Protocol summary

Study title	**Intra-operative vessel and bone acquisition, towards ultrasound registration for surgical navigation** NL: Intra-operatieve beeldvorming van de vaten en botten, voor toekomstige navigatie chirurgie met ultrasound registratie
Study coordinator	M.A.J. Hiep, MSc
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Rationale	Image-guided navigation surgery allows for full utilization of pre-operative imaging during surgery and has the potential of reducing both irradical resections and morbidity. To use navigation, a registration procedure is required to correlate pre-operative imaging with the patient's position on the operating room (OR). Currently, registration is done by Cone-Beam CT (CBCT) scanning on the OR prior to navigation surgery. However, the main limitation of the CBCT method is that it cannot compensate for per-operative changes such as bed rotation, retractor placement and tissue displacement due to the surgery. Alternatively, by using intra-operative tracked ultrasound and vessel-based patient registration, changing conditions during surgery can better be dealt with. This improved patient registration method could lead to an increased navigation accuracy and improved clinical usability and outcomes. The main difference between CBCT and proposed ultrasound registration is that CBCT is based on bones, while the ultrasound is based on vessels. Bones can be very easily imaged on the CBCT and therefore used for bone-bone registration with pre-operative CT-scans. However, vessels are more difficult to acquire, especially with ultrasound, and an automatic registration process with pre-operative imaging is needed for efficient clinical usability. For this, the vessels need to be extracted from the tracked ultrasound images to create a 3D representation that can be registered. Therefore, an algorithm needs to be developed that can automatically segment the vessels from ultrasound images.
Objectives	Primary objective: • To develop an automatic segmentation algorithm using artificial intelligence for real-time intra-operative vessel segmentation Secondary objectives: • Post-operative evaluating the accuracy of different registration

	methods, such as 3D model or centerline registration • The usability of the tracked ultrasound setup (SUS-score)
Study design	A single center observational feasibility study
Methodology	This is a feasibility study, without any impacts on the surgical procedure itself. The total study-related delay of the surgical procedure will be approximately 10 minutes. Participation in the study will not involve additional visits to the hospital or additional radiation dose for the included patients. Informed consent will be obtained during the pre-operative outpatient clinic appointment or upon admission to the hospital at least one day before operation. Surgery starts according to the standard procedure, which includes incision and preparation of the internal tissue required for the surgery. For this study, optimal ultrasound image acquisition of the vessels (without compressing the tissue with the ultrasound probe) is required. For laparotomy, the abdominal cavity will partly be filled with standard warm saline. Subsequently, intra-abdominal ultrasound is acquired using the BK ultrasound system linked to the NDI Aurora electromagnetic tracking system. For robotic assisted lymph node dissections, intra-operative ultrasound could be acquired percutaneously and/or intra-abdominal using a drop-in ultrasound transducer. If accessible, the abdominal aorta, left and right iliac arteries and both internal and external iliac arteries will be imaged as well as the pubic bone, sacrum and iliac crests; or other relevant arteries and bones close to the target area. For offline validation of the registration accuracy, a sterile electromagnetic pointer is used to pinpoint several anatomical landmarks, such as the aortic bifurcation or lymph nodes. All ultrasound and tracking data will be recorded during the measurements and post-operatively analyzed and used to train an automatic vessel segmentation algorithm.
Inclusion criteria	• Age ≥ 18 • Patients scheduled for laparotomy (first 30 patients) or robotic assisted lymph node dissection (second 20 patients) • A pre-operative CT scan is available • Patients provide written ‘informed consent’
Exclusion criteria	• Metal implants which could influence the vessel segmentation or tracking accuracy • Pacemaker or defibrillator • Patient received treatment, e.g. surgery or radiotherapy, between the pre-operative CT scan and surgery, which might altered the patient’s anatomy
Number of patients	50 (firstly 30 laparotomy patients, secondly 20 robotic assisted lymph node dissection patients)
Study duration	2 years

Evaluation criteria	• Number and quality of ultrasound sweeps for automatic segmentation of the vessels • Localization of clinical targets with an electromagnetically tracked pointer to compute a target registration error
Statistical methods	The main study parameter is the development of an algorithm that can automatically segment the vessels from US imaging. With this study, we want to obtain intra-operative US data to train such algorithm. Statistically, we want to test if the created algorithm is able to successfully segment the vessels from US images. This can be done by comparing the automatically segmented vessel with the ground truth. The segmentation will be defined successful for a Dice coefficient ≥ 0.7. Since we are interested in the proportion of vessels found on US images, the sample size was calculated with a power calculation based on the number of US sweeps. It is assumed that the US image quality and the number of found vessels are equally correlated across different patients, since we use a scanning protocol to visualize the same vessel segments in each patient. The segmentation of an US sweep will be defined successful for a Dice coefficient ≥ 0.7 of that sweep. We estimate a success rate of the network to successfully segment the main pelvic arteries in all sweeps combined of 93% (P). According to the binomial calculation using a 95% confidence interval for proportion with a width of 0.1, a sample size of 118 US sweeps is required. In this study, at least 4 US sweeps will be made per patient, which means that 30 patients should be included for a total of 120 US sweeps. After successful evaluation of these 30 laparotomy patients, the same methods will be applied to 20 patients scheduled for robotic assisted lymph node dissection. In addition, the registration accuracy will be determined by computing the target registration error. The usability of the tracked ultrasound setup will be evaluated using standard questionnaires, resulting in a score between 1 and 100.
Quality of Life	N.A.
Pharmakinetics (PK)	N.A.
Translational research (TR)	N.A.
Risk evaluation	No additional burden or risks are expected apart from to the extended surgery time, approximately 10 minutes, for the included patients. Ultrasound imaging takes place in the same way that conventional intra-operative ultrasound is acquired (for example during liver surgeries), using the same standardized sterile cover or sterilized US transducer. The electromagnetic tracking system (NDI Aurora) including the tracked pointer is the same system as applied during conventional abdominal navigated surgeries at the NKI-AvL and multiple navigation studies.