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Review

Next Generation Digital Pathology: Emerging Trends and Measurement Challenges for Molecular Pathology

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Abstract: Digital pathology is revolutionising the analysis of histological features and is becoming more and more widespread in both the clinic and research. Molecular pathology extends the tissue morphology information provided by conventional histopathology by providing spatially resolved molecular information to complement the structural information provided by histopathology. The multidimensional nature of the molecular data poses significant challenge for data processing, mining, and analysis. One of the key challenges faced by new and existing pathology practitioners is how to choose the most suitable molecular pathology technique for a given diagnosis. By providing a comparison of different methods, this narrative review aims to introduce the field of molecular pathology, providing a high-level overview of many different methods. Since each pixel of an image contains a wealth of molecular information, data processing in molecular pathology is more complex. The key data processing steps and variables, and their effect on the data, are also discussed.

Keywords: digital pathology; molecular imaging; mass spectrometry imaging; Raman microscopy; spatial transcriptomics; spatial metabolomics

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1. What Are Digital and Molecular Pathology?

Digital pathology can refer to any form of disease diagnostics that includes some form of computer assistance. This can include, but is not limited to, automated histological image capture (and associated metadata) [1,2]; computer-assisted image analysis [3] and instrument calibration [4]; artificial-intelligence (AI)-based diagnosis and classification [5]; and acquisition, analysis, and interpretation of other modalities such as molecular pathology [6,7]. Molecular pathology is the acquisition of images of molecular features such as specific tagged proteins or RNA or full metabolic, proteomic, or transcriptomic imaging. Just as with histopathology, digital pathology methods can be applied to molecular pathology imaging.

2. Why Is It Important?

Digitising the pathology process provides virtual records that can be associated with historical pathologies, and can improve efficiency in a clinical setting, reducing the cost and time between biopsy and diagnosis. Gleaning the most information in pathology is fundamental in moving towards enabling personalised medicine [8]. Previous studies show improvements in efficiency by performing whole-slide imaging (WSI), and analysing results digitally [9,10]. This is the simple case of using existing pathology workflows and digitising the information where possible. Further to this, machine learning (ML) and AI can be used to classify and diagnose from digital slides. This has the potential to reduce inter-operative variability [11], with strong diagnostic accuracy [12] in addition to saving time. By digitising the information contained in a histology slide, rapid sharing of information across the whole world (telepathology) can also be achieved. This may enable expert pathological review of samples acquired in remote locations far from the pathologist's place of work, or even on smart phones [13]. This can also be used for crowdsourcing efforts to gain insight from multiple pathologists [14], and for the purpose of training new pathologists [15]. In some diseases, standard approaches are insufficient to accurately diagnose and, therefore, select appropriate treatment regimens. As such, novel methods such as molecular pathology are required [16]. For example, complex intra- and inter-tumour heterogeneity can be measured using metabolic imaging [6].

3. Classical Digital Pathology

When referring to digital pathology, the most common topic discussed is the automatic acquisition, and analysis of histopathology slides, usually haematoxylin and eosin (H&E) and complementary IHC staining of thin tissue sections. Digital pathology can refer to the digitisation of any of the processes involved in this type of pathological examination; from whole-slide scanning for digitisation to automation of classification using AI (Figure 1). Within each of these different steps, there are measurement challenges that could impact the end diagnostic result. There are also many parallels and commonalities between the steps in digital pathology and molecular pathology, such as common challenges in data storage and machine learning, which are discussed in more detail.

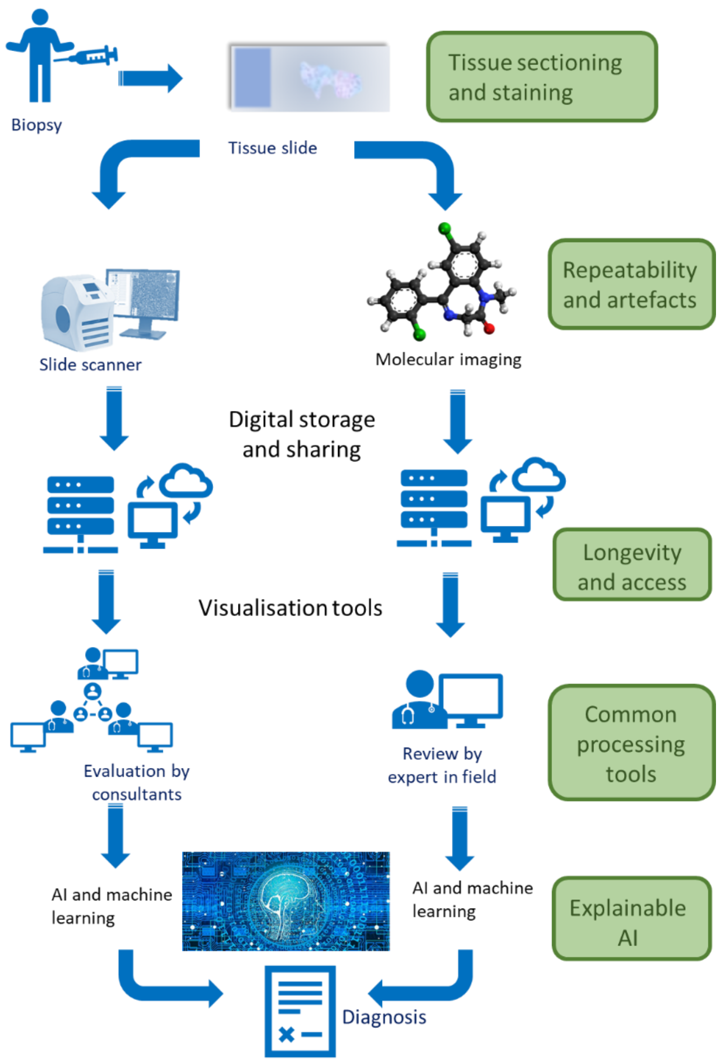

Figure 1. Example of a digital pathology workflow (left), and its equivalent molecular pathology workflow (right). Many of the steps involved have similar challenges, as highlighted in the green boxes.

3.1. Slide Scanning

The first step in a digitised pathology workflow is to acquire a digital image of the entire slide using whole-slide imaging (WSI) technology. These images can then be reviewed virtually using software to mimic the experience of analysing the slide under a microscope. This presents measurement challenges that are not observed during classical pathology. First, the resolution with which to scan the slide must be determined. In some cases, a low-resolution scan may be sufficient to diagnose disease [17], but for very small features such as microorganisms, higher resolution scans must be acquired [18]. This increases the size of data by the increase in resolution squared and, as such, rapidly increases the requirements for large-scale data storage as the resolution is increased. Second, artefacts may be introduced in the scanning process that are not derived from the tissue preparation step. Methods to automatically detect these artefacts, and identify the slides to be rescanned, were reported [19], but such methods are still in development and are not routinely available. The potential time that can be saved by this, however, is extremely promising. These challenges seen in digital pathology are mirrored in analysis by molecular pathology (Figure 1), with potential additional complications of increased, or non-standardised, sample preparation, or more complex imaging instrumentation.

3.2. Guided Visualisation

Visualisation tools and machine learning can be used to aid a pathologist's interpretation of whole-slide images. On a base level, this is a platform for interactive viewing and manual annotation of histological slides analogous to what a pathologist would see under a microscope. Modern advancements in AI and machine learning can provide a wealth of additional information and tools to a pathologist. For example, some tools can perform unsupervised or supervised segmentation, which can then be further refined by a pathologist [20], or can perform tasks such as nuclear segmentation and allow for distances between nuclei to be calculated [21]. This reduces the time required to manually draw annotations, especially in very complex and detailed tissue architecture such as calculating multiple nuclei distances. However, this introduces another potential source of uncertainty into the decision-making process [22]. Some software packages allow a pathologist to annotate the different tissue types on a slide and then classify the remainder of the slide, or other slides [3,20]. The key aspect of any visualisation tool for digital pathology is that it must be easily used by pathologists, to enable sufficient uptake to bring digital pathology into a more clinical setting. An example of how interactive guided visualisation would be performed is illustrated in Figure 2.

Some of these visualisation tools can also interact directly with molecular pathology data. For example, QuPath directly imports images from mass spectrometry imaging (MSI) data, as well as exports annotations that can be imported into MSI-specific software [20]. This cross-technique software integration is vital in enabling the use of molecular pathology by practitioners, as it provides minimal barriers to their incorporation into existing workflows.

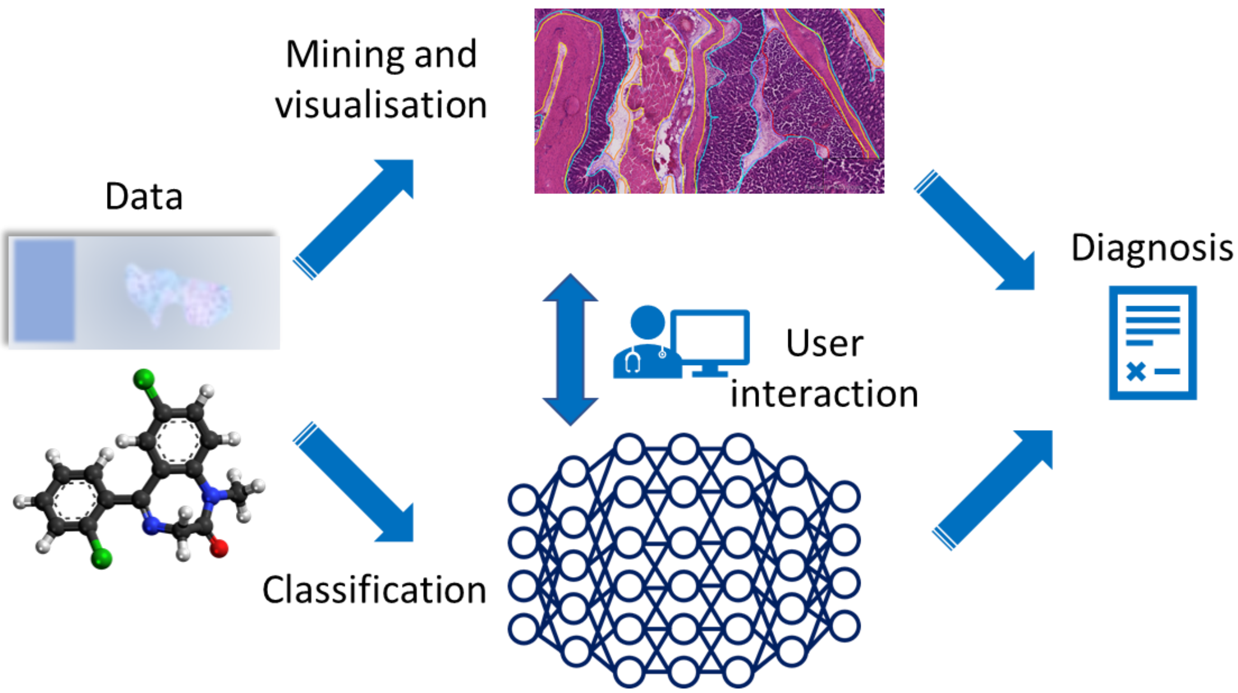

Figure 2. Example of how software for visualisation and data mining can improve the information obtained in a digital pathology workflow.

3.3. AI for Classification

The next step in machine learning and AI in digital pathology is to perform automatic classification of tissues. This has been applied to many different diseases such as fatty liver disease [23], nephropathology [24], and bacterial diseases [25]. By far the most widely applied area is digital pathology for oncology [26–28], likely due to a combination of prevalence and the diverse range of tissues and features that are observed in cancer.

One of the biggest challenges in classification for digital pathology is adequate labelled data for either training when using supervised methods, or performance evaluation when using unsupervised methods. Manual annotation by an expert pathologist is time-consuming and, therefore, costly. Large resources exist for certain cases such as glioblastoma [29], and breast carcinoma [30,31] but this is even more difficult for less prevalent diseases. In examples where data are limited, data augmentation through image transformation can be used to artificially increase the size of the available training data, but this approach does not always capture the full variability that is observed in larger training datasets. As mentioned, one advantage of digital pathology is the ability to crowdsource annotations to multiple experts, which can alleviate this problem [14]. This presents its own potential problems, particularly those around quality control. There are guidelines and best practice that can be followed to ensure that efforts to crowdsource in digital pathology are rigorous [32,33].

As well as requiring pathologist input for training data, validation of results via expert comparison is also required to evaluate the accuracy of classification in digital pathology, as well as to manually review regions and tissues that show discrepancies. One of the key recent developments is explainable AI for digital pathology. Explainable AI not only gives a classification diagnosis, but also determines the driving factors behind this classification. This allows a pathologist to understand and analyse the underlying reason behind the classification process to further aid in diagnosis, as well as to determine confidence in the diagnosis. There are many different methods to perform this, and a full survey of explainable AI for digital pathology was written by Pocevičiūtė et al. [34].

3.4. Metadata

Digital pathology is more than just a set of digital images that can be collected and analysed. Metadata around sample, storage, and acquisition are associated alongside the images themselves. These associated metadata can then be mined independently of the images. In the field of radiology, Santos et al. analysed the sensitivity and radiation exposure at different sites and over time to discover inter-site and temporal differences [35]. Furthermore, imaging and metadata can be combined to enhance the classification accuracy when using AI models [36,37]. This additional level of information is another way that digital pathology can elevate above classical histopathology. Extending metadata inclusion and mining into molecular pathology is particularly challenging, as each technique has its own unique parameters and variables to capture, as well as different proprietary or community formats to store these in.

4. Molecular Pathology

There are several non-standard imaging technologies that are being increasingly applied to disease diagnostics. These methods typically aim to measure molecular information (metabolomics, proteomics, etc.) from discrete spatial locations across a tissue specimen. The overall process in molecular pathology can look remarkably similar to that of digital pathology including sample preparation, image generation, informatics, and review (Figure 1). Unlike digital pathology, many of these methods capture tens to thousands of measurements at every pixel of an image to obtain spatially resolved molecular information. These include techniques that acquire spectral absorption/emission information such as Raman and infrared (IR) microscopy, and hyperspectral imaging. Coherent Raman scattering (CRS) techniques enable much more rapid imaging, and can be performed simultaneously with other label-free optical techniques such as second and third harmonic generation and two-photon-excited fluorescence (TPEF), which provide label-free contrast for connective tissues and structural features (e.g., collagen) [38,39], and can provide three-dimensional information. Others acquire multiple measurements through multiplexing of previously single analyses, such as multiplex fluorescence in situ hybridization (FISH), multiplex immunohistochemistry (IHC), and imaging mass cytometry (IMC). In addition to this, tissue microdissection can be performed, followed by analysis by RNA sequencing (RNA-seq) to obtain spatially resolved maps of transcriptome [40]. A detailed review of each method individually is outside of scope for this review; for detailed reviews of these different methods, see references [41] (FISH and RNA-seq), [42] (Raman and IR), [43] (multiplex IHC), [44] (IMC), and [45] (MSI). In addition to molecular imaging methods, there are other methods that can measure other properties of the tissue such as optical scattering using optical coherent tomography (OCT) [46], or speed of sound attenuation through photoacoustic imaging [47]. These provide an additional layer of information that can be complementary to molecular and morphological information.

These methods are suited towards the analysis of complex diseases and those that display molecular differences in areas that are histologically homogeneous [6]. In particular, cancer is known to be an extremely complex disease, and variations in tumour microenvironments can drastically alter the efficacy of different treatments [48]. One of the key challenges in the use of molecular pathology is the selection of the best method to use for a given diagnosis. By providing a comprehensive comparison of different methods, this review aims to guide practitioners as to what methods are most suited to a given challenge. There are no specific rules on a given method for a suspected diagnosis, but a greater understanding of the techniques available enables practitioners to use molecular pathology more regularly.

Some methods, such as IR and Raman microscopy and MSI require no chemical labelling of the tissues and, as such, are particularly useful in analysing pathologies where labelling may alter the information obtained [49]. Other methods such as multiplex IHC, FISH, and IMC require labelling via antibodies and, as such, are dependent on the availability, binding affinity, and specificity of the antibodies used. Many of these methods can be minimally to non-destructive, allowing additional analysis such as H&E staining to be applied to the same sample [50]. These methods vary in their target molecules or functional groups, as well as in sensitivity, specificity, and spatial resolution. A summary of these properties is provided in Table 1.

Table 1. Summary of different techniques that can be used for molecular pathology, and their key properties relevant to clinical diagnostics for digital pathology.

Technique	Measurements	Specificity	Sensitivity	Spatial Resolution	Labelled	Spectral Channels
Raman microscopy	Bond vibration	Medium	Medium	<1 µm	Unlabelled	100–1000
IR microscopy	Bond vibration	Medium	Medium	1 µm	Unlabelled	100–1000
Hyperspectral imaging	Light absorption	Low	Low	100 nm	Unlabelled	10–100
Multiplex IHC	Labelled antibodies	High	High	100 nm	Labelled	10
Multiplex FISH	Labelled fluorophores	High	High	100 nm	Labelled	10
IMC	Labelled antibodies	High	High	1 µm	Labelled	52
MSI	Ionised molecules	High	Medium	10 µm	Unlabelled	1000–100,000
Microdissection and RNA-seq	Gene expression	High	High	1 µm	Unlabelled	1000–100,000

4.1. Spatial Resolution

Spatial resolution is a key driver of the use of molecular pathology in certain areas. As previously mentioned, for certain features, classification can be performed on low-resolution (tens of microns) images [17]. However, to classify small features such as micro-organisms, nanometre spatial resolution is required [18]. This can be overcome by the metabolic, proteomic, or transcriptomic information afforded by molecular pathology, such as how molecular profiles from mass spectrometry can determine bacterial type [51].

Some of these molecular pathology imaging techniques, such as Raman microscopy, hyperspectral imaging, and IHC, are capable of acquiring images with the same spatial resolution as classical histopathology (diffraction limited) and, as such, are well-suited towards diagnostics that have small features. Others, such as MSI and microdissection RNA-seq, typically provide lower spatial resolution information, but higher levels of spectral (molecular or transcriptome) information. It is also worth noting that sensitivity sometimes limits spatial resolution in some techniques. For example, in MSI, if there is Insufficient sensitivity for the features of interest, then this may require a decrease in spatial resolution. Analogous to the data size challenge with resolution in classical digital pathology, sensitivity requirements increase with the square of spatial resolution; therefore, this becomes particularly critical when observing very small features.

4.2. Data Analysis

The nature of molecular pathology data is more complex than classical histopathology. Molecular pathology data contain tens to millions of measurements in every pixel of an image. The increase in complexity and dimensionality of molecular pathology data is both a benefit and challenge for data analysis. High dimensionality provides huge amounts of information to perform tasks such as classification, which can improve accuracies of diagnostics [52]. Where classification of H&E images is performed in patches, hyperspectral data can be classified on a pixel by pixel basis by determining spectral similarities [53].

However, the calculation of some measures of similarities are difficult in high-dimensional data. This is referred to as the 'curse of dimensionality' [54], which necessitates additional dimensionality reduction steps prior to classification.

Typical workflows for data processing in molecular pathology include the following steps: pre-processing, feature selection (spectral and spatial), segmentation, classification, and, finally, validation and review. Each of these steps are discussed in the following sections.

4.2.1. Pre-Processing

Pre-processing is fundamental to any digital workflow; the often used phrase is "garbage in—garbage out" [55]. Poor-quality input data leads to poor-quality results, and could introduce unintentional bias that may affect the end interpretation. The goal of pre-processing is to remove physical and computational artefacts to improve any subsequent analysis. Pre-processing is technique-specific, so this review does not detail methods for all techniques described here; for more details on pre-processing for each method described, see references [56] (IR microscopy), [57] (Raman), [58] (MSI), [59] (FISH), [60] (IHC), and [61] (RNA-seq).

4.2.2. Feature Selection

For many of the molecular pathology methods, it is not possible or appropriate to perform machine learning on the entire spectral information. This can be reduced by either targeted selection of specific features (IR/Raman wavenumbers, MS peaks of interest, genes of interest, or spatial features), or by untargeted dimensionality reduction methods.

The simplest methods to select features for subsequent analysis are to select peaks either manually, from predetermined lists, or using statistical tests. Manual selection or selecting from predetermined lists requires prior knowledge of features of interest, but can provide greater biological insight from the results obtained [62]. In comparison, if spatial features are known, then discriminating spectral features can be selected using statistical tests such as receiver operator characteristics (ROC), and t-tests [63,64]. It is critical when performing such feature selection that the data fit any assumptions in the tests performed, such as expectations of normal distributions in the case of certain statistical tests.

Instead of selecting individual features from different criteria, unsupervised dimensionality reduction can be performed. These methods aim to reduce the dimensionality of the data while retaining key features present. For example, principal component analysis (PCA) aims to reduce the data, such that the first component maximises the variance of the projected data, and subsequent components maximise the remaining variance orthogonal to prior components [65]. In comparison, t-distributed stochastic neighbour embedding increases the probability of high-dimensionally similar pixels being closer in low-dimensional space to one another [66]. Dimensionality reduction methods can be broadly categorised into two types, linear and non-linear. Linear methods, such as PCA and non-negative matrix factorisation (NMF), assume that there is a linear relationship between variables in the data. In comparison, non-linear methods are not constrained by this, but are often more complex and computationally costly. A detailed review of different dimensionality reduction algorithms can be found here [67]. Dimensionality reduction for molecular pathology often needs to be memory-efficient to cope with the large volumes of data that can be acquired in clinical settings. These can include methods for subsampling [68], or sparse representations [69].

Spatial features may also be selected to remove unwanted information, such as the removal of background pixels. This can be achieved by various methods such as semi-supervised classification and clustering [70]. The main advantage of performing such a reduction is to reduce data size and speed up subsequent data analysis.

4.2.3. Segmentation

Segmentation involves the grouping together of similar pixels or spectral features based on some measure of spatial or spectral similarity. This is used to differentiate anatomies [71], diseased vs. healthy [72], or disease grading and subtyping [73]. As with dimensionality reduction, it is often necessary to develop memory-efficient methods, such as subsampling, to perform segmentation on molecular pathology data. due to its large size [74].

There are many different algorithms used for segmentation in molecular pathology and, as such, appropriate selection of the correct or optimal algorithm for a given task is necessary. The main difficulty with this is that in digital pathology applications, samples are biologically derived and, therefore, there is not an absolute ground truth to evaluate against. One way to alleviate this is to use synthetic data, but it is a challenging to create data that contain similar variability to biology in a controlled manner. This can be achieved by analysing the underlying distributions of the biological data and randomly sampling from the same distributions [75].

4.2.4. Classification

Classification, as with classical digital pathology, involves the assignment of data to different groupings; i.e., diseased vs. healthy, or disease grading. Unlike classical pathology, however, molecular pathology data contain rich spectral information at every pixel and, therefore, classification can be performed on a pixel by pixel basis rather than on whole data or patches, which improves diagnostic accuracy [76]. In addition to providing potentially greater classification accuracy, it can be easier to determine and understand the driving contributors to differentiation by molecular pathology. For example, classification performed on RNA-seq data can not only diagnose a disease, but can determine the driving genomic factors, which could lead to more personalised medicine [77].

These classification methods applied to ex vivo tissue can also be translated to in vivo measurements made during surgeries. For example, Raman microscopy data are used to generate classification models that can be applied to Raman data acquired during endoscopy [78]. Similarly, stimulated Raman histology has been combined with deep neural networks for near-real-time intra-operative brain tumour diagnoses [79]. Mass spectrometry data are used to classify tumour and healthy tissue, which can then be determined during cutting via electrosurgical knife [80].

4.2.5. Validation and Review

The final step in data analysis for molecular pathology, as it currently stands, is to validate methods and review the results. As with AI-based classification in histopathology, one of the main barriers to validation in molecular pathology is access to large volumes of annotated training data. Initiatives to create repositories for these data are ongoing, but will take time to establish. In addition to this, interpretation and review of molecular imaging modalities often requires specific expertise. A future development of these methods is to improve on the translation of information to a clinician.

4.2.6. Metadata in Molecular Pathology

As mentioned, metadata in molecular pathology are additionally challenging. due to the wide number of techniques available and a lack of common variables and data formats. In the field of MSI, the imzML format (an extension of the mass spectrometry mzML) was developed, which captures many aspects of metadata available [81]. More recently, conversion methods were developed to incorporate Raman imaging data into the imzML format as well [82]. For methods that use microscopy-based techniques, such as multiplexed immunohistochemistry, open standards such as DICOM whole-slide imaging or Open Microscopy Environment TIFF can be used [83], and could be implemented in the clinic.

4.3. Barriers to Molecular Pathology

The main barriers to molecular pathology are the need for specific instrumentation and expertise, uptake by pathologists, and validation and acceptance by regulating bodies. The key in using molecular pathology in clinical settings is to first determine the appropriate technique that should be used for a given application. However, since molecular pathology is not standard, there is a lack of knowledge as to what could or should be used in any given situation. Furthermore, most labs may not have access to all of the techniques and, as such, will only use those that are more readily available.

In some cases, when attempting to validate molecular pathology against histopathology, there may be regions that are histologically homogeneous but there may be underlying molecular differences in different regions [39,84]. This means that histology may not always be suitable to validate these methods when they attempt to provide additional information. It is worth noting that, in many cases, performing molecular pathology may not be necessary as classical pathology (especially in a digital workflow) may be much faster and provide adequate diagnosis accuracy. However, in some cases, the incorporation of molecular pathology can improve diagnostic accuracy over classical methods. It is important to determine what the added benefit of molecular pathology would be to a study and select the appropriate methods accordingly.

4.4. Integration of Molecular Pathology with Classical Histopathology

Molecular pathology can offer many benefits over existing methods, such as improved diagnostic accuracy or insight into disease. This does not replace the need for classical histopathology, however. Many of the methods still make use of histological examination, either to make comparisons of molecular information to morphological features [76], or to select for examination [85]. Much, if not all, of the evaluation of diagnostic accuracy of emerging molecular pathology modalities is based upon a comparison with histology, and there is a wealth of information from historical studies and samples using these methods. Integrating these new technologies with histology, and bringing together practitioners of molecular pathology with pathologists, is a vital step in realising the full potential of these methods in a clinical setting.

4.5. Routes to Standards in Molecular Pathology

One of the key requirements for the wider uptake of molecular pathology in clinical settings is the approval of methodologies by regulating bodies. This is underpinned by a fundamental basis of standards that allow quantitative characterisation of performance i.e., diagnosis accuracy, false positive and negative rates, and repeatability and reproducibility. For all laboratory-based methods, assurance procedures should be based on a system of standards, validation, and accreditation. The ISO/IEC 17025:2005 standard specifies general requirements for the competence of testing and calibration laboratories [86], and ISO 15189 sets out standards required for quality and competence in medical, including pathology, laboratories [87]. Initial accreditation of pathology laboratories began three decades ago in the UK [88], as well as in the USA and Canada [89], and is now standard in most practicing clinical pathology laboratories. Initially focused on the need for reliable pathology services for physicians, the current trend towards establishing comprehensive specialty centres, particularly cancer centres, provided a resurgence towards the accreditation of pathology labs to broaden the scope [90]. The development of such specialty centres introduces a greater need for novel diagnostic techniques such as molecular pathology, and, as such, a need to incorporate these techniques into accreditation. Assessing measurement uncertainty is an integral part of laboratory quality valuation because every measurement is subject to some uncertainty, which should be expressed as the quantified doubt about the result of a measurement. Where required, measurement traceability ensures that all steps in a procedure can be queried and validated by reference to documented results, calibrations, and standards, through an unbroken chain of comparisons that all have stated measurement uncertainties. There are many possible sources of uncertainty in digital and molecular pathology, including the sample preparation (e.g., section thickness and artefacts) [91], measuring instrument (e.g., bias, drift, noise), 'imported' uncertainties (e.g., operator skill), computational uncertainty (e.g., performance of classification algorithms with random elements) [92], and the laboratory environment (e.g., temperature and air pressure). Methods for evaluating uncertainty from individual components include uncertainty estimates using statistics (usually from repeated readings), and uncertainty estimates from any other information (e.g., from past experience of the measurements, from calibration certificates, manufacturer's specifications, from calculations, or from published information). As described by Tzankov et al., even current standard pathology has more limited access to certified or validated commercial procedures [90]. This is even more true for molecular pathology, where instrumentation and methodologies are rapidly changing. Such methods are permitted by ISO, provided they are verified (objective evidence that specified requirements are fulfilled), validated (objective evidence, that the requirements for a specific intended use or application are fulfilled), and qualitative (the degree to which a set of inherent characteristics fulfils requirements). In addition to measuring uncertainty in molecular pathology, comprehensive reporting is required to ensure developments adhere to FAIR principles (findable, accessible, interoperable, and reusable) [93]. This requires minimal reporting standards, which are present in some areas but still in development in others [94]. This is particularly challenging in continually evolving fields where the reporting requirements may become obsolete as new developments are made.

5. Conclusions and Future Directions

Digital pathology has the potential to revolutionise the diagnosis and understanding of disease in the near future. While the basis for histological investigation may seem to have not changed much in the last hundred years, there have been dramatic changes recently to digitise the pathological workflow. Future pathology will involve a much greater amount of digitisation, and the next generations of pathologists will have many more computational tools available to them to perform diagnoses. Emerging technologies such as molecular pathology changed the very basis by which pathological analyses are carried out. This is a continually evolving landscape, and although the focus in this article is on techniques that are currently used in clinical settings, there are lots in development and many of which are going through clinical trials. The ability to acquire data from multiple complementary label-free methods will provide powerful new insight in improving online diagnostics during surgery, saving valuable operation time, increasing throughput and precision for a successful operation. Additionally, with the use of AI tools, prognostic models may be created to enhance precise and accurate diagnostics using multidimensional information, and could incorporate new types of grading and staging systems [95]. The core advantage of molecular imaging is that derived information from the technique of interest is not only related to a single condition, but potentially could be associated with multiple pathologies and potentially identify multiple conditions. Standardisation across different platforms is needed to enable access to a wider pool of data that, with the appropriate data tools, may offer more precise diagnostics. This is foundational to future developments in personalised medicine. Further developments in standardisation and regulation will enable more use of molecular pathology in a wider clinical setting. Pathology already looks very different now than it did a decade ago, and it is likely that the future of pathology will look very different in the decades to come.

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