

Value of SPECT/CT for Detection and Anatomic Localization of Sentinel Lymph Nodes Before Laparoscopic Sentinel Node Lymphadenectomy in Prostate Carcinoma

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Laparoscopic evaluation of sentinel nodes is useful for staging prostate cancer, but preoperative localization of deep abdominal sentinel nodes with planar lymphoscintigraphy is difficult. We evaluated the value of SPECT/CT for detecting and localizing sentinel nodes in prostate cancer. **Methods:** ^{99m}Tc-nanocolloid was injected peri- and intratumorally, guided by transrectal ultrasonography, in 46 patients with prostate cancer of intermediate prognosis. Patients underwent planar imaging after 15 min and 2 h, SPECT/CT after 2 h, and laparoscopic sentinel node lymphadenectomy on the same day. SPECT was fused with CT and analyzed using 2-dimensional orthogonal slicing and 3-dimensional volume rendering. We evaluated the number of extra sentinel nodes found by SPECT/CT, the number of sentinel nodes found by SPECT/CT outside the area of the extended pelvic lymphadenectomy, and the anatomic information provided by SPECT/CT. Furthermore, we classified the value of the additional SPECT/CT images into 3 categories (no advantage, presumable advantage, and definite advantage) according to the extra anatomic information given and whether additional sentinel nodes were found by SPECT/CT. **Results:** The patients had a mean age of 64 y (range, 53–74 y) and received a mean injected dose of 218 MBq (range, 147–286 MBq). The sentinel node visualization rate was 91% (42 patients) for planar imaging and 98% (45 patients) for SPECT/CT. In 29 of the 46 patients (63%), SPECT/CT revealed additional sentinel nodes (especially lymph nodes near the injection area) not seen on planar imaging. In 7 patients, those additional sentinel nodes were positive for metastasis (being the exclusive metastatic sentinel node in 4 patients). Overall, 15 patients (33%) had positive sentinel nodes. Sentinel nodes outside the area of extended pelvic lymphadenectomy were found in 16 patients (35%), whereas in 56% of these patients those nodes were not seen on planar imaging. Performing SPECT/CT had no advantage in 13% of the patients, a presumable advantage in 24%, and a definite advantage in 63%. Urologic surgeons used the SPECT/CT images to guide their trocar insertion sites and sentinel node finding with the probe. **Conclusion:** More sentinel nodes can be detected with

SPECT/CT than with planar imaging alone. In comparison with planar imaging, SPECT/CT especially reveals extra sentinel nodes near the prostate and outside the area of the extended pelvic lymphadenectomy. Furthermore, the modality provides useful additional information about the anatomic location of sentinel nodes within and outside the pelvic area, leading to improved intraoperative sentinel node identification.

Key Words: prostate cancer; radionuclide imaging; single-photon emission computed tomography; SPECT/CT; sentinel lymph node; sentinel lymphadenectomy

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Lymph node involvement may influence treatment decisions, such as decisions about the extent of the radiotherapy target volume or about the length of adjuvant hormonal treatment (1). Sentinel node lymphadenectomy has been shown to be accurate for lymph node staging in prostate cancer (1). Several groups have validated sentinel node lymphadenectomy with open surgery (2–5) or laparoscopy (6–8). In our center, laparoscopic sentinel node lymphadenectomy is preferred because it is minimally invasive and has proven to be a reliable diagnostic tool (8). We perform lymph node staging on patients in the intermediate-prognosis group (clinical stage > T2b, prostate serum antigen level > 10.0 ng/mL, or Gleason sum score > 6) who elect to be treated with radiotherapy, because in this group of patients this staging procedure has therapeutic consequences.

A clear advantage of sentinel node lymphadenectomy in prostate cancer is the fact that sentinel nodes outside the area routinely dissected (the obturator fossa and the region around the external iliac vein) and even outside the extended pelvic lymphadenectomy region can also be localized and removed (2,7). We consider the extended pelvic lymphadenectomy area to be the regions between the external iliac arteries, the obturator fossa, the pelvic wall, the common iliac arteries up

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to the ureteric crossing, and the internal iliac arteries down to (just caudal of) the superior vesical artery.

It is relevant to know the location of the sentinel node in relation to other structures (mainly the large vessels) in order to be able to locate and identify the sentinel node successfully and safely during surgery. In prostate cancer, the tumor generally drains to the pelvic lymph nodes, but drainage outside the area of extended pelvic lymphadenectomy (e.g., aortoiliac junction) is also observed (2). Planar lymphoscintigraphy is the routine choice to provide surgeons with information about the location of the sentinel nodes (2,7). But because this modality is able to provide only 2-dimensional information, exact anatomic localization is usually impossible.

Integrated SPECT/CT allows 3-dimensional visualization without overprojection of the injection site. With the combination of SPECT and CT in a single device, the nodal tracer uptake detected by SPECT can be fused with CT, providing the surgeon with better information on the anatomic location of the sentinel node. We introduced the use of SPECT/CT in addition to planar imaging in prostate cancer patients undergoing sentinel node lymphadenectomy. Here, we report our experience with this imaging modality. The purpose of the study was to determine the additional value of SPECT/CT in preoperative sentinel lymph node mapping in prostate cancer patients, especially for localizing sentinel nodes in relation to the area of extended pelvic lymphadenectomy.

MATERIALS AND METHODS

Patients

We evaluated the use of SPECT/CT in 46 patients with prostate cancer of intermediate prognosis. The criteria for inclusion were the presence of one or more of the following characteristics: clinical stage greater than T2b, prostate serum antigen level greater than 10.0 ng/mL, or Gleason sum score greater than 6.

The patients elected to be treated with external radiotherapy in the Netherlands Cancer Institute between June 2006 and September 2008, and the sentinel node lymphadenectomy took place before the radiotherapy.

Before sentinel node lymphadenectomy, the patients underwent routine planar imaging and additional SPECT/CT. At our center, performing SPECT/CT after planar imaging is routine for patients who undergo sentinel lymph node mapping and who are expected to have intraabdominal drainage. The patients were included after giving informed consent.

Image Acquisition and Sentinel Node Localization

Preoperative planar imaging and SPECT/CT were performed after injection of ^{99m}Tc -nanocolloid (Amersham Cygne). The tracer was injected peri- and intratumorally; 0.1 mL was injected in each quadrant of the prostate. Administration was guided by transrectal ultrasonography, and each 0.1-mL injection was followed by flushing with approximately 0.7 mL of saline. The remaining radioactivity in the injection device was subtracted from the total dose to calculate the net injected dose.

Planar imaging was performed at 15 min and again at 2 h after injection of the tracer.

After the delayed planar images had been obtained, SPECT and CT images were acquired using a hybrid camera (Symbia T; Siemens). This system consists of a dual-head variable-angle γ -camera equipped with low-energy high-resolution collimators and a multislice spiral CT component optimized for rapid rotation. The SPECT acquisition (128 \times 128 matrix, 60 frames, 25 s/frame) was performed using 6° angular steps in a 20-s time frame. For CT (130 kV, 17 mAs, B60s kernel), 5-mm slices were obtained.

After correction for attenuation and scatter, corresponding SPECT and CT axial 5-mm slices were generated using an Esoft 2000 application package (Siemens). Images were fused using an Osirix Dicom viewer in a Unix-based operating system (MAC OS X, MacPro; Apple Inc.).

Furthermore, the images were analyzed using 2-dimensional orthogonal reslicing in axial, sagittal, and coronal directions. Also, a 3-dimensional presentation, using volume rendering, was generated to localize sentinel nodes in relation to anatomic structures.

All images were available on a separate SPECT/CT screen in the operation theater.

The first nodes in each station appearing on early planar imaging were considered to be the sentinel nodes. Nodes appearing later in the same stations were considered to be second-echelon nodes. If SPECT/CT showed additional hot spots in caudal areas or on a side with no other drainage or without previous drainage, those hot spots were also considered to be sentinel nodes. Radio-guided sentinel node lymphadenectomy was assisted by a laparoscopic γ -probe (Europrobe; Euro Medical Instruments) and a portable mini γ -camera (Sentinella, S102; GE Healthcare).

The extended pelvic lymphadenectomy area concerned the regions between the external iliac arteries, the obturator fossa, the pelvic wall, the common iliac arteries up to the ureteric crossing, and the internal iliac arteries up to (just caudal of) the superior vesical artery.

Therapeutic Consequences

Sentinel nodes were examined postoperatively by experienced pathologists. Frozen sections were not examined. The nodes were fixed in formalin, bisected, embedded in paraffin, and cut at a minimum of 6 levels at 50- to 150- μm intervals. Pathologic evaluation included hematoxylin-eosin staining and immunohistochemical staining with CAM5.2.

All sentinel node-negative patients received external-beam radiation therapy to the prostate (78 Gy) and 6 mo of hormonal treatment. For sentinel node-positive patients, our policy was to perform external-beam radiation therapy to the prostate (70 Gy) and pelvic area (50 Gy) and give 3 y of hormonal therapy.

Analysis

Primary tumor characteristics were recorded, as well as the results of the preoperative imaging procedures. Primary outcome characteristics were classified as preoperative detection of sentinel nodes outside the extended pelvic lymphadenectomy area (inguinal, near the aortoiliac junction, presacral, or near the umbilical ligament in the abdominal wall) by SPECT/CT and anatomic localization of these nodes by SPECT/CT. Furthermore, we evaluated if SPECT/CT detected more sentinel nodes in general and if it provided better localization information (e.g., a location definitely near great vessels). Anatomic localization information was regarded as useful if nuclear medicine physicians could preoperatively provide the urologic surgeon with the exact location of the sentinel node near great vessels (e.g., "at the aortoiliac junction")

TABLE 1. Characteristics of the 46 Patients	
Characteristic	Value
Mean age (y)	64 (median, 65; range, 53–74)
Mean prostate serum antigen (ng/mL)	23 (median, 15; range, 2.1–208)
Mean Gleason score	7 (median, 7; range, 5–9)
T category	
T1	2 patients
T2	6 patients
T3	36 patients
T4	2 patients

or “near the external iliac artery”) or a ligament (e.g., “near the umbilical ligament in the abdominal wall”) on the basis of SPECT/CT images, whereas this information could not be provided on the basis of planar images alone. If nodes appeared to be in a different location on the basis of SPECT/CT results (e.g., superficial inguinal node instead of drainage to parailiac area), this anatomic localization information was also regarded as useful.

To classify the additional value of SPECT/CT in each patient, we categorized the SPECT/CT yield as being of no advantage (if no extra sentinel nodes were found and planar imaging could have provided the surgeon with enough information on the location of the sentinel node), of presumable advantage (if no extra sentinel nodes were detected on SPECT/CT but localization information on SPECT/CT was more useful than that on planar imaging), or of definite advantage (if more sentinel nodes were detected on SPECT/CT, including cases of nonvisualization on planar imaging and visualization of drainage on SPECT/CT).

RESULTS

Forty-six patients (mean age, 64 y; range, 53–74 y) were investigated, and the mean injected dose of ^{99m}Tc -nanocolloid

was 218 MBq (range, 147–286 MBq). Clinical patient characteristics are summarized in Table 1, and the results, in Table 2.

Visualization rates were 91% (42/46) for planar imaging and 98% (45/46) for SPECT/CT. In 4 patients, planar imaging showed no sentinel node, but in 3 of these cases, SPECT/CT showed sentinel nodes (3, 3, and 6 sentinel nodes). In one patient, SPECT/CT also did not show any drainage.

Planar imaging visualized a mean of 2.2 sentinel nodes per patient. In 37% of the patients, all sentinel nodes had already been visualized on the early planar images, and in the other 63% the late images after 2 h showed additional drainage to sentinel nodes. In many of those patients, the early images were useful for distinguishing between first- and second-echelon nodes.

SPECT/CT visualized a mean of 4.3 sentinel nodes per patient. In 29 of the 46 patients (63%), SPECT/CT revealed additional sentinel nodes not seen on planar imaging. Sentinel lymph nodes near the injection area were better visualized on SPECT/CT but were easily missed on planar imaging. This was the case in 6 patients whose presacral sentinel nodes were detected only on SPECT/CT.

Sixteen patients (35%) had sentinel nodes outside the extended pelvic lymphadenectomy area (inguinal, near the aortoiliac junction, presacral, or near the umbilical ligament in the abdominal wall). In 9 patients (56%), these sentinel nodes were detected only on SPECT/CT and would have been missed if only planar imaging had been performed. Pathologic examination revealed in one patient a nodal metastasis with a sentinel node outside the extended pelvic lymphadenectomy area and seen only on SPECT/CT. In the other patients, the sentinel nodes outside the ex-

TABLE 2. Results for the 46 Patients	
Parameter	Result
Mean injected dose (MBq)	219 (median, 219; range, 147–286)
Total number of sentinel nodes visualized with planar imaging	102 (and 8 uncertain sentinel nodes, probably second-echelon) Sentinel nodes detected on early images: 37% Additional sentinel nodes visible on late images: 63%
Total number of sentinel nodes visualized with SPECT/CT	196 (and 1 uncertain sentinel node, probably second-echelon)
Number of patients with additional sentinel nodes localized by SPECT/CT	29 (63%)
Importance of SPECT/CT	No advantage: 6 (13%) Presumable advantage: 11 (24%) Definite advantage: 29 (63%)
Patients with uncommonly located sentinel nodes (outside pelvic area)	16 (35% of all patients): Visible on planar imaging: 7 (44%) Detected by SPECT/CT only: 9 (56%)
Node-positive patients	15 (33%) Metastasis in only sentinel nodes seen on planar images: 8 (53%) Metastasis in sentinel nodes exclusively detected by SPECT/CT: 7 (47%) Only positive sentinel nodes: 4 (27%)*

*In 4 of 7 patients with sentinel node metastasis in sentinel nodes that were exclusively seen on SPECT/CT, this sentinel node was the only positive sentinel node. Those patients (27% of all node-positive patients) were upstaged, and adjuvant therapy was given.

tended pelvic lymphadenectomy area were negative for metastases.

Of the node-positive patients, 47% had a metastasis in a sentinel node detected only on SPECT/CT. In 4 of those patients (27% of all node-positive patients; 9% of all prostate cancer patients), the metastasis in the sentinel node detected only on SPECT/CT was the only nodal metastasis.

Performing additional SPECT/CT for detection and localization of sentinel nodes provided a definite advantage in 63% of our patients, a presumable advantage in 26%, and no advantage in 13%.

Figures 1–3 and Supplemental Figure 1 (supplemental materials are available online only at <http://jnm.snmjournals.org>) show different examples of the additional value of SPECT/CT in preoperative localization of sentinel nodes in prostate cancer patients.

DISCUSSION

Our results emphasize the significant value of SPECT/CT in localizing sentinel nodes preoperatively. In our population, SPECT/CT revealed additional sentinel nodes in 63% of all prostate cancer patients, leading to excision of more sentinel nodes and thus complete staging. The relevance of excising those nodes is shown by the fact that in almost half of all tumor-positive patients, a sentinel node that was missed on planar images showed tumor positivity. Some of those patients also had another tumor-positive sentinel node (a sentinel node visible on the planar images). However, in 4 patients (9% of all prostate cancer patients), the sentinel node additionally detected on SPECT/CT was the only tumor-positive sentinel node, leading to upstaging and alteration of the treatment regime.

Furthermore, 35% of the patients had sentinel nodes outside the pelvic area. In 56% of the cases, those nodes were detected only on SPECT/CT, including one tumor-

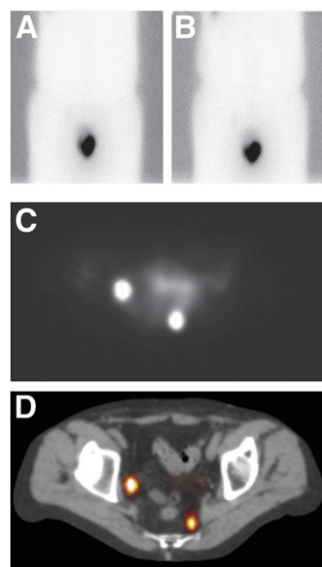


FIGURE 1. (A and B) No distinct drainage is seen on planar imaging at 15 min (A) or 2 h (B). (C) SPECT shows localization of 2 sentinel nodes. (D) Those nodes are localized with SPECT/CT, which clearly shows one sentinel node in left presacral area and another in right iliac area.

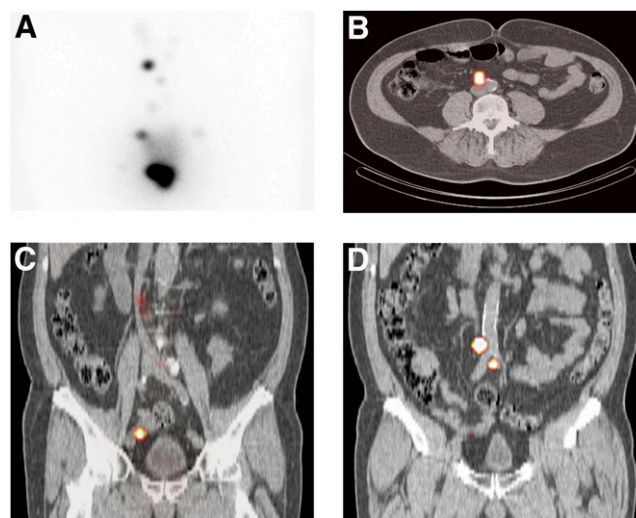


FIGURE 2. (A) Planar imaging at 2 h shows drainage to pelvic lymph node and to node high in abdomen. This latter node had already been seen on planar imaging at 15 min. (C) On fused coronal SPECT/CT, right sentinel node is seen in parailiac area. Another section showed sentinel node in left parailiac area as well. (B) On transversal image, sentinel node high in abdomen appears to be near abdominal aorta. (D) On coronal section, this sentinel node is clearly seen to be just above aortoiliac junction. Furthermore, another node just below aortoiliac junction is visible. This lymph node, appearing only on delayed planar images, was considered second-echelon node.

bearing sentinel node. If we had not added SPECT/CT to the preoperative imaging procedure, in 20% of all patients a sentinel node would have been missed even if sentinel node lymphadenectomy based on planar imaging had been combined with extended pelvic lymphadenectomy.

If SPECT/CT and planar imaging do not show the sentinel node, extended pelvic lymphadenectomy is the best remaining option for accurate staging, although not 100% accurate and with greater morbidity. In our population, extended pelvic lymphadenectomy could be prevented in 3 of 4 patients, because although planar imaging showed no drainage, SPECT/CT showed the sentinel node.

Furthermore, the intraoperative probe does not always pick up a sufficient signal to localize the sentinel node. In that case, the sentinel node information and anatomic reference points on the SPECT/CT images will guide the surgeon as to the relevant area to dissect, and the radioactive node can then be identified *ex vivo*.

During the validation phase of sentinel node biopsy for prostate cancer at our center (8), we noticed no added value from images obtained more than 2 h after injection of the tracer. Furthermore, the sooner patients undergo surgery after injection, the higher the radioactivity within the sentinel nodes and the higher the probability of easy localization of those nodes. Therefore, all patients receive the injection in the morning and undergo surgery on the afternoon of the same day, using a 1-d protocol.

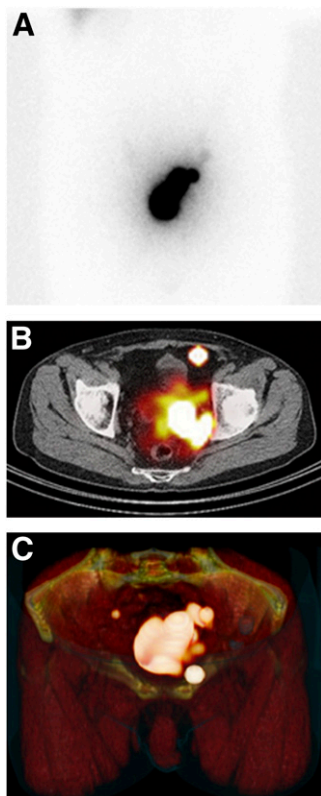


FIGURE 3. Patient with atypical sentinel node in abdominal wall. (A) Anterior planar imaging at 2 h vaguely shows right and left parailiac drainage. (B) In contrast, SPECT/CT with 2-dimensional orthogonal slicing clearly showed parailiac lymph nodes, but a node near the abdominal wall is also visible. (C) Three-dimensional volume-rendered reconstruction depicts this sentinel node in relation to injection site and iliac nodes. At laparoscopy, this sentinel node was found near left medial umbilical ligament.

Previous reports on the use of SPECT/CT in sentinel node detection also showed favorable results for this modality. Lerman et al. studied the use of SPECT/CT in 157 patients with breast cancer (9). They concluded that SPECT/CT may improve preoperative localization of sentinel nodes and may detect hot nodes missed by planar imaging. Furthermore, some nonnodal false-positive sites of uptake could be excluded and the nodes could be accurately localized (9). van der Ploeg et al. concluded that SPECT/CT in breast cancer patients and melanoma patients was especially useful in patients with inconclusive planar imaging findings and patients without drainage on planar images. In those patients, SPECT/CT detected additional sentinel nodes and, besides, was useful in finding the exact location of sentinel nodes (10). In another study, van der Ploeg described the use of SPECT/CT in hidden sentinel nodes: SPECT/CT visualized lymphatic drainage in 8 of 15 breast cancer patients (53%) with nonvisualization on planar imaging (including 3 tumor-positive sentinel nodes) (11).

Besides breast cancer, the use of SPECT/CT has been quite well described in sentinel node lymphadenectomy for head and neck cancer (12–17). Because of complex lymph drainage systems and the presence of several vital structures such as vessels and nerves, preoperative imaging in this region is essential. Several authors have concluded that the additional use of SPECT/CT in head and neck cancer leads to detection of more sentinel nodes and better anatomic localization of the sentinel nodes (12–17).

The value of SPECT/CT for sentinel node lymphadenectomy in malignancies with pelvic drainage has been less

extensively studied. Sherif et al. reported on the use of SPECT/CT in 6 patients with bladder cancer (18) and concluded that the addition of SPECT/CT could markedly increase the detection of sentinel nodes. Beneder et al. reported that the use of SPECT/CT in vulvar cancer revealed additional information in 7 of 10 patients (19). With regard to the use of SPECT/CT in prostate cancer, Kizu et al. were the first to describe fusion of images from those 2 modalities (20). In 11 patients, fusion images correlated reasonably well with intraoperative findings: 87% of the lymph node locations visualized on SPECT/CT fusion images were confirmed by the surgeons (20). Furthermore, Krenkli et al. described how preoperative imaging of lymph drainage with SPECT/CT in prostate cancer patients can alter the radiotherapy regime and lead to optimization of pelvic irradiation (21).

Because the literature confirms the importance of additional imaging in sentinel node identification, we advise that SPECT/CT be performed on all patients undergoing sentinel node procedures for malignancies with intraabdominal drainage. If SPECT/CT is not available, planar imaging can be used, but in that case physicians have to accept that sentinel nodes will be missed, especially those near the injection area. To distinguish between first- and second-echelon nodes, sequential planar images remain useful. Earlier-appearing nodes in each station are considered to be first-echelon nodes, whereas later-appearing nodes, located cranially in the same station, are identified as second-echelon nodes.

CONCLUSION

Accurate staging with sentinel node lymphadenectomy can be achieved only if all sentinel nodes are detected. Because the lymph drainage of tumors draining deeply in the abdomen, such as prostate carcinoma, is often complex, preoperative localization is mandatory. SPECT/CT not only provides useful anatomic information about the localization of sentinel nodes but also has been proven to detect additional sentinel nodes. This is especially relevant for sentinel nodes outside the extended pelvic lymphadenectomy area and sentinel nodes near the prostate; a significant number of such nodes will be missed without SPECT/CT.

Sequential planar imaging will remain important for preoperatively identifying early-appearing lymph nodes as sentinel nodes. Anatomic localization of these sentinel nodes, however, is achieved by SPECT/CT. Because the introduction of SPECT/CT in sentinel node procedures for prostate cancer has markedly improved sentinel node detection and localization, we advise the routine use of this modality in malignancies with deep intraabdominal drainage.

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