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Visualization of Histopathological Decision Making Using a Roadbook Metaphor

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***Abstract*—Since pathology is supported by information technology new opportunities and questions have arisen. The digital age enables analyzing histopathological data with artificial intelligence methods to reveal further information and correlations. In this paper existing approaches to visualization of medical decision processes are presented as well as the relevance of explainability in decision making. The first step for implementing decision-paths in systems is to retrace an experienced pathologist's diagnosis finding process. Recording a route through a landscape composed of human tissue in terms of a roadbook is one possible approach to collect information on how diagnoses are found.**

Choosing the roadbook metaphor provides a simple schema, that holds basic directions enriched with metadata regarding landmarks on a rally - in the context of pathology such landmarks provide information on the decision finding process.

***Index Terms*—explainability, artificial intelligence, medical decision vizualisation, digital pathology roadbook**

I. Introduction

Being able to automatically describe the process of what pathologists use as *relevant* information in medical decision making is a challenging task, however it will have enormous impact in the future, for instance in the development of urgently needed novel user interfaces for digital pathology [1] [2], in the development of explainable AI solutions [3] and in the development of sophisticated educational tools and e-learning systems.

Modern pathology was founded by Rudolf Virchow (1821-1902) in the mid of the 19th century. In his collection of lectures on Cellular Pathology (1858) he set the basis of modern medical science and established the "microscopic thinking" still applied today by every pathologist.

According to [4] in pathology routine microscopy work the level of expertise corresponds with differences in search, perception, and reasoning components of the tasks; several discrete steps occur on the path to competence and encompasses a) appropriate search strategies, b) rapid recognition of anatomic locations, c) acquisition of visual data interpretation skills, and d) transitory reliance on explicit feature identification. Astonishingly little is known about human factors influencing the cognitive skills of pathologists - contrary to radiologists [5].

In histopathology a biopsy or surgical specimen is examined by a pathologist, after the specimen has been processed and histological sections have been placed onto glass slides and in cytopathology either free cells (fluids) or tissue microfragments are "smeared" on a slide without cutting a tissue.

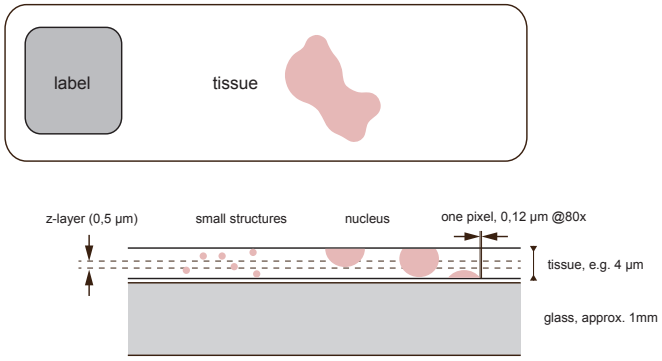

Fig. 1. Schematic view of a histopathological slide, when scanned a pixel represents 0.125 1.55 µm at the highest resolution (80x)

Pathology today allows storing and processing slides as digital images which lays the foundation for digital pathology. The analysis of histological sections is now supported by information technology via e.g. high-resolution slide scanners as well as computer vision techniques and image analysis software to detect conspicuous mutation in tissue samples. The discipline digital pathology brings challenges, like the density of the scanned whole slide images (WSI), and opportunities, like putting data in new contexts [6]. Digital data facilitates

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re-combining, annotating and enriching image-data. Primarily to support the pathologists making diagnosis based upon that additional information. The next logical step is annotating the available image data with data of the diagnosis process by tracking a pathologist's steps and findings. By analysing examination methods and visualization of a professional's tour through a slide, ongoing pathologists are able to trace a "learning path" and machines might learn from other's experiences.

II. Related Work

A. Visualization of Electronic Health Records

A comprehensive overview on visualization methods for electronic health records and temporal patient data was done by Aigner and Miksch [7], including an analysis of graphical patient record summary by Powsner [8], time lines and life lines by Plaisant [9]. A glyph based visualization of patient records based on ICD10 classification was developed by Müller et al. [10] "AnamneVis" [11] is a framework for the visualization of patient history and medical diagnostics chains, which is based on patient's detailed anamnesis the physician follows through a medical diagnostics chain that includes requests for further investigation and examinations ending in a report of treatment outcome.

Müller et al. [12] further developed multilevel data glyphs for the visualization of large medical data sets, where the data glyphs provide three levels of detail (semantic zoom) suitable for a different screen space, and a validation of the data variable mapping.

The system AnamneVis represents a patient's past and presents health conditions to be overviewed within a radial sunburst visualization. A stylized body map represents the patient's body and provides detail when zooming into it. The reasoning chain is visualized through multi-stage flow charts enriched with examination data. Devarakonda et al. developed a visualization method based on summarisation of Electronic Medical Records (EMRs) created by Watson analytics, which relates a patient's problem to relevant clinical data [13]. Dabek et al. [14] described methods for aggregating and summarizing of electronic health records. In their approach they integrate analytic models, machine learning summarisation with graphical interfaces. The proposed timeline-based visualization allows easy skimming, jumping through time, filtering and compare different time frames. However, visualization is just the final step in the whole knowledge discovery pipeline, before that it needs a concerted effort of various topics, ranging from data pre-processing, data fusion, data integration and data mapping to interactive visualization [15].

B. Visual Languages

Most of today's human–computer interfaces are based on the visual communication paradigm, which in many aspects is superior to pure textual representation. One reason is that they are often far more convenient to the end-user than textual languages [16]. Otto Neurath developed 1936 the ISOTYPE visualizations method [17] and a large number of attempts to construct communication systems based on symbols have been developed since. For a historic survey of the main approaches in computer based visual language solutions see [18]. When the building blocks (icons, images, animations, graphics) of a visual statement can change and adapt according to the needs of the (human) receiver the user interface gets adaptive [19]. Such interfaces do not exist in isolation, but rather improve their ability to interact by constructing an user model based on the interaction. This brings the problem of adaptive interfaces close to the area of machine learning where the user plays the role of the environment in which the learning occurs and the user model corresponds to the learning knowledge base [20].

In such a scenario the interaction acts as performance task, on which learning should lead to improvements [21]. An innovative approach are Adaptive Visual Symbols (AVS) [22], which consist of an intended denotation coding (the semantics of the message), a set of adaptive visual signs and a method for the analysis of the receiver reactions. In order to achieve the overall goal - congruence between the intended denotation and the constructed denotation at the receiver - the presentation process (rendering, level of detail, presentation speed, additional explanations) can be adapted. The fundamental innovation of an AVS lies in a clear distinction between the semantics of a message and the used visual sign [23].

C. Visualization of Medical Decisions

Visualization and explanation of decision making is a key facilitator for AI algorithms in medical applications, particularly to facilitate transparency and trust [24].

A detailed design, user experience and usability (DUXU) study for NGS applications with a special focus on clinical and diagnostic settings can be found in [25]. The DUXO study evaluates with eye tracking methods [26], [27] a data driven GUI and visualization framework parameterized by (a) the user role and experience and (b) the outcome of the patient counseling and attributes of related medical events. Currently, more and more researchers emphasize the importance of explainability in AI [28].

III. The Process of histopathological decision making

Each histopathological diagnosis starts with a medical question and a corresponding underlying initial hypothesis. The pathologist refines this hypothesis in an iterative process, consequently looking for known patterns in a systematic way in order to confirm, extend or reject his/her initial hypothesis. Unconsciously, the pathologist asks the question *"What is relevant?"* and zooms purposefully into the - according to his/her opinion - essential areas of the cuts. The duration and the error rate in this step vary greatly between inexperienced and experienced pathologists.

Through a precise classification and quantification of selected areas in the sections, the central hypothesis is either clearly confirmed or rejected. In this case, the pathologist has to consider that the entire information of the sections is

no longer taken into account, but only areas relevant to the decision are involved. It is also quite possible that one goes back to the initial hypothesis step by step and changes their strategy or consults another expert, if no statement can be made on the basis of the classifications. Finally the pathologist combines the recognized features to a diagnosis.

The following tables summarize the most relevant concepts in liver pathology and show the logical structure as an ante-hoc explanation [29]. Please note, that for complex findings only the most common alternatives are listed here.

TABLE I
MACROSCOPIC EVALUATION OF THE HISTOLOGICAL SECTION

Concept	**Finding Attributes**
Type, Number, Size of Specimens	Description
Tissue Cohesion of Biopsies	Description
Staining and Staining Quality	H&E, CAB, Sirius Red, Iron, PAS, Immunohsistochemistry
Already visible exogenous tissue (tumor)	Yes, No, Partly

TABLE II
MICROSCOPIC EVALUATION AT LOW MAGNIFICATIONN

Concept	**Finding Attributes**
Lobular Architecture	Preserved, Disturbed, Destroyed
Number of Portal Fields	optimal 10–15 per slide
Liver Cell (hepatocyte) plates	one cell layer, several cell layers
Inflammatory Changes lobular peripheral,lobular central	portal,lobular,combined
Presence or Absence of tissue	Description

IV. VIDEO RECORDING OF MICROSCOPIC EVALUATION

The video of the microscope is captured with a resolution of $4096\,\mathrm{x}2160\,\mathrm{in}$ 60fps. The microscope is equipped with 5 objectives (4x, 10x, 20x, 40x, 60x). For the pathologist working with the ocular directly an additional magnification of 10x is added. The slides are scanned on a 3D-Histech Pannoramic 1000, with a $40\,\mathrm{x}$ objective, $1.6\,\mathrm{x}$ camera adapter and a resolution of $1.25\,\mu\mathrm{m/pixel}$ single layer.

Fig. 2. Setup of the video acquisition

TABLE III
MICROSCOPIC EVALUATION AT HIGHER MAGNIFICATIONN

Concept	**Finding Attributes**
Portal tracts	regular, extended, fibrotic, rounded, edematous
Connective tissue parenchyma border	sharp, unsharp
Parenchymatous border plate	preserved, partially destroyed, mostly destroyed, nonexistent in flammatory, infiltrates portal, periportal interface, sparse, tight, ...
Abnormal content of the portal field	tumourcells, foreignbodies, parasites
Portal vessels	present, expanded, narrowed, inflammatory
Bile ducts	present, elongated, absent, single-layer, multi-layer , polymorphic ...
Ductal reaction	absent, low, pronounced, ductalcholestasis
Lobulus, liver parenchyma	livercells large, balloonized, small-atrophic, anisocytosis, apoptosis
Cytoplasm	granular, net-like, light cytoplasmic glycogen-rich, diffuse homogenized, focally homogenized
Cytoplasmic inclusions	fat large droplet, fat small droplet, lipofuscin granules, siderin granules, Mallory Denk bodies (MDB), bilirubin, ...
Necroses	disseminated, confluent, lobularcentral, lobularperiphery, bridgingporto-central, bridgingcentro- central, massive
Liver cell nuclei	anisocaryosis, pycnosis, punchcores, "sandcores", coreinclusions
Kupffer cells	focally increased (nodular)/diffus increased, enlarged, inclusions
Star cells (stellate cells)	increased, non increased
Central vein lumen	open, narrowed, obliterated, inflamed, wall fibrosis
Fibrosis	portal, perisinusoida, pericellular, perivenular, septal, meshed wire fibrosis, incomplete cirrhosis, cirrhosis, ...

The recorded video is structured into cuts and scenes, where a scene represents a specific event in decision making. The scenes are shown as paragraph and annotated in the "Video Book" viewer [30], see figure 3. The path analysis of the captured video is done by feature extraction of the video's key frames. Each image is compared with the slide image. Template matching has been realized with the open source software library "Open CV", which implements the SURF-algorithm (Speeded-Up Robust Features) for key feature detection, to meet the requirements of variable zoom levels in the video as well as minor changes in orientation. For each key frame the matching picture detail as well as the coordinates within the slide image are stored, to visualize the findings on a web-based GUI. The web front end presents the original video and the corresponding slide image in a new way: based

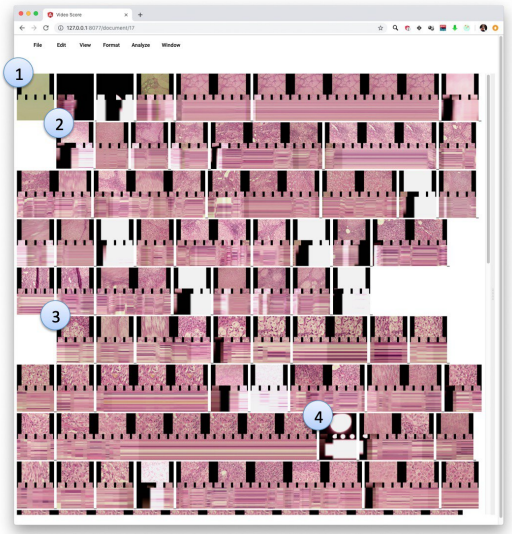

Fig. 3. Structure of a recorded video, each items represents a cut, a paragraph denotes one event in the decision making.

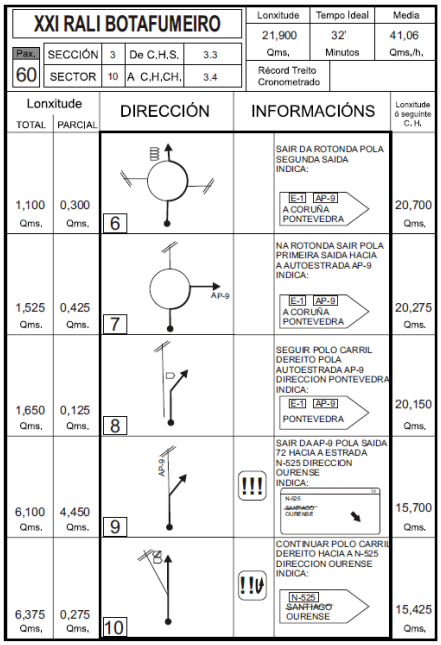

Fig. 5. Example of a roadbooks / pacenotes as used in motorsport [31]

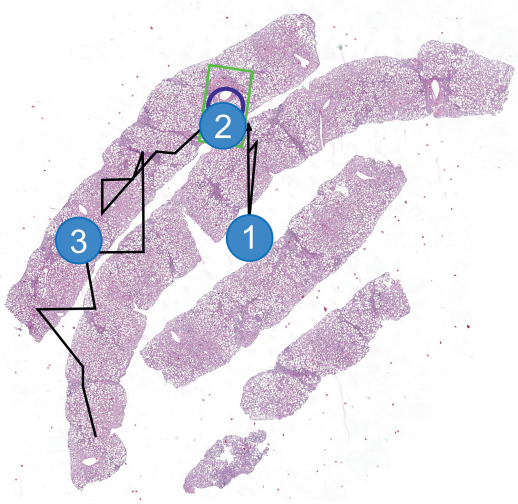

Fig. 4. Path of a pathologist's "navigation" through a slide, blue circles denote the events (one line in the roadbook) the green rectangle illustrates the viewing window at a specific event

on the video position and the visible key frame the template coordinates are highlighted in the slide image as well as a slide snippet.

Additionally, it's possible to overlay a map layer with all template findings on the original slide as well as the path that has been followed by the pathologist. The trace of a pathologist's elaborated searching method within the human tissue landscape is visualized in 3 ways: highlights in the slide image while playing the video, display of the path, cut out picture details chronologically arranged.

V. The "Roadbook Metaphor"

The Greek term "metahpora" can be translated into "transfer" - it refers to a well-known term that is figuratively transferred into a new context to increase traceability and understanding of complex issues. The use of metaphors allows us to apply the comprehension of one area to another field - drawing literally a picture facilitates understanding, representation and therefore communication. Averbukh et. al describe interface metaphor as the basic idea of likening between interactive objects and model objects of the application domain, and visualization metaphors as a map establishing the correspondence between concepts and objects of the application domain under modeling and a system of some similarities and analogies [32]. We chose to use the roadbook metaphor to approach a visualization of implicit knowledge of a pathologist.

Roadbooks or pacenotes are typically used for rallies. They include - besides exact directions referring to the 2nd dimension - information about any peculiarity that might be essential and should be taken into consideration while manoeuvring like radius and severity of curves, changes in the route concerning the 3rd dimension and even temporary challenges due to the weather. This level of detail in combination with a speed event needs an efficient notation that can be read to the driver while a rally. A roadbook allows two people to synchronize their view and navigation exactly within a landscape. While examining a slide a pathologist also navigates through a landscape that is composed of human tissue.

Though there isn't a common standard on how to symbolize a rally path, so called "tulip diagrams" are a wide spread system to note down directions. Those diagrams are composed

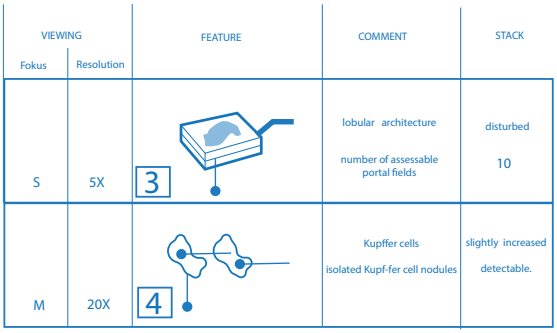

Fig. 6. Structure of an event in histopathological decision making

of simple symbols like lines, arrows and circles to illustrate the actual position and the upcoming direction - chronologically ordered from start to goal. Tulip arrows can be positioned according to a map or turned and related to the navigator's actual position.

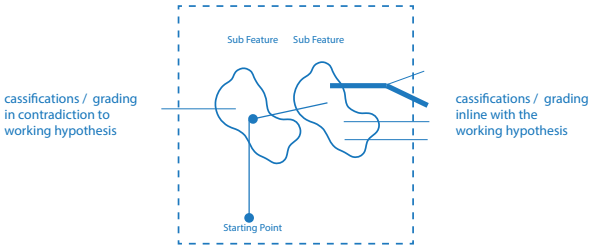

Fig. 7. "Feature Crossing"

VI. Results

We asked an experienced pathologist to record the *relevant* steps when making a diagnosis. A very small portion of the histological sections are shown in figure 4 as illustration. For this specific diagnosis the pathologist gave the following explanation:

- Liver biopsy; plenty of material (length: ~1,5cm; diameter: ~1mm); macroscopically good tissue cohesion.
- The lobular architecture is disturbed.
- The portal fields (numerous, well assessable) are extended and fibrotic.
- The liver cells are arranged properly.
- There is an increase in connective tissue septa, mostly portoportal. Some septa can be found, which enforce the entire biopsy material.
- The portal fields are formed regular. (interlobular bile duct, artery and a branch of vena portae detectable).
- Sharp connective tissue parenchyma border. Only in places individual inflammatory cells (lymphocytes), which spread to the lobular parenchyma in the sense of "spill-over".
- The liver cells are markedly fatty with large droplets.
- The parenchymal fatty degeneration amounts to approx. 60% of the parenchymal area.
- Frequently there are some droplets of fat in the liver parenchyma, which are surrounded by lymphocytes and neutrophil granulocytes. (so-called resorption nodules)
- Kupffer cells are not activated noteworthy.
- The Berliner blue staining is negative.
- The chromotrope aniline blue staining (CAB) shows that fibrosis is initiated. (dynamically interpreted)

For a specific case values of all above features contribute to the diagnosis with different weights and causal relations present in the human model on liver pathology, which an expert acquired by training and experience. Figure 8 shows a presentation of the findings within a histopathological roadbook.

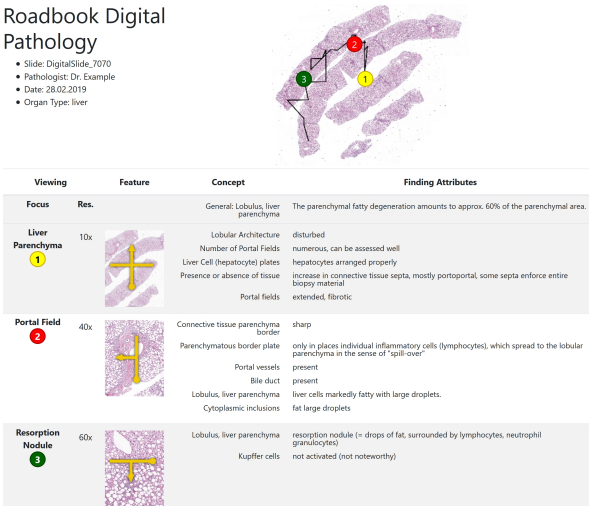

Fig. 8. Roadbook for specific diagnosis; Hematoxylin and Eosin (HE) staining

VII. Summary and Outlook

Our work shows an approach to make human decisions in diagnosis processes visible. A pathologist's microscopic evaluation has been recorded on video and then analyzed. The gathered data of the guided navigation serves as base for creating a roadbook that is usable for a) orientation to other pathologists or students who will learn from other's experiences and b) future AI applications and their traceability. The comprehension on how a decision is made by systems is a vital factor in system verification and further improvement. Capturing human interaction while microscopic examination on a high level of expertise and in detailed steps is a significant resource for the future training of machine learning models when applying our approach to a larger set of video examination documentations.

A further future task will be an interactive version of the roadbook that allows a flight through a whole slide image to illustrate a pathologist's "journey". Getting zoomed immediately into essential areas of a slide will accelerate learning

outcomes and reduces straying in inconspicuous zones. This approach literally meets the proverb "to pick someone's brain" as the interactive roadbook provides a look onto human tissue through someone else's eyes intending to improve the user's inherent pattern recognition.

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