Real-time intraoperative digital pathology for surgical oncology

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Accurate decision-making during surgical resection of various human cancers is reliant on good communication between surgeon and pathologist. The frozen section is essentially unchanged since described by pathologist Dr Louis B. Wilson in 1905 at the request of surgeon Dr William Mayo, one of the founders of the Mayo Clinic.

Despite the historic value of the frozen section, many surgeons and pathologists alike question its utility, arguing that assessing the ex vivo resection or the surgical bed is of greater clinical benefit. Various studies support these varying approaches in distinct cancer types including head and neck, breast and brain.

The need to re-appraise current surgical oncological practice is upon us, driven in part by the digital revolution whereby techniques not previously available or imaginable

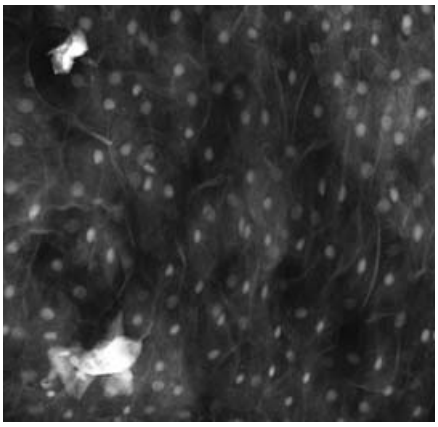

Figure 1

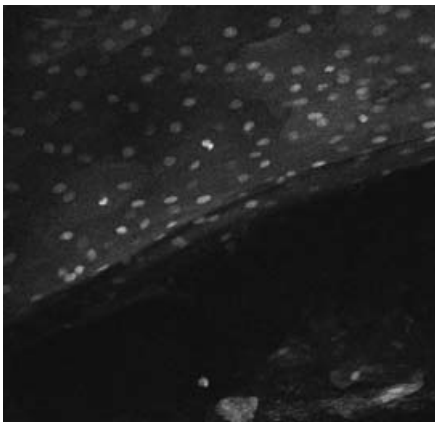

Figure 2

Key messages

- Real-time intraoperative digital pathology can be used to determine tissue histoarchitecture and surgical clearance of tumours
- Handheld fluorescence-based miniaturised confocal endomicroscopy with telepathology is at least 23 times faster than frozen section assessment
- Intraoperative video-flow digital pathology coupled with telepathology achieves near perfect concordance with permanent hematoxylin and eosin stain (H&E) tissue sections but in real-time.

are now a reality and easily applicable in theatre. A recently published US study examined the utility of real-time intraoperative surgery using confocal laser endomicroscopy (CLE) and telepathology for navigating a series of 11 patients with brain masses.

Handheld CLE devices enable in vivo digital visualisation of tissue histoarchitecture with absolute recapitulation of standard histomicroscopy allowing real-time assessment of pathological tissues and clearance of resection margins, with on-the-fly communication between surgeon and pathologist.

In the recently published study, neurosurgeons used CLE to treat six patients with gliomas, three with other primary brain tumours, one with metastasis, and one with reactive brain tissue.

Video-flow images were generated of the operative field during surgery, while pathologists viewed the images simultaneously outside the operating theatre at distant sites. One was in another state, four were at home, and six were elsewhere in the hospital. All video and still CLE images were correlated to corresponding frozen section and standard H&E histology sections.

Video-flow CLE allowed correct tissue histoarchitecture interpretation in 96% of digital biopsies. This was possible in a fraction of the time taken to undertaken frozen section assessment. The duration of application of the CLE system was one minute per case and 0.25 seconds per digital biopsy, with the first image that demonstrated identifiable histopathological features being acquired within six seconds. Frozen sections were processed within 23 minutes, which was statistically significantly longer than CLE imaging.

Intraoperative digital pathology with CLE allowed real-time assessment of tissue histoarchitecture without taking tissue biopsies, facilitated communication between surgeon and pathologist, and permitted accurate decision-making during oncological surgery. Overall, it resulted in immediate informed decisions with significant advantages over frozen section assessment.

An example of this approach in the context of head and neck pathology is provided here, where a moderately dysplastic oral epithelial lesion is imaged before resection (Fig. 1), after which the peripheral mucosal (Fig. 2) and deep surgical (Figs. 3-5) margins were imaged. The peripheral mucosal margin demonstrates normal squamous epithelial histoarchitecture transitioning to the surgical bed, while the deep margin demonstrates fine elastin fibres and collagen bundles (Fig. 3), muscle (Fig. 4) and underlying adipose tissue (Fig. 5), all imaged from different parts of the surgical bed.

Removal of all premalignant epithelium was established before wound closure and confirmed on standard H&E sections.

The benefits of intraoperative digital pathology during oncological surgery extend beyond good communication between surgeon and pathologist. They include reduced operating time, greater accuracy of pathological diagnosis, better surgical clearance with normal tissue margins, efficiency in

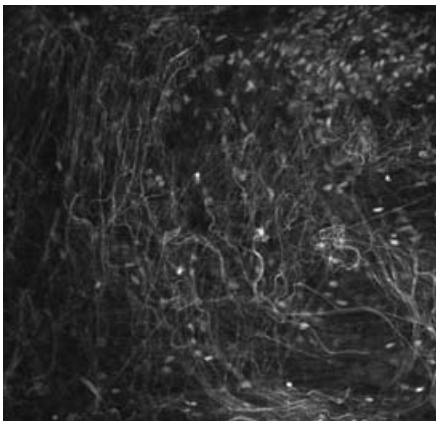

Figure 3

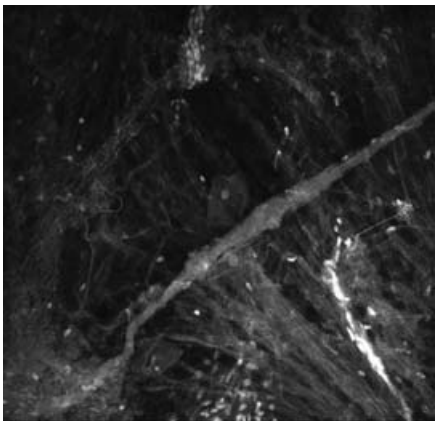

Figure 4

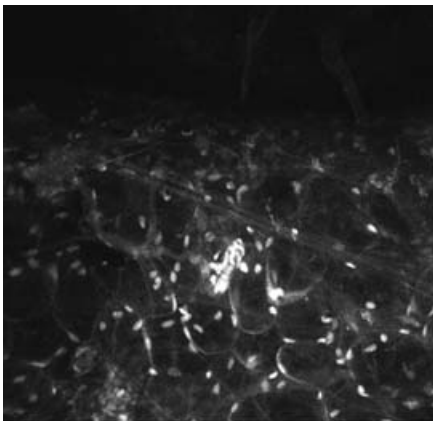

Figure 5

operating theatre utility, reduced pathologist travel time, ability to interrogate the complete surgical bed, limited impact by blood in the surgical field, reduced need for repeat surgery, reduced need for adjuvant therapies, better patient outcomes, and better health economics.

Importantly, digital workflows allow the integration of artificial intelligence with image-guided surgery and computer-assisted diagnostics, whereby each surgical case is utilised as another opportunity for continuous training and refinement of both surgical approaches and pathological diagnoses.

This further improves diagnostic and prognostic accuracy for patients while simultaneously building a repository of knowledge for surgeons and pathologists to refine their surgical procedures and diagnostic interpretations.

Although many of these parameters require validation in different oncological settings, the imperatives of contemporary patient care necessitate adoption of procedures, processes and technologies that enable a digitally driven sustainable healthcare system. Dr William Mayo would have been the first to recognise the central role that digital pathology would play in shaping future medical practice. mf

– References available on request

Author competing interests – the author is CEO & Managing Director of Optiscan Imaging Ltd, an ASX-listed Australian company which has developed, manufactured, and commercialised handheld fluorescence confocal laser endomicroscopes for real-time intraoperative digital pathology applications.