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Health Technology Evaluation

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

Draft scope

Draft remit and evaluation objective

To appraise the clinical and cost effectiveness of artificial intelligence (AI) technologies that assist the histopathological diagnosis of breast cancer in biopsies from people with suspected breast cancer, who have not been referred from the NHS Breast Screening Programme.

Background

Breast cancer starts in the tissues of the ducts or lobules of the breast. It is the most common cancer in women in the UK, and accounts for 15% of all new cancer diagnoses. Approximately 56,800 new cases of breast cancer are diagnosed each year in the UK. It is predominantly found in women, but 1% of diagnoses are in men (NICE Clinical Knowledge Summary, 2025).

Survival is linked to the stage of the disease at diagnosis. Stages 1 to 3 are called early and locally advanced breast cancer. Early breast cancers (stages 1 and 2) are diagnosed when it is restricted to the breast, or the breast and nearby lymph nodes, or both. Locally advanced breast cancer (stage 3) is diagnosed when the cancer has spread from the breast to the lymph nodes close to the breast, to the skin of the breast or to the chest wall. Stage 4, or advanced cancer, is diagnosed when it has spread to other parts of the body. The five-year survival rate in England between 2016 and 2020 was almost 100% in women diagnosed with stage 1 breast cancer, 90% with stage 2, 70% with stage 3 and 25% with stage 4 (Cancer Research UK).

There are several types of breast cancer. Invasive breast cancer means that the cancer cells have grown through the lining of the ducts into the surrounding breast tissue. Invasive cancer (no special type) is the most common, accounting for about 70 to 80% of all breast cancer diagnoses in the UK (Cancer Research UK). Ductal carcinoma in situ (DCIS) means that some cells have started to turn into cancer, but these cells are all contained inside the ducts. If left untreated DCIS could become invasive. Around 7,300 women are diagnosed with DCIS in the UK each year (Cancer Research UK).

A glossary of terms is included at the end of the document.

Initial diagnosis of breast cancer

Clinical examination and medical imaging are used to identify areas suspicious for cancer. But, definitive diagnosis of breast cancer can only be done with

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histopathology analysis. For initial diagnosis, this involves microscopic examination of a small sample of tissue (biopsy). What type of biopsy is done depends on the appearance, size and location of the suspicious region. Core needle and vacuum assisted biopsies (VAB) are most commonly done for initial diagnosis. About 65,000 breast biopsies were histologically tested for breast cancer between 2023 and 2024 (estimate derived from the National Disease Registration Service procedure activity extracts and National Cost Collection activity).

Histopathological reporting for initial diagnosis of breast cancer

The Royal College of Pathologists Guidelines for non-operative diagnostic procedures and reporting in breast cancer screening (2021) outline a minimum dataset that should be reported for histopathological analyses of core biopsies and VAB for breast cancer diagnosis. Key information that should be reported includes:

- Overall histological categorisation, rated B1 (normal) to B5 (malignant). Lesions with a B5 rating should be specified whether they are in situ or invasive carcinoma. In situ carcinoma should be identified as ductal or lobular, and invasive carcinoma type should be identified.
- Histological grade is reported when any carcinoma is identified. DCIS is graded as high, intermediate or low based on how abnormal the cells look. Invasive carcinoma is graded using the Elston and Ellis method, also known as Nottingham Grading.
- Biomarker status is reported when invasive carcinoma is detected. It is used for treatment planning and decisions on further genetic testing. The NICE guideline for early and locally advanced breast cancer: diagnosis and management (last updated in 2025) recommends oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) status should be reported quantitatively for all invasive breast cancers at the time of initial histopathological diagnosis. If HER2 status is inconclusive from immunohistochemistry (IHC) staining, a type of genetic test called in situ hybridisation (ISH/FISH) may be done to determine this.
- When a biopsy is taken to investigate a calcification, it should be reported if a calcification was histologically identified. This informs whether the biopsy likely includes the mammographically identified target lesion and is suitable for diagnostic assessment.
- Cytology and lymph node biopsy findings are reported if available, but these are not routinely present for initial diagnosis. 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.

Currently, a minimum of haematoxylin and eosin (H&E) staining and IHC staining must be done for histopathology analysis for suspected breast cancer. All processed tissue samples are routinely stained with H&E to detect regions of tumour and calcification, and for grading when carcinoma is found. 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.

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The delay between H&E and IHC slide review for the same person with suspected cancer can be several days. If HER2 status is inconclusive and ISH/FISH testing is needed, it can take up to 7 days for a histopathology report to be finalised.

Pathways for initial diagnosis of breast cancer

Initial diagnosis of breast cancer in the NHS can be via the NHS Breast Screening Programme (NHS BSP) or NHS symptomatic breast services.

NHS symptomatic breast services do diagnostic investigations for people who go to their GP or A&E with symptoms of breast cancer, and people who have a suspicious finding detected during surveillance for breast cancer outside of the NHS BSP. A GIRFT report on breast surgery from 2021 estimated that 60% of cancers are diagnosed following GP referrals, 4 to 5% from emergency services and 30% as a result of the NHS BSP. About 30,000 of an estimated 65,000 biopsies were histologically tested outside of the NHS BSP between 2023 and 2024.

- People having surveillance for breast cancer may have ultrasound or mammography scans at prespecified intervals. This could be because of a personal or familial history of breast cancer. Recommended conditions and schedules for surveillance are outlined in NICE's guideline on early and locally advanced breast cancer and NICE's guideline on familial breast cancer. If a suspicious finding is detected with imaging, the person should be given an urgent referral for suspected breast cancer.

- NICE's guideline on suspected cancer: recognition and referral defines criteria for urgent referral for people who have symptoms of breast cancer. Symptoms can include an unexplained lump in the breast or axilla, or changes to a nipple or the skin on the breast. Criteria for urgent referral are different in Scotland than in England, Wales and Northern Ireland (Cancer Research UK). People who are initially referred to non-suspected cancer pathway could be given an urgent referral if they present with red flag symptoms.

NHS England's faster diagnostic pathway applies to NHS symptomatic breast services when breast cancer is suspected. This standard recommends a maximum of 28 days from referral for a person to get a confirmed diagnosis or ruling out of breast cancer. Key points for histopathology in the faster diagnosis timeline for breast cancer are:

- by day 10, people should be seen in a 'one stop clinic' with same-day access to clinical examination, mammography, ultrasound and biopsy

- by day 17, histopathology results including ER, PR and HER2 status should be available for multidisciplinary team (MDT) discussion

- by day 24, when relevant, additional histopathology results for ISH/FISH should be available for MDT discussion

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- by day 28, the person should be informed of diagnosis or cancer ruled out, and treatment options discussed.

MDTs include breast and plastic surgeons, oncologists, specialist nurses, radiologists and pathologists.

Royal College of Pathologist standards and datasets for reporting cancers state that histopathology cases must be reported, confirmed and authorised within 7 to 10 calendar days of the biopsy procedure.

Treatment

NICE's guidance on early and locally advanced breast cancer (last updated in 2025) and NICE's guideline on advanced breast cancer (last updated in 2025) give recommendations for breast cancer management. Treatment options depend on multiple clinical factors and patient choice. Clinical factors include tumour type, location, size, grade, receptor status, whether it has spread, and characteristics of the person with breast cancer. The MDT discusses treatment options, considering the person alongside medical imaging and histopathology findings.

People usually have a combination of treatments. The main treatments for early and locally advanced breast cancer include:

- surgery
- chemotherapy
- radiotherapy
- hormonal therapy
- targeted cancer drugs and immunotherapy
- bone strengthening drugs (bisphosphonates)

Treatments for advanced breast cancer may focus on managing symptoms and slowing down the spread of cancer.

Unmet need

Breast cancer is the most common cancer in women in the UK. Early and accurate diagnosis leads to better patient outcomes. Waiting for a diagnosis can cause anxiety and frustration. NHS Faster Diagnosis Standards recognise the need to reduce unwarranted variation between services in the time taken to reach diagnosis. The standards aim to give people a confirmed diagnosis or have cancer ruled out within 28 days of referral for investigation.

When breast cancer is detected, IHC and sometimes ISH/FISH analyses need to be done. These are expensive tests that can cause delays in histopathology reporting. In current laboratory workflows, these tests are not done until cancer is confirmed by a histopathologist, so the results must be interpreted by in a second or third sitting,

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before the histopathology report is complete. Interpretation of some histopathology analyses may sometimes need a second opinion from another histopathologist for quality assurance. Differences in current infrastructure to support digital sharing of slide images, and the degree of expertise and subspecialisation of professionals working in NHS pathology centres, may contribute to variation between centres.

A Royal College of Pathologists 2025 workforce census found that 47% of pathologists are aged 50 and over and 60% of consultant pathologists in the UK are typically working beyond their contracted hours each week. Most pathologists do not believe current staffing levels are adequate to ensure long-term stability of pathology services and to meet growing demand. In response to workforce shortages, the Royal College of Pathologists 2025 to 2028 workforce strategy aims to transform current models of working for pathology. This includes developing best practice recommendations on automation, digital and AI to improve the efficacy and efficiency of workflows.

The Royal College of Pathologists position statement on the use of digital pathology and AI states that there is an increasing body of research and interest in use of AI for assisting pathologists in diagnosis, and potential to transform working models which could improve healthcare. The statement highlights the potential for AI to free highly trained pathologists from more routine and repetitive work, and to improve accuracy and consistency in pathology diagnosis.

A GIRFT 2025 summary of diagnostics findings and recommendations supported innovation in AI for pathology. This aligns with the broader NHS long term plan (2025) commitment to introducing AI to increase efficiency in NHS services, including those committed to faster diagnosis of disease. Accurate, efficient and timely results from histopathology for diagnosis of breast cancer is central to achieving the Faster Diagnosis Standard 28-day target, whilst meeting quality standards in the face of increasing demand and workforce shortages.

The technologies

Technologies that use AI for histopathology analyse digitised images of tissue samples, called whole slide images (WSI). AI technologies that assist diagnosis of breast cancer can automate a range of analyses that are usually done by one or more histopathologists.

This assessment will focus on analyses done for the initial diagnosis of breast cancer. Initial diagnosis is the point at which the highest volume of histopathology analyses is done in the pathway, so it is where the technologies could demonstrate the most impact on the unmet need.

Technologies for initial histopathological diagnosis of breast cancer may do one or more of the following analyses:

- detection and classification of regions of tumour and calcification

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- grading or subtasks needed for grading, including mitotic count
- biomarker status for ER, PR and HER2.

This assessment will focus on AI technologies that do a minimum of tumour detection. Clinical experts indicated that most benefit would be gained from technologies that can do tumour detection because when cancer is found, additional IHC testing must be done. If IHC tests can be ordered so that all results are available for histopathologist review in 1 sitting, this could reduce overall case review time by days.

Additional effects of included technologies that do analyses to determine HER2 status will also be assessed. Clinical experts indicated that additional benefit could come from technologies that do biomarker analysis to report HER2 status. Identifying low and ultra-low HER2 status is technically challenging, and if a histopathologist reports equivocal HER2 status (2+), ISH/FISH testing must be done. These tests can add up to 7 days to the histopathology reporting timeline. Additional MDT discussion is sometimes needed if ISH/FISH tests are not done in time. Some algorithms do HER2 status analysis with IHC-stained slides and some do this directly from H&E-stained slides, which could deliver additional time and cost savings.

All technologies included for assessment 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.

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:

- analysis of other biomarkers
- analysis of lymph node biopsies
- analysis of excisions and resections
- risk stratification and prediction of response to treatment
- streamlining of laboratory workflow
- quality assurance in slide preparation.

Technologies that only do one or more of these analyses will be excluded from this assessment. 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. Technologies that are not specifically designed and indicated for use in breast cancer diagnosis will be excluded from this assessment.

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Appendix B

Digital pathology is a pre-requisite for AI technologies used to assist histopathological diagnosis of breast cancer. This will be considered the standard of care, so the technologies used for digital pathology alone will not be explicitly examined during this assessment.

Key functions of technologies included in this assessment are summarised in Table 1.

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Appendix B

Table 1. Technologies included in the assessment

Technology name (Company)	Deployment options	Stain and sample type	Tumour detection and typing	Grading	Biomarker analysis	Other functions	Regulatory approval	NHS use
Aiforia Breast Cancer Suite (Aiforia Technologies Plc)	Cloud-based or on-site	Core needle biopsies and surgical resections H&E (grading module) IHC (biomarker analysis modules)	Grading module: identifies invasive carcinoma and DCIS	Grading module: Nottingham Grading with component level findings	ER, PR and HER2 modules	Triage urgent cases Operators can customise automated reports of analysis outputs	Grading: CE-IVD (IVDR Class C) ER: CE-IVDD (CE-IVDR Class C approval will be sought before guidance publication) PR: CE-IVDD (CE-IVDR Class C approval will be sought before guidance publication) HER2: CE-IVD (IVDR Class C)	Yes

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Technology name (Company)	Deployment options	Stain and sample type	Tumour detection and typing	Grading	Biomarker analysis	Other functions	Regulatory approval	NHS use
AIRABreast (AIRA Matrix Private Limited)	Cloud-based or on-site	Core needle biopsies, lumpectomies, and mastectomy specimens H&E (tumour region detection algorithms) IHC (biomarker algorithms)	Identifies tumour regions and quantifies tumour burden	Not supported	Percent positivity and intensity scoring for ER and PR HER2 classification Heterogeneous staining patterns are highlighted	Automated report generation	CE-IVDR approval is planned before guidance publication	No
Ibex Breast, Ibex Breast IHC (Ibex Medical Analytics)	Cloud-based	Core needle biopsy, VAB and excision samples H&E and hematoxylin-eosin-saffron (HES) (Ibex Breast), IHC	Ibex Breast: categorises slides as benign or suspicious for cancer; predicts biopsy or excision-level	Ibex Breast: grades in situ cancer.	Ibex Breast IHC: scores ER, PR, HER2 stained slides.	Ibex Breast: can prioritise urgent cases based on detection of tumour and trigger ordering of	The Ibex Platform has CE-IVDR approval which covers Ibex Breast and HER2 diagnostic testing.	Yes

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Technology name (Company)	Deployment options	Stain and sample type	Tumour detection and typing	Grading	Biomarker analysis	Other functions	Regulatory approval	NHS use
		(Ibex Breast IHC)	cancer classification. Detects invasive and in-situ tumours and pre-cancerous and suspicious lesions. Subtypes invasive cancer.			other diagnostic and IHC tests. Slide and case-level reporting is available.	Ibex IHC modules are not currently regulated for use in the UK.	
Mindpeak Breast Suite (Mindpeak GmbH)	Cloud-based or on-site	Core needle biopsies or resections H&E (H&E module), IHC (biomarker modules)	H&E module: detects invasive carcinoma and in situ lesions without pathologist identification of RoI	Not supported	ER/PR module: detection, classification and counting of stained or not stained tumour cells. The pathologist does not need to identify a RoI.	Not applicable	H&E: Research use only. ER/PR: CE-IVD HER2 RoI: CE-IVD	No

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Technology name (Company)	Deployment options	Stain and sample type	Tumour detection and typing	Grading	Biomarker analysis	Other functions	Regulatory approval	NHS use
					HER2 RoI: HER2 score is based on staining within the RoI. HER2: HER2 score calculated automatically from the WSI. The pathologist does not need to identify a RoI.		HER2: Research use only.	
OptraSCAN Breast carcinoma analysis (OptraSCAN Inc.)	Unclear	Unclear what tissue samples are supported Unclear what stains	Detects and quantifies invasive carcinoma and DCIS	Not supported	An embedded biomarker analysis module gives ER, PR and HER2 scores	Automatic report generation	Regulatory status is unclear	Unknown
Cleo Breast (Primaa)	Unclear	Biopsy and excision H&E (all modules)	Detects and measures in situ and invasive carcinoma,	Mitosis hotspots are highlighted and counted	Not currently supported	Prioritises slides	CE-marked according to website	Unknown

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Technology name (Company)	Deployment options	Stain and sample type	Tumour detection and typing	Grading	Biomarker analysis	Other functions	Regulatory approval	NHS use
			and calcifications					
Paige Breast Suite (Tempus-Paige)	Cloud-based or on-site	Biopsies and excisions H&E (all modules)	Paige Breast Detect: identifies and classifies foci suspicious for cancer	Paige Breast Mitosis: detects mitotic figures and quantifies mitotic activity	HER2Complete: measures expression directly from H&E samples	Different slide overlays available for Paige Breast Detect Embedded in the information system to streamline reporting	CE-IVD marked	Unknown
Breast cancer AI algorithms (Virasoft)	Cloud-based or on-site	Unclear what tissue samples are supported H&E (detection and grading modules), IHC (biomarker modules)	Invasive region detection module highlights regions of invasive tumour, used as a precursor to	Developed for Nottingham grading including: Nuclei detection module, Mitosis detection	ER nuclear analysis module PR nuclear analysis module HER2 membrane analysis	Case triage may be available	ER, PR, HER2 modules are CE-IVD marked according to the website. Regulatory status of other	Unknown

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Technology name (Company)	Deployment options	Stain and sample type	Tumour detection and typing	Grading	Biomarker analysis	Other functions	Regulatory approval	NHS use
			grading modules	module, Tubule detection module, Nuclear pleomorphism module	FISH analysis		modules is unclear.	

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Place of the technology in the pathway

Histopathological analysis happens at more than one point in the breast cancer pathway. Histopathology is done on different types of sample, like biopsies, excisions and resections, from different tissues, including the breast and lymph nodes. Multiple histopathology analyses may be done at each stage and on each tissue type.

This assessment will evaluate the impact of included technologies for analysis on biopsies of breast tissue, done for initial diagnosis. If surgery is done, additional histopathology on resected or excised tissues from the breast and lymph nodes will be done to understand more about the size, type, stage and grade of cancer. This information informs adjuvant treatment strategies and prognosis but is not necessary for initial diagnosis. Costs and effects of technologies on post-surgical histopathology will not be evaluated in this assessment.

Centres may use AI in different ways depending on analysis type and individual laboratory practices (for example, as triage, first or second read). The assessment will consider these alternatives where appropriate.

Intervention(s)	AI technologies that assist histopathological detection of breast cancer in WSI of core or vacuum assisted biopsies for initial diagnosis, including: • Aiforia Breast Cancer Suite (Aiforia Technologies Plc) • AIRABreast (AIRA Matrix Private Limited) • Ibex Breast, Ibex Breast IHC (Ibex Medical Analytics) • Mindpeak Breast Suite (Mindpeak GmbH) • OptraSCAN Breast carcinoma analysis (OptraSCAN Inc.) • Cleo Breast (Primaa) • Paige Breast Suite (Tempus (Paige)) • Breast cancer AI algorithms (Virasoft)
Population(s)	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. Adults who have previously been treated for breast cancer and did not have any tumour present when discharged from that episode are included.
Subgroups	No subgroups were identified.

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Comparators	Histopathologist review of WSI of breast core needle or vacuum assisted biopsies for initial diagnosis of breast cancer, without AI assistance.
Outcomes	The outcome measures to be considered include: **Intermediate outcomes** • diagnostic accuracy (sensitivity, specificity, positive predictive value and negative predictive value) • case review time (slide review time, time to produce report for MDT, time to MDT diagnosis) • concordance between AI and pathologist review • need for or use of additional tests (repeat biopsies, repeat IHC, genetic testing) • need for second pathologist read • proportion of slides not appropriate for AI review • adverse events or technical failure **Clinical outcomes** • impact on clinical decision-making including staging and treatment selection • time to initiate treatment • stage of cancer at detection • overall survival • progression free survival • adverse effects including under or overtreatment **Patient reported outcomes** • health-related quality of life • service user and carer acceptability, views, experience and satisfaction **Other** • clinical user acceptability **Resource use** • cost of technology • cost of training • cost of data storage • costs of additional tests (for example, for IHCs) • cost of second reads

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	• cost of managing cancer, related to missed cancers or overdiagnosis
Setting	NHS histopathology services that use digital pathology for breast cancer diagnosis, outside of the NHS BSP, with interpretation in MDTs.
Economic analysis	The NICE reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The NICE reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
Other considerations	Guidance will only be issued in accordance with the CE or UKCA marking. **Digital infrastructure** Infrastructure for digital pathology is a pre-requisite of AI for histopathology. Current digital pathology usage is not widespread in the NHS. NHS IT compatibility and capacity issues may be a barrier to the implementation of AI software in some NHS Trusts. Some technologies have minimum requirements for image quality and magnification to run the analysis. Some technologies can only integrate with certain digital pathology hardware and software. Some technologies can integrate with existing laboratory information management systems that are in NHS use. Data security is essential when deploying AI technologies for histopathology as they require access to patient data. There may be challenges around confidentiality, integrity, and governance. Issues relating to data ownership and custodianship, risks of re-identification of depersonalised data, unauthorised access and system vulnerabilities, and consent and data sharing should be considered. The location of data storage and processing (e.g., on-site or cloud-based), and the security measures employed are key to these concerns. **Training** Workforce training is required for the safe and optimal use of AI technologies in this pathway. Most technologies report that they provide training delivery packages alongside user guides, and support services which should be used in

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	conjunction with local competency sign offs. **Sustainability** AI assisted workflows claim to increase efficiency and reduce waste associated with laboratory processes. **AI acceptability** Work by the Academy of Medical Sciences suggests that patients strongly support the use of AI in healthcare provided it improves quality and frees up time. The Royal College of Pathologists advise there is a need for more engagement with patients about the potential use of AI in their healthcare in order to maintain broad public support (Royal College of Pathologists, 2024). From a user perspective, optimal integration with existing workflows is key to successful deployment of AI in laboratories. **Other** Clinical pathways for breast cancer diagnosis vary across the devolved nations. Recommendations for diagnoses made within the NHS BSP are within the remit of the National Screening Committee (NSC). NICE does not make recommendations for people within NSC programmes.
Equality considerations	People with cancer are protected under the Equality Act 2010 from the point of diagnosis. **Detection rates and outcomes** Deprivation: cancer death rates are nearly 60% higher for those living in the most deprived areas of the UK compared with the least deprived. People in less deprived areas have earlier detection due to higher screening rates. Although breast cancer incidence rates are lower among people living in the most deprived areas, they are more likely to be diagnosed with late-stage breast cancer. Geography: outcomes in the north of England are worse than the south. People living in rural areas face greater travel burdens for treatment. There are also variations in service availability across the country. Ethnicity: women with a black and South Asian background are more likely to be diagnosed at an advanced stage. Age: most breast cancer is diagnosed in people over 50. Although people over 70 can self-refer for screening, they are not automatically invited. They are more likely to present with advanced stage breast cancer than younger age groups. Sex: men with breast cancer often present later and with more advanced disease. Gender: Some trans people may be at increased risk due to hormone treatment. Eligible trans and non-binary people

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	may miss out on screening because the system only invites those who are registered as female with their GPs. Disabilities: Many people with disabilities experience delayed diagnosis, present with advanced-stage breast cancers and have poorer outcomes. People with disabilities may have barriers in communication, support and access to breast screening services and treatment. Inclusion health groups: many inclusion health groups are at higher risk of breast cancer because they may have challenges in registering with a GP and may not receive invitations for breast cancer screening. Breast screening services lack a system for identifying eligible people from these groups. More detail is available in the NICE Inequalities briefing for Breast Cancer (2024). This was done for the 2025 update for NICE Guideline Early and locally advanced breast cancer: diagnosis and management. **Technology features** If AI technologies can improve workflow, they could help to reduce variability linked to local workforce constraints. Smaller district NHS histopathology services tend to be most affected by workforce constraints. AI technologies could help to standardise assessment and reduce inter-rater variability in diagnosis caused by subjectivity. This could help deliver more equitable diagnostic quality across regions. This is particularly important for people with borderline hormone and HER2 status, because accurate detection and quantification is needed to optimise treatment planning. **Technology validity for the assessment population** The validity of AI algorithms depends on the data on which they are trained. Cases with significant artefacts may reduce performance and interpretation of technologies. The quality of reporting for AI assisted biopsies should be audited as part of laboratory practice (Royal College of Pathologists, 2024). When available, information will be reported on the representativeness of training and validation datasets for 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. Information about the representativeness of sex, ethnicity and rare tumour morphologies in training and validation datasets will be sought. When groups are not represented, the assessment will consider the potential to exacerbate or introduce new health inequalities.

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	Some technologies are not indicated for use in men, some cancer subtypes, or after treatment. **Groups with high inter-rater variability** The technologies may have additional benefits for some groups that often have high inter-rater variability. Evidence for the following groups will be considered when available: • People with low ER or PR positivity • People with borderline HER2 (2+) status
Related NICE recommendations	**Related HealthTech guidance:** Tumour profiling tests to guide adjuvant chemotherapy decisions in early breast cancer (2024) NICE HealthTech guidance 719 **Related technology appraisals:** There are 44 published Technology Appraisals on breast cancer and 23 in development Technology Appraisals on breast cancer. Many of these are indicated for breast cancers with specific biomarker status, so may rely on the contribution of outputs from technologies included in this assessment. **Related NICE guidelines:** Early and locally advanced breast cancer: diagnosis and management (2018) NICE guideline 101 Last updated: 14 April 2025 Suspected cancer: recognition and referral (2015) NICE guideline 12 Last updated: 12 January 2026 Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer (2013) NICE guideline CG164. Last updated 14 November 2023 Advanced breast cancer: diagnosis and treatment (2009) NICE guideline 81 Last updated: 19 February 2025 **Related NICE guidelines in development:** Suspected Cancer: recognition and referral (update). NICE guideline. Publication expected March 2026

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	Advanced breast cancer: diagnosis and management (Partial update). NICE guideline. Publication expected 29 May 2026 Familial Breast Cancer: initial assessment and genetic testing (update). NICE guideline. Publication expected April 2027 **Related quality standards:** Suspected cancer (2016) Quality standard 124 Last updated: 05 December 2017 Breast cancer (2011) Quality standard 12 Last updated: 16 June 2016 **Related clinical knowledge summaries:** Breast cancer - recognition and referral (2025) NICE clinical knowledge summary Breast cancer - managing FH (2024) NICE clinical knowledge summary Breast screening (2022) NICE clinical knowledge summary

Questions for consultation

1. Is the proposed title for this assessment appropriate?
2. Is the proposed population described appropriately?
    - Is it appropriate to include people who have previously been treated for breast cancer?
    - Is it appropriate to restrict the population to adults?
    - Are there any other subgroups for whom you would expect the clinical and cost effectiveness of the intervention to differ?
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?
    - Are there any technologies you feel should be added to the scope? If so, why?
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)?
5. Is the comparator appropriate?
6. Are all the outcomes and costs suitable for inclusion in the assessment? Are there any additional outcomes or costs we should consider?
7. What level of evidence is there for the use of these technologies for initial diagnosis of breast cancer?
8. Which of these technologies are currently in use in the NHS?
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.

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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.
11. Are there any other stakeholders NICE should be aware of for this topic?

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Glossary of terms

Biopsy
A sample of tissue from the body to assist in diagnosis of disease.

Calcification
Small spots of calcium in the breast that do not cause symptoms. Macrocalcifications are benign and not linked to cancer. Microcalcifications can be a sign of pre-cancerous changes or early breast cancer, if found in a cluster.

Core biopsy reporting categories
Biopsies are rated B1 (normal) to B5 (malignant) in the Royal College of Pathologists reporting proformas. B2 indicates a benign lesion, B3 indicates an atypia with uncertain malignant potential and B4 indicates a lesion suspicious for malignancy.

Digital pathology
Digital pathology includes the acquisition, management, sharing and interpretation of pathology information, including whole slide images (WSI), in a digital environment. WSI are captured with a scanning device. The device produces a high-resolution image that can be viewed on a computer screen or mobile device.

Ductal carcinoma in situ (DCIS)
DCIS is an early breast cancer. It is diagnosed when some cells in the lining of the ducts of the breast tissue have started to turn into cancer cells. The cancer cells are contained inside the ducts and have not spread.

Fluorescence in situ hybridisation (FISH)
If HER2 status is inconclusive from IHC staining and analysis, in situ hybridisation (ISH) or fluorescence in situ hybridisation (FISH) may be done to determine HER2 status. ISH is a technique that detects and counts extra copies of the HER2 gene in cancer cells. FISH is a type of ISH technique in which a fluorescent probe is attached to the DNA.

Histological grade
Histological grade is reported when carcinoma is identified. DCIS is graded as high, intermediate or low based on how abnormal the cells look. Invasive carcinoma is graded using the Elston and Ellis method, also known as Nottingham Grading. A score between 3 and 9 is reached by considering the percentage of the tumour that forms tubular gland (scored 1 to 3), how much the cancer cell nuclei differ from normal cells (scored 1 to 3), and mitotic count which is the frequency of dividing cells in the most active part of the tumour (scored 1 to 3). Total scores of 3 to 5 points indicates grade 1 tumour (low grade), 6 to 7 points indicates grade 2 tumour (intermediate grade) and 8 or 9 is grade 3 (high grade).

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Haematoxylin and eosin (H&E) and haematoxylin, eosin and saffron (HES) staining
H&E is a routine histological stain used to show the structure and morphology of cells and tissues. It helps pathologists assess how normal or abnormal a tissue looks. Haematoxylin stains cell nuclei, eosin stains cytoplasm and extracellular matrix. Sometimes, HES is used. The addition of saffron staining can distinguish connective tissue from muscle.

Histopathology
The microscopic examination of biological tissues to study, diagnose, and understand the manifestations of disease

Human epidermal growth factor 2 (HER2)
Some breast cancers have large amounts of a protein called HER2. Testing breast cancer cells for the HER2 protein can help to show whether targeted drugs might work. Targeted cancer drugs are treatments that change the way cells work and help the body control the growth of cancer. The drugs attach to the HER2 protein and stop the cells from growing and dividing. Breast cancers that have large amounts of HER2 are called HER2 positive breast cancers.

Immunohistochemistry (IHC) testing
IHC is the recommended method for assessing receptor status in breast cancer. It uses antibodies that bind to specific proteins (ER, PR and HER2) in tumour tissue. The antibodies stain the tissue and show if and how much of the receptor is present.

Inclusion health groups
Inclusion health is an umbrella term used to describe people who are socially excluded, who typically experience multiple overlapping risk factors for poor health, such as poverty, violence and complex trauma. This includes people who experience homelessness, drug and alcohol dependence, vulnerable migrants, Gypsy, Roma and Traveller communities, sex workers, people in contact with the justice system and victims of modern slavery. People in inclusion groups tend to have very poor health outcomes compared with the general population, and a lower average age of death. This contributes considerably to increasing health inequalities. The way healthcare services are delivered may result in poor access to health and care services and negative experiences. More detail is on the NHS England website.

Mitotic count
Mitotic count is the frequency of dividing cells in the most active part of the tumour. Higher mitotic count indicates a faster growing and more aggressive type of cancer. This information is used to grade the tumour.

NHS Breast Screening Programme
The NHS BSP invites all women aged between 50 and 70 for breast screening mammography every 3 years. Women aged over 70 can self-refer to this service. The NHS BSP also outlines eligibility criteria and screening protocols for women at

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very high risk for breast cancer. If mammography or ultrasound screening identifies suspicious lesions, further tests that may include a biopsy will be done at an assessment clinic.

Oestrogen receptor (ER) status

Most breast cancers have receptors for the hormone oestrogen (ER). They are called ER positive breast cancer. Breast cancers that have less than 1% ER are called ER negative breast cancers. This is determined at initial diagnosis because hormone therapy is only likely to work for cancers that are ER-positive. Hormone therapies work by stopping oestrogen from stimulating the cancer cells to grow and divide.

Progesterone receptor (PR) status

Progesterone receptor (PR) status indicates if breast cancer cells contain receptors for the hormone progesterone. Unlike ER, PR is not a predictive factor for response to adjuvant hormone therapy but it does give prognostic information for people with ER-positive tumours. It may also act as a quality control marker because ER-negative, PR-positive tumours are very rare. If tests show this combination of hormone receptors the quality of ER-stained sections should be reviewed.

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