

Review

The future of pathology is digital

J.D. Pallua^{a,*}, A. Brunner^a, B. Zelger^a, M. Schirmer^d, J. Haybaeck^{a,b,c}^a Department of Pathology, Neuropathology and Molecular Pathology, Medical University of Innsbruck, Müllerstraße 44, A-6020, Innsbruck, Austria^b Department of Pathology, Medical Faculty, Otto-von-Guericke University Magdeburg, Leipzigerstrasse 44, D-Magdeburg, Germany^c Diagnostic & Research Center for Molecular BioMedicine, Institute of Pathology, Medical University of Graz, Neue Stiftingtalstrasse 6, A-8010, Graz, Austria^d Department of Internal Medicine, Clinic II, Medical University of Innsbruck, Anichstrasse 35, A-6020, Innsbruck, Austria

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ABSTRACT

Information, archives, and intelligent artificial systems are part of everyday life in modern medicine. They already support medical staff by mapping their workflows with shared availability of cases' referral information, as needed for example, by the pathologist, and this support will be increased in the future even more.

In radiology, established standards define information models, data transmission mechanisms, and workflows. Other disciplines, such as pathology, cardiology, and radiation therapy, now define further demands in addition to these established standards. Pathology may have the highest technical demands on the systems, with very complex workflows, and the digitization of slides generating enormous amounts of data up to Gigabytes per biopsy. This requires enormous amounts of data to be generated per biopsy, up to the gigabyte range.

Digital pathology allows a change from classical histopathological diagnosis with microscopes and glass slides to virtual microscopy on the computer, with multiple tools using artificial intelligence and machine learning to support pathologists in their future work.

1. Introduction

The term “digital pathology” (DP) was first introduced in 1986 by Weinstein [67]. DP is defined as a pathological diagnosis transmitted over a distance, together with specific digital images of micro- and macroscopic preparations, clinical data, and information on cases sent to a pathologist via a data link [37,70]. This system allows both the transfer of images and live video recordings [35]. DP is the integrated use of information technology to assist in the creation, sharing, and exchange of information, including data and images, and to support the complex workflow, which ranges from receipt of study material to submission of the final data. For these purposes, DP requires the development of an infrastructure that enables collaboration between different pathology facilities or health systems by allowing multimodal and multi-level pathology data to be shared by all specialists involved.

In this review, we summarize current developments and aims of DP, considering recent publications on compatible hardware, software, and other applications, as well as current opportunities and limitations of DP.

2. Status quo in the digitalization process of pathology

Technical progress in diagnostic disciplines has enormously

increased during recent years. Unlike laboratory medicine, diagnostics in pathology is very comprehensive. The task of the pathologist is to identify characteristics and patterns of cells and tissues for pathological changes, with the microscope still considered to be the gold standard. For the pathologist's diagnosis and classification, assessment of morphology and characteristic changes at the molecular level of the patient's sample are essential - with important consequences for the following therapeutic decisions. Also, preparation strongly depends on the material examined, including body fluids and small biopsies, as well as complex surgical specimens and amputates. Therefore, automation in pathology primarily focuses on specific aspects of pre-analytic and analytic sample processing and staining, respectively.

The knowledge of tissue selection (macroscopic), preparation of microscopic sections (paraffin sections / frozen sections), and the final pathological diagnosis and classification are achievements made by skilled laboratory and medical personnel [23]. Today, the pathologist's assessment is based on the histological patterns as well as cell counting. Therefore, computer-generated tumor grading should not and cannot replace human expertise. For specific prespecified purposes, however, computers can fulfill the same task more objectively [4] and more rapidly. Computer algorithms can help pathologists to screen the sample for predefined morphological findings and to assess samples more precisely using established scores, thus reducing the differences

* Corresponding author.

E-mail address: johannes.pallua@i-med.ac.at (J.D. Pallua).

between the experts' assessments – to make pathology more comparable worldwide.

DP could also help in the scientific exchange with colleagues in multidisciplinary tumor board (MTB) conferences. The mentioned conferences represent a multidisciplinary approach to the care of cancer patients, which is commonly incorporated in academic institutions. MTBs are formal, regularly-scheduled meetings of specialized medical oncologists, radiation oncologists, surgeons, radiologists, and pathologists devoted to the care of cancer patients. These teams then review patients diagnosed with cancer, patients at high risk for cancer or patients with complex management questions, discuss diagnosis, and formulate management plans using an evidence-based approach [45,46]. It could be demonstrated that MTBs improve diagnostic accuracy, adherence to clinical practice guidelines, and some clinical outcomes [44].

Future DP-related advantages for the patients are obvious: As cancer and other therapies are becoming more and more personalized, DP allows the pathologist to consult specialists within seconds. As more sophisticated pathological diagnoses can be made earlier, the appropriate treatment can be started at an early stage of the disease. However, DP has not yet caught on in routine pathological diagnostics, and the process of digitization poses new challenges to pathology. Light microscopy is still considered the gold standard in pathology. It can only be speculated that the high costs for necessary infrastructure with rapid scanners, large storage spaces, and full integration in medical information systems are the main reasons. Also, it is necessary to standardize the scanner systems, image processing systems, image formats, as well as the interfaces of virtual microscopy with pathology and clinical information systems, or the integration of molecular pathology subsystems.

At present, whole slide imaging (WSI) is introduced in routine pathology departments. WSI means that prepared biopsies of tissue samples and cytological preparations are scanned, digitized, and displayed [47]. When several layers of a sample are imaged, even the spatial dimension of a sample becomes visible. Thus, the pathologist's evaluation quality is comparable to that of a modern microscope. The "virtual" microscope simply replaces the conventional microscope. Both methods have been compared in several studies [3,9,38,53,54], indicating that WSI can be considered as an equivalent to the conventional microscope and as a gold standard. As a consequence, WSIs facilitate remote primary diagnosis, teleconsultation, improved workload efficiency and balancing, collaborations with sub-specialists, and allows central clinical trial reviews, development of artificial image analyses, practical education, and lead to other innovative research perspectives [27,47].

However, WSI still raises only modest interest, mainly due to regulatory data security, technical challenges, and increased non-personal costs [21]. So, although DP is faster, it is associated with higher expenditure than conventional pathology, at least in the initial implementation phase. Nevertheless, digitalization is progressing and will lead to new working methods in modern pathology. More and more pathologists can use high-performance systems to scan tissue sections and analyze them on a screen.

3. Influence of digitization on pathology in Austria

In Austria, 299 specialists actively practice pathology, most of them at the age of around 58 years. Thus, in 10 years, 48 percent of all active pathologists will reach the age of retirement. Since there are hardly any young pathologists, these retirements will not be compensated easily. However, the need for pathologists is growing due to the progressively more complex examinations and the increasing importance of personalized therapies. Even today, the 144 apprenticeship training positions for pathologists approved by the Medical Association and the Ministry of Health cannot be filled according to the old training regulations (see also Table 1) [8].

Table 1
Apprenticeship training position listed by province.

Province	Approved apprenticeship training positions	Occupied apprenticeship training positions
Burgenland	3	0
Carinthia	6	0
Lower Austria	15	6
Upper Austria	17	6
Salzburg	6	3
Styria	36	8
Tyrol	6	0
Vorarlberg	4	2
Vienna	51	12

Therefore, it is necessary to make pathology more attractive and to give young pathologists an understanding of this discipline. One possibility could be the digitization of histological slides with potential further developments of supporting tools to be used by the younger generation. These tools have to present detailed information about disease processes, which is essential for both clinical diagnosis and medical research. Advances in the processing of large volumes of data now make it possible to systematically standardize digital information from complex images of tissue sections and clinical disease courses. In the future, this should make it possible to utilize a previously unexplored source of information from histological sections generated within the framework of pathological research, diagnostics and medical teaching [4,23].

4. Purposes and aims of Digital Pathology (DP)

DP promises an extension of the traditional light microscopy. Traditionally, glass slides must be physically brought from the laboratory to the pathologist; the light microscope is then used for one single slide to be investigated by the pathologist. This single-view could change fundamentally using WSI. Glass slides are then scanned in the laboratory, and WSIs are immediately available without using the usual transport routes. Virtual microscopy and deciding about the diagnosis takes place on the screen, even with simultaneous assessment of several slides [22]. The daily routine will thus be facilitated:

Advantages of diagnosis and classification:

- Improved standardization and optimization of microscopic methods
- A simultaneous and rapid examination of several regions and several staining procedures in any magnification
- Simplification of morphological findings through digital tools, such as annotations, measurements, and counts
- Support of the assessment process by certified digital quantification of diagnostic and predictive markers and use of other validated artificial intelligence applications, classification systems, and other decision aids
- Provision of detailed clinical information, including clinical, morphological and radiological details in one data-set, thus assuring the submission of full patients' records to the pathologist (on request)

Organizational advantages:

- Support of accreditation processes
- Digital archiving: easy and fast access to WSIs in the digital archive
- Error-free allocation of slice preparations provide higher patient safety
- Location independence: consultation with other pathologists around the world - faster and easier network cooperations between pathologists, especially in areas with few specialists available
- Spatially and temporally more flexible job opportunities (home office)

- Optional development of new artificial intelligence applications for the analysis of existing image archives, classification systems for diagnostics, research, teaching, and other new decision aids

At present, the main areas of application of diagnostic DP are intraoperative frozen sections and consultations of a colleague [14,16,36,51,52,69]. Teleconsultation is suitable for the technically simple transmission of digitized image sections of a histological specimen by e-mail, providing a safe data-transfer. The implementation of intraoperative frozen sections for diagnosis requires a more sophisticated technical and organizational approach [68]. At least, a remotely controllable microscope equipped with a digital video camera and an online data connection is required to transmit a live video stream [71]. A telepathology system consists of a personal computer, a remotely controllable telemicroscope with an attached digital camera, and an optional macroscopic workstation with a video camera.

Future applications are already under discussion and are likely to go far beyond the points mentioned above [12]. In particular, quantification of biomarkers and the tedious search for diagnostically relevant and representative tumor areas can be automated by computer programs. Specific patterns are recognized and stored to support and accelerate the pathologists' work. Machine learning approaches designed for comparing other samples with the same histological pattern will allow more precise decision-making.

In brief, it can be anticipated that the new possibilities and advantages of DP will enable pathologists to solve tedious and repetitive tasks much more efficiently [40]. However, it is essential to note that digitalization can support but definitely not replace the pathologists' knowledge. The pathologists' expertise, in combination with the technical advances of DP, including artificial intelligence and machine learning tools, will then provide the best diagnostic accuracy, thus supporting correct clinical decisions in the future.

The applications of digital images in DP are manifold and can be subdivided into three major categories: clinical services, education/teaching, and research [17].

4.1. Clinical routine services

A rapidly growing area in pathology is the integration of WSI for clinical diagnostic and consultation purposes [17]. This applies to the primary diagnosis, frozen section consultations [6,11,56] and second opinion consultations for challenging cases [5,31]. By using automatic image analysis tools, pathologists could be supported for complex routine activities, such as cell count. The use of DP should also help to accelerate the creation of pathological reports. Standardized, structured

reports can accelerate and even improve communication and cooperation between various institutions involved in the patient's treatment. Additional clinical procedures include quality assurance, data retrieval/electronic medical records, and autopsy reports [17].

The main obstacle to applying automatic image analysis tools in routine pathology is the lack of digitalization. However, even if digital images are available, vast amounts of data have to be processed (even much more than in radiology). It has already been shown that the use of digital images will probably prevail in the long term. Even the problem of large data volumes can already be solved by multi-resolution approaches and the ever-increasing computing power.

Although legal and safety issues have to be considered and may increase administrative efforts, it can be anticipated that quality and research issues become easier using DP.

4.2. Digital Pathology for teaching purposes

The collection and integration of WSI can be used as an essential teaching tool. Collections then contain typical phenomena and unusual, novel cases. Such an extensive image collection will be useful for academic pathology. Digital microscopic images should make students independent of microscopes and glass slides. Furthermore, images can be extracted from the databank for conference presentations, for scientific publications, self-study, and continuing medical education purposes [17].

4.3. Research agenda in digital pathology

The fields for the possible use of automatic image analysis tools in DP are multiple and diverse, although most of them are not yet considered as research priorities. Automatic image analysis can already quantify phenomena that a pathologist can only describe using qualitative statements. With the help of image analysis, new and clinically relevant, predefined limits could be determined more precisely even in clinical routine.

More and more research projects integrate digital slides into tissue microarray (TMA) databases [29,32,43]. Other research areas include biomarker testing with immunohistochemistry, immunofluorescence, or fluorescence in situ hybridization (FISH) [10,28,64].

5. Technical issues in digital pathology

DP enables the responsible processing of a microscopic slide over any distance, provided that both sites are equipped with the appropriate technical facilities. DP requires the generation, distribution and

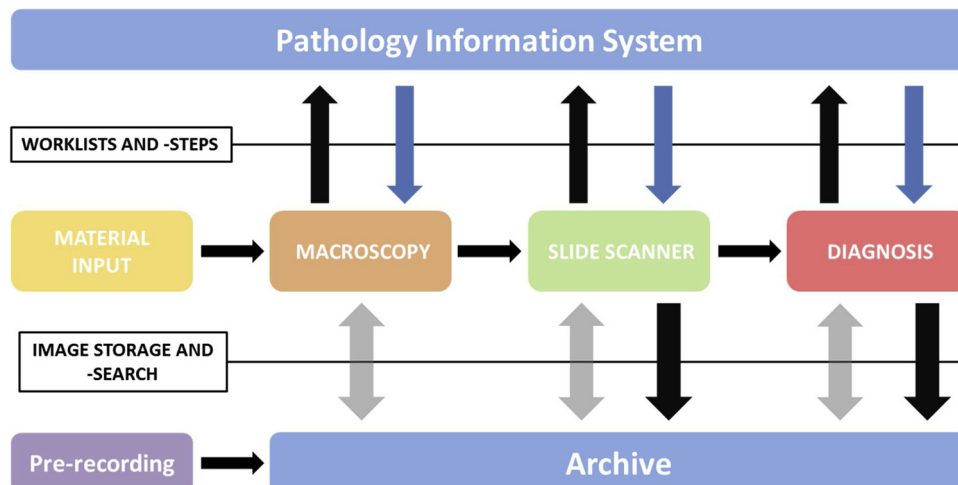


Fig. 1. Functional diagram of necessary technical layers with information and data flows in DP.

Table 2
System Goals of Digital Pathology.

System	Tasks	Aims
Pathology information system	Support for complete work processes	Reduction of administrative work and improvement of work processes
Material-management / documentation subsystem	Case creation, image and document capture	Improvement and organization of documentation
Microscopy subsystem	Microscopic findings	Digital capture, distribution, display of slides
Diagnostic subsystem	Case-based presentation and editing of all image and case information	Fully digital visualization, assessment, and observation of information available on a case
Archive	Digital case-based archiving	Organization and distribution of all images and information

archivation of large images like WSIs, as well as the digital processing of the pathological workflow in the form of a distributed system with components and interfaces for many different situations. An overview is outlined in Fig. 1.

5.1. Pathological information systems and issues on data storage

A pathological information system is designed to manage case-oriented objects and procedures, material usage, and documentation of work steps, which have to be integrated into DP, as summarized in Table 2.

By using digital image processing, even small pathologies can reduce the efforts necessary to document material input and macroscopy. This requires a robust and straightforward image capture and archiving. Requirements for image processing are so high that they can currently only be met by federal institutions, such as university departments, partly by integrating already existing infrastructure. However, this will become more profitable as more options for storage and network resources are available. It appears that the benefits of virtual microscopy for consultation and medical training are significant enough to justify the effort, even if only a fraction of the cases are entirely processed digitally.

5.2. The scanning process - crucial for the quality of reproducibility

Further insights into DP are possible by the advances made in information technology [68,71]. Today several models of scanners are available, differentiating between high-volume and low-volume scanning systems (as examples outlined in Table 3).

5.3. Whole slide imaging as a prerequisite for Digital Pathology

WSI's means that the entire slide is scanned to be then available in a digital archive. Consequently, a simultaneous and rapid examination of several regions and several staining procedures in any magnification is possible (see Figs. 2 and 3). Access to the image data can be achieved using imaging software, which also allows access from a different workplace. The use of a standardized form guarantees this image distribution. Access to image data becomes more efficient as the

mechanical control of the microscope is eliminated. The conventional microscope is replaced by its virtual counterpart, which allows several parties to have access to the same preparations. Access is also possible at any time because the specimen can be examined without a microscope.

WSI has decisive advantages: Instead of photographing the specific regions, the entire slides are digitized. This is the basis for creating a data archive. The original slides are, therefore no longer necessary. Regions of interest can be viewed without placing the slide under the microscope, and simultaneous presentations can easily compare different slide scans. If a server-side image distribution is used for vendor-independent protocols, then the client-side does not need any special software, which broadens the range of users practically without limitations, thus combining the advantages of static and interactive telepathology. WSI also offers new possibilities, such as the linkage of diagnosis data and image content in structured form or the constant availability for automated image analysis [1,47,68].

6. Analytical approaches

A variety of different approaches for digital image analysis have emerged, which are suitable for medical questions with prespecified objectives. A successful analysis depends on (a) the staining, (b) the scanning technology and (c) the image analysis. Various questions have to be answered to select the right method.

- How many and what (structure, biomarker, etc.) will be analyzed?
- What is the spatial expression profile?
- How many samples will be analyzed?
- Which staining strategy and which image evaluation strategy should be used?

These criteria primarily relate to the question of statistical significance which is expected for the sample under investigation. Analyses in DP are only irregularly in clinical use and currently used more in research. In clinical studies, such analyses are already applied with the aim of a quantitative, objective recording of immunopathological parameters. There is a general procedure for these evaluations, but individual processing steps are not enough automated

Table 3
Scanning systems for Whole Slide Images, grouped according to their scanning capacity (in alphabetical order).

Low volume (2 – 6 slides)	Medium volume (10 – 60 slides)	High volume (> 100 slides)
PreciPoint (M8)	Motic (EasyScan)	Huron (TissueScope LE120)
Objective Imaging (Glissando)	Hamamatsu (Nanozoomer S60)	OpraScan (OS-FCL)
Mikroscan (SL5)	3DHistech (Panoramic MIDI)	Leica (Aperio AT2)
Sakura (VisionTek M6)	Huron (TissueScope LE)	3D Histech (Panoramic 1000)
Leica (Aperio LV1)		Philips (UltraFast)
Hamamatsu (Nanozoomer SQ)		Hamamatsu (Nanozoomer S210)
Roche (Ventana DP 200)		Roche (iScan HT) Olympus (VS120)
3DHistech (Panoramic Desk II)		
Huron (TissueScope PE)		
Motic (EasyScan)		
Grundium (Ocus)		

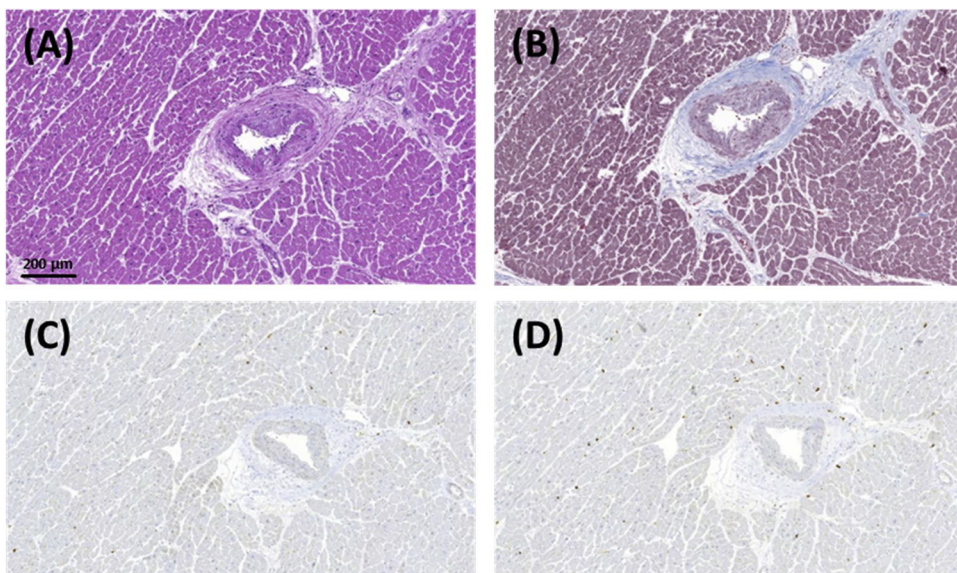


Fig. 2. Region of interest of a WSI scanned myocardial tissue section affected by myocarditis. Image captured using a whole slide scanner Olympus V120. Digitized at 20-fold resolution and displayed at a 5-fold resolution. Tissues are stained with (A) HE and (B) Trichrome, as well as immunostained with (C) anti-CD3- and (D) anti-CD45-antibodies.

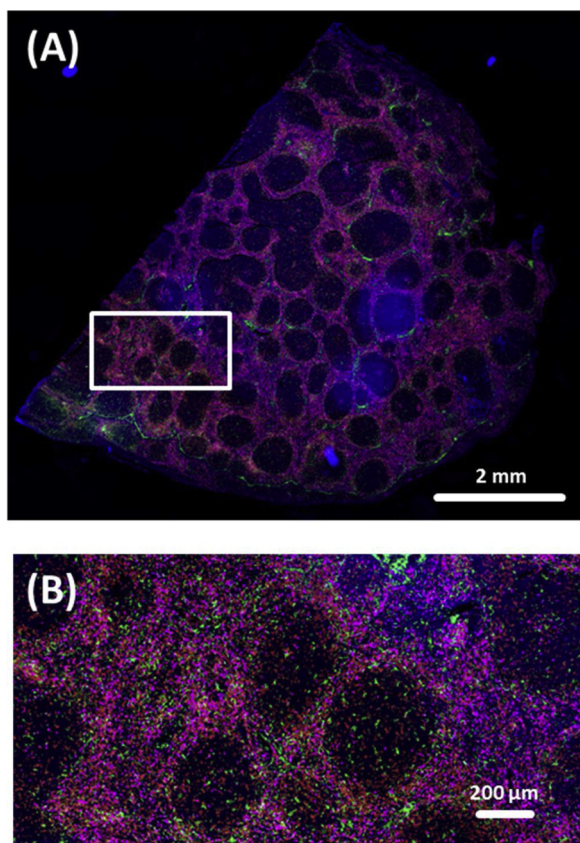


Fig. 3. Example of WSI of a follicular lymphoma tissue section with a multiplex Staining for CD3, CD8 and PDL1 using a whole slide scanner Olympus V120, digitized at 20-fold resolution. (A) whole-slide (B) inlet at a 5-fold resolution.

to handle extensive studies effectively.

Most algorithms in DP are so-called classifiers for one of two rough analysis steps. Classifiers assign a specific object class to an image region or a cell. Classification of the image regions is called image segmentation. This step can also be done by manual drawing. In the segmentation step, the tissue is first recognized, tumors are annotated and then spatially divided. Fully automatic segmentation algorithms are available.

6.1. Computer-assisted diagnosis (CAD)

CAD refers to technical procedures using computer algorithms to assist medical diagnoses. During the past 25 years, CAD has evolved into a frequently used research tool and has meanwhile been implemented in many clinical practices for various imaging techniques, such as mammography, radiography, computed tomography, and magnetic resonance imaging [13,39,50,60]. CAD is becoming one of the major research areas in medical imaging and has been the inspiration for significant advances in many areas, such as image processing, machine learning, user interfaces, and clinical systems integration.

Within histopathology, CAD systems are applied more frequently [7,48,62,73], helping pathologists to find pathological changes. One of the aims is to replace the second evaluation of an additional expert. Currently, such a second evaluation is made whenever the number of false-positive test results has to be minimized, for example, in the case of malignant neoplasms. Replacement of the second opinion by a CAD system is especially crucial for mass examinations, such as cytopathology. Given the high number of cases, it is difficult to find enough experts for a second opinion. Also, patients usually have to wait longer for the result, especially if the two reviewers work in different places.

Usually, histological images are more challenging to handle than radiological images. Histological images contain large numbers of different cells that form a variety of different structures. Therefore, the manual interpretation of histological images is time-consuming and requires a lot of skill and experience. Identifying specific histological structures is one of the prerequisites for cancer grading. Quantitative and qualitative data regarding the presence, extent, size, and shape of structures, such as cell membranes, cytoplasm or nuclei, can be essential indicators for treatment prediction and prognosis.

Studies have demonstrated that the use of a microscope for interpretation and scoring of stained specimens is both labor-intensive and also a highly visual and subjective process [2,57,58]. Despite efforts achieved in standardizing the scoring processes, the inter- and intra-observer reproducibility of histopathological scoring by pathologists is not optimal [30,61,63,66]. Also, with the increasing importance of molecular biomarkers, quantitative studies are somewhat limited to the practical limitations involved in traditional microscopy. The use of computer-assisted analysis of histological images seems to promise a simplification of the workflow, because of automation and consistent interpretation [18,24,49].

The combination of computational power, high-quality digital cameras, and WSI scanners, together with the improvement of image

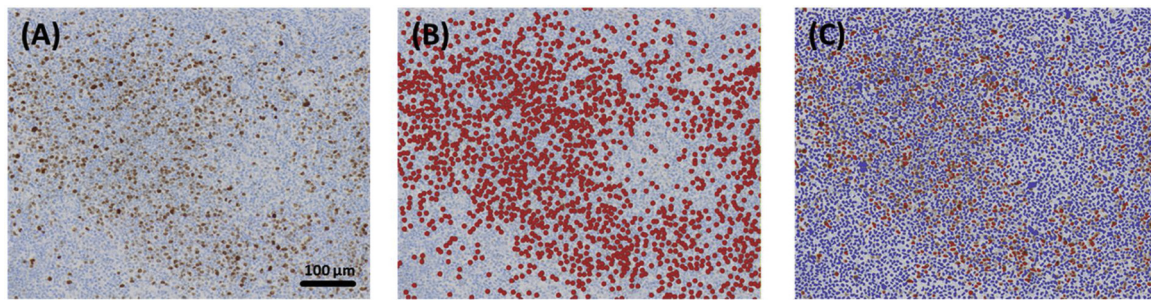


Fig. 4. Example of the resulting image from a free web application (ImageJ, Qupath) for automated image analysis of Ki67 immunohistochemically stained and digitally scanned follicular lymphoma tissue section. (A) the original image, (B) pseudo-colored image shows the segmented staining component for Ki67 (red) and (C) pseudo-colored image shows the segmented staining components for Ki67 (red) and hematoxylin (blue).

analytical algorithms during the last decade, has allowed the development of many powerful computer-assisted approaches to histological data [19,47,48]. The new methods offer not only a successful and robust quantification of protein expression but also objectivity and reproducibility [26,33,55,65]. Currently, most algorithms include all of the pattern recognition procedures, texture analysis, densitometry, and digital signal processing that compare and analyze patterns, as well as colors of the pixels making up the image.

Algorithms are now simple enough to run on standard laptops or desktop computers. Modern software distinguishes between tumor and non-tumor tissue, requires relatively few manual commands before analysis, and presents the data in a quick, systematic, and comprehensible way [25,41,42]. Costs range from free open source-solutions where users can add, change, and develop new applications (e.g., ImageJ, Fiji, Qupath, Cell profiler, Ilastik, Orbit, Icy, Cytomine) to advanced licensed software (see Fig. 4).

For example, quantitative histomorphometry (QH) is a rapidly growing field that aims at introducing advanced image analytics into the histopathological workflow. QH is the conversion of a digitized histopathology slide into a series of quantitative measurements of tumor morphology and is tightly coupled with the first steps of DP [72]. Early applications of quantitative DP required necessary measurements, such as cell count, object size measurement, and light absorption characteristics [34]. QH is starting to gain popularity in clinical practice but is often limited to identifying the extent of staining in IHC-stained images. Routine hematoxylin and eosin (H & E) staining accounts for the vast majority of histopathology studies, but the development of robust QH tools for large-scale diagnostic and prognostic analysis of H & E images has proven to be difficult [41].

A major limitation is that available software still has to be adapted to the different file formats as each manufacturer of scanners tends to use his unique image compression standard. Furthermore, the software is not widely accessible to the pathology community. As a consequence, software solutions are either complicated and challenging for their users, or poorly supported by the companies. Moreover, users of advanced image analysis software often have to make a compromise between simplicity of use and flexibility for diverse and complex research applications. Optimized, validated, and certified digital image analysis techniques should then be available and incorporated into the daily workflow of pathologists and researchers.

6.2. Artificial intelligence going into routine work

DP can be considered as one of the pioneers of applied artificial intelligence (AI). In particular, multilayer neural networks are on the way to routine as diagnostic assistance systems. An obstacle to overcome is the black box character of the algorithms; this black box does not allow easy understanding of the predictions and is therefore met with skepticism among medical professionals. Apart from this, AI enables simple, efficient as well as robust pattern recognition. An essential

distinction is made between two approaches:

- **knowledge-based systems** the knowledge is entered explicitly by experts
- **self-learning systems:** the knowledge is trained using sample data sets

AI has great potential as a data-driven DP approach. Indeed, the use of AI in DP is referred to as the third major revolution in pathology after the introduction of immunohistochemistry in the 1980s and molecular pathology in the 1990s [59]. Researchers have already demonstrated the potential of this technology for the automation of diagnostic tasks [15]. The ability and robustness of AI depend on the amount of underlying data, which is still minimal. In order to get broadly applicable classifiers for specific questions, databases must now be built up. This is currently done mainly in isolated initiatives and there are hardly any standardized approaches. This complicates the standardization of diagnostic and therapy standards [20]. An important step for DP standardization was achieved by the creation of a guide for DP from the Association of German Pathologists [27].

Overall, it is highly unlikely that any kind of AI will replace pathologists in the foreseeable future. Software and hardware developments have made rapid progress in recent years and first applications in pathology are being tested, but they cover only a fraction of this highly complex field of pathology. As noted above, current AI strategies primarily depend on a large number of high-quality and annotated training examples. For rare entities, it is questionable whether there will ever be enough annotated training examples to achieve the accuracy values required for diagnosis. Even the already existing image data in digital form are not available for broad use yet.

Moreover, even if the digitization of the pathological examination material is being massively promoted, only a fraction of the histological data produced daily in pathologies worldwide are then available as digital images in the near future. So it is likely that AI will not diagnose alone, but simultaneously with the pathologists, e.g., as part of a so-called clinical decision support system. Particularly in view of an expected shortage of qualified specialist personnel and at the same time a rather increase of workload with higher numbers of examinations in the future, the developments of DP should be recognized as an important opportunity.

Before DP can ever independently generate and release a finding, a crucial question must be answered: What happens if this finding is incorrect? Precisely these medical-legal aspects may represent an insurmountable hurdle for an autonomous diagnosis based on AI. Last but not least, the patient's wishes also count. It remains to be seen whom they trust more: a computer or their pathologist.

7. Outlook and future perspectives

DP will open up new possibilities. Differentiated work processes of

DP with real-time integration in existing clinical infrastructures will allow a practical and widely accepted implementation of DP based on international standards. Telemedical applications of DP, automated image evaluations, or three-dimensional views are developed and will be validated for specific purposes. It can be anticipated that patient care will benefit as much as medical education - directly and indirectly.

8. Summary

Clinical pathology applies histological, immunohistological, and molecular techniques, and all of these can be simultaneously presented to the pathologists after digitization. Depending on the specimen and the scanner, large amounts of data are generated and need proper storage. Since the microscopic resolution is very demanding, WSI occupies even more storage space than needed in radiology.

While digitization in pathology is currently less common and still less standardized than in some other areas of medicine, the development of advanced CAD-based applications will provide tremendous potential for cost-saving measures through increased efficiency and patient safety. Integration of images and results in larger information systems is not yet standard, but will significantly contribute to the acceptance of digital pathology as part of the clinical workup.

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