Just In Time Pattern Recognition Image Analysis (PRIA) Morphology Recommendation Transfer Among Specialists

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Research Report

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ROI viewing patterns vary significantly among pathologists. The viewing is guided by the pathologist's experience that the disease state morphologies are likely to be visually identified. We present a reliable method which learns to assist identifying disease relevant ROIs, based on information available in such viewing patterns. Our approach enables accumulating learned morphologies into dictionaries and organizing them into atlases. The ability to learn such atlases from scratch following an installation, eliminates the need to support a vast range of calibrations and clinical settings. Such atlases can be automatically consulted to transfer this knowledge into ROI recommendations, thus reducing the probability of errors through collaboration. Ultimately, these atlases facilitate dramatically improving patient care.

1 INTRODUCTION

ROI viewing patterns exhibit low concordance among pathologists, per Ezgi *et al*, 2016 [1]. The viewing is guided by the experience of the pathologist focusing on areas with higher likelihood that disease state morphologies may be visually identified. Due to the low concordance of viewing patterns, combining the experience of multiple pathologists, through collaboration, may reduce error rates exponentially. As observed by Halabi et al 2018 [2], significant error reduction can be achieved through collaboration of radiologists, due to dramatically reduced probability that independent specialists experience the same error.

Our proposal is to develop methods that enable specialists to project their experience of identifying ROIs with disease relevant morphology patterns. We propose to organize into atlases the morphology patterns collected though analysis of viewing pattern traces. Such atlases ultimately facilitate organizing cases as collections of ROIs, consistent with the workflow recommended by Fine 2014 [3].

2 METHODS

The analysis performed by Ezgi *et al*, 2016 [1] visualizes the differences between viewing patterns using a heatmap, using colors to encode the time spent in each region of the slide, as depicted in **Figure 1**. The grey areas are the least viewed and the yellow areas are the most viewed. The observed viewing patterns of different pathologists often focus on totally different areas of the slide. Thus, errors experienced in one area are unlikely to repeat on others.

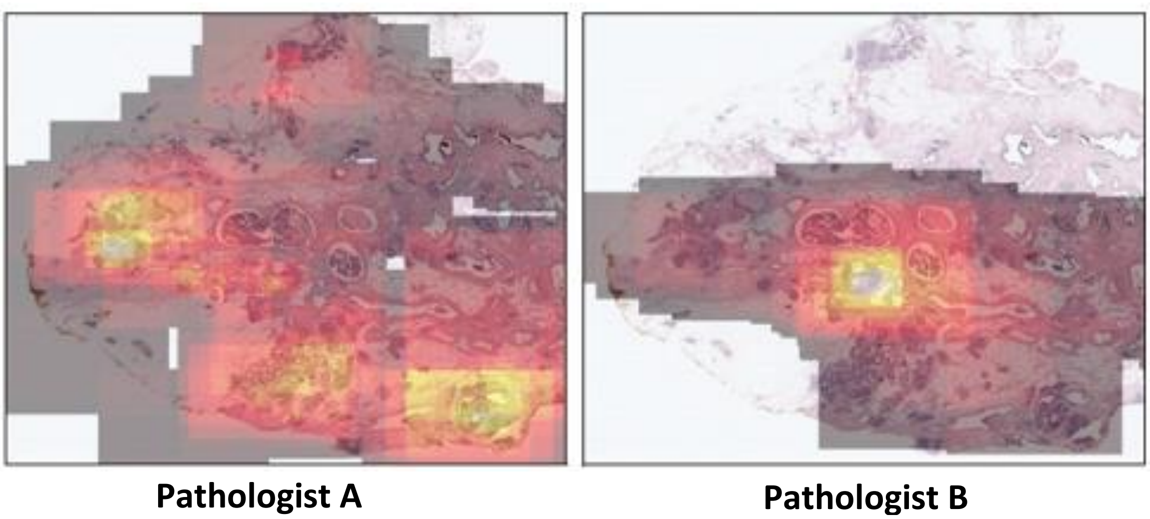


Figure 1: Visualizing viewing pattern: 'grey' as least viewed, 'yellow' as most viewed (Ezgi *et al*, 2016 [1]).

The low concordance implies that combining the viewing patterns of two pathologists can dramatically reduce the errors and, as a consequence, improve patient care. As an example, as depicted in **Figure 2**, for challenging situations in which there is a 30% chance of an error by a single pathologist, the error rate may be reduced to 10% when using two pathologists.

Further error reduction are possible when combined with a Deep Learning based recommendation system. The quantitative analysis performed by Halabi et al 2018 [2] shows that, whereas the CheXNet (Radiologist-Level Pneumonia Detection on Chest X-Rays with Deep Learning) can achieve 60% diagnostic accuracy on its own, it is possible to reduce the error rate to 20% when CheXNet was used as a recommendation input to a group of collaborating radiologists.

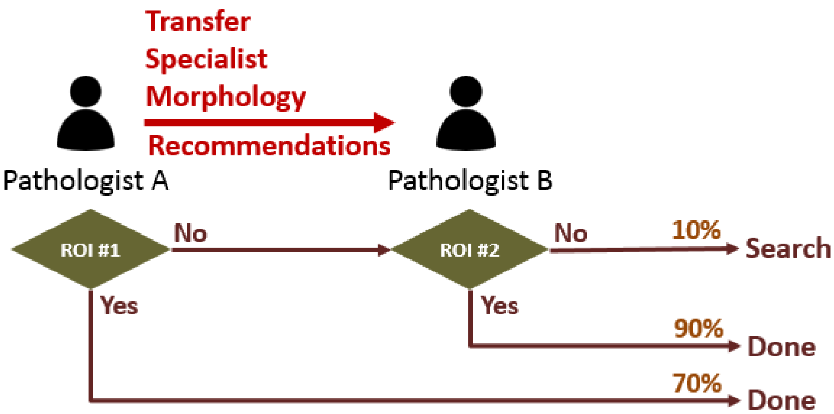


Figure 2: Exploiting low concordance to reduce errors by combining readings from two pathologists.

Building on those observations we propose to leverage Deep Learning to support an end-to-end recommendation system, whereby viewing patterns of multiple collaborating pathologists are combined to produce a heatmap of relevant morphologies. As depicted in **Figure 3**, the process starts with a morphology dictionary assembled from a pathologist's viewing patterns. These dictionaries are linked to the source ROIs and can used for Content Based Image Retrieval (CBIR). These morphologies are subsequently combined with pathologist preferences, extracted from viewing patterns, using collaborative filtering algorithms. The resulting customized recommendations are visualized as a heatmap, as depicted in **Figure 3**.

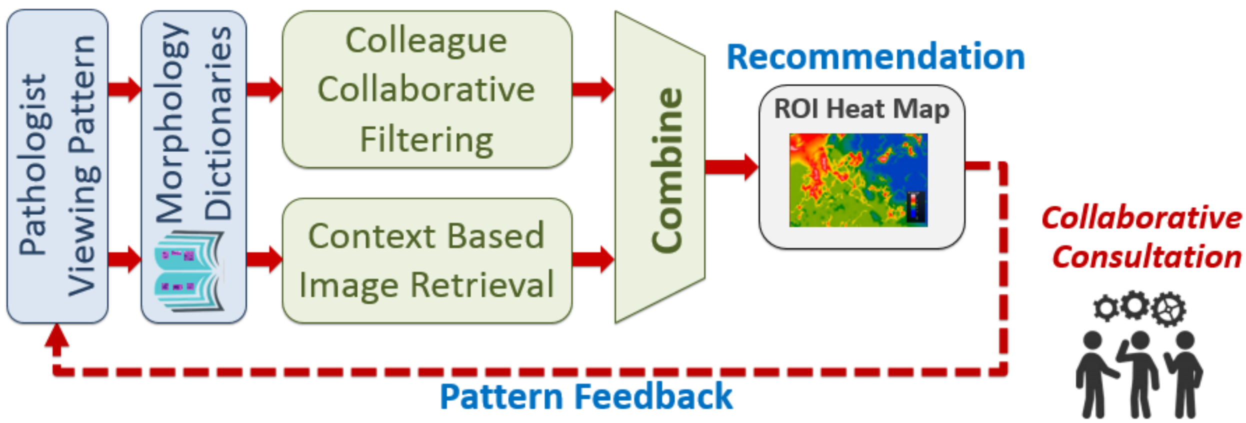
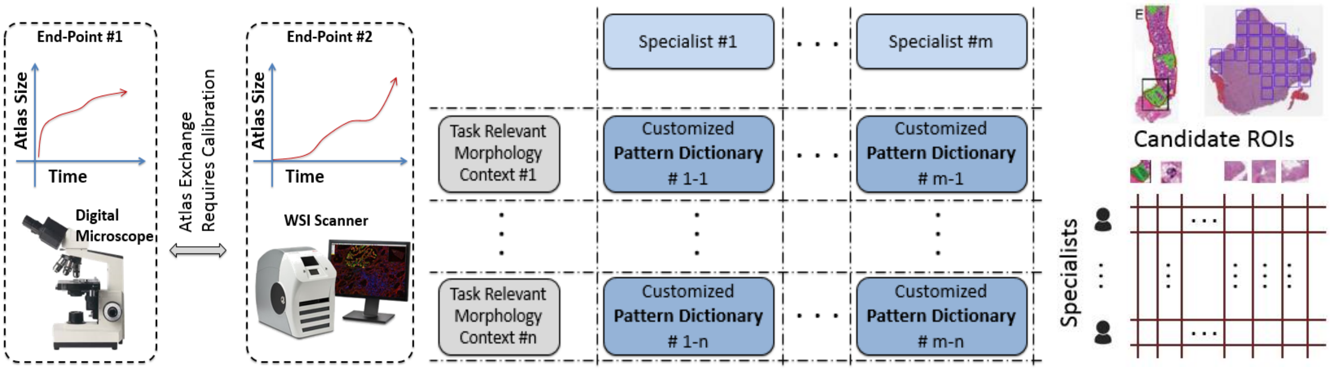


Figure 3: Context sensitive selection of morphology dictionary using recommendation engine methods.

A key weakness of Deep Learning methods is the need to train and validate across a vast range of lab processes, scanner calibrations and clinical settings. Our approach neutralizes this weakness as follows: Each new end-point deployment starts with an empty atlas. Following an end-point installation, accumulation of morphology dictionaries begins as pathologists use the system and accumulate viewing patterns, as depicted in **Figure 4a**. Each incrementally learned morphology pattern is labeled with the originating lab process, scanner calibration and clinical setting associated with that end point; atlas exchange across end-points is challenging and requires calibration. The learned atlases are endowed with a wealth of meta-data comprising of detailed Anatomic Pathology Lab Information System (APLIS) lineage and clinical context, enabling reliable relevance analysis and reliable selection of applicable ROI recommendation. Such a data strategy enables quantifying the impact of context, process and settings.

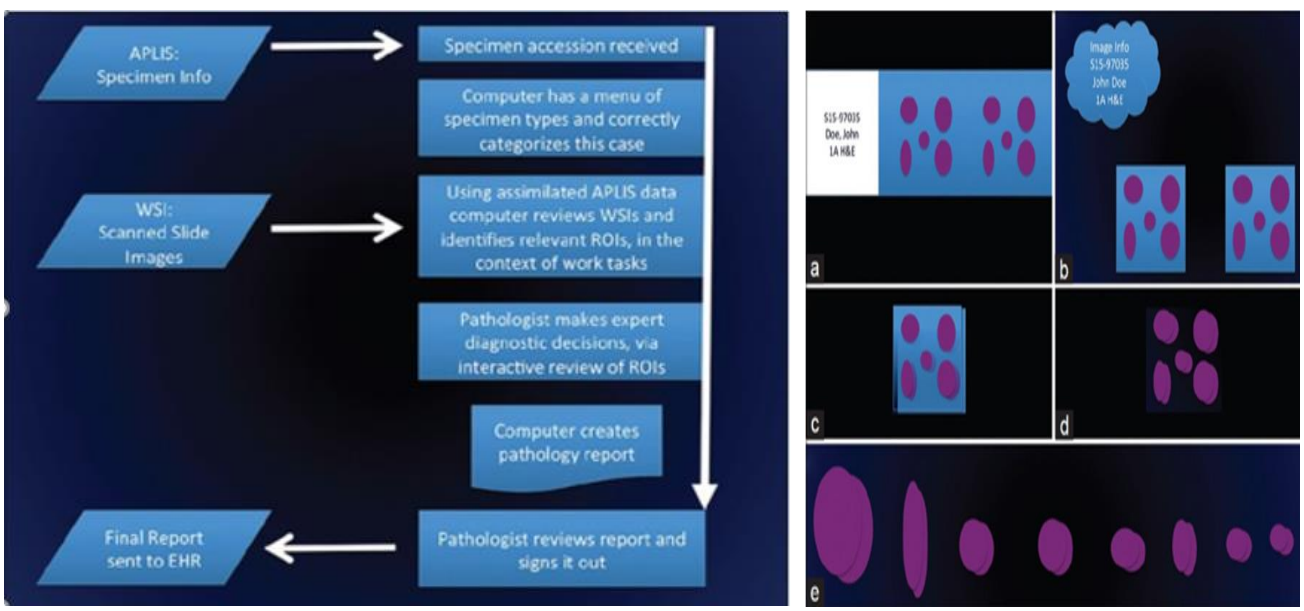
With this approach, collaboration occurs between pathologists sharing the same end-point as well as across end-points. The implied specialist recommendation matrix, depicted in **Figure 4b**, assigns each pathologist weights representing the relevance of each atlas morphology to the task at hand. Conversely, each atlas morphology is assigned a weight representing its utility to ROIs and specialists, as depicted in **Figure 4c**. As a result, the collaborative filtering approach enables learning the context-sensitive utility of morphologies from their collective viewing patterns.



(a) Distributed Atlas Acquisition **(b)** Specialist-Recommendation Matrix **(c)** Morphology-ROI Matrix

Figure 4: Collaboration approach at the end-point and across end-points.

With the presence of an ROI recommendation engine, the ROI-centric workflow depicted in **Figure 5a** is preferred to a slide-centric workflow. According to Fine 2014 [3], an ROI-centric workflow starts with accessioning and categorizing within an Anatomic Pathology Lab Information System (APLIS), as is done today. Subsequently, rather than read form the physical slide, the improved workflow continues with scanning to obtain a digital manual partial slide scan or an automated Whole Slide Image (WSI) scan, and an algorithm which decomposes it into context specific Regions Of Interest (ROI). At this point, our proposed online ROI recommendation approach is able to automatically organize the ROIs according to their relevance to the disease state or diagnostic task at hand. The output from that step is the ROI-centric view of a case, as depicted in **Figure 5b**. Subsequently, the pathologist can review the ROI recommendation provided in terms of heatmap, and renders an expert opinion. The key to the improved patient care is *the reduction of error through the use of Deep Learning methods to project uncorrelated viewing patterns of multiple pathologists and produce a reliable heatmap*.



(a) ROI-centric Workflow **(b)** ROI-centric view of a case

Figure 5: The preferred ROI-centric workflow as described in Fine 2014 [3].

To evaluate our approach, we ask specialists to manually analyze 21 WSIs and identify location centers for 19 Basal Cell Carcinoma (BCC) relevant morphologies. Using only information about centers of morphology patterns, which can be otherwise be extracted from pathologist viewing patterns, we extracted >1800 structure specific patterns representing those morphologies. Subsequently, we partitioned those patterns into groups A and B. We use a DNN to learn the morphology patterns in Group A, and project those onto Group B. The morphologies in Group A would be identified through aggregating multiple viewing patterns.

3 RESULTS

We observe that Deep Neural Networks (DNN) have the capability to reliably learn the morphology patterns in group A, and project them onto group B. We analyzed the cohesion of each of the 19 BCC morphology patterns separately. The t-distribution Stochastic Neighbor Embedding (SNE) in **Figure 6** shows general lack of cohesion, implying that determining pattern similarity is very difficult. Despite the low cohesion, we observe in **Figure 7** that *a single DNN* projected from A onto B *all* 19 BCC morphologies with *>97% Area Under the Curve (AUC)*. The ability of *a single DNN* model to reliably project all *19 patterns* implies a significant opportunity for model reuse. The resulting pattern dictionaries can subsequently be used for unsupervised segmentation of unseen images for educational purposes and to support longitudinal studies. An example of leveraging the learned atlas to perform such segmentation is depicted in **Figure 8**.

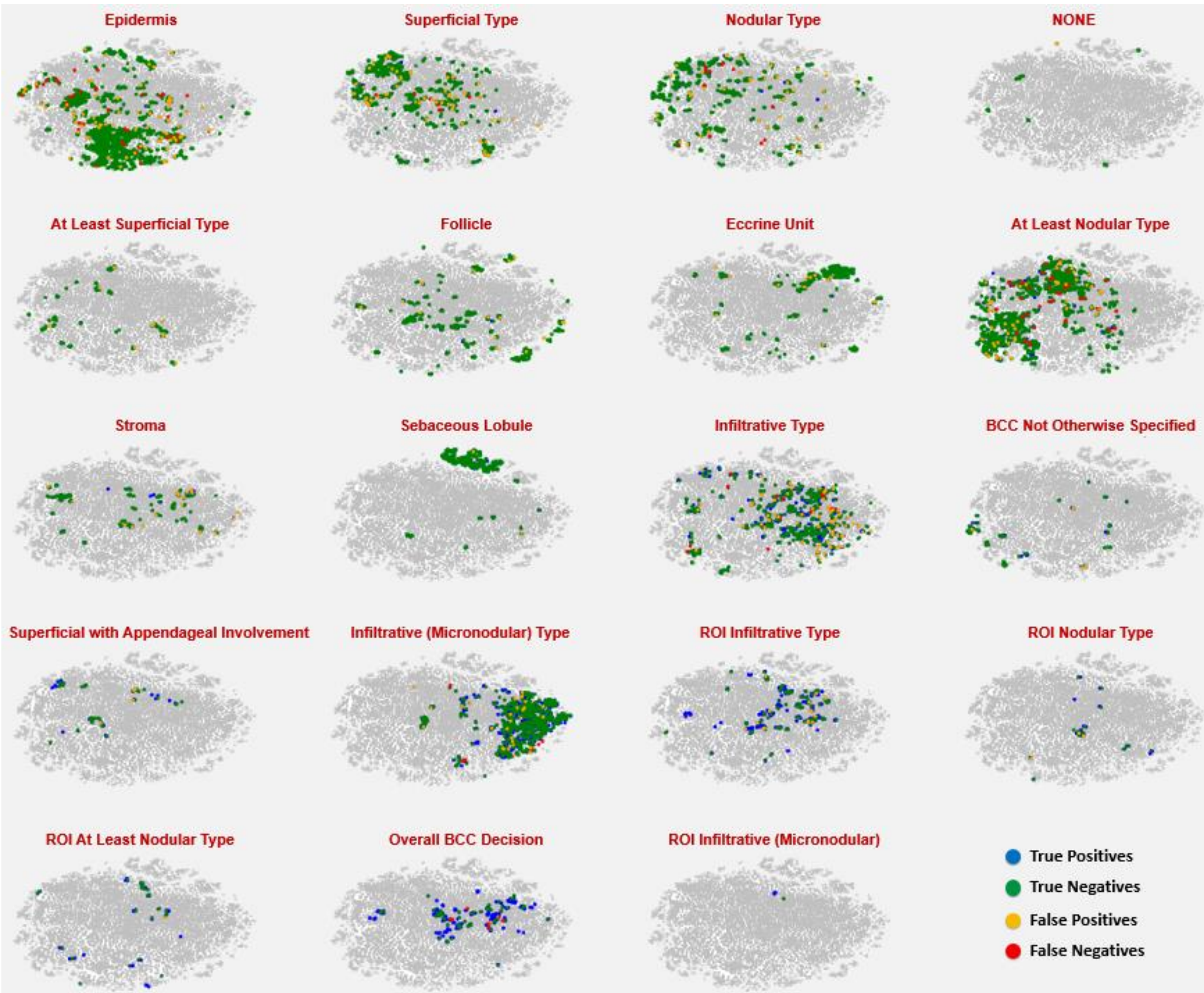


Figure 6: Group A patterns show multiple distinct clusters per morphology using t-SNE visualization.

4 REFERENCES

[1] Ezgi Mercan, Selim Aksoyy, Linda G. Shapiro, Donald L. Weaverx, Tad Brunye, Joann G. Elmorez (2016). "**Localization of Diagnostically Relevant Regions of Interest in WSI**", *Journal of Digital Imaging* 29:496, Aug 2016, ISSN 0897-1889

[2] Safwan Halabi, MD, Stanford University; Matthew Lungren, MD, MPH; Louis Rosenberg, PhD; David Baltaxe; Bhavik Patel, MD; Jayne Seekins, MD; Francis Blakenberg, MD; David Mong, MD; Timothy Amrhein, MD;Pranav Raipurkar, MS; David Larson, MD, MBA; Jeremy Irvin; Robyn Ball; Curtis P. Langlotz, MD, PhD, FSIIM;Gregg Willcox, "**Radiology SWARM: Novel Crowdsourcing Tool for CheXNet Algorithm Validation**", 2018 Conf.Machine Learning in Medical imaging.

[3] Jeffrey L. Fine (2014), "**21st century workflow: A proposal**", Journal of Pathology Informatics 5:44, Nov 2014, PMCID: PMC4260324

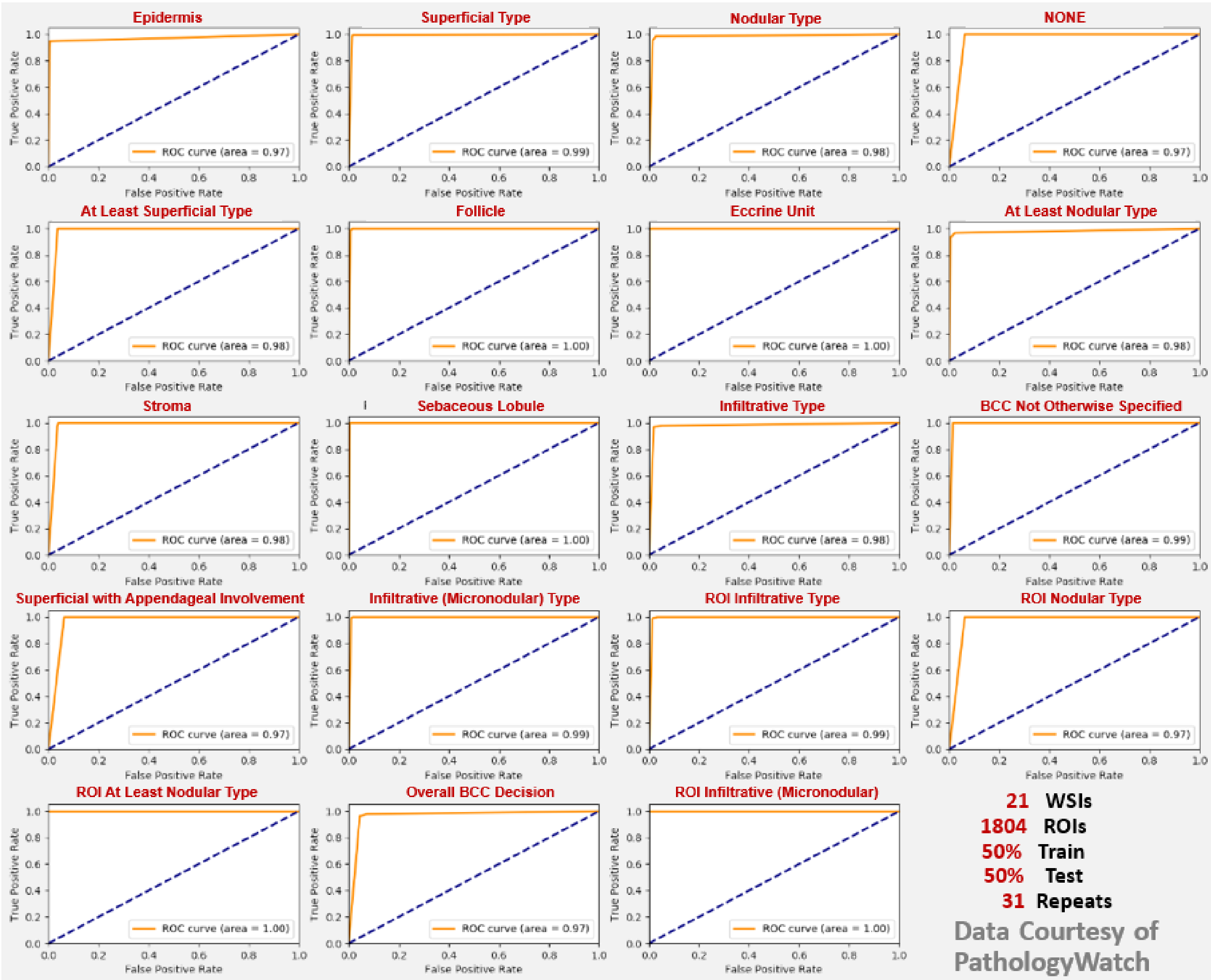


Figure 7: Reliability of recommendation transfer to Group B shows >97% AUC for all morphologies.

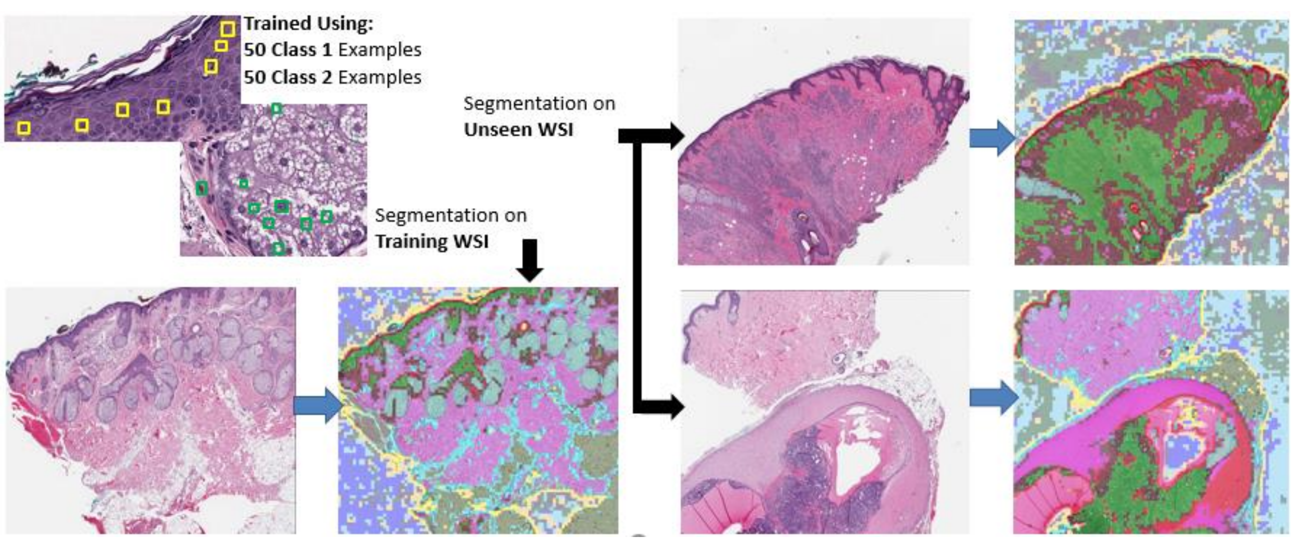


Figure 8: Reliable segmentation using morphology dictionaries which can be gleaned from viewing patterns.