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IS THERE A PREDICTIVE ROLE FOR BIODISTRIBUTION SPECT/CT OBTAINED AFTER THE FIRST [¹⁷⁷Lu]Lu-PSMA-617 RADIOLIGAND THERAPY IN PROGRESSIVE MCRPC?

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Background/Aim: Radioligand therapy (RLT) is an effective treatment strategy for progressive metastatic castration-resistant prostate cancer (mCRPC). Post-treatment single-photon emission computed tomography/computed tomography (SPECT/CT) permits the appraisal of [¹⁷⁷Lu] Lutetium-prostate-specific membrane antigen-617 ([¹⁷⁷Lu]Lu-PSMA-617) biodistribution at the individual-lesion level. This preliminary study evaluated whether lesion-level parameters derived from SPECT/CT after the

first cycle of [¹⁷⁷Lu]Lu-PSMA-617 RLT could predict subsequent lesion response. *Patients and Methods:* We retrospectively evaluated consecutive patients with mCRPC who received at least two cycles of [¹⁷⁷Lu]Lu-PSMA-617 RLT at Messina University between February 2022 and January 2026 and underwent SPECT/CT covering all known disease sites after the first treatment cycle. Each PSMA-positive lesion was semiautomatically segmented using a 40% threshold to derive maximum and mean standardized uptake values (SUVmax and SUVmean), total lesion volume (TLV), and total lesion activity (TLA=SUVmean × TLV). The SPECT/CT parameters for every lesion were then correlated with the single-lesion response at the final RLT cycle, classified as progressive (PD) or non-PD (partial/complete response, stable disease) according to the qualitative RECIP 1.0 and quantitative PPP criteria. Receiver operating characteristic (ROC) curve analysis was used to identify the optimal cutoff values for the SPECT/CT parameters, which were then exploratorily validated in an external cohort from the University of Genoa. *Results:* The training cohort included 19 mCRPC patients (245 lesions: 205 osteomedullary, 34 lymph nodal, 6 visceral) and the external validation cohort included four patients and 45 lesions. At the final cycle, there were 52/245 PD lesions, while 193/245 did not progress to RLT. After the first cycle, SUVmax, SUVmean, TLV, and TLA were significantly higher in non-progressive lesions than in PD lesions ($p<0.001$). ROC analysis of TLA yielded an AUC of 0.825 (best cut-off=61.7), SUVmax of 0.800 (best cut-off=11.8), SUVmean of 0.795 (best cut-off=6), and TLV of 0.650 (best cut-off=7.1 ml). In the exploratory external validation cohort, cutoffs were applied such that values below each threshold identified progressive (PD) lesions, yielding the following sensitivity and specificity: TLA cutoff of 61.7, sensitivity 67.6% and specificity 100%; SUVmax cutoff of 11.8, sensitivity 100% and specificity 87.5%; SUVmean cutoff of 6.0, sensitivity 97.3% and specificity 100%. In contrast, a TLV cutoff



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of 7.1 ml showed unsatisfactory performance, with sensitivity below 50% and specificity of 100%. *Conclusion:* Lesion-level TLA, SUVmax, SUVmean, and TLV measured on SPECT/CT after the first cycle of [¹⁷⁷Lu]Lu-PSMA-617 RLT were associated with subsequent lesion response, with significantly higher values observed in non-progressive than in progressive lesions. This showed a potential association between PSMA expression and RLT response, which is well-known for PSMA PET, where higher receptor expression (quantified through SUVmean) predicts a response to [¹⁷⁷Lu]Lu-PSMA-617 RLT (1, 2). The association between higher TLA and response may reflect the combined contribution of PSMA expression and lesion volume, suggesting that even large lesions may respond favorably when they demonstrate high PSMA uptake. Our preliminary findings suggest that SPECT/CT parameters obtained after the first RLT cycle, which reflect PSMA expression, may serve as early lesion-level predictors of treatment response.

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OUTCOMES OF CRYOABLATION FOR RENAL MASSES: A THREE-YEAR SINGLE-CENTRE RETROSPECTIVE COHORT STUDY

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Background/Aim: Percutaneous renal ablation represents a minimally invasive treatment option for renal masses, particularly in elderly patients or those with significant comorbidities. The aim of this study was to evaluate oncological outcomes, safety, and histological characterization of renal tumors treated with percutaneous cryoablation at our institution. *Materials and Methods:* We retrospectively reviewed all renal ablation procedures performed between July 2022 and September 2025 at the Hospital of Ravenna. Both radiofrequency ablation (RFA) and cryoablation procedures were performed, but only cryoablation procedures were included in this study. Demographic, clinical, tumor-related, procedural, and outcome data were collected. Descriptive statistics were used. The primary endpoint was local recurrence, while secondary endpoints included peri-procedural complications. *Results:* Forty renal ablation procedures were performed in 39 patients, with one patient undergoing repeat treatments. Mean age was 74.7±7.6 years, and the majority of patients were male (57.5%). The mean Charlson Comorbidity Index was 4.53±1.92. Mean tumor size was 30.6±9.1 mm, with left-sided lesions being slightly more common (52.5%). Percutaneous biopsy was performed in 65% of procedures, revealing predominantly renal cell carcinoma, mainly clear cell and papillary subtypes. Complications occurred in 12.5% of procedures, including 7.5% major complications (Clavien-Dindo II-

IIIa). No procedure-related mortality was reported. Mean hospital stay was 1.78 ± 1.40 days. During follow-up, recurrence or disease progression occurred in 5% of patients. *Conclusion:* Renal ablation at our center demonstrated a favorable safety profile, short hospitalization, and acceptable short-term oncological outcomes. It represents a valuable treatment option in patients with a relevant comorbidity burden, as assessed by the Charlson Comorbidity Index, who are poor candidates for surgical resection. Longer follow-up and larger cohorts are required to confirm long-term efficacy.

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REAL-WORLD EFFICACY, SAFETY, AND QUALITY-OF-LIFE OUTCOMES OF ENFORTUMAB VEDOTIN IN METASTATIC UROTHELIAL CARCINOMA: PREDICTORS OF RESPONSE FROM THE MARCHE REGION (EV-OLUTION TRIAL)

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Background/Aim: Enfortumab Vedotin (EV) is a Nectin-4-directed antibody–drug conjugate that has transformed the treatment landscape of metastatic urothelial carcinoma

(mUC). Registrational trials (EV-301 and EV-302) demonstrated survival benefits over standard chemotherapy, establishing EV as a key option in advanced disease (1, 2). Clinical trials often enroll selected populations; real-world evidence is essential to assess outcomes in routine practice. Metabolic heterogeneity and patient factors such as body mass index (BMI), sarcopenia, and sarcopenic obesity may affect drug exposure, toxicity, and efficacy. Additionally, treatment-emergent neurotoxicity could reflect drug pharmacodynamics and serve as a predictor of response, but its role in clinical outcomes remains underexplored. The EV-olution trial is a multicenter real-world study evaluating EV efficacy, safety, and quality-of-life outcomes across oncology centers in the Marche region, Italy. The study specifically investigates the prognostic impact of BMI, sarcopenia, neurotoxicity, and other clinical and metabolic factors, while assessing longitudinal patient-reported outcomes (PROs) to understand the treatment's effect on health-related quality of life (HRQoL). The aim of this study was to identify metabolic and patient-related predictors, including neurotoxicity, to optimize patient selection and toxicity management strategies. *Materials and Methods:* This ambispective multicenter study included 43 patients with mUC treated with EV. Efficacy endpoints were overall survival (OS) and progression-free survival (PFS), calculated from treatment initiation using Kaplan–Meier methods. Safety was evaluated according to CTCAE criteria, focusing on treatment-emergent adverse events (TEAEs). Baseline BMI and sarcopenia were recorded and analyzed as potential predictors of clinical outcomes. HRQoL was longitudinally assessed using validated patient-reported outcome instruments, including the EORTC QLQ-C30 and EQ-5D-5L questionnaires, administered during treatment cycles. Multivariate analyses explored associations between BMI, sarcopenia, neurotoxicity, and other clinical and metabolic factors with survival outcomes. *Results:* At a median follow-up of 16.8 months, median OS was 14.5 months and median PFS 6.4 months. Higher BMI ($p=0.0021$) and treatment-emergent peripheral neurotoxicity ($p=0.034$) were independent predictors of improved OS and PFS. Patients with baseline sarcopenia or sarcopenic obesity experienced

higher rates of Grade 3 toxicities, indicating increased vulnerability. PRO analysis revealed a “well-being window” during the first three months, with rapid symptom relief and improved functional scores. HRQoL declined later, primarily due to cumulative neurotoxicity, which reached Grade ≥ 3 in 15-23% of patients. Hyperglycemia and cutaneous reactions were frequent but manageable with dose adjustments and supportive care. *Conclusion:* The EV-olution trial confirms high clinical activity of EV in a real-world mUC population, with outcomes comparable to registrational trials. BMI, sarcopenia, neurotoxicity, and other metabolic and clinical factors emerged as potential predictors of treatment efficacy and response to EV. Early HRQoL improvements highlight EV’s rapid symptomatic benefit, while cumulative neurotoxicity remains the main limitation to long-term therapy. These findings underscore the importance of a multidisciplinary management strategy, including nutritional assessment and proactive neurological monitoring, to optimize treatment outcomes and preserve quality of life. Integration of metabolic, clinical, and treatment-related parameters, including neurotoxicity, may guide personalized therapy and patient selection. Prospective studies are warranted to validate these observations and refine predictive biomarkers for ADC-treated patients.

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FEASIBILITY AND TOLERANCE OF STEREOTACTIC ABLATIVE BODY RADIOTHERAPY WITH COMPLETE-ARC VOLUMETRIC MODULATED ARC THERAPY (VMAT) FOR PROSTATE CARCINOMA IN PATIENTS WITH BILATERAL HIP PROSTHESES

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Background/Aim: The number of hip replacement procedures has increased in the last decades and patients undergoing this type of surgery are often elderly, an age group with an increased incidence of prostate cancer. Stereotactic body radiation therapy (SBRT) is increasingly accepted in the treatment of prostate cancer and has demonstrated non-inferiority to conventionally fractionated radiotherapy and moderately fractionated radiotherapy, with a good toxicity profile. However, bilateral hip replacement may compromise radiotherapy feasibility because metallic implants generate artifacts on the computed tomography (CT) images used for treatment simulation and planning. These artifacts may impair the accurate delineation of target volumes and organs at risk and introduce dosimetric uncertainties because of inaccurate modeling of radiation scattering and attenuation. Commercially available metal artifact reduction (MAR) algorithms may improve treatment planning in patients with hip prostheses. This retrospective study evaluated the feasibility, treatment tolerance, and preliminary outcomes of prostate SBRT in patients with bilateral hip prostheses. *Patients and Methods:* Six patients with bilateral hip prostheses treated with SBRT for prostate cancer were

retrospectively evaluated. All patients received 36.25 Gy in 5 fractions (7.25 Gy/fraction) once-weekly using 6-MV flattening filter-free photons and volumetric modulated arc therapy (VMAT). The once-weekly schedule was chosen because of the patients' comorbidity status. SBRT was delivered to the prostate gland only, without pelvic lymph-node irradiation. Before simulation, all patients underwent intraprostatic fiducial marker implantation for image-guided radiotherapy (IGRT). All patients were treated with complete-arc VMAT; beam entry through the hip prostheses was minimized using an avoidance optimization structure extending 1 cm around each implant with a dose constraint of 5 Gy. For simulation, all patients underwent a planning CT with MAR. No hydrogel rectal spacers were used. Patient positioning was verified before each fraction using cone-beam CT, with image matching based on the intraprostatic fiducial markers. No patient received androgen deprivation therapy. Acute and long-term toxicities were assessed according to the Common Terminology Criteria for Adverse Events (CTCAE). International Prostatic Symptom Score (IPSS) was used to assess baseline urinary status before SBRT. Performance status was assessed using Karnofsky Performance Status (KPS) scale. Treatment response was monitored through periodic clinical examinations and prostate-specific antigen measurements. **Results:** Six patients were available for retrospective analysis. Median age at diagnosis was 77 years (range=68-84 years). Median IPSS before the start of SBRT was 4 (range=1-7). Median KPS was 90 (range=90-100). One patient was low risk, four patients were intermediate risk, and one patient was high risk. Median follow-up was 21 months (range=8-28) (Table I). All patients responded to treatment and, at the time of this data analysis, no patient has recurred. The median acute genitourinary (GU) toxicity was grade 0 (range=0-1). The median acute gastro-intestinal (GI) toxicity was grade 0 (range=0-1) and median long-term GU toxicity was grade 0 (range=0-1). The median long-term GI toxicity was grade 0 (range=0-1) (Table II). **Conclusion:** Despite the preliminary nature of these findings, the limited follow-up, and the potential biases associated with the retrospective design and small sample size, once-weekly prostate SBRT was feasible and well

Table I. *Patients' characteristics.*

Patient n°	6
Median age (years)	77 (range=68-84)
Median IPSS	4 (range=1-7)
Median KPS	90 (range=90-100)

Table II. *Acute and late toxicities.*

Toxicity		Grade	N° of cases
Acute	GI	G0	5
		G1	1
	GU	G0	5
		G1	1
Late	GI	G0	5
		G1	1
	GU	G0	5
		G1	1

tolerated in patients with bilateral hip prostheses. No recurrences were observed during the available follow-up. The use of advanced technologies, including MAR algorithms, VMAT, and fiducial marker-based image-guided radiotherapy, is essential for minimizing uncertainties in target and organ-at-risk delineation and dose calculation. Hydrogel rectal spacers may provide additional rectal sparing in appropriately selected patients. These findings suggest that bilateral hip prostheses do not necessarily preclude prostate SBRT; however, prospective confirmation in larger cohorts is required. Alternative treatment options, including prostatectomy, should also be considered within a multidisciplinary decision-making process.

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EXOGENOUS EXPRESSION OF WILD-TYPE AND P53 VARIANTS DIFFERENTIALLY MODULATES CELL DEATH AND HIF-1A STATUS IN KJ29 AND CAKI-2 KIDNEY CARCINOMA CELLS

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Background/Aim: Renal cell carcinoma (RCC) accounts for approximately 2-3% of all human malignancies, with clear cell RCC (ccRCC) representing the most common histological subtype, comprising about 70-80% of cases. Currently, combinations of immune checkpoint inhibitors (ICIs), either as doublets or in association with tyrosine kinase inhibitors (TKIs), represent the preferred first-line treatment options for metastatic disease. However, the development of drug-resistance mechanisms limits treatment efficacy and patient survival. The tumor suppressor p53 is expressed at relatively low levels in ccRCC cells, although TP53 mutations are uncommon in this malignancy. This study investigated the functional effects of wild-type p53 and the naturally occurring p53 mutants R175H and R273H in ccRCC cells. **Materials and Methods:** Caki-2 and KJ29 ccRCC cells were seeded in duplicate in six-well plates and transfected with plasmids encoding wild-type (WT) or mutant (R175H and R273H) p53 for 24 h in DMEM/F12 supplemented with 1% FBS. Control cells were transfected with an irrelevant plasmid encoding the photoprotein aequorin. After transfection, cell morphology was evaluated using phase-contrast microscopy; images were acquired with a digital camera and processed using ImageJ software. Next, cells were lysed in a buffer containing 1% Triton X-100 and a cocktail of protease and phosphatase inhibitors. Following protein electrophoresis, HIF-1 α and p53 expression was assessed by western blot using specific antibodies. Levels of p53 and HIF-1 α were calculated as band intensity ratio between the protein of interest and β -actin. Statistical analysis was performed using GraphPad Prism software and an unpaired *t*-test. A *p*-value <0.05 was considered statistically significant. **Results:** KJ29 and Caki-2 cells transfected with the control plasmid (CTRL) displayed a normal morphology (Figure 1A). In contrast, expression of wild-type p53 and

the R273H variant induced a marked cell detachment, with cell rounding and reduced cell volume in both ccRCC cell lines (Figure 1A). Notably, the expression of the p53 mutant R175H did not affect cell morphology, which remained comparable to CTRL cells (Figure 1A). Western blot analysis confirmed that cells transfected with p53 WT, R175H, and R273H exhibited higher levels of p53 protein than CTRL cells (Figure 1B). Interestingly, the expression of both wild-type p53 and R273H variant induced a significant down-regulation of HIF-1 α compared with CTRL cells (Figure 1B). In contrast, the p53 R175H variant did not alter HIF-1 α expression, showing levels comparable to those observed in CTRL cells (Figure 1B). **Conclusion:** Although p53 mutations are relatively rare in ccRCC, we have previously demonstrated that p53 expression is lower in ccRCC cells than in normal kidney cells. This suggests that p53 dysfunction may contribute to tumor development and progression in kidney cancer. In the present study, wild-type p53 and the R273H variant induced marked morphological changes consistent with reduced cell viability and significantly suppressed HIF-1 α expression. In contrast, the expression of p53 R175H mutant did not affect cell morphology, which remained similar to control cells, suggesting a loss of functional activity. We also evaluated the expression of the angiogenic factor hypoxia-inducible factor 1 α (HIF-1 α), which is constitutively activated in most ccRCC cases. As expected, control cells exhibited elevated levels of this transcription factor, whereas cells expressing wild-type p53 and the R273H variant showed a marked reduction in HIF-1 α expression. No significant changes in HIF-1 α levels were observed in cells expressing the p53 R175H mutant, further supporting its loss of function. In conclusion, our findings indicate that wild-type p53 induces cell death and suppresses HIF-1 α expression in ccRCC cells. Notably, the p53 R273H variant appears to retain these functional properties, whereas the R175H mutant does not exhibit antitumor activity. These results suggest that the restoration of wild-type p53 function or the reactivation of p53 mutants could represent a promising therapeutic strategy for patients with metastatic RCC.

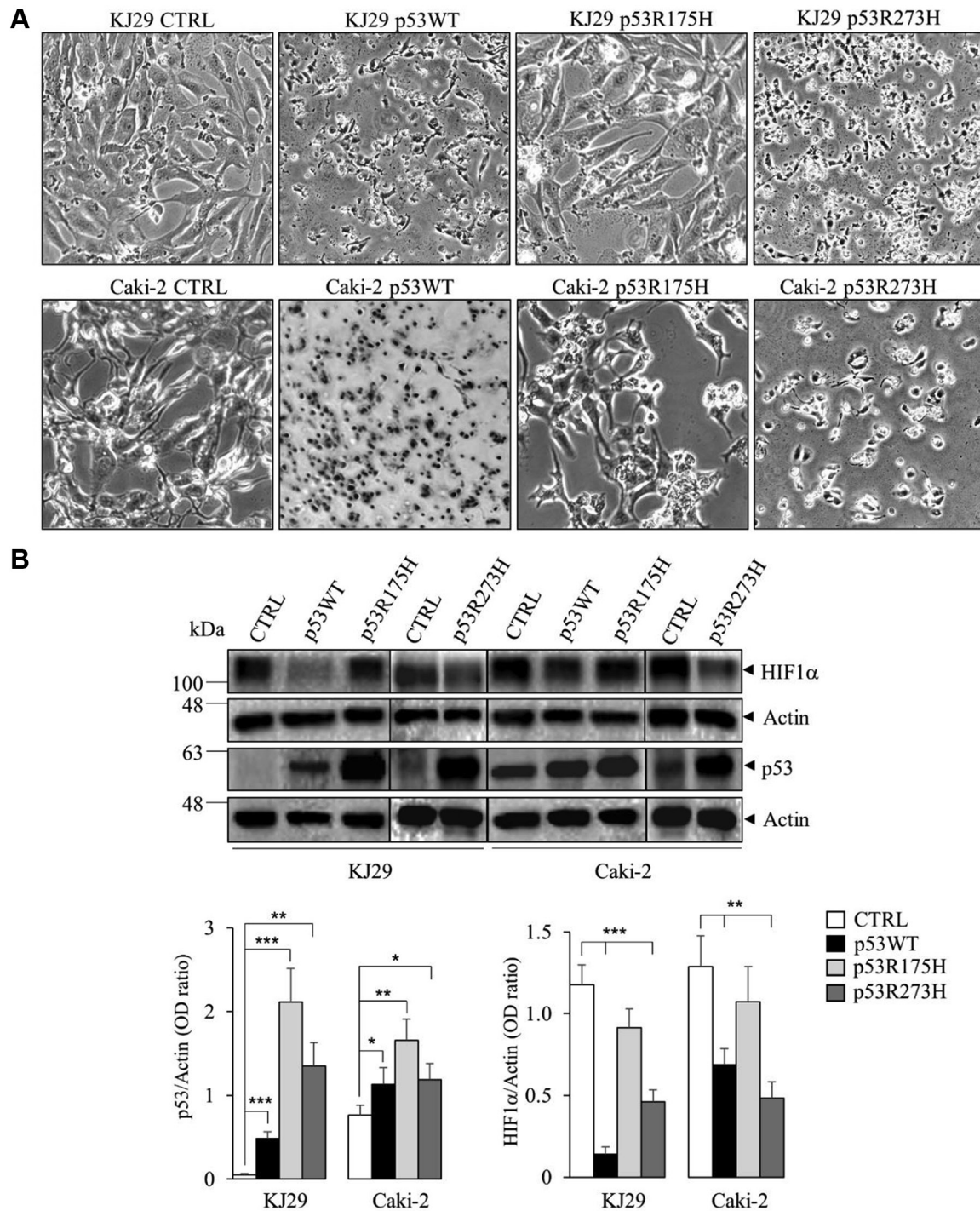


Figure 1. Analysis of cell morphology and HIF-1 α expression in clear cell renal cell carcinoma cells expressing p53 wild type (WT) and two naturally occurring variants. (A) The expression of p53WT induced marked cell death, as evidenced by extensive cell detachment in both cell lines compared with control cells (CTRL). (B) The expression of HIF-1 α , p53 WT, and p53 mutants was analyzed by western blotting. Levels of wild type and mutated forms of p53 are increased in KJ29 and Caki-2 cells transfected with the corresponding plasmids compared with those transfected with the control vector (CTRL). Notably, the presence of wild type p53 strongly reduces the expression of HIF-1 α in both cell lines, whereas the expression of p53 R175H variant does not affect the levels of this transcription factor.

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PROSTATE CANCER: AN EPIDEMIOLOGICAL ASSESSMENT

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Background/Aim: According to the 2024 report of the Lancet Commission on Prostate Cancer, new prostate cancer diagnoses are estimated to double by 2040, exceeding 2.9 million annual cases due to the progressive aging of the population. This global trend, although more pronounced in developing economies, is reflected in the Italian landscape with a 14% increase over the last three years. This study aimed to verify this epidemiological evolution by analyzing incidence data collected at an Apulian hospital pharmacy (serving a catchment area of 60,000 users). *Materials and Methods:* The analysis considered the number of patients as of December 31st of each year from 2021 to 2025, as well as the active ingredients indicated for the treatment of: Newly diagnosed high-risk metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT), Asymptomatic or mildly symptomatic metastatic castration-resistant prostate cancer (mCRPC) after failure of androgen deprivation therapy and for whom chemotherapy is not yet clinically indicated, mCRPC in adult men whose disease has progressed during or after a docetaxel-based chemotherapy regimen, and non-metastatic castration-resistant prostate cancer (nmCRPC) at high risk of developing metastatic disease. *Results:* The annual numbers of treated patients, stratified by active pharmaceutical ingredient, were as follows: 12 patients in 2021, including 7 treated with abiraterone and 5 with enzalutamide; 13 patients in 2022, including 6 treated with abiraterone, 3 with apalutamide, and 4 with enzalutamide; 28 patients in 2023, including 5 treated with abiraterone, 11 with apalutamide, and 12 with enzalutamide; and 35 patients in 2024, including 7 treated with abiraterone, 16 with apalutamide, 11 with enzalutamide, and 1 with

darolutamide. In 2025, 5 patients received abiraterone, 26 received apalutamide, 15 received enzalutamide, and 2 received darolutamide. Overall, the data showed a marked increase in the number of patients receiving systemic treatment for advanced prostate cancer, accompanied by increasing use of apalutamide and the introduction of darolutamide. *Conclusion:* This local analysis supports the broader trend toward an increasing number of patients requiring systemic treatment for advanced prostate cancer. The evolution of the therapeutic landscape, characterized by the growing use of apalutamide and the introduction of darolutamide, mandates rigorous guideline implementation. To ensure equitable and sustainable innovation, investments in specialized training and health literacy programs for the male population are required. In this setting, the Hospital Pharmacist serves as a key figure, providing the clinical expertise necessary to guide patients through their care pathway and follow-up monitoring.

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ANALYSIS OF DRUG UTILIZATION IN PROSTATE CANCER: IMPACT AND OPPORTUNITIES OF GENERIC THERAPIES

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Background/Aim: In line with the projections of the Lancet Commission on Prostate Cancer (1), which predict a doubling of global diagnoses by 2040 (2.9 million/year) due to progressive demographic aging, Italy is already recording a 14% increase over the last three years. This study aims to translate this epidemiological evidence into a local pharmacoeconomic analysis by monitoring consumption volumes and the impact on pharmaceutical expenditure at an Apulian Hospital Pharmacy (serving a catchment area of 60,000 users). *Materials and Methods:* The analysis considered consumption data from 2021 to 2025 for active

ingredients indicated for the treatment of: Newly diagnosed high-risk metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT), Asymptomatic or mildly symptomatic metastatic castration-resistant prostate cancer (mCRPC) after failure of androgen deprivation therapy and for whom chemotherapy is not yet clinically indicated, mCRPC in adult men whose disease has progressed during or after a docetaxel-based chemotherapy regimen and Non-metastatic castration-resistant prostate cancer (nmCRPC) at high risk of developing metastatic disease. *Results:* Aggregated data show a significant evolution in expenditure and therapeutic mix. In 2021, for 12 patients, expenditure was €271,577, sustained almost entirely by Abiraterone and Enzalutamide. In 2023, despite the doubling of patients (28), expenditure remained nearly unchanged (€277,766) due to the collapse of costs for Abiraterone (from €167k to €17k), attributable to the use of the generic drug. These cost savings allowed for the absorption of the introduction of apalutamide and darolutamide, whose combined expenditure reached approximately €434,000 in 2025 out of a total of €587,897 for 53 treated patients. *Conclusion:* Data extrapolation confirms a strong growth trend within the analyzed context. Although an overall increase in treatments was observed, rising from 12 in 2021 to 53 in 2025 (+341%), the growing number of patients did not lead to a proportional increase in costs, which rose from €271,577.03 to €587,897.31 (+116.5%) over the same period. Despite the expansion of the therapeutic spectrum, expenditure containment was ensured by the introduction of generic drugs, which proved crucial for NHS sustainability, alongside the ability of hospital pharmacists to adapt promptly.

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10 **DEFINING PATIENT SELECTION FOR** **METASTASIS-DIRECTED THERAPY IN** **OLIGOMETASTATIC UROTHELIAL CANCER:** **THE OMERO MULTICENTER STUDY**

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Background/Aim: The role of metastasis-directed therapy (MDT) in oligometastatic urothelial cancer (OUC) remains controversial, and robust evidence to guide patient selection is lacking. In the context of evolving systemic treatment strategies, real-world data are needed to clarify the potential role of stereotactic body radiation therapy (SBRT) as part of a biologically-driven MDT approach. **Patients and Methods:** We conducted a retrospective multicenter study including patients with OUC treated with SBRT for one to three extracranial metastatic lesions. Clinical outcomes included local control (LC), progression-free survival (PFS), overall survival (OS), treatment-related side effects, and predictive factors associated with clinical benefit. **Results:** A total of 163 patients with 237 metastatic lesions were included. Most patients had bladder cancer (82.8%) and metachronous oligometastatic disease (79.8%). Ninety-five patients

received systemic therapy before SBRT, and 60 received concomitant systemic treatment. After a median follow-up of 14.4 months, median LC and time to polymetastatic progression were not reached. LC rates at 1, 3, and 5 years were 82.9%, 73.8%, and 67.2%, respectively. Median PFS was 10.7 months, while median OS was 51.2 months, with a 3-year OS rate of 55.3%. Bone metastases were independently associated with shorter PFS and OS, whereas patients with lymph node-only disease and metachronous metastases experienced significantly improved survival. SBRT was well tolerated, with no grade ≥ 3 treatment-related side effects observed. **Conclusion:** In this large multicenter real-world cohort, SBRT as MDT was associated with durable LC and favorable survival outcomes in selected patients with OUC. These results highlight the importance of clinical selection, as outcomes may not exclusively reflect the effect of MDT but also an intrinsic biological selection. Our findings support the integration of MDT within contemporary systemic treatment paradigms and highlight the need for prospective trials to refine patient selection and optimize the combination of SBRT with modern systemic therapies.

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ROLE OF MRI IN PENILE CANCER: ACCURACY IN LOCAL AND NODAL STAGING AND IMPACT ON SURGICAL DECISION-MAKING

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Background/Aim: Penile cancer is a rare malignancy carrying a substantial psychosocial burden. A reliable preoperative diagnostic pathway is essential to balance oncological control with organ preservation. This study aimed to assess the accuracy of magnetic resonance imaging (MRI) in evaluating local tumour invasion and nodal status, and its role in guiding therapeutic decisions. **Patients and Methods:** We retrospectively reviewed 120 consecutive patients with penile cancer who underwent preoperative MRI at our institution (1999-2024). Patients were stratified into Group A (radical surgery, namely glansectomy or penectomy; n=62, 52%) and Group B [penile-sparing surgery (PSS); n=58, 48%]. A subgroup analysis was performed on the 24 Group B patients who subsequently underwent radical surgery. Continuous variables are reported as median (Q1-Q3); comparisons used Wilcoxon rank-sum, Fisher's exact or Pearson's chi-squared tests, as appropriate. Multivariable logistic regression models identified independent predictors of treatment selection. **Results:** Group A patients were older (63 vs. 58 years; $p=0.019$) and harboured larger tumours (35 vs. 21 mm; $p<0.001$). MRI revealed higher rates of cT3 (29% vs. 5.2%) and cN2-3 (26% vs. 0%) in Group A ($p<0.001$). Pathology confirmed locally advanced disease (pT2-T4) in 76% vs. 33% ($p<0.001$). Positive margins and intraoperative radicalization driven by frozen-section margin assessment rates were comparable between groups. Overall MRI-pT concordance was 50.8% (61/120), highest for pT3 (60%), and lowest for pT2 (42%; with 45% of upstaging at final pathology) ($p=0.001$). Among 24 patients requiring radical surgery after PSS, MRI understaged 72% of initial cT0-Tis-T1 cases ($p=0.035$). In this subgroup, all cT0-Tis-T1 patients achieved negative margins, whereas 40% of cT2-T3 had positive margins ($p=0.043$). MRI-US and MRI-CT concordance for nodal staging were high (95% and 87%). Overall MRI-pN concordance was 67%. The same rate of concordance (67%) was identified for US/CT-pN. Pathological nodal distribution differed significantly between concordant and discordant cases: 65% of discordant patients were pN+, indicating nodal understaging as the predominant pattern

($p=0.001$). At multivariable analysis, age (OR 0.94, 95%CI=0.90-0.98; $p=0.008$), tumour size (OR 0.94, 95%CI=0.90-0.98; $p=0.014$), and MRI cT stage (cT2-T3 vs. cT0-Tis-T1: OR 0.34, 95%CI=0.12-0.91, $p=0.033$) were independent predictors of treatment selection. **Conclusion:** MRI cT staging influenced surgical treatment choice. While cT3-pT3 concordance was strong, MRI substantially understaged early-stage tumours. Nodal understaging was the predominant discordance pattern ($p=0.001$), and MRI did not outperform US/CT for nodal assessment. These findings support MRI integration in preoperative evaluation while emphasizing cautious selection for organ-sparing surgery.

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EXTRAPERITONEAL VS. TRANSVESICAL SINGLE-PORT ROBOT-ASSISTED RADICAL PROSTATECTOMY: PRELIMINARY PERIOPERATIVE, ONCOLOGICAL AND EARLY FUNCTIONAL OUTCOMES

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Background/Aim: Single-port (SP) robot-assisted radical prostatectomy (RARP) has broadened the minimally invasive setting for localized prostate cancer, with extraperitoneal (EP) and transvesical (TV) access emerging as the most promising approaches thanks to peritoneal-cavity sparing, shorter length of stay (LOS),

and improved pain control. Comparative evidence between the two remains limited and mostly derived from high-volume North American series. The current study compares perioperative, oncological and early functional outcomes of SP EP *versus* SP TV RARP at a European tertiary referral center. *Patients and Methods:* We retrospectively reviewed 176 consecutive patients who underwent SP RARP with the da Vinci SP platform at our institution. Patients were stratified by approach: EP (n=159, 90%) and TV (n=17, 10%). Baseline characteristics, perioperative variables, pathological findings, and early functional outcomes were collected. Continuous variables are reported as median (Q1-Q3); comparisons used Wilcoxon rank-sum, Fisher's exact or Pearson's chi-squared tests, as appropriate. *Results:* Cohorts were balanced for age (64 vs. 62 years; $p=0.092$), BMI (25.3 vs. 24.6; $p=0.2$), prostate volume (44 vs. 42 ml; $p=0.3$) and EAU risk classification ($p=0.4$). Operative time was slightly longer in the TV group (224 vs. 210 min; $p=0.4$). Bilateral nerve-sparing was performed in the entire TV cohort (100 % vs. 87% in EP; $p=0.5$), while pelvic lymph node dissection was performed exclusively in the EP group (17%). Slightly higher positive surgical margins rate was observed in the TV group (16% vs. 24%; $p=0.7$), but PSA persistency was higher in the EP group (3.4% vs. 0%; $p>0.9$). Assistant port was used almost in all TV cases, while in fewer than half of EP cases (plus-one 94% vs. 40%; $p<0.001$). LOS was virtually the same in both cohorts (2 [2-4] days). We recorded a higher number of postoperative complications in TV groups (47 % vs. 29 %; $p=0.12$), with a statistically significant higher rate of Clavien–Dindo 2 events (35% vs. 8.8%; $p=0.013$). Despite the marked population imbalance and lack of statistical significance, TV showed a consistent trend toward superior early functional recovery: 0-1 pad continence at 1 and 6 months reached 86% vs. 67% ($p=0.3$) and 100% vs. 86% ($p=0.7$). This impact was not assessed for potency recovery at 1 month, where erectile dysfunction was 71% vs. 64%, respectively for TV vs. EP groups. Conversely ED at 12 months was 0% vs. 39%, respectively for TV vs. EP groups. *Conclusion:* The current study is limited by its

small sample size, which frequently resulted in insufficient statistical power to detect significant differences. Nevertheless, both SP EP and SP TV RARP appeared feasible and oncologically safe, with comparable positive surgical margin and persistent prostate-specific antigen rates. The TV approach showed a trend toward improved continence and erectile-function recovery, whereas postoperative complications, particularly Clavien–Dindo grade II events, were less frequent following the EP approach. The higher complication rate observed with TV RARP may partly reflect the learning curve associated with this technique. Larger prospective comparative studies with longer follow-up are required.

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SINGLE-PORT ROBOTIC UNILATERAL RETROPERITONEAL LYMPH NODE DISSECTION FOR TESTICULAR GERM CELL TUMORS: A PRELIMINARY MONOCENTRIC EXPERIENCE

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Background/Aim: Retroperitoneal lymph node dissection (RPLND) is a cornerstone in testicular germ cell tumors (GCT), particularly for stage IIA/B non-seminomatous disease and post-chemotherapy residual masses. Multi-port robotic RPLND has reduced morbidity while preserving oncological radicality, and unilateral nerve-

sparing templates have lowered anejaculation rates. The da Vinci Single-Port (SP) platform, with single-incision multichannel access, may further improve cosmesis, pain and recovery; however, SP experience in RPLND is limited. We report the preliminary data of a single-center series of SP unilateral RPLND for GCT. **Materials and Methods:** We prospectively collected and retrospectively analysed data from six consecutive patients who underwent left unilateral SP robotic RPLND (June 2025–March 2026) for stage IB–IIIB GCT, with/without neoadjuvant PEB, at our Institution. In supine position, patients received a superior-anterior retroperitoneal access (SARA). AirSeal insufflation and one 12-mm assistant port were used. Unilateral template with inferior mesenteric artery (IMA) sparing was adopted. Demographic, oncological, intra/peri-operative, pathological, functional and Clavien-Dindo data were analyzed. Median (Q1, Q3) and n (%) were reported. **Results:** Six patients (median age 26 yrs, IQR 19-28), with normal BMI (25.1) and no other comorbidities, were treated. Primary histology was embryonal carcinoma in four cases (66%), one case of yolk sac (17%) and one of mesothelioma (17%). Most patients harbored a pT2 cN1 disease at diagnosis (83%), and half received neoadjuvant chemotherapy (namely PEB). All procedures were completed *via* a left unilateral SP approach, with no conversions or intra-operative complications. Median operative time was 194 min (135-350 min) and blood loss negligible in all cases (EBL max 50 cc); the IMA was spared in every patient, cord radicalization performed in half, and a drain placed in 83%. Pathology confirmed adequate nodal clearance (11 nodes, 10-15) with two positive nodes per patient. In one case we recorded a final pN0, pN1 and pN2 in two cases respectively, and pN3 in the last case. Median LOS was 4.5 days (2-7 days), drains were removed after four days and no patients required opioid analgesia. A prophylactic hypolipidic diet was routinely adopted, with one chylous ascites (17%) managed conservatively. One minor in-hospital event (<Clavien II) and one post-discharge Clavien IIIa (drained lymphocele) occurred. Erectile function and antegrade ejaculation were preserved in 100% of cases. At follow-up, five out six patients were

disease-free; one PEB-naive patient had a scrotal recurrence on the cord stump. **Conclusion:** In this preliminary series, SP-RPLND was feasible and was associated with operative time, lymph-node yield, and major complication rates comparable to those reported for contemporary multi-port robotic series. The unilateral nerve-sparing template preserved erectile function and antegrade ejaculation in all patients. The short hospital stay and absence of opioid requirements may represent potential benefits of the SP approach. However, given the small cohort, short follow-up, and occurrence of postoperative complications and one recurrence, these findings should be interpreted cautiously. Further studies involving larger cohorts and longer follow-up are required to confirm the safety, oncological efficacy, and potential advantages of SP-RPLND in appropriately selected patients treated at high-volume centers.

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IMPACT OF LYMPHADENECTOMY ON PERIOPERATIVE OUTCOMES IN SINGLE-PORT ROBOT-ASSISTED RADICAL PROSTATECTOMY: A SINGLE-CENTER EXPERIENCE

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Background/Aim: Single-port robot-assisted radical prostatectomy (SP-RARP) is an emerging minimally invasive approach for the treatment of localized prostate cancer.

However, the impact of lymphadenectomy on perioperative outcomes in this setting is still unclear. The aim of this study was to compare perioperative outcomes and complication rates in patients undergoing SP-RARP with and without lymph node dissection (LND). *Patients and Methods:* A retrospective analysis was conducted on 176 consecutive patients who underwent SP-RARP at a single referral center. Data were prospectively collected and retrospectively analysed. Complications were graded according to the Clavien-Dindo classification. Patients were divided into LND (15%) and non-LND (85%) groups. Variables analysed included age, body mass index (BMI), prostate volume, operative time, length of stay (LOS), time to catheter removal, surgical margin status, prostate-specific antigen (PSA) persistence, intraoperative and postoperative complications and readmission. Results are reported as median and interquartile range or frequencies and percentages. *Results:* Median age was 64 years in both groups. No significant differences were observed in BMI (25.3 vs. 25.3; $p=0.8$) or prostate volume (44 vs. 42 ml; $p=0.8$). Operative time was significantly longer in patients undergoing LND (239 vs. 205 minutes; $p=0.002$). LOS was comparable (2 vs. 2 days; $p=0.5$), as was time to catheter removal (5 vs. 5 days; $p=0.7$). Positive surgical margins were similar between groups (15% vs. 17%; $p>0.9$). PSA persistence was observed in 8.3% versus 2.2% ($p=0.2$). Intraoperative complications occurred in 3.7% of LND patients versus 1.3% of non-LND patients ($p=0.4$), including bleeding requiring transfusion, conversion to multiport, and gas embolism. However, these complications were not directly linked to the LND procedure. Postoperative complications were higher in the LND group (52% vs. 27%; $p=0.010$), with more Clavien-Dindo grade ≥ 3 a events (19% vs. 1.3%; $p=0.001$). Common complications included subcutaneous emphysema, fever, and lymphocele. Hospital readmission occurred in 10 patients (5.7%) and was higher in the LND group (14.8% vs. 4.0%; $p=0.048$), mainly due to lymphocele and thromboembolic events. *Conclusion:* SP-RARP is a safe and feasible procedure. Lymphadenectomy is associated with increased operative time, postoperative complications, particularly major ones, and readmission rate, without differences in early oncological outcomes. Careful patient selection is warranted.

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DOES SURGEON EXPERIENCE MATTER IN SINGLE-PORT RADICAL PROSTATECTOMY? A COMPARATIVE ANALYSIS OF PERIOPERATIVE, ONCOLOGICAL, AND FUNCTIONAL OUTCOMES

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Background/Aim: The aim of this study was to compare perioperative, oncological and functional outcomes between a highly experienced single surgeon [who had performed more than 2000 multiport robot-assisted radical prostatectomies (RARP)] versus less-experienced surgeons (who had performed less than 500 multiport RARP) in patients undergoing RARP using Da Vinci Single Port (SP) Platform. *Patients and Methods:* A retrospective analysis was performed on 93 consecutive patients undergoing SP RARP. Patients were divided into two groups according to surgeon experience: high-experience surgeon ($n=46$, 49%) versus low-experience surgeons ($n=47$, 51%). Baseline characteristics, intraoperative variables, pathological outcomes as well as postoperative functional results were compared. Continuous variables were expressed as median and interquartile range and categorical variables as number and percentage. Statistical significance was set at $p<0.05$. *Results:* Patients treated by young surgeons were older (66 vs. 62 years, $p=0.002$), with higher body mass index (26.37 vs. 24.53, $p=0.008$) and larger prostate volume (49 vs. 39 milliliters, $p=0.008$). Operative time was significantly longer in the young surgeons' group (246 vs. 186 minutes, $p<0.001$),

and time to catheter removal was also longer (6 vs. 5 days, $p=0.034$), while length of hospital stay was similar (2 days in both groups, $p=0.9$). Lymph node dissection was performed more frequently by the high-experience surgeon (26% vs. 6%, $p=0.010$). Positive surgical margins were comparable (11% vs. 13%, $p=0.5$), as well as prostate specific antigen persistence (2.5% vs. 4.5%, $p>0.9$). No intraoperative complications were reported in either group. Postoperative complications occurred in 22% and 26% of patients in high-experience *versus* low-experience surgeons, respectively ($p=0.7$). Urinary continence rates were similar at 1 month (0-1pad use: 66% vs. 72%, $p=0.7$) and at 6 months (80% vs. 86%, $p=0.9$). Erectile function recovery at 6 months with or without pharmacological support was lower in the young surgeons' group (64% vs. 73%, $p=0.030$), while no significant difference was observed at 12 months ($p=0.2$). **Conclusion:** Surgical experience significantly influenced operative time and perioperative management, with shorter procedures and earlier catheter removal in the high-volume surgeon group. However, oncological outcomes, complication rates as well as urinary continence were comparable between the two groups. Overall, radical prostatectomy with Da Vinci Single Port Platform performed by lower experience surgeons achieved outcomes similar to those of a high-experience surgeon, despite less favorable baseline patient characteristics.

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IMPACT OF PROSTATE VOLUME ON INTRAOPERATIVE AND POSTOPERATIVE OUTCOMES AFTER ROBOT-ASSISTED RADICAL PROSTATECTOMY USING THE DA VINCI SINGLE-PORT PLATFORM

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Aim: This study aimed to evaluate intraoperative and postoperative outcomes in patients undergoing robot-assisted radical prostatectomy (RARP) for localized prostate cancer (PCa) using the Da Vinci Single-Port (SP) robotic platform according to prostate volume (PV). **Materials and Methods:** We identified 176 patients with localized PCa treated with RARP using the Da Vinci SP platform at our tertiary referral center. Patients were stratified according to PV (≥ 50 ml vs. <50 ml). Descriptive analyses of patients' baseline characteristics, intraoperative and post-operative outcomes were performed. Continuous variables are reported as median (Q1-Q3); comparisons used Wilcoxon rank-sum, Fisher's exact or Pearson's chi-squared tests, as appropriate. **Results:** Among 176 RARP SP patients, 56 (32%) had PV ≥ 50 ml. Patients with PV ≥ 50 ml were older (67 vs. 63 years; $p<0.001$) and exhibited a higher prevalence of preoperative erectile dysfunction (32 vs. 14%; $p=0.009$). EAU risk classification was comparable between the two groups ($p=0.8$). Assessment of intraoperative outcomes showed longer operative times in patients with PV ≥ 50 ml (238 vs. 200 min; $p<0.001$), while no significant differences were observed in the use of an assistant trocar ($p=0.3$), nerve-sparing modality ($p=0.2$), positive surgical margins on intraoperative frozen section analysis ($p=0.8$), or intraoperative complications ($p=0.2$). Postoperative outcomes analysis revealed comparable rates of length of stay ($p=0.6$), time to catheter removal ($p=0.1$), complications ($p=0.2$), Clavien-Dindo complication classification ($p=0.5$), PSA persistency ($p=0.7$) and urinary incontinence rates at 1 month (30 vs. 33%, $p=0.7$) and 6 months (16 vs. 9%, $p=0.8$). The rate of non-potent patients at 1 month was higher in patients with PV ≥ 50 ml (80 vs. 57%; $p=0.017$), whereas sexual potency at 6 months was comparable between the two groups (57 vs. 32% $p=0.4$). **Conclusion:** The Da Vinci SP platform provides a safe and

feasible option for radical prostatectomy regardless of PV. Although patients with PV ≥ 50 ml were older, had longer operative times, and showed a higher rate of early postoperative erectile dysfunction, no significant differences were observed in intraoperative complications, postoperative complications, length of stay, time to catheter removal, PSA persistency, urinary continence, or mid-term sexual function recovery. Larger PV may increase surgical complexity without negatively affecting overall perioperative outcomes.

18 POSTOPERATIVE PAIN AND BOWEL RECOVERY AFTER SINGLE PORT VS. MULTI-PORT ROBOT ASSISTED RADICAL PROSTATECTOMY: A COMPARATIVE STUDY

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Background/Aim: Single-port (SP) robot-assisted radical prostatectomy (RARP) has emerged as a minimally invasive alternative to the conventional multiport (MP) approach, with the potential to improve postoperative recovery. By minimizing abdominal incisions, the SP technique may offer advantages in terms of postoperative pain control and faster return of bowel function. This study aimed to compare bowel function recovery and postoperative pain between SP and MP approaches, in order to better define the potential clinical benefits of the SP surgery. *Materials and Methods:* We retrospectively analyzed 95 patients undergoing MP (n=63 [66%]) and

SP (n=32 [34%]) RARP in a high-volume center. Primary endpoints were bowel recovery and postoperative pain. Bowel recovery was assessed by time to first flatus and first bowel movement. Postoperative pain was assessed in terms of intensity, measured for each patient using a 0-10 numeric rating scale (NRS), and analgesic requirement. *Results:* Baseline characteristics were comparable between the two groups, with no significant differences in preoperative variables. Median operative time was 214 minutes, and median length of stay (LOS) was 2 days in both groups. Early bowel recovery, defined as time to first flatus <24 hours, was more frequent in the SP group compared to the MP group (97% vs. 81%; $p=0.05$). However, no significant difference was observed in time to first bowel movement ($p>0.9$). Median postoperative pain intensity was lower in the SP group compared to MP (2 vs. 3), although the difference was not statistically significant ($p=0.2$). Similarly, no significant differences were observed in terms of postoperative analgesic requirements ($p=0.2$). *Conclusion:* SP RARP was associated with a trend toward faster recovery of bowel function compared to the MP approach. Postoperative pain outcomes were comparable between groups. These findings suggest a potential advantage of the SP approach in early postoperative recovery, although larger prospective studies are needed to confirm these results.

19 PSMA-PET RE-EVALUATION IN A MULTIDISCIPLINARY TUMOR BOARD: IMPACT ON STAGING AND TREATMENT OF PROSTATE CANCER

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Background/Aim: Real-world concordance between prostate-specific membrane antigen-positron emission tomography (PSMA-PET) readers at non-academic centres and expert readers at academic institutions is unexplored, and the clinical impact of expert second-opinion review on staging and treatment remains unknown. This study aimed to assess the impact of PSMA-PET re-evaluation within a multidisciplinary tumor board (MDT) on disease staging and subsequent treatment of newly diagnosed prostate cancer (PC) in a real-world referral network. **Patients and Methods:** This retrospective analysis included 168 patients with newly diagnosed prostate cancer who underwent PSMA-PET for primary staging at non-academic centers between 2021 and 2024 and were subsequently discussed by our multidisciplinary team. All scans were re-evaluated by expert nuclear medicine readers, unblinded to clinical-pathological data and to the original report, to reflect routine decision-making rather than a blinded reader-to-reader comparison. Agreement between original and revised scans was tested with Cohen's κ (95%CI) for separate N, M1a, M1b, and M1c stages, overall M stage (M0/M1a/M1b/M1c), overall M classification (M0/low-volume/high-volume), overall disease staging (N0M0/N1M0/

NanyM1a/NanyM1b/NanyM1c), and planned treatments [robot-assisted radical prostatectomy or radiotherapy (RALP/RT) vs. radiotherapy plus hormone therapy (RT+HT) vs. radiotherapy plus hormone therapy plus androgen receptor-targeted agent (RT+HT+ARTA) vs. chemotherapy plus hormone therapy plus androgen receptor-targeted agent (CHT+HT+ARTA)]. Follow-up data after treatment were tabulated. **Results:** The radiotracer used was fluorine-18-labelled prostate-specific membrane antigen-1007 ($[^{18}\text{F}]$ PSMA-1007) in 106 examinations (63%) and gallium-68-labelled prostate-specific membrane antigen-1007 ($[^{68}\text{Ga}]$ Ga-PSMA-11) in 25 (15%); the radiotracer was not specified in 37 examinations (22%). Only 11 external reports (6.5%) followed a structured reporting format. Agreement between the external reports and multidisciplinary team reassessment was substantial for N stage [74 (44.0%) vs. 59 (35.1%); $\kappa=0.77$] and M1a disease [43 (25.6%) vs. 29 (17.3%); $\kappa=0.65$], but poor for M1b [113 (67.3%) vs. 49 (29.2%); $\kappa=0.25$] and M1c disease [8 (4.8%) vs. 2 (1.2%); $\kappa=0.18$]. Overall disease staging showed only slight agreement ($\kappa=0.18$): N0M0, N1M0, NanyM1a, NanyM1b and NanyM1c were reported in 16 (9.5%) vs. 81 (48.2%), 12 (7.1%) vs. 20 (11.9%), 22 (13.1%) vs. 17 (10.1%), 110 (65.5%) vs. 48 (28.6%), and 8 (4.8%) vs. 2 (1.2%) original vs. revised scans, respectively. Management plans (RALP/RT, RT+HT, RT+HT+ARTA, CHT+HT+ARTA) changed from 28 (16.7%), 22 (13.1%), 87 (51.8%) and 31 (18.5%) to 101 (60.1%), 17 (10.1%), 36 (21.4%) and 14 (8.3%), respectively ($\kappa=0.26$). Discrepancies were mainly driven by downstaging of suspected M1b lesions and translated into clinically relevant shifts from systemic therapy to definitive local treatment. **Conclusion:** Expert MDT re-evaluation of externally performed PSMA-PET scans led to extensive stage migration and substantial changes in PC management. The clinical utility of PSMA-PET at a network level depends not only on access to the technology, but also on reader expertise, structured reporting, and integration within multidisciplinary care pathways.

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SINGLE-PORT ROBOT-ASSISTED RADICAL PROSTATECTOMY: SHORT-TERM OUTCOMES AND LEARNING CURVE ASSESSMENT

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Background/Aim: Single-port robot-assisted radical prostatectomy (SP-RARP) is an emerging minimally invasive option for localized prostate cancer. The extraperitoneal approach (EP) avoids bowel manipulation, reduces hospital stay and opioid use, and is particularly suited to the SP platform. However, distinctive features of SP surgery – narrow working space, altered triangulation and reduced instrument strength – may influence the learning curve (LC), even for surgeons experienced with multi-port (MP) RARP. This study aimed to evaluate perioperative, oncological and early functional outcomes of extraperitoneal SP-RARP, focusing on the learning curve (LC) impact, in a series performed by a surgeon with >500 MP-RARP. **Patients and Methods:** We retrospectively reviewed 46 consecutive patients who underwent EP SP-RARP by a single surgeon at a tertiary centre. Continence was defined as 0-1 safety pad/day. To assess the LC, the first 20 cases (LC group) were compared with the subsequent 26 (proficiency group) using Wilcoxon rank-sum, Fisher's exact and chi-squared tests. **Results:** Median age was 62 years (IQR=58-66), BMI 24.5 (22.8-26.3) and prostate volume 39 ml (28-50). By EAU risk, 13% were low-, 85% intermediate, and 2% high-risk. Median operative time was

186 min (167-211 min), length of stay two days, and catheter removal on day 5. Bilateral nerve-sparing was performed in 91% and pelvic lymphadenectomy in 26%. No intraoperative complications or conversions occurred. Positive surgical margin (PSM) rate was 11% (5/46). Comparing LC vs. proficiency group, no significant differences emerged in operative time (183 vs. 187 min, $p=0.3$), bilateral nerve-sparing (90% vs. 92%, $p=0.8$), PSM (10% vs. 12%, $p>0.9$) or intraoperative events. A significant reduction in the use of accessory assistant ports was observed with increasing experience (40% vs. 4% of "+1 port" cases, $p=0.005$), reflecting progressive technical autonomy. Postoperative complications occurred in 5% vs. 35% ($p=0.028$), though almost entirely low-grade (Clavien-Dindo I 15%, II 4.3%, IIIa 2.2%; no CD $\geq$ IIIb), likely related to closer structured follow-up and adoption of more complex cases in later patients. At 1 month, continence (0-1 pad) was achieved in 69% vs. 63% ($p>0.9$) and potency (with/without PDE5-i) in 75% vs. 71% ($p>0.9$), with no significant differences. **Conclusion:** In experienced MP-RARP surgeons, extraperitoneal SP-RARP is safe, feasible and reproducible, with rapid skill transferability. The LC did not adversely affect operative time, oncological or early functional outcomes. The progressive reduction in assistant port use supports the achievement of technical autonomy within the first 20 cases. These findings endorse the integration of SP-RARP into established MP-RARP programs, although longer follow-up is warranted to confirm durable functional and oncological outcomes.

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EARLY FUNCTIONAL AND ONCOLOGICAL OUTCOMES OF SINGLE-PORT ROBOT-ASSISTED RADICAL PROSTATECTOMY: INITIAL EXPERIENCE

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Background/Aim: Single-port (SP) robot-assisted radical prostatectomy (RARP) has emerged as a minimally invasive approach for localized prostate cancer. We report early functional and oncological outcomes of a consecutive series performed at a high-volume referral center. **Materials and Methods:** We retrospectively analyzed 176 consecutive patients who underwent SP-RARP. Baseline characteristics, postoperative and follow-up data were collected. Early functional outcomes included continence and potency. Oncological outcomes included positive surgical margins (PSM), PSA persistence, and biochemical recurrence (BCR). **Results:** Median (IQR) age was 64 years (range=60-68 years) and median (IQR) prostate volume was 44 ml (range=33-57 ml). Most patients had intermediate-risk disease according to EAU risk categories (82%), with PIRADS ≥ 4 in 80% of cases. Bilateral nerve-sparing was performed in 88% of patients. Final pathology showed ISUP grade group ≥ 3 in 30.4% of patients and pT3 disease in 31.3%. Early continence rates (0-1 pad) were 69% at 1 month and 87% at 6 months, with pad-free rates of 27% and 58%, respectively. At 6 months, erectile function was recovered in 50% of patients (39% with pharmacological assistance and 11% spontaneously). At 12 months, potency outcomes further improved with 63% of patients achieving erections (27% with pharmacological assistance and 37% spontaneously). PSM were observed in 18.3% of cases. PSA persistence occurred in 3.1% of patients, while BCR was recorded in 0.6% at a median time of 6 months. **Conclusion:** In this initial experience, SP-RARP appeared safe and feasible, with favorable early functional outcomes along with low rates of PSA persistence and BCR. Longer follow-up is required to confirm these results.

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PERIOPERATIVE OUTCOMES AND COMPLICATION PROFILE OF SINGLE-PORT ROBOT-ASSISTED RADICAL PROSTATECTOMY: A SINGLE-CENTER EXPERIENCE

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Background/Aim: Single-port robot-assisted radical prostatectomy (SP-RARP) is an emerging minimally invasive approach for localized prostate cancer. We report the perioperative outcomes and complication profile of a consecutive series performed at a single referral center. **Patients and Methods:** We retrospectively analyzed 176 consecutive patients who underwent SP-RARP. Baseline characteristics, intraoperative data, and postoperative complications were recorded. Complications were graded according to the Clavien-Dindo (CD) classification. **Results:** Median patient age was 64 years (IQR 60-68) and median prostate volume was 44 ml (IQR 33-57). The majority of patients had a CCI class 3-4 (69%) and a BMI consistent with pre-obesity or normal weight (46% and 44%, respectively). Most cases were PIRADS 4 (63%), and the predominant EAU risk category was intermediate-favorable (58%). The extraperitoneal approach was employed in 90% of cases, with transvesical access in the remaining 9.7%. Bilateral nerve-sparing was performed in 88% of patients. Median operative time was 210 minutes (IQR=182-246), median length of stay was 2 days (IQR 2-3), and median time to catheter removal was 5 days (IQR=5-7).

Lymphadenectomy was performed in 15% of patients. Intraoperative complications occurred in 3 patients (1.7%), consisting of bleeding (n=2) and a technical issue requiring conversion to multiport (n=1). Postoperative complications were recorded in 54 patients (31%), the vast majority being early (<30 days, 96%). The most frequent complication was subcutaneous emphysema (13%), followed by fever without sepsis (3.4%), lymphocele (2.8%), hematuria (2.3%), and pneumothorax (2.3%). Late complications (≥30 days) occurred in two patients (1.1%), both presenting with urethral stricture. According to CD classification, grade 1 complications were most frequent (16%), followed by grade 2 (11%) and grade 3a (4%). No grade 4 or 5 events were recorded. Hospital readmission was required in 10 patients (5.7%). *Conclusion:* SP-RARP is a safe and feasible procedure with a low intraoperative complication rate and an acceptable postoperative morbidity profile. The majority of complications were minor and managed conservatively, with no severe or fatal events observed.

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ASSESSING THE VALUE OF GRADE HETEROGENEITY AMONG PRIMARY TUMOR AND VENOUS TUMOR THROMBUS IN CLEAR CELL RENAL-CELL CARCINOMA

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Background/Aim: Recent evidence demonstrated the presence of nuclear grade heterogeneity between primary tumor (PT) and venous tumor thrombus (VTT) in clear-cell renal cell carcinoma (ccRCC). This study aimed to assess the

rate of tumor grade discrepancy (GD) between PT and VTT in a cohort of ccRCC and the association with disease-free survival (DFS), overall survival (OS), and cancer-specific survival (CSS). *Materials and Methods:* This retrospective analysis was based on two prospectively collected databases from high-referral centers. Pathology slides were centrally reviewed. GD, a bidirectional variable (up-grading or down-grading), was numerically defined as the VTT grade minus the PT grade. Multivariable models were built to predict DFS, OS, and CSS. The Kaplan–Meier method and the log-rank test were applied to assess differences in survival. *Results:* In this study, data from 88 patients with locally advanced ccRCC and VTT were analyzed. GD was identified in 47 (53.5%) cases. VTT upgrading occurred in 27 (30.6%) patients, while downgrading was observed in 20 (22.9%) patients. The presence of GD was independently associated with significantly worse oncologic outcomes across all endpoints, regardless of the direction of the discrepancy. Multivariable Cox regression analysis revealed that GD correlated with a lower probability of DFS (HR=1.74), CSS (HR=1.68), and OS (HR=1.91). Specifically, VTT upgrading (GD +1 or +2) emerged as the most adverse prognostic indicator, with GD +2 patients facing the highest risk of recurrence (HR=1.88). These findings suggest that integrating thrombus-specific grading into postoperative frameworks could enhance risk stratification and help personalize adjuvant therapy strategies. *Conclusion:* Routine reporting of PT and VTT grade in locally-advanced ccRCC can facilitate more informed treatment decisions by tailoring strategies to an individual patient's risk of progression.

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SYSTEMIC IMMUNE MODULATION INDUCED BY METASTASIS-DIRECTED STEREOTACTIC BODY RADIOTHERAPY IN OLIGOMETASTATIC PROSTATE CANCER: RESULTS FROM THE PROSPECTIVE I.OSCAR STUDY

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Background/Aim: Stereotactic body radiotherapy (SBRT) is increasingly used as metastasis-directed therapy (MDT) in oligometastatic prostate cancer (PCa), providing high rates of local control and delaying systemic treatment escalation (1). Beyond tumor ablation, SBRT may exert systemic immunomodulatory effects (2, 3). However, prospective data characterizing immune dynamics in this setting remain limited. I.OSCAR is a prospective pilot study investigating systemic immune modulation in patients with oligorecurrent or oligoprogressive PCa treated with SBRT. **Patients and Methods:** Peripheral blood samples were collected at baseline (T0), at the end of SBRT (T1), and one week after treatment (T2). Multiparametric flow cytometry was used to characterize lymphoid and myeloid cell populations. Associations between immune parameters and clinical outcomes, including progression-free survival (PFS) and overall survival (OS), were explored using Cox regression models. **Results:** Thirty-seven patients were included. SBRT achieved high local control rates (94.0% at 12 months), while median PFS was 28.25 months. Early post-treatment PSA levels were significantly associated with OS. Baseline immune profiling revealed that patients who developed disease progression had reduced adaptive immune components and increased markers of T-cell differentiation and exhaustion. SBRT induced modest but measurable systemic immune changes, predominantly within the myeloid compartment, including expansion of circulating monocytes with features of alternative activation. In the lymphoid compartment, treatment was associated with functional modulation, including increased TIGIT expression on CD8⁺ T cells and reduced CTLA-4 expression on CD4⁺ T cells. Exploratory analyses suggested that androgen deprivation therapy was associated with expansion of T-cell

populations, although no clear correlation with clinical outcomes was observed. **Conclusion:** SBRT induces measurable systemic immune modulation in oligometastatic PCa, with baseline immune profiles and treatment-induced changes potentially influencing clinical outcomes. These findings support further investigation of immune-based biomarkers and combinatorial strategies integrating SBRT with immunomodulatory approaches.

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PROSTATE RE-IRRADIATION: A MULTICENTER EXPERIENCE ON EFFECTIVENESS, ADVERSE EVENTS, AND THE INTEGRATION OF ANDROGEN DEPRIVATION THERAPY IN A REAL WORLD POPULATION

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Background/Aim: The management of local recurrence of prostate cancer (PCa) after previous radiotherapy (RT) remains a clinical challenge. Re-irradiation (reRT) is emerging as a promising salvage option, but consolidated data on its efficacy, safety, and optimal integration with androgen deprivation therapy (ADT) are lacking. This multicenter retrospective study aims to analyze the outcomes of prostate reRT with stereotactic body radiotherapy (SBRT) in a real-world patient cohort. **Patients and Methods:** We retrospectively analyzed data from 32 patients from three centers, with intraprostatic or prostatic bed PCa recurrence, treated with SBRT reRT between 2014 and 2024 after a previous course of RT. The primary outcome was local relapse-free survival (LRFS). Secondary outcomes included biochemical response at 3 (3mBR) and 6 months (6mBR), biochemical relapse-free survival (BRFS), metastasis-free survival (MFS), overall survival (OS), and acute and late adverse events (AEs), assessed according to CTCAE v5.0 criteria. **Results:** With a median follow-up of 42 months, median LRFS was 81.6 months, with 1-, 2-, and 5-year rates of 100%, 88.8%, and 66.7%. High-risk disease per NCCN classification was the only factor significantly associated with local relapse at both univariate (HR=10.12, 95%CI=1.2-82.5, $p=0.03$) and multivariate analysis (HR=14.24, 95%CI=1.64-123.09, $p=0.01$). Biochemical response occurred in 46.9% and 78% of patients at 3 and 6 months. Median BRFS and MFS were 41.6 and 59.2 months. Median OS was not reached; two deaths occurred (one treatment-related, one disease-related). The treatment was well-tolerated, with low rates of severe (Grade ≥ 2) AEs: ≥ 2 acute genitourinary (GU) and gastrointestinal (GI) AEs occurred in 31.2% and

15.6% of patients, respectively. Clinically relevant late GU and GIAEs occurred in 34.3% and 15.6%, respectively. A single G5 late event (3.1%) was recorded. The majority of patients (84.3%) did not receive concomitant ADT. **Conclusion:** Prostate reRT with SBRT is confirmed as an effective and relatively safe salvage option, capable of providing high rates of LC with an acceptable safety profile. Careful patient selection, the use of advanced imaging, and meticulous dosimetric planning are essential to optimize outcomes and minimize risks. The role of concomitant ADT requires further investigation in prospective trials.

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LAPAROSCOPIC RADICAL VS. PARTIAL NEPHRECTOMY FOR T2 RENAL CELL CARCINOMA

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Background/Aim: Laparoscopic radical nephrectomy (RN) continues to be the standard treatment for cT2 renal cell carcinoma (RCC), but partial nephrectomy (PN) has emerged as a viable alternative with the advancement of lap and robot-assisted techniques. However, comprehensive comparative data between lap and robot-assisted partial nephrectomy (LPN and RAPN) and LRN for larger renal tumors remain scarce. **Materials and Methods:** We conducted a multicenter prospective study utilizing prospectively collected data. Patients undergoing LPN and RAPN or LRN for cT2M0 RCC were matched 1:1 using propensity scores based on clinical and tumor characteristics. The primary outcome was 5-year disease-free survival (DFS). Secondary endpoints included overall survival (OS), renal function, perioperative outcomes, complications, and achievement of the Trifecta. **Results:**

Among the 778 patients included, 390 LPN + RAPN and 388 LRN were matched. The median tumor size was 7.8 cm vs. 8.1 cm respectively. Oncological outcomes were comparable: five-year DFS was 63.5% for LPN and RAPN and 57.0% for LRN ($p=0.09$), cancer-specific survival (CSS) was 87.5% for LPN and RAPN and 91.0% for LRN ($p=0.35$), metastasis-free survival (MFS) was 70.0% for LPN and RAPN and 62.5% for LRN ($p=0.029$), and OS was 80.0% for RAPN and LPN compared to 79.0% for LRN ($p=0.55$). RAPN and LPN were associated with enhanced preservation of renal function (mean $\Delta eGFR$ at 5 years: -12.8 vs. -28.4 ml/min/1.73 m², $p<0.001$), fewer migrations to chronic kidney disease (CKD) stages, and a reduction in acute kidney injury. Major complications occurred more frequently following RAPN (7.0% vs. 3.0%, $p=0.015$). The Trifecta outcome was achieved in 46.3% of RAPN cases. **Conclusion:** RAPN and LPN are safe and functionally advantageous alternatives to LRN for selected cT2 RCC patients. While there is a higher incidence of perioperative morbidity associated with RAPN, these risks are considered acceptable in specialized centers and are mitigated by long-term nephron-sparing benefits.

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LAPAROSCOPIC VS. ROBOTIC ADRENALECTOMY

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Background/Aim: The comparative effectiveness of different surgical approaches for adrenocortical carcinoma (ACC) remains a topic of debate. This multicentric prospective study aimed to compare overall survival (OS) and disease-free survival (DFS) between laparoscopic adrenalectomy (LA) and robotic adrenalectomy (RA). **Materials and Methods:** Between

2021 and 2025, we conducted a retrospective analysis of 112 patients with stage I-III ACC who underwent either LA or RA. Propensity score matching (PSM) was utilized to balance baseline characteristics across the LA and RA groups. The primary outcomes evaluated were OS and DFS. Survival analyses were performed using the Kaplan–Meier method, and the log-rank test was applied to compare survival curves. Univariate and multivariate Cox proportional hazards models were employed to identify factors influencing OS and DFS. **Results:** When considering perioperative and survival outcomes, the RA group exhibited significantly shorter operative times compared to the LA group, with marked differences observed in both unmatched ($p<0.001$) and matched cohorts ($p=0.002$). Additionally, patients in the RA group experienced a reduced length of hospital stay, again reflected in both unmatched ($p=0.002$) and matched cohorts ($p=0.015$). Importantly, despite these advantages in terms of operative efficiency and recovery, there were no significant differences in the incidence of tumor rupture, mortality rates, OS, recurrence, or DFS between the LA and RA groups. A further comparison between retroperitoneal laparoscopic adrenalectomy (RLA) and transabdominal laparoscopic adrenalectomy (TLA) revealed that RLA was associated with shorter operative times, yet no significant differences in other clinical outcomes between the two laparoscopic techniques were found. Overall, long-term survival analyses demonstrated no substantial differences in OS or DFS outcomes when comparing both the matched and unmatched cohorts for LA and RA approaches. Additionally, the type of laparoscopic technique employed did not have a significant impact on OS or DFS. Notably, tumor size and T stage emerged as significant predictors of poorer survival outcomes across both surgical cohorts. **Conclusion:** For localized ACC (stage I-III), both LA and RA provide comparable long-term oncological outcomes regarding OS and DFS. Both TLA and RLA are safe and effective surgical options for managing localized ACC.

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CLINICAL IMPACT OF BIOPSY AND FIDUCIAL MARKER POSITIONING BEFORE STEREOTACTIC BODY RADIOTHERAPY IN PATIENTS TREATED WITH PRIMARY KIDNEY CARCINOMA

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Background/Aim: Stereotactic body radiation therapy (SBRT) is a non-invasive alternative approach for patients with kidney cancer who are unfit for surgery for medical reasons or decline surgery. Pre-treatment biopsy may confirm malignancy and prevent unnecessary treatment of benign lesions that mimic renal cancer on imaging. Fiducial markers can be implanted during the same procedure and used for image-guided radiotherapy (IGRT), potentially

allowing more accurate patient positioning and smaller planning margins, thereby reducing irradiation of the surrounding healthy renal tissue. This study evaluated the clinical role of renal mass biopsy and fiducial marker placement before SBRT for primary renal tumors. **Patients and Methods:** We retrospectively analysed 22 patients (sixteen male and five female). Median age at diagnosis was 79 years (range=52-89 years). Median ECOG performance status was 0-1 in all patients. All renal masses were unifocal. Lateralization was left in 13 patients and right in nine patients. All patients were discussed in a multidisciplinary setting before SBRT was proposed to the patients. Biopsy before SBRT was performed in 14 patients: eight were clear cell renal carcinoma, three were papillary, one was medullary and three were benign oncocytomas. Eleven patients underwent a fiducial marker positioning procedure before SBRT the same day of renal biopsy, and no significant side effects were reported (Figure 1A and B). Biopsy was ultrasound-guided in all cases. Patients proceeding to treatment received SBRT using volumetric modulated arc therapy. Daily IGRT was performed using cone-beam computed tomography, with image registration based on the fiducial markers in patients in whom they had been implanted. **Results:** In the 14 patients who underwent biopsy, three patients (14%) had a benign lesion and were spared

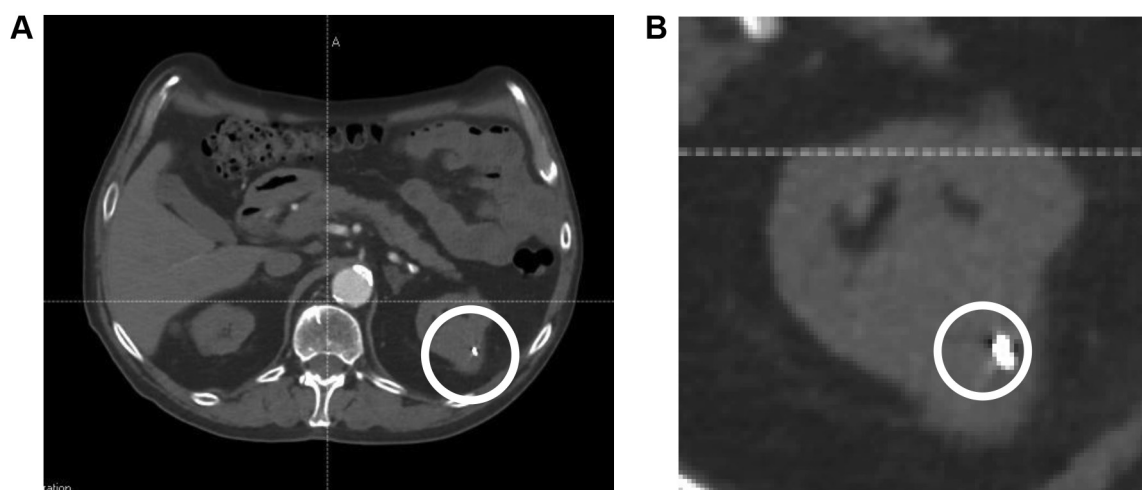


Figure 1. Fiducial marker positioning in a patient with renal carcinoma candidate to stereotactic radiotherapy. A) Fiducial marker (white circle) positioned next to a left renal lesion. B) Magnified view of the fiducial marker (white circle).

SBRT since they were asymptomatic; they started a follow-up program consisting of an abdominal contrast-enhanced computed tomography once a year. Median tumor volume was overall 20.2 cc (range=4.4-60.4 cc), while it was 22 cc (range=4.4-60.4 cc) for malignant tumors and 15.5 cc (range=14-17 cc) for benign tumors. In the subset of 11 patients who underwent fiducial marker positioning, median positioning shifts measured with IGRT were respectively 3.4 mm (range=0-13.2 mm) laterally, 4.6 mm (range=0-14.3 mm) cranio-caudally, and 6 mm (range=0-20 mm) antero-posteriorly. Retrospective positioning data were unavailable for patients without fiducial markers, precluding a direct comparison between the two groups. *Conclusion:* SBRT is an emerging treatment option for medically inoperable primary renal cancer and can be delivered non-invasively in an outpatient setting. In this series, pre-treatment biopsy identified benign oncocytomas that would otherwise have been treated on the basis of imaging findings alone, thereby preventing unnecessary irradiation and its potential adverse effects. Fiducial marker implantation performed during the biopsy procedure was feasible and was not associated with clinically significant complications. The observed positioning corrections suggest that fiducial markers may support accurate image guidance during renal SBRT. However, because positioning data were unavailable for patients without fiducial markers, no conclusions can be drawn regarding their comparative benefit or their ability to reduce treatment margins. Pre-treatment biopsy should therefore be considered in patients undergoing SBRT for presumed primary renal cancer, while the potential advantages of fiducial marker guidance require confirmation in larger comparative studies.

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LOCAL CONTROL AND TOXICITY IN A COHORT OF PATIENTS TREATED WITH STEREOTACTIC BODY RADIOTHERAPY FOR PRIMARY KIDNEY CARCINOMA

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Background/Aim: Stereotactic body radiation therapy (SBRT) is a non-invasive treatment approach for patients with kidney cancer who are not candidates for nephrectomy (either partial or total) for medical reasons or who decline surgery. In this study, we report outcomes and feasibility of SBRT for primary renal cancer with a focus on renal function after SBRT. *Patients and Methods:* We retrospectively analysed data for 19 patients. Fourteen were males and five were females. Median age at diagnosis was 79 (range=52-89) years. Median Eastern Cooperative Oncology Group performance status was 0-1 for all patients. Clinical stage was T1a, T1b and T2a in 12, 6 and 1 patient, respectively. All renal masses were unifocal. Lateralization was left in 12 patients and right in 7. Three patients had positive history for renal surgery (one contralateral total nephrectomy and two homolateral partial nephrectomies). All patients were discussed in a multidisciplinary setting before SBRT was proposed. Biopsy before SBRT was performed in 12 patients: 8 cases were clear-cell renal carcinoma, 3 were papillary and 1 was medullary. Eleven patients underwent a fiducial marker positioning procedure before SBRT on the same day of renal biopsy: non significant side-effects were reported. All patients were given stereotactic radiotherapy and volumetric-modulated arc therapy was planned for all cases; 18 patients were given 42 Gy/3 fractions and 1 patient 50 Gy/5 fractions. Follow-up consisted of clinical examination creatinine and estimated glomerular filtration rate (eGFR) and imaging every 6 months. Toxicity was graded according to the Common Terminology Criteria for Adverse Events (version 5.0). *Results:* Data regarding outcome and tolerance were available for 18 patients. Local control was achieved for all patients after a median follow-up of 12 (range=6-24) months. There was one

case of G1 acute gastrointestinal toxicity consisting of mild nausea. One suspected G3 late gastrointestinal toxicity requiring hemicolectomy for ischaemic damage was reported. Creatinine and eGFR before SBRT were 1.14 (range=0.74-3.6) ng/ml and 61 (range=15.3-91.2) ml/min/1.73m². Creatinine and eGFR after SBRT were 1.22 (range=0.65-4.25) ng/ml and 55 (range=12-101.7) ml/min/1.73m² at 6 (range=0.94-2.1) months, and 1.3 ng/ml and 52 (range=36-74.1) ml/min/1.73m² at 12 months (data at 12 months were available for 9 patients). *Discussion and Conclusion:* In this cohort, SBRT showed favourable outcomes and tolerance; renal function was overall stable at 12 months. SBRT appears to be a non-invasive alternative for patients with renal clear-cell carcinoma who are inoperable due to comorbidities.

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THE INSIDE STUDY: MAPPING DNA DAMAGE RESPONSE GAPS BEYOND *BRCA* TO OPTIMIZE PRECISION MEDICINE IN HIGH-RISK ADVANCED PROSTATE CANCER

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Background/Aim: Despite recent therapeutic advances, prostate cancer (PC) remains associated with suboptimal response rates and the development of treatment resistance, which significantly contribute to mortality. Genomic analyses reveal DNA-damage response (DDR) alterations in approximately 10-19% of primary PCs, increasing to 23-27% in metastatic castration-resistant PC. While *BRCA* DNA repair-associated (*BRCA*) alterations and their predictive value for response to poly (ADP-ribose) polymerase (PARP) inhibitor are well established in metastatic castration-resistant PC (1), prospective data in high-risk advanced PC are lacking. Furthermore, the clinical significance of DDR alterations beyond *BRCA* remains poorly defined. In the context of precision oncology, there is a critical need for experimental models that capture tumor heterogeneity. Patient-derived 3D organoids represent a promising platform for this purpose (2). The ongoing INSIDE study aims to identify actionable DDR vulnerabilities beyond *BRCA* and to assess their clinical relevance in high-risk advanced PC. *Materials and Methods:* The INSIDE study is a prospective observational trial led by the Candiolo Cancer Institute, FPO-IRCCS, with San Luigi Hospital as a satellite center. Since March 2023, 97 patients with high-risk PC have been enrolled. Among the 90 patients with available diagnostic data, Gleason scores (GS) were distributed as follows: GS 7 (45%), GS 9 (41%), GS 8 (13%), and GS 10 (1%). Tumor samples are collected for patient-derived 3D organoid generation, molecular characterization, and pharmacological profiling. Genomic analysis is performed using the TruSight Oncology 500 HRD (TSO500-HRD) assay, enabling assessment of genomic alterations and genomic instability scores, with a focus on DDR-related pathways. *Results:* Comprehensive genomic profiling of the initial cohort revealed a heterogeneous DDR landscape. Preliminary analysis of 48 tumor samples identified variants across multiple DNA-repair pathways, including missense mutations in base excision repair and nucleotide excision repair genes. Beyond *BRCA* alterations, additional aberrations were observed in homologous recombination genes. Notably, alterations in replication stress pathways were also identified. To functionally characterize these

findings, we established a pharmacological screening platform using patient-derived PC organoids, allowing correlation between genomic alterations and drug sensitivity. Preliminary results suggest a potential association between non-*BRCA* homologous recombination gene alterations and sensitivity to the PARP inhibitor olaparib. Furthermore, candidate biomarkers predictive of response to ataxia-telangiectasia mutated (ATM) and ataxia-telangiectasia and RAD3-related (ATR) inhibitors have been identified. *Discussion and Conclusion:* The INSIDE study underscores the clinical relevance of DDR alterations across multiple repair pathways in high-risk PC and highlights novel therapeutic vulnerabilities beyond *BRCA*. The integration of genomic profiling with functional drug screening in patient-derived PC organoids provides a robust framework for patient stratification and supports the development of more effective precision medicine strategies.

1 Longoria O, Beije N, de Bono JS: PARP inhibitors for prostate cancer. *Semin Oncol* 51(1-2): 25-35, 2024. DOI: 10.1053/j.seminoncol.2023.09.003

2 De Lazzari G, Opattova A, Arena S: Novel frontiers in urogenital cancers: From molecular bases to preclinical models to tailor personalized treatments in ovarian and prostate cancer patients. *J Exp Clin Cancer Res* 43(1):146, 2024. DOI: 10.1186/s13046-024-03065-0

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VIRTUAL REALITY IN LAPAROSCOPIC PARTIAL NEPHRECTOMY: SUPERIOR PREDICTIVE ACCURACY AND IMPROVED PERIOPERATIVE OUTCOMES IN A PROSPECTIVE COHORT

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Background/Aim: Laparoscopic partial nephrectomy is recognized as the gold standard treatment for T1 renal tumors, achieving favorable oncological and functional outcomes. However, traditional computed tomography (CT) imaging may not adequately visualize complex vascular and spatial anatomy. The application of virtual reality (VR)-based 3D reconstruction offers an immersive anatomical visualization, which could potentially enhance preoperative planning. This study aimed to evaluate the efficacy of VR-assisted planning in predicting the feasibility of laparoscopic partial nephrectomy and improving perioperative outcomes. *Materials and Methods:* A prospective study was conducted involving patients with solid renal masses from June 2023 to June 2025. Contrast-enhanced CT datasets were reconstructed into interactive VR models. Key perioperative metrics such as operative time, blood loss, conversion to radical nephrectomy, and complications (Clavien–Dindo grade $\geq$ II) were compared between VR-assisted and conventional CT-based planning. Predictive accuracy was assessed using receiver operating characteristics and area under the curve (AUC) statistics, with significance set at $p < 0.05$. *Results:* A total of 212 patients were included. VR-assisted planning (105 patients) was associated with significant perioperative improvements vs. the non-VR group (107 patients). Operative time was reduced (92 ± 22 vs. 131 ± 34 minutes; $p = 0.017$), as was blood loss (180 ± 67 vs. 325 ± 55 ml; $p = 0.028$). Conversion to radical nephrectomy was lower (1.9% vs. 9.3%; $p = 0.029$), and major complications less frequent (3.8% vs. 11.2%; $p = 0.037$). In 26.6% of cases, VR mapping influenced the surgical approach, particularly hilar dissection and clamping sequence. Predictive modeling using VR-derived parameters (tumor-vessel distance, polar location, RENAL score) showed superior

diagnostic accuracy (AUC=0.91, 95% confidence interval=0.83-0.98) over CT-based planning (AUC=0.74, 95% confidence interval=0.63-0.84; $p=0.008$). VR assistance was also an independent predictor of reduced operative time ($\beta=-0.42$; $p=0.014$) and blood loss ($\beta=-0.38$; $p=0.027$). No vascular injuries or unexpected anatomical findings occurred in the VR group. *Conclusion*: Three-dimensional VR imaging significantly enhances anatomical comprehension, improves the accuracy of surgical planning, and reduces operative time, blood loss, and complication rates. Its robust predictive capability (AUC=0.91) validates the integration of VR into preoperative assessments for complex renal masses.

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LAPAROSCOPIC PARTIAL NEPHRECTOMY WITHOUT ARTERIAL CLAMPING USING INNOLCON VERSUS ROBOTIC PARTIAL NEPHRECTOMY WITH CLAMPAGE: PERIOPERATIVE EFFICIENCY, TUMOR COMPLEXITY, AND MID-TERM RENAL FUNCTIONAL OUTCOME

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Background/Aim: Partial nephrectomy can be performed laparoscopically (LPN) or robotically (RPN). RPN with warm ischemia allows precise excision but increases costs due to robotic instrumentation and longer operative times. LPN without pedicle clamping using Innolcon avoids ischemia

and may improve renal preservation, with potential cost advantages. This study compared the direct hospital costs of LPN versus RPN in the same patient cohort. *Materials and Methods*: A prospective analysis considered 147 patients undergoing PN between 2021-2024: 75 LPN without clamping using Innolcon, and 72 RPN with conventional clamping. Cost components included: Operating room time: €19.8 per minute; consumables: €1,205.6 per LPN case vs. €3,487.3 per RPN case; blood transfusion: €198.7 per unit (average of 0.16 ± 0.12 units in LPN vs. 0.05 ± 0.07 units in RPN); hospital stay: €804.3 per day (mean stay of 3.12 ± 1.08 days for LPN vs. 2.95 ± 1.05 days for RPN); and costs for management of complications. *Results*: Considering all cost components together, the overall cost per case was significantly lower for LPN without arterial clamping using Innolcon compared with RPN with clamping. Major contributors to savings were the reduced cost of consumables and avoidance of robotic instrumentation. Shorter operative times further reduced operating room costs, while slightly higher blood loss did not translate into clinically relevant transfusion needs. Hospital stay and complication costs were similar for the two groups. The functional and efficiency benefits of Innolcon make LPN both clinically and economically advantageous. *Conclusion*: LPN without arterial clamping using Innolcon is a safe, efficient, and cost-effective alternative to RPN with clamping. Adoption of ischemia-sparing, energy-assisted LPN can reduce hospital expenditures without compromising patient outcomes, supporting its broader implementation for appropriate patients.

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PERIOPERATIVE AND FUNCTIONAL OUTCOMES OF OFF-CLAMP LAPAROSCOPIC PARTIAL NEPHRECTOMY: A SINGLE-SURGEON SERIES OF 375 CONSECUTIVE CASES WITH ANALYSIS OF LEARNING CURVE AND TEMPORAL TRENDS

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Background/Aim: Off-clamp laparoscopic partial nephrectomy has been proposed to minimize renal ischemia-related injury while preserving surgical efficacy. We report perioperative and functional outcomes of 375 consecutive such procedures performed by a single high-volume surgeon, focusing on temporal trends and perioperative outcomes. **Materials and Methods:** Baseline, intraoperative and postoperative data were prospectively collected. Continuous variables were expressed as medians with interquartile range, and compared across quintiles (Q1-Q5) using the Kruskal-Wallis test; categorical variables were analyzed using the chi-squared or Fisher's exact test, as appropriate. LOWESS smoothing was applied to depict changes in operative time, hemoglobin, estimated glomerular filtration rate, and hospital stay for the 375 cases. All procedures were performed using KarlStorz lap instrumentations, with a 0° or 30° camera and using Ultracision as a dissecting tool. **Results:** Median age was 66.4 (42-74) years, body mass index 27.3 (21.3-32.5) kg/m², and tumor size 3.7 (1.8-6.8) cm; 20% of patients had American Society of Anesthesiologists score ≥3. Sutureless off-clamp laparoscopic partial nephrectomy was performed in 42% of cases. Median operative time and hospital stay were 74 (45-112) min and 2.2 (2-4) days, respectively. Major bleeding events occurred in 12%, and complications of Clavien-Dindo grade ≥3 were experienced by 0.5%. Median baseline and discharge estimated glomerular

filtration rate were 81.7 and 79.1 ml/min/1.73 m², respectively. Over time, there was an increase in case complexity, reflecting the surgeon's growing experience. LOWESS curves confirmed a significant reduction in operating time with increasing experience ($p=0.02$). **Conclusion:** Purely off-clamp laparoscopic partial nephrectomy is a safe and effective technique that provides excellent perioperative and functional outcomes when performed by experienced surgeons. Progressive expertise allows for the successful management of increasingly complex cases without compromising renal preservation or patient safety.

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HIGH BASELINE PSMA TUMOR VOLUME INDEPENDENTLY PREDICTS EARLY BIOCHEMICAL PROGRESSION IN ADVANCED PROSTATE CANCER: PRELIMINARY RESULTS OF THE PELICAN STUDY

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Background/Aim: The management of advanced prostate cancer (PC) requires accurate biomarkers to predict

response to systemic therapies and optimize the patient's course. The ongoing Italian multicenter prospective PELICAN study (NCT07089550) is evaluating patients with metastatic PC undergoing baseline prostate-specific membrane antigen (PSMA) positron-emission tomography (PET)/computed tomography (CT) before initiating systemic treatment (androgen receptor pathway inhibitor, chemotherapy, or radioligand therapy). This preliminary analysis aimed to compare the predictive value of baseline tumor burden (PSMA-TV) and total lesion (TL-PSMA) against traditional clinical and laboratory markers for early treatment failure across different clinical settings (hormone-sensitive PC and castration-resistant PC). **Materials and Methods:** Patients were stratified into biochemical responders, defined by a prostate-specific antigen nadir ≤ 0.2 ng/ml at 3 months post-treatment initiation, and non-responders. Baseline PSMA PET/CT scans were segmented semi-automatically utilizing an absolute standard uptake value threshold ($SUV \geq 2$) to extract SUVmax, PSMA-TV, and TL-PSMA. Clinical, laboratory, and imaging differences between groups were assessed using non-parametric tests, followed by a multivariate logistic regression model to identify independent predictors. **Results:** The final cohort included 74 patients (median age=72 years, IQR=65-77 years; 70% hormone-sensitive PC, 30% castration-resistant PC; median follow-up=10 months), divided into 38 (51%) responders and 36 (49%) non-responders. Responders exhibited a significantly lower baseline tumor burden: PSMA-TV (median: 32.4 vs. 257.6 ml, $p=0.0001$) and TL-PSMA (179.0 vs. 1451.9, $p=0.0003$). At univariate analysis, non-responders presented with significantly lower hemoglobin ($p=0.028$) and higher alkaline phosphatase ($p=0.045$) levels. Notably, baseline prostate-specific antigen showed only a trend towards significance ($p=0.054$), and SUVmax was not associated with response ($p=0.52$). In the subgroup treated with first-line apalutamide ($n=34$), responders maintained a markedly reduced PSMA-TV (43.6 vs. 188.8 ml, $p=0.022$) and TL-PSMA (193.3 vs. 1272.6, $p=0.008$). In patients with baseline distant metastases (M+), PSMA-TV showed a strong trend towards being lower

in responders, approaching statistical significance (32.1 vs. 256.7 ml, $p=0.054$). At multivariate analysis, a high baseline PSMA-TV ($p=0.003$) and having castration-resistant PC ($p=0.003$) emerged as the sole independent predictors of early treatment failure, nullifying the significance of classic laboratory biomarkers. **Discussion and Conclusion:** The striking superiority of baseline PSMA-TV and TL-PSMA over standard imaging metrics (SUVmax) underscores a crucial biological premise: three-dimensional tumor volume more accurately captures disease heterogeneity and the overall burden of therapy-resistant clones in advanced PC. Furthermore, while standard biochemical markers (prostate-specific antigen, alkaline phosphatase) showed univariate significance, they failed to maintain independent predictive value when spatial tumor volume was accounted for in the multivariate model. These findings have immediate clinical implications for the uro-oncological patient. By identifying patients at high risk of early systemic therapy failure before treatment initiation, baseline PSMA PET/CT volumetry provides a critical window for early therapeutic intensification or enrollment in combination clinical trials. In conclusion, PSMA-derived volumetric parameters are robust, independent prognostic biomarkers, promoting a paradigm shift for PSMA PET/CT from a staging modality to an indispensable tool for prognostic stratification and personalized management.

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IMPACT OF ADT DURATION ACCORDING TO PSMA PET/CT FINDINGS IN HIGH-RISK BIOCHEMICAL RECURRENCE AFTER RADICAL PROSTATECTOMY

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Background/Aim: High-risk biochemical recurrence (BCR) after radical prostatectomy is associated with a substantial risk of metastatic progression and prostate cancer-specific mortality. In contemporary practice, prostate-specific membrane antigen positron-emission tomography/computed tomography (PSMA PET/CT) guides treatment selection, including the use and duration of androgen deprivation therapy (ADT). However, whether the effect of ADT duration differs according to PSMA PET/CT findings remains incompletely defined. We evaluated outcomes in patients with high-risk BCR managed according to a PSMA PET-guided multidisciplinary strategy, focusing on the relationship between PET-defined disease extent and ADT duration. **Materials and Methods:** We retrospectively analyzed consecutive patients with high-risk BCR after radical prostatectomy discussed within a multidisciplinary tumor board at a tertiary referral center. All patients underwent PSMA PET/CT at recurrence, which guided treatment allocation. Primary endpoints were second biochemical recurrence-free survival and progression-free survival, both measured from the date of PSMA PET/CT. Progression-free survival was assessed exclusively using PSMA PET/CT. Outcomes were analyzed using

Kaplan Meier estimates, multivariable Cox regression, and model-based estimates of 36-month progression probability according to ADT duration and PSMA PET/CT category. **Results:** A total of 136 patients were included. At PSMA PET/CT, 35% had negative findings or isolated local recurrence, 18% had pelvic nodal recurrence [molecular imaging (mi)N1M0], and 47% had distant metastatic disease (miNanyM1). Median ADT duration differed across PET categories, being 24 months in patients with negative/local recurrence, 24 months in those with miN1M0 disease, and 29 months in those with miNanyM1 disease. Concomitant ADT was administered in 42%, 42%, and 76% of patients, respectively. Among patients receiving PET-guided treatment, PSMA PET/CT findings were the strongest independent predictors of clinical progression: compared with negative/local recurrence, the risk was significantly higher for those with miN1M0 disease [hazard ratio(HR)=2.53, 95% confidence interval (CI)=1.05-6.10; $p=0.036$] and markedly higher for those with miNanyM1 disease (HR=5.07, 95% CI=2.51-10.21; $p<0.001$). Concomitant ADT was independently associated with a lower risk of progression (HR=0.70, 95% CI=0.51-0.89; $p<0.001$). The LOWESS function suggested that the effect of ADT duration varied according to PET-defined disease burden. In particular, longer ADT duration was associated with a marked reduction in the predicted probability of PSMA PET progression by 36 months in patients with miN1M0 disease, whereas this effect appeared less pronounced in patients with negative/local recurrence. **Conclusion:** In high-risk BCR after radical prostatectomy, the prognostic effect of ADT appears to depend on PSMA PET/CT findings. While metastatic disease remains associated with the highest risk of progression despite more frequent and prolonged ADT exposure, patients with nodal-only recurrence may derive the greatest relative benefit from longer treatment duration. These findings support a PET-adapted approach to ADT use and duration and suggest that molecular imaging may help refine treatment intensity in this setting.

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ENHANCING THE AWAKE ROBOTIC SURGERY EXPERIENCE: VIRTUAL REALITY DURING NEURAXIAL ANESTHESIA FOR SINGLE-PORT RADICAL PROSTATECTOMY REDUCES ANXIETY AND MAINTAINS OPTIMAL COMFORT

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Aim: To quantify anxiety, pain perception, tolerability, and patient-reported experience associated with virtual reality support during extraperitoneal single-port robot-assisted radical prostatectomy (SP-RARP) performed under combined spinal-epidural anesthesia. *Materials and Methods:* A prospective cohort study included 14 consecutive patients undergoing extraperitoneal SP-RARP under combined spinal-epidural anesthesia with immersive virtual reality support. Patients selected a virtual scenario preoperatively and used the device throughout the procedure when tolerated. Anxiety was measured using the State-Trait Anxiety Inventory-State questionnaire before admission, before surgery, immediately after surgery, and at 24 h after surgery. Pain and anxiety perception were assessed using a 10-point Visual Analog Scale. Usability and satisfaction were evaluated using the Health Information Technology Usability Evaluation Scale. *Results:* Thirteen out

of 14 patients (92.9%) completed the entire procedure wearing the virtual reality headset. One patient (7.1%) required removal due to intolerance. Complete isolation from the external environment was reported for 12 patients (85.7%). The median State-Trait Anxiety Inventory-State score increased from 40 before admission to 54 before surgery, and decreased to 46 immediately after surgery, and 34 at 24 h. Median anxiety score decreased from 66 preoperatively to 49 intraoperatively, and 47 postoperatively. Median intraoperative pain score was 0/10, and no patient required additional analgesia. Median overall satisfaction score was 9/10; 12 out of 14 patients (85.7%) reported high satisfaction (score ≥ 8), confirming a positive overall experience. Lower ratings were observed for three patients (21.4%), mainly related to suboptimal headset comfort and incomplete acoustic isolation, without affecting completion of the procedure. *Conclusion:* Virtual reality support during combined spinal-epidural anesthesia was feasible in 92.9% of patients and was associated with a reduction in perioperative anxiety and absence of intraoperative pain. High satisfaction scores confirm good patient acceptance of this approach, supporting its role in improving the patient experience during awake SP-RARP.

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AWAKE SINGLE-PORT ROBOTIC RADICAL PROSTATECTOMY: PERIOPERATIVE AND EARLY ONCOLOGICAL OUTCOMES OF EXTRAPERITONEAL SURGERY UNDER NEURAXIAL ANESTHESIA WITH VIRTUAL REALITY SUPPORT

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Aim: To evaluate feasibility, anesthesiological safety, perioperative outcomes, and early oncological results of extraperitoneal single-port robot-assisted radical prostatectomy (SP-RARP) performed under combined spinal-epidural anesthesia within a virtual reality-assisted setting. **Materials and Methods:** A prospective single-center study was conducted on 14 consecutive patients with low- or intermediate-risk localized prostate cancer treated with extraperitoneal SP-RARP under combined spinal-epidural anesthesia with virtual reality support. Inclusion criteria were prostate volume <80 ml, body mass index <30 kg/m², and American Society of Anesthesiologists score 1-3. All procedures were performed by a single experienced surgeon. Patients maintained spontaneous breathing with supplemental oxygen and light sedation. A virtual reality device was used intraoperatively. Primary endpoints were completion of surgery without conversion to general anesthesia and intraoperative safety. Secondary endpoints included operative time, blood loss, postoperative pain and complications (Clavien–Dindo classification), length of stay, catheterization time, and surgical margin status. **Results:** All 14 procedures (100%) were completed under combined spinal-epidural anesthesia, with no conversion to general anesthesia or open surgery. No intraoperative interruptions due to patient movement occurred. Two patients (14.3%) experienced transient hypotension, resolved with pharmacological treatment. No bradycardia or respiratory complications were recorded. Median operative time was 92 min, median estimated blood loss was 75 ml, and median length of stay was 2 days. Median postoperative pain score was 0/10. No postoperative complications grade ≥2 occurred within 30 days. Median catheterization time was 5 days. Surgical margins were negative in 13 out of 14 patients (92.9%). The use of virtual reality did not interfere

with anesthesiological management or surgical workflow. **Conclusion:** Extraperitoneal SP-RARP performed under combined spinal-epidural anesthesia within a virtual reality-assisted setting was feasible in 100% of cases, with low morbidity, no conversions, and a 92.9% rate of negative surgical margins. The integration of virtual reality did not affect intraoperative safety or perioperative outcomes, supporting the feasibility of an ‘awake’ robotic surgery model.

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NEUROAXIAL VERSUS GENERAL ANESTHESIA DURING SINGLE-PORT ROBOT-ASSISTED RADICAL PROSTATECTOMY: A COMPARATIVE ANALYSIS OF PERIOPERATIVE OUTCOMES

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Background/Aim: Single-port robot-assisted radical prostatectomy (SP-RARP) is traditionally performed under general anesthesia (GA). However, neuroaxial anesthesia (NA) may represent a feasible alternative in selected patients, potentially reducing perioperative morbidity and opioid use. This study aimed to compare the feasibility, safety, and perioperative outcomes of SP-RARP performed under NA

versus GA. **Materials and Methods:** A prospective comparative analysis was conducted including patients undergoing SP-RARP between May 2024 and March 2026. Patients were stratified into two groups according to the anesthesia protocol performed during surgery. Exclusion criteria for NA included body mass index $>30 \text{ kg/m}^2$, significant pulmonary disease, obstructive sleep apnea, or contraindications to NA. Demographic, intraoperative, and postoperative variables were collected, including operative time, estimated blood loss, need for conversion to GA, intraoperative complications, postoperative pain control (Visual Analog Scale score), opioid consumption, time to ambulation, length of stay, and complications (Clavien–Dindo classification). **Results:** A total of 102 patients were included (NA=23; GA=79). Baseline characteristics were comparable between groups (age: 65.8 ± 3.7 vs. 67.1 ± 2.1 years; body mass index: 27.4 ± 2.8 vs. $25.3 \pm 4.1 \text{ kg/m}^2$; $p > 0.05$). All procedures in the NA group were successfully completed without conversion to GA. No additional ports or open conversions were required in either group. Operative time was 109.3 ± 10.3 vs. 105.5 ± 15.7 min ($p > 0.05$), and estimated blood loss was 210.2 ± 34.1 vs. $188.2 \pm 13.5 \text{ ml}$ ($p > 0.05$) in NA vs. GA groups, respectively. No intraoperative complications were recorded. Transient patient movement was observed in 8.6% of NA cases, without impacting surgical performance. Postoperative pain scores at 3 h were significantly lower for the NA group: 2 [interquartile range (IQR)=2-3] vs. 3 (IQR=2-4) ($p = 0.04$), with reduced opioid requirement (17.3% vs. 63.2%; $p = 0.001$). Early recovery parameters favored NA, including shorter time to ambulation (12.3 ± 1.2 vs. $20.4 \pm 2.1 \text{ h}$; $p = 0.02$) and reduced length of stay [2 (IQR=1-3) vs. 4 (IQR=3-5) days; $p = 0.03$]. Overall complication rates were similar (8.6% vs. 11.3%; $p = 0.23$), with all the complications graded as Clavien–Dindo grade I or II, and no anesthesia-related adverse events were reported for the NA group. **Conclusion:** NA during SP-RARP is a feasible and safe alternative to GA in selected patients. It provides comparable intraoperative outcomes with potential advantages in postoperative recovery and reduced opioid use. Larger studies are warranted to confirm these findings and better define patient selection criteria.

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FIRST ITALIAN SURGICAL CASE-SERIES TREATED USING THE EDGE ROBOTIC PLATFORM: A PROSPECTIVE SERIES ACROSS MULTIPLE UROLOGICAL PROCEDURES

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Aim: To report the first Italian surgical case-series treated using the EDGE robotic platform, evaluating feasibility, intraoperative performance, and perioperative outcomes across different urological procedures. **Materials and Methods:** A prospective observational study was conducted including 26 consecutive patients undergoing robotic surgery with the EDGE platform at a single tertiary referral center, all performed from January to March 2026. All procedures were performed by a single experienced robotic surgeon. Procedures included robot-assisted radical prostatectomy (RARP) (n=19), robot-assisted radical nephrectomy (n=1), robot-assisted partial nephrectomy (RAPN) (n=4), robot-assisted simple prostatectomy (n=1), and robot-assisted radical cystectomy (n=1). Perioperative variables analyzed included estimated console time, estimated blood loss, intraoperative complications, conversion to open surgery, length of hospital stay, postoperative complications (according to Clavien–Dindo

classification), and surgical margin status. *Results:* All 26 procedures (100%) were successfully completed using the EDGE platform without conversion to open surgery. No intraoperative complications were recorded (0%), and no procedure required interruption or change in surgical strategy. The median dressing time was 5 [interquartile range (IQR)=3-7] min, the median docking time was 4 (IQR=4-6) min, and the median operative time was 73 (IQR=58-88) min. Median estimated blood loss was 160 ml (IQR=100-190). Median length of hospital stay was 4 (IQR=3-5) days. No major postoperative complications were observed within 30 days (0%). Postoperative minor complications were 4/26 (15%), including one lymphocele, one episode of acute urinary retention, and one febrile event during the postoperative stay after RARP, as well as one case of anemia requiring transfusion in the RAPN cohort. Surgical margin status was negative in RARP for 16/19 cases (84%) and in RAPN for 0/4 cases (100%). *Conclusion:* In this first Italian case-series, the EDGE robotic platform was used in 26 consecutive urological procedures with a 100% completion rate, no intraoperative or postoperative major complications, and no need for conversion to open surgery. Median console time and length of stay were within expected ranges for robotic surgery, even though at the beginning of the learning curve. These findings support the feasibility and safety of the EDGE platform across different urological procedures in the early adoption phase.

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HYCAPP TRIAL: A PROSPECTIVE RANDOMIZED TRIAL TO EVALUATE THE IMPACT OF HYPNOTIC COMMUNICATION ON ANXIETY, PAIN AND PERCEPTION OF CARE ON PATIENTS UNDERGOING PROSTATIC BIOPSY

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Background/Aim: Prostate biopsy is a common outpatient procedure frequently associated with significant pain and anxiety, negatively impacting patient experience. Non-pharmacological strategies to improve procedural tolerability are increasingly needed. This study aimed to evaluate the impact of hypnotic communication (HYC) on anxiety, pain, and perception of care in patients undergoing prostate biopsy. *Materials and Methods:* We conducted a single-center prospective randomized controlled trial including patients undergoing prostate biopsy, randomized 1:1 to HYC or standard care. Primary endpoints were peri-procedural anxiety (Visual Analog Scale-A and vital parameters), pain (Visual Analog Scale), and perception of care (Likert scale). Secondary endpoints included use of analgesia, perceived procedural duration, complications, and time to resumption of daily activities. Repeated-measures analyses were performed to assess temporal trends. *Results:* A total of 101 patients were analyzed (52 HYC, 49 standard care). Baseline anxiety levels were comparable between groups. HYC was associated with a significant reduction in anxiety at 30 min and 36 h post-procedure (1.2 vs. 2.8; $p=0.004$; and 0.4 vs. 1.3; $p=0.01$), with a greater decrease from baseline. Pain scores were significantly lower for the HYC group both during and after biopsy (3.1 vs. 4.2; $p=0.02$ and 0.5 vs. 1.5; $p=0.002$). Patients receiving HYC reported a better perception of care (median 4.8 vs. 4.2; $p<0.001$) and a shorter perceived procedural duration ($p<0.0001$). No differences were observed in complications or analgesic use. *Conclusion:* HYC significantly improved patient

experience during prostate biopsy by reducing anxiety and pain and enhancing perception of care. This simple, non-pharmacological approach may be integrated into routine urological practice to optimize patient-centered outcomes.

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TOXICITY AND OUTCOMES OF PROSTATE STEREOTACTIC BODY RADIOTHERAPY (SBRT) WITH DIFFERENT TRACKING TECHNIQUES: A MULTICENTER RETROSPECTIVE ANALYSIS

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Aim: To evaluate the safety and efficacy of stereotactic body radiotherapy (SBRT) for localized prostate cancer, comparing different prostate tracking techniques. **Materials and Methods:** This multicenter retrospective study included 43 patients treated with prostate SBRT between February 2023 and March 2026. Median age was 76 (range=63-81) years, with a median baseline prostate-specific antigen of 7.43 (range=4.23-43) ng/ml. Risk stratification included 3 favorable intermediate-, 24 unfavorable intermediate-, and 16 high-risk patients. The median International Prostate Symptom Score was 5 (range=0-14). Target delineation was performed using magnetic resonance imaging fusion according to shared protocols. Anisotropic planning target volume margins were applied (5 mm, reduced to 3-4 mm posteriorly). All patients received 36.25 Gy in 5 fractions

delivered on alternate days; two patients received a boost to the dominant intraprostatic lesion. Treatments were delivered using ultrasound-guided tracking, fiducial-based tracking, or without tracking in 19, 17, and 7 patients, respectively. Toxicity was assessed according to Radiation Therapy Oncology Group criteria. **Results:** With a median follow-up of 23 (range=1-35) months, no local or distant recurrences were observed; three high-risk patients (7%) developed locoregional nodal recurrence (positive prostate-specific membrane antigen positron-emission tomography). No acute or late ≥G3 genitourinary toxicity and no acute ≥G3 gastrointestinal toxicity were observed; one late G3 gastrointestinal event was reported. Acute genitourinary G1-G2 toxicity occurred in 30 patients (69.7%): 4 (57%) in the no-tracking group, 14 (73%) in the ultrasound-guided tracking group, and 12 (70%) in the fiducial-based group. Acute G1-G2 gastrointestinal toxicity occurred in four patients (18%): three (42.8%) in the no-tracking group, and one (5%) in the fiducial group. Comparative analysis using Fisher's exact test showed no statistically significant differences among groups. No correlation was observed between toxicity and organ-at-risk doses (rectum: V18, V29, V36.25 Gy; bladder: V18, V36.25 Gy; urethra: V36.25 Gy; bowel: V18, V30 Gy). **Conclusion:** Prostate SBRT is safe, effective, and well tolerated. In this cohort, tracking technique did not significantly affect toxicity. Further studies and longer follow-up are needed to confirm these findings.

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AI-DRIVEN RECONSTRUCTION OF THE PERIPROSTATIC NEUROVASCULAR NETWORK FROM MRI FOR PERSONALIZED NERVE SPARING DURING ROBOT-ASSISTED RADICAL PROSTATECTOMY: A PILOT FEASIBILITY STUDY

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Background/Aim: Precision surgery in prostate cancer has evolved with 3D reconstruction, enabling accurate tumor localization and tailored planning. However, current imaging provides limited information on periprostatic neurovascular anatomy, restricting personalization of nerve-sparing strategies aimed at preserving functional outcomes. We aimed to develop and evaluate a workflow integrating advanced magnetic resonance imaging (MRI) and artificial intelligence to reconstruct the periprostatic neurovascular network for patient-specific planning of nerve-sparing robot-assisted radical prostatectomy. **Materials and Methods:** We developed a workflow integrating MRI acquisition, manual segmentation, and artificial intelligence-based reconstruction of the periprostatic neurovascular network. Preoperative multiparametric MRI included high-resolution sequences optimized for nerve visualization, including diffusion-based imaging and 3D-Short Tau Inversion Recovery (STIR) sequences. A biomedical engineer manually segmented visible neurovascular elements, generating a discontinuous 3D model due to signal fragmentation. Segmented data were processed using skeletonization and cost-based pathfinding algorithms. Skeletonization extracted centerlines preserving topology, while pathfinding iteratively identified the most probable connections between segments by minimizing a cost function based on spatial distance and signal intensity, reconstructing continuous nerve trajectories. The model was refined, smoothed, and converted into a parametric tubular

3D representation. Final patient-specific models were integrated into preoperative planning to visualize tumor-nerve relationships and support intraoperative nerve-sparing. **Results:** Fourteen consecutive patients with low-risk prostate cancer were included (mean age±standard deviation=67±5.4 years). All had MRI-visible disease; tumor contact with the capsule was observed in 10/14 (71%), with no extracapsular extension. Median preoperative International Index of Erectile Function-5 was 20 (interquartile range=18-22). Neurovascular reconstruction was successfully achieved in 12/14 (85.7%). In 2/14 cases (14.3%), reconstruction was not feasible due to suboptimal image acquisition, with insufficient nerve signal visualization on diffusion-based and 3D-STIR sequences. In reconstructed cases, the workflow provided detailed neurovascular bundle mapping, enabling tailored nerve-sparing: bilateral full NS in 6/14 (42.9%), unilateral partial with contralateral full NS in 5/14 (35.7%), and bilateral partial NS in 1/14 (7.1%). Final pathology confirmed prostate cancer with International Society of Urological Pathology grade 2 in 10/14 (71%) and 3 in 4/14 (29%). One positive margin (7.1%) occurred in a pT3a tumor; not involving reconstructed neurovascular bundle. At 3 months, prostate-specific antigen was undetectable in all patients (100%), with recovery of erectile function in 10/14 (71%). **Conclusion:** This study demonstrates the feasibility of an artificial intelligence-driven workflow for reconstruction of the periprostatic neurovascular network from MRI. Despite technical limitations related to image quality, this approach enables patient-specific nerve-sparing and represents a step toward precision, function-preserving surgery.

45 ROBOT-ASSISTED TRANSPERINEAL TARGETED PROSTATE BIOPSY WITH BIOBOT MONA LISA 2.0 SYSTEM

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Background/Aim: Recent advances in imaging and robotic technologies have profoundly transformed the diagnostic approach to prostate cancer (PC). The implementation of multiparametric magnetic resonance imaging (MRI) has enabled targeted biopsy (TB) strategies that improve the detection of clinically significant PC compared to standard systematic biopsy (SB). However, SB is still recommended in combination with TB, as some clinically significant PC may be missed by TB alone. The transperineal route is increasingly favored for its superior safety profile, although it remains technically demanding and time-consuming, particularly when both TB and SB are performed. In this evolving context, the Mona Lisa 2.0 system (Biobot Surgical, Singapore) has been developed as a next-generation robotic MRI/ultrasound (US) fusion platform designed to enhance biopsy precision, reproducibility, and workflow efficiency. By integrating robotic guidance, artificial intelligence-assisted prostate segmentation, real-time image fusion, and automated calculation of needle trajectory and depth, the system aims to achieve accurate and reproducible sampling while maintaining the safety of the transperineal approach. This study presents our clinical experience with the Mona Lisa 2.0 platform for

robot-assisted TB. **Materials and Methods:** Up to October April 2026, 30 patients with MRI-visible prostate lesions underwent robot-assisted TB using the Mona Lisa 2.0 system at IRCCS-FPO Candiolo Cancer Center. Pre-procedural T2-weighted MRI images were uploaded for prostate and lesion segmentation, generating a 3D model used for biopsy planning. On the day of the procedure, real-time transrectal US was fused with the MRI model, allowing precise selection of target and optional perilesional cores. The robotic arm automatically calculated and positioned the optimal angle and depth for each puncture. Biopsies were performed transperineally under general anesthesia using disposable 18-gauge needles. Data collected included prostate volume, lesion diameter, number and positivity of biopsy cores, procedure time, and complications. Diagnostic performance and safety were assessed descriptively. **Results:** The mean prostate volume was 62.2 ± 19.2 ml, and the mean lesion diameter was 10 ± 3 mm. Five patients presented with an anterior lesion, and 25 with posterolateral ones. The mean number of target and standard cores was 7 ± 4 and 9 ± 4 , respectively; the mean number of positive target and standard cores was 4 ± 2 and 2 ± 2 , respectively. Twenty-three (76.6%) robot-assisted TB samples were positive for clinically significant PC, while robot-assisted SB detected only non-significant PC in six cases (20%), with positive cores located close to the target area ('penumbral' effect). No peri- or post-procedural complications were observed. The mean biopsy duration was 12.9 ± 2.0 min. All samples were of high histological quality, with a mean core length of 10.2 ± 1 mm. **Conclusion:** This experience demonstrates that the Mona Lisa 2.0 robotic platform is a safe, feasible, and precise tool for transperineal MRI/US fusion-guided prostate biopsy. Robotic automation ensures consistent and reproducible sampling while minimizing operator variability and procedural invasiveness. Despite the small cohort and initial learning curve, the system achieved a high rate of detection of clinically significant PC in the target area and penumbra, suggesting its potential for reducing or omitting systematic sampling.

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**THREE-DIMENSIONAL GUIDANCE OPTIMIZES
ROBOT-ASSISTED PARTIAL NEPHRECTOMY IN
HORSESHOE KIDNEYS: RESULTS FROM
A MULTICENTER YAU-RCC EXPERIENCE**

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Aim: To evaluate the impact of three-dimensional (3D)
virtual models on surgical planning and outcomes of robot-

assisted partial nephrectomy (RAPN) for renal tumors in
horseshoe kidneys, a setting characterized by complex
vascular anatomy and challenging surgical exposure.
Materials and Methods: This retrospective multicenter
study was conducted by the Young Academic Urologists
Renal Cancer (YAU-RCC) Working Group and included 27
consecutive patients treated between January 2018 and
November 2025. All patients underwent RAPN with
preoperative patient-specific 3D models derived from
multiphase computed tomography. 3D reconstructions
were used to identify arterial and venous anatomy, tumor
relationships, and to guide surgical strategy, including
clamping approach and resection technique. Models were
available intraoperatively for real-time reference. Collected
variables included demographic and tumor characteristics,
intraoperative parameters (operative time, estimated
blood loss, ischemia strategy), postoperative outcomes
(complications according to Clavien–Dindo classification,
length of stay), functional outcomes (estimated glomerular
filtration rate), and oncological outcomes. **Results:** Median
tumor size was 5.5 [interquartile range (IQR)=4.0-7.0] cm,
with a median RENAL score of 9 (IQR=7-10), and the
median number of renal arteries was 3 (IQR=2-4),
confirming high anatomical complexity. A clampless
approach was performed in 14/27 patients (52%),
including cases with selective devascularization of tumor-
specific branches, while clamping was required in 13/27
(48%), with a median warm ischemia time of 23 (IQR=21-
26) min. Median operative time was 235 (IQR=160-290)
min and median estimated blood loss was 480 (IQR=150-
720) ml. No conversions to open surgery or radical
nephrectomy occurred (0/27, 0%). Overall complications
were observed in 8/27 patients (30%), including major
complications in 2/27 (7%). Median length of stay was 4
(IQR=3-5) days. Median decline in estimated glomerular
filtration rate was 5.0 (IQR=0-12) ml/min/1.73 m² at last
follow-up. Positive surgical margins were reported in 2/27
patients (7%). At a median follow-up of 20 (IQR=7-30)
months, no local or distant recurrences were observed
(0/27). Trifecta outcomes were achieved in 14/27 patients
(52%). **Conclusion:** In this multicenter YAU-RCC Working

Group experience, 3D-assisted RAPN for tumors in horseshoe kidneys is feasible and safe, allowing detailed preoperative understanding of vascular anatomy and tailored ischemia strategies. The use of 3D models may facilitate nephron-sparing approaches, reduce intraoperative uncertainty, and support favorable functional and oncological outcomes in anatomically complex cases.

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UNVEILING THE PARADOX: LOW URINARY PSA LEVEL AS A STRONGER INDICATOR OF PROSTATE CANCER RISK COMPARED WITH ELEVATED SERUM PSA

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Background/Aim: Prostate cancer screening is commonly based on the measurement of serum prostate-specific antigen (PSA), with an elevated level of circulating PSA traditionally considered indicative of an increased risk of malignancy. However, serum PSA may also rise in several benign prostatic conditions, resulting in a substantial number of false-positive findings and potentially unnecessary prostate biopsies. Conversely, during neoplastic transformation, prostate cells may progressively lose their ability to produce and release PSA. Accordingly, reduced PSA

levels in prostate tissue and urine have been reported to correlate with the presence of prostate cancer. This apparent paradox underscores the need for a more comprehensive understanding of PSA dynamics to improve the diagnostic accuracy of prostate cancer screening. The aim of this study was to compare the association of urinary PSA, serum PSA, and PSA density with prostate cancer presence and aggressiveness. **Materials and Methods:** Following a standardized 20-s prostate massage, urine samples were collected from 200 individuals scheduled to undergo prostate biopsy on the basis of conventional clinical parameters, including serum PSA, digital rectal examination, age, and multiparametric magnetic resonance imaging. Urinary PSA concentrations were measured using optimized commercially available assays. PSA density (PSAD) was calculated by dividing the serum PSA value by the prostate volume. **Results:** Both PSAD and serum PSA showed strong positive correlation with the Gleason score, whereas urinary PSA demonstrated a significantly inverse correlation with increasing Gleason score (all $p < 0.0001$). As Gleason score increased, the urinary PSA value significantly progressively decreased in patients with prostate cancer compared with those without. For PSAD, a significant difference compared with patients without prostate cancer was observed only for patients with Gleason score 7 (4+3) and Gleason scores 8-9. For serum PSA, statistical significance was reached only for those with Gleason scores 8-9. Receiver operating characteristic curve analysis showed an area under the curve of 0.50 for serum PSA, compared with 0.68 for PSAD and 0.72 for urinary PSA. Both PSAD and urinary PSA demonstrated statistically superior diagnostic performance compared with serum PSA. When PSAD and urinary PSA were individually combined with the PI-RADS score obtained from multiparametric magnetic resonance imaging, the corresponding area under the curve values increased to 0.79 and 0.82, respectively. **Conclusion:** Urinary PSA measurement demonstrated a noteworthy ability to discriminate between individuals with and without prostate cancer. Its diagnostic performance was significantly superior to that of serum PSA alone and comparable to that of PSAD. These findings suggest that urinary PSA may provide clinically relevant diagnostic

information even when data on prostate volume are unavailable, supporting its potential use as a tool for improving the accuracy of prostate cancer screening.

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OPTIMIZED URINE 'SMART TEST' FOR EARLY DETECTION OF PROSTATE CANCER

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Background/Aim: Rapid diagnostic tests provide *in-vitro* results within a short time and can be performed at the point of care by non-specialized personnel. These tools may therefore support the decentralization of first-line diagnostic assessments from hospitals to local healthcare settings. The aim of this study was to validate the diagnostic performance of a rapid test based on urinary prostate-specific antigen (PSA) and zinc and to investigate its potential role in improving the early detection of prostate cancer. *Materials and Methods:* Urine samples were collected from 174 patients scheduled to undergo prostate biopsy on the basis of standard clinical parameters, including serum PSA level, digital rectal examination, and multiparametric magnetic resonance imaging. Written informed consent was obtained from all participants. Urinary PSA and zinc levels were assessed using an

optimized device combining a lateral-flow immunoassay for PSA with a colorimetric dipstick assay for zinc. The results were subsequently confirmed using commercially available assays. *Results:* The urinary PSA and zinc tests were optimized according to the values observed in previous studies, generating a semiquantitative intensity scale ranging from 0 to 4 based on the amount of each analyte detected in the urine sample. Signal intensity was evaluated both visually and through image-based readers, with an overall concordance of 88%. Multivariate receiver operating characteristic analysis combining rapid-test intensity with routine clinical parameters (serum PSA, age, and digital rectal examination), collectively defined as the standard of care, and the Prostate Imaging-Reporting and Data System score obtained by multiparametric magnetic resonance imaging resulted in an area under the curve of 0.861. This value was statistically significantly higher than those obtained using the standard of care or Prostate Imaging-Reporting and Data System alone (area under the curve values of 0.643 and 0.761, respectively). *Conclusion:* These findings suggest that an optimized rapid urine test combining PSA and zinc measurements may be clinically useful for detecting neoplastic changes in the prostate and may help avoid unnecessary invasive diagnostic procedures in patients without prostate cancer.

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URINARY PSA AND ZINC RAPID TEST FOR IDENTIFYING PROGRESSIVE DISEASE DURING ACTIVE SURVEILLANCE

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Background/Aim: Active surveillance is a standard management strategy for patients with low-risk prostate cancer, aiming to avoid overtreatment while promptly identifying disease progression. Current monitoring protocols are mainly based on serial blood prostate-specific antigen (PSA) testing, multiparametric magnetic resonance imaging, and scheduled repeat biopsies. However, blood PSA kinetics and imaging findings often fail to clearly discriminate progressive tumors from indolent disease. The objective of this study was to evaluate the performance of a rapid urine test measuring PSA and zinc in identifying progressive prostate cancer at the beginning of active surveillance, with the aim of supporting personalized monitoring protocols and reducing unnecessary repeat biopsies. **Materials and Methods:** Ninety men diagnosed with low-risk prostate cancer and enrolled in an active surveillance protocol were included. The protocol included serum PSA testing every 3 months, multiparametric magnetic resonance imaging every 6 months, and repeat prostate biopsy at 12 months. All patients underwent the urinary PSA and zinc rapid test at entry into active surveillance. Disease progression was defined by histological upgrading at the 12-month repeat biopsy. Based on biopsy results, patients were classified as having progressive or indolent disease. The ability of serum PSA changes, Prostate Imaging-Reporting and Data System (PIRADS) score variations, and the urinary test result to discriminate between progressive and indolent tumors was assessed. **Results:** Of the 90 patients included, 37 (41%) showed disease progression confirmed by repeat biopsy at 12 months. An increase in serum PSA during the first 12 months was observed in 43% of patients with progressive disease and in 28% of patients with indolent disease. An increase in the PIRADS score during surveillance was observed in 3% of those with progressive tumors and in

10% of those with indolent tumors. The urinary PSA and zinc test yielded positive results in 80% of patients with progressive disease, compared with 43% of those with indolent disease. Among the 34 patients with indolent disease who tested negative at entry into active surveillance, 97% remained non-progressive after 4 years of follow-up. **Conclusion:** During active surveillance, changes in serum PSA level and magnetic resonance imaging findings showed limited ability to discriminate progressive prostate cancer from indolent disease. In contrast, a rapid urinary test measuring PSA and zinc demonstrated a higher capacity to identify patients with progressive tumors at entry into active surveillance and to reliably classify patients with stable disease. These results suggest that the urinary test may support personalized surveillance strategies, potentially allowing the reduction or postponement of repeat biopsies in patients with indolent prostate cancer and guiding the use of more intensive monitoring tools in those at higher risk of progression.

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INTEGRATION OF RPCRC RISK CALCULATOR AND A RAPID URINARY PSA AND ZINC TEST TO REDUCE UNNECESSARY BIOPSIES

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Background/Aim: Risk-based strategies are increasingly being adopted to improve patient selection for prostate biopsy and to reduce overdiagnosis and unnecessary invasive procedures. The Rotterdam Prostate Cancer Risk Calculator is designed to estimate the individual probability of prostate cancer and guide biopsy decisions. However, residual false-negative cases remain a relevant limitation. The objective of this study was to evaluate whether the integration of a previously validated rapid urine test measuring prostate-specific antigen (PSA) and zinc improves diagnostic accuracy and allows further optimization of prostate biopsy selection when combined with the risk calculator. **Materials and Methods:** A cohort of 170 men meeting the eligibility criteria required for the application of the Rotterdam Prostate Cancer Risk Calculator-4 were analyzed. For each patient, biopsy indication was assessed using the risk calculator. In the same cohort, a rapid urine test measuring PSA and zinc was applied. Three diagnostic strategies were compared: Risk calculator alone, urine test alone, and the combination of both tools. Outcomes included the percentage of avoided unnecessary biopsies, false-negative rate, International Society of Urological Pathology (ISUP) grade of missed cancer, positive predictive value, negative predictive value, and number needed to screen. **Results:** The risk calculator alone reduced unnecessary prostate biopsies but showed a false-negative rate of 16%. Missed prostate cancer included two patients with ISUP grade 3, 11 with grade 2, and 3 with grade 1 disease. The rapid urine test alone reduced unnecessary biopsies by 59% whilst missing 13 cases with prostate cancer. The combined strategy reduced unnecessary biopsies by 52%, with a false-negative rate of 9%. Missed cancer in the combined approach included eight patients with ISUP grade 2 and 1 with grade 1 disease. Positive predictive and negative predictive values improved from 66% and 67% with the risk calculator alone to 72% and 81%, respectively, with the combined strategy. The number needed to screen decreased from 6.4 using the risk calculator alone to 4.1 with the combined approach. **Conclusion:** The integration of a rapid urinary PSA and zinc test into a validated risk-based diagnostic pathway significantly

improves prostate biopsy selection. The combined strategy reduced unnecessary biopsies, improved predictive values, lowered the number of men to be screened, and limited the proportion of missed clinically significant prostate cancer. These results support the inclusion of non-invasive urinary biomarkers alongside established risk calculators to enhance precision and efficiency in prostate cancer diagnostic assessment.

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PRELIMINARY EVALUATION OF CIRCULATING *MIR-371A-3P* IN YOUNG PATIENTS WITH GENETIC CONDITIONS AT RISK FOR TESTICULAR LESIONS

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Background/Aim: Circulating *miR-371a-3p* has recently emerged as a highly sensitive and specific biomarker for testicular germ cell tumor (GCT). However, its role in some hereditary conditions such as disorders of sex development, congenital adrenal hyperplasia (CAH), and other syndromes associated with increased testicular tumor risk, including Carney complex, remains unexplored. In androgen insensitivity syndrome (AIS) residual gonadal tissue is associated with an increased GCT risk, requiring regular surveillance. Similarly, in CAH, testicular adrenal rest tumor (TART) may represent a diagnostic challenge due to its similarity to malignant lesions. In this context, circulating *miR-371a-3p* may represent a useful non-invasive biomarker for follow-up and for distinguishing benign from malignant lesions.

Materials and Methods: We conducted an ongoing preliminary observational study, initiated in March 2024, including 11 patients enrolled to date: nine with AIS (partial to complete forms), referred by the Pediatric Endocrinology Unit of the University of Pisa; one with CAH and bilateral TART; and one with Carney complex, a condition associated with increased testicular tumor risk. The patient with CAH, previously presenting at our Pediatric Department but non-adherent to therapy and follow-up, was later referred for bilateral orchiectomy by a private urologist. The patient with Carney complex had a history of childhood testicular surgery and bilateral adrenalectomy for Cushing syndrome. The age of patients ranged from 3 to 21 years (median of 15 years). *miR-371a-3p* levels were measured to assess possible GCT development. A total of 22 serum samples (1-4 per patient) were analyzed. All patients underwent abdominal and, when applicable, testicular ultrasound. **Results:** All patients with AIS had *miR-371a-3p* levels below the established relative quantification (RQ) positivity threshold of 5, except for one patient, who presented minimal elevation (RQ=5.06). This finding was considered clinically non-significant and managed conservatively, repeating the test after a few months; the value normalized at subsequent follow-up. No patients showed clinical, biochemical or radiological evidence of GCT during follow-up. The patient with bilateral TART also had *miR-371a-3p* levels consistently below the positivity threshold of RQ 5, despite ultrasound findings suggestive of bilateral testicular masses. Serial *miR-371a-3p* measurements (at least 4 over a 2-year follow-up) confirmed levels were persistently below the threshold, while ultrasound findings remained stable. The patient with Carney complex presented testicular calcifications on ultrasound and persistently showed *miR-371a-3p* levels of RQ<5, with no evidence of tumour on imaging during follow-up. **Conclusion:** In this preliminary cohort, circulating *miR-371a-3p* levels were consistently below the threshold across AIS, CAH with bilateral TART, and Carney complex with testicular calcifications, supporting its potential role as non-invasive biomarker for excluding GCT in high-risk populations.

Overall, *miR-371a-3p* may be useful in the clinical evaluation of testicular lesions in hereditary conditions, helping to distinguish benign findings from malignant GCT. Larger studies are needed to validate these observations.

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VALIDATION OF THE PRI-MUS SCORE FOR THE DETECTION OF CLINICALLY SIGNIFICANT PROSTATE CANCER: A SINGLE-CENTER ANALYSIS

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Background/Aim: Micro-ultrasound (MUS) has emerged as a novel imaging modality for prostate cancer (PC) detection. The PRI-MUS score was developed to standardize lesion assessment, but real-world validation remains limited. **Materials and Methods:** We retrospectively analyzed 457 consecutive patients undergoing prostate biopsy with MUS evaluation. The PRI-MUS score was defined as the highest score per patient. The primary endpoint was detection of clinically significant PC (csPC). Associations between PRI-MUS score and csPC were assessed using logistic regression. Discriminative ability was evaluated using receiver operating characteristics analysis. **Results:** Overall, 201/457 patients (44.0%) were diagnosed with csPC. The rate of csPC increased with higher PRI-MUS score: 42.3% for PRI-MUS 3, 72.1% for PRI-MUS 4, and 90.6% for PRI-MUS 5 ($p<0.001$). Notably, 63 out of 165 patients (27.6%) with negative MUS harbored csPC at systematic biopsy. Using clinically relevant cut-offs, PRI-MUS ≥ 3 and ≥ 4 were strongly associated with csPC (odds ratios of 4.0 and 7.0, respectively; both $p<0.001$).

At multivariable analysis, PRI-MUS remained an independent predictor of csPC (odds ratio of 2.35 per point increase, 95% confidence interval=1.83-3.04; $p<0.001$), after adjusting for prostate-specific antigen density, age, and prostate volume. The PRI-MUS score showed good discriminative ability for csPC (area under the receiver operating characteristics curve=0.71). *Conclusion:* The PRI-MUS score is strongly associated with csPC and demonstrates good discriminative performance. Risk of csPC increases progressively with higher PRI-MUS categories, supporting its use as a reliable tool for risk stratification and biopsy decision-making.

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NOT ALL HIGH-RISK BIOCHEMICAL RECURRENCE IS THE SAME: PATIENTS HARBORING BOTH EAU BCR RISK FACTORS ARE MORE LIKELY TO HAVE DISTANT DISEASE AND WORSE PROGRESSION-FREE SURVIVAL

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Background/Aim: Patients with high-risk biochemical recurrence (BCR) after radical prostatectomy are commonly grouped into a single clinical category, although their risk of metastatic disease and subsequent progression is likely heterogeneous. We assessed whether harboring both risk factors of BCR, namely International Society of Urological Pathology (ISUP) grade group ≥ 4 and prostate-specific antigen doubling time (PSAdt) <12 months) identified patients at higher risk of distant disease on prostate-specific membrane antigen positron-emission tomography/computed tomography (PSMA PET/CT) and worse progression-free survival (PFS). *Materials and Methods:* We retrospectively analyzed patients with high-risk BCR after radical prostatectomy who underwent PSMA PET/CT at recurrence. Two adverse features were considered: ISUP Grade Group ≥ 4 and PSAdt <12 months. Patients were stratified according to the presence of 1 vs. 2 risk factors. The primary analyses assessed the association between risk group and distant disease at PSMA PET/CT using logistic regression, and the association with PFS using Kaplan-Meier estimates and Cox regression. *Results:* A total of 135 evaluable patients were included, of whom 82 had 1 risk factor and 53 had 2 risk factors. Patients with two risk factors showed a more aggressive clinical profile, including a shorter median time to first BCR (68.0 vs. 112.0 months), a lower use of salvage radiotherapy (29% vs. 62%), and more frequent treatment intensification with concomitant androgen-deprivation therapy (74% vs. 49%) and androgen receptor-targeted agents (28% vs. 2%). Median duration of androgen-deprivation therapy was longer for the group with 2 risk factors (24.0 vs. 18.0 months). Patients harboring both risk factors were substantially more likely to present with distant disease on PSMA PET/CT than those with one risk factor (69.8% vs. 32.9%). On multivariable logistic regression, the presence of 2 risk factors was strongly associated with metastatic disease at recurrence (odds ratio=4.71, 95% confidence interval=2.27-10.15; $p<0.001$). This simple clinical stratification also translated into significantly different oncological outcomes. On multivariable Cox regression,

patients with 2 risk factors had worse PFS than those with 1 (hazard ratio=1.66, 95% confidence interval=1.03-2.67; $p=0.039$) after adjusting for well-known confounders. *Conclusion:* Not all patients with high-risk BCR after radical prostatectomy carry the same biological or clinical risk. A simple model combining ISUP Grade Group ≥ 4 and PSAdt <12 months identifies a subgroup with a markedly higher likelihood of distant disease on PSMA PET/CT, greater treatment intensification, and significantly worse PFS. These findings support a more refined risk stratification within high-risk BCR in the PSMA PET era.

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CAN MICRO ULTRASOUND IDENTIFY CLINICALLY SIGNIFICANT CANCER IN PATIENTS WITH NEGATIVE MPMRI? A SINGLE-CENTER EXPLORATORY ANALYSIS

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Background/Aim: Multiparametric magnetic resonance imaging (mpMRI) has a high negative predictive value, yet a non-negligible proportion of clinically significant prostate cancer (csPC) remains undetected. Micro-ultrasound (MUS) may provide additional diagnostic information in this setting. *Materials and Methods:* We retrospectively analyzed patients undergoing prostate biopsy with pre-biopsy mpMRI and MUS evaluation (457 patients). Patients with negative/non-significant mpMRI (PI-RADS ≤ 2) and prostate-specific antigen (PSA) ≥ 3 ng/ml were included. The primary endpoint was overall detection of csPC. Secondary endpoints included detection of any PC and the association between MUS positivity and csPC. *Results:*

Among 73 patients with negative/non-significant mpMRI, 62 had PSA ≥ 3 ng/ml and were included. MUS was positive in 9/62 patients (14.5%). Overall, while PC was detected in 26/62 (41.9%), csPC was detected in 13/62 patients (21.0%). Among MUS-positive patients, 5/9 (55.6%) harbored csPC at MUS targeted biopsy (8.1% of the cohort), compared with 8/53 (15.1%) among MUS-negative patients (odds ratio=6.7, $p=0.02$). PC was identified at MUS targeted biopsy in 6/9 patients (66.7%). A sensitivity analysis was performed in patients with PSA density ≥ 0.15 ng/ml ($n=14$), showing consistent trends. *Conclusion:* In patients with negative/non-significant mpMRI but persistent clinical suspicion, the risk of csPC remains non-negligible. MUS positivity identifies a subgroup at higher risk and may provide additional value in the diagnostic pathway of mpMRI-negative patients. Larger prospective studies are warranted.

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INVESTIGATING THE COMBINED VALUE OF PSA AT BIOCHEMICAL RECURRENCE AND PSMA PET/CT RESULTS IN HIGH-RISK RECURRENCE AFTER RADICAL PROSTATECTOMY

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Background/Aim: High-risk biochemical recurrence (BCR) after radical prostatectomy is associated with an increased risk of metastatic progression and prostate cancer-specific mortality. Although prostate-specific membrane antigen positron-emission tomography/computed tomography (PSMA PET/CT) is increasingly used to guide treatment in this setting, the additional prognostic role of prostate-specific antigen (PSA) at recurrence remains incompletely defined. We evaluated oncological outcomes in patients with high-risk BCR managed according to a PSMA PET-guided multidisciplinary strategy, focusing on the complementary prognostic role of PSA at first recurrence. **Materials and Methods:** We retrospectively analyzed consecutive patients with high-risk BCR after radical prostatectomy discussed within a multidisciplinary tumor board at a tertiary referral center. All patients underwent PSMA PET/CT at recurrence, which guided treatment allocation. Primary endpoints were second biochemical recurrence-free survival and progression-free survival, both measured from the date of PSMA PET/CT. Progression-free survival was assessed exclusively by PSMA PET/CT. Outcomes were analyzed using Kaplan–Meier estimates, multivariable Cox regression, and LOWESS analysis. **Results:** A total of 136 patients were included. At PSMA PET/CT, 35% had negative findings or isolated local recurrence, 18% had pelvic nodal recurrence [molecular imaging (mi) N1M0], and 47% had distant metastatic disease (miNanyM1). Median PSA at first BCR increased across PSMA PET categories, from 0.3 ng/ml in patients with negative/local recurrence to 0.4 ng/ml in those with miN1M0 disease and 0.7 ng/ml in those with miNanyM1 disease, supporting an association between biochemical burden and imaging extent of disease. On multivariable analysis, PSMA PET findings were the strongest independent predictors of clinical progression, with hazard ratios of 2.53 for miN1M0 and 5.07 for miNanyM1 *versus* negative/local recurrence. Importantly, PSA at first BCR independently predicted progression beyond imaging

findings (hazard ratio=1.07, 95% confidence interval=1.00-1.15; $p=0.049$), whereas PSA doubling time did not. Model-based estimates further showed that among patients with miN1M0 disease, rising PSA values were associated with a 36-month predicted probability of PSMA PET progression that approached that of metastatic disease. **Conclusion:** In high-risk BCR after radical prostatectomy, PSMA PET/CT provides robust prognostic stratification, while PSA at recurrence adds independent prognostic information beyond imaging alone. The combination of PSA level and PSMA PET findings may improve risk assessment in patients with miN1M0 disease. These findings also highlight the need for caution when interpreting intermediate oncologic endpoints in the PSMA PET era.

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LEARNING CURVE OF NODAL PSMA PET ACCURACY OVER TIME: STABLE RULE-OUT PERFORMANCE BUT NO CLEAR IMPROVEMENT IN POSITIVE PREDICTIVE VALUE

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Background/Aim: Not all nodal prostate-specific membrane antigen positron emission tomography (PSMA PET) uptakes correspond to true pathological lymph node involvement. As multidisciplinary teams gain experience

with image interpretation, improvements in the ability to distinguish true- from false-positive nodal uptake may be expected. We evaluated the temporal learning curve of nodal PSMA PET accuracy, with particular focus on positive predictive value (PPV) and negative predictive value (NPV), using pathological nodal status as the reference standard. *Materials and Methods:* We retrospectively analyzed patients who underwent PSMA PET before radical prostatectomy with pelvic lymph node dissection and had available pathological nodal assessment. All PSMA PET scans were read by a single experienced nuclear medicine physician at a tertiary referral center. Nodal PSMA PET findings were classified as positive or negative and compared with the final nodal pathology. Accuracy metrics included PPV, NPV, sensitivity, and specificity. Temporal trends were assessed overall, by calendar year, and by splitting the cohort into early and late periods according to chronological case order. A cumulative learning curve of PPV and NPV over time was also generated. *Results:* A total of 101 evaluable patients were included. Overall, nodal PSMA PET showed a PPV of 52.2%, an NPV of 88.5%, a sensitivity of 57.1%, and a specificity of 86.2%. Thus, while a negative nodal PSMA PET finding was frequently confirmed at pathology, nearly half of the positive nodal uptakes were not associated with pathological nodal involvement. When stratified by year, PPV was 42.9% in 2023 and 40.0% in 2024, whereas NPV remained consistently high at 88.2% and 90.9%, respectively. In the early *versus* late comparison, PPV remained largely unchanged (54.5% vs. 50.0%), while NPV was stable or slightly higher over time (87.2% vs. 89.7%). Fisher's exact test restricted to PET-positive cases did not show a significant temporal improvement in pathological confirmation of positive uptake ($p=0.155$). The cumulative learning curve confirmed persistently high NPV across chronological cases, whereas PPV remained modest and did not display a clear upward trend over time. *Conclusion:* In the examined cohort, nodal PSMA PET demonstrated high and stable rule-out performance, but only moderate rule-in accuracy. Despite

increasing institutional experience, no clear learning curve emerged for improving the pathological reliability of positive nodal uptake interpretation. These findings suggest that false-positive nodal PSMA PET findings remain clinically relevant and that positive uptake should be interpreted cautiously, particularly when treatment escalation or nodal dissection decisions are being considered.

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FATAL CHOLANGITIS FROM ADJUVANT PEMBROLIZUMAB IN INTERMEDIATE-HIGH-RISK CLEAR CELL RENAL CARCINOMA: A CASE REPORT

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Background/Aim: One year of adjuvant pembrolizumab has become a standard option in intermediate/high-risk, clear cell renal carcinoma (RCC) after surgery. However, immune-related adverse events can affect multiple organs, including the liver and the kidney, and may sometimes have adverse outcomes notwithstanding high-dose (HD) of corticosteroids and other immunosuppressive drugs, with a global mortality rate of around 1-2%. *Case Report:* This is the case of an elderly patient who underwent radical left nephrectomy for high-risk, clear cell RCC, followed by adjuvant pembrolizumab. He rapidly developed renal failure and cholangitis, he was treated with HD steroids, and

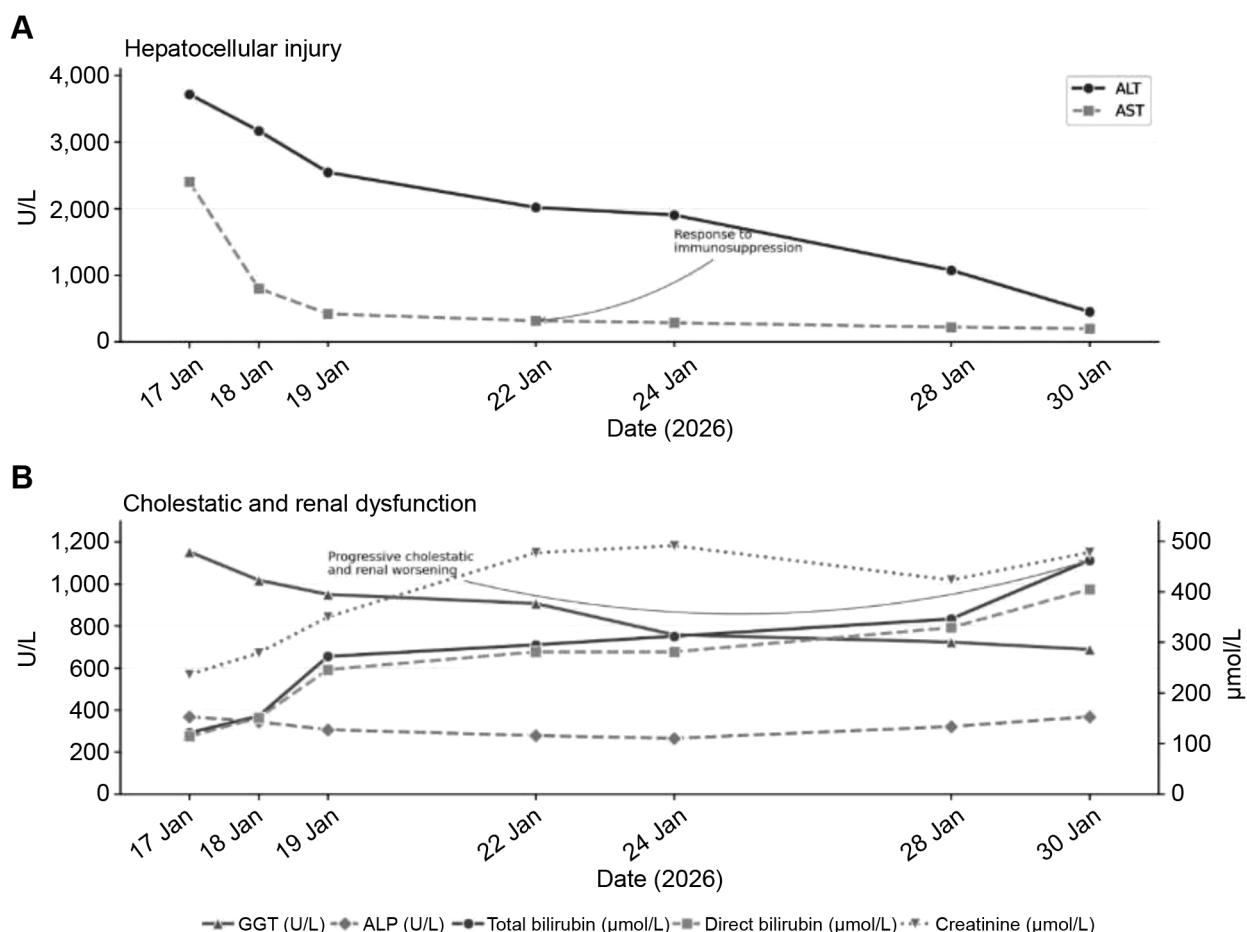


Figure 1. (A) The trend of serum transaminases. (B) The trend of biliary-cholestatic markers and renal function.

mycophenolate mofetil with no recovery. In April 2025, a 72-year-old man complained of back pain and underwent an abdominal CT scan, which showed a huge left renal lesion with renal vein thrombosis. He then underwent radical left nephrectomy for clear cell RCC with rhabdoid features, pT3a, with no evidence of metastatic disease at postoperative CT scan of chest and abdomen. He did not have relevant comorbidities and had never experienced autoimmune disorders. He started adjuvant pembrolizumab in September 2025. Just after three doses, he experienced a creatinine elevation to G2 according to CTCAE 5.0. Abdominal ultrasound was normal, and therefore, immune-related renal toxicity was hypothesized. Oral prednisone at 37.5 mg/day was started, resulting in a rapid recovery of

renal function. Steroids were tapered to 12.5 mg/day, but new lab tests showed G4 hypertransaminasemia, G3 hyperbilirubinemia, G2 cholestasis indices, and G2 hypercreatinemia. The patient was immediately admitted to our inpatient ward and started intravenous hydration with saline solutions and intravenous methylprednisolone at 2 mg/day for two days, with no improvement. Mycophenolate mofetil 1 g/BID was added, but only a minor reduction of AST and ALT was obtained; renal function and bilirubin levels further worsened (Figure 1). The Nephrologist hypothesized the contribution of bile cast nephropathy, so intravenous hydration was increased. Magnetic resonance of the liver revealed diffuse thickening of the bile duct walls, with alternating focal expansion and

stenosis, confirming diffuse cholangitis. Hepatic biopsy excluded metastases, and showed evidence of hepatobiliary cholestasis in the acinar parenchyma. *Results:* Despite immunosuppression and supportive care, the patient's general condition deteriorated, renal function further worsened, resulting in hypoxic respiratory failure and multi-organ dysfunction syndrome. Broad-spectrum antibiotics were added for suspicion of an opportunistic lung infection, without improvement. The patient was transferred to the Intensive Care Unit. Despite high doses of vasoactive amines and mechanical ventilation, the patient died. *Conclusion:* Pembrolizumab has improved disease-free and overall survival of clear cell RCC, but complex immune-related adverse events (irAEs) may appear after treatment initiation. While skin, hepatic, and pulmonary immune-related toxicities are well documented, rare entities like immune-related cholangitis and nephropathy remain poorly characterized (1, 2). Cholangitis is an uncommon, often steroid-refractory irAE that may require intensified immunosuppression. Severe cholestasis can also induce secondary renal injury through bile nephropathy by tubular bile acid toxicity and bile cast formation (3). In our case report, the occurrence of concomitant steroid-refractory cholangitis and progressive renal dysfunction highlights the complex interplay between immune-mediated injury and metabolic damage. Despite prompt HD corticosteroids and mycophenolate mofetil, only partial biochemical improvement in transaminases was achieved, with persistent cholestasis and worsening renal function, underscoring the limited efficacy of standard immunosuppression and the uncertainty regarding optimal escalation. Our case underscores the importance of early recognition of atypical irAEs, the unmet need for alternative treatment options for steroid-refractory immune-related events within a multidisciplinary approach. Management is challenged by the need to balance immunosuppression against the risk of opportunistic infections. Further studies are essential to identify patients who are at increased risk of irAEs, in order to have a more accurate discussion of pros and cons of adjuvant pembrolizumab, which is administered to patients who may have already been cured by surgery.

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- 2 Karamchandani DM, Chetty R: Immune checkpoint inhibitor-induced gastrointestinal and hepatic injury. *Semin Diagn Pathol* 36(6): 453-461, 2019. DOI: 10.1136/jclinpath-2018-205143
- 3 Van Slambrouck CM, Salem F, Meehan SM, Chang A: Bile cast nephropathy is a common pathologic finding for kidney injury associated with severe liver dysfunction. *Kidney Int* 84(6): 1247-1252, 2013. DOI: 10.1038/ki.2013.78

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STEREOTACTIC BODY RADIOTHERAPY FOR PANCREATIC OLIGOPROGRESSION FROM RENAL CELL CARCINOMA: DELAYING SYSTEMIC THERAPY THROUGH DURABLE LOCAL CONTROL

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Background/Aim: Renal cell carcinoma (RCC) may exhibit an indolent course with late metastases to uncommon sites, including the pancreas. In oligometastatic or oligoprogressive

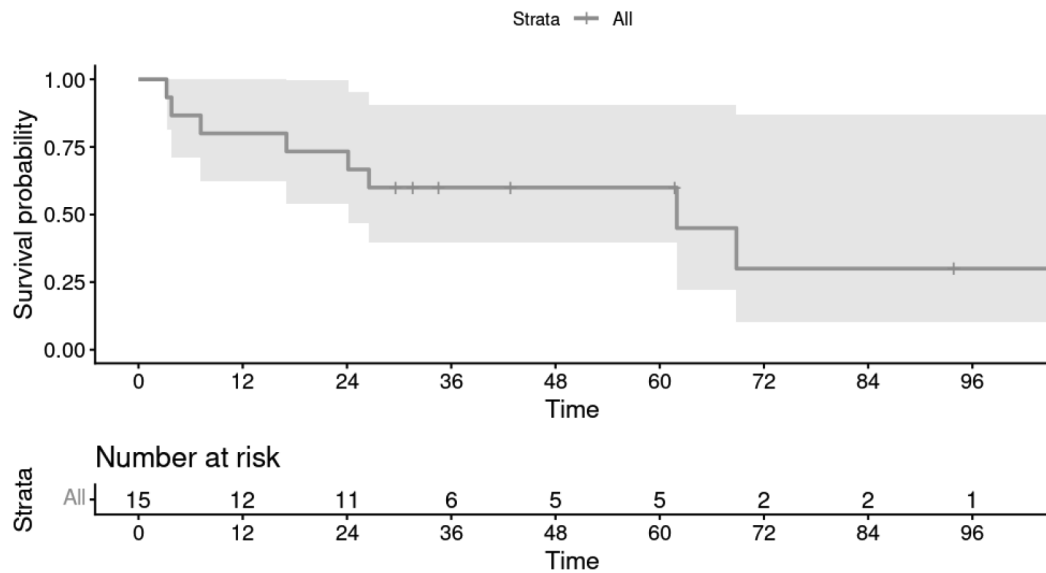


Figure 1. Kaplan-Meier curve for local control.

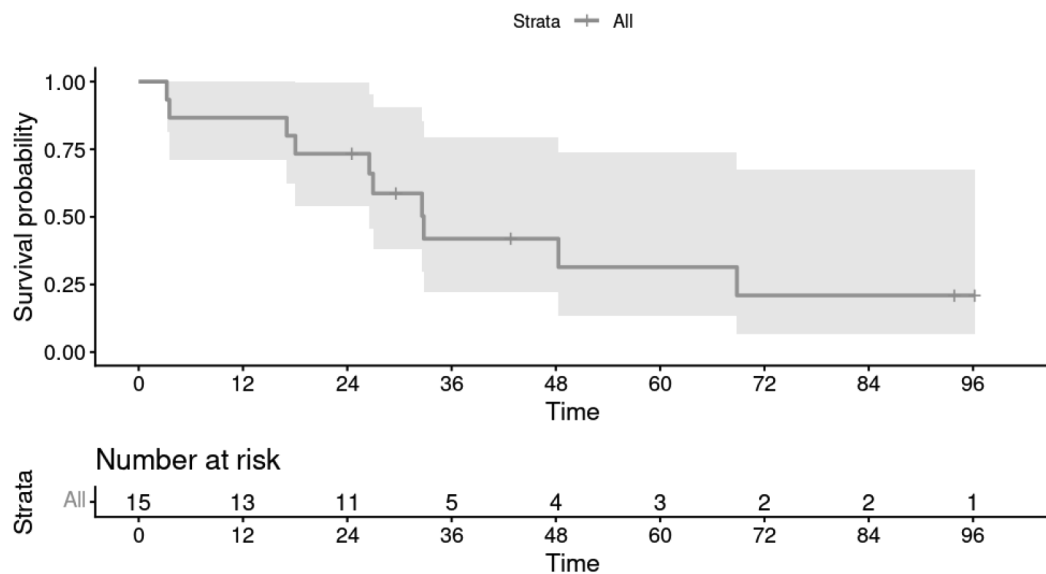


Figure 2. Kaplan-Meier curve for progression-free survival.

settings, stereotactic body radiotherapy (SBRT) represents a non-invasive ablative approach capable of achieving durable local control (LC), potentially delaying the initiation or escalation of systemic therapy. We report our institutional experience with SBRT for pancreatic oligometastases from RCC. *Materials and Methods:* We retrospectively analyzed

oligometastatic RCC patients treated with SBRT between 2013 and 2023 at our Institution. SBRT was delivered with a total dose of 25-40 Gy in 3-8 fractions. The primary endpoint was LC, assessed by computed tomography scan (CTscan) or magnetic resonance imaging (MRI) according to RECIST-like criteria and estimated using the Kaplan-Meier

Table I. Patient and treatment characteristics.

Age at SBRT, median (range) [years]	70.0 (52-79)
KPS (range)	90-100
CCI age-adjusted	3-5
Systemic therapy at SBRT	
Yes	3 pts
No	12 pts
SBRT dose	
25 Gy in 5 fx	6 pts
27 Gy in 3 fx	1 pt
30 Gy in 5 fx	5 pts
32 Gy in 4 fx	1 pt
35 Gy in 5 fx	1 pt
40 Gy in 8 fx	1 pt
FUP, median (range) [months]	42.8 (7.4-117.6)
LC, median (range) [months]	31.5 (3.2-108.2)
PFS, median (range) [months]	29.5 (3.2-96.2)

CCI: Charlson Comorbidity Index; FUP: follow-up; KPS: Karnofsky performance status; LC: local control; PFS: progression-free survival; SBRT: stereotactic body radiotherapy, pt: patient.

method from the end of radiotherapy to local progression or last follow-up (FUP). The secondary endpoint was progression-free survival (PFS), calculated from the end of SBRT to disease progression at any site or last FUP. *Results:* Among 121 metastatic RCC patients, 15 (12.4%) with pancreatic oligoprogression treated with SBRT were included. After a median FUP of 42.8 months (IQR=33.0-101.7), local progression occurred in 8 patients (53.3%). Median LC was 31.5 months (IQR=20.6-61.8), with 1- and 2-year LC rates of 80% and 73.3%, respectively. Median PFS was 29.5 months (IQR=21.3-45.6), with 1- and 2-year rates of 86.7% and 73.3%, respectively. Kaplan–Meier curves for LC and PFS are shown in Figure 1 and Figure 2. Four patients (26.7%) did not require systemic therapy, while in the remaining 11 (73.3%) SBRT allowed its postponement or modification. Patterns of failure were predominantly distant. Best local responses were mainly partial response or stable disease. Treatment was well tolerated, with no CTCAE v5.0 ≥ G2 toxicity observed (only one episode of self-limiting vomiting). At last FUP, most patients were alive with active disease; one death of unknown cause occurred during ongoing targeted therapy. Patient and treatment characteristics are summarized in Table I. *Conclusion:* SBRT appears to be a safe and effective local treatment for

pancreatic oligoprogression from RCC, providing durable LC with a median exceeding 2 years. These findings support its role within a multidisciplinary strategy aimed at delaying disease progression, deferring systemic therapy, and prolonging treatment-free intervals. Prospective studies with larger cohorts are warranted to optimize dose and fractionation and to better define their impact on clinical outcomes.

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**COMBINED NODAL PSMA PET AND PLND
FINDINGS STRATIFY THE PROBABILITY OF
UNDETECTABLE POSTOPERATIVE PSA
AFTER RADICAL PROSTATECTOMY**

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Background/Aim: The prognostic significance of discordant nodal findings between prostate-specific membrane antigen positron emission tomography (PSMA PET) and pelvic lymph node dissection (PLND) remains incompletely defined. We evaluated whether the combination of preoperative nodal PSMA PET status and final nodal pathology identifies distinct groups with

different probabilities of achieving undetectable postoperative prostate-specific antigen (PSA) after radical prostatectomy, and whether PSMA PET or PLND results better predict PSA persistence. *Materials and Methods:* We retrospectively analyzed patients undergoing radical prostatectomy and PLND with available nodal PSMA PET findings, final nodal pathology, and first postoperative PSA value. Undetectable postoperative PSA was defined as <0.1 ng/ml. Patients were stratified into four groups according to nodal PSMA PET and PLND results: PET-/PLND-, PET+/PLND-, PET-/PLND+, and PET+/PLND+. Group comparisons were performed using Chi-squared and Fisher's exact tests. Logistic regression was used to assess the association between group assignment and undetectable postoperative PSA, using PET-/PLND- as a reference. An ordinal trend model was also tested across the four categories. *Results:* A total of 86 evaluable patients were included: 56 were PET-/PLND-, 9 PET+/PLND-, 9 PET-/PLND+, and 12 PET+/PLND+. Rates of undetectable postoperative PSA differed significantly across groups (Chi-squared $p=2.4 \times 10^{-6}$; Fisher $p=6.1 \times 10^{-6}$). The highest rate of undetectable PSA was observed in PET+/PLND- and PET-/PLND- patients (89.3%). In contrast, undetectable PSA was achieved in only 55.6% of PET-/PLND+ patients and 25.0% of PET+/PLND+ patients. Compared to PET-/PLND- patients, those with occult nodal disease despite negative PET (PET-/PLND+) had significantly lower odds of undetectable PSA (OR=0.15, 95% CI=-0.03-0.74; $p=0.017$), while patients with concordant PET-positive and pathologically node-positive disease (PET+/PLND+) had the lowest likelihood of postoperative undetectable PSA (OR=-0.04, 95% CI=-0.007-0.17; $p<0.001$). The PET+/PLND- group had no cases of postoperative detectable PSA, precluding a stable effect estimate, but showed a uniformly favorable biochemical outcome. When analyzed separately, both nodal PSMA PET and PLND status were associated with PSA persistence, but the association was markedly stronger for pathological nodal involvement. PSA persistence was observed in 42.9% of PET-positive versus

15.4% of PET-negative patients, compared with 61.9% of PLND-positive versus 9.2% of PLND-negative patients. *Conclusion:* The combination of nodal PSMA PET and PLND findings identifies biologically and clinically distinct groups after radical prostatectomy. Patients with pathologically confirmed nodal disease, particularly when concordant with PET positivity, had a markedly lower probability of achieving undetectable postoperative PSA. In contrast, discordant groups suggest that pathological nodal status may be more informative than PSMA PET alone in predicting PSA persistence. Integrating imaging and pathology may therefore improve postoperative biochemical risk stratification beyond either modality alone.

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REAL-WORLD PERFORMANCE OF MIR-371A-3P IN DETECTING RECURRENCE DURING FOLLOW-UP OF TESTICULAR GERM CELL TUMOURS

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Background/Aim: The current cornerstones of clinical management of testicular germ cell tumour (GCT) are surgery, imaging and serum tumour markers such as alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (beta-HCG) and lactate dehydrogenase (LDH). Given the young age of these patients and the need

for long-term surveillance, more accurate tumour markers are required to improve early detection and guide clinical management. Recently, miRNA-371a-3p (M371) has emerged as a highly promising biomarker, showing superior diagnostic performance compared to conventional markers. This study aimed to evaluate its real-world accuracy in detection of recurrence of GCT during follow-up, compared to the conventional tumour markers. *Materials and Methods:* We prospectively analysed 81 patients under follow-up for GCT (52 seminomas, 29 non-seminomas, 14 metastatic at diagnosis). Clinical data, imaging/histology results, and serum levels of AFP, β -hCG, LDH, and M371 were collected. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratios (LQ+, LQ-), and ROC curves were calculated and compared. *Results:* After a mean follow-up of 33.4 months, 31 recurrences occurred in 23 patients. M371 showed a sensitivity of 93.5% and a specificity of 92.0%. Sensitivity was significantly higher than AFP (32.3%), β -hCG (32.4%), and LDH (35.5%) ($p=0.0001$). Specificity was 100% for β -hCG, 94.9% for AFP, and 85.0% for LDH. For M371, PPV was 72.5% and NPV was 98.4% (LR+ 11.64; LR- 0.07). ROC analysis showed an AUC of 0.966 for M371, compared with 0.72, 0.75, and 0.65 for AFP, β -hCG, and LDH, respectively. Diagnostic accuracy was higher in seminomas (AUC 0.99) than in non-seminomas (AUC 0.94). The optimal cut-off for M371 was RQ=5.2. Postoperative elevation of M371 may indicate the presence of occult metastases. *Conclusion:* The M371 test demonstrated excellent diagnostic performance in detecting GCT recurrence under real-life conditions and outperforms conventional markers. Its integration in the follow-up could reduce the need for imaging and patient radiation exposure, improving their long-term safety. Postoperative elevation of M371 may suggest the presence of occult metastases and may contribute to decision-making regarding adjuvant treatment. Larger prospective multicentre studies are needed to confirm these findings and to better define its role in the clinical decisions.

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ACCURACY OF PSMA PET/CT FOR LYMPH NODE STAGING IN PROSTATE CANCER: RESULTS FROM A HIGH-VOLUME SINGLE CENTER

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Background/Aim: Prostate-specific membrane antigen positron emission tomography/computer tomography (PSMA PET/CT) has become a key tool for assessing pelvic lymph node metastases in prostate cancer and is now widely used in preoperative staging. However, its diagnostic accuracy in the primary staging setting remains debated. This study aimed to evaluate the diagnostic accuracy of PSMA PET/CT for lymph node detection in a high-volume center. *Materials and Methods:* This single-center retrospective study included patients who underwent PSMA PET/CT and subsequent robot-assisted radical prostatectomy with pelvic lymph node dissection between 2018 and 2025. The diagnostic performance of PSMA PET/CT was evaluated using final pathological nodal status as the reference standard. Sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and overall accuracy were assessed, along with agreement using Cohen's kappa coefficient. Subgroup analyses were performed according to International Society of Urological Pathology grade group and D'Amico risk classification. Patients with distant metastases or missing data were excluded. *Results:* Overall, 609 patients were identified. The prevalence of pathological lymph node involvement was 20.7% (126/609). In the overall cohort, PSMA PET/CT showed a sensitivity of 50.8%, specificity of 90.1%, PPV of 57.1%, NPV of 87.5%, and overall accuracy of

81.9%. Agreement with final pathology was moderate, with a Cohen's kappa coefficient of 0.426. Stratifying our cohort by the D'Amico risk classification, the prevalence of lymph node involvement was 8.8% in the low-risk group; 9.6% in the intermediate-risk group and 30.6% in the high-risk group. Sensitivity was 33.3%, 15.8%, and 59.1% in the low-, intermediate-, and high-risk groups, respectively. Specificity remained high across all groups, at 93.5% in low-risk, 90.4% in intermediate-risk, and 89.1% in high-risk patients. PPV was 33.3% in low-risk, 15.0% in intermediate-risk, and 70.5% in high-risk patients. NPV was 93.5%, 91.0%, and 83.2% in the low-, intermediate-, and high-risk groups, respectively. Overall accuracy was 88.2% in low-risk, 83.2% in intermediate-risk, and 79.9% in high-risk patients. Agreement with pathology was low in the intermediate-risk group (Cohen's kappa 0.061), moderate in the low-risk group (0.269), and higher in the high-risk group (0.505). *Conclusion:* PSMA PET/CT demonstrated high specificity and NPV, but limited sensitivity for lymph node staging in prostate cancer. Diagnostic performance varied across risk groups, with higher sensitivity and PPV in high-risk patients, while remaining suboptimal in low- and intermediate-risk groups. These findings indicate that, although PSMA PET/CT is reliable for confirming nodal disease when positive, its limited sensitivity and NPV reduce its ability to safely exclude lymph node involvement and it cannot replace pelvic lymph node dissection for accurate staging.

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EFFECT OF PRE-OPERATIVE HORMONAL THERAPY ON PSMA PET/CT ACCURACY FOR LYMPH NODE STAGING IN PROSTATE CANCER

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Background/Aim: The PSMA-PET/CT scan is widely recognized for detecting pelvic lymph node metastasis in prostate cancer (PCa). However, the use of a pre-operative androgen deprivation therapy (ADT), even if not recommended by guidelines, may affect its diagnostic accuracy. This study aimed to evaluate the impact of pre-operative ADT on the diagnostic performance of PSMA-PET/CT scan for lymph node staging. *Materials and Methods:* This single-center retrospective study included patients who underwent PSMA PET/CT followed by RARP with pelvic lymph node dissection between 2018 and 2025 at the European Institute of Oncology, Milan (Italy). Patients were stratified according to the use of pre-operative ADT. Only unfavorable intermediate- and high-risk patients according to the D'Amico classification were included. The diagnostic performance of PSMA-PET/CT was evaluated using final pathological nodal status as a reference standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), overall accuracy, and agreement using Cohen's kappa coefficient were assessed. *Results:* A total of 540 patients with unfavorable intermediate- and high-risk PCa were included. Of these, 457 patients (85%) were untreated, while 83 (15%) underwent neoadjuvant treatment. Overall, pathological lymph node involvement was observed in 125 of 531 evaluable patients (24%), with a higher prevalence in the treated group (36% vs. 21%, $p=0.003$). In the overall cohort, PSMA PET/CT demonstrated a sensitivity of 47.8% and specificity of 90.6% in untreated versus 65.5% and 79.2% in treated patients. PPV was 57.3% vs. 65.5%, and NPV was 86.8% vs. 79.2%, respectively. Overall accuracy was 81.6% in patients without hormonal therapy and 74.0% in the treated group. Agreement with final pathology was moderate in both groups (Cohen's kappa 0.409 vs. 0.447). In the high-risk subgroup, sensitivity was 54.9% without therapy and 66.7% with therapy, while specificity was 89.5% and 84.4%, respectively. PPV was 66.1% vs. 78.3%, and NPV was 84.2% vs. 75.0%. Accuracy was 80.2% in

untreated and 76.3% in treated patients, with moderate agreement (Cohen's kappa 0.470 vs. 0.516). In the unfavorable intermediate-risk subgroup, sensitivity increased from 21.1% in untreated patients to 50.0% in those receiving neoadjuvant therapy, while specificity decreased from 91.9% to 68.8%. PPV was 25.0% vs. 16.7%, and NPV was 90.1% vs. 91.7%, respectively. Overall accuracy was 83.9% without therapy and 66.7% with therapy. *Conclusion:* Pre-operative ADT affects the diagnostic performance of PSMA PET/CT scan, increasing the sensitivity but reducing the specificity and the overall accuracy. Although the NPV remains relatively high, it decreases after the pre-operative treatment, limiting the reliability of a negative scan to exclude lymph node metastases. Therefore, the PSMA PET/CT cannot completely replace pelvic lymph node dissection for accurate nodal staging, particularly in patients receiving pre-operative ADT.

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COMBINING PSA DENSITY AND PRI-MUS SCORE IMPROVES RISK STRATIFICATION FOR CLINICALLY SIGNIFICANT PROSTATE CANCER: A SINGLE-CENTER ANALYSIS

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Background/Aim: Both prostate-specific antigen (PSA) density and micro-ultrasound (microUS) findings are

associated with prostate cancer risk. Their combined value for clinically significant prostate cancer (csPCa) risk stratification remains poorly defined. *Materials and Methods:* We retrospectively analyzed 432 patients with complete clinical, biopsy, and microUS data. The highest PRI-MUS score per patient was considered. The primary endpoint was detection of csPCa. Univariable and multivariable logistic regression analyses were performed to assess the association of PSA density and PRI-MUS with csPCa. Discriminative ability was evaluated using ROC analysis. A combined risk stratification model was also developed using PSA density and PRI-MUS categories (low-risk group: PSA density <0.15 and PRIMUS ≤3; intermediate-risk group: PSA density ≥0.15 or PRI-MUS ≥4; high-risk group PSA density ≥0.15 and PRI-MUS ≥4). Optimal PSA density thresholds were calculated using ROC curve analysis and the Youden index in the overall population and in the PRI-MUS 3 subgroup. *Results:* Overall, 188/432 patients (43.5%) were diagnosed with csPCa. Median PSA density was 0.11 ng/ml² (IQR=0.08-0.17). MicroUS was negative in 218 patients (50%), PRI-MUS 3 in 104 patients (24%), PRI-MUS 4 in 80 patients (19%) and PRI-MUS 5 in 30 patients (7%). PSA density was significantly higher in patients with csPCa than in those without ($p<0.001$). Using a clinically relevant threshold, PSA density ≥0.15 was associated with csPCa (OR=2.59, 95% CI=1.68-4.01, $p<0.001$). PRI-MUS ≥4 was also strongly associated with csPCa (OR=7.19, 95%CI=4.27-12.47, $p<0.001$). ROC analysis identified an optimal PSA density cut-off of 0.125, with a sensitivity of 53.7% and specificity of 68.0%. At multivariable analysis, both PSA density (OR=21.8, 95% CI=2.68-251.46, $p=0.008$) and PRI-MUS score (OR=2.35 per point increase, 95% CI=1.83-3.04, $p<0.001$) remained independent predictors of csPCa, together with age and prostate volume. The combined model showed significantly better discrimination for csPCa than PSA density alone (AUC 0.753 vs. 0.656, $p<0.001$) and PRI-MUS alone (AUC 0.753 vs. 0.721, $p=0.005$). When combining PSA density and PRI-MUS into three clinical risk groups, the rate of csPCa was 27.5% in the low-risk group, 52.6% in the intermediate-

risk group, and 91.5% in the high-risk group. Among patients with PRI-MUS 3 lesions, PSA density further stratified the risk of csPCa. Using an optimal threshold of 0.115, csPCa rates increased from 34.5% to 54.3% ($p=0.049$). **Conclusion:** Combining PSA density and PRI-MUS score significantly improves risk stratification for clinically significant prostate cancer compared with either parameter alone. While PSA density alone showed moderate discriminatory ability, its integration with PRI-MUS enhances clinical decision-making, particularly in patients with intermediate-risk (PRI-MUS 3) lesions.

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PRE-TREATMENT BLADDER ULTRASOUND IN PROSTATE CANCER RADIOTHERAPY: A SIMPLE STRATEGY TO SIGNIFICANTLY REDUCE REPEATED CONE-BEAM COMPUTED TOMOGRAPHY SCANS

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Background/Aim: Daily pre-treatment cone-beam computed tomography (CBCT) is routinely used in prostate cancer radiotherapy to verify target positioning and assess pelvic organs at risk. The position of the prostate gland, or prostatic bed in post-operative patients, is strongly influenced by bladder and rectal volume variations. Adequate bladder filling is associated with reduced radiation dose to the bladder and a lower risk of genitourinary (GU) toxicity (1). However, achieving consistent bladder filling remains challenging in daily

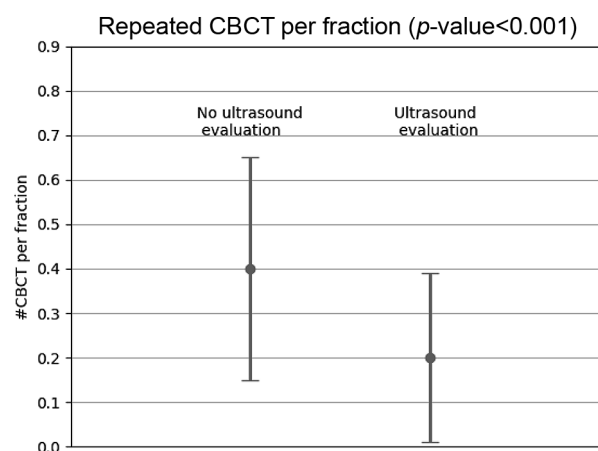


Figure 1. Mean of exceeding CBCT per fraction with standard deviation in the two groups. CBCT: Cone beam computed tomography.

clinical practice, often resulting in repeated CBCT acquisitions, treatment delays, and reduced workflow efficiency. The aim of this study was to evaluate whether the pre-treatment ultrasound (US) assessment of the bladder could reduce the number of repeated CBCT scans and to assess its impact on treatment tolerability. **Materials and Methods:** Since October 2024, a pre-treatment bladder US assessment using a hand-held device (Cerbero 4,0 – ATL s.r.l., Milan, Italy) has been introduced in our Department for prostate cancer patients undergoing pelvic radiotherapy. We retrospectively analyzed data from 100 prostate cancer patients treated between September 2024 and April 2026 with radical or adjuvant pelvic radiotherapy. Patients were divided into two groups: 50 treated without pre-treatment ultrasound assessment and 50 treated with daily bladder US assessment prior to CBCT. We collected clinical and treatment data, including the number of repeated CBCT scans per fraction for any reason (*e.g.*, inadequate bladder or rectal preparation or target misalignment). The number of repeated CBCTs was normalized per fraction. Statistical analysis was performed using the Mann-Whitney *U*-test. Acute GU and gastrointestinal (GI) toxicities were also recorded and compared between the two subgroups. **Results:** The mean number of repeated CBCT scans per fraction was 0.4 in the

group without US and 0.2 in the US group, with a statistically significant difference according to the Mann–Whitney *U*-test (Figure 1). From a safety perspective, treatment was well tolerated. The majority of patients did not experience any acute or late GU or GI toxicity in both groups. No grade ≥ 3 acute or late GU and GI toxicities were reported. Moreover, no statistically significant differences in toxicity were observed between the two groups, as expected. *Conclusion:* In this retrospective analysis, the implementation of a simple, low-cost pre-treatment bladder US assessment was associated with a significant reduction in repeated CBCT scans, with approximately a two-fold decrease in the number of repeated acquisitions, without reducing the already low GU and GI toxicity. These findings are in line with previously reported literature data (2, 3) and support the role of the bladder US assessment in improving daily workflow efficiency and patient compliance. Nevertheless, the large variability observed within both groups suggests that repeated CBCT scans and treatment reproducibility remain critical issues, likely influenced by patient bowel preparation or other patient-related factors. Further prospective studies may help to optimize bladder and rectal preparation protocols.

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EFFECTIVENESS AND SAFETY OF 5-FRACTION STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR LOCALIZED PROSTATE CANCER: A PROSPECTIVE OBSERVATIONAL STUDY

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Background/Aim: Stereotactic body radiation therapy (SBRT) has become a primary treatment modality for localized prostate cancer (PCa), exploiting the tissue-specific radiobiological sensitivity to high radiation dose per fraction. As its clinical adoption expands, prospective data are essential to confirm the SBRT safety profile and oncological efficacy (1, 2). This study evaluated the clinical outcomes and treatment-related adverse events of a five-fraction linear accelerator (linac)-based SBRT protocol in a prospective cohort of patients with localized PC. *Materials and Methods:* Patients with localized PCa prospectively enrolled and treated with SBRT at University Hospital of Parma from 2022 to 2024 were included in the analysis.

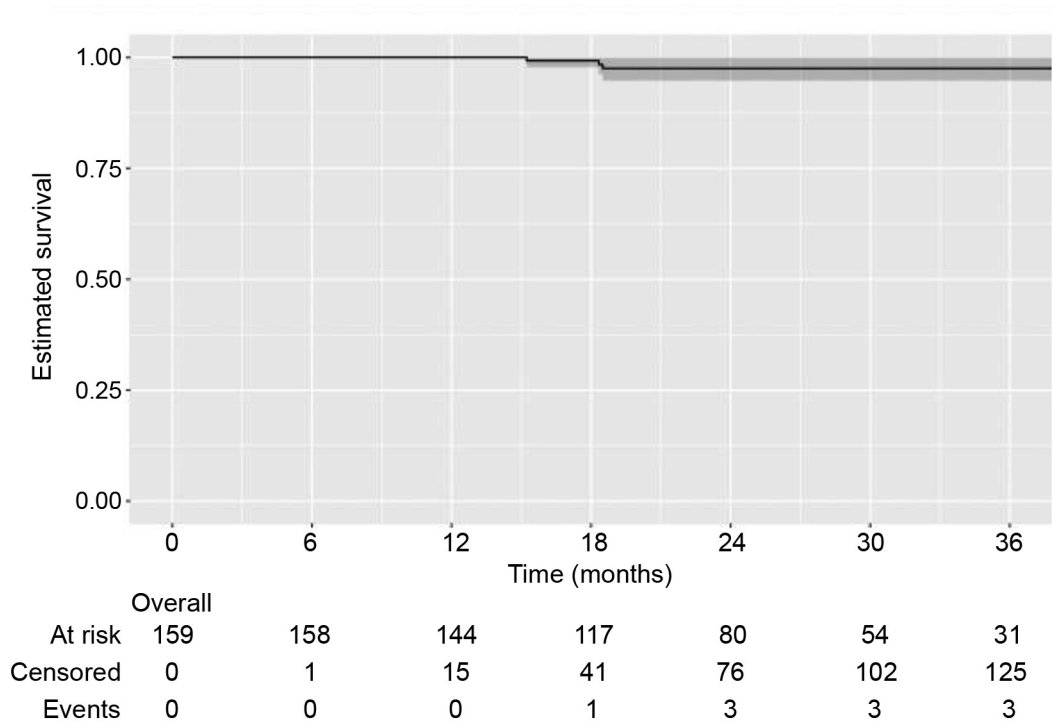


Figure 1. Kaplan-Meier survival curve for biochemical recurrence-free survival.

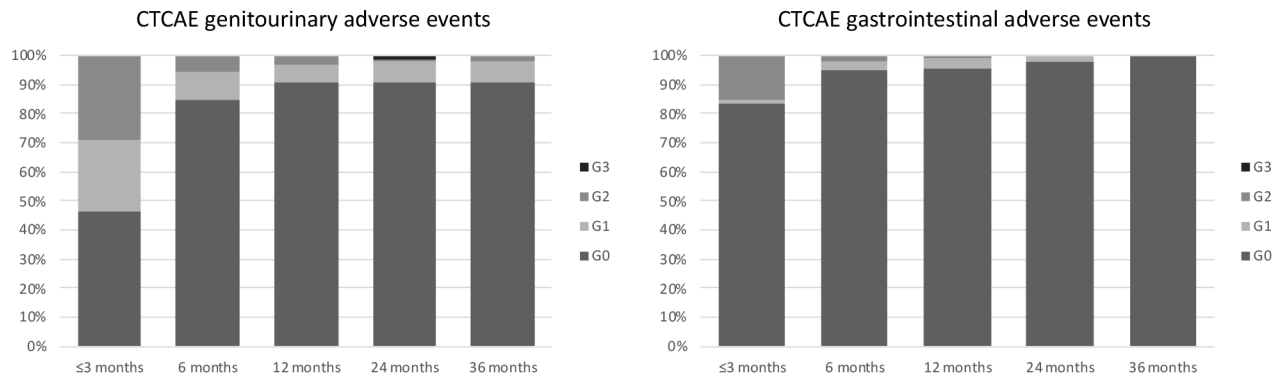


Figure 2. Common Terminology Criteria for Adverse Events toxicity for genitourinary and gastrointestinal systems

SBRT was delivered with volumetric modulated arc radiotherapy (VMAT) and flattening filter free (FFF) beam technique, administering 36.25 Gy in 5 fractions every other day to the Planning Target Volume (PTV). A simultaneous integrated boost (SIB) of 40 Gy to the prostate was adopted for intermediate- and high-risk patients. All

patients underwent intraprostatic fiducial marker placement with real-time automatic beam hold (ABH) tracking. Biochemical recurrence was defined according to the Phoenix criteria, as an increase of ≥ 2 ng/ml above the post-SBRT PSA nadir. Genitourinary (GU) and gastrointestinal (GI) adverse events were reported

according to the Common Terminology Criteria for Adverse Events (CTCAE) scoring criteria. *Results:* A total of 159 patients were included in the analysis. Median patient age was 75 years (IQR=71-78), and median baseline PSA (iPSA) was 8.8 ng/ml (IQR=5.9-13.0). Overall, 15.7%, 64.8% and 19.5% of cases were classified as low-, intermediate, and high-risk according to D'Amico/NCCN risk group, respectively. In 51.1% of patients, androgen deprivation therapy (ADT) was administered in accordance with class risk group. All patients (100%) completed the SBRT prescribed treatment, in a median time of 10 days (IQR=9-13). At a median estimated follow up of 24.6 months (95% CI=22.4-26.7), biochemical relapse occurred in 3 (1.9%) patients, with a 1-, 2- and 3-year biochemical recurrence-free survival (bRFS) rate of 100% (95% CI=100-100), 97.5% (95% CI=94.8-100) and 97.5% (95% CI=94.8-100), respectively (Figure 1). At ≤3, 6, 12, 24, and 36 months from SBRT, G≥2 GU toxicity was observed in 28.9%, 5.7%, 3.4%, 2.2% and 2.3% of patients, respectively, while G≥2 GI toxicity was reported in 15.1%, 1.9%, 0.7%, 0.0%, and 0.0%, respectively, at the same time-point (Figure 2). One (0.6%) case of G3 urethral stenosis with obstruction occurred 24 months after SBRT. At last follow up, no cancer-specific death occurred, while five (3.1%) patients had died from competing causes. One-, 2- and 3-year overall survival (OS) rate for the entire cohort was 98.1% (95% CI=95.9-100), 98.1% (95% CI=95.9-100) and 94.6% (95% CI=89.6-99.9), respectively. *Conclusion:* This prospective study confirms that five-fraction linac-based SBRT with fiducials tracking is an effective and safe treatment approach for localized prostate cancer. The low rates of adverse events and the excellent medium-term biochemical control align with results from major randomized controlled trials, supporting the routine use of this ultra-hypofractionated regimen in clinical practice.

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IMPACT OF PRIOR TURP ON GENITOURINARY ADVERSE EVENTS AND OUTCOMES FOLLOWING STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR PROSTATE CANCER

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Background/Aim: The impact of prior transurethral resection of the prostate (TURP) on patients receiving SBRT for localized prostate cancer (PCa) remains unclear. This study aimed to evaluate the association between prior TURP and SBRT-related genitourinary (GU) adverse events (AEs), as well as oncologic outcomes. *Materials and Methods:* Patients with localized PCa treated with linac-based SBRT were retrospectively analyzed, regardless of risk group or prostate volume. Maximum GU AEs (CTCAE

Table I. AEs (CTCAE v5.0) profile distribution in the analyzed population.

	G0	G1	G2	G3	G4-5
Acute AEs	16 (48.5%)	9 (27.3%)	8 (24.2%)	0	0
Late AEs	16 (48.5%)	11 (33.3%)	5 (15.2%)	1 (3.0%)	0

AEs: Adverse events.

v5.0) and PSA levels were recorded at baseline and during follow-up at Fondazione IRCCS San Gerardo dei Tintori, in Monza, Italy. Logistic regression models identified predictors of AEs, including clinical and dosimetric variables. PSA kinetics were assessed using linear mixed-effects models. Statistical analyses were performed with Stata v13.0, with $p < 0.05$ considered significant. **Results:** A total of 33 patients with prior TURP/enucleation were included. Median age at SBRT was 69 years (range=59-83 years). ISUP grade distribution was as follows: grade 1 in 6 patients, grade 2 in 11, grade 3 in 9, and grade ≥ 4 in 7. Median follow-up was 19 months (range=6-53 months). The maximum GU AE grade was G1 in 13 patients, G2 in 9, and G3 in 1. At univariate analysis, a shorter interval between TURP and SBRT was associated with higher risk of AEs: patients experiencing $\geq G2$ AEs had a median interval of 33 months compared to 91 months in those with $\leq G1$ AEs ($p=0.014$). Bladder dosimetric parameters were also predictive: median bladder V18 Gy was 25.1% in patients with G1+ AEs *versus* 21.3% in G0 ($p=0.009$), while median bladder D50% was 7.7 Gy vs. 4.2 Gy ($p=0.004$). At multivariate analysis, both a shorter time from TURP ($p=0.041$) and higher bladder D50% ($p=0.046$) independently predicted G1+ AEs. Urinary incontinence occurred in 30.3% (7 G1, 3 G2). Acute and late AEs profiles are summarized in Table I. No biochemical or local recurrences were observed. Median PSA decreased from 9.4 ng/ml (range=1.1-66.0 ng/ml) to 0.2 ng/ml (range=0-3.9 ng/ml) at nadir, reached at a median of 13 months. PSA declined at an average of 11% per month ($p < 0.001$). ADT use was associated with a faster decline, whereas higher ISUP grade and NCCN risk group were associated with slower PSA kinetics. **Conclusion:** SBRT after TURP achieved excellent short-term oncologic control in

patients with localized PCa. GU AEs were mainly influenced by the interval between TURP and SBRT, as well as bladder dosimetric parameters, highlighting the need for careful patient selection and optimized treatment planning.

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THREE-FRACTION ULTRA-HYPOFRACTIONATED PROSTATE STEREOTACTIC BODY RADIATION THERAPY (SBRT) WITH 4D TRANSPERINEAL ULTRASOUND INTRA-FRACTION MOTION MONITORING: CLINICAL RESULTS AND SAFETY

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Background/Aim: This prospective study evaluated adverse events (AEs), quality of life (QoL) and biochemical control in patients affected by localized prostate cancer (PCa) and treated with Three-Fraction SBRT. Intra-fraction motion was monitored using 4D Transperineal US. **Materials and Methods:** All patients, regardless of the risk class, received linac-based SBRT to a total dose of 30 Gy in 3 fractions (fx) (EQD2_{1.5} 99 Gy, EQD2₃ 78 Gy), delivered on alternate days. The CTV was isotropically expanded by 3 mm to generate PTV. Real-time 4D US tracking (Clarity®Autoscan) enabled beam gating. IPSS,

Table I. AEs profile among population.

Toxicities	G0	G1	G2	G3	G4-5
Acute GU	31 (43%)	16 (22.2%)	24 (33.3%)	1 (1.4%)	0
Acute GI	56 (77.8%)	10 (13.9%)	6 (8.3%)	0	0
Late GU	48 (66.7%)	14 (19.4%)	9 (12.5%)	1 (1.4%)	0
Late GI	67 (93%)	2 (2.8%)	3 (4.2%)	0	0

AEs: Adverse events; GU: genitourinary; GI: gastrointestinal.

EPIC-CP and IIEF5 were collected at baseline and during follow-up (FUP). Longitudinal changes were analyzed using linear mixed-effects models and categorized as acute or late subgroups. Minimal important difference (MID) was defined as a change $\geq 0.5 + SD$ from baseline and used to assess clinical relevance. AEs (CTCAEv5.0) were recorded and predictors were identified through a logistic regression model. PSA levels were recorded at baseline and during FUP. Biochemical relapse-free survival (BRFS) was evaluated using Cox regression. A p -value < 0.05 was considered statistically significant. *Results:* Seventy-two patients were enrolled with a median age of 78 years; among them 58.3% had ISUP GG1-2 disease, 25% ISUP GG3, 16.7% ISUP GG4-5 and 41.7% received ADT. Median FUP was 16 months (6-27). The AEs profile is summarized in Table I. At multivariate analysis, acute GU AEs were significantly associated with higher IPSS at baseline, with a median score of 8.5 in patients with $\geq G2$ acute GU AEs *versus* 5 in those with $< G2$ AEs ($p=0.019$). Median PSA dropped from 7.9 ng/ml (range=1.5-65 ng/ml) at baseline to 0.44 ng/ml (range=0.01-26 ng/ml) at last FUP. BRFS was 98.2% at 12months and 96.1% at 24 months; 2 patients developed BCR. Regarding patient-reported outcomes, GU AEs (IPSS, obstructive symptoms and incontinence) worsened at late FUP, hormone-related symptoms showed early deterioration, and sexual function declined early and then stabilized. QoL showed a persistent decline, whereas bowel function remained stable. Although all deviations from baseline were statistically significant, none reached clinical relevance according to MID. *Conclusion:* Three-fraction SBRT with 4D transperineal US guidance appears to be a safe and effective treatment for localized PCa, achieving excellent

biochemical control with a favorable AEs profile. Despite statistically significant changes in QoL measures, no MID deterioration was observed. Longer FUP and additional data are needed to confirm these findings.

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SEE-AND-TREAT OFFICE-BASED DIODE LASER ABLATION WITHOUT ANESTHESIA IN RECURRENT LOW-GRADE NON-MUSCLE-INVASIVE BLADDER CANCER

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Background/Aim: Office-based management of recurrent Ta low-grade non-muscle-invasive bladder cancer (NMIBC) represents an evolving paradigm aiming to minimise procedural burden while preserving oncological integrity. We evaluated the feasibility, safety, tolerability, and short-term oncological outcomes of outpatient transurethral laser ablation (TULA) using the LEONARDO® Mini Dual diode laser (980/1740 nm) in a prospective single-centre cohort. *Materials and Methods:* Sixty consecutive patients [mean age=72 years (range=65-82 years)] with suspected recurrent low-grade NMIBC underwent TULA during diagnostic flexible cystoscopy without pre-scheduling or intravesical anaesthesia. A cold-cup biopsy preceded each ablation for mandatory histological confirmation. Pain was quantified

via visual analogue scale (VAS). Patient preference versus conventional transurethral resection of bladder tumour (TURBT) was systematically recorded. Complications were graded according to the Clavien–Dindo classification. *Results:* Pre-ablation biopsy confirmed pTa low-grade NMIBC in 66.7% of cases, with carcinoma *in situ* identified in 4 patients (6.7%), underscoring the oncological relevance of systematic tissue sampling. Mean energy delivered was 336 J (range 15-1414 J). No procedure required hospitalisation; all patients were discharged within two hours. Grade I haematuria occurred in 4 patients (6.7%); no Grade II or higher complications were recorded. Notably, despite 13.3% of patients receiving anticoagulant therapy and 30.0% antiplatelet therapy, none of the variables analysed demonstrated a clinically meaningful association with bleeding risk on Fisher's exact test, further supporting the favourable haemostatic profile of dual-wavelength diode laser energy; these findings remain exploratory given the limited event number. Median VAS pain score was 2 (IQR=1-2). Overall, 96.7% of patients preferred outpatient TULA over TURBT under general or spinal anaesthesia, primarily attributing this preference to immediate same-session treatment availability. At 3-month follow-up cystoscopy, recurrence rate was 5.0% (n=3), all managed with repeat TULA followed by intravesical mitomycin C induction. *Conclusion:* Outpatient diode laser ablation constitutes a safe and well-tolerated alternative to TURBT for recurrent low-grade NMIBC, achievable without dedicated laser training or intravesical anaesthesia. The incidental CIS detection in 6.7% of cases reinforces the indispensable role of pre-ablation biopsy. This strategy optimises institutional resource allocation and reduces operating room occupancy, supporting its broader integration into contemporary bladder cancer surveillance pathways.

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BLADDER BIOPSY PRIOR TO OUTPATIENT LASER ABLATION OF RECURRENT NMIBC IDENTIFIES OCCULT HIGH-RISK DISEASE AND CHANGES CLINICAL MANAGEMENT

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Background/Aim: Non-muscle invasive bladder cancer (NMIBC) represents approximately 75% of new bladder cancer (BC) diagnoses and is typically treated with transurethral resection of bladder tumor (TURB-T), followed by endovesical instillations. The cornerstone of follow-up consists of repeated cystoscopies to enable early detection and treatment of recurrences. Frequent recurrences of low-grade (LG) tumors represent a common global challenge due to the need for repeated TURB-T procedures and multiple endovesical instillations, which increase healthcare-related costs. Several strategies have been proposed to reduce the surgical burden on patients and associated costs; among these, transurethral laser ablation (TULA) of small LG NMIBC recurrences is a promising option. This procedure allows immediate and definitive treatment without the need for a new surgical intervention. *Material and Methods:* At our Centre (Division Of Urology, Ao Santa Croce e Carle, Cuneo, Italy), we perform a bladder biopsy prior to TULA to confirm the diagnosis and assess for any histological changes in the tumor; although this is not indicated in international guidelines or previous publications. We use flexible biopsy forceps to obtain a sample of the lesion, followed by ablation of the tumour with a diode laser; performed in a 'see-and-treat' approach during follow-up cystoscopy in the same outpatient setting. *Results:* To date, we have performed this procedure in 47 patients without the need for any form of anesthesia, achieving excellent results in terms of tolerability and efficacy. In 5 cases (10%), the pathologist reported the presence of carcinoma *in situ* (CIS) in the specimen. All patients therefore started endovesical instillations with Bacillus Calmette–Guérin (BCG), with no evidence of recurrence at 6 months. *Conclusion:* Early identification of progression from LG NMIBC to high-grade urothelial carcinoma results in a significant change in patient

management. Specifically, this enables the prompt initiation of intravesical BCG therapy and a more intensive cystoscopic surveillance schedule, as patients are reclassified as high-risk according to EAU risk stratification criteria, thereby optimizing treatment outcomes. In our experience, performing a bladder biopsy in patients undergoing TULA is quick and feasible in an outpatient setting, and facilitates early detection of high-grade tumors in patients with a history of LG NMIBC. This approach may allow timely initiation of appropriate treatment and contribute to a more efficient use of healthcare resources.

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SBRT WITH SIMULTANEOUS FOCAL BOOST FOR LOCALIZED PROSTATE CANCER: EARLY OUTCOMES AND IMPACT OF RECTAL SPACING FROM A PROSPECTIVE STUDY

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Background/Aim: Dose escalation to the dominant intraprostatic lesion (DIL) represents a promising strategy to enhance the therapeutic ratio of Stereotactic Body Radiotherapy (SBRT) in prostate cancer. This study aimed to evaluate the early oncological outcomes and the impact of rectal spacer placement in patients undergoing prostate SBRT with a Simultaneous Integrated Boost (SIB) to the DIL (SBRT-SIB_{DIL}). *Materials and Methods:* This prospective

observational study enrolled patients with histologically confirmed localized prostate adenocarcinoma and a gland volume of ≤ 90 ml. The DIL was identified utilizing multiparametric magnetic resonance imaging (mpMRI), specifically incorporating T2-weighted, diffusion, and perfusion sequences. The prescribed SBRT dose was 36.25 Gy delivered in 5 fractions to the Planning Target Volume (PTV), with a SIB escalating the dose to the DIL up to 45 Gy. The analysis evaluated genitourinary (GU) and gastrointestinal (GI) side effects, planning dosimetric data, and biochemical responses. *Results:* Between June 2022 and August 2024, 41 men treated with prostate SBRT-SIB_{DIL} at our Institution were prospectively analyzed. The median patient age was 76 years (IQR=73-78). According to the D'Amico/NCCN risk classification, 7 patients (17.1%) were low-risk, 29 (70.7%) were intermediate-risk, and 5 (12.2%) were high-risk. The DIL was located in the peripheral zone in 32 cases (72.7%), and 3 patients (7.3%) presented with two distinct DILs. All patients (100%) were treated using volumetric modulated arc radiotherapy (VMAT) with fiducial marker tracking (Figure 1). The insertion of a rectal spacer was optional and performed in 24 patients (58.5%). Androgen deprivation therapy (ADT) was administered to 14 patients (34.1%). At a median estimated follow-up of 21.0 months (95% CI=18.5-28.3), no Grade 3 or higher side effects were observed. The cumulative rates for Grade 2 GU and GI adverse events were 24.4% and 14.6%, respectively (Table I). A summary of DIL dosimetric parameters and Organs at Risk constraints is outlined in Table II. The utilization of a rectal spacer significantly improved rectal dosimetric parameters compared to cases without spacer: V38Gy: 0.0 cc vs. 0.2 cc ($p<0.001$); V36Gy: 0.0 ml vs. 1.7 ml ($p<0.001$); V24Gy: 5.9% vs. 15.3% ($p<0.001$). Despite these dosimetric improvements, the difference in Grade 2 rectal side effects between the spacer and no-spacer cohorts was not statistically significant (23.5% vs. 8.3%, $p=0.175$). A biochemical response was achieved in all patients. Furthermore, patient-reported Quality of Life (QoL) metrics at the last follow-up showed no significant deviation from their pre-SBRT baseline. *Conclusion:* Prostate SBRT delivering a focal boost to the DIL up to 45 Gy is associated



Figure 1. Prostate SBRT plan with Simultaneous Integrated Boost (SIB) to the DIL. The prescribed dose is 36.25 Gy in 5 fractions to the whole gland (PTVprostate, continuous line) with a 45 Gy focal boost to the dominant lesion (PTVboost, dash-dot line, Dmax 49.3 Gy). Hot spots to the urethra (dotted line) are avoided (D_{max} 41.9 Gy).

Table I. Cumulative CTCAE genitourinary (GU) and gastrointestinal (GI) toxicity.

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

CTCAE: Common Terminology Criteria for Adverse Events.

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

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

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

with favorable early safety and efficacy outcomes. The use of rectal spacer significantly enhances dosimetric parameters, with a corresponding non-significant reduction in rectal side effects.

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THREE-YEAR EXPERIENCE WITH VI-RADS MULTI-PARAMETRIC MAGNETIC RESONANCE IMAGING (MPMRI) IN DIFFERENTIATING MUSCLE-INVASIVE BLADDER CANCER (MIBC) FROM NON-MUSCLE-INVASIVE BLADDER CANCER (NMIBC): A SINGLE-CENTRE STUDY

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Background/Aim: Vesical imaging-reporting and data system (VI-RADS) is a standardized scoring system developed to assess the likelihood of muscle-invasive bladder cancer (MIBC) using multiparametric magnetic resonance imaging (mpMRI). Our aim was to describe our three-year experience in using mpMRI to differentiate MIBC from non-muscle invasive bladder cancer (NMIBC). All radiological reports were generated using the VI-RADS score. *Materials and Methods:* Patients with a ≥ 15 -mm finding suspicious for bladder cancer on ultrasound, computed tomography, or flexible cystoscopy underwent mpMRI before transurethral resection of bladder tumor (TURBT). We used a five-point VI-RADS score, derived using T2-weighted MRI, diffusion-weighted imaging, and dynamic contrast enhancement. MRI was 1.5T. In these three years images were analyzed by MRI dedicated radiologists and all TURBTs were performed by expert urologists adhering to the European guidelines' recommendations in order to strive for high-quality resections. Accuracy was determined using histopathology as the reference standard. *Results:* A

total of 90 patients were analyzed, both primary and recurrent. Overall accuracy of the complete mpMRI protocol was 87% in differentiating NMIBC from MIBC. Better accuracy was achieved for ≥ 25 mm (92%) and lateral wall sided (91%) lesions, while a lower one was recorded for dome tumours (86%). Hematuria, cytology, class of risks, focality and patients' features did not impact on results. No differences were recorded for histological variants. *Conclusion:* Mp-MRI is considered effective in determining muscle invasion in cases of urinary bladder cancer, a standpoint confirmed by our encouraging data. Therefore VI-RADS scoring system represents an easy-to-learn tool and a good way to standardize reports. Greater experience and improved instrumentation, such as a 3T-MRI, can further enhance our preliminary results.

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LINEAR ACCELERATOR (LINAC)-BASED STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR LOCALIZED PROSTATE CANCER: ONCOLOGICAL OUTCOMES AND TOXICITY IN A 201-PATIENT SINGLE-INSTITUTION EXPERIENCE

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Background/Aim: This retrospective single-institution study aimed to evaluate safety and oncological outcomes of pts with localized prostate cancer (PCa) treated with linac-based SBRT. We assessed the correlation between genitourinary toxicity (GU tox) and baseline parameters, namely International Prostate Symptom Score (IPSS) and prostate volume (PV) and investigated factors influencing

Table I. Distribution of acute and late GU and GI toxicity in patients treated with SBRT.

	Toxicities	G0-1	G2	G3	G4-5
36.25 Gy/5fx	Acute GU	65 (67.0%)	29 (29.9%)	3 (3.1%)	0
	Acute GI	87 (89.6%)	10 (10.3%)	0	0
	Late GU	86 (88.7%)	8 (8.2%)	3 (3.1%)	0
	Late GI	96 (98.9%)	1 (1%)	0	0
42.7 Gy/7fx	Acute GU	70 (67.3%)	30 (28.8%)	4 (3.8%)	0
	Acute GI	93 (89.4%)	11 (10.6%)	0	0
	Late GU	91 (87.5%)	9 (8.7%)	4 (3.8%)	0
	Late GI	104 (100%)	0	0	0

Biochemical Relapse Free Survival (BRFS). **Materials and Methods:** We retrospectively analyzed patients with PCa cT1b–cT3bN0M0 treated with SBRT to prostate and seminal vesicles (SV). SV coverage and hormonal therapy (HT) were tailored according to NCCN Risk Class. RT regimens were 36.25 Gy in 5 fractions (fx) or 42.7 Gy in 7 fx, delivered every other day. Pts were instructed to maintain a full bladder and empty rectum, performing an enema before simulation and each fx, and following a standardized diet. After SBRT, pts underwent trimestral PSA $\pm$ testosterone monitoring. Baseline PV and IPSS were collected. Acute toxicity was graded per CTCAE v5, with G2+ events considered clinically relevant. Multivariable logistic regression (MVA) was performed adjusting for fractionation, HT, treatment duration, and comorbidities. ROC analyses were used for risk stratification. BRFS was evaluated using Cox regression. **Results:** A total of 201 pts were treated: 97 received 36.25 Gy/5 fx (BED_{1.5} 211.46, EQD2 90.63), mainly low/favourable-intermediate risk; 104 received 42.7 Gy/7 fx (BED_{1.5} 216.35, EQD2 92.72), mainly unfavourable-intermediate/high risk. Median follow-up was 27.4 months (8.4–64.3). Median PSA was 8.42 ng/ml (6.2 in 5-fx, 3.9 in 7-fx). Median IPSS was 9 (0–28): 8 in 5-fx and 10 in 7-fx. Median PV was 62 ml (5-fx) vs. 52 cc (7-fx). At multivariable analyses (MVA), larger prostate volume (PV) was associated with higher risk of acute GU tox (OR=1.03, $p<0.001$), independent of fractionation, hormonal therapy (HT) and comorbidities. Acute GU tox was higher in pts with PV ≥ 60 ml vs. <60 cc (42.7% vs. 25.0%, $p=0.006$; AUC=0.67). A weaker association was seen for late GU tox (OR=1.02, $p=0.044$), with higher

median PV in pts with $\geq G2$ GU tox vs without (69 vs. 57 cc, $p=0.046$; AUC0.63). BRFS was 98.3% at 12 months, 95.7% at 24 months, and 91.4% at 36 months. Cox regression showed a significant association between risk class and BRFS (HR=2.11, $p=0.003$). Details about toxicity are provided in Table I. **Conclusion:** Linac-based SBRT provides excellent early disease control and acceptable toxicity in localized PCa. GU tox seems to be influenced by prostate volume, while risk class remains a key determinant of biochemical outcome.

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A RETROSPECTIVE STUDY ON THE CORRELATION BETWEEN THE PIRADS SCORE AND THE HISTOLOGICAL FINDINGS IN THE MPMRI (MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING) OF THE PROSTATE CANCER

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Background/Aim: Multiparametric magnetic resonance imaging (mpMRI) is the method of choice to evaluate the prostate, allowing to delineate the structure and morphology of its different parts and examine its behavior following the administration of contrast medium. mpMRI can detect suspicious areas that necessitate targeted biopsy, in order to

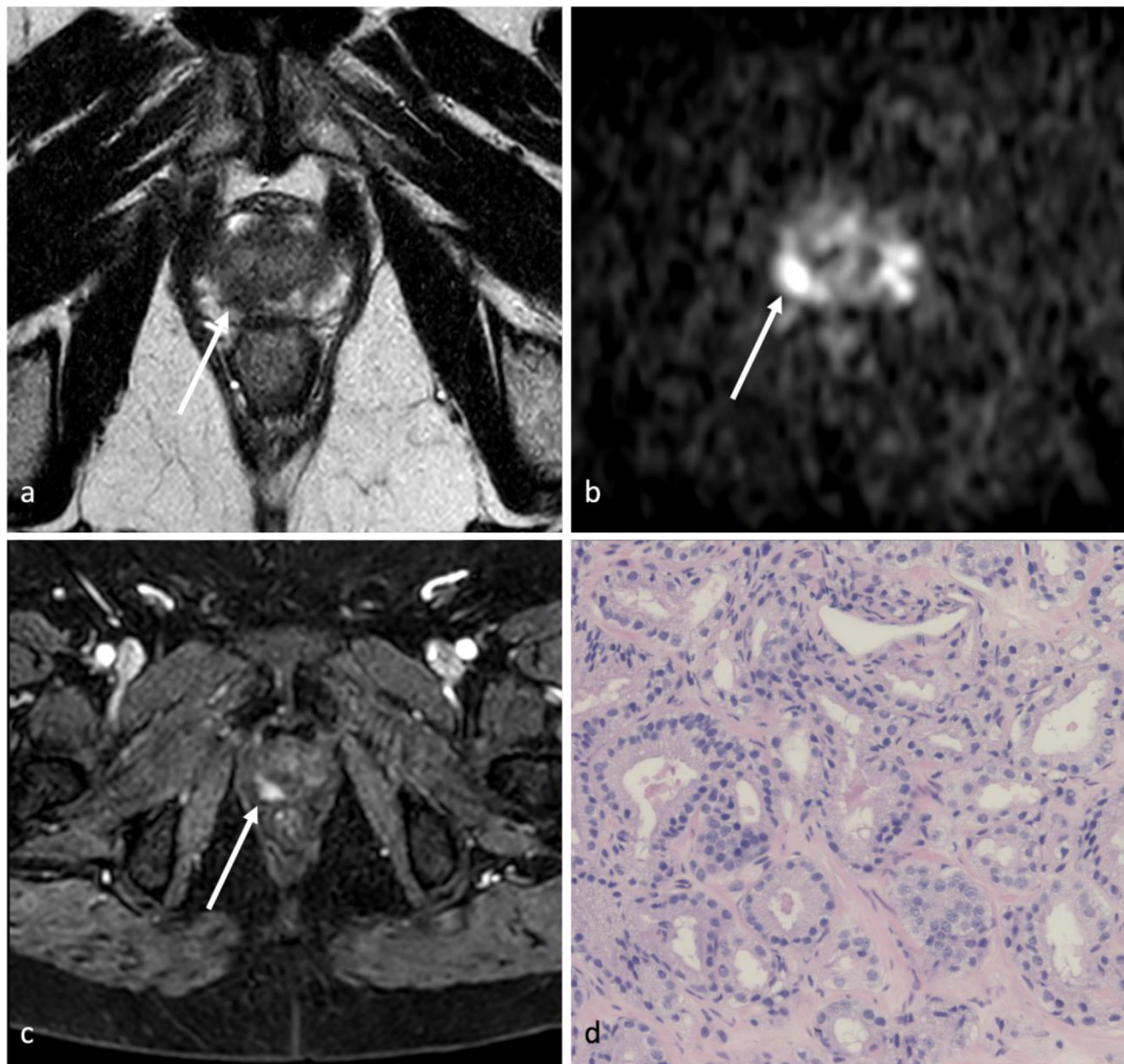


Figure 1. Lesion in the posterolateral portion of the prostate that was biopsied and histologically confirmed as prostate cancer.

increase accuracy and reduce unnecessary procedures on patients. An essential aspect in prostate MRI is structured reporting through the use of PI-RADS v2 criteria (1), enabling the definition of a score (1-5) that estimates the likelihood of clinically significant prostate cancer, stratifying risk and thereby dictating subsequent management. PI-RADS criteria

also allow studies from different institutions to be compared, facilitating prostate cancer research. However, inaccuracies can arise from the incorrect interpretation of images, which may reduce concordance with histological results. The aim of our work is to examine the agreement between radiological and pathological findings in patients with

suspected prostate cancer. *Patients and Methods:* We performed a retrospective evaluation of patients who underwent prostate mpMRI at our institution between May 2025 and March 2026, excluding negative cases (PI-RADS 2). Our technical protocol for mpMRI includes morphological T1w and T2w sequences (in particular the T2w images are obtained following the axial, coronal and sagittal planes), diffusion-weighted-imaging (DWI) with 4 different b values (50, 800, 1,500, 2,000) and perfusion dynamic sequences, both with narrow and wide field-of-view. The PI-RADS score and characteristics of every lesion were noted. We then compared radiological findings in the various suspicious areas with the actual histological results reported by our pathological anatomy unit on the same patients. *Results:* Our analysis retrieved 201 patients subjected to mpMRI, with a total of 216 suspicious lesions, among which 102 (47%) were classified as a PIRADS 3, 85 (39%) as PIRADS 4 and only 25 (13%) as PIRADS 5. The vast majority of lesions were located in the peripheral zone (80% vs 20% in the transition zone). Upon comparison with pathological reports, the reliability of PIRADS score by mpMRI at our center was found to be elevated (Figure 1), with a limited number of cases that did not match the histological data. Such disagreements were mostly stemming from areas of acute or chronic prostatitis, which is also associated with diffusion restriction and focal enhancement. *Conclusion:* Although the agreement between radiological reports and pathological results at our institution appears to be satisfactory, it is undeniable that some inaccuracies or misinterpretations occurred due to several pitfalls related to the study of the prostate with MRI. Such pitfalls may arise from different factors: (i) misinterpretation of the appearance of normal anatomic structures within and around the prostate (neurovascular bundles, central zone); (ii) benign pathology mimicking cancer such as prostatitis or ectopic adenoma; (iii) technical artifacts (2). One limitation of our study is the inability to access the histological results of patients who did not undergo biopsy at our hospital, significantly limiting the effective size of our sample. However, our study is expected to continue, adding more data in an attempt to further investigate the accuracy of prostate cancer diagnosis with

mpMRI and raising awareness around the most common mistakes that can occur while interpreting images to ultimately obtain bulletproof reports in the future.

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IMPACT OF HYDROGEL SPACER QUALITATIVE DISTRIBUTION ON RECTAL DOSIMETRY AND ADVERSE EVENTS IN PROSTATE STEREOTACTIC RADIOTHERAPY

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Background/Aim: To evaluate how the qualitative distribution of hydrogel rectal spacers (HRS) impacts rectal

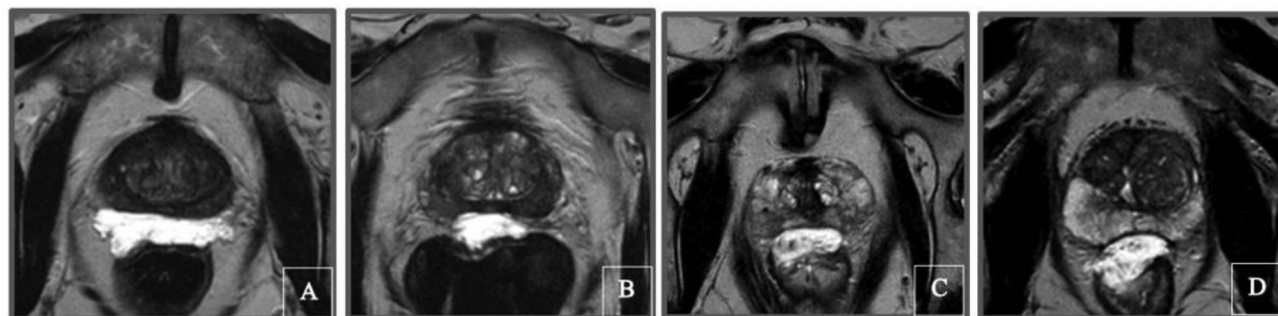


Figure 1. Representative axial T2-weighted MR images of a hydrogel spacer implant with RWI score (A) 0, (B) 1, (C) 2, (D) 3.

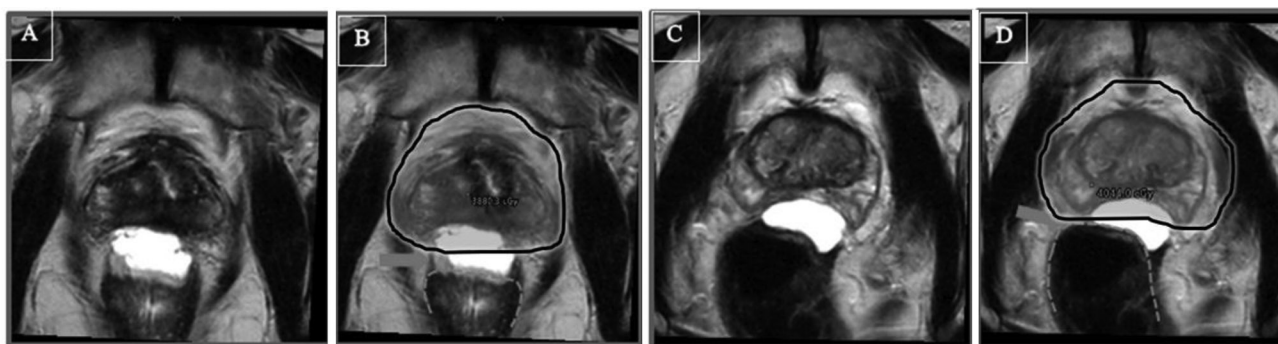


Figure 2. Midgland axial T2-weighted magnetic resonance images of a patient with SQS 2, SYM score 1 and the corresponding 38 Gy dose distribution (A-B). High-quality distribution scores correlate with improvement in rectal dose sparing. A Patient with SQS 1, SYM score 3 and the corresponding 38 Gy dose distribution; asymmetrical lateral placement of rectal spacer and lower SQS do not permit optimal rectal sparing (arrow) (C-D).

dosimetry and acute toxicity in patients undergoing stereotactic body radiation therapy (SBRT) for localized prostate cancer (PCa). **Materials and Methods:** This analysis was part of a prospective observational study that included localized PCa patients who received transperineal HRS insertion prior to SBRT at our Institution. The qualitative distribution of the hydrogel was evaluated on post-implant T2-weighted magnetic resonance imaging (MRI) using three distinct metrics: Spacer Quality Score (SQS), Symmetry Score (SYM), and Rectal Wall Infiltration Score (RWI) (Figure 1). These scores were then analyzed for correlations with rectal dosimetric parameters and acute rectal adverse events (defined as presenting within 6 months post-SBRT). **Results:** Between 2022 and 2024, 76 patients with localized PCa underwent HRS implantation followed by SBRT. The prescribed planning target volume

(PTV) dose was 36.25 Gy in 5 fractions for 17 patients (22.4%), while the remaining 59 patients (77.6%) received a concomitant prostate boost of ≥ 40 Gy. The median anteroposterior separation achieved between the midgland of the prostate and the rectum was 10 mm (range=4-20 mm). SQS distributions were scored as 0 ("inadequate") in 3 patients (3.9%), 1 ("good") in 48 (63.2%), and 2 ("excellent") in 25 (32.9%). A significant correlation was found between the SQS and rectal Dmax ($p=0.003$), maximum dose to 1 ml ($p=0.003$), V36 Gy ($p=0.018$), V30 Gy ($p=0.002$), and V18Gy ($p=0.002$) (Figure 2). SYM scores ranged from 1 ("best") to 5 ("worst"), with 52 (68.4%), 17 (22.4%), 2 (2.6%), 3 (4.0%), and 2 (2.6%) patients in categories 1 through 5, respectively. The SYM score demonstrated a significant correlation with rectal V40 ($p=0.009$). RWI was graded as 0 (no abnormality) in

56 cases (73.7%), 1 (rectal wall edema) in 2 (2.6%), and 2 (superficial infiltration) in 18 (23.7%), with no deep infiltrations (grade 3) observed. Acute rectal side effects were reported in 18 patients (23.7%), comprising 3 Grade 1 (16.7%) and 15 Grade 2 (83.3%) events according to CTCAE. The incidence of these acute toxicities was significantly associated with the SQS score ($p=0.004$), whereas no correlation was found with RWI categories ($p=0.672$). *Conclusion:* The study demonstrated that a high-quality HRS distribution is significantly associated with improved rectal dosimetry and a decreased incidence of acute adverse events in localized PCa patients treated with SBRT. Although rectal wall infiltration was observed in nearly one-quarter of the cohort, it did not correlate with an increased risk of acute rectal side-effects.

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HYPERTHERMIC INTRAVESICAL CHEMOTHERAPY (HIVEC™) FOR BCG-UNRESPONSIVE AND BCG-INTOLERANT NON-MUSCLE INVASIVE BLADDER CANCER: EARLY ONCOLOGICAL AND SAFETY OUTCOMES

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Background/Aim: The management of high-risk non-muscle-invasive bladder cancer (HR-NMIBC) presents a challenge in preserving the bladder whilst preventing progression to muscle-invasive or metastatic disease. For patients who have failed Bacillus Calmette-Guérin (BCG) therapy, radical cystectomy (RC) remains the standard of care. However, this is associated with high morbidity,

meaning that some patients are not eligible for surgery due to their comorbidities. Little is known about the optimal treatment for patients with high-risk tumors who have been unable to complete BCG instillations due to intolerance; furthermore, the management of high-risk BCG-unresponsive patients who are ineligible for radical cystectomy due to comorbidities or who refuse surgery remains undoubtedly complex. In all these cases, there may be a role for technologies that enhance the efficacy of alternative treatments to BCG, such as Hyperthermic IntraVesical Chemotherapy (HIVEC™). The aim of our study was to evaluate the safety and efficacy of HIVEC protocol for BCG-unresponsive and BCG intolerant non-muscle invasive bladder cancer in a cohort of patients enrolled at our center. *Materials and Methods:* At our Center, from July 2023 to January 2026, the HIVEC protocol with the COMBAT system was offered to patients with HR-NMIBC who were not eligible for intravesical BCG therapy or who could not tolerate BCG due to side effects, as well as to patients who were ineligible for radical cystectomy due to comorbidities or who refused surgical intervention for high-risk disease unresponsive to BCG. *Results:* A total of 17 patients were enrolled in the study, of whom 9 were BCG-intolerant and 8 were BCG-unresponsive. The treatment was generally well tolerated; only 1 patient withdrew from the protocol due to irritative symptoms (6%). Among the BCG-intolerant patients, 6 were found to be recurrence-free at the 12-month follow-up after the maintenance cycle (66%), 2 were negative at the 6-month follow-up, and only 1 experienced disease progression and therefore underwent RC. Eight BCG-unresponsive patients were enrolled in the protocol. Of these, 3 were disease-free at 12 months, 2 at 9 months (62.5% in total), whilst 3 experienced high-risk disease recurrence. *Conclusion:* Based on these data, HIVEC treatment yielded satisfactory results in patients with HR-NMIBC (81% disease-free at 6 months, 56% at 12 months), offering a valid alternative to BCG in patients who are intolerant to it and a treatment option for BCG-unresponsive patients who are ineligible for cystectomy or who refuse the procedure, following thorough counselling on the risk of disease progression.

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