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Advancing surgical guidance: from (hybrid) molecule to man and beyond

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CHAPTER 5

A HYBRID RADIOACTIVE AND FLUORESCENT TRACER FOR SENTINEL NODE BIOPSY IN PENILE CARCINOMA AS A POTENTIAL REPLACEMENT FOR BLUE DYE

Adapted from: Brouwer OR*, van den Berg NS*, Mathéron HM, van der Poel HG, van Rhijn BW, Bex A, Valdés Olmos RA, van Leeuwen FWB, Horenblas S. Eur Urol. 2014;65:600-609.
* = Shared first authorship.

ABSTRACT

BACKGROUND Sentinel node (SN) biopsy in penile cancer is typically performed using a combination of radiocolloid and blue dye. Recently, the hybrid radioactive and fluorescent tracer indocyanine green (ICG)-^{99m}Tc-nanocolloid was developed to combine the beneficial properties of both radio-guidance and fluorescence imaging.

OBJECTIVE To explore the added value of SN biopsy using ICG-^{99m}Tc-nanocolloid in patients with penile carcinoma.

DESIGN, SETTING, AND PARTICIPANTS
Sixty-five patients with penile squamous cell carcinoma were prospectively included (January 2011 to December 2012). Preoperative SN mapping was performed using lymphoscintigraphy and single-proton emission computed tomography supplemented with computed tomography (SPECT/CT) after peritumoural injection of ICG-^{99m}Tc-nanocolloid. During surgery, SNs were initially approached using a gamma probe, followed by patent blue dye and/or fluorescence imaging. A portable gamma camera was used to confirm excision of all SNs.

SURGICAL PROCEDURE Patients underwent SN biopsy of the cN0 groin and treatment of the primary tumor.

OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS The number and location of preoperatively identified SNs were documented. Intraoperative SN identification rates using radio- and/or fluorescence guidance were assessed and compared with blue dye. Statistical evaluation was performed using a two-sample test for equality of proportions with continuity correction.

RESULTS AND LIMITATIONS Preoperative imaging after injection of ICG-^{99m}Tc-nanocolloid enabled SN identification in all patients (a total of 183 SNs dispersed over 119 groins). Intraoperatively, all SNs identified by preoperative SN mapping were localized using combined radio-, fluorescence-, and blue dye guidance. Fluorescence imaging enabled visualization of 96.8% of SNs, while only 55.7% was stained by blue dye ($p<0.0001$). The tissue penetration of the fluorescent signal, and the rapid flow of blue dye limited the detection sensitivity. A tumor-positive SN was found in seven patients.

CONCLUSIONS ICG-^{99m}Tc-nanocolloid allows for both preoperative SN mapping and combined radio- and fluorescence-guided SN biopsy in penile carcinoma patients and significantly improves optical SN detection compared with blue dye.

INTRODUCTION

Penile carcinoma predominantly shows metastatic spread via the lymphatic system. As a consequence, lymph node staging in penile carcinoma has strong prognostic implications [1]. Since only 20-25% of patients have regional metastases, performing a complete lymph node dissection (LND) may be overtreatment, resulting in considerable morbidity [2]. Sentinel node (SN) biopsy is a validated procedure to detect (micro-)metastases in clinically node-negative groins without the morbidity associated with a complete lymph node dissection. Yet the reliability of SN biopsy depends on successful pre-, intra-, and postoperative identification of all (tumor-positive) SNs [3,4].

Generally, SNs are preoperatively identified using lymphoscintigraphy after a peritumoral injection of a radioactive tracer (^{99m}Tc-nanocolloid is the gold standard in Europe). With the introduction of single photon emission computed tomography supplemented with computed tomography (SPECT/CT), it has become possible to detect the SNs in their anatomic context [5]. This three-dimensional (3D) information can be used to accurately plan the surgical approach.

The intraoperative procedure traditionally relies on localization of the radioactive signal using a handheld gamma-ray detection probe (hereafter referred to as gamma probe) that generates an acoustic readout. A portable gamma camera has been introduced with the ability to acquire intraoperative overview images of radioactive hot spots. Unfortunately, the current portable gamma cameras are unable to provide adequate anatomic information, leaving the radioactive signal depicted against a two-dimensional black background [6]. To anatomically visualize the SNs within the surgical field, a second injection with blue dye is usually administered shortly before surgery. However, one of the disadvantages of blue dye is that preoperatively defined (radioactive) SNs may not always be stained blue at the time of excision [7]. Moreover, blue dyes stain the injection site, potentially hindering tumor resection, which is generally performed after SN biopsy.

The use of near-infrared fluorescence imaging has characteristics that can be advantageous for intraoperative SN detection: an improved tissue penetration compared to blue dye, and the fluorescent signal is only visible using a dedicated near-infrared fluorescence camera system, leaving the surgical field unstained [8]. Similar to blue dye, fluorescence imaging normally also requires an additional injection of, for example, the clinically approved indocyanine green (ICG). Like blue dye, ICG migrates quickly through the lymphatic system, resulting in a limited diagnostic window. The larger radioactive ^{99m}Tc-nanocolloid does not have this limitation [9].

To combine the beneficial properties of both radio guidance and fluorescence imaging, ICG-^{99m}Tc-nanocolloid was developed [9,10]. This hybrid tracer expands the gold standard radiotracer ^{99m}Tc-nanocolloid with a near-infrared fluorescent component (ICG) without altering the well-validated tracer kinetics of the gold standard [11]. Pilot studies have demonstrated the feasibility of this hybrid approach in head-and-neck malignancies and prostate cancer [12-14]. Its added value, however, remains to be assessed in a more extensive study population. The purpose of this study was to evaluate the added value of

SN biopsy using ICG-^{99m}Tc-nanocolloid compared with blue dye in a large cohort of patients with penile carcinoma.

METHODS

PATIENTS

A total of 84 consecutive patients presenting with ≥T1G2 tumors were prospectively included. The SN procedure was performed following the European Association of Urology penile cancer guidelines [15]. The study protocol was approved by the institutions' medical ethics committees (N09DRF, NL 26699.031.09).

Seventeen patients were excluded from the study. Nine patients were previously included in a reproducibility study [11]. In five patients, excised SNs were only evaluated ex vivo. In one patient no blue dye was used, one patient presented with a penile melanoma and another patient presented with a carcinoma of the urethra.

Characteristics of the remaining 65 evaluated patients are listed in Table 1. Only patients with at least one cN0 groin were enrolled. In patients with proven unilateral nodal involvement (n=10) or with a previous unilateral lymph node dissection (n=1), only the contralateral cN0 groin was included for SN biopsy, resulting in a total of 119 included groins. Patients were scheduled for SN biopsy or repeat SN biopsy (n=6) in case of a recurrent tumor, followed by treatment of the primary tumor or for SN biopsy only in case of previous penile surgery in another center.

Table 1. Patient characteristics

No of included patients	65
Average age (years)	67 (range 34-93, median 66)
Recurrence (repeat SN biopsy), no.	6
Tumor stage	
- T1	25
- T2	34
- T3	6
Groins	
- cN0 (with or without) FNAC	119
- cN1 (tumor + FNAC)	10
- Previous LND	1
Total included groins for SN biopsy	119

SN = sentinel node; FNAC = fine needle aspiration cytology; LND = lymph node dissection.

TRACER PREPARATION

ICG-^{99m}Tc-nanocolloid was prepared as previously described [11]. Subsequently, approximately 90 MBq±10% was subtracted from the vial containing the ICG-^{99m}Tc-nanocolloid solution. Saline was then added to reach a total volume of 0.4 mL in the syringe. All procedures were performed under good manufacturing practice (GMP-z) and under supervision of the institution's pharmacist.

PREOPERATIVE PROCEDURE

A schematic overview of the study setup is given in Figure 1. ICG-^{99m}Tc-nanocolloid was intradermally injected proximally around the tumor in three or four deposits on the same day or on the day before surgery. No adverse reactions were observed.

Dynamic lymphoscintigraphy was performed during 10 min immediately after injection, using a dual-head gamma camera (Symbia T; Siemens, Erlangen, Germany). Static planar gamma camera images were acquired 15 min post-injection (early) and 2 h post-injection (late), followed by SPECT/CT imaging (Symbia T; Siemens, Erlangen, Germany). Lymph nodes draining from the site of injection through an own lymphatic vessel or a single radioactive lymph node in the groin were identified as SNs [16]. SNs were anatomically localized using multiplanar reconstruction, which enabled comparison of fused SPECT/CT

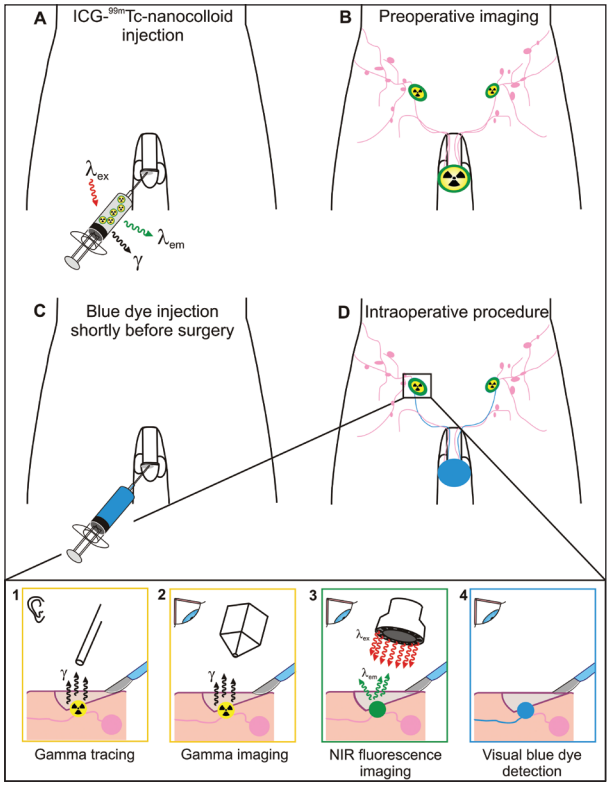

Figure 1. Schematic overview of the study setup. A) After injection of indocyanine green (ICG)-^{99m}Tc-nanocolloid, preoperative imaging of the sentinel nodes (SNs) is performed using lymphoscintigraphy and B) single-proton emission computed tomography supplemented with computed tomography. C) Shortly before surgery, blue dye is also administered. D) Intraoperatively, the radioactive component of the hybrid tracer allows for radioguided SN localization using (1) a gamma-ray detection probe and (2) the portable gamma camera. In addition, the fluorescent component allows for SN visualization using (3) a near-infrared fluorescence camera. (4) Intraoperative SN identification rates using radio- and/or fluorescence guidance were assessed and compared with blue dye. SN = sentinel node. γ = gamma; λ_{ex} = excitation light; λ_{em} = emission light; NIR = near-infrared.

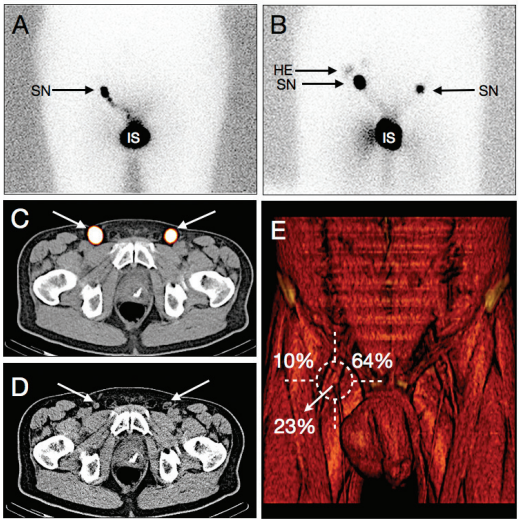

Figure 2. Sentinel node mapping after indocyanine green-^{99m}Tc-nanocolloid injection using lymphoscinti graphy and single proton emission computed tomography supplemented with computed tomography (SPECT/CT). A) Early lymphoscintigram showing drainage to a right inguinal SN (arrow); B) Late lymphoscintigraphy also reveals drainage to the left-side SN, as well as higher (iliac) echelon drainage on the right side (arrows). C) Axial fused SPECT/CT images depicting both radioactive SNs; D) Corresponding CT showing the lymph nodes (arrows). E) Drainage in penile cancer and the five inguinal zones of Daseler: In this study, most of the SNs (64.2%) were located in the medial superior zone, 10.1% in the lateral superior zone, and 23.5% in the central zone, which is concordant with the expected drainage pattern using ^{99m}Tc-nanocolloid alone [5]. SN = sentinel node; HE = higher-echelon node; IS = injection site.

images with the concomitant CT. Additionally, 3D SPECT/CT display of SNs in relation to the anatomic structures was accomplished using volume rendering. Distribution of the SNs on SPECT/CT was determined by dividing the groin into five different zones, according to Daseler (Figure 2E).

INTRAOPERATIVE PROCEDURE

Shortly before surgery, approximately 1.0 mL patent blue dye V (Laboratoire Guerbet, Aulnay-Sous-Bois, France) was intradermally administered in all patients in the same way as the ICG-^{99m}Tc-nanocolloid injection. A portable gamma camera (Sentinella; OncoVision, Valencia, Spain) (Figure 3A) was then used to acquire a pre-incision reference image, as previously described [17]. After incision, SNs were initially pursued with a gamma probe (Neoprobe; Johnson & Johnson Medical, Hamburg, Germany). During surgical exploration, alternating attempts were made to optically visualize the SNs via near-infrared fluorescence imaging using a handheld fluorescence camera (PhotoDynamic Eye; Hamamatsu Photonics K.K., Hamamatsu, Japan) (Figures 3C and 4) and/or visual detection of the blue dye. Fluorescence imaging required the lights in the operating room to be dimmed for a brief period to minimize the background signal. After excision of the SNs, the surgical area was scanned using the gamma probe and palpated to search for clinically suspicious nodes. Subsequently, a second image was acquired with the portable gamma camera to verify complete SN removal.

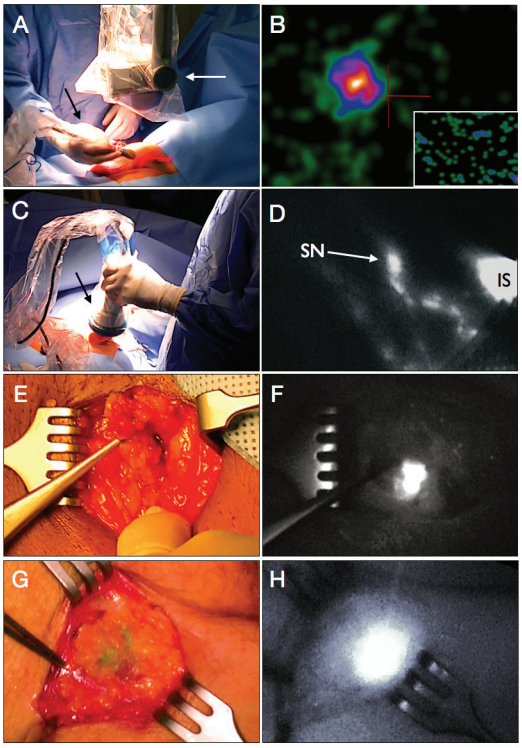

Figure 3. Combined intraoperative radio- and fluorescence-guided sentinel node biopsy. A) The radioactive signature of the hybrid tracer enables initial SN detection using a conventional gamma probe (black arrow) and a portable gamma camera (orange arrow); B) The portable gamma camera provides an overview image of the SNs that can be used to verify complete SN removal after excision (figure inlay); C) As the SN is approached, the fluorescent signature of the hybrid tracer enables SN visualization using a near-infrared fluorescence camera; D) In some patients, the SN (arrow) and its afferent lymphatic duct, as well as the injection site, could be visualized through the intact skin; E-F) A radioactive, non-blue SN clearly seen via fluorescence imaging of the hybrid tracer; G-H) The improved tissue penetration of the fluorescence signal enables clearer visualization of the SN and its borders compared to blue dye. SN = sentinel node.

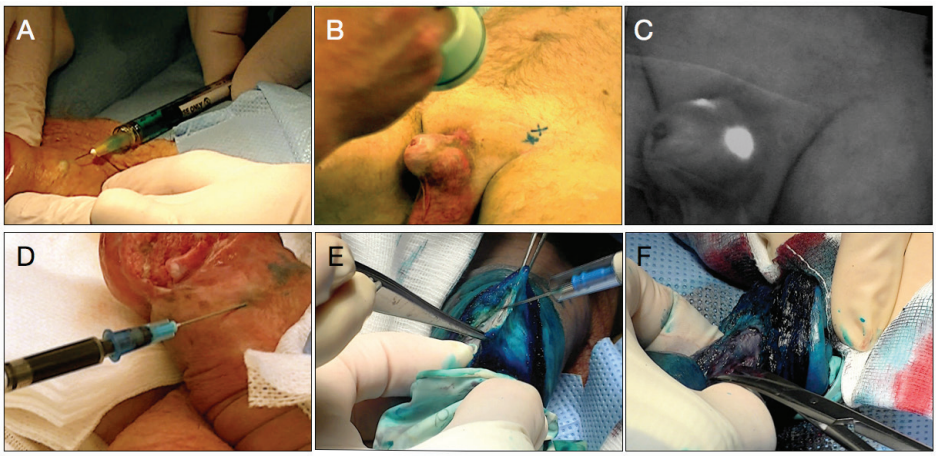

Figure 4. The fluorescent signal is only visible using a dedicated near-infrared fluorescence camera system, leaving the surgical field unstained. A) Hybrid tracer administration; B-C) The injection sites are only visible when using the fluorescence camera; D) Intraoperative blue dye injection; E-F) Blue dye stains the surgical field blue, which may be a hindrance during penile surgery.

If remaining radioactivity was observed at the site of a previously excised SN, it was considered part of a cluster of multiple SNs close together and, thus, as an additional SN, which was also harvested. Intraoperative SN identification rates using radio- and/or fluorescence guidance were assessed and compared with blue dye. Statistical evaluation of the difference between the number of fluorescent- and blue dye stained nodes was performed using a two-sample test for equality of proportions with continuity correction.

PATHOLOGY AND EX VIVO ANALYSES

Harvested SNs were bisected, formalin-fixed, paraffin-embedded, and cut at six or more levels (50-150 µm intervals). Paraffin sections were stained with hematoxylin and eosin and with cytokeratin using an anticytokeratin antibody, clone AE1/AE3 (cat. no. MS-343-P; Thermo Fisher Scientific Inc., Waltham, MA, USA).

To study the distribution of ICG-^{99m}Tc-nanocolloid in tumor-positive SNs, 5-mm sections of four tumor-positive SNs (two patients) were cut and deparaffinized with xylene (twice, 10 min) and rehydrated in 100% ethyl alcohol (EtOH) (twice, 10 min), 70% EtOH (twice, 5 min), and water (twice, 5 min). Slides were subsequently air dried for 2 h and scanned on an Odyssey scanner (LI-COR Biosciences, Lincoln, NE, USA) for the presence of ICG (setting: 800 nm; focus offset: 0 mm; intensity: 10).

RESULTS

PREOPERATIVE RESULTS

An average dose of 79 MBq ICG-^{99m}Tc-nanocolloid was preoperatively injected on the same day (n=38) or on the day before surgery (n=27). Lymphoscintigraphy and SPECT/CT visualized at least one SN in all patients (100% visualization rate). Only 89 SNs (48.5%) were visible on the early planar lymphoscintigrams, whereas 160 SNs (87.4%) were identified on the late planar lymphoscintigrams. One patient declined to undergo SPECT/CT due to claustrophobia (four SNs at lymphoscintigraphy). In the remaining 64 patients, SPECT/CT revealed 26 SNs in 18 patients that were not seen on the lymphoscintigrams. Furthermore, SPECT/CT helped to define three nodes (in three patients) as iliac higher-echelon nodes (these were considered as inguinal SNs based on lymphoscintigraphy). In sum, a total of 183 SNs were preoperatively identified dispersed over 119 groins (median: three SNs per patient; range 1-6) (Table 2).

Table 2. Results

Preoperative SN results	
- Lymphoscintigraphy, early	89
- Lymphoscintigraphy, late	160
- SPECT/CT*	179
Total number of identified SNs	183 (average 2.9; median 3, range 1-6)
Location of SNs, no.	
- Medial superior zone	115 (64.2%)
- Lateral superior zone	18 (10.1%)
- Central zone	42 (23.5%)
- Medial inferior zone	3 (1.7%)
- Lateral inferior zone	1 (0.6%)
Total	179*
Intraoperative SN results	
- Traceable with probe (in vivo)	215 (97.3%)
- Radioactive (ex vivo)	220 (99,6%)
- Fluorescent (in vivo)	214 (96.8%)**
- Fluorescent (ex vivo)-	220 (99.6%)
- Blue (+ radioactive/fluorescent)	123 (55.7%)**
- Blue (non-radioactive/non-fluorescent)	1 (0.45%)
Total number of excised SNs	221 (average 3.4; median 3, range 1-9)
Pathology	
Total number of SNs	221 (average 3.4; median 3, range 1-9)
Total number of lymph nodes	239
Number of tumor-positive SNs	10 (7 patients, 7 groins)

*One patient refused to undergo SPECT/CT. **Statistical significant difference between surgically visualized fluorescent and blue SNs ($p<0.0001$). SN = sentinel node; SPECT/CT = single photon emission computed tomography combined with computed tomography.

Bilateral drainage was observed in 52 of the 54 patients (96.3%) with clinically N0 groins. The remaining two patients received tracer re-injection; lymphoscintigraphy 1 h later showed bilateral drainage in both cases. In seven of the ten patients with a clinically N1 groin based on ultrasound and fine-needle aspiration cytology, bilateral drainage was observed. The remaining three patients only showed drainage to the unaffected groin. One patient who presented with a recurrent tumor already had received a previous unilateral lymph node dissection and only showed drainage to the contralateral side.

Most of the SNs (64.2%) were located in the medial superior zone of the groin, 10.1% was located in the lateral superior zone and 23.5% in the central zone (Figure 2E). Drainage to an inferior quadrant was seen in four patients (2.2%) with a recurrent tumor who had already received a previous SN biopsy, which may have caused an altered lymphatic drainage pattern.

INTRAOPERATIVE RESULTS

SN biopsy was started 3-27 h (mean: 13 h; median: 7 h) after injection of ICG-^{99m}Tc-nanocolloid. All 183 preoperatively defined SNs could be localized using a combination of radio- and fluorescence guidance. Only one blue node was found during surgery that was neither radioactive nor fluorescent. This node was also considered a SN and harvested.

Post-excision imaging with the portable gamma camera revealed remaining activity at the location of the previously excised SN in 22 of 65 patients (33.8%). In these patients, the area was explored once again, yielding 37 additional SNs. In six of these cases, a remaining SN was identified using the portable gamma camera after no residual activity was detected during initial scanning with the gamma probe (Figure 5).

Of the total of 221 excised SNs (Table 2, Figure 6), 97.3% could be roughly localized using the gamma probe. The remaining 2.7% (in four patients) could not be detected using the gamma probe because the radioactive signal was too weak due to radioactive decay (surgery was performed >24 h after tracer injection and relatively low tracer uptake in these SNs was observed on preoperative images). These nodes were localized using fluorescence imaging, which does not suffer from decay.

In total, 96.8% of the excised SNs were intraoperatively visualized with the fluorescence camera during surgery; 55.7% had stained blue at the time of excision. This means that 41.1% more SNs could be optically identified via fluorescence imaging ($p<0.0001$). In only 22 patients, all of the preoperatively defined radioactive SNs were also stained blue. In eight patients, no blue SN was found at all, whereas a fluorescent SN could be visualized in every patient. Fluorescence imaging offered an improved tissue penetration compared with blue dye, allowing earlier visualization of the SNs. This was exemplified by cases in which superficially located SNs were visible through the skin (Figure 3).

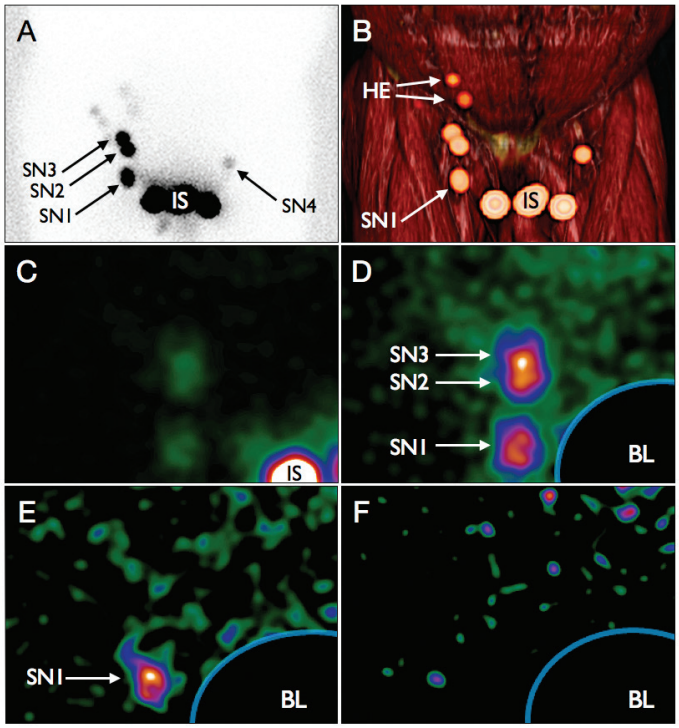

Figure 5. Post-excision confirmation of complete sentinel node removal using a portable gamma camera. A) Lymphoscintigram showing the injection site (IS) and three SNs on the right side and on SN on the left side; B) 3D volume-rendered SPECT/CT image revealing that the most caudal SN on the right side is located in an inferior Daseler zone; C) Initial image acquired with the portable gamma during surgery mainly depicting the high radioactive signal coming from the injection site (IS); D) Blocking the injection site using the Sentinella suite software visualizes the three SNs on the right side; E) Post-excision image after removal of three radioactive and fluorescent nodes shows that the most caudal SN is still in situ; F) After excision of the remaining SN, which proved to be tumor-positive at histopathology, complete SN removal is verified. SN = sentinel node; HE = higher-echelon node; BL = blocked injection site using Sentinella suite software. 3D = three-dimension, IS = injection site.

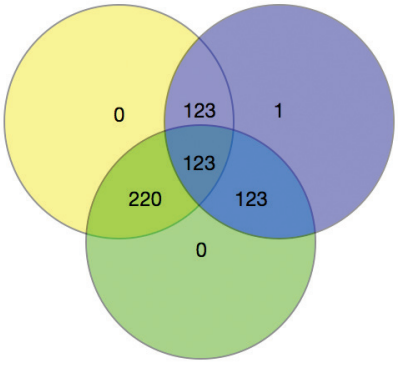

Figure 6. Ex vivo sentinel node evaluation. Excised nodes were radioactive (yellow circle), fluorescent (green circle) and/or blue (blue circle). Of the excised SNs, 220 were both radioactive and fluorescent. Of these SNs 123 were also blue. Only one SN was non-radioactive, non-fluorescent, but blue. SN = sentinel node.

HISTOPATHOLOGY FINDINGS AND EX VIVO ANALYSES

Pathologic analyses of the excised SNs revealed metastases in 10 SNs (seven of 65 patients (19.8%), seven of 119 groins (6%)). Three patients with a tumor-positive SN also had a tumor-positive node at ultrasound guided fine needle aspiration cytology in the contralateral groin, for which they received an LND in the same session. All seven patients with a tumor-positive SN were scheduled for an LND of the affected groin.

The median size of the SN metastases was 8 mm (mean: 7.94 mm; range: 1.5-14 mm). In one patient, one of the tumor-positive SNs was an additional SN, which was excised after being identified using the portable gamma camera (Figure 5). While all 10 tumor-positive SNs were both radioactive and fluorescent only seven stained blue. The single non-radioactive and non-fluorescent SN that was blue was tumor-negative.

Additional ex vivo examination of four tumor-positive SNs revealed that the fluorescent signal was mainly present in the unaffected lymphatic tissue of the SN (Figure 7).

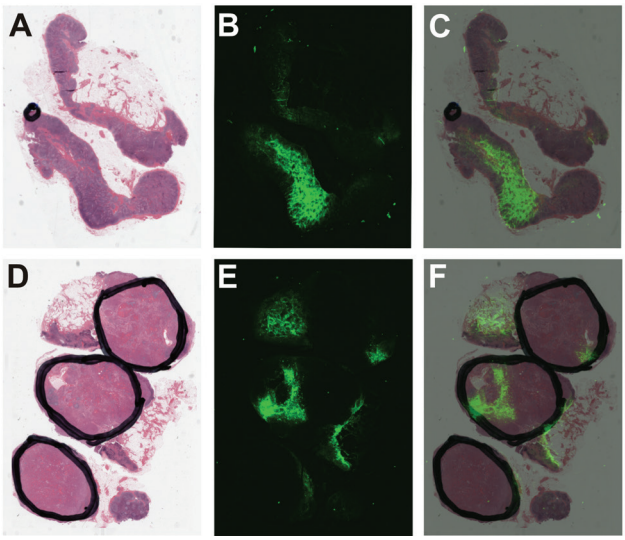

Figure 7. Ex vivo examination of the fluorescent signal in tumor-positive sentinel nodes. A) A SN containing a micrometastases (black circle); B-C) Ex vivo fluorescence imaging reveals that the fluorescent signal is mainly present in the remaining unaffected lymphatic tissue of the node; D) A SN containing a macrometastases (black circle); E-F) Ex vivo fluorescence imaging.

DISCUSSION

SN biopsy for penile carcinoma, using a radiocolloid (^{99m}Tc-nanocolloid) in combination with blue dye, is a well-established procedure to accurately stage clinically node-negative groins [7,15,18]. Here, we demonstrate that the hybrid tracer ICG-^{99m}Tc-nanocolloid improves optical SN detection in comparison with blue dye. In our series of 65 patients, all of whom were injected with both the hybrid tracer ICG-^{99m}Tc-nanocolloid and blue dye, 96.8% of the SNs could be intraoperatively visualized using fluorescence imaging, whereas merely 55.7% of the SNs were stained blue at time of excision ($p<0.0001$). This statistically significant difference suggests that optical SN detection using ICG-^{99m}Tc-nanocolloid can potentially replace blue dye. The low percentage of blue-stained nodes identified in this study is in line with a recent meta-analysis of 19 studies by Sadeghi et al. that reported a pooled SN detection rate of 60% for blue dye alone [7].

There are several potential explanations as to why >40% of the SNs that were identified using ICG-^{99m}Tc-nanocolloid were not stained blue. Consistent with previous reports in areas with rapid lymphatic drainage (e.g., the head-and-neck region), the blue dye may already have passed the SN at the time of excision [13,19]. However, lymphatic drainage in penile carcinoma can also be more delayed, as demonstrated by the limited number of visualized SNs on early lymphoscintigraphy in this series. Hence, the blue dye may not yet have reached the SN at the time of excision in some cases. Together these factors limit the diagnostic window and potentially require timed (re-)injections prior to, or during, the operation. It is also important to note that only 70% of the tumor-positive SNs identified with ICG-^{99m}Tc-nanocolloid stained blue, whereas the single SN (0.45%) that was blue, but did not contain ICG-^{99m}Tc-nanocolloid, was tumor-negative.

SN distribution in this study was similar to a previous anatomic SN mapping study using SPECT/CT, showing that drainage was mainly directed to the superior and central inguinal zones [5]. The current study further substantiates results from a previous reproducibility study showing that ICG-^{99m}Tc-nanocolloid preserves the gold standard in preoperative SN mapping (lymphoscintigraphy and SPECT/CT) [11]. The addition of the fluorescent moiety extends the window for optical SN detection using fluorescence imaging up to (or possibly even beyond) 27 h after tracer injection. This enables the use of ICG-^{99m}Tc-nanocolloid in both one- and two-day protocols, without the need for additional injections during surgery.

Ex vivo fluorescence imaging confirmed the presence of fluorescence in all radioactive SNs. Therefore, the 3.2% of SNs that could not be visualized intraoperatively using the near-infrared fluorescence camera were probably covered with overlying (fatty) tissue so the fluorescent signal was blocked. This illustrates that while the tissue penetration of near-infrared fluorescence imaging is superior to blue dye, it is still limited compared with the radioactive signal. This is further demonstrated by the finding that SNs were only visible through the skin when located superficially in patients with a low body mass index (Figure 3), which is in line with a previous report on the use of ICG in patients with vulvar

cancer [20]. Improvement of near-infrared fluorescence camera systems may help further expand the applicability of intraoperative fluorescence guidance [21]. For the time being, the radioactive signature of the hybrid tracer still remains crucial to enable reliable SN mapping. For example, the ability to acquire an overview image with the portable gamma camera during surgery allowed the identification of residual SNs that could have been missed with the gamma probe or near-infrared fluorescence camera (Figure 5), thereby providing confirmation of complete SN removal in the operating room.

The fluorescent signature of ICG-^{99m}Tc-nanocolloid provides the unique possibility to study tracer distribution in ex vivo tissue specimens, long after the radioactive signal has decayed [22]. In this study, ex vivo imaging using a sensitive fluorescence camera confirmed the presence of a fluorescent signal in all tumor-positive SNs with metastases ≤14 mm (Figure 7). Apparently, when unaffected lymphatic tissue is still present, the presence of tumor tissue in a node does not necessarily cause rerouting of the lymph flow [23].

CONCLUSION

ICG-^{99m}Tc-nanocolloid allows for combined radio- and fluorescence-guided SN biopsy in penile carcinoma patients while retaining the properties of the radiocolloid that are optimal for preoperative SN identification using lymphoscintigraphy and SPECT/CT. The fluorescent component significantly improved intraoperative optical SN identification compared with blue dye, indicating that by using this hybrid approach, blue dye may be omitted.

SURGERY IN MOTION

The Surgery in Motion video accompanying this article can be found in the online version at http://dx.doi.org/10.1016/j.eururo.2013.11.014 and via www.europeanurology.com.

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