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Original Research Article

After neoadjuvant therapy, axillary sentinel lymph node frozen sections from breast cancer patients are accurately diagnosed using telepathology

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ABSTRACT

Context: Telepathology is a digital, microscope-independent method of diagnosing pathology from scanned slides. Frozen sections (FS) can be performed and read by a pathologist at any site. At our institution, telepathology is used for diagnosis of frozen sections of sentinel lymph nodes (SLN) in patients who have undergone neoadjuvant chemotherapy and are enrolled in a clinical trial.

Objective: We investigated the accuracy of diagnosing SLN frozen sections in the neoadjuvant setting using telepathology.

Design: SLN were entirely submitted for frozen section. A pathology assistant prepared the frozen and scanned the slides using VisionTek M6 digital microscope ecosystem (East Dundee, IL). Cases were interpreted by trained, board-certified pathologists. All frozen sections remnants were submitted for formalin-fixed paraffin-embedded permanent sections. Frozen section diagnoses using telepathology were compared to final pathology. Turn-around time from specimen collection to frozen section diagnosis was recorded.

Results: 54 SLN from 22 breast neoadjuvant cases were diagnosed via telepathology from March 2017 to July 2019. 95% of SLNs interpreted as negative on frozen section and on permanents. A definitive diagnosis could not be rendered on six SLNs; diagnosed "atypical" at frozen. Sensitivity and specificity were 80% and 100% respectively with accuracy of 95.8%. The false-negative rate was 5%. There were no false positives. The average turn-around time was over an hour.

Conclusions: Telepathology is an accurate method of diagnosing SLN frozen sections in the neoadjuvant setting, but lobular carcinomas and treatment effect pose diagnostic challenges and the time to report results is increased compared to standard microscopy.

Introduction

Telepathology is a relatively new technique that enables pathologists to review digital images of glass slides without a microscope. Using telepathology for diagnosis has advantages. Pathologists can evaluate slides in real time from any computer or even a phone, and do not have to be at a microscope; multiple pathologists can view the slides at the same time; and domestic and international consults can be done without the need to mail slides to distant locations. Another benefit is to perform intraoperative frozen section consultation at remote locations that cannot be staffed with a pathologist. Potential disadvantages of the technology include lack of comfort by the pathologist reviewing slides on the computer rather than a microscope, sluggish internet resulting in less-than-optimal digital slide quality, and the amount of time needed to make a diagnosis. It has previously has been reported in the literature that telepathology for frozen sections has acceptable diagnostic accuracy.[1] However, it has not been reported for special circumstances, such as evaluating lymph nodes following neoadjuvant therapy.

Sentinel lymph node (SLN) excision is a limited evaluation of the first draining lymph nodes in the axilla and it is the standard of care for axillary surgical management.[2–4] Evaluation of these lymph nodes, which are localized by radioactive or colored tracers, determine whether axillary dissection is indicated. Frozen sections are performed on SLN in order to guide intraoperative surgical decisions about axillary management. The eighth edition of the American Joint Committee on Cancer (AJCC) classifies regional lymph node metastasis by size: isolated tumor cells (ITCs) are <200 tumor cells or < 0.2 mm, micrometastases are 0.2 mm - 2.0 mm, and macrometastases are >2.0 mm.[5] Intraoperative frozen section diagnosis of sentinel lymph nodes in surgical breast cancer cases by standard microscopy has been shown to offer a reasonable sensitivity and accuracy

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for diagnosing macrometastases, but low sensitivity (19%) for detecting micrometastases.[6–8]

Neoadjuvant treatment, including chemotherapy and endocrine therapy, is used for certain breast cancers to reduce tumor size, enable better surgical and cosmetic outcomes, and to obtain upfront prognostic information about the tumor.[9] After neoadjuvant chemotherapy, lymph nodes may regress and be difficult to identify.[10–12] Additionally, ITCs and micrometastases are more common after treatment, making frozen section diagnoses challenging.[13]

There are significant morbidities associated with axillary dissection, and in 2011, the ACOSOG Z0011 (Alliance) clinical trial, found that for patients undergoing lumpectomy followed by radiation with limited SLN involvement (1–2 nodes), axillary dissection did not provide added survival benefit.[2,14] With this information, and additional confirmational studies, there has been a shift in clinical practice to perform sentinel lymph node excision only, when certain criteria are met. Another ongoing clinical trial A011202 (Alliance), of which our institution is a participant, compares axillary radiation to axillary dissection after neoadjuvant chemotherapy. Patients enrolled in this trial have a pre-treatment biopsy proven lymph node metastasis and are treated with neoadjuvant chemotherapy. At the time of surgery, a pathologist evaluates SLN's by frozen section and if there is at least one positive lymph node (>0.2 mm), patients are intraoperatively randomized to receive either axillary dissection or axillary radiation.[15] For patients not enrolled in this trial who have metastatic cancer in a sentinel node after neoadjuvant chemotherapy the standard surgical treatment is axillary lymph node dissection.

At our institution, we have a central hospital staffed with pathologists, but also have two satellite hospitals, which are not staffed with pathology assistants (PA) or pathologists, and couriers take specimens back to the main hospital. The only frozen sections requested are SLN from breast cancer patients who have received neoadjuvant chemotherapy. Many of these patients are enrolled in the A011202 trial. The use of telepathology to diagnose SLNs in breast cancer during frozen section has been shown to be equivalent to onsite microscopy,[16–18] but the accuracy of telepathology frozen section diagnosis of SLNs after neoadjuvant therapy has not been reported. Our hospital structure and use of telepathology provided a unique opportunity to evaluate the accuracy of using telepathology in the neoadjuvant setting.

Methods

Our system for intraoperative sentinel lymph node review from our satellite hospitals is the following: The surgeon provides advanced notification that a case will require a frozen section at the satellite hospital. A PA travels to the satellite hospital and prepares the frozen using standard protocols. SLN are serially sectioned perpendicular to the long axis into 2 mm thickness sections and entirely submitted for frozen section intraoperative diagnosis. The sections are embedded in Optimal Cooling Temperature (OCT) (Sakura Finetek, Torrance, CA) media. The frozen embedded tissue is cut to 5 μm thickness and at least three levels are cut of each section. The cut sections are stained by rapid H&E and the whole slides is scanned using the VisionTek M6 digital microscope ecosystem (East Dundee, IL). A board-certified pathologist is assigned to "frozen call" to cover virtual and onsite frozen sections one week at a time and is divided between approximately 10 pathologists with a wide range of experience levels (from new-in-practice to >15 years of experience). All pathologists completed training on the VisionTek system. The assigned pathologist is given advanced notification of the case and is notified by the PA when the slides are ready to be scanned. The pathologist logs into the system (VisionTek viewing system) and interprets the digital telepathology slides from a personal office computer. The pathologist has the ability to zoom in and out of the digital image and move to different areas of the image to visualize all of the tissue on the slide, similar to microscopy. Deeper level sections can be requested by the pathologist when needed. All remnants of frozen sections are then thawed and submitted for formalin-fixed paraffin-embedded permanent sections. Results are called in to the surgeon and written on printed paperwork for each case. The time at diagnosis is recorded.

For this study, a retrospective search was performed in the pathology database for patients from 2017 to 2019 who were treated with neoadjuvant chemotherapy and had frozen sections of sentinel lymph nodes diagnosed by telepathology. Patient characteristics and demographics as well as tumor characteristics such as the Nottingham score were recorded. If no residual tumor remained after neoadjuvant therapy, the grading from the pre-treatment biopsy was recorded, if available. This was an IRB approved study.

Results of SLN frozen section diagnosis made by telepathology and the final diagnosis made by standard microscopy including the remnant frozen section were compared. Frozen section results were considered inconsistent if the telepathology frozen section was interpreted as negative and the slide during standard microscopy revealed a micro- or macrometastasis. A negative interpretation at frozen section and either a negative result or ITCs identified at permanent section were considered concordant (per clinical trial protocol). A frozen section diagnosis of positive and a diagnosis of negative on final review was also considered inconsistent.

The false-negative rate was calculated using the number of SLNs found to have micro- or macrometastases by microscopy that were not identified during telepathology frozen section over the total number of negative SLN diagnosed at frozen section.

Turn-around time was determined from collection in the operating room to telepathology frozen section diagnosis reported to the surgeon, which was recorded for each case. For comparison's sake, a small retrospective search from January 2019 to July 2019 of frozen sections of SLN after neoadjuvant therapy by standard microscopy was undertaken to record the time to diagnosis of those cases. The comparison cases were onsite cases for the same pathologist covering telepathology cases.

Results

Twenty-two patients meeting criteria for the study were found retrospectively after performing a search in the pathology database. All patients had biopsy-proven breast cancer prior to neoadjuvant therapy. Patient and tumor characteristics are reported in Table 1. All patients were women. The average patient age at surgery was 52 years with a range of 28–71 years. Residual tumor was present in the resection specimen in 14 of 22 patients. The predominant tumor type was invasive ductal carcinoma (17/22). Two patients did not have their outside pathology reviewed at our institution. One (Case 15) did not include a breast resection specimen because surgery was aborted after the frozen section was performed, and the other (Case 19) had a complete response to presurgical treatment and for clinical reasons, the completion surgery was not performed.

Frozen section diagnosis by telepathology was performed on a total of 54 SLNs (Fig. 1). The majority of SLNs were interpreted as negative at frozen section (40/54). Eight SLN were interpreted as positive (8/54), and six SLNs were called atypical and were deferred to permanent sections (6/54). Of the SLNs diagnosed as negative at frozen section, two were later found to have macrometastases that required immunohistochemistry for diagnosis on permanent sections (2/31) (Fig. 2). The permanent sections from the six SLNs with deferred ("atypical") diagnosis revealed three positive SLNs (two macrometastases, one micrometastases) and three negative SLNs (one ITC). Three of the SLNs with deferred diagnosis at frozen section were from a single case of invasive lobular carcinoma. One SLN with deferred diagnosis at frozen section still underwent axillary lymph node dissection at the same surgery due to concern by the surgeon, but the SLN was negative on permanent section, showing extensive treatment effect. There were no false positives in this study. The sensitivity was 80%, specificity was 100%, and the accuracy was 95.8%. The false-negative rate was 5%.

The number of SLNs sent for frozen section diagnosis ranged from 1 to 4 per case. Case 10 did not report the time of diagnosis communicated to the surgeon and is not included in turn-around time analysis. The average turn-around time was 1 h, 16 min per frozen section and the median turn-around time was 1 h, 14 min. The range for turn-around time was 37 min–2 h, 5 min. A comparison of turn-around time was made of neoadjuvant breast

Table 1
Characteristics of patients and tumors. The average age of at surgery was 52 years. Invasive ductal carcinoma was the majority tumor type (17/22). Residual tumor in the breast was identified in 14/22 cases. Case 15 did not include a resection specimen. Case 19 had a complete response to presurgical treatment, but we did not have access to the patient's prior biopsy. The tumor type and Nottingham grade are shown. Residual tumor indicates if there was residual cancer in the breast resection specimen. If no residual tumor was identified in the breast resection specimen, the grading from the biopsy was used. The number of sentinel lymph nodes (SLN) sent for frozen section diagnosis, the number of SLN diagnosed as positive or atypical at frozen section, and the number of positive SLN on permeants are listed. UNKN = unknown; Mam = mammary.

Case #	Age	Type	Grade	Residual tumor	# SLN frozen	# SLN positive or atypical at frozen section	# SLN positive on permeant
1	32	Ductal	2	Y	2	1	2
2	45	Ductal	2	Y	3	0	0
3	60	Ductal	3	N	2	0	0
4	71	Mam	2	Y	2	2	2
5	54	Ductal	3	Y	1	1	1
6	28	Ductal	3	Y	1	1	1
7	56	Ductal	1	Y	2	1	1
8	58	Lobular	2	Y	3	3 – Atypical	2
9	73	Lobular	2	Y	2	0	0
10	56	Ductal	2	Y	3	1	1
11	46	Ductal	3	Y	2	0	0
12	74	Ductal	3	Y	4	1 – Atypical	1
13	28	Ductal	3	N	3	0	0
14	43	Ductal	3	N	4	0	0
15	42	UNKN	UNKN	UNKN	2	1	2
16	46	Ductal	3	N	2	1 – Atypical	0
17	59	Ductal	3	N	3	0	0
18	69	Ductal	3	Y	3	1 – Atypical	0
19	48	UNKN	UNKN	N	1	0	0
20	50	Ductal	2	Y	3	0	0
21	55	Ductal	2	Y	2	0	0
22	49	Ductal	3	N	4	0	0

cancer cases which had frozen section of SLNs by standard microscopy covered by the same group of pathologists (Fig. 3). There were 33 cases with a total of 88 SLN frozen sections. These were found to have an average turnaround time of 37 min per frozen section.

Discussion

Pathology practices are varied. Many receive pathology specimens from multiple hospitals in different locations. Staffing at remote sites can be challenging for departments due to logistics and expense. Our institution is an academic, tertiary care and comprehensive cancer care health system, which has expanded in recent years. Two satellite hospitals, which are 40 min to an hour drive away from the central hospital depending on traffic, were opened to accommodate regular health-care needs and cancer care to surrounding areas. Surgery is performed at these two locations, and specimens are couriered to the pathology department at the central facility. The only surgery requiring frozen sections at this time has been breast sentinel lymph nodes, which are not frequent enough to warrant staffing the gross room at these hospitals with a PA or a pathologist. In order to handle the sentinel lymph node frozen sections, a telepathology system was purchased (VisionTek M6 digital microscope). A protocol was established with the surgeon to provide advanced notice of any remote cases requiring a frozen section, so that a PA and a pathologist could be made available. A PA travels to the hospital where the surgery is performed, prepares the specimens for frozen section and alerts the pathologist to examine the scanned digital whole slide images. The pathologist calls in results to the surgeon in the OR the same as they do with standard frozen sections.

Frozen sections of axillary SLNs for breast cancer by standard microscopy is challenging for many pathologists. With neoadjuvant treatment, the difficulty is magnified by treatment effect, biopsy site changes and reactive changes to lymphoid cells, which make interpretation difficult.[13,19,20] Determining whether a small residual tumor focus is a micrometastasis or isolated tumor cells in this setting can be challenging, but is important, as positive lymph nodes of any size (micrometastasis or macrometastasis) may trigger axillary dissection.[3–5,21]

In this study, we show that telepathology has comparable accuracy to standard microscopy for interpreting frozen sections of sentinel lymph nodes from breast cancer patients who had neoadjuvant therapy (94.9%)[13] and similar accuracy to a prior study that analyzed telepathology of breast cancer SLN without neoadjuvant therapy.[18] Treatment effect and lobular carcinomas contributed to false negatives and non-diagnostic (atypical) results.

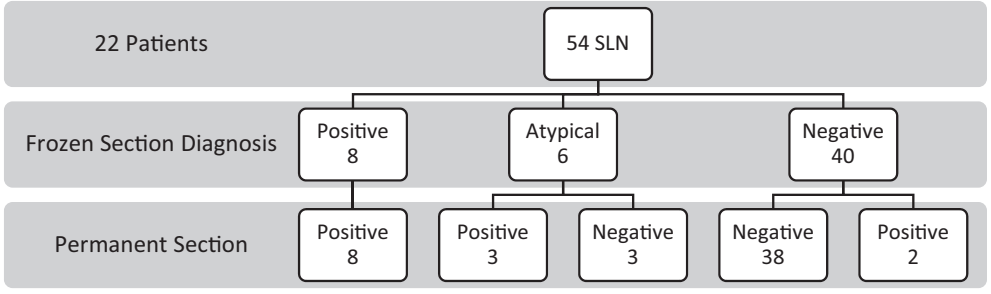

Fig. 1. Sentinel lymph nodes (SLN) sent for frozen section diagnosis via telepathology that have been treated with neoadjuvant therapy. 54 SLN were sent for frozen section diagnosis from 22 patients. The majority of SLN interpreted as negative at frozen section were negative at permanent section (38/40). The two false-negative SLN required the use of immunohistochemistry to identify the metastatic cells. All SLN interpreted as positive at frozen section were positive on permanent section (8/8). Of the six SLN with diagnosis deferred at frozen section, half were positive at permanent (3/6).

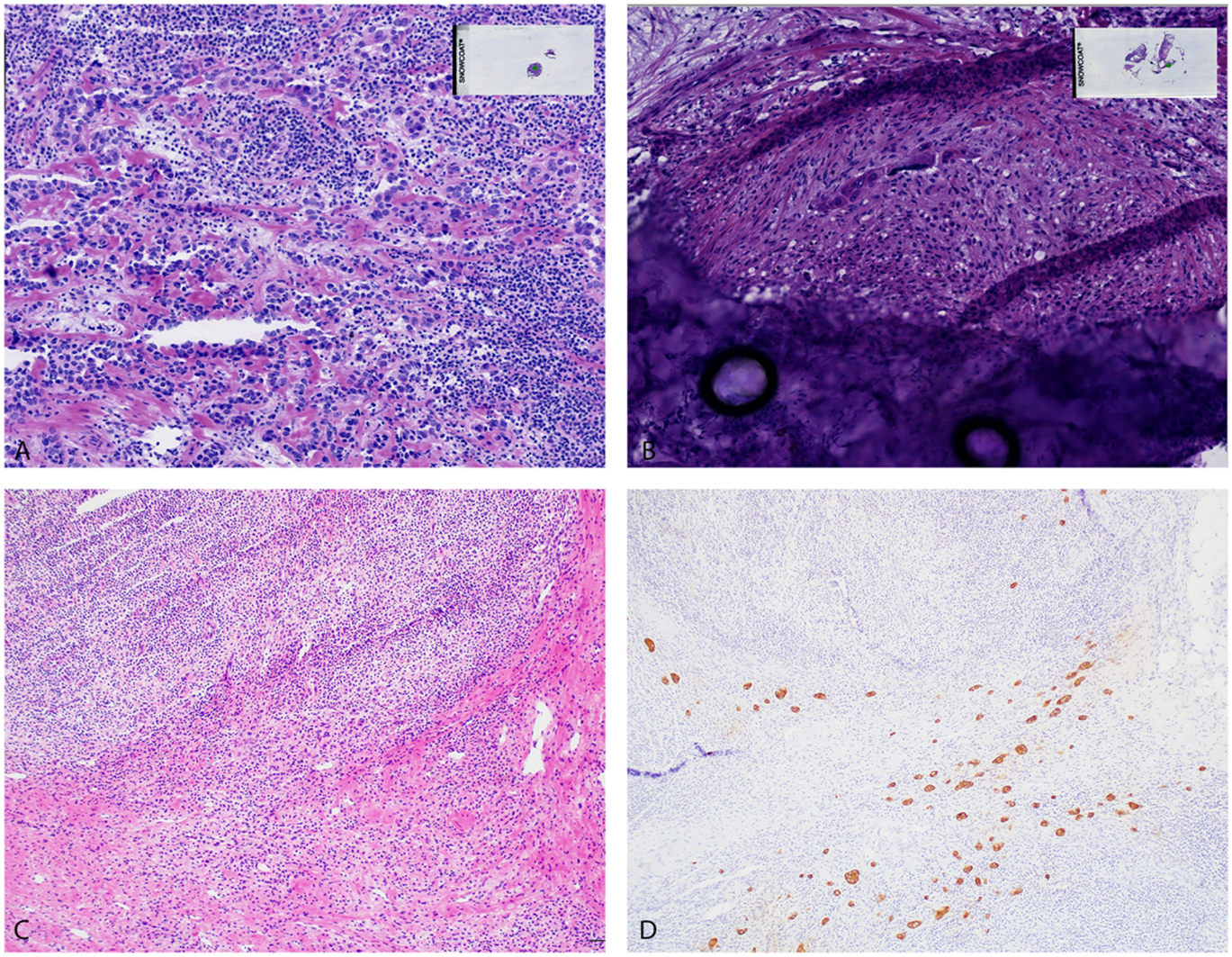

Fig. 2. Representative images from cases. (A, B) Images taken during frozen section telepathology from Case 4 (A) and Case 6 (B). (C, D) Representative photos of false-negative lymph node. (C) Section shows a fibrotic lymph node with clusters of cells at 10× (C) Immunohistochemical AE1,3 keratin stain (10×) highlights small keratin positive clusters and single cells (D).

While accuracy of diagnosis is important, so too are the time to diagnosis and comfort with making the diagnosis. Surgeons wait for frozen section diagnoses to determine intraoperative lymph node management. The turn-around time for the diagnosis is important, since the patient must remain under anesthesia while the histology is evaluated. We found that telepathology frozen section results on average take 39 more minutes than non-telepathology cases. Though we did not specifically study this, the amount of time appears to be related to the number of lymph nodes sent, each with multiple levels, and the time needed to review the digital images. We are also limited by computer speed and network issues; however, exact network speeds and firewall issues were not documented during the study. Our pathologists complain of pixelated images that take time to come into focus. Although each pathologist was trained on how to use the system, many months may pass between using it, so our pathologists have not become faster or more adept by seeing more cases. While this has not affected diagnostic accuracy, it adds time and a feeling of unease with looking at whole slide images on a screen rather than standard microscopy. Our study was not undertaken to perform a root cause analysis to improve telepathology turn-around time or pathologists' comfort with the system, but it did reveal that this is an area for improvement. Despite the added time to the cases, our breast surgeon who operates at the remote sites has communicated that, while not ideal, the benefit of receiving a frozen section diagnosis outweighs the cost of the delay.

There were two obvious weaknesses of this study. The first is having a relatively small sample size to analyze. The second is that it would be interesting to have a direct comparison of telepathology with standard microscopy. This would require looking at a microscope and the computer concurrently at the time of a frozen section and was not possible during actual surgical cases. Retrospectively, this could be done with existing slides, and might provide additional data about the comfort level of pathologists with the digital system when reading frozen sections in the neoadjuvant setting.

Telepathology optimizes patient care by providing access to pathologists who are not on-sitewhere a surgery is performed. While telepathology has previously been shown to have high diagnostic accuracy in a variety of settings, our study contributes that diagnostic accuracy is maintained during the evaluation of sentinel lymph nodes following neoadjuvant chemotherapy for breast cancer. However, our study also found thatthat the turn-around time to diagnosis can be much longer than standard microscopy in this se ing, which should be considered in the adaptation of this technology.

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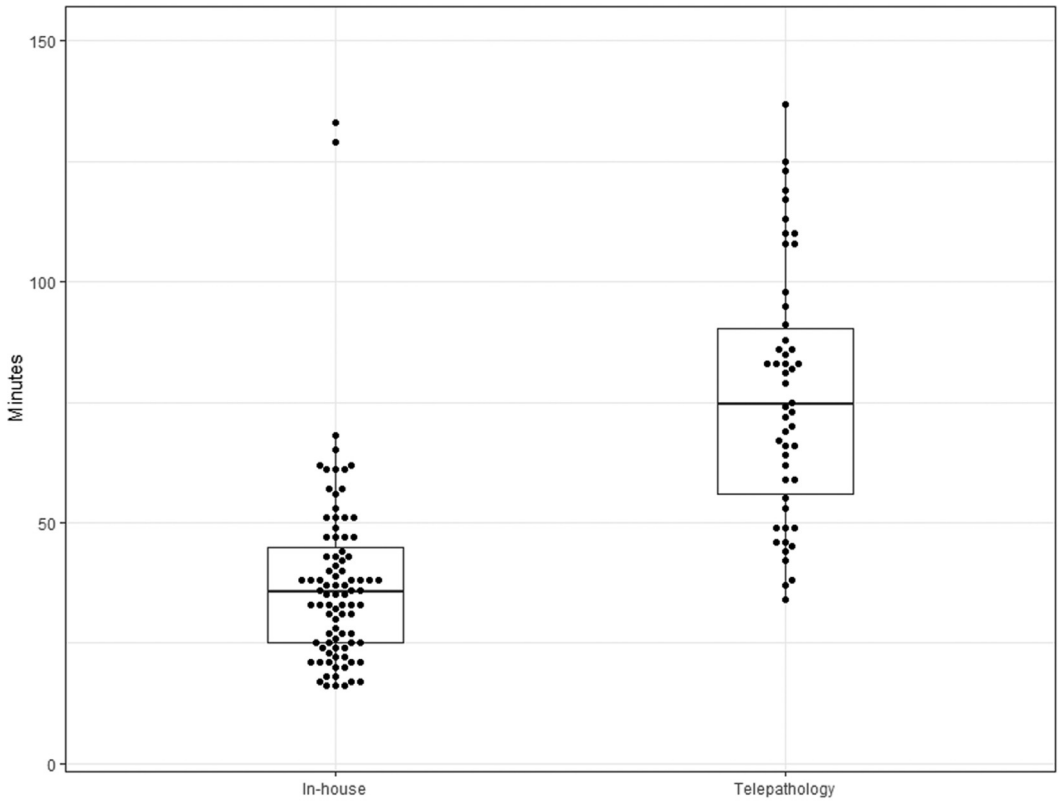

Fig. 3. Turn-around time (TAT) in minutes per frozen section. Turn-around time is defined as collection time in the operating room to diagnosis report to the surgeon. In-house neoadjuvant SLN frozen sections had an average TAT of 37 min per frozen section for 88 SLNs. When telepathology was used, the average TAT was 76 min per frozen section for 54 SLNs.

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References:

1. Dietz RL, Hartman DJ, Pantanowitz L. Systematic review of the use of telepathology during intraoperative consultation. Am J Clin Pathol October 2019;aqz155. https://doi.org/10.1093/ajcp/aqz155.
2. Giuliano AE, Ballman KV, McCall L, et al. Effect of axillary dissection vs no axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: the ACOSOG Z0011 (Alliance) randomized clinical trial. JAMA 2017;318(10):918. https://doi.org/10.1001/jama.2017.11470.
3. Canavese G, Catturich A, Vecchio C, et al. Sentinel node biopsy compared with complete axillary dissection for staging early breast cancer with clinically negative lymph nodes: results of randomized trial. Ann Oncol 2009;20(6):1001–1007. https://doi.org/10.1093/annonc/mdn746.
4. Krag DN, Anderson SJ, Julian TB, et al. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol 2010;11(10):927–933. https://doi.org/10.1016/S1470-2045(10)70207-2.
5. Amin MB, Edge S, Greene F, et al, eds. AJCC Cancer Staging Manual. 8th ed. Chicago, IL: Springer International Publishing; 2017.
6. Lombardi A, Nigri G, Maggi S, et al. Role of frozen section in sentinel lymph node biopsy for breast cancer in the era of the ACOSOG Z0011 and IBCSG 23-10 trials. The Surgeon 2018;16(4):232–236. https://doi.org/10.1016/j.surge.2017.11.003.
7. Cipolla C, Graceffa G, Cabibi D, et al. Current role of intraoperative frozen section examination of sentinel lymph node in early breast cancer. Anticancer Res 2020;40(3):1711–1717. https://doi.org/10.21873/anticanres.14124.
8. Francissen CMTP, van la Parra RFD, Mulder AH, Bosch AM, de Roos WK. Evaluation of the benefit of routine intraoperative frozen section analysis of sentinel lymph nodes in breast cancer. ISRN Oncol 2013;2013:1–5. https://doi.org/10.1155/2013/843793.
9. Asselain B, Barlow W, Bartlett J, et al. Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials. Lancet Oncol 2018;19(1):27–39. https://doi.org/10.1016/S1470-2045(17)30777-5.
10. Yu Y, Cui N, Li H-Y, et al. Sentinel lymph node biopsy after neoadjuvant chemotherapy for breast cancer: retrospective comparative evaluation of clinically axillary lymph node positive and negative patients, including those with axillary lymph node metastases confirmed by fine needle aspiration. BMC Cancer 2016;16(1):808. https://doi.org/10.1186/s12885-016-2829-5.
11. Boughey JC, Ballman KV, Le-Petross HT, et al. Identification and resection of clipped node decreases the false-negative rate of sentinel lymph node surgery in patients presenting with node-positive breast cancer (T0–T4, N1–N2) who receive neoadjuvant chemotherapy: results from ACOSOG Z1071 (Alliance). Ann Surg 2016;263(4):802–807. https://doi.org/10.1097/SLA.0000000000001375.
12. Boughey JC. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial. JAMA 2013;310(14):1455. https://doi.org/10.1001/jama.2013.278932.
13. Grabenstetter A, Moo T-A, Hajiyeva S, et al. Accuracy of intraoperative frozen section of sentinel lymph nodes after neoadjuvant chemotherapy for breast carcinoma. Am J Surg Pathol 2019;43(10):1377–1383. https://doi.org/10.1097/PAS.0000000000001311.
14. Giuliano AE, Hunt KK, Ballman KV, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. JAMA 2011;305(6):569–575. https://doi.org/10.1001/jama.2011.90.
15. National Library of Medicine (U.S.). Comparison of Axillary Lymph Node Dissection With Axillary Radiation for Patients With Node-Positive Breast Cancer Treated With Chemotherapy. https://clinicaltrials.gov/ct2/show/NCT01901094.
16. Huang YT, Renne SL, Sollai M, et al. Clinical application of a real-time telepathology system for frozen section diagnosis in comparison with optical microscope. Front Med 2019;6:215. https://doi.org/10.3389/fmed.2019.00215.
17. Menter T, Nicolet S, Baumhoer D, Tolnay M, Tzankov A. Intraoperative frozen section consultation by remote whole-slide imaging analysis –validation and comparison to robotic remote microscopy. J Clin Pathol November 2019. https://doi.org/10.1136/jclinpath-2019-206261.jclinpath-2019-206261.
18. Gifford AJ, Colebatch AJ, Litkouhi S, et al. Remote frozen section examination of breast sentinel lymph nodes by telepathology: remote analysis of breast sentinel nodes. ANZ J Surg 2012;82(11):803–808. https://doi.org/10.1111/j.1445-2197.2012.06191.x.
19. Brown AS, Hunt KK, Shen J, et al. Histologic changes associated with false-negative sentinel lymph nodes after preoperative chemotherapy in patients with confirmed lymph node-positive breast cancer before treatment. Cancer 2010;116(12):2878–2883. https://doi.org/10.1002/cncr.25066.
20. Tee SR, Devane LA, Evoy D, et al. Meta-analysis of sentinel lymph node biopsy after neoadjuvant chemotherapy in patients with initial biopsy-proven node-positive breast cancer: sentinel lymph node biopsy after neoadjuvant chemotherapy in patients with initial biopsy-proven node-positive breast cancer. Br J Surg 2018;105(12):1541–1552. https://doi.org/10.1002/bjs.10986.
21. Boileau J-F, Poirier B, Basik M, et al. Sentinel node biopsy after neoadjuvant chemotherapy in biopsy-proven node-positive breast cancer: the SN FNAC study. J Clin Oncol 2015;33(3):258–264. https://doi.org/10.1200/JCO.2014.55.7827.