Engineering precision surgery: Design and implementation of surgical guidance technologies

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CHAPTER 10

SUMMARY

In the quest to achieve precision surgery, the work described in this thesis introduces several novel (hybrid) detection and navigation modalities. All the presented engineering efforts focused on optimal detection and localization of cancer-related tissue using the complementary tracer signatures of either nuclear and fluorescence radiation, or a combination thereof, using so-called hybrid tracers. These newly developed image-guided surgery technologies were evaluated in different settings, ranging from phantom work to pre-clinical and even clinical studies.

Part one of this thesis covered several surgical navigation concepts. In **chapter 2** the general concepts for a typical surgical navigation workflow were introduced. Important requirements are: 1) some form of imaging, providing a 3D map of the disease; 2) computer-aided planning using the patient map; 3) registration of the patient map to the actual patient on the operating table; 4) position and orientation tracking of the patient and surgical tools in the operating room; and 5) navigation of the surgical tools towards the tissue of interest. This all constitutes to a workflow wherein the surgeon knows exactly where the surgical tools are on the patient map, relative to the targeted tissue. Apart from the fields of neurosurgery, radiotherapy and perhaps orthopedic surgery, the application of navigation remains experimental, mainly due to the inability to cope with, or compensate enough for, tissue-deformation-induced inaccuracy of the navigation workflow. Nevertheless, the studies shown, combined with the advances in the underlying technology, suggest that the use of surgical navigation will be much more widespread in the near future.

Chapter 3 demonstrated the concept of using nuclear-based navigation to position the robot integrated fluorescence laparoscope within the vicinity of the targeted lesion during robot-assisted laparoscopic surgery, using the hybrid tracer ICG-^{99m}Tc-nanocolloid, which is both radioactive and fluorescent. Phantom evaluations showed a navigation accuracy of 2.25 mm (coronal plane) and 2.08 mm (sagittal plane) when navigation was based on preoperative SPECT/CT scans. When navigation was based on freehand SPECT (fhSPECT) scans, these accuracies were 1.92 mm (coronal plane) and 2.83 mm (sagittal plane). In comparison to the <1 cm detection limit of fluorescence imaging, this would indicate that the navigation inaccuracies could be compensated using the real-time fluorescence feedback as provided by the fluorescence laparoscope. Therefore, these initial phantom experiments suggest that SPECT-based navigation of the robot-integrated fluorescence laparoscope has the potential to aid fluorescence-guided surgery procedures for lesions positioned deep within the patient anatomy.

In **chapter 4**, the navigated fluorescence camera concept was translated to a system applicable for both open and laparoscopic surgery, using a detachable exoscope and laparoscope respectively. Initial phantom evaluations revealed an overall tool-to-target distance accuracy of 2.1 mm for SPECT/CT-based and

3.2 mm for fhSPECT-based navigation. The augmented reality registration accuracy was found to be 1.1 and 2.2 mm, respectively. Evaluations in open (penile cancer) and laparoscopic (prostate cancer) navigation were successful and accurate enough to localize the fluorescence signals of the targeted tissues in vivo. This proof-of-concept study suggest that the single hybrid navigation setup studied is applicable in various open and laparoscopic surgical applications.

The studies evaluated in chapter 3 and 4, combined with the work of KleinJan et al. [1], revealed that using near-infrared optical tracking, obstructed fluorescence imaging of open surgery fluorescence cameras. **Chapter 5** thoroughly investigated the different components of this interference aspect and recommended possible solutions. The different measurements performed indicated that interference was caused by: (1) spectral overlap between the optical tracking system (OTS) light emitted and the fluorescence camera detection range, (2) OTS light intensity, (3) OTS duty cycle, (4) OTS emission frequency, (5) fluorescence camera measurement frequency, and (6) fluorescence camera sensitivity. Optimization of points 2-4 already indicated OTS and fluorescence camera compatibility can be used to support the navigated fluorescence guidance concept, even in open surgical procedures.

Part two of this thesis introduced several detection modalities, further supporting the translation of molecular imaging towards intraoperative guidance. **Chapter 6** described the engineering of a multimodal animal imaging platform, capable of imaging bioluminescence, fluorescence and SPECT emission signatures, optimally supporting preclinical hybrid tracer development. Phantom and in vivo mice evaluations indicated accurate imaging of all three signals (i.e. bioluminescence, fluorescence and SPECT). Hereby, the acquired SPECT and bioluminescence scans were used to place the fluorescence imaging results in to perspective: for example, by showing tracer accumulation in non-target organs such as the liver and kidneys (SPECT) and by giving a semi-quantitative read-out of the tumor spread (bioluminescence). This revealed the advantages of a fully integrated imaging platform, optimally using the complementary scans to improve data interpretation during research.

Chapter 7 explored how the generation of a novel freehand Fluorescence (fhFluo) imaging approach could complement fhSPECT in a hybrid setup. Next to the generation of fhSPECT scans, the conceived hybrid modality was capable of creating (pseudo-)3D fluorescence tomography scans. The imaging resolution of fhFluo (1 mm) was found to be superior to that of fhSPECT (6 mm), however, fhFluo was confined to a maximum depth of 0.5 cm, while fhSPECT imaging was usable at all depths (evaluated $\leq$2 cm). Both fhSPECT and fhFluo allowed for augmented- and virtual-reality navigation towards tracer hotspots, segmented in the image. Imaging in prostate and sentinel lymph node specimens confirmed these trends: fhSPECT has a lower resolution but a more in-depth detectability, while fhFluo harbors a superior resolution, but only supplies superficial detectability. Overall, using radioactive and fluorescent (hybrid) tracers, this chapter showed that fhFluo has complementary value to fhSPECT, rendering a unique hybrid imaging/navigation modality.

Chapter 8 focused specifically on improving detection of the nuclear tracer emissions during robot-assisted laparoscopic surgery. To this end, a tethered and highly flexible DROP-IN gamma probe was developed which could optimally benefit from the flexible wrists of a (robot-assisted) laparoscopic forceps, increasing intra-abdominal maneuverability. In comparison to a conventional laparoscopic gamma probe (allowing for movements with 4 degrees of freedom (DOF)), a DROP-IN combination allowed for 6 DOF with a robotic forceps. Phantom experiments underlined the importance of this maneuverability, showing that distinguishing a low radioactive lesion (e.g. SN) from a high radioactive background (e.g. prostate) was only possible with the detector faced ≥90° away from the high background source. Further evaluation in phantom, ex vivo clinical (i.e. prostate and SN specimens) and in vivo porcine studies all influenced the different prototype designs of the DROP-IN geometry. After thorough investigation of the probe pick up grip design, the surgeon favored a 45°-grip at the distal end of the probe. Introduction and optimization of the first DROP-IN gamma probe prototypes indicated a better integration of using radioguidance during (robot-assisted) laparoscopic surgery. The clinical potential of this technology was recently demonstrated during prostate cancer related robot-assisted laparoscopic SN procedures [2].

In **chapter 9**, the **outlook** of this thesis, the introduced (hybrid) detection and navigation modalities were linked to an overview of the general research developments made for virtual- and augmented-reality computer-assisted procedures in urological interventions. Many different approaches were shown for both the urinary system (including nephrolithotomy and nephrectomy) and the reproductive organs (including primary tumor lesions and lymphatic spread). Within these fields, the detailed surgical roadmaps were created with pre- or intra-operative forms of (cone-beam) CT, MRI, ultrasound and SPECT imaging modalities. Registration of these surgical roadmaps with the real-life surgical view was performed using mainly electromagnetic, mechanical, vision or near-infrared optical-based tracking techniques, whereby the combination of approaches was suggested to provide superior outcome. Unfortunately, soft-tissue deformations remain one of the most challenging obstacles in this field of soft-tissue surgery, demanding the use of confirmatory interventional detection modalities. This has resulted in the introduction of new intraoperative detection modalities such as DROP-IN US, transurethral US, (DROP-IN) gamma probes and fluorescence cameras. Although most techniques are evaluated in small patient groups and there is still a lot of room for refinement, the presented navigation efforts might provide the first steps towards a promising future for computer-assisted surgery in urology, hopefully improving surgical accuracy and clinical outcome.

In conclusion, the different detection and navigation modalities engineered and investigated in this thesis, all used the complementary values of nuclear and fluorescence tracer signatures to optimally guide the surgeon during the resection of cancer-related tissue. Hopefully, these image guided surgery approaches can all help to move the field towards a more precise, less invasive and more effective surgical procedure. While initial clinical evaluations were tailored towards SN procedures in urology (i.e. prostate and penile cancer), all presented techniques are of such a nature, that they could easily be applied in many different (hybrid) tracer-based surgical procedures. Such procedure already include hybrid SN procedures in head and neck cancer [3,4], SN in cervical cancer [5], SN in breast cancer [6] and radioguided occult lesion localization procedures [7]. Recent developments of tumor-receptor targeted hybrid tracers should open up many other applications in the (nearby) future, including localization of the primary tumor and metastatic spread in renal cancer (e.g. using an ^{111}In-girentuximab-IRDye800CW tracer) [8], neuroendocrine tumors (e.g. using a Cy5-^{111}In-DTPA-Tyr3-octreotate tracer) [9] and prostate cancer (e.g. using a PSMA I&F tracer) [10]. Alternatively, modalities like the introduced DROP-IN technology have also proven value during receptor targeted surgery, in specific PSMA guided resection of lymphatic metastases [11].

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