Real-world digital pathology: considerations and ruminations of four young pathologists

Digital pathology offers the opportunity to improve all aspects of pathology by introducing recent technical advancements in daily diagnostic practice.[1] Its introduction in routine work, especially as part of a fully digitised workflow, allows for the creation of a smoother, traceable and interconnected environment where primary diagnoses can be rendered directly on digital slides.[2] Besides its main use as a diagnostic tool, however, digital pathology has a role in enhancing education of trainees and in research activities.[3]

In this letter, we present the impressions of two pathology residents and two young pathologists after exposing them to a fully digital workflow.

Figure 1 The workspace of the digital pathologist comprises at least two computer monitors, so that one can show the laboratory information system (left, for clinical data and report writing), while another is free to display the whole-slide image at full-screen resolution (right). Comparing multiple slides (eg, immunohistochemistry to standard H&E) is also feasible, either splitting a monitor in half or using multiple monitors.

AM: ROUTINE PRACTICE

When I started working in Caltagirone, primary diagnosis on whole slide images was already the standard for routine histology and most cytology cases. I had doubts about the feasibility of this and I thought that image quality could not be compared to traditional optical microscopy.

These doubts were dispelled in a few days of actual experience in my new workplace. At first it was almost like getting lost inside the digital slide: everything looked bigger and thus more suspicious of malignancy to me. After a few days of practice, however, I realised that I really did not need to cross-check glass slides anymore. The ease of glancing at the whole mount and then progressively looking at the finer details was also something that became second nature very quickly (figure 1).

In time I noticed that there were many more features to digital pathology that I did not think of at first. Digital annotations are definitely easier and more precise than ink-writing on the glass slide. The ability to access all the previous histological examinations and clinical history for every patient in just a few clicks is an invaluable tool for the pathologist. It does not matter if the previous examination is 1 week or 20 years old, it is ready for viewing.

AC: WORKFLOW

The next-generation digital workflow stands on the shoulders of workflow research and augments it with the latest technologies.

For example, digital pictures document each stage of specimen life (figure 2).[2 4 5] These are automatically shown in the laboratory information system (LIS), giving operators an opportunity to (1) quickly notice if an error occurs, (2) determine exactly when it happened and thus (3) amend it and take actions to prevent similar future errors. Common errors thus detected include not cutting deep enough into the paraffin to reveal all fragments in the block and malfunctions in the scanner excluding pieces of tissue from the digital slide.

When reporting, the pathologist is shown a colour-coded, sorted and complete inventory of work. New cases appear on the dashboard in real time, as soon as they are finished scanning, and cases waiting for additional techniques are moved to a different list to avoid clogging the main view. When a pathologist requests an immunohistochemical (IHC) stain with a few clicks, an entry instantly shows up in the dashboard of a technician. A small handheld device guides the technician to the correct room, then to the correct shelf and finally to the tissue block to retrieve. At the microtome, scanning the block causes an adjacent printer to spit out slides for each stain that was requested, already labelled.

The speed and accuracy of a fully digital lab mean faster and better care for patients. But this has an unsettling corollary. How many patients are treated too late due to delays caused by messy workflows? How many diagnoses are missed, left underneath a layer of paraffin?

BB: RESEARCH

Pathology is increasingly recognised as the core of precision medicine research. The need for high-throughput approaches integrating different layers of information and enabling complex analyses clashes with the intrinsic qualitative nature of morphological evaluation and reporting. Digitalisation of pathology data has infringed these limitations, opening a full spectrum of opportunities for tissue-based investigations.

The integrated adoption of pathologist-guided and/or artificial intelligence (AI)-assisted segmentation of tissue structures and cell components conjugates the suitability of analytical methods proper of single-cell resolved science (eg, clustering analyses, dimensionality reduction methods) with spatial information, offering an unprecedented

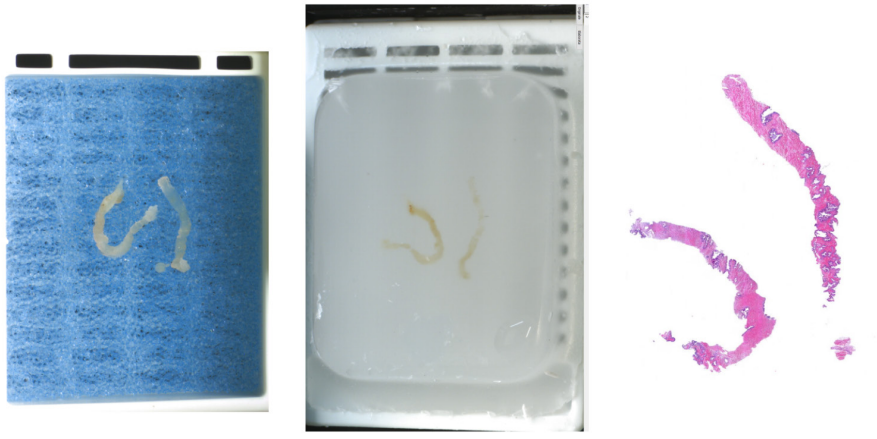

Figure 2 Pictures documenting the life of a specimen in a digital pathology lab. In the grossing room, a digital camera takes pictures of the specimen to document the grossing procedure. Similarly, prior to closing the lid, the filled cassettes are also photographed by a dedicated device (left). Later, these pictures are joined by those of the paraffin surface after microtome sectioning (middle), by the slide macroimage after scanning (right) and of course by the whole-slide image.

level of insight into the biology of normal and diseased tissues.[6]

High-resolution tissue imaging based on new generation slide scanners further extends the inference of pieces of information beyond the quantitative analysis of cell morphotype/phenotype and cell–cell or cell–contexture interactions, opening a window over topographic organisation of nuclear content and related mechanobiology.[7]

The possibility to exploit in situ transcriptional analyses to discover and validate the correspondence between emerging digital patterns and the underlying molecular networks represents the current edge of tissue-driven research, with genome-level assays making their way into the field.[8] In the scenario of such a multiomics harmonisation—now including what we can identify as pathomics—preanalytical phases and quality controls of surgical pathology lab best practices represent the cornerstones. The confluence of mergeable digital pathology data into repositories for proper comparison and data analysis routines will likely represent the bottleneck of pathomics in the forthcoming years, when tissue-driven research will face the rapid refinement of tissue-based molecular/genetics methods and the exponential increase in the availability of digital pathology platforms.

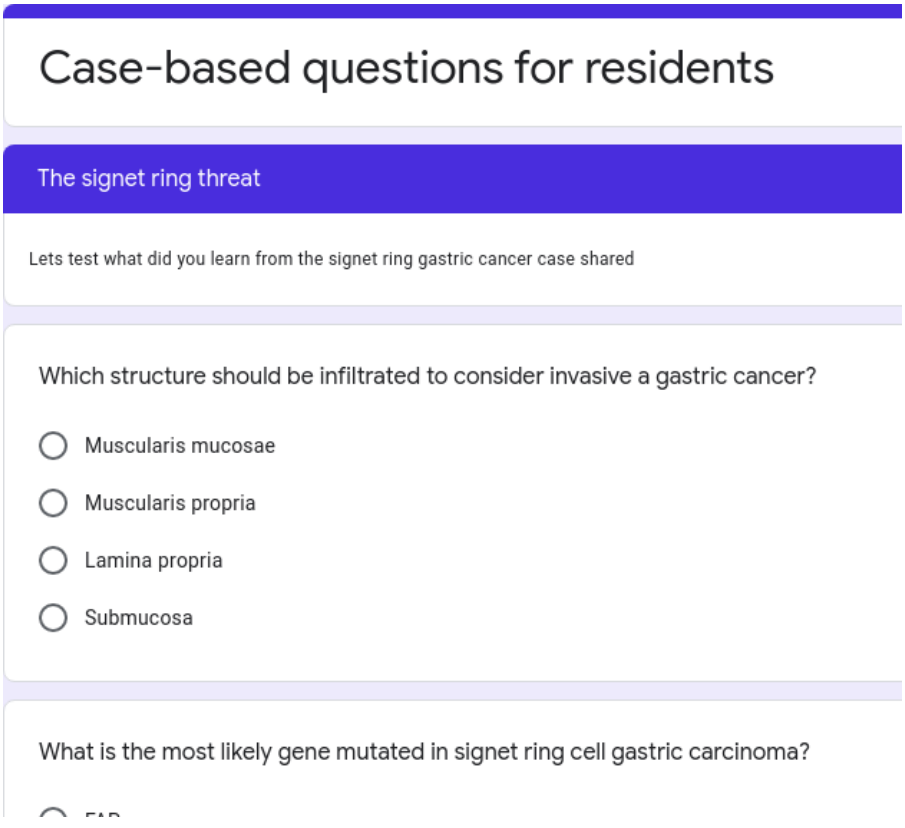

Figure 3 Collections of whole-slide images can be shared with trainees together with an accompanying questionnaire to stimulate thinking, enhance retention and simulate application of knowledge to real-world scenarios.

FG: EDUCATION

As a first-year pathology resident, who had only previously visited 'traditional analogue working' pathology departments, experiencing a fully digitised pathology environment for the first time felt like being projected many years into the future. In this setting, digital pathology acted as a second term of comparison that encouraged me to better understand the shortcomings and the potential points of improvement of the 'traditional working' practice, in the face of a growingly demanding modern world.

From the educational point of view of a trainee, a whole-slide image (WSI) on screen is a valuable substitute for a multiviewing microscope, and it is indispensable in scenarios where no such microscopes are available. As a trainee, I could be assigned a series of cases to study on my own at my computer workstation and leave notes directly on the virtual slide whenever I encountered parts of it that left me puzzled. A senior pathologist could later review my annotations and provide me with a targeted clarification. Additionally, without the constraint of a physical glass slide and a microscope, challenging cases of educational interest could be shared digitally and be viewed at different workstations, even simultaneously, no matter the geographical distance, creating a flexible and interconnected training environment.

Despite all these potential contributions, digital pathology is still not widely recognised at the academic level to the point of being made a consistent part of the training course of pathology trainees. No formal teaching sessions on virtual microscopy are generally provided to improve diagnostic decision analysis with WSI, and little opportunity is given to show digital pathology as a valid alternative to the classical workflow. Perhaps, promoting a wider introduction to digital pathology

in training programmes will help build trust in its potentials and encourage wider acceptance among institutions (figure 3).

CONCLUSION

In contrast with some previous reports highlighting the scepticism of pathologists and technicians towards digital pathology, herein we present four positive opinions of young pathologists after their first encounter with digital pathology. It is interesting to note that while some people fear the switch to digital, these four pathologists think it is overdue and they are instead concerned about making it happen as soon as possible.

In addition to the improvements in primary diagnosis,[9] digital pathology enhances education by making slides and their annotations readily accessible anywhere in the world, by any number of people at the same time. Research can similarly benefit from the adoption of digital pathology by, for example, having terabytes of scanned slides at one's disposal—a precious resource in the age of AI and computer-aided pathology. Raising the awareness of young pathologists about digital pathology is fundamental to ensure the switch happens as soon and as completely as possible. In our opinion, the earlier, the better.

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