National Institute for Health and Care Excellence

Technology Appraisal

Artificial intelligence (AI) technologies to assist histopathology for breast cancer diagnosis [ID6732]

Response to stakeholder organisation comments on the draft remit and draft scope

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Comments on the draft remit and proposed process- appropriateness of an evaluation and proposed evaluation route

No.	Stakeholder	Comments [sic]	Response
1	Sectra Imaging IT Solutions	No comment	n/a
2	Aiforia Technologies Plc	No comments	n/a
3	Tempus/Paige	We support this evaluation but recommend the adoption of a hierarchy of evidence that prioritizes **NHS data** over other non-NHS studies. We believe it is critical to evaluate technologies based on their ability to support service provision on the NHS population.	Thank you for your comment. The external assessment group (EAG) will produce a protocol,

No.	Stakeholder	Comments [sic]	Response
			which will include a hierarchy of evidence.
4	DiaDeep	DiaDeep strongly supports this evaluation. AI-assisted histopathology for breast cancer addresses a critical unmet need given NHS pathology workforce shortages and the imperative to meet the 28-day Faster Diagnosis Standard. The Technology Appraisal route is appropriate given the potential for these technologies to affect treatment decisions and patient outcomes at scale across NHS pathology services.	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
5	Mindpeak GmbH	No comment Why not include the biomarker Ki67 in the technology analysed. You claim in the introduction the fact that The proliferation marker Ki-67 is also assessed as part of breast cancer histopathology in some NHS centres. This is not routine practice as currently there is no standardised methodology. Using AI can support the standardization of this biomarker assessment and can be another advantage of AI technologies Even if we marked confidential on the RFI, I think it's important to add also for these 2 tools that H&E and HER2 will be sought CE-IVDR Class C approval before guidance publication. Like all Mindpeak Breast Suite tools.	Thank you for your comment. Ki-67 analysis not standard practice as it is not included in the NICE Guideline for Early and locally advanced breast cancer: diagnosis and management, or a mandatory field in the Royal College of Pathologists minimum dataset for non-operative diagnostic procedures for breast cancer. Clinicians agreed it is appropriate to focus the assessment on the added value of AI for analysis done and outputs used in the standard care pathway. Regulatory status of Mindpeak's technologies has been updated in the scope.
6	Breast Cancer Now	The proposed topic and evaluation route is appropriate.	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
7	Stratipath AB	The evaluation is narrowed down to assist the diagnosis of breast cancer in biopsies, and only includes AI technologies for cancer detection, routine biomarkers and grading. There is a limitation with not including risk stratification AI technologies (using H&E WSI) that can add additional prognostic value in form of independent risk stratification at the time of diagnosis to support more informed decisions at the MDT discussion and treatment planning.	Thank you for your comment. Feedback from clinicians indicates that the NHS histopathologist workforce shortage and the impact this is having on histopathology turnaround time is the key unmet need that this assessment should aim to address. This assessment is focusing on AI technologies that can address this unmet need in the standard care pathway. AI technologies for novel risk profiling in breast cancer do not address this decision question. NICE recognises that risk profiling technologies for breast cancer could address an unmet need in the NHS, and the NICE prioritisation board selected a separate topic for HealthTech guidance production that will be assessing novel risk profiling technologies to guide adjuvant chemotherapy decisions in early breast cancer. The decision has been published on the NICE website. Details of technologies that may be relevant for this topic have been passed to the topic team.

No.	Stakeholder	Comments [sic]	Response
8	AIRA Matrix Private Limited	AI-based tools in digital pathology, including quality control and analytical algorithms, should be evaluated through a proportionate approach that reflects their role within the clinical workflow. Evaluation should focus on analytical and technical performance, robustness across diverse datasets and laboratory conditions, usability, and impact on workflow efficiency and standardization. For non-diagnostic or adjunctive tools, the primary value lies in improving the reliability and consistency of downstream processes rather than directly influencing patient outcomes. Therefore, an appropriate evaluation route may emphasize early value assessment, technical validation, and real-world evidence generation, ensuring safe integration into clinical workflows while supporting scalable adoption.	Thank you for your comment. Key outcomes that will be assessed where evidence permits are listed in the scope, and the external assessment group will critically appraise the quality and relevance of the evidence. Further details on the methods and processes for NICE technology appraisals are in NICE technology appraisal and highly specialised technologies guidance: the manual. This topic has been routed to the National HealthTech Access Programme for guidance production. The committee can make recommendations for further evidence generation or research if this is appropriate. These recommendations are explained in Section 6.4 of NICE technology appraisal and highly specialised technologies guidance: the manual.

9	Artera Inc	As described in the NHS 10-year health plan, digital and artificial intelligence (AI) technologies will offer patients significantly more personalised care and are “among the clearest routes to secure the productivity gains that will ensure the NHS’s financial sustainability”. Therefore, we consider the choice of topic of ‘AI for histopathology’ to be a highly appropriate priority area. However, as described in more detail below, we are concerned that the remit misunderstands clinical practice in breast cancer histopathology and imposes an artificial concept of ‘histopathology for the diagnosis’ of breast cancer based on biopsies, that does not reflect clinical practice. Specifically, the remit does not take into account: 1. that histopathology cannot be meaningfully separated into ‘diagnostic’ and ‘prognostic’ functions, because the assessment of pathological features to establish diagnosis also directly guides risk assessment and treatment selection. 2. that ‘diagnosis’ of breast cancer does not end at the first biopsy. It is an integrated process that begins with assessment of biopsy, which informs whether surgery is required, and is then refined by histopathologic examination of resected tissue. As described in the background section of the draft scope, as part of the RCPath minimum dataset (2021), biomarker status is reported when invasive carcinoma is detected, and is used for treatment planning and decisions on further genetic testing. Excluding UKCA marked AI digital histopathology technologies that can be integrated into the histopathology care pathway either at biopsy or post-surgery to enhance the information already provided under standard care, without substantially altering the	Thank you for your comment. Please refer to the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis. Feedback from clinicians indicated that the NHS histopathologist workforce shortage and the impact this is having on histopathology turnaround time is the key unmet need that this assessment should aim to address. This assessment will focus on the impact of technologies on the analysis of biopsies done for initial diagnostic assessment and biomarker analysis, as this is the highest volume of work for histopathology in the pathway. The primary inclusion criteria for functionality is on technologies that could support triage of cases and enable initial diagnosis and biomarker analysis for relevant cases to happen in 1 histopathologist session. Included technologies support this by detecting presence of invasive cancer and DCIS. This could enable laboratories to prioritise cases and order IHC staining for further analysis. AI for biomarker

No.	Stakeholder	Comments [sic]	Response
		histopathology workload, represents a missed opportunity to positively impact multiple outcomes listed in the draft scope, including: • impact on clinical decision-making including staging and treatment selection • overall survival • time to initiate treatment • progression-free survival • adverse effects of treatment, including under- or over-treatment • health-related quality of life • cost of managing cancer, related to missed cancers or overdiagnosis Therefore, failing to include these technologies in the draft scope represents a missed opportunity to benefit patients directly, via personalised treatment decision-making, and to reduce costs and time to treatment compared with standard care.	analysis will be included where available for technologies that also meet the primary inclusion criteria for functionality. Focusing the assessment in this way will maximise the benefit of the assessment with the limited resources available.

No.	Stakeholder	Comments [sic]	Response
10	Digistain Ltd	The proposed evaluation route is appropriate; however, the current draft remit risks being too narrowly defined to capture the most clinically impactful applications of AI within histopathology workflows. In response to the draft scope, we conducted a rapid UK clinician survey over the past week (n = 648 breast clinicians). The findings were highly consistent and clinically significant: **88.2%** reported that post-surgical risk stratification delays treatment decisions by at least one week **64.6%** identified risk stratification as the **single greatest source of delay** in the breast cancer care pathway **70.6%** indicated that innovation in this area would improve the patient pathway These findings suggest that while AI-assisted diagnostic interpretation is valuable, the **greatest system-level inefficiencies occur downstream**, particularly at the stage of tumour risk assessment that informs MDT decision-making. Restricting the evaluation to initial diagnostic use risks focusing on a part of the pathway where timelines are already relatively efficient, while excluding areas where delays are longer, more variable, and more impactful on patient experience and treatment timelines.	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis. Please see the response to comment 9 with respect to focusing the assessment on initial diagnosis and biomarker analysis.

No.	Stakeholder	Comments [sic]	Response
11	NHS England	NHS England considers the proposed evaluation route appropriate and supports NICE undertaking a Technology Appraisal of AI technologies supporting histopathology in breast cancer diagnosis.	Thank you for your comment.
12	Roche Diagnostics UK	Roche strongly supports the evaluation of AI technologies supporting the histopathological diagnosis of breast cancer and considers the proposed evaluation route both appropriate and timely. Roche recognises that people referred through the NHS Breast Screening Programme fall under the remit of the NSC; however, if histopathological assessment of biopsy samples is similar regardless of referral route, excluding this population may risk creating variation in access to AI-supported diagnostic tools.	Thank you for your comment. NICE cannot make recommendations for biopsies done via the NHS Breast Screening Programme; this is considered by the National Screening Committee (NICE-wide topic prioritisation: the manual, Section 3.9). However, data from studies that include people from the screening programme will not be excluded from the assessment report. The external assessment group's protocol will detail how evidence will be selected and prioritised.

13	Visiopharm	Visiopharm supports the development of this assessment and agrees that evaluating AI technologies in breast cancer histopathology is both timely and important. The proposed approach is sensible and addresses many of the key components of the diagnostic pathway. We do, however, believe that two areas of the scope may benefit from reconsideration or clarification to ensure that the full value of AI is captured for patients and NHS services. 1. Value opportunities from additional use cases in breast pathology. We recognise the clinical importance of using AI in the initial diagnosis. However, we would like to highlight the significance clinical and operational value through other critical components of the pathway, such as biomarker assessment, mitotic counting, or quality assurance tasks. In practice, tumour detection and downstream processes (e.g., automated IHC ordering, case prioritisation) depend on integration with laboratory information systems and digital pathology platforms, which can vary widely across the NHS. Because these dependencies fall outside the scope of the assessment, there is a risk that valuable technologies that address other clinically significant steps are unintentionally omitted. Ensuring flexibility in the inclusion criteria would allow NICE to capture the broader range of innovations that support accuracy, efficiency, and consistency in breast cancer diagnosis — even when their primary function is not tumour detection.	Thank you for your comment. Feedback from NHS clinicians was clear that AI technologies that could enable initial diagnosis and biomarker analysis for relevant cases to happen in 1 histopathologist session and that can assist with triaging of cases are likely to have the greatest impact on the unmet need. So, only technologies that do detection of invasive cancer and ductal carcinoma in situ as a minimum will be included in this assessment. But, NICE acknowledges feedback that there is potential value of AI for analyses to support other proforma reporting requirements at this step in the pathway, including biomarker analysis and tasks for grading. The scope specifically acknowledges that technologies that assist more accurate assessment of HER2 status could reduce the amount of ISH/FISH testing done. So, the effects of AI to assist these analyses will be assessed as appropriate for technologies included in scope.

No.	Stakeholder	Comments [sic]	Response
		2.Exclusion of Lymph Node Assessment We acknowledge that the current focus is on initial diagnosis based on core or vacuum-assisted biopsies. However, it may be worth signalling that lymph node assessment, although outside the primary scope, represents a substantial diagnostic workload with high clinical impact. Lymph node evaluation can take considerably longer than tumour detection in the breast core biopsy itself and carries important implications for staging, treatment decisions, and patient outcomes. In real-world clinical use (e.g., UMC Utrecht), the technology achieved **35–39% reductions in review time,** improving overall workflow efficiency and reducing laboratory burden (Published nature paper shared in original RFI submission). While this may not need to be incorporated into the immediate scope, we recommend NICE consider whether lymph node analysis should be addressed in future extensions of this work to ensure that the most resource-intensive and clinically consequential tasks are not overlooked. We believe the scope would benefit from a more flexible definition of the included technologies so that the evaluation fully reflects the breadth of AI driven value across the breast cancer histopathology pathway. A broader approach would help ensure that innovations improving diagnostic accuracy, reducing variation, and addressing workload challenges across multiple steps of	Feedback from clinicians indicates that the NHS histopathologist workforce shortage and the impact this is having on histopathology turnaround time is the key unmet need that this assessment should aim to address. This assessment will focus on the impact of technologies that assist histopathologist assessment of initial biopsies as this is the highest volume sample type in the pathway. Quality assurance checks for slide preparation are pre-analytical tasks that happen before histopathologist review. Most people do not have a lymph node biopsy done for initial diagnosis, so the effects of technologies that do lymph node analysis will not be assessed for this topic. Companies can submit notifications about technologies for these use cases through the NHS Innovation Service.

No.	Stakeholder	Comments [sic]	Response
		the process are captured, not only those performing tumour detection.	

No.	Stakeholder	Comments [sic]	Response
14	The Royal College of Pathologists	Evaluation is needed the scope seems overly restricted. In addition to tumour detection distinction between in-situ and invasive disease and detection of vascular invasion would be worthwhile including pathologists spend time evaluating slides for these features prior identification may improve efficiency and accuracy.	Thank you for your comment. All included technologies will have a minimum requirement to detect presence of invasive cancer or DCIS to triage cases and order IHC staining for further analysis. Lymphovascular invasion is usually reported from surgical specimens, and is not standard practice for the initial diagnosis from biopsy. It is not included in the NICE Guideline for Early and locally advanced breast cancer: diagnosis and management, or a mandatory field in the Royal College of Pathologists minimum dataset for non-operative diagnostic procedures for breast cancer. So, this function is not a minimum requirement for inclusion and will not be assessed.
15	ROVI Biotech Ltd	We fully support the evaluation of this topic. Breast cancer diagnosis can be transformed by measured adoption of AI diagnostic support in digital pathology.	Thank you for your comment.
16	Primaa	Primaa confirms that Cleo Breast is CE-marked for biopsy and excision analysis. It specifically assists in detecting invasive and in situ carcinoma while highlighting mitosis hotspots. We can provide further technical details on its	Thank you for your comment. This information will be used to update

No.	Stakeholder	Comments [sic]	Response
		deployment options (Cloud/On-site) during the assessment.	the description of Cleo Breast in the scope.

The draft remit and proposed process- Additional comments on the draft remit

No.	Stakeholder	Comments [sic]	Response
17	Sectra Imaging IT Solutions	No comment	n/a

No.	Stakeholder	Comments [sic]	Response
18	DiaDeep	DiaDeep considers the draft remit broadly appropriate. We respectfully request that the remit be extended to explicitly include AI technologies for automated biomarker quantification on confirmed cancer specimens, as a complementary capability alongside tumour detection. Accurate and reproducible biomarker scoring (ER, PR, HER2, Ki-67, mitoses) directly determines treatment eligibility and is a recognised source of inter-laboratory variability with documented impact on patient outcomes.	Thank you for your comment. Please see the response to comment 13 with respect to the minimum functionality of included technologies and the assessment of other proforma reporting requirements.
19	Mindpeak GmbH	Done above	n/a

20	NHS England	National screening programme exclusion query The National screening programme is a planned exclusion currently, but it is suggested the draft scope be reflective of the eventual requirement for future inclusion as AI pathway will be appropriate for screening. Clarification would be helpful regarding exclusion of cases arising from the NHS Breast Screening Programme as: • Breast screening accounts for a significant proportion of histopathology workload in breast pathology services. • The screening population differs somewhat from symptomatic referral pathways, but the histopathology assessment and diagnostic processes remain broadly similar. • Evaluating AI technologies across both screening and symptomatic pathways could generate valuable evidence to support future service implementation. It is recognised that recommendations from the UK National Screening Committee may underpin the current exclusion of screening populations from the scope. However, while screening and symptomatic pathways differ operationally in terms of reporting processes and programme governance, the underlying histopathology diagnostic approach remains largely the same. NHS England would therefore recommend further discussion with the national screening programme as part of the development work for the TA, to clarify whether:	Thank you for your comment. Please see the response to comment 12 with respect to the inclusion of people from the screening programme.

No.	Stakeholder	Comments [sic]	Response
		• Screening cases should be included within the scope of this evaluation, or • Screening cases should remain excluded but acknowledged as a potential future application area for AI-supported histopathology. Even if screening populations remain out of scope for this evaluation, the draft remit should recognise that AI-supported histopathology technologies are likely to be relevant to the screening pathway in the future.	
21	Roche Diagnostics UK	N/A	n/a

22	Ibex Medical Analytics	Ibex would like to understand more regarding the following: Breast 1. **How does the evaluation framework assess different types of AI solutions**, including: (a) Clinical and morphological features identified by the AI (e.g., an AI model that only detects breast cancer vs. a model that identifies and classifies invasive ductal and lobular carcinoma, DCIS, lobular neoplasia, ALI/LVI, microcalcifications and additional findings), (b) The accuracy of the AI solution (per clinical findings); (c) Integration capabilities with other systems within the workflow (e.g., LIS, scanners, IMS); (d) Workflow, usability, user-interface features. Are these assessed together as a whole category (e.g., for all AI solutions for breast H&E) or individually per feature/capability/solution? 2. How is **evidence categorised and weighted**, especially when comparing regulatory evidence, real-world data evidence, research-based evaluation, multi-centre evaluations, independent evaluations in clinical settings? Is there specific focus on evidence from NHS labs? 3. **How do you ensure fair comparison** when some solutions present substantially more evidence than others and offer different sets of features or capabilities? Is there any structured comparison	Thank you for your comment. NICE's methods for evidence assessment and economic analysis in technology appraisals are described in sections 3 and 4 of NICE technology appraisal and highly specialised technologies guidance: the manual. The external assessment group will produce a protocol which will give further information on the approach to evidence selection and assessment, and economic evaluation. This will be published on the NICE website. Technologies are assessed individually, not as a class, unless there is evidence to support clinical equivalence between technologies. NICE's methods state that fully incremental analysis is preferred (4.10.8). However, pairwise comparisons (each technology versus the comparator) may be presented when relevant and justified. For example, when there is not enough evidence to inform a fully incremental analysis. Factors that the committee considers when making its

No.	Stakeholder	Comments [sic]	Response
		process at all, or are solutions evaluated independently? 4. **How are accuracy and performance metrics assessed, and which features are evaluated?** For example: cancer/no cancer detection, or additional subcategories such as invasive cancer (inc. Invasive Ductal carcinoma / Invasive Lobular carcinoma, DCIS (inc. grading of DCIS) - are these assessed per feature/module? 5. **How do you evaluate different solution features and capabilities**, for example: automation vs manual solutions, workflow-integrated vs standalone tools? How are upfront costs, capabilities, and evidence requirements incorporated into the overall cost-benefit assessment? 6. **What are the key criteria that drive your final decision**, such as clinical effectiveness, safety, cost-effectiveness, usability, and integration feasibility? Is the main focus to decrease costs, e.g., by reducing pathologist review time and unnecessary IHC tests (while maintaining diagnostic accuracy, of course)? Is it to improve the accuracy and consistency of diagnosis? Improve treatment decisions and patient outcomes?	decision are detailed in section 6 of the manual.

The draft scope- background information

No.	Stakeholder	Comments [sic]	Response
23	Sectra Imaging IT Solutions	No comments	n/a
24	Aiforia Technologies Plc	Yes. We find the pathway for initial diagnosis and treatment of breast cancer to be correctly described.	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
25	DiaDeep	The background and care pathway description are accurate and comprehensive. We wish to highlight that biomarker quantification introduces significant inter-observer variability beyond what is acknowledged in the draft: manual Ki-67 hotspot ICC is 0.737 across 30 institutions (Chung et al., 2016), HER2 IHC overall percent agreement is as low as 28.8% among 18 pathologists (Rimm et al., 2017), and PD-L1 CPS ICC is 0.45-0.57 among 12 pathologists (Schallenberg et al., 2023). These figures underscore that variability in biomarker scoring represents a significant source of inconsistent patient management in the NHS.	Thank you for your comment. Please see the response to comment 13 with respect to the minimum functionality required for inclusion in this evaluation and the assessment of included technologies to support other proforma reporting requirements. Please see the response to comment 5 with respect to Ki-67 analysis. The same principle applies to PD-L1 marker analysis, so the effects of this analysis will not be assessed for included AI technologies.
26	Mindpeak GmbH	yes It's clearly described	Thank you for your comment.
27	Breast Cancer Now	We would suggest including information about the distinction between ductal and lobular breast cancer, since this is referred to later in the document	Thank you for your comment. Additional text (in **bold** below) describing this has been added to the background. **"**There are several types of breast cancer. **Most often, breast cancer starts in the milk ducts (ductal carcinoma). Sometimes it starts in the milk-producing glands, or lobules of the breast (lobular carcinoma)."**

No.	Stakeholder	Comments [sic]	Response
28	Stratipath AB	No comment. See also ‘additional comments’ below.	n/a
29	AIRA Matrix Private Limited	The described care pathway is broadly appropriate and reflects current digital pathology workflows; however, it may benefit from minor refinements to ensure completeness and clarity. In particular, the pathway should explicitly distinguish between pre-analytical (slide scanning, image quality control, and algorithmic analysis), and post-analytical (pathologist review and reporting) stages.	Thank you for your comment. Additional text (in **bold**, below) describing this has been added to the scope**:** “NICE is aware of other AI technologies for histopathology of biopsies for suspected breast cancer that do analyses that are not always done for initial diagnosis, or that do not do diagnostic analyses. These include:”…”**pre-analytical tests including** quality assurance in slide preparation.”

30	Artera Inc	In terms of the role of histopathology in the care pathway, the background information correctly identifies core items to be reported on as a minimum when performing histopathology on breast biopsies. However, although the draft text does acknowledge that biomarker status is reported in order to inform treatment planning and decisions on further testing, the overall framing of the role of histopathology is for 'initial diagnosis' of breast cancer. This is an incomplete description that does not adequately reflect clinical practice. In breast cancer, histopathology cannot be meaningfully separated into 'diagnostic' and 'prognostic' functions, because, as acknowledged in the draft background, the assessment of pathological features to establish diagnosis also directly guides risk assessment and treatment selection. Furthermore, this diagnostic process does not end at biopsy analysis but is further refined based on pathologist assessment of surgical samples; this is particularly important given the reported discordance rates for biomarkers between core needle biopsies and surgical excision specimens.1,2 By imposing an artificial division to separate 'diagnostic' histopathology, the scope fails to consider the clinical implications of the minimum histopathology dataset also including features that provide prognostic/risk stratification information e.g. grading, biomarker status. Risk stratification is an essential and inseparable part of breast cancer histopathology, therefore it is not consistent with current clinical practice to exclude AI digital histopathology technologies that can be integrated into the current workflow to provide risk stratification information. Including prognostic/risk stratification AI digital histopathology technologies would also support NICE's existing guidance on management of early and locally advanced breast cancer and on advanced breast cancer. We suggest the following:	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis.

No.	Stakeholder	Comments [sic]	Response
		The unmet need section references the RCPath position statement on digital pathology and AI but omits their broader view of the potential role of AI in histopathology services: “The College supports the use of digital pathology and AI to improve patient care. AI is a very powerful technology with the potential to improve pathology diagnosis and / or provide novel prognostic or predictive information.” Therefore, we suggest that the unmet need section is updated to reflect the full view of the College as outlined in their position statement. Similarly, the section currently references the GIRFT 2025 summary of diagnostics findings and recommendations which supports innovation in AI for pathology. The GIRFT summary includes a specific focus on decision support tools and AI being developed to aid interpretation, with the recommendation to “embrace innovation in pathology, particularly in AI and improved decision support”. The summary highlights the unmet need for tools that can aid interpretation, which should be reflected in the scope. Finally, this section references the commitment in the NHS long term plan to introducing AI to increase efficient NHS services. The plan specifically references AI use to deliver personalised, precision care and treatment to identify the most effective interventions. AI risk stratification tools in histopathology have the potential to directly address this commitment, therefore we would suggest that this is specifically incorporated into this section. The remainder of the background information is accurate and complete in terms of the current draft scope; however, we suggest that the draft scope is incomplete (as described above) and therefore the section describing the technologies and the section describing the place of the technology in the pathway should be revised to include AI digital	

No.	Stakeholder	Comments [sic]	Response
		histopathology technologies that provide prognostic/risk stratification information throughout the diagnostic pathway.	

31	Digistain Ltd	The background information accurately describes the role of AI in supporting histopathological diagnosis, particularly in relation to tumour detection and classification. However, it is not fully complete in reflecting where the most significant delays occur in the real-world breast cancer care pathway. As shared above our rapid UK clinician survey conducted in response to this consultation (n = 648 breast clinicians) found that: • 64.6% identified post-surgical tumour risk stratification as the single greatest source of delay in the pathway • 88.2% reported that this stage delays treatment decisions by at least one week These findings suggest that the current background section is weighted toward earlier diagnostic steps, while under-representing downstream tumour assessment processes that have a greater impact on treatment timelines and patient experience. The care pathway is broadly correct; however, it is incomplete in its emphasis. The current description focuses on initial biopsy interpretation and diagnostic classification. In practice, these steps are typically delivered within relatively short and well-defined timeframes across NHS breast services. By contrast, the stage following diagnosis — where additional tumour information is required to support MDT decision-making — introduces greater variability and longer delays. This includes processes such as tumour risk assessment and other forms of biological characterisation that inform treatment decisions. As the clinical utility of histopathological diagnosis is realised only through its impact on downstream treatment decisions the pathway would be more accurately described by explicitly recognising this downstream stage as a key contributor to overall time to treatment decision.	Thank you for your comment. Please refer to the response to comment 9 with respect to focusing the assessment on initial diagnosis and biomarker analysis. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis.
32	NHS England	The description of the care pathway is accurate and appropriate.	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
33	Roche Diagnostics UK	Roche considers the background information to be accurate and the care pathway to be appropriately described for the purposes of this evaluation.	Thank you for your comment.
34	Visiopharm	Yes, the care pathway is clear and correctly described	Thank you for your comment.
35	Ibex Medical Analytics	Overall it is correctly described. We provide some comments on the following sentences: Page 2: *"Currently, a minimum of haematoxylin and eosin (H&E) staining and IHC staining must be done for histopathology analysis for suspected breast cancer."* – This is not entirely correct, as Ductal Carcinoma in Situ (DCIS) is often diagnosed without extra IHCs. Page 2: "*In standard practice, IHC staining to determine biomarker status (ER, PR and HER2) is not ordered until a histopathologist has reviewed H&E-stained slides and confirmed presence of cancer."* – Some Trusts implemented as system where they can pre-order IHCs based on Radiology findings. Others, use Ibex AI to pre-order based on the AI findings, shortening TAT and reducing double reads from Pathologists. Page 3: *"it can take up to 7 days for a histopathology report to be finalised."* – Experimental findings show also 10 days or more. Overall it is confusing, however, we can rely on RCPATH - *standard: 80% of cases must be reported within seven calendar days and 90% within ten calendar days.* (RCPATH) or on GOV UK: *The diagnostic report of 90% of non-operative specimens should be available within 5 working days and 90% of surgical specimen diagnostic reports should be available*	Thank you for your comment. The following amendments (in **bold**) have been made: Initial histopathological diagnosis and biomarker analysis of breast cancer section: "Currently, a minimum of haematoxylin and eosin (H&E) staining **is done for suspected breast cancer**. IHC staining **for biomarker analysis must also be done when invasive cancer is detected**". Unmet need section: "~~In standard practice~~ **Usually,** IHC staining to determine biomarker status (ER, PR and HER2) is not ordered until a histopathologist has reviewed H&E-stained slides and confirmed presence of **invasive** cancer**."**

No.	Stakeholder	Comments [sic]	Response
		within 10 working days has been removed from the guidance. Services should comply with national cancer waiting times standards. (GOV UK)	Considerations section: **"Some trusts have implemented a system where radiologists can flag cases with a high suspicion of invasive cancer so that laboratories can pre-order IHC staining.**" Unmet need section: "The delay between H&E and IHC slide review for the same person with suspected **invasive** cancer can be several days. If HER2 status is inconclusive and ISH/FISH testing is needed, ~~it can take up to 7 days for~~ **more delays are incurred before** a histopathology report can be finalised." Patient pathways for initial diagnosis of breast cancer section: "Royal College of Pathologist standards and datasets for reporting cancers state that **they expect 80% of cases to be reported, confirmed and authorised within 7 calendar days of the biopsy procedure, and 90% within 10 days**."

No.	Stakeholder	Comments [sic]	Response
36	The Royal College of Pathologists	Appropriate	Thank you for your comment.
37	ROVI Biotech Ltd	Yes. The care pathway is correctly described as we understand it.	Thank you for your comment.

Comments on the draft scope- population

No.	Stakeholder	Comments [sic]	Response
38	Sectra Imaging IT Solutions	No comment	n/a
39	Aiforia Technologies Plc	Yes. Adults who have had core needle or vacuum assisted biopsy and are awaiting initial diagnosis for suspected breast cancer outside of the NHS BSP pathway.	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
40	DiaDeep	The population definition is appropriate. We support inclusion of adults awaiting initial diagnosis outside the NHS BSP and previously treated patients. We suggest the scope clarify that patients with confirmed invasive carcinoma requiring biomarker testing (ER/PR/HER2, Ki-67, PD-L1) are explicitly included, as these represent the population most directly affected by variability in manual biomarker quantification.	Thank you for your comment. People with invasive carcinoma are included within the population defined in the scope so no change to the wording has been implemented. Please see the response to comment 13 with respect to the minimum functionality required for inclusion in this evaluation and assessment of technologies that support other proforma reporting requirements including biomarker analysis.
41	Mindpeak GmbH	Can you leverage why the population defined is scoped outside of the NHS BSP pathway? If after a mammogram, a breast cancer is detected, the patient still needs to have a core needle or vacuum assisted biopsy and are awaiting initial diagnosis for suspected breast cancer. So why remove this population ? Except that the population is clearly defined and we agree it's appropriate to include people who have previously been treated for breast cancer and to restrict the population to adults.	Thank you for your comment. Please see the response to comment 12 with respect to the inclusion of people from the screening programme.
42	Breast Cancer Now	**Is it appropriate to include people who have previously been treated for breast cancer?** We are not aware of evidence to suggest that people with a previous breast cancer diagnosis should be excluded	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
43	Stratipath AB	Yes	Thank you for your comment.
44	AIRA Matrix Private Limited	The defined population is broadly appropriate	Thank you for your comment.
45	Artera Inc	As described, the draft remit does not reflect that diagnostic and prognostic/risk stratification information are not separable in the histopathology workup for breast cancer, therefore we would suggest that the following is added to the population: Adults who have had surgical excision or resection of breast cancer.	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis. Please see the response to comment 9 with respect to focusing the assessment on initial diagnosis and biomarker analysis.
46	Digistain Ltd	The population definition (adults undergoing biopsy for suspected breast cancer) is appropriate for technologies focused on diagnostic classification. However, if the scope were broadened to include AI technologies that derive additional tumour information from histopathology samples, the relevant population would extend to patients following initial diagnosis, particularly those requiring further tumour characterisation to inform treatment decisions. This represents a substantial proportion of patients within breast cancer care pathways and is therefore highly relevant to overall system performance.	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis. Please see the response to comment 9 with respect to focusing the assessment on initial diagnosis and biomarker analysis.
47	NHS England	No additional comments	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
48	Roche Diagnostics UK	Roche considers the population to be defined appropriately for the purposes of this evaluation. Roche recognises that people referred through the NHS Breast Screening Programme fall under the remit of the NSC; however, if histopathological assessment of biopsy samples is similar regardless of referral route, excluding this population may risk creating variation in access to AI-supported diagnostic tools.	Thank you for your comment. Please see the response to comment 12 with respect to the inclusion of people from the screening programme.
49	Visiopharm	Yes, the population would appear to be defined correctly and avoid cross over with breast screening programme. Additional questions from scope document Is it appropriate to include people who have previously been treated for breast cancer? Yes, as they are part of the workload for the histopathology department. Is it appropriate to restrict the population to adults? Yes, very small numbers of non-adult breast cancer.	Thank you for your comment.
50	Ibex Medical Analytics	No — we believe it should be clearly stated when the population refers specifically to adult females aged >18 years. Some technologies may be CE-marked and registered with the MHRA exclusively for female use, given the severe underrepresentation of males.	Thank you for your comment. The scope population specifies adults are included, which means people aged 18 and over according to the NICE Style Guide. The scope has not been amended to only include women in the included population. Although some technologies may only be indicated for use in women, some are

No.	Stakeholder	Comments [sic]	Response
			indicated for use in breast tissue without specifying the sex of the person. Final NICE Guidance will include a description of each technology evaluated including the indications for use (see section 5.8.63 of the technology appraisals manual). Also, the Equality and Health Inequality Impact Assessment form and the considerations section of the scope state that information about the representativeness of sex, ethnicity and rare tumour morphologies in training and validation datasets will be sought.
51	The Royal College of Pathologists	I think data may need enriching for minority ethnic groups	Thank you for your comment. NICE recognises that the characteristics of people included in the AI training datasets may not be representative of the population seen in clinical practice. The Equality and Health Inequality Impact Assessment form and the considerations section of the scope state that information about the representativeness of sex, ethnicity and rare tumour morphologies in training and validation datasets will be sought.

No.	Stakeholder	Comments [sic]	Response
52	ROVI Biotech Ltd	Yes	Thank you for your comment.

Comments on the draft scope- sub-groups

No.	Stakeholder	Comments [sic]	Response
53	Sectra Imaging IT Solutions	Yes, NHG 2 population is an example where using AI for further stratification between patients would be valuable. We have added Stratipath as a Stakeholder providing an AI for this specific population	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis.
54	Aiforia Technologies Plc	No	Thank you for your comment.
55	Tempus/Paige	We suggest a subgroup analysis based on geographic region and laboratory sub-specialization. We have evidence that shows that AI offers the greatest marginal benefit when deployed among general, non-specialist pathologists by comparison to specialist breast pathologists. Specialists already operate at or near peak diagnostic accuracy and while AI demonstrates improvements here, the biggest performance improvements are seen in the non-specialist setting, which is typical in many regional hospitals in the UK. AI therefore has the potential to narrow the performance gap, effectively standardising quality across a broader and more varied pathologist population. This has significant implications for health systems in the UK.	Thank you for your comment. The following statements have been added to the scope to reflect this (new text in **bold**): • Place of the technology in the pathway section: "…centres may use AI in different ways depending on analysis type and individual laboratory practices, **laboratory size and subspecialisation of staff** (for example, as triage, first or second read). The assessment will consider

No.	Stakeholder	Comments [sic]	Response
			these alternatives where appropriate." • Considerations section: "**The benefits seen from adoption of AI technologies may vary depending on the laboratory it is used in. Factors may include the scale of the laboratory, accreditation, sub-specialisation, integration with existing digital infrastructure, use of the technology as a triage tool and first or second reads."** The external assessment group may explore these factors in scenario analyses depending on the evidence available.
56	Mindpeak GmbH	Having no subgroups is the appropriate option.	Thank you for your comment.
57	Breast Cancer Now	**Are there any other subgroups for whom you would expect the clinical and cost effectiveness of the intervention to differ?** Groups with high inter-rater availability, for example people with low ER or PR positivity or people with borderline HER2 status	Thank you for your comment. The considerations section of scope states "The technologies may have additional benefits for the following groups if they increase accuracy, so

No.	Stakeholder	Comments [sic]	Response
			evidence will be considered when available: • People with low ER or PR positivity • People with borderline HER2 (2+) status".
58	Stratipath AB	No	Thank you for your comment.
59	AIRA Matrix Private Limited	Yes, there are subgroups within the population that may warrant separate consideration, primarily driven by variability in workflow, image characteristics, and potential impact on efficiency rather than differences in direct clinical outcomes. For example, subgroups based on specimen type (e.g., biopsy vs. resection specimens), staining protocols (e.g., H&E versus special stains or IHC), and scanner platforms or imaging settings may influence algorithm performance and therefore could be considered separately. Additionally, laboratories with high case volumes or fully digital workflows may derive greater operational and cost-effectiveness benefits due to increased scalability and reduction in manual quality control burden. Variability in site-specific practices, including tissue processing and slide preparation, may also impact the performance and utility of such technologies.	Thank you for your comment. The effects of factors listed in this comment will be captured in several ways. Effect of WSI quality and acquisition methods on accuracy has been added to the list of outcomes to be considered, which may include effects of scanner platforms, image settings, slide preparation, tissue processing and quality control for slide preparation. Please see the response to comment 55 with respect to exploring the effects of differences between laboratories. Please see the response to comment 13 with respect to the

No.	Stakeholder	Comments [sic]	Response
			minimum functionality required for inclusion in this evaluation, and approach to biomarker analysis. Only histopathology done for biopsies are included in this assessment. Please refer to the response to comment 9 with respect to focusing the assessment on initial diagnosis and biomarker analysis.
60	Artera Inc	No	Thank you for your comment.
61	Digistain Ltd	No specific subgroups are currently defined in the draft scope. If the scope remains limited to diagnostic applications, subgroup considerations may be less critical. However, if expanded to include technologies supporting tumour characterisation and risk stratification, it may be appropriate to consider subgroups such as: • patients with early-stage disease where treatment decisions are uncertain • patients requiring additional tumour assessment to guide systemic therapy	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis.

No.	Stakeholder	Comments [sic]	Response
		• These groups are particularly affected by delays in downstream pathology workflows.	
62	NHS England	No additional comments	Thank you for your comment.
63	Roche Diagnostics UK and Ireland	Roche considers it appropriate that no subgroups were identified for the purposes of this evaluation.	Thank you for your comment.
64	Visiopharm	No further comments	Thank you for your comment.
65	Ibex Medical Analytics	No to the best of my knowledge	Thank you for your comment.
66	ROVI Biotech Ltd	No	Thank you for your comment.

Comments on the draft scope- comparators

No.	Stakeholder	Comments [sic]	Response
67	Sectra Imaging IT Solutions	No comment	n/a
68	Aiforia Technologies Plc	The current standard treatment is visual evaluation. The comparators are relevant.	Thank you for your comment. Centralised investment and rollout are supporting uptake of digital pathology, nationally. Published evidence from an NHS multicentre blinded crossover comparison study (Snead et al 2025), and a systematic review and meta-analysis (Azam et al 2021) supports equivalence of reporting when using

No.	Stakeholder	Comments [sic]	Response
			digital pathology compared with light microscopy. Other UK national guidance acknowledges that digital pathology is a suitable option for breast pathology analysis in the screening population (National Screening Committee, 2023). But, clinical experts indicated that comparisons between light microscopy and AI may be useful to consider in the evidence base. The scope has been updated to reflect that both light microscopy and digital pathology will be included as comparators.
69	Tempus/Paige	For the reason stated above, we suggest a subgroup analysis based on sub-specialization.	Thank you for your comment. Please see response to comment 55 with respect to subspecialisation.
70	DiaDeep	The comparator is appropriate. DiaDeep suggests the assessment also consider scenarios where AI is used as a second read or for quality assurance alongside primary pathologist review, as this reflects common real-world deployment models for biomarker quantification.	Thank you for your comment. Please see the response to comment 55 with respect to the exploring different laboratory practices. Please see the response to comment 13 with respect to AI to

No.	Stakeholder	Comments [sic]	Response
			support quality assurance in slide preparation.
71	Mindpeak GmbH	Using pathologists without AI is the right gold standard.	Thank you for your comment.
72	Breast Cancer Now	Yes	Thank you for your comment.
73	Stratipath AB	Yes	Thank you for your comment.
74	AIRA Matrix Private Limited	The comparators listed are broadly appropriate and reflect current standard practice within the NHS, where quality control and assessment of histopathology slides are predominantly performed through manual visual review by laboratory personnel and pathologists as part of routine workflows. This represents the primary comparator for technologies such as AIRABreast and other AI tools. For downstream AI tools (e.g., diagnostic or prognostic algorithms), comparators may also include standard-of-care assessment by pathologists without AI assistance, and where relevant, existing validated scoring systems or clinical risk models.	Thank you for your comment. Please see response to comment 79 with respect to the comparator for this assessment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis. Note that “effect of WSI quality and acquisition methods on accuracy” has been added to the list of outcomes to be considered.
75	Artera Inc	As described, the draft remit does not reflect that diagnostic and prognostic/risk stratification information are not separable in the	Thank you for your comment. Please see the response to comment 7 with respect to the

No.	Stakeholder	Comments [sic]	Response
		histopathology workup for breast cancer, therefore we would suggest that the following amendment to the comparator: Histopathologist review of WSI of breast core needle or vacuum assisted biopsies or surgical tissue for breast cancer, without AI assistance.	assessment of AI for risk stratification and prognosis. Please refer to the response to comment 9 with respect to focusing the assessment on initial diagnosis and biomarker analysis.
75	Digistain Ltd	The current comparator of histopathologist review without AI assistance is appropriate for technologies assisting diagnostic interpretation. However, where AI technologies provide additional tumour information beyond detection and classification, it may be relevant to consider comparison with existing downstream testing approaches that are currently used to obtain similar information from tumour samples. This would allow the evaluation to capture the broader system impact of such technologies, particularly in terms of: ● reducing additional testing steps ● shortening time to MDT decision ● reducing pathway variability	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis. Please refer to the response to comment 9 with respect to focusing the assessment on initial diagnosis and biomarker analysis.
77	NHS England	The proposed comparators reflect current NHS practice and are appropriate.	Thank you for your comment.
78	Roche Diagnostics UK	Roche considers the comparator to be defined appropriately for the purposes of this evaluation.	Thank you for your comment.
79	Visiopharm	The comparator to manual assessment either by viewing whole slide image on a screen or reviewing the case on a microscope is the only alternative.	Thank you for your comment. Centralised investment and rollout are supporting uptake of digital

No.	Stakeholder	Comments [sic]	Response
			pathology, nationally. Published evidence from an NHS multicentre blinded crossover comparison study (Snead et al 2025), and a systematic review and meta-analysis (Azam et al 2021) supports equivalence of reporting when using digital pathology compared with light microscopy. Other UK national guidance acknowledges that digital pathology is a suitable option for breast pathology analysis in the screening population (National Screening Committee, 2023). But, clinical experts indicated that comparisons between light microscopy and AI may be useful to consider in the evidence base. The scope has been updated to reflect that both light microscopy and digital pathology will be included as comparators.
80	Ibex Medical Analytics	The comparator should be WSI reviewed digitally. Directly comparing the standard of care using a microscope with a Digital + AI workflow may be challenging.	Thank you for your comment. Please see response to comment 79 with respect to the comparator for this assessment.
81	The Royal College of Pathologists	appropriate	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
82	ROVI Biotech Ltd	Yes	Thank you for your comment.

Comments on the draft scope- outcomes

No.	Stakeholder	Comments [sic]	Response
83	Sectra Imaging IT Solutions	Again coming back to Stratipath's solution; this app can be used instead of NGS. The app has potential to both shorten turn-around-time and save money (how much of the latter of course depends on what they charge though)	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis.
84	Aiforia Technologies Plc	Yes. The outcomes listed are seen as appropriate	Thank you for your comment.
85	DiaDeep	The outcomes are comprehensive. We recommend additions: (1) Inter-laboratory concordance rates for biomarker scoring (ER, PR, HER2, Ki-67, PD-L1), directly capturing the standardisation benefit of AI; (2) Rate of ISH/FISH referral for HER2 equivocal (2+) cases - AI-assisted HER2 scoring can reduce equivocal calls avoiding the 7-day ISH/FISH delay; (3) Repeatability and reproducibility of AI-generated biomarker scores, given that deterministic AI scoring (0% repeatability variation) represents a qualitative improvement over inherently variable manual quantification.	Thank you for your comment. The following key outcomes are listed in the scope for consideration (text in **bold** indicates additions for the final scope): • concordance between AI and pathologist review • need for or use of additional tests (repeat biopsies, repeat IHC, **ISH/FISH** testing) • Diagnostic accuracy, for which the external assessment group will consider the quality of the ground truth in the evidence. Outcomes not listed in the scope may be considered if present in the

No.	Stakeholder	Comments [sic]	Response
			evidence and considered important for analysis by the external assessment group or committee.

No.	Stakeholder	Comments [sic]	Response
86	Mindpeak GmbH	All the outcomes proposed will capture the benefits of the technology.	Thank you for your comment.
87	Breast Cancer Now	Yes	Thank you for your comment.
88	Stratipath AB	Yes	Thank you for your comment.
89	AIRA Matrix Private Limited	In addition to general measures, outcomes should include analytical and clinical performance metrics, such as agreement with pathologist assessment, prognostic accuracy (e.g., ability to stratify patients by risk of disease progression or metastasis), and comparison with existing clinicopathological risk models. **Clinical utility outcomes** are also important, including the impact on treatment decision-making (e.g., changes in management strategies), alignment with multidisciplinary team (MDT) decisions, and potential to reduce overtreatment or undertreatment. Where feasible, longer-term outcomes such as progression-free survival or metastasis-free survival may be considered, although these may be supported through retrospective or validation studies. Overall, the outcomes are appropriate in principle, but ensuring inclusion of prognostic performance, clinical utility, and decision impact measures, alongside system-level benefits and risks, will provide a more comprehensive evaluation of AIRABreast's value within the NHS.	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis. The following outcomes are listed in the scope for consideration (text in **bold** indicates additions for the final scope): • concordance between AI and pathologist review • impact on clinical decision-making including staging and treatment selection, which includes MDT decisions • adverse effects including under or overtreatment • progression-free survival, **disease-free and distant disease-free survival**

No.	Stakeholder	Comments [sic]	Response
90	Artera Inc	We agree that the outcomes listed are in general appropriate. We would suggest that for many breast cancers (i.e. those treated with curative intent), disease-free survival and distant disease-free survival are highly relevant endpoints that should be added to the outcomes.	Thank you for your comment. Disease-free and distant disease-free survival have been added to the list of outcomes for consideration.

91	Digistain Ltd	The outcomes listed in the draft scope (including diagnostic accuracy, reporting time, and concordance) are appropriate for technologies assisting initial diagnostic interpretation. However, they do not fully capture the most important **system-level and patient-level impacts** associated with delays in the breast cancer care pathway. The clinician survey referenced above indicates that the most significant delays occur **after initial diagnosis**, at the stage where additional tumour information is required to inform treatment decisions. These delays directly affect: • time from diagnosis to MDT decision • time to initiation of systemic therapy • patient experience during the decision-making period To ensure that the evaluation captures the full impact of AI technologies operating within histopathology workflows, it would be helpful to include additional outcomes such as: • **time from diagnosis to treatment decision** • **effects of over/undertreatment (where risk stratification plays a uniquely important role)** • **time from diagnosis to treatment initiation (this was explicitly identified as a core focus in the scoping briefing)** • **variability in pathway duration across centres** • **impact on downstream testing requirements** Including these outcomes would allow NICE to assess not only diagnostic efficiency, but also the potential of AI technologies to reduce delays across the broader care pathway. It is therefore ultimately in the interest of the committee to consider risk stratification when evaluating the effectiveness of the proposed scope for these measures	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis. The following outcomes are listed in the scope for consideration (text in **bold** indicates additions for the final scope): • case review time/ **turnaround time** (including slide review time/**number of cases reviewed per session**, time to produce report for MDT) • time to diagnosis (**referral to diagnosis, biopsy to MDT**) • time to initiate treatment • service user and carer acceptability and views • adverse effects including under or overtreatment • need for or use of additional tests (repeat

No.	Stakeholder	Comments [sic]	Response
			biopsies, repeat IHC, **ISH/FISH** testing)

No.	Stakeholder	Comments [sic]	Response
92	NHS England	No additional outcomes proposed.	Thank you for your comment.
93	Roche Diagnostics UK	Roche believes the outcomes listed are appropriate. Additional outcomes relevant to this evaluation could include: • Time to diagnosis • Time to final histopathology report including further testing • Inter-observer variability • Capacity outcomes, such as waitlist times • Workforce productivity outcomes, such as number of cases reviewed per pathologist unit time, time spent biomarker scoring, laboratory throughput, pathologist workload and overtime hours	Thank you for your comment. The following outcomes are listed in the scope for consideration (text in **bold** indicates additions for the final scope): • case review time/ **turnaround time** (including slide review time/**number of cases reviewed per session**, time to produce report for MDT) • time to diagnosis (**referral to diagnosis, biopsy to MDT**) Note the above are examples of clinician productivity measures and if others are present in the evidence they will be considered**.** • concordance between AI and pathologist review
94	Visiopharm	Yes, it seems quite comprehensive but as described earlier in the response. Visiopharm believes that a broader scope might help identify further benefits.	Thank you for your comment. Please see responses to your previous comments.

No.	Stakeholder	Comments [sic]	Response
95	Ibex Medical Analytics	Yes — however, capturing the case review time field may be challenging. Departments are staffed using a standard point-based system (RCPATH)., and it will be difficult to demonstrate that staff supported by AI work 20–50% faster than those without AI. In practice, this would translate into handling 20–50% more workload with the same resources. It is also difficult to assess this experimentally: *time to produce report for MDT, time to MDT diagnosis*. Cancer pathways are well-established, and MDTs typically involve 10–15 medical specialists, often at consultant level. Introducing a new technology makes it challenging to alter such schedules and processes. While feasible, any change is likely to be slow and gradual.	Thank you for your comment. Several options for how workforce productivity might be captured are given in the scope. These are examples of productivity measures and if other relevant outcomes are present in the evidence they will be considered. The limitations of these outcomes will be discussed where relevant in the assessment report by the EAG.

No.	Stakeholder	Comments [sic]	Response
96	Cancer Research UK	Some of the outcomes, listed either as intermediate outcomes or clinical outcomes, are not relevant to the intervention., e.g., overall survival.	Thank you for your comment. NICE's reference case for modelling cost-effectiveness states that the time horizon for estimating clinical effectiveness and value for money should be long enough to reflect all important differences in costs or outcomes between the technologies being compared. Diagnostic technologies like these do have the potential to have effects on costs and outcomes over a person's lifetime because they inform clinical decision making and treatment planning. In these circumstances, a lifetime time horizon is usually appropriate. We acknowledge that many studies done for these technologies may not report long-term outcomes, but NICE uses a linked evidence approach, whereby evidence on the technology and short-term outcomes is linked with data from other studies that report long-term outcomes so that we can assess this.
97	The Royal College of Pathologists	appropriate	Thank you for your comment.

98	ROVI Biotech Ltd	Yes. In addition to diagnostic performance, it would be important that the scope considers several practical requirements for implementation in real-world pathology services: • Interoperability with existing digital pathology infrastructure, including compatibility with widely used slide scanners and Laboratory Information Management Systems (LIMS). • Integration into existing pathology workflows, ensuring that AI tools support rather than disrupt routine diagnostic practice. • Regulatory compliance, particularly alignment with UK regulatory frameworks and international standards such as CE-IVD / IVDR where applicable. • Transparency and explainability of AI outputs, allowing pathologists to understand how algorithmic suggestions are generated. • Performance monitoring and post-deployment validation, ensuring that diagnostic performance remains consistent across institutions and patient populations. These elements are critical to ensure safe, scalable, and sustainable implementation within NHS pathology services.	Thank you for your comment. The considerations section of the scope includes the following points: • Digital infrastructure requirements. • AI acceptability, including that optimal integration with existing workflows is key to successful deployment of AI in laboratories. Also, the following text has been added to this section: "**Transparency and explainability of outputs may be important to develop confidence in the technologies**." • The following statement has been added to the considerations section of the scope: "**Performance monitoring and post-deployment validation is necessary to ensure diagnostic performance remains consistent across institutions and patient populations."**

No.	Stakeholder	Comments [sic]	Response
			In addition, ease of use/user acceptability, which can capture the extent to which use of the AI disrupts usual workflows, is listed in the final scope for consideration. Section 5.3.16 of NICE technology appraisal and highly specialised technologies guidance: the manual states that NICE will not publish final guidance on a technology until UK regulatory approval has been granted.

Comments on the draft scope- equality

No.	Stakeholder	Comments [sic]	Response
99	Sectra Imaging IT Solutions	No comment	Thank you for your comment.
100	Aiforia Technologies Plc	Standardising cancer pathology ensures that every patient receives the same rigorous diagnostic precision.	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
101	DiaDeep	We support the equality considerations outlined. Cloud-based AI solutions requiring no on-premise GPU hardware can be deployed in smaller district general hospitals serving underserved populations, providing standardised quantification regardless of institutional size or sub-specialist expertise. This is especially important for borderline biomarker cases (HER2-low, Ki-67 intermediate, PD-L1 near-threshold). The assessment should seek evidence on representativeness of AI training datasets across ethnicity, sex, and rare tumour subtypes.	Thank you for your comment. A statement on deployment options has been added to the considerations section of the scope: "**Technologies vary as to whether they offer on-site or cloud-based deployment options, or both. Flexibility may facilitate uptake and implementation in smaller district general hospitals**." Please see the response to comment 51 with respect to considerations on sex, ethnicity and rare tumour morphologies.
102	Mindpeak GmbH	We believe the current wording of the draft remit and scope is appropriate and already addresses the stated aims; therefore, no changes are necessary.	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
103	Breast Cancer Now	AI models are trained on the data that is shown to them. The scope does not offer information on how the models being considered have been trained. This information needs to be transparent, and the data used should be representative of the population they will serve. The AI tools used must be able to perform to the same level of accuracy and consistency across different populations. Understanding whether the accuracy of AI tools varies depending on breast tissue density may also have equity implications as some groups are more likely to have dense breasts based on age or ethnicity. New AI tools for confirming and characterising breast cancers must be able to accurately assess pathology samples from women with dense breast tissue.	Thank you for your comment. Please see the response to comment 51 with respect to considerations on generalisability of the technologies and sex, ethnicity and rare tumour morphologies. Clinical experts advised that breast density was a concern for radiological detection of cancer but not for histopathological assessment of biopsy tissue.
104	Stratipath AB	No comment	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
105	AIRA Matrix Private Limited	AI-based digital pathology tools, including AIRABreast, rely on the quality and representativeness of training and validation datasets. There is a potential risk that under-representation of certain demographic groups(e.g., based on ethnicity or age) in development datasets could impact performance and generalisability. It would therefore be important to ensure that evidence is generated to demonstrate consistent performance across diverse patient populations, including groups protected by equality legislation. For people with disabilities, particularly those affecting vision or digital interaction, consideration should be given to user interface accessibility and usability, ensuring compatibility with assistive technologies where applicable. Thoughts: **Performance across demographic subgroups**, including ethnicity, age, and other relevant characteristics **Multi-site validation data** reflecting variability in NHS settings **Usability and human factors evaluations**, including accessibility considerations **Implementation considerations**, including potential disparities in access to digital pathology infrastructure	Thank you for your comment. Please see the response to comment 51 with respect to validity and generalisability of training and validation datasets. With respect to multi-site validation data, this comment has been noted and the external assessment group will produce a protocol which will include their approach to hierarchy and selection of evidence. A statement on usability has been added to the equality considerations section of the scope: "**Accessibility and compatibility of technologies with assistive technologies for users with disabilities affecting vision or digital interaction should be considered**". Note also that "ease of use/ user acceptability" is listed in the outcomes to be considered in the final scope. The considerations section of the scope includes a statement on digital infrastructure requirements and considerations.

No.	Stakeholder	Comments [sic]	Response
106	Artera Inc	By excluding AI digital histopathology technologies that report prognosis/risk stratification, the draft remit and scope excludes from consideration the potential for these technologies to address the following inequalities: • Improvements in care in areas with higher levels of deprivation and ethnic diversity. It is known that in these areas, there is greater use of more intensive combination treatment, including tumour resection, radiotherapy, and chemotherapy. While this may be because there is lower uptake of screening and therefore patients present with more advanced disease, requiring more intensive treatment regimens, additional prognostic and predictive information may reduce overtreatment with chemotherapy in this population.3 • Improvements in care for older patients. Technologies validated as predictive for chemotherapy benefit in older (post-menopausal) patients provide additional information for shared decision-making regarding the appropriateness of chemotherapy for older patients, helping overcome documented issues around access to chemotherapy due to ageism.3 • As highlighted in the draft scope, people living in rural areas face greater travel burdens for treatment. Providing additional risk stratification to inform treatment decision-making could allow some patients to avoid adjuvant therapy, reducing this burden.	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis.

No.	Stakeholder	Comments [sic]	Response
107	Digistain Ltd	The draft scope appropriately recognises the importance of equality considerations. However, limiting the evaluation to technologies that assist initial diagnostic interpretation may risk **excluding technologies that could address inequalities arising later in the pathway**, particularly those associated with delays in accessing additional tumour assessment. In practice, access to downstream tumour characterisation can vary across NHS trusts due to differences in infrastructure, resources, and commissioning practices. These variations may disproportionately affect: • patients treated in resource-constrained settings • patients in geographically dispersed regions • populations already experiencing disparities in cancer outcomes The clinician survey findings suggest that delays in this part of the pathway are both common and clinically significant. Excluding technologies that could reduce these delays may therefore limit NICE's ability to fully consider solutions that could improve equity of access to timely treatment decision-making. To support evaluation of equality impacts, it would be helpful to consider evidence relating to: • variation in time to treatment decision across different NHS settings • access to additional tumour assessment across regions and populations • the potential for workflow-integrated technologies to reduce these variations	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis.
108	NHS England	No equality concerns or comments	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
109	Roche Diagnostics UK	Roche does not anticipate that the draft remit or scope would adversely impact people with protected characteristics. However, it may be important to consider the representativeness of training and validation datasets used for AI technologies, to ensure consistent performance across different demographic groups. In addition, variation in digital pathology infrastructure between NHS centres could influence access to AI-enabled diagnostics and may warrant consideration to ensure equitable implementation.	Thank you for your comment. Please see the response to comment 51 with respect to validity and generalisability of training and validation datasets. Please see response to comment 79 with respect to digital pathology as a comparator for this assessment. The considerations section of the scope includes a statement on digital infrastructure requirements and considerations.
110	Visiopharm	The draft remit seems to comprehensively cover equality and will not intentionally exclude any people from the study.	Thank you for your comment.
111	Ibex Medical Analytics	We did not experience any specific biases in our trials.	Thank you for your comment.
112	The Royal College of Pathologists	See comment above regarding ethnic minorities	Thank you for your comment. Please see the response to comment 51.

No.	Stakeholder	Comments [sic]	Response
113	ROVI Biotech Ltd	We do not believe the current scope excludes any protected groups. However, we highlight that for AI technologies to promote equality, it is essential that the evidence base (training and validation datasets) reflects the diverse demographic reality of the UK population, including ethnicity and age. We recommend that the committee monitors potential 'algorithmic bias' to ensure that diagnostic precision remains consistent across all patient groups, particularly those who may have been underrepresented in early digital pathology research. Cells IA is committed to transparency in dataset composition to mitigate these risks.	Thank you for your comment. Please see the response to comment 51 with respect to validity and generalisability of training and validation datasets. Please see the response to comment 98 with respect to algorithm transparency and performance monitoring and post-deployment validation.

Comments on the draft scope- other considerations

No.	Stakeholder	Comments [sic]	Response
114	Sectra Imaging IT Solutions	No comment	n/a
115	Aiforia Technologies Plc	A reasonable evaluation should be of transparent visualization of the results and manual editing if needed, keeping pathologists in the driving seat of the diagnostic process.	Thank you for your comment. Please see the response to comment 98 with respect to algorithm transparency.
116	Tempus/Paige	As mentioned above, We urge NICE to prioritize **evidence conducted within the NHS setting**. Tempus/Paige has completed a retrospective study in the NHS that demonstrates these tangible benefits (manuscript in preparation).	Thank you for your comment. This comment has been noted and the external assessment group will produce a protocol which will include

No.	Stakeholder	Comments [sic]	Response
			their approach to hierarchy and selection of evidence.
117	DiaDeep	DiaDeep requests that subgroups with high inter-observer variability be explicitly included: (1) Ki-67 intermediate-range tumours (5-30%), treatment-determining for Luminal A vs B subtyping; (2) HER2 equivocal (2+) cases where AI may reduce unnecessary ISH/FISH referrals; (3) PD-L1 expression near clinically relevant thresholds (CPS near 1, 5, or 10 in TNBC), where manual inter-observer ICC is as low as 0.45.	Thank you for your comment. The considerations section of the scope acknowledges potential benefits for groups with high interobserver variability including people with borderline HER2 (2+) status. Ki-67 and PD-L1 are not routinely assessed for the Royal College of Pathologists proforma dataset, and technologies to support these analyses will not be included in this assessment (please see the response to comment 5).
118	Mindpeak GmbH	No other consideration	n/a
119	Stratipath AB	See below	n/a
120	AIRA Matrix Private Limited	No comments	n/a
121	Artera Inc	N/A	n/a
122	Digistain Ltd	The draft scope distinguishes between AI technologies that assist diagnostic interpretation and those that provide additional tumour information for treatment decision-making. In practice, this distinction may not reflect how these technologies are used within clinical workflows. AI tools that analyse histopathology samples to derive tumour biology information:	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis.

No.	Stakeholder	Comments [sic]	Response
		• operate on the same tissue samples as diagnostic tools • integrate into the same pathology workflows • are subject to the same workforce and capacity constraints • influence the same MDT decision-making processes As such, these technologies represent an extension of digital histopathology rather than a separate category. Given the strong clinician-reported evidence that delays are greatest at the stage of tumour characterisation, it may be appropriate for the evaluation to consider AI technologies across the **full histopathology workflow**, rather than limiting the scope to initial diagnostic interpretation alone.	
123	NHS England	The scope should reflect the rapid growth in digital pathology infrastructure within the NHS. Digital histopathology has had significant central investment by NHS England through the national diagnostics and pathology programmes, and uptake is increasing across pathology networks in England. Digital infrastructure is a prerequisite for the implementation of AI technologies in histopathology, and therefore the level of digital adoption is directly relevant to implementation feasibility. The current wording in the draft scope does not fully reflect the current position: “Current digital pathology usage is not widespread in the NHS”	Thank you for your comment. The scope wording relating to current digital pathology usage has been amended to acknowledge the ongoing rollout. This includes explicit reference to the need for digital infrastructure for AI implementation (new text added to the scope is in **bold**): “Infrastructure for digital pathology is a pre-requisite of AI for histopathology. **In line with national priorities for diagnostic and cancer services, centralised investment and rollout are supporting uptake of digital pathology nationally. Current adoption data indicates:**

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		Whilst a smaller proportion of trusts are reporting the majority of cases digitally, most pathology networks have begun digital reporting and national rollout continues. Current position (February 2026): • 25 of 27 pathology networks have begun digital reporting • 106 of 132 acute and specialist trusts are using digital images for primary diagnosis • 51 trusts are digitally reporting more than 50% of cases The rollout of AI technologies could risk reinforcing existing variation in diagnostic pathways if digital adoption is not also considered. Key barriers to full digital adoption include: • Training and assessment requirements still based on glass slides • Storage and infrastructure requirements for whole slide imaging • Variation in information governance arrangements across organisations There are also strong links to national priorities, including: • National diagnostics productivity targets • Cancer pathway improvement programmes • National plans supporting the use of AI in diagnostics • National target for 98% of histopathology tests to be reported within 10 days by March 2029 Recognition of these factors would improve the accuracy and context of the scope.	**25 of 27 pathology networks have begun digital reporting, approximately 80% of acute and specialist trusts are using digital images for primary diagnosis and about 51 trusts are digitally reporting more than 50% of cases. Level of digital adoption underpins the implementation of AI technologies included in the assessment**."

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124	Roche Diagnostics UK	Roche suggests that the role of digital pathology software platforms in enabling the implementation of AI technologies within routine histopathology workflows should be considered as an important aspect of the evaluation. Successful deployment of AI-assisted diagnostics requires an integrated digital pathology infrastructure, including software platforms capable of integrating with laboratory information systems and deploying multiple AI algorithms within a single environment. Consideration of these implementation factors are important to ensure reliable performance, reproducibility and practical adoption within NHS laboratories. The navify Digital Pathology platform supports the deployment and management of multiple AI applications across different tissue types, including breast cancer algorithms within the scope of this evaluation as well as additional Roche and third-party AI solutions. Platforms that integrate licensing, workflow management, and deployment within a single environment may facilitate AI adoption and reduce the need for separate integrations, reducing time to adoption and cost. The role of such enabling infrastructure may therefore be relevant to the evaluation, especially as it can influence the performance of the algorithms.	Thank you for your comment. The considerations section of the scope acknowledges that compatibility with digital infrastructure may be a barrier to implementation. Please see response to comment 98 with respect to digital compatibility and user acceptability and integration with workflow.
125	Visiopharm	No further comment	n/a
126	Ibex Medical Analytics	**Diagnostic benefits.** The appraisal does not account for the potential diagnostic advantages	Thank you for your comment and reference to available datasets.

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		of integrating AI into the clinical pathway. Establishing an accurate baseline is difficult due to limited data availability and the ethical constraints inherent in study design. Nonetheless, the latest National Audit on Breast Screening in England reported a core-biopsy miss rate—defined as cancers with prior core biopsies classified as B1 or B2—ranging from 0% to 0.76% for benign lesions (B1 + B2). When intermediate categories (B3) are also considered, it is reasonable to project that this rate could reach 1% or higher. Such misses can have substantial consequences, including lost productivity, hospitalisation, delayed treatment, misdiagnosis, reputational harm, additional testing, legal costs, and a significant burden on patients, families, and the healthcare system.	The assessment aims to capture diagnostic accuracy and the downstream impacts of clinical decision-making based on the testing (see suggested clinical and cost outcomes in the scope). NICE does not include outcomes on reputational harm or legal costs.
127	ROVI Biotech Ltd	The current evidence landscape is characterised by high technical proficiency but an "implementation gap" in routine practice. While retrospective validation on digitised whole-slide images has reached a high degree of maturity, we must be grounded in the fact that prospective, large-scale evidence within the unique operational pressures of the NHS remains limited. In our view, the existing data—largely derived from reader-assist studies—clearly demonstrates the potential to: • Standardise outcomes: Increase diagnostic consistency, especially in grading tasks where inter-observer variability is traditionally high. • Enhance sensitivity: Improve the detection of clinically significant breast cancer that might otherwise be overlooked in high-volume settings. • Optimise time: Measurably reduce slide review time, allowing pathologists to focus on complex cases.	Thank you for your comment. This comment has been noted and the external assessment group will produce a protocol which will include their approach to hierarchy and selection of evidence. They will discuss the limitations of the evidence in their assessment report. The committee will consider the limitations of the evidence in their decision-making and have a range of recommendation options to handle this (see Section 6 of NICE technology appraisal and highly specialised technologies guidance: the manual). Several outcomes have been listed in the scope for

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		However, for Cells IA (as part of Rovi), the next frontier is operational validation. Future evidence must shift from "can the algorithm see the cancer?" to "how does the algorithm improve the patient pathway and laboratory resilience in a live NHS environment?	consideration that may capture the potential benefits (outcomes added to the final scope are in **bold**): • diagnostic accuracy (sensitivity, specificity, positive and negative predictive value) • concordance between AI and pathologist review • case review time/ **turnaround time** (including slide review time/**number of cases reviewed per session**, time to produce report for MDT) • time to diagnosis (**referral to diagnosis, biopsy to MDT**)

Questions for consultation

No.	Stakeholder	Comments [sic]	Response
128	Sectra Imaging IT Solutions	No comment	n/a
129	Tempus/Paige	No comments	n/a
130	DiaDeep	Q3 - Technologies to add: DiaDeep formally requests inclusion of DiaKwant (DiaDeep) in this evaluation. DiaKwant is CE-IVDR Class C certified AI software for automated quantitative scoring of ER, PR, HER2, Ki-67, Mitoses, and PD-L1 on breast carcinoma WSI. Although	Thank you for your comment.

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		the draft scope requires tumour detection as a minimum, DiaKwant incorporates automated tumour region identification as an integral precursor to biomarker quantification - functionally equivalent to tumour detection within the IHC workflow. Validated across 833 slides from multiple independent laboratories: HER2 89% vs 82% routine, PD-L1 CPS 87% vs 75%, Mitosis 77% vs 65% (IFU-DK V05). Achieves 0% repeatability variation, cross-scanner ICC >= 0.7. UK launch planned H2 2026 via Roche navify Digital Pathology and Sectra UniView. Q7 - Evidence: Retrospective multi-laboratory validation studies are available. DiaDeep would welcome the opportunity to submit a full evidence package. Q8 - NHS use: DiaKwant is not yet in NHS use; EU commercial launch completed. UK launch H2 2026.	Please see the response to comment 13 with respect to the assessment of AI to support other proforma reporting requirements. Clarification has been added to the scope that technologies included on the basis of being able to detect invasive cancer or DCIS must do this from H&E-stained slides, so that IHC staining is not unnecessarily ordered for cases that do not need it (for example, if there is no cancer or DCIS is detected).
131	Mindpeak GmbH	1. Is the proposed title for this assessment appropriate? **YES** 2. Is the description of the intervention appropriate? **YES** 3. Are there any technologies currently included in scope that you think should not be? If so, why? **NO** 4. What level of evidence is there for the use of these technologies for initial diagnosis of breast cancer? T**he CE-IVD level provides a strong foundation of evidence. The planned economic study is a crucial addition to this evidence base, directly addressing the need for AI tools to demonstrate their value for adoption in routine clinical practice.** 5. Do you consider that the use AI for histopathology to assist diagnosis of breast cancer can result in any potential substantial health-related benefits that are unlikely to be captured by a generic quality of life measure? • Please identify	Thank you for your comment. Companies that are included in the final scope will be contacted by NICE to complete the request for evidence document. The user guide contains information on what evidence can be submitted. The user guide and a draft request for evidence document have already been circulated to companies included in the draft scope.

No.	Stakeholder	Comments [sic]	Response
		the nature of the data which you understand to be available to enable the committee to take account of these benefits. **Using standard, generic quality-of-life measurements is appropriate. Employing such measures will help establish that AI is equivalent to other IVD solutions and offers significant added value to pathologists.**	
132	Breast Cancer Now	**6. Are there any additional outcomes or costs we should consider?** Digital pathology is not widespread in the NHS. System readiness and the cost of rolling this out should be considered in the assessment to reduce the risk of variation in access to new technologies. This consideration should include the cost of any upgrades to general IT software that would be needed to utilise AI tools, as well as the cost of the tools themselves. **8. Which of these technologies are currently in use in the NHS?** The table in appendix B shows that Aiforia Breast Cancer Suite and Ibex Breast are currently in use on the NHS. We can also see that an AI technology by Ibex Breast, Galon Breast, is in trial at Cambridge University Hospitals NHS Foundation Trust, Nottingham University Hospitals, North West Anglia NHS Foundation Trust, Betsi Cadwaladr University Health Board and University Hospitals Birmingham. We are not aware of any other usage of these technologies in the NHS.	Thank you for your comment. Please see the response to comment 123 with respect to the rollout of digital pathology and pre-requisites for AI implementation in the histopathology workflow. Please also see response to comment 79 with respect to the comparator for this assessment. NICE has been informed that Galon Breast is a predecessor technology of Ibex Breast.
133	Stratipath AB	Description of the intervention: There are several AI technologies for prognostic risk stratification that should be included (such as	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
		Stratipath Breast) since they add independent prognostic information which is of clinical value at the point of diagnosis in for the treatment decision-making.	Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis.
134	AIRA Matrix Private Limited	No comments	n/a
135	Artera Inc	1. Is the proposed title for this assessment appropriate? We suggest amending the title to “Artificial Intelligence technologies to assist histopathology for breast cancer” 2. Is the proposed population described appropriately? Is it appropriate to include people who have previously been treated for breast cancer? Yes, this would be appropriate. Some patients with diagnosed breast cancer who have had surgery may benefit from adjuvant therapies. Appropriate risk stratification, which is informed by histopathology under current standard of care and could be enhanced by the implementation of AI digital histopathology technologies, is essential to informing these treatment decisions and should be included within the scope. Is it appropriate to restrict the population to adults? Yes, this is appropriate. Are there any other subgroups for whom you would expect the clinical and cost effectiveness of the intervention to differ? N/A 3. Is the description of the intervention appropriate? Are there any technologies currently included in scope that you think should not be? If so, why? N/A	Thank you for your comment. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis and the response to comment 9 with respect to focusing the assessment on initial diagnosis and biomarker analysis. For these reasons, the title will not be amended. NICE assessments take the perspective of the NHS and personal social services and so are unable to account for wider societal costs such as productivity (see 4.2.9 of NICE technology appraisal and highly specialised technologies guidance: the manual). However, other health-related effects, system benefits and qualitative outcomes are intended to be captured in the

No.	Stakeholder	Comments [sic]	Response
		Are there any technologies you feel should be added to the scope? If so, why? As described above, we consider that the scope is not consistent with the role of histopathology in breast cancer diagnosis and does not reflect the inseparability of diagnostic and prognostic/risk stratification information. AI digital histopathology technologies that enhance the prognostic/risk stratification elements of the histopathology workflow should be included in the scope; for example, the ArteraAI Breast Cancer Assay. 4. Is the usage of AI technologies in the breast cancer pathway appropriately described (i.e. that they can be used as tools for triage, first or second read)? No, as described in more detail above, the scope does not fully reflect that histopathology in the breast cancer pathway inseparably provides information that informs both diagnosis and prognosis/risk stratification. This is partially reflected in the understanding that grading and biomarker detection are an important part of breast histopathology, as this informs prognosis and treatment management. Therefore, the usage of AI digital histopathology technologies in the breast cancer pathway should reflect this clinical reality and include technologies that also inform prognosis/risk stratification. 5. Is the comparator appropriate? Covered in the above section. 6. Are all the outcomes and costs suitable for inclusion in the assessment? Are there any additional outcomes or costs we should consider? The outcomes included are suitable (although we have suggested some additional relevant outcomes above), and we would like to highlight that	assessment through the following outcomes: • Case review time • Time to diagnosis • Time to initiate treatment • Clinical user acceptability • Service user and carer acceptability and views Further issues and considerations relating to equality and health inequality are reported in the scope and Equality and Health Inequality Impact Assessment form.

No.	Stakeholder	Comments [sic]	Response
		many of the long-term outcomes included will primarily benefit from tools that provide complete prognostic information. 7. What level of evidence is there for the use of these technologies for initial diagnosis of breast cancer? N/A 8. Which of these technologies are currently in use in the NHS? N/A 9. Do you consider that the use AI for histopathology to assist diagnosis of breast cancer can result in any potential substantial health-related benefits that are unlikely to be captured by a generic quality of life measure? Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. As described above, there is considerable evidence that diagnosis and treatment of breast cancer is inequitable, disadvantaging a range of groups. AI digital histopathology technologies have the potential to address these inequalities, but this is unlikely to be captured in the QALY. Breast cancer generates a substantial societal burden that extends beyond direct healthcare costs, particularly through impacts on informal carers and wider participation in work and family life. Beyond carer impacts, breast cancer also imposes wider societal costs through reduced productivity, early retirement, and changes in household and caregiving roles. These impacts may be due to the disease itself or to treatment side-effects. Therefore, technologies that inform clinical decision making have the potential to direct treatment decisions appropriately and therefore ameliorate these societal burdens; however, this benefit will not be captured in the QALY.	

No.	Stakeholder	Comments [sic]	Response
		10. NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if, in addition to the equality considerations in the decision problem table, the proposed remit and scope: could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which capsule sponge tests will be used; could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology; could have any adverse impact on people with a particular disability or disabilities if there are any additional equality considerations we should be aware of? please tell us what evidence should be obtained to enable the committee to identify and consider such impacts. Covered in the above section. 11. Are there any other stakeholders NICE should be aware of for this topic? N/A	
136	Digistain Ltd	The consultation question regarding whether the scope should include additional AI applications within histopathology is particularly relevant.	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
		Based on both clinical practice and the survey findings, there is a clear rationale for including AI technologies that: • analyse histopathology samples beyond tumour detection • provide clinically relevant tumour characteristics • support MDT decision-making within the same workflow Restricting the evaluation to diagnostic applications alone risks focusing on a part of the pathway where timelines are already relatively efficient, while excluding technologies that may have a greater impact on reducing delays in treatment decision-making. As such, a linked evidence approach would be more appropriate to capture the full pathway impact, connecting diagnostic performance to changes in treatment allocation and ultimately patient outcomes. We therefore suggest that the scope is expanded, or explicitly structured, to reflect this diagnostic–decision linkage, particularly in populations where additional risk stratification is standard practice, to ensure that the evaluation reflects real-world clinical pathways and does not underestimate the value of technologies that influence decision-making beyond initial diagnosis.	Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis. Please see the response to comment 13 with respect to the assessment of AI to support other proforma reporting requirements.
137	NHS England	**1. Is the proposed title for this assessment appropriate?** No - If cases from the NHS Breast Screening Programme are excluded, the title should be amended to clarify this. E.g. - ***AI technologies to assist histopathology for non-screening breast cancer diagnosis -*** This would provide clarity regarding the population covered by the evaluation. **2. Is the proposed population described appropriately?** **• Is it appropriate to include people who have previously been treated for breast cancer?**	Thank you for your comment. Please see the response to comment 12 with respect to the inclusion of people from the screening programme. Given that it is routine for NICE not to make recommendations for programmes overseen by the National Screening

No.	Stakeholder	Comments [sic]	Response
		Yes - inclusion may be appropriate where patients previously treated for breast cancer are disease-free and undergoing new diagnostic assessment. • **Is it appropriate to restrict the population to adults?** Yes • **Are there any other subgroups for whom you would expect the clinical and cost effectiveness of the intervention to differ?** Yes – it may differ in male breast cancer **3. Is the description of the intervention appropriate?** • **Are there any technologies currently included in scope that you think should not be?** No – there are no technologies that should be removed from the scope. • **Are there any technologies you feel should be added to the scope?** No – there are no technologies that should be added to the scope. **4. Is the usage of AI technologies in the breast cancer pathway appropriately described (i.e. that they can be used as tools for triage, first or second read)?** Yes **5**. **Is the comparator appropriate?** Yes - The comparator reflects current standard practice and is appropriate. **6. Are all the outcomes and costs suitable for inclusion in the assessment?** Yes - The outcomes and costs proposed for the evaluation are appropriate. **Are there any additional outcomes or costs we should consider?**	Committee, the title will not be amended to reflect this. People who have been previously treated and are undergoing diagnosis for a new suspected breast cancer episode will be included, but in response to feedback at the scoping workshop, this group will be listed in the subgroup section of the scope to understand if previous treatment that may affect cell morphology could affect AI performance. Please see the response to comment 51 with respect to considerations on sex, ethnicity and rare tumour morphologies. Please see the response to comment 135 with respect to effects not captured in the QALY; the outcomes listed in this comment are listed in the scope. Please see response to comment 96 with respect to NICE's linked evidence approach to enable long-term outcomes to be captured in health economic modelling.

No.	Stakeholder	Comments [sic]	Response
		No – there are no additional outcomes or costs proposed. **7. What level of evidence is there for the use of these technologies for initial diagnosis of breast cancer?** There are a variety of clinical trials published in peer-reviewed journals evaluating AI-assisted histopathology for breast cancer diagnosis. Relevant literature can be identified through databases such as PubMed. 8. **Which of these technologies are currently in use in the NHS** **Ibex** were awarded £1.5 million in NHS AI Awards Phase 4 funding. Deployment sites include: • Nottingham University Hospitals • Cambridge University Hospitals • North West Anglia NHS Foundation Trust • Betsi Cadwaladr University Health Board • University Hospitals Birmingham **9. Do you consider that the use AI for histopathology to assist diagnosis of breast cancer can result in any potential substantial health-related benefits that are unlikely to be captured by a generic quality of life measure?** Yes **• Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** AI-supported histopathology may deliver system and patient benefits not fully captured by QALY measures, including: Short-term benefits: • Reduced time to histological diagnosis • Reduced time to treatment	Additional relevant stakeholders will be added to the stakeholder list, thank you.

No.	Stakeholder	Comments [sic]	Response
		Longer-term benefits (more difficult to capture in short studies): • Time to disease-free status • Risk of recurrence • Life expectancy following treatment Short-term operational metrics are likely to be the most feasible to measure within evaluation studies. **10. NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if, in addition to the equality considerations in the decision problem table, the proposed remit and scope:** **• could exclude from full consideration any people protected by the equality** **legislation who fall within the patient population for which capsule sponge** **tests will be used;** No **• could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access theTechnology** No **• could have any adverse impact on people with a particular disability or Disabilities** No **• if there are any additional equality considerations we should be aware of?** No	

No.	Stakeholder	Comments [sic]	Response
		• please tell us what evidence should be obtained to enable the committee to identify and consider such impacts No **11. Are there any other stakeholders NICE should be aware of for this topic?** • Royal College of Pathologists • Institute of Biomedical Science • Royal College of Radiologists • Association of Breast Pathology • Association of Breast Surgery • NHS England National Pathology Programme • Pathology networks in England • Digital pathology programme leads	
138	Roche Diagnostics UK	**Are there any technologies you feel should be added to the scope? If so, why?** The draft scope specifies that only technologies which perform “a minimum of tumour detection” will be considered. Roche recognises that tumour detection is an important step in histopathological diagnosis; however, this requirement may unintentionally exclude technologies that support other essential elements of the initial diagnostic workflow. Excluding these technologies may therefore affect outcomes such as time to initiate treatment and clinical decision-making. Roche believes that a broader scope may be necessary to realise the full potential impact of AI technologies in improving efficiency across the diagnostic pathway.	Thank you for your comment. Please see the response to comment 13 with respect to the assessment of AI to support other minimum reporting requirements, and the response to comment 9 with respect to focusing the assessment on initial diagnosis and biomarker analysis. Please see the response to comment 130 with respect to clarification that detection must be done from H&E stained slides for inclusion.

No.	Stakeholder	Comments [sic]	Response
		As noted in the draft scope, biomarker determination for ER, PR and HER2 forms part of routine histopathological reporting during the initial diagnosis of breast cancer. Royal College of Pathologists guidance states that these biomarkers can be assessed on diagnostic core biopsy specimens once invasive carcinoma is identified (1). This is also reflected in NHS England's Faster Diagnostic Standard, which requires histopathology results including ER, PR and HER2 status to be available for the initial multidisciplinary team (MDT) discussion by day 17 following referral (2). This demonstrates that biomarker assessment is expected to be completed within the initial diagnostic timeframe. However, this component of the diagnostic pathway can introduce delays. The draft scope notes that IHC staining to determine ER, PR and HER2 can add around 2–3 days between H&E and IHC review, potentially contributing to delays (3). Evidence also suggests that turnaround time targets are not always met; for example, FOI data from an NHS trust indicated that 11% of HER2 IHC cases did not meet the 7-day reporting target (4). As highlighted by clinical experts in the scope and supported by the literature, technologies that perform biomarker analysis may bring several benefits to the diagnostic pathway, including minimising inter-observer variation between pathologists and supporting standardisation of biomarker scoring (7), improving accuracy and consistency while speeding up the assessment process (8), reducing time to result and enhancing reproducibility (9), and improving overall efficiency (10). If technologies that perform biomarker analysis are not	Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis. Most technologies in scope do HER2 analysis. One potential benefit of introducing AI for HER2 analysis is to reduce the need for ISH/FISH testing. Need for and cost of additional tests are included as outcomes for consideration in the scope.

No.	Stakeholder	Comments [sic]	Response
		prioritised within the evaluation, there may be a missed opportunity to address delays within this part of the diagnostic pathway. Furthermore, some AI technologies designed for biomarker analysis on IHC slides can identify tumour regions directly as part of the analysis workflow, without requiring manual tumour annotation. In such cases, tumour detection is effectively integrated within the biomarker assessment step. In addition, some algorithms can also identify tumour regions on H&E slides (e.g., highlighting invasive cancer regions) which can support downstream biomarker analysis. Together, this suggests that technologies supporting biomarker interpretation may also incorporate tumour detection within their functionality. The draft scope also notes that when HER2 status is inconclusive following immunohistochemistry, additional in situ hybridisation (ISH/FISH) testing may be required to determine HER2 gene amplification. According to the Faster Diagnostic Standard, these additional results should be available by day 24 for MDT discussion, prior to the patient being informed of their diagnosis and treatment options by day 28, indicating that this testing forms part of the initial diagnostic stage (2). The scope notes that the ISH/FISH step itself can add up to 7 days to the histopathology reporting timeline. This represents a significant burden in the process and leaves little margin to meet the day-24 reporting target if delays occur. In addition, ISH/FISH testing is a	

No.	Stakeholder	Comments [sic]	Response
		specialised and technically complex procedure that can be time-consuming to perform and interpret. As a result, some laboratories may outsource this testing, which can introduce further delays. Technologies that support interpretation of HER2 IHC or ISH analyses on diagnostic biopsy specimens may therefore play an important role in reducing these significant turnaround times and improving access where specialist testing capacity is limited. For example, the HER2 Dual ISH algorithm follows the same workflow to IHC for staining, slide scanning and algorithm-based analysis, allowing it to be used alongside other biomarker algorithms, while enhancing diagnostic consistency in breast cancer. (11) Furthermore, the draft scope excludes technologies that perform risk stratification or prediction of treatment response. However, risk stratification typically follows immediately after a positive diagnosis and is required to support treatment planning discussions with patients. This part of the diagnostic process often incurs the longest delay. Key literature and clinical experts have recognised that incorporating additional risk stratification via AI into the diagnostic pathway may be valuable in supporting more informed treatment decisions. (12) Excluding technologies that support risk stratification may therefore risk shifting bottlenecks further along the pathway, rather than addressing delays in producing the full set of information needed for clinical decision-making. Overall, biomarker determination, including IHC staining and additional ISH/FISH testing where required, forms part of the diagnostic	

No.	Stakeholder	Comments [sic]	Response
		information reviewed by the MDT before a diagnosis and treatment options are communicated to the patient (2). Limiting the scope to technologies that perform tumour detection may risk overlooking this stage of the pathway where significant delays occur, potentially shifting bottlenecks further along the diagnostic process. Broadening the scope to include AI technologies that assist interpretation of biomarker analyses, even if they do not perform tumour detection, would allow consideration of technologies addressing the full initial histopathological diagnostic process and help reduce the overall turnaround time for finalising histopathology reports. This may be particularly relevant given current workforce pressures in pathology, given that biomarker interpretation, including HER2 scoring, can be complex and subjective, meaning delays may disproportionately occur at this stage of the pathway. Recent studies suggest that AI-based biomarker prediction approaches may reduce biomarker reporting turnaround times by up to 45% (6). The importance of this is highlighted by evidence that suggests that delays in biomarker testing can influence treatment decisions, including decisions not to prescribe targeted therapies, and therefore have real consequences for patients. (4) Furthermore, consideration of related analyses, such as risk stratification, may also help ensure that improvements in diagnostic efficiency translate into more timely treatment decision-making. Roche therefore encourages consideration of a broader scope to enable the full potential of AI technologies to improve efficiency across the diagnostic pathway.	

No.	Stakeholder	Comments [sic]	Response
		1. Royal College of Pathologists (2021) *Guidelines for non-operative diagnostic procedures and reporting in breast cancer screening (G150).* London: Royal College of Pathologists. Available at:https://www.rcpath.org/static/4b16f19c-f7bd-456c-b212f557f8040f66/G150-Non-op-reporting-breast-cancer-screening.pdf 2. NHS England (2024) *Faster diagnostic pathways: implementing a timed breast cancer diagnostic pathway – guidance for local health and social care systems.* Available at: https://www.england.nhs.uk/long-read/faster-diagnostic-pathways-implementing-a-timed-breast-cancer-diagnostic-pathway-guidance-for-local-health-and-social-care-systems/ 3. Taniere, P. *et al*., 2024. *Landscape of cancer biomarker testing in England following genomic services reconfiguration: insights from a nationwide pathologist survey.* **Journal of Clinical Pathology**, 77(7), pp.486–492. https://pmc.ncbi.nlm.nih.gov/articles/PMC11228219/ 4. University Hospitals of North Midlands NHS Trust, 2021. Freedom of Information request ref: 029-2021: Breast cancer reporting and digital pathology questionnaire response. Available at: https://www.uhnm.nhs.uk/media/tmzc2mhu/20200518-foi-request-ref-029-2021-final-2-of-2.pdf 5. Taniere, P. *et al*., 2024. *Landscape of cancer biomarker testing in England following genomic services reconfiguration: insights from a nationwide pathologist survey.* **Journal of Clinical Pathology**, 77(7), pp.486–492.https://pmc.ncbi.nlm.nih.gov/articles/PMC11228219/	

No.	Stakeholder	Comments [sic]	Response
		6. Ruelle, T. et al., 2026. How artificial intelligence applied to digital pathology could transform biomarker assessment and diagnostic workflows in oncology. ESMO Real World Data and Digital Oncology. Available at: https://www.esmorwd.org/article/S2949-8201(25)00551-X/fulltext 7. Rönnlund, C., Sifakis, E.G., Schagerholm, C. *et al.* Prognostic impact of HER2 biomarker levels in trastuzumab-treated early HER2-positive breast cancer. *Breast Cancer Res* 26, 24 (2024). https://doi.org/10.1186/s13058-024-01779-9 8. Gough, M. *et al.* (2023) 'Improved concordance of challenging human epidermal growth factor receptor 2 dual in-situ hybridisation cases with the use of a digital image analysis algorithm in breast cancer', *Histopathology*, 83, pp. 647–656. 9. Kapadia, M. *et al.* (2022) 'Artificial intelligence-based whole slide scoring of nuclear breast cancer IHC markers Ki67, ER, and PR matches performance of manual clinical scoring', *Cancer Research*, 82(4 Suppl.), P1-02-17. 10. 33rd European Congress of Pathology – Abstracts. *Virchows Arch* 479 (Suppl 1), 1–320 (2021). https://doi.org/10.1007/s00428-021-03157-8 11. Yoder, A. *et al.* (2022) 'Computer-aided scoring of erb-b2 receptor tyrosine kinase 2 (HER2) gene amplification status in breast cancer', *Journal of Pathology Informatics*, 13, p. 100116. 12. McCaffrey, C. *et al.* (2024) 'Artificial intelligence in digital histopathology for predicting patient prognosis and treatment efficacy in breast cancer', *Expert Review of Molecular Diagnostics*, 24(5), pp. 363–377.	

No.	Stakeholder	Comments [sic]	Response
139	Visiopharm	Is the proposed title for this assessment appropriate? Yes, this is appropriate Is the description of the intervention appropriate? Are there any technologies currently included in scope that you think should not be? If so, why? Visiopharm agree that technologies currently in the scope should be included but believe that the mandatory requirement of tumor detection should not be the only mandatory requirement which potentially excludes other technologies or fails to capture the full benefit of the technology. Are there any technologies you feel should be added to the scope? If so, why? Visiopharm would propose the inclusion of a IHC staining quality control platform, Qualitopix. This platform is recommended by UKNEQAS to manage the drift observed in IHC staining over time and alert labs to potential clinical risks caused by issues such as antibody lot malfunctions or manufacture malfunctions of stainers. As analysis of biomarkers is dependent on the assay performed, which will differ from site to site and day to day. Then the benefits of these analysis, especially something like HER2-low, will be underpinned by the performance of these assays and a way to control those or flag a potential issue might be extremely beneficial. At least of 30% of patient cases use a standardised control cell line which is compatible with	Thank you for your comment. Please see the response to comment 13 with respect to the assessment of AI to support other minimum reporting requirements, and with respect to AI to support quality assurance for slide preparation. The potential benefits of AI to support biomarker analysis are captured in the list of outcomes for consideration in the scope. Also, “proportion of slides not appropriate for AI review/ repeat slide scanning” and “effect of WSI quality and acquisition methods on accuracy” are listed as outcomes for consideration to help understand the effects of quality control on AI included in scope. The following text has been added to the scope to reflect that the technologies in scope are supportive not autonomous: • The technologies section: “**The technologies are intended to support pathologists review and should not be used for**

No.	Stakeholder	Comments [sic]	Response
		Qualitopix. Around 20 NHS labs are already using Qualitopix in routine practice for markers such as HER2. Is the usage of AI technologies in the breast cancer pathway appropriately described (i.e. that they can be used as tools for triage, first or second read)? Yes, the usage of AI technologies in the breast cancer pathway is appropriately described, including their roles in triage, first read, and second read. We suggest adding a clarification that these tools function as diagnostic support systems, with the final interpretation and responsibility for clinical decisions, including ordering any additional tests, always remaining with the reporting pathologist. It may also be helpful to highlight that AI tools used for biomarker quantification operate in a similar support role within the pathway. Unlike tumour detection and grading, where AI typically supplements processes already performed by pathologists, biomarker quantification can offer capabilities beyond manual assessment, such as counting significantly larger numbers of cells and providing consistent quantitative outputs. These quantitative measures can be clinically significant for informing treatment decisions. Recognising this parallel role would help ensure the scope fully reflects where AI provides diagnostic value across the pathway. What level of evidence is there for the use of these technologies for initial diagnosis of breast cancer?	**final decision-making without pathologist oversight**." • Place of the technology in the pathway section: "**AI technologies in scope are intended for use as diagnostic support systems. Responsibility for the final interpretation remains with the pathologist**." With respect to the current level of evidence, this comment has been noted and the external assessment group will produce a protocol which will include their approach to hierarchy and selection of evidence.

No.	Stakeholder	Comments [sic]	Response
		There is predominantly early-stage feasibility and validation studies, with limited long-term real-world evidence due to early adoption. These are often small research studies and have not considered the full production use of algorithms in clinical practice. There are a small number of labs predominately in Europe, which have shown the use of these algorithms in daily practice who may not have published all their findings. Which of these technologies are currently in use in the NHS? Visiopharm have described several NHS trusts which are using our technology already in our RFI response. Do you consider that the use AI for histopathology to assist diagnosis of breast cancer can result in any potential substantial health-related benefits that are unlikely to be captured by a generic quality of life measure? No comment Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. There are several published papers which show the use of this technology and its potential clinical benefit. We don't believe there has been significant studies on cost benefit analysis due to the limited implementation of the technology over a long period of time. There are a few cutting-edge laboratories who have been at the forefront of the use	

No.	Stakeholder	Comments [sic]	Response
		of this technology such as UMC Utrecht who would be a beneficial reference site to discuss with the role of this technology. There have also published and presented at several conferences on return on investment analysis.	
140	The Royal College of Pathologists	I am not sure what regulatory approval or in process of achieving regulatory approval means in this context. It should mean at least UK CA or CE IVDR approval. In process of being awarded should not be evaluated as it is impossible to define what this means.	Thank you for your comment. To be included in the scope, technologies must have appropriate regulatory approval or be in the process of obtaining this. They must also be available to the NHS or be in the process of preparing to enter the UK market. But, NICE cannot publish guidance on a technology that does not have regulatory approval by the time of guidance publication (see section 5.3.16 of NICE technology appraisal and highly specialised technologies guidance: the manual).
141	ROVI Biotech Ltd	7. What level of evidence is there for the use of these technologies for initial diagnosis of breast cancer? While technical accuracy is proven, there is still a "lack of prospective data" on whether AI-assisted diagnosis leads to better long-term survival or quality of life compared to standard care. 8. Which of these technologies are currently in use in the NHS?	Thank you for your comment. With respect to the current level of evidence, this comment has been noted and the external assessment group will produce a protocol which will include their approach to hierarchy and selection of evidence. Please see response to comment 96 with respect to NICE's linked

No.	Stakeholder	Comments [sic]	Response
		Adoption across the NHS is currently heterogeneous and typically driven by local digital maturity or specific research mandates. We recognise the pioneering work of platforms like Ibex (Galen), Indica Labs, and Tempus (Paige AI), which have been evaluated in various pilot deployments and digital pathology Centres of Excellence. That said, the landscape is evolving beyond these initial pilots. The widespread deployment of digital pathology infrastructure—such as the various NHS Digital Pathology Networks—is creating a fertile ground for more modular and specialised AI assistants. At Cells IA, we observe that while these early movers have paved the way, there is a clear and growing demand for solutions that prioritise seamless LIMS integration and user-centric design to move from "pilot phase" to "routine standard of care 9. Do you consider that the use AI for histopathology to assist diagnosis of breast cancer can result in any potential substantial health-related benefits that are unlikely to be captured by a generic quality of life measure? While improved overall survival through earlier detection is a primary goal, the use of AI in histopathology offers substantial benefits that generic measures like EQ-5D often overlook. Specifically, AI-driven workflows can significantly shorten the diagnostic waiting period, mitigating acute psychological distress that standard QoL snapshots miss. Furthermore, AI provides standardised objectivity, reducing inter-observer variability. This ensures higher diagnostic 'correctness,' preventing the physical and mental morbidity associated with misclassification and subsequent over- or under-treatment, which are	evidence approach to enable long-term outcomes to be captured in health economic modelling. Please see the response to comment 123 with respect to the description of the digital pathology rollout in the NHS. Also, the scope acknowledges the need to integrate with digital infrastructure and the importance of user acceptability in the considerations section. Ease of use or user acceptability is also listed as an outcome. Other health-related effects, system benefits and qualitative outcomes are intended to be captured in the assessment, beyond those captured in the QALY, through the following outcomes: • time to diagnosis (referral to diagnosis, biopsy to MDT) • service user and carer acceptability and views • diagnostic accuracy

No.	Stakeholder	Comments [sic]	Response
		benefits that go beyond the sensitivity of generic health-state instruments. To enable the committee to account for these benefits, we suggest the following data are available: Concordance Data: Comparative analysis of inter-observer variability (Kappa scores) showing how AI-assisted grading provides a more consistent baseline for treatment than manual review alone. Reclassification Analysis: Real-world evidence (RWE) or retrospective cohort data identifying the frequency with which AI-driven biomarker quantification (e.g., HER2 or Ki-67) leads to treatment plan adjustments. Workflow Throughput Data: Comparative 'time-to-result' metrics from pilot implementations, demonstrating the capacity released within the pathology department. Qualitative Patient Data: Targeted PREMs or literature-based evidence quantifying the psychological impact of reduced diagnostic wait-times, which generic instruments like EQ-5D lack the sensitivity to capture.	• impact on clinical decision-making including staging and treatment selection • concordance between AI and pathologist review • case review time/ **turnaround time** (slide review time/**number of cases reviewed per session**, time to produce report for MDT) • time to diagnosis (**referral to diagnosis, biopsy to MDT**)

Additional comments on the draft scope

No.	Stakeholder	Comments [sic]	Response
142	Sectra Imaging IT Solutions	No comment	n/a

No.	Stakeholder	Comments [sic]	Response
143	DiaDeep	The scope would benefit from a clearer distinction between two complementary technology functions: (1) tumour detection/classification on H&E slides, and (2) biomarker quantification on IHC slides. Both address distinct but equally important bottlenecks in the diagnostic pathway and should be evaluated independently to enable robust assessment of technologies specialising in either or both capabilities.	Thank you for your comment. Please see the response to comment 13 with respect to the assessment of AI to support other minimum reporting requirements, including biomarker analysis.
144	Mindpeak GmbH	No	n/a
145	Stratipath AB	As mentioned, there are existing variabilities in biomarker scoring, but also for grading of invasive breast cancer (Acs B Cancers 2021 https://doi.org/10.3390/cancers13051166; van Dooijeweert C Intl Journal of Cancer 2020 https://doi.org/10.1002/ijc.32330). There is an even larger variability in pathologist's grading of biopsies than the surgical excised tumours. As described, all clinical factors at the diagnosis are combined for the treatment decision making, but for a large group of especially ER+/HER2- patients there is often insufficient information. The AI technology Stratipath Breast provides an independent risk stratification of the invasive cancer which is available without prolonging the diagnostic workup and is to be used in conjunction with the clinical factors to improve informed decision-making at the MDT.	Thank you for your comment. Please refer to the response to comment 9 with respect to focusing the assessment on initial diagnosis and biomarker analysis, and the response to comment 13 with respect to the assessment of AI to support other minimum reporting requirements, including grading and biomarker analysis. Please see the response to comment 7 with respect to the assessment of AI for risk stratification and prognosis.

Comments on the provisional stakeholder list

No.	Stakeholder	Comments [sic]	Response
146	Sectra Imaging IT Solutions	We suggest to consider the following additional stakeholders: -Visiopharm with their apps for ER, PR and HER2	Thank you for your comment.

No.	Stakeholder	Comments [sic]	Response
		-Stratipath with their app Stratipath Breast for NHG 2 patients -Panakeia with their PanProfiler, an application finding biomarkers based on H&E stains	Companies with technologies included in the final scope will be listed as consultee stakeholders. These companies will be invited to respond to a request for evidence, respond to consultations, nominate clinical experts and have the right to appeal against the Final Draft Guidance. Companies that do not have a technology in the final scope and do not support digital pathology infrastructure will not be invited to register as stakeholders. However, they will still have the opportunity to participate as follows: • respond to the public consultation on draft guidance • apply to observe committee meetings as public observers. Consultee or commentator stakeholders are provisional until a signed Confidentiality Agreement & Undertaking form is submitted to NICE at the evaluation stage.

No.	Stakeholder	Comments [sic]	Response
147	DiaDeep	DiaDeep is not currently on the provisional stakeholder list. Given our participation in the related TA6684 consultation and our CE-IVDR certified technology directly relevant to this evaluation, we respectfully request that DiaDeep be added as a Provisional Consultee in the Company category. We are committed to full participation in this evaluation process.	Thank you for your comment. Please see the response to comment 146 with respect to companies that will be included on the stakeholder list.
148	Stratipath AB	Based on Comment 1 and 2 above, we suggest that Stratipath with Stratipath Breast for biopsy should be added to the provisional stakeholder list.	Thank you for your comment. Please see the response to comment 146 with respect to companies that will be included on the stakeholder list.
149	Artera Inc	Artera Inc would like to continue to be considered a stakeholder due to the relevance of our technology to the histopathology care pathway in breast cancer.	Thank you for your comment. Please see the response to comment 146 with respect to companies that will be included on the stakeholder list.
150	Digstain Ltd	No additional organisations are suggested.	Thank you for your comment.
151	NHS England	Comments on the provisional stakeholder list • FujiFilm • Leica • Indica • Sectra • Siemens • Sysmex • Philips	Thank you for your comment. Companies that support digital pathology infrastructure will be added to the stakeholder list and invited to register as commentators. Commentators are not asked to prepare an evidence submission or statement, but are able to respond

No.	Stakeholder	Comments [sic]	Response
		• Roche	to consultations and they receive the final draft guidance for information only, without right of appeal. Consultee or commentator stakeholders are provisional until a signed Confidentiality Agreement & Undertaking form is submitted to NICE at the evaluation stage.
152	Roche Diagnostics UK	Roche Diagnostics UK and Ireland believe that they are appropriate to include as a stakeholder in this evaluation. Roche Diagnostics provides both AI algorithms and digital pathology software platforms that support the deployment of Roche and third-party AI applications within histopathology workflows.	Thank you for your comment. Roche has technologies that support digital pathology and third-party AI technologies, so will be added to the stakeholder list as a commentator. See response to comment 151 with respect to the role of commentators.
153	Ibex Medical Analytics	We were not sure of the appropriate time to put forward suggestions for the expert reviewers. However Ibex would like to suggest the following individuals who have experience in the field of Breast AI in Histopathology. [redacted]	Thank you for your comment. Companies that provide the technologies in the final scope will be invited to make an evidence submission and nominate clinical experts (see the response to comment 146). The project management team will be in contact in due course to facilitate this process.

No.	Stakeholder	Comments [sic]	Response
154	The Royal College of Pathologists	Appropriate	Thank you for your comment.
155	ROVI Biotech Ltd	We would like to see ROVI Biotech Ltd. (Cells IA) added to the list of Companies under Provisional Consultees.	Thank you for your comment. Please see the response to comments 146 and 151 with respect to companies that can be included on the provisional stakeholder list.