Paraaortic Sentinel Lymph Nodes: Toward Optimal Detection and Intraoperative Localization Using SPECT/CT and Intraoperative Real-Time Imaging

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Paraaortic sentinel node biopsy may be a challenging procedure because the sentinel nodes are located retroperitoneally in close proximity to vital structures. The purpose of this study was to describe and evaluate the value of preoperative SPECT/CT for lymphatic mapping, and a portable γ-camera for intraoperative radioguidance, in patients with paraaortic sentinel nodes. **Methods:** We evaluated our practice in 18 patients, who were treated at The Netherlands Cancer Institute with sentinel lymphadenectomy for different urologic malignancies and showed paraaortic drainage on preoperative images. After intratumoral injection of ^{99m}Tc-nanocolloid, the patients underwent sequential planar lymphoscintigraphy, hybrid SPECT/CT, and sentinel lymphadenectomy. Intraoperative node detection and localization were guided by a laparoscopic γ-probe and a portable γ-camera. This γ-camera was set to display both the ^{99m}Tc signal and the ^{125}I-seed signal. This ^{125}I seed was placed on top of the γ-probe, functioning as a pointer on screen, thus enabling real-time sentinel node localization with the γ-camera. **Results:** In 16 patients with midabdominal drainage on planar images and in 2 patients with nonvisualization on planar images, SPECT/CT showed clear localization of paraaortic sentinel nodes in relation to the abdominal vessels. Five patients underwent open surgery, and 13 patients underwent laparoscopy. The paraaortic sentinel nodes were successfully localized and removed in 15 patients with the help of the portable γ-camera and γ-probe and in 3 patients with the γ-probe only. In 1 patient, the paraaortic sentinel node showed a metastasis. **Conclusion:** If retroperitoneal drainage is expected, SPECT/CT provides good detection and clear localization of sentinel nodes in relation to anatomic structures. Detection and removal of paraaortic sentinel nodes by means of a laparoscopic γ-probe and real-time imaging with a portable γ-camera is a successful method with high intraoperative detection rates.

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In recent decades, the use of sentinel lymph node biopsy has been introduced as a possible staging procedure in several solid malignancies (*1–3*). Sentinel node biopsy is now widely used for breast cancer and melanoma staging (*4,5*), and its possible value in several other malignancies is a reason for worldwide ongoing research. The concept of sentinel node biopsy is based on the sequential spread of metastatic cancer cells through lymphatic flow. The value of this procedure is based on the idea that if the first draining lymph node from the tumor (sentinel node) is free of metastases, the remaining nodes in the same nodal basin will be as well. Sentinel lymph node mapping is now used as a minimally invasive staging method in several malignancies to spare many node-negative patients the significant comorbidity caused by regional lymph node dissection.

Sentinel node biopsies from axillary and inguinal nodal basins have been shown to be safe and quick (*6–8*), probably in consequence of the superficial location of these nodes and the widespread experience of surgeons with these cases.

As the use of sentinel lymph node mapping is extending, so is the variety of lymph node basins containing the sentinel nodes. Experience with sentinel lymph node mapping of retroperitoneal and intraabdominal nodal basins is less widespread but increasing. The feasibility and value of sentinel lymph node mapping in prostate cancer, with drainage mainly to pelvic sentinel nodes, has been well described (*9,10*). Furthermore, sentinel lymphadenectomy in cervical cancer, endometrial cancer, ovarian cancer, and testicular cancer has been studied with different results

(*11,12*). Its possible role in gastric cancer and colorectal cancer is reason for debate (*13,14*).

Exact lymphatic drainage patterns from tumors with expected retroperitoneal drainage have not been clearly identified yet, and considerable interpersonal variation can be observed. From several abdominal tumors, though, drainage to paraaortic sentinel lymph nodes might be expected. Precise localization and removal of those paraaortic nodes is a requisite to achieve successful staging but can be challenging because they are near vital structures. The purpose of the current study was to describe and evaluate our approach to paraaortic sentinel nodes with preoperative SPECT/CT and the introduction of a portable γ-camera for intraoperative radioguidance.

MATERIALS AND METHODS

Patients

We evaluated our practice of sentinel node detection, localization, and excision in 18 patients with paraaortic sentinel nodes. The median age of these patients was 57 y (range, 31–71 y). Four patients have also been included in a pilot study of the value of a portable γ-camera for intraoperative imaging of sentinel nodes (*15*). In all patients, the malignancy was diagnosed at The Netherlands Cancer Institute between January 2006 and July 2009, and all patients were included in different studies regarding the value and feasibility of sentinel lymphadenectomy. Patients were included in the current study if preoperative imaging showed paraaortic sentinel nodes. In the case of preoperative nonvisualization, patients were excluded from this analysis. The result was inclusion of all patients with visualized paraaortic sentinel nodes since the introduction of SPECT/CT and intraoperative imaging: 8 prostate cancer patients, 6 patients with renal cell carcinoma, and 4 patients with testicular cancer. Patient characteristics and results per tumor are outlined in Table 1.

Preoperative Sentinel Node Detection

Patients underwent preoperative lymphoscintigraphy after injection of ^{99m}Tc-nanocolloid (GE Healthcare).

In prostate cancer patients, the tracer was injected, 1 depot of 0.1 mL per quadrant of the prostate, guided by transrectal ultrasonography. Each depot of 0.1 mL was followed by flushing with approximately 0.7 mL of saline. In renal cell carcinoma, intratumoral injection, in 2 depots of 0.2 mL, was guided by ultrasonography, and in testicular cancer, 1 depot of 0.2 mL was injected intratesticularly. The remaining radioactivity in the injection device was subtracted from the injected dose to calculate the net injected dose. The median injected dose was 205 MBq of ^{99m}Tc-nanocolloid (range, 59–243 MBq).

All patients underwent planar lymphoscintigraphy and SPECT/CT to evaluate lymphatic drainage. Planar lymphoscintigraphy was performed at least twice: 15 min and 2 h after injection of the radiopharmaceutical. Planar images after 4 h were acquired only in the case of renal cell carcinoma, because for these tumors sentinel node mapping protocols have not been validated yet and we wanted to ensure that we would not miss any drainage.

After the delayed planar images, SPECT and low-dose CT were performed, using a hybrid camera (SymbiaT; 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 × 128 matrix, 60 frames, 25 s/frame) was performed using 6° angular steps in a 20-s time frame. For CT (130 kV, 40 mAs, B30s 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/Mi Apps application package (Siemens). An iterative reconstruction was performed using 3-dimensional fast low-angle shot (8.4-mm gaussian). 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.

If a lymphatic channel leading to a paraaortic node was seen, this node was regarded as the sentinel node. If no lymphatic channel was visualized, the node or nodes that were the first to appear intensely on early planar images were defined as the sentinel node or 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 previous drainage or no other drainage, those hot spots were also considered to be sentinel nodes. For prostate cancer patients, this implied that if an intense hot spot was seen in the paraaortic area before or simultaneously with pelvic nodes, this paraaortic node was considered to be a sentinel node. If this paraaortic hot spot appeared after visualization of intense pelvic nodes, it was regarded as a node further downstream and those patients were not included in this study.

Intraoperative Sentinel-Node Detection

All patients with prostate cancer and testicular cancer underwent surgery within 6 h after injection of the tracer. Patients with renal cell carcinoma underwent surgery the next morning, because for logistic reasons late planar images up to 4 h after injection could not be combined with an operation on the same day.

Sentinel nodes were removed laparoscopically in patients with prostate cancer and testicular cancer. In renal cell carcinoma, the sentinel lymph node biopsy was performed laparoscopically or through open surgery, depending on the primary tumor, other patient characteristics, and the surgeon's preference.

For intraoperative sentinel node localization, we introduced the use of a portable γ-camera (Sentinella, S102; Oncovision), in combination with the γ-probe (Europrobe; Euro Medical Instruments, and Neoprobe; Johnson&Johnson Medical). The portable γ-camera was equipped with a 4-mm pinhole collimator and has a field of view of 4 × 4 cm, which increases to 20 × 20 cm when the camera is placed at a distance of 15 cm from the patient's body. It uses a CsI(Na) continuously scintillating crystal and has a 1.3-mm intrinsic resolution (*15*).

Before the start of sentinel node seeking, a ^{125}I seed (>10 MBq) was placed on the top of the γ-probe. In the case of laparoscopic sentinel lymphadenectomy, the ^{125}I seed was placed on the laparoscopic probe. During the operation, this ^{125}I seed was used as a pointer, being displayed separately (as a green circle) on the screen of the portable γ-camera. To provide better orientation for the surgeon and to avoid attenuation of the signal, the location

TABLE 1 Patient Characteristics and Results

Type of malignancy	*n*	Age (y)	Injected dose (MBq)	Findings: Planar images	Findings: SPECT/CT	Findings: Surgery	Intraoperative localization	Postoperative course	Pathology
Prostate cancer	8	Median: 68; range: 56–71	Median: 205; range: 147–239	8 midabdominal SNs; 16 pelvic or presacral SNs	8 SNs around aortic bifurcation (exact localization); localization of 20 other SNs	Laparoscopic sentinel lymphade-nectomy	Detection and localization of all SNs with portable γ-camera and probe	Uncomplicated: 7 pts; lymphocele: 1 pt	Paraaortic SN positive: 1 pt; parailiac SN positive: 2 pts
Renal cell carcinoma	6	Median: 54; range: 45–59	Median: 224; range: 95–243	4 midabdominal SNs; 1 parasternal SN; nonvis: 2 pts	8 para- and interaortocaval SNs (exact localization); 1 parasternal SN	Laparoscopic nephrectomy and sentinel lymphade-nectomy: 1 pt; open procedure: 5 pts	Visualization of SN with portable γ-camera: 3 pts; detection possible only with γ-probe: 3 pts; detection of additional hot node in 1 pt*	Uncomplicated: 4 pts; infected wound: 1 pt; cicatricial hernia of nephrectomy wound:1 pt	All SNs negative
Testicular cancer	4	Median: 32; range: 31–40	Median: 77; range: 59–97	7 midabdominal SNs	5 interaortocaval SNs; 2 left paraaortic SNs; 1 SN along testicular vein (exact localization); localization of 1 parailiac SN	Laparoscopic sentinel lymphade-nectomy	Detection and localization of all SNs with portable γ-camera and probe	Uncomplicated: 3 pts; hydronephrosis: 1 pt	All SNs negative

*Two paraaortic sentinel nodes were found and removed during surgery, whereas preoperative SPECT/CT had visualized only 1 paraaortic sentinel node.
Nonvis = nonvisualization; Pt = patient; SN = sentinel node.

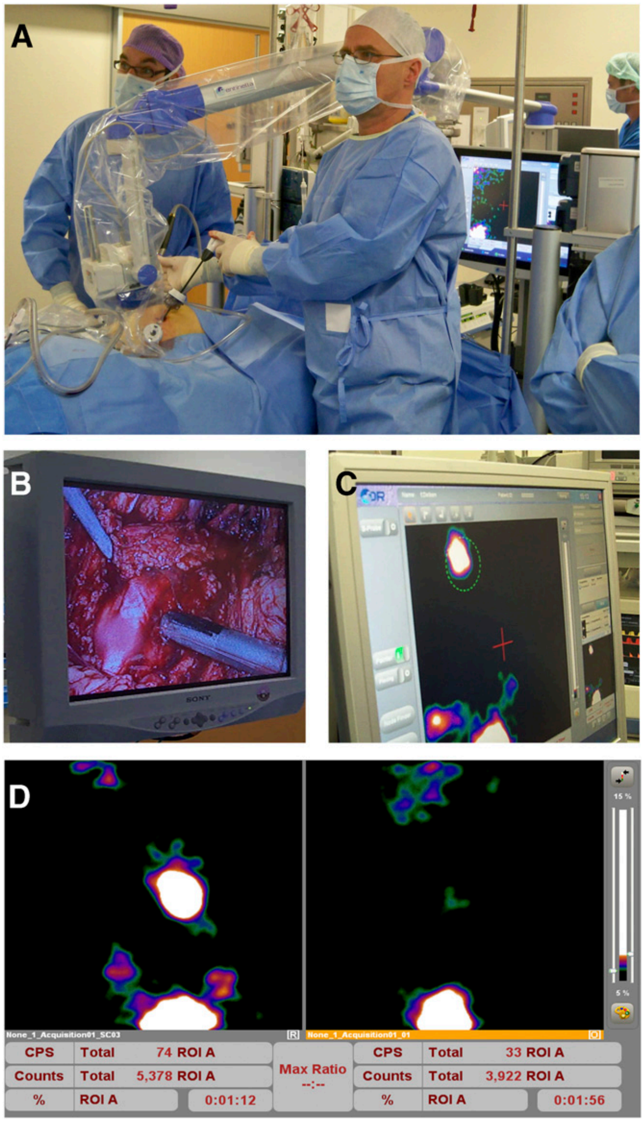

FIGURE 1. Use of portable γ-camera for localization of paraaortic sentinel node. Portable γ-camera was used for intraoperative sentinel node display in patient with prostate cancer (A). Laparoscopic probe with ^{125}I seed placed on top was used for sentinel node localization (B). ^{99m}Tc signal (sentinel node) and seed-pointer signal are displayed separately on screen of portable γ-camera. Injection area is visualized caudally on screen as well as sentinel nodes on both sides of pelvic area. More cranially on screen, hot paraaortic node was visualized. ^{125}I seed on probe functioned as pointer and matched with paraaortic sentinel node, indicating exact location of sentinel node (C), and subsequently this node was removed. Portable γ-camera can show remaining radioactivity after removal of each node. In this example (D), situation before and after removal of all sentinel nodes is compared. Radioactivity in injection area and liver remained, as well as weak background radioactivity at site of excision of paraaortic sentinel node (lymphatic channel or higher-echelon node).

of the ^{125}I seed on the top of the γ-probe was marked with a thin black line. In this way, the location of the seed on the probe was visible. In the case of laparoscopy, the thin black line was applied to the top of the laparoscopic γ-probe and to the grip of the laparoscopic probe. In this way, the surgeon could see where on the probe the seed was located.

The collimator of the γ-camera was sterile-wrapped to allow manipulation by the surgeon and was placed above the previously marked sentinel node levels, using a laser pointer. Then, the camera was set to display the 2 different signals: the ^{99m}Tc signal for sentinel node localization and the ^{125}I signal displayed as a green circle, functioning as a pointer. Matching of the 2 signals on the screen of the portable γ-camera indicated correct localization of the sentinel node, which was subsequently removed. This intraoperative procedure is further explained in Figure 1.

All detected hot spots near the marked areas (sentinel node levels) were considered to be sentinel nodes and therefore were localized with the help of the γ-camera and removed. Second-echelon nodes, as identified preoperatively, were left in place. All removed nodes were examined by experienced pathologists.

RESULTS

In 16 patients with an abdominal or midabdominal sentinel node seen on planar lymphoscintigraphy, SPECT/CT showed the paraaortic sentinel node in relation to the abdominal vessels (aortic artery, caval vein, or renal vessels). In the 2 other patients with paraaortic sentinel nodes, those sentinel nodes were seen only on SPECT/CT; planar imaging did not show drainage. Figure 2 shows an example of paraaortic sentinel nodes in a patient with nonvisualization on planar images.

In testicular cancer patients and patients with renal cell carcinoma, the sentinel nodes were located mainly along the abdominal aorta and caval vein. In prostate cancer, most patients showed drainage to pelvic sentinel nodes, but 9 of 67 (13%) also showed direct drainage to a paraaortic sentinel node. Eight of these were included in this study because they underwent surgery in the period that SPECT/CT and intraoperative radioguidance with a γ-camera were used for paraaortic node detection. The localization of the paraaortic sentinel nodes, as found with preoperative imaging by means of SPECT/CT, is shown in Figure 3.

In all patients, the paraaortic sentinel nodes were successfully localized and removed during surgery: in 5 patients through open surgery (all renal cell carcinoma

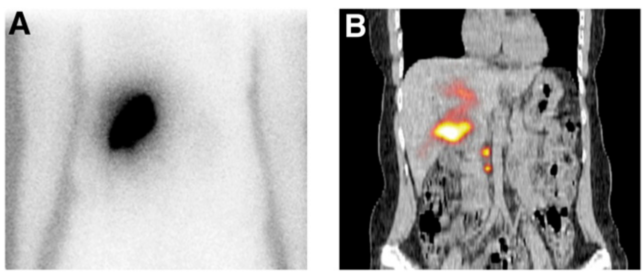

FIGURE 2. Patient with renal cell cancer of right kidney. Planar images after 15 min, 2 h, and 4 h (A) showed no visualization of lymphatic drainage. SPECT/CT (B) showed 2 paraaortic sentinel nodes between aortic artery and caval vein.

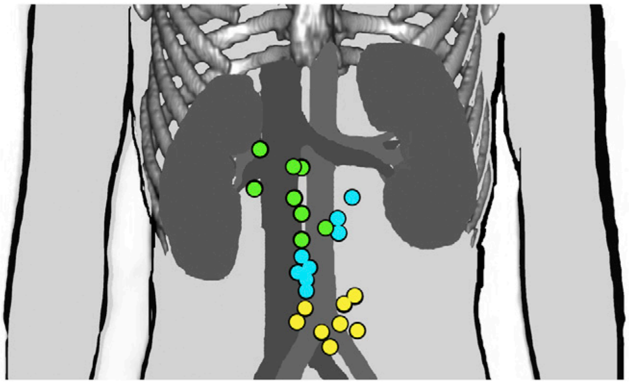

FIGURE 3. Paraaortic sentinel nodes as seen in our patient population. Green nodes are sentinel nodes seen in renal cell carcinoma, blue nodes in testicular cancer, and yellow nodes in prostate cancer. All nodes were successfully detected and removed intraoperatively with guidance of laparoscopic γ-probe and portable γ-camera.

patients) and in 13 patients through laparoscopy. In 15 patients (83%), the portable γ-camera provided intraoperative real-time sentinel node identification and localization, as shown in Figure 1. After removal of the paraaortic sentinel nodes in these patients, the portable γ-camera showed remaining background activity only, confirming removal of the correct (sentinel) node.

In patients with strong tracer uptake, sentinel nodes were visualized within a few seconds, whereas nodes with weak uptake took 30–50 s to visualize. In 3 patients (the two with nonvisualization on planar images and one with weak sentinel node visualization), the γ-camera was of no additional value because the node could not be visualized. All 3 patients received open sentinel lymphadenectomy for renal cell carcinoma, and in these patients nodal tracer uptake was too weak for adequate intraoperative real-time imaging.

DISCUSSION

Experience with retroperitoneal lymphadenectomies has been described mainly in gynecologic and urologic tumors. Paraaortic lymphadenectomy has been performed safely in large patient cohorts for cervical cancer (*16*), testicular cancer (*17*), and renal cell carcinoma (*18*). In some of those cancers, sentinel lymphadenectomy has also been described, although in small groups or with sentinel lymph node detection and labeling preceding total lymphadenectomy (*19–21*). Sentinel lymph node mapping is a less invasive procedure, but detection, localization, and removal of the correct node or nodes are challenging. Finding the sentinel node is requisite, though, to provide accurate staging with sentinel lymphadenectomy.

In large studies on cervical cancer and prostate cancer, much experience has been gained with sentinel node procedures in pelvic areas (*9,10,19,20*). Many studies, however, did not describe paraaortic sentinel node dissection but performed a regional paraaortic lymphadenectomy in the case of paraaortic drainage.

In a study by Kushner et al., 2 paraaortic sentinel nodes were safely and successfully removed, followed by pelvic lymphadenectomy (*21*), and Tanis et al. described the successful laparoscopic removal of 2 paraaortic sentinel nodes (*22*). Satoh et al. were able to localize paraaortic sentinel nodes in 21 of 22 patients with testicular carcinoma undergoing completion lymph node dissection, although the sentinel nodes were not separately excised (*12*). The current study shows good intraoperative detection of paraaortic sentinel nodes after SPECT/CT and the introduction of intraoperative radioguidance.

We use SPECT/CT for all patients with retroperitoneal and intraabdominal drainage. The contribution of this imaging modality has been described before in breast cancer and melanoma (*23,24*), head and neck tumors (*25,26*), and prostate carcinoma (*27*). Our results underline the importance of SPECT/CT in patients with paraaortic sentinel nodes. All nodes found by planar imaging could be localized in relation to the aortic artery and caval vein by SPECT/CT. On planar images, the relationship between the sentinel node and the aorta or caval vein is not clear. A laparoscopic procedure is thus challenging, because for decisions on port placement it is important to know this relationship. With the laparoscopic probe, it cannot be decided if a sentinel node is located anterior or posterior to the large vessels, whereas SPECT/CT can visualize the accurate location. Supplemental Figure 1 (supplemental materials are available online only at http://jnm.snmjournals.org) shows an example of the localization of a paraaortic sentinel node on planar images, compared with on SPECT/CT. Furthermore, SPECT/CT appeared to be more sensitive than planar imaging in detecting sentinel nodes. SPECT/CT detected paraaortic sentinel nodes in 2 patients with nonvisualization on planar images.

Besides using SPECT/CT, we introduced a portable γ-camera for intraoperative radioguidance and real-time imaging. The use of this γ-camera has been described for radioguided surgery in parathyroidectomy (*28,29*) and radioguided occult lesion localization (*30*) in breast cancer. Mathelin et al. described the use of the portable γ-camera for preoperative identification of sentinel nodes in breast cancer and were able to successfully estimate the depth of the nodes with the γ-camera (*31*). The first results with the portable γ-camera for intraoperative sentinel node localization in patients with urologic tumors showed clear sentinel node visualization in 90% of the patients (*15*).

A main advantage of the intraoperative use of the portable γ-camera in our patients appeared to be the ability to monitor the paraaortic area before and after removal of the hot nodes, as visualized in Figures 1 and 4. The γ-camera could be used to check if the sentinel node had actually been removed and only background radioactivity remained or if there was a hot (sentinel) node left in this area. Because weak hot spots will not be visualized within

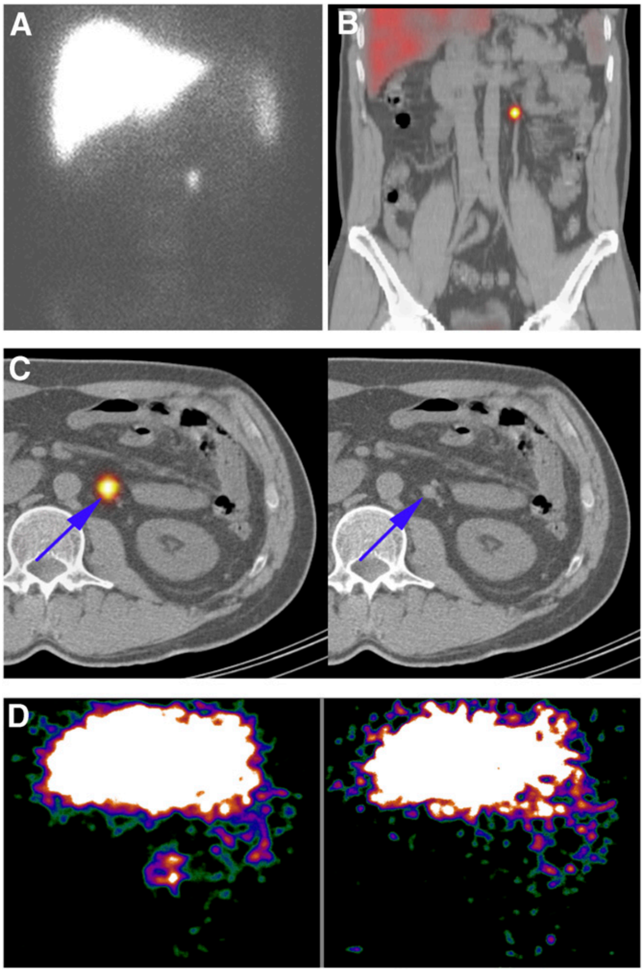

FIGURE 4. Patient with testicular cancer. Planar images at 2 h showed drainage to sentinel node in abdomen and tracer uptake in liver and spleen (A). Intense uptake in liver and spleen might be due to partial intravascular injection of radiotracer. With 2-dimensional SPECT/CT fusion images (B), sentinel node was clearly localized alongside testicular vein, 1.5 cm caudal to renal vessels. On axial sections, node was clearly visualized, and node could also be identified on CT scan (C). During surgery, sentinel node was clearly depicted with portable γ-camera (D). After localization with ^{125}I-seed pointer, node was removed and only radioactivity in liver and spleen remained (D), confirming excision of only the radioactive hot spot.

a few seconds, we decided that imaging of at least 1 min is required for accurate postexcision monitoring. However, whether a very hot node has been correctly removed will be clear within 20–30 s.

In laparoscopic procedures, where spatial mobility is limited, SPECT/CT images and the visualization of the ^{125}I seed on the laparoscopic probe can lead the surgeon to the sentinel node. In this way, intraoperative identification and localization of the sentinel nodes appears to improve. The portable γ-camera can visualize and identify sentinel nodes close to the injection area, which is nearly impossible with the γ-probe. The ^{125}I-seed signal is not hampered by the ^{99m}Tc signal from the injection area, and therefore, especially nodes near the injection area are more easily localized with this method. If underneath the injection area, however, the node is not visible on the screen of the portable γ-camera. That situation was never the case in our group of patients because the primary tumors were not in the preaortic region.

In 3 patients with weak nodal tracer uptake, the paraaortic sentinel nodes could not be depicted on the screen of the portable γ-camera. Sufficient tracer uptake is required for adequate intraoperative real-time imaging with γ-cameras.

In our practice, there are no additional costs for the use of the ^{125}I seed as a pointer, because remaining seeds that have become too weak for brachytherapy can be used as long as radioactivity is above 10 MBq. We choose to use an iodine source because it is freely available at our institute. Another reason is that the energy peak of ^{125}I (35 keV) differs greatly from the energy peak of ^{99m}Tc (140 keV), making optimal separation of the 2 signals on the screen of the portable γ-camera possible. Other γ-ray–emitting sources (e.g., barium, armarium, or gadolinium) could also be used as a pointer on the screen of the portable γ-camera. However, to be able to distinguish both signals, the energy peak from the isotope used as the point source should differ substantially from the energy peak of the tracer (^{99m}Tc).

CONCLUSION

If preoperative planar lymphoscintigraphy shows possible paraaortic lymph nodes, SPECT/CT will show the exact location of those nodes in relation to abdominal anatomic structures (mainly the large vessels) and will therefore moderate intraoperative tracing of those nodes. Furthermore, SPECT/CT can detect sentinel nodes if they are not visualized on planar images. If drainage to retroperitoneal nodes is expected, routine use of SPECT/CT is advisable. Intraoperative localization of paraaortic sentinel nodes by means of a laparoscopic γ-probe and intraoperative real-time imaging with a portable γ-camera has shown good detection and removal rates in our population. The portable γ-camera can also provide certainty about the completeness of the sentinel lymphadenectomy, showing remaining radioactivity after removal of the node.

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