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Radio-Guided Lymph Node Resection With Prostate-Specific Membrane Antigen in Prostate Cancer: Initial Experience

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Radical prostatectomy with extended lymphadenectomy is a cornerstone in the treatment of high risk and locally advanced prostate cancer (PCa).[1] Current international guidelines recommend staging these patients using prostate-specific membrane antigen (PSMA)-positron emission tomography. However, access to this technique is limited in public institutions, leading to the continued use of conventional imaging for staging. Radio-guided surgery with technetium-99m PSMA (99mTc-PSMA) is useful for lymph node salvage in biochemical recurrence and for guiding lymphadenectomy in patients with de novo N1 and M1a disease.[2] This study aimed to evaluate the correlation between positive lymph node lesions detected using single photon emission computed tomography (SPECT)-PSMA during initial staging and histopathological analysis of intraoperative 99mTc-PSMA radio-guided lymphadenectomy.

Patient selection included patients with PCa limited to the prostate and locally advanced diseases, including lymph nodes close to the pelvis. Patients with distant lymph node metastases were excluded. Staging of our patients was performed using SPECT-PSMA or conventional imaging. Twenty to 25 mCi of 99mTc-PSMA was administered intravenously 16–18 hours before the procedure and correlated with preoperative SPECT-PSMA 2 hours after administration. All patients underwent open radical prostatectomy and bilateral pelvic extended radio-guided lymphadenectomy with 99mTc-PSMA, with maximal cytoreductive intent in patients with cN1 disease and as part of the standard treatment in patients with cN0 disease. A gamma probe (NuclearLab R) was used for lymph node detection. The baseline uptake intensity count of the subcutaneous adipose tissue was set as a reference, and a value greater than or equal to its double was considered positive. Lymph node groups were sent separately for pathological studies, and their uptake was recorded using a gamma probe.

The initial experiment included 4 patients. One patient had an unfavorable intermediate risk, 1 had a high risk, 1 presented with pelvic lymphadenopathy in the adenomegalic range (locally advanced), and 1 was considered metastatic 1a due to adenopathy in the adenomegalic range at the aortic bifurcation, as shown in Table 1. The mean age of the patients at diagnosis was 67 years.

Baseline uptake counts were 45 for patients 1 and 2 and 40 for patients 3 and 4. Forty lymph nodes were resected, of which 7 were positive for metastatic infiltration. Among these, 5 showed hyperuptake in the gamma probe; the 2 samples that were not positive for marking belonged to patients 1 and 4 and were 3 and 4 mm, respectively. The sensitivity, specificity, positive predictive value, and negative predictive value were 71.42%, 100%, 100%, and 77.78%, respectively. The lymphadenectomy findings of the 4 patients are detailed in Table 1. In patients 2 and 3, no hyperuptake was observed in the lymph nodes; therefore, the ranges of both gamma probe counts and resected lymph node sizes were detailed.

Patient 1 presented with the largest lymph node (40 mm) on the posterior aspect of the aortic bifurcation (outside the extended lymphadenectomy template), which was successfully resected using this method, aiding its localization, as shown in Fig. 1.

The average diameter of lymph nodes was 10.87 mm (range, 3–40 mm). Upstaging was detected in 2 patients (1 and 4), and downstaging was detected in 1 patient (3) in the primary tumor histopathology. The average surgical time was 150 minutes (range, 120–185 minutes), with an average of 22 minutes (range, 18–25 minutes) for gamma probe use. Two Clavien-Dindo II lesions were observed in the immediate postoperative period, which resolved without complications.

Approximately 40% of patients with PCa treated with curative intent experience prostate-specific antigen persistence and/or biochemical recurrence.[3] Pelvic lymph nodes are the most frequent site of biochemical recurrence and radio-guided resection, which identifies hyperactive microadenopathies,[4] could potentially reduce this risk. According to the OSPREY study, PSMA-positron emission tomography has a mean sensitivity of 40.3% for positive lymph nodes, with an overall sensitivity of 97.9%, positive predictive value of 86.7%, and negative predictive value of 83.2%.[5] Mix et al. used this radiopharmaceutical in extended lymphadenectomies as a primary treatment, analyzing 3 variables in the resected tissue (weight, gamma probe uptake, and imaging uptake), and compared them between unaffected and metastatic lymph nodes. The sensitivity, specificity, positive predictive value, and negative predictive value were 76%, 94%, 89%, and 86%, respectively. An increase in all 3 analyzed variables was observed in favor of samples with tumor presence.[6] Because of the variable lymphatic drainage of the prostate, 40% of lymphadenectomies present positive lymph nodes in atypical areas outside the predetermined template.[7] Radio-guided surgery enables the detection and resection of these otherwise undetected lymph nodes; however, lesions ≤4 mm usually do not take up PSMA and may therefore escape detection.[8,9] Preliminary results of a prospective

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Table 1

Results of lymphadenectomy.

Patients	Gamma probe count	Lymph node size	Pathology report	Final result
1	1400	40	Metastatic infiltration with capsular invasion	True positive
	80	3	Metastatic infiltration without capsular invasion	False negative
	600	20	Metastatic infiltration without capsular invasion	True positive
	24	5	Reactive adenitis	True negative
	50	5	Reactive adenitis	True negative
	25	6	Reactive adenitis	True negative
	600	17	Metastatic infiltration with capsular invasion	True positive
	210	17	Metastatic infiltration without capsular invasion	True positive
	175	15	Metastatic infiltration without capsular invasion	True positive
	50	5	Reactive adenitis	True negative
2	25–45	6–8	Reactive adenitis	True negative
3	35–50	5–9	Reactive adenitis	True negative
4	30	9	Reactive adenitis	True negative
	40	4	Metastatic infiltration with capsular invasion	False negative

phase 2 study analyzing the ability of Tc-PSMA radio-guided surgery to detect metastatic lymph node involvement in robotic radical prostatectomy with lymphadenectomy have been published, and preliminary results have shown that it is a safe technique with minor complications and 63% sensitivity.[10]

Radio-guided surgery is feasible in an Argentine public hospital and is an easy-to-implement technique with low-severity complications. This study confirmed that the lesions correlated with preoperative images with 100% specificity.

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Statement of ethics

This study was approved by the ethics committee of Hospital Durand. All patients agreed to participate in the study and remain anonymous as agreed. All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

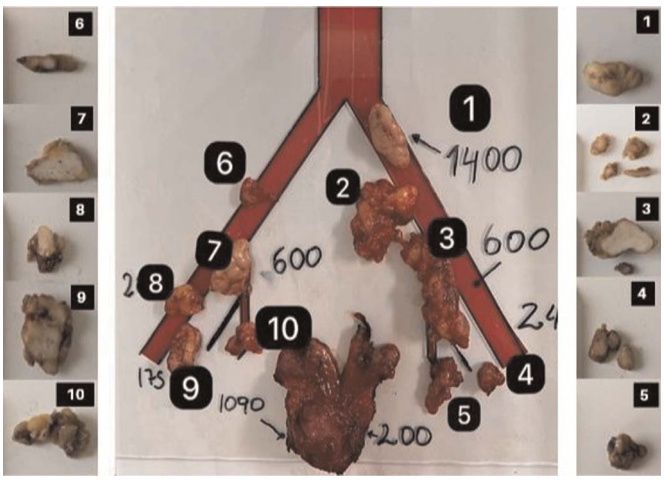

Figure 1. Patient 1 lymphadenectomy.

Conflict of interest statement

None.

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Author contributions

Cristian Carlos Gonzalez: Data curation, writing, methodology;
Rodrigo Medel, Walter De Bonis, Claudio Graziano: Supervision;
Luis Garcia Barrios, Marcos Gramajo Feijoo, Bernardo Sanchez Naranjo, Cesar Vargas Calle, Luis Palma Sabando: Data curation;
Silvina Racioppi: Methodology;
Diego Barreiro: Supervision, data analysis, final draft writing, methodology.

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