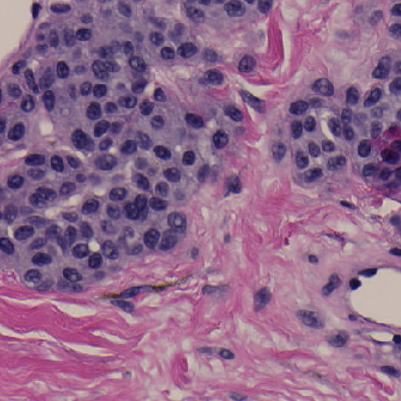
Whole slide imaging (WSI) involves scanning microscope slides and converting them into high-resolution digital files. In this way, image viewing is more flexible and image transfer is much more efficient. A WSI system consists of the scanner, viewer, and display components. A scanner scans slides and converts them into a standard file format, which can be opened by viewer software and its data converted to color values, which are then sent to the display for pathologists to examine. Currently, only two whole-system WSI devices have been cleared by the FDA. Recently, third-party vendors submitted independent WSI viewer software as alternatives to replace factory viewer components in preapproved devices. The basis of these submissions is that the third-party viewer software should be interoperable with the cleared devices – since the output of a scanner is a standard file format and the input to the display is color values, as long as a viewer can convert the data in the file to color values, it should be able to replace any other viewer, since they are not fundamentally different. However, the results of this study show that this is clearly not the case. Comparing the color data between viewers on the pixel level shows significant color differences between certain viewers.

To compare viewers, the following procedure was devised. A WSI file produced by a Hamamatsu scanner was opened in four separate viewers, including the factory Hamamatsu viewer, NDP.view 2, as well as Sedeen from Pathcore, and two open-source viewers, QuPath from Queen’s University Belfast, and ASAP, from Radboud University. After adjusting the field of view in each viewer to show the region of interest, screenshots of each viewer were taken using Microsoft Snipping Tool. Snipping Tool captures the digital color data sent to the display, without involving the display, which was verified by a previous study [1]. The screenshots were registered, then scanned pixel by pixel to calculate color difference, as defined by the International Commission on Illumination (CIE). The metric, ΔE, is based on human perception of color.

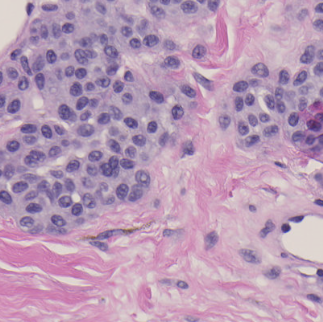
The following registered samples were compared in the study:

ΔE information was presented in the form of heat maps and histograms. Average ΔE and standard deviation were also associated with each comparison. A box plot was also generated.



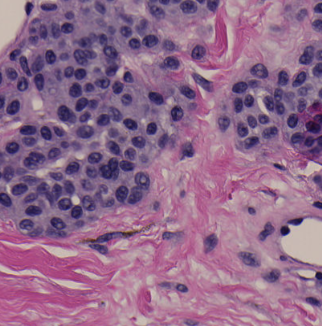
ASAP

Radboud U



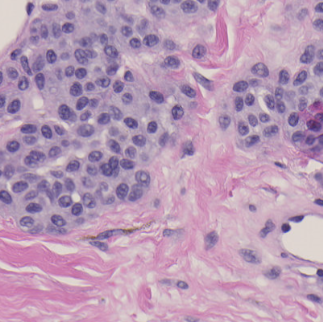
NDP.view2

Hamamatsu



QuPath

Queen’s U

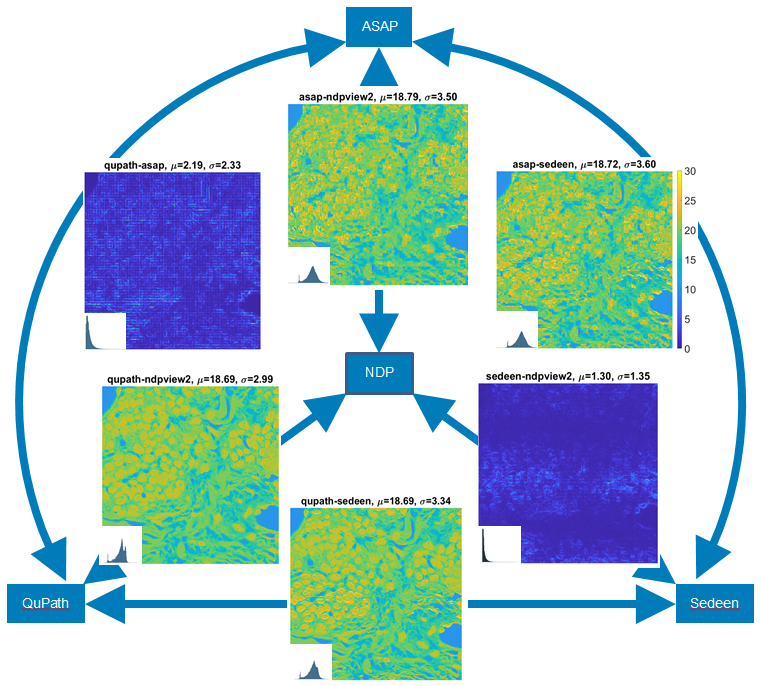


Sedeen

PathCore







The results of the study show that there are significant differences in color between the reference Hamamatsu NDP.view 2 viewer and QuPath and NDP.view 2 and ASAP. Comparing between Sedeen and QuPath and Sedeen and ASAP give similar results. These color differences seem to correlate with tissue structure, with nuclei, stroma, and background sections having different levels of ΔE. Sedeen was much closer in color to NDP.view 2, but there were still slight differences almost imperceptible to the human eye. In addition, there were strange stitching errors that showed up on the Sedeen viewer. ASAP was also problematic; when comparing ASAP with other viewers, noticeable "pixelized" ΔE patterns show. This could be a sign of differences in decompression.

For the same input file, four different WSI viewers generated four different images, which confirms that it is a fallacy to assume that any WSI viewer can reproduce digital images identically. The concept of interoperability between WSI components needs to be revisited to include image integrity on the pixel level. Before a WSI file format is standardized, third-party viewer vendors should work with the scanner manufacturer instead of relying on untested free libraries. More adequate bench testing data are needed for 510(k) WSI viewer submissions. In the future, more work needs to be done to determine the sources of these observed differences, as well as including the two FDA cleared WSI devices. Ultimately, bench test methods and acceptable criteria for determining substantial equivalence in terms of color performance among viewers should be established.