

REVIEW

Strategies for laboratory cost containment and for pathologist shortage: centralised pathology laboratories with microwave-stimulated histoprocessing and telepathology

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The imposition of laboratory cost containment, often from external forces, dictates the necessity to develop strategies to meet laboratory cost savings. In addition, the national and worldwide shortage of anatomical pathologists makes it imperative to examine our current practice and laboratory set-ups. Some of the strategies employed in other areas of pathology and laboratory medicine include improvements in staff productivity and the adoption of technological developments that reduce manual intervention. However, such opportunities in anatomical pathology are few and far between. Centralisation has been an effective approach in bringing economies of scale, the adoption of 'best practices' and the consolidation of pathologists, but this has not been possible in anatomical pathology because conventional histoprocessing takes a minimum of 14 hours and clinical turnaround time requirements necessitate that the laboratory and pathologist be in proximity and on site. While centralisation of laboratories for clinical chemistry, haematology and even microbiology has been successful in Australia and other countries, the essential requirements for anatomical pathology laboratories are different. In addition to efficient synchronised courier networks, a method of ultra-rapid tissue processing and some expedient system of returning the prepared tissue sections to the remote laboratory are essential to maintain the turnaround times mandatory for optimal clinical management. The advent of microwave-stimulated tissue processing that can be completed in 30–60 minutes and the immediate availability of compressed digital images of entire tissue sections via telepathology completes the final components of the equation necessary for making centralised anatomical pathology laboratories a reality.

Key words: Microwaves, histoprocessing, telepathology, centralised laboratories, ultrarapid processing, cost containment.

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INTRODUCTION

Many pathology laboratories in Australia and worldwide are staffed by a single pathologist who has responsibility for anatomical pathology as well as the haematology, biochemistry, microbiology and immunology services. While all these services are largely automated, anatomical pathology is essentially a manual, labour-intensive

discipline that requires the pathologist to personally carry out grossing, dissection and cut-up of specimens, and reporting. In addition, one technologist, and often two because of leave coverage, are required for tissue processing and section preparation, and to assist during specimen cut-up. Such solo practices may accession up to 5000 surgical biopsies per year, taking up most of the pathologist's time and effort. In large laboratories with trainees/residents, the latter perform the grossing/cut-ups as part of their training, allowing pathologists to conduct other duties additional to the reporting of biopsies. More importantly, there is a national and worldwide shortage of pathologists, particularly anatomical pathologists, so there is an immediate need to rationalise and consolidate this resource.

It is estimated that maintenance of such small, one-pathologist laboratories for histopathology is in the region of AU\$170 000 per annum, comprising \$80 000 for technologists' salaries (1.5 full-time equivalent [FTE]), \$40 000 for consumables and equipment maintenance, and \$50 000 for laboratory space and overheads. These laboratories are necessary because conventional histoprocessing requires a minimum of 14 hours and histoprocessing has to be conducted on site for expediency.

The rising cost of medical care has seen efforts to reduce and contain pathology laboratory budgets. Laboratory costs generally account for no more than 5% of total healthcare costs and it sometimes appears that pathology receives disproportionate attention, perhaps because laboratory activities seem more amenable to measurement and analysis. Even if external forces do not impose restriction of laboratory costs, there are potential virtues in laboratory cost containment; saved money can be invested in the modernisation of facilities such as laboratory information systems and computers, development of new diagnostic tests and technologies, establishment of new positions or competitive salaries to attract and retain valuable professionals, and improvements in the work environment, to name a few.

The consolidation of personnel resources provides for long-term staff shortages in peripheral laboratories and short-term back-up during periods of shortage due to planned and emergency leave for pathologists and technical staff.

There are at least three essential components for the successful centralisation of pathology laboratories; namely, an efficient and speedy network of couriers, rapid

processing of specimens and a rapid method of returning the results to the remote laboratory. All three components currently operate for most disciplines of pathology other than anatomical pathology. Efficient courier services exist, automated processors in clinical chemistry, haematology and immunology enable rapid specimen turnaround and the use of the fax machine or automatic server downloads via the Internet allow many private laboratories to consolidate through laboratory centralisation. However, this has not been possible in anatomical pathology except perhaps for a small proportion of specimens of mostly small biopsies.

This paper examines some of the strategies for laboratory cost containment and focuses on the potential for centralisation of anatomical pathology laboratories in order to accommodate the current shortage of anatomical pathologists.

EFFICIENCIES AND WORK FLOW PATTERNS

There are many strategies for cost savings in the pathology laboratory. Personnel costs are usually in the region of 60% or more of total costs and constitute the single largest component of the laboratory budget. However, lowering personnel salaries is not a feasible strategy in the current climate of an impending shortage of qualified professional staff. Instead, efforts directed at improvements in the productivity of staff, and changes in technology and skill-mix levels to extend the productivity of existing staff, remain the more viable alternatives. For example, competent pathology assistants can be trained and, under supervision, can conduct many tasks previously performed by pathologists, including the grossing and transfer of small biopsy specimens, and autopsy dissections. New technological developments such as automated vision systems that are designed for cytology screening can reduce cytopathology workforce requirements significantly and conduct quality assurance tasks. Other technological innovations in anatomical pathology that reduce manual intervention and demands on technologists' time include cassette and slide label printers, automated tissue processors, automated routine slide stainers and pathologist-operated digital photography units. However, despite this significant list, major technological innovations in anatomical pathology are few and far between compared with other disciplines of pathology and laboratory medicine.

The re-engineering of processes is one opportunity for cost containment that is often overlooked. Most processes can be studied and subjected to time and motion analysis. For example, the receipt/accessioning of biopsy specimens in the laboratory, through tissue processing and preparation of stained slides, through to the signed surgical pathology report for small and large biopsy specimens can be quite different. As such, specimens should be triaged and handled differently according to the time of day received, processing requirements and clinical urgency.

The familiar pattern of work in anatomical pathology laboratories has peak activity in the morning when overnight histoprocessing is completed and paraffin blocks are sectioned and stained. Activity subsides significantly in the afternoons when only re-cuts, special stains and grossing are the major functions in the laboratory. Continuous and

even flow of activity would allow greater efficiencies than the conventional pattern of peaks and troughs that almost all laboratories experience. Component processes linked by commonalities such as specimen size and therefore processing requirements, time of arrival, clinical turnaround time requirements, transcription, etc., can be identified, allowing batching of specimens and greater efficiencies. Each of these processes will have productive time and time spent waiting for something to happen. If ways to remove waiting and non-productive time can be devised, the entire flow can be compressed into a shorter time period, making individual contributions more efficient. Voice transcription reporting has met with varying success but computer validation and editing of anatomical pathology reports by pathologists is well established and contributes to expediency.

CENTRALISATION/CONSOLIDATION OF LABORATORIES

Partnerships and consolidations is another approach. In general, larger laboratory size brings economies of scale. Reagent and instrument costs should be volume-dependent and common laboratory information systems not only save on costs but also allow seamless transitions between laboratories both for pathology reports, specimen tracking and billing.

Two different laboratories would invariably have different practices and approaches to the 'default' number of blocks and slides on particular types of cases/specimens, laboratory information systems, staining protocols and processing laboratories. The major consolidation strategy would involve adopting the 'best practices' between the laboratories, including the best laboratory information system as well as single-site consolidation of histopathology processing and preparation, and cytopathology screening. Equally important is the establishment of single leadership at the levels of director and supervisors so that 'best practice' decisions can be made quickly and efficiently. Centralisation of anatomical pathology laboratories has the potential for significant cost savings but this has not been possible in the past because clinical turnaround time requirements necessitate that the laboratory and pathologist be in proximity and on site. Histoprocessing required a minimum of 14 hours and any delays in report generation would impact on patient care and hospital bed costs, the latter between \$1000 and \$2500/bed/day.

SYNCHRONISED COURIER SERVICE

Many private pathology services have successfully established sophisticated courier networks that employ road and air services. The majority of couriered specimens are blood and body fluids, results of which can be faxed to the source or accessed from a central database. When processing of tissues is centralised it generally results in delays because of the mandatory time required by conventional tissue processing and because the prepared tissue sections need to be couriered back to the source laboratory.

An integral component of our proposed system is a well-synchronised and efficient courier system that delivers by

road or rail within 6 hours, allowing coverage of a radius up to 600 km from the central laboratory, and a much greater distance by air. Specimens can thus arrive in the central laboratory before midnight and, following dissection and sampling, can be processed in the early hours of the morning. Specimens should be triaged according to urgency, originating laboratory, and separated according to size into small and large specimens. Small biopsies can be processed almost immediately without the attention of a pathologist, while large specimens can be fixed up to facilitate dissection by microwave irradiation in normal saline.⁵

ULTRA-RAPID TISSUE PROCESSING

Ultra-rapid tissue processing is essential to the concept of histopathology laboratory centralisation. Such instruments and protocols are now well established and available. Tissue fixation requires a minimum of 8 hours immersion in 10% buffered formalin for small biopsies and up to 14 hours for large specimens to be effective.⁶ This process can be greatly accelerated by exposure to microwaves (MW). Whole large specimens can be irradiated to 70°C in normal saline to solidify and facilitate dissection.⁵ The fixation of sampled tissue blocks and small biopsies can be completed whatever their state of fixation at time of receipt by similarly irradiating in normal saline or 10% buffered formalin to 70°C for 10 minutes.⁷

We have previously described a MW-stimulated protocol that completes histoprocessing of both small and larger biopsies within 30–60 minutes.⁸ In essence, the fixed tissue blocks are immediately irradiated to 70°C for 20 minutes in a proprietary solution comprising absolute alcohol, isopropyl alcohol and a long chain hydrocarbon. Irradiation is performed under 2 bar pressure to prevent boiling of the reagent, this single step serving to remove water and lipids simultaneously. By reducing the pressure to 0.1 bar, the reagent is vaporised before final wax impregnation by irradiating in molten paraffin to 85°C for a further 15 minutes at 0.1 bar.⁸ This protocol has resulted in a second-generation MW tissue processor (Milestone RHS-2; Milestone, Italy) that does not require pressure changes. In a one-step procedure, lipids and water are removed by irradiation in the same proprietary solution to 68°C for 20 minutes, followed by transfer to molten wax and irradiation to 85°C for 10 minutes. This instrument is capable of processing 120 tissue blocks, and small and large blocks are processed in 30 and 60 minutes, respectively. A completely automated processor is currently in production.

Recently, another MW-stimulated protocol for ultra-rapid tissue processing has been described⁹ and a fully automated instrument employing this method is also commercially available. The use of such MW-accelerated histoprocessing instruments significantly reduces both tissue processing and reporting turnaround times, the latter because prepared sections are available to pathologists for reporting at more convenient times.^{10,11} In our hands, compared with a TAT of almost 21 hours from specimen accession to slide production with conventional tissue processing, MW processing took 6.5 hours. With the introduction of MW processing, 88% of small biopsies were reported within 48 hours of accessioning compared

with 71% previously, with remaining specimens taking longer because of interruption by weekends and holidays.^{12,13} In another study employing a different MW processing protocol over a 1-year period, same day reporting was achieved in 55% of cases compared with <1% before implementation of MW processing.¹⁰ The quality of morphology and histochemical and immunohistochemical stains with both MW processing instruments was indistinguishable from that obtained with conventional 6–8-hour formalin fixation and 14-hour histoprocessing.

Ultra-rapid MW tissue processing will thus make up for any time lost by couriering specimens to a centralised laboratory.

IMAGE ACQUISITION

Telepathology makes it possible to transmit macroscopic and microscopic images to remote sites for diagnosis and consultation almost instantaneously and without significant cost.^{1–4} Adoption of this resource will allow the reporting pathologist to be at a site remote to the processing laboratory. The pathologist could remain at the source hospital to supervise the other aspects of automated pathology and laboratory medicine while reporting on the images acquired from the remote processing laboratory via telepathology and maintaining direct liaison with clinicians. Such a practice is not as radical as it seems and is currently practised in a simplified form by private pathology services that courier specimens to a centralised laboratory and courier back prepared sections to the remotely sited pathologist for reporting.

The use of networked digitised images of whole tissue sections has an additional benefit. Single pathologist practices cannot offer the full range of expertise in all areas of pathology and consultations are currently conducted through the examination of glass slides. This method is dependant on postal and courier services but can be circumvented when digitised slide images are available on a network for immediate access by the consultant in the centralised laboratory or elsewhere.

Good quality general-use digital cameras with image capabilities of up to 6 megapixels are now available at reasonable costs and extensive use of macro photography with such cameras¹⁴ provides sufficient images for the reporting pathologist to enable correlation without the need to view or dissect the specimen personally. Digital camera systems linked to computers and appropriate software that permit images to be accessed at different terminals are also commercially available. Such systems allow annotations on the images, automatic sizing or measurements, as well as indication of the sampling site,¹⁵ so that gross descriptions and sampling block keys can be replaced by digital images, further reducing costs and delays imposed by transcription of dictation.

The acquisition of microscopic images, their storage and access is another component integral to the success of laboratory centralisation. Still image acquisition is labour-intensive and the images acquired represent a fraction of the total area of tissue section. If the digital slide is to replace the glass slide there is a need to represent the entire section in digital format. The true virtual slide is one that contains a digital representation of the entire tissue section

at a resolution adequate to display the diagnostic cytomorphological features. The latter requirement is subjective but is generally accepted to be equivalent to at least $\times 20$ objective magnification.

For the digital slide to be useful in a high-volume pathology laboratory, automated image acquisition is essential. Although there are several unique and innovative approaches to acquisition that have involved re-engineering the microscope as pathologists conventionally know it, the majority of digital slide systems rely on components added to a conventional microscope. Computer software controls the mechanical stage, which moves in the vertical plane for focusing, and in the horizontal plane to scan the entire slide as a montage of images or 'tiles'. Tens of thousands of individual image tiles may be required to cover the entire section area. This latter approach has become commonplace insofar as there are now many vendors offering the hardware necessary to retrofit an existing microscope with a motorised stage, digital video camera and computer with interface for the camera.

With a retrofitted mechanical stage, a digital camera and talented programmer, any organisation can build its own digital slide system. This is of course oversimplification, but for every commercial vendor offering a digital microscopy kit, there is probably an equal number of 'home-grown' solutions.

Today, it is possible to purchase hardware interfaces which will control a video camera and acquire up to 30 images per second. Early systems took much longer.^{16,17} When synchronised with robotic stage movement, it becomes possible to scan a 20×25 -mm tissue area at $\times 20$ objective magnification in 3 minutes or less. However, there is trade off between speed of image acquisition, and accuracy of focus and tile alignment. Few systems can achieve seamless blending of adjacent image tiles and the incidence of misalignments and poor focusing appears proportional to the speed of image acquisition. Robust calibration of the motorised stage is also essential. To be useful for high-volume work a digital slide system should be able to reliably handle multiple stacked slides, requiring only a few minutes for each slide.

Three commercial systems will be discussed, each for their special qualities. The Bacus Laboratories Inc. Slide Scanner (BLISS; Bacus Laboratories, USA) is probably the oldest commercial system. The design is 'conventional' in that it comprises a robotic microscope (motorised stage, objectives, autofocus, substage condenser, etc.) with Windows PC and the completed digital slide is composed of several thousand image tiles acquired at user-defined size and spatial resolution. The digital slide is saved in 'WebSlide' format, a proprietary multi-resolution format that can be delivered to multiple users via a proprietary server (WebSlide) or catalogued with its 'SlideTray' software application. The images can be viewed through the WebSlide Browser thin client software and a WebSlide Viewer Java applet allows viewing from within a webpage. Bacus Laboratories continues to improve the speed of its digital slide acquisition and supporting software suite. A Webslide Transfer program provides the technical novice with a straightforward way of transferring digital slides across the Internet (a form of store-and-forward telepathology) and there is software for quantitative

immunohistochemistry on the virtual slides (IHCscore) and tissue microarrays (TMA score).

Nikon has played an important role in reducing the cost of entry-level digital microscopy through the introduction of the Coolpix consumer digital camera range. Other vendors including Olympus have followed suit, driving down the price of entry-level dedicated digital microscopy cameras, which provide immediate results and have far lower running costs than chemical photography.¹⁸

The Nikon Coolscope (Nikon, Japan) was introduced in 2003 to address the demand for low-cost, simple-to-use digital microscopy. It is a 'microscope in a box', and externally resembles a PC tower casing. Inside, the microscope parts are essentially similar to a regular microscope integrated to a 5-megapixel digital camera. The initial product provided the ability to demonstrate cases live on a television monitor or on a networked computer or through the Internet (real-time telepathology). Automated full slide scanning with the Coolscope is now possible through a licensing agreement with Bacus Laboratories, effectively allowing a Coolscope user to create Bacus Laboratories 'WebSlides'.

DMetrix is a spinout company from the University of Arizona Optical Sciences Center and will be notable in the history of microscopy for its development of a radically new microscope, designed purely for the purpose of creating digital slides. Its background in optics and proximity to an internationally renowned centre for optical design and manufacture (the Optical Sciences Center produces mirrors for the largest telescopes in the world), combined with genuine innovation, has allowed it to create a unique device in which the microscope optics are no greater than several millimeters across and there is not one lens but a miniature array of lenses no larger than a 10 cent coin. By stacking three of these arrays (like a stack of three coins), a microscopy slide can be scanned in a single pass in seconds, at a resolution equivalent to a numerical aperture of 0.20 (somewhere between a good $\times 20$ and $\times 40$ objective). The acquired digital images show good nuclear detail and are indistinguishable from those acquired with conventional optics. The DMetrix system provides the fastest method of microscopy data acquisition currently available.

Both the Bacus Laboratories and DMetrix systems have automated slide loaders that allow digitisation of slides in batches. However, innovative designs come at a price. Expect to pay more than US\$100 000 for a system that transcends conventional microscope design. There are also additional costs for items such as an automatic batch slide scanner system and additional software.

IMAGE STORAGE AND DELIVERY

There is a great deal of data on a single tissue section. Conservatively, this is in the range of 20 gigabytes uncompressed for a single focal plane. Image storage is one of the areas which initially posed significant problems; however, these are now largely resolved. When compressed, the images from a single case can be contained in one DVD-ROM that provides about 1 gigabyte capacity. While this method of storage is robust and suitable for circulation like a glass slide, it is not a viable option for the large

volume of routine daily work. Clearly, a busy pathology laboratory would consume several hundred terabytes of data storage in a short period of time. This is no longer a significant obstacle as image compression strategies can dramatically reduce the size of the data, and even in the absence of this, vendors such as IBM (USA) and Hewlett-Packard (USA) offer scaleable networked storage setups which are capable of readily handling this data volume. Thus, data storage issues are significant but no longer the limiting factor.

The most viable strategy is for the data, automatically acquired by scanning the glass slides, to be stored on networked high-volume hard drive arrays such as those from IBM or Hewlett-Packard. With these systems, capacities in the orders of petabytes (1 million gigabytes) are entirely feasible. Pathologists at remote sites can access the data in the storage area network (SAN); this has storage devices placed throughout a network which are accessed as if they are on a single device. Alternatively, GRID computing provides for repositories of data and computing power throughout the network and allows seamless access to the data from remote sites throughout the country.

A digital slide is incomplete without an interface to view the data. Ideally, this should simulate a microscope and the pathologist should be able to interact with the data, as if with a microscope, in real time. Dedicated client software can be made quite sophisticated but it is difficult to enable widespread dissemination and installation. The best kind of client software is one that does not need any installation, i.e., a 'self-executable' (.exe) file. This overcomes technical difficulties with installation, and administrator's privileges and access rights to hospital/laboratory workstations. Most vendors now provide both client software and a web-based means of viewing the data, the latter allowing cases to be viewed on any browser-equipped networked workstation through secure or encrypted web-interface.

CONCLUSIONS

Digital microscopy is an enabling tool that will permit better handling and dissemination of pathology images. Once laboratories fully utilise the digital slide, the range of applications will expand exponentially and the technology becomes ubiquitous. The availability of the virtual slide completes the requirements to enable successful centralisation of anatomical pathology laboratories both as a measure to alleviate the impact of pathologist shortage and for cost containment. Together with existing efficient courier networks, ultra-rapid MW stimulated histoprocessing and the rapid access to whole slide digitisation data

stored on a networked high-volume hard drive array, the scene is set for pathology laboratories of the future.

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