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Virtual reality Powerwall versus conventional microscope for viewing pathology slides: an experimental comparison

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ABSTRACT

Background

Virtual slides could replace the conventional microscope. However it currently takes 60% longer to make a diagnosis with a virtual slide, due to the small display size and inappropriate user interface of current systems.

Aims

To create and test a virtual reality (VR) microscope using a Powerwall (a high resolution array of 28 computer screens) for viewing virtual slides more efficiently.

Methods

A controlled user experiment was performed to compare the Powerwall with the microscope for four types of task: 1. a simple diagnosis, 2. a decision about a lymph node, 3. finding small objects, 4. score a tissue microarray. User behaviour was recorded with video and a questionnaire.

Results

Time taken to perform all 4 tasks and diagnostic confidence was similar using the Powerwall and conventional microscope.

Conclusions

After just a few minutes familiarization, a VR Powerwall allowed tasks to be performed as quickly and confidently as a microscope. Behavioural data indicated how histopathologists should be trained to make the best use of the large display provided by the VR microscope. Together with the potential for further improvements in the design of the VR microscope, future virtual slide systems could out-perform conventional microscopes in histopathology diagnosis.

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INTRODUCTION

Virtual slides are obtained by scanning glass slides at high resolution to produce a digital image which contains detail that is comparable to when the original slide is viewed at high magnification (up to 800x) through a conventional microscope. The virtual slides used in pathology are very large (typically 100,000 x 100,000 pixel images; 30 gigabytes when uncompressed) but offer great potential to improve pathology in both research and diagnosis. They could increase laboratory efficiency, make obtaining second opinions easier, and be incorporated into other systems including e-learning, image analysis and computer aided diagnosis systems.

Unfortunately, in their current form virtual slides are not an acceptable alternative to the microscope. There are several reasons for this, including a lack of formal approval for clinical use (e.g. US Food and Drugs Administration (FDA) approval), lack of evidence for what constitutes acceptable image quality, a lack of underlying infrastructure in health systems to support digital imaging, and a lack of training (typically pathologists in the UK see between 2000 and 10000 slides per year – possibly many more, but very few pathologists have seen more than a handful of virtual slides).

None of the above is insurmountable, but even if they were all solved one fundamental problem would remain. It currently takes much longer to examine tissue with a virtual slide than it does with a conventional microscope. In previous work we showed that diagnoses took 60% longer with virtual slides than with a conventional microscope, and there was a particularly large difference for tasks involving searching for small objects -

searching for asbestos fibres took over 3 times longer with the virtual slide compared to the microscope.[1]

The two main reasons for the inefficiency of virtual slides are:

1. The display size

A conventional light microscope offers the pathologist an immersive experience which fills much of their field of view with image (e.g. 57 degrees for a Leica DMRB microscope.[2] By contrast, a high resolution computer monitor (1600x1200 pixels) shows only 21% of the viewable area of a typical microscope[1], and most of the computers used in today's hospitals show an even smaller area. Therefore to view the same area of tissue at a comparable resolution would take many more individual views with a virtual slide than with a microscope.

2. The user interface

The user interface is determined by the hardware and software design of the virtual slide application which the pathologist uses to view the slide. Almost all virtual slide user interfaces to date are based on approaches borrowed from image editing software - i.e. a central large image controlled by on-screen buttons on toolbars toward the top of the

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[1] Virtual slides are scanned so that one pixel in the image corresponds to one arc minute (the limit of human visual acuity) of what is seen when the same slide is viewed at an equivalent magnification with a conventional microscope. Thus, the "field of view" of a virtual slide system is dictated by the display resolution.

screen; zooming by pressing buttons with fixed magnification; panning by clicking and dragging the slide or by clicking on thumbnails.

While such interfaces are suitable for viewing and annotating photographs and other such material, they are poorly suited for use with the giant images required for diagnostic pathology because the processes of navigating across a slide, and switching back and forth between regions of interest takes a long time. As a result, most pathologists find using virtual slides to be a slow and frustrating experience.

A VIRTUAL REALITY POWERWALL

A Powerwall is a large, high resolution computer display. It should not be confused with normal projectors which simply display what is visible on a monitor onto a large screen - in this case the resolution of the projected display is the same as the monitor's.

The Powerwall that is installed in the University of Leeds' School of Computing [3] comprises an array of twenty-eight 20-inch TFT screens that provide an overall image size of 3 x 1.3m and resolution of 53 million pixels (see Figure 1).

We developed our own virtual slide application, which ran on the Powerwall and addressed both aspects of diagnostic efficiency that were identified above. First, the very high resolution of the Powerwall meant that it displayed six times more than a microscope in any given view. Second, by implementing techniques developed for virtual reality applications [4], the application was able to render virtual pathology slides in real time so users could pan and zoom into/out of the slides without any noticeable lag. Control was provided by a wireless Logitech Rumblepad 2 [5] (commonly used for computer games, and available from most computer retailers), with one joystick used for

panning and the other for zooming. A movie demonstrating use of the Powerwall is available in supplementary material 1.

EVALUATION

A controlled user experiment was run to compare the Powerwall with a conventional microscope for four types of microscope task. Each participant performed four diagnostic tasks, first with one of the systems (e.g., Powerwall) and then with the other (e.g., microscope). Two sets of slides were used for this, and a third set was used for training (see below). The virtual versions of the slides in each set scanned with an Aperio T3 scanner [6] with a 40x objective lens and compressed with JPEG compression at quality 50. The order in which the two systems were used and the test slide set that was used on each system were counterbalanced between participants.

MATERIALS AND METHODS

Local institutional ethical approval was obtained for the study. Eight pathologists participated (four trainees and four consultants) and performed four diagnostic tasks using both the interfaces. Median experience of pathology was 4.5 years (range 3-5 years) for the trainees and 11 years (range 7-22 years) for the consultants.

For the microscope tasks, a Leica DMRB microscope with 2.5x, 5x, 10x, 20x and 40x objectives was used. An external video camera recorded the pathologists' hand actions as they worked, and a second camera attached to the microscope C-mount recorded the view seen by the pathologist. The recordings were later analysed in detail to record the

microscope lens used at all times during the tasks, details of the frequency and timing of pan and focus actions used and time between fixations.

The virtual reality Powerwall is described above. In contrast to a microscope which allows only fixed magnifications, the Powerwall allowed a slide to be displayed at any magnification, so the zooming action was smooth. The Powerwall software recorded all pan and zoom actions together with a timestamp, including time between fixations. In addition a video camera recorded the physical actions taken by the pathologist as they used the Powerwall. Analysis of this video recording was performed to investigate the physical movements of the pathologists as they used the Powerwall.

The tasks were chosen to test a range of diagnostic and research uses of the microscope as follows (see Figure 2):

1. Make a simple diagnosis

Pathologists were asked to make a simple diagnosis - e.g. a basal cell carcinoma or squamous cell carcinoma of skin.

2. Make a decision about a lymph node

Pathologists were asked to examine a slide containing a number of lymph nodes (from colorectal cancer or breast cancer resection cases) and to count the number of nodes involved by cancer and total number of nodes present.

3. Find small objects

Pathologists were asked to examine a slide of cancer (colorectal cancer or endometrial cancer) and count as many mitoses as possible in 4 minutes.

4. Score a tissue microarray

Pathologists were asked to examine a tissue microarray (of colorectal cancer stained with ki67 immunostain) and assess a 6 x 6 core area using the scale 0 = none; 1 = 1-33%; 2 = 34 -66%; 4 => 67%.

Each pathologist participated in two sessions, one involving usage of the Powerwall and the other a microscope. Participants were shown how to use the Powerwall but were not directed to use it in a prescriptive way.

The procedure for each session was as follows. First, a pathologist was given a short training period with the training slide set, to illustrate the four tasks. Next, the participant was asked to perform the four experimental tasks with the instruction to perform them as if they were a diagnostic case from their daily workload. They were informed that the time they take to perform the task and their actions would be recorded. At the end of each task they were asked for their diagnosis or decision on the slide, and their level of diagnostic confidence on a scale from 0 (no confidence) to 100 (complete confidence).

Once both sessions had been completed, the pathologist was asked for their feedback on the interface used with a questionnaire. Their preferred interface for each task (microscope or Powerwall), and their perceived acceptability for use of the Powerwall in training and diagnosis were recorded on a 10 point Likert scale.

RESULTS

Initial analyses confirmed that participants' performance and diagnostic accuracy was similar with both test sets of slides, similar for expert and trainee pathologists, and not affected by the order in which the systems (Powerwall and microscope) were used. The data below were analysed using analyses of variance (ANOVA), a standard statistical

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techniques for analyzing the results of user evaluations.[7] In the ANOVAs, the interface (Powerwall vs. microscope) and task (simple diagnosis, lymph node, small objects and microarray) were within participants factors, and the grade of pathologist (expert vs. trainee) and the order in which the interfaces were used (Powerwall first vs. microscope first) were between participants factors..

For Tasks 1, 2 and 4 a participant's performance was measured by the time taken to complete the task, whereas performance in Task 3 was measured by calculating the average time taken to find four mitoses (this gave a performance measure that was similar in magnitude to the other tasks). An ANOVA showed that performance with the Powerwall and microscope was similar ($F(1, 4) = 0.20, p > .05$) (see Figure 3).

A second ANOVA showed that participants' confidence in diagnoses made with the Powerwall and microscope was similar ($F(1, 4) = 0.10, p > .05$), but there was a significant effect of task ($F(3, 12) = 8.70, p < .01$) and a significant interaction between these two factors ($F(3, 12) = 4.86, p < .05$). This was caused a tendency by participants to be less confident in task 3 (find small objects) on the Powerwall (possibly related to perceived difficulties in detecting mitoses in a digital image), and difficulties navigating rows and columns accurately in task 4 (score a tissue microarray) with the microscope (see figure 4).

This study was not intended or designed to assess diagnostic accuracy, but there were no errors in the diagnostic task (task 1) in either the microscope or Powerwall trials.

Analysis of the video recordings allowed every pan and zoom action to be identified, and the rate at which these were performed to be calculated (due to a recording error, this rate could not be calculated when one participant did Task 4 on the Powerwall). An

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ANOVA showed that the time interval between pan/zoom actions was higher with the Powerwall than a microscope ($F(1, 3) = 16.19$, $p < .05$) and varied across the tasks ($F(3, 9) = 40.17$, $p < .01$) (see Figure 5). In other words, participants tended to exploit the large display area of the Powerwall by dwelling for a time on each image, whereas a microscope diagnosis involved making many small pan and zoom actions (see also comments on efficient usage of the Powerwall, below).

Qualitative analysis of the videos of the pathologists using the Powerwall showed distinct patterns of efficient and inefficient use. Efficient use was characterised by standing less than 1 metre from the Powerwall (this allowed full advantage to be gained from the detail provided by the Powerwall's very high resolution), and appropriate use of so-called "physical navigation" (i.e. turning the head, moving the eyes and physically walking along the Powerwall to inspect different parts of the display) to minimise minimize the time required for diagnoses (see [8]).

Inefficient usage involved standing too far away from the Powerwall and/or making many small panning/zooming movements to navigate a slide, which mimics the way a conventional microscope has to be used (e.g., locating a target, centering it on the screen, zooming in to view it, adjusting the centering, zooming some more, and so on).

For example figure 6a demonstrates efficient use of the Powerwall during diagnosis of an intradermal naevus. The pathologist used the full field of view provided by the Powerwall, assessing the entire lesion at a medium magnification (about 30% of native resolution, roughly equivalent to 10-15x magnification) and making only 6 pans. In contrast figure 6b demonstrates inefficient (microscope-like) use of the Powerwall for the

same diagnosis, with repeated panning and zooming being used to assess the lesion so that, in total, 45 pans, 5 zooms, and 5 physical steps were made.

Finally, user feedback gathered from the questionnaire showed that pathologists would use the Powerwall for teaching in preference to the microscope, but were neutral in their preference for diagnostic use (Figure 6).

DISCUSSION

If virtual slides are to replace the conventional light microscope in diagnostic pathology, research and teaching then major improvements are needed in the design of virtual slide systems. In particular, the user interface of these systems needs to be radically improved so that tasks can be performed as quickly (and preferably quicker) than with a microscope.

Previously our research has shown that diagnoses take an average of 60% longer when a virtual slide is viewed on a desktop PC than when a glass slide is viewed through a microscope.[1]

The present study showed that, after just a few minutes familiarization, use of a virtual reality Powerwall allowed tasks to be performed as quickly and confidently as with a microscope, and diagnostic errors were not made with the Powerwall (though the study was not designed or powered to test diagnostic accuracy). The reasons for this large performance improvement are: (1) the very large amount of a slide that can be seen in a single view (six times what was visible in the microscope's field of view, allowing the pathologist to assess large areas of tissue with minimal activity), and (2) the fact that

pathologists could pan and zoom into/out of the slides smoothly and without any noticeable lag.

The present study also highlighted the type of strategy that help pathologists to exploit the large display area of a Powerwall to make rapid, accurate diagnoses. The key elements of an effective strategy are standing close to the display (it is designed to be viewed from a similar distance as a desktop PC) and, where possible, physically moving ones eyes, head and body to scan the display instead of mimicking the way that a conventional microscope is used and making many small movements with the interface device (e.g., mouse or gamepad). With simple training and more understanding of how a large display works, all pathologists could learn efficient patterns of use – just as they have with the conventional microscope over many years.

Finally, we plan further research involving "intelligent navigation" that automatically guides the pathologist around regions of interest in the tissue, and refinements of our Powerwall interface. With these developments, we expect that Powerwalls will soon provide a more efficient way to examine tissue than the conventional light microscope, increasing both their acceptability to pathologists and the likelihood that they will replace the microscope in clinical, research and teaching use.

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Figure captions

Fig 1: The 53-million pixel Powerwall used to view virtual slides. Each of the 28 TFT screens has a resolution of 1600x1200 pixels. The "thumbnail" image (displayed on four screens; top right hand side of the Powerwall) shows the whole slide and allows a pathologists to identify the part of the slide that is shown on the main display. The pathologist controls the Powerwall display with a cordless joystick. In this image the same virtual slide shown in figure 6 is being viewed (a specimen of skin showing an intradermal naevus).
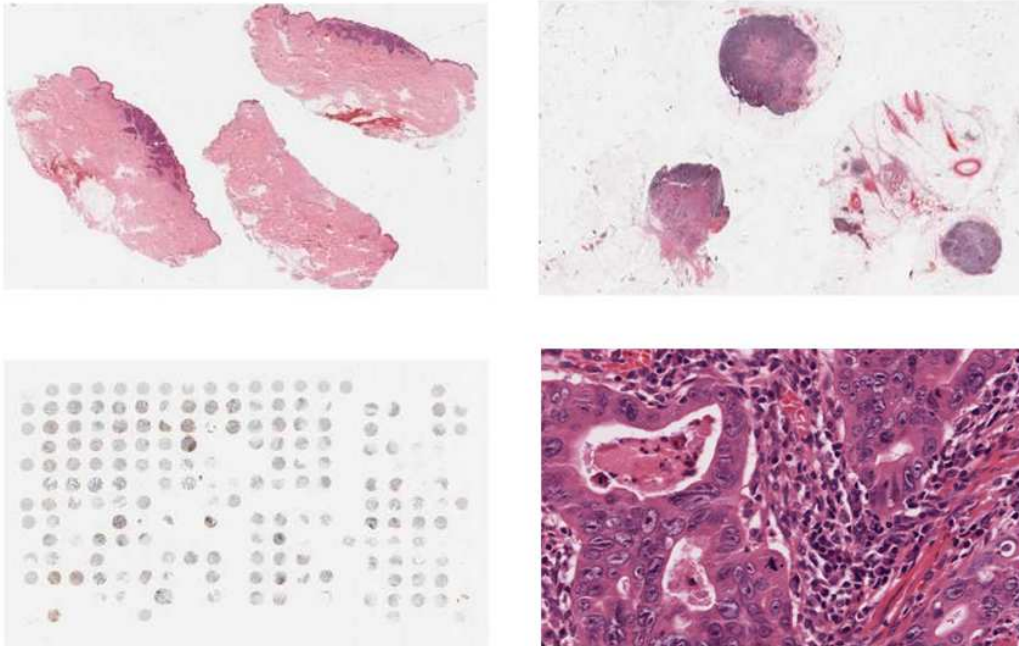
Fig 2: Examples of the virtual slides used, clockwise from top left: 1. Make a simple diagnosis, 2. Make a decision about a lymph node, 3. Find small objects, 4. Score a tissue microarray. Further information about the specific tasks is in the Methods section.
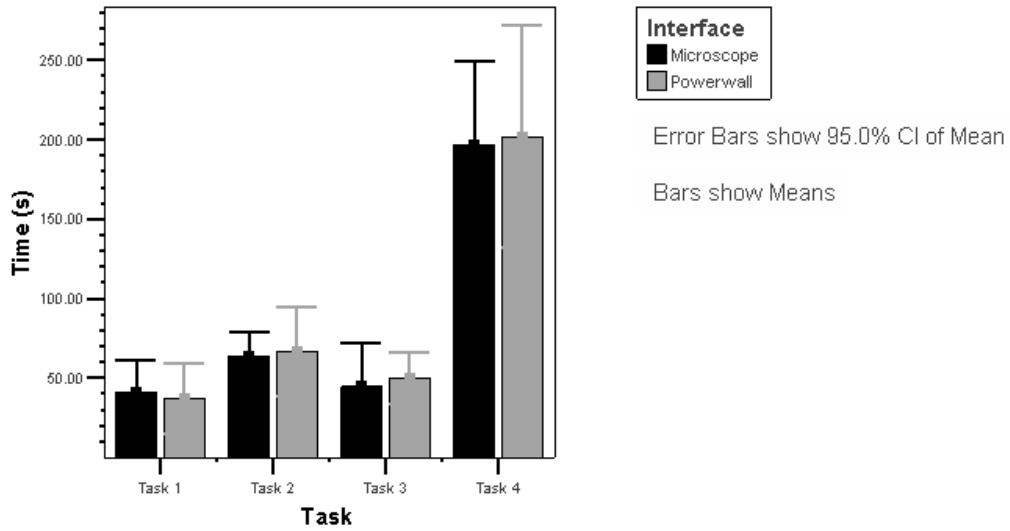
Fig 3: Participants' mean performance (time taken to complete Tasks 1, 2 & 4; time to find 4 mitoses in Task 3) with the Powerwall and conventional microscope. Error bars show 95.0% confidence interval (CI) of the mean.
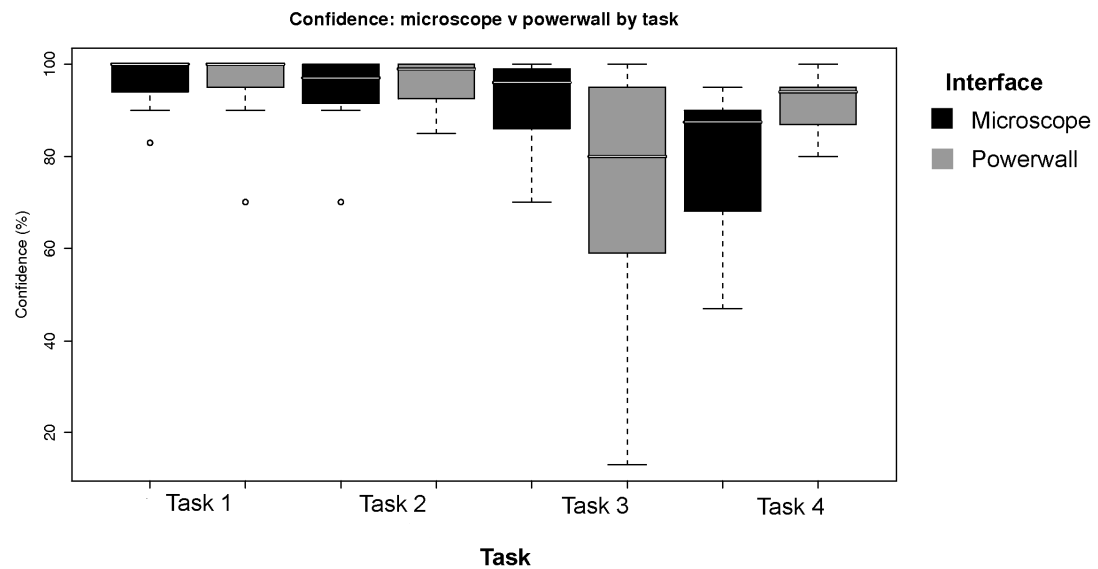
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Fig 4: Participants' mean confidence in making diagnoses with the Powerwall and conventional microscope. Error bars show 95.0% CI.

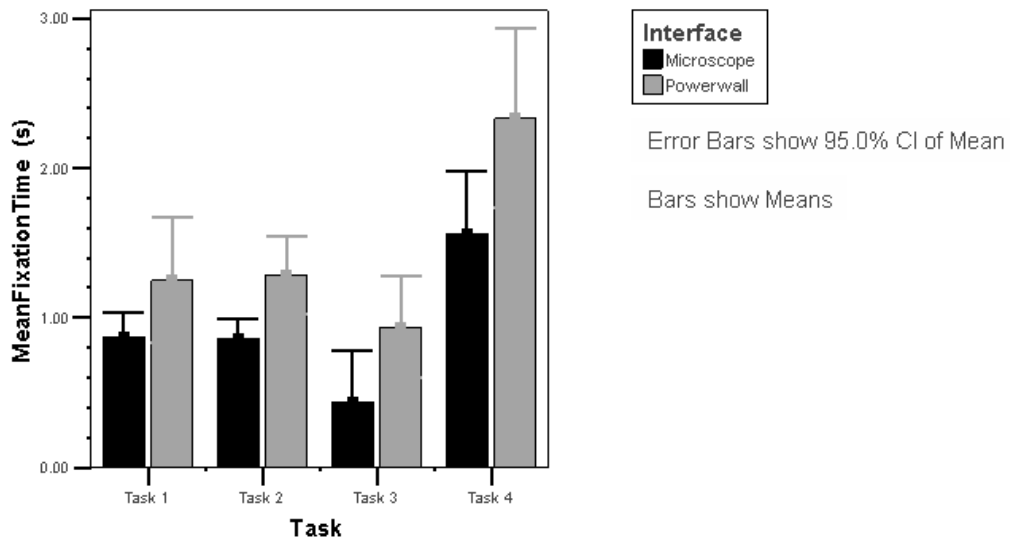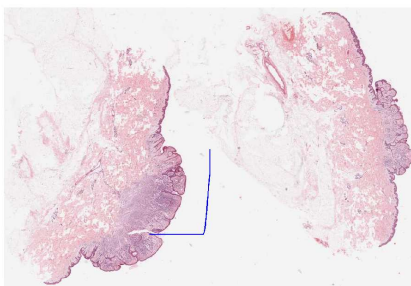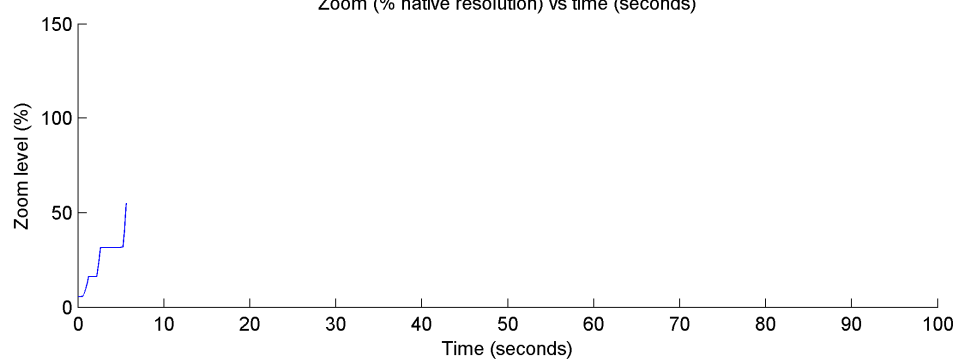Fig 5: Mean fixation time (time between each pan and zoom action performed) for the Powerwall and conventional microscope. Error bars show 95.0% CI.

Path taken to view slide

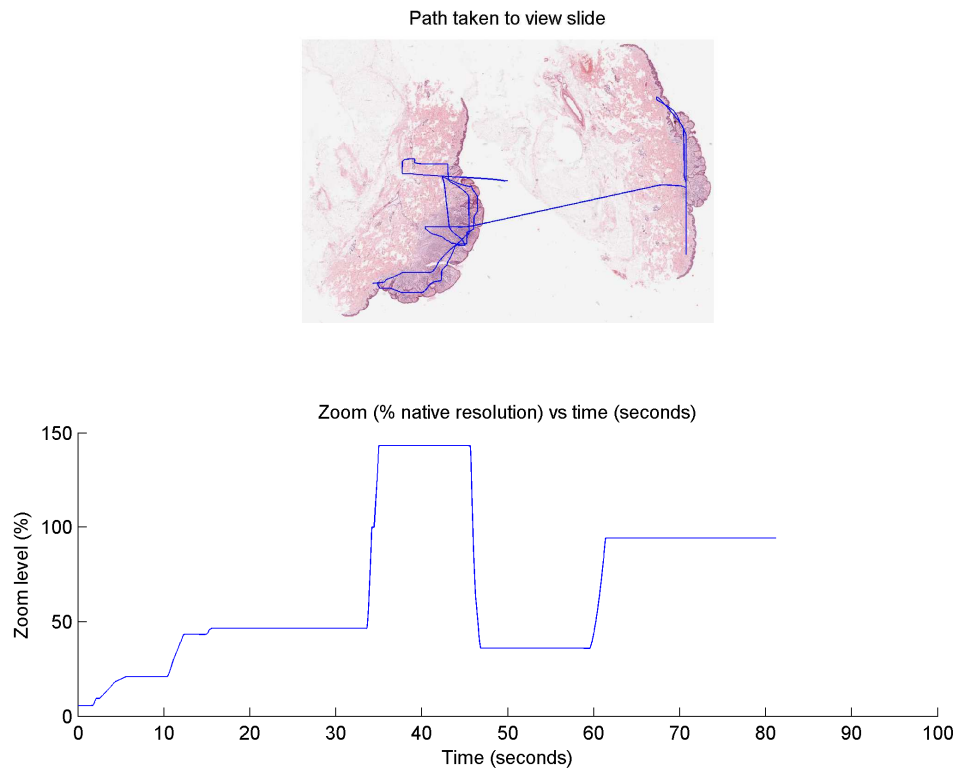Zoom (% native resolution) vs time (seconds)

Fig 6: Examples of efficient (a) and inefficient (b) use of the Powerwall. The path taken while viewing the slide is superimposed on a snapshot of the slide (above), and the magnification used during the task is plotted against time below. Magnification (zoom level) is expressed as percentage of native resolution – the slides were scanned with a 40x objective lens, so 100% is 40x, 50% is 20x, 25% is 10x etc.
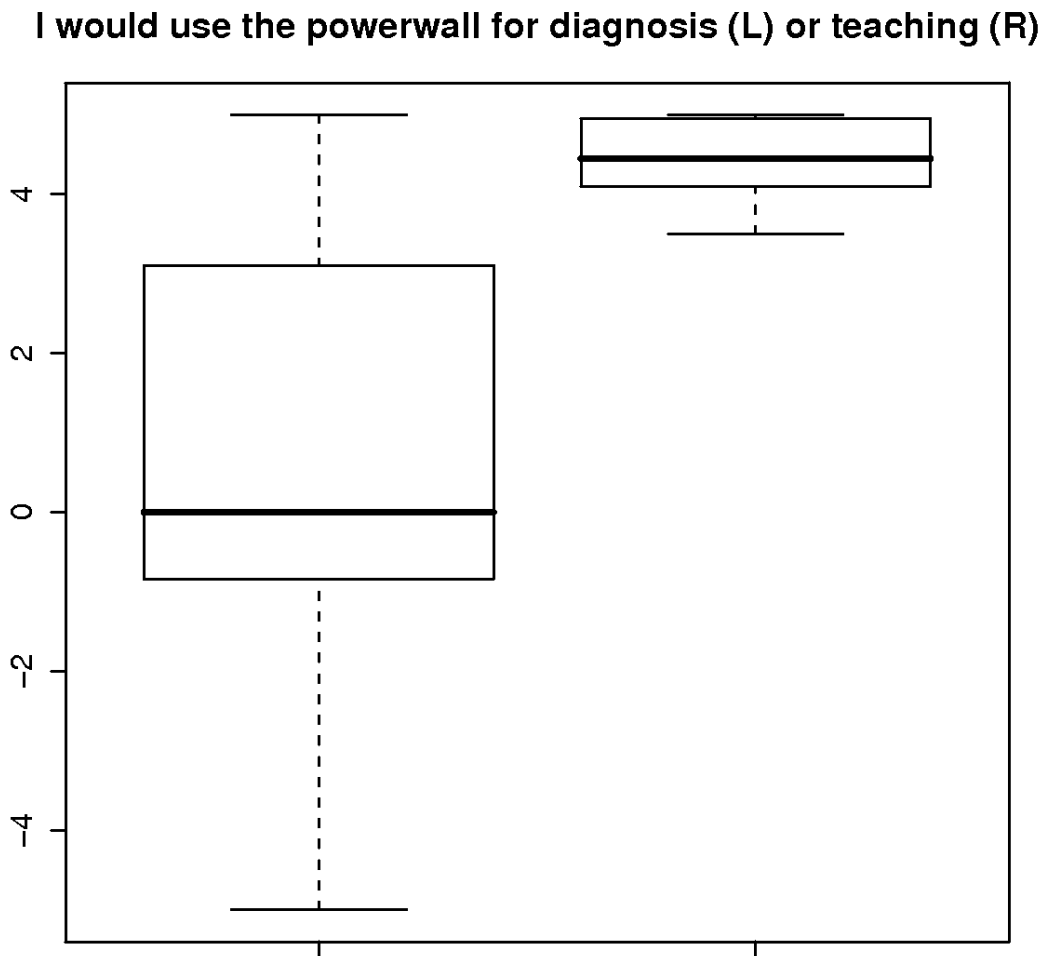
I would use the powerwall for diagnosis (L) or teaching (R)

Fig 7: Acceptability of Powerwall for diagnostic or teaching use. A boxplot showing pathologists agreement with the statement "I would use the Powerwall for diagnosis (left) or teaching (right)", where 0 is neutral, -5 is strongly disagree and +5 is strongly agree.

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