ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

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Current and Future Uses of Digital Pathology in Oncology

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H&O What is digital pathology?

AP Digital pathology entails the digitizing of standard diagnostic pathologic information and decentralization of pathologic review. For example, pathologists may be able to review cases from different sites at a single digital pathology workstation, obviating the need to be physically present at an off-site location to view a glass slide under a microscope. My colleagues and I are researching ways to use algorithms, machine learning techniques, and artificial intelligence to extract information from pathologic images. This endeavor has been assisted by the growth of the clinical digital pathology domain. There has been a tremendous increase in the volume of digital health information that is being collected and stored. Eventually, this information will serve as potential building blocks for the implementation of algorithmic-based diagnostics.

H&O How is digital pathology used in hematology and oncology?

AP Currently, digital pathology is being used by pathologists to assist the diagnostic workflow in both cancer and noncancer applications. A digitized version of a suspicious sample can be assessed in the same way as a glass slide image; the pathologist can provide input regarding the diagnosis, characteristics, grading, and other factors. With the right clinical setup, the process can be performed at the same clinical speed as needed for glass slides.

From a research and data perspective, I think it is much easier to keep a digital imaging repository compared with a repository of glass slides. As researchers are building information repositories, it is helpful to use digital forms as opposed to physical glass slides.

H&O What are the other advantages of digital pathology?

AP Digital pathology is becoming more economical as clinicians increase the throughput. At my institution and many others, glass slides can be evaluated, captured, and stored in a digital format. Access to the digital files becomes extremely quick if they can be pulled up through a network. For glass slides, in contrast, a technician might need to visit an off-site repository and search through hundreds of thousands of samples, depending on the location and institution.

H&O How is digital pathology currently being used to practice precision medicine?

AP The use of digital pathology as a biomarker of genomic data is in early stages. For example, my colleagues and I recently published data regarding the potential for detecting actionable mutations directly from digital histology, and we validated the ability to detect microsatellite instability directly from digital slides. There is no current digital pathology signature that is generally acknowledged to directly indicate a molecular profile or a precision-medicine class. However, there has been a huge increase in research in this area, and these concepts are forthcoming.

H&O Are there any barriers to the use of digital pathology as a component of precision medicine in clinical practice?

AP The primary barrier is the availability of strong, representative data to build models. It is essential that the data used to train models are representative of the intended application population in order to develop unbiased artificial intelligence applications in medicine. Another barrier is that digital pathology–based precision medicine or a machine learning–based model must be validated in the prospective setting. It will be necessary to confirm that the model is performing as expected throughout a wide variety of patient types and end users. A third barrier is building the digital pathology infrastructure to enable deployment of such a model. Such infrastructure requires microscopy instruments, digitization equipment, and networks that can communicate to a central model housing server.

H&O Do you anticipate that the application of digital pathology and precision medicine will evolve?

AP Digital pathology is part of a larger schema of digital medicine that is rapidly expanding. Other components include radiology, clinical data, wearable devices that track biomarkers, and audio information. As we learn how to evaluate and synergize all of these different inputs, it will be possible to move toward rapid, accurate diagnostics that permit personalized assessments of prognosis. A key factor in developing applications of machine learning for digital pathology is the availability of clinical researchers who are willing to learn about emerging computational methods.

H&O What is machine learning curiosity?

AP Machine learning curiosity for clinical research is the willingness of clinical researchers to learn about and apply new computational algorithms to human health problems. We are in the early stages of the development of a new biomarker paradigm that can be derived using machine learning–based tools. A unique aspect of machine learning algorithms is that the digital streams of information I discussed earlier could be used to develop models that are not necessarily intuitive in terms of their predictions. For example, patterns in a computed tomography scan might be able to automatically predict severity in a patient with COVID-19.

To maximize the benefits of this evolving class of modeling techniques and the large amount of digital information that will become available, an important goal is for practicing oncologists with an interest in this field to collaborate with data scientists to create clinically useful models. There will be a need for clinical researchers who are able to conceptualize how to best use machine learning–based techniques to build models that are of maximum clinical applicability for patients in their specific areas of oncology.

H&O How will machine learning curiosity impact research in hematology and oncology?

AP The most important aspects, in terms of impact, will be to bring modeling technology into the clinic and to use machine learning–based models in a similar way to genomic or traditional clinical models. For example, machine learning techniques will require rigorous biomarker validation, as was required for other types of clinical research and predictive models. The researchers who will validate these biomarkers are the ones who are treating patients in the clinic and ensuring that best practices are followed.

H&O Do you have any recommendations on how to incorporate these technologies into research and clinical practice?

AP The best way to raise awareness of these rapidly emerging modeling techniques is to include some exposure to machine learning as a part of training for subspecialists. These new machine learning–based concepts are just starting to move into the clinic. It will be important to ensure that trainees have exposure to current developments within different types of machine learning–based models. This type of education will break down barriers and increase comfort levels as these sometimes opaque, nonintuitive computational models are brought from the research domain into clinical practice.

Another essential component is to ensure that the stream of data can be collected in the most efficient way. At many institutions, digital pathology and radiology are already part of the clinical workflow. The electronic health record is also gathered in a digital format. Some institutions, however, lack the protocols for the rapid, simultaneous utilization of these disparate threads of information. An important opportunity is to find a way to either prospectively or retrospectively organize and annotate information across these different domains using a platform that can be deployed for research.

An important priority of research in the next 10 years will be to ensure that there is a group of clinical researchers with domain expertise in subspecialized practices throughout oncology who are comfortable partnering with machine learning practitioners. These clinicians can

help ensure that the best new models and data computation algorithms become available in the coming years.

H&O What is next for these technologies?

AP Deployment of these technologies is starting. In the European Union, a machine learning–assisted digital pathology tool received the "CE" designation for breast cancer and prostate cancer, indicating that it met certain health, safety, and environmental protection requirements. (These tools are known as the Paige Prostate Clinical [CE-IVD] and Paige Breast Clinical [CE-IVD] devices). As models continue to improve, it may be possible to reliably extract "hidden" molecular information from samples in a rapid, efficient way. The goal is to decrease the time and cost that is required to obtain accurate, personalized information to guide the treatment of patients. Machine learning–based digital models have the potential to be transformative in the development of these new domains.

Disclosure

Dr Pearson is a member of the advisory board of Prelude Therapeutics.

Suggested Readings

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