Journal of Nuclear Medicine, published on May 26, 2016 as doi:10.2967/jnumed.115.171645

Towards (hybrid) navigation of a fluorescence camera in an open surgery setting

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Running head

Fluorescence camera navigation

Synopsis

Fluorescence guidance is limited by its superficial nature. By integrating fluorescence with radioguidance, and using a navigation set-up, in-depth information can be used to provide directional guidance during fluorescence camera placement.

Word count

2492

Abstract (max. 150 words: 150)

Introduction With the introduction of the hybrid tracer indocyanine green (ICG)-^{99m}Tc-nanocolloid, a direct relation between preoperative imaging and intraoperative fluorescence-guidance was established. However, fluorescence guidance is limited by its superficial nature. This study evaluated the feasibility of a nuclear medicine-based navigation concept that allowed intraoperative positioning of a fluorescence camera (FC) in the vicinity of preoperatively defined ICG-^{99m}Tc-nanocolloid containing sentinel nodes (SNs).

Methods Five patients with penile cancer scheduled for SN biopsy were injected with ICG-^{99m}Tc-nanocolloid followed by preoperative SPECT/CT imaging. The navigation device was used to provide a real-time augmented reality overlay of the SPECT/CT images and video output of the FC. This overlay was then used for FC navigation.

Results SPECT/CT identified thirteen SNs in nine groins. FC navigation was successful for all twelve intraoperatively evaluated SNs (average error: 8.8 mm, range: 0-20 mm).

Conclusion This study reveals the potential benefits of FC navigation during open surgery procedures.

Key words

Augmented-reality, Sentinel node biopsy, Navigation, Fluorescence imaging, SPECT/CT

Introduction

While interventional guidance can be provided using multiple modalities, due its appealing possibility to provide detailed and real-time guidance, fluorescence imaging (FI) is receiving increasing interest. FI is highly effective in superficial applications at known locations, but has a limited in-depth potential *(1)*. Radioguidance technologies on the other hand have been shown to have a great in-depth potential and even allow for preoperative confirmation of tracer uptake using e.g. single photon emission computed tomography combined with computed tomography (SPECT/CT) *(2)*.

When separate approaches are used to provide pre- and intraoperative guidance, information may get lost between diagnostic imaging and the operation theatre. Discrepancies in findings may subsequently result in over- or under-treatment of the patient. To solve these translational issues, and to enable a “best of both worlds” scenario, a hybrid surgical guidance concept is advocated. This concept is based on integrating multiple complementary features that are of value for preoperative imaging (nuclear medicine) and intraoperative (fluorescence) image-guided surgery *(3)*. This can, in part, be realized by using a hybrid tracer that contain two distinct signals, e.g. the sentinel node (SN) tracer indocyanine green (ICG)-^{99m}Tc-nanocolloid *(1)*. Recently, this hybrid concept was expanded beyond the field of tracer development to hardware-based integration of radioguidance and FI modalities *(4,5)*.

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Surgical navigation using three dimensional (3D) nuclear medicine findings has been used to provide directional movement to the lesion of interest, in the form of in-depth information. This technology was considered particularly valuable during SN biopsy procedures *(6–8)*. Apart from navigation of a gamma-probe, the navigation set-up has also been usef for laparoscope *(4),* gamma camera *(7)*, and ultrasound probe *(9)* positioning. We thus reasoned it should be possible to also navigate a fluorescence camera (FC) in an open surgery setting (Fig.1).

For penile cancer SN biopsy we have previously demonstrated that ICG-^{99m}Tc-nanocolloid provides superior optical guidance towards SNs compared to blue dye *(10).* However, in patients with increased fatty tissue surrounding the SNs, the limited tissue penetration of the fluorescent signal was not always sufficient to optically identify the SN(s) via fluorescence guidance *(10)*. Although rhe conventional radioguided approach was effective in identifying these SNs, these modalities provided no depth information to the target. By integrating navigation into the procedure, we made an attempt to overcome these shortcomings for penile cancer patients that were to undergo a SN biopsy procedure.

Methods

Patients

Five patients with cT1-2N0Mx penile cancer *(11)* scheduled for SN biopsy and subsequent treatment of the primary tumor were prospectively included. All included groins were clinically node-negative *(10)*.

The institutional review board of the The Netherlands Cancer Institute - Antoni van Leeuwenhoek approved this study and all subjects signed a written informed consent. Procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki declaration of 1975, as revised in 2008.

Hybrid tracer preparation, injection and preoperative sentinel node mapping and (histo)pathology

Hybrid tracer preparation, injection and preoperative SN mapping as well as (histo)pathological analysis protocols can be found in the Supplemental Information (SI) .

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Specifications of navigation device and fluorescence camera (software and hardware)

A prototype FC, the modified-PhotoDynamicEye (m-PDE; Hamamatsu Photonics KK, Hamamatsu, Japan) was used to provide fluorescence guidance. This FC has the ability to switch between white light and near-infrared FI mode and works under ambient light conditions (12).

As navigation device, the declipseSPECT (SurgicEye, Munich, Germany) was used in which DICOM files of preoperatively acquired SPECT/CT data-sets can be loaded *(4,8)*.

To allow the FC to be tracked and navigated in the preoperative SPECT/CT images, a navigation display similar to the one generated for the conventional gamma probe was used (8). Herein an overlay of the 3D SPECT/CT images onto the patient was displayed in the video-feed of the FC. This same view also showed the distance from the tip of the FC to the designated targets (SNs).

A more detailed technical description of the navigation set-up and the reference trackers can be found in the SI.

Surgical procedure: Intraoperative navigation to the sentinel node(s)

Before incision, the FC was navigated in the preoperatively acquired SPECT/CT images towards the SN(s) in the groin. During this process the distance between the FC and the center of the SN was provided. If the SN was not visible through the skin via FI, the gamma probe (Neoprobe; Johnson & Johnson Medical, Hamburg, Germany) was used to determine the site for incision.

After incision, alternating gamma tracing and FI allowed localization of the SN(s) in the groin. Upon localization of the SN, the FC was again navigated to determine the correlation between the acquired fluorescence image and the projected SPECT/CT image. The error of navigation (in the coronal plane) was determined by measuring the distance between the center of the radioactive hotspot and the center of the fluorescence hotspot as seen on-screen from the perspective of the FC.

Results

Preoperative sentinel node mapping

Preoperative imaging revealed bilateral drainage in four of the five included patients. In the remaining patient only unilateral drainage was seen. With SPECT/CT imaging a total of 13 SNs, dispersed over nine groins, was identified of which 30.8% could already be visualized on the lymphoscintigrams acquired 15 min post-injection of the hybrid tracer (Table SI1).

Navigation

In the navigation set-up, the overlay of the SPECT/CT images and the FC video feed was displayed on-screen (Fig. 1, Fig. 2 and Fig. 3). Intraoperatively, twelve of the thirteen SNs seen on preoperative imaging were navigated to with the FC (See supplemental movie file) with an average navigation error of 8.8 ± 9.1 mm (median 7.5 mm; range 0-20 mm). The one SN that was resected without using navigation was omitted due to logistical reasons. Intraoperative repositioning of the $RT_{patient}$ directly resulted in a large navigation error (see table S1 patient 3 and 4). Only in patient 4 we were able to correct this $RT_{patient}$ placement using the preoperative placed skin markings, thereby reducing the navigation error for the other SNs of this patient to 0 mm (Table SI1).

In two patients (patient 2 and 3), upon localization of the SN we experienced that the hotspot in the preoperative images contained multiple (clustered) SNs. This resulted in the intraoperative identification of two additional SNs.

Overall, the navigation procedure was not found to be of influence on the length of the operation (average operation time: 91 min, including the primary tumor treatment).

Discussion

In this proof-of-concept study during open surgical SN biopsy procedures, we demonstrate the feasibility of the hybrid navigator concept. This integrated approach provides an important step in the evolution of hybrid surgical guidance as it allows preoperative imaging information to be physically linked to FI in the intraoperative setting. Not only does merging of modalities help prevent a mismatch in findings, it also provides a step towards reducing space (e.g. in m^2 they take up in the operation theatre).

A fairly ideal evaluation set-up was found in penile cancer patients since SNs were rather easy to locate because of their superficial location. The main advantage of adding navigation in the hybrid surgical guidance concept was the improved directional feedback including depth estimation. As demonstrated in the current study, with the FC the accuracy of the navigation process could be confirmed or corrected. Similar to as previously reported, the navigation error strongly depended on the accuracy with which we could replace the $RT_{patient}$ during the surgical procedure *(7,8)*. This is further elaborated on in the SI.

By including patients that undergo SN procedures in other anatomies, e.g. in the head-and-neck or axilla, the value of this technique can be further evaluated. Alternative to navigating towards a SN one may also think of using this approach for hybrid tracer-based radioguided occult lesion localization (ROLL) or for a seed-localization set-up wherein hybrid marker seeds are applied *(13,14).* PET-based navigation in combination with intraoperative Cerenkov imaging could also provide an interesting extension *(15)*.

Conclusion

Navigation-based integration of preoperative 3D SPECT/CT information with real-time FI provides an interesting next step in the hybrid surgical guidance concept. If the technology evolves further, its implementation may be extended to other (hybrid) tracers and anatomies.

Acknowledgements

We gratefully acknowledge the surgical staff and the department of nuclear medicine of the Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital for their support and assistance.

Disclosure

This work was partially supported by a Eurostars grant (Hybrid Navigator; Grant No. E! 7555), an NWO-STW-VIDI grant (Grant No. STW BGT11272), and a European Research Council under the European Union's Seventh Framework Program (FP7/2007-2013) grant (Grant No. 2012-306890).

The m-PDE fluorescence camera used in this study was provided by Hamamatsu Photonics K.K. (Hamamatsu, Japan). SurgicEye (Munich, Germany) provided the prototype software for the navigation device.

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Figures

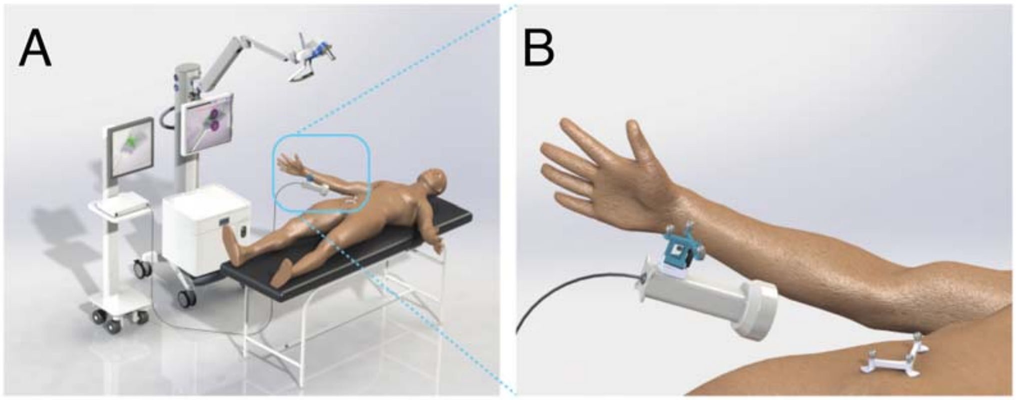

Figure 1. Navigation setup

A: Set-up in the operation theatre. B: A reference tracker is placed on both the patient and the fluorescence camera. Consequently the navigation system is able to localize the fluorescence camera with respect to the position of the patient and the overlayed SPECT/CT images.

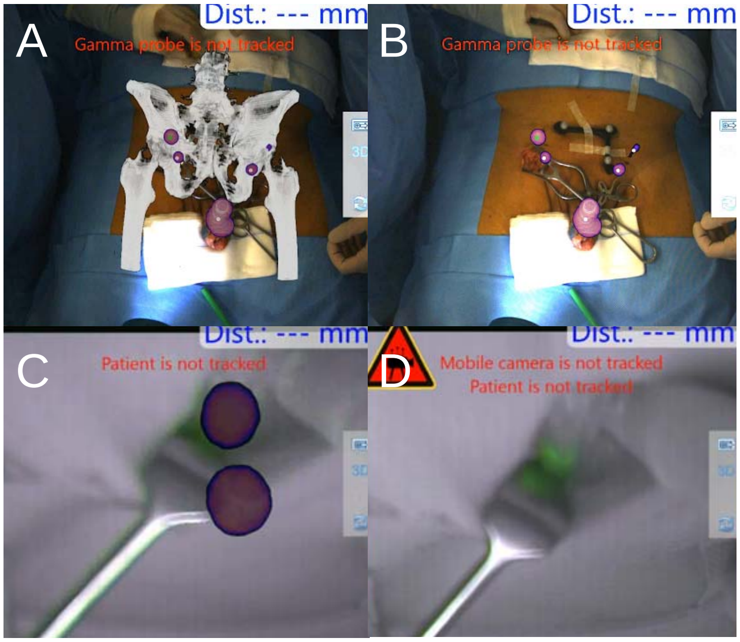

Figure 2. Navigation of the fluorescence camera

The video signal of the overhead camera of the navigation system allows projection of the SPECT/CT (A) or SPECT (B) onto the patient; Bony structures (low-dose CT) and SNs/injection site (SPECT) are shown. C: Overlay of the SPECT on the infrared video signal of fluorescence camera showing 2 SNs; D: Fluorescence imaging optically visualized the SN and thus allowed confirmation of fluorescence camera navigation accuracy.

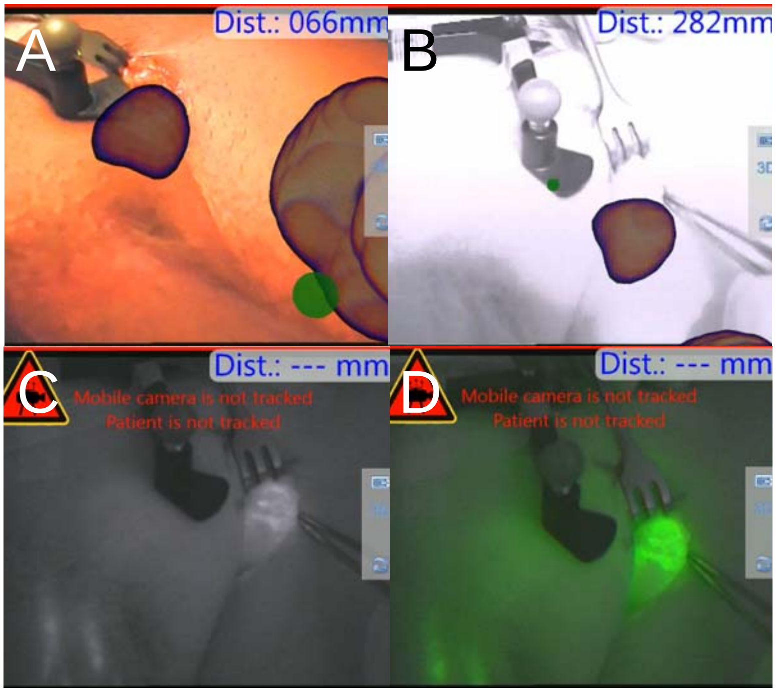

Figure 3. Fluorescence imaging with integrated overlay

A: Preoperative overlay of the SPECT onto the patient from the perspective of the fluorescence camera (white light imaging mode). The primary injected tumor and close to the reference tracker the SN are shown; B: Preoperative overlay of the SPECT onto the patient from the perspective of the fluorescence camera (fluroescence imaging mode) illustrating the influence the flickering caused by the tracking signal of the navigation device has on the ability to visualize the fluorescence signal in the SN (C and D, in black-and-white or pseudo-colored green, respectively).