A Feasibility Study of Multisite Networked Digital Pathology Reporting in England

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Abstract

Background: The objective of the project was to evaluate the feasibility of introducing a single-networked digital histopathology reporting platform in the Southwest Peninsula region of England by allowing pathologists to experience the technology and recording their perceptions. This information was then used in planning future service development. The project was funded by the National Health Service (NHS) Peninsula Cancer Alliance and took place in 2020 during the COVID-19 pandemic. **Materials and Methods:** Digital slides of 500 cases from Taunton were reported remotely in Truro, Plymouth, Exeter, Bristol, or Bath by using a single remote reporting platform located on the secure Health and Social Care Network (HSCN) that links NHS sites. These were mainly small gastrointestinal, skin, and gynecological specimens. The digital diagnoses were compared with the diagnoses issued on reporting the glass slides. At the end of the project, the pathologists completed a Google Forms questionnaire of their perceptions of digital pathology. The results were presented at a meeting with the funder and discussed. **Results:** From the 500 cases there were nine cases of significant diagnostic discrepancy, seven of which involved the misrecognition of *Helicobacter pylori* in gastric biopsies. The questionnaire at the end of the project showed that there was a general agreement that the platform was easy to use, and the image quality was acceptable. It was agreed that extra work, such as deeper levels, was easy to request on the software platform. Most pathologists did not agree that digital reporting was quicker than glass slide reporting. Some were less confident in their digital diagnoses than glass diagnoses. They agreed that some types of specimens cannot easily be reported digitally. All users indicated that they would like to report at least half of their work digitally in the future if they could, and all strongly agreed that digital pathology would improve access to expert opinions, teaching, and multidisciplinary meetings. It was difficult to find pathologists with time to undertake remote digital reporting, in addition to their existing commitments. **Conclusions:** Overall, the pathologists developed a positive perception of digital pathology and wished to continue using it.

Keywords: Cancer diagnosis, digital pathology, information technology, software

Background

In the United Kingdom, most cellular pathology laboratories are run by the state-owned NHS, usually at an NHS hospital site. The legal entity that owns and operates these laboratories is usually an NHS trust. This is a public sector body with responsibility for the provision of state-funded health care in a particular geographic region, or occasionally a highly specialist area of care. Typically, an NHS trust will operate only one pathology laboratory to support its health-care activities. Despite these laboratories all being state-owned and funded, sharing work between them is difficult as they are managed independently, usually with no shared staff. In addition, they operate a wide variety of different laboratory information systems that are not interconnected. Transportation of glass slides between these laboratories can be complex to administer and slow. Digital pathology has been in use in the United Kingdom for about 10 years but has not yet been widely adopted. However, it seems to have the potential to improve cooperation between NHS laboratories, allowing them to share capacity and expertise. The objective of the project was to evaluate the feasibility of introducing

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a single-networked digital histopathology reporting platform in the Southwest Peninsula region of England by allowing pathologists to experience the technology and understand its benefits and shortcomings. This project was funded by the NHS Peninsula Cancer Alliance and involved seven NHS pathologists at five hospital sites in the Southwest of England over a period from March to December 2020, during the COVID-19 pandemic.

Materials and Methods

Digital slides of 500 cases from Taunton were reported remotely in Truro, Plymouth, Exeter, Bristol, and Bath (see authors' institutions above and [Figure 1]) by using a single remote reporting platform located on the secure HSCN that links NHS sites. At the start of the project, scanning was performed on a GE / Omnyx scanning platform, but this was replaced about one-third of the way through the project with a Sysmex / 3D Histech platform, due to the Omnyx platform reaching the end of its maintenance cover with the vendor. Scanning was at the "x40 objective" setting on both platforms. All of the participating NHS sites had pathology laboratories that were accredited by The United Kingdom Accreditation Service. Seven remote pathologists volunteered to assist in the study, all with consultant grade posts in the NHS. These pathologists logged onto the Free D Path reporting platform remotely via the HSCN and selected cases from a list of unallocated pending work [Figure 2]. Pathologists were free to avoid cases that were not within their specialty experience and training. One pathologist only reported breast specimens. Each case was reported by only one remote pathologist. Pathologists used the existing equipment provided by their NHS site, and this equipment varied from site to site. No specialist equipment was installed at the remote reporting sites. Some pathologists used voice recognition software. The reporting platform linked the cases, via a hyperlink, to the relevant images on a separate server, and also handled the administration of the cases and extra work requests. Connection could be via client software installed on the pathologist's computer, or a web browser. If the pathologist was reporting away from an NHS site, for example from home, then a VPN connection to the HSCN was used. Most of the specimens were simple, nonurgent samples of the type that are commonly accumulated in reporting backlogs. Most could be reported without additional laboratory work such as immunohistochemistry. The reports from the remote digital pathologists were not published or used for clinical management but were compared with the conventional glass slide reports by a different pathologist, and discrepancies were noted. Pathologists were given the opportunity to review the glass slides of cases for which there was discrepancy with the digital diagnosis. Information was collected on accuracy of diagnoses but this was not easily comparable with other studies of the accuracy of digital pathology as some of the pathologists in our study had had no prior experience of, or training

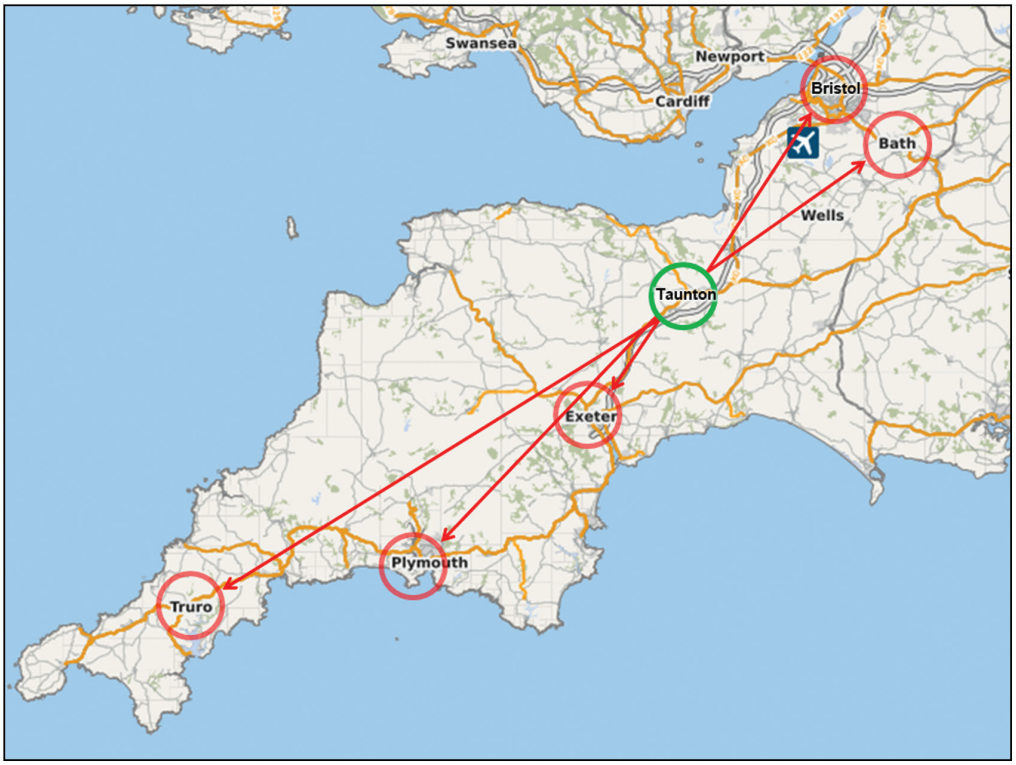


Figure 1: The study involved NHS sites in the Southwest Peninsula of England. Digital slides scanned in Taunton were reported remotely in Truro, Plymouth, Exeter, Bristol, and Bath by using the Free D Path networked reporting platform. (Map© OpenStreetMap contributors)

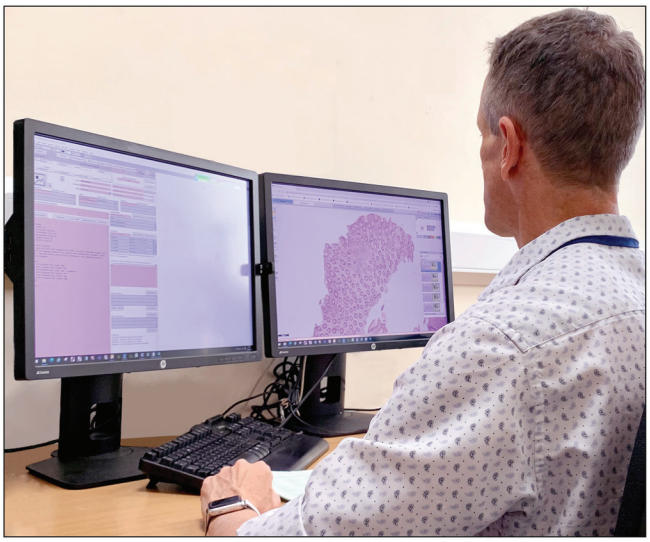


Figure 2: A pathologist reporting a digital slide (right) using the Free D Path software platform (left). This model allowed multiple remote NHS sites to run on a single server using the HSCN secure network. The server was located in Taunton. (original image)

in, digital pathology, and they were using suboptimal equipment. Also, digital and glass slide interpretations of the cases were by different pathologists, and the study was small, involving only 500 cases divided between seven pathologists. The assessment of diagnostic accuracy was not the principal purpose of the study.

At the end of the project, the participating pathologists filled out a Google Forms questionnaire regarding their perception of the reporting platform and digital pathology in general, so as to inform plans for future use in the region. The project coincided with the start of the COVID-19 pandemic, spanned the first two "lock-downs" in England, and, consequently, attracted some interest as a tool to allow pathologists to keep reporting while isolating at home.

Results

Technical aspects

The main purpose of this study was to gather information to more fully understand the difficulties and benefits that might be encountered when introducing a multisite digital pathology platform. It was anticipated that access to the network platform might be hindered by the local information technology protocols at each of the participating sites. For this reason we chose to use a platform that had a fully functional web browser mode, thus avoiding dependence on local IT support or the need to install client software locally on the pathologists' computers. For two sites the server IP address needed to be authorized by the site's local IT administration. This permission should take only a few minutes to implement, but in practice can take some weeks to negotiate. Fortunately, the other sites were able to access the server immediately without requesting any IT support. The platform required a password-protected user login; it incorporated user activity tracking and record-level access control to prevent users from seeing cases that were not part of the project. We were able to use the platform and start digital reporting within a month of the funding being approved.

Specimen types

Of the 500 cases, the most common five specimen types were large bowel biopsies (n = 126), skin excisions and biopsies (n = 65), stomach biopsies (n = 60), duodenal biopsies (n = 56), and endometrial samples (n = 50). Overall, 72 cases had at least one extra work requested. The most common request was for extra levels (n = 27) and the next most common was diastase PAS for fungi (n = 12), mainly for esophageal biopsies.

Process errors

These were technical errors in the digital scanning and reporting pathway. There were six, including slides being out of focus, incorrect digital slide hyperlinks, and one or more slides missing. The linking of the slides to the cases on the reporting platform was a partially manual process and could be improved by automation. Imperfect focus often involved only part of the slide. Another potential problem with digital pathology can be nonrecognition of tissue. This is when the scanner mistakes pale tissue, such as fat, mucus, or sparsely cellular tissue, for an empty background and does not include it in the territory that is scanned. However, this was not noticed in any of the cases in the project.

Minor diagnostic discrepancy

This is a reporting issue that involves a minor discrepancy in diagnosis that would not have a significant impact on clinical management. There were seven examples. Most involved the distinction between hyperplastic polyps and sessile serrated lesions in large bowel biopsies. This is a well-known area of subjectivity in gastrointestinal pathology and is unlikely to be related solely to digital reporting.

Significant diagnostic discrepancy

This is a reporting issue that involves a discrepancy in diagnosis that could have an impact on clinical management. There were nine of these, seven of which involved the misrecognition of *Helicobacter pylori* in gastric biopsies. There was also a case involving the distinction between reactive changes and dysplasia in a gastric biopsy, and a case in which a gastric neuroendocrine tumor was not recognized on digital reporting.

Review of diagnosis

In all cases with a discrepancy between the glass and digital result, the glass result was accepted as correct on review.

Pathologist availability

This study involved reporting 500 cases digitally over a period of nine months at five sites. Although this is not a large volume of work, it was difficult to find pathologists with the time to do it, in addition to their routine work.

User perceptions and acceptability of the platform

The pathologists involved in the study participated in an end-of-study questionnaire, collected using Google Forms [Figures 3–18]. Most of the pathologists had limited previous experience of digital pathology. There was an agreement that the platform was easy to use, and the image quality was good. It was agreed that extra work, such as deeper levels and immunohistochemistry, was easy to request. Most pathologists did not agree that digital reporting was quicker than glass slide reporting. Some were less confident in their digital diagnoses than glass diagnoses. They agreed that some types of specimens cannot easily be reported digitally. All users indicated that they would like to report at least half of their work digitally in the future if they could, and all strongly agreed that digital pathology would improve access to expert opinions, teaching, and multidisciplinary meetings.

Discussion

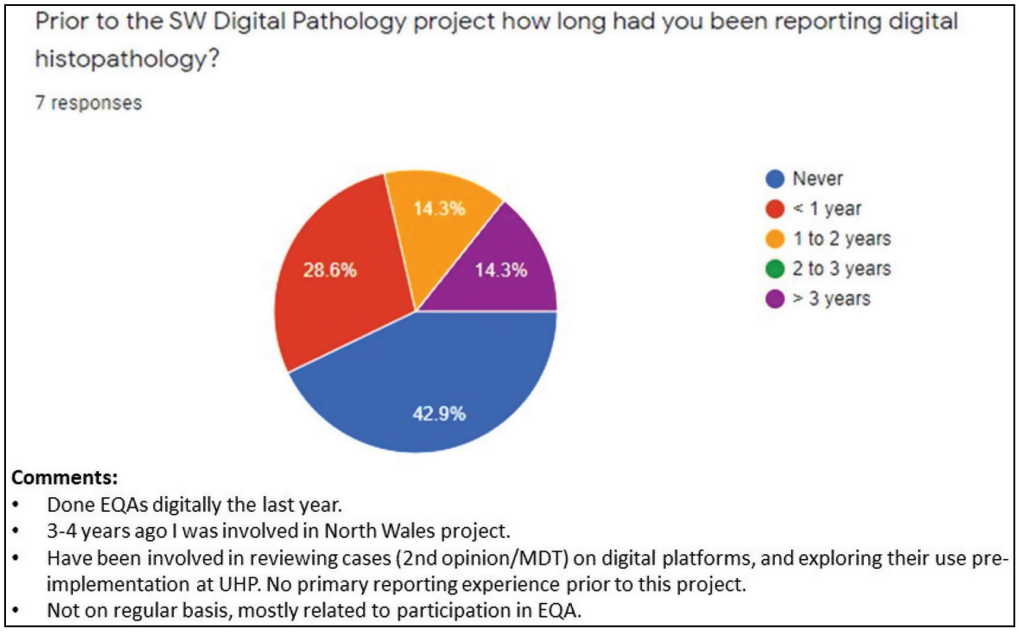
This was a service evaluation study of a networked digital reporting model; it was not principally designed to compare the digital and glass slide reporting, particularly as the digital and glass slides were not reported by the same pathologist and some of the discrepancies could be due to variations in interpretation between pathologists rather than due to the slide type. We found that where there was a discrepancy between the digital and glass slide diagnosis, the latter was correct in all cases. It has previously been found that for cases with a discrepancy between glass and digital diagnoses, the glass diagnosis was preferred in 85%, increasing to 93% for a discrepancy that has the potential to cause moderate or severe patient harm.[1]

A good deal of data has already been published on the accuracy of digital pathology, although an assessment by the Royal College of Pathologists[2] concluded that the overall quality of the evidence was not high, and many studies were small. One study reviewed 1,155 abstracts, of which 38 papers were included in a systematic analysis.[3] The overall diagnostic concordance between digital pathology and conventional microscopy ranged from 63% to 100%, with a weighted mean of 92.4%. A large 2017 study in the United Kingdom included 3,017 cases[4] with a noninferiority design and prior sample size calculation. It demonstrated no inferiority of digital diagnosis compared with the light microscope and complete concordance or no clinical difference in 99.3% of cases (95% confidence interval 99.0% to 99.6%). Another study conducted in the United States with a wide range of specimen types also demonstrated no inferiority.[5] For the cases in our small and limited study, significant diagnostic discrepancy (i.e. discrepancy with a clinical difference) was absent in 98.6%. However, the difficulty in recognizing *Helicobacter pylori* was well known[4,6] before the project started and if it had been avoided by not including gastric biopsies or performing reflex *Helicobacter pylori* immunohistochemistry on gastric biopsies, then the percentage could have increased to 99.6%. The pathologists used their existing equipment, and this varied from site to site. However, this was not the reason that helicobacter could not be seen in some cases as when these cases were reviewed on specialist monitors in the department in which they were scanned and the organisms could still not be seen on the Giemsa stain, even with the knowledge that they were there. *Helicobacter* associated gastritis has a characteristic pattern of inflammatory infiltrate that will usually prompt a pathologist to make a careful search of the digital slides for the organisms. If the pathologists in this study were to progress to using digital pathology in a "live" diagnostic setting, then they would most likely adhere to recommendations on digital reporting published by The Royal College of Pathologists, the professional body of pathologists in the United Kingdom. It is notable that this guidance was recently updated in response to COVID-19 and now acknowledges that "Pathologists who have limited or no validation, or who have not used digital pathology before will find that they can confidently report some or many cases digitally, without undertaking a formal 1 - 2 month validation comparing glass and digital, but should be aware of the risks and mitigate this risk where possible."[7] Our study tends to support this view. The pathologists' performance was good despite them being mainly unfamiliar with digital reporting.

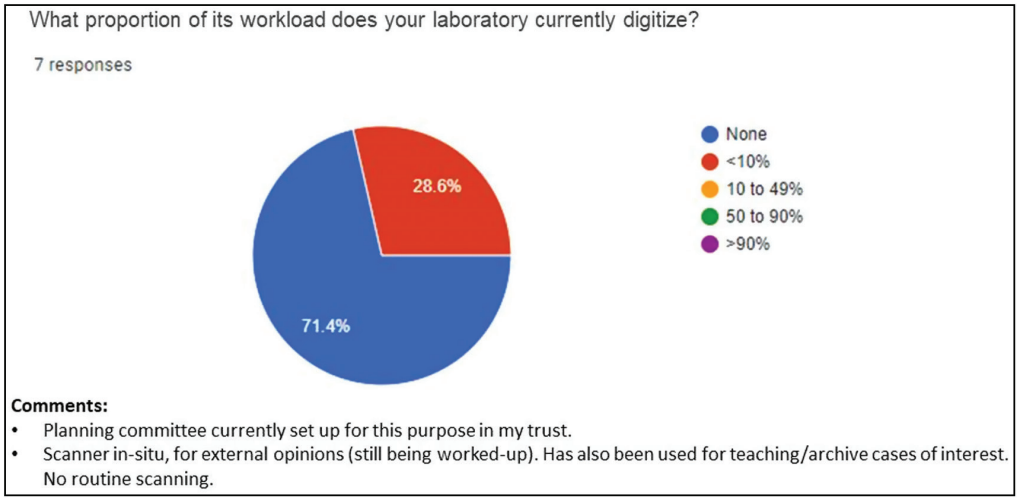
It should be noted that this study focused on simple, nonurgent samples of the type that commonly accumulate in reporting backlogs. Digital pathology also has an important potential role in allowing specialist expert groups to share and co-report complex cases, such as lymphomas, across a network. In England, some types of specialist cases are usually double reported, but sending glass slides offsite for another opinion adds delay when the nature or disease requires rapid diagnosis and treatment. In this scenario, remote digital reporting can be particularly valuable.

Most pathologists did not agree that digital reporting was quicker than glass slide reporting. Some were less confident in their digital diagnoses than glass diagnoses. However, these were pathologists with only limited experience of digital reporting and both speed and confidence are likely to improve with practice.

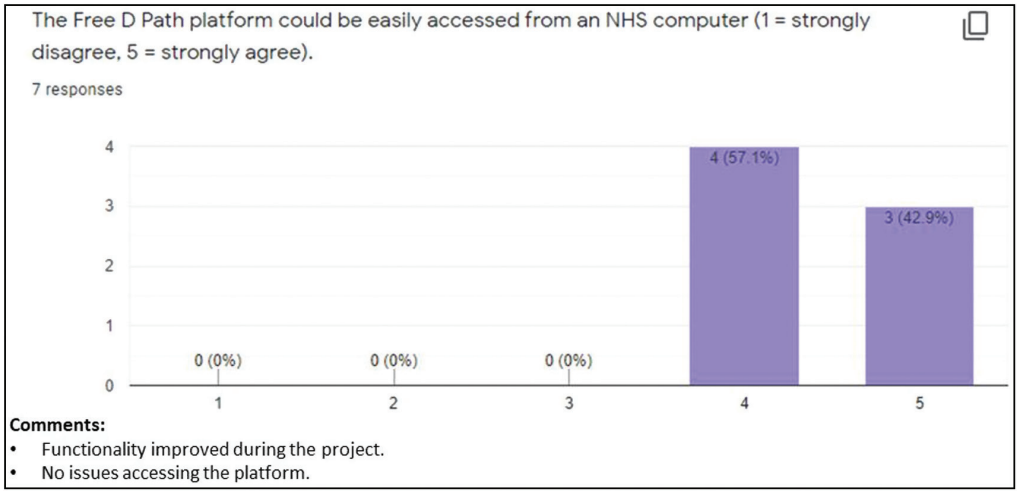
This service evaluation study could be a template to be copied in other regions, before introducing a digital pathology platform. It allows a group of potential users



Comments:
- Done EQAs digitally the last year.
- 3-4 years ago I was involved in North Wales project.
- Have been involved in reviewing cases (2nd opinion/MDT) on digital platforms, and exploring their use pre-implementation at UHP. No primary reporting experience prior to this project.
- Not on regular basis, mostly related to participation in EQA.

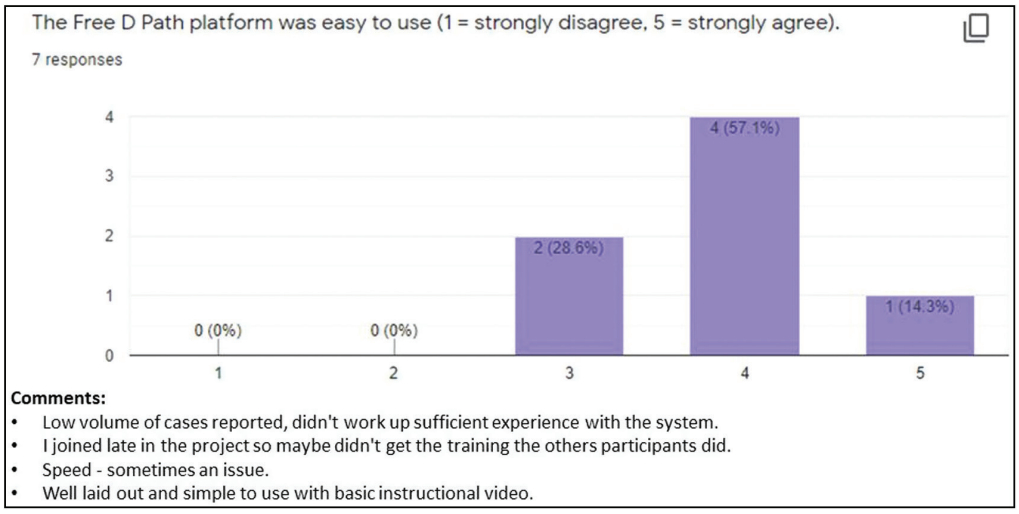


Comments:
- Planning committee currently set up for this purpose in my trust.
- Scanner in-situ, for external opinions (still being worked-up). Has also been used for teaching/archive cases of interest. No routine scanning.



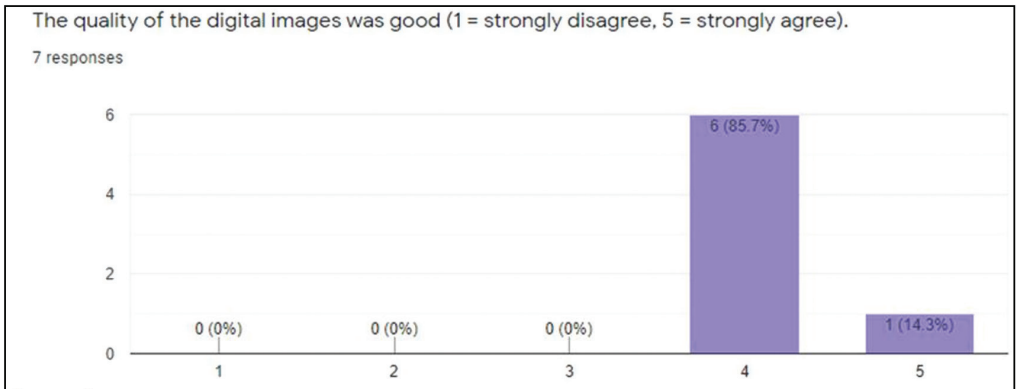
Comments:
- Functionality improved during the project.
- No issues accessing the platform.

Figure 3–18: Questions and responses that reporting pathologists gave regarding the study. These were collected by using Google Forms. The comments include some abbreviations. SW = Southwest, EQA = external quality assessment, MDT = multidisciplinary meeting, UHP = University Hospital Plymouth, Free D Path = the networked reporting software, RCT = Royal Cornwall Hospital, H&E = hematoxylin & eosin stain, IHC = immunohistochemistry, HPB = hepatobiliary, GI = gastrointestinal, UGI = upper GI



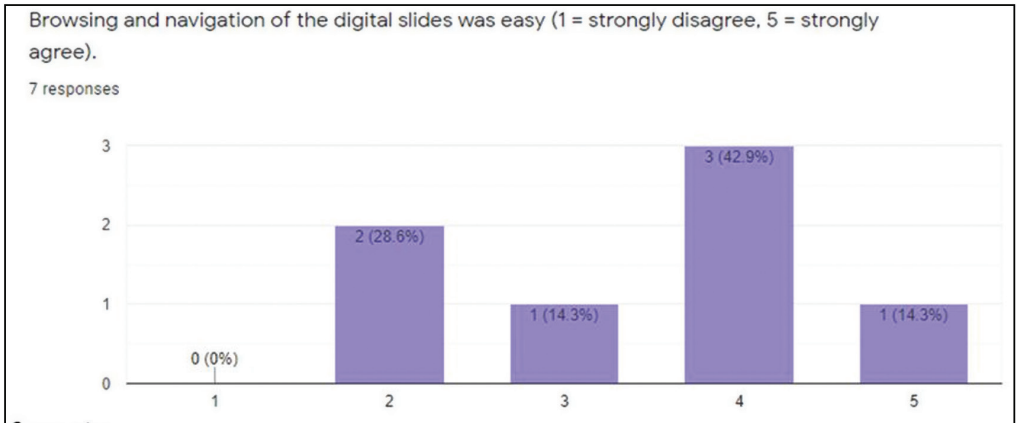
Comments:

- Low volume of cases reported, didn't work up sufficient experience with the system.
- I joined late in the project so maybe didn't get the training the others participants did.
- Speed - sometimes an issue.
- Well laid out and simple to use with basic instructional video.



Comments:

- I find pale H&E stains more difficult on digital and glass and Taunton's (like RCHT) are quite pale to my eye.
- Adequate. Quite pale staining with a lack of contrast.
- Mostly good images.



Comments:

- Images opening in new window/tab confusing.
- I prefer the Sysmex slides to the original Omnyx system you were previously using which didn't pan toward your mouse pointer.
- My only concern was that zooming was not cursor centered but slide centered so that when I zoomed I lost the area what I was looking at.
- Slow and cumbersome on my work computer.
- Connection speed via VPN form home was slower, but feasible. May be due to local network setup (WiFi), as fine on hospital network.
- It takes more time compared to microscope for moving slides. A 3D mouse or something similar to microscope stage can be helpful.

Figure 3–18: Continued

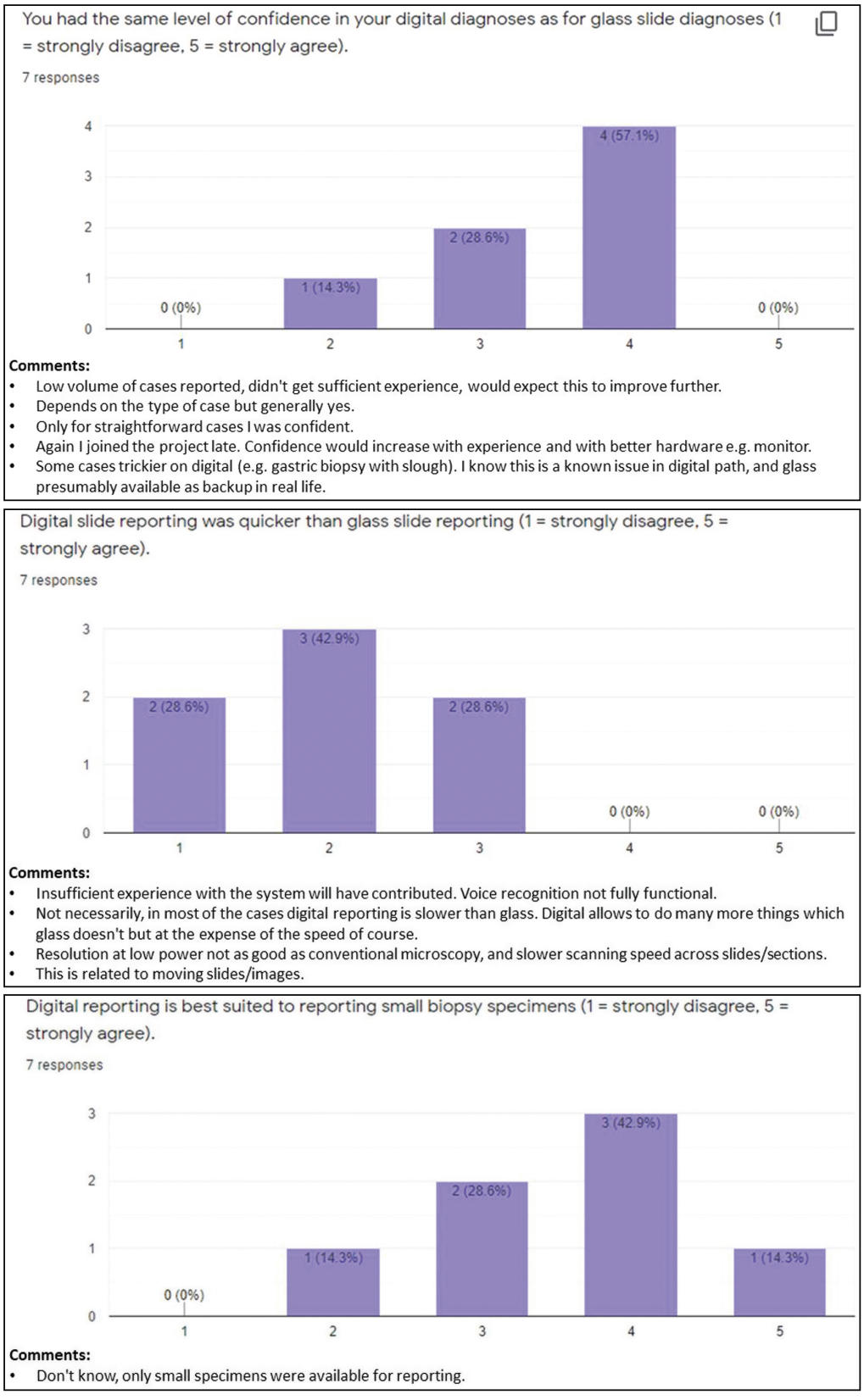
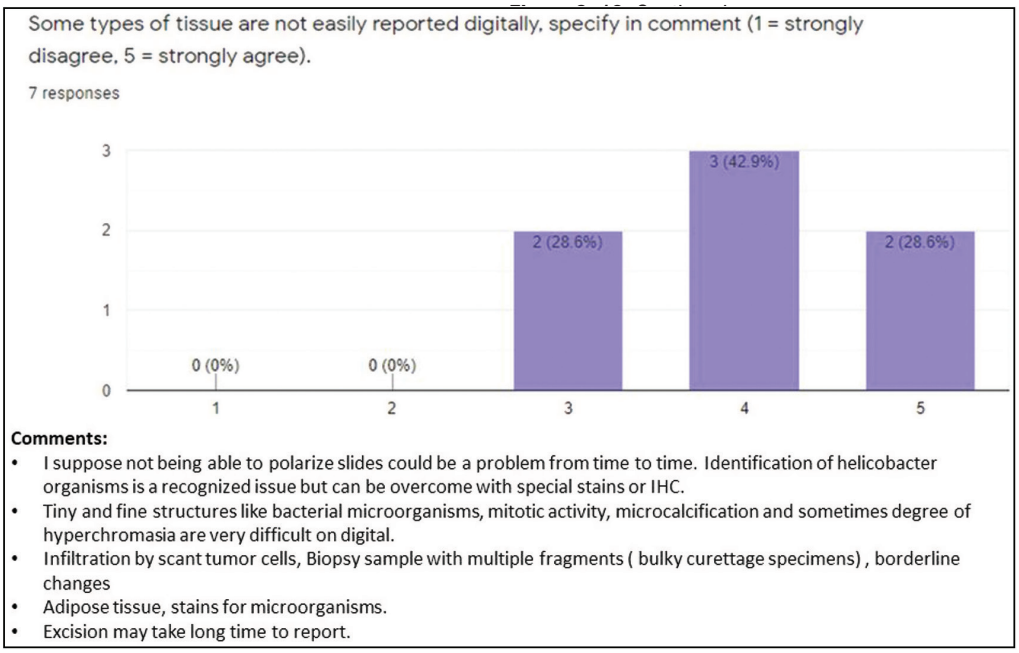
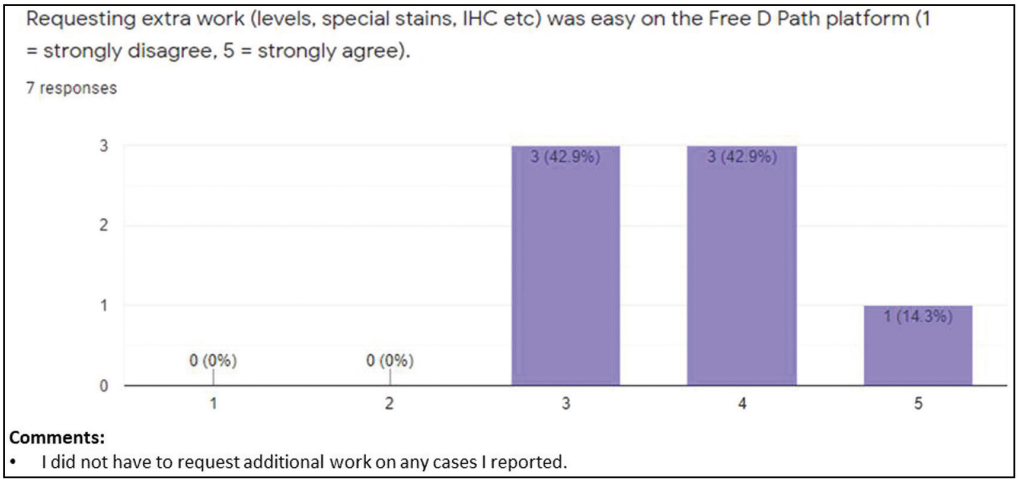


Figure 3–18: Continued



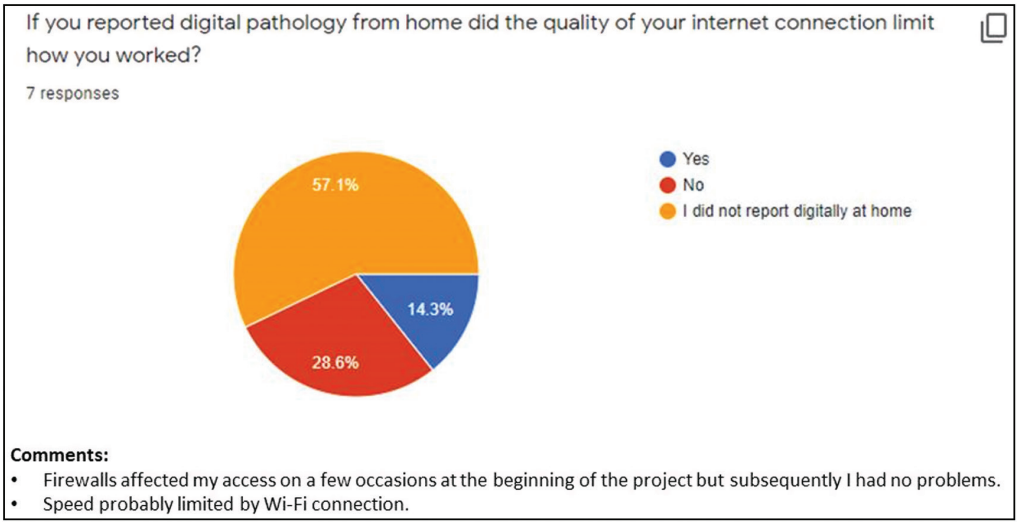
Comments:

- I suppose not being able to polarize slides could be a problem from time to time. Identification of helicobacter organisms is a recognized issue but can be overcome with special stains or IHC.
- Tiny and fine structures like bacterial microorganisms, mitotic activity, microcalcification and sometimes degree of hyperchromasia are very difficult on digital.
- Infiltration by scant tumor cells, Biopsy sample with multiple fragments (bulky curettage specimens) , borderline changes
- Adipose tissue, stains for microorganisms.
- Excision may take long time to report.



Comments:

- I did not have to request additional work on any cases I reported.



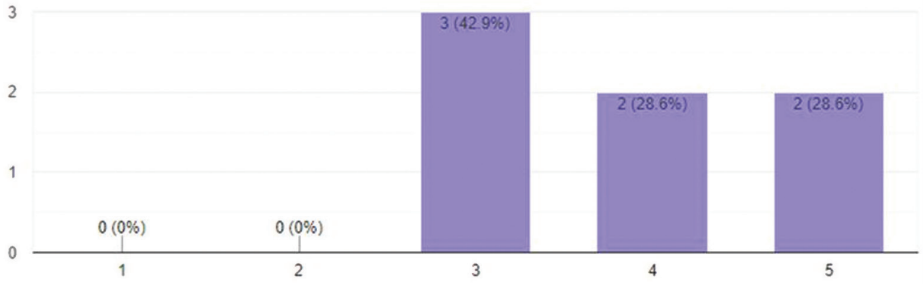
Comments:

- Firewalls affected my access on a few occasions at the beginning of the project but subsequently I had no problems.
- Speed probably limited by Wi-Fi connection.

Figure 3–18: Continued

If your department could digitize slides how much of your work would you like to report digitally? (1 = none, 5 = all).

7 responses

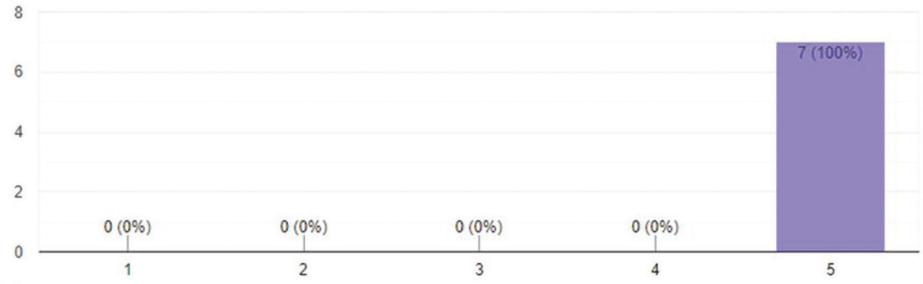


Comments:

- But only if a fully integrated system is in place.
- Ideally I would like to digitize all the work if there were no limitations on this.
- I hope 50%.
- Difficult to know from this pilot using ordinary computer, network and monitor.
- About 50%. Happy to report all endometrial biopsies, cervical biopsies, upper GI biopsies, malignant colonic biopsies. Personally I would like to have glass for cases that require sampling in more than three slides.
- I'd be happy to report a majority of work via digital pathology.
- It depends on availability of 3D mouse or something similar to microscope stage.

If your department could digitize slides would you use them to obtain expert opinions or validate difficult diagnoses with pathologists at remote sites? (1 = strongly disagree, 5= strongly agree).

7 responses



Comments:

- Regional training has always been hampered by geographic location, and centralization of certain services (e.g. HPB/UGI/Thoracic). This can be mitigated by digital slides. The Radiology Academy worked so well for radiologists because of this kind of technological advance, creation of archives, teaching sets etc.

If your department could digitize slides would you use them for teaching? (1 = strongly disagree, 5= strongly agree).

7 responses

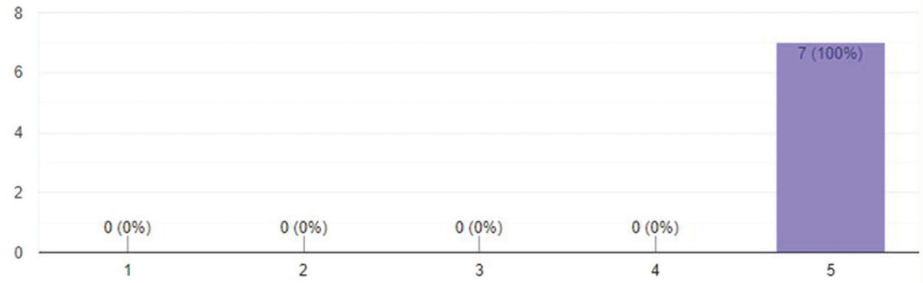


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Figure 3–18: Continued

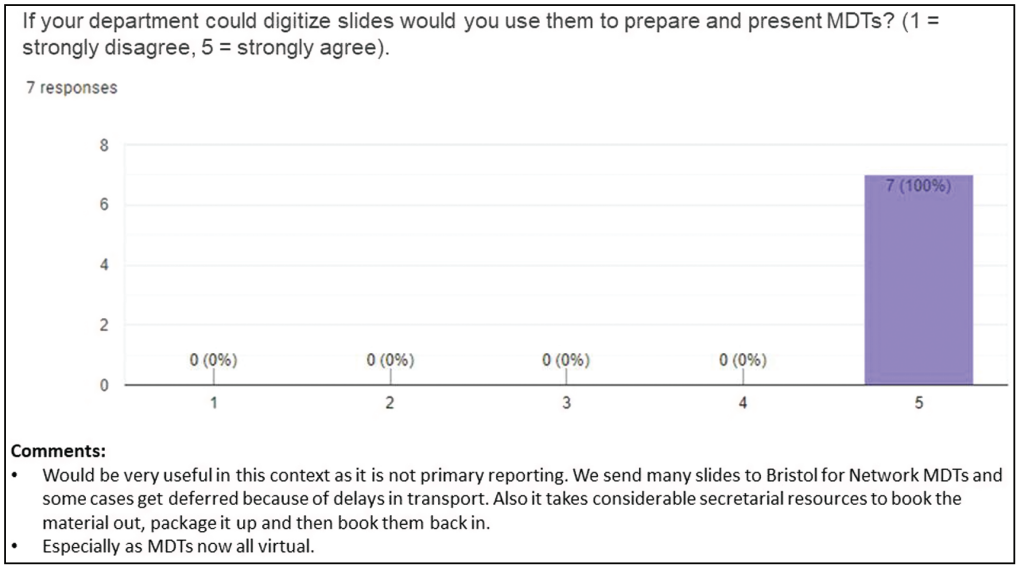

Figure 3–18: Continued

to understand the likely benefits and limitations before committing to the expense and additional complexity of digital slide reporting. Potential users sometimes have unrealistic expectations and do not appreciate the extent to which digital reporting relies not just on the scanner but also on supporting technology. Scanner platforms require integration with other laboratory databases and hardware. Without full integration, the reporting process can be slow, cumbersome, and even unsafe. Tracking and bar-coding is required to enable a robust link between all digitally scanned slides and the reporting system. A digital pathology platform needs to be easily but securely accessible from remote sites. In the NHS, this is often done using the HSCN between NHS sites. During the COVID-19 pandemic, there was heightened interest in the advantages of being able to report from home. This can be attempted with a VPN connection to the HSCN, but users may find that the data speed over a VPN is limited at busy times of the day as there are many other medical users sharing the connection. This VPN-choking can be an issue even when the remote user has high speed Internet, and for those with rural Internet reporting can be slow or impossible. In our study, most users avoided these difficulties by reporting from an NHS hospital site with high-speed network access. New users are often surprised by the amount of maintenance that scanners need to keep them operational, and they do not anticipate the difficulties caused by outages. A feasibility study can bring these and other issues to the fore before a commitment to digital pathology is made.

At the end of the study, the funder and the participants met online to discuss the outcomes and some of the following associated issues:

Should there be a single reporting platform for the region?

This could have the benefit of simplicity and allow pathologists to share the reporting of cases across the network, load balancing capacity, and demand. However, on the other hand, some sites have particular reporting practices that their local clinicians are accustomed to.

Could one platform serve the whole region with a central image repository?

This would simplify access and the sharing of reporting, together with easy review of diagnoses for patients transferred between sites. However, it is unclear whether funding would be available for a single procurement for multiple sites.

Should the reporting platform support both glass and digital reporting?

It was agreed that a regional reporting platform should support reporting for both glass and digital cases.

Who should be the platform provider?

This is unclear. Practically speaking there needs to be a single legal entity that is the administrator and owner for the platform.

How could the pathologists be employed when reporting network cases from another site?

Currently, pathologists are employed by an NHS trust to work at a particular site. If a multisite network were to be introduced for routine work, then there would need to be quite a complicated financial agreement between multiple parties, and perhaps the creation of a single legal entity to contract with the reporting pathologists.

How could a single-networked platform be interfaced with various remote hospital laboratory information systems?

The quickest and most cost-effective way to do this is with robotic process automation software, as it avoids the difficulties and costs of working with the laboratory information system (LIMS) provider. Typically, robotic process automation takes about three to five days per site to complete, depending on whether the LIMS is of a type that has been connected earlier. For a more elegant long-term solution, it may be better to work with the LIMS provider to develop a bespoke interface. However, in the United Kingdom, many LIMS systems are antiquated and do not support modern database connectivity protocols.

Does the proposed platform improve capacity by load-balancing across the network? This project showed that there was little spare pathologist capacity in the region. Despite there being only 500 cases to report, it was difficult to find enough pathologists to do the reporting. Pathologists often had local overtime arrangements that took priority. Being able to load balance work across multiple sites is often cited as a potential advantage of digital pathology, but in reality the sites that participated in this study might be more interested in sending work away than in receiving it. In another environment, with a more diverse mixture of well-staffed departments and understaffed departments, a digital network could allow work to be redistributed to pathologists with spare capacity.

Conclusion

This service evaluation study, conducted during the COVID-19 pandemic, showed that pathologists with little previous experience of digital pathology were able to report digital slides remotely at multiple sites on a networked platform. Accuracy was good despite minimal preparation and training. Digital pathology was perceived as being particularly useful for access to expert opinions, teaching, and multidisciplinary meetings, but it was also perceived as not being as quick as glass slide reporting and some pathologists were less confident of their diagnoses. It was difficult to find pathologists with time to undertake remote digital reporting, in addition to their existing commitments. Overall, the pathologists developed a positive perception of digital pathology and wished to continue using it.

Competing interests

Frederick Mayall is a director and shareholder of Diagnostic Path Solutions Ltd, an IT company that is partly owned by the NHS and that received funding from the NHS to provide the Free D Path software and technical support for the project, and to engage and manage the reporting pathologists.

Authors' contributions

Study concept and design: Mayall. Funding obtained: Mayall. Conduct of the study and method development: Mayall, Smethurst, Semkin, Mandalia, Sohail, Hadden, and Biddlestone. Analysis and interpretation of data: Mayall. Drafting of the article: Mayall. Critical revision of the article for important intellectual content: Mayall, Smethurst, Semkin, Mandalia, Sohail, Hadden, and Biddlestone. Study supervision: Mayall.

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Conflicts of interest

There are no conflicts of interest.

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