

Image-Guided Navigation in Lymph Node Biopsy

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ABSTRACT

Background and Objectives: Image-guided navigation is an effective intra-operative technology in select surgical subspecialties. Laparoscopic and open lymph node biopsy are frequently undertaken to obtain adequate tissue of difficult lesions. Image-guided navigation may positively augment the precision and success of surgical lymph node biopsies.

Methods: In this prospective pilot study, pre-operative imaging was uploaded into the navigation platform software, which superimposed the imaging and the subject's real-time anatomy. This required anatomical landmarks on the subject's body to be spatially registered with the platform using an infrared camera. This was then used to guide dissection and biopsy in laparoscopic and subcutaneous biopsies.

Results: Image-guided lymph node biopsy was undertaken in 15 cases. Successful biopsy locations included: retroperitoneum, porta hepatis, mesentery, iliac region, para-aortic, axilla, and inguinal region. There was an 87% total absolute success rate in biopsies (89% in laparoscopic image-guided navigation [LIGN] and 83% in subcutaneous image-guided navigation [SIGN]). There was a 92% absolute success rate in lesions with fixed locations. There was a 67% absolute success rate in lesions with mobile locations.

Conclusion: The investigators successfully incorporated image-guidance into surgical biopsy of lymph nodes in a diverse variety of locations. This image-guided technique for surgical biopsy can accurately and safely localize target lesions minimizing unnecessary dissection, conversion to open procedure, and re-operation for further tissue characterization. This technique was useful in the morbidly obese, instances of limited foci of disease, PET-active lesions, identifying areas of highest PET-avidity, and lesions with critical surrounding anatomy.

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Disclosure: The StealthStation (Medtronic, Minneapolis, Minnesota, USA) was used in the study in a way for which it is not technically labeled.

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INTRODUCTION

Image-guided navigation (IGN) involves syncing perioperative imaging to the patient's real-time anatomy on the operating room (OR) table to guide dissection relative to the position of surgical instruments. Use of IGN has become widespread in craniofacial and spinal procedures, but has also shown theoretical feasibility in other surgical fields.¹⁻⁵ In 2004, Mårvik et al⁶ proposed the use of 3-dimensional (3D) navigation technology based on preoperative magnetic resonance imaging (MRI) or computed tomography (CT) in combination with a laparoscopic navigation pointer in laparoscopic surgery. Chen et al⁷ first showed the feasibility of thoracoscopic localization of pulmonary nodules in a porcine model using the StealthStation (Medtronic, Minneapolis, Minnesota, USA) surgical navigation system, which is used extensively in craniofacial and spinal surgery.⁷ This technology may have clinical feasibility and efficacy in surgical lymph node biopsy.

Laparoscopic biopsy is frequently undertaken to obtain adequate tissue sampling of a lesion when percutaneous methods fail or are not feasible. Laparoscopic lymph node biopsy has been well described in the abdomen, pelvis, and retroperitoneum, leading to diagnosis, immunohistochemical analysis, and staging of lymphoma, metastatic abdominal malignancies, and metastatic genitourinary malignancies.^{8,9} Laparoscopic biopsy has proven more efficacious than percutaneous biopsy in intra-abdominal lymphoma and superior to open biopsy of nodal metastasis of colon cancer.^{10,11} Targeted surgical biopsy approaches using image-guidance may lead to faster, safer diagnoses and more rapid initiation of treatment.

The goal of this study was to explore the feasibility and efficacy of combining laparoscopic and open lymph node biopsies with intraoperative IGN. Laparoscopic image-guided navigation (LIGN) and subcutaneous image-guided navigation (SIGN) may lead to financial and outcome benefits by streamlining the diagnosis of malignancies and minimizing perioperative patient morbidity. Clinical feasibility of LIGN and SIGN in lymph node biopsy may also lead to the study of this technology in different surgical procedures throughout the body.

MATERIALS AND METHODS

A prospective interventional pilot study was undertaken. All biopsies were performed by the principal investigator (PI) at a single institution with an intraoperative navigation platform and trained support personnel readily available (Stealth-Station). All subjects had preoperative imaging with CT or positron emission tomography (PET)-CT. This experimental investigation of human subjects underwent an appropriate and thorough institutional review board (IRB) process. All subjects were appropriately educated about the study, with all questions and concerns addressed, and gave informed consent to be involved in the study by signing a detailed consent form approved by the IRB.

Preoperative images (CT, PET-CT) were first uploaded into the navigation software platform. This platform was then brought into the OR with a connected infrared camera on an articulating arm (**Figure 1**). At least 4 of the following standardized anatomic reference locations were used to sync preoperative imaging to real-time anatomy: sternal notch, clavicular heads, xiphoid process, costal margins, pubic symphysis, umbilicus, and anterior superior iliac spine (ASIS). Within the platform, the investigators tagged any combination of these locations on the preoperative imaging study and registered the same location on the subject's anatomy with an infrared reflecting pointer (**Figure 2**). These points on the subject's body had to register in the platform via the infrared camera within an acceptable margin of error in relation to the tagged points on the preoperative imaging.

At this point, the spatial location of the lesion was approximately the same in both the subject's body on the OR table



Figure 1. The navigation platform and the infrared camera interface attached by an articulating arm overlooking the patient's real-time anatomy.



Figure 2. Top: before surgery, the anatomical landmarks were stored in the navigation platform, shown by the red dot and red arrow. Bottom: the identical anatomical landmarks were subsequently synced to real-time anatomy with an infrared reflective pointer.

and the preoperative image within the navigation platform. Infrared reflecting spheres were then affixed to the surgical instruments, and the spatial orientation of the instruments was registered. After following all of these steps, upon entry of the laparoscope into the peritoneum, the investigators had a camera view with a simultaneous view showing the corresponding CT or PET-CT cut relative to the location of the instrument tip. The investigators were then able to scan through the surgical field to localize the lesion of interest and begin dissection for biopsy. For open biopsy, the investigators were able to guide incision placement over the lesion and scan through the subcutaneous tissue toward the lesion. **Figures 3** and **4** show example views from the OR of retroperitoneal lymph node biopsies obtained with the use of LIGN. **Figure 5** displays laparoscopic pictures from a targeted LIGN retroperitoneal dissection (case 4) with the ureter coursing directly on top of a target lymph node. With a less precise dissection, ureteral injury would have been more difficult to avoid. Once the specimen was obtained, it was confirmed by fresh-frozen pathology intraoperatively and then further characterized through a formal histopathologic evaluation.

RESULTS

This technique was applied to 15 cases (5 men, 10 women) with age range of 30–80 (median, 56) years and body mass index (BMI) range of 18.1–45.9 (median, 27.6) kg/m². **Table 1** shows case details of the LIGN biopsies. Indications for

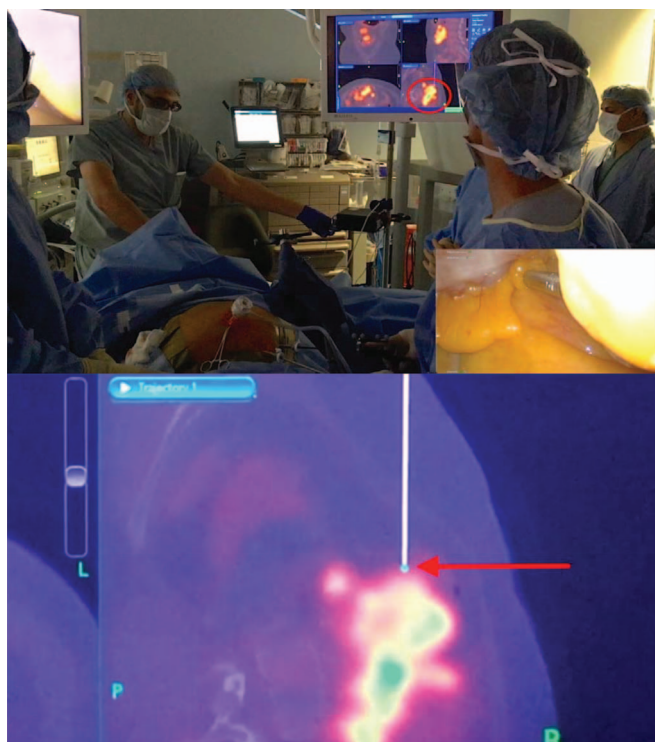


Figure 3. Top: from the surgeon's point of view, the ability to simultaneously scan through the synced preoperative PET-CT and the laparoscopic camera view. Here, the instrument tip is shown abutting the mesenteric PET-avid lesion in the platform view (red circle) and in the laparoscopic view (close-up). Bottom: close-up of the platform view shows the location of the lesion of interest in relation to the tip of the synced laparoscopic instrument shown by the red arrow.

biopsy included lymphadenopathy, work-up of lymphoma recurrence, breast cancer metastasis, and further tissue characterization after a previously inadequate biopsy. Lesion locations included retroperitoneum, porta hepatis, mesentery, iliac region, para-aortic, axilla, and the inguinal region. Biopsy results included reactive lymph node, diffuse large B-cell lymphoma, follicular lymphoma, small lymphocytic lymphoma, marginal zone B-cell lymphoma, and Hodgkin lymphoma. **Table 2** displays biopsy statistics. There were no surgical complications. Two cases were converted to open: 1 was planned to have an open component of the surgery because the lesion encased the aorta and vena cava. IGN could not be used in 2 cases, because the platform did not properly sync the subject's anatomy within an acceptable margin of error—defined as platform failure.

Nine cases were laparoscopic biopsies, and there was an 89% (8/9) absolute success rate—defined as achieving adequate tissue for diagnosis and immunohistochemical analysis

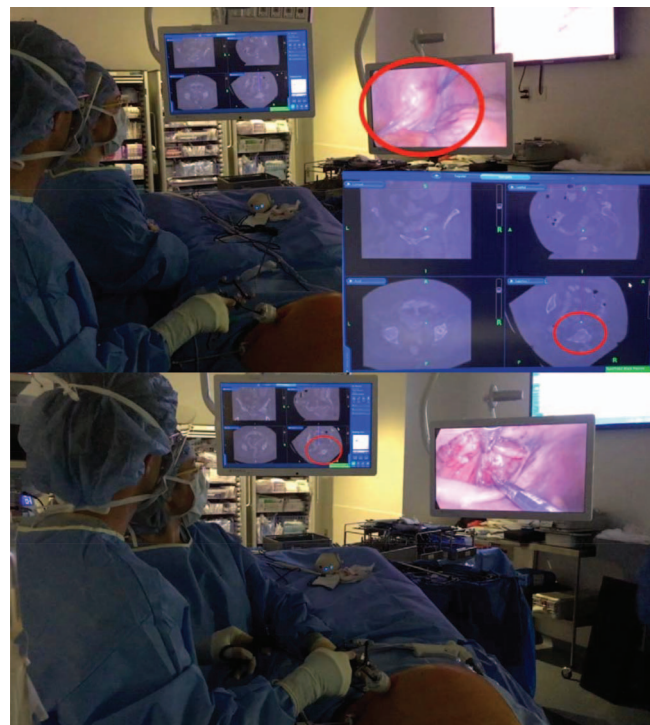


Figure 4. Top: from the surgeon's point of view, the lesion of interest (red circles) is found with the synced laparoscopic instrument tip on both the platform view of the preoperative CT (close-up shown) and the laparoscopic view. Bottom: from the surgeon's point of view, the image-guided dissection of the peritoneum is performed, and the lesion location is confirmed again before biopsy on the platform view (red circle) with the synced laparoscopic instrument tip.

as planned. In 2 cases that were converted to open, an adequate biopsy was still achieved (22%), and 1 case had a platform failure that disallowed image-guided biopsy (11%). Six cases were open subcutaneous biopsies with an 83% (5/6) absolute success rate, and 1 case had a platform failure that disallowed image-guided biopsy (17%). Twelve of the cases involved lesions in fixed anatomic locations. Of these cases, there was a 92% (11/12) absolute success rate, 1 case had a platform failure (8%), and 1 case was converted to open, but adequate biopsy was achieved (8%). Three of the cases involved lesions in mobile anatomic locations. Of those cases, there was a 67% (2/3) absolute success rate: 1 case had a platform failure (33%), and 1 case was converted to open, but adequate biopsy was achieved (33%).

DISCUSSION

This prospective pilot study supports the use of IGN in surgical biopsy of lymph nodes as feasible and efficacious. In

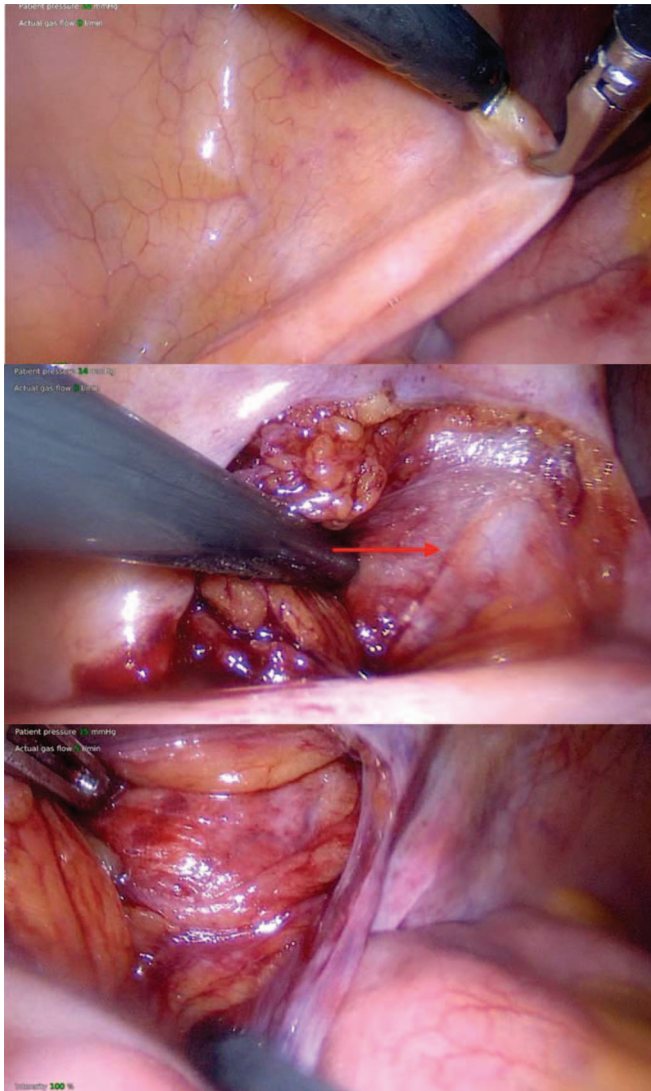


Figure 5. Top: laparoscopic view, the lesion of interest has been precisely located by using LIGN, and peritoneal dissection begins. Middle: laparoscopic view, the image-guided dissection of the peritoneum is performed, and the ureter directly overlying the lesion is seen to vermiculate (red arrow). Bottom: laparoscopic view, the ureter is gently swept away exposing the underlying lymph node.

the investigators' experience, these very difficult biopsies were immensely aided, if not entirely made possible, by image guidance. Based on these findings, IGN is best used when the lesion has limited foci of disease and has a complex anatomic location, in the setting of morbid obesity, and when there is a preoperative expectation of extensive dissection or extended time under anesthesia. Minimizing dissection reduces risk of bleeding and injury to adjacent structures (**Figure 5**). When the target lesion is a solitary node, or

a node in a chain with the highest PET avidity, IGN can direct dissection toward this high-yield lesion. IGN can expedite the diagnosis of difficult intra-abdominal, retroperitoneal, and subcutaneous lymphomas. However, it can also expedite the diagnosis of a negative or purely reactive lymph node, minimizing the likelihood that a patient will receive further unnecessary and potentially harmful medical or surgical treatments. Or, as in case 15, it can help diagnose lymphoma after a previous biopsy showed a purely reactive lymph node.

Based on the findings, LIGN and SIGN are best used in fixed lesions. Fixed lesions have a high probability of residing in the identical spatial position throughout time: both in the real-time anatomy and the anatomy of the patient during the preoperative imaging. If the lesion is in a mobile location, such as the mesentery, small bowel, or the axillary–breast complex, there is a higher degree of variability in where the lesion is position spatially in real-time surgical anatomy compared to where it was in preoperative imaging—depending on the different external physical forces acting in these scenarios. For example, axillary dissection and biopsies were aided more by SIGN when the lesion was adherent to the chest wall, rather than in mobile and redundant soft tissue. PET-CT obtained with thin cuts was preferred by the investigators for maximizing precision in IGN biopsy to a standard CT scan. A PET-CT was sometimes obtained after traditional CT in the preoperative period, often because of the patient's diagnosis.

It is worth mentioning that some of the initial cases were purposely chosen to test the feasibility of this technology: for example, a very large retroperitoneal lymphoma requiring more extensive tissue sampling that was an obvious abnormality as soon as the laparoscope entered the body. This lesion would not have been difficult to biopsy without IGN, but it helped show that IGN is a feasible adjunct. With proven feasibility, IGN was applied in several of the later cases where the lesions were much more concealed—for instance, a small lymphoma at the porta hepatis of a morbidly obese patient. In more difficult cases like such as that one, LIGN and SIGN were minimally invasive adjuncts that decidedly aided in lesion localization and biopsy success.

This clinical review is limited by the fact that the technology used was not designed to aid in laparoscopic or subcutaneous biopsy; it was designed for craniofacial and spinal surgery. The high absolute success rate despite this fact (in very difficult biopsies) shows great potential for IGN in laparoscopic and subcutaneous biopsy. In the future, IGN may also have the potential to augment other difficult surgical dissections, such as in parathyroid iden-

Table 1. Case Information and Results of Biopsies Including Biopsy Pathology

Case	Gender	Age (years)	BMI (kg/m ²)	Indication for Biopsy	Diagnostic Imaging	Repeat Imaging	Lesion Location	Procedure	Notes	Result
1	F	80	24.8	Retroperitoneal lymphadenopathy	CT	PET-CT	Retroperitoneum	LIGN	—	Diffuse large B-cell lymphoma
2	M	63	24.8	Abdominal lymphadenopathy	CT	No	Porta hepatitis	LIGN	—	Reactive lymph node
3	F	30	33.6	Lymphoma recurrence	CT	PET-CT	Mesentery	LIGN	—	Diffuse large B-cell lymphoma
4	F	70	42.9	Iliac lymphadenopathy	CT	No	Iliac chain	LIGN	—	Reactive lymph node
5	F	68	23.0	Retroperitoneal lymphadenopathy	CT	No	Retroperitoneum	LIGN	—	Follicular lymphoma
6	F	68	41.86	Lymphoma recurrence	PET-CT	No	Porta hepatitis	LIGN	—	Small lymphocytic lymphoma
7	F	56	25.8	Lymphoma recurrence	PET-CT	No	Mesentery	LIGN	Conversion to open	Follicular lymphoma
8	F	56	28.5	Breast cancer metastasis	PET-CT	No	Axilla	SIGN	Platform failure	—
9	F	46	45.9	Lymphoma recurrence	CT	PET-CT	Axilla	SIGN	—	Reactive lymph node
10	M	41	27.2	Further tissue characterization	CT	No	Iliac chain	LIGN	Platform failure	—
11	M	50	24.9	Lymphoma recurrence	PET-CT	No	Inguinal region	SIGN	—	Follicular lymphoma
12	M	38	18.1	Lymphoma recurrence	PET-CT	No	Inguinal region	SIGN	—	Marginal zone B-cell lymphoma
13	M	63	27.6	Lymphoma recurrence	PET-CT	No	Retroperitoneum	LIGN	Conversion to open	Hodgkin lymphoma
14	F	46	45.9	Lymphoma recurrence	PET-CT	No	Axilla	SIGN	—	Reactive lymph node
15	F	46	45.9	Lymphoma recurrence	PET-CT	No	Inguinal region	SIGN	—	Hodgkin lymphoma

Cases 9, 14, and 15 involved 3 separate image-guided biopsies on the same patient.

Table 2.

Statistical Results of the Image-Guided Biopsies

Biopsy and Lesion Type	Success Rate
Image-guided Biopsies	
Laparoscopic	89 (8/9)
Open	83 (5/6)
Lesion	
Fixed anatomic location	92 (11/12)
Mobile anatomic location	67 (2/3)
Overall	87 (13/15)

Notably, fixed lesions were easier to biopsy with navigation. Data are the percentage of successes in the total group (number of successful biopsies/total attempted).

tification or reoperative surgery. However, the off-label application in this clinical review also reveals an open marketplace for IGN software designed specifically for the abdomen, retroperitoneum, pelvis, thorax, neck, and subcutaneous tissues, among others, which could lead to even greater surgical precision in these locations. Furthermore, this study is limited as a single-investigator study with a small subject population.

CONCLUSION

Image guidance was successfully and safely incorporated into surgical biopsy of lymph nodes in a diverse variety of locations. Adequate biopsy was achieved in 13 of 15 cases. No patient was harmed during the study. Two operations were converted to open, and these lesions were in very challenging locations. Nearly all difficult biopsies were positively enhanced by the technology. The investigators believe that this image-guided technique for surgical lymph node biopsy can more accurately and safely localize target lesions in properly selected cases, minimizing unnecessary dissection, conversion to open procedure, and reoperation for further tissue characterization. This technique was useful in the morbidly obese, instances of limited foci of disease, lesions with critical surrounding anatomy, PET-active lesions, and in identifying lesions of highest PET avidity. The investigators believe that the success shown in this prospective interventional pilot study using IGN for surgical biopsy of lymph nodes may lead to further investigation of applying image guidance as a surgical navigation technology outside of craniofacial and spinal surgery. Further success using IGN may lead to the development of navigation software platforms created specifically for different anatomic locations.

IGN is likely to become integrated into robotic surgery interfaces, as well. More advanced image-guidance software may also eventually aid in extensive, complicated abdominal, thoracic, pelvic, soft tissue, and neck resections.

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