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The Ethical Challenges of Artificial Intelligence - Driven Digital Pathology

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Abstract :

With the availability of extensive health data, artificial intelligence has immense potential to accelerate medical discoveries and improve healthcare. The digitization of clinical histopathology services through the scanning and storage of pathology slides has opened up new possibilities for health care in recent years, especially as it brings opportunities for artificial intelligence (AI)-driven research. It is also set to improve medical practice soon. However, acknowledging that there is little scholarly debate on the ethics of digital pathology when used for AI research, this paper summarizes four key ethical issues to consider when deploying AI infrastructures in pathology, what is seen as such, namely, privacy, choice, equity, and trust. These arise from (1) the tension between artificial intelligence (AI) research-with its hunger for more and more data-and the default preference in data ethics and data protection law for the minimisation of personal data collection and processing; (2) the fact that digital pathology lends itself to kinds of data fusion that go against data ethics norms and some norms of bio banking; (3) the fact that AI methods are esoteric and produce results that are sometimes unexplainable (the so-called 'black box' problem) and (4) the fact that digital pathology is particularly dependent on scanning technology manufacturers with interests of their own in profit-making from data collection. We shall suggest that most of these issues are resolvable.

Keywords : Artificial intelligence, digital pathology, privacy, choice, equity, bias, commercial interest, trust

Introduction :

Digital pathology nowadays plays an increasingly important role in basic, translational, and clinical pathology research and in routine clinical practice. Digital pathology is cellular pathology conducted with digital whole slide images (WSIs) rather than tissue sections and light microscopes. The use of WSI prevents transportation and physical sharing of tissue samples, with cost savings and a reduction in, or loss of, glass slides.WSIs are generally clear and detailed, even at low levels of magnification and allow rotation, panning and zooming. WSIs can improve clinical workflow. They can aid collaboration: a few experts in different places can work at the same time on analyses of the same slide images for diagnostic and prognostic purposes.

Digital pathology is not entirely free of ethical issues. For one thing, if it is collaborative, it can involve sharing sensitive personal data, which is subject to distinctive ethical and legal norms. There is also the fact that the scanners used to make WSIs are a new technology only recently permitted for use by regulators in the USA and the UK following large-scale validation studies.

In digital pathology, WSI images provide very rich and complex information about tissue or disease characteristics, which require advanced computational methods for effective image analysis. Deep

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learning that learns multilevel abstract representations can explore high-dimensional WSI data and discover complex hidden patterns or complicated relationship between image appearance and disease expression. Crucially, we focus on machine learning applied to WSIs-as opposed to pathologists' use of WSIs for slides and light microscopes. After briefly giving examples from the recent literature of advances in computational pathology, we consider some of the ethical problems that could be thought to arise.

Digital Pathology :

Digital pathology is the process of digitizing glass slides using a whole slide image scanner and then analyzing the digital images using an image viewer, typically on a computer monitor or mobile device. An image viewer functions similarly to a conventional standard light microscope, allowing pathologists to move slides in the same way.

While basic viewing functionality hasn't changed drastically, digital pathology has made amazing strides for pathology lab efficiency, workflow, and revenue growth.

Method for digital pathology used today

There are three main ways in which digital pathology is used today.

1. Research institutions, such as pharmaceutical companies, CROs, and academic medical centers, use digital pathology in robust study design, data collection, and database management for the millions of specimen that they currently manage and seek to leverage.
2. Clinical labs use digital pathology on select cases for remote consultations, education, or quantitative analysis.
3. The third and fastest-growing use case centers on clinical labs moving to an all-digital workflow. These labs use computatioanlly - enabled digital pathology powered by AI to help assign cases to pathologists, manage the workflow into work lists, offer quantitative image analysis for specific case types, integrate information into their existing Lab Information System (LIS), and expand access to cases beyond the brick-and-mortar walls of the lab itself. With digital pathology, diagnosis no longer needs to be delayed by the physical shipment of tissue samples or the wait times that result when pathologists are out of the office.

Types and fundamental structure of AI

1) **Machine learning-** AI is a broad term used for certain types of computer technology, some of which is called machine learning. Machine learning refers to a system in which a computer repeatedly learns from data, and the computer can derive an answer by the learning effect without a person providing any guidance. There is a technique in machine learning called deep learning, in which artificial neural networks of calculating "cells" are multilayered to resemble the human brain .

   Machine learning builds predictive models from data to identify patterns or perform tasks such as regression or classification. There are two main types of machine learning methods-supervised learning and unsupervised learning. In supervised learning, data are structured as paired features (e.g., images or other measurements) and their labels (ground truth).

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2) **Deep learning -** Deep learning most often refers to a neural network composed of many layers (hence the description "deep"). These adaptive algorithms have demonstrated a remarkable ability to learn from complex data like images with unrivaled accuracy. One way to conceptualize these algorithms is that each layer transforms the data to produce a new representation of the problem. As these layers are stacked, the algorithm can learn to represent complex phenomena through successive transformation of the input data via the layers and by repeated exposure to the data during training. This characteristic enables learning directly from "raw" data like images without needing any intermediate representation.\

   Prior to this development, research in machine learning for pathology focused on developing methods to transform pathology images into intermediate features that capture what humans think is important. In contrast to deep learning, this approach has the advantage of being transparent and explainable. The accuracy of these methods is typically inferior since the definition of features is not adaptive. Deep learning avoids this bias, learning features in a way that is entirely driven by labels in an unbiased manner. As a consequence, trained deep learning algorithms cannot be readily explained and are referred to as "black box" algorithms. This lack of specification presents problems for verification, and black box algorithms can fail in unexpected ways that are dangerous in clinical applications.

3) **Convolutional neural networks (CNNs) -** CNNs are a type of neural network for processing images. These networks explicitly model the spatial structure of images using convolution operations. The introduction of deep CNNs (DCNN) in the 2010s led to significant improvements in many image analysis tasks and so DCNNs have become the predominant approach for image analysis today. To describe how CNNs function we first introduce neural networks and then describe the convolution operation.

4) **Generative neural networks -** Recently, generative AI, including variational autoencoder and generative adversarial network (GAN) techniques, have attracted attention for its various applications. An autoencoder is a neural network that encodes data into lower-dimensional embeddings and decodes embeddings back to the original data. Typically, encoded embeddings have lower dimensions than the original data. Thus, they handle and maintain the original information and can be used in other analyses.

Ethical Issues of Digital Pathology :

1. **Privacy -** Traditionally, histopathologists have diagnosed disease by examining sections of tissue on glass slides with a light microscope. With the introduction of whole slide image (WSI) scanners, however, glass slides can be captured as high-resolution digital images, stored and transmitted electronically, and viewed on workstations allowing pathologists to make their diagnosis using an enlarged digital image on their computer screen. Databases of the captured images can also be used to train machine learning algorithms.

   The process begins with specimen retrieval and preparation through fixing, cut-up/ trimming/ grossing, embedding, microtomy, staining, and drying. High?resolution digital scans (×40) of the glass slide are then taken and 'stitched' into one 'WSI'. Next, the digital images are uploaded to a server and viewed by the pathologist on their workstation so that they can determine their diagnosis and input a digital report. The pathologist may also, at this point, add annotations and labels to the images as part of their reporting. That information is saved with the image and report, and stored in the cloud where it can be accessed, along with other linked data, by third parties for the purposes of research. While there are several ethical issues that may arise throughout the workflow, the ethical challenges related to AI are primarily associated with the pooling and sharing of data for research (research here may involve multiple uses of patient data, whether AI driven or not, but it is expected that AI will be the most common contribution due to its facility in analysing large data sets). Here, the issue that has seen the most attention is data privacy and its protection through de-identification practices.

Data privacy can be assured in several ways, for instance, by managing access to the data, through de-identification techniques (i.e. by removing data that could identify a patient), and by legally binding third parties to maintaining secure information governance practices.

2. **Choice -** Many legal and bioethical precedents allow for the sharing of de-identified patient data without explicit opt-in consent from the patient. If data no longer identifies a patient, the argument goes, it poses no harm to them if shared, and so can be done so freely. This does not mean, however, that patients hold no interests in de-identified data. From our experience, many patients express a desire for some kind of choice in how pathology data flows even if they cannot be identified from it. This is often due to general social concerns about how such data is being used - they may wish not to support, for instance, what they perceive as certain inappropriate uses of data.

   It is a well-established principle of medical law and ethics that patients provide informed consent for their treatment. Individual opt-in consent is, as noted above, also required when sharing personal data unless sharing it falls under one of the aforementioned exceptions or the implied consent needed for direct care.

   Providing some degree of control over data sharing would go a long way to improving public confidence and acceptability of big data and AI driven digital pathology, though there is no clear and easy answer on how to do it.

3. **Equity -** Given the low risks to patient confidentiality, the public benefits of sharing data, and the availability of opt-out, we contend that the above approach functions well for protecting individual data subjects' interests for privacy and autonomy. However, there are broader social challenges of AI-driven digital pathology concerning equity that need to be mentioned.

   The motivation for digitising pathology services is to improve patient care and patients are justified in their need to be reassured of the centrality of this value. It should also be remembered that digital pathology can also be an advantage in this regard, as it can play a role in reducing health disparities overall by enabling new forms of expertise and delivery to hard to reach areas through remote assessment.

4. **Trust-** Both commercial involvement and bias have further implications for public trust. Thus, for trust to exist, an individual or organisation makes decisions that are in the best interests of another, whose trust must be earned, not obliged. Trustworthiness similarly means being able to demonstrate

that goodwill. Though there are no studies of public trust in AI?driven digital pathology, multiple studies show differing degrees of awareness and trust around AI. The issue facing the future of digital pathology is how to evidence that it is trustworthy. Strengthening commitments to privacy, choice, and equity can all help in that regard, by highlighting that digital pathology is motivated by the right kind of values. In addition, we think there is much to be done in the area of patient and public involvement and engagement including developing and validating an integrated model which leverages existing approaches; namely, lay representation on data access committees (DACs), through patient and public involvement (PPI) groups, and through deliberative democratic projects such as citizens' juries, citizen panels, citizen assemblies, etc. - what we collectively call "citizen forums".

Role of Regulatory Agencies :

Government regulation is one important mechanism for enforcing ethical behavior. The Health and Human Services Office of Civil Rights enforces rules related to patient information privacy and security. Regulatory agencies such as these will need to develop new processes to address the patient safety and ethical issues introduced and/or complicated by AI.

Ethics, however, should not be confused with regulatory compliance. The process of developing regulations is slow and deliberative, and there can be a considerable time lag between the emergence of new technologies and comprehensive laws to govern them. In addition, creative individuals and organizations can often find technically legal mechanisms (ie, loopholes) for ethically questionable actions. Conflating ethics and regulatory compliance might actually give moral cover to loophole-seeking behavior. A better approach is to consider regulatory compliance as a subset of ethical behavior. Individuals and organizations should also seek opportunities to engage with regulatory agencies, professional societies, and trade groups during the deliberation phase of designing new rules.

Digital pathology enhance the value of whole slide imaging :

AI applications can "read" a entire slide image and apply specialized algorithms that can perform a number of useful clinical tasks to augment the role of the pathologist. It is well known that there is fundamental prognostic data embedded in pathology images. Software applications can now measure aspects of tissue often invisible to humans even under a microscope to predict the likely diagnosis, the aggressiveness of tumors, and ultimately, patient outcomes. These AI applications, under the umbrella of computational pathology, are redefining why labs are quickly adopting digital pathology.

Digital pathology and commercial interest :

We come finally to the ethical issues arising from the role of commercial firms in digital and computational pathology. These issues have a specific character when commercial companies use data from a public health service, with unique and valuable data sets, and where the consequences of misuse can be particularly damaging to an institution at the heart of a national welfare state.

Scanner manufacturers are a major type of business partner in digital pathology. Their equipment produces WSIs, and the more widely distributed it is in hospitals or laboratories, the more money they make.

Impact of COVID-19 on the adoption of digital pathology :

Digital pathology was developed decades ago to allow pathologists to remotely collaborate on cases and improve the accuracy of diagnostic techniques by sharing digital images across laboratories. Prior to COVID-19 pandemic, the United States lagged behind most other developed countries in the adoption of digital pathology adoption due to strict federal regulations of the US Food and Drug Administration (FDA) and the Clinical Laboratory Improvement Amendments (CLIA) from the Centers for Medicare & Medicaid Services (CMS). Thus, the COVID-19 pandemic accelerated the widespread adoption of digital pathology for remotely pathology diagnoses. This imaging technology has provided pathologists and pathologists-in-training with a variety of resources to help them continue to remotely care for patients, collaborate, and support virtual education.

Challenges and limitations of AI in pathology :

Artificial intelligence in medical applications is always faced with a series of difficulties. The challenges range from the quality of input data and model performance to ethical problems. Some key challenges include:

1) **Poor quality data -** Major applications of AI include using digital pathology slides with image analysis algorithms for accurate diagnosis. However, preparing slide images is a cumbersome process involving embedding, cutting, staining, and scanning the tissue sample. Due to this, only a few datasets are available for adequate training.

   Moreover, the image preparation process is so complex that the slide samples can become distorted. Elements such as dust, hair, and air bubbles can easily make their way into the slides undetected. This results in poor-quality data and weakly supervised deep-learning models.

2) **Data dimensionality and hardware limitations -** Whole slide imaging deals with data in the size of giga-pixels. A typical slide scan spans around 100,000 by 100,000 pixels in size.

   Deep learning algorithms, on the other hand, are often trained using images of around 250 by 250 pixels. This is because the computer hardware used for training cannot store such large-sized files.

3) **Lack of clinical and technical expertise -** Building an AI model requires experts in clinical-grade computational pathology, statistics, artificial intelligence, and on-field medical professionals. The process consists of the collection and preparation of clinical data, annotation, model training, and, finally, validation.

   Each of these experts plays a vital role in the entire process. Medical practitioners guide researchers regarding data analysis. Their guidance helps collect data and annotate the most complex cases.

4) **Lack of transparency -** Despite their success in numerous fields, deep learning algorithms are often "black box models"-little information is provided on how the results are achieved.

   Transparency and accountability are absolutely crucial for medical experts. Practitioners must provide proper reasoning and justifications for why a certain decision was made. Since AI models do not provide clear reasoning, building trust with their outcomes is difficult.

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Benefits of digital pathology :

There are a number of advantages related to the use of digital pathology, these advantages are helping the practice become more widely adopted, and commonplace in lab settings.

1) **Improved analysis -** To begin with, digital pathology offers improved analysis. It provides algorithms to be used for automated slide analysis, which is objective, rapid, and accurate.

2) **Reduction in errors -** The use of digital pathology means fewer errors are made, mistakes such as misidentification are reduced, and because the images are stored digitally, breakages do not threaten data.

3) **Enhancing imaging -** The practice also offers better views of the samples, it allows scientists to magnify to slides and look at them from different angles.

4) **Improved productivity -** Productivity is one of the main benefits that has helped digital pathology gain popularity. It improves workflow by enabling wide-scale collaboration, offering central storage of data and easy access, minimizing the need for outsourcing and facilitates automation.

   Also, it improves turnaround times by enabling rapid access to digital slides held in the archives, speeding up the processes of retrieving, organizing, and matching data.

5) **More innovation -** Innovation is another key benefit of digital pathology. The process facilitates more innovation by encouraging pathologists to become specialized, giving scientists access to better tools and information, and sharing practices with broader geographies.

6) **Better patient outcomes -** A main role of pathologists is to establish a diagnosis for a patient based on their tissue samples, leaving a critical decision up to a single person, or small group of people. Diagnosis in this way is vulnerable to human error, even if the person reviewing the samples is an expert, they are still not immune from human error.

7) **Reduces long-term costs -** Finally, digital pathology can greatly reduce costs in the long-term. This is because it can speed up the workflow, eliminate the need for couriers, reduce the requirement for scientists to travel, and reduce time and resources spent analyzing and interpreting data.

Conclusion :

AI has the potential to provide gains in quality, accuracy, and efficiency through the automation of tasks such as detecting metastases, identifying tumor cells, and counting mitoses in the not so distant future. The introduction of AI as a device assisting pathological diagnosis is expected to not only reduce the workload of pathologists but also to help standardize the otherwise subjective diagnosis that can lead to sub optimal treatment of patients.

Risks in deploying AI in daily clinical diagnostics include leakage of personal information, high operating costs, mis diagnosis, and assignment of responsibility for such mis dagnosis. In its current state, AI will need to be closely supervised in diagnostic tasks. However, with the use of advanced algorithms, AI should be able to perform diagnoses in collaboration with human pathologists. Developing integrative platforms that bring together multimodal data to suggest prognosis and/or the choice of therapy will be another substantial benefit of digitization and provide an additional sanity check on AI generated predictions.

When such advanced ("next generation") pathological diagnosis will enter medical practice, it is likely that demands of clinicians would not be satisfied with the level of current pathological diagnosis offered by pathologists using solely a microscope. Pathologists who reject digital pathology and AI may face a diminished role in the future pathology practice.

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