Whole slide imaging software

At a minimum, software for WSIs includes software to run the scan and software to view the slides. Scanning software permits a user to stitch together multiple tiled images of the slide or takes a long picture of one linear pass of the slide, regardless of the method, these images overlap enough that the software can piece them together in one image. Whole slide imaging is typically associated with high-resolution cameras, which capture images that contain options to export to JPEG2000 or an uncompressed TIFF. An open source software, OpenSlide, reads the majority of proprietary formats. An example of a scanned slide can be seen in figure 1.

The file size depends on the magnification at which the slide was scanned, the degree of compression of the file (which varies between the proprietary formats), the number of ‘z-levels’ (scanning the same slide at a different plane of focus), and the size of the scanned area. A 20x scan has a resolution of 0.5 microns per pixel (1.2 billion pixels for a 2.0 x 1.5 cm slide), typically resulting in an image of 0.5 x 2.0 GB for a compressed proprietary format. A 40x (2.4 billion pixels for a 2.0 x 1.5 cm slide), resulting in an image of 1.0-2.0 GB. These files can be archived, stored on a local disk or a network, or can be assessed using computer algorithms. In terms of file storage, a sensible option is to store the most recent cases in a low latency network for quick loading times. Long-term storage can be on high-storage, low-speed drives. Some file properties can be adjusted, including hue and saturation.

Parity with conventional microscopy

For digital pathology to become the primary method of diagnosis, it must be comparable to conventional microscopy in regard to its ability to give the pathologist enough information to make a correct diagnosis in a time- and resource-efficient manner. The literature shows that there is a 90-100% concordance rate between digital and conventional microscopy. Histologic features that cause difficulty include fungus and H. pylori. eosinophilic granules, atypia, apoptosis, and mitotic figures. Pathologic concepts that show a high inter-observer variability with conventional microscopy (e.g. breast ductal lesions) continue to have this variability in digital microscopy, with some studies showing a slightly increased level of variability.

Studies comparing diagnostic time are mixed, with some studies showing shorter times for reading digital slides, assuming optimal hardware and software, and others showing longer times. This variance is largely explained by the observation that the field of view in a microscope is generally much larger than the number of pixels on most computer screens. For a 40x objective viewed through a 22mm 10x eyepiece, the field of view is 0.55mm (550 microns); the number of pixels in this field of view is 2,200 pixels in diameter (1,800,000 pixels in area), and a 21” monitor displays 1680 x 1050 pixels (1,764,600 pixels in area, or 46% of the area visible in the eyepiece). The use of larger, high-resolution screens (2,560 x 1600) or multiple monitors in order to have the same field of view as a microscope appears to improve the speed at which a digital slide can be assessed. Having multiple high or multiple-pinned screens generally also requires that a better graphics processing unit (GPU) is installed in a computer, along with a good network connection to the data being displayed. Some studies have studied efficient viewing patterns, which could explain the variability in time. Many design also play a role, and methods exist to make conventional microscopy and WSI take similar amounts of time.

Machine learning

Each pixel of any image contains data; a digital slide can contain billions of pixels that each contain data about color. This data can be processed by high-performing computers to correlate specific patterns present in the slide with other features or clinical outcomes. While previous computing techniques might use explicit algorithms (if x, then y), these solutions are typically context-specific and non-generalizable. Machine learning allows for the training of a computer to accomplish a specific task or goal while reducing error. For example, if the task is to identify the specific histomorphometric patterns of malignant cells, the human can give the computer images of H&E slides and either label the epithelium or give the computer a stain for cytokeratins (the establishment of "ground truth"). A computer capable of machine learning can assess the data associated with epithelium and find patterns associated with it, and after sufficient training, should be able to identify epithelium without the human establishing ground truth.

The specific mechanisms of machine learning vary, but many are centered around the creation of a neural network. Convolutional neural networks (see figure 3, right) are frequently used. These programs mimic the human visual neural structure, wherein a single neuron obtains information from several different receptors and weigh the information obtained from each according to their context. Additionally, adjacent neurons may connect to some of the same receptors as its neighbors, with different weights associated with that information. From a computing standpoint, the assessment of a pixel in a digital slide is likely to be shaped by that pixel's relationship to the pixels around it. One example could be the assessment of chromatin density in a nuclear pixels that represent an area of clumped chromatin are going to have different relationships to each other than in otherwise normal nuclei, or in unclumped areas.

The benefits of machine learning in pathology are becoming increasingly evident, and these benefits will most easily be realized by individuals or institutions with a predominantly digital workflow. When assessing a WSI, the pathologist may be able to apply a filter that generates a heat map of the most relevant areas of the image (i.e., mitotic activity, areas of decreased differentiation, locations of entity-specific features such as their neighbors, with different weights associated with that information. From a computing standpoint, the assessment of a pixel in a digital slide is likely to be shaped by that pixel's relationship to the pixels around it. One example could be the assessment of chromatin density in a nuclear pixels that represent an area of clumped chromatin are going to have different relationships to each other than in otherwise normal nuclei, or in unclumped areas.

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Conclusions

Digital pathology has the potential to substantially change the way that pathology is practiced. Major barriers to its adoption—costs, technological deficiencies (such as correcting for poor staining or artifacts), federal and state regulations—are not insurmountable and will likely be addressed over the next couple of decades. Given advances made in other technologies like digital photography and virtual reality, the possibility that digital pathology will be an omnipresent part of pathology in the near future is very real. In the near term, pathology laboratories without prior experience with digital histology will prepare itself through continuing education and assist current residents in obtaining experience with digital pathology.

Disclaimer: authors BV, MH, and RS are on the medical board of directors of PathPresenter.com.

References

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