Lessons Learnt in the use of whole slide images for image analysis in a diagnostic laboratory practice

Heng Seow Ye, Sng Shi Hui Adeline, Cheng Chee Leong
Singapore General Hospital, Department of Anatomical Pathology

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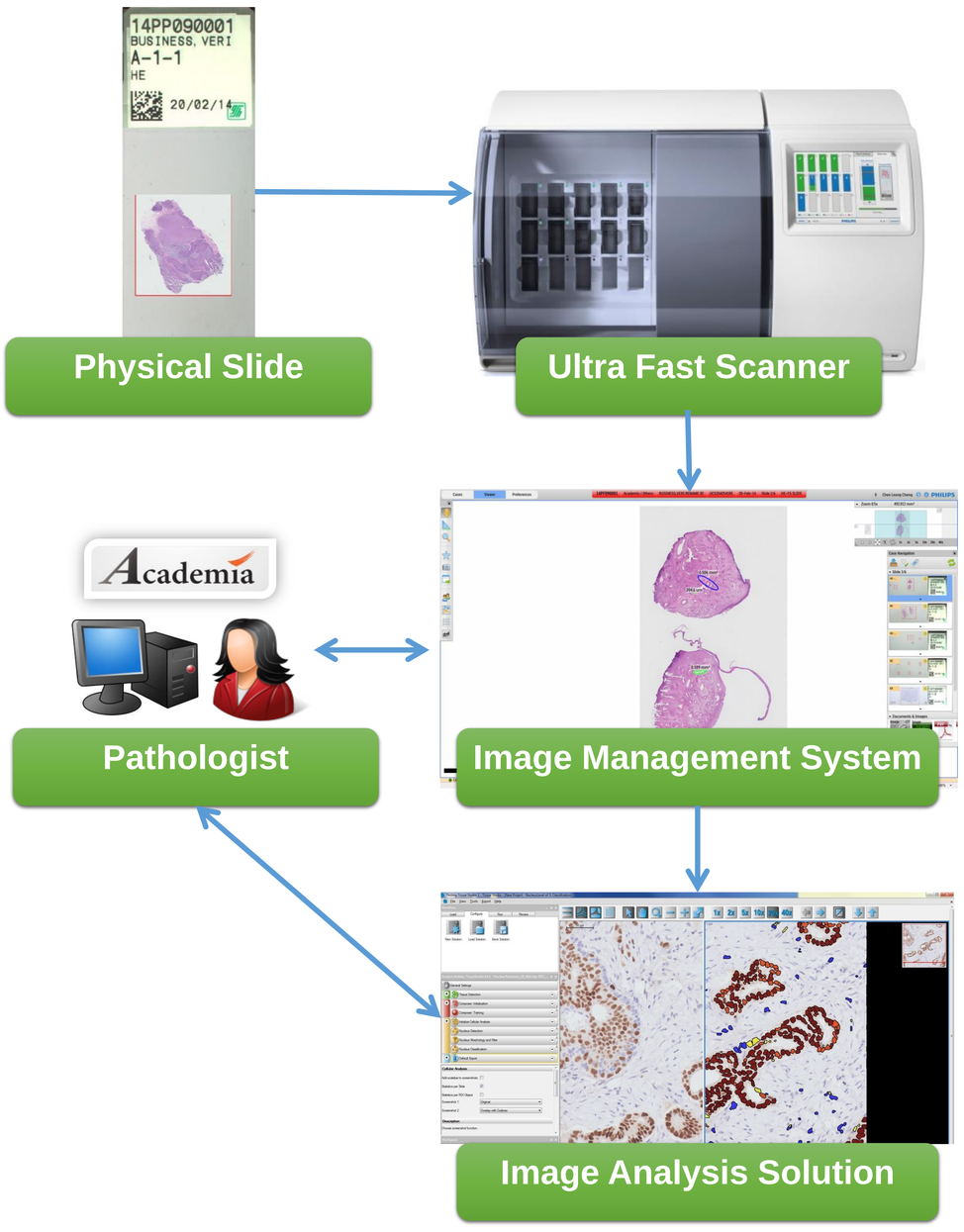
Singapore General Hospital
SingHealth

Introduction

Digital pathology solution (DPS) allows the production of high magnification virtual image of microscopic slides known as whole slide images (WSI), examinable using image management system, in a manner comparable to a conventional microscope. The capability of creating these virtual slides with the ultra fast scanner allows the concurrent use of the WSI for multiple purposes at the same time, as the users are no longer bound by the physical constraints of the glass slides. One application of the WSI is image analysis by image analysis solution, which can be performed even while the WSI of the case is being examined by the pathologist.

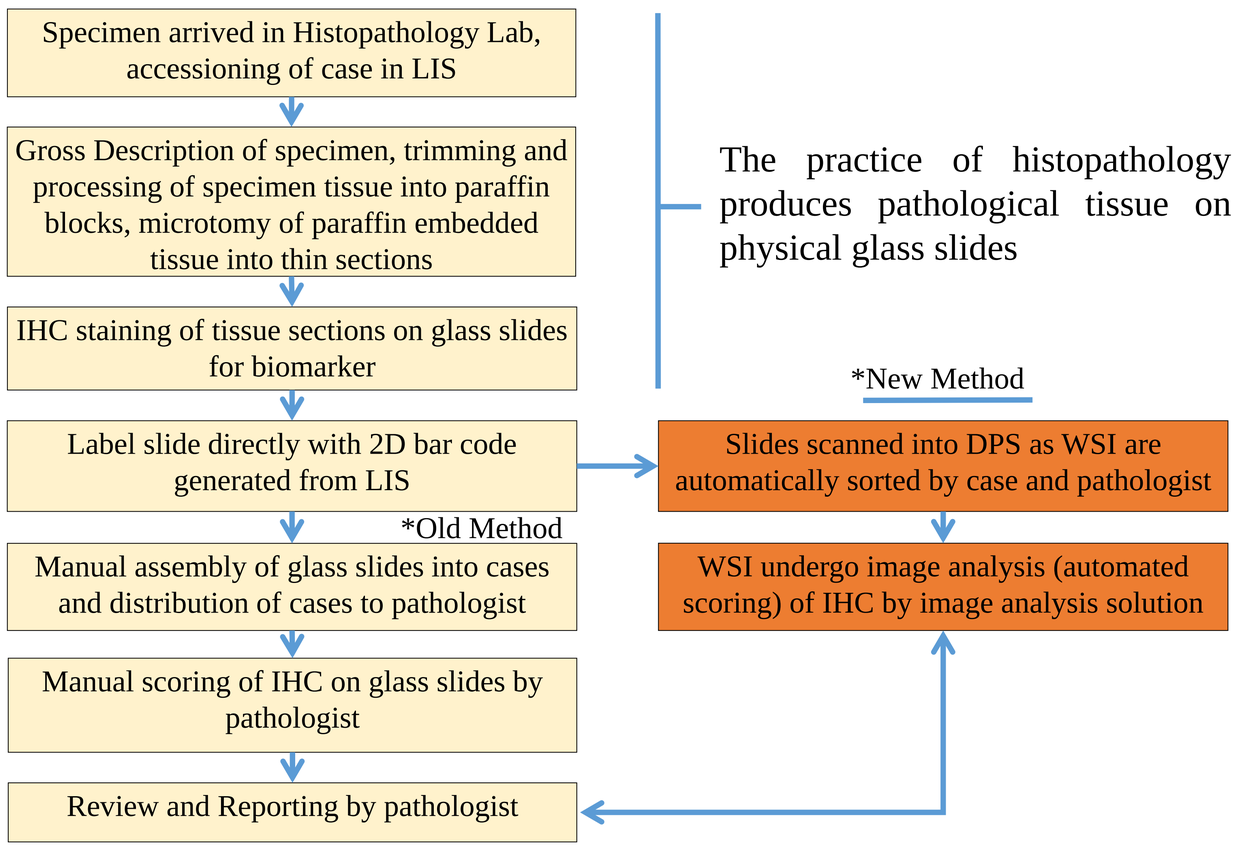


Aim

❖ Describe the use of WSI for image analysis on immunohistochemically (IHC) stained sections of breast core biopsies.
❖ Summarise lessons learnt from the use of image analysis in diagnostic detection of IHC biomarkers such as nuclear markers ER, PR, Ki-67 and membrane marker CerbB2.
❖Describe the resolution of the challenges faced during the optimisation and performance of image analysis.

Methodology

The DPS used for our study is the Philips IntelliSite Pathology Solution (PIPS), which comprises of the PIPS Image Management System (IMS) and the PIPS Ultra Fast Scanner (UFS).
In the practice of histopathology, pathological tissue is sectioned and stained onto physical glass slide, the slide is then scanned as digital WSI by the UFS. These WSI can be viewed as an virtual image of microscopic slide on the web-based IMS and also be retrieved directly for image processing and analysis.
The image analysis solution used is the Definiens Tissue Studio, which is able to detect regions of interest and distinguishes cell types and cellular compartments within target regions of our WSI , without the need to separately acquire image snapshots. It determines morphology and expression profiles per individual cell or cellular compartment, based on pre-determined parameters optimised within the software.



Result and Challenges

Traditionally, pathologist uses the method of manual scoring of IHC staining on glass slides, which is time consuming, inefficient and inherently subjective. The use of WSI for image analysis in the diagnostic setting allows an efficient and consistent tumour detection, cellular compartment detection, statistical analysis and generation of results based on pre-determined parameters optimised within the image analysis solution. It also alleviates the issues related to inter-pathologists and intra-pathologists variations, but there are still issues and challenges related to the technology such as:

❖ Variable stain intensity: This generally applies to haematoxylin counterstain and will affect the cellular detection of negatively stained nuclei, hence affecting the overall percentage scoring of positive versus negatively stained nuclei. This issue can be resolved by following appropriate staining standards to reduce variability in intensity of the counterstain.
❖ Tissue artefacts: This refer to the presence of various artefacts on the tissue such as tissue folds (Refer to Figure 1) that will provide an non-accurate representation of the pathological tissue, hence leading to false detection of cell types by the image analysis solution. This issue can be resolved by doing tissue quality check to reject tissue of non-acceptable quality.
❖ Detection of cellular compartments: This refers to calibration and optimisation of pre-determined parameters in the image analysis solution for detection of tumour region and cellular compartments. If not done properly with sufficient representative materials, this will result in non-accurate detection of regions of interest and cellular compartments on the pathological tissue. This issue can be resolved by optimising parameter range on sufficient training set materials and validation by pathologists.

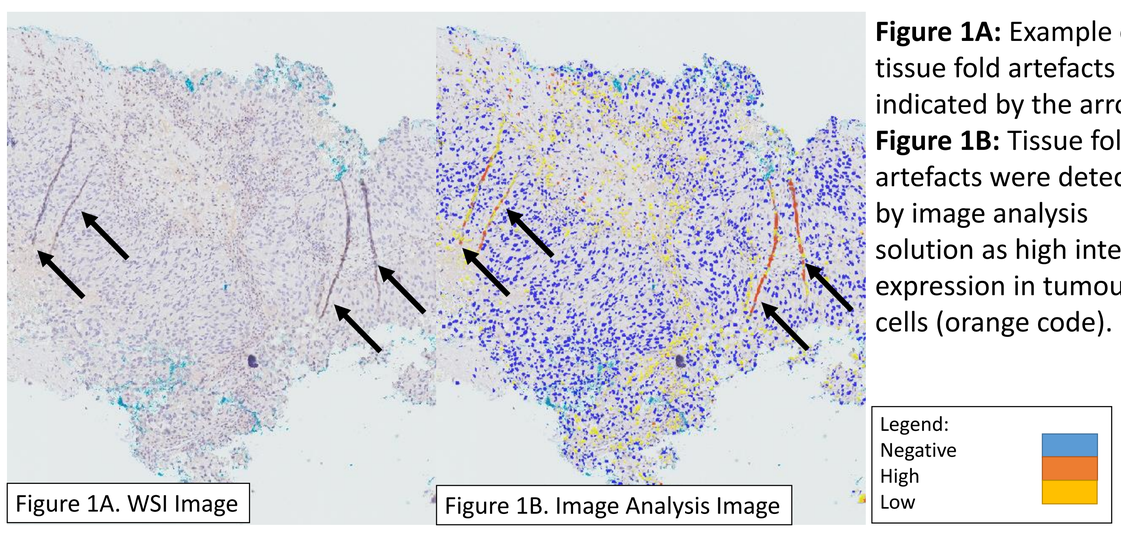


Figure 1A. WSI Image
Figure 1B. Image Analysis Image

Figure 1A: Example of tissue fold artefacts indicated by the arrows. **Figure 1B:** Tissue fold artefacts were detected by image analysis solution as high intensity expression in tumour cells (orange code).

Conclusion

The use of WSI for image analysis in a diagnostic laboratory practice requires quality tissue section of appropriate staining standards, coupled with numerous rounds of calibration on training sets comprising representative materials to optimise the algorithms and parameter settings related to specific biomarkers.