Detection of Pelvic Lymph Node Metastases in Patients With Clinically Localized Prostate Cancer: Comparison of [^{18}F]Fluorocholine Positron Emission Tomography-Computerized Tomography and Laparoscopic Radioisotope Guided Sentinel Lymph Node Dissection

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Purpose: Accurate detection of lymph node metastases in prostate cancer has important implications for prognosis and approach to treatment. We investigated whether preoperative [^{18}F]fluorocholine combined in-line positron emission tomography-computerized tomography and intraoperative laparoscopic radioisotope guided sentinel pelvic lymph node dissection can detect pelvic lymph node metastases in patients with clinically localized prostate cancer as reliably as extended pelvic lymph node dissection.

Materials and Methods: A total of 20 patients (mean age 63.9 ± 6.7 years, range 52 to 75) with clinically localized prostate cancer, prostate specific antigen greater than 10 ng/ml, and/or a Gleason score sum of 7 or greater and negative bone scan were enrolled in the study. [^{18}F]fluorocholine combined in-line positron emission tomography-computerized tomography was performed before surgery. Sentinel pelvic lymph node dissection preceded extended pelvic lymph node dissection including the area of the obturator fossa, external iliac artery/vein and internal iliac artery/vein up to the bifurcation of the common iliac artery. Laparoscopic radical prostatectomy was performed afterward.

Results: In 10 of the 20 patients (50%) lymph node metastases were detected, and were exclusively found outside the obturator fossa in 62%. These metastases would not have been identified with standard lymph node dissection of the obturator fossa only. [^{18}F]fluorocholine combined in-line positron emission tomography-computerized tomography was true positive in 1, false-positive in 2, false-negative in 9 and true negative in 8 patients. The largest lymph node metastasis not seen with [^{18}F]fluorocholine combined in-line positron emission tomography-computerized tomography was 8 mm. Laparoscopic sentinel guided lymph node dissection revealed lymph node metastases in 8 of 10 patients. In the other 2 patients sentinel lymph node dissection was not conclusive. In 1 patient normal nodal tissue was completely replaced by cancer and, therefore, there was no tracer uptake in the involved pelvic sidewall/node, and the other patient had no tracer activity at all in the involved pelvic sidewall. Extended pelvic lymph node dissection missed 1 lymph node metastasis (2 mm diameter near pudendal artery) which was detected by sentinel pelvic lymph node dissection only.

Conclusions: Extended pelvic lymph node dissection reveals a higher number of lymph node metastases as described for obturator fossa dissection only. [^{18}F]fluorocholine combined in-line positron emission tomography-computerized tomography is not useful in searching for occult lymph node metastases in clinically localized prostate cancer. Sentinel guided pelvic lymph node dissection allows the detection of even small lymph node metastases. The accuracy of sentinel pelvic lymph node dissection is comparable to that of extended pelvic lymph node dissection when the limitations of the method are taken into consideration.

Key Words: prostatic neoplasms, lymphatic metastasis, laparoscopy, prostatectomy, positron-emission tomography

The presence of pelvic LNM in men diagnosed with prostate cancer has an adverse prognosis. Accurate identification of clinically occult LNM may have important implications on the treatment strategy during the operation and on the initiation of adjuvant therapy regimens.[1] To date PLND is still the most accurate staging procedure. However, homogeneous surgical standards of PLND cannot be found in the current literature and no consensus exists as to the extent of dissection. Recent data

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For another article on a related topic see page 2274.

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suggest that E-PLND can detect a significant number of occult positive nodes outside the obturator fossa.[2–5] To decrease the morbidity of E-PLND while maintaining its sensitivity, the concept of radioisotope guided S-PLND was introduced and validated by Wawroschek et al for prostate cancer.[6] We recently demonstrated the feasibility of the technique with laparoscopy.[7]

Computerized tomography and magnetic resonance imaging are insensitive for the preoperative detection of small LNM. Recently FCH PET-CT has shown promising results as a noninvasive metabolic imaging modality for prostate cancer cells.[8] In this prospective study we investigated whether FCH PET-CT and intraoperative laparoscopic sentinel LND are able to detect occult pelvic LNM as reliably as extended PLND in patients with clinically localized prostate cancer.

MATERIALS AND METHODS

Patients

A selected group of 20 patients with biopsy proven and clinically localized prostate cancer suitable for laparoscopic radical prostatectomy were recruited for this prospective study performed from April 2004 to November 2005. Further inclusion criteria were a PSA of 10 ng/ml or greater or a biopsy Gleason score sum of 7 or greater. A positive bone scan was an exclusion criterion. All 20 men gave informed written consent and completed the study. Patient characteristics are presented in table 1.

Radiochemical Synthesis of FCH

FCH ([^{18}F]fluorocholine—IASOcholine®) was synthesized from N,N-dimethylethanolamine and [^{18}F]fluoromethyl triflate in a fully automated solid phase fluoromethylation reaction by ARGOS Zyklotron Company Linz.[9] Dimethylethanolamine concentration (average less than 1 μg/ml) as well as radiochemical purity (greater than 99%) were determined by high performance liquid chromatography.[10]

PET-CT Acquisition Protocol and Processing

Imaging was performed on an integrated PET-CT system (Discovery LS®) which combines a third-generation multislice spiral CT with a dedicated full-ring bismuth germinate PET scanner (transaxial FOV 55 cm, axial FOV 15.2 cm, 35 image slices at an axial sampling of 4.25 mm per slice). Images were acquired in a 2-dimensional mode (4 minutes emission per bed position) and were reconstructed using an iterative reconstruction algorithm. The CT scanner (transaxial FOV 50 cm) is operated in 4-slice helical mode with a slice thickness of 4.25 mm. CT data were used for attenuation correction (140 kV, 80 mA, 6:1 pitch, 0.5 seconds per revolution). The reconstructed attenuation corrected PET (128×128 pixels matrix), CT (512×512 pixels) and fused images are available for reading in axial, coronal and sagittal images, and in maximum intensity projections as 3-dimensional cine mode. Acquisition started 1 minute after intravenous injection of FCH (4.07 MBq/kg body weight) with dynamic PET images in the pelvic region for 8 minutes (1 minute frames) followed by a static acquisition from thigh to base of skull.[11]

TABLE 1. *Patient characteristics*

	Mean ± SD (range)
Preop data (20 pts):	
Age	63.9 ± 6.7 (52–75)
PSA (ng/ml)	27.1 ± 27.5 (9.2–100)
Biopsy Gleason sum	7 ± 1 (5–9)
Postop data (18 pts):	
pT stage:	
pT2	7
pT3	11
pT4	0
Pathology specimen Gleason sum:	7.6 ± 1 (6–9)
Gl 5	2
Gl 6	5
Gl 7	6
Gl 8	3
Gl 9	2
LNs removed by E-PLND	14.0 ± 5.4 (7–27)

PET-CT Interpretation

Precise co-registration using PET-CT can reduce the number of false-positive lesions in comparison with PET diagnosis alone. On conventional CT, LNs were classified as malignant according to the standard criteria of no fatty hilus, round configuration, diameter more than 10 mm and/or CT enhancement. Performing dynamic acquisition is helpful to differentiate focal ureter activity vs pathological lymph nodes in the pelvis. Focal FCH uptake from the beginning (minutes 1 to 4) has to be interpreted as malignant lymph nodes (**a/o** bone metastases), while that occurring in later frames (minutes 5 to 8) has to be interpreted as tracer in the ureter. In the bladder FCH also appears approximately 5 to 8 minutes after injection. In metastatic lymph nodes increased tracer uptake still remains in the whole body and/or late images.[11] The PET-CT images were interpreted by 2 experienced PET physicians who were blinded to the clinical data.

Intraoperative Sentinel and Extended LND

The technique of preoperative tracer injection and γ camera imaging was described in detail previously.[7] The tracer (2 ml/200 MBq of ^{99m}Tc labeled human serum albumin colloid; mean particle size 205 nm, range 100 to 600) was injected according to sextant biopsies in 3 locations each of both prostatic lobes under transrectal ultrasound guidance the day before surgery (18 to 22 hours).

Laparoscopic surgery consisted of radioisotope guided sentinel PLND and extended LND followed by radical prostatectomy. A laparoscopic γ detection probe (diameter 11 mm) with a lateral energy window at 90 degrees was used to detect radioactivity signals in situ. The pelvic sidewall was systematically scanned (area of obturator fossa along the external and internal iliac artery/vein up to the ureter and down to the epigastric artery, along the pudendal artery and the presacral region). Initially only LNs sending radioactive signals were dissected and removed. The radioactivity in the node was reevaluated after removal and the pelvic sidewall was rescanned to confirm that the correct nodal pack had been removed.

Following S-PLND standardized E-PLND was performed. This template included the external and internal iliac artery up to the common iliac artery and down to the epigastric artery. Laterally the dissection was carried to the ilioinguinal nerve. The posterior extent included the tissue surrounding the obturator nerve, obturator vessels and internal iliac vein.

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