Multi-Biomarker Analysis for Hodgkin Lymphoma using Automatic Registration

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Background. Hodgkin lymphoma (HL) affects 8500 people annually in the United States, which is nearly 10.2% of all lymphoma cases [1]. An accurate and timely diagnosis of HL is critical for an appropriate treatment plan [1]. For the accurate diagnosis, joint analysis of multiple protein expressions and tissue morphology is performed by the pathologists using hematoxylin and eosin (H&E) staining, as well as immunohistochemical biomarkers including CD20, CD30, and Pax5. Currently, pathologists manually examine the co-localized areas across IHC and H&E slides for a final diagnosis [2], which is a tedious and challenging task because of the morphological deformations introduced during slide preparation and also large variations on cell appearance and tissue morphology across different stainings. It is, therefore, an important task to align all the IHC and H&E images for easy and accurate analysis.

Methods. We propose a two-step automatic feature-based cross-staining WSI registration to enable the localization of metastatic foci in the assessment of HL. In the first step, WSI pairs were aligned allowing for translation, rotation, and scaling using affine transformation. The registration was performed automatically by first detecting landmarks in both source and target images, using the scale-invariant image transform (SIFT), followed by the fast sample consensus (FSC) protocol for finding point correspondences and finally aligned the images [3]. In the second step, rigidly aligned source and target images are vertically divided into three sections to get the landmarks evenly distributed over the tissue region. These automatically detected landmarks are then used as the control points for non-rigid transformation using local weight mean (LWM) transformation.

Results. For evaluation, we used 47 pairs of images registered automatically, and manually to compare the performance of the proposed system. The images were acquired from the Grand River Hospital, Ontario Canada. The specimens are taken from different parts of the body. Jaccard similarity index for each manual and automatically registered pair is calculated to evaluate the proposed system. Average Jaccard similarity index for 47 pairs was 0.92. Moreover, few registered samples from the data are shown in Fig. 1.

Conclusion. Multi-protein cross-stain analysis is pivotal for disease diagnosis such as HL for suitable prognosis. For this, we propose a fully automatic and accurate stain registration method to align IHC biomarkers with H&E for an accurate diagnosis.

References:

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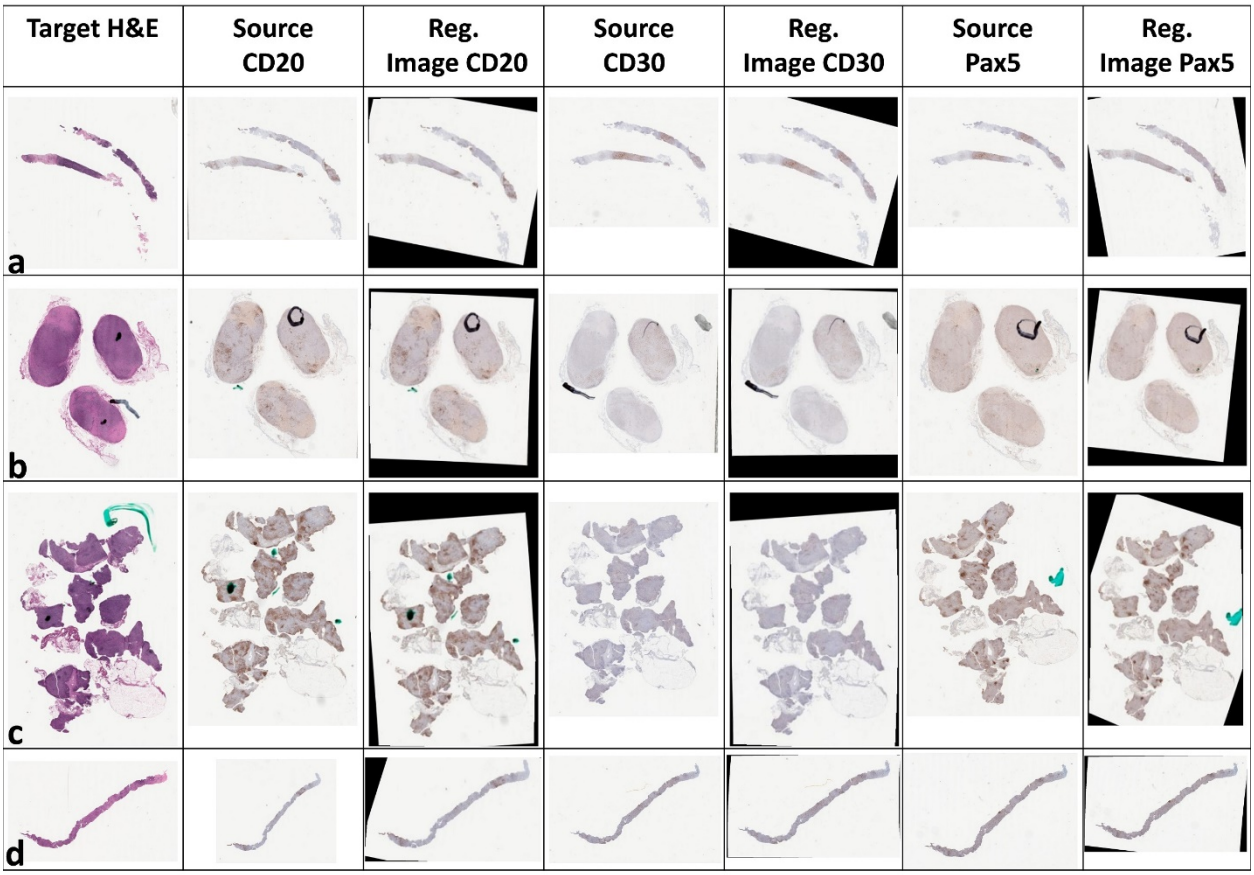

Figure 1 Illustrates few examples of registered biomarkers according to the target H&E Image.