UK National Screening Committee (UK NSC)

Use of digital pathology in breast, bowel and cervical cancer screening

Date: 10 November 2023

Contents

Aim

To ask the UK National Screening Committee (UK NSC) to make a recommendation, based on the evidence presented in this document, on the use digital pathology as an option in the national breast, bowel and cervical screening programmes.

Background

In 2020, the UK NSC was asked by the National Coordinating Committee for Breast Pathology and by the Royal College of Pathologists to consider the evidence regarding the use of whole slide imaging (WSI) for the preoperative diagnosis of tissue specimens from the NHS Breast Cancer Screening Programme. Digital pathology is a technology that allows glass histopathology slides to be reviewed digitally on a computer screen, rather than with a microscope. As a first step, a preliminary evidence map was commissioned to evaluate the volume and type of evidence since the 2017 systematic review on key issues related to the use of digital pathology in breast cancer screening. Following internal discussions with the Screening Programmes, it was agreed to extend the scope of the evidence map to include bowel and cervical cancer screening. Based on the conclusion of the evidence map, the Adult Reference Group (ARG) agreed that an evidence summary on the use of digital pathology in breast and cervical cancer screening only should be commissioned. The volume and type of evidence related to the use of digital pathology for bowel cancer screening was insufficient to justify further work at the time.

The 2021 evidence summary

The 2021 evidence summary was carried out by Solutions for Public Health. The review found that:

- the bulk of the available evidence regarding the accuracy of digital pathology was related to breast cancer, although evidence specifically relating to the accuracy of digital pathology in cases detected by screening was limited
- the interpretation of the evidence base was also limited by the small number of cases involved and differences in the designs, statistical parameters and process used in the studies
- similarly, the evidence on the use of digital pathology in cervical cancer screening was limited
- evidence relating to the acceptability of digital pathology among pathologists in the UK was mixed with both positive views and concerns identified
- no studies on the cost-effectiveness of digital pathology compared to light microscopy were identified

A Health Technology Assessment (HTA) primary study was ongoing when the UK NSC examined the evidence on the use of digital pathology in breast, bowel and cervical cancer screening. There was an expectation that this work would produce useful evidence on the performance of digital pathology in cancer screening. The UK NSC agreed to consider this evidence when published.

The HTA multi-site study

The findings of the HTA multi-site study from the UK were discussed at the ARG meeting on 11 May 2023 and subsequently at the UK NSC meeting on 15 June 2023. In total, 6 NHS sites and 16 pathologists took part. The study recruited 2,024 cases (608 breast, 607 GI, 609 skin, 200 renal), including 207 breast screening and 250 bowel cancer screening samples. This sample size was chosen to obtain precise estimates of percentage clinical management concordance (CMC), meaning identical diagnoses plus discordant diagnoses which do not affect patient management. Findings were interpreted with reference to 98.3% CMC as an acceptable threshold. For overall light microscopy vs digital pathology comparisons, CMC rates were 99.95% (95%CI 99.90-99.97) for all groups and 98.96 (98.42-99.32) for cancer screening samples. The multi-site study concluded that comparing light microscopy and digital pathology CMC, overall rates exceed the reference 98.3%, showing that pathologists provide equivalent results for both routine and cancer screening samples irrespective of the modality used.

Consultation

The results of the HTA and extensive expert discussion at the ARG led the reference group to agree that digital pathology performs as well as light microscopy for

histopathology. ARG was also confident that, while the work focussed on breast and bowel cancer, the findings and the current use in service were such that they were likely to be extended to cervix histopathology. The UK NSC did not carry out a cost effectiveness exercise.

Following on from this, the UK NSC consulted on the recommendation that commissioners and service providers can safely use digital pathology in place of light microscopy in the national screening programmes (excluding cytology) if they wish.

The UK NSC sought views on whether stakeholders:

- are aware of any studies/papers which conflict with the findings of the UK HTA study
- fundamentally disagree with the use of digital pathology in existing cancer screening programmes, excluding cytology

A 6-week consultation was hosted on the GOV.UK. Direct emails were sent to 32 stakeholders. (Annex A)

The public consultation opened on 7 August and ended on 15 September 2023.

The total number of consultation responses received was 31.

Comments were received from the following 31 stakeholders (see Annex B for comments):

- Bowel Cancer UK
- Roche Diagnostics UK
- Royal College of Pathologists
- 16 consultant histopathologists
- 4 co-authors of the HTA multi-study
- Two consultant cyto/histopathologists
- One retired member of the public previously working in the Diabetic Eye Screening (DES) Programme
- One clinical director
- One service manager (pathology services at NHS Trust)
- One consultant gynaecological pathologist
- One consultant surgical pathologist
- One professor of diagnostic histopathology

Key points raised by stakeholders are summarised below:

- None of the respondents were aware of any studies/papers contradicting the findings of the UK HTA study
- Bowel Cancer UK and the Royal College of Pathologists support the use of digital pathology in histopathology diagnosis, including its use in cancer

screening. Similarly, other responses were broadly positive and in favour of the use of digital pathology with some pointing out the need to maintain access to light microscopy especially in difficult cases. Benefits of digital pathology cited include: gaining second opinions more quickly, helping with the workflow within the lab, improved turnaround times, allowing reporting offsite, easier measurement of some pathological features, quicker diagnosis for patients. Two stakeholders raised some concerns in relation to bowel cancer, about the amount of non-concordance with regards to low grade dysplasia (LGD) and high-grade dysplasia (HGD), about HGD vs cancer and about the identification of malignant polyps. These responses suggested that uncertainties such as these should be addressed within implementation strategies, for example through use of pilots and / or by ensuring second opinions can be accessed when malignancy is suspected.

- Three stakeholders focused their responses on the use of digital pathology on cervical screening. One stakeholder (Consultant in Cellular pathology and Clinical Advisor to NHSE) was fully satisfied that the evidence currently available supports the use of digital pathology for reporting cervical histopathology. A second stakeholder (Consultant Gynaecological Pathologist) stated that it is unclear whether the results of the HTA multi-site study can be extrapolated to cervical screening, adding that cervical histopathology should have been part of the HTA multi-site study and that a similar study ought to be repeated for cervical histology and include cervical biopsies as well as loop excisions and some hysterectomy samples. A third stakeholder (Jo's Cervical Cancer Trust) acknowledged the potential of digital pathology to help improve cancer screening pathways and support timely diagnosis. However, the stakeholder also expressed concern that there remains little research specifically examining the use of digital pathology in diagnosing cervical cancer, and in diagnosing and grading cervical cell changes. The stakeholder also pointed at the acceptability of digital pathology amongst pathologists being mixed, that there is no evidence on the acceptability amongst the public or amongst pathologists of using digital pathology specifically in cancer screening programmes, and that they would like to see more research into this. Ultimately, Jo's Cervical Cancer Trust noted that, if a decision is made to embed digital pathology in the cervical screening programme, that this should be only to supplement the current pathology services and not to replace light microscopy.
- According to one consultant histopathologist, this consultation came too early because as a first step, a vast majority of pathologists need to be validated, then all hospitals need to have access to digital pathology and only after these two conditions are met, moving screening to digital pathology can be considered. A second consultant histopathologist shared similar concerns noting that the introduction and application of digital images is variable between hospitals across the country and that therefore, the UK is not ready to systematically use digital pathology in regular reporting of cancer in the screening setting.

- Roche Diagnostics UK stated that they agree that digital pathology performs as well as light microscopy for histopathology. They added that digital pathology enables the deployment of artificial intelligence (AI) algorithms to augment the diagnostic capabilities of pathologists and asked for the inclusion and importance of AI to be highlighted in addition to digital pathology as a standalone technology.
- One consultant histopathologist noted they were unable to comment on this consultation as their organisation was in process of going digital and expected to complete this process by the end of the year.
- Some concerns and/or limitations of digital pathology were raised in some responses:
    - time implications for lab staff having to upload the slides (leaving less time to prepare them) and for pathologists to do the necessary training amidst staff shortages
    - potential negative workforce implications and negative impact on turnaround times
    - funding associated with the purchase and maintenance of equipment
    - importance of the display screen' resolution and of workstation's design to avoid eye fatigue and postural muscular tension
    - insufficient evidence regarding public acceptance, cost effectiveness and the role of AI in digital pathology
    - poorer quality communication between pathologists and clinicians as a result of more remote reporting with digital pathology

UK NSC Response: The UK NSC thanks all stakeholders for their contribution to the consultation process.

The proposal that digital pathology could be employed in a screening programme's diagnostic pathway was generally accepted by the stakeholders. There were some comments suggesting that the fact that the UK NSC does not mandate the use of digital pathology but allows for its implementation, if considered appropriate by local preferences and circumstances, needed to be more clearly explained. The final recommendation has been written to take this into account. Some stakeholders suggested that, considering the paucity of evidence for the use of digital pathology in cervical screening programmes, some primary research in this field might be necessary. This was discussed by the ARG members, and it was agreed that when used in screening programmes, the implementation of digital pathology should be audited to evaluate its effectiveness.

This was particularly the case for cervical screening where the generation of real world evidence might mitigate any uncertainties arising from the very limited volume of available research evidence. In addition, the ARG noted that one respondent had expressed a willingness to undertake a study of digital pathology in cervical samples. The ARG would welcome this development but considered that the evidence from other cancer sites was generalisable to cervical cancer. Because of this, the ARG

was concerned to emphasise that requiring further evidence on CMC in the cervical cancer setting prior to a recommendation could be disproportionate to any uncertainties on digital pathology's performance.

In light of the consultation comments received and expert input from the ARG, the Committee makes the recommendation as stated below.

Recommendation

The Committee is satisfied that digital pathology can represent a safe option for commissioners and providers of diagnostic pathways in the breast, bowel and cervical screening programmes. The Committee does not suggest that the use of light microscopy should be discontinued.

Furthermore, the UK NSC recommends that there should be regular audits to gauge the performance of digital pathology in the screening programmes, as part of implementation. This will be of particular value in relation to its use in the cervical screening programme as it will provide important additional data.

Annex A: List of Organisations Contacted

1. Association for Clinical Biochemistry and Laboratory Medicine
2. Bowel Cancer UK
3. Bowel Cancer Wales
4. Breast Cancer Care
5. Breast Cancer Now
6. British Association for Cytopathology
7. British Association of Surgical Oncology
8. British Society of Gastroenterology
9. Cancer Research UK
10. Faculty of Public Health
11. Joint Advisory Group on GI Endoscopy
12. Jo's Cervical Cancer Trust
13. Lynn's Bowel Cancer Campaign
14. Macmillan
15. Medical Research Council
16. Northern Ireland Cancer Network
17. Royal College of General Practitioners
18. Royal College of Nursing
19. Royal College of Pathologists
20. Royal College of Physicians
21. Royal College of Physicians and Surgeons of Glasgow
22. Royal College of Physicians of Edinburgh
23. Royal College of Radiologists
24. Royal College of Surgeons

25. Royal College of Surgeons of Edinburgh
26. Society and College of Radiographers
27. The Association of Coloproctology of Great Britain and Ireland
28. The British Association for Cancer Research
29. The British Association of Urological Surgeons
30. The British Society for Colposcopy and Cervical Pathology
31. Urostomy Association
32. Yorkshire Cancer Research

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Annex B: Consultation Responses

1. **XXXX XXXX, Consultant Histopathologist, Professor, Division of Clinical Medicine, Head & Neck & Thyroid MDT Lead Pathologist, Screening and Symptomatic MDT Breast Lead Pathologist, Professional Clinical Advisor for Breast Pathology, Surrey Pathology Services, XXXX XXXX XXXX, XXXX**

I have read the documents about the use of digital pathology in breast, bowel and cervical cancer screening.

I agree digital pathology can perform like assessment on glass slides.

I am concerned of the time implications for both lab staff (uploading slides will leave less time to actually prepare them) and for breast pathologists (the training will require more time to assess slides AND digital imaging)

I currently do not have any extra time. Thank you

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2. XXXX XXX, Member of the Public

I am responding as a member of the public who used to work in a Diabetic Eye Screening (DES) Programme prior to retirement. The programme screened people with diabetes in order to detect early changes that could lead to diabetic retinopathy (DR) or check for evidence of retinopathy in those people who delayed getting medical advice despite being symptomatic.

I am sure I won't be the only one to highlight that retinal images have been successfully graded digitally for many years. DES programmes are subject to regular Quality Assurance inspections and the system has worked very well, helping those who are found to have retinal changes manage their diabetes or referring to Ophthalmology for further assessment and or treatment*.

I am sure that digital examination in other screening programmes will be similarly effective, as shown by the multisite study that has been carried out.

* https://www.gov.uk/government/collections/diabetic-eye-screening-information-leaflets

Kind regards

UK National Screening Committee

3. XXXX XXXX, **Director at** XXX XXXX **and co-author of the HTA multi-site study**

I write to support the use of digital pathology in the reporting of cancer screening samples. In our NIHR funded study NIHR 17/84/07 Ref 126020 Multi-centred validation of digital whole slide imaging for routine diagnosis, we examined 2024 cases with 8 replicate readings by four pathologists. The results were presented to the ARG meeting, European Congress of Digital Pathology and Pathological society and now available as a pre-print on the SSRN web site

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4487130

a slightly revised version of this paper is now under review at the journal Histopathology.

In summary this study established

• agreement overall between digital pathology and glass slide reporting was very high (99.95%) and similarly high for cancer screening samples (98.96%).

• Differences detected in breast and large bowel cancer screening samples we seen most commonly in areas where disagreement between pathologists is commonly recognised.

• These differences did not show any trend towards either light microscopy or digital pathology and agreement to the consensus ground truth was similar for both modalities.

Therefore examining the data from multiple perspectives we see no evidence to suggest reports produced with digital pathology would be any different to those issued using light microscopy. It is also worth stressing the allowing the use of digital pathology by those pathologists who wish to use it can improve workflow and reduce the time to diagnosis for patients, improve peer review discussion of difficult cases and mutli-disciplinary team review. All of these points are widely acknowledged by those departments which have already made the change to digital.

Finally allowing the use of digital pathology does not preclude the use of light microscopy where this remains useful. So, for those occasions where objects are uncertain or too small to be clearly discriminated on digital images, light microscopy is still available to be used.

I summary I believe there is now considerable evidence to suggest digital pathology is a perfectly safe modality for reporting cancer screening samples, and we should not fear or obstruct its use since this is going to improve the service overall.

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4. XX XXX. Professor of Cancer Pathology, The XXXX XXXX XXXX XXXX, and co-author of the HTA multi-site study

I write to support the use of digital pathology in the reporting of cancer screening samples. In our NIHR funded study NIHR 17/84/07 Ref 126020 Multi-centred validation of digital whole slide imaging for routine diagnosis, we examined 2024 cases with 8 replicate readings by four pathologists. The results were presented to the ARG meeting, European Congress of Digital Pathology and Pathological society and now available as a pre-print on the SSRN web site

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I summary I believe there is now considerable evidence to suggest digital pathology is a perfectly safe modality for reporting cancer screening samples, and we should not fear or obstruct its use since this is going to improve the service overall.

5. XXXX XXXX XXXX, **Consultant Histopathologist, Honorary Lecturer (Teaching)** XXXX XXXX XXXX XXXX, XXXX XXXX **Hospital; Diagnostics & Pharmacy Group – The Northern Care Alliance NHS Group**

Hi,

We are in the process of setting up digital pathology and are in the stage of validation. Our group has set up 20 cases from s symptomatic centre as use of digital pathology in screening was not advised.

The below results published is very promising and hopefully below 100% is still valid for routine reporting. There will always be cases where the glass slides will have to be looked into initially more, than less and less as one gains experience.. However, it is not clear which equipment's were used for scanning and analysing the images. The resolution of the display screen is very important as well as the ergonomic design of the work station. Constant scanning of digital images can lead to eye fatigue, postural muscular tension etc. I hope these are also looked in to.

(In breast cancer screening comparison between LM v DP for CMC was 96.27% which is very high but slightly below the reference of 98.3%. However the comparison to the GT for these samples shows slightly better agreement seen with DP (99.89) as opposed to LM (97.57), indicating, along with the lower inter-class correlation scores, these variances are more likely to be due to differences in interpretation of challenging biopsies than the modality.)

From this

Thank you

Best Wishes

6. XXXX XXXX, **Consultant Surgical Pathologist, Hon Senior Lecturer, Clinical Director,** XXXX XXXX XXXX XXXX XXXX **of Medicine,** XXXX XXXX XXXX XXXX **NHS Foundation Trust**

Bowel and cervix- more accurate in measurement and overall assessment particularly for early cervical cancers

Breast- as above except for mitoses which is not identical in assessment as analogue and Ki67 proliferation is overestimated.

I am just writing as a follow up to my previous comments as I realise that several non-pathologists- or who are not practicing digital pathology, screening pathology or any pathology- analogue or digital are responding to the consultation. It is my concern that comments from non practitioners can skew the consultation either to inflation for or deflation against digital pathology which has some limitations but great deal of advantages when applied judiciously taking cognisance of the limitations.

7. XXXX XXXX, Consultant Pathologist, XXXX Hospital

I am not aware of any papers which contradict the HTA (Lancet publication pending)

We have been glass slide free for several months and I am lead for both breast screening and bowel screening – there have been no issues and only very infrequent recourse to requesting glass slides from archive….even Weddelite is often appreciable on digital

8. XXXX XXX, **Consultant Histopathologist, Lead Gynaecology and Colposcopy Pathologist,** XXXX XXXX XXXX **Hospital**

We are in process of going digital and are expecting to go digital by the end of this year (hopefully). So, I'm unable to comment on this consultation.

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9. XXXX XXXX , Service Manager, Cellular Sciences XXXX XXXX XXXX XXXX NHS Trust

I am responding to the UK NSC comments on whether stakeholders: are aware of any studies/papers contradicting the findings of the UK HTA study and fundamentally disagree with the use of digital pathology in existing cancer screening programmes, excluding cytology

I can confirm:

• I am **not** aware of any studies/papers contradicting the findings of the UK HTA study

• I am **fully** supportive of the use of digital pathology in existing cancer screening programmes, excluding cytology

10. XXXX XXXX, Clinical Director, XXXX XXXX XXXX XXXX Bowel Cancer Screening Centre

Thank you so much for sharing the Consultation and Multi-site findings.

Given that my Centre in 2022 submitted nearly 4000 samples for histology, is this study for bowel cancer screening of large enough size to recommend use?

I have concerns over the amount of non-concordance with regards Low Grade Dysplasia (LGD) and High Grade dysplasia (HGD) BUT unless I missed it, what about HGD vs Cancer?

Not clear whether samples were resected polyps only, biopsies of tissue only or polyps and biopsies. No comment seen on whether R0 (completely excised) polyps, which may not change clinical diagnosis BUT may well impact upon surveillance

In terms of operational impact, will DP have negative impact upon histology TAT's. What are the workforce implications?

I am not against the use of DP, but that use should be piloted within Bowel Cancer Screen Centres and should take into account ongoing work within NBCSP with regards optical diagnosis for 'Resect and Discard' modality for diminutive polyps.

11. XXXX XXXX XXXX, Consultant Histopathologist, XXXX NHS Trust, and co-author of the HTA multi-site study

Thank you for acknowledging the usefulness of digital pathology.

I have been using digital pathology for over 5 years now and am confident that screening cases will benefit immensely, as digital pathology allows for more resourceful sharing of pathologist services.

The quality of digital pathology images are very good and I have been involved in 2 validation studies both of which have shown comparable results with digital and glass slides.

I should have mentioned this earlier but can I add that measurements are much more accurate using digital pathology and this has significance in bowel cancer screening as polyp size can determine the frequency of surveillance.

12. XXXX XXXX, Consultant Histopathologist and Lead Histopathologist for Cervical Screening, XXXX XXXX XXXX XXXX Teaching Hospitals NHS Trust

I have no concerns regarding the accuracy of digitally scanned slides compared to light microscopy. To achieve the highest level of accuracy I prefer maintaining access to light microscopy in difficult cases. However, there is insufficient evidence regarding public acceptance, cost effectiveness and the role of Artificial Intelligence in digital pathology.

13. XXXX XXXX XXXX **, Consultant Histopathologist, University** XXXX XXXX XXXX XXXX

We have been successfully reporting digitally at our hospital (see address below) since 2016 across a wide range of specimens. There is minimal difference between reporting digitally and using the light microscope.

We have found digital reporting very helpful in sharing difficult cases between ourselves and externally. It also helps in the workflow within the lab as there is no need to retrieve several large cases for the MDT meetings etc.

14. XXX XXXX XXXX**, Consultant in Histopathology,** XXXX **Hospital,** XXXX

I would suggest that digital pathology should be the standard way to report all histology cases.

15. XXXX XXXX XXXX, Consultant Histopathologist, XXXX – XXXX XXXX Hospital

That's a very good study. I agree that both modalities should be available to the pathologists for reporting.

A few things to know:

1. Can we use polariser for amyloid/ collagen.
2. Are the images provided separately In this paper.
3. What is the authors experience regarding DP in assessing difficult cases like invasion or pseudoinvasion.

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16. XXXX XXXX, Consultant in Cellular pathology, XXXX XXXX XXXX, XXXX XXXX NHS Trust; chair of the Laboratory clinical and professional group for Cervical Screening and Professional Clinical Advisor to NHSE

Thank you for consulting on this matter

I am the chair of the Laboratory clinical and professional group for Cervical Screening and a Professional Clinical Advisor to NHSE. I am a histo/cytopathologist with many years experience of cervical histology reporting, and former Regional Head of Screening Quality Assurance for PHE.

I am fully satisfied that the evidence currently available supports the use of digital pathology for reporting cervical histopathology.

NHS England have been clear that digital conversion is mandatory for histopathology reporting in general and I see no reason why cervical histopathology should be any different.

Protocols for implementation include internal validation, and the ability to default to conventional microscopy in the case of diagnostic difficulty.

In my view there is no significant risk to implementing digital reporting and significant risk to not implementing it, especially when this would mean that screening programme histopathology was the only part of the histology repertoire not using digital reporting.

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17. XXXX XXXX, Consultant Gynaecological Pathologist, XXXX University Hospitals NHS Foundation Trust

This is my feedback for the consultation document on the use of digital pathology for screening histopathology.

I am not sure that what has been found in this paper extrapolates to cervical screening and I am amazed that all this hard work was undertaken, and cervical histopathology was left out. Cervical histology forms a large part of the gynaecological pathology workload, and it is reckless not to include it in any project looking at the use of digital pathology.

I believe this entire exercise needs to be repeated for cervical histology and to include cervical biopsies as well as loop excisions and also some hysterectomy samples.

I am prepared to lead this if needed.

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18. XXXX XXXX XXXX, Consultant Histopathologist, XXXX XXXX Hospital

In response to the consultation on the use of digital pathology in analysis of cancer screening samples.

Although I have worked with the three types of screening before (bowel cancer, breast and cervix), we have becoming subspecialised and at the moment I only do BCSP.

For BCSP I see no problem in interpreting the results from digital pathology samples.

If you need further information from me please let me know.

19. XXXX XXXX, Consultant Histopathologist, XXXX XXXX Hospital, and co-author of the HTA multi-site study

I am the lead pathologist for the XXXX breast cancer screening service and I fully support the use of digital pathology in analysis and diagnosis of cancer screening samples.

As a disclosure of interests, I am part of the NIHR study group on the breast arm of "Digital pathology for reporting histopathology samples, including cancer screening samples – definitive evidence from a multi-site study" and co-author of the paper. As the evidence in the study shows, digital pathology is a comparable and valid diagnostic method compared with the current gold standard of light microscopy.

Further to my work on the above research project, we have employed digital pathology for the diagnosis and MDT review of non-screening samples across multiple disciplines in my department in Lincoln for a number of years. Provided that pathologists are trained to use the software and undergo a formative validation process to ensure they are familiar with the platform and confident to us it we have encountered no issues. The glass slides are always available should the pathologist want to defer to glass.

There are benefits to using digital pathology in terms of quality governance and improved turn-around times. Digital pathology allows second opinions from local, regional and national colleagues without the need to send glass slides between pathologists. This increases the opportunity to collate a range of further opinions on difficult and contentious cases. Digital pathology also allows remote offsite reporting so even if a pathologist is away from their base hospital urgent cases can be reviewed and reported without the need to wait for glass slides to be physically transported. Fewer cases miss MDT discussion due to delays improving the patient diagnostic and treatment pathway.

I have seen no evidence that there is an increased risk of diagnostic errors when using digital pathology versus conventional light microscopy.

These are the reasons that I support the use of digital pathology in cancer screening samples for primary diagnosis and review.

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20. XXX XXXX, Consultant Histopathologist, XXXX XXXX Hospital

Thank you for the opportunity to participate in this consultation.

Digital pathology adds an additional step prior to the slides reaching the pathologist. With the quick turnaround times expected for breast biopsies this could potentially delay the reporting process with the added stress for pathologists. As mentioned in the documents circulated, the introduction and application of digital images is variable between hospitals. In my opinion we are not ready in the UK to systematically use DP in regular reporting of cancer in the screening setting.

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21. XXXX XXXX, Consultant Histopathologist, Professional Clinical Advisor in Pathology, XXXX XXXX XXXX XXXX XXXX

I am a GI pathologist (and PCA to the BCSP) who reports BCSP cases and my comments are restricted to the use of digital pathology in the bowel cancer screening programme.

1. After reading Professor Snead's article in press and from my own knowledge of the digital pathology literature I am satisfied that reporting using digital images for GI cases is as accurate and reliable as reporting using a microscope and glass slides for the vast majority of BCSP cases. My only concern is the identification of malignant polyps. In the study presented by Professor Snead there was no information as to how many malignant colorectal polyps were included in their sample and in Table 6, in the error category TA versus malignant polyp, both erroneous diagnoses were made using scanned images. It would be helpful to know how many malignant polyps were included in the GI series and how consistent diagnosis was between the 2 methods of examination. It may be that where malignancy in a polyp is suspected , a second opinion using glass slides should be mandated.

2. My principal concern about the introduction of digital pathology into routine pathology practice, including screening however, is that :

a. There is no good evidence at present that digital reporting is more efficient/faster than using a light microscope in a properly staffed and equipped department, though I appreciate that in the current circumstances where many laboratories are struggling to meet TATs and have to outsource reporting, digitisation of slides has a number of advantages.

b. Digital pathology, by facilitating more remote reporting, will accelerate the uncoupling of pathologists from their clinical colleagues and hospitals in which they work, potentially leading to less access to important clinical information required for diagnosis and poorer quality communication between pathologists and clinicians. The latter is particularly important where diagnoses are difficult and clinicians have a limited understanding of pathological interpretation and the pathologist's degree of confidence in their diagnosis.

I appreciate however, that the latter two points are outwith the terms of reference of this consultation and have little or no bearing on the decision to allow the use of WSI in the screening programme.

22. XXXX XXXX, Consultant Histopathologist, BCSP Pathology Lead, Lead Medical Examiner, XXXX XXXX XXXX Foundation Trust

Apologies if I've missed the specific questions being asked, but I strongly support the use of digital pathology for reporting BCSP specimens (I don't report cervical or breast screening specimens). Digital pathology is validated for all non-screening specimens so is the usual method of reporting for many pathologists. It allows rapid and accurate measurement of lesions and enables pathologists to share images without delay. Obtaining second opinions, both within and outside the department, is much easier. When we currently want an opinion from the Expert Panel we have to post slides to one member, and they have to post them to the next, who then posts them to the third. With digital pathology we could share images immediately with all 3 panel members and have a consensus opinion within hours instead of weeks. It would also support the new ways of working with pathologists increasingly working from home. I currently have to drive 40 minutes to the hospital to pick up BCSP slides as I can't report them digitally, as I can everything else. This is poor use of consultant time and not very ecologically friendly. If I need a second opinion eg high grade dysplasia or invasive carcinoma, I can't show the slides to another pathologist until the following working day if I have them at home with me. With pressure on turnaround times, digital reporting will minimise delays.

23. XXXX XXXX, Professor of Diagnostic Histopathology and Honorary Consultant Histopathologist, The University of XXXX

I fully support the use of digital pathology in screening pathology.

I report thousands of cases a year both digitally and using glass slides. I prefer digital reporting as it gives a much better low power view of the slides and means areas with pathology are much less likely to be missed. Digital pathology also applies compression algorithms to the image which sharpens borders and makes some features stand out more easily than when viewing glass slides. I report several hundred colorectal polyps a year digitally in a non-screening setting and have found no problems, only advantages, to using digital pathology.

There is also the possibility than AI will become clinically useful for classifying colorectal polyps in the near future, there are already large well-carried out Scandnavian studies showing that AI can triage all low risk polyps out from a mixed lab population with no misclassification of high risk polyps. AI is already being used in clonoscopy for polyp identification.

24.XXX XXXX, Consultant Pathologist, XXXX XXXX Hospitals NHS Trust

Regarding the use of digital pathology for bowel Cancer screening samples.

There is no evidence to suggest digital diagnosis for the samples will be inferior to diagnosis on glass slides.

In the current climate of staffing crises histopathology, it would be sensible to be able to digital outsourced screening samples when necessary, and in particular the ability to gain remote second opinions both within one's own organisation and outside the organisation would be extremely beneficial and resulting reduced turnaround times (consensus diagnosis of high-grade dysplasia and adenocarcinoma in BCSP samples is currently mandated), particularly when reporting pathologists are working from home.

It is nonsensical to me that the BCSP EQA is an online system using digital slides and yet primary digital reporting is not currently accepted.

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25. Bowel Cancer UK

Dear Sir/Madam

Thank you for the opportunity to comment upon the United Kingdom National Screening Committee's proposal to consider recommending the use of digital pathology in existing cancer screening programmes, excluding cytology.

It is encouraging to note the multi-site study, which included investigations regarding bowel cancer pathology, concluded that the quality with digital slides has been demonstrated to be as good as conventional slides.

Benefits of digital pathology include the possibility it provides to enable easier reviews within the screening programme. For example, in complex scenarios a further review by a different Trust/Board histopathology lead would be much easier to facilitate through digital pathology as opposed to the complex processes required if physical samples require to be transferred.

Similarly, another benefit is that shared learning within the programme relating to histopathology samples would be likely to be facilitated through digital pathology, as opposed to hindered by this change. Additionally, the ultimate beneficiary is that patients may profit from earlier diagnosis and therefore more timely access to treatment. It is well established that as bowel cancers become more advanced, the less likely positive outcomes are, making earlier diagnosis and treatment imperative when looking to improve bowel cancer survival[1].

Currently pathway capacity, including within histopathology, has resulted in severe delays related to the treatment of bowel cancers patients, innovative technologies such as digital pathology could help reduce these.

Furthermore, advances in digital and computational pathology unlocks new avenues for personalised healthcare solutions that address the unmet medical needs of patients.

Harnessing the power of imaging technology and artificial intelligence (AI), pathology will bring about a new era of precision medicine advantageous to both clinicians and patients alike.

As with all new interventions there are also challenges to overcome including funding associated with the purchase and maintenance of equipment and training of pathologists, however it is the opinion of Bowel Cancer UK that the disadvantages are far outweighed by the benefits of what could be achieved by greater access to digital pathology. We work upon the assumption however that the process will include regular dip sampling comparisons between digital and conventional slides.

We are not aware of any studies/findings which would conflict with the UK HTA study.

I hope this clarifies the position of Bowel Cancer UK which is based upon the findings of the UK HTA study and opinion of the membership of the Royal College of Pathologists.

Should you require any further clarification please do not hesitate to contact me.

[1] https://crukcancerintelligence.shinyapps.io/EarlyDiagnosis/

26. XXXX XXXX, Consultant Histopathologist, Clinical Lead - National Pathology Programme, Interim Clinical Board Director, CD&T, University XXXX XXXX

I am a consultant histopathologist at the University Hospital XXXX XXXX. I currently report in the NHS using light microscopy, however, I am familiar with digital pathology through reporting cases for Cyted and EQA schemes, as well as being the health board representative on the XXXX Digital Pathology Project. I am clinical lead for the national pathology programme who manage the DCP project. I was involved in phase 1 of the digital pathology project where we validated whole slide imaging (digital pathology) for 3001 cases, comparing light microscopy to the digital image (published - Verification and Validation of Digital Pathology (Whole Slide Imaging) for Primary Histopathological Diagnosis: All Wales Experience - PubMed (nih.gov)). Subsequent phases of the project are rolling out and expanding the use of digital pathology across the country. Despite there being a few diagnostic differences in material from screening populations the concordance between light and digital media will translate between routine and screening pathology. The faster training and faster second opinions that digital images afford are benefits that need to be realised by using digital technology as soon as possible in the screening programme.

27. Roche Diagnostics UK

Roche Diagnostics UK welcomes the opportunity to contribute to the consultation and strongly agrees with the expert opinions of the ARG.

The main point that we are in agreement is that Digital pathology performs as well as light microscopy for histopathology.

Digital pathology (DP) involves the visualisation and analysis of digitised glass slides for the diagnostic and treatment stratification of patients with cancer. **DP enables the deployment of state-of-the-art artificial intelligence (AI) algorithms to augment the diagnostic capabilities of pathologists**.

Roche Diagnostics respectfully asks for the inclusion and importance of Artificial Intelligence (AI) algorithms to be highlighted in addition to Digital Pathology as a standalone technology.

As stated on the NHS Transform website, ‘AI has the potential to make a significant difference in health and care settings through its ability to analyse large quantities of complex information.’ Roche Diagnostics are in a unique position to support transformation of pathology services to digital to enable this realisation.

'Days to minutes': a study published in Lancet Oncology, 2020 reported that an AI system for diagnosing colorectal cancer included 1,330 patients showing a significant reduction in the time for diagnosis. It has since been implemented in clinical practice in the UK, improving diagnostic efficiency and reducing waiting times.

An AI solution implemented in the UK for Breast Cancer has shown increased diagnostic accuracy, reducing the need for repeat biopsies, reducing the burden of planned hospital care including bed occupancy.

The Royal College of Pathologists also highlighted it’s support for the role of AI in Digital Pathology in a position statement released in March 2023.

https://www.rcpath.org/discover-pathology/news/position-statement-from-the-royal-college-of-pathologists-rcpath-on-artificial-intelligence-ai-and-digital-pathology.html

Many thanks again for the opportunity to input into the consultation

UK National Screening Committee

28. XX XXXX , Consultant Histopathologist, XXXX NHS Trust

These are my answers to the consultation, that I only learned about today:

One of the problems is that only a fraction of hospitals have access to digital pathology (at the moment) **and the present gold standard** for reporting is glass.

Would it not be wise to transform the screening into digital only after **all** pathology departments have converted to digital? How is this going to be managed, in terms of QA etc if (for example) only 25% of pathologists can screen on digital and 75% will have to continue using glass slides?

Validation of reporting on digital pathology is far from being complete, in fact most hospitals have not done it yet. The majority of pathologists have been trained on glass and took their exams on glass. Their practice has been the same for a long time. Validation is the answer, but validation varies wildly between departments. Would it not be better to centralise validation (let it be run by RCP, as it is the entity that also runs the exams that allow us to report)?

In my opinion this consultation comes too early: first a **vast majority of pathologists need to be validated**, then **all hospitals need to have access to digital pathology** and only after these two conditions are met can we start considering how screening can move to digital.

I also think this consultation should have been widely advertised and designed to be more user friendly (web-based questionnaire for example)

29. XXX XXXX XXXX, Consultant Cyto/histopathologist, The XXXX XXXX Hospital

I have been using digital pathology for some while and report breast cases on slides and using digital pathology. I am very comfortable doing this. I have read all of the information and attended the ABP discussion today.

I think that it would be safe practice and evidence based to use digital slides for reporting in the breast screening programme.

30. Jo's Cervical Cancer Trust

Jo's Cervical Cancer Trust response to the UK National Screening Committee consultation on the use of digital pathology in analysis of cancer screening samples

Histopathology in cervical screening

Last year in England, over 167,000 women were diagnosed with cervical cell changes[i] – detected by successful cytological and histological testing by the NHS cervical screening programme. The cervical screening pathway involves multiple, successive tiers of testing, which identifies those with high-risk HPV, before using liquid-based cytology to test for cervical cell changes and identify the severity (grade) of these cell changes. Where cell changes are identified, a biopsy of the cells may be taken. This cervical biopsy will be examined by a histopathologist, to confirm the diagnosis and determine a patient's risk of cervical cancer[ii]. This diagnosis will inform what treatment or monitoring the patient will receive next.

Digital pathology

Digital pathology is a technology that allows pathologists to review glass histopathology slides digitally on a computer screen, rather than with a light microscope. The key technology enabling digital pathology is 'whole slide imaging', a technology which creates a digital image of the entire glass slide with a scanning device to provide a high-resolution image that can be stored and viewed on a computer screen or mobile device for later review.

It is reported that the use of digital pathology would benefit screening by allowing for more streamlined distribution of screening cases to pathologists and faster access to archived cases for comparison. There is a severe shortage of pathologists in the UK – with vacancies of 10-12%, and a growing demand for pathology services[iii]. A 2020 Cancer Research UK report indicates that a 45% staff increase is needed across seven cancer-related professions to meet Health Education England's (HEE) aim to provide world-class services for cancer patients by 2029.

It is therefore increasingly important to optimise the existing and future histopathology workforce across the UK's screening programmes. Moving to whole slide imaging would enable the NHS to distribute the workload of pathologists across regions – as the digital images could be easily shared across the country - reducing the burden on specific NHS trusts. This would support in the faster processing of results, leading to faster diagnosis and earlier enrolment in treatment, where necessary. Furthermore, in cases where histopathological diagnoses prove complicated for local pathologists, digital pathology provides avenues of support, enabling faster peer review by senior pathologists.

Digital pathology for cervical screening and cervical cancer diagnosis

As noted by the UK National Screening Committee, the bulk of available evidence – and the focus of the 2023 Health Technology Assessment (HTA) multi-site study – is mainly regarding breast and bowel cancers. It is also noted that, "The evidence specifically relating to the accuracy of digital pathology in cases detected by screening is limited."[iv]

The only specific mention of cervical cancer throughout the HTA multi-site study is the assertion that, "Reporting cancer screening cases is based on the same principles regardless of the tumour site, so there is every reason to believe the results presented here will translate to other cancer screening samples such as uterine cervix and lung.[v]"

The Solutions for Public health evidence review from 2021, on the use of digital pathology, also highlights some key concerns with regards to cervical cancer screening and diagnosis. This includes that a potential concern about the use of digital pathology in cancer screening is "whether the digital images would allow the accurate identification of subtler morphologies such as precancers, atypia and early-stage cancers."

The accurate grading of cervical cell changes is essential for women to receive timely and effective treatment, to prevent the development of cervical cancer, and to prevent the over-treatment of low-grade cell changes. On this topic, the evidence review notes that "Case agreement rates by diagnostic category were reported in one study, which reported that agreement with the reference standard was statistically significantly higher for glass slides than digital whole slide images for most of the diagnostic categories." This suggests that the use of digital pathology may provide less accuracy in the grading of cervical cell changes, though the summary also highlights that there was limited evidence identified on this aspect.

Only a single piece of research from 2015 looked specifically at the application of digital pathology in cervical screening. This small study included 157 cases and noted major discrepancies of 5.1% and minor discrepancies of 8.3% in diagnoses made between light microscopy and whole slide imaging[vi]. The evidence review concludes that "The evidence available on the accuracy of digital pathology in cervical cancer was limited to a single small study, restricting any conclusions that can be drawn on the use of digital pathology in this area."

The 2021 evidence review summarises that, "The conclusion of this evidence summary was that there is not enough evidence to recommend the use of digital pathology in breast cancer or cervical cancer screening programmes." While the HTA multi-site study added to the evidence base for the use of digital pathology in breast, gastrointestinal, skin, and renal cancer diagnosis, it offers no additional evidence to support the use of digital pathology in cervical cancer screening programmes.

Response

It is clear that digital pathology has great potential to help improve cancer screening pathways, and support in more efficient and timely diagnosis. However, we are concerned that there remains so little research specifically examining the use of digital pathology in diagnosing cervical cancer, and in diagnosing and grading cervical cell changes. The Solutions for Public Health evidence review from 2021 highlighted that the available research was limited, and that there was not enough evidence to support a recommendation, and we believe that this is still the case. There appears to be no additional research into the use of digital pathology in the cervical cancer screening programme to provide evidence – supportive or otherwise – to inform a decision.

A key feature of the cervical screening programme is the ability to accurately diagnose cervical cell changes before they become cancerous. Accurately grading these cell changes is essential for determining whether patients will be monitored (when the cell changes are deemed likely to regress on their own) or treated (when the cell changes are deemed likely to develop into cancer). Data from telepathology services in Northern Tanzania highlighted inconsistent accuracy in the diagnosis and grading of CIN2,[vii] which could have significant clinical implications – leading to either over-treatment or under-treatment. The Ordi et al. study, referenced in the evidence summary, highlights that 89% of the discrepancies observed involved high-grade cell changes being diagnosed as low-grade cell changes, or as negative or reactive changes in the cervix[viii]. This is concerning, as high-grade cell changes are those most likely to develop into cervical cancer. We would hope to see more research that outlines and confirms the accuracy of using digital pathology when grading cervical cell changes.

The Ordi et al. study highlights that there are different levels of reproducibility for punch biopsy specimens compared to loop excision procedure specimens, when examined using light microscopy. This is an area where we would also like to see more research, to establish whether different biopsy types are more, or less, suitable for diagnosis and grading with digital pathology.

The evidence review also notes that the acceptability of digital pathology amongst pathologists is mixed, and that there is no evidence on the acceptability amongst the public or amongst pathologists of using digital pathology specifically in cancer screening programmes. We would like to see more research into the acceptability of this – amongst a broad range of stakeholders – as confidence in the programme is crucial for ensuring the uptake of screening tests.

If the decision is made to embed digital pathology in the cervical screening programme, we would urge that it is only to supplement the current pathology services, until there is enough evidence to show that it is at least as effective and sensitive. We agree that there are benefits to the use of digital pathology in screening programmes – particularly in terms of distributing workloads, facilitating collaboration between pathologists, and in keeping samples safe – but until there is more data on its performance in identifying and accurately grading cervical cell changes and cervical cancer, we would object to a move away from light microscopy.

For more information, please contact media@jostrust.org.uk.

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[iii] The Royal College of Pathologists, The pathology workforce, [Accessed online 14.09.23] https://www.rcpath.org/discover-pathology/public-affairs/the-pathology-workforce.html

[iv] UK National Screening Committee, Evidence summary on the use of digital pathology in breast and cervical cancer screening, External review against programme appraisal criteria for the UK National Screening Committee, Solutions for Public Health,

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https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1176412/UK_NSC_review_digital_pathology_3.0_November_2021.pdf

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[vii] Mremi A, Bentzer NK, Mchome B, Mlay J, Blaakær J, et al. (2022) The role of telepathology in diagnosis of pre-malignant and malignant cervical lesions: Implementation at a tertiary hospital in Northern Tanzania. PLOS ONE 17(4): e0266649. https://doi.org/10.1371/journal.pone.0266649

[viii] Ordi J, Castillo P, Saco A, Del Pino M, Ordi O, Rodríguez-Carunchio L, Ramírez J. Validation of whole slide imaging in the primary diagnosis of gynaecological pathology in a University Hospital. J Clin Pathol. (2015). https://jcp.bmj.com/content/68/1/33

31. Royal College of Pathologists

15th September 2023

In response to UK National Screening Committee Use of digital pathology in breast, bowel and cervical cancer screening

The Royal College of Pathologists supports the use of digital pathology in histopathology diagnosis, including its use in cancer screening.

The Royal College of Pathologists position on digital pathology is summarised in our Digital Pathology Strategy (which states that "The College supports the use of digital pathology in diagnosis, research, education and training". Our high level objectives in this strategy include a commitment to:

- **support Fellows [i.e. Pathologists] wishing to use digital pathology in clinical practice and coordinate training in relation to digital pathology**
- **ensure that high standards of practice are maintained by departments implementing digital pathology**
- **support the deployment of digital pathology across laboratories**

The College has created best practice guidelines for pathologists on the deployment of digital pathology to ensure the safe adoption of digital pathology for all histopathology specimens, regardless of whether they are screening samples.

These guidelines take a cautious approach to digital pathology to ensure that diagnoses made on digital are not inferior to those made on glass slides with a microscope. They include comparison with the glass slide, emphasise the importance of learning over time, and promote risk reduction strategies and ongoing monitoring to ensure safety.

At the time of the best practice guidelines publication (2018) there was a lack of high quality evidence and relatively little clinical experience of digital pathology.

Since then we have seen digital pathology deployed successfully across multiple sites in the NHS and across the world, with pathologists more confident about digital diagnosis. Several labs have used the College guidelines to achieve ISO15189 accreditation from UKAS for digital diagnosis.

There are also now further publications demonstrating research evidence of safety, including the NIHR HTA study 17/84/07 Ref 126020 “Multi-centred validation of digital whole slide imaging for routine diagnosis commissioned to examine the safety of digital pathology in screening”.

Furthermore, digital pathology, rather than simply replicating the light microscope, brings additional benefits including:

- **Facilitating access to second opinions, improving overall diagnostic quality**
- **Supporting under-resourced laboratories by sharing work across hospitals or regions, facilitating service provision and avoiding service failure**
- **Easier measurement of pathological features (e.g. polyp size, as mandated by the Bowel Cancer Screening Program)**
- **Better evaluation of low power architectural features better than the microscope (e.g. the degree of villousness of polyps)**
- **Creating a digital foundation for the future use of artificial intelligence which has the potential to increase the speed and accuracy of diagnosis**

The Royal College of Pathologists therefore supports the use of digital pathology in cancer screening programs.