

2014-05-02

Digital Imaging in Pathology

Horn, Christopher Lee

Horn, C. L. (2014). Digital Imaging in Pathology (Master's thesis, University of Calgary, Calgary, Canada). Retrieved from <https://prism.ucalgary.ca>. doi:10.11575/PRISM/25713

<http://hdl.handle.net/11023/1480>

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UNIVERSITY OF CALGARY

Digital Imaging in Pathology

by

Christopher Lee Horn

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE
DEGREE OF MASTER OF SCIENCES

MEDICAL SCIENCE GRADUATE PROGRAM

CALGARY, ALBERTA

April, 2014

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Abstract

A large component of pathology informatics is the usage and utility of digital images. The main objectives of this thesis involve many different applications related to digital imaging and anatomic pathology.

An initial literature review identifies the delivery and applications of digital images and current imaging systems related to pathology including hematopathology, and whole slide imaging platforms. Telepathology as the future delivery model of pathology digital images is examined as well.

Pathology staff across Canada currently utilizes gross digital images for regular documentation and educational reasons. They also indicate that the technology will be needed for future applications in teaching, consultation and medico-legal purposes.

Currently, there is no resource available to match up typical gross features with the appropriate gross descriptive term. This is accomplished in this thesis and can be used as an educational tool for pathology professionals.

Preface

This preface lists the publications by the author of this thesis which include the materials and ideas presented in the thesis.

1. Horn, C.L., DeKoning, L., Klonowski, P., Naugler, C., *Current usage and future trends in gross digital photography in Canada*. BMC Med Educ, 2014. **14**(1): p. 11.
2. Horn, C.L., Mansoor, A., Wood, B., Nelson, H., Higa, D., Lee, L.H., Naugler, C., *Performance of the CellaVision[®] DM96 system for detecting red blood cell morphologic abnormalities*. Submitted to Journal of Pathology Informatics, Feb 2014.

Acknowledgements

I would like to thank my program director Dr. Amy Bromley for her help and encouragement during the duration of this program.

I would also like to thank Dr. Jim Wright for his vision and willingness to implement a much needed PA program here in Western Canada. Thank you also for trusting me to be the “guinea pig” in this endeavour.

I want to thank Dr. Larry DeKoning and Dr. Paul Klonowski for their knowledge and guidance for the projects associated with this thesis and other projects not directly related.

I want to acknowledge Dr. Christopher Naugler who provided me with everything I needed to succeed in this program, and afterwards as I continue on in my career. In particular, Dr. Naugler was always there to lend his support and guidance to me, day or night. His genuine concern to see me succeed has been noticeable. In addition, Dr. Naugler has taught me what it is to become a true lab professional. This work would not be possible without your help, support and encouragement.

Finally, I want to thank Calgary Laboratory Services for providing me with the resources needed to complete my studies and other independent research projects.

Dedication

I dedicate this thesis work to my friends and co-workers who have shown considerable support for me in my journey to complete my studies.

To my parents, Larry and Jeannette, thank you for raising me with the values and work ethic that is necessary to become successful at this level. You have given me the much needed confidence to believe in my abilities and to strive for so much more academically and personally.

I want to give special thanks to Sonja, Doug & Paulette. Your continued love, support and encouragement during this time made the process so much easier for me and my family.

Special dedication goes out to my wonderful children, Genevieve, Justin and Samantha who have shown incredible patience and understanding during the time of my studies. I hope to inspire unto you, what so many have done for me.

To my wonderful wife, Dana, your support throughout my studies has been nothing short of remarkable. Thank you for your love and understanding during this time. Couldn't have done it without you!

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List of Symbols, Abbreviations and Nomenclature

Symbol	Definition
CD ROM	Compact Disc Read-Only Memory
CDSS	Clinical Decision Support System
CME	Continuing Medical Education
CLL	Chronic Lymphocytic Leukemia
CLS	Calgary Laboratory Services
CT	Computed Tomography
DICOM	Digital Imaging and Communications in Medicine
DSLR	Digital Single-lens Reflex
EIS	Enterprise Image Server
EXIF	Exchangeable Image File
FDA	Food and Drug Administration
FISH	Fluorescence in situ hybridization
FMC	Foothills Medical Centre
GPS	Global Positioning System
HD	High Definition
H&E	Hematoxylin and Eosin
IHC	Immunohistochemistry
ISO	International Standards Organization
IT	Information Technology
LCD	Liquid Crystal Display
LED	Light-Emitting Diode
LIS	Laboratory Information System
OR	Operating Room
OS	Operating System
PACS	Picture Archive and Communication System
PC	Personal Computer
QA	Quality Assurance
QC	Quality Control
RBC	Red Blood Cell
SIVQ	Spatially Invariant Vector Quantization
SSI's	Surgical Site Infections
TMA	Tissue MicroArray
WBC	White Blood Cell

Chapter One: Introduction

1.1 Pathology as a Visual Specialty

Among the many functions of a pathologist are diagnosis, consultation, documentation, and education. Implicit in these activities is the necessity to document morphological findings both at the macroscopic and microscopic level [1]. Traditionally, this has been accomplished through the process of descriptive prose with inherent idiosyncratic variations in the style, vocabulary and abilities of individual pathologists and other staff performing tasks such as surgical gross dissection [2]. Frequently, the difference between making a specific diagnosis and a generic pathological process is determined by the gross description including what the gross lesion looked like, where the lesion occurred and how the lesions were distributed [3]. This is accomplished through descriptive prose dictated to a pathology report and can be accompanied with photographs of the specimen itself.

Photographs capture unbiased appearances of pathological changes and may reduce many of the inaccuracies resulting from discrepancies in descriptive ability [2]. Each specimen is unique and thus requires variation in description and handling procedures [4]. This makes the accurate description and interpretation of the findings critical because that is what remains in the permanent record as the basis for later historical, medical and legal review and interpretation [3]. In this respect, descriptive pathology, including gross photographs, can be considered a road map for what should be done next. Proper gross description, with accompanying gross photos, provides a permanent, written and legal documentation of the medical problems of the patient [3]. To acquire precision and efficiency in the pathologic diagnosis of disease and maximize the results of the gross findings, the lab staff presenting the gross description must accurately

observe, describe, record and communicate the results of the case to the pathologist for interpretation and diagnosis [3].

The use of pathology informatics as a diagnostic tool, and specifically digital imaging, is on the rise in Canada [5]. Digital imaging in pathology is defined as the storage of anatomical pathology information in an electronic format and is one of the most commonly used tools of informatics [6]. A large component of pathology relies upon processing visual information, often using digital imaging [7]. This information can be collected as either microscopic slides or as gross pictures of surgically removed specimens (gross digital pathology).

Since pathology is a visual science, the inclusion of quality images into lectures, teaching handouts and electronic documents is crucial [8]. With advancing technology, these images have transitioned into a digital format. When incorporated with synoptic texts, reports are more complete, hopefully adding to their overall accuracy and conciseness [9]. In addition, block keys and hand-drawn diagrams can be replaced with digital photographs [2]. In this way, digital photography has changed the face of the pathology report significantly [10], allowing the incorporation of coloured prints of the gross specimen as well as of relevant microscopic features, thereby enhancing the reproducibility of the findings and greatly improving the quality of the pathology report.

As time goes on, pathology informatics and the technology associated with it will continue to advance at a rapid pace. As this technology continues to move forward, we must gauge the current usage and application and anticipate the future needs in order to use this information and maximize it to our benefit. In the following sections of this chapter, I review research motivations, objectives, novelty and significance, contributions and methodology of this thesis: the final section outlines the structure of the thesis.

1.2 Motivations

As previously mentioned, pathology informatics is rapidly ascending in Canada and all over the world [5]. Pathology informatics is now considered a pathology subspecialty with its own association [11], publication journal [12] and board certified fellowship examination [13]. Included within the realm of pathology informatics are technologies associated with digital imaging for both macroscopic and microscopic purposes. As technology advances, existing systems will improve and new systems will develop. It is important to gauge current applications and technologies and utilize them as much as possible, including for medical education purposes. As the technology continues to improve at a rapid pace, an in-depth knowledge is needed to utilize current methods and anticipate future needs.

1.3 Research Objectives

The objectives of this thesis involve many different applications related to digital imaging and anatomic pathology. The first objective is to assess the applications and obtain a snapshot of the current use of digital gross photography in pathology laboratory settings across Canada. The second objective is to design and develop a database of gross digital images showing particular gross features and using it as an educational tool for new laboratory staff including pathology residents and pathologists' assistant students. The final objective is to provide an inventory of modern imaging systems which are currently utilized in different areas of pathology.

1.4 Research Novelty and Significance

The usage and implementation of gross digital photography is not novel in pathology laboratories in Canada or around the world. However, the exact usage, utility and future direction of gross digital images across Canada is relatively unknown. The survey we have crafted for this project (chapter three) is intended to accomplish these objectives. In addition, the establishment of gross digital databanks across the country is not unique, but the application of these images showing particular gross features and using them as an educational tool is (chapter four). This thesis will gauge the future direction of gross digital photography in Canada to hopefully help organizations to plan and develop their systems to anticipate future needs identified in this paper. Also, the gross digital databank from this thesis can be used by institutions to help train staff to help identify particular gross features of pathology specimens and standardize methods of gross description.

1.5 Research Contributions

This research has the following contributions:

- Identify the current and future usage and utility of gross digital images in Canadian pathology laboratories.
- Develop a comprehensive list of gross descriptive terms required for pathology laboratory staff performing surgical dissection.
- Provide a basic overview and comparison of commercially available pathology macro imaging stations.
- Develop a gross digital image databank of particular gross abnormalities seen in surgical and autopsy specimens commonly seen in the pathology laboratory.

- Provide a brief background and explanation of each gross abnormality that has been digitally photographed for the databank.

1.6 Research Methodology

The gross digital images used in this research are a combination of images retrieved from a pre-existing databank and of specimens specifically photographed for their gross appearances as they enter the pathology department at the Foothills Medical Centre (FMC) in Calgary, Alberta. All images retrieved for the purposes of this project, and future usage, are used by permission from the Department of Laboratory Medicine, University of Calgary and Calgary Laboratory Services (CLS). Approximately 158 images were retrieved for this project, and modifications of the images to enhance particular features and/or remove patient information were done through Adobe Photoshop software.

1.7 Structure of the Thesis

Following is a brief description of the chapters of the thesis. The thesis is structured as follows:

Chapter two contains background regarding digital images. This includes comparisons of digital imaging vs. traditional still photography images and macrophotography vs. microphotography. In addition, there is an overview of current digital pathology imaging systems including those used at Calgary Laboratory Services (CLS). Lastly, there is a brief overview of the applications of gross digital images including educational, clinical and remote applications of the technology.

Chapter three contains the previously described survey regarding the usage, utility and future direction of gross digital images in Canada. The chapter contains a brief discussion, methods, results and discussion of the survey. Included in this chapter is a copy of the survey questions.

Chapter four presents a gross digital image databank as an educational tool for the pathology lab. Included in this chapter is a comparison of different camera types and commercially available macro imaging systems. Also, as an attempt to gauge novelty of this project, there is a list of current gross pathology images available through print and electronic delivery. Additionally, there is a section discussing digital imaging and archiving, which is an important step in the process of acquiring gross digital images. The final section of this chapter is dedicated to the actual gross digital image databank for educational purposes including an attachment of all of the images themselves, with accompanying descriptions of each pathological process.

Chapter five presents the final conclusions, limitations and future direction of gross digital images.

Chapter Two: Literature Review and Related Works

2.1 Digital Imaging vs. Still Photography Images

Photographing specimens as a means of documentation in the pathology department has been done for decades [14]. This has traditionally been accomplished by analog (i.e. 35-mm film) photographs. However, there has been a tremendous shift over the past ten to fifteen years to document these findings into a digital format [15]. By comparing the two different formats, there is no doubt as to the increased advantages of digital imaging over traditional analog photography [2].

The first major advantage digital photographs possess over analog photographs is the improved cost efficiencies. The development of digital photography and the rapidly decreasing costs of good quality digital cameras has had a major impact on our traditional way of documenting pathological findings at both the gross and microscopic level [2]. There are some initial start-up costs associated with converting from analog to digital format. For instance, purchasing new camera devices and accompanying software is necessary to download these pictures into a protected harddrive. However, basic digital photograph systems can be relatively inexpensive when compared to analog format, which needs expensive processing and development. Additionally, storage and retrieval of analog photographs requires time and manpower, which may require dedicated staff and thus, requires additional expense. This is different from digital photographs which are archived and retrieved almost immediately by the user from a sharable network or hard drive which requires little time and no extra manpower, thereby negating the additional expenses. Thus, a compelling reason to convert to digital technology is the lower running costs and shorter image production turnaround times [2].

Some other significant advantages are the overall ease of use and versatility of digital photographs when compared to analog photographs. Digital images permit the image quality and content to be assessed at the time of capture, have no developing delays or costs, are easily duplicated and manipulated, and facilitate image storage, cataloguing, retrieval, sharing and applications [2, 6, 7]. Also, images can be directed into long term storage at acquisition, decreasing the risk of misfiling.

Patient care is enhanced by the transmission of digital images to other individuals for consultation and education, and by the inclusion of these images in patient care documents [8]. Digital images do not utilize photographic film and these images are immediately available for incorporation into web sites or digital publications, printing, transfer to other individuals by email, or other educational applications [8]. Specifically, these applications in education are abundant and include conference presentations, publication, undergraduate and postgraduate teaching as well as remote consultation through telepathology, and quality assurance (QA) programmes [2]. These items will be discussed at further length later in this thesis.

On a broader scale, the transition to digital images from analog has allowed for a more improved workflow in the pathology laboratory. A digital imaging network allows decentralization of pathologists and pathology departments as images can be accessed from any image capable personal computer (PC) or device connected to the network. Thus, images are immediately available for review by attending pathologist and clinical teams. Additionally, digital images are easily duplicated to enhance reporting, consultation and educational purposes.

2.2 Macro vs. Micro

Digital pathology images consist of either gross (macro) photos or microphotography (histologic photography). The distinction in pathology between the two is quite clear. Gross pathology concentrates on the organ or whole patient [3]. Thus gross digital pathology would refer to digital photographs of organs, organ systems or the entire patient. On the other hand, histopathology refers to the study of the microscopic anatomical changes in diseased tissue [16]. Consequently, digital microphotography in pathologic terms refers to digital images of tissues and cells as seen through a microscope [3]. Both types of images, either independently or together, can correlate with clinical disease or support a presumptive diagnosis [3].

2.3 Current Digital Pathology Systems

There are currently several commercially available digital pathology systems for use in pathology departments. These systems are intended to augment and supplement manual methods for routine diagnosis while keeping up with the steady increase in workflow. In particular, haematology departments have been utilizing modern hematopathology imaging systems as automated diagnostic tools. At Calgary Laboratory Services (CLS) in Calgary, Alberta, the various haematology departments across the city use the CellaVision[®]DM96 to screen for white blood cell (WBC) and red blood cell (RBC) abnormalities. Another digital pathology system being utilized at CLS is the Aperio ScanScope system which is used to scan glass histology slides into a digital format. Once digitized, these slides can be utilized for remote viewing, consultation and telepathology purposes.

Specific for anatomic pathology are systems which integrate gross and microscopic images of surgical and autopsy specimens into network accessible databases for clinicians. In

particular, there has been some discussion to incorporate these images through already established radiology image systems, called Picture Archive and Communication System (PACS). This can be established through the Digital Imaging and Communications in Medicine (DICOM) format before they can be archived into a PACS system. Each of the above mentioned pathology imaging systems is discussed in greater detail below.

2.3.1 Hematopathology Imaging Systems

There are several recently developed hematopathology imaging systems which show significant potential in automated peripheral blood film interpretation and reporting. All of these systems incorporate a whole slide scanner coupled with image analysis software. The software program “pre-classifies” cells into basic cell types which can then be assessed by the user. In general, these systems perform fairly well for white blood cell (WBC) morphology assessment [17-21] and platelet counts [22], but it has been more challenging for red blood cell (RBC) morphology (HORN et al, submitted to Journal of Pathology Informatics, 2014-02-04).

The most widely established system and the one used primarily at CLS is the CellaVision[®]DM96, which is an automated system for in-vitro diagnostic practice. It works in conjunction with an analyzer (e.g. Coulter LH 780 analyzer) to screen for RBC and WBC abnormalities. Blood samples are initially screened by the analyzer, and then if an abnormality arises, a blood smear slide is prepared (usually by an automated slide smear machine). The blood smear slide is next scanned into the CellaVision[®]DM96 for automated analysis.

The CellaVision[®]DM96 system scans a user-defined portion of a microscopy slide and automatically locates and presents images of cells on blood smears. A peripheral blood application is specified for differential count of WBC's, classification of RBC morphology and

platelet estimation. The CellaVision®DM96 system overlays the digitized image with a grid to facilitate accurate cell counting. The operator recognizes and verifies the recommended classification of all cells according to types specified in a pre-existing database [23]. For RBC morphology, the CellaVision®DM96 system scans one zone equivalent to eight fields using a 100X objective. The CellaVision®DM96 system is outfitted with four flag levels to discriminate between six morphological abnormalities of size and colour of RBCs including hypochromasia, polychromasia, microcytosis, macrocytosis, anisocytosis and poikilocytosis [19], and has the ability to characterize several more [23].

There are several other digital hematology platforms available, but do not yet have FDA approval. HemaCAM is one such system, which is currently available in Europe [24, 25]. This platform was developed by a German publically funded research institute, Fraunhofer IIS, and was certified for in vitro diagnostic service in 2010. The Nextslide Digital Review Network was developed as a collaboration between the Department of Hospital Laboratories, University of Massachusetts Memorial Medical Centre and Nextslide Imaging (Cleveland, Ohio). Initially published Nextslide Digital Review Network evaluations have shown excellent correlation compared to both CellaVision and manual differentials [26]. Finally, the Bloodhound Integrated Hematology System also uses whole slide imaging to detect cells of interest but differs in that it integrates a cell counter, slide maker and image analysis software into a single instrument.

2.3.2 Whole Slide Imaging (WSI)

The traditional microscope, combined with the "routine" hematoxylin and eosin (H & E) stain, continues to be the gold standard for diagnosis of cancer and other diseases [27]. However, there has been an exponential period of growth for digital imaging in pathology which has been

catalyzed by changes in **imaging** hardware and advances in computational processing [28]. This modernization, called whole slide imaging (WSI), has allowed the digitization of entire glass slides at near the optical resolution limits of light to occur in about one minute per slide [28]. In addition, whole slides can be imaged in fluorescence or can be used for multispectral **image** analysis [28, 29] and Immunohistochemistry (IHC) [27]. As a result, **digital imaging** is revealing the potential to combine primary image characteristics into high-dimensional genomic assays by advancing microscopic analysis into the digital age [28]. There are at least 10 different vendors that offer commercially available WSI systems on the market today [28]. The most popular and the one used at CLS is the Aperio ScanScope™ system.

2.3.2.1 Aperio ScanScope™

The Aperio ScanScope™ group of systems are brightfield scanners that digitize whole histology microscope slides at 20x and 40x magnification and provides excellent high resolution images (~ 0.5 microns/pixel for 20x and ~ 0.25 microns/pixel for 40x scans) [29]. Image files can be up to 100,000 by 100,000 pixels in size, resulting in multiple gigabyte files. However, they are JPEG2000 compressed down to a few hundred megabytes for an average-sized slide [29]. Once these images are captured, they can be easily viewed using Aperio's free image viewer, called ImageScope™, which lets you to take snapshots and perform quantitative analysis [29].

The ScanScope™ system works in conjunction with a number of software applications for optimal use. The Aperio ImageScope™ software is needed to open and view the images. **In addition, the** Aperio Genie Histology Pattern Recognition™ software allows you to train the system to identify different tissue types based on their patterns [29]. For example, it can be

trained to recognize tumour regions, then algorithms from the software can be used to quantify items such as nuclear staining in the tumour regions [29].

2.3.2.2 Advantages/ Disadvantages of Whole Slide Imaging

There are many advantages of WSI over traditional manual histologic analysis. Some of the major advantages include:

- 1) Traditional analysis entails “hunting” around with a microscope, trying to find representative image fields to capture. With WSI, this time consuming and labour intensive step is replaced with a fast, automated scan of the entire slide.
- 2) After they have been captured, digital slides are available for use on a sharable network by any number of users to view and analyze.
- 3) WSI digital images are stored as a single file, usually in a tiff format, that allows prompt access to any image location at any magnification.
- 4) WSI allows the user to view the digital slide faster than conventional methods. This is because you can zoom to any magnification very rapidly and select regions for analysis in just a few seconds [28, 29].

- 5) WSI allows the user to scan and analyze entire slides. This is advantageous because you can work more efficiently and also because you are not limited to analyzing only small representative portions of a specimen [29]. This also eliminates the potential pitfall of selection bias which is inherent in static digital microscopy (Naugler, C – Imaging in Clinical Pathology – In submission).
- 6) For WSI there are tools available to analyze the entire digital slide or exclusive regions. After the user designates both the analysis region and desired software algorithm, a single click starts the analysis – all results appear on the screen upon completion[29].
- 7) WSI analysis results are stored with the image and can be reviewed for accuracy at any time. An example is pseudo-color mark-up images where the image shows exactly how the algorithm is performed and includes immediate confirmation that the algorithm results are accurate. This information is readily available for review at any point for a study or other purposes.
- 8) WSI analysis can be repeated for any digital slide and the results can be compared in just a few minutes. Additionally, different algorithms and parameter settings or algorithms can be processed for comparison. The user can even add or exclude regions and repeat the entire analysis.
- 9) WSI quantitative results for individual slides, as well as for slide sets, can be exported into a single data file, for additional analysis with popular tools like Excel Microsoft [29].
- 10) For WSI, each image can potentially contain a single set of analysis results that are readily viewed in an overlay fashion on the input slide image. This eliminates numerous

file folders full of snapshots, each with their own set of analysis results that have to be collated and combined into a single result set [29].

11) WSI and associated software allow for algorithms for Immunohistochemistry (IHC) and stain intensity. Specifically, the Aperio analysis package includes algorithms for Nuclear, Membrane, Micrometastasis and Staining Intensity quantification [29]. These are highly advanced algorithms based upon morphological image processing methods.

12) WSI is a versatile, high resolution system which has standard 20X scanning and can even go up to 40X. This allows the user to measure and count cellular structures, as well as area and intensity of staining [29].

13) WSI, and specifically the ScanScopeTM system, allows the user to export results to a common file format that can be imported into popular application software, such as Microsoft Excel. This allows the user to look for correlations between specimens, or for graphical representations of the numerical data [29].

14) An advantage of WSI is that multiple images can be viewed simultaneously. In particular, this is advantageous for analyzing IHC-stained slides, where more than one assay has been prepared [29].

Despite the obvious advantages, there are many barriers to the widespread implementation of WSI including operational, production and cost benefit analysis. There is an increased awareness that use and acceptance of WSI for diagnostic purposes necessitates that workflow and operational challenges are addressed [30-33]. Cost analysis of WSI have traditionally been based only on direct costs and diagnostic accuracy [31], which can be quite costly [34]. However, these analyses often disregard cost and workflow issues that develop because of

redundancy, the need for extra staffing, operational challenges and customized software development when WSI is integrated into routine practice. In addition, initial start-up costs (in excess of US\$100,000 to \$150,000 per scanner [28]), service contracts, technical support, regulatory and licence issues must also be addressed. Consequently, pathology laboratories may find it problematic to implement a realistic cost-benefit analysis of adding WSI to their department and were possibly much greater than first anticipated [31, 35].

There are also challenges with respect to validation of the quality and reliability, and overcoming perceptions associated with digital images. Validation of digital images is necessary to assess diagnostic performance issues when transitioning from traditional microscopic diagnosis to a digital platform. As an example, evaluation of the standard H & E stain is necessary so that diagnostic performance by pathologists is not compromised when they transition to WSI instead of traditional stained tissues on glass slides [27]. In addition, the most significant limiting factor is the perception among pathologists that WSI systems are inferior in performance when compared with light microscopes [28]. Given that pathologists have carried out their work with light microscopes for over 100 years, WSI is perceived as a disruptive technology [28].

Perhaps the biggest obstacles to date are the regulatory issues surrounding WSI implementation. The US Food and Drug administration has ruled that WSI imaging devices are class III (highest risk) medical devices. In practical terms, this means a more stringent regulatory approval process and a prolonged timeline for implementation of WSI imaging systems for primary diagnosis. It appears that FDA approval of the first WSI systems for primary diagnosis could be at least 5 years away [36].

There appears to be no doubt that WSI will become commonplace in the pathology laboratory in the very near future as evidenced by the emergence of more than 10 different WSI vendors over the past 5 years [28], and over 30 different scanning platforms on the market [37]. Additionally, because of the simplicity involved in file sharing and the interactive nature of viewing images, WSI is extremely effective for education [38]. However, digital platforms for WSI implementation have been slow for the pathology community. As a result, WSI applications have been limited to education, research, and specific areas in clinical practice [27, 28]. To achieve widespread implementation and acceptance of WSI technology for diagnostic purposes, there is much work to be done before WSI technology for diagnostic purposes can be widely adopted [6, 39, 40].

2.3.3 Picture Archive and Communication System (PACS)

In radiology, an electronic picture archive and communications system (PACS) has multiple uses including storage, rapid retrieval and extensive access to digital images [41, 42]. PACS is offered by virtually all major radiology vendors and is captured by multiple modalities (e.g., magnetic resonance imaging, computed tomography, positive emission tomography scan) with users at many remote sites having simultaneous access to these images [7, 43]. Additionally, both electronic images and reports are able to be digitally transmitted via PACS [43]. The main constituents of a PACS are the imaging modalities, workstations for interpreting and reviewing images, a secured network for the transmission of patient information and servers for storage and retrieval of images and reports [43]. PACS offers capabilities for off-site viewing and reporting and provides the electronic platform for radiology images to be interfaced with other information systems including the electronic medical record [7, 43]. Another key

aspect of PACS is its role in radiology workflow management. In particular, it is used to manage the workflow of patient examinations [7, 43].

Initially, PACS was developed primarily for radiologists and their requirements for image interpretation and diagnosis [7, 43]. However, more recently imaging informatics at the enterprise level has transitioned toward the development of novel multimedia and communication tools targeted toward the requirements of other users such as pathologists, surgeons, cardiologists and even patients themselves [44, 45].

2.3.4 Integration of gross digital images into PACS via DICOM

As previously stated, radiology departments have been successful in utilizing PACS for storage, rapid retrieval and widespread access to digital images [41, 42]. Digital Imaging and Communications in Medicine (DICOM) is the universal format for PACS image storage and transfer, synonymous with International Organization for Standardization (ISO) standard 12052 [7]. DICOM defines information objects not only for images, but also for patients, studies, reports and other data combinations [7]. Digital images from a pathology-based LIS must be compatible with the DICOM format before they can be successfully integrated into an enterprise-wide PACS [43]. In other words, DICOM is essential for integrating gross digital images into PACS.

There have been some recent initiatives that have helped create a DICOM imaging standard so that pathology images can be included in PACS [46, 47]. For example, the DICOM supplements 122 and 145 provide flexible object information definitions devoted to pathology specimen description and whole slide imaging (WSI) acquisition, storage and display [48].

There are very few authors who have addressed the potential benefits of a PACS specifically for pathology [45, 49, 50]. Furthermore, the actual integration of digital pathology images into an enterprise-wide PACS has not yet been widely implemented [7]. Limitations of previous PACS-systems in pathology were that they were limited in scope and had restricted access to only the pathology department or a exclusive group of medical subspecialties [43]. The benefits of integrating digital pathology images into pre-existing electronic health records are suggested to include greater accessibility to these images by all clinicians, and incorporation of clinical findings for patient care, education and research [43]. In addition, sharing of pathology images has traditionally been achieved by paper (printed photos) and/or e-mail-based (e-mail with attached image files) systems. However, this is time consuming work for the pathologist, leaving less time available for clinical service responsibilities [43]. Other limitations of these systems include minimal documentation, patient traceability and a deficiency of institution-wide access [43].

The integration of gross pathology digital images into PACS was successfully achieved by Amin et al [43]. They were able to automatically transmit almost 27,000 gross images from their LIS into their PACS enterprise image server (EIS) in 2012, with a very low fail rate of 0.5%, those of which had to be manually entered into PACS [43]. Once transmitted, these images were immediately available to institution-wide PACS users.

The benefits of digital gross images available on the PACS network are numerous. First, because of the expedient availability of these images, the surgeons were able to more quickly determine follow-up treatment protocols for their patients (e.g. transplant trials based on the amount of resected tissue) [43]. Secondly, surgeons no longer had to continually contact pathologists to request gross pathology images of the specimens they surgically resected [43].

Thirdly, gross digital images were accessible for immediate review in subspecialty-based surgical oncology conferences and for counselling specific patients during clinic appointments [43]. An additional benefit was that by accessing these gross digital images, surgeons could more easily interpret the text-based gross description of the pathology reports, including the orientation of the specimen and the location of the lesion [43].

Potential limitations were also identified when attaching gross digital images to a PACS network. As with any radiology image, users with privileged access to the PACS can copy or save any gross digital image, such as for a presentation or publication, without obtaining permission from the pathology department [43]. Another limitation is that there is no direct user interface that permits PACS users (including pathologists) to remove an image from the EIS. In other words, once an image is permanently archived it cannot be removed from the system. It is possible that the IT department managing the service could “remove” an unwanted image from the user interface. However, they cannot be truly deleted once they are permanently stored as the digital image with associated information on the EIS [43]. Additionally, since the PACS relies on an automated process, if the person who captured the image decides to post-process and re-upload an image at a later time, both the original and edited image will appear in the medical record, and a manual request must be obtained to remove the original image [43]. Despite these limitations, reports of unauthorized use, security breaches or patient-image-data mismatches have not yet been documented since the initiation of the enterprise-wide sharing of digital gross pathology images in the Amin, et al. study [43].

As previously discussed, an advantage of implementing gross digital images into PACS is that every obtained image will be automatically accessible, without restrictions, institution-wide. However, accompanying this “advantage” are possible drawbacks. For example, images

with inadequate focus or composition that have not been deleted from the pathology image server will automatically appear on the EIS [43]. As clinicians access these poor quality images, they may be inclined to become dissatisfied with the pathology service [43]. Given this potential, all pathology laboratory staff responsible for capturing these gross digital images should be educated and adequately trained on the importance of taking quality gross images, and replacing any suboptimal images with more effective ones [43].

Of particular importance is that all gross digital images may be open to misinterpretation by any non-pathologist [43]. For example, a resection margin that appears grossly negative may be microscopically involved, or a tumour appearing grossly benign may indeed be malignant upon histologic assessment. To date there is no known literature that has sufficiently investigated this specific pitfall in pathology [43]. However, the issue has been examined in radiology with noteworthy results. In particular, Boyle, et al. conducted a cross-sectional study evaluating the interpretation of computed tomography (CT) scans for head trauma by “middle grade and consultant” emergency physicians [51]. In the study it was recommended that these physicians not interpret these radiologic images without additional training [51]. Additionally, other radiology type studies have also recommended that non-radiologists (fellowship trainees and generalist staff) do not interpret radiology images due to “significant differences” and “higher discrepancy rates” in reporting and consequent “negligible changes in clinical management” when compared to radiologists [52, 53]. As a result, it is recommended that communication between pathologists and clinicians is crucial when interpreting gross digital images and final diagnosis reporting to avoid subsequent misguided patient care [43].

2.4 Applications of Digital Images

In a general sense, the applications of digital images in the pathology laboratory can be divided into three major categories which are medical education, clinical services and pathology research [6]. These areas can be independent, but often overlap.

2.4.1 Education

The collection and integration of digital image collections in the pathology laboratory can be used as an important teaching tool. Collections can contain typically seen appearances and interesting, novel cases alike. Both have educational purposes for either new laboratory staff, or more seasoned senior trainees and staff. This wide-ranging image collection would be particularly useful in academic pathology settings where the vastness of both laboratory professionals and medical professionals is evident. Regular pathology staff are often wide-ranging in specialty which include Laboratory Assistants, Laboratory technologists, Pathologists' Assistants, Pathology residents, Pathology fellows, Medical students and Pathologists. In addition, there are often rotating research graduate students and residents from other medical specialties that have elective rotations in the department. All of these different medical professionals can benefit from a large collection of diverse images.

Specifically, these images can be used for a number of different reasons. In addition to hands-on teaching in the laboratory environment, images can be extracted from the databank for conference presentations. Additionally, images can be used for scientific publications, self-study and continuing medical education (CME) purposes [6].

2.4.2 Clinical

An interesting and rapidly growing area in pathology is the integration of digital images for clinical diagnostic and consultation purposes [6]. This may be for primary diagnosis and may include frozen section consultation [54-56] and second opinion consultation for challenging cases [57, 58]. Additional clinical uses include quality assurance (QA), data retrieval/electronic medical records and autopsy reporting [6]. An important clinical feature is that there are permanent digital archives of gross and microscopic images of patient cases [6].

2.4.3 Research

A majority of the literature in regards to digital images and research focus on the microscopic applications. For example, many bioinformatics research projects are increasingly integrating digital slides into tissue microarray (TMA) databases [59, 60]. These computer-driven systems are available for not only creating TMAs and TMA databases, but can link sample and staining data in addition to analyzing their results [7]. Other areas of microscopic digital photography research include biomarker testing with immunohistochemistry (IHC), immunofluorescence (IF) or fluorescence in situ hybridization (FISH) for WSI [7, 61].

In regards to gross digital images, there are a number of opportunities for research. Areas for study include case study compilation, metastudy analysis, and availability of digitized images for quantitative analysis and permanent/reusable image records for archival study [62]. In addition, there are applications for algorithm analysis for gross digital images particularly for forensic pathology [63] (specifically addressed in chapter 5).

2.4.4 Applications of Gross Digital Images

There are some specific applications unique to gross digital photography which include specimen retention advantages and in diagnostic documentation/reporting. Gross digital images are accurate representations of surgical specimens and are not subject to the same retention guidelines required for organ and tissue retention [64]. Consequently, they do not require maintenance or physical space for storage [64]. Additionally, gross digital images allow the acquisition of images and their incorporation into the respective reports, which is a hallmark of modern information systems [3][4].

2.4.5 Telepathology and Remote applications

2.4.5.1 Telepathology

The process of transmitting digital images (macroscopic or microscopic) for pathologic purposes via telecommunication links is referred to as “telepathology” [34]. Included in these pathologic purposes are remote interpretations (telediagnosis), consultations or second opinions (teleconsultation) and for educational purposes [65-69]. In telepathology, the original material (gross sample, glass microscopic slide, etc) is separated by distance from the remote consultant (telepathologist) [34]. Remotely viewed digital or analog images, or WSI, get interpreted by the telepathologist on a electronic device (Smartphone, tablet or computer screen) rather than through a conventional light microscope [34]. Today, virtually ubiquitous Internet access, or to other broadband telecommunications linkages, on most continents, facilitates nearly worldwide image sharing [34]. As a result, telepathology has been used to aid a growing amount of pathology laboratory services over great distances, and has even been utilized by others to increase the effectiveness of services between hospitals less than a mile apart [70].

With increasing pathology subspecialisation, the use of telepathology to access subspecialists (e.g. dermatopathologists, neuropathologists) is also on the rise and is demonstrating to be cost-effective in at least certain settings [39, 71-75]. In addition, telepathology is not limited to rendering diagnosis, but can also play important roles in other areas such as QA (e.g. re-review of cases) and teaching and research [72, 75].

Telepathology can be classified into four major modes which are static image, dynamic, hybrid and virtual slide (WSI). Static image telepathology, also known as store-and-forward, is the assessment of precaptured still digital images that can be transmitted via email or stored on a shared server [34]. Dynamic telepathology, also termed real-time, involves the examination of live images or a sequence of images in real-time by means of a live telecommunications link [34]. In general, dynamic systems offer greater accuracy [76]. Hybrid telepathology is a mixture of static and dynamic modes which combines speed with high-resolution imaging [77-79]. In hybrid systems, dynamic viewing of a static image is possible whereby selected fields of interest can be viewed at higher magnification [34]. Lastly, WSI telepathology involves multiple devices including a slide loader, microscope with different objectives, digital camera, robotics and software [34]. Scanners that do not have robotics only capture and forward static images of digital slides [34]. However, with the appropriate equipment, telepathologists are able to remotely control and view digital images at different magnifications to render a remarkably suitable diagnosis [70, 74, 80, 81].

Currently, static image telepathology is still used for rendering diagnosis, primarily in developing countries [34]. Static digital images are also valuable when presenting a microscopic “field of interest” to colleagues for consultation purposes. In particular, they can show these microscopic field images to laboratory subspecialty pathologists for rendering a complete

diagnosis. Additionally, static digital images are being included into surgical pathology reports, but this is often done as a laboratory service marketing strategy directed to nonpathologist clinicians [34]. However, the future of telepathology appears to lie in WSI. WSI technology allows surgical pathology cases to be securely posted on the internet, which is the ideal way to present surgical pathology cases to reference laboratory subspecialty pathologists, to clinicians, or at multisite “virtual” surgical pathology conferences [34].

2.4.5.2 Remote Applications

Probably the greatest challenge facing healthcare delivery in most low and middle income countries is how to provide adequate medical services to the remotest locations [82]. In many of these third world countries the majority of the population live in rural areas, where socioeconomic conditions and the means of communication are considered rudimentary [83]. In particular, there is a serious deficit in Pathology services in these developing countries because even in those centers where pathology laboratories exist, they are often the least developed clinical specialty [82]. Medical services located in these regions are restricted in the treatment they provide by the shortage of pathologists and most of these institutions have ill-equipped laboratories with an inadequate number of staff [82]. As a result of these deficiencies, rendering the correct pathologic diagnosis for patients proves difficult and has resulted in serious consequences for patients in the past [84]. Additionally, because of the significant distances between some rural and referral centers in these developing nations, consultation with an expert pathologist is rare, time consuming and expensive [82].

The implementation of a telepathology service for these remote locations could vastly improve the quality of laboratory services. The prerequisites for success of a telepathology

service are basic infrastructure coupled with skilled and experienced staff [85]. Once established, telepathology systems will allow for remote diagnosis (intra-operative frozen section and permanent section), subspecialty consultations, and better educational feedback[82]. Second opinions, including even worldwide remote consultation, are not only technically possible but also considered user friendly [75]. In addition, these advantages have influenced the decision of some developed countries to make it a priority to include telepathology applications in their healthcare systems in an effort to improve services [82]. Most importantly, however, there is widespread enthusiasm from local laboratory personnel in developing nations to improve the quality of pathological diagnosis and this should be of significant incentive and motivation to organizations with interest in these kind of partnerships [82].

2.4.5.3 Barriers to telepathology in the developing world

The widespread utilization of telepathology to these underdeveloped nations is impeded by several factors, some of which are listed here:

- 1) Socio-cultural barriers – these factors may be political, cultural or religious in nature or even just a natural tendency to of the staff to initially resist any new technology. For example, local physicians and health care workers may be concerned that telepathology systems may be invasive, time-consuming and generate unnecessary extra work.
- 2) Inadequate laboratory infrastructure – Since pathology, and by extension telepathology, is not the main governmental focus, funds are traditionally allocated to on high-profile capital projects. Thus, essential telepathology components may not be readily available.

- 3) Archaic telecommunication facilities – modern telecommunication facilities may be poorly developed or not developed at all. Without this, telepathology would be difficult or impossible to introduce or sustain in developing countries.
- 4) Funding and sustainability – financial support is an important determinant to the sustainability of telepathology systems [82]. Steady funding is needed to cover project costs, which include equipment, maintenance, telecommunications charges, supplies, travel and staff training.
- 5) Shortage of personnel - the rapidly increasing demand for pathology services is not matched with the availability of skilled laboratory personnel in most underdeveloped nations [82]. Also, additional training for staff is necessary for proper implementation of a telepathology system. Thus, adequate staff amounts are needed to both cover the initial workload and to handle extra services associated with telepathology.
- 6) Poor technical quality of slides – this is a limiting factor in rendering adequate diagnosis. Technical difficulties in preparing slides have a very negative effect on the subsequent quality of a telepathology consultation.
- 7) Unresolved legal issues – regulatory approval for telepathology systems would be an issue in many developing countries [82]. In addition, problems are generally related to concerns of privacy, reliability and to the quality of health data [82]. Also, concerns may be raised surrounding medical liability, but European scholars have suggested that the practice of telepathology be assigned to the site of the practitioner, not the patient [86].

2.4.5.4 Future developments in telepathology

In reality, the bulk of people living in developing countries do not have access to modern diagnostic services due to a host of factors, as listed above. So the impact of telepathology in diagnostic work, consultation or medical education is yet to be completely felt [82]. It was estimated that in 2008, only about 0.1% of the potential telemedicine demand from the developing world was being met [87]. With this in mind, the expansion of telepathology in the developing world is delayed for reasons which are beyond the control of local healthcare providers. However, the number of institutions that have adopted telepathology in the developing nations is on the rise, and there are attempts by these institutions to integrate the technology into the healthcare systems of these low resource nations [82].

Chapter Three: Survey Regarding the Current Use and Future Trends of Gross Digital Images in Canada.

3.1 Background

In Canada the exact usage and applications of gross digital images are not very well known. Therefore, standardized methods and applications of these methods are not identified or are thought to be under utilized in Pathology laboratories across the country. A standardized method of obtaining, storing and sharing digital images is needed and can lead to better diagnostic techniques and consultation methods for Pathology diagnosis [10, 48, 88, 89], however these procedures have yet to materialize [10, 36, 90, 91]. Additionally, utilizing digital images for teaching and consultation can be more effective for storage purposes and have easier accessibility as compared to glass slides. There is very little data assessing the utilization of gross digital images in Canada. This survey will attempt to give a better overall picture of the current usage and utilization of gross digital images in Canada and examine the perceived future direction of the technology. It may also identify opportunities for further education, research, and software development in this field.

3.2 Methods

To obtain current information regarding the usage of digital imaging from across Canada, a survey was used. A 23 question survey was designed and focused on the type of respondent, knowledge of gross digital photography, current usage, strengths and weaknesses and perceived future direction of digital photography in the pathology laboratory (Figure 1). The survey was designed through Survey Monkey and the link to this survey was emailed to all available contacts.

Figure 1 - Survey Regarding the Utilization and Application of Gross Digital Images in the Pathology Laboratory

1. Level of Practice

- Laboratory Technologist
- Pathologists' Assistant
- Resident
- Pathologist with 0-5 years of practice
- Pathologist with 6-10 years of practice
- Pathologist with 11-20 years of practice
- Pathologist with 20+ years of practice
- Other (please specify)

2. What is the name of your institution?

3. What type of centre do you practice?

- Academic
- Urban non-academic
- Community

Other (please specify)

4. Do you use digital pathology in your practice?

- Yes
- No

5. Is digital pathology of gross specimens (Gross Digital Photography) used in at your institution?

- Yes

No

6. How do you define gross digital pathology?

- photography of gross specimens with digital camera
- photography of microscopic images with digital camera
- storage of pathology images into digital format
- sharing of pathology digital images for teaching/ consultation of diagnosis

Other (please specify)

7. Are you aware of/ read about gross digital pathology in the literature?

- Yes
- No

8. Do you see a need for routine digital imaging of gross surgical specimens in your practice?

- Yes
- No

9. If yes to Question 8, who is the primary user of the gross digital images at your institution?

- Laboratory Technologists
- Pathologists' Assistants
- Residents
- Pathologists
- Clinical Colleagues
- Scientists

Other (please specify)

10. If yes to question 8, in what capacity is the technology used? (choose all that apply)

- Teaching
- OR/ Frozen section consult
- Routine diagnosis
- Consult service
- QA
- Interesting/ complex cases

Medico-legal cases
Other (please specify)

11. How often do you use Gross Digital Photography?

- Every case
- Routinely
- Daily
- Rarely
- Never
- Only for certain types of cases

12. Estimate which percentage of Gross specimens are photographed

- <10%
- 25%
- 50%
- 75%
- 100%

13. What types of Gross specimens are digitally photographed?

- All cases
- All cases of a particular type or for a particular subspecialty
- Interesting cases
- Complicated cases only
- Medico-legal cases

14. What sorts of Gross Digital Images are taken? (choose all that apply)

- Of intact gross specimen (before fixation)
 - Of intact gross specimen (after fixation)
 - Of specimen after it has been sectioned
 - Of specific features within section(s)
- Other (please specify)

15. If yes to question 8, how are the images stored?

- Central database
- Individual hard drive
- Memory card/ stick etc.

Other (please specify)

16. Who has access to your Digital Gross Images?

- Only I do
- All employees
- Residents
- Medical Staff
- Pathologists' Assistants

Other (please specify)

17. If yes to question 8, what are your observed advantages in using Gross Digital Images (please select all that apply).

- Allows me to observe the specimen from a remote location
- Faster (than non-digital images, eg. kodachrome)
- Conservation of physical space (as compared to non-digital images)
- Cheaper (as compared to non-digital images)
- Easier access (as compared to non-digital images)
- N/A

Other (please specify)

18. If you use gross digital images for teaching, in what teaching environments is it used?

- CAP PIP or ASCA Check Path or CME activities
- Conferences
- Resident Education
- Clinical Rounds/ Tumor boards

Other (please specify)

19. What do you think should be the application(s) of Gross Digital Pathology? (choose all that apply)

- Teaching

- OR/ frozen consult
- Routine Diagnosis
- Consult service
- QA
- Medico-legal documentation
- Tumor boards/ clinical rounds

Other (please specify)

20. Have you ever requested a second opinion/ consult using a Gross Digital Image?

- Yes
- No
- N/A

21. In your opinion, what are the disadvantages in using Gross Digital Images? (select all that apply)

- Cost
- Compromise diagnostic quality
- Security
- Not representative (ie. quality is compromised)
- Increased time to make diagnosis
- I am not comfortable with the technology
- I am concerned about image quality
- It would take too long to learn how to use the technology
- There is not a perceived need for the service
- Storage space issues

Other (please specify)

22. Would you favour having an on-line digital library to review features of challenging or rare cases of gross specimens?

- Yes
- No

23. Do you perform gross-microscopic correlation with the aid of Gross Digital Images?

- Yes
- No
- N/A

Additional Comments

The survey was first distributed to current employees known to be involved in digital pathology practices throughout various sites within the Calgary Laboratory Services (CLS) network. Additionally, surveys were then distributed amongst contacts known to myself and my supervisor throughout pathology labs across Canada, with a focus on getting feedback from all parts of the country. These surveys were directed at, but not limited to, pathologists, pathology residents, pathologists' assistants and laboratory technologists who were known to have direct involvement in handling surgical pathology specimens for preparation and gross dissection. Also, these contacts were asked to distribute the survey link to their colleagues who they could identify as directly involved in handling the surgical pathology specimens in the pathology lab. These individuals were targeted for the survey because they would decide if the specimens required special procedures before formalin fixation, including selection for photography. Emails contained an invitation to participate in the survey and a link to the survey to be administered through the Survey Monkey web service. In all, it is estimated that over 100 people were sent the link to the survey. This project was approved by the University of Calgary Conjoint Research Ethics Board (Ethics ID#E-25044).

3.3 Results

Overall, I gathered 60 completed survey results (est. 60% response rate) representing most provinces across Canada. In the first portion of the study, I focused on the classification and geographical location of the respondents. The majority of the respondents were pathologists' assistants (50.0%), pathologists (25.0%) and pathology residents (23.3%), with one medical laboratory technologist, all with various degrees of experience (Fig 1). I was able to gather responses from most of the areas of the country geographically as follows: British Columbia (2), Alberta (24), Manitoba (1), Ontario (24), Quebec (1), Nova Scotia (4), New Brunswick (1) and Prince Edward Island (1). Two of the respondents did not give a location where they practice. Some of the respondents practice in community (30.4%) and urban, non-academic settings while most were practicing from Academic centres (58.9%), which are usually indicative of larger, urban centres. The second portion of the survey focuses on the respondent's knowledge and application of gross digital photography. Most of the respondents are frequent users of gross digital pathology (86.2%), with most of the sites reporting that it is utilized at their institution (90.0%). A large majority (91.5%) defined gross digital photography as photography of gross specimens with digital camera. Another large majority of respondents use digital pathology in their practice (86.2%), with even more stating that gross digital pathology is used at their institution (90.0%). Additionally, they were less likely to have heard or read about gross photography in the literature (60.0%). The large majority of users are the Pathologists (88.0%), and to a lesser extent, pathology residents (50.0%) and pathologists' assistants (54.0%). However, there seems to be an awareness regarding the technology as a majority of the

respondents feel that there is a need for routine digital imaging of gross surgical specimens in their practice (80.0%).

The major themes of this survey are summarized in Figures 2-5 as follows: Current usage (Fig 2), reported advantages (Fig 3) and disadvantages (Fig 4) of gross digital photographs and the applications and future direction of gross digital photography (Fig 5).

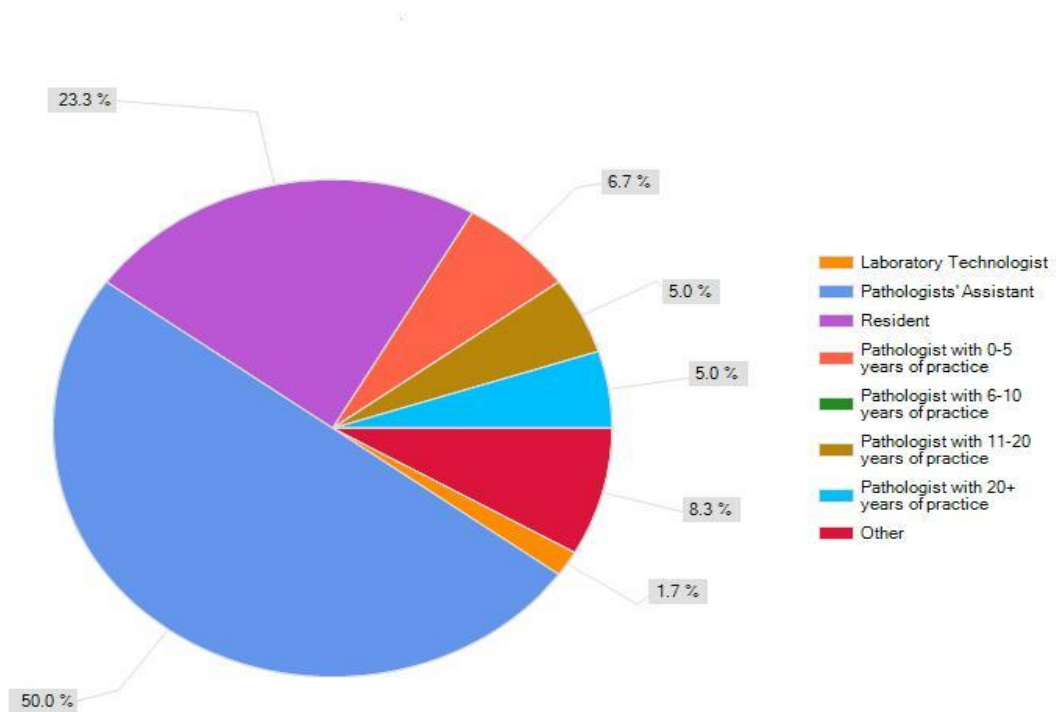


Figure 2 - Summary of survey respondents by level of practice

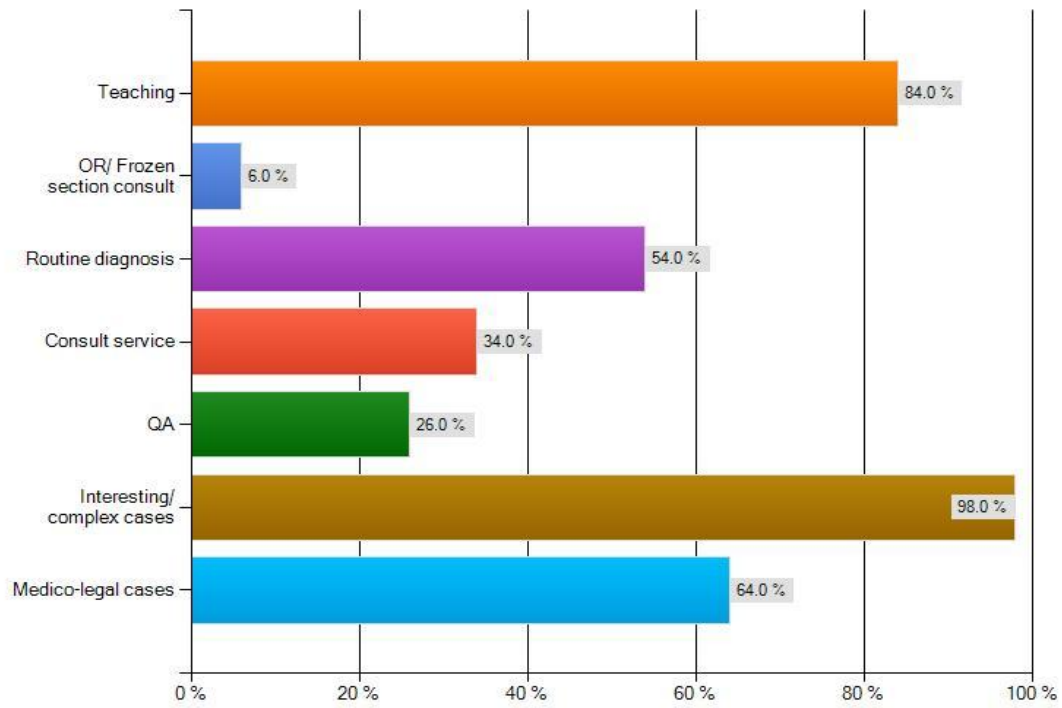


Figure 3 - Current applications of gross digital photography

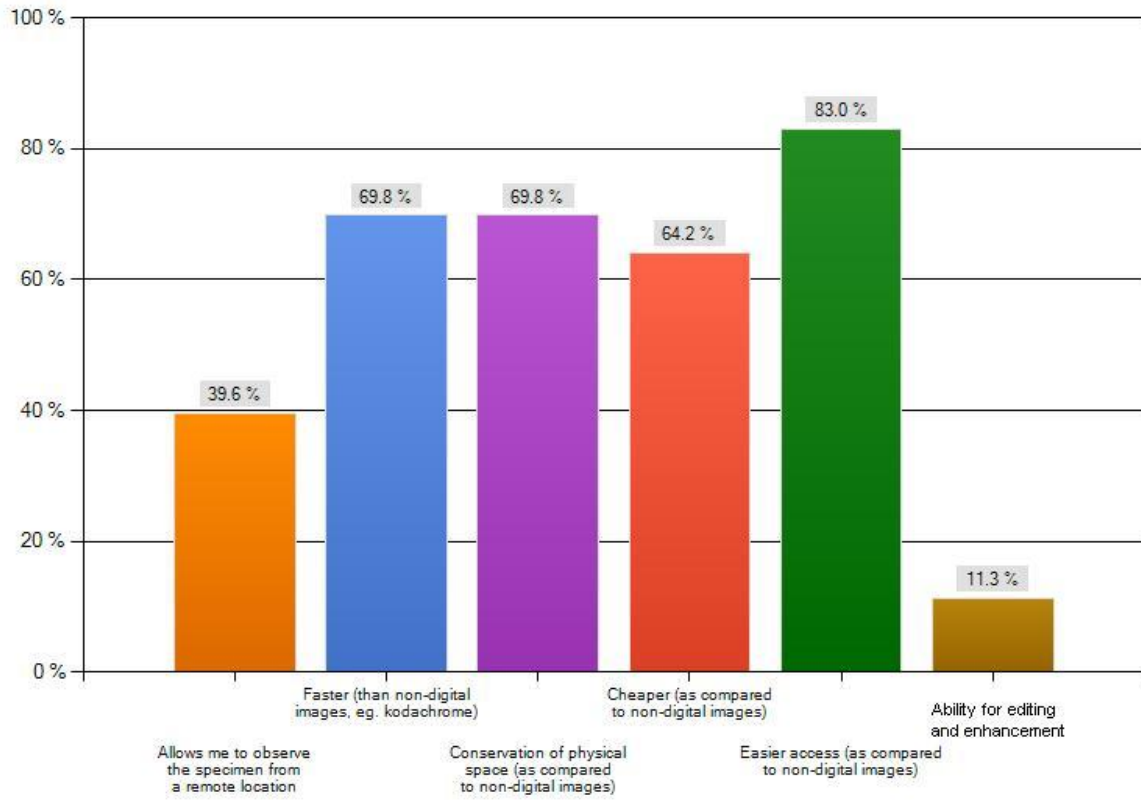


Figure 4 - Reported advantages of gross digital photography

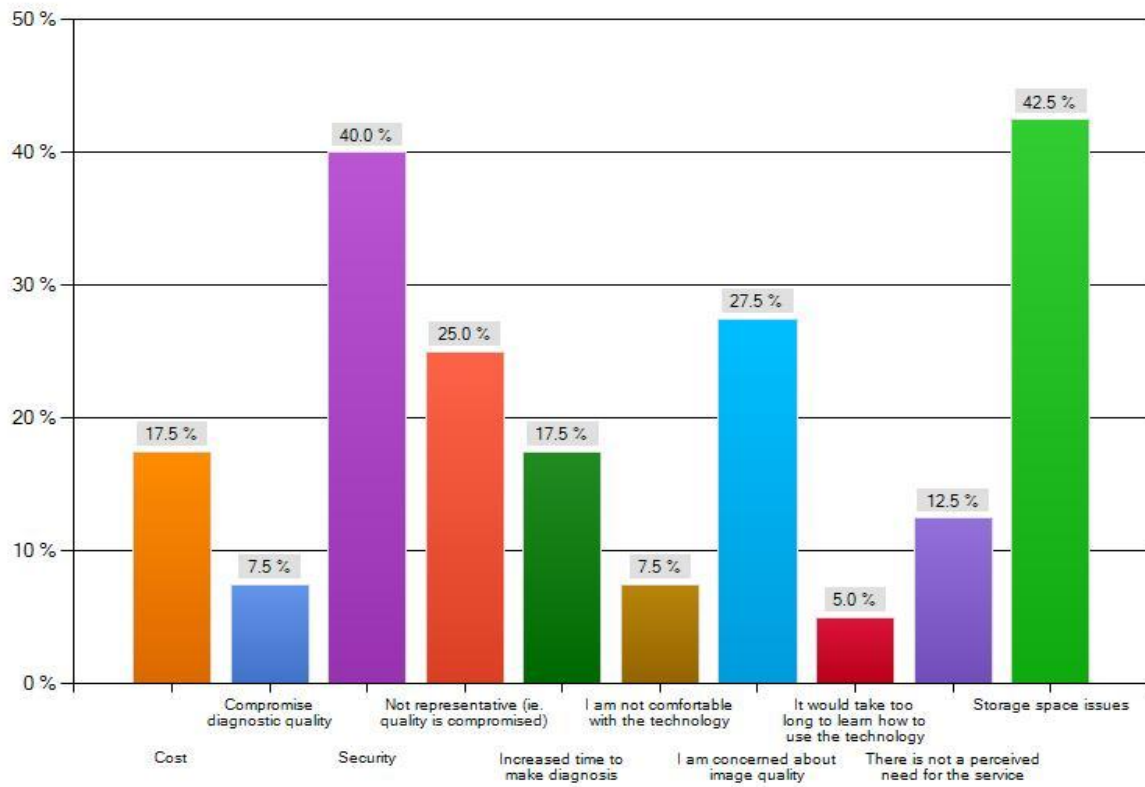


Figure 5 - Reported disadvantages of gross digital photography

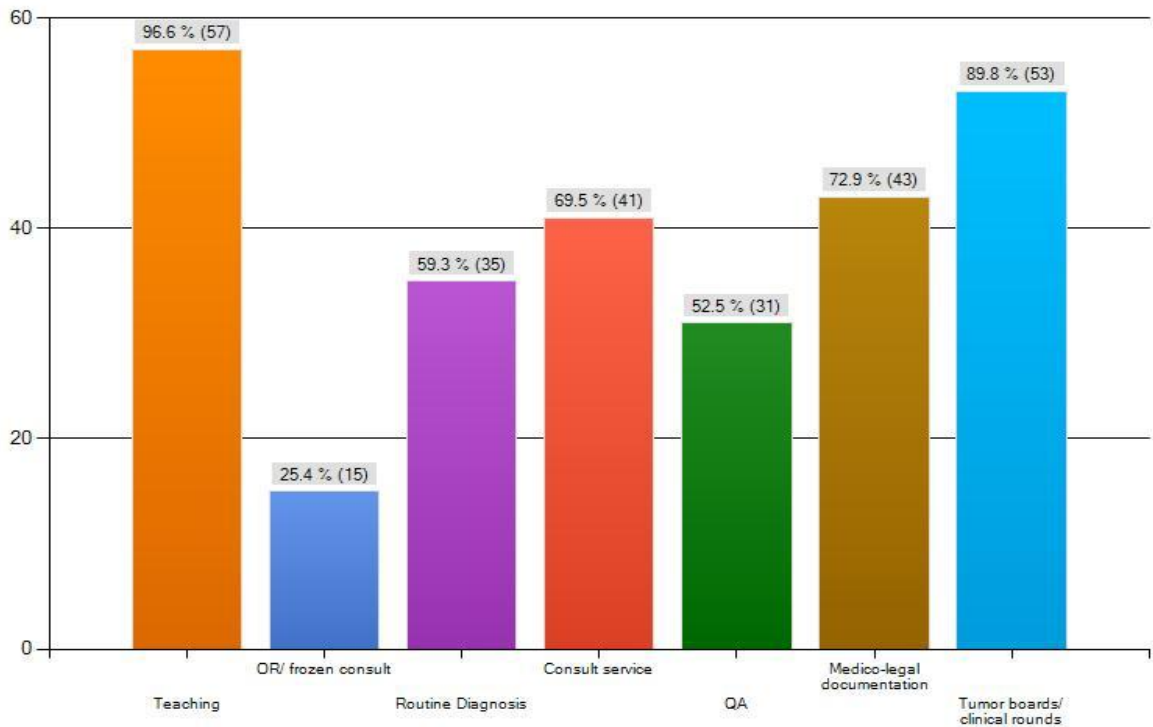


Figure 6 - Respondents opinion on the future of gross digital photography

Gross digital images are seldom taken on a routine basis (30.0%) and when they are taken, it is only for specific types of pathology cases (31.7%). Additionally, it is extremely rare in pathology labs across Canada that all specimens are selected for gross digital photography (1.7%). Overall, most respondents stated that less than 10% of total specimens received are being digitally photographed (61.0%), while others said approximately 25% (33.9%), and to a lesser extent 50% (3.4%).

There is a wide range of the types of cases being selected for gross digital photography. Most respondents stated a need for photography of interesting/complex cases (88.1%), medico-legal documentation (61.0%), complicated cases (55.9%) and cases of a particular type or

belonging to a particular subspecialty (e.g. Gynaecological Oncology) (52.5%). Additionally, surgical specimens are photographed at any point of the process, from intact specimens before fixation (79.7%), after fixation (83.1%), after sectioning (81.4%) and of specific features within sections (71.2%).

The gross digital images are usually stored onto a central database (79.6%), with other forms of storage also used including individual hard drives (14.8%), and memory sticks (18.5%). Access to these images is varied amongst institutions as pathologists' assistants (64.9%) and medical staff (57.9%) makes up the majority, while all staff members (26.3%), individual access (8.8%) and administrative staff (3.3%) are the minority. It is also worth mentioning that one respondent did not know who was accessing the images.

Respondents were also asked to expand on the teaching aspect, and in particular - in what teaching environments is it used? The large majority answered clinical rounds/tumour board presentations (90.2%) and resident education (72.5%) as the primary environment. Conference presentation of gross digital images (56.9%) and Continuing Medical Education (CME) type of activities (25.5%) were used, but to a lesser extent. However, a huge majority felt that an on-line digital library of gross digital images would be helpful to review features of challenging or rare cases of gross specimens (96.6%).

An overwhelming amount of the respondents felt that the current application of gross digital photography is for teaching purposes (96.6%) and clinical rounds (89.8%). Additionally, medico-legal documentation (72.9%) and consult services (69.5%) also ranked high. A majority of the respondents also felt that the images were needed for routine diagnosis (59.3%) and Quality Assurance (QA) purposes (52.5%). For example, in breast lumpectomy cases, slices are numbered and photographed. Sections taken are hand-drawn onto the printed photograph for

mapping purposes. Also, current utilization of gross digital images for gross-microscopic correlation is used frequently (51.7%) while consultation/second opinion diagnosis usage is rare (18.6%).

3.4 Conclusion

Overall, pathology informatics, and specifically gross digital photography has become commonplace in pathology labs across Canada. The majority of the users, which are pathologists, residents and pathologists' assistants, photograph (document) gross specimens with a digital camera. The images are then commonly stored digitally into a centralized database that is easily accessible for lab personnel. In most institutions, less than 10% of all surgical cases are digitally photographed which are usually classified (documented) as interesting, medico-legal or complicated. After being archived, the digital images are usually accessed by pathologists' assistants, residents and medical staff for teaching in clinical rounds, resident education and conferences. Additionally, they are accessed for medico-legal and consultation purposes.

There is a wide range of perceived disadvantages to gross digital photography. Storage issues are a major concern among the respondents. Archiving of gross digital images is extremely important for multiple reasons. First, the complexity of archiving will increase with multiple users and acquisition devices plus the ease of retrieval and utilization of these images needs to be managed successfully [7]. Secondly, image files can be quite large and should be stored onto a centralized database. This can be circumvented by file compression, the compaction of an image by removal of redundant information which helps with image processing, storage and transmission [7]. Ideally, acquired pictures should be embedded into

pathology reports [92] and then captured directly into a Laboratory Information System (LIS) [7].

Image quality also appears to be of major concern for the respondents. It is essential for gross digital Images to be a good quality representation of the original source [7]. Generally speaking, a good quality image can be taken with a lower end camera producing 3-5 megapixel image [15]. This is necessary to avoid the possible compromise of diagnostic accuracy due to reduced image quality or under representation of the lesion in the digital image [10]. Therefore it is essential to prepare for good gross digital photography by having a well-lit specimen and a clean background [7]. But, most importantly, a high resolution mega-pixel camera with good macro lens with a long barrel for close focusing is essential for optimal gross digital images [7].

Another area of concern appears to be the cost association of gross digital photography. In fact, the most important issues in pathology informatics are challenges associated with the cost of electronic storage [6]. The majority of the costs are associated with building of the new system and training of the pathology health staff which require significant spending [6]. However, after the initial capital investment, the additional operating costs are minimal and can be balanced by the elimination of expenses associated with storage and retrieval of physical (i.e. Kodachrome) images [6]. Reduced costs and extensive applications make the adoption of digital imaging in anatomical pathology laboratories an essential consideration [2, 4].

A major concern identified in the survey was an absence of need for gross digital photography. In fact, other studies show that a significant percentage of pathology staff is not in favour [6, 10] or not aware of the need of the transition into digital practice. Indeed, in our survey, 10% of the respondents do not use digital photography, indicating reliance on older

kodachrome images or no photography used at all at their institution. This may be attributed to a lack of understanding of the applications of gross digital photography and the associated limitations and reduced control over this technology [6]. However, a failure to adopt a digital imaging technology may be considered a deficiency of practice [15]. Indeed, if the reporting pathologist does not employ such a system for proper documentation, back-up or quality assurance it may be considered as negligence in a court of law [2].

One particular area not specifically addressed by this survey is in relation to ethical issues associated with digital photography. In particular, the issue of fraudulent digital image manipulation has emerged as a particular area of concern [7, 10, 93, 94]. Critics of digital imaging claim that any image manipulation, willingly or unknowingly, alters digital data which causes a misrepresentation of the original information [95]. The critics go on to say that this manipulation is equivalent to scientific fraud [94]. However, fraudulent activities existed long before the arrival of digital imaging and there are undoubtedly easier ways of falsifying scientific data [2].

There is no doubt as to the current usefulness and future applications of gross digital photography in the pathology lab. This survey has shown that the technology is being utilized consistently by pathologists, residents, pathologists' assistants for documentation and educational purposes of diagnostic specimens. According to this survey, the majority of pathology lab personnel in Canada feel that gross digital photography should be utilized for educational purposes including teaching and round presentation, which is consistent with previous reports [10]. Also, it is needed for medico-legal documentation, consultation, QA and routine diagnostic services. Respondents of the survey identify future applications of gross digital photography in Canada as teaching, consultation and medico-legal documentation. There

is less excitement indicated for telepathology, and three-dimensional digital pathology methods, both of which were previously identified as an emerging trend in pathology informatics [6, 7, 10, 96-98].

Chapter three of this thesis has been published in a peer-reviewed, open-access publication:

Horn, C.L., DeKoning, L., Klonowski, P., Naugler, C., *Current usage and future trends in gross digital photography in Canada*. BMC Med Educ, 2014. **14**(1): p. 11.

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Chapter Four: Building a Gross Digital Image Bank as an Educational Tool

4.1 Introduction

Currently in many pathology laboratories, including Calgary Laboratory Services (CLS), if anyone is interested in examining an image of a particular gross appearance or abnormality they will rely on an internet search or more commonly, through pathology textbooks. In addition, at CLS, gross digital images are collected usually for interesting cases, or for tumour board/ round presentations. Gross digital images are not captured or filed by particular gross abnormalities or typical gross presentations. Usually, they are archived according to surgical accession number only. There are thousands of images compiled in the CLS databank, many of which can be used for teaching and education. However, because they are not accessible according to gross abnormality or appearance, this databank of images is virtually useless in order to be accessed as a teaching tool for new pathology staff.

The objective of this project in part is to design and develop a database of gross digital images showing particular gross features and use it them as an educational tool for new laboratory staff including pathology residents and pathologists' assistant students. Initially, a list of typical gross abnormalities commonly seen in the pathology lab was collected from pathology websites and textbooks. Then corresponding images were extracted, organized and archived from the CLS gross digital image databank. Lastly, a brief description of the gross appearance and disease process was attached to each photograph. For new pathology trainees, this collection of images could become invaluable as a teaching tool when transitioning from theoretical learning to actual "hands-on" gross pathology practice.

Relevant to this project is an overview of the different types of cameras, commercially available systems and set-ups available for pathology gross areas to capture gross digital images.

Additionally, we will briefly explore the different literature, both in print and online, of the current available gross digital photographs and how they are presented. Lastly, we will present our collection of gross digital images and corresponding descriptions of typical gross appearance and disease processes commonly observed in the pathology laboratory.

4.2 Cameras

There are a variety of types of digital cameras available for use in the pathology lab today. They include compact cameras (often referred to as “point and shoot”), digital single-lens reflex (DSLR), mobile device cameras (e.g. iPhones), desktop cameras (webcam), light microscope cameras and more specialized cameras for advanced imaging (e.g. multispectral imaging) [8]. The most commonly used devices in gross digital photography are the compact cameras and DSLR that are integrated within the pathology grossing area. However, the future direction of the technology may lie in mobile device systems with their Wi-Fi capabilities and for the webcam devices which can give “real-time” assessment and direct connection to LIS.

4.2.1 Compact Cameras

These cameras are liked because of their portability and cheaper price point. Compact cameras are generally “hand held” devices which can be useful when taking various angles of photography for gross digital images. In addition, instead of investing in multiple cameras for each gross station, a single compact camera can be shared amongst multiple users and workstations. Another great feature is that they are relatively easy to use and are sometimes referred to as “point and shoot” devices because of this. Also, compact cameras usually contain liquid crystal display (LCD) screens and image management software which allows the user to

select and edit images as they are captured. Probably the most advantageous feature is their low price point. Compact cameras are available for under \$100 for a 16.1 megapixel device [99]. In general, the quality of image from a compact camera with higher resolution can be considered of “good” quality digital image [7].

However, because of their lower price point, and subsequent inferior quality, compact cameras generally do not perform as well when compared to the other available devices [7]. Also, they usually do not have many options when it comes to lens selections, which can also limit their quality capabilities. Another drawback is no “hands free” options for when you are working with very bloody or dirty gross surgical specimens. This forces the user into changing gloves multiple times while handling the specimen and camera to avoid contamination. Some users may avoid changing gloves altogether and contaminate the device anyway. Another major drawback would be that compact cameras are not connected to a Laboratory Information System (LIS), which would automatically link the image to the specimen and its corresponding accession number. Instead, the images from a compact camera would need to be downloaded by an individual and manually assigned to either a centralized database or to the surgical accession number. This method would be subject to user error and digital images may not be stored correctly or lost altogether.

4.2.2 Digital Single-Lens Reflex (DSLR)

DSLR cameras offer advantages that compact cameras do not for gross digital imaging. For instance, due to their larger sensors, they offer superior performance in low-light situations [7]. In addition, DSLR cameras have interchangeable lenses which allow the user the option to select lenses which are best suited for gross macro photography [7]. Like the compact cameras,

DSLR cameras offer versatility in regards to different angles to photograph specimens as they are also hand held devices. Similarly, they are not fixed to one location and can be shared amongst users in the lab. Thus, one DSLR camera should be sufficient at each site which should drastically reduce the overall cost. The big advantage over compact cameras is that DSLR cameras are known for having superior flexibility and the potential for higher image quality [100]. Commercially available DSLR cameras can reach up to 36.3 megapixels of resolution for a recognizable affordable brand name to up to 80 megapixels for a top end professional model [101].

However, DSLR cameras also have some of the similar drawbacks that compact cameras have. In particular, unless the camera is directly mounted to the gross station, then there is not a “hands free” option, thereby increasing the chances of blood and body fluid contamination of the device. Even if mounted to the station, the user is still required to touch the camera to turn it on/off and for focusing. Also similar to the compact camera, the images taken by the DSLR have to be downloaded to a separate file and are not automatically attached to the LIS. And with higher resolution images, the amount of storage space needed for these images is substantial and would require some planning to accommodate the increase in needed storage space [102].

Currently at the FMC site in the CLS network, we have a DSLR set-up that is connected directly to a sharable network drive. The cameras are mounted to each grossing station and are directly connected to a local personal computer (PC). Each computer has a software program installed which allows for on-screen assessment, focusing and zoom applications of the digital image. In addition, the software program has a “log-in” feature which allows you to manually enter information which will be tagged with the image including surgical accession number, preliminary diagnosis and assigned pathologist. Once the digital image is captured, the software

application files it according to the surgical accession number into a centralized, sharable database within the CLS network. Any employee within the CLS network who has admittance to this sharable drive has access to these digital images.

4.2.3 Mobile Devices

Mobile devices are similar to compact cameras in size and capability, but differ in other areas. A mobile device is a small, handheld computing device typically having a display screen with touch input and/or a miniature keyboard and weighing less than 2 pounds. These devices are primarily personal hand held devices that have multi-functional applications. A handheld computing device has an operating system (OS), and can run various types of application software, known as apps. Most handheld devices can also be equipped with Wi-Fi, Bluetooth, and Global Positioning System (GPS) capabilities that can allow connections to the Internet and other Bluetooth-capable devices, such as an automobile or a microphone headset. A camera or media player feature for video or music files can also be typically found on these devices along with a stable battery power source such as a lithium battery. Typically, the cameras in these devices are similar to compact cameras in resolution and quality, however there is one model of mobile camera device which has a 41 megapixel camera [103].

There are specific advantages in sharing of digital images that these devices have over the compact camera and DSLR cameras. Once the images are captured they can be easily sent via text message, email or through Wi-Fi to whomever the operator chooses. Thus there are great advantages when sharing the images with other pathologists and clinicians. However, this might raise privacy concerns over the use of the images.

The ease of distribution may entice operators to be more promiscuous with the digital images, thereby bypassing confidentiality rules in regards to such things. Similar to other health care organizations, CLS employees and other individuals performing work on behalf of CLS are not permitted to disclose any business, Health, and/or Personal Information of other CLS employees, contractors, patients/clients, or another aspect of their position within CLS they are not specifically authorized to disclose [104]. This would include the use of gross digital images captured at any of the sites in the CLS network. In other words, captured digital images should only be shared with proper authorization.

Disadvantages of mobile devices are similar to that of compact and DSLR cameras. To date, there does not appear to be a Wi-Fi capability allowing mobile devices to be automatically linked up to the LIS. Similarly, they must be downloaded by the operator and attached to the specimen documentation manually. Also, similar to the other compact and DSLR cameras, the mobile devices are entirely hand operated. Therefore, similar concerns are raised in regards to contamination of the device with blood and body fluids.

4.2.4 Webcam

Webcams are relatively new to grossing-based digital pathology applications. These systems are comprised of high definition (HD) camera systems with several functions in addition to still gross digital images. Other capabilities include streaming images in real-time, capturing video, annotation and measure gross specimens [105, 106]. The advantages of the webcam are numerous when comparing them to the compact, DSLR and mobile camera devices. The most obvious one involves the live sample imaging communication features. The device allows the laboratory staff to connect directly to the surgical suite and/or pathology subspecialty opinions,

which creates the possibility for real-time consultation [105, 106]. This live feedback option allows the entire team of pathologists, laboratory staff and OR staff to come together and have immediate resolution of orientation and diagnostic questions that are presented during surgical procedures [106].

Another unique feature of the webcam device is the ability of the device for teleconferencing purposes. This feature allows for effective video conferencing to provide pathologists and laboratory staff with methods for immediate archiving and retrieval of key procedural images. This would be beneficial for referencing, quality assurance (QA), quality control (QC) and liability case support [106].

Another advantage of the webcam over the other devices is that they are capable of integrating with a pre-existing LIS. This would allow for automatic linkage of gross digital images to the surgical report, thereby bypassing the manual uploading and archiving of these images. This would greatly quicken the overall process and eliminate the chance of order entry error by the user.

Additionally, these devices are typically a “hands free” operation which virtually eliminates the blood and body fluid contamination. Operators can operate the camera functions, including zoom and focusing, either through the touch screen, footswitch or remote control[105, 106]. Thus, the capturing of digital images is “clean” because manipulation of the camera with dirty gloves is not required during the process.

On a clinical note, an interesting advantage that the manufacturers of these webcam devices claim is the ability of these devices to reduce surgical site infections (SSI's), and therefore hospital mortality rates [105]. SPOT Imaging Solutions states that their webcam device, when connected directly to the OR, can reduce the intra-operative consultation and

surgical procedure time by 10-20 minutes [105]. They claim that this is the “scrub out” time that it takes the surgeon to leave the OR, bring the specimen to the pathology laboratory for orientation and discussion, then re-enter the OR. Patients that are exposed to this additional time are at increased risk of SSI’s [107]. The SPOT system allows for real time consultation between the OR and pathology lab. Therefore, intra-operative video conference systems, like the SPOT product, eliminate the need for surgeons to leave the OR for consultation and its associated surgical delays which reduces the amount of potential SSI’s [106, 107].

4.3 Commercially Available Systems

There are many different companies that offer digital camera systems for pathology laboratory use and specifically for gross digital images (macro imaging). Each of these systems serves the same purpose when capturing and saving the digital images. These companies offer systems that can integrate all aspects of digital imaging from the macroscopic to the microscopic level and include these images into the official pathology report. In addition, some of these systems offer unique ways to edit these images to show how the specimen was handled when it entered the pathology laboratory.

After reviewing the products available on the market today, there appears to be some consistencies with what is being offered among the companies. A list of the commercially available systems and their features are compared in Table 3.1.

Table 1 - Comparison of commercially available digital camera systems

Features	Spot Imaging Solutions			RMT iMedHD™	Nikon Macro Imaging Station			MacroPATH		PAXcam	
	PathStand	Pathstation2	Pathwall		AdvancedPath	SmartPath	SimplePath	Pro	Lean	Gross Imaging System	Macrostand
Washable Stands (sealed)	X	X	X		X	X		X	X		
Transfer to LIS	X	X	X			X		X	X		
Free standing	X				X	X	X	X	X		X
Wall-mounted			X					X	X	X	
Gross station Mount		X		X				X	X	X	
Zoom Lenses	X	X	X	X	X	X	X	X	X	X	X
Light Source	X		X		X			X		X	X
HD Camera		X		X							
Autofocus		X		X		X		X	X		X
Touch screen	X	X	X		X		X	X	X		
Teleconference Software		X				X	X				
Motorized lens	X	X	X		X	X		X	X		X
Foot switch control (software or camera)	X	X	X		X			X	X	X	X
Barcode input	X	X	X		X	X	X	X	X		
On-screen image preview and image editing	X	X	X			X		X	X		
On-screen annotation, sample and section labelling	X	X	X	X		X		X	X	X	
Calibrated Image capture for length measurement	X	X	X	X	X	X		X	X		X
Video Capture				X				X	X		
Audio Capture								X			
Remotely Controlled				X							
Telepathology		X		X		X		X	X	X	

4.4 Set-up

Commercial digital imaging systems typically come in three different set-up options. They include the wall-mounted camera, free-standing macro stations and stands that fit into, or are mounted directly to the grossing station [105, 106, 108-111]. Many of the companies listed above offer each of the different set-up options. The main differences between the systems depend on specific features (Table 3.1) and which system is suitable for a particular gross area. For example, the most expensive set-up systems are the independent stand-alone stations that have most of the options (listed on Table 3.1) and are considered ideal for labs with large spaces. However for laboratory areas with small spaces, a wall-mounted or gross station mounted imaging system is the most efficient option, but has fewer features (Table 3.1).

Gross photography imaging stations appear to be the gold standard among the different imaging set-up options. In general, these systems offer more features as compared to the wall-mount and gross station mount set-up systems (Table 3.1). In particular, these stations are often enclosed and washable, which provides a clean, safe environment to capture, document and measure gross specimens [106, 109, 111]. These stations also provide an independent light source which helps create consistent photos which are bright, sharp and offer improved detail [109]. In addition, the newer models have high-intensity LED lighting ensuring that the gross specimens will not be damaged by heat that is emitted by conventional light sources [106, 108, 109].

Another viable option for gross digital photography set-up is the wall-mount digital imaging systems. These systems are recommended for smaller laboratories that cannot accommodate the larger imaging stations, or cannot afford them. The wall-mount digital systems offer many of the features as the other options (table 3.1), with the added bonus of being able to “push away” the system when it is not in use [106]. Also, the wall-mount systems can be mounted in-between grossing stations, allowing for sharing between multiple users and workstations [106].

The third option is a digital imaging system that can fit inside, or is directly mounted to the grossing station. These systems are designed to allow for specimen handling in a controlled environment, providing a completely uninterrupted workflow [110]. This is in direct contrast to the free standing stations where specimens are constantly moved back and forth from the grossing station. A drawback to these systems is that in general they are not sealable and therefore, subject to contamination. This is of particular concern because of the continuous contact with pathologic specimens and the fluids associated with them. However, these stations reduce the risk of contamination by using water and splash resistant workstation surfaces, mouse, keyboard and touch-screen PC's so that they can be wiped clean after use [106, 108].

4.5 Web Sites/Books – Available literature

The idea of collecting images with corresponding pathological diagnosis is not novel to the world of pathology. Indeed, after an internet search (Google) of the terms “atlas”, “pathology”, “gross”, “digital” and “images” there exist some 2.3 million matching results. One of the links is a blog which narrows down the specific pathologic image print books down to

93 titles both of print and e-book format [112]. Upon examining the literature and researching the books through Amazon.ca, there are a few specific publications which are dedicated to having a large number of macroscopic photographs. Again, these books are more likely to centre around the type of pathologic diagnosis and then include corresponding macroscopic, and in most cases, some microscopic appearance [113, 114]. A large majority of these are atlas type of publications which document a particular disease type with the corresponding images [112]. The images contained in these publications are both macroscopic and microscopic, but are mostly microscopic. A list of the most relevant titles for gross digital images in both print and electronic format is provided in Table 2.

Table 2 - Gross pathology images available through print and electronic delivery

Title	Price (CAN\$) (Amazon.ca)	Book (B) or Website (W)
Atlas of Gross Pathology: With Histologic Correlation	136.27	B
Color Atlas of Gross Placental Pathology	156.90	B
An Atlas of Gross Pathology	206.87	B
Gross Pathology: A Color Atlas	162.11	B
Atlas of Orthopedic Pathology: With Clinical and Radiologic Correlations	52.41	B
Atlas of Gross Neurosurgical Pathology	75.67	B
Colour Atlas of Pathology	419.24	B
An Atlas of Gross Neuropathology	49.31	B
Atlas of Orthopaedic Pathology: With Clinical and Radiologic Correlations	119.97	B
Colour Atlas of Anatomical Pathology	16.19	B
Atlas of Surgical Pathology of the Colon, Rectum, and Anus	216.24	B
A Colour Atlas of Cardiac Pathology	22.00	B
Atlases of Demonstrations in Surgical Pathology: Alimentary System v. 1	70.38	B
Atlas of Clinical Dermatology	328.15	B
Atlas of Neuropathology	363.86	B

A Colour Atlas of Neuropathology	26.60	B
A Colour Atlas of Peripheral Vascular Diseases	15.22	B
A Colour Atlas of Thymus and Lymph Node Histopathology with Ultrasound	22.00	B
A Colour Atlas of Adult Congenital Heart Disease	52.00	B
A Colour Atlas of Liver Disease	22.00	B
Sandritter Macropathology: Text & Color Atlas	165.43	B
Robins and Cotran Atlas of Pathology and Robbins Basic Pathology	110.10	B
The Placenta: To Know Me is to Love Me. A Reference Guide for Gross Placental Examination	165.79	B
Manual of Pathology of the Human Placenta: Second Edition	59.06	B
Anderson's Colour Atlas of Pathology	N/A	B
Color Atlas and Text of Neuropathology	N/A	B
Colour Atlas and Textbook of Macropathology	N/A	B
Pathology of the Placenta	228.26	B
Pathology of the Human Placenta	239.53	B
Eye Pathology: An Atlas and Basic Text	148.18	B
Digital Atlas of Gynecologic Pathology	N/A	W
Digital Atlas of Breast Pathology	N/A	W
Digital Pathology, Brown University	N/A	W
PathPedia.com	N/A	W
The Internet Pathology Laboratory for Medical Education	N/A	W
Pathology Atlas of Gross and Microscopic Images	N/A	W
Atlas of Pathology	N/A	W
The Urbana Atlas of Pathology	N/A	W

In addition to printed books and e-books, there are many websites that are dedicated to using digital pathology images as a teaching tool. The focus for the majority of these websites is to classify images according to diagnosis with both macro and micro photography [115-124]. These websites are also listed on Table 3.2. One of these websites has a section devoted to gross pathology, but is very limited in variety and overall completeness as they display only 9 anatomical sites and 54 total images, including 25 of kidney alone [118].

4.6 Digital Image Archiving and Sharing

4.6.1 Archiving

Archiving of gross digital images is perhaps the most important step in the process of acquiring gross digital images. As time goes on, the complexity of archiving increases with multiple users and acquisition devices [7]. Additionally, major consideration should be given to having the appropriate amount of available storage space. Once the storage of digital images is taken care of, image management becomes the next important stage. Image management can be divided into two main areas which are retrieval and utilization.

Particular attention must be given to how easily digital images are to be retrieved after they have been acquired. When stored correctly, the images are easily retrieved. When the digital image is captured, the camera automatically records additional information which is tagged with the image in an exchangeable image file (EXIF) format [7]. This information includes date, time, ISO speed, file size, etc. [7]. As the digital image is saved, the taxonomy used should include standardized file format, directory format and file names [7]. Currently at the FMC, images are saved onto a centralized database on a sharable network. As the files are

saved, they can be manually assigned a surgical accession number. The above information of the images are stored with the image, but they are primarily organized according to this accession number.

Ideally, gross digital images should be saved and managed in an LIS [7]. Although ideal, this may be the most difficult components in all of digital pathology [7]. This may be due, in part, to the multiple types of LIS systems, and linking them up with a digital image capturing software may become complex. And as technology advances and system upgrades are being implemented, this may compound the problem even further [7].

Despite the challenges, there are two particular ways to manage integration of digital images into a LIS, which are to include integrated and modular imaging [7]. In an integrated imaging solution, the LIS vendor supplies commercial software or an application module to incorporate and manage digital images in the LIS [7]. With this method, limited acquisition devices can often be supported and if images from a new device (e.g. new webcam) are to be captured in the LIS, a new interface is typically necessary. Another huge limitation is a dependence on the vendor for software, image storage format may which are often limiting and/or proprietary, and access to these images for users may be restricted and closely linked to this information system [7].

To avoid these proprietary issues, some institutions have chosen to use a modular imaging solution using separate image acquisition and storage procedures [125]. This method has dual-image storage locations with automated filing of images on servers using integrated Web-Reference based viewing solutions [126]. This set-up has been successfully implemented, allowing several authorized users in an institution's Intranet to acquire access to these images[126]. In addition, determining which digital images to purge or back-up could possibly

raise the cost of owning a digital imaging solution for the laboratory [7]. Storing images that frequently get backed up off site to an enterprise server in the Information Technology (IT) department can suddenly become an expensive operation, particularly as you constantly capture and save more images [7]. Besides the scalability of the system, other areas to consider when launching a digital archive are reliability, ease of access to these images and security.

4.6.2 Sharing

Once the digital images are captured, they can be utilized many different ways. For instance, they can be printed out on printers, displayed on a computer monitor or projector, integrated into surgical pathology reports, transmitted over networks for remote viewing, or imported into presentation software (e.g. PowerPoint, Keynote) [7]. With their versatility, digital images can be utilized for lectures, presentations, diagnostic purposes, in atlases and publications. There is an increasing movement towards embedding digital images, both macroscopic and microscopic, into pathology reports [92]. To accomplish this, a connection is necessary between the digital archive and LIS [7]. When a successful implementation of the digital images has been employed, it has been verified as a constructive addition to autopsy reports, serving to enhance the clinician's understanding and usefulness of these reports [127]. However, some concerns have arisen over the possible interruption of the workflow, which may not be currently reimbursed, and also the potential increase in medical-legal exposure [128].

4.7 Image Databank

A list of commonly identified gross descriptive terms and appearances was collected (Figure 3.1). With this list in mind, I scoured the CLS digital image databank in search of digital

gross photos which exemplify each of the terms. The CLS digital image databank consists of thousands of images collected from several pathology laboratory sites in Calgary since 2001.

The database of gross digital images at the FMC centres around specimens received in the pathology lab directly from the operating room. My collection targets specific gross appearances, as listed in Table 3, which are commonly seen in the gross area.

Table 3 - List of commonly used gross descriptive terms

Abrasion	Exophytic	Mucocele	Sloughed
Abscess/ Purulent/ Suppurating	Exudate	Multicystic	Smooth
Adhesion	Everted	Multifaceted	Solid-cystic
“Apple-core”	Excrescence	Multifocal	Stellate
Amorphous/ Irregular	Fat necrosis	Multilobular	Stenosis
Annular	Fenestrated	Multiparous	Streaked
Anthroctic pigment	Fibrofatty	Mummified	Striated
Asymmetrical	Fibrous	Necrotic	Submucosal
Bilateral	Firm	Nodular	Subserosal
Bile-stained	Flat	Nodule	Symmetrical
Bivalved	Flecked	Non-intact	Thickened
Blister	Fleshy	Nulliparous	Trabeculated
Bosselated	Fluid (fluid-filled)	Obstructed	Translucent
Botryoid	Fistula	Oval	Transparent
Bulla	Focal	Ovoid	Ulcerated
Calculi	Fractured	Papillated	Uniform
Caseous	Friable	Papillary	Unilateral
Centrally-located	Fungating	Papule	Variable-sized
Chalky	Gangrenous	Patent	Velvety
Circular	Granulated	Peau d’ orange	Vermiform
Circumferential	Gritty	Pedunculated	Verrucous
Circumscribed	Hairy	Petechia	Vesicle
Clot/ Thrombus	Hemorrhagic	Perforated	Well-healed
Coalescing	Heterogenous	Pigmented	Wrinkled
Cobblestone	Homogenous	Plaque	Whorled
Congested	Ill-defined	Prominent	
Crystalline	Incised	Protruding	
Cystic	Indrawn	Pseudocyst	
Cylindrical	Indurated	Pseudopolyps	
Defect	Infarct	Puckered	
Dense/ Solid	Infiltrated	Pultaceous/ Sebaceous	

Degeneration	Intact	Pus	
Depressed	Intracavitary	Pustule	
Demarcated	Intralumen	Raised	
Diffuse	Invasive	Reniform	
Dilated	Inverted	Roughened	
Discoloration	Irregular/Amorphous	Ruptured	
Distended	Ischemic	Scale	
Diverticuli	Laceration	Segmental	
Eccentric	Linear	Serpiginous	
Edematous	Lobulated	Septate	
Ellipse	Loculated	Serosal	
Elongated	Macule	Serous	
Encapsulated	Mottled	Serrated	
Eroded	Mucinous	Sessile	

As I collected these images they were classified according to their gross appearance and were not classified according to specific diagnosis like the previously described books and websites. In addition a brief commentary stating the gross appearance, underlying disease process and common sites of the body in which it appears was noted with the photograph. In this way, the collection is unique and can be helpful for new staff and students in the pathology laboratory who need to have gross surgical pathology training, as well as providing a valuable new resource for PA trainees, residents and medical students. The collection of these images and corresponding information is listed in Appendix A. This project was approved by the University of Calgary Conjoint Research Ethics Board (Ethics ID: CHREB13-0714).

Modifications and alterations of these images for enhancement purposes were accomplished by using Adobe Photoshop CS6 Version 13.0 x64 software. Modifications included cropping of images to focus on specific areas and to eliminate patient information included on the original photographs (e.g. surgical accession numbers). In addition, brightness, contrast and sharpening were adjusted for each photograph to improve overall picture quality.

Lastly, the “spot healing brush tool” was used to eliminate background debris such as blood, extraneous portions of tissue and other fluids that were on the original photograph.

Chapter Five: Conclusions and Future Work

In this chapter I will conclude this thesis with a summary of the main achievements, results and contributions. This will be followed by future works of the themes associated with this study which show the “big picture” of the extendibility and applicability of first, digital photography, and then specifically gross digital photography in pathology.

5.1 Conclusions

The need for pathology informatics is crucial to modern medicine across the entire continuum of patient care [129]. The laboratory provides consultation services and information management through reliable, reproducible, large scale quantitative data that is used comprehensively to screen populations, diagnose disease, estimate prognosis, guide therapy and measure outcomes [130]. For these reasons, pathology informatics is on the rise and may become a dominant specialty in future. A large component of pathology informatics is the usage and utility of digital images.

Pathologists are required to document morphological findings both at the macroscopic and microscopic level [1]. Photographs capture unbiased appearances of pathological changes and may reduce many of the inaccuracies resulting from discrepancies in descriptive ability [2]. Transitioning from an analog to digital format has transformed the way pathology labs can utilize photography. As this technology advances, existing systems will improve and new systems will develop. It is important to gauge current applications and technologies and utilize them as much as possible, including for medical education purposes. As the technology continues to improve at a rapid pace, an in-depth knowledge is needed to utilize current methods and anticipate future

needs. Chapter one outlines the objectives of this research, which are to examine many different applications related to digital imaging and anatomic pathology. In addition, we assess the novelty and significance, research contributions and methodology of the project.

Chapter two is a literature review section initially discussing digital imaging and the advantages it possesses in direct comparison to traditional still images. Next the discussion focused on the specific applications of digital imaging in the pathology laboratory setting. In particular, the differences between macro and micro photography are established. Next, an overview of some of the currently utilized digital pathology systems is discussed, with heavy emphasis on hematopathology, WSI and the incorporation of images into PACS. Additionally, the application of digital images is explored for education, clinical and research. Lastly, an overview of telepathology in relation to its remote site, developing world applications and future direction of the technology is examined.

The survey discussed in chapter three has shown that the technology is being utilized consistently by pathologists, residents, pathologists' assistants in Canada for documentation and educational purposes of diagnostic specimens. According to this survey, the majority of pathology lab personnel in Canada feel that gross digital photography should be utilized for educational purposes including teaching and round presentations. Also, it is needed for medico-legal documentation, consultation, quality assurance and routine diagnostic services. Respondents of the survey identify future applications of gross digital photography in Canada as teaching, consultation and medico-legal documentation. Interestingly, there is less excitement indicated for telepathology and three-dimensional digital pathology methods, both of which were previously identified as emerging trends in pathology informatics [6, 7, 10, 96-98].

Chapter four was dedicated to the design and development of a database of gross digital images showing particular gross features and their use as an educational tool for new laboratory staff including pathology residents and pathologists' assistant students. Relevant to this project is an overview of the different types of cameras, commercially available systems and set-ups available for pathology gross areas to capture gross digital images. Initially, a list of typical gross abnormalities commonly seen in the pathology lab was collected from pathology websites and textbooks. Then corresponding images were extracted, organized and archived from the CLS gross digital image databank. Lastly, a brief description of the gross appearance and disease process was attached to each photograph. For new pathology trainees, this collection of images will become invaluable as a teaching tool when transitioning from theoretical learning to actual "hands-on" gross pathology practice. Additionally, we explored the different literature, both in print and online, of the current available gross digital photographs and how they are presented.

5.2 Future Work

Image analysis algorithms, as discussed in chapter two, will likely gain increased importance in pathology laboratories. WSI and associated software allow for algorithms for IHC and stain intensity. The Aperio analysis package includes algorithms for Nuclear, Membrane, Micrometastasis and Staining Intensity quantification [29]. These are highly advanced algorithms based upon morphological image processing methods. Since manual analysis of IHC is a tedious, time-consuming subjective process with inherent intra- and interobserver variability [131, 132], image analysis algorithm systems could alleviate these issues and bring about a standardized method of reporting.

Although the gold standard is likely to remain the pathologist's eye, computational quantification of IHC staining is beginning to be accepted in the histological community and even in the clinic [133]. There are increasing publications validating these methods, so this industry is likely to continue growing in the coming years [134, 135]. Similar systems are being developed to quantify FISH staining, IF and to identify rare events in a population of cells or sections [133]. New areas focusing on diagnosis or recognition of pathological lesions caused by drug toxicity are emerging, with image analysis systems being developed to segment images and annotate regions of disease, such as necrosis or hypertrophy [133]. Institutions are also acknowledging the potential of this technology, and are implementing systems that can both manage and analyze their digital images using algorithms and can be shared across networks or even the Internet [133].

Of all areas in digital pathology, hematopathology, and in particular peripheral blood smears are perhaps closest to realizing the full benefits of automated image analysis. As previously mentioned in chapter two, performance has been rated well in classifying images for blood cell abnormalities. In addition, recent work has been done to detect Chronic Lymphocytic Leukemia (CLL) through a flexible and adaptable Clinical Decision Support System (CDSS) using algorithm image analysis software [136]. However, further development work is necessary for RBC morphology and also bone marrow interpretation to reach the automation of peripheral blood smears. If current analytical and regulatory issues are conquered then slideless hematopathology labs may become a reality in the next decade [36, 137]. However, even though these technological advancements are years away, digital pathology currently fulfills important roles in hematopathology including education, quality control and continuing professional development [138, 139].

For gross digital pictures, there are promising future image analysis applications. In particular, algorithm analysis and gross digital pictures can be used to assist and support the work of the forensic physician and add a quantitative component to analyzing these images[63]. A study by Levy et al. demonstrated the technique of Spatially Invariant Vector Quantization (SIVQ) in the analysis of gross forensic images. SIVQ is a pattern recognition algorithm which is employed by the forensic pathologist to analyze gross forensic images from gunshot wounds, burns and patterned contusions [63]. After the user defined the features, the algorithm was able to detect both the gunshot wound and its marginal abrasion, calculate the surface area of a gunshot wound defect, distinguish between a thermal burn and the surrounding areas of healing, analyze a patterned contusion, and both identify and calculate the density of gunpowder stippling[63]. This research has demonstrated that SIVQ is able to easily identify features of interest in gross forensic images. However, further work needs to be done to fully investigate the potential for this technology to the practice of forensic pathology.

The applications of using gross images as a teaching tool, as discussed in chapter four, can have immediate educational utility. The list of gross descriptive terms and corresponding gross digital images collected in this thesis is comprehensive. These terms and images can be made available to medical laboratories and trainees as a resource for standardizing gross descriptions for surgical and autopsy specimens. This resource can be available as a website, e-book, CD ROM, or printed textbook.

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