Virtual Microscopy in Undergraduate Pathology Education

An early transformative experience in clinical reasoning

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Abstract

Objectives: Whole-slide imaging (WSI) and virtual microscopy (VM) have revolutionized teaching, diagnosis and research in histopathology. The aims of this study were to establish the feasibility of achieving early integration of clinical reasoning with undergraduate pathology teaching on a virtual microscopy platform and, to determine its student-centricity through student feedback. Methods: Thirty-eight VM-centered clinical cases were introduced to forty-nine students in an integrated undergraduate medical curriculum. The cases were aligned to curricular objectives, reinforced the pathologic basis of disease with critical thinking and were delivered across fifteen interactive small-group sessions. A simulated cross-disciplinary integration and judicious choice of pertinent diagnostic investigations was linked to principles of management. Feedback was obtained through a mixed-methods approach. Results: User-friendliness, gradual learning curve of VM and annotation-capacity were scored 4-5 on a Likert scale of 1-5 by 91.84%, 87.75% and 83.67% students respectively. Students agreed on content-match to the stage of learning (81.63%), theme of the week (91.84%) and development of a strong clinical foundation (77.5%). Integration (85.71%) and clinico-pathological correlation (83.67%) were strengths of this educational effort. High student attendance (~100%) and
improved assessment scores on critical thinking (80%) were observed. Software lacunae included frequent logouts and lack of note-taking tools. Easy access was a significant student-centric advantage. **Conclusion:** A VM-centered approach with clinico-pathological correlation has been successfully introduced to inculcate integrated learning. Using the pathologic basis of disease as fulcrum and critical reasoning as anchor, a digitally-enabled generation of medical students have embraced this educational tool for tutor-guided, student-centered learning.

**Keywords:** virtual, digital, pathology, microscopy, medical education

**Advances to Knowledge**
- Digital pathology is an enabler of integrated undergraduate medical education, blending clinical presentations with morphologic evidence of disease to reinforce its pathophysiologic basis.
- Judicious use of VM in health professions education is invaluable in preparing health professionals of the future.
- Electronic tools are vital to student-centered learning in contemporary medical education

**Application to Patient Care**
- Virtual microscopy is increasingly being adopted in diagnostic practice, revolutionizing modern histopathology laboratories.
- It is appropriate that doctors of the future are sensitized to its manifold applications, while enhancing student-centered learning in today’s digital generation.

**Introduction**
The teaching of diseased conditions in undergraduate medical education has been dominated for more than two centuries by macroscopic display of specimens mounted in pathology museums and microscopic cellular changes on glass slides. Over the last quarter-century, museums have reinvented learning through audio-visual compositions and tours. The 21st century witnessed transformation of microscopic demonstration of
disease through the marriage of digital image capture (whole slide imaging; WSI) with software capabilities (virtual microscopy; VM). This has resulted in a revolutionary transition in learning, liberating students from laboratory bench-top microscopes for conventional light microscopy (CLM).\textsuperscript{3,4} Pathology instructors have utilized this opportunity to design innovative teaching modules whereas the student-millennials have discovered ease and interest in tapping into this platform on-the-go, through computers and hand-held computing devices\textsuperscript{5}.

The vertical integration of undergraduate learning with postgraduate training and subsequent entry into physician practice or academic career paths, demands a nuanced, stage-specific exposure to modern technology. Digital microscopy has provided an opportunity for a second opinion on challenging diagnoses through remote consultation: several centres shifting completely to virtual histopathology\textsuperscript{6}. Quality control programs have increasingly transited to virtual slides to maintain speciality accreditation norms in histopathology. Sound underpinnings of microscopic evidence of disease prepare physicians, irrespective of their chosen speciality to make more informed decisions through multidisciplinary team meetings. Thus, it makes sense to embrace technology-enhanced microscopy and blend it with clinical emphasis to prepare future doctors.

This study was carried out in a newly established College of Medicine which has an accredited, integrated medical curriculum with a student-centered, tutor-enabled, educational philosophy. Digital learning and electronic assessment underpin the curricular experience. The six-year MBBS program has nine program learning outcomes (PLOs) to graduate a safe and competent doctor who practices evidence-based medicine with ethical attributes and knowledge of modern healthcare systems. Good communication, advocacy and teamwork are essential hallmarks of this future physician with a strong capacity for self-directed learning. In the first pre-clinical year, students are introduced to structure and function, essentials of medical practice, bioethics, epidemiology and biostatistics. Years-two and -three integrate clinical manifestations and principles of management with disease morphology and its pathophysiologic basis.
This study was undertaken within a 4-credit General Pathology course in the first semester of year-two. The course introduces disease mechanisms and manifestation and specifically aligns with the PLOs in terms of knowledge and competency with clinicopathological correlation, communication, advocacy, peer education and self-directed learning. There is a spiral continuum with preceding basic sciences and succeeding clinical, stepwise learning. The emphasis is on clinical case-based teaching and early clinical-skills orientation in tandem, through simulation and hospital experience. Thus, this study was based on the constructivist theory of learning to enhance the spiral nature of the medical curriculum.

This study on digital pathology and VM as an educational intervention aimed to a. establish the feasibility of achieving early integration of clinical reasoning with pathology teaching on a virtual microscopy platform and, b. determine student-centricity of this teaching modality through student feedback. The objectives, design, delivery, student experience and assessment on this e-learning platform were analysed in this study.

The likely impact of this innovative educational intervention is early integration of clinical reasoning with fundamentals of disease and digital empowerment of 21st century medical practitioners. The intent is to establish a continuum of undergraduate-postgraduate medical education.

**Methods**

An educational innovation of e-learning through virtual microscopy, was established at the College of Medicine (CoM), Mohammed Bin Rashid University of Medicine and Health Sciences (MBRU), Dubai Healthcare City, United Arab Emirates. This is a new medical school with its first cohort intake in 2016. The six-year MBBS program has three pre-clinical years followed by three clinical years. The first cohort intake had 54 students. Forty-nine students who progressed to year-2, participated in this study between August and December 2017. Students were introduced to VM through integrated clinical case-based tutorials in the General Pathology course which runs in the first semester of year-two. IRB exempt review was approved for this educational research.
A web-based platform, Philips Pathology Education Tutor software was utilised for this educational delivery, accessed through an institutional subscription. It provided a whole scanned microscopic slide (WSI) inventory comprising histology and histopathology slides illustrating a range of common disease processes across organ systems. Dynamic virtual microscopic viewing was accessed from the cloud. The software tools enabled building of clinical case content by tutors, through combining text and static pictures (clinical, radiology, electrophysiologic, macroscopic disease, multimedia, tables etc.) and linking them with dynamic VM. Tutor-training and student orientation formed part of the initiation process.

VM-centered clinical case teaching was introduced in two-hour practical sessions within the ‘General Pathology’ course. The cases illustrated the week’s teaching theme and objectives e.g. cell injury, inflammation, oedema and thrombosis through fatty change, acute appendicitis, pulmonary edema and thrombo-embolism, respectively. One case example of the twenty-five clinical scenarios, taught during the semester is illustrated in Fig 1. Additional images and multimedia (e.g. Radiology, ECG, Haematology and Microbiology reports etc.) were included, as appropriate. The clinical cases were designed in-house to inculcate an early clinico-pathophysiologic-morphologic integration with resultant ability to optimize choice of investigation and rationalize diagnosis and management. WSI were uploaded to the case either alone or with normal histology slides to contrast normal with abnormal (e.g. normal myocardium with ischaemic necrosis in infarction) or features of two disease processes (e.g. lobar pneumonia vs. bronchopneumonia). Slides were annotated to allow students to identify and discuss disease changes with the tutor and peers. Clinical complexity was appropriate to the stage of learning and integrated with students’ parallel learning of clinical skills and other diagnostic disciplines eg. Radiology, Haematology, Biochemistry, Microbiology etc.

Ten interactive teaching sessions lasting two hours each, in small group format, were sited in a well-equipped computer laboratory (Fig. 2). Students had access to prepared cases on the website on-the-go through their laptops, ahead of the formal scheduled discussion. The tutor projected the web page live while students conducted the
discussion. Tutor and student-annotated areas on VM were addressed. Case content was probed through interactive questions directed towards clinico-pathological correlation, critical reasoning and logical thinking, focused on identifying gaps in knowledge and comprehension. Follow-up enquiries from students, individually or through forums closed the loop.

Student feedback was obtained at mid-semester through anonymous tutor-designed surveys and end-semester through formal, University-enabled, electronic feedback on the courses. The surveys elicited the students’ experience with virtual microscopy (4 questions) and content (5 questions) through a mixed-methods approach. Quantitative responses on satisfaction with the VM experience on a 4-item questionnaire were measured on a Likert scale of 1-5; where 1 = lowest and 5 = highest. A 5-item questionnaire on case content was scored from 1-3 as agree, partly agree and disagree (Fig. 3 and 4). Qualitative responses sought anonymous, open-ended comments addressing lacunae and positive learning experiences for improvement of the module and reinforcement of strengths respectively.

Tutor feedback entailed inputs with regard to: course-appropriate case creation; learning curve on IT tools (including expertise and time management); navigation and ease of teaching on the web-based program; mutual satisfaction between teacher and taught in handling the one-on-one computer sessions; software support and troubleshooting by the website maintenance team.

An Objective structured practical examinations (OSPE) was conducted through the Tutor software’s OLT portal. It was weighted at 15% of the course semester assessment. Students were provided formative guidance to e-assessment of skills and question format. The skill domain was tested through OSPE stations that mirrored the teaching. Analysis of clinical vignettes centered on VM, explored students’ identification of disease morphology for example granulomas with clinicopathologic correlation and pathophysiologic interpretation of disease patterns. The format included VM slide-based annotations, MCQs and short answers. A sample question is illustrated in Fig. 5.
emphasis was not on mastery over histologic diagnosis, but on stage-appropriate knowledge of pathologic change that explains a clinical or radiologic manifestation or functional alteration due to disease.

**Results**

*Student feedback on the virtual microscopy* (Fig 3)

For user friendliness, 45/49 (91.84%) students scored ease of software-use between 4-5. Specific suggestions for improvement related to frustration with the ‘time-out’ mode which required repeated log-in. The inability to write ‘notes’ on the same webpage while class discussions were ongoing was a challenge. The capacity to manipulate VM images showed a gradual learning curve. A Likert score of 4-5 was accorded to this attribute by 43/49 (87.75%) students. A part of the learning-adaptation was the gradual recognition of cellular patterns from normal to abnormal. Annotation usage by students earned a score of 4-5 by 41/49 (83.67%) students. The interactive capacity of this tool, especially in out-of-class feedback, was especially useful, demonstrating self-directed learning.

*Student feedback on case content* (Fig 4)

This course was the students’ first introduction to disease concepts and clinico-pathological correlation. Forty of forty-nine students (81.63%) agreed that the content matched the stage of learning. The correlation of practical cases to the didactic theme of the week was agreed to by 45/49 students (91.84%). The role of the course in laying down a clinical foundation was acknowledged by 38/49 students (77.55%). In qualitative feedback, students expressed their initial struggle with clinical reasoning and a self-perceived gradual growth in capacity as they reached the end of the course, specifically attributed to case content. They identified frequent cross-integration with clinical skill learning in a simulated setting within the same semester. Forty-two of forty-nine students (85.71%) expressed satisfaction with cross-integration of pathology cases with other diagnostic modalities. The feedback acknowledged developing specific links with haematology, biochemistry and microbiology and critical learning of laboratory
investigations in specific diseases. Students made particular mention of achieving vertical integration of disease identification in Pathology with previous sensitization to imaging in Anatomy. Clinico-pathological correlation appeared to be a strength of this teaching format with 41/49 students (83.67%) satisfied with development of logical analysis of a clinical presentation. Student engagement was demonstrated by a near-100% attendance across 15 face-to-face sessions.

Content design, developed in-house, was intellectually stimulating, resulting in robust synthesis with course learning objectives. At each step, clinical reasoning, as the ultimate goal of pathology teaching, remained the guiding principle. Creation of case scenarios, familiarization with software and IT trouble shooting was demanding. The most rewarding aspect was the interactive delivery and the steady improvement in student’s analytical abilities over the period under study.

Initial hurdles in software manipulation and annotation, were reported to the website support team who responded with software update solutions. This made the educational delivery smooth and event-free. The software assessment format, which allowed for complex assembly of text, VM, annotations and static images, was effective in creating items that tested disease recognition and critical thinking.

The mean OSPE score of 82.14% (range 60-100%) was similar to the average of the final semester theory examination. In the OSPE, students performed best on questions that integrated the analysis of symptoms, signs and radiology (80%), with a lower average on functional correlates with organ disease (75%), reflective of the early stage of learning. Assessment, in turn, provided an opportunity for formative feedback - individually and collectively - to address lacunae in fundamental disease concepts.

**Discussion**

Digital technology is ubiquitous; an essential fact of human existence today, social or professional. In the early 20th century conventional light microscopy (CLM) display, at first through analog and later digital video cameras, led to the evolution of telemedicine
as a means of distance education. It was utilized by diagnostic disciplines like radiology and anatomic pathology to enable second-opinion consultations by experts or for diagnostic coverage to remote areas. However, in educational terms, telepathology restricted display and manipulation to the instructor-operator. This prevented the exploratory learning that determines knowledge-skill integration. Pioneering efforts were made to explore replacing CLM with virtual microscopy (VM) a decade and a half back. Over the next few years it became clear that the next logical step would be its application to medical teaching and diagnostic practice with the advancement of resolution in whole slide imaging. It has, today, become an enabling force in pathology education in many medical schools across the world, while efforts for standardizing its usage in diagnostic practice are ongoing. Multicentric validation studies in recent times have provided impetus to its acceptance both in routine diagnostic reporting and for off-site frozen-section reporting. It will play a vital role in sharing of whole slide images for research-access across the scientific community as this facility expands, bridging opportunities across developing and developed nations.

In pathology education, WSI and VM have overcome several shortcomings of the traditional microscope: the need for producing multiple glass slides from limited tissues for individual viewing by a large number of students; limitation on number of slides in cytology preparation; replenishment of slides for faded stains, broken/lost slides; individual supervision during the learning process; and laboratory-bound access to learning. There are, in addition, two potent arguments for virtual microscopy in undergraduate medical education: the ease with which a generation born to the digital age accepts and enjoys it and the robust shift from tutor-directed to student-centered learning as it is a take-anywhere, use-anytime tool. The ergonomic ease of VM over CLM can hardly be overemphasized.

In the setting of a new medical school, the use of VM ab initio, provided all these advantages. The students in this study cohort had limited parallel experience on microscope hardware usage in two practicals each of Microbiology and Haematology courses delivered in the same semester. But students showed rapid engagement with the
web-based platform which provided ease of access and content exploration. Microscopic slide resolution was excellent and matched glass slide clarity in teaching. While the students have excellent digital skills growing up as a digitally enabled generation, virtual microscopy was virgin territory. Once mastered, the ease of image manipulation provided a gaming effect to stimulate student learning. An interesting off-shoot was the high rate of student attendance validating enthusiasm for this simulated learning platform and its perceived benefits.

Marchevsky reported the switchover to case-based teaching of pulmonary pathophysiology on digitized images aided by text and audio recordings in University of California-Los Angeles (UCLA) guided by a pathologist-pulmonologist tutor team. Observation over a four year period reported stimulated student interest upping attendance from 30-40% to 100% and progressive student satisfaction. In the current study cohort, student attendance has been unprecedented, validating student interest. A John Hopkins study illustrating cytopathology applications in clinical practice to second year students, using ten electronic, interactive modules and evaluation by multiple choice questions (MCQs) showed demonstrable student satisfaction. Whole slide imaging (WSI) and virtual microscopy adaptive tutorials (VMATs) were used in a randomized crossover trial as tools to introduce cytopathology to senior medical students completely naïve to the subject matter previously at the University of New South Wales.

Physician assistants exposed to video-assisted microscopy showed significantly higher practical examination scores compared to 5 previous cohorts that used conventional microscopy. This is attributed largely to two processes: first, the discussions that go beyond textbook facts to real-life simulated cases and problem-solving capability allow students to take ownership of the process; and second, the design of assessment itself stimulates critical-thinking: a consequence of the students’ approach to these sessions. At a new medical school, introduction of virtual microscopy right from the beginning, when creating an integrated curriculum and choosing a digital format of delivery, was a well-considered decision. The continuum of learning normal histology in tandem with histopathology on a dynamic image mode was perceived by students as an enriching
experience. Students’ interpretive capacity improved from their first exposure continually through the semester and dramatically in the next semesters as they have followed pathology learning in the organ systems (data not shown). Students had the freedom to explore and annotate images within the construct of clinical cases: the simulation provided an enriched, clinically-relevant interpretation of disease while encouraging collaborative peer-learning, as also reported by others.\textsuperscript{17}

The focus on clinical reasoning on the one hand, takes away the tedium of looking at static images of morphologic changes and learning by rote to ‘spot’ diseased cells and tissues; on the other, it avoids the ocular adaptation challenges to the physical microscope and its restricted availability, confined to the educational site.

There is a strategic approach to graduate students from simple disease-based integrative learning initially, to the complexities of presentation-based differential diagnosis in year three with increasing clinical maturity. The foundation laid in year 2 transited to pathology teaching within six integrated organ-systems courses over the next three semesters (years two and three) of the curriculum. In this way, within and across the organ systems spiral learning was achieved. A VM-centered approach enhances this learning journey and will lead students to the clerkship years, armed with robust understanding of disease.

VM has already entered the arena of graduate medical education in histopathology, haematology and dermatology wherein large libraries of digitized slides, available open access or through subscription, enable mastery of a range of disease diagnosis beyond the confines of clinical training sites.\textsuperscript{18,19} In a nation-wide survey in USA across 52 histopathology residency programs 82\% used web-based digital slide collections.\textsuperscript{18} In-training and certification exams now use a VM platform. In addition, anatomic pathology and cytopathology quality assurance programs have already adopted it to ensure safe diagnostic expertise.\textsuperscript{20,21} Thus the continuum of undergraduate-postgraduate learning of VM is now an established need. Continuing efforts and validation have brought VM into
the realm of diagnostic histopathology with some centers having taken the leap to exclusive digital practice.²²,²³

Medical practice, whatever the chosen specialty, rests on sound knowledge, skills and attitudes. Visual demonstrations of disease recognition whether clinical or in diseased organs, assume multiple forms and the VM mode has brought another nuance to learning styles. Almost all hospital based specialty practice entails multidisciplinary team (MDT) meetings to secure rational, comprehensive, management decisions. VM in one form or another today occupies center-stage in MDT’s to the ultimate aim of making informed decisions on patient management.⁶ Irrespective of the chosen specialty, it will become a vital cog in the learning wheel of the life of a competent medical professional when practicing safe medical care, hence its use early in the educational process seems entirely appropriate.

This study has two limitations. One, the instructional strategy was implemented in the first cohort of students of a new medical school, hence lacks a comparison with a control group which underwent simultaneous conventional microscopy teaching. Second, the analyses can be improved by a survey of the same cohort once they enter clinical clerkship to reflect back on the value of early clinical reasoning integrated with student-centered teaching of virtual microscopic pathology.

**Conclusion**

Digital Pathology and virtual microscopy (VM) span the continuum of learning of disease mechanisms and appearance from undergraduate, postgraduate to continued medical education. The art of its usage relies on careful construct of teaching content, to make it the backbone for clinical reasoning and critical thinking. This study demonstrates its successful implementation in integrated clinical teaching in a new medical school and establishes its utility through student satisfaction and assessment. Its usage finds vindication in the current COVID-19 pandemic in 2020, when remote digital delivery has proved the savior for education. VM is today, an integral part of quality assurance, research and multidisciplinary meetings for patient management. Its introduction into
diagnostic practice and specialized cross-consult is a work in progress subject to validation and regulation. The growing digital platform, integrated with advances in high resolution images holds the future in education, research and patient care.

**Conflict of Interest**
The author declares no conflicts of interest.

**Funding**
No funding was received for this study.

**References**


Figure 1: Composite illustration of a VM-centered prototype case: Acute appendicitis. A clinical vignette integrates the anatomical basis of location of pain and the gross appearance of the operated appendix. Microscopic comparison of a normal and diseased...
appendix at low magnification (upper right); transmural neutrophilic infiltration (higher magnification)

Figure 2: An interactive VM session in progress in the computer laboratory. Students dynamically manipulate the virtual microscope and discuss the questions and annotations with the tutor

Figure 3: Student experience with virtual microscopy: quantitative responses to a 4-item questionnaire on a Likert scale (1=lowest; 5=highest)
**Figure 4:** Student feedback on case content: a 5-item questionnaire scaled quantitatively as agree; partly agree; disagree

**Figure 5:** Assessment on VM software: a question that integrates clinical reasoning with disease morphology