

# Efficient Visualization of Whole Slide Images in Web-based Viewers for Digital Pathology

Peter J. Schüffler, DS; Evangelos Stamelos, MS; Ishtiaque Ahmed, BS; D. Vijay K. Yarlagadda, MS; Orly Ardon, MSc, MBA, PhD; Matthew G. Hanna, MD; Victor E. Reuter, MD; David S. Klimstra, MD; Meera Hameed, MD

• **Context.**—Wide adoption of digital pathology requires efficient visualization and navigation in Web-based digital slide viewers, which is poorly defined.

**Objective.**—To define and quantify relevant performance metrics for efficient visualization of cases and slides in digital slide viewers.

**Design.**—With a universal slide viewer used in clinical routine diagnostics, we evaluated the impact of slide caching, compression type, tile, and block size of whole slide images generated from Philips, Leica, and 3DHistech scanners on streaming performance on case, slide, and field of view levels.

**Results.**—Two hundred thirty-nine pathologists routinely reviewed 60 080 whole slide images over 3 months. The median time to open a case's slides from the laboratory information system was less than 4 seconds, the time to change to a slide within the case was less than 1 second, and the time to render the adjacent field of view when

navigating the slide was less than one-quarter of a second. A whole slide image's block size and a viewer tile size of 1024 pixels showed best performance to display a field of view and was preferable over smaller tiles due to fewer mosaic effects. For Philips, fastest median slide streaming pace was 238 ms per field of view and for 3DHistech, 125 ms. For Leica, the fastest pace of 108 ms per field of view was established with block serving without decompression.

**Conclusions.**—This is the first study to systematically assess user-centric slide visualization performance metrics for digital viewers, including time to open a case, time to change a slide, and time to change a field of view. These metrics help to improve the viewer's configuration, leading to an efficient visualization baseline that is widely accepted among pathologists using routine digital pathology.

(*Arch Pathol Lab Med.* 2022;146:1273–1280; doi: 10.5858/arpa.2021-0197-OA)

More and more pathology laboratories are considering digital workflows for routine clinical practice including scanning, reviewing, and storing of digital pathology slides. Digital pathology (DP) gained popularity in recent years as a powerful technology<sup>1</sup> for routine primary diagnosis.<sup>2–6</sup> DP attracted even more attention during the recent COVID-19 pandemic, when pathologists were working remotely or from home to reduce risk of infection.<sup>3,7</sup> Still, DP has a reputation to slow down the efficiency of pathologists<sup>2</sup> due to technical constraints of image visualization on a computer screen and a computer mouse as input device.

In DP, slides are digitized to whole slide images (WSIs) by high-resolution scanners from various vendors. To date, no standard file format exists for WSIs, and the vendors employ different viewer software to visualize and navigate their proprietary WSIs. The viewers can either be local desktop programs or Web-based applications. For labs that use whole slide scanners from different vendors, this can result in a variety of different viewers that the pathologists will have to interact with. Furthermore, owing to their proprietary nature, these vendors' systems do not easily integrate into existing hospital systems, such as molecular pathology databases, research databases, or others.

To overcome these issues, we developed a vendor-agnostic Web-based slide viewer that integrates into our department's anatomic pathology laboratory information system (LIS), molecular pathology LIS (MPath), genetic research database (cBioPortal), and research tissue biobank.<sup>8</sup> This integration allows for the opening of complete cases or individual images in a single WSI viewer, regardless of the file type or image format. The system has been operational for more than 3 years, and multiple changes have been made to increase speed and performance.

Web-based digital slide viewing systems orchestrate the complex synergy of file formats, data storage, network performance, Web-server architecture, and Web-browser limitations, while considering image compression and tile stitching of gigabyte-sized images. The efficiency of such

Accepted for publication September 7, 2021.

Published online January 3, 2022.

From the Institute of Pathology, Technical University of Munich, Munich, Germany (Schüffler); and the Department of Pathology, Memorial Sloan Kettering Cancer Center, New York City, New York (Schüffler, Stamelos, Ahmed, Yarlagadda, Ardon, Hanna, Reuter, Klimstra, Hameed).

This research was funded in part through the NIH/NCI Cancer Center Support Grant P30 CA008748.

Schüffler is co-founder of and consultant for Paige and Hanna is consultant for Paige and PathPresenter; the work presented has not been funded by these 2 companies. The other authors have no relevant financial interest in the products or companies described in this article.

Corresponding author: Peter J. Schüffler, DS, Institute of Pathology, Technical University of Munich, Trogerstrasse 18, Munich, Bavaria 81675 Germany (email: peter.schueffler@tum.de).

systems therefore depends very much on the local infrastructure. In this work, we highlight the most important improvements made in our Web-based solution for efficient streaming of cases and slides. To quantify efficiency, we define 3 key metrics relevant to pathologists for their DP workflow as follows: (1) the time it takes to open a case in the viewer, (2) the time to open an image, and (3) the time to navigate the image. We further provide insights and relationships between specific viewer configurations and visualization performance and lessons learned while building the system.

### Related Work

The efficiency of 3 proprietary Web-based viewers has been evaluated in 2008<sup>9</sup> comparing their pace to open an image (3–4 seconds) and display a field of view (FOV) (2–6 seconds). However, the included viewers and their underlying technologies do not exist anymore. Further, the authors compared the viewers based on 8 randomly selected slides, which provides limited statistical significance, and they did not include opening a case from an LIS, which is a crucial process for integrated DP. Finally, the authors did not discuss implementation details to explain or improve the performance.

Another aspect of viewer performance is image reproducibility and quality, for which the US Food and Drug Administration recently published official guidelines.<sup>10,11</sup> In contrast, our work focuses on streaming efficiency specifically for which no guidelines exist.

We describe our system setup and the performance metric definitions in the following Methods section. In the Results section, we report important relationships between specific viewer configurations and visualization changes using the metrics. We finalize the paper with a discussion of the results and their implications.

### METHODS

Our home-grown, Web-based slide viewer server runs in the hospital's data center. The server uses an internal solid-state-drive cache to store served image tiles, thumbnails, macros, label images, and other metadata. It is connected via 10-Gigabit Ethernet to the digital slide storage (Dell, EMC Isilon H500-NAS-Platform).

Pathologists access the viewer via the LIS (Cerner, CoPath Plus) on their workstations using a consumer-grade 24" monitor with a resolution of 1920 × 1200 pixels. Workstations are connected via 1-Gigabit Ethernet with the hospital's backbone network. When opening digital images from within the LIS, the LIS launches a small local executable on the pathologist's machine that (1) receives the message file containing the selected image identifiers from the LIS, (2) signs the message via the hospital's active directory and a shared secret for automatic user authentication, (3) pushes the message to the viewer server, and (4) opens the local Web browser (such as Google Chrome, version 89) with a unique viewer URL to open the selected images. The viewer then displays the case including (1) the first WSI with its thumbnail, macro, label image, and image tiles needed to compose the first full-screen FOV, and (2) the thumbnail, macro, and slide labels of the remaining WSI in a virtual slide tray. To collect these data, each WSI has initially to be opened with its specific software development kit (SDK), which can be time consuming (on the order of seconds), such that the user has to wait for the case to be fully displayed. The time to launch slides of a given case and view the first image is part of our benchmark.

To visualize WSIs from the 4 different scanner models, Aperio AT2, Aperio GT450 (Leica Biosystems, Buffalo Grove, Illinois), IntelliSite Ultra Fast Scanner (Philips, Eindhoven, Netherlands), and Panoramic 1000 (3DHitech Ltd., Budapest, Hungary), the

vendor-agnostic viewer uses the open-source libraries OpenSlide (OS)<sup>12</sup> and OpenSeadragon (OSD),<sup>13</sup> as well as the vendors' proprietary SDKs from Philips<sup>14</sup> and 3DHitech.<sup>15</sup> OS and OSD are commonly used in Web-based slide viewers<sup>16–21</sup> as they are well suited to visualize and navigate a broad range of WSIs, being compatible with many slide formats. However, their impact on the WSI visualization speed has never been quantified.

### Performance Metrics

To assess the viewer performance for this study, we defined 3 user-centric metrics and 1 technical metric to evaluate the turnaround time performance for Web-based slide viewers as shown in the following.

**Time to Open a Case.**—The time between opening the images of a case in the LIS and displaying the first digital slide in the viewer is defined as time to open a case. It is measured automatically in the viewer as the time between calling the viewer's API from the LIS and the full rendering of the first slide of the case.

**Time to Change a Slide.**—The time between selecting a new WSI in the viewer's slide tray and displaying the corresponding slide in the viewer is defined as time to change a slide. It is measured automatically as the time between clicking on another slide of the case and the full rendering of that slide.

**Time to Show a Field of View.**—The time between zooming or panning to a different FOV and fully rendering that FOV is defined as time to show a field of view (TFOV). It is measured automatically in the viewer as the time between the start of a navigation and the completed rendering of the new FOV.

Note that this measure depends on the size of the FOV, as larger FOVs have to load more image tiles. To be comparable across experiments, we included only navigation events with an FOV size of 1920 × 790–1040 pixels, which corresponds to a full-screen view on the hospital workstations. Further, to exclude continuous zooming and panning events that we did not want to consider in this study, we included only FOV events with an effective number of loaded tiles between 0.5 and 2 times the number of expected tiles for the FOV size.

**Time Per Tile (Technical).**—The time between querying and displaying a single tile is defined as time per tile. This is measured as the time between querying a tile for an FOV and receiving this tile. This metric is technically interesting for specific experiments in our work, but not directly relevant for pathologists, as they are not reviewing individual tiles, but rather a whole FOV.

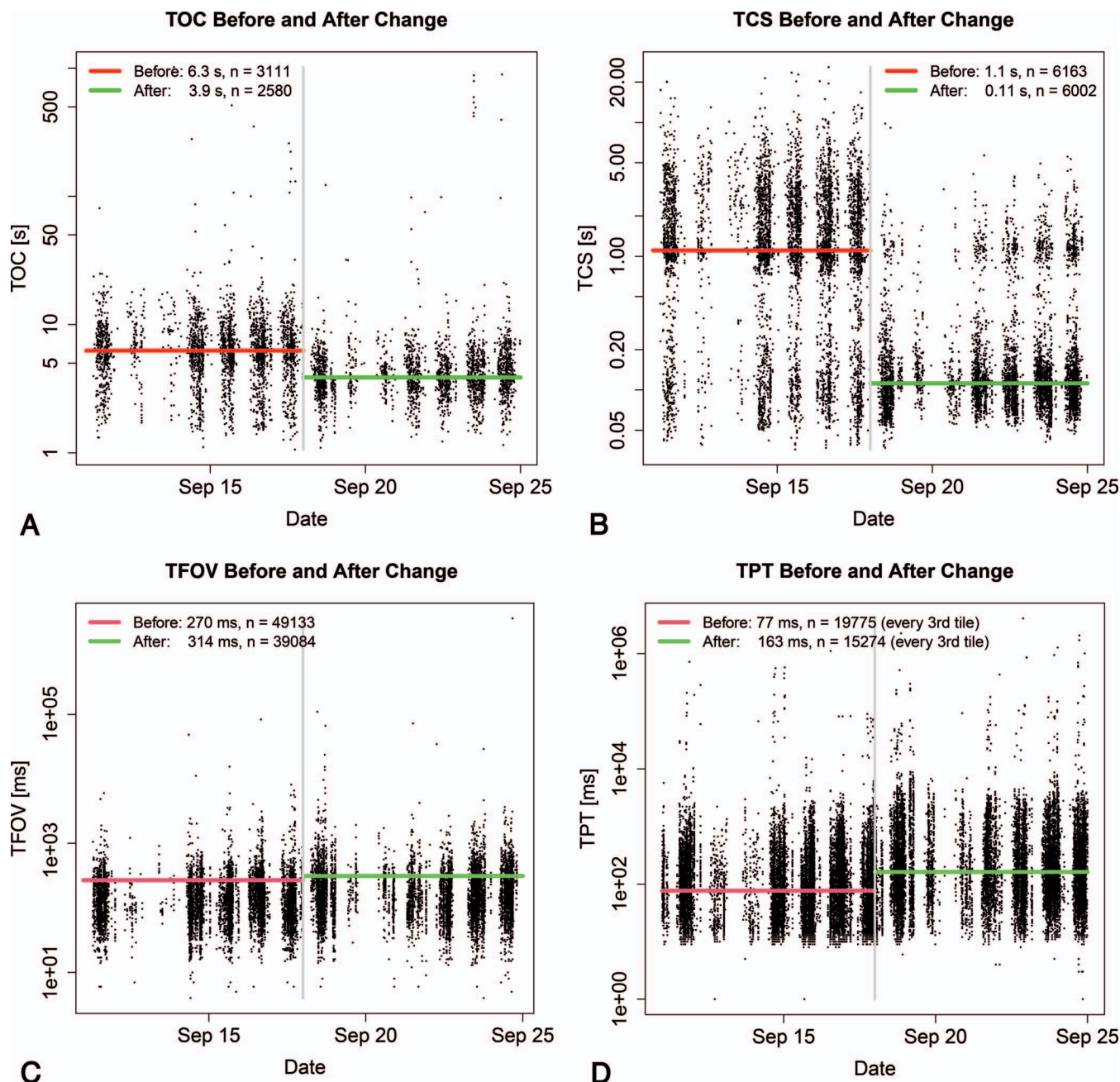
All metrics were automatically measured using the viewer's JavaScript code and the specified events, and empirically collected in the running system over 3 months. We illustrate the significant influence of specific caching strategies, different compression techniques, and block and tile size configurations on these metrics and show how we improved our setup accordingly.

### Blocks and Tiles

We use the word "block" to refer to the static image patches stored in the WSI file as they are generated during the scanning process. After scanning, they cannot be changed. We use the word "tiles" to refer to the image rectangles that compose the viewer's FOV. Tiles are generated by stitching and cropping blocks to the configured viewer's tile size.

### RESULTS

During our study period of 3 months, 239 distinct pathologists reviewed a total of 60 080 WSIs (37 570 from Leica AT2, 20 899 from Leica GT450, 781 from Philips UFS, 830 from 3DHitech P1000). All slides were scanned at ×40 except for Leica AT2 slides scanned at ×20. In the following sections, we describe specific scanner and viewer settings that had measurable influence on the performance to visualize WSIs from a user-centric point of view.



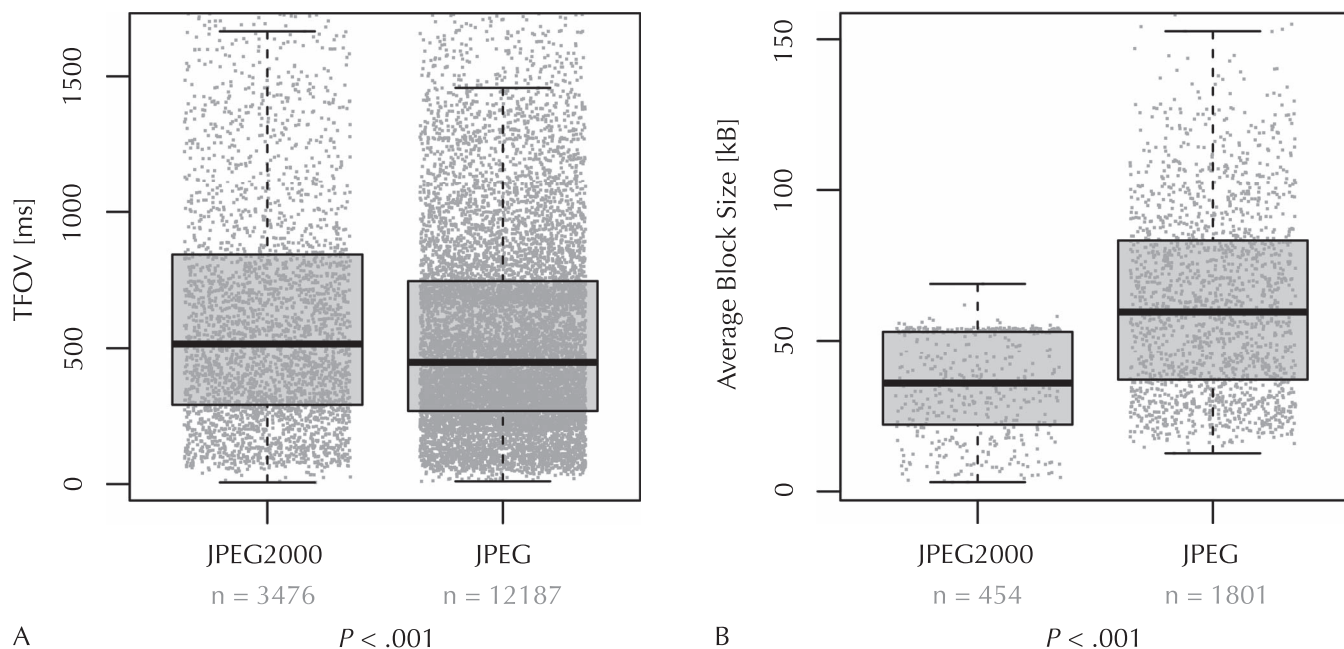
**Figure 1.** Time to open a case (TOC), time to change a slide (TCS), time to show a field of view (TFOV), and time per tile (TPT) with and without caching of whole slide images (WSIs). Red line: Median time of event with caching of WSI. Gray vertical line: We switched off caching of WSI on September 18, 2020. Green line: Median time of event without caching of WSI. A, TOC. Every case opened by a pathologist in the viewer from the laboratory information system is represented by a black dot ( $n = 5691$ ). B, TCS. Every slide changed to in the viewer is represented by a black dot ( $n = 12\,165$ ). C, TFOV. Every slide navigation in the viewer queries a new FOV represented by a black dot ( $n = 88\,217$ ). D, TPT. Every tile queried in the viewer is represented by a black dot ( $n = 35\,049$ ). The performance gain to open a case by 2.4 seconds and to change a slide by 1.0 second when not caching the WSI outweighs the loss of slower retrieval of subsequent FOVs by 44 ms and tiles by 86 ms. Therefore, we do not cache WSIs going forward.

### Influence of WSI Caching on Time to Open a Case and Time to Change a Slide

Our scanners store the WSIs on a dedicated storage connected via 10-Gigabit Ethernet. Viewers can either stream WSIs directly from their original location on the storage cluster or alternatively cache them first temporarily on the viewer server at the time of accessing the corresponding case. With prior caching, the viewer server

will first download the complete WSI from the storage to provide a faster streaming to the client afterward. Of note, download of the first WSI of a case must happen before visualization of the case to avoid concurrent access of the file for visualization, thumbnail generation, and label file extraction. Download of additional WSIs in the same case can happen in parallel in background while the first WSI is being displayed and navigated.





**Figure 2.** Compression of whole slide images (WSIs) influences field of view (FOV) loading speed (time to show an FOV [TFOV]) and file size. A, JPEG2000-compressed WSIs need significantly longer to load an FOV (median 515 ms) than JPEG-compressed WSIs (median 446 ms) ( $N = 15\,663$  measured FOV). B, JPEG2000 compression leads to smaller files with a median of 36 kB per block compared with JPEG with a median of 60 kB per block ( $N = 2255$  WSIs). All WSIs use a block size of 512 pixels and a compression quality factor of  $Q = 70$ . P value: 2-sample t-test.

The viewer server will maintain cached versions of the WSIs and their thumbnails, macros, labels, and all previously visited tiles. When visiting a cached slide, the WSI does not need to be opened with the SDK, as the metadata are already prepared. Hence, the slide can be opened faster. This cache is cleared regularly every night on the server to save disk space.

Note that if a user opens a case in the same browser again, the browser might even reuse cached versions of the corresponding images, thereby increasing the speed of displaying the case further. However, Web-based viewers must rely on (limited) browser caching controls, optimized for websites and not necessarily for WSI visualization. This is a major difference from local desktop application viewers with advanced client-based caching strategies.

Figure 1, A through C, illustrates the tradeoff between opening of a case and tile streaming with and without WSI caching. While cases are opened quicker when disabling WSI caching (Figure 1, A and B), tiles are streamed slower (Figure 1, C and D) as each tile has to be generated on a remote file share attached via network. This data set includes 5691 cases with 12 165 WSIs accessed by our pathologists from the LIS between September 11 and September 24, 2020. On September 18, we enabled caching of the entire WSI in the viewer settings, and thereafter, we disabled caching. For the accessed WSIs, we measured 29 399 FOV and 35 049 tiles loaded (every third tile measured). We find that disabling WSI caching accelerates opening of a case significantly from 6.3 to 3.9 seconds and changing to another slide from 1.1 to 0.1 seconds, both improvements noticeable by the user. At the same time, directly streaming the WSI from the storage slightly decelerates the viewer performance at the FOV level (from 270–314 ms) and on a single tile level (77–163 ms). Because the performance gain to open cases and slides greatly outweighs the loss in streaming, we decided to keep WSI caching disabled.

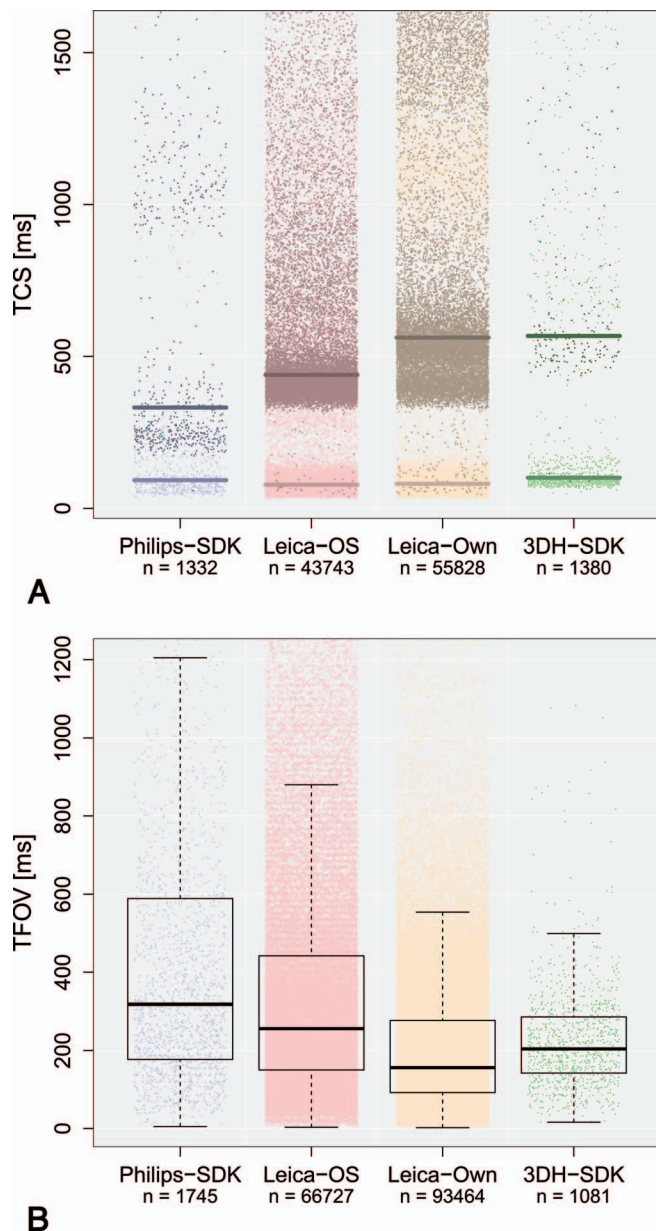
### Influence of Image Compression on TFOV and File Size

WSIs from Leica AT2 Scanners can be compressed with either the JPEG or JPEG2000 standard. We evaluated how the alternative compression techniques affect the streaming of a Web-based viewer. The data set used in this experiment is a total of 2255 Leica files for which the viewer uses OS to access the WSI. The slides have an internal default block size of 512 pixels and a compression quality factor of  $Q = 70$ . Figure 2, A, indicates that JPEG2000-compressed slides need 515 ms to change the FOV of such a WSI, while JPEG-compressed slides need 446 ms to change each FOV. This time difference might be hardly noticeable by the user. On the other hand, JPEG2000-compressed slides use on average a remarkable 40% less space on disk with 36 kB per block instead of 60 kB per block for JPEG-compressed WSIs (Figure 2, B). The superior compression rate of JPEG2000 comes at the cost of a longer decompression time due to a higher complexity.

### Influence of Scanner Type, SDKs, and OS on Time to Change a Slide and TFOV

We included WSIs from the scanners Philips UFS, Leica AT2, Leica GT450, and 3DHitech P1000 to evaluate the influence of the file format on the visualization performance in our viewer. Note that this comparison does not include the native vendors' viewers, but our home-grown, Web-based slide viewer. Therefore, this experiment does not make any claim about the particular vendors' systems. Rather, it gives an impression of how well one can use the file formats outside of their native systems.

To access JPEG-compressed Leica SVS files, we use both OS and alternatively our own implementation of an SVS reader. This implementation uses a byte reader that points to the SVS file and streams the individual JPEG-compressed blocks in the WSI. As a result, the viewer server can send the



**Figure 3.** Viewer performance for different vendors' whole slide images (WSIs). *A*, Time to change a slide (TCS). In all cases, we can differentiate between first-time access of a WSI (darker color) and consecutive access (lighter color). While the first-time accesses need in the median 333 ms (Philips-SDK), 439 ms (Leica-OS), 562 ms (Leica-Own), or 568 ms (3DHistech-SDK) for the change to that slide, returning to those slides greatly improves their loading time to 93 ms (Philips-SDK), 78 ms (Leica-OS), 81 ms (Leica-Own), or 101 ms (3DHistech-SDK) as their slide objects are already instantiated. *B*, Time to show a field of view (TFOV). Median times to display a new FOV are 318 ms (Philips-SDK), 256 ms (Leica-OS), 156 ms (Leica-Own), and 204 ms (3DHistech-SDK).

blocks directly to the client as they are saved in the WSI, without any additional decompression and compression as is done in OS to stitch and crop the blocks to the queried tiles. While this is fast and efficient, it limits the viewer's tile width to be identical with the WSI's block width, as horizontal block stitching would require decompression and recompression of the blocks. For the tile height, we can

stitch multiple blocks together without decompression leading to nonquadratic tiles.

Figure 3, A and B, shows the viewer performance of all 3 scanner types on all 60 080 distinct WSIs reviewed by our pathologists. All WSIs were directly accessed from the storage cluster (ie, without prior caching on the viewer server). In total, 102 302 change-to-slide events were recorded (Figure 3, A). For changing to a slide in the viewer, it is important to differentiate between first-time access and consecutive access of the same slide. For the first-time access, the slide object has to be instantiated on the server (first call of OS, SVS Reader, or SDK). This takes a median of 333 ms for iSyntax files using Philips' SDK, 439 ms for SVS files using OS, 562 ms for SVS files using our byte reader, and 568 ms for MRXS files using 3DHistech's SDK. If a user reopens a case that has been opened earlier, the slides of all 4 vendors are visible almost immediately (below 100 ms). For the impact of the slide type on slide navigation, we measured a total of 163 017 relevant FOV events in the viewer (Figure 3, B). Loading FOVs showed a median of 318 ms for iSyntax files using Philips' SDK, 256 ms for SVS files using OS, 156 ms for SVS files using our byte reader, and 204 ms for MRXS files using 3DHistech's SDK.

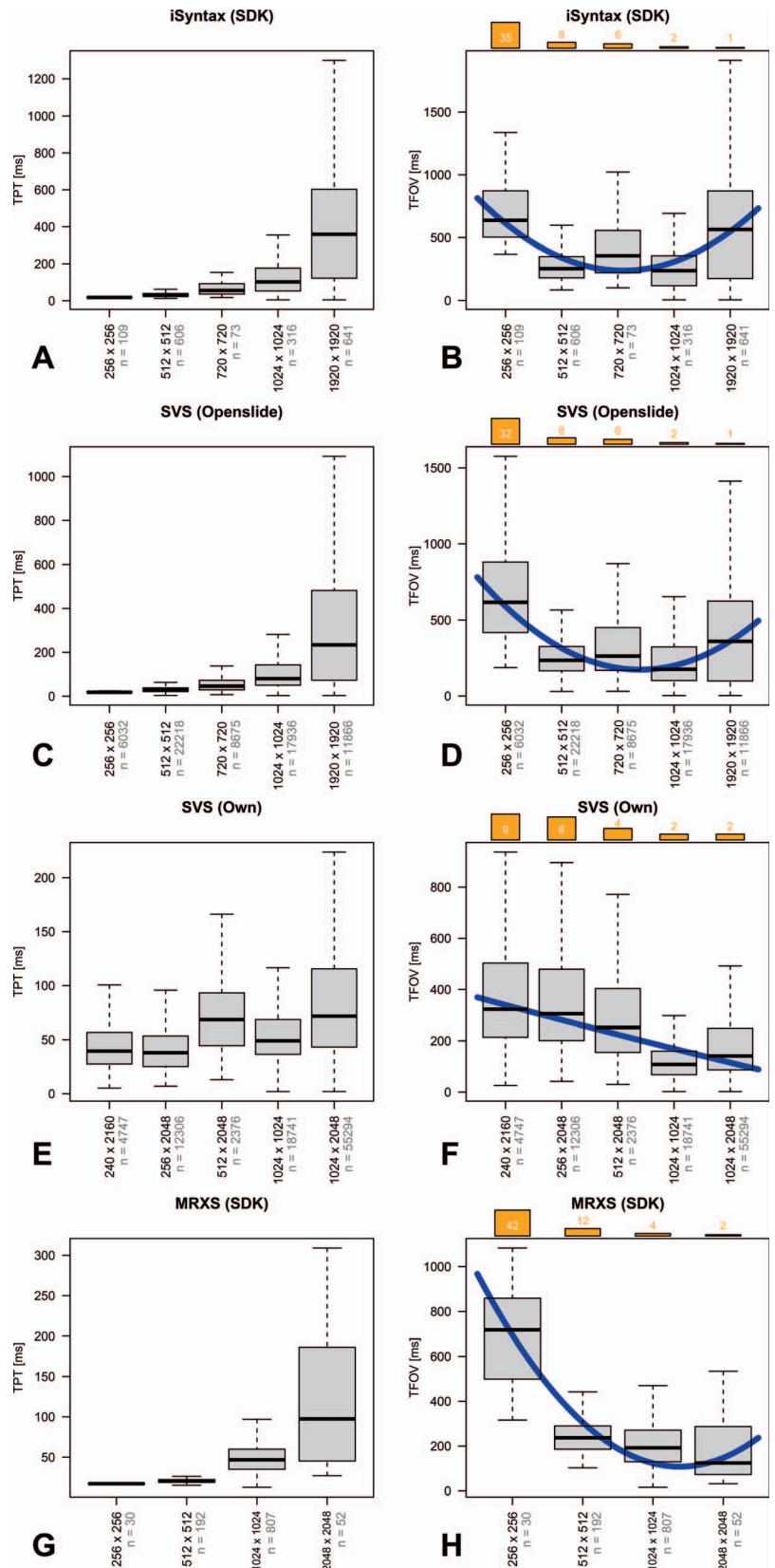
#### Influence of Tile Size on Time Per Tile and TFOV

When serving tiles in an FOV in a Web-based viewer, the tile size directly influences the performance of the viewer; with smaller tiles, an FOV can be served in parallel, but multiple network requests and file accesses are needed to provide the tiles. If there are too many tiles, browser limitations for concurrent requests per client come into play. On the other hand, with larger tiles, fewer tiles are requested for the FOV, but tiles are larger in size and need longer to be generated and transferred. We therefore investigated if there is an optimal tile size for efficient FOV loading. We separated all FOVs served in the viewer by WSI vendor (Philips, Leica, 3DHistech), WSI reader (OS, own, or vendor's SDK), and tile size (240, 256, 512, 720, 1024, and 1902 pixels) and illustrate this relationship in Figure 4, A through H. In the left column, the time per tile is plotted against the different tile sizes for the Philips (Figure 4, A and B), Leica (Figure 4, C through F), and 3DHistech (Figure 4, G and H) slides. As expected, small tiles are the fastest to be delivered in the viewer for all vendors. However, the right column plotting the TFOV demonstrates that small tiles still do not necessarily lead to faster FOVs. Throughout all vendors, there is an empirically optimal TFOV at a tile size of 1024 pixels. Further, for all vendors' slides, the time it takes to generate the FOV is approximately equal to the time per tile multiplied by the number of tiles loaded (yellow bars), indicating that OS, our own implementation, and the SDKs serve the tile queries in sequence rather than in parallel.

When experimenting with different tile sizes in the viewer, we received the following valuable feedback from our users: when small tiles were loaded in an FOV, there was a visible mosaic effect in the FOV that was perceived as disturbing. Larger tiles of 1024 pixels and above, instead, reduced this mosaic effect greatly, which was preferred by our users.

Finally, we investigated the relationship between block size and tile size when generating the FOV. The Leica scanners allow for the control of the block size, and we changed their configuration to use a block size of 240

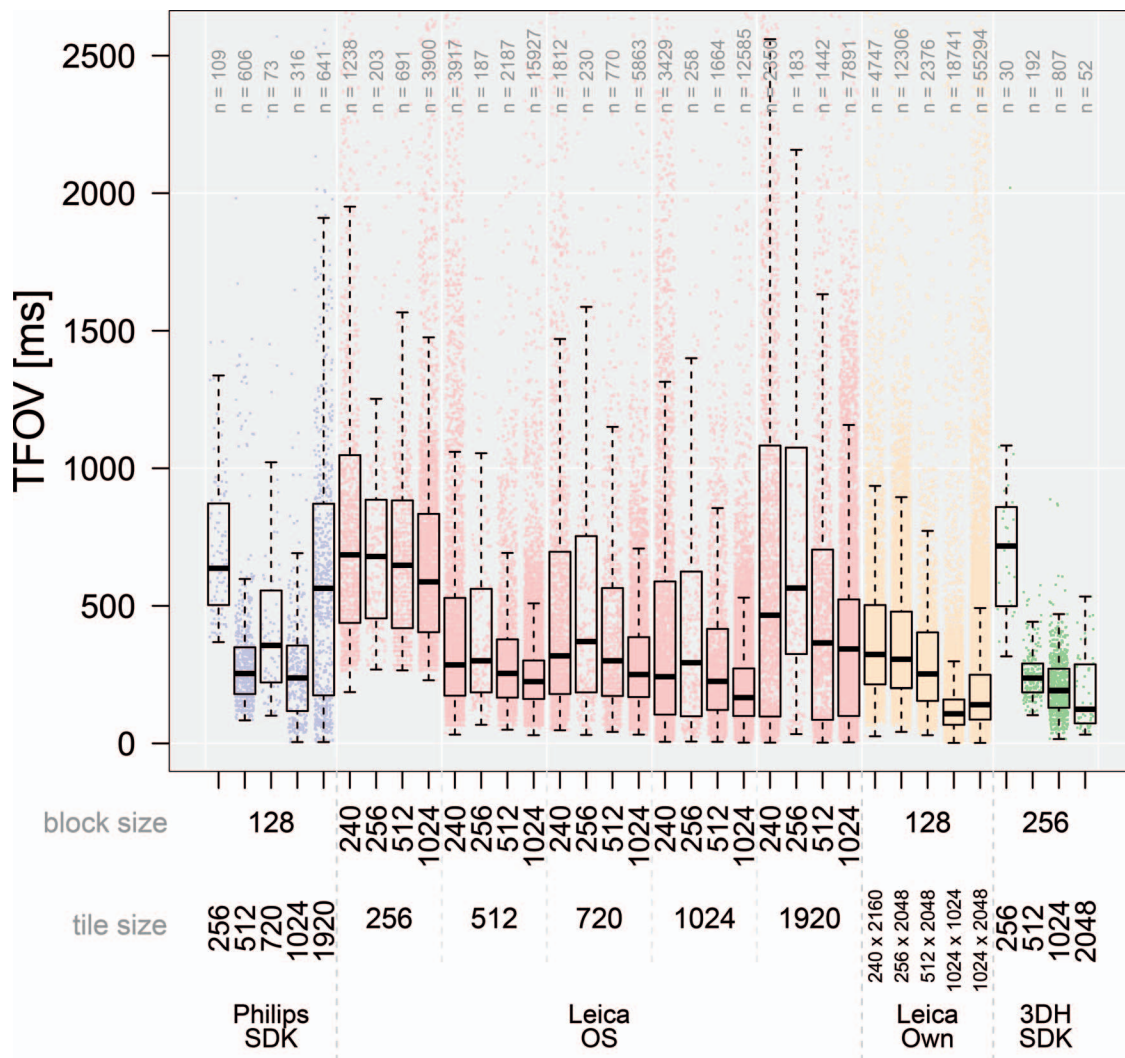
**Figure 4.** Relationship between tile size and time per tile (TPT, left column) or time to show a field of view (TFOV, right column). Tile sizes are given as width  $\times$  height, and are typically quadratic, except for our own SVS byte reader. As expected, larger tiles need more time to be generated and transferred over the network, consistently throughout all tested file formats. Still, the FOV generation profits from larger tiles up to a size of 1024 pixels, because fewer tiles have to be loaded to display the FOV. A and B, Philips iSyntax files (accessed with Philips' software development kit [SDK]). C and D, Leica SVS files (accessed with our own byte reader). E and F, Leica SVS files (accessed with OpenSlide). G and H, 3DHistech MRXS files (accessed with 3DHistech's SDK). Blue: polynomial regression line. Orange: median number of tiles loaded per FOV as measured in the viewer. Abbreviation: N, number of measured FOV events.



(original), 256, 512, or 1024 pixels. This setting was not configurable for Philips or 3DHistech scanners and was preset to 128 and 256 pixels, respectively. After 3 months, our pathologists reviewed 22 345 WSIs included for this

experiment. Figure 5 shows the TFOV stratified by block size and tile size. Similar as before, we observe an optimal block size for Leica WSI at 1024 pixels for fastest FOV streaming (median 167 ms per FOV) when using OS and a tile size of





**Figure 5.** Time to show a field of view (TFOV), stratified by slides of Philips (software development kit [SDK], blue,  $N_{WSI} = 209$ ), Leica (OS, red,  $N_{WSI} = 9018$ ), Leica (Own, yellow,  $N_{WSI} = 12\,846$ ), and 3DHistech (SDK, green,  $N_{WSI} = 272$ ) and by tile size in the viewer and block size in the whole slide image (WSI). WSIs were streamed with a random tile size per WSI. Leica scanners had been configured to use different block sizes. Philips and 3DHistech scanners could not be configured and used fixed block sizes. All measured FOVs were  $1920 \times 915$  pixels. Abbreviation: N, number of relevant FOV events (total 163 017).

1024 pixels. When using our own streaming technique without decompression and compression, this can be further reduced to 108 ms per FOV. The fastest configurations for Philips and 3DHistech WSIs in our viewer were tile sizes of 1024 pixels (median 238 ms per FOV) and 2048 pixels (median 125 ms per FOV), respectively.

## DISCUSSION

For wide adoption of DP, digital slide viewers must be able to efficiently open cases and display and navigate slides. While microscopes visualize glass slides instantaneously, digital viewers are affected by slide loading times, image rendering times, and mosaic effects. Therefore, improved slide streaming techniques to accelerate loading and visualization times are needed. Owing to the large size of digital slides of several gigabytes compressed image data and due to their random access during slide review, these streaming techniques need specific considerations for pathology data, such as intelligent caching, efficient tiling and close connection of image data, and viewer servers. Still,

little effort is done to systematically quantify relevant key measures for reviewing cases and slides, and therewith to discover common bottlenecks.

A most optimal viewer would have an ideal response time of zero seconds for all user interactions. This is of course not reachable, but it has been shown that response times below 1 second increase user productivity significantly (commonly known as *Doherty's 400 ms threshold*).<sup>22</sup>

To our knowledge, we present the first study to define and systematically quantify visualization efficiency via 3 user-centric key metrics for opening a case from the LIS, opening an individual image, and rendering an FOV. These metrics were measured in a Web-based digital viewer in a production system for routine pathology diagnostics at a large academic medical center with 60 080 different slides reviewed by 239 pathologists. Our results indicate an overall acceptable benchmark performance of less than 4 seconds (3.9 seconds) to open a case from the LIS, less than 1 second (333–568 ms) to change to another slide within the viewer, and less than one-fourth of a second (108–238 ms) to

change the FOV. This is not only faster than what has been reported before,<sup>9</sup> but also reaches productive reaction times.<sup>22</sup> Further improvements should be made for the time to open the case, which still takes most of the loading time.

This setup further allows for the comparing of different WSI file formats and critical system configurations, such as caching strategies, tile sizes, and even block sizes. We find that a relatively large block and tile size of 1024 pixels is favorable to both the speed to load an FOV and the user's perception (fewer mosaics). Conventional scanners and viewers use a block and tile size of 128 to 512 pixels, which might be optimal for smaller FOVs. Considering that computer screens get larger with higher resolution in future, we propose to adjust scanners and viewers accordingly.

Of note, we did not compare different viewers with each other, including the native viewers of the vendors' file formats. The reported numbers therefore do not reflect the overall performance of the specific file formats in their native systems, but only of these formats in our own Web-based viewer. While we can measure the proposed metrics in our home-grown system easily, no other viewer reports similar statistics of its own performance over time. With this study, we define key metrics that are meaningful to pathologists, provide a first baseline on what Web viewers can achieve on these metrics with nonstandard configurations, and encourage viewer developers to consider these metrics in their development to make viewers comparable to each other. We give insight in technical details on how to improve DP workflows with specific scanner and viewer configurations.

Not all improvements presented in this study have the same impact. While disabling slide caching accelerated case opening most notably in the order of seconds, changing the block and tile sizes increased the rendering of an FOV in the order of milliseconds, hardly noticeable by the user. Still, it provided a positive association due to reduced mosaic effects. However, the provided metrics will enable us to objectively compare further system configurations and additional viewers and scanners, to drive the development toward a seamless DP workflow. For example, further improvements of digital viewers that were not discussed in this study include pretiling of WSIs, new image compression techniques,<sup>23,24</sup> and advanced Web streaming.<sup>25,26</sup> With improved digital systems, we hypothesize, digital sign out will be on par or even more efficient than with a microscope.

## References

1. Pantanowitz L. Digital images and the future of digital pathology. *J Pathol Inform.* 2010;1(1):15. doi:10.4103/2153-3539.68332
2. Hanna MG, Reuter VE, Hameed MR, et al. Whole slide imaging equivalency and efficiency study: experience at a large academic center. *Mod Pathol.* 2019;32(7):916–928. doi:10.1038/s41379-019-0205-0
3. Hanna MG, Reuter VE, Ardon O, et al. Validation of a digital pathology system including remote review during the COVID-19 pandemic. *Mod Pathol.* 2020;33(11):2115–2127. doi:10.1038/s41379-020-0601-5
4. Buck TP, Dilorio R, Havrilla L, O'Neill DG. Validation of a whole slide imaging system for primary diagnosis in surgical pathology: a community

- hospital experience. *J Pathol Inform.* 2014;5(1):43. doi:10.4103/2153-3539.145731
5. Bauer TW, Schoenfield L, Slaw RJ, Yeran L, Sun Z, Henricks WH. Validation of whole slide imaging for primary diagnosis in surgical pathology. *Arch Pathol Lab Med.* 2013;137(4):518–524. doi:10.5858/arpa.2011-0678-OA
6. Gilbertson JR, Ho J, Anthony L, Jukic DM, Yagi Y, Parwani AV. Primary histologic diagnosis using automated whole slide imaging: a validation study. *BMC Clin Pathol.* 2006;6:4. doi:10.1186/1472-6890-6-4
7. Ardon O, Reuter VE, Hameed M, et al. Digital pathology operations at an NYC Tertiary Cancer Center during the first 4 months of COVID-19 pandemic response. *Acad Pathol.* 2021;8. doi:10.1177/23742895211010276
8. Schöffler PJ, Geneslaw L, Yarlagaadda DVK, et al. Integrated digital pathology at scale: a solution for clinical diagnostics and cancer research at a large academic medical center. *J Am Med Inform Assoc.* 2021;28(9):1874–1884. doi:10.1093/jamia/ocab085
9. Rojo MG, Gallardo AJ, González L, et al. Reading virtual slide using web viewers: results of subjective experience with three different solutions. *Diagn Pathol.* 2008;3(Suppl 1):S23. doi:10.1186/1746-1596-3-S1-S23
10. Technical performance assessment of digital pathology whole slide imaging devices - guidance for industry and Food and Drug administration staff. Food and Drug Administration Web site. <https://www.fda.gov/media/90791/download>. Accessed November 12, 2020.
11. Cheng W-C, Wu C-L, Badano A. Quantitative assessment of color tracking and gray tracking in color medical displays. *Color Imaging Conf.* 2019;2019(1):349–354. doi:10.2352/issn.2169-2629.2019.27.63
12. Goode A, Gilbert B, Harkes J, Jukic D, Satyanarayanan M. OpenSlide: a vendor-neutral software foundation for digital pathology. *J Pathol Inform.* 2013;4(1):27. doi:10.4103/2153-3539.119005
13. OpenSeadragon - an open-source, Web-based viewer for high-resolution zoomable images, implemented in pure JavaScript, for desktop and mobile. OpenSeadragon Web site. <http://openseadragon.github.io/>. Accessed May 10, 2020.
14. Philips Open Pathology Portal. Philips Open Pathology Web site. <https://www.openpathology.philips.com/>. Accessed May 13, 2020.
15. Software Downloads. 3DHISTECH Web site. <https://www.3dhitech.com/software-downloads>. Accessed May 13, 2020.
16. McLendon R, Friedman A, Bigner D, et al. Comprehensive genomic characterization defines human glioblastoma genes and core pathways. *Nature.* 2008;455(7216):1061–1068. doi:10.1038/nature07385
17. Virtual Pathology at the University of Leeds project website. Virtual Pathology at the University of Leeds Web site. [https://www.virtualpathology.leeds.ac.uk/slides/library/view.php?path=%2FResearch\\_4%2FTeaching%2FEQA%2FGeneral\\_Histopathology%2FHisto\\_EQA\\_CircW\\_Set6%2F149712.svs](https://www.virtualpathology.leeds.ac.uk/slides/library/view.php?path=%2FResearch_4%2FTeaching%2FEQA%2FGeneral_Histopathology%2FHisto_EQA_CircW_Set6%2F149712.svs). Accessed February 12, 2021.
18. Digital slide archive (DSA). Cancer Digital Slide Web site. <https://cancer.digitalarchive.org/#!/CDSA/acc/TCGA-OR-A5J1/TCGA-OR-A5J1-01A-01-TS1?slide=TCGA-OR-A5J1-01A-01-TS1.CFE08710-54B8-45B0-86AE-500D6E36D8A5.svs>. Accessed February 12, 2021.
19. Pathpresenter public. Pathpresenter Web site. <https://pathpresenter.net/home>. Accessed February 12, 2021.
20. Objective whole slide image server. Objective Web site. [https://the.pathology.network/view.aspx?global=/CANP%2F2020%2FCase%208&View=/CANP%2F2020%2FCase%208/Case\\_08\\_1.zif](https://the.pathology.network/view.aspx?global=/CANP%2F2020%2FCase%208&View=/CANP%2F2020%2FCase%208/Case_08_1.zif). Accessed September 1, 2021.
21. Organpathologie-Atlas | el-IPH. Universität Heidelberg Web site. <https://eliph.klinikum.uni-heidelberg.de/atlas/?c=05-schilddruese&context=image&pg=1>. Accessed February 12, 2021.
22. Doherty WJ, Thadani AJ. The economic value of rapid response time. <https://jlellioton.blogspot.com/p/the-economic-value-of-rapid-response.html>. Accessed August 10, 2021.
23. Habib RU. Optimal compression of medical images. *Int J Adv Comput Sci Appl IJACSA.* 2019;10(4). doi:10.14569/IJACSA.2019.0100415
24. Helin H, Tolonen T, Ylinen O, Tolonen P, Näpänkangas J, Isola J. Optimized JPEG 2000 compression for efficient storage of histopathological whole-slide images. *J Pathol Inform.* 2018;9:20. doi:10.4103/jpi.jpi\_69\_17
25. Hulsken B. Fast Compression method for medical images on the web. Cornell University Web site. <http://arxiv.org/abs/2005.08713>. Accessed September 28, 2021.
26. Schöffler PJ, Ozcan GG, Al-Ahmadie H, Fuchs TJ. Flextilesource: an openseadragon extension for efficient whole-slide image visualization. *J Pathol Inform.* 2021;12:31. doi:10.4103/jpi.jpi\_13\_21