

Navigated breast tumor excision using electromagnetically tracked ultrasound and surgical instruments

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Abstract— Objective: Lumpectomy, breast conserving tumor excision, is the standard surgical treatment in early stage breast cancer. A common problem with lumpectomy is that the tumor may not be completely excised, and additional surgery becomes necessary. We investigated if a surgical navigation system using intraoperative ultrasound improves the outcomes of lumpectomy, and if such a system can be implemented in the clinical environment. **Methods:** Position sensors were applied on the tumor localization needle, the ultrasound probe, and the cautery, and three-dimensional navigation views were generated using real time tracking information. The system was tested against standard wire-localization procedures on phantom breast models by eight surgical residents. Clinical safety and feasibility was tested in six palpable tumor patients undergoing lumpectomy by two experienced surgical oncologists. **Results:** Navigation resulted in significantly less tissue excised compared to control procedures (10.3 ± 4.4 vs. 18.6 ± 8.7 g, $p = 0.01$) and lower number of tumor-positive margins (1/8 vs. 4/8) in the phantom experiments. Excision-tumor distance was also more consistently outside the tumor margins with navigation in phantoms. The navigation system has been successfully integrated in an operating room, and user experience was rated positively by surgical oncologists. **Conclusion:** Electromagnetic navigation may improve the outcomes of lumpectomy by making the tumor excision more accurate. **Significance:** Breast cancer is the most common cancer in women, and lumpectomy is its first choice treatment. Therefore, improvement of lumpectomy outcomes have a significant impact on a large patient population.

Index Terms—Image-guidance, Computer-assisted surgery, Sonography, Surgical oncology.

I. INTRODUCTION

BREAST cancer is the leading cancer in women worldwide. When it is discovered in its early stage, the first therapeutic approach is lumpectomy. The tumor is removed from the breast while sparing as much healthy tissue as possible. Long-term survival of lumpectomy is equivalent to mastectomy, but it is preferred due to improved cosmesis [1][2][3]. A common problem with lumpectomy is that the tumor may not be

completely excised. Therefore, the excision margins undergo histological analysis after surgery. When cancer-positive margins are found, additional surgery is needed to remove the remaining tumor, in order to minimize the chance of cancer recurrence [4]. Positive margin rate is reported between 15 and 50% of the cases [5][6]. Additional operations invoke more cost, delay adjuvant therapy, and cause additional trauma to the patient because the second operation is usually total mastectomy. Due to the large number of breast cancer patients, reduction of positive margin rates may have a significant impact on population health and the cost of healthcare.

The high rate of positive margins is caused by two main characteristics of breast cancer. Tumors are often not palpable, therefore surgeons have no direct visual or tactile feedback to ensure that the entire tumor is included in the excision. Breast tissue is also very deformable, allowing tumor movements. Therefore, tumor location assessed on preoperative images may only give approximate information on the tumor location during surgery. The current standard approach in lumpectomy is wire localization technique. A needle with a hooked wire is inserted and fixed in the tumor under ultrasound or X-ray guidance before surgery. The radiologist informs the surgeon about the size and position of the tumor relative to the needle. But it is often difficult to estimate the position of the wire during surgery. The surgeon operates with insufficient spatial awareness about the tumor, which results in the current high rate of positive margins.

Intraoperative ultrasound has been reported to reduce the rate of positive margins in lumpectomy in several studies. Continuous Ultrasound-guided Breast Excision (CUBE) is feasible in some tumors with promising initial results [7]. In this technique, ultrasound is used by surgeons continuously during excision to estimate the distance between the cautery and the tumor margin in the ultrasound image. Despite abundant evidence that ultrasound localization reduces the rate of positive margins [8], intraoperative ultrasound is still not the routine clinical practice. Ultrasound-guided surgery requires a combination of sonography and coordination skills that have

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difficult learning curves, and are traditionally not included in surgical curricula. Furthermore, there is a significant rate of positive margins even when ultrasound is used. Computerized navigation has been beneficial in surgical areas such as orthopedic [9] and neurosurgery [10]. Real time position tracking has also been used for marking breast tumors under magnetic resonance image (MRI)-guidance before lumpectomy [11]. If the cautery was similarly navigated during surgery around the ultrasound-visible tumor margins, it may be helpful in maintaining negative surgical margins and prevent unnecessary removal of excessive healthy breast tissue.

This study aimed to determine whether tracked ultrasound-based surgical navigation can improve the outcomes of lumpectomy performed on breast tumor phantom models, using amount of removed tissue and minimum excision-tumor distance as primary outcomes. A further aim was to determine if the navigation technique is safe and feasible in the clinical environment as assessed by experienced surgical oncologists.

II. MATERIALS AND METHODS

A. Operation Workflow

The navigated surgical technique derives from the standard lumpectomy wire localization method. The localization needle is inserted under ultrasound guidance to or near the tumor. Hooked wires are deployed through the needle to lock the tumor to the needle tip and prevent the needle from slipping out of the breast. The needle creates a rigid relationship between the tumor and the needle base, allowing tumor position tracking by a position sensor on the needle base. Although needles with direct electromagnetic tip tracking are commercially available, our tumor localization needles were short (50 mm) and did not bend significantly during usage, which allowed us to use lower cost tracker attachment at the base. When the localization needle is in place, a skin incision is made across the point where the needle enters the breast. Then two skin flaps are created on both sides of the incision by separating the skin layer from the underlying tissue. The dissection is performed under the flaps downward around the tumor, until the tumor can be separated from the surrounding tissue and removed from the patient.

B. Navigation System Overview

The navigation system consists of an ultrasound machine, a real time position tracker, and a computer running the navigation software. The PLUS software tool interfaces with a wide range of ultrasound and tracker devices that can be interchanged in our system by modifying the PLUS configuration file [12]. In this study we used a SonixTouch ultrasound machine with SonixGPS electromagnetic position tracker (Analogic Corporation, Peabody, MA, USA) and additional electromagnetic position sensors mounted on the surgical tools (Figure 1). The navigation system can be built using any ultrasound machine by directly connecting an external tracker to the navigation computer. A tablet computer (Microsoft Surface Pro 3) was also connected to the navigation computer through a wireless network to provide a convenient user interface for surgeons (Figure 2).

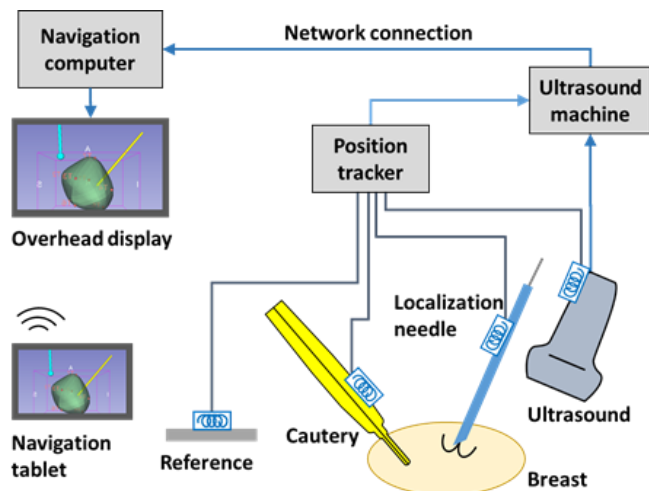


Fig. 1. Overview of the hardware components in the navigation system. Blue coils represent electromagnetic position sensors. The navigation tablet is wirelessly connected to the navigation computer to allow table-side viewing and control.

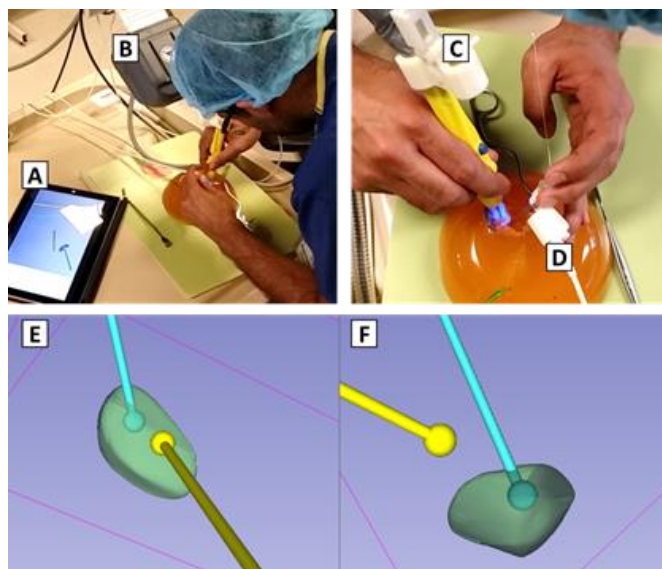


Fig. 2. Phantom experiment setup. The navigation display is shown on a tablet computer (A). The EM tracked transmitter (B) is outside the operating area. EM tracker sensors are mounted on the cautery (C) and the localization needle (D) inserted in the phantom. The tablet displays navigation scenes from the surgeon's point of view (E), and side view (F). The yellow model represents the cautery, the light blue model represents the localization needle. The tumor margin is shown in green.

There are two software applications in our system. The Plus Server application (www.plustoolkit.org) runs on the ultrasound computer. It is responsible for spatial and temporal calibration and collecting and synchronizing real-time data from the ultrasound and the tracker [12]. Synchronized tracked ultrasound is streamed through a local network to the navigation computer. The navigation computer runs another application, 3D Slicer with the SlicerIGT extension (www.slicerigt.org). 3D Slicer is an open-source application platform for medical image processing that support quick application prototyping and distribution through an online extension manager [13].

Schematics of the coordinate systems in the navigation system are illustrated separately for tumor model definition and

tumor excision (Figure 3). The tumor margin was outlined in the live ultrasound images by marking 15-20 points at the tumor boundary while moving the image into different cross sections of the tumor. A three-dimensional boundary surface was generated from the points by Delaunay triangulation followed by smoothing using the 8-point Butterfly Scheme [14]. The tumor boundary points were saved in the needle's coordinate system, therefore even as the tumor moved, the needle – and the tumor model that was defined relative to the needle position – moved along with it. This way tumor motions were compensated by needle tracking during both margin definition and later during surgical excision. Tumor deformations relative to the needle are generally limited because tumor tissue is less elastic compared to healthy breast tissue, and the wire hooks provide additional mechanical support. However, to compensate for potential errors due to tumor deformations, a 1 mm safety zone was added around the visible tumor when defining the surgical margins.

Surgical navigation required presentation of the target area and the relative position of the surgical tools in a simple, intuitive layout. The first three-dimensional navigation scene was presented by a virtual camera from the operator's point of view. An additional view from an orthogonal camera angle and to the right of the operator was shown for depth perception. The surgeon set up the views by activating virtual camera control mode in the software and then moving the tracked cautery as if it was a video camera: the position and orientation of the cautery determined the viewpoint position and orientation. The camera up direction was defined in the direction of the cautery buttons. The virtual camera position could not be linked to the needle position sensor, because changes in needle orientation during the procedure would have resulted in camera rotations, making the navigation display less intuitive for the surgeon. Therefore, an additional position sensor was taped on the patient's sternum in a consistent anatomical orientation and used as a reference coordinate system for the virtual cameras.

The navigation software is released in the form of open-source modules for the 3D Slicer application, with a license allowing academic and commercial use and modification without obligations (www.slicerigt.org). Furthermore, hardware design for surgical tools are also released as editable files under the same permissive license (www.plustoolkit.org). The navigation system can be replicated without programming using any ultrasound machine and a wide range of position trackers due to the device abstraction feature of the PLUS software toolkit [12].

C. Navigation Workflow

The navigation software is used in three workflow steps during this surgery. 1) Prior to start of the procedure, the reference position sensor is placed on the patient's sternum for correct anatomical orientations in the navigation display. Cautery tracker calibration is performed by placing the cautery tip on the sterile needle tracker, and pivoting the cautery around its tip for 5 seconds. The cautery orientation relative to the

cautery tracker is defined in the mechanical design of the tracker clip, therefore only the position of the tip needs to be computed intraoperatively. We use a closed form pivot calibration problem algorithm based on singular value decomposition. For implementation details see source code of our Pivot Calibration software module¹. 2) The needle is inserted in the tumor and wire hooks are deployed. A three-dimensional tumor margin model is defined on tracked ultrasound images displayed on the tablet computer. The surgeon defines the tumor model by tapping on the visible margins. A three-dimensional contour enclosing these margin points is computed automatically after each new point is added (Figure 4). 3) Before the first incision, virtual camera orientations are adjusted to the surgeon's point of view for navigation.

During excision, the navigation system provided audiovisual cues to the surgeon when the cautery tip came close to the tumor margins. The cautery tip position relative to the tumor margins

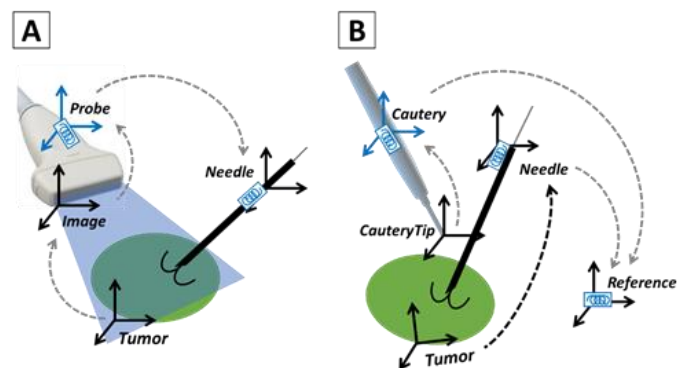


Fig. 3. Coordinate systems and transformations during tumor contouring (A) and tumor excision (B). Blue coils indicate position sensors. Dashed arrows indicate transformations between coordinate systems. Tumor margins are saved in the Needle coordinate system, and rigid connection (black dashed arrow) is assumed during excision.

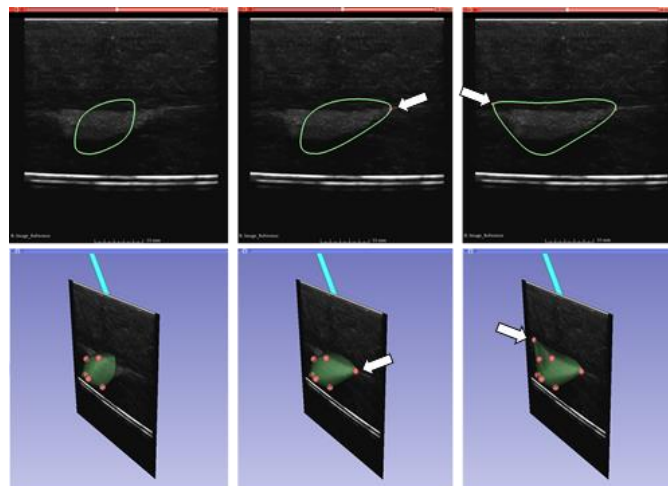


Fig. 4. Tumor margins are represented by a three-dimensional surface (green) including tumor margin points (red) picked by the user. As new points are added on the 2-dimensional ultrasound images (top row), the three-dimensional margin model (bottom row) is updated automatically. Light blue stick represents the localization needle. White arrows point to new tumor margin points defined by the user.

¹ <https://github.com/SlicerIGT/SlicerIGT/tree/master/PivotCalibration>

was shown in the three-dimensional scenes (Figure 2). When the cautery tip crossed the planned margin, the margin model turned from green to red in the navigation display and a warning sound was played on the speakers of the navigation computer. This warning sound drew the surgeon’s attention to the potential risk of cutting into the tumor. The surgeon could then look at the navigation display to assess an optimal route to avoid cutting into the tumor.

D. Phantom Experiments

Phantom experiments were designed to test the effect of navigation on outcomes of lumpectomy. Eight surgical residents familiar with wire-localization lumpectomy technique volunteered to participate in the phantom study. Tumor contouring involved at least two images in two approximately orthogonal scanning orientations, e.g. cranial-caudal and left-right, but additional contour points were allowed until the operator was confident that the entire tumor is inside the contour with at least 1 mm safety margins. Typically 6-8 contour points were marked on each ultrasound image. Each participant performed two lumpectomies on phantom models; a Control procedure by conventional wire localization method

and a Navigated procedure using the navigation system. Four participants started with the Control and four with the Navigated procedure to avoid learning bias. Sterile technique was not relevant for the outcomes of the phantom study, therefore sterile bagging of tracking instruments were omitted.

Phantom models were constructed from plastisol liquid plastic (M+F Manufacturing, Fort Worth, TX, USA), adding 1/4 part softener to match the mechanical characteristics of biological tissue [15]. Three phantom parts were created using different additional materials. The bottom layer was transparent to allow measurement of excision-tumor distance after surgery by inspecting the phantom from the bottom side. The upper part of the phantom modelled normal breast. Cellulose 1 g / 300 ml was added to the liquid plastic for realistic ultrasound speckle, and to make the phantom opaque to the surgeon looking from the top side. The third component was for the tumor model. The amount of cellulose was doubled in the tumor material to create ultrasound visible tumor contrast. The tumor material was also marked with EP2-19 phosphorescent powder (Judikins, Gardena, CA, USA), 0.5 g / 300 ml so that we could check for complete tumor removal by examining the specimens in the dark. All tumor models were cylinder shaped with 5 mm diameter and 10 mm length, weighing approximately 0.2 g. They were placed in the phantoms with their long axis in the horizontal plane, in random orientation around the vertical axis.

To evaluate the effect of navigation in the phantom lumpectomies, we measured total weight of excised tissue, tumor presence at excision margins, and minimum excision-tumor distance. The durations of navigation system setup (tumor contouring and navigation view setup) and excision were recorded. Additionally, participants filled out a survey after the procedures to rate their experience with both control and navigated procedures.

E. Data Analysis

Weight of excised tissue was compared using paired T-test. Original data is reported for tumor presence at excision margins and minimum excision-tumor distance. Results of the survey were analyzed using Wilcoxon rank-sum test. Survey analysis uses Bonferroni correction for the significance level of $p=0.05$ to account for multiple comparisons.

F. Clinical Safety and Feasibility Study

The study protocol was approved by our institutional ethics review board. Clinical feasibility was tested in patients undergoing lumpectomy with palpable breast tumors. Since palpable tumors can be safely excised solely relying on tactile feedback, surgeons could test the navigation system without additional risks to the patients. After written informed consent, six patients participated in the feasibility test. Two experienced surgical oncologists tested the system during palpable tumor lumpectomies. After the operations, the surgeons' feedback was recorded on a questionnaire. Usability was rated on a scale of 1-5 (very difficult – very easy). Steps of the operations were timed to assess if navigation affects the procedure time.

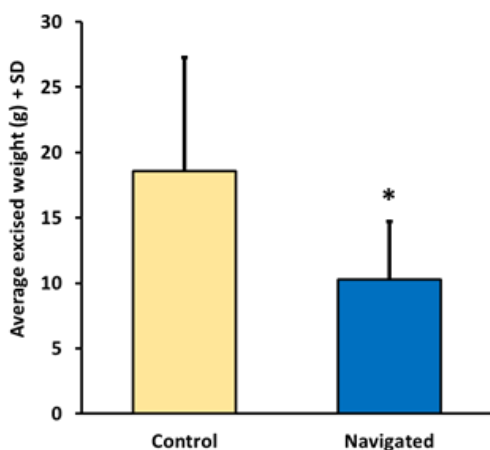


Fig. 5. Average weight of excised tissue in the two study groups. * $p<0.05$ vs. Control group at 95% confidence interval.

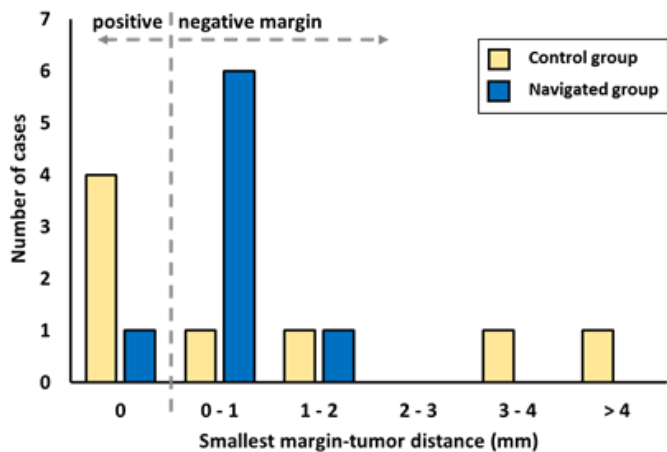


Fig. 6. Distribution of smallest excision-tumor distances in the excision cases in both study groups.

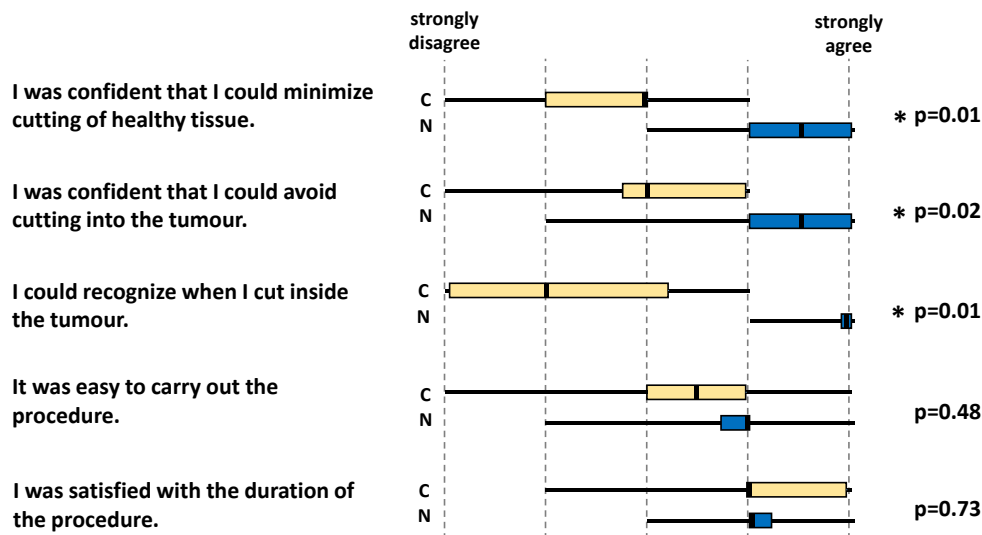


Fig. 7. Summary of results from the questionnaire. Box and whiskers diagram represents minimum, 25th percentile, median, 75th percentile, and maximum. Upper bars (C) represent answers from the Control group. Lower bars (N) represent answers from the Navigated group. * p < 0.02 Navigated group vs. Control group.

III. RESULTS

A. Phantom Study

In lumpectomies performed on phantom models, excised tissue weight was significantly lower in the Navigated group compared to the Control group (10.3 ± 4.4 vs. 18.6 ± 8.7 g, average \pm SD, $p = 0.01$) (Figure 5).

The positive margin rate was 12.5% (1/8) in the Navigated group, and 50% (4/8) in the Control group. The minimum excision-tumor distance was consistently around 1 mm in the Navigated group, while it was approximately evenly distributed in a 5 mm radius around the tumor margin for the Control group (Figure 6). The excision time from first incision to removal of tumor tissue was 4.3 ± 2.3 min in the Navigated group, and 4.0 ± 1.5 min in the Control group (average \pm SD). There was an additional average 3.4 min spent on tumor margin definition and navigation view setup before excision in the Navigated group.

Participants were significantly more confident that they could minimize healthy tissue damage, cutting into the tumor, and recognize tumor margin breach in the Navigated group (Figure 7). No significant difference was found in the perceived difficulty of the two procedures.

B. Clinical Safety and Feasibility

The navigation system successfully passed infection control inspection, and was approved for a safety and feasibility study by our institutional ethics review board. The system was integrated in the operation room environment without interfering with the standard arrangement of other equipment (Figure 8). Six lumpectomies for palpable tumors have been completed using the navigation system. Setup and calibration of the system could be completed during preparation of the patient. Cautery pivot calibration and tumor contouring on tracked ultrasound are the only steps that the navigation system adds to the standard procedure time. The total operation time from patient draping to incision closure was 51 ± 16 min (average \pm SD), within the standard operation time for

lumpectomy. Experienced surgeons rated the navigation system as easy (4 out of 6) or very easy (2 out of 6) to use. No breach of sterile barriers was detected after sterile bagging of the tracking instruments. Lumpectomy was completed in all patients with histologically confirmed tumor-negative margins.

IV. DISCUSSION

Our results indicate that navigation improves measurable outcomes in a phantom lumpectomy model, and surgeons rate it as a helpful adjunct to the conventional wire localization method. We have also successfully verified that the system is feasible in a clinical environment.

Tracked ultrasound-based navigation is one of several methods that have been developed to reduce the rate of positive margins in lumpectomy. Another common approach is to check the excised tissue margins during surgery. Intraoperative frozen section histology was found to improve the clean margin rate of lumpectomy. However, it adds significant time and cost to the routine procedures, since it requires a pathologist to be available near the operating room at the time of surgery [16].

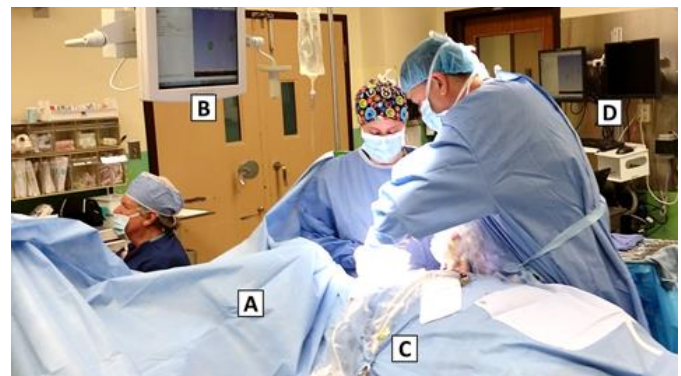


Fig. 8. Navigation system in use during lumpectomy operation. Picture shows ultrasound machine and electromagnetic tracker under sterile drape on the opposite side of the surgeons (A); Overhanging monitor with navigation display (B); tracker sensor cables in sterile bags (C); and computer running the navigation software (D).

Navigation does not require additional staff, and can be implemented with inexpensive instruments. Intraoperative margins can also be analyzed using the electrical properties of tissue by a handheld device, but this method has limitations in both sensitivity and specificity [17]. Another approach to more accurate lumpectomy is tumor marking with a radioactive seed. The surgeon can localize the markers using a gamma counter during surgery. The reduction in positive margin rate is limited, even when the seed is confirmed to be in the excision [18]. Radioactive markers cannot model the three-dimensional tumor for precise navigation. An expensive but promising method for image-guided lumpectomy is MRI guidance. The breast can be fixed with a thermoplastic shell, and the skin can be marked based on the tumor location on the MRI image. However, lumpectomy after MRI-based skin marking still resulted in 21% positive margin rate [19]. MRI-guided surgery may be improved in the future by combining it with navigation. An MRI-compatible needle may be implanted in the tumor. MRI-derived tumor contours could be defined with respect to the needle, and used during navigated lumpectomy. This could be an alternative solution for navigation tumor excision when the tumor margins cannot be assessed in ultrasound.

The greatest technical challenge in developing the navigation system for lumpectomy is that tumor motions are possible any time during imaging, contouring, or excision due to the deformable nature of breast tissue. Although moving anatomical targets have been accounted for in published navigation techniques, these methods cannot be applied directly in breast surgery. Ventilation during general anesthesia is associated with predictable motion patterns in internal organs [20]. Real-time navigation can also be combined with respiratory gating [21]. However, patients may only be sedated during lumpectomy, and tissue deformations in open surgical procedures depend on factors independent of breathing, e.g. physical interaction with tissues. A more straightforward approach to the moving target problem has comprised tracking the target by insertion of a position sensor in or near the target area. This has been extensively tested in liver tumor ablation [22][23]. Although methods developed for liver ablation and liver surgery are closely related to our current approach, our approach does not require spatial registration of a preoperative image or tumor model. Furthermore it does not require multiple needles that would make cutting around and removing the tumor more challenging. Liver surgery navigation uses preoperative CT imaging, and the liver shape does not significantly deform after imaging. Unfortunately neither of these applies to ultrasound imaging and breast tissue. In breast tissue, the target tumor may move relative to the reference position sensor even during the registration process between the tumor margins and the needle position sensor. In contrast to existing surgical planning systems, the presented tumor model definition in the needle's coordinate system accounts for tumor motions even during the construction of the model. A similar approach to our presented method is used in liver tumors in ultrasound-guided interventions [24]. Although this method provides near real-time visualization of the tumor without previous registration, repeated tumor margin definitions during

lumpectomy at every suspected tumor movement would significantly increase the procedure time. Another approach uses a preoperative tumor model that is intraoperatively registered to tracker placed directly in the tumor [25] using tracked ultrasound imaging. In contrast, our method does not need such a registration step, leaving less room for inaccuracies and procedure failure. An electromagnetic tracker was also used to navigate a needle into the kidney using a rendezvous approach with a tracked needle [26]. This method eliminates image registration from the navigation workflow, but is only suitable to track a single target point, not a tumor contour.

Our method also allows real-time extension of the tumor margins by adding additional margin points during surgery. This may become an important feature when advanced real-time tumor detection techniques, such as optical coherence tomography, fluorescent markers, or other real-time chemical analysis of the tissue become feasible with commercial cautery tools. Real-time adjustment of tumor margins would minimize the risk of tumor deformations, or undetected tumor regions in ultrasound. Another advantage of our method is that it does not require preoperative volumetric imaging, or that special markers be placed in the patient before surgery. This may be an important aspect in patient management, because surgery scheduling would not depend on other procedures before lumpectomy.

A limitation of our methods is that tissue deformations have not been analyzed or estimated. Deformations larger than the safety zone kept around the tumor when defining the tumor model may allow actual tumor tissue to be outside the tracked margins. Mechanical properties of our phantom models were close to real breast tissue, but future studies in biological samples should analyze the amount of deformations under typical surgical manipulations and various tumor sizes. Although our methods may be applicable in any tumor size, larger tumors will likely require larger safety margins due to larger deformations. Large safety margins may limit the benefit of navigation compared to conventional wire-localization. It is also known that about half of breast tumors are not directly visible in ultrasound images. The tumor location can still be made visible for ultrasound during tumor biopsy before surgery. Hematoma, a side effect of biopsy, is visible in ultrasound for up to 5 weeks, and it can be used as an ultrasound landmark during surgery. Hematoma as a marker has shown to reduce the rate of positive margins compared to the conventional wire localization method from 47% to 24% in a single-center study [27]. Synthetic gel markers are more predictable tissue markers for preoperative ultrasound localization [28]. Advanced ultrasound imaging techniques may be integrated in the navigation system to differentiate a wider range of cancers from normal tissue [29].

We used electromagnetic tracking, because the relatively larger markers of optical trackers would interfere with the surgical workspace, or may bend the localization needle. Electromagnetic tracking is known to be affected by ferromagnetic objects and electrical instruments in the tracking field. Steel retractors and the electrosurgical cautery may distort the tracking field, therefore we analyzed the tracker accuracy in

the presence of these tools [30]. Optical tracking was used to provide simultaneous true position for electromagnetic tracker testing [31]. Accuracy was not affected by retractors due to the distance between tools and their position sensors. The operating cautery did not affect tracking accuracy either, probably due to the difference between the cautery and the tracker electromagnetic signal frequency. In our system tracking accuracy is most important at the tumor margins. This was not directly measured, but the excision-tumor distance and tumor presence at the margins are indirect indicators that tumor margin tracking was sufficiently accurate during excision.

There was one positive margin among the results of the Navigated group in our phantom study. Although we are uncertain whether this was caused by human or machine error, this indicates that our navigation system alone does not guarantee successful procedures, and further system improvements may lead to better outcomes.

V. CONCLUSION

The presented navigation method may become a routine clinical technique to reduce the rate of positive margins. Open-source release of all software and hardware will hopefully foster research collaboration and incremental results towards our goal of lower tumor recurrence after lumpectomy, and more efficient treatment in this large patient population. Since the presented method is not limited to breast, or non-palpable tumors, future studies should be conducted to explore its full potentials in surgical oncology.

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