Innovating image-guided surgery: Introducing multimodal approaches for sentinel node detection

Brouwer, O.R.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: https://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Image navigation as a means to expand the boundaries of fluorescence guided surgery


Purpose: To provide a proof of how intraoperative navigation based on preoperative SPECT/CT images may help improve hybrid radio- and fluorescence guided surgery.

Methods: A hybrid navigation approach based on optical tracking of a fluorescence endoscope was applied in a phantom study and one clinical pilot case. After placing/injection of a hybrid radioactive and fluorescent tracer consisting of $^{99m}$Tc-nanocolloid and the fluorescent dye indocyanine green, preoperative SPECT/CT images are acquired with a fixed reference target placed on a rigid structure on the phantom/patient. By also attaching a reference target to the fluorescence endoscope, the preoperative SPECT/CT can be processed by the navigation system to a virtual view of the SPECT/CT images from the perspective of the endoscope.

Results: After feeding the SPECT/CT images to the navigation system, optical tracking could be used to position the tip of the fluorescence endoscope relative to the preoperative 3D imaging data. This hybrid navigation approach allowed us to accurately identify marker seeds in a phantom setup. In addition, the approach was used to navigate towards the prostate in a patient undergoing robot assisted prostatectomy. Navigation of the tracked fluorescence endoscope towards the target identified on SPECT/CT resulted in real-time gradual visualization of the fluorescent signal in the prostate, thus providing an intraoperative confirmation of the navigation accuracy.

Conclusion: Image navigation in hybrid surgical guidance procedures appears to be technically feasible, and may be a next step to fine-tune the hybrid surgical guidance process.
INTRODUCTION

Fluorescence based surgical guidance is a rapidly growing field of clinical research, that has been predominantly focused on the near-infrared (NIR) dye indocyanine green (ICG).\textsuperscript{1,2} The visible dye fluorescein, which has very limited tissue penetration, has also shown its clinical potential in selected indications.\textsuperscript{3-5} However, even with a 1-1.5 cm penetration of the NIR emission of ICG in tissue, fluorescence guidance is suboptimal for the localization of deep lesions and ends up requiring an exploratory surgical approach.\textsuperscript{6} Furthermore, fluorescence imaging does not enable the acquisition of preoperative images for surgical planning, which could help minimize the region of exploration. It is for this reason that to date, clinical fluorescence guidance has mostly been restricted to superficial sentinel nodes (SNs) of e.g. the breast or to lesions on the surface of an organ.\textsuperscript{7-11}

To extend the use of currently available fluorophores for fluorescence guided surgery to deeper structures, our group introduced the use of a hybrid tracer that is both radioactive and fluorescent.\textsuperscript{12,13} The radioactive signal emitted by this tracer allows for the identification and localization of the lesions in 3D prior to the intervention using imaging modalities such as Single Photon Emission Computed Tomography with X-ray computed tomography (SPECT/CT), thereby facilitating preoperative surgical planning. Intraoperatively, the radioactive label helps the surgeon to identify the region of interest using gamma-tracing techniques.\textsuperscript{14-16} On top of this radio-guidance, the hybrid tracer enables additional fluorescence guidance. Fluorescence is used to visualize the exact location of the lesion and its margins during the excision. This hybrid-guidance concept was clinically introduced for the visualization of deeply situated pelvic SNs\textsuperscript{17} and SNs in the head and neck region.\textsuperscript{18}

Preclinically, our group has shown that this technology can be expanded to the use of radioactive and fluorescent marker seeds and the visualization of specific tumor biomarkers.\textsuperscript{19-21} By targeting the tumor, this hybrid technology can be exploited to its full potential as it may provide guidance towards both the primary tumor and distant metastases.

Still, even when fluorescence imaging is combined with preoperative surgical planning based on SPECT/CT and intraoperative gamma ray detection, surgical orientation in minimally invasive surgery can be difficult. In our previous study, focused on laparoscopic biopsy of pelvic SNs in prostate cancer patients, the limited tissue penetration of the fluorescent emission of ICG prevented intraoperative visualization of deeper lying or tissue embedded nodes (4 out of 27 SNs).\textsuperscript{17}

In addition, SN identification using the laparoscopic gamma probe was sometimes hindered by background signals from the nearby injection site. This practical experience suggests that more accurate intraoperative image navigation towards the areas of interest, e.g. based on the intraoperative use of 3D scintigraphic images, could help to further improve SN identification in complex areas.\textsuperscript{22}

Rigid navigation is common in surgical guidance towards lesions in the brain, spine and in musculoskeletal surgery.\textsuperscript{23} However, navigation alone does not always
provide exact localization of the target lesions in soft movable tissues like in pelvic SN procedures. In these areas, the intervention may alter the position of the lesions of interest relative to more rigid reference points such as the skeleton. Current navigation systems cannot compensate for such deformation, rendering them less accurate. As such, an additional modality for intraoperative confirmation of the navigation accuracy (e.g. via fluorescence imaging) remains desirable.

In this manuscript we provide a proof of concept using phantom studies and one clinical pilot case to illustrate how intraoperative navigation based on preoperative 3D scintigraphic images may help improve hybrid radio- and fluorescence guided surgery.

METHODS

General system set-up

The concept of the hybrid navigation approach is to combine rigid navigation based on preoperative SPECT/CT data with real-time intraoperative detection of fluorescent light. For the rigid navigation we use reference targets (fiducials) fixed both on the phantom/patient and on a fluorescence endoscope, which are clearly distinguishable by CT and by an optical tracking system (Figure 1). By generating a 3D view of the SPECT/CT data from the perspective of the endoscope, the endoscope can be navigated to the target lesions identified by SPECT/CT.

SPECT/CT

For preoperative surgical planning, a SPECT/CT data set was acquired. To enable intraoperative navigation, fiducials where fixed to the phantom/patient before acquiring the CT to serve as reference targets. These fiducials are clearly distinguishable on the CT images and also are detectable by the optical tracking system. The registered coordinates of these optically tracked fiducials are later used for the navigation process.

For the acquisition of the SPECT/CT a dual head gamma-camera SPECT/CT system was used (Symbia T, Siemens, Erlangen, Germany), providing the data-processing unit with 2 3D images (the SPECT and the CT image) and the relative transformation between them in order to be properly fused (the relative position and orientation of the 2 images can be completely specified by a 4x4 transformation matrix $S^{\text{SPECT}}_{CT}$ which describes the rigid transformation in homogeneous coordinates from any point in the coordinate system of the CT to its corresponding point in the coordinate system of the SPECT). The SPECT was acquired using LEAP collimators, 30s/view, 20 views, an OSEM based iterative reconstruction – Siemens’ “Flash 3D” reconstruction for a matrix of 128x128 with voxels of 4.8x4.8x5mm and a 8.4mm Gauss filter. For the CT; 130kV, 40mAs, a B30s medium kernel and 2mm slices were used. As mentioned above, the CT was performed with a 3-fiducial reference target fixed to the patient/phantom within the field of the CT as shown in figure 1b. The fiducials (see below) used in the patient/phantom reference
target were placed at 50.33, 83.29 and 67.27 mm from each other forming an asymmetric triangle for unambiguous tracking.

Fluorescence endoscope
In the fluorescence imaging system, light emitted by an internal Xenon light source is guided through a special fluid light cable to an infrared-optimized rigid laparoscope (D-light system, Karl Storz Endoscopes, Tuttingen, Germany) containing an optical filter system that can differentiate between, white light, auto-fluorescence (AF-settings), and ICG (ICG-settings). The laparoscopic system provides two light settings, one with 410 nm excitation light to visualize fluorescein (max emission wavelength 520 nm) and one with 760 nm excitation light to visualize ICG (max emission wavelength 820 nm). The optics of the laparoscope are placed under a 30° angle.

With the aim of enabling navigation of the fluorescence laparoscope, this device was also equipped with a second 3-fiducial reference target using an ad-hoc designed interface that enabled to work under sterile conditions without the need of recalibrating the endoscope tip after each use (see figure 1a). This target could also be detected by the optical tracking system. The interface for mounting the reference target consisted on a rounded asymmetric conic male connector fixed rigidly to the camera housing and one corresponding rounded asymmetric cone female connector on the side of the fiducials, both kept together by a clamping mechanism. Such interface was designed in a way that the camera could be covered by the sterile draping. This avoids having to sterilize the camera, while the fiducials can be mounted over the cover in order to guarantee visibility by the optical tracking system. In the case of this ‘endoscope’ reference target, the fiducials were placed at 50.00, 56.60 and 78.34 mm from each other forming an asymmetric triangle for proper tracking. After a rigid calibration, the position of the tip of the endoscope could be determined in real-time (see below).

Images were recorded using a single Storz CCD camera that can detect both visible and NIR emissions. To improve the detection accuracy of the ICG detection, the blue and green cables of the RGB output were swapped places. Swapping RGB cables allows for visualization of the ICG emission in green (originally in blue which is not optimally visible by the human eye) and depicts the signal from fluorescein (which can be seen by the bare eye as yellow/green) in bright blue.

Optical tracking system
The aforementioned fiducials were configured in so called “reference targets”. These reference targets (made of mat surgical degree stainless steel or medical degree PEEK, SurgicEye, Munich, Germany) are unique asymmetric configurations of at least three fiducials. In the system used in this project, the fiducials are infrared reflectors (11.5 mm diameter retro-reflective spheres of polyurethane and polyvinyl-chloride covered with retro-reflective tape, also called fiducials, figure 1a) which can
be detected by the infrared cameras of the optical tracking system (OTS; Polaris Vicra, Northern Digital, Waterloo, Canada), integrated in the declipseSPECT system (SurgicEye, Munich, Germany, figure 1c,d). The identification of the reference targets by the OTS is based on detection of white round spots in the infrared images as the fiducials significantly reflect the infrared light emitted by the OTS. By firstly loading their mechanical drawings to the image processing software the configurations of each reference target are known to the OTS. The OTS output is the 3D position and orientation of the individual components (here; endoscope reference target – ERT and patient/phantom reference target – PRT). The 3D position and orientation of an object is a 6D vector, which is often referred to as 3D pose. Such a pose can be rewritten as a 3D rigid transformation 4x4 matrix from the coordinate system of the OTS to the coordinate system of the respective targets \( \begin{bmatrix} ERT_{OTS} \end{bmatrix} \) and \( \begin{bmatrix} PRT_{OTS} \end{bmatrix} \), respectively, figure 1). These matrices are then used to calculate the transformation between each reference target according to: \( ERT_{PRT} = ERT_{OTS} \cdot PRT\cdot T_{OTS}^{-1} \).

To determine the pose of the tip of the endoscope in relation to the reference target, calibration was needed. Calibration was performed using a mechanical construction (a “calibrator”) with a 12mm bore of 30mm depth with a tolerance of 0.1mm in which the 12mm tip of the endoscope could be placed. Via a 3-fiducial reference target with known geometry, this mechanical construction could also be detected by the OTS system. The axis of the bore and its bottom position (obtained from the mechanical drawing of this calibrator) were fed to the OTS in the coordinates of the calibrator’s reference target. Once the endoscope was fixed to the calibrator, the pose of the endoscope was assumed to be the same as the pose of the center of the construction and was stored. The calibration process does not correct for the 30° viewing angle of the laparoscope, it merely calibrates the tip of the laparoscope. The quantitative error of the calibration relative to the reference target on the CCD camera was evaluated by repeating the calibration procedure 200 times and analyzing the standard deviation of the transformation pose. In our set-up the pose standard deviation was 0.53°, 0.35mm in the axis of the endoscope and 4.42mm in the plane of camera (equivalent lever was 476mm).

The static bias was derived from the construction tolerance of the calibrator to be 0.2mm. The calibration step described above provides a 4x4 transformation matrix from the ERT to the tip of the endoscope – TE (matrix \( \begin{bmatrix} T_{E} \end{bmatrix} \)), which further enables the relative transformation from the endoscope tip to the patient/phantom reference target according to: \( T_{E} \cdot T_{PRT} = T_{E} \cdot T_{E} \cdot T_{PRT} \).

The OTS used in the present study works with a tracking frequency of 20 Hz and a pulsed wavelength of 980 nm. The infrared light used by the OTS does not excite the fluorophores. As such, it does not interfere during the surgical procedure. The tracking accuracy of the system (for non-occluded or partially occluded fiducials within the tracking volume) is 0.2mm RMS, 1.0mm maximum and the tracking volume is approximately 50x50x50cm³.
Display system
The system set-up included 2 (RGB) displays, one for depicting the video image generated by the endoscope (toggling between fluorescent and white imaging, figure 1f, analogue display) and one for displaying the 3D render of the SPECT/CT data from the perspective of the endoscope (figure 1e, digital 1280x1024 display).

Data processing
In our set-up, the SPECT/CT data and the pose data of the OTS are fed to a data processing unit consisting of an i7 processor with 8GB RAM running Windows 7 (figure 1d). The data processing unit has the task to generate a view of the SPECT/CT data from the perspective of the (calibrated) endoscope. This view can then be used to navigate the tip of the endoscope to the target radioactive/fluorescent structures.

Registration of patient/phantom pose data to the SPECT/CT images
In conventional navigation, the imaging data (here SPECT/CT) has to be put in the coordinate system of the tracking device (here the coordinate system of the OTS). This step is called registration. In the proposed setup the registration can be performed automatically as we use fiducials that are visible with CT and also can be detected by the OTS.

After acquiring the SPECT/CT image with the reference target fixed to the patient/phantom, the CT data is segmented in order to define the pose of the reference target on the CT image. Subsequently, the 4x4 transformation matrix between CT image coordinates and PRT coordinates can be calculated (matrix $CT_{PRT}$, figure 1). In the experimental set-up we used a threshold-based segmentation for detecting the reference targets as they are built from known material (i.e. their Hounsfield units are known). An automatic ‘grow region’ algorithm was then used to dilate the detected fiducial “candidates” and a centroid algorithm provided their 3D position in the CT image. The segmented image was then registered to the geometry of the PRT by point matching and the Umeyama registration algorithm running on the fiducial candidates. Finally the transformation from CT coordinates to the tip of the endoscope could be calculated according to: $T_{ET_{CT}} = T_{ET_{PRT}} T_{PRT_{CT}}$. The average registration error for the PRT and the CT was calculated to be 0.49mm with a standard deviation of 0.18mm. This error was measured from a set of several CT scans acquired with the hardware of the used set-up and the residual error provided by the Umeyama registration.

Furthermore, since the transformation between SPECT and CT can be read from the DICOM tags of the fused SPECT/CT data (patient image position and patient image orientation tags), the 4x4 transformation matrix of the CT to the SPECT (matrix $SPECT_{CT}$) can also be calculated. By performing this registration, the intraoperative pose data of the ERT can be related to the SPECT/CT image and as such, it can be used for intraoperative navigation using: $T_{ET_{SPECT}} = T_{ET_{CT}} T_{CT_{SPECT}}$. 
Generation of SPECT/CT render from view of endoscope

Visualizing the SPECT/CT images from the perspective of the endoscope is the essence of the proposed navigation approach. The visualization of 3D imaging data from a particular perspective is called rendering. Here we render the SPECT/CT images in real-time using the perspective of the tracked endoscope calculated by the OTS.

In order to render the SPECT/CT images properly on the 3D data display, a virtual view from the tip of the endoscope can be used. The virtual view (VV) can be a 3D render of the combined volumetric CT and SPECT data from the perspective of a virtual camera using different 4D transfer functions (RGB and transparency channel) and a 3x4 projection matrix \( \mathbf{WP}_{CT} \) and \( \mathbf{WP}_{SPECT} \) respectively. In our set-up, this virtual camera was set to have an equivalent 8mm optics (for a \( \frac{1}{2} '' \) sensor) point with a 0° angle from the TE. These parameters were used to compute the projection matrix from the TE to the VV (matrix \( \mathbf{WP}_{TE} \)) following the standard photometric model of a camera. As a result the projection matrices for the 3D images are provided following: \( \mathbf{WP}_{CT} = \mathbf{WP}_{TE} \mathbf{T}_{CT} \) and \( \mathbf{WP}_{SPECT} = \mathbf{WP}_{TE} \mathbf{T}_{SPECT} \).

For volume rendering a standard ray casting algorithm was used and adapted for SPECT/CT in order to be able to render both the CT and SPECT fused. For the CT data different transfer functions were implemented. Transfer functions provide color values to different CT values. Here, a trapezoid transfer function similar to the bone window used in Osirix was used (Pixmeo, Bernex, Switzerland). For the SPECT a maximum intensity projection (MIP) was used in which the transfer function consisted of an adjustable linear color scale which enables the operator to optimally set the proper contrast and brightness. A dark blue to light pink color scale was used for the SPECT data. Thus, low radioactive structures were seen as dark blue while high radioactive structures were depicted as pink (see Figure 1e).

Experimental set-up

In order to validate the feasibility of the hybrid navigation system set-up, phantom experiments were performed followed by a proof of concept experiment in a prostate cancer patient.

Phantom experiment

Small multimodal marker seeds were made out of glass capillaries (diameter 1.0mm, length 8.0mm), as described in a previously reported procedure. Larger seeds consisted of sealable plastic 1.5ml Eppendorf vials. The marker seeds were filled with a mixture of: 100µl ICG (1mg/ml) + 100µl fluorescein (1mg/ml) + 50µl Magnevist (Gd-DTPA; used as MRI contrast medium, 1/100 diluted from clinical stock) + 15µl \(^{99m}\text{Tc}\) (200 MBq / 50µl). After closure the small seeds contained approximately 10µl of the tracer mixture, whereas the large seeds were filled with 100µl of the mixture.

A 20cm x 14cm x 10.5cm piece of pork, including a rib segment, was fixed to
a plate of Styrofoam using three wooden pins (figure 2a). Two large and 2 small markers seeds were placed at different positions in this phantom (figure 2b-f). The smaller seeds were implanted using a hollow implantation needle (AccuNeedle; 18G, 20cm; Oncura, Brussels, Belgium). The larger seeds were implanted after making a small incision. Similar to the preoperative routine we used during our preclinical and clinical studies using hybrid tracers and/or marker seeds for surgical guidance, an initial SPECT/CT was made to plan the 'surgical procedure’, only this time with a reference target for optical tracking fixed to the Styrofoam plate (figure 2a, b).

Clinical pilot case
To evaluate the preclinical phantom approach in a clinical setting, a 63 year old patient with prostate cancer (cT2cN0Mx, Gleason score 7) scheduled for robot assisted prostatectomy was included after informed consent was obtained. For this clinical pilot case, we used the clinically approved hybrid radioactive/fluorescent tracer (ICG-\textsuperscript{99}mTc-nanocolloid), which was prepared as previously described.\textsuperscript{17} Approximately 4 hours prior to surgery, the tracer was transrectally injected (197MBq; 0.4mL; 4 injections) into both lobes of the prostate guided by ultrasound. Subsequently, preoperative lymphoscintigraphic imaging was performed followed by SPECT/CT. Before the start of the SPECT/CT acquisition, the reference target was fixed on the patient’s skin adjacent to the right superior anterior iliac spine using medical tape, and the location was marked with indelible ink. In the operating room, a sterilized PRT was placed at the previously marked position on the patient’s skin and fixed with sterile tape. Similarly, a sterilized ERT was placed over the sterile cover on the calibrated fluorescence laparoscope using the clipping mechanism (figure 5b).

In previous experiments we measured the repositioning error of the PRT as well as the error due to breathing and changes in leg positioning separately in a group of test subjects. The repositioning error in that series was 1.08mm for 10s acquisitions, the maximum error being 2.15mm. For the pelvic area the breathing and deformation due to different patient positioning was 244mm with maximum error of 6.02mm.
RESULTS

Phantom experiment

The radioactive component within all four marker seeds could be visualized within the phantom by SPECT/CT (figure 2b). The average error found in the registration (in 3D) as provided by SPECT/CT was 1.89mm (SD 0.81mm). This error was quantified using a manual segmentation of the SPECT and CT images of the radioactive seeds and a posterior error analysis of the centroids of these seeds using Osirix. After feeding the DICOM files of the SPECT/CT images to the navigation system, the latter could be used to help position the tip of the endoscope relative to the 3D imaging data. This enabled accurate navigation towards the radioactive hot spots (figure 3). During the exposure of the marker seeds, the endoscope (in its ICG setting) was used to excite ICG and gradually enable the fluorescent visualization of the marker seed. This combined approach allowed us to accurately identify all the marker seeds that were positioned in the phantom.

Since we incorporated 2 dyes in the marker seeds (fluorescein and ICG), which have a different degree of tissue penetration, the navigation process could be accurately visualized via multispectral fluorescence imaging. As the tip of the tracked endoscope was gradually navigated towards the fluorescent marker, the NIR emission with a signal penetration <1.5cm could be detected first. When the tip of the scope was navigated on top of a marker seed (<2mm distance), it could be visualized using both the fluorescein settings (blue; figure 4b) and the ICG settings (green; figure 4c). Because the tissue penetration of fluorescein is limited, it could only be detected very superficially, improving the resolution range in which the margins of the marker seed can be visualized. Removal of the markers was further aided by the fact that superficially, the fluorescence emission of fluorescein can also be detected by eye (green; figure 4d).

Clinical pilot case

After providing the proof of concept in phantom tissues, the next challenge was to apply the navigation approach in a clinical setting. Following our previous experiences in hybrid surgical guidance during robot assisted procedures, we initially focused our clinical proof of concept on laparoscopic navigation towards the tracer deposits in the prostate. In spite of the challenging logistics and robotic arms blocking the detection of the reference targets (both the ERT and the PRT) by the OTS at certain times, it was possible to use the navigation system during a robot assisted laparoscopic prostatectomy procedure (figure 5a). To maximize the intraoperative navigation accuracy, a relatively rigid location (superior anterior iliac spine) near to the location where the fluorescence endoscope is inserted was found to be most suitable for the placement of the reference target (figure 5b). During surgery, the navigation system enabled accurate navigation to the prostate and was able to provide real-time distance estimations of the tip of the fluorescence endoscope to the center of radioactivity/fluorescence within the
prostate (figure 5c,d). Navigation of the tracked fluorescence endoscope towards
the target identified on SPECT/CT resulted in real-time gradual visualization of the
fluorescent signal in the prostate. Herein the fluorescent signal provided intraoper-
ative confirmation that the navigation accuracy is within the <10-15mm penetration
rate of the ICG emission in soft tissue (figure 5e,f).

**DISCUSSION**

This pilot study demonstrates the feasibility of combined rigid navigation based on
preoperative SPECT/CT images and intraoperative fluorescence imaging for soft
tissue navigation within a small range of deformation in complex surgical proce-
dures. When combined with the use of hybrid (radioactive and fluorescent) tracers,
such a navigation set-up may enable preoperative surgical planning as well as
intraoperative image navigation towards the lesions using the radioactive signature,
while accurate target localization and visualization can take place using the fluo-
rescent signature. The ability to perform navigation with a multispectral camera system
allows for the simultaneous use of the 2 most common and clinically approved
dyes used for optical surgical guidance, namely fluorescein and ICG.

One important feature provided by the SPECT/CT based navigation made possible
using hybrid tracers, is on one hand that the limited tissue penetration of the
fluorescent signal is of less influence on the surgical guidance towards the target
lesion. On the other hand, the limited accuracy of surgical navigation based on
preoperative data is of less influence on the surgical procedure too as the intraop-
erative real-time fluorescence helps the surgeon to compensate for deformations,
positioning errors and changes in the anatomy from the moment of imaging and
the surgical procedure. In this sense the main premise for an approach like the one
presented here is that the penetration of the fluorescence signal should be greater
than the registration error of the preoperative images. In this setup, such a premise
can be achieved. In addition, the ability to include different fluorescent signals,
which each give different degrees of tissue penetration opens up possibilities to
intraoperatively monitor the surgical safety margins in real-time using a so-called
“traffic light approach”.19

As our initial studies were based on our experiences with radioactive gamma
emitters and fluorescent hybrid tracers, the surgical planning and navigation in
this study was based on SPECT/CT.12,17 However, it should be noted that such
a system can also be expanded to other imaging modalities. For example, the
navigation system can also be used to help provide ultrasound guided navigation
towards radioactive lesions or for instance help place marker seeds in or around
a lesion (figure 2d).19 Alternatively, imaging modalities like MRI can be included,
which provide better soft tissue contrast and can include functional information on
e.g. vascular physiology and tissue spectroscopy. MRI can be used as a basis for
navigation or as an alternative for CT in fused form with SPECT information (figure
2e-f). Realizing that switching the isotope in a marker seed or on an imaging agent
to a positron emitter is relatively straightforward, this opens the way to include positron emitted tomography with computed tomography (PET/CT), or even PET/MRI in the guidance process. Furthermore, next to navigation based on preoperative imaging modalities, intraoperatively acquired images using the previously described freehand SPECT system could also be used for navigation in the current phantom study (figure 2c, data not shown), but is not yet available for laparoscopic procedures.\textsuperscript{22}

As stated in the introduction, non-rigid surgical navigation is challenging. A hybrid navigation approach like the one presented here may provide a way to avoid complex deformable registration methods and still provide accurate (hybrid) intraoperative guidance. Although we encountered logistical challenges that need further optimization; such as the positioning of the PRT and the positioning of the OTS relative to the patient and the endoscope, the current study provides a proof of concept of the hybrid navigation approach. Further studies are needed in order to determine the overall accuracy and sources of error so that the process can be optimized for routine use. A larger study to substantiate these preliminary findings is currently in preparation.

CONCLUSION

Image navigation in hybrid surgical guidance procedures appears to be technically feasible and can be performed with an error lower than the tissue penetration of the used fluorophores. We believe that such an approach makes optimal use of all available preoperative data and may be a next step to fine-tune the hybrid surgical guidance process.

ACKNOWLEDGEMENTS

This research is supported, in part, by a KWF-translational research award (Grant No. PGF 2009-4344; FvL) and via a FP7-HYPERImage (grant no. 201651; TB). The authors would also like to thank also the SurgicEye team; in particular Stefan Wiesner and Moritz Hoyer for the implementation of software and hardware modifications needed for the current experimental set-up.
Figure 1. Hybrid navigation approach. (a,b) The set-up includes two different input systems: the reference targets shown in figure 1a are placed on the patient and fluorescence endoscope. The preoperative SPECT/CT images are acquired with a fixed reference target placed on a rigid structure on the patient/phantom (figure 1b, white circle). (c) An optical tracking system (OTS) determines the pose of the reference targets. (d,e) The preoperative SPECT/CT and the poses determined by the OTS are processed by the data-processing unit to a virtual view of the SPECT/CT images from the perspective of the endoscope, as shown in figure 1e. (f) Navigation of the tracked fluorescence endoscope towards the target identified on SPECT/CT (figure 1e) results in real-time gradual visualization of the fluorescent signal on a second display (figure 1f), thus providing confirmation of the navigation accuracy.

Figure 2. Current and future incorporation of imaging modalities in the hybrid navigation procedures. (a) The phantom is imaged with a fixed reference target for later pose matching enabling intraoperative navigation. (b) SPECT/CT image displaying the radioactive component in the four multimodal marker seeds. (c) Using a tracked gamma probe, real-time freehand SPECT images can also be acquired for navigation. (d) Visualization of the marker seeds using ultrasound (arrow). (e,f) High resolution of the tissue morphology using MRI can be matched with the SPECT data (SPECT/MRI) increasing the amount of detail even further.
Figure 3. Endoscopic navigation procedure. (a,b,c) As the tracked fluorescence endoscope approaches the phantom; (d,e,f) the data-processing unit enables navigation towards the lesion based on the preoperative SPECT/CT images. (g,h,i) Synchronously, the fluorescence camera system enables stepwise visualization of the fluorescent signal of the hybrid tracer.

Figure 4. Multispectral fluorescence guidance. (a) Based on the SPECT/CT images the laparoscope can be navigated towards the lesion. (b,c) The multispectral nature of the near-infrared optimized fluorescence endoscope enables visualization of both fluorescein (blue) and ICG (green). Note: the RGB input of the endoscopic signal is altered (green/blue cables swapped place), therefore, fluorescein appears blue instead of green. (d) The visual fluorescence emitted by fluorescein can be readily detected by the naked eye.
Figure 5. Laparoscopic navigation towards the prostate in a patient undergoing robot assisted prostatectomy. (a) Intraoperative set-up depicting the surgical robot system, the navigation system display (1), the fluorescence camera system display (2), and the position of the optical tracking system (3). The area within the white circle is enlarged in figure 5b. (b) The reference targets are placed on the patient and fluorescence endoscope. The latter is inserted through a separate access port. (c,d) Based on the preoperative SPECT/CT, the fluorescence endoscope can be navigated towards the prostate, while the system provides distance estimations in mm. (e,f) Navigation of the tracked fluorescence endoscope towards the target identified on SPECT/CT resulted in real-time gradual visualization of the fluorescent signal in the prostate, thus providing an intraoperative confirmation of the navigation accuracy.
REFERENCES


