Block-Centric Visualization of Histological Whole Slide Images With Application to Revealing Growth-Patterns of Early Colorectal Adenomas and Aberrant Crypt Foci

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Introduction:

Comfortable navigation through diagnostic images is a prospective challenge for the acceptance of virtual microscopy applications in routine pathology [1],[2]. Tracing different regions of interest through multiple sections on one or several slides is a typical task in diagnostic slide examination (Fig. 1). This laborious and time-consuming co-localization is currently executed by pathologists. Retaining the relative positions of tissue structures while alternating between multiple slides is still not feasible in a satisfactory manner in conventional nor virtual microscopy.

To address this issue we present a more comfortable and intuitive method to read slides using computer-assisted navigation. Furthermore, we demonstrate the strengths of our method by applying it to large series of serial colorectal tissue sections, creating new kinds of visualizations of different adenomatous mucosal architectures in human tissue, while looking for human correlates of lesions recently described in mice[3].

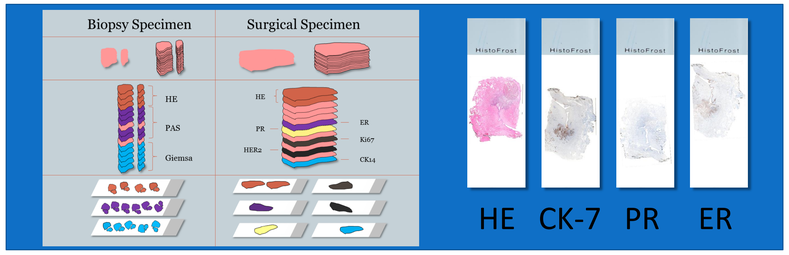

Figure 1: Tissue preparation process using mammary tissue as an example.

Materials and Methods:

Histological images contain multiple distortions from different sources in the laboratory and digitalization process. An interconnection model was created to describe distortions by several layers, providing a normalized tissue representation. Layers were associated with specific distortions with each layer serving as a new level of abstraction. The first layers enabled a coarse alignment of tissue sections. Further alignment is achieved by piece-wise, multi-resolution, SIFT-based [4] correspondence extraction (Fig. 2) and refinement. Inside the convex hull of all fiducial points local affine transformations were applied whereas a global affine transformation was used on the outside.

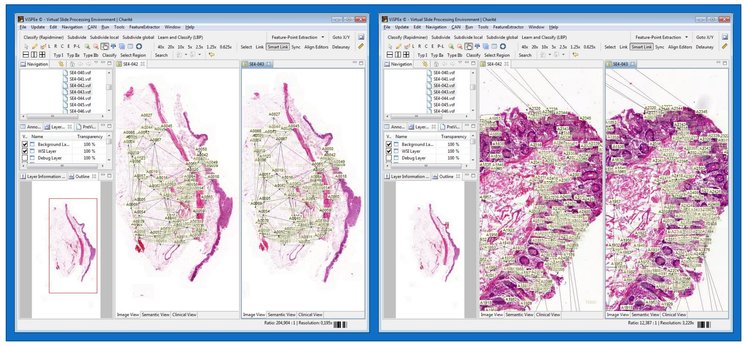

Figure 2: Feature-based, multi-resolution correspondence refinement.

Animated stacks were generated for regions of interest using local rigid transformations to preserve exact morphological coherences. For subsequent creation of 3D models, the relevant histological objects within these images were annotated by a pathologists, partly using computer assisted segmentation based on active contours [5]. These annotations were used subsequently to create simplified 3D models by applying VTK [6].

Results:

The presented methods provide an efficient means to retrieve correspondences and additional spatial information from serial sections of histological slides. They also show good applicability for specimen from different origin. Alignment methods can be applied to generate block-centric visualizations such as parallel (Fig. 3) and transparent (Fig. 4) viewing of multiple stains .

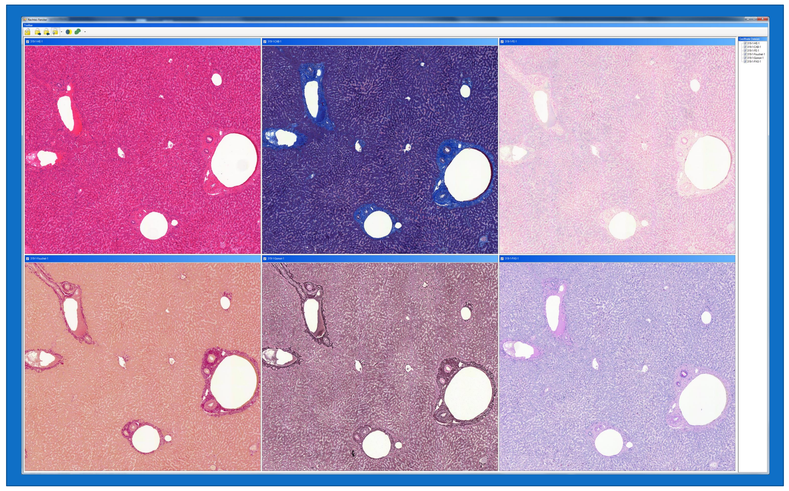

Figure 3: Parallel, block-centric navigation through liver tissue (HE, CAB, FE, Fouchet, Gomori, PAS)

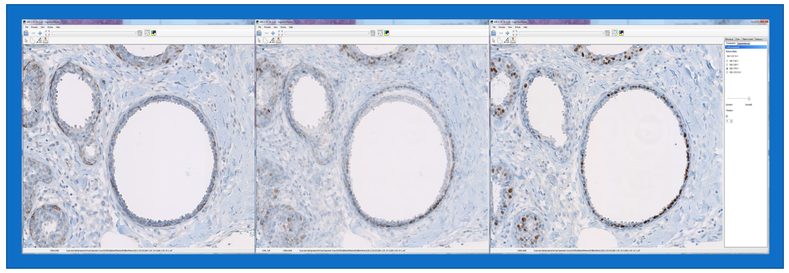

Figure 4: Transparent overlapping of mammary tissue (CK14, CK14 and PR, PR)

Moreover, the generated stack videos and 3D models demonstrate the very good accuracy of section alignment even in large series. The visualizations enable pathologists and researchers to grasp the 3D structural relationships in the tissue at a glance, providing an excellent tool to communicate more complex histomorphological findings. Interestingly, we see two kinds of tubular adenomas, which could imply multiple ways to tubular adenoma formation in FAP-patients, possibly akin to the recent observations in mice [3].

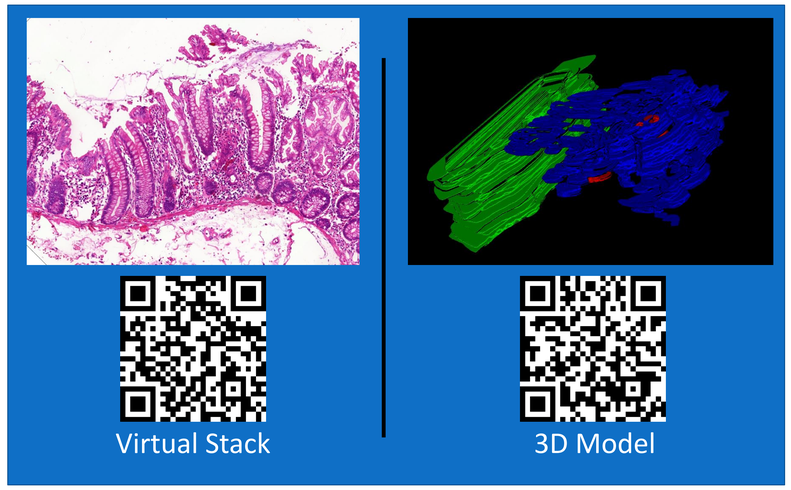

Figure 5: Advanced visualizations to reveal growth patterns of different adenomatous epithelia.

The most important challenges are the time consuming scanning process as well as the creation of contours. In addition, advanced visualizations are susceptible to any artifacts introduced during preparation process such as missing sections, overlap of tissue and inhomogeneous staining.

Conclusions:

Computer-assisted navigation together with advanced visualizations provide an excellent tool to enhance clinical pathology and research. In addition, an automated alignment of serial slides enables pathologists to examine tissue sections of the same block independent of laboratory- and scanner-based linear distortions. These features can facilitate a shift from a slide-centric towards a block-centric perspective in tissue examination.

Acknowledgements:

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