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**Title:** Image guided surgery: clinical validation of lesion identification technologies and exploration of nerve sparing approaches
**Issue Date:** 2018-03-08
Figure 1. Fluorescence camera navigation

Figure 2. Navigation of the FC. Video signal of the overhead camera of navigation system allows projection of 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 near-infrared video signal of the FC showing 2 SNs. (D) Fluorescence imaging optically visualized the SN and thus allowed confirmation of FC navigation accuracy.

Figure 3. Fluorescence imaging with integrated overlay. (A) Preoperative overlay of the SPECT onto the patient from the perspective of the FC (white light imaging mode) showing the primary injected tumor and, close to the reference tracker, the SN. (B) Preoperative overlay of the SPECT onto the patient from the perspective of the FC (fluorescence 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 pseudocolored green, respectively).
General introduction
and outline of this thesis
IMAGE GUIDED SURGERY: CLINICAL VALIDATION OF LESION IDENTIFICATION TECHNOLOGIES AND EXPLORATION OF NERVE SPARING APPROACHES

GENERAL INTRODUCTION
Surgery is considered the golden standard to treat the primary tumour and regional spread of many different cancer types. In addition to the pathological evaluation of surgical margins, the evaluation of lymph nodes is needed to stage the metastatic dissemination of the disease [1,2]. Both these aspects are critical in accomplishing radical excision and are, as such, providing true prognosis. However, the quest for complete cure should be in balance with the desire for minimally invasive surgery [3–5]. Hereby it can be assumed that surgical side effects may negatively influence the patient’s quality of life.

Advanced image guided surgery technologies can be used to improve the surgical resection and to minimize the invasive nature of the procedure [6]. In this thesis both these technologies are discussed. Hereby we focussed on the locoregional assessment of the lymphatic tumour spread via sentinel lymph node procedures [7–11]. In addition technologies that support nerve-sparing surgery have been pursued. To realize these ambitious goals, a combination of imaging modalities has been used, ranging from fluorescence to nuclear imaging and hybrid combinations of the same.
OUTLINE OF THIS THESIS

In part one the hybrid surgical guidance concept for sentinel lymph node (SN) resection using the hybrid tracers ICG-\textsuperscript{99m}Tc-nanocolloid is discussed. In chapter 2 the potential of hybrid tracers in radioguided surgery is discussed. The study described in chapter 3 underlines the potential of hybrid tracers discussing the summarizing of the use of a hybrid SN tracer in 501 procedures performed in varying malignancies. Here SNs were identified based on the hybrid combination of gamma tracing and fluorescence. Hereby the fluorescence emission of the hybrid tracer allowed highly sensitive intraoperative identification of the exact same nodes as those defined using preoperative SPECT/CT. Chapter 4 describes how technical improvements to the sensitivity and visualization-settings help increase the clinical usability of a fluorescence laparoscope during pelvic surgery. In chapter 5 the hybrid surgical guidance procedure and laparoscopic fluorescence detection has been fully integrated in a robot-assisted setting. These two chapters indicate that both fluorescence camera optimization and integration of the technology in surgical routine help to provide added benefit.

Chapter 6 evaluates the relation between hybrid tracer dose and the ability to obtain fluorescence guidance. This relation was studied both during open and laparoscopic procedures and in vivo and \textit{ex vivo} fluorescence guidance was benchmarked against visibility on SPECT/CT.

Part two describes new surgical modalities that can be used during the hybrid surgical concept. Since a hybrid tracer was used to integrate pre- and intraoperative imaging findings using nuclear and fluorescence signatures, an attempt was also made to create hybrid analogues of the intraoperative hardware. In Chapter 7 the first-in-human evaluation of physically integrating radio- and fluorescence modalities is reported on. Two hybrid detection modalities were created whereby one combined fluorescence- with gamma-imaging, while the other one combined fluorescence-imaging with acoustic gamma tracing. Chapter 8 presents a different type of hardware integration, namely the geometrical tracking of a fluorescence camera in a SPECT-based navigation set-up for open surgery. Alternatively, in chapter 9, surgical navigation based on intraoperative freehandSPECT in combination with a handheld gamma camera is described. Here the intraoperative radioguidance provides a surgical roadmap for fluorescence guidance.
Part three of this thesis describes technologies that help advance nerve sparing surgery. In chapter 10 the direct relation between intraoperative fascia preservation and postoperative erectile function was determined in a large cohort of prostate cancer patients. Based on the findings a nomogram was developed to predict the functional outcome after robot-assisted prostatectomy. In an attempt to visualize nerves prior to surgery the use of a magnetic resonance based imaging technique was pursued in the head and neck area (Chapter 11). With so-called D-Prep MRI it was possible to accurately visualize the anatomical variation in nerve distributions. At the same time, the technology assisted in the more accurate visualization of lymph nodes and their distribution. Alternatively, fluorescence imaging was used to pursue intraoperative detection of peripheral-nerves. To this end in chapter 12, lectin-based fluorescence tracers were evaluated for their nerve staining capacities following local administration.

In chapter 13 a summary of both parts is provided and suggestions for future research directions have been given.
REFERENCES


Part one
Clinical evaluation of hybrid surgical guidance during sentinel lymph node procedures