Daniel Visscher, M.D.
Professor of Pathology
Director of Surgical Pathology

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Dear Sirs/Madams:

I am a Surgical Pathologist and currently the Director of Surgical Pathology at the University of Michigan. I have practiced for approximately 20 years at a number of institutions including Henry Ford Hospital, the Detroit Medical Center and Mayo Clinic Rochester. Although I specialize in breast pathology, I consider myself a general pathologist and I participate widely in our services including performing frozen sections and directed consultations sent in from colleagues at other institutions. Since the beginning of my career I have been actively involved with resident and medical student instruction. I give a number of talks around the country every year, mostly about diagnostic breast pathology.

My relationship to Aperio is mostly that of a customer; we use Aperio devices in order to teach Anatomic Pathology using scanned digitized slides that are projected in Anatomical Pathology Laboratories to second year medical students. We also utilize digitized images at our annual Frontiers in Pathology CME course. Our department is currently performing research with Aperio in order to determine whether digitized slides are similar to glass slides in the context of diagnosing difficult breast lesions. Finally, our division utilizes scanned images in the context of telepathology, generally with reviewing difficult frozen sections in real time with colleagues via a continuous web streaming camera system.

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I am writing to express my experiences to date with digital pathology. As I have worked with digital images for a number of years, I have developed some opinions. However, I realize that my impressions at this point are preliminary owing to the fact that we are still exploring the potential of this technology, the technical quality of which is developing rapidly.

Digital pathology has a number of obvious advantages over conventional microscopy; most importantly, it provides the opportunity for multiple people to review the same slide, either conjointly or at separate times. In many ways, digital pathology is easier to use than a microscope. Even a computer novice can quickly learn how to navigate images and review slides at low and high magnifications. Digital images are more easily annotated, photographed or quantitated than conventional microscopic slides and, obviously, but not incidentally, require only a computer screen (as opposed to a microscope). At low and mid magnifications the quality of a digitized image is outstanding if not superior to that of a conventional microscope. At higher magnifications (400x) I think that the microscope still maintains a significant although narrow advantage. I would estimate that I can reach a definitive diagnosis on a digitized image in about 95-98% of cases. The remaining few are those that would require high magnification examination.

One should bear in mind that a microscopic slide is only part of what is required for making a diagnosis. Nearly any Surgical Pathologist would tell you that, when taken out

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of context, a slide or image can represent a very confusing and disorienting examination. Indeed, Surgical Pathology regularly makes use of multiple slides, knowledge of the clinical findings and gross description of the excised tissue. To my knowledge, there are no studies which critically evaluate even microscopes for the ability to render accurate diagnoses out of context from these clinical and gross microscopic parameters. Thus, we should be careful when evaluating the "accuracy" of assessing a digitized image.

There is tremendous potential for future developments in digital pathology. First, and foremost, a digitized slide is a very convenient format in which to obtain consultation about a case. Sending an image and reviewing it with a second pathologist "online" would allow both individuals to review and discuss a case together in real time, a manner which could never be achieved with a single glass slide. Further, glass slides are subject to breakage and stain oxidation; they are therefore perishable. I strongly emphasize that digital pathology consultation can performed on a "real time" basis opposed to the delay associated with slide and/or personnel transport.

One of the obvious advantages of dual slide review is quality assurance. It is well known that there are many diagnoses for which often pathologists differ in opinion, such as melanocytic lesions, thyroid nodules and problematic hyperplastic lesions of the breast. Digital pathology would potentially provide the basis for two pathologists to simultaneously or blindly review difficult cases, thereby providing invaluable and prospective insights into problematic cases or errors (i.e. in time to prevent patient injury). One of the real weaknesses in my profession has been our inefficiency at

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learning from one another. Digital pathology provides a nearly infinite spectrum of opportunities for improved development of diagnostic criteria. This applies to conceptual as well as, possibly, development of more objective and quantitative parameters.

As noted earlier, I am an investigator with Aperio in "Project Pink". This study seeks to evaluate the diagnostic accuracy of digital microscopy in review of routine and difficult breast lesions. As noted, I was able to definitively evaluate at least 95% of cases using the scanned images. I suspect that percentage may increase still further with greater experience and with technical improvements allowing greater resolution at high magnifications. I don't know for sure yet because we haven't evaluated our data, but I suspect that interobserver variation in diagnoses of these difficult cases will probably represent a greater factor than discrepancies due to the technical difference between routine microscopic and digital pathology.

I appreciate the opportunity to make my views known to you about digital pathology. Thank you for considering my opinions and views on this important matter.

Sincerely,

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