

Commentary: Impact of Digital Pathology in the Field of Intraoperative Neuropathology: Master the Tool

The use of telepathology for intraoperative consultation dates back to >20 years ago, and it has been steadily increasing given both the limited availability of expert pathologists and the development of even more advanced and performing technological solutions.^[1] Some subspecialties of pathology are particularly likely to benefit from the implementation of a telepathology service, such as neuropathology,^[2,3] gynecological pathology,^[4] and transplant pathology.^[5] These fields of pathology indeed represent a niche where there is a scarcity of pathologists with specific expertise and at the same time a growing demand due to the increase of surgical activity even in small- and medium-sized institutions.^[3,6]

The recently published article of Baskota *et al.*^[7] on the implementation of an intraoperative teleneuropathology system has received attention. The authors of this study aimed to describe both the development of the teleneuropathology systems at their institution and the results of the newly deployed system in terms of diagnostic performance. Indeed, the authors describe their practice setting composed of academic and community hospitals, with differences among the several hospitals in terms of neuropathology workload. This reflects a typical setting where telepathology can be deployed to provide a consultation service for a field of pathology with scarce personnel availability. Furthermore, the authors briefly report on the three different eras of teleneuropathology at their institution, starting in 2002 with a static nonrobotic system controlled by a local pathologist, passing in 2003–2006 to robotic remote-controlled microscopy to the complete system of robotic microscopy workstations until 2017.^[8,9] The authors state that final discrepancies between conventional light microscopy (LM) and telepathology were uncommon, and performance improved slightly with the adoption of newer technology and pathologist experience.^[7] Then, a new system with a hybrid scanner comprising real-time robotic microscopy and whole-slide imaging (WSI) with better optics and software has been starting to be used. The study is aimed to evaluate the impact of the new device on concordance and deferral rate on a population of overall 503 intraoperative consultation cases. Many aspects and issues of teleneuropathology are explored in the article, with conclusions on the feasibility and usefulness of such a system for neuropathology.

THE SPECIMENS AND THE TECHNOLOGY

Neuropathology often requires the pathologist to establish an intraoperative diagnosis on a very small amount of tissue with the need for ensuring maximal preservation for the definitive diagnosis in permanent sections and further analysis. Cytological smears and frozen sections (FS) are considered

complementary in many cases, and both have advantages and limitations. In most cases, however, cytology alone can allow making the diagnosis with relevant sparing of time and tissue. Cytological smears do not introduce freezing artifacts, provide invaluable detailed cellular and nuclear features suggesting the tissue pattern, of particular help in highlighting glial fibrillary architecture. Finally, cytological smears require less equipment than a FS and can be prepared faster even in the absence of a pathologist on-site.^[10,11] Limitations of cytology for intraoperative diagnosis of the central nervous system (CNS) lesions are less important and reside mainly in the potential presence of debris, air bubbles, and/or excessive thickness of the cellular layers that can hamper the examination in comparison with a histological slide.^[10] When coming to the digitization of cytological specimens, these limitations are indeed the main issues encountered in studies dealing with cytological diagnoses on WSI slides, with the importance of correct focusing of cellular groups of different thickness to evaluate cellular and nuclear detail and the need for extra scanning time to digitize all the slide area covered by the smear.^[12] The authors state that majority of their neuropathology consultations consisted of cytological smears despite not reporting the numbers and acknowledge the already mentioned difficulties in digitizing brain smears. They report however how using robotic microscopy allowed to overcome these focus issues, as well as other artifacts encountered during FS (e.g. air bubbles, tissue folds, and excess obscuring mounting medium).

THE CONCORDANCE AND THE RELIABILITY OF TELEPATHOLOGY

The concordance rate of telepathology diagnosis with WSI has been reported to be high in most experiences, as highlighted in a recent review.^[13] Baskota *et al.* reported a trend toward improvement of diagnostic concordance with reference diagnosis through the several eras of the telepathology service, mainly to be attributed to more advanced technology, adherence to recommendations and guidelines^[14] for validation and confidence and expertise of handling pathologists. There was a slightly increased although not statistically significant deferral rate for the telepathology cohort in comparison with the conventional LM cohort (27% vs. 22%), suggesting at first that a case likely to be deferred in telepathology is a case which is likely to be deferred also with conventional microscopy. Higher proportions of diagnostic categories labeled as “wrong pathologic process” or “no lesional tissue” or “inadequate” were present among the deferred cases. This is not surprising, but it would have been of interest if deferred cases had been

stratified also according to their belong to the telepathology versus the conventional LM cohort. However, when coming to the concordance rates, the authors report a concordance rate of 93% for teleneuropathology, with no statistically significant difference in concordance rate between telepathology and conventional LM assessment (7% vs. 9%). Furthermore, most importantly, they highlighted no statistically significant differences in the subclassification of major and minor discordances between telepathology and conventional LM assessment (38.5% vs. 28.6%). These results are in line with other reported in the literature and reinforce the evidence that telepathology is a reliable mode to provide an intraoperative consultation service in practice settings where the demand is high and the availability of expert pathologists on-site is scarce.

CRITICAL POINTS WITH BOTH MODALITIES: WHOLE-SLIDE IMAGING AND LIGHT MICROSCOPY

Baskota *et al.* reported then also the major discordant cases and it is interesting to note that they are similarly distributed in the telepathology and conventional LM cohorts. Indeed, in both cohorts, there were cases of B-cell lymphoma misclassified at intraoperative consultation as glioma, and false-positive cases of gliosis/inflammation/normal tissue diagnosed at intraoperative consultation as glioma. These are common challenges in the differential diagnosis for CNS lesions that have a relevant impact on subsequent surgery and patient's management.^[10] For example, the detection of lymphoma would limit the surgery and prevent unnecessary resection, while the false-positive diagnosis of glioma could have led to overtreatment. It is; however, somehow comforting that the critical differential diagnoses are the same in both telepathology and conventional LM: indeed, as clearly stated by the authors, the discordances were not related to technical issues with robotic microscopy, but all were related to the nature of the intraoperative diagnostics employed in the evaluation of stereotactic needle biopsy of the brain.^[7] This is in our opinion another point in favor of the deployment of teleneuropathology, given that no increased diagnostic difficulties are encountered with digital slides. Finally, the critical point of turn around time in intraoperative consultation. It has to be considered then that WSI scanners can fail in detecting small and pale pieces of tissues and as discussed above concerning cytological smears, longer scanning times are needed to digitize a large portion of a slide covered by the smear. Although the authors did not report on scanning and/or reporting times, they mentioned that pathologists usually render a diagnosis faster with LM. However, in our opinion, the time spent to digitize a CNS biopsy case series can be returned when the general pathologist on-site can consult live the expert pathologist who does not need to reach the operating room but can provide the diagnosis at distance with the same reliability of LM.

In conclusion, the study of Baskota *et al.* keeps together important consideration concerning the deployment of

teleneuropathology system. In the field of intraoperative neuropathology, experienced hands are needed to reach correct diagnoses which affect the management of the patient. Safe use of digital pathology requires calibration, validation, and practical guidelines. Technology has now evolved to sustain the increasing demand for telepathology services at multiple hospitals and has shown to be as effective as performing intraoperative consultation with conventional LM. The chance to deliver neuropathology and other specific expertise with technological solutions can also contribute to attracting financial resources and to the growth of an institution, in terms of quality of care provided.

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