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The Royal College of Pathologists of Australasia

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA (RCPA)

Guidelines for Digital Microscopy in Anatomical Pathology and Cytology

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Revision history

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Scope

This document describes the guidelines for the safe implementation of digital microscopy into diagnostic laboratories in Australia, and provides an understanding of the potential factors to be taken into consideration when implementing digital microscopy systems for diagnostic use in anatomical pathology and cytology.

The main drivers of these guidelines are the recent technological advances in digital microscopy systems, storage devices, and communication technology, and the potential use of digital microscopy systems for diagnosis.

These guidelines are relevant to digital microscopy for the intended uses of diagnosis, consultation, education, training and quality assurance, and will indicate factors for consideration that may affect their safety and effectiveness for these purposes.

The RCPA recognises the rapid development in digital microscopy systems, and so we anticipate that these guidelines may need to adapt as the technology advances.

This document excludes image acquisition by other means such as single field photography, video and robotics.

This document excludes the use of digital microscopy in other disciplines of pathology such as Haematology and Microbiology.

This document excludes some features that may be currently available with some digital microscopy systems, such as image analysis and decision support features.

These exclusions may be addressed in the future.

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Abbreviations

CAP	College of American Pathologists
CPD	Continuing Professional Development
DICOM	Digital Imaging and Communications in Medicine standard
DPA	Digital Pathology Association
EQA	External Quality Assurance
FISH	Fluorescence in situ hydrisation
HL7	Health Level Seven. See HL7 Australia.
IQA	Internal Quality Assurance
LAN	Local Area Network
LIS	Laboratory Information System
NATA	National Association of Testing Authorities, Australia
NPAAC	National Pathology Accreditation Advisory Council
RCPA	The Royal College of Pathologists of Australasia
RCPA QAP	RCPA Quality Assurance Programs
TGA	Therapeutic Goods Administration
VPN	Virtual Private Network
WAN	Wide Area Network

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Definitions

ADSL	ADSL is an asymmetric digital subscriber line. ADSL is a type of broadband communications technology used for connecting to the Internet.
DICOM	Digital Imaging and Communications in Medicine standard for handling, storing, printing, and transmitting information in medical images and related information (ISO 12052). It defines the formats for medical digital slide images that can be exchanged with the data and quality necessary for clinical use.[1]
Digital microscopy	The scanning of a whole glass slide containing cut and stained human tissue and glass slide cytology preparations, then converting into a high-resolution quality digital image, which can be viewed by a pathologist on a viewer application with panning and zooming functions which can be used to simulate the use of a conventional microscope. Images can be acquired in 2 dimensions (x- and y-axes) with the option of z-stacked (3-D) annotations).
Interoperability	The ability for two or more systems, devices or applications to exchange, and mutually use, information.
Lossy compression	A file compression where the file size is reduced often by removing information not relevant to the image's intended use. When uncompressed image is reconstructed often there is a degree of loss of quality. Example of lossy compression image files is JPEG.
Lossless compression	A file compression where the file size is reduced but with no loss of quality when the image is uncompressed. Examples of lossless compression image files are JPEG2000, RAW, etc.
Telepathology	A type of telemedicine. It is the process by which diagnostic pathology is performed on transmitted digital slide images that are viewed at a distant site in real-time on a display screen rather than by conventional light microscopy with glass slides. Telepathology can be used for histopathology and cytopathology specimens, blood films / bone marrow morphology, immunofluorence and microbiological assessments of cultures.[2]
Z-stacking	Z-stacking is when multiple images are captured at different focal planes.[1]

Introduction

This document has been developed by the Royal College of Pathologists of Australasia (RCPA) and is intended to offer best practice guidance to laboratories in Australia that are considering using digital microscopy for diagnosis. These guidelines follow the published RCPA Position statement *Telepathology*[2] and a workshop the College held in October 2014. The workshop engaged a variety of digital microscopy stakeholders to discuss related issues in digital microscopy and develop quality standards for digital microscopy when used for diagnostic purposes.

This document presents a set of guidelines to be used in conjunction with other reference materials to promote quality, accuracy, security and privacy in digital microscopy. Existing NPAAC requirements and relevant jurisdictional and other regulatory requirements must apply to all diagnostic laboratories.

Background

Digital microscopy shows great potential to improve peer sharing of diagnostic materials and has been used in Australia for quality assurance and education purposes for many years. Although it has not yet been used for diagnostic purposes in Australia, this is occurring in other countries such as the USA, Canada and Sweden[3].

"Virtual" microscopy has been in use by RCPA QAP since 2007, with all diagnostic modules now using this as the only means of providing images to participants.

With increasing numbers of implementations in Australia laboratories, the need for standards and guidelines has arisen, as it is imperative to ensure that the accuracy of diagnosis and quality of patient care are not compromised when these systems are used for diagnostic use.

The main drivers for a laboratory implementing digital microscopy for diagnostic use include:

- Recent technological advances in scanners, diagnostic tools, storage devices, communication, etc.;
- Ability to work remotely, this may assist geographically dispersed laboratories and pathologists;
- Ease of sharing images for collaboration such as for second opinions (internal and external), multi-disciplinary team, etc.;
- Improved tools for research, teaching and quality assurance.

There are a number of challenges to be addressed before digital microscopy can be adopted for diagnostic use in a pathology laboratory, these include:

- No formalised standards exist for digital slide image colour, resolution, quality, file format and compression, storage, etc.;
- Network bandwidth - significant bandwidth of network is required to handle the fast transfer of very large digital slide image files;
- Ergonomic issues related to physical environment, software and navigational controls;
- Patient privacy issues when using laptops, smartphones, tablets and other devices for viewing digital slide images;

- Medio-legal issues with sharing digital slide images between pathologists from different organisations or countries.

There are other issues that are common to all forms of pathology for diagnosis and include such areas as patient identification and chain of custody, training and education, validation, security and storage of images to name a few. Critically, there is a need for engagement with technology providers and technicians to ensure that the standards expected in current laboratory processes are translated into the digital domain.

These guidelines present the framework of concepts for consideration to assist the safe and reproducible implementation of digital microscopy into diagnostic laboratories for anatomical pathology and cytology.

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1   Technical specifications

The College recognises that establishing technical requirements is challenging due to the rapid advances being made in the field of digital microscopy, so these guidelines aim to provide guidance for key technical factors to bear in mind when implementing digital microscopy for diagnostic use in anatomical pathology and cytology, to ensure end-to-end quality, performance and effectiveness of the digital microscopy system.

Generally, the digital microscopy system may comprise of a slide feeder, scanner, storage server and computer environment. The image acquisition is performed by a scanner (combination of hardware and software) which scans the whole glass slide, capturing a series of images, then uses software to combine or "stitch" the digital slide images together to create a high resolution image.

Due to the size of the file, the image is often compressed and stored in a manner that enables it be reconstructed quickly on a viewer. If the digital microscopy system has the ability to communicate with the Laboratory Information Systems (LIS), it will retrieve request and patient data either by push/pull communication method from the LIS.

1.1   Background set-up requirements

When considering a digital microscopy system for diagnostic use, consider:

- determining labour requirements - assess whether additional or specific skilled staff are required; costs of training, etc.;
- additional costs that may be incurred for quality assurance, purchasing workstation equipment (e.g. chairs, monitors), etc.;
- performing analysis of time taken to diagnose using digital microscopy versus conventional microscopy (for the modalities that digital microscopy is intended to be used in).

Additionally it is important to engage pathologists, laboratory staff and IT to assess requirements to ensure the system is scalable to meet future increases in workload. For example, it is important to have your IT department determine the following:

- Assess interoperability with existing systems including the LIS;
- Estimate file storage requirements (short and long term storage, archiving, etc.);
- Assess network and communications requirements including secure workstations, storage devices, etc. that may be either local or distributed on wide area network with remote connections via VPN or internet (e.g. ADSL or wireless broadband, etc.).
- Estimate network bandwidth and assess the impact of transmitting large size files on the current network. For example, the Digital Pathology Association recommends the LAN network bandwidth to be 100Mbps[4] and the WAN bandwidth to a minimum suitable for the screen resolution, image compression and tissue types so the pathologist can work productively with the displayed images.
- Assess privacy and security requirements to ensure the digital microscopy system meets jurisdictional legislation and the organisation's privacy and security policies.
- Determine if additional software (i.e. interfaces, virus scanners, firewalls, etc.) need to be written or sourced;
- Assess and cost additional hardware that may need to be acquired, including tablets, smartphones, monitors (consider screen size, graphics cards, graphic drivers, etc.), navigation devices and storage devices;
  Note: To date there have been no studies that have examined the accuracy of diagnosis when a digital slide is viewed on small devices such as Smart phones and

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tablets, and so extensive validation is required before these devices are used for diagnostic purposes. Additionally there is an issue with patient confidentiality that must also be considered before these mobile devices are used for diagnostic purposes.

- Assess IT expertise required for the support of interfaces, operating systems, databases, hardware and software configuration, network, etc.

Physical characteristics should be considered in conjunction with the technical characteristics as these may affect the performance and usability of the system, and be mindful of the optimal operation conditions recommended by the manufacturer. Physical factors to consider include:

- Ensuring sufficient space for the digital microscopy system, workstations and other utilities; bench space to store slides before and after loading, distance between workstations, etc.
- Optimal conditions as specified by the manufacturer i.e. room temperature, bench and floor stability, lighting, optimal size of the section on slide (typical size is 15mm x 15mm), etc.;
- Noise and sounds when the equipment is in operation i.e. alarms, mechanical parts, system fans, etc.;
- Workstation requirements such as adequate chairs with back and neck support; also consider glare from lights, sunlight onto monitors, etc.;
- System instructions and labelling i.e. instructions may be on the system, in operating manuals or via online help.

Additionally the physical work areas must be safe and ergonomic. For more details see RCPA Position statement, Ergonomics.[5]

G1.1   The manufacturer **must** provide adequate labelling, including on equipment warning labels/instructions, operation and maintenance manuals, etc.

G1.2   The laboratory should have an understanding of the technical support requirements for the operation of the digital microscopy system including networking, interfaces and operating systems.

G1.3   The laboratory should have a service agreement in place with the manufacturer or designated support agent, which will cover routine maintenance and breakdown of equipment.

G1.4   There should be a documented routine maintenance plan for the equipment.

G1.5   There should be a log to document all maintenance performed for the life of the equipment.

1.2 Image acquisition

Glass slides of the diagnostic tissue are prepared in the usual way as for conventional microscopy, i.e. using haematoxylin and eosin, immunohistochemical or other visible stains; and the thickness of the section should be as prepared for conventional microscopy. It is recommended to consult with the scanner manufacturer for the optimal size of the tissue section but typically it is 15mm x 15mm. Note: The larger the tissue section on the slide to be scanned, the larger the final file size of the digital slide.

The scanner is a device that may use a tile or linear scanning pattern to scan the entire glass slide at one or more resolutions to create a digital slide image file. The scanner may have the capability to capture images through brightfield or fluorescence, or both. After the images are captured by the scanner, software then "stitches" the images into a single large image.

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G1.6   The digital microscopy system **must** capture a high quality and resolution image of the glass slide.

     CG1.6(i)   Poorly prepared slides can result in poor quality and re-work. As for conventional microscopy factors that may affect the quality of the slide include:

- thickness and size of the section;
- slide staining and drying time;
- artefacts on the glass slides (e.g. dust, fingerprints);
- air bubbles under coverslip.

     CG1.6(ii)   The resolution and quality of the captured image can be affected by a number of factors:

- Method of scanning the slide i.e. tile or linear scanning pattern;
- Number of axes scanned i.e. multiple-axis (X Y axis) or multiple stacked axes (X Y and Z-axis) or Z-stacking;

    NOTE: Z-stacking could be useful for slides for cytology, lymphoma pathology or FISH. Z-stacking may provide depth of focus but will lead to larger file sizes[6].

- Distribution of focal points across the scanned tissue area;
- Number and dimensions of pixels of the scanner;
- Scanning magnification – the scanner should at least be able to scan at 20x and 40x magnification. The scanning magnification will be set to the lowest magnification that provides all information needed for accurate diagnosis. This may be determined by the type of case, pathologist preference or laboratory procedures. For example, the _RCPA Invasive Breast Cancer structured reporting protocol_[7] states to use 40x objective to perform the mitotic score. Magnifications of 60x may be useful in cytology and lymphoma pathology.
- The viewable resolution is limited by the scanned resolution. Typical scanned resolutions are 0.5 micron/pixel (20x) and 0.25 micron/pixel (40x);
- Colour depth, which is typically 24-bit colour. Consider the availability of software tools for colour, white balance, contrast, exposure, etc. It should be possible to also adjust these in the view, like adjusting a microscope.

    Note: The image colour can be influenced by other factors such as staining (type of stain, overstaining or understaining, etc.), software manipulation, etc.

    Care must be taken when manipulating a digital image (i.e. Rotating, and adjusting brightness and colour of an image) to ensure that the manipulation does not affect diagnosis[8].

G1.7   The scanning system should perform reliably and be capable of high performance for diagnostic use.

     CG1.7(i)   Reliability and performance factors to be considered include:

- Slide feeder should be reliable and be able feed the scanner without damaging the slide;
- Scanning speed should be adequate for the expected laboratory workload– this may be dependent on the size of the tissue area to

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scan, magnification and scanner. For example, 20x objectives may vary from 30 seconds to 5 minutes.

- High scan read rates of slides and barcode/metadata. For the system to function reliably it is recommended that the read rates for the slide and barcode/metadata are >95%. NOTE: The barcode read rate may be affected by the print quality, format, placement of barcode label, etc., and it is recommended that slide is labelled with legible information (e.g. unique number identification, patient name).
- The scanner should support common barcode formats (e.g. 1D, 2D, etc.).
- The network connection between the scanner and the storage device/s should be capable of transmitting as fast as the scanner can send the image file.

CG1.7(ii)   The scanning system should be able to operate off-line if there is a network or LIS outage.

CG1.7(iii)   The user should have the ability to manage and monitor the mechanics of the scanning system.

1.3 Image file and compression

The file size of the captured image is dependent on the size of the section, magnification of the lens and number of z-planes. The typical size ranges from 1-20GB (uncompressed), to in an extreme case a 50mm x 25mm tissue size, captured at 0.1 micron/pixel (100X) with 10 Z-planes (375 GB per plane) = 3.75TB per image.[1]

Many digital microscopy systems will use file compression for storage and transmission of a file. The compression ratio i.e. ratio of uncompressed to compressed file size, will determine the file size, for example:
- A 20x 0.5micron/pixel, 15mm x 15mm section has an uncompressed file size of 2.51GB. With compression (e.g. lossy compression JPEG) with 1:20 compression the file size becomes 128 MB; or with 1:10 compression, 256 MB.
- A 40x 0.25micron/pixel, 15mm x 15mm section has an uncompressed file size of 10.1GB. With compression (e.g. lossy compression JPEG) with 1:20 compression the file size becomes 502 MB; or with 1:10 compression, 1GB.

Pyramidal images are also captured by most scanners which will store images of lower magnification and these extra images can take up to 30% of additional space within each image file. Whatever file format and file compression is adopted by the digital microscopy system it is essential that these factors do not impact the image quality when displayed on a viewer.

G1.8   The digital slide image **must** be captured in an appropriate file format and viewable at all times.

CG1.8(i)   File format should be open (e.g. TIFF, Big TIFF etc.). Open licence file compression algorithms such as JPEG should be used.

CG1.8(ii)   The file **must** be stored and viewable on the system for at least the minimum retention time for glass slides as outlined in NPAAC publication *Requirements for the retention of laboratory records and diagnostic material*[9].

G1.9   If image compression is used, it should be an efficient file compression should be applied, ensuring the digital slide can be reconstructed on a standard image viewer

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without compromising image quality.

CG1.9(i)   As the sizes of the captured image are very large an efficient compression method should be used for storing and transmitting the image.

CG1.9(ii)   The compression **must** not affect the quality of the image to the extent it becomes unsuitable to perform a reliable diagnosis. So when the image is recreated on a standard image viewer it is done so without compromising the quality of the image. Compression algorithms and resultant degree of acceptable loss should be validated to be diagnostically accurate.

There are 2 types of file compression:
-   Lossless compression reduces the size of the file without loss of quality when the image is uncompressed. There is typically 3x-5x reduction in file size. Lossless compression is allowed as there is no loss of quality when uncompressed;
-   Lossy compression reduces the size of the file by eliminating some data and when the image is recreated on a viewer there is often a degree of loss of quality. There is typically 10x-50x reduction in file size. Lossy compression may be used only if the quality of the image is suitable to perform a reliable diagnosis. Studies by Foran, et al and Kupinksi, et al show that varying degrees of lossy compression can be applied without significant decrease in quality relative to light microscopy.[9,10] The verification and validation process in section 4.1 can be used to determine the degree of compression that will still allow reliable diagnosis taking into account the local specimen mix and diagnostic tasks required.

1.4 File storage and archive

G1.10   All images used for diagnostic purposes **must** be stored on a secured device in a secure location.

CG1.10   The storage device/s (including database servers, backup devices, etc.) used for storing / archiving images and related case information, must be kept in a secure location.

G1.11   There **must** be an efficient and reliable method for storing and retrieving images (including from online and archive file systems).

CG1.11(i)   Data integrity must be maintained, so the storage device must ensure that the data is stored reliably, and there is no data loss or corruption if the storage device fails. An appropriate archive and backup process should also be put in place to protect image data and associated metadata according to regulated preservation guidelines and durations.

CG1.11(ii) The storage device should be able to store as fast as the scanner can transmit the image file. If the storage system is connected to an LIS, then the storage device should also be able to store as fast as the LIS can transmit data.

CG1.11(iii) The digital microscopy system may store images using an appropriate file organisation. For example, single frame organisation or tiled image organisation (preferred).[1]

CG1.11(iv) Long term storage or archived data must be stored on robust storage devices. It is not recommended to use a portable media format (such

as laptop, smartphone, tablet, USB stick, etc.) as it is subject to being misplaced or damaged.

CG1.11(v) The case data (including digital slide images, patient and clinical information) must not be able to be modified or deleted after it has been archived, without appropriate tracking.

NOTE: The system should provide the ability to copy a de-identified digital slide images and related case data for teaching, quality assurance, presentations or research purposes.

CG1.11(vi) A secure transmission protocol should be used for image and data transfer such as Hypertext Transfer Protocol (HTTP) across networks.

G1.12 The stored digital slide image must be associated with the machine readable identifier.

CG1.12(i) Storage must be able to associate the scanned machine readable identifier to the scanned image, and depending on the communication with the LIS the patient metadata may also be linked to the record.

CG1.12(ii) If the digital microscopy system is integrated with a LIS, the minimum information to be stored in the digital microscopy system storage for each case includes:

- Patient identifiers (minimum of two) - e.g. patient ID, medical record number, patient name, etc.;
- Patient data - e.g. date of birth;
- Slide information - e.g. accession number, block number, stain type, etc.;
- Appropriate timestamps of transmission records - e.g. date and time of receiving request/patient data from LIS or other system; date and time of transmission of results to LIS, etc.;
- Pathologist comments (if available);
- Audit functionality if any data is modified by a user or the system – e.g. If pathologist comments or annotations are entered or updated, then pathologist login details, date and time for any actions must be stored. It also good practice to store the reason for the modification.

Each scanned image should contain a record of the following information at a minimum:

- File dimensions;
- Colour depth;
- Image resolution;
- Creation date and time.

CG1.12(iii) Each image captured for a given identifier should be stored and be able to be viewed or deleted by the user, as required, with appropriate tracking.

G1.13 The stored image and related case data **must** be available for the minimum retention time.

CG1.13(i) When digital slide images are used for diagnostic use, the storage of the digital image and associated diagnostic material must satisfy the existing retention times for glass slides as stated in the NPAAC publication *Requirements for the retention of laboratory records and diagnostic material[11]*.

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CG1.13(ii)   Glass slides must also be kept for the minimum retention time, as stated in the NPAAC publication *Requirements for the retention of laboratory records and diagnostic material[11]*.

1.5 Pathologist workstation

The computer environment includes network communications; hardware and software components of the device used for managing, retrieving and viewing digital slide images and associated metadata for a given case. The image display device could be a laptop/monitor, tablet or smartphone typically connected via a network to the storage and archive devices and LIS. This remote connection to the LIS and digital microscopy system would allow pathologists to report and provide comments remotely via a secure network.

Workstation configuration and issues such as visual strain associated with prolonged engagement with a computer screen are important considerations. Voice recognition may assist with dictation during reporting.

G1.14   The digital slide image should be retrieved on a reliable high-quality display monitor.

CG1.14(i)   The monitor should provide the same quality characteristics when viewing a digital slide as viewing a glass slide under a microscope. The Digital Pathology Association (DPA)[4] suggests the optimal requirements are:

- Screen size: 24" monitor
- Resolution: 1920x1200
- Pixel pitch: 0.27 mm

Other considerations for the workstation include:

- Colour depth support: 24bit or 30bit.
- User defined colour and image settings
- Availability of monitor colour calibration.

G1.15   The pathologist should have access to an ergonomic navigation control device.

CG1.15(i)   The navigation control device must provide adequate speed, panning and zooming capabilities, with no pixelation of the image.

CG1.15(ii)   Common navigation control devices should be supported i.e. trackball, mouse and joystick. Other navigation control devices may be available, such as 3D cad mouse, touch screen, position / motion detectors and eye tracking. Ergonomically designed navigation devices are an important consideration to minimise constant large repetitive movements of wrists, thumb and index finger.

1.6 Image review application

Pathologists will spend long hours reviewing digital slides and so the efficiency and effectiveness of the pathologist may depend on the performance and usability of the application used for viewing the slides. The following design features should be considered when purchasing an image review system for diagnostic use:

- Routine diagnostic workflow – this may include dynamic worklists, ability to configure structured reporting templates, etc. See the published structured reporting templates on the Royal College of Pathologists of Australasia (RCPA) website: https://www.rcpa.edu.au/Library/Practising-Pathology/Structured-Pathology-Reporting-of-Cancer/Cancer-Protocols

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- Software interaction, e.g.
  - data entry (spell check, ways to prevent data entry errors);
  - steps required to perform a diagnosis, etc.;
  - response time to retrieve images and metadata from storage.

- Screen display, e.g.
  - screen layout and complexity of the screen (a complex screen may cause confusion or frustration) [12];
  - field of view of displayed slide;
  - size of text;
  - use of thumbnails, menu options, keyboard shortcuts, etc.;

- Software functions (ease of use and speed) e.g.
  - moving between cases;
  - selecting fields of interest;
  - selecting and changing magnification of an image;
  - image manipulation functions such as colour alterations (adjust colour, white balance, etc.).

- Navigation controls (ease of use and speed) e.g.
  - provision of different types of navigation such as keyboard (including shortcuts, arrows, etc.), mouse, joystick, touch screens, etc.;
  - consider ergonomics, pathologists may spend many hours of repetitive use of the navigation tool fatigue is an important consideration.

G1.16   The web-browser or desktop image review application **must** display a high quality image.

CG1.16(i)   The image quality **must** be maintained at all selected magnifications.

CG1.16(ii)   There **must** be no pixelation or distortion of the image after panning and zooming an image.

G1.17   A secure web-browser or desktop image review application should allow local and remote network access to view the stored image file.

CG1.17(i)   The software application should seamlessly connect to the storage system anywhere on the network including remote access using VPN where a web-interface is not used, etc.

CG1.17(ii)   The local and remote software application must provide security access and be able to verify a valid user login. See *Privacy, confidentiality and security* section for more details.

CG1.17(iii)   The software application should access data from a secure storage system and must not store patient data on the viewing device.

CG1.17(iv)   The software application should provide access locally or remotely to view images on a variety of devices such as computer monitors, tablets, or smartphones. The laboratory must ensure thorough testing on all intended devices before using the device for diagnostic purposes.

G1.18   The web-browser or desktop image review application should provide a configurable, user-friendly and intuitive interface to assist diagnostic workflow.

CG1.18(i)   The software application must provide a clear screen layout with adequate field of view of displayed image.

CG1.18(ii)   The software application should have both icon and font size configurable by the user, to ensure easy viewing on different sized device screens, to suit individual user preferences.

CG1.18(iii)   The software application should provide functionality to assist routine workflow similar to that used by pathologists when viewing slides under conventional light microscope, such as:

- Easy selection of magnification level for panning and zooming of an image;
- Ability of user to select areas of interest.

CG1.18(iv)   The software application must have the capability to display the minimum stored information on the screen, see G1.11(iii).

Note: If the case has been archived, then archived status should be visible at a minimum, but could also indicate the date/timestamp of the archived record.

CG1.18(v)   The software application may provide user-friendly functionality for the diagnostic viewing and reporting of a case. Such functionality may include:

- variety of annotation tools such as the ability to circle, highlight and add free text comments;
- image manipulation functions such as colour alterations (adjust colour, white balance, etc.); image sharpening functions (if z-stacking is available);
- calibrated ruler to measure tumour size, margins, etc., and ability to add these measurements to the case;
- calibrated standard area such as 1 square mm to 5 square mm for mitotic count per area. For example, facility to drag out a 1mm square box or circle to enable counting of mitoses.
- user defined template fields to capture data for structured reporting.
- facility for simultaneous viewing of a slide by multiple pathologists;
- ability to compare multiple slides for a case;
- dictation facility via speech recognition.

NOTE: Ideally an un-annotated version of the image should be stored.

G1.19   The web-browser or desktop image review application should deliver optimal speed performance when retrieving and navigating an image.

CG1.19(i)   The display for any randomly accessed field of view within the digital slide image, at any level of magnification, and associated information for a case should be within:

- 0-2 seconds (local area network)[4];
- 0-5 seconds (WAN, internet, VPN).

NOTE: Response times may vary when displaying images remotely on computer monitors, tablets or smartphones as it is dependent on the network speed and bandwidth.

CG1.19(ii)   The software application should provide a fast response time with continuous panning and zooming of an image; and also moving between images.

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G1.20   The web-browser or desktop image review application should provide the ability to copy, de-identify and share a digital slide image and related case data, for use in teaching, quality assurance, presentations or research.

CG1.20(i)   The web-browser or desktop image review application should provide the ability to copy and de-identify a digital slide image slide and related case data, for teaching, quality assurance, presentations or research purposes from the users workstation. This computer is likely to be remote from the slide scanner, acquisition computer and the server.

NOTE: Care must be taken when copying digital slide images as patient metadata may be embedded in the file, in these cases the patient metadata must be either removed or de-identified on the copied image file.

CG1.20(ii)   The software application should allow a de-identified copy of a digital slide image to be stored either on the digital microscopy system or downloaded to local workstation.

CG1.20(iii)   The software application should allow the online sharing of a stored de-identified digital slide image and related case data, for teaching, quality assurance, presentations or research purposes. For example, a laboratory may like to share a fixed URL link of a de-identified digital slide image with another application such as RCPA eCases for educational purposes.

G1.21   Quantitative data and other decision support from digital microscopy systems **must not** be used for diagnostic use until further clinical validation studies are performed except as covered by CG1.18.

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2 Communications and networks

Communication and network configurations are important considerations before acquiring a digital microscopy system for diagnosis as there will be large amounts of data transmitted across the network from scanners to workstations (local or remote), storage devices and the LIS. For the safe and effective use of the digital microscopy, the IT infrastructure must be able to cope with the increased data traffic, transmit the data securely to protect patient confidentiality and reduce risk of data loss.

G2.1   Systems **must** ensure the secure and confidential transmission of information (e.g. images, patient data) across private and public networks.

CG2.1(i)   Transmission of data across networks should use secure encryption protocols (e.g. SSL, PKI, etc.) for authentication and to transmit all patient and case data (including case accession slide labels, patient / case / specimen information, etc.) [13].

CG2.1(ii)   A robust firewall should be considered for protection. For example, a web application firewall used to block unauthorised applications (e.g. server plugins, etc.).

G2.2   The digital microscopy system should be capable of integration with existing systems (LIS, etc.).

CG2.2(i)   The system should be integrated with the LIS to ensure that there is no need for double entry of comments.

CG2.2(ii)   The system should ensure the completeness, accuracy and integrity of messages between the digital microscopy system and the LIS at all times.

NOTE: Information from the LIS may include patient information, clinical history, specimen information, etc. It is good practice to ensure that any changes to this information are sent to the LIS so the systems are synchronised.

CG2.2(iii)   The digital microscopy systems should support an open format that can be transformed to DICOM in the future when the DICOM licensing terms are fully known.

CG2.2(iv)   A standard messaging protocol (e.g. HL7) should be used for transmission of information between the digital microscopy system or middleware and LIS. If HL7 is used then it **must** be compliant to *AS4700.2 Implementation of Health Level Seven*.

For more details on information communication requirements for accredited pathology laboratories see NPAAC *Requirements for information communication* (2013).

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3 Privacy, confidentiality and security

G3.1   The digital microscopy system **must** ensure the privacy, confidentiality and integrity of records is maintained at all times.

    CG3.1(i)   The system **must** comply with national and state privacy regulations.

    CG3.1(ii)   Digital slide images may be embedded with patient metadata so digital slide images **must** be stored and displayed on devices that provide privacy features. Portable storage devices, such as USB sticks, etc. must also comply with all privacy and security requirements.

    CG3.1(iii)   Devices used to display digital slide images should be positioned so they cannot be seen by unauthorised people. This is especially important when using smartphones, tablets and other mobile devices for remote diagnosis.

G3.2   The digital microscopy system and supporting utilities should be secured and maintained, both on-site or if taken off-site.

G3.3   The digital microscopy system **must** incorporate reasonable measures to protect all images and case information from misuse, unauthorised access, modification and improper disclosure.

    CG3.3(i)   The system **must** authenticate all access to information by verifying user access.

    CG3.3(ii)   Restricting access by multi-factor authentication including a passphrase is highly recommended.

    CG3.3(iii)   The system should provide a user-defined no activity timeout periods of less than 15 minutes.

    CG3.3(iv)   The system should have protection from malicious software (e.g. viruses, Trojans or worms).

    CG3.3(v)   Other security considerations include:

- Ability to remotely disable or wipe devices;
- Periodic purging of digital microscopy files and data from remote devices;
- Logging and investigating all security breaches;
- Internal audits of all devices.

The following provide more in-depth information on how privacy and security are controlled and regulated in Australia for accredited pathology laboratories:

- NPAAC *Requirements for information communication* (2013)
- RCPA guidelines, Managing privacy information in laboratories
- AS/ISO17799 *Information Security Management*
- HB174 *Information Security Management Implementation Guide for the Health Sector*

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4   Quality and compliance

4.1   Verification and validation

G4.1   Functional verification of the digital microscopy system **must** be performed to assess the performance and ensure it is operating in accordance with the manufacturer's specification.

CG4.1(i)   Verification of the digital microscopy system should ensure it is operating in accordance with the manufacturer's specifications as documented in accompanying user and technical manuals.

CG4.1(ii)   All verification results **must** be documented and kept for the life of the equipment.

CG4.1(iii)   The supervising pathologist **must** assess whether re-verification is required when there is a significant change of IT infrastructure (network, etc.), hardware or software for either the LIS or digital microscopy systems.

G4.2   Validation **must** be performed on the digital microscopy system to assess the performance and ensure it meets the intended use and process. If the digital microscopy system is intended for diagnostic use then validation must include demonstrating the equivalent diagnosis is made between conventional and digital microscopy.

CG4.2(i)   Validation testing **must** be supervised by an adequately trained pathologist and involve all relevant stakeholders (e.g. pathologists, laboratory staff, IT, vendor technicians, etc.).

CG4.2(ii)   The validation method should be appropriate for the intended use/s (i.e. diagnostic, teaching, research, etc.), and it is recommended that:

- Testing **must** simulate the intended operation and process. Documented use case scenarios and test plans should be written to test the entire digital microscopy system and intended process. NOTE: This includes testing on all intended viewing devices such as tablets, smartphones, etc.
- A sufficient sample set is used when testing with a reasonable coverage of different scan magnifications, stains, specimen types and histological features (i.e. cytoplasmic, membranous, nuclear immunoreaction*).* [14]
- Consideration is given to repeatability/reproducibility parameters such as:
  - Agreement of diagnosis between different pathologists for a select number of digital microscopy slides;
  - Consistency of diagnosis when viewing cases through conventional and digital microscopy. To reduce bias consider:
    - sufficient washout period between viewing slides through conventional and digital microscopy; NOTE: CAP recommends a washout period of 2 weeks. [14,15]
    - viewing slides in random order.
- Assessment of performance goals by assessing potential failure points/function (e.g. barcode read errors, slide scan errors, transmission errors to/from LIS; time studies on viewing images on viewer, etc.);
- Monitor mechanical functions such as luminance or light

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intensity; and chromaticity or colour temperature.[16]

CG4.2(iii)   The supervising pathologist **must** assess whether re-validation of the digital microscopy system is required when there is a significant change of IT infrastructure (network, etc.), hardware or software for either the LIS or digital microscopy systems.

G4.3   The record of validation method, test results and final approval **must** be documented and comply with accreditation standards (e.g. NATA).

CG4.3   Final approval of validation **must** be documented and signed by the supervising pathologist.

G4.4   Each pathologist **must** be given an adequate transition period between using conventional and changing to digital microscopy for diagnostic use.

NOTE: Allow a sufficient time for doubling up conventional and digital microscopy workflows until the pathologist has confidence with the new process (see Section 5).

4.2 Quality management

G4.5   The intended use and procedures for the digital microscopy system **must** be clearly defined and documented.

CG4.5(i)   There **must** be clearly defined and documented procedures covering the workflow and equipment operation.

CG4.5(ii)   There **must** be clearly defined and documented procedures for quality control activities, including:

- image quality standards for image resolution, colour depth, scan rate, barcode read rate, display response time, etc.;
- use of system tests and calibration tools to measure image quality (if applicable).

NOTE: Vendors should provide information and training on the supplied system tests and calibration tools.

CG4.5(iii)   There **must** be clearly defined and documented procedures for business continuity during mechanical or communication downtime. This may include steps to revert to conventional diagnostic microscopy in the event of equipment failure.

CG4.5(iv)   There **must** be clearly defined and documented procedures for the backup and archive of data.

CG4.5(v)   The procedures should be evaluated and updated as required when:

- new major releases of software and/or hardware are released;
- changes are made to associated standards such as DICOM, HL7, etc.;
- changes are made to compliance regulations such as NPAAC, national or state Privacy legislations, TGA medical device regulations, NATA, etc.

G4.6   An ongoing audit, issues and root cause analysis framework **must** be part of the laboratory quality control program.

CG4.6   Examples of issues that need to be documented include:

- Data integrity issues (e.g. incorrect or incomplete patient metadata in digital microscopy system, incorrect or incomplete

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report data in LIS after transmission).
- Quality issues (e.g. poor/inconsistent staining, slide damages, incorrect/incomplete transmission errors, etc.);
- Performance issues (e.g. high barcode error rates, scan rates, poor display response times, network performance issues, etc.);
- Mechanical malfunctions and unanticipated errors;
- Operating system and software crashes and unanticipated errors messages.

4.3 Regulations and compliance

G4.7   The laboratory **must** comply with all relevant regulatory and governing bodies, and privacy legislations before using a digital microscopy system for diagnostic use.

CG4.7   When implementing digital microscopy systems for diagnostic use, the laboratory **must** ensure they comply with all national / state regulatory and governing bodies (i.e. NPAAC, NATA, TGA, etc.); and, Commonwealth, State and Territory privacy legislations, especially in regard to:

- Storage and retention of digital slides and associated metadata;
- Security;
- Privacy;
- Communication messaging;
- Audit trial.

G4.8   The manufacturer of the digital microscopy system **must** comply with all relevant national / state regulatory and governing bodies for a medical device; and Commonwealth, State and Territory privacy legislations.

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5 Professional practice, training and competency

G5.1 Pathologists should undertake adequate professional practice activities, including training, participation in Internal Quality Assurance (IQA) and External Quality Assurance (EQA), and Continuing Professional Development (CPD).

CG5.1 When implementing a digital microscopy systems for diagnostic use consider professional practice issues such as:

- Human resourcing, which includes:
  - Resource requirements during the transition period;

    NOTE: There should be a double-up of conventional and digital processes initially to ensure each pathologist acquires competency in digital microscopy.

  - Workload and the hours of work;
  - Issues relating to remote practice such as:
    – Level of remote supervision of cases (such as cut-up, slide preparation, slide scanner magnification settings, etc.);
    – Professional isolation;
    – The RCPA Reporting of Histopathology and Non-Gynaecological Cytopathology Specimens outside the Laboratory and the organisation's policies on reporting outside the laboratory.
- Handling of peer reviews or second opinions for cases.

  NOTE: It is recommended to have a policy for the use of digital microscopy for professional second opinions, that considers situations such as cases from:

  - Same organisation but different locations / time zones / disciplines;
  - Different organisations;
  - Cross border (NOTE: there should be a separate policy for cross-border pathology).
  NOTE: The sending/receiving organisations should comply with this guideline with respect to all elements of digital microscopy.

G5.2 Each pathologist should undertake adequate training and accreditation.

CG5.2 Before using digital microscopy for diagnostic purposes each pathologist must:

- Undertake appropriate training from the vendor;
- Be proficient in using digital slide images and be able to:
  - assess the quality of the digital slide image;
  - understand the system limitations, including situations where turnaround times are longer or accuracy is lower using the digital system;
  - understand the system features such as how to navigate the digital slide, add annotations, etc.
  - understand patient confidentiality pertaining to digital pathology;
  - remove metadata from a digital slide file in order to copy for teaching sets and educational purposes.
- Credentialing of pathologists and certification of technicians is

recommended.

G5.3   The pathologist should decide the best method for diagnosing each case, i.e. digital or conventional microscopy or a combination of both according to their clinical judgement.

G5.4   Pathologists should incorporate digital microscopy to their continuing professional development (CPD). This development could include training from the RCPA, industry or in-house training, especially in the area of informatics or bioinformatics.

G5.5   The new digital microscopy system should create no additional medico-legal liability[17,18] issues for the reporting pathologist. Pathologists must adhere to all existing supervision and accreditation requirements when using digital microscopy for diagnostic purposes and be cognisant of any additional obligations incurred by electronic transmission and storage of patient information.

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