SEXUAL FUNCTION IN PENILE CANCER: A SINGLE-CENTER COMPARATIVE STUDY

Omid Sedigh, Carlo Ceruti, Massimiliano Timpano, Marco Falcone, Mirko Preto, Maurizio Barale, Giuseppe Pizzuto, Simone Agosti and Paolo Gontero

Division of Urology, Città Della Salute e Della Scienza, University of Turin, Turin, Italy

Background/Aim: Penile cancer is a rare neoplasia with a potential for local invasion and metastatic extension. Penile cancer can be cured in over 80% of cases if diagnosed early. However, local treatment can be mutilating and devastating for the patient's psychological well-being. In localized penile cancer the radical treatment can offer even better oncological outcomes but glansectomy can destroy the sexual life of a patient. Recent advances in surgical techniques and technologies have allowed for many organ-sparing techniques with acceptable psychosexual and oncological outcomes. Following the EAU Guidelines the glans-sparing approach or wide local excision (WLE) has been offered to more and more patients lately. We want to evaluate the oncological and sexual outcomes in patients with localized penile cancer comparing two techniques: wide local excision and glansectomy. *Patients and Methods:* We compared retrospectively the postoperative functions in patients affected by localized (<T2a) penile cancer and treated with wide local excision (group A) or glansectomy and uretroglanduloplasty (group B). All patient with palpable adenopathy were excluded. A total of 49 patients underwent surgery between January 2016 and January 2019 and surgery was performed by a single surgeon. Patients with a severe erectile dysfunction or not interested in maintaining an active sexual life were excluded. We evaluated the stretched length and the sexual function was assessed by international index of erectile function (IIEF) and sex encounter profile (SEP). All patients were asked to complete a questionnaire before surgery and 6 months after. Oncological follow-up was at least 10 months and consists in physical examination and inguinal US at 3, 6 and 9 months. Statistical analysis was performed by two-tailed tests: Student's *t*-test and Chi Squared test. *Results:* The median patient's age at the presentation was 54 years (range=39-77 years). Pre-operative stretched length was 13 cm for both groups. Pre-operative IIEF was 21 for group A (15-25), 19 for group B (14-25). A total of five (30%) patients underwent WLE and 34 patients underwent glansectomy with uretroglanduloplasty. The stretched length loss was 12 mm in group A, 27 mm in group B. A decrease in post-operative IIEF was recorded in both groups, but was statistically significant only in group B. SEP was not significantly modified in group A while group B reported a significant loss in achieving penetrative intercourse. Oncological outcomes were excellent for both groups: histopathological examination of the specimen confirmed squamous cell carcinoma and tumor-free surgical margins were obtained in all cases. One patient scheduled for WLE had a positive margin at the definitive histological examination and underwent glansectomy. Four patients developed recurrence (after 13-28 months), one from group A, three from group B and not significant differences were found. *Conclusion:* The diagnosis of penile cancer does not mean the end of sexual life for a patient. With careful patient selection and meticulous follow-up, most patients with localized penile carcinoma can be offered glans preserving surgery. Obviously, this kind of surgery has to be managed in a reference center. When feasible for the features of neoplasia, WLE should be performed and lead to better functional outcomes and better sexual health without adding oncological risk for recurrences.

67

ANTITUMOR EFFECTS OF PAK4-INHIBITION IN *IN VIVO* AND *IN VITRO* PROSTATE CANCER MODELS

Alessandro Colapietro[1], Andrea Mancini[1], Alessandra Rossetti[1], Vincenzo Mattei[2], Stefano Martellucci[2], Adriano Angelucci[3], Giovanni Luca Gravina[4] and Claudio Festuccia[1]

[1]Laboratory of Radiobiology, Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy; [2]Biomedicine and Advanced Technologies Rieti Center, Sabina University, Rieti, Italy; [3]Laboratory of General Pathology, Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy; [4]Radiotherapy Unit, Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy

Background: Prostate cancer represents 11% of all cancers and 9% of cancer-related deaths in European men (1, 2). The treatment of prostate cancer includes radical prostatectomy, radiations and hormonal therapy (3). To date, although the improvements of care and of outcome of the disease, further efforts must to be put in place for increase the efficacy of treatment and reduction of the relapse. So, in the last years have been identified different molecular targets in prostate cancer, useful for the generation of new therapeutic strategies (4, 5). Among these new targets PAK4 raised a great interest for its importance in prostate cancer progression and survival (6, 7). In our work we resumed the antitumor effects of PAK4 inhibition in four prostate cancer cells (PC3, DU145 and 22RV1) through *in vivo* and *in vitro* experiments. *Materials and Methods*: PC3, DU145, and 22RV1 prostate cancer cells were subcutaneously injected in the flank of nu/nu CD1 mice, treated with PAK4-inhibitor and monitored over the time for tumor growth rate respect to untreated animals. In parallel, the prostate cancer cells were cultured and treated for the evaluation of different properties, such as proliferation, cell death induction, autophagy, migration, through western blotting, FACS analysis, and wound healing repair assays. *Results: In vivo* experiments showed that KPT-8752 reduced cancer growth of about 25-60% in relation to the cell line, respect to the untreated group. Indeed, 22RV1 cell lines seemed to be the most sensitive, while the PC3 cell line resulted to be very less sensitive to the inhibitor. The *in vitro* results, defined that apoptosis occurred in 22RV1 and DU145 cells when KPT8752 was administered proven by caspase 3 cleaved appearance, while in PC3 cells the activation of the autophagy program was very clear, testified by the increase of Beclin1 and LC3IIb levels. In all the cell lines the wound healing repair assay showed a reduction of migratory capacity, in a dose-dependent way with the inhibitor. *Discussion*: Our results indicate that PAK4-inhibitor KPT-8752 delayed tumor growth in treated mice, respect to the control group. In association to this, the overall tumor weight in treated animals resulted to be lower in comparison to untreated animals. Regarding *in vitro* results, they showed that the three prostate cancer cells exhibited a different behavior when exposed to the PAK4-inhibitor. Indeed, by the evaluation of two important mechanisms related to cancer survival, such as apoptosis and autophagy, the different prostate cancer cell seemed to be undertaking different faith. This, could be explained by the different genetic asset own of the cells. Moreover, in all the three cell lines used is evident a reduction of the migration when compared to control cells, when KPT-8752 was administered. *Conclusion:* Our results, in agreement with previous studies, confirm that PAK4 is a suitable therapeutic target for prostate cancer. The role of PAK4 in tumorigenesis and sustenance of prostate cancer is well known and these results spur us to continue to investigate the implication of the inhibition of this marker and identify new strategies for counteract its functions in the disease.

1 Bray F, Sankila R, Ferlay J and Parkin DM: Estimates of cancer incidence and mortality in Europe in 1995. Eur J Cancer *38*: 99-166, 2002. PMID: 11750846.

2 Black RJ, Bray F, Ferlay J, Parkin DM: Cancer incidence and mortality in the European Union: Cancer registry data and estimates of national incidence for 1990. Eur J Cancer *33*: 1075-1107, 1997. PMID: 9376190.

3 Aus G, Abbou CC, Bolla M, Heidenreich A, Schmid HP, van Poppel H, Wolff J, Zattoni F and European Association of Urology: EAU guidelines on prostate cancer. Eur Urol *48*: 546-551, 2005. PMID: 16046052.

4 Saad F, Shore N, Zhang T, Sharma S, Cho HK and Jacobs IA: Emerging therapeutic targets for patients with advanced prostate cancer. Cancer Treat Rev *76*: 1-9, 2019. PMID: 30913454.

5 Fujii S and Kagechika H: Androgen receptor modulators: a review of recent patents and reports (2012-2018). Expert Opin Ther Pat *6*: 439-453, 2019. PMID: 31092069.

6 Won SY, Park JJ, Shin EY and Kim EG: PAK4 signaling in health and disease: defining the PAK4-CREB axis. Exp Mol Med *51(2)*: 11, 2019. PMID: 30755582. DOI: 10.1038/s12276-018-0204-0

7 King H, Nicholas NS and Wells CM: Role of p-21-activated kinases in cancer progression. Int Rev Cell Mol Biol *309*: 347-387, 2014. PMID: 24529727. DOI: 10.1016/B978-0-12-800255-1.00007-7

68

NEOADJUVANT CHEMOTHERAPY PLUS RADICAL CYSTECTOMY *VERSUS* RADICAL CYSTECTOMY IN CT2 BLADDER CANCER: A MULTICENTER STUDY

Andrea Giordano[1], Peter Black[2], Adrian Fairey[3], Michael Cookson[4], Evan Yu[5], Wassim Kassouf[6], Marc Dall'Era[7], Srikala Sridhar[8], John McGrath[9], Jonathan Wright[10], Andrew Thorpe[11], Todd Morgan[12], Siamak Daneshmand[13], Jeff Holzbeierlein[14], Trinity Bivalacqua[15], Scott North[16], Daniel Barocas[17], Yair Lotan[18], Petros Grivas[19], Andrew Stephenson[20], Jay Shah[21], Bas Van Rhijn[22], Philippe Spiess[23], Shahrokh Shariat[24], Francesco Soria[1] and Paolo Gontero[1]

[1]Division of Urology, Department of Surgical Sciences, Torino School of Medicine, Turin, Italy;
[2]Division of Urology, Department of Urologic Sciences, University of British Columbia, Vancouver, BC, Canada;
[3]Division of Urology, University of Alberta, Edmonton, AB, Canada;
[4]Division of Urology, Department of Urology, University of Oklahoma College of Medicine, Oklahoma, OK, U.S.A.;
[5]Division of Oncology, Department of Medicine, Division of Oncology, University of Washington School of Medicine and Fred Hutchinson, Seattle, WA, U.S.A.;
[6]Division of Urology, Department of Surgery, McGill University Health Center, Montreal, MO, Canada;
[7]Division of Urology, Department of Urology, University of California at Davis, Davis Medical Center, Sacramento, CA, U.S.A.;
[8]Division of Urology, Princess Margaret Hospital, Toronto, ON, Canada;
[9]Division of Urology, Department of Surgery, Exeter Surgical Health Services Research Unit, Royal Devon And Exeter NHS Trust, Exeter, U.K.;
[10]Division of Urology, Department of Urology, University of Washington, Seattle, WA, U.S.A.;
[11]Division of Urology, Department of Urology, Freeman Hospital, Newcastle Upon Tyne, U.K.;
[12]Division of Urology, Department of Urology, University of Michigan Health System, Ann Arbor, MI, U.S.A.;
[13]Division of Urology, USC/Norris Comprehensive Cancer Center, Institute of Urology, University of Southern California, Los Angeles, CA, U.S.A.;
[14]Division of Urology, Department of Urology, University of Kansas Medical Center, Kansas City, KS, U.S.A.;
[15]Division of Urology, Department of Urology, The James Buchanan Brady Urological Institute, The Johns Hopkins School of Medicine, Baltimore, MD, U.S.A.;
[16]Division of Urology, Cross Cancer Institute, Edmonton, AB, Canada;
[17]Division of Urology, Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, TN, U.S.A.;
[18]Division of Urology, Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX, U.S.A.;
[19]Division of Medicine, Department of Hematology and Medical Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH, U.S.A.;
[20]Division of Urology, Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, OH, U.S.A.;
[21]Division of Urology, Department of Urology, Stanford University School of Medicine, Stanford, CA, U.S.A.;
[22]Division of Urology Department of Urology, The Netherlands Cancer Institute - Antoni Van Leeuwenhoek Hospital, Amsterdam, the Netherlands;
[23]Division of Urology, Department of Genitourinary Oncology, H Lee Moffitt Cancer Center and Research Institute, Tampa, FL, U.S.A.;
[24]Division of Urology, Department of Urology, Medical University of Vienna, Vienna General Hospital, Vienna, Austria

Background: Cisplatin-based neoadjuvant chemotherapy (NAC) followed by radical cystectomy (RC) is the standard and recommended treatment for clinical T2-T4aN0M0 bladder cancer (BCa). However, due to several reasons and despite high-level evidence in favor of NAC, compliance with this recommendation remains low, especially in cT2 disease. Actually, data from prospective randomized clinical trials (SWOG 8710 and BA06 30894) showed a greater survival benefit for patients with ^{3}cT3 disease compared to those with cT2 (survival gain of 42 *vs*. 19 months, respectively). Several attempts have been made with the aim to risk-stratify patients with muscle-invasive bladder cancer based on the presence of different preoperative risk factors such as clinical tumor stage, preoperative hydronephrosis, presence of lymphovascular invasion (LVI), histological variants and carcinoma *in situ* (CIS) at the time of transurethral resection (TURB). However, these trials have been usually conducted on patients who only underwent RC without NAC and, therefore, the related results should be considered with caution and mainly informative. Given the complexity of conducting a new RCT and the lack of direct comparisons in patients with clinical T2 disease, the aim of our study was to compare the efficacy of NAC and RC vs RC alone in a large multicenter cohort of cT2 patients without preoperative hydronephrosis. *Patients and Methods:* Patients were identified retrospectively from 21 Centers across Europe, Canada and the USA. Only patients with cT2N0M0 urothelial carcinoma of the bladder without preoperative hydronephrosis and with complete data regarding final pathology at RC were retained for the purpose of this study. Patients who received less than three cycles of NAC were excluded from the analyses. The primary and secondary endpoints of the study were pathological

response and overall survival, respectively. Complete response was defined as the absence of disease at surgery (pT0 pN0) while partial response as the presence of non-muscle invasive bladder cancer (pTa-Tis-T1 pN0) at RC. Multiple imputation was used to handle missing data for preoperative variables that were assumed to be missing at random for all covariates. To account for potential selection bias, observed differences in baseline characteristics between the two groups were controlled with inverse probability of treatment weighting (IPTW) analysis. IPTW-multivariable-adjusted analyses were performed to determine the independent predictive value of NAC on pathological and survival outcomes. *Results:* Overall, 619 patients (316 receiving NAC and RC and 303 treated only with RC) with complete data regarding final pathology were included in the study. Overall, 29% of patients receiving NAC and 3% of patients treated with only RC were classified as complete responders at RC. Partial response was observed in 22% of patients treated with NAC and in 21% of those without NAC. After IPTW-adjusted analysis, no differences between the groups in terms of preoperative characteristics such as age, gender, body-mass index (BMI), Charlson comorbidity index (CCI), performance status, smoking status and presence of variant histology, LVI or CIS at TURB were observed. On IPTW-adjusted multivariable logistic regression analyses that adjusted for the effect of standard prognosticators NAC was independently associated with complete response (HR=9.21, $p<0.001$). After a median follow up of 20 months (IQR=8-41), 123 patients experienced disease recurrence and 168 died. On IPTW-adjusted multivariable cox regression analysis NAC was not associated with overall survival ($p>0.05$). *Discussion and Conclusion:* In our multicenter retrospective propensity score-based analysis, NAC showed to be associated with pathologic complete response at RC even in patients with clinical T2 and absence of preoperative hydronephrosis, thus generating new evidence in favor of NAC also in low-risk patients. However, we were not able to demonstrate a survival gain in favor of NAC. Limitations are inherent to the retrospective nature of the study.

71
CLAMP-LESS PARTIAL ROBOTIC NEPHRECTOMY (RPN): SURGICAL FEASIBILITY, PERCENTAGE OF POSITIVE MARGINS AND INTRA- AND POST-OPERATIVE COMPLICATIONS

Gianluigi Taverna[1,2], Matteo Zanoni[1], Paolo Vota[1], Matteo Justich[1], Giovanni Toia[1], Giuseppe Malagola[1], Alberto Mandressi[1], Fabio Grizzi[2] and Giorgio Guazzoni[2]

[1]Department of Urology, Humanitas Mater Domini, Rozzano, Italy;
[2]Department of Urology, Humanitas Clinical and Research Center, Rozzano, Italy

Background/Aim: Robotic partial nephrectomy (RPN) has emerged as an attractive minimally-invasive nephron-sparing surgical option. However, on-going concerns about RPN include: prolonged ischemia time with potential implications on renal functional outcomes. We detail the technique and present perioperative outcomes of our technique of zero-ischemia RPN for renal tumours (Clamp-less robotic surgery). *Patients and Methods:* From January 2011 to September 2019, 181 patients underwent PN Clamp-Less robotic assisted care. RPN was offered to all patients with even partially exotic lesions, regardless of renal-vascular anatomy, contralateral kidney characteristics or renal function. A total of 5/181 had dual unilateral tumours. A total of 7/181 had monorene. The mean diameter of the neoplasms was 3.9 cm (2.5-5.5 cm), the lesions were localized: 101 right kidney, 80 left kidney, 47 upper polar, 53 middle, 80 lower. The operating technique involved the use of 3 robotic doors (camera + scissors and Prograsp) + 1 accessory door. After isolation of the kidney and the lesion, hot enucle/tumorectomy was performed with subsequent diathermocoagulation of the enucleoresezine bed with positioning of fibrin glue and haemostatic material. *Results:* The RPN zero-ischemia has been successful in all cases without the need for hilar clamping. The size of the median tumor (range) was 3.9 (2.5-5.5) cm. The time of warm ischemia was zero in all cases. The mean operating time was 60 (45-100) min, the estimated blood loss was 120 (50-300) ml. The average hospital stay was 4 (3-6) days. There were no intraoperative complications; 4/181 (0.02%) patients presented a post-operative haemorrhage that required a decisive laparotomy. None of the 4 patients had bleeding from the resection margins. A total of 2 patients was bleeding from kidney fat and 2 from a robotic port. All tumour samples had negative surgical margins. The absolute median decrease in serum creatinine and the estimated glomerular filtration rate at discharge were 0 (0.2-0.7) mg/dl ($p=0.4$) and 5 (-16-29) ml/min for 1.73 m (2) ($p=0.8$), respectively. *Conclusion:* Zero-ischemic RPN for kidney cancer is safe and feasible. The elimination of hot ischemia can optimally preserve renal function. Randomized prospective studies are required to confirm any renal functional advantages of RPN without clamping.

72
PERCUTANEOUS RADIOFREQUENCY ABLATION OF SMALL RENAL MASSES DOES NOT SIGNIFICANTLY REDUCE RENAL VOLUME IN HEREDITARY RENAL CELL TUMOUR PATIENTS

Mattia Sibona[1], Marco Allasia[1], Carlo Gazzera[2], Luca Alois[2], Marco Calandri[2], Giancarlo Marra[1], Maurizio Barale[1] and Paolo Gontero[1]

[1]Division of Urology, Department of Surgical Sciences, A.O.U. Città della Salute e della Scienza – Molinette Hospital, University of Turin, Turin, Italy;
[2]Division of Radiology, A.O.U. Città della Salute e della Scienza – Molinette Hospital, University of Turin, Turin, Italy

Background/*Aim:* Patients affected by hereditary renal cell tumour syndromes [*i.e.* Von Hippel – Lindau (VHL) syndrome, hereditary papillary renal tumour syndrome] are characterized by high incidence of small renal masses. Differently from nonhereditary small renal masses, percutaneous radiofrequency (RF) can be considered a first line therapy in these patients, due to its lower impact on healthy renal parenchyma, compared to surgery. The aim of our study was to objectify the effect of RF by comparison of pre and postprocedural, MRI-determined, renal volumes. *Patients and Methods:* We considered 18 small renal masses, diagnosed in 7 different patients attending our multidisciplinary Centre for hereditary renal cell tumours care at the Molinette Hospital in Turin. A total of 6 patients were affected by VHL syndrome, 1 was affected by hereditary papillary tumour syndrome. Preoperative imaging was obtained with renal MRI. In case of synchronous lesions, each renal mass was considered separately for the volumetric analysis. Postoperative imaging was also obtained with renal MRI. We did not include in our analysis cases of re – treatment of persistent disease foci after the first RF. *Results:* The median (IQR) age of the patients was 37 (31-45) years. Seven lesions were unique at diagnosis, while 11 presented as synchronous to one or two other lesions, either in the same or contralateral kidney. The median (IQR) maximum diameter of the lesions was 20 (10.25-23.75) mm. The median (IQR) volume of the lesions was 2.08 (0.57-4.38) cm^3. RF ablation of the lesions was achieved through US guided, percutaneous approach in all cases. In 1 case, a trans-hepatic approach was needed due to the unfavourable position of the tumour. First postoperative imaging with renal MRI was obtained after a median time of 93 days. The ablation was complete in 16 cases (89%). In 2 cases, postoperative imaging revealed persistent disease, which was successfully treated with a subsequent re – do RF. No major post-operative complications were recorded. In 2 cases, a Clavien I complication (post-procedural flank pain) was noticed. The median (IQR) maximum diameter of the scar resulting from the RF was 20.5 (17-27.75) mm, while its median (IQR) volume was 1.88 (1.46-6.20) cm^3. The median (IQR) preoperative renal volume was 157.3 (150.8-200.2) cm^3; the median (IQR) postoperative renal volume was 152.0 (147.7-200.9) cm^3. The comparative analysis showed no significant difference between pre and postoperative renal volume (p=0.84). Moreover, also the volume of the post-operative scar did not differ significantly from that of the original lesion (p=0.41). *Conclusion:* Percutaneous RF did not cause a significant renal volume reduction when performed for the treatment of small renal masses in patients affected by hereditary renal cell tumours.

74

DOES PHOTODYNAMIC DIAGNOSIS (PDD) IMPROVE THE QUALITY OF TURB BY DIMINISHING RESIDUAL DISEASE RATE?

Gianluigi Taverna[1], Fabio Grizzi[2], Matteo Zanoni[1], Paolo Vota[1], Matteo Justich[1], Giovanni Toia[1], Linda M. Thiel[3], Brian Stork[4], Desiree L. Miller[5], Lorenzo Tidu[6], Alberto Mandressi[1] and Giorgio Guazzoni[7]

[1]Department of Urology, Humanitas Mater Domini, Castellanza, Italy;
[2]Department of Immunology and Inflammation, Humanitas Clinical and Research Center, Milan, Italy;
[3]McAuley School of Nursing, College of Health Professions, University of Detroit Mercy, Detroit, MI, U.S.A.;
[4]Department of Urology, University of Michigan, School of Medicine, Ann Arbor, MI, U.S.A.;
[5]Mercy Health Visiting Nurses Services and Hospice Services, Muskegon, MI, U.S.A.;
[6]Military Veterinary Center, CEMIVET, Grosseto, Italy;
[7]Department of Urology, Humanitas Clinical and Research Center, Milan, Italy

Background: Thanks to the continuous research in the field of the detection of bladder cancer (BCa), the role of photodynamic diagnosis (PDD) applied in its diagnosis is well nowadays established. In the literature PDD has shown to improve overall BCa detection of about 20% when compared to white light (WL), with an additional detection rate of around 40% in case of carcinoma *in situ* (CIS). When moving from a diagnostic to an operative setting, little evidence exists regarding the impact of photodynamic diagnosis on transurethral resection of the bladder (TURB). Therefore, the aim of our study was to evaluate the ability of PDD compared to white light to enhance the quality of transurethral resection of bladder by improving the completeness and precision, diminishing residual disease rate, of the endoscopic resection. To reach this aim we presented the experience of our Center. *Patients and Methods:* We performed a prospective single-center analysis of patients undergoing transurethral resection of the bladder for primary bladder cancer (tumor size >1 cm). The trial was performed by a single expert surgeon in two-steps. First, cystoscopy and complete TURB were performed

under white light; bladder biopsies were taken in case of suspected areas outside the main lesion. Then, in a second moment and only when the procedure was deemed complete by the surgeon, a PDD-guided cystoscopy was performed. In case of PDD-positivity in the area of the transurethral resection of the bladder (at the level of the resection bed or perilesional), the resection was continued until no evidence of residual fluorescence was demonstrated, so until the endoscopic finding was completely negative. The specimens obtained from the photodynamic diagnosis transurethral resection of the bladder were sent separately for pathologic assessment. PDD-guided biopsies were taken in the case of carcinoma *in situ*-suspected areas. The main endpoint of the study was to evaluate the presence of residual disease at the time of photodynamic diagnosis-transurethral resection of the bladder (PDD-TURB). *Results:* Overall, 42 patients underwent the two-step procedure we described above. When PDD was added and used after the completion of the first step, a residual fluorescence at the level of the previous resection site (in white light) was found in 15 patients (36%). The presence of residual disease was pathologically confirmed at the specimen in 6 out of 15 patients (40%). The pathological analysis revealed the presence of Ta, CIS and T1 residual tumor in 2, 1 and 3 patients, respectively. Notably, in two cases the addition of PDD changed the risk-category of the tumor: in one patient the diagnosis changed from Ta low-grade (LG) to T1 high-grade disease while in the other patient from TaLG to TaLG+CIS. Moreover, photodynamic diagnosis confirmed the ability to improve the BCa diagnosis and, especially, that of CIS. Actually, the evaluation of the pathology of the biopsies performed on PDD-suspected lesions outside the resection area revealed the presence of concomitant carcinoma *in situ* (CIS) in 5 cases and of Ta and T1 tumors in 3 and 2 patients, respectively. *Discussion and Conclusion:* In this exploratory prospective study, we showed our experience with this diagnostic tool used in the detection of bladder cancer. Transurethral resection of bladder performed under white light showed to be not complete in one out of seven patients. The addiction of PDD during the resection showed to enhance the quality of the transurethral resection of bladder by improving its completeness. Based on these preliminary data, photodynamic diagnosis may be used not only as a diagnostic tool but also as an instrument to improve the quality of transurethral resection of bladder (TURB) and to diminish the presence and the rate of residual disease.

77
HIGHLY-TRAINED DOGS' OLFACTORY SYSTEM DOES NOT DISCRIMINATE LOW- AND HIGH-RISK PROSTATE CANCER IN URINE SAMPLES

Gianluigi Taverna[1], Lorenzo Tidu[2], Fabio Grizzi[3], Alberto Mandressi[1], Paolo Sardella[2], Giuseppe La Torre[4], Matteo Zanoni[1], Paolo Vota[1], Matteo Justich[1], Giovanni Toia[1], Giuseppe Malagola[1] and Giorgio Guazzoni[4]

[1]Department of Urology, Humanitas Mater Domini, Castellanza, Italy; [2]Italian Ministry of Defences, Military Veterinary Center, CEMIVET, Grosseto, Italy; Departments of [3]Immunology and Inflammation and [4]Urology, Humanitas Clinical and Research Center, Rozzano, Italy

Background/Aim: To establish the diagnostic accuracy, in terms of sensitivity and specificity at which a rigorously trained canine olfactory system can discriminate high-risk prostate cancer (HPC) *versus* low risk prostate cancer (LPC) specific volatile organic compounds (VOCs) in urine samples (1-3). *Materials and Methods:* Two female and one male German Shepherd explosive detection dogs were trained to identify HPC-specific VOCs in urine samples and tested on 550 subjects (165 with HPC *vs*. 385 with LPC). This cross-sectional design for diagnostic accuracy involved Humanitas Mater Domini and the Italian Ministry of Defense's, Military Veterinary Center. *Results:* The dogs achieved the following performances: Dog 1 achieved a sensitivity of 1% and specificity of 0.7% Dog 2 achieved a sensitivity of 0,2% and specificity of 0.1% Dog 3 achieved a sensitivity of 0.1% and specificity of 0.7%. *Conclusion:* A trained canine olfactory system did not discriminate between HPC and LPC. Evidently, for highly-trained dogs' olfactory system, high-risk cases did not differ in terms of VOCs compared to LPC. Apparently, the VOCs metabolism is the same for HPC and LPC.

1 Taverna G, Tidu L and Grizzi F: Sniffing out prostate cancer: a new clinical opportunity. Cent European J Urol *68(3)*: 308-310, 2015. PMID: 26568871. DOI: 10.5173/ceju.2015.593

2 Taverna G, Tidu L, Grizzi F, Torri V, Mandressi A, Sardella P, La Torre G, Cocciolone G, Seveso M, Giusti G, Hurle R, Santoro A and Graziotti P: Olfactory system of highly trained dogs detects prostate cancer in urine samples. J Urol *193(4)*: 1382-1387, 2015. PMID: 25264338. DOI: 10.1016/j.juro.2014.09.099

3 Taverna G, Tidu L, Grizzi F, Stork B, Mandressi A, Seveso M, Bozzini G, Sardella P, Latorre G, Lughezzani G, Buffi N, Casale P, Fiorini G, Lazzeri M and Guazzoni G: Highly-trained dogs' olfactory system for detecting biochemical recurrence following radical prostatectomy Clin Chem Lab Med *54(3)*: e67-70, 2016. PMID: 26402886. DOI: 10.1515/cclm-2015-0717

78

SAFETY AND EFFICACY OF BLADDER-PRESERVING THERAPY FOR MUSCLE INVASIVE BLADDER CANCER: A MONOINSTITUTIONAL EXPERIENCE

Luca Frassinelli[1], Ercole Mazzeo[1], Roberto Sabbatini[2], Claudia Mucciarini[3], Giulia Alicino[1], Marco Vernaleone[1], Massimiliano Nicolini[4], Frank Lohr[1] and Alessio Bruni[1]

[1]Radiotherapy Unit, Department of Oncology And Hematology, University Hospital "Policlinico of Modena", Modena, Italy;
[2]Medical Oncology Unit, Department of Oncology And Hematology, University Hospital "Policlinico of Modena", Modena, Italy;
[3]Medical Oncology Unit, "Ramazzini Hospital", Carpi-Modena, Italy;
[4]Medical Oncology Unit, AUSL Modena – District of Sassuolo, Modena, Italy

Background/Aim: Bladder cancer is a common neoplasm worldwide particularly frequent in the older age and in the western countries (1). Men are more often diagnosed than women. At the time of diagnosis of bladder cancer 70% had not had a muscle invasive type, while 30% had muscle invasive (2). Non-muscle invasive bladder cancer can be treated with local radical surgical approach such as transurethral resection of bladder tumor with adjuvant intravescical instillation of an active agent (BCG). On the other side, for the muscle invasive disease two different therapeutic options should be proposed: radical cystectomy with or without neoadjuvant/adjuvant chemotherapy or a trimodality approach (endoscopic transurethral resection of macroscopic bladder tumor followed by concomitant radiotherapy and platinum-based chemotherapy). Bimodal approach (surgery followed by adjuvant radiotherapy) is an alternative option that could be considered in a selected setting such as frail or older patients (3). The aim of this study was to retrospectively evaluate acute side-effects and efficacy of a multimodal approach characterized by radical radiotherapy with or without concurrent chemotherapy after transurethral resection of bladder tumor in patients with non-metastatic muscle-invasive bladder cancer. *Patients and Methods:* Between August 2012 and December 2018, 9 patients (pts) were submitted to cystoscopy with histological diagnosis of muscle-invasive bladder cancer. Median age was 75 years (range=63-85 years). Eight pts were male and one female. Four pts were former smokers, while 4 were still active smokers at time of treatment; only one patient was a never smoker. Eight pts had a performance status equal to 0 or 1 (according to ECOG scale) and only one had a performance status equal to 2. All pts were submitted to a complete restaging with post-surgery cystoscopy and chest abdominal CT scan; furthermore, four pts were submitted to 18 FDG PET CT and one to bone scintigraphy. All pts had not distant metastasis while 2 patients had loco-regional disease at the final staging. All pts were submitted to single transurethral resection of bladder cancer (TURB), while only one was submitted to reTURB without evidence of residual tumour. Six patients had macroscopic residual tumour. Histological examination revealed high grade urothelial papillary carcinoma in all pts. Four pts were unfit to surgery approach while five pts choose bladder preserving treatment. All pts were submitted to radiotherapy with radical intent, receiving doses ranging from 56 Gy and 66 Gy: one patient was treated with doses lower than 60 Gy, while eight pts with 60 Gy or more. Six pts were submitted to radiotherapy in combination with chemotherapy (3 pts whit 5-fluorouracil plus mitomycine C, 1 pt with gemcitabine and 2 pts whit cisplatin), 1 patient received chemotherapy before radical radiotherapy. *Results:* At a median follow-up of 10 months (range=8-34 months) eight pts are still alive, while 1 died due to other causes. After ending radical treatment 8 pts were restaged through cystoscopy, while 9 through chest abdominal CT scan and one also to 18 FDG PET CT scan. Two pts showed a complete response, four patients a partial response, one had an apparent local disease progression after CT scan imaging with negative urinary cytology (histological specimen not obtained due to deterioration of ECOG performance status that did not allow cystoscopy). One patient had local recurrence and another showed locoregional lymph node progression. All pts completed the radiotherapy course without any treatment delay. Eight pts showed G1 or G2 acute toxicity, no G3 or more toxicity were registered according to CTCAE scale v4.0. Five pts had urinary diseases (dysuria and strangury in 3 pts and 1 pt respectively), 3 pts had diarrhea, one had proctitis while 3 pts had haematological toxicity. Regarding late toxicities 1 pts presented G1 or G2 toxicity, no G3 or more were reported. *Discussion and Conclusion:* In our single-institution retrospective analysis, trimodality or bimodality approach appeared to be safe and effective in the short-term management of muscle invasive bladder cancer in selected patients. Longer follow-up is needed to definitely validate these findings. Prospective or randomized clinical trial are still requested to compare this conservative approach to radical surgical approach.

1 Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J and Jemal A: Global cancer statistics, 2012. CA Cancer J Clin *68*: 87-108, 2015. PMID: 25651787. DOI: 10.3322/caac.21262
2 Vaidya A, Soloway MS, Hawke C, Tiguert R and Civantos F: *De novo* muscle invasive bladder cancer: is there a change in trend? J Urol *165(1)*: 47-50, 2001. PMID: 11125361.
3 Linee Guida AIRO-AIRB 2018: Neoplasia della vescica. Tumori *104(2S)*: S5-S7, 2018. PMID: 29893173. DOI: 10.1177/0300891618766104

79

EFFECTS OF BLADDER NECK RECONSTRUCTION ON URINARY CONTINENCE AFTER ROBOTIC ASSISTED LAPROSCOPIC PROSTATECTOMY: PRELIMINARY RESULTS OF A RETROSPECTIVE STUDY

Alessio Tognarelli, Tommaso Di Vico, Jacopo Durante, Alessandro Perotti, Francesco De Vita, Lorenzo Tesi, Susanna Lunardini, Simone Malloggi and Cesare Selli

Urology Unit, University of Pisa, University of Pisa, Pisa, Italy

Background/Aim: Vesico-urethral anastomosis (VUA) is one of the critical steps during laparoscopic radical prostatectomy (LRP) and robotic-assisted laparoscopic prostatectomy (RALP). Hoznek *et al*. (1) first described a continuous running suture for VUA, used to decrease operating time. Van Velthoven *et al*. (2) further simplified this technique, describing the preparation of the first anastomotic knot extracorporeally. This modification was soon adopted and popularized by many centres of expertise. Nevertheless, before this critical step, it is essential to deal with the bladder neck. Although the direct parachute-suture technique is an alternative option for some surgeons, in case of large volume prostates it is common to produce a wide bladder neck after the RP. In these situations, we consider it essential to reduce the bladder neck diameter before starting the VUA. Tennis-racket or anterior bladder-tube reconstruction have been described as technical options to manage the bladder neck during open RP (3). However, few publications using the aforementioned techniques can be found in the series of LRP or RALP. One of the reasons is the difficult visualization of the posterior bladder wall during LRP or RALP, which makes it challenging to reconstruct the bladder neck using these techniques. With the aim of simplifying bladder neck reconstruction, we describe a transverse bladder neck plication technique during RALP. The aim of the present study was to evaluate the effects of bladder neck reconstruction on continence after robotic assisted laparoscopic prostatectomy (RALP) in large volume prostates. *Patients and Methods:* This non-randomized retrospective study analyzed data concerning a consecutive series of thirty-five RALP performed in our Department between January 2017 and March 2018. Exclusion criteria were preoperative urinary incontinence, previous history of external beam radiotherapy, previous TURP and other concomitant diseases possibly affecting urinary continence. All the procedures were performed by two experienced robotic surgeons through a transperitoneal approach. When needed, bladder neck reconstruction was performed through a one- or two-sided running suture. Demographic and pre-, peri- and post-operative data were collected and continence evaluated at 1, 3 and 6 months after surgery comparing patients receiving bladder neck reconstruction (Group R) and patients who did not (Group C). *Results:* Thirty-five patients were enrolled in the study. The mean follow-up was 25 months and mean age was 68.3+4.9 years. In 18 patients (51%) reconstruction of the bladder neck was deemed necessary (Group R). Operative time, length of hospitalization, complication rates did not significantly differ between the two groups; mean prostate volume in the Group R was significantly higher (71 ml *vs*. 53 ml). Continence rates at 1, 3 and 6 months of follow-up were not significantly different between the two groups. *Conclusion:* Bladder neck reconstruction in great volume prostates allows to reach similar continence at early and late stages of follow-up, in comparison with smaller prostates. One- or two-sided bladder neck closure is a reliable way of facilitating suture prior to vesico-urethral anastomosis.

1 Hoznek A, Salomon L, Rabii R, Ben Slama MR, Cicco A, Antiphon P and Abbou CC: Vesicourethral anastomosis during laparoscopic radical prostatectomy: the running suture method. J Endourol *14*: 749-753, 2000. PMID: 11110570. DOI: 10.1089/end.2000.14.749

2 Van Velthoven RF, Ahlering TE, Peltier A, Skarecky DW and Clayman RV: Technique for laparoscopic running urethrovesical anastomosis: the single knot method. Urology *61*: 699-702, 2003. PMID: 12670546. DOI: 10.1016/s0090-4295(02)02543-8

3 Seaman EK and Benson MC: Improved continence with tubularized bladder neck reconstruction following radical retropubic prostatectomy. Urology *47*: 532-535, 1996. PMID: 8638363. DOI: 10.1016/S0090-4295(99)80490-7

80

TRIFECTA IN OPEN *VERSUS* LAPAROSCOPIC PARTIAL NEPHRECTOMY: A COMPARISON BASED ON FERRARA SINGLE-CENTRE EXPERIENCE

Giulio Rossini[1], Giovanni Christian Rocca[1], Elena Forini[2], Gaetano Capparelli[1], Emmanuele Vece[1], Andrea Gobbo[1], Laura Fornasari[1] and Carmelo Ippolito[1]

[1]Division of Urology, Az. Ospedaliera Universitaria Ferrara, Ferrara, Italy; [2]Medical Statistics, Az. Ospedaliera Universitaria Ferrara, Ferrara, Italy

Background/Aim: According to the EAU's guide lines, renal cell carcinoma is nowadays considered the most lethal urological malignant tumour; moreover, RCC represents a relevant percentage of incidence and mortality among neoplastic diseases in Italian population. Due to widespread

Table I. *Trifecta rates in LPN and OPN cohorts.*

		LPN		OPN		*p*-Value
Gender	Male	63	67.02%	17	62.96%	0.871281
	Female	31	32.98%	10	37.04%	
Age, mean (SD)		62.6	(10.9)	65.5	(10.8)	0.222711
BMI, mean (SD)		28.03	(5.35)	28.8	(4.1)	0.429773
ASA score (n.)	1	1	1.06%	1	3.70%	0.085815
	2	38	40.43%	4	14.81%	
	3	47	50.00%	19	70.37%	
	4	8	8.51%	3	11.11%	
Surgical indication (n.)	Elective	91	96.81%	14	51.85%	<0.000001
	Rel. Imperative	1	1.06%	7	25.93%	
	Imperative	2	2.13%	6	22.22%	
Tumoral localization (n.)	Upper pole	24	25.53%	9	33.33%	0.599215
	Mesorenal	33	35.11%	10	37.04%	
	Lower pole	37	39.36%	8	29.63%	
PADUA score (n.)	5	1	1.06%	0	0.00%	0.030536
	6	26	27.66%	4	14.81%	
	7	27	28.72%	5	18.52%	
	8	24	25.53%	7	25.93%	
	9	6	6.38%	6	22.22%	
	10	2	2.13%	4	14.81%	
	11	6	6.38%	1	3.70%	
	12	2	2.13%	0	0.00%	
PADUA score stratification (n.)	Score ≤7	54	57.45%	9	33.33%	0.046362
	Score >7	40	42.55%	18	66.67%	
RENAL score (n.)	4	26	27.66%	4	14.81%	0.007835
	5	18	19.15%	1	3.70%	
	6	20	21.28%	8	29.63%	
	7	16	17.02%	4	14.81%	
	8	5	5.32%	1	3.70%	
	9	3	3.19%	6	22.22%	
	10	6	6.38%	2	7.41%	
	11	0	0.00%	1	3.70%	
RENAL score stratification (n.)	Score ≤5	44	46.81%	5	18.52%	0.015649
	Score >5	50	53.19%	22	81.48%	
Clinical dimensions (cT) (n.)	cT1a	83	88.30%	20	74.07%	0.319283
	cT1b	7	7.45%	5	18.52%	
	cT2a	2	2.13%	1	3.70%	
	cT2b	2	2.13%	1	3.70%	
Surgical techinque (n.)	Open		---	27	22.31%	<0.000001
	VLP	94	77.69%		---	
Warm ischemia time (WIT) stratification (n.)	No ischemia	65	69.15%	13	48.15%	0.049544
	≤25 min.	15	15.96%	11	40.74%	
	>25 min.	13	13.83%	3	11.11%	
	No data	1	1.06%	0	0.00%	
Clavien-Dindo score stratification (n.)	1 (CDS I-II)	86	91.50%	24	88.89%	0.799011
	2 (CDS III-IV)	8	8.51%	3	11.11%	
Surgical margins (n.)	M–	78	82.98%	23	85.19%	0.982558
	M+	16	17.02%	4	14.81%	
Trifecta achievement (n.)	Reached	60	63.83%	17	62.96%	0.885167
	Not reached	34	36.17%	10	37.04%	

use of imaging techniques in many modern medicine fields (especially emergency) the diagnosis number of small renal masses is increasing; as a consequence, the number of patients undergoing conservative renal surgery (partial nephrectomy) is constantly rising. This background leads to the need to determine which conservative renal surgical approach is the best for single patients when partial nephrectomy is indicated. The concept of Trifecta for Partial

Table II. *Univariate analysis for OPN cohort*.

		Trifecta reached		Trifecta not reached		*p*-Value
Gender	Male	11	64.71%	6	35.29%	0.866496
	Female	6	60.00%	4	40.00%	
Age, mean (SD)		65.06	(11.66)	66.30	(9.86)	0.770842
BMI, mean (SD)		29.02	(4.32)	28.43	(3.95)	0.72243
ASA score (n.)	1	0	0.00%	1	100%	0.082561
	2	4	100%	0	0.00%	
	3	10	52.63%	9	47.37%	
	4	3	100%	0	0.00%	
Surgical indication (n.)	Elective	9	64.29%	5	35.71%	0.31797
	Rel. Imperative	3	42.86%	4	57.14%	
	Imperative	5	83.33%	1	16.67%	
Tumoral localization (n.)	Upper pole	7	77.78%	2	22.22%	0.456489
	Mesorenal	5	50.00%	5	50.00%	
	Lower pole	5	62.50%	3	37.50%	
PADUA score (n.)	6	4	100%	0	0.00%	0.102352
	7	1	20.00%	4	80.00%	
	8	6	85.71%	1	14.29%	
	9	3	50.00%	3	50.00%	
	10	2	50.00%	2	50.00%	
	11	1	100%	0	0.00%	
PADUA score stratification (n.)	Score ≤7	12	66.67%	4	44.44%	0.887949
	Score >7	5	55.56%	6	33.33%	
RENAL score (n.)	4	4	100%	0	0.00%	0.411711
	5	0	0.00%	1	100%	
	6	5	62.50%	3	37.50%	
	7	3	75.00%	1	25.00%	
	8	1	100%	0	0.00%	
	9	3	50.00%	3	50.00%	
	10	1	50.00%	1	50.00%	
	11	0	0.00%	1	100%	
RENAL score stratification (n.)	Score ≤5	4	80.00%	1	20.00%	0.718113
	Score >5	13	59.09%	9	40.91%	
Clinical dimension (cT) (n.)	cT1a	14	70.00%	6	30.00%	0.135162
	cT1b	1	20.00%	4	80.00%	
	cT2a	1	100%	0	0.00%	
	cT2b	1	100%	0	0.00%	
Surgical technique (n.)	Open	17	62.96%	10	37.04%	1
	VLP		---		---	
Warm ischemia time (WIT) stratification (n.)	No ischemia	9	69.23%	4	30.77%	0.05589
	≤25 min.	8	72.73%	3	27.27%	
	>25 min.	0	0.00%	3	100%	
Clavien-Dindo score stratification (n.)	1 (CDS I-II)	17	70.83%	7	29.17%	0.078195
	2 (CDS III-IV)	0	0.00%	3	100%	
Surgical margins (n.)	M–	17	73.91%	6	26.09%	0.023547
	M+	0	0.00%	4	100%	
Trifecta achievement (n.)	Reached	17		---		<0.000001
	Not reached	---		10		

Nephrectomy is currently the main parameter for the evaluation of surgical outcome; Trifecta is defined by (1) absence of major perioperative complications, (2) negative surgical margins and (3) intraoperative ischaemia time ≤25 minutes: Trifecta achievement can be considered as the main target when Partial Nephrectomy is performed. Our study has the purpose of comparing Open and Laparoscopic Partial Nephrectomy, aiming to provide a useful instrument to urological surgeons when choosing the correct surgical approach for individual patients. *Materials and Methods*: The whole study was based and developed on our single-centre experience (Department of Urology, University of Ferrara).

Table III. *Univariate analysis for LPN cohort.*

		Trifecta reached		Trifecta not reached		*p*-Value
Gender	Male	42	66.67%	21	33.33%	0.556709
	Female	18	58.06%	13	41.94%	
Age, mean (SD)		63.12	(11.23)	61.65	(10.36)	0.523555
BMI, mean (SD)		28.11	(5.12)	27.88	(5.82)	0.847925
ASA score (n.)	1	1	100%	0	0.00%	0.426826
	2	23	60.53%	15	39.47%	
	3	29	61.70%	18	38.30%	
	4	7	87.50%	1	12.50%	
Surgical indication (n.)	Elective	58	63.74%	33	36.26%	0.693261
	Rel. imperative	1	100%	0	0.00%	
	Imperative	1	50.00%	1	50.00%	
Tumoral localization (n.)	Upper pole	16	66.67%	8	33.33%	0.882773
	Mesorenal	20	60.61%	13	39.39%	
	Lower pole	24	64.86%	13	35.14%	
PADUA score (n.)	5	0	0.00%	1	100%	0.423995
	6	16	61.54%	10	38.46%	
	7	19	70.37%	8	29.63%	
	8	15	62.50%	9	37.50%	
	9	2	33.33%	4	66.67%	
	10	2	100%	0	0.00%	
	11	5	83.33%	1	16.67%	
	12	1	50.00%	1	50.00%	
PADUA scorestratification (n.)	Score ≤7	35	64.81%	19	35.19%	0.988945
	Score >7	25	62.50%	15	37.50%	
RENAL score (n.)	4	20	76.92%	6	23.08%	0.304024
	5	7	38.89%	11	61.11%	
	6	14	70.00%	6	30.00%	
	7	10	62.50%	6	37.50%	
	8	3	60.00%	2	40.00%	
	9	2	66.67%	1	33.33%	
	10	4	66.67%	2	33.33%	
RENAL score stratification (n.)	≤5	27	61.36%	17	38.64%	0.801265
	>5	33	66.00%	17	34.00%	
Clinical dimension (cT) (n.)	cT1a	52	62.65%	31	37.35%	0.483986
	cT1b	4	57.14%	3	42.86%	
	cT2a	2	100%	0	0.00%	
	cT2b	2	100%	0	0.00%	
Surgical technique (n.)	Open		---		---	1
	VLP	60	63.83%	34	36.17%	
Warm ischemia time (WIT) stratification (n.)	No ischemia	51	78.46%	14	21.54%	<0.000001
	≤25 min.	9	60.00%	6	40.00%	
	>25 min.	0	0.00%	13	100%	
	Dato assente	0	0.00%	1	100%	
Clavien-Dindo score stratification (n.)	1 (CDS I-II)	60	69.77%	26	30.23%	0.000153
	2 (CDS III-IV)	0	0.00%	8	100%	
Surgical margins (n.)	M–	60	76.92%	18	23.08%	<0.000001
	M+	0	0.00%	16	100%	
Trifecta achievement (n.)	Reached		60		---	<0.000001
	Not reached		---		34	

We collected data from January 2013 to March 2019 of 121 patients that underwent Laparoscopic Partial Nephrectomy (LPN) and Open Partial Nephrectomy (OPN) in our centre. Afterwards, we match-compared LPN group with OPN group: through this comparison we evaluated possible variables that could influence surgical approach choice (OPN *vs*. LPN); we considered the following variables: anthropometric data (gender, age, BMI), neoplasia

Table IV. *Ischemia rates vs. masses complexity.*

	Ischemia		No ischemia		RR	95% CI	*p*-Value
PADUA score >7							
LPN	15	37.50%	25	62.50%	0.737	0.40-1.32	0.318266
OPN	10	55.56%	8	44.44%	1.356	2.44-0.75	
PADUA score ≤7							
LPN	14	25.93%	40	74.07%	0.625	0.24-1.63	0.459265
OPN	4	44.44%	5	55.56%	1.601	4.16-0.61	

characteristics (polar/middle localization, clinical dimension cT, RENAL score, PADUA score), preoperative data (ASA score, surgical indication), intraoperative data (Open/Laparoscopic surgical approach, Warm Ischaemia Time WIT), postoperative data (Clavien-Dindo score, surgical margins evaluation). Trifecta was defined by simultaneous achievement of (1) negative surgical margins, (2) Clavien-Dindoscore ≤grade II and (3) WIT ≤25 min. Trifecta outcome has been considered as our benchmark in this comparative evaluation. Secondly, we searched for predictive factors for Trifecta achievement in both cohorts. In this second part of our work we considered the same aforementioned variables. Statistical analysis was carried out through univariate analysis respect to surgical approach (OPN *vs*. LPN) and positive/negative Trifecta achievement in both cohorts. Pearson's Chi Squared test was used to compare categorical variables, while Student's *t*-test was used for continuous variables. Statistical significance was defined by *p*-value<0.05. All statistical analysis was performed using the SPSS software. *Results:* We reached an overall identity in Trifecta achievement rates between the two surgical techniques (Table I: 63.83% LPN *vs*. 62.96% OPN, *p*>0.05). This result places our Urological Department in line with other centres that conducted similar studies, according to published literature (1, 2). We obtained statistically significant results for OPN cohort: OPN patients were associated to an higher anatomic-surgical complexity at RENAL and PADUA scores (Table I: RENAL score >6: 31.9% LPN *vs*. 51.85% OPN, *p*=0.09; PADUA score >7: LPN 42.5% *vs*. OPN 66.7%, *p*<0.05) and a lower rate of "zero ischaemia" surgery (Table I: 48.2% OPN *vs*. 69.2% LPN, LPN *vs*. 21.4 min. OPN, *p*>0.05). None of the considered factors resulted as predictive for Trifecta achievement in both OPN (Table II) and LPN (Table III) groups at univariate analysis. *Discussion and Conclusion:* According to our results, there are no significant differences in Trifecta achievement rates between OPN and LPN approach. We evaluated if there was any correlation between the higher complexity of OPN cohort masses and the lower rate of clamp-less surgery (Table IV): for this purpose, we divided our population in two cohorts depending on PADUA scores (PADUA ≤7 group *vs*. PADUA >7 group); then we evaluated patients from both groups searching for warm ischaemia performance and surgical technique: we found that OPN patients underwent warm ischaemia with higher rates than LPN patients independently from masses complexity (Table IV: for PADUA ≤7 group ischaemia was performed with rates: 25.9% LPN *vs*. 44.4% OPN, *p*=0.46; for PADUA >7 group ischaemia was performed with rates: 37.5% LPN *vs*. 55.6% OPN, *p*=0.32). We reported a RR =1.601 (95% CI=4.16-0.61) for PADUA ≤7 group and a RR=1.356 (95%CI=2.44-0.75) for PADUA >7 group regarding warm ischaemia execution in OPN cohort compared to LPN cohort (Table IV). We also observed an opposite trend between OPN/LPN in Trifecta achievement rates as neoplasia complexity increases: while LPN cohort Trifecta rates decrease as complexity increases (PADUA score ≤7: 65% Trifecta achievement; PADUA score >7: 62.5% Trifecta achievement, *p*>0.05), OPN cohort shows an opposite trend (PADUA score ≤7: 55% Trifecta achievement; PADUA score >7: 66.7% Trifecta achievement, *p*>0.05). Nevertheless, this result did not reach statistical significance. According to our results and considering scientific literature currently present about this topic, we achieved the following conclusions: 1) Surgical technique (OPN *vs*. LPN) does not influence Trifecta achievement rates; 2) High-complexity masses are more frequently associated to OPN surgery; low-complexity masses are more frequently associated to LPN surgery; 3) "Zero ischaemia" surgery is more frequently associated with LPN. OPN is associated with warm ischaemia execution, independently from masses complexity. This should be kept in mind when surgery is performed on patients with low preoperative eGFR or with relative-imperative surgical indication (*i.e*. patients with comorbidities as diabetes, hypertension and lithiasis that can affect postoperative renal function) (3). *Conclusion:* a) LPN should be considered as first choice for low-complexity masses: LPN leads to higher chances of "zero ischaemia" surgery, shorter hospitalization time, better postoperative health and faster recovery of daily activities, with same Trifecta achievement rates compared to OPN surgery; b) OPN should be

considered as an alternative approach to LPN for high-complexity masses: OPN leads to higher surgical safety (*i.e.* lower rates of intraoperative complications and no risk of conversions to Open, easier management of intraoperative complications, lower risks of surgical failure) keeping on the other hand the same Trifecta achievement rates of LPN surgery. Limitations in our study are its retrospective nature and consequently the lack of randomization; furthermore, we couldn't perform multivariate analysis due to low statistical significance and limited dimension of our sample.

1 Osaka K, Makiyama K, Nakaigawa N and Yao M: Predictors of trifecta outcomes in laparoscopic partial nephrectomy for clinical T1a renal masses. Int J Urol *22(11)*: 1000-1005, 2015. PMID: 26251228. DOI: 10.1111/iju.12893

2 Minervini A, Siena G, Antonelli A, Bianchi G, Bocciardi AM, Cosciani Cunico S, Ficarra V, Fiori C, Fusco F, Mari A, Martorana G, Medica M, Mirone V, Morgia G, Porpiglia F, Rocco F, Rovereto B, Schiavina R, Simeone C, Terrone C, Volpe A, Carini M, Serni S; Members of the RECORd Project-LUNA Foundation: Open *versus* laparoscopic partial nephrectomy for clinical T1a renal masses: a matched-pair comparison of 280 patients with TRIFECTA outcomes (RECORd Project). World J Urol *32(1)*: 257–263, 2014. PMID: 24013181. DOI: 10.1007/s00345-013-1155-7

3 Bolton E and Lynch T: Impact of warm ischaemia time during partial nephrectomy on renal function - is it really a matter of time? BJU Int *121(1)*: 3-4, 2018. PMID: 29314540. DOI: 10.1111/bju.14085

81

IMPACT OF CHEMO-IMMUNOTHERAPY FOR NON-MUSCLE INVASIVE BLADDER CANCER ON SEXUAL FUNCTION AND QUALITY OF LIFE

Tommaso Di Vico, Alessio Tognarelli, Jacopo Durante, Tiziana Fidecicchi, Paola Gattuso, Damiano Bracchitta and Luca Brizzi

Urology Unit, University of Pisa, Urology Unit, University of Pisa, Pisa, Italy

Background/Aim: Bladder cancer is the fourth most common malignancy in male adult patients. Common presentation of bladder cancer is non-muscle invasive bladder cancer (NMIBC), that represents about 75% of new diagnoses. Intravesical immunotherapy with Bacillus Calmette- Guérin (BCG) or intravesical chemotherapy with mytomicin C (MMC) are indicated for the management of intermediate and high-risk NMIBC. The main purpose of this study was to evaluate changes of sexual functions and quality of life in patients who underwent intravesical immuno-chemotherapy for non-muscle invasive bladder cancer. *Patients and Methods:* Between January 2017 and December 2017, we selected forty-five male patients (with a maximum age of 65 years) who underwent TURB (transurethral resection of the bladder) who had received a first diagnosis of NMIBC. Selected patients were assessed for sexual functions, lower urinary tract symptoms and quality of life before and after a 6-week cycle of induction therapy with MMC or BCG. We have evaluated these aspects using validated Italian versions of international sexual function index (IIEF-5) and international prostate symptom score (IPSS) questionnaires. *Results:* Thirty-one patients were treated with BCG while fourteen patients were treated with MMC. Median age in BCG group was 59 (IQR=55-65), while in MMC group was 61 (57-65). Average IIEF-5 score before instillation in BCG group was 19.3±3.5, after the last instillation was 15±5. Average IIEF-5 score in MMC group before instillation was 23±2.5, after instillation was 23±2.5. IPSS score in BCG group before instillation was 7.5±4 after instillation was 11.5±5.5. IPSS score in MMC group before instillation was 6.5±3, after instillation 8±5.5. *Discussion*: We found worse sexual and quality of life outcomes in patients treated with BCG compared to MMC. This result implies the necessity of a multidisciplinary counseling (involving psychologists and sexologist) and supporting therapy (hyaluronic acid instillation or oral PDE5 inhibitors). A more complete assessment by the urologist investigating basic comorbidity of the "young" patient is undoubtedly necessary: moreover, other urological functional disorders should be studied (overactive bladder, LUTS, initial ED) and, on the other hand, we should also consider concurrent pathology such as diabetes mellitus or high blood pressure. *Conclusion:* The overall assessment of the patient before instillation therapy and its clinical history is a daring objective. In order to guarantee an improvement (or a conservation) of patients' quality of life and sexuality, alongside a proper oncological assessment and treatment. This work is a further confirmation of what is already presented in the literature and should be new basis for subsequent studies aiming to find solutions for the management of patients with a diagnosis of NMIBC.

82

THE MANAGEMENT OF NEWLY-DIAGNOSED OLIGOMETASTIC PROSTATE CANCER: A CASE REPORT

Sara Nanni, Simona Borghesi, Andrea Rampini, Serena Nucciarelli, Silvia Bertocci, Pietro Giovanni Gennari, Paola Pernici, Carmine Iermano and Enrico Tucci

Radiotherapy Unit, San Donato Hospital and Santa Maria alla Gruccia, Arezzo, Italy

Background: The management of oligometastatic prostate cancer (PCa) at presentation is a challenging and debatable

topic. The STAMPEDE trial has proven that local radiotherapy (RT) can improve overall survival (OS) in oligometastatic PCa. *Case Report:* A 68-year-old patient with high-risk PCa [PSA 80 ng/ml and GS 9 (4+5)] was referred to our Radiotherapy Unit in 2017. He underwent bone scan, whole-body CT and 11C choline-PET/CT that showed a cT3b N0 M1 PCa, with a sacroiliac metastasis, confirmed on ^{68}Ga-PMSA PET/CT. He received androgen-deprivation therapy (ADT) with LHRH analog with decreasing PSA levels until April 2019, when PSA failure occurred (3.9 ng/ml). On May 2019, ^{68}Ga-PMSA PET/CT revealed an increased uptake of bone metastasis and primary tumour, so we proposed to the patient to continue ADT and to undergo moderate hypofractionated RT to prostate and seminal vesicles (60 Gy; 3 Gy per fraction) and stereotactic body RT (SBRT) to bone metastasis (36 Gy; 12 Gy per fractions). On September 2019 PSA was 0.16 ng/ml. *Discussion*: The STAMPEDE trial showed a 3-year OS benefit of 8% in the RT group, although RT was only directed to the primary. The oligometastatic paradigm suggests that some patients with a limited number of metastases might be cured if all lesions are eradicated with SBRT. In SABR COMET trial, SBRT was associated with an OS improvement. We, therefore, hypothesized that combining RT to the prostate and SBRT to oligometastasis would have yielded the greatest benefit. *Conclusion:* Adding moderately hypofractionated RT to the primary tumour and SBRT to oligometastases is an emerging therapeutic modality in this setting of patients treated with systemic treatment (ADT alone or in combination with docetaxel or abiraterone).

83

INTER-OBSERVER VARIABILITY OF DIFFERENT NEPHROMETRY SCORE SYSTEMS IN PREOPERATIVE SETTING OF CONSERVATIVE RENAL SURGERY: COMPARATIVE ANALYSIS BETWEEN UROLOGISTS AND RADIOLOGISTS

Simone Scarcella[1], Andrea Rochira[2], Lucio Dell'Atti[1], Giulio Milanese[1], Erika Palagonia[1] and Andrea Galosi[1]

[1]Department of Urology, Ancona
University Hospital, Ancona, Italy;
[2]Department of Public Health, Bologna
University Hospital S. Orsola, Bologna, Italy

Background/Aim: During the last decade, the advances in imaging diagnostic techniques led to an increased incidence of small renal masses diagnosis. In this context, we observed a shift regarding surgical indications for the treatment of renal cancer with a prevalence of nephron-sparing surgery (NSS) over radical nephrectomy. Moreover, the use of minimally-invasive techniques such as robot-assisted/laparoscopic partial nephrectomy, cryoablation or experimental trial of active surveillance guaranteed same oncological outcomes with better perioperative results (lower blood losses and length of hospital stay). Preoperative imaging evaluation is necessary to plan the best surgical technique depending on the anatomy of the patient and the specific characteristics of the renal lesion. Different renal scoring systems have been proposed and tested for predicting surgical complexity and post-procedural outcomes in NSS. Numerous studies reported the superiority of one scoring system over the others; however, the lack of consensus regarding a gold-standard scoring system could be misleading. To date, it has not been determined how these scoring systems vary between specialists with different backgrounds and levels of expertise. The aim of this study was the evaluation of the reproducibility of four different nephrometry scoring systems comparing the scores assigned by radiologists and urologists. *Patients and Methods:* Between November 2018 and November 2019, 64 patients were referred to our urology unit with a radiological diagnosis of renal mass. All patients were treated with a nephron sparing surgical approach: robot-assisted or open technique according to surgeon's preference. All preoperative computed tomography (CT) images were retrospectively evaluated. Three urologists and three radiologists analysed the scans of each patient and assigned independently the estimated nephrometry scores. Four scoring systems were included in the study: RENAL, PADUA, C–Index and ABC. All continuous variables were analysed with median and interquartile range, while categorical variables with frequencies. Urologists and Radiologists scores were then compared using the Mann-Whitney test; the intra-class correlation coefficient (ICC) was used for the comparison of continuous variables while for categorical scores the Cohen's kappa (k) was used. *Results:* RENAL and PADUA scores were characterized by a higher ICC among all readers while for C-Index and ABC scores it was lower. Considering the specific professional background, nephrometry scores assigned by Urologists were defined by an intra-class correlation index higher than 0.85 points, while for the Radiologist group only Renal and PADUA scores were comparable. In opposition to these results, C-Index and ABC nephrometry scores showed lower ICC in both groups of specialists. Overall, the mean differences in score assigned between the two groups of specialists differ respectively of 1 and 0.6 point for the RENAL score (p=0.012) and the C-Index (p<0.001) while no statistical differences were observed for PADUA and ABC scores (p>0.05). *Discussion and Conclusion:* Nephrometry scoring systems are determined by anatomical characteristics, dimension and localization of the renal masses. In our experience scoring systems based on anatomical characteristics, such as P.A.D.U.A and R.E.N.A.L. score, seem to be characterized by a higher reproducibility even between specialists with

different backgrounds. On the contrary, scoring systems based on specific algorithms like the C-Index tend to vary significantly between urologists and radiologists, even between specialists with the same backgrounds. According to our results nephrometry scoring systems based on anatomical characteristics should be preferred for the higher reproducibility resulting in a better stratification of patients according to surgical risks.

84

A MULTICENTER PROSPECTIVE STUDY OF 1,008 PATIENTS UNDERGOING MPMRI FUSION-TARGETED BIOPSIES UNDER LOCAL ANESTHESIA: OUTCOMES AND PREDICTORS OF PAIN

Alessandro Marquis[1], Junlong Zhuang[2], Giancarlo Marra[1], Mattia Beltrami[1], Xiaozhi Zhao[2], Giorgio Calleris[1], Yansheng Kan[2], Marco Oderda[1], Haifeng Huang[2], Riccardo Faletti[3], Qing Zhang[2], Luca Molinaro[4], Wei Wang[2], Laura Bergamasco[3], Hongqian Guo[2] and Paolo Gontero[1]

[1]Department of Urology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy;
[2]Department of Urology, Drum Tower Hospital, Medical School of Nanjing University, Nanjing University, Nanjing, P.R. China;
[3]Department of Radiology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy;
[4]Department of Pathology, San Giovanni Battista Hospital, Città della Salute e della Scienza and University of Turin, Turin, Italy

Background/Aim: Low tolerability due to peri-procedural pain is considered a major argument against use of transperineal (TP) biopsy in an in-office setting using local anesthesia (LA). However, no large cohorts detailed mpMRI-TP fusion biopsies (TPFBx) pain outcomes and factors influencing pain. Materials and Methods: We performed a multicenter prospective study from 2016 to 2019 in men undergoing TPFBx under LA. Primary outcomes were: i) pain scores in different procedural phases; ii) identification factors associated with severe pain. Secondary outcome was

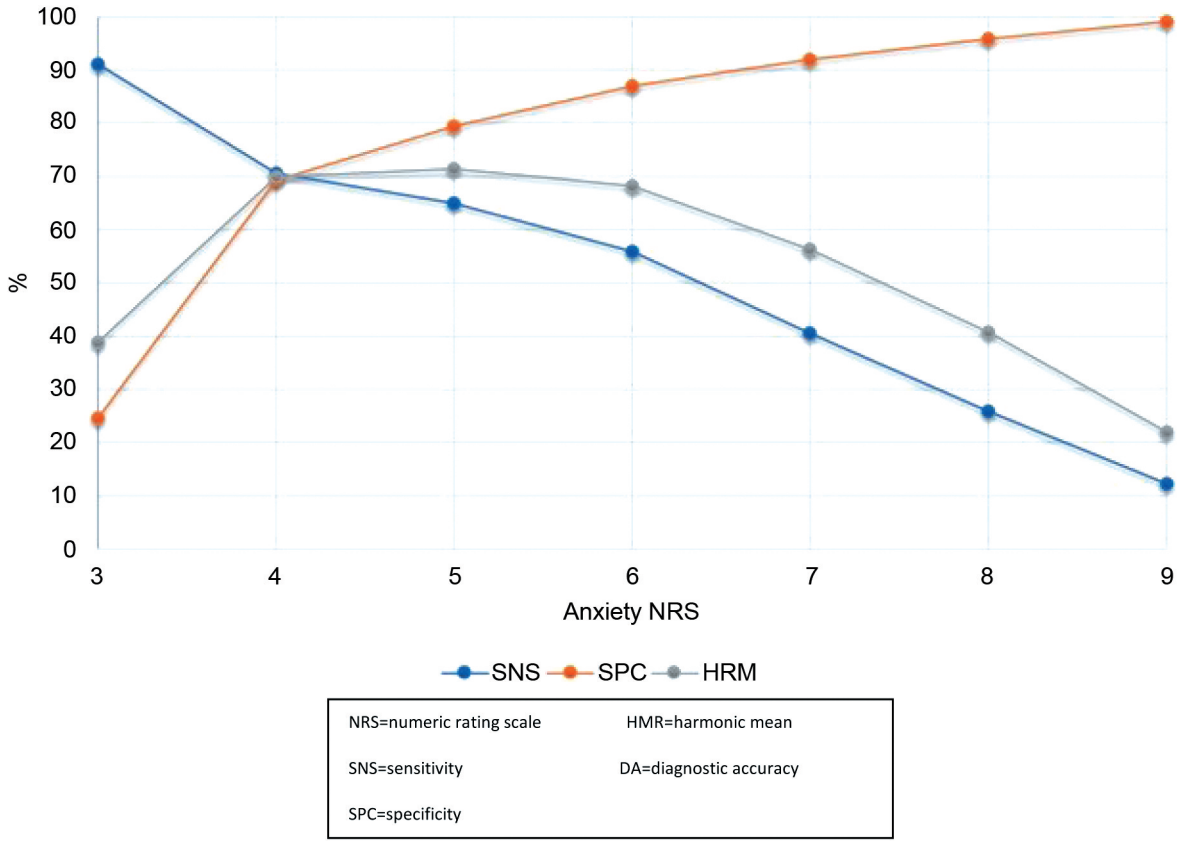

Figure 1. *Anxiety and severe pain.*

to develop a model able to identify men at higher risk of experiencing severe pain based on most-relevant pre-procedural factors. Pain scores were recorded using a numeric rating scale (NRS) at the time of: i) transrectal US probe insertion; ii) local anesthesia; iii) prostate biopsy. Severe pain and pre-procedural anxiety were defined as NRS >6. *Results:* We included 1,008 men undergoing TPFBx under LA. Mean NRS pain scores were 3.9±2.1 for LA, 3.1±2.3 for Bx; maximum mean experienced pain was 4.7±2.1. On multivariate analysis age and severe anxiety were a protective and risk factor respectively, both for severe biopsy (age OR=0.96, 95% CI=0.94-0.99; anxiety >6 OR=2.99, 95% CI=1.83-4.89) and for severe maximum pain (age OR=0.96, 95% CI=0.94-0.98; anxiety >6 OR=2.82, 95% CI=1.87-4.27). Procedural time was also associated with an increased risk of experiencing severe Bx (OR=1.04, 95% CI=1.00-1.08) and maximum pain (OR=1.03, 95% CI=1.01-1.06). Amongst different anxiety cut-offs to predict severe pain (Figure 1) best anxiety cut-off to predict severe pain was 5 (SEN: 65%, SPE: 79.45%). Nonetheless, from a clinical perspective, if aiming to test possible anxiety preventive measures effects on pain, an anxiety cut off >6 NRS would decrease to 13% the number of patients being treated whilst identifying 56% of those experiencing severe pain. *Conclusion:* TPFBx under LA are tolerable, with highest pain scores being recorded during LA. Severe anxiety predicts anesthesia, biopsy and maximum severe pain levels and may be used to identify those at higher risk of experiencing severe pain and to test the effect of possible anxiety preventive measures to reduce pain in these patients. Future studies are needed to validate our findings.

86
ONCOLOGICAL OUTCOMES IN CT2A RENAL TUMORS TREATED WITH MINIMALLY INVASIVE PARTIAL NEPHRECTOMY: EXPERIENCE OF A TERTIARY CENTER

Daniele Amparore[1], Enrico Checcucci[1], Matteo Manfredi[1], Federico Piramide[1], Diletta Garrou[1], Enrico Bollito[2], Cristian Fiori[1] and Francesco Porpiglia[1]

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

Background/Aim: Indications for partial nephrectomy (PN) have been established as the gold standard for cT1 tumors, but the nephron sparing approach for higher stage renal masses is still debated. In our study we evaluated the perioperative, pathological and oncological outcomes compare to clinical T2a (cT2a) and clinical T1b (cT1b) renal tumors treated with PN. *Patients and Methods:* We extracted data from our prospective maintained database of patients who underwent minimally invasive PN between 06/2008 and 06/2018 for cT1b (group A) and cT2a (group B) renal tumours. The same surgeon performed all the PN. We evaluated and analyzed: demographics, perioperative (size and PADUA score of the masses, solitary kidney, operative time - OT, estimated blood loss - EBL, ischemia time, intra and postoperative complications – classified by Clavien, length of stay - LOS), pathological (tumor pathology, pT, positive surgical margin – PSM, ISUP grade and pT3a upstaging) and follow up data (recurrence and survival). We also registered the overall survival (OS), the cancer specific survival (CSS), and the recurrence free survival (RFS). Statistical analysis was performed using *t*-test and Mann Whitney *U*-test to compare the two groups. To compare the oncologic outcomes, we built a Kaplan-Meier survival analysis (KMSA). *Results:* We included 234 patients; we found 190 malignant lesions (81.2%), with PSM rate of 2.1% (4/190). Median ISUP grade was 2 (IQR=2-3). 34/190 cases (17.8%) had a pT3a upstaging. The median follow-up of the whole cohort was 36 (IQR=20-63) months. 11/190 pts had a recurrence (5.8%). Considering clinical stage, 188 pts were cT1b and 46 pts were cT2a. We did not find any differences between the two groups for all the variables considered except: age (61.7+12.3 *vs*. 56.2+13.6 yrs, p=0.018), tumor size (51+7 *vs*. 79+7 mm, p<0.001) and ISUP grade [2 (IQR 1) *vs*. 3 (IQR 2), p=0.025]. KMSAs for 5-year OS were 94% and 93% for cT1b and cT2a respectively (p=0.83), for 5-year CSS 98% and 94% (p=0.31), and for 5-year RFS 89% and 90% (p=0.13). *Conclusion:* The present study suggested that PN is a viable and safe treatment option for larger renal tumors if performed by experienced hands. Further studies with larger samples are needed in order to confirm these findings.

Authors Index*

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