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Special Section on Telepathology

Primary frozen section diagnosis by robotic microscopy and virtual slide telepathology: the University Health Network experience

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Summary Although telepathology (TP) has not been widely implemented for primary frozen section diagnoses, interest in its use is growing as we move into an age of increasing subspecialization and centralization of pathology services. University Health Network is a 3-site academic institution in downtown Toronto. The pathology department is consolidated at its Toronto General Hospital (TGH) site. The Toronto Western Hospital (TWH), located 1 mile to west of TGH, has no on-site pathologist, and generates 5 to 10 frozen section cases per week. More than 95% of these frozen sections are submitted by neurosurgeons, in most cases to confirm the presence of lesional tissue and establish a tissue diagnosis. In 2004, we implemented a robotic microscopy (RM) TP system to cover these frozen sections. In 2006, we changed to a virtual slide (VS) TP system. Between November 2004 and September 2006, 350 primary frozen section diagnoses were made by RM. An additional 633 have been reported by VS TP since October 2006, giving a total of 983 frozen sections from 790 patients. Of these cases, 88% have been single specimens with total turnaround times averaging 19.98 and 15.68 minutes per case by RM and VS TP, respectively ($P < .0001$). Pathologists required an average of 9.65 minutes to review a slide by RM. This decreased 4-fold to 2.25 minutes after the change to VS TP ($P < .00001$). Diagnostic accuracy has been 98% with both modalities, and our overall deferral rate has been 7.7%. Midcase technical failure has occurred in 3 cases (0.3%) resulting in a delay, where a pathologist went to TWH to report the frozen section. Discrepant cases have typically involved minor interpretive errors related to tumor type. None of our discrepant TP diagnoses has had clinical impact to date. We have found TP to be reliable and accurate for frozen section diagnoses. In addition to its superior speed and image quality, the VS approach readily facilitates consultation with colleagues on difficult cases. As a result, there has been greater overall pathologist satisfaction with VS TP.

1. Introduction

Telepathology (TP), a term introduced in 1986 by Dr Ronald Weinstein [1,2], refers to the delivery of pathology services over a distance. A more contemporary definition of

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TP would include the use of the internet to link a pathologist to a glass slide. Some centers have used TP extensively for routine surgical pathology [3-6], whereas others have used it more selectively for pathologist-to-pathologist consultation with frozen sections [7,8]. TP was first used for primary frozen section diagnosis in 1989 in Norway [9], where videotelemicroscopy was used to provide intraoperative coverage with 100% accuracy to 5 remote hospitals. In spite of the success of the Norwegian program and others that have followed [7,10-18], the pathology community as a whole has been slow to adopt this technology.

The major barriers preventing more widespread use of TP for primary diagnostic purposes, including frozen sections, were identified by Weinstein et al [19] in 2001 and are still relevant today. Firstly, the cost and time required to implement and maintain a TP program can be prohibitive in the absence of a solid business case. Secondly, there has been a general perception that TP is unacceptably slow and would not allow for the timely reporting of frozen sections. Finally, pathologists have generally been of the opinion that the technique will be inaccurate and that suboptimal image quality will result in errors with adverse patient outcomes and medicolegal consequences. The latter concern persists in spite of the existence of several retrospective validation studies demonstrating an average accuracy rate of 95% (range, 84.1%-100%) [20-24] (Table 1) for TP frozen section diagnoses. Furthermore, there have been at least 11 reports published between 1991 and 2007 showing an average diagnostic accuracy of 96% (range, 89%-100%) when TP was used for primary frozen section diagnosis [7,10-18] (Table 2). With the exception of a few outliers [10,11,22], most articles have reported diagnostic accuracy values that fall within the accuracy range for frozen sections reported by conventional light microscopy [25].

The imaging technology used for TP has evolved significantly from the low resolution videotelemicroscopy used by Nordrum et al [9], to include static microscopy involving the transmission of selected images [23,26,27] and dynamic robotic microscopy (RM). Most of the TP systems summarized in Tables 1 and 2 have used dynamic or static/dynamic RM whereby the viewing pathologist assumes remote control of the microscope. Although such systems provide image quality that is more than adequate for diagnostic purposes, RM tends to be much slower than light microscopy and patience on the part of the pathologist is required if an accurate diagnosis is to be rendered. The development of virtual slide (VS) technology represents a marked advance in the remote assessment of histologic slides. VS systems (Aperio, Vista, CA; DMetrix, Tucson, AZ; Olympus, Center Valley, PA; BioImagene Inc, Cupertino, CA) use slide scanners that can rapidly digitize histologic sections on glass slides from low to high magnification to produce images of outstanding quality that can be viewed over the Internet. Validation studies with VS technology on formalin-fixed, paraffin-embedded tissue sections have reported excellent results in diagnostic accuracy, when compared to conventional light microscopy [28-30]. Data on the performance of VS systems on frozen sections are limited to a single pilot study of 15 cases [31].

Table 1 TP frozen section validation studies

Year	Primary author	Accuracy (%)	Deferral (%)	Time (min/slide)
2000	Winokur [20]	97	3	NA
2001	Demichelis [24]	95	11	6.2
2002	Kaplan [21]	100	NA	2.8
2003	Moser [22]	84.1	7.4	14.2
2007	Frierson [23]	95	NA	NA

Table 2 Primary frozen section diagnoses by TP

Year	Primary author	Accuracy (%)	Deferral (%)	Time (min/slide)
1991	Nordrum [9]	100	0	15
1995	Oberholzer [10]	90.3	6 [a]	20-40
1997	Steffen [11]	89	4 [a]	NA
1999	Della Mea [12]	100	NA	4.5
2000	Dawson [13]	97	NA	3
2003	Hutarew [17]	99.4	NA	1-36
2003	Terpe [15]	98	NA	15
2005	Sukal [16]	NA [b]	NA	NA
2005	Hitchcock [18]	95.3	NA	NA
2006	Hutarew [14]	97.9	0	10.7
2007	Horbinski [7]	95.5-96.9	12-20	NA

Abbreviation: NA indicates not available.

[a] These reports did not provide deferral rates but rather the percentage of cases during which technical problems were encountered.

[b] This report did not provide diagnostic accuracy data but concluded that TP was a useful adjunct in Mohs surgery.

University Health Network (UHN) is a 3-site academic medical center located in downtown Toronto, comprising Toronto General Hospital (TGH), Princess Margaret Hospital (PMH), and Toronto Western Hospital (TWH). TGH and PMH are located directly across from each other, whereas TWH is located approximately 1 mile (1.6 km) to the west of TGH. TWH, home to the Krembil Neuroscience Center, has had no regular on-site anatomical pathologist for more than 12 years and no regular on-site neuropathologist since our department consolidated at TGH in early 2006.

The surgical services at TWH have historically generated up to 10 frozen section cases per week, most of these requested by neurosurgeons. Because most of our routine reporting, teaching, and research activities take place at TGH or PMH, sending a single pathologist over to TWH to cover a small volume of frozen sections was inefficient from a workflow perspective. In addition, there was no easy method of consulting with a colleague on difficult cases. Sending tissue by ground transportation from TWH to TGH for frozen section assessment was slow and unreliable. TP was viewed as a viable solution, and a solid business case could be made in support of its implementation.