# The Next Generation Robotic Microscopy for Intraoperative Teleneuropathology Consultation

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|------------------------|----------------------|-----------------------|------------------------|
| Abstract               |                      |                       |                        |

**Introduction:** Teleneuropathology at our institution evolved over the last 17 years from using static to dynamic robotic microscopy. Historically (2003–2007), using older technology, the deferral rate was 19.7%, and the concordance was 81% with the final diagnosis. Two years ago, we switched to use hybrid robotic devices to perform these intraoperative (IO) consultations because our older devices were obsolete. The aim of this study was to evaluate the impact this change had on our deferral and concordance rates with teleneuropathology using this newer instrument. **Materials and Methods:** Aperio LV1 4-slide capacity hybrid robotic scanners with an attached desktop console (Leica Biosystems, Vista, CA, USA) and GoToAssist (v4.5.0.1620, Boston, MA, USA) were used for IO telepathology cases. A cross-sectional comparative study was conducted comparing teleneuropathology from three remote hospitals (193 cases) to IO neuropathology consultation performed by conventional glass slide examination at a light microscope (310 cases) from the host hospital. Deferral and concordance rates were compared to final histopathological diagnoses. **Results:** The deferral rate for IO teleneuropathology was 26% and conventional glass slide 24.24% (*P* = 0.58). The concordance rate for teleneuropathology was 93.94%, which was slightly higher than 89.09% for conventional glass slides (*P* = 0.047). **Conclusion:** The new hybrid robotic device for performing IO teleneuropathology interpretations at our institution was as effective as conventional glass slide interpretation. While we did observe a noticeable change in the deferral rate compared to prior years, we did appreciate the marked improvement of the concordance rate using this new hybrid scanner.

**Keywords:** Digital pathology, frozen section, hybrid scanner, intraoperative consultation, neuropathology, robotic microscopy, teleneuropathology, telepathology

## INTRODUCTION

Telepathology has been used for many years by many institutions to remotely manage intraoperative (IO) consultations such as frozen sections. The use of telepathology for this purpose has been steadily increasing because of the limited availability of pathologists and demand for pathologists with subspecialty expertise.<sup>[1]</sup> The concordance of telepathology for IO consultations with the reference standard is excellent, showing a weighted mean of 96.9%.<sup>[2]</sup> There are several technological categories of telepathology that include static, dynamic, robotic, whole slide imaging (WSI), and hybrid methods.<sup>[3-5]</sup> Most of these methods have offered diagnostic accuracy rates similar to conventional microscopy.<sup>[6]</sup> At our institution, the University of Pittsburgh Medical Center (UPMC), the vast majority of IO consultations handled by telepathology have been for neuropathology cases.<sup>[7]</sup>

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Over the years, to meet the growing demand for teleneuropathology frozen sections in different hospitals, we utilized different modes of telepathology.<sup>[8,9]</sup> From January 2002 to August 2003, we deployed a nonrobotic hybrid (high-resolution static/low-resolution dynamic) microscopy system (DN100 Digital Network Camera System, Nikon). During this era, local pathologists at the host hospital initiated the consultation and controlled the microscope while the neuropathologist remotely viewed

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transmitted images using a standard web browser. From September 2003 to December 2006, we switched to using robotic remote-controlled microscopy (COOLSCOPE, Nikon). The COOLSCOPE tray could only handle one slide at a time. This allowed our neuropathologists to remotely control slide navigation and focus in real time. From 2007 to 2017, several ZEISS (previously Trestle SL4 scanner) robotic microscopes were strategically placed within frozen section rooms at our different facilities. The ZEISS system had the ability to load four slides at a time, offered faster image transmission, had higher resolution, and contained five separate objectives ( $\times 2$ ,  $\times 4$ ,  $\times 10$ ,  $\times 20$ , and  $\times 40$ ). Accompanying software (MedMicroscopy) to access and remotely control this robotic microscope was readily available from any workstation. Table 1 summarizes the diagnostic outcome from this earlier period when comparing conventional neuropathology frozen sections to those performed by telepathology. Intraoperative final discrepancies were uncommon, and performance improved slightly with the adoption of newer technology and pathologist experience.

Eventually, the vendor support for our ZEISS systems ended, and these instruments thus became obsolete. To maintain our teleneuropathology service in 2018, we switched to use Aperio LV1 instruments (Leica Biosystems). This 4-slide capacity device is a desktop hybrid scanner that supports both real-time robotic microscopy plus WSI. Compared to our prior robotic microscopy instruments, this newer device offered better optics ( $\times 2.5$ ,  $\times 5$ ,  $\times 10$ ,  $\times 20$ ,  $\times 40$ , and  $\times 63$ ) and software (e.g., simultaneous live viewing of multiple regions on the same slide). A preliminary validation study conducted at one of our hospitals showed that compared to the ZEISS robotic microscope, the LV1 device had a faster loading time, less lag phase when navigating or changing magnification, and had less downtime errors.<sup>[10]</sup>

The few publications to date reporting on the performance of employing the LV1 device for frozen section telepathology have been favorable.<sup>[11]</sup> The aim of the current study was to evaluate the impact that changes to the LV1 device had on our deferral and concordance rates with teleneuropathology.

# MATERIALS AND METHODS

## Teleneuropathology practice setting and case collection

UPMC is an integrated health-care network comprised of academic and community hospitals, each geographically separated. Our neuropathology division is located at the UPMC Presbyterian (PUH) location. However, neurosurgery is also performed at eight other facilities. At PUH, IO neuropathology consultations are handled on site by a neuropathologist manually examining a glass slide with a conventional light microscope (glass method). For all other locations, teleneuropathology is employed for IO consults (digital method). For the purposes of this study, we included only three different sites in our cross-sectional analysis: UPMC Shadyside Hospital (SHY), UPMC Mercy hospital (Mercy), and Children's Hospital of Pittsburgh (CHP). Since the majority of adult teleneuropathology cases take place at UPMC Shadyside and UPMC Mercy, those two hospital sites were chosen. UPMC Children's hospital was incorporated in the study to include pediatric neuropathology cases. A total of 503 IO neuropathology consultations were performed at these hospitals for 1 year. Those performed by the conventional glass method (n = 310) at PUH hospital were compared to the rest (n = 193) performed by telepathology at SHY (n = 137), Mercy (n = 26), and CHP (n = 30). The glass slides produced for IO neuropathology consultation cases by physician assistants included mostly hematoxylin and eosin (H and E) stained smears, and when required H and E stained frozen sections. Both types of slide preparation are suitable for teleneuropathology.<sup>[12]</sup> Our neuropathologists had access to the patient neuroradiology imaging. No gross specimen telepathology was available. Archival clinicopathological data, including IO and final diagnoses, were retrieved for our 1-year study period from our laboratory information system database (CoPath, Cerner). We did not record the number of pathologists per case/different cases nor did we track the number of cases sought for second consultation with colleagues in this study. In general, for 80% of cases, an attending neuropathologist and the fellow review slides together, in 10% two neuropathologists may review slides and in 10% only one neuropathologist.

## **Technology deployed**

Aperio LV1 4-slide capacity hybrid scanners with an attached desktop console (Leica Biosystems, Vista, CA, USA) were used for teleneuropathology [Figure 1]. Neuropathologists only used the live robotic microscopy mode. The GoToAssist application (v4.5.0.1620, Boston, MA, USA) through Citrix was used for remote access and viewing cases.

## **Technology validation**

All Aperio LV1 hybrid scanners were validated individually at each site before being deployed for clinical use. We prospectively

Table 1: Historical performance of teleneuropathology (digital) compared to conventional light microscope (glass) intraoperative consultations at University of Pittsburgh Medical Center

| Study period | Telepathology technology  | Deferral rate (%) |              | Concordance rate (%) |         | Reference                          |
|--------------|---|-------------------|--------------|----------------------|---------|------------------------------------|
|              |   | Glass             | Digital      | Glass                | Digital |                                    |
| 2002-2006    | Dynamic: Video (DN100 camera, Nikon)<br>and Robotic microscopy (Coolscope, Nikon) | 10.6              | 19.7         | 85-87                | 81      | Horbinski et al. <sup>[9]</sup>    |
| 2007-2008    | Robotic microscopy (Trestle SL4 scanner)  | Not reported      | Not reported | 70-72                | 60      | Horbinski and Wiley <sup>[8]</sup> |
|              |   | 1                 |              |                      |         |                                    |



Figure 1: The Aperio LV1 hybrid scanner and attached desktop console that was used for teleneuropathology

validated 60 neuropathology cases at UPMC Shadyside and then 20 cases each at UPMC Mercy and UPMC Children's hospital by a single-experienced neuropathologist (CW). For brevity, validation data are limited to UPMC Shadyside. There was 93% concordance (n = 56/60) between the glass slide and digitally rendered diagnoses. In one case, a technical problem due to a slipped glass slide was recorded. For the discordant cases (n = 4), two were considered to be a major discordance; however, one case of high-grade glioma was correctly diagnosed with the LV1 but was called benign by manual glass slide review, and the other case was also a high-grade glioma that was correctly diagnosed by glass slide examination but was called metastatic carcinoma using the LV1. The remaining two cases had only minor discrepancies.

#### **Telepathology performance measures**

The metrics used to measure telepathology performance included deferral, concordance, and discordance rates. These rates were compared between the telepathology (TP) and no TP (NOTP) groups. A case was categorized as deferred when the IO interpretation documented in the final pathology report included the word "defer." Concordance refers to a case in which the same diagnosis (or diagnostic category) was reported in both the IO assessment field and the final diagnosis of the pathology report at sign out. Concordance was further categorized into six different categories: inadequate for diagnosis, no lesional tissue present, correct category, exact diagnosis, wrong pathologic process, and wrong tumor. A case was categorized for this study as "inadequate for diagnosis" whenever there was insufficient material to render a specific diagnosis. The term "no lesional tissue present" was used when the tissue submitted was enough but did not represent the lesion described by radiology and the expected clinical interpretation. A case was designated as being in the "correct category" when the IO and final diagnosis fell into the same diagnostic group according to the World Health Organization tumors of the Central Nervous System 2016 categorization,<sup>[13]</sup> but differed only in grade or histologic subtype. "Exact diagnosis" was used when both the IO and final interpretation matched completely, including the tumor grade and histologic subtype. A case was classified as "wrong pathologic process" when there was a discordant interpretation between the IO and final interpretation. For example, if a case was interpreted as benign or inflammatory by IO interpretation and subsequently signed out as a neoplasm in the final report, this was categorized as "wrong pathologic process." "Wrong tumor" was used if the IO and final interpretations differed with respect to tumor type. Discordance was defined as a disagreement between IO and final diagnosis, and these were then further subclassified as a major or minor discordance. A case was categorized as a major discordance if the diagnosis was considered to potentially have a significant impact on clinical management. The discordant cases were also subcategorized into false-negative, false-positive, and misclassified cases. The false-negative group was comprised of neoplastic cases that were falsely classified as inadequate or nonneoplastic for the IO diagnosis. False-positive cases were comprised of specimens that were classified as neoplastic at the time of IO assessment but subsequently turned out to be nonneoplastic in the final report. Misclassification was used for the group of cases that were identified as a tumor but reported to be a tumor that was different from the final designation.

#### **Statistical analysis**

A Chi-square test was used to determine if the proportion of concordance and discordance was different among the TP and NOTP groups. Further assessment using the Chi-square test was done to determine if the deferral rate contributed to any significance between the six different concordance categories. Statistical significance was assumed at  $P \le 0.01$ . The analysis was performed using Microsoft Excel 365 and IBM SPSS Statistics 22 (Armonk, New York, United States).

## RESULTS

A total of 503 cases were included in the study from April 2018 to March 2019. TP was performed in 193 cases (38.4%) and NOTP in the remaining 310 cases (61.6%). Patients included 48% (n = 243) males and 52% (n = 260) females (male: female sex ratio = 0.93:1). The average mean age of these patients was 55.9 years (range 22–91 years). The total percentage of patients below 21 years was 7% (n = 36), and 48% (n = 240) were over 61 years. Table 2 summarizes the incidence of IO diagnoses by TP and NOTP at the various UPMC facilities. Almost all NOTP procedures were undertaken at UPMC Presbyterian Hospital. Most IO consultations by TP were performed at UPMC Shadyside.

A breakdown of the six diagnostic categories for concordance between the IO diagnosis and final diagnosis is shown in Figure 2. Among these six diagnostic assessment categories, the majority of cases for both the IO (41.2%, n = 207) and final report (78.0%, n = 390) fell into the *exact diagnosis* category. The second-most common group was the *correct category* that comprised 41.4% (n = 208) of IO interpretations and 10.9% (n = 37) for final rendered diagnoses. Table 3

| Table 2: Incidence of neuropathology intraoperative consultations at each University of Pittsburgh Medical Center facility |  |                                  |                                     |  |  |  |
|--|--|----------------------------------|-------------------------------------|--|--|--|
| UPMC facility  | Total patients (n=503), n (%)          | Intraoperative TP (n=193), n (%) | Intraoperative NOTP, (n=310), n (%) |  |  |  |
| Children's hospital  | 30 (6.0)                               | 30 (16.0)                        | 0 (0.0)                             |  |  |  |
| Mercy hospital   | 26 (5.0)                               | 26 (13)                          | 0 (0.0)                             |  |  |  |
| Presbyterian hospital  | 309 (61.0)                             | 0 (0.0)                          | 309 (99.8)                          |  |  |  |
| Shadyside hospital   | 138 (27.0)                             | 137 (71.0)                       | 1 (0.2)                             |  |  |  |
| NOTP: No telepathology 7   | P. Telenathology LIPMC · University of | of Pittsburgh Medical Center     |                                     |  |  |  |

P: No telepathology, TP: Telepathology, UPMC: University of Pittsburgh Medical

| Table  | 3:  | Deferral | rate | by | telepathology | versus | no |
|--------|-----|----------|------|----|---------------|--------|----|
| telepa | the | ology    |      |    |               |        |    |

| Diagnosis                                 | TP ( <i>n</i> =193),<br><i>n</i> (%) | NOTP ( <i>n</i> =310),<br><i>n</i> (%) | Total ( <i>n</i> =503),<br><i>n</i> (%) | Р     |  |
|---|--------------------------------------|--|---|-------|--|
| Defer                                     | 53 (27.0)                            | 68 (22.0)                              | 121 (24.0)                              | 0.159 |  |
| No defer                                  | 140 (73.0)                           | 242 (78.0)                             | 382 (76.0)                              |       |  |
| NOTP: No telepathology, TP: Telepathology |                                      |  |   |       |  |

summarizes the deferral rate between IO TP and NOTP cases. There was a slightly increased deferral rate to permanent slide interpretation for the TP group (27.0%, n = 53) compared to the NOTP group (22.0%, n = 68), but this difference was not statistically significant (P = 0.159).

Figure 3 summarizes studied cases according to their deferral rate. The deferral rate was calculated for each of the six diagnostic categories. There is a statistically significant (P < 0.001) higher proportion of deferred cases with an IO diagnostic assessment of no lesional tissue present (36%) than cases that were not deferred (4%). There is also a statistically significantly (P < 0.001) lower proportion of deferred cases with an IO diagnostic assessment of exact diagnosis (14%) than cases that were not deferred (50%). In addition, there is a statistically significant (P = 0.003) higher proportion of deferred cases with an IO diagnostic assessment of the wrong type of pathological process (7%) than cases that were not deferred (2%). Finally, there is a statistically significantly (P < 0.001) higher proportion of deferred cases with an IO diagnostic assessment of inadequate for diagnosis (5%) than cases that were not deferred (0%). Some examples of diagnoses in various deferral scenarios include inadequate glial tissue in a case of gliosis, subtle reactive changes in a case of reactive gliosis, infarct in a case that turned out to be a ruptured Rathke's cleft cyst with associated granulomatous reaction, necrosis in a case of or glioblastoma multiforme, atypical cells in a case of ganglioglioma, and a neoplasm not further subtyped during IO consultation that was later signed out as an atypical meningioma.

Table 4 shows the rate of discordance between the TP and NOTP groups. While there were slightly fewer discordant cases in the TP group (7.0%) compared to the NOTP group (9.0%), this difference was not statistically significant (P = 0.360). For 11 of the discordant cases, there was insufficient tissue submitted for ancillary studies. Figure 4 depicts the subdivision of discordant cases based on the reason for the discrepancy. The most common reason was due to false-negative cases (44%, n = 18), followed



Figure 2: Proportion of cases in different concordance diagnostic assessment categories

by misclassified cases (24%, n = 10). Those cases that fell into other categories (10%, n=4) were signed out in the final report as inflammatory or reactive lesions. The discordant cases were further subdivided into major and minor discordances based on the clinical impact of the diagnosis. Of 41 discordant cases, 31.7% (n = 13) were major and 68.3% (n = 28) of minor impact. There was no statistically significant difference (P = 0.527) between TP versus NOTP groups and their subclassification as major and minor discordances [Figure 5]. In the TP group, 38.5% (n = 5) of cases had a major discordance and 61.5% (*n* = 8) of cases were of minor discordance. For NOTP cases, 28.6% (n = 8) were of major and 71.4% (n = 20) were of minor discordance. Of 28 discordant cases, 89.3% (n = 25) that were deferred were in the minor discordant category in contrast to 0.0% (n = 0) cases in the major discordant category (P < 0.001). Table 5 summarizes the major discordant cases. There were seven such cases in the misclassified category and six cases placed into the false-positive category. The most common incorrect IO diagnosis was glioma (53.8%, n = 7). Figures 6 and 7 offer examples of major discordant cases in both the TP and NOTP groups.

# DISCUSSION

TP remains one of the key applications of digital pathology. Enabling laboratories to easily share their digital images has become vital today to supply subspecialized expertise such as neuropathology.<sup>[14]</sup> The revenue generated by neurosurgeons for an institution who rely on IO consultations far outweighs the expense of purchasing and maintaining a TP system.[15] At our institution, the teleneuropathology service has steadily grown over the years.<sup>[16]</sup> In 2002, around 5% of IO neuropathology consults were handled by TP. In 2016, up to 45% of IO consultations at UPMC were performed by TP. While the vast majority of teleneuropathology activity is undertaken between UPMC hospitals, we eventually expanded our practice to cross

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Figure 3: Diagnostic assessment based on case deferral



Figure 5: Summary of discordant cases

## Table 4: Discordance rate in telepathology versus no telepathology groups

| Correlation                               | TP ( <i>n</i> =193),<br><i>n</i> (%) | NOTP ( <i>n</i> =310),<br><i>n</i> (%) | Total (n=503),<br>n (%) | Р     |  |
|---|--------------------------------------|--|-------------------------|-------|--|
| Concordance                               | 180 (93.0)                           | 282 (91.0)                             | 462 (92.0)              | 0.360 |  |
| Discordance                               | 13 (7.0)                             | 28 (9.0)                               | 41 (8.0)                |       |  |
| NOTP: No telepathology, TP: Telepathology |                                      |  |                         |       |  |

state lines in the USA and began offering interinstitutional and interstate teleneuropathology.[17]

In the field of digital pathology, hardware and software platforms evolve continually. Fortunately, today there are several excellent commercial TP solutions to select from. As evidenced by our experience, there was a need to change as old technology became obsolete. There is a long-standing history of teleneuropathology. Prior to WSI, the two basic systems utilized for performing remote neuropathology examinations included static and dynamic modalities.<sup>[3]</sup> Static systems typically cost less, are technically easier to use, deal with small manageable files, and tend to be vendor independent. However, the pathologist has no remote control and thus the host needs to have some expertise. Acquiring static images is also labor intensive and there is the possibility of sampling and focus errors. Dynamic (real-time, robotic) TP provides the remote pathologist with access to the entire slide, but can be more expensive as both the host and consultant require integrated software as well as a need for high bandwidth. Remote video microscopy for teleneuropathology is also feasible, but as reported by Becker et al. require a lot of effort on the part of the referring pathologist who can



Figure 4: Different discordant categories



Figure 6: Major discordant case in the telepathology group. The patient was a 59-year-old female with a remote history of follicular non-Hodgkin lymphoma and vulvar cancer postchemotherapy and radiation therapy, presenting with multiple enhancing intracranial lesions within the supratentorial and infratentorial hemispheres. The right parietal brain stereotactic biopsies were performed. (a) Intraoperative brain smear interpreted as glioma (H and E,  $\times$ 20). (b) Final diagnosis of CD20 positive follicular non-Hodgkin lymphoma (H and E,  $\times 20$ ). The portion of tissue chosen for intraoperative preparation contained a high percentage of reactive gliotic tissue surrounding the principal lesion

spend up to 16 min per case selecting representative areas for transmission.<sup>[18]</sup> WSI is advantageous because it not only provides access to an entire slide, or set of slides from a case but also offers automated scanning and generation of high resolution images. Menter et al.[19] showed that with their validation study, the median specimen handling time for robotic microscopy was

| Discordant category Intraoperative diagnosis |  | Final diagnosis                              | TP/NOTP | Number of cases |  |  |
|--|--|--|---------|-----------------|--|--|
| Misclassified                                | Glioma                                   | Atypical teratoid rhabdoid tumor             | TP      | 2               |  |  |
| Misclassified                                | Glioma                                   | CD20+ large B-cell lymphoma                  | TP      | 1               |  |  |
| Misclassified                                | Medulloblastoma                          | Juvenile pilocytic astrocytoma               | TP      | 1               |  |  |
| Misclassified                                | Glioma                                   | CD20+ large B-cell lymphoma                  | NOTP    | 1               |  |  |
| Misclassified                                | Metastasis                               | CD20+ large B-cell lymphoma                  | NOTP    | 1               |  |  |
| Misclassified                                | Chondrosarcoma                           | Chordoma                                     | NOTP    | 1               |  |  |
| False positive                               | Glioma                                   | Cerebellar cortex                            | TP      | 1               |  |  |
| False positive                               | Glioma                                   | Gliosis                                      | NOTP    | 1               |  |  |
| False positive                               | Glioma                                   | Acute and chronic inflammation               | NOTP    | 1               |  |  |
| False positive                               | Rare atypical cells                      | No tumor                                     | NOTP    | 2               |  |  |
| False positive                               | Acellular scar with nodule of high-grade | Proliferative granulation tissue with severe | NOTP    | 1               |  |  |
|  | tumor                                    | atypia                                       |         |                 |  |  |

NOTP: No telepathology, TP: Telepathology



Table 5: Intraonerative and final diagnoses for major discordant cases

**Figure 7:** Major discordant case in the no telepathology group (i.e., performed by conventional light microscopy). The patient was a 73-year-old male with a homogeneously enhancing infiltrating tumor in the anterior aspect of the hypothalamus. Suprasellar/third ventricle mass brain biopsies were performed. (a) Intraoperative brain smear interpreted as glioma (H and E,  $\times$ 20). (b) Final diagnosis of CD-20 positive large B-cell lymphoma (H and E,  $\times$ 20). The intraoperative smear was thick and only a small proportion was involved by the neoplastic process

19 min, compared to just 6 min with WSI. However, the time to perform an IO evaluation will depend on case complexity. For example, Cima *et al.*<sup>[20]</sup> reported that the average scan and viewing/reporting time were 12 and 3 min for their cancer cases versus 18 and 5 min for transplant cases. While we did not record turnaround time in this study, in general, our experience is that pathologists tend to reach a diagnosis faster with glass slides. Of course, this does not take into account the length of time it

takes a neuropathologist to reach the operating room. WSI is also more expensive, can have lengthy scan times, may miss scanning small and pale pieces of tissue, and generates large digital files.

While other groups have chosen to use WSI for teleneuropathology,<sup>[21]</sup> we opted to use robotic microscopy. In general, user acceptance of robotic TP has always been high.<sup>[22]</sup> No noteworthy technical performance problems (e.g., pixilation) were reported with the LV1 devices. Many of our neuropathology IO cases typically utilize brain smear preparations, and sometimes a frozen section slide that may introduce artifact. We did not record the number of smears and/or frozen section slides prepared per case. However, when a pathology assistant prepares slides instead of a pathologist, there is a tendency for some of our neuropathologists to request both a smear and a frozen section. A s is the case with cytology material,<sup>[23]</sup> digitizing brain smears poses challenges with focusing due to thick areas, three dimensional cell groups, and obscuring blood. For this reason, using robotic microscopy allowed us to overcome these focus issues, as well as other artifacts encountered during frozen sections (e.g., air bubbles, tissue folds, and excess obscuring mounting medium).

With increased experience in TP by our neuropathology division over the years, coupled with technology advances, we anticipated an improvement in the performance metrics for teleneuropathology. Indeed, the concordance rate at our institution from 2002 to 2006 for TP (digital) cases was 81% with TP compared to 93% calculated during the current 2018–2019 study. While this represents a modest improvement, we are still pleased with the upward trend, which helps justify our decision to transition to a new TP platform. Long-term experience with teleneuropathology by other groups has also been positive and advocated for similar use of this technology. Hutarew *et al.* from Austria, for example, reported a diagnostic accuracy for TP of 97.9% for 343 IO frozen section diagnoses.<sup>[24]</sup>

The deferral rate at our institution from 2002 to 2006 for TP (digital) cases was 19.7% compared to 27% calculated in the current 2018–2019 study period. Of note, the deferred cases

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were not seen in the major discordant category. Our deferral rate is also high compared to studies from other institutions. For example, Evans *et al.*<sup>[25]</sup> reported a deferral rate of 7.6% in a study done with 983 frozen sections, out of which 97% were neuropathology frozen performed at the University Health Network in Toronto, Canada. While the reasons for this difference are worthy of exploring to guide future process improvement (e.g., re-training), in our opinion they are not attributable to a flaw of the technology, and rather represent differences in case mix at different institutions as well as how a "deferred" diagnosis is defined (e.g., at our institution, if suspicious cells are identified in a minute tissue fragment the diagnosis tends to be deferred to either obtaining more tissue or later evaluation of permanently fixed material).

Reviewing the discrepancies in our study, we identified three categories of issues responsible for diagnostic differences. None of these categories related to technical issues with robotic microscopy, but all were related to the nature of the IO diagnostics employed in the evaluation of stereotactic needle biopsy of the brain. Stereotactic brain biopsy is a procedure that generates small amounts of tissue (i.e., 0.5 cm in length and 2 mm in diameter). The goal of the procedure is to get diagnostic tissue with minimal invasiveness. The goal of the IO consultation is to confirm lesional tissue and preserve as much material as possible for later permanent evaluation to fulfill a full diagnostic workup (frequently requiring 6–12 immunostains and nucleic acid extraction for the next generation sequencing). The three categories responsible for diagnostic differences are as follows:

- 1. Diagnostic refinement: Three cases (e.g., chondrosarcoma for IO diagnosis versus chordoma after permanent evaluation), in which the final diagnoses required immunohistochemistry
- 2. Histologic mimics: Four cases where the tumor was identified, but there was not enough utilized during the IO procedure to correctly classify the lesion; however, enough material was available to complete diagnostics with the permanent slide preparation
- 3. Overcall or undercall: Six cases where inadequate tissue was used during the IO procedure to obtain a correct diagnosis and the neurosurgeons elected to preserve material for permanent assessment only.

# CONCLUSION

We found that switching to a new hybrid robotic device for IO consultations through teleneuropathology sustained our service of remotely supplying neuropathology expertise and is as effective as performing these interpretations with a conventional light microscope.

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### **Conflicts of interest**

Dr. Pantanowitz is on the medical advisory board for Leica, Hologic, and Ibex and consults for Hamamatsu.

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