Real-time Telepathology Is Substantially Equivalent to In-Person Intraoperative Frozen Section Diagnosis

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• ***Context.***—**Intraoperative diagnosis by frozen section is a mainstay of surgical pathology practice, providing immediate feedback to the surgical team. Despite good accuracy with modern methods, access to intraoperative surgical pathology with an appropriate turnaround time (TAT) has been a limiting factor for small or remote surgical centers, with negative impacts on cost and patient care. Telepathology offers immediate expert anatomic pathology consultation to sites without an in-house or subspecialized pathologist.**

Objective.—**To assess the utility of live telepathology in frozen section practice.**

Design.—**Frozen section diagnoses by telemicroscopy from 2 tertiary care centers with combined 3 satellite hospitals were queried for anatomic site, TAT per block, pathologist, and concordance with paraffin diagnosis. TAT and concordance were compared to glass diagnoses in the same period.**

Results.—**For 748 intraoperative diagnoses by telemicroscopy, 694 had TATs with a mean of 18 minutes 56 seconds ± 8 minutes 45 seconds, which was slower than on glass (14 minutes 25 seconds ± 7 minutes 8 seconds, $P < .001$). Twenty-two (2.89% of available) were discordant, which was not significantly different from the on-glass rate ($P = .44$) or categorical distribution ($P = .31$). Two cases (0.27%) had technical failures.**

Conclusions.—**Although in-person diagnoses were statistically faster, the great majority of telemicroscopic diagnoses were returned in less than 20 minutes. This remained true through numerous pathologists, pathology assistants and/or technicians, different hospitals, and during a combined 6 years. The concentration of discordant diagnoses among relatively few pathologists suggests individual comfort with telepathology and/or frozen section diagnosis. In rare cases, technologic issues prevented telemicroscopic diagnosis. Overall, this justifies continued use and expansion of telemicroscopic services in primary intraoperative diagnoses.**

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Frozen section diagnosis is a necessary part of anatomic pathologic practice owing to the need for rapid assessment of clinical variables that change surgical requirements. These include distance of tumor from margin, histologic features and attributes, and other variables. The current approach using modern mounting-medium, hematoxylin-eosin–based methodologies were first codified in 1931.[1] Practices for the last 50 years have and continue to demonstrate high overall accuracy and good interobserver agreement,[2–4] providing operating physicians with timely information necessary to appropriately triage the patients during their surgeries. However, just as with all other medical subspecialties, access to intraoperative diagnosis requires access to skilled pathologists, grossing staff, and the institutions where they practice. Thus, patient populations served outside of major medical centers or urban areas have less access to time-sensitive pathology services. This trend has been noted for the last 40 years and throughout the world, not just in the United States and Canada[5,6] but also in the United Kingdom,[7] Australia,[8] the United Arab Emirates,[9] and Tanzania.[10] Further, even within academic medical centers, such expertise may not be available at all sites at all time, further necessitating the need for telepathology services.

To address issues pertaining to geographic access to intraoperative care, telepathology systems have been created and creatively used.[11,12] These systems have demonstrably increased access to intraoperative pathology services without decreasing accuracy and with turnaround time (TAT) within acceptable limits. Dedicated telemicroscopy/telepathology systems were once outside of the realm of feasibility for most medical centers owing to cost, rarity, and the requirement for individual programming for both local[13] and distant use.[14] In the past decade, such systems have also become more commonplace and much more affordable.

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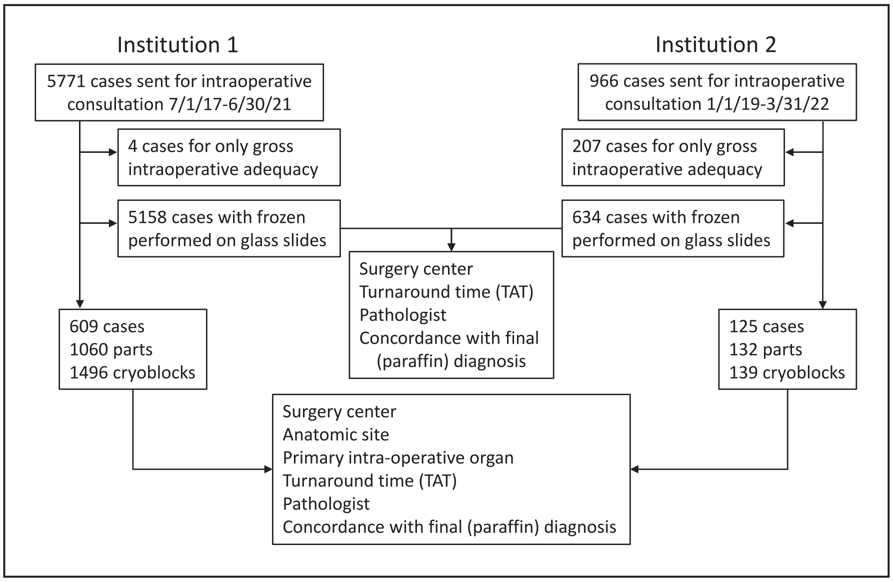

Figure 1. *Analysis pipeline. The respective laboratory information systems were queried at each institution. For all blocks, the surgery center, the turnaround time per block, reading pathologist, and concordance data were recorded. For those cases performed by telemicroscopy, the anatomic site of surgery and the primary intraoperative organ were also recorded. "Frozen" refers to the intraoperative diagnosis performed on frozen tissue.*

Our institutions offer intraoperative pathology services to geographically distant satellite hospitals. At one institution, a pathologist is always on-site, and a telemicroscope is available for subspecialty consultation from the parent hospital. The other institution has pathology assistants on-site who prepare frozen section slides for planned intraoperative diagnosis by pathologists at the parent hospital; no pathologist is present for this institution. All satellite centers use a dedicated, commercially available telemicroscope where field, focus, and magnification are controlled by the computer at the parent institution.

After a combined 6.5 years of utilization of this system, we sought to clarify whether there were distinct measurable outcomes between the telepathology and standard, glass intraoperative diagnoses at our institutions.

MATERIALS AND METHODS

Figure 1 demonstrates the informatics workflow. Records at 2 tertiary care centers that use the same telemicroscope setup (SL5, Mikroscan, Carlsbad, California; http://www.mikroscan.com/mikroscan-sl5) at combined 3 referral sites were included. The hardware/telemicrosope is present only at the distance site, and HIPAA (Health Insurance Portability and Accountability Act)–compliant software is installed on the single distance and every receiving computer. Computers are not required to be dedicated, and send/receive functions within a standard high-speed Internet setup are more than adequate for our use. No specific network configuration is required. All screens must have a minimum resolution (1920 × 1080 pixels) for appropriate utilization. As no image is retained, there is no format, DICOM or otherwise; an image is streamed in real time only, and is viewed through the provided software. Of note, this system is exclusively a telemicroscope with no built-in mechanism for sharing gross images; it neither obviates nor replaces either a standard gross pathology station or skilled gross pathology skills to generate the slides that undergo telemicroscopic diagnosis.

Records were queried for all frozen sections for surgical center, TAT, pathologist, and concordance with final (paraffin) diagnosis in the available time frames. At both institutions, the primary pathologist for telepathologic diagnosis was the same as for nondistance diagnoses on any given day; however, at institution 1, some skin cases were triaged directly to a dermatopathologist. Notification of telepathologic diagnosis to the attending/responsible pathologist differed by location; at institution 1, the primary pathology assistant notified the frozen section pathologist of impending cases by page or phone call, whereas at institution 2, the primary pathologist at the distance site was ultimately responsible for notifying the consultant pathologist by page or phone call. After intraoperative diagnoses were rendered, the attending pathologist was ultimately responsible for notifying the surgeons, usually directly by phone, but infrequently the pathology assistant was asked to notify the surgeons at institution 1.

For cases performed by telemicroscopy, anatomic site of frozen section performed and intraoperative organ site were also annotated. For institution 1, which is the center of referral for 2 satellite hospitals, all frozen section diagnoses in the complete 4-year period following implementation of routine telemicroscopy were included. For institution 2, which serves as the referral site for a single satellite hospital, all frozen section diagnoses with available data, consisting of a 27-month period, were included. TAT on glass was only available for 695 blocks. For cases with multiple frozen tissues, only the main specimen (eg, cancer resection) was included in calculations from institution 1, whereas cases with multiple parts, with each requiring telemicroscopic consultation, were included from institution 2. All calculations and comparisons were performed per block in order to normalize for multiblock, single-part versus multiblock, multipart frozen tissues. Comparisons were performed by 2-way analysis of variance (ANOVA), *t* test with Welch correction, and χ^2 tests as appropriate, and graphs and tables were constructed in Microsoft Excel version 18.2110.13110.0 (Microsoft Corporation, Redmond, Washington) and Graphpad Prism, version 9.3.1 (Graphpad, San Diego, California). This study was performed following the principles of the Declaration of Helsinki; it exclusively uses data previously collected for internal institutional quality assurance use and does not involve human subjects.

RESULTS

For institution 1, a total of 5771 cases were identified in a 4-year period, of which 609 were performed by telemicroscopy. For institution 2, a total of 966 cases were identified in the 27 months available, of which 125 had a total of 139 blocks where any portion of the intraoperative diagnoses was performed by telemicroscopy. A total, therefore, of 734 cases with 748 relevant blocks performed by telepathology were identified between the 3 satellite hospitals, consisting of 17 uniquely annotated anatomic sites (Table 1). A markedly varied distribution of primary site was identified between hospitals and between institutions.

Table 1. Tissue Site and Turnaround Time (TAT) for Telemicroscopic Cases by Hospital/Surgical Center[a]															
	Institution 1									Institution 2					
	Hospital 1			Hospital 2			Combined			Hospital 1			Overall		
Anatomic Site	No.	n With TAT	TAT	No.	n With TAT	TAT	No.	n With TAT	TAT	No.	n With TAT	TAT	No.	n With TAT	TAT
Parathyroid	243	234	18:01	18	18	15:07	261	252	17:49	2	2	30:00	263	254	17:55
Skin	213	182	13:08	1	0	N/A	214	182	13:08	1	1	32:30	215	183	13:14
Lymph node	66	59	23:14	31	30	19:15	97	89	21:53	3	3	33:00	100	92	22:15
Brain	0	0	N/A	1	0	N/A	1	0	N/A	51	50	30:40	52	50	30:40
ENT	15	14	20:04	2	2	24:30	17	16	20:37	34	34	24:55	51	50	23:32
Prostate	0	0	N/A	0	0	N/A	0	0	N/A	15	15	22:10	15	15	22:10
Ovary	0	0	N/A	1	1	23:00	1	1	23:00	7	7	21:20	8	8	21:33
Thyroid	1	1	18:00	6	5	22:00	7	6	21:20	1	1	25:00	8	7	21:51
Soft tissue	0	0	N/A	4	3	27:20	4	3	27:20	4	4	23:45	8	7	25:17
Neuro	0	0	N/A	0	0	N/A	0	0	N/A	7	7	24:25	7	7	24:25
Joint	0	0	N/A	6	6	13:02	6	6	13:02	0	0	N/A	6	6	13:02
GI	0	0	N/A	0	0	N/A	0	0	N/A	4	4	20:35	4	4	20:35
GU	0	0	N/A	0	0	N/A	0	0	N/A	3	3	21:25	3	3	21:25
GYN	0	0	N/A	0	0	N/A	0	0	N/A	3	3	25:50	3	3	25:50
Breast	0	0	N/A	0	0	N/A	0	0	N/A	2	2	20:30	2	2	20:30
Liver	0	0	N/A	1	1	13:00	1	1	13:00	1	1	31:00	2	2	22:00
Bone	0	0	N/A	0	0	N/A	0	0	N/A	1	1	30:00	1	1	30:00
Total/average	**538**	**490**	16:53	**71**	**66**	18:15	**609**	**556**	17:03	**139**	**138**	26:32	**748**	**694**	18:56

Abbreviations: ENT, otorhinolaryngologic (ear, nose, and throat); GI, gastrointestinal; GU, genitourinary; GYN, gynecologic specimens separate from ovary; N/A, not applicable; Neuro, extracranial neurological specimens ("Brain" indicates intracranial).

[a] The distribution by organ undergoing frozen section diagnosis with the respective TAT (in minutes:seconds) as available is included. Institution 1 serves 2 satellite hospitals.

For institution 1, which comprised 2 satellite hospitals, the greatest proportion of frozen sections was performed on parathyroids (261 of 609, 42.86%) and skins (214, 35.14%). For institution 2, the greatest proportion was composed of brain (51 of 139, 36.69%) followed by otorhinolaryngologic (ear, nose, and throat) specimens (34, 24.46%).

Recorded TAT per block likewise varied dramatically, ranging from less than 5 minutes to 1 hour 2 minutes at institution 1 and 10 to 44 minutes at institution 2. The average TAT by institution and anatomic site is shown in Table 1, and the distribution of anatomic sites with TAT is shown in Figure 2, A and B. Times are defined by minutes and seconds. Overall TAT was 18 minutes 56 seconds $\pm$ 8 minutes 45 seconds, with 17 minutes 3 seconds $\pm$ 8 minutes 3 seconds at institution 1 and 26 minutes 32 seconds $\pm$ 7 minutes 13 seconds at institution 2. Compared to glass diagnoses performed at each institution in the same time frame, the turnaround by telepathology was significantly slower ($P < .001$; Table 2). Significant differences in TAT by anatomic site were noted (overall $P = .01$), with wide ranges of TAT within anatomic sites as well. Two cases at institution 1 (0.33% of institutional total) noted computer technical issues that did not allow a frozen diagnosis to be rendered; no such instances occurred at institution 2.

Next, concordance with final diagnosis for telemicroscopic frozen diagnoses was compared to concordance in the same time frame by glass at each institution. Twenty-two of 760 total discordant cases (2.89%) were identified. For institution 1: 557 of 609 cases (91.46%) had available concordance data, and 19 (3.03% of available) were discordant. In the same time frame, 262 of 6539 frozen diagnoses rendered on glass (4.00%) were discordant. For institution 2: 3 of 151 cases (1.99%) were discordant on telemicroscopy, compared to 51 of 1692 (3.01%) by glass. No significant difference in rate or distribution of discordance grade was identified when compared overall as well as within each institution (all $P \geq .11$; Table 3).

The specialty of each frozen section pathologist for each telemicroscopy interpretation is delineated in Table 4. Thirty-seven unique pathologists read an average of 20 (mode, 2; range, 1–131) frozen telemicroscope cases between both institutions. Discordant reads were present for 10 of these pathologists, with a mean of 2.2 (range, 1–4). The available reason for each discordant diagnosis was individually examined (Table 5). No trend in anatomic site or reason for discordance was discerned.

DISCUSSION

We report substantial equivalency between intraoperative frozen section diagnoses performed at our institutions by telepathology and by standard practices on glass. This remained true over a combined nearly 6.5 years; among 37 unique reading pathologists with a variety of subspecialty pathology areas of practice; between numerous pathologists, pathology assistants, and/or technicians performing the gross pathology and loading the telemicroscope; and for 3 different satellite sites served by the 2 separate hospital systems. No difference in discrepancy rate, or trend in reason for discrepancy, was noted. To our knowledge, this study also encompasses the greatest number of cases, anatomic sites, reading pathologists, and time frame of any attempt to interrogate this question to date.

The relative concentration of discordant diagnoses among a small proportion of the reading pathologists suggests differences in individuals' degree of comfort with the telepathology system or with frozen section, as opposed to

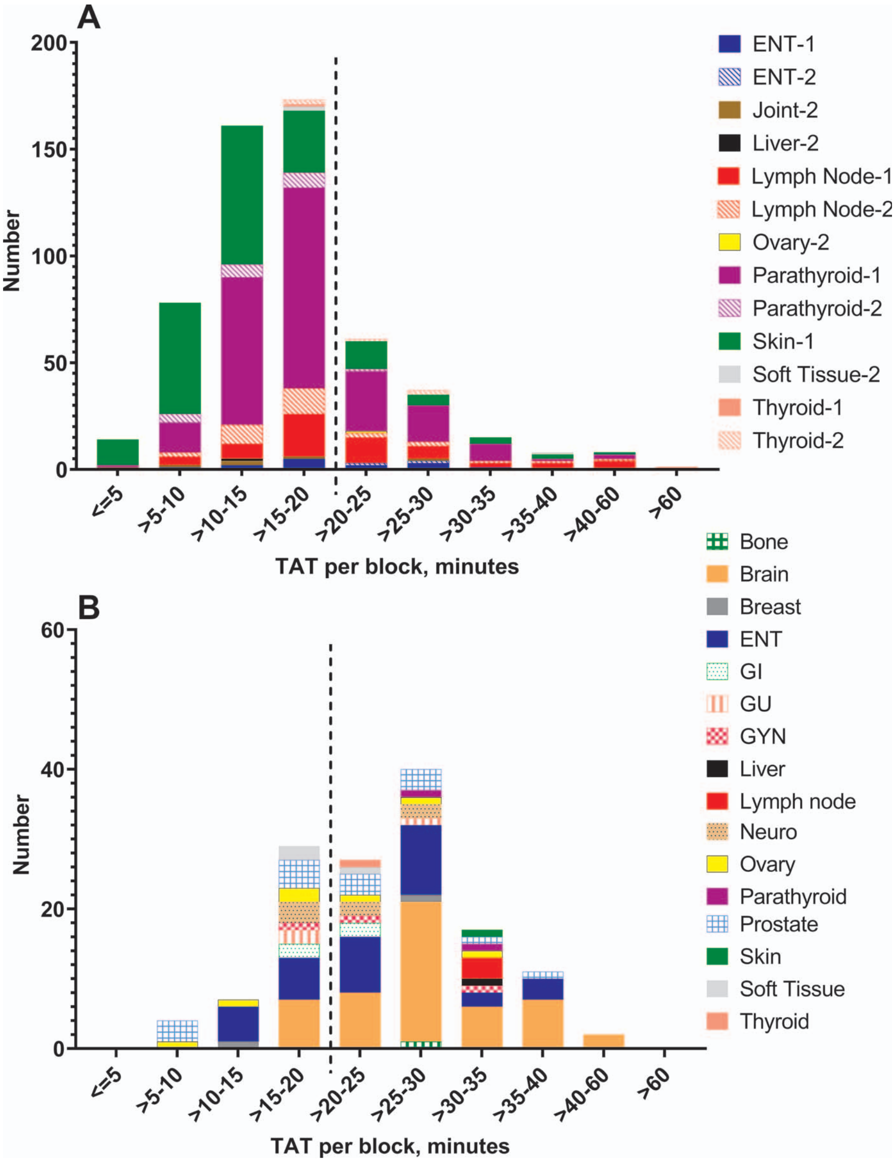

Figure 2. *TAT per block for anatomic site and hospital. The distribution of anatomic site and TAT at institution 1 (A) and institution 2 (B) are delineated. Institution 1 serves 2 satellite hospitals, and those centers' respective contributions are indicated by the numbers following the sites in the legend. Abbreviations: ENT, otorhinolaryngologic (ear, nose, and throat); GI, gastrointestinal; GU, genitourinary; GYN, gynecologic specimens separate from ovary; Neuro, extracranial neurological specimens ("Brain" indicates intracranial); TAT, turnaround time.*

a systemic issue with the telemicroscope. Subspecialty does not appear to contribute either; 5 of the Category A discrepancies were read by subspecialized pathologists of the organ in question. The overall low numbers also suggest that the noted errors may simply represent the approximate expected level of error in intraoperative diagnosis. This is borne out by the lack of statistical difference of glass versus telemicroscopic discrepancy rate and distribution.

The outcomes between glass and telemicroscopic services were similar but not identical. There was a statistically meaningful increase in TAT at both institutions when performing telepathology. For institution 2, this brought

Table 2. Telemicroscopy Versus Glass Turnaround Time (TAT) by Institution[a]

	Institution 1		Institution 2		Overall	
	Telemicroscopy	Glass	Telemicroscopy	Glass	Telemicroscopy	Glass
Mean TAT, min:s	17:03	14:17	25:30	15:24	18:14	14:25
SD	08:03	07:07	07:16	07:08	07:28	07:08
P	<.001		<.001		<.001	
No. of blocks <20 min, n (%)	427/556 (76.80)	4812/5432 (88.59)	62/91 (68.13)	595/695 (85.61)	489/647 (75.58)	5407/6127 (88.25)
P	<.001		<.001		<.001	

[a] The means and SDs for each institution and the combined are indicated. For both institutions and overall, the glass diagnoses were faster ($P < .001$). Glass diagnoses also had a greater proportion returned in less than 20 minutes than telemicroscopy ($P < .001$). These data include only the TAT by telemicroscopy at institution 2 that parallels the time frame during which the data for glass diagnoses were available. Comparisons were performed within each institution and overall/in combination as indicated.

Table 3. Concordance for Telemicroscopy Versus Glass Diagnosis for Each Institution[a]

	Institution 1			Institution 2		
	Glass	Hospital 1	Hospital 2	Glass	Hospital 1	Overall *P*
Concordant	6539	494	63	1641	136	.44
Discordant	262	16	3	51	3	
A	90	7	1	44	3	.31
B	140	7	1	7	0	
C	32	2	1	0	0	
P		.11			.34	

[a] A total of 22 discordant reads were identified between both institutions. No significant difference was identified between the proportion of discordance between glass and telemicroscopy, or among the distribution of discordance categories, for either institution. Comparisons were performed combining both institutions (overall, values on the right side) and within institution (values on bottom).

the mean above the quality metric of 20 minutes. However, in our experience, this apparent increased TAT has not been met with surgeon or other customer concerns. All 3 sites are satellite suburban hospitals that serve as extensions of their main, tertiary care academic institutions. The surgeons and hospitals, and by extension patients, who are served by telepathology seem to appreciate the ability to have more simultaneous operations, and to have those surgical suites closer to where the patients and/or operating staff may live.

Interestingly, our 2 institutions use telepathology slightly differently. Institution 1 preferentially schedules expected noncomplicated surgeries, including simple anticipated frozen sections, at its 2 satellite hospitals, and requests large specimens or complicated cases be performed at the main campus with the in-house pathologists including all service consultation. No pathologist is on-site at either external location, and the external frozen section diagnosis is covered by the rotating pathologist independently of subspecialty practice. Contrarily, institution 2 only uses the telemicroscope for particularly difficult cases, when the on-site pathologists seek additional subspecialty pathologist input. We believe that this explains the difference between the 2 institutions' recorded TAT. Whereas institution 1 selects for simple cases for telemicroscopic diagnosis, institution 2 selects for complicated ones. Additionally, time is added when the primary pathologist at institution 2 must connect with the referral pathologist. This may also inform why institution 1 had technical failures, whereas institution 2 did not; for cases that may otherwise have had technical problems with the telemicroscope, the on-site pathologist was still present to render a diagnosis, and therefore any issue would not have been encoded.

Compared to slide scanning, telemicroscopy offers other definitive advantages and disadvantages. Beyond the instrument itself and a standard frozen section setup, the only physical needs are a computer on the receiving end to host the software and a high-speed Internet connection. The cost of servers, storage, and random-access memory, which is obligatory for scanned slide analysis, is not required with this telemicroscopic system. Likewise, the time delay with scanning, uploading, and downloading is eliminated. However, scanning offers the distinct advantage of saving the image for future reference, which is of use in the medical record as well as for quality control and

Table 4. Telemicroscopy Performed by Reading Pathologist and Discordance[a]

			Category			
Pathologist	Specialty	Total Counts	A	B	C	Total
1	Derm	131				**0**
2	Derm	73				**0**
3	Surg	47	3		1	**4**
4	ENT	42	2			**2**
5	GI	42	2	1		**3**
6	B/G	41	2	2		**4**
7	GI	40	1			**1**
8	GI	40				**0**
9	GI	39		2		**2**
10	Surg	37		1		**1**
11	Neuro	29				**0**
12	Neuro	23				**0**
13	GI	22		1	2	**3**
14	B/G	22				**0**
15	Neuro	16				**0**
16	Surg	14				**0**
17	GU	8				**0**
18	ENT	8	1			**1**
19	B/G	7				**0**
20	Neuro	8				**0**
21	Soft tissue	7				**0**
22	Soft tissue	5				**0**
23	B/G	4				**0**
24	Surg	6		1		**1**
25	Surg	6				**0**
26	Surg	5				**0**
27	GU	5				**0**
28	B/G	4				**0**
29	ENT	3				**0**
30	GI	2				**0**
31	GI	2				**0**
32	Surg	2				**0**
33	Surg	2				**0**
34	Surg	2				**0**
35	GI	2				**0**
36	Surg	1				**0**
37	GYN	1				**0**
Total		**748**	**11**	**8**	**3**	**22**

Abbreviations: B/G, breast/gynecologic pathology; Derm, dermatopathology; ENT, otorhinolaryngologic (ear, nose, and throat); GI, gastrointestinal; GU, genitourinary; GYN, gynecologic; Neuro, neuropathology; Surg, general surgical pathology.

[a] The 37 unique pathologists had an average of 20 intraoperative diagnoses rendered by telemicroscopy (range, 1–131). The 22 discordant reads were concentrated among 10 pathologists with varied subspecialty areas.

especially in light of an ever-increasing digital pathology workflow. Although the system we use does have the capacity to perform slide scanning as well, we have not used it for that purpose.

Rapid telepathology can also theoretically eliminate the geographic requirements for slide-based consultation. The most immediate use is to provide surgical pathology intraoperative consultation for anywhere in our catchment areas, or even more widely. However, an extension may be beyond frozen sections. As long as the originating institution

Category	Anatomic Site	No.	Narrative	Specialty
A	Lymph node	2	Additional node positive for breast carcinoma	B/G ×2
			One case already known positive by frozen section	
			One case negative on frozen section with isolated carcinoma cells on levels	
		1	Additional node negative for breast carcinoma	GI
	Skin	1	Focal positive margin > negative margin	Surg
		1	Possible tumor > negative	GI
	ENT	2	Invasive squamous cell carcinoma identified on permanent only	ENT ×2
		1	High-grade squamous dysplasia on permanent only	ENT
	Parathyroid	1	Misreport weight/more parathyroid in fat	Surg
		1	No parathyroid > small parathyroid	GI
		1	Parathyroid > thyroid	GI
B	Skin	3	Focal positive margin (BCC, SCC) > negative margin	GI ×2, B/G
		1	Actinic keratosis > in situ squamous cell carcinoma	GI
		1	Negative margin > focal positive margin	GI
	Lymph node	2	Negative for breast carcinoma > positive	Surg, B/G
	ENT	1	Negative for squamous cell carcinoma > positive	Surg
C	Thyroid	1	Lymphocytic thyroiditis with focal papillary change > follicular thyroid carcinoma	Surg
	Parathyroid	1	Endocrine tissue, favor parathyroid > thyroid	GI
	Skin	1	Negative margin > positive margin	GI

Table 5. Narrative of Discordant Reads[a]

Abbreviations: BCC, basal cell carcinoma; B/G, breast/gynecologic pathology; ENT, otorhinolaryngologic (ear, nose, and throat); GI, gastrointestinal; SCC, squamous cell carcinoma; Surg, general surgical pathology.

[a] All 22 cases with discordant reads distributed among 10 reading pathologists were specifically interrogated. The errors are distributed among anatomic site and type of error.

can create the slide and load it, the receiving institution can see the image and help interpret it from anywhere in the world. This setup does not necessarily make sense for daily sign-out, but it certainly could hold merit for a smaller or more remote general pathology practice that wishes subspecialty consultation and can avoid the significant delay with sending slides to a referral center.

This telemicroscopic system is a microscope, not a full grossing setup, and therefore still requires the technical knowledge and people to gross correctly just as in standard practice. It does not include a mechanism to share gross images. At our institutions, it fits into our intraoperative offerings because we have skilled pathology assistants and/or pathologists to perform the gross examination and frozen sectioning. Institution 1 in particular chooses to schedule expected noncomplicated surgeries (eg, skin, parathyroid) preferentially at these distance sites to minimize the need for gross consultation, while institution 2 uses the system exclusively for the more complicated cases. In both locations, however, the use of telepathology can only occur *after* standard, high-quality gross examination. There is the serious possibility in cases or organs requiring careful selection of the areas to freeze that important areas may be missed because of sampling error, the same way that sampling error can occur absent a telemicroscopic setup. This system as we use it does not replace anybody or reduce the need for trained pathology staff; it simply expands the time frame and locations of intraoperative consultations we can offer. The availability of commercially available systems lends itself to expanding services, both as a consumer and as a consultant.

Ultimately, our data support the noninferiority and utility of telepathology for intraoperative frozen section diagnosis in daily practice.

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