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Original contribution

Evaluation of whole slide image immunohistochemistry interpretation in challenging prostate needle biopsies ☆

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Summary Whole slide images (WSIs), also known as virtual slides, can support electronic distribution of immunohistochemistry (IHC) stains to pathologists that rely on remote sites for these services. This may lead to improvement in turnaround times, reduction of courier costs, fewer errors in slide distribution, and automated image analyses. Although this approach is practiced de facto today in some large laboratories, there are no clinical validation studies on this approach. Our retrospective study evaluated the interpretation of IHC stains performed in difficult prostate biopsies using WSIs. The study included 30 foci with IHC stains identified by the original pathologist as both difficult and pivotal to the final diagnosis. WSIs were created from the glass slides using a scanning robot (T2, Aperio Technologies, Vista, CA). An evaluation form was designed to capture data in 2 phases: (1) interpretation of WSIs and (2) interpretation of glass slides. Data included stain interpretations, diagnoses, and other parameters such as time required to diagnose and image/slide quality. Data were also collected from an expert prostate pathologist, consensus meetings, and a poststudy focus group. WSI diagnostic validity (intraobserver pairwise κ statistics) was "almost perfect" for 1 pathologist, "substantial" for 3 pathologists, and "moderate" for 1 pathologist. Diagnostic agreement between the final/consensus diagnoses of the group and those of the domain expert was "almost perfect" (κ = 0.817). Except for one instance, WSI technology was not felt to be the cause of disagreements. These results are encouraging and compare favorably with other efforts to quantify diagnostic variability in surgical pathology. With thorough training, careful validation of specific applications, and regular

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postsignout review of glass IHC slides (eg, quality assurance review), WSI technology can be used for IHC stain interpretation.

1. Introduction

Whole slide images (WSIs), also known as virtual slides, are digital facsimiles of entire histopathologic sections originally mounted on glass microscope slides [1,2]. These images are viewed using interactive software, termed "virtual microscopy software," which enables the user to adjust magnification and navigate to any portion of the image (Fig. 1). Until recently, application of WSI technology has primarily been limited to education and proficiency testing [3,4], but newer studies describe its potential usefulness in quality assurance activities and in the analysis of pathologists' diagnostic decision making [5,6].

A small number of previously published validation studies, including our own, support the clinical effectiveness of WSIs in settings and situations in which static and dynamic digital imaging telepathology have been shown to be useful [7-10]. Feasibility studies demonstrating the use of WSIs in real-time anatomic pathology practice are needed before integration of this technology into day-to-day practice may practicably occur, but such studies are lacking in this relatively recent imaging modality.

Pathologists interested in digital imaging at the University of Pittsburgh Medical Center (UPMC) have been actively involved in the development and evaluation of novel WSI applications and resources [5,7], with the goal of improving the

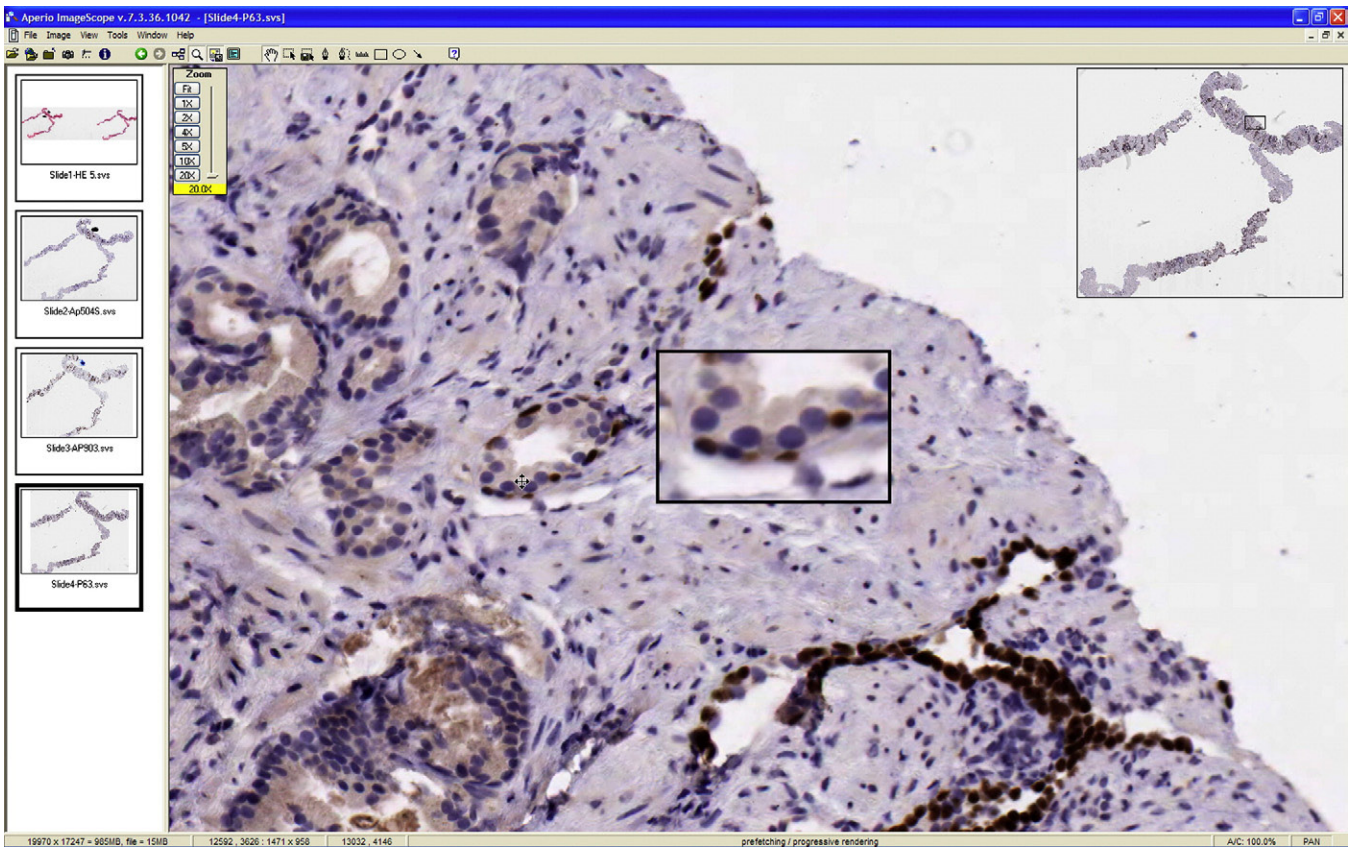

Fig. 1 WSI viewing software, also known as "virtual microscopy" software (ImageScope, version 7.3.36.1042, Aperio Technologies). This is a prostate biopsy (prostate adenocarcinoma) stained with p63 that was originally scanned at 20× objective magnification, zoomed in to maximum magnification. The configuration is typical, with a low-magnification thumbnail image in the upper right corner, a high-magnification image comprising most of the viewing area, magnification controls in the upper left area, and several "annotation" tool buttons (ie, for measuring or marking the WSI). The user can navigate to any portion of the image using the computer mouse (ie, "click and drag"); magnification can be changed by rolling the mouse wheel or by clicking on the visible magnification controls. Also present are thumbnails of other available images (left side) permitting rapid switching between different stains in this case. Finally, a magnification tool is present (thick-lined rectangle near center); this tool permits even more magnification of interesting areas and aids detection of subtle features such as faint nucleoli.