**Title:** The potential utility of abbreviated breast MRI (FAST MRI) as a tool for breast cancer screening: a systematic review and meta-analysis

**Running title:** FAST MRI: a systematic review and meta-analysis

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**Aim:** To synthesise evidence comparing abbreviated breast MRI (abMRI) to full-protocol MRI (fpMRI) in breast cancer screening.

**Materials and methods:** A systematic search was undertaken in multiple databases. Cohort studies without enrichment, presenting accuracy data of abMRI in screening, for any level of risk (population, moderate, high risk) were included. Level of evidence was assessed using The Grading of Recommendations Assessment, Development and Evaluation (GRADE). Meta-analyses (bivariate random effects model) were performed:

- for abMRI, with fpMRI and histology from fpMRI positive cases as reference standard, and
- with follow up to symptomatic detection added to the fpMRI.

The review also covers evidence comparing abMRI with mammographic modalities.

**Results:** Title and abstract review retrieved 23 articles. Five studies (6 articles) were included (2,763 women, 3,251 screening rounds). GRADE assessment of the evidence was very low because the reference standard was interpreted with knowledge of the index test and biopsy was not obtained for all abMRI positives. The overall sensitivity for abMRI, with fpMRI (and histology for fpMRI positives) as reference standard, was 94.8% (95% CI 85.5-98.2) and specificity as 94.6% (95% CI 91.5-96.6). Three studies (1,450 women, 1,613 screening rounds) presented follow up data, enabling comparison between abMRI and fpMRI. Sensitivities for abMRI did not significantly differ from those for fpMRI (p=0.83) nor did specificities (p=0.37).

**Conclusion:** A very low level of evidence suggests abMRI could be accurate for breast cancer screening. Research is required, with follow up to interval cancer, to determine the effect its use could have on clinical outcome.

# Introduction

Magnetic resonance imaging (MRI) is the most sensitive imaging modality for the detection of breast cancer[1,2], and can find small cancers of 5mm and smaller[3–5]. As a screening tool for breast cancer in the very high risk population (>30% lifetime risk) it increases both early cancer detection and metastases-free survival[6] and is the standard of care for these women in the UK and internationally. Nevertheless, breast MRI is a high cost investigation, secondary to its long scan acquisition time and the time taken for image interpretation. This limits its cost effectiveness for use as a screening tool in other populations of women with lower breast cancer prevalence, despite evidence that it could provide for them increased early cancer detection and reduced interval cancer rate[7,8]. In addition, the length of time spent inside the MRI scanner during a breast MRI examination has been shown to be a significant source of discomfort in over a third of women undergoing the investigation[9,10] and so a reduction in the scan time would potentially improve the screening clients' experience.

In 2014 Kuhl et al. introduced the concept of an abbreviated protocol for breast MRI (abMRI): First post contrast Acquisition SubTracted (FAST) protocol[11]. This proof of concept study investigated whether a single pre and post contrast acquisition with derived images (FAST) and maximum-intensity projection (MIP) was suitable as an alternative to the full protocol (fpMRI) for screening. Their published results were promising, with the MRI acquisition time reduced to just 3 minutes and an image interpretation time of <30 seconds whilst diagnostic accuracy was maintained, equivalent to the fpMRI. As a consequence of Kuhl's original research, several authors have published articles exploring the utilisation of an abMRI for detecting breast cancer[12–20], including several variations of the original FAST format in an attempt to increase specificity. These variations include adding T2 sequences

and diffusion weighted imaging and a number of reviews have been written about the technique[21–24].

Parallel to Kuhl's development of the FAST protocol abMRI for use in breast screening, Mann et al. suggested that an "ultrafast" abMRI protocol, originally described by Hermann et al. in 2011[25], utilising a time resolved magnetic resonance angiography technique (Time-resolved angiography With Stochastic Trajectories (TWIST)) that provided additional kinetic information, could be used for the same indication[26]. They concluded that calculating the maximum slope of the relative enhancement-versus-time curve obtained from the TWIST sequences allowed discrimination of benign and malignant breast lesions with high accuracy. This early study on Ultrafast MRI has been supported by subsequent studies confirming that a steep slope and a short time to enhancement both correlate with malignancy[27–31].

With the advent of personalised screening, women are likely to be stratified, according to their level of risk, to different screening regimes/imaging modalities with the potential to increase the number of women offered a screening modality more sensitive than mammography[32]. Published studies of abMRI techniques have used expert MRI readers for interpretation, and this has been a potential barrier to expansion of the technique for personalised screening with abMRI[24]. However, with a single day's standardised training[33] to interpret the simplest of the abMRI techniques (FAST MRI), an early study suggests that professionals who are already competent at reading mammograms can achieve similar levels of accuracy of interpretation of abMRI to that of expert breast MRI readers[34]. If these results should be validated in subsequent studies[35], limitation to expansion of the role of abMRI (FAST protocol) on the grounds of workforce feasibility will have been reduced.

Although individual studies of abMRI have suggested it might offer a diagnostic accuracy similar to fpMRI with acquisition and reporting times nearer to those of mammography, there

has been little direct comparison of abMRI with mammography reported in the literature. In order to decide whether abMRI could replace fpMRI for high risk population screening, we need to understand how it compares in diagnostic accuracy. There is also a potential role for abMRI to replace mammograms for moderate risk screening although for this to be cost effective its diagnostic accuracy would need to be demonstrably sufficiently greater than that of mammograms to justify its higher cost.

The primary objective of this systematic review was to assimilate published evidence to compare the diagnostic accuracy of breast cancer detection of abMRI (that includes the FAST protocol) with that of fpMRI in the screening setting.

The secondary objectives were:

- To compare the abMRI and fpMRI scanning acquisition and reporting times
- To compare the diagnostic accuracy of abMRI with that of any mammographic modality (standard digital mammography, digital breast tomosynthesis and contrast enhanced spectral mammography).
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## Materials and methods

The systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidance[36].

### Search strategy

A systematic literature search for relevant articles was performed in November 2019. The keywords utilised in the literature search and an example database search are included in

**Appendix 1**. The searches were performed using Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Embase, Medline. The search was limited to articles published in the English language after the year 2000. De-duplication was performed in Endnote and then title and abstract screening was performed manually by a single author to identify eligible articles. Full text screening was performed by 2 authors.

## Eligibility criteria:

Studies were included in the systematic review and meta-analysis if they fulfilled the following inclusion criteria:

1) Studies investigated the diagnostic accuracy of an abMRI that included the FAST sequence[11].
2) Studies included a comparison with an appropriate reference standard, either the fpMRI or appropriate follow up/histological analysis.
3) Studies were performed in the screening setting

Screening studies of women at high risk, moderate risk, population risk and at mixed risk of developing breast cancer were included. Cross-sectional and cohort studies, including retrospective cohort studies were included but case control studies and cohorts which were enriched with a greater proportion of cancer cases were excluded.

## Quality assessment

The quality appraisal tools used in this review were selected to be relevant to diagnostic test studies[37,38]. Two authors performed data extraction and quality assessment, initially this was performed by each author independently and any discrepancies were discussed, and a

consensus opinion was made in discussion with a third author. Judgements were made on the level of evidence provided using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for diagnostic tests and strategies[39–42] including the assessment of risk of bias, directness of evidence and of consistency and precision of results.

## Data extraction

Included studies were summarised to detail: number of women, study population, number of scans, format of abMRI, reference standard used, sensitivity, specificity, PPV and NPV for the abMRI and also for the fpMRI if there was sufficient follow up, time to read abMRI and fpMRI, scan acquisition time, sources of bias.

## Meta-analysis

A meta-analysis of accuracy of abMRI was performed for the similar studies. The reference standard was fpMRI results with histology for fpMRI positives. Forest plots of the sensitivities and specificities were constructed. To account for the dependency between the sensitivity and specificity, a bivariate random effect model[43] was fitted using the R package "mada" for performing meta-analyses of diagnostic accuracy[44] to obtain the pooled sensitivity and specificity estimates and associated 95% confidence intervals (95% CI). The bivariate random effect model was also used to assess any differences in the sensitivity and specificity between the studies with only high risk patients and those with population and moderate risk patients. Similar methodology was used to conduct a meta-analysis comparing abMRI with fpMRI for studies with additional follow-up.

## Results

The results of the literature search are illustrated as a PRISMA flowchart in **Figure 1**[45]. 7 articles (6 studies) met the selection criteria for inclusion in the review[11,46–51]; One study was reported in two articles[48,49]. **Table 1** summarises the participant demographic of the 7 articles. The average age of the participants included in the studies ranged from 44.3 years[51] to 54.2 years[11].

**Table 2** shows the quality assessment results for the 7 included articles. All 7 fulfilled the inclusion quality criteria for validity and applicability except that none of the studies validated the tool (abMRI) within the study. However, it could be considered that each study provided some validity for the others. **Table 3** demonstrates the MRI specifications of the abMRI scans used in the studies. The table shows variation in the protocols used by the different studies, including, for example, that results from both 1.5T and 3T scanners were included in three studies[47,50,51], 1.5T alone was used in one study[11] and 3T alone in one study (two articles)[48,49] and for one study the strength of magnet was not specified[46].

### Study population

The included studies varied in study population (**Table 1**). Three of the studies included solely women described as being at "high risk" of developing breast cancer[46,47,51]. These 3 studies described multiple reasons for inclusion of a participant in their study under the heading of high risk, including BRCA gene mutation, family history, personal past history of breast cancer and previous atypical histology on biopsy. However, in none of these studies was the percentage lifetime or ten-year risk defined. Both articles by Chen et al focused on

women who had dense breasts on mammography but were otherwise at population risk[48,49], although the mechanism for classification of density was not defined in either article. Choi et al. included women with a personal past history of breast cancer as their study population[50], and the study population in Kuhl's study was women of mixed risk, above population risk (mild, moderate and high) including women with family history, women with personal past history of breast cancer and those with no other risk factor than dense breasts[11].

## Study design

In one study[11] all data was acquired prospectively, while for the other 5 studies[46–51] images from consecutive screening examinations were identified retrospectively and then re-interpreted prospectively.

## Reading protocol

AbMRIs and fpMRIs were single reported by radiologists who were expert in breast MRI interpretation in 5 studies[11,46,47,50,51]. In contrast, in both articles by Chen et al.[48,49] both the abMRIs and fpMRIs were double reported, the reporting performed independently by two radiologists, both expert in breast MRI interpretation, with any discordant interpretations being arbitrated by an experienced third, arbitrating reader. All studies had a paired design, with each reader examining both abMRI and fpMRI for a series of women.

Chen's two articles[48,49] describe an attempt to reduce recall bias by reporting the abMRI and fpMRI in two separate sessions, at least one month apart, and randomising the order of the cases presented to readers at each session. Four studies[11,46,47,51] describe sequential reading of the two scans for each case with readers interpreting the abMRI first and then fpMRI

immediately afterwards. In one study only an abMRI, and no fpMRI was acquired[50] (reference standard = histology or follow up).

Four articles (3 studies) failed to state whether mammograms were available to readers during abMRI and fpMRI interpretation[46,48,49,51]. In 2 studies mammograms were available to readers reading both abMRI and fpMRI[47,50] and in one study they were not available to readers at all[11].

## Diagnostic accuracy

Six of 7 articles compared abMRI results with fpMRI (including histology of fpMRI positive cases) as reference standard. However, 3 of these 6 articles provided no follow up data[46,49,51], one provided single year follow up data for a subset of scans only[47] and two provided 2 years follow up data[11,48]. In addition, in all 6 articles, histology was performed for fpMRI positive scans but not for abMRI positive scans (unless there was concordance). A comparative accuracy assessment of abMRI with fpMRI was therefore not possible. Instead an analysis was performed of the accuracy of abMRI using fpMRI and histology of fpMRI positives as reference standard.

One study reported in 2 papers[48,49]. Therefore, a total of 3,251 breast MRI scans were performed in 5 studies[11,46,47,49,51], and detected a total of 58 cancers by fpMRI (43/58 invasive (73.6%))(cancer detection rate = 17.8/1000). All but one of the 58 cancers were detected by abMRI (57/58 = 98%). It was not specified whether the cancer missed by abMRI was invasive or not. The diagnostic accuracy data for the 5 studies are summarised in **Table 4**. The sensitivity for the abMRI in comparison with the fpMRI (and histology of fpMRI positives) is 100% for all but one study (Chen et al 93.8%)[49]. Specificity for the abMRI ranged from 88.3% to 97.0% of that achieved by the fpMRI.

Only one study[50] reported rates for abMRI of early call to abMRI at 6 months (76/799 (9.5%)), recall rate (19/799 (2.4%)) and biopsy rate 17/799 (2%) for a cancer detection rate by abMRI of 15/1000 women screened (12/799).

## Meta-analysis

Meta-analysis was performed of the accuracy of abMRI on the 5 similar studies which used fpMRI (and histology of fpMRI positives) as reference standard[11,46,47,49,51], interpretable as the abMRI's exact deficiencies versus fpMRI (**Figure 2**). The overall sensitivity was estimated as 94.8% (95% CI 85.5-98.2) and the specificity as 94.6% (95% CI 91.5-96.6) for the abMRI (**Figure 2**). The sensitivities did not significantly differ between the studies that involved high risk patients and those that did not (p=0.98) nor the specificities (p=0.58).

## Comparison of abMRI with full protocol (fpMRI)

Three studies had additional follow up (1 or 2 years) [11,47,48] that allowed the comparison of abMRI with fpMRI; only one of these studies identified any interval cancers [47]. Two interval cancers were missed by both the abMRI and fpMRI [47]. The data are summarised in **Table 5**. The overall sensitivity over these 3 studies was estimated as 92.1% (95% CI 68.6-98.4) and the specificity as 93.8% (95% CI 85.4-97.5) for the abMRI compared to an overall sensitivity of 91.4% (95% CI 68.1-98.1) and specificity of 96.0% (95% CI 93.4-97.7) for the fpMRI (**Figure 3**). The sensitivities for abMRI did not significantly differ from those for fpMRI (p=0.83) nor did the specificities (p=0.37).

## Judgements made on level of evidence for studies included in the meta-analysis

The GRADE approach[39–42] to quality assessment was applied to the 5 studies that used fpMRI, with histology for fpMRI positives, as reference standard. Assessment of different

aspects of the studies, including design, risk of bias, indirectness, inconsistency, imprecision and quality of evidence, yielded assessments of evidence quality ranging from High through Moderate and Low to Very Low (**Table 6**). The main sources of bias identified were that the index tests were not undertaken independently, that readers had knowledge of the index test when interpreting the reference standard and that only fpMRI positive cases were biopsied so that the reference standard differed by index test. In addition, there was lack of clarity in the definition of population studied and imprecision, seen as large confidence intervals demonstrated for sensitivity. The short or absent follow up of cases presented by studies further lowered the overall evidence quality. The confidence we can have in the comparative diagnostic accuracy results, and therefore our overall level of certainty that abMRI and fpMRI have a similar level of diagnostic accuracy, was assessed as very low.

## Time taken to acquire and read the scans

The times taken to acquire and to interpret the abMRI and fpMRI protocols are summarised in **Table 7**. For all 3 studies[11,46,47] that compared acquisition times of abMRI with fpMRI, the acquisition time for abMRI (range: 180-264 seconds) was consistently less than that for fpMRI (1024-1440). For all 3 studies[46,47,49] that compared interpretation times of abMRI with fpMRI, the average interpretation time for the abMRI (range: 42-144 seconds) was consistently less than that for fpMRI (192-396).

## Grade and stage of cancers detected

Four articles included information on grade of cancers detected[11,46–48] (Table 8a) and 4 articles included full or partial information on stage of cancers detected[11,47,48,50] (Table 8). In all studies the majority of cancers were invasive (48/68 (71%))(range within studies 58-86%). Across the studies that reported grade, only a small proportion of invasive cancers were

Grade 1 (4/34 (12%)), and two thirds of in situ cases detected were high grade DCIS (8/12 (67%)). Across the studies that reported stage or size, the majority of invasive cancers detected were small, measuring less than or equal to 1cm diameter (26/51 (51%)) and no invasive cancers measured greater than 2cm diameter.

### Comparison of abMRI with mammography

No articles were identified that directly compared abMRI with mammographic modalities (digital mammography, digital breast tomosynthesis and contrast enhanced spectral mammography). However, of the studies included in this systematic review, three studies[11,47,49] documented a recent normal screening mammogram as an inclusion criterion for their participants. Therefore, all cancers identified by abMRI in these three studies were not identified by mammography. The additional cancer yield (invasive and non-invasive disease) over mammography achieved by the abMRI in these three articles was stated as 18.15/1000 women screened[11], and 13.3/1000[47], and calculated from the study's published figures as 31.4/1000 (15/478)[49]. However, in none of these articles was the original cancer detection rate by mammography presented for comparison.

## Discussion

This systematic review has assimilated data from 6 studies, published as 7 articles, which compare the diagnostic accuracy, for breast cancer detection, of abMRI (protocols that include the FAST protocol) with acceptable reference standards, most commonly fpMRI, in a breast cancer screening setting. The original intention of the review had been to present the comparative accuracy of abMRI versus fpMRI, but to meet that need the ideal study would

refer for histology if either test recommended it and then follow up for a number of years. No studies with this ideal design were found, and therefore the results of our meta-analysis are interpretable as abMRI's exact deficiencies versus fpMRI and include 5 published studies.

The GRADE approach determined that the overall quality of the current evidence available about whether abMRI and fpMRI have a similar diagnostic accuracy is very low. Four studies were published with incomplete or no follow up data[46–49,51], one study published one year's follow up data[50] and one study published two years' follow up[11]. Without sufficient follow up data, levels of absolute sensitivity for both abMRI and fpMRI are likely to be overestimated. For the smaller numbers of cases that had follow up data reported (within 3 studies that compared abMRI with fpMRI[11,47,48]) the risk of bias, inconsistency, imprecision, study design and flow is otherwise unchanged and the overall assessment of the quality of evidence remains very low.

Although, in all 7 articles abMRI interpretation was appropriately blinded to the reference standard, during 4 studies[11,46,47,51], interpretation of the fpMRI (reference standard) was performed directly after interpretation of abMRI by the same reader. This study design includes a risk of bias, since the results of the fpMRI may have been influenced by knowledge of the abMRI and this could have unpredictable confounding effects. In addition to there being a mixture of study populations, the included studies either mixed or failed to specify prevalent or incident screening rounds. Together these factors resulted in a heterogenous pre-test probability both within and between studies. The small numbers of participants and the very small numbers of cancers detected during each study led to wide confidence intervals, particularly in the assessment of sensitivity, that have contributed to imprecision. These factors together necessitated the downgrading of the overall quality of evidence to very low by GRADE criteria.

Measured times to acquire and to interpret the two protocols were reported by 3 studies[11,46,47] and by 3 studies[46–49], respectively, and consistently demonstrated shorter times required for both acquisition and interpretation of abMRI than fpMRI. The large magnitude of reduction in time required to acquire and to report abMRI in comparison with fpMRI makes it more likely that these findings are real.

Although no articles were identified that directly compared abMRI, that include the FAST protocol, with mammographic modalities, indirect evidence from 3 studies suggested that abMRI is likely to perform better at diagnostic accuracy than mammograms[11,47–49]. Of note, one of these studies[48,49] included only women assessed as having dense breasts on mammography for whom we know the sensitivity for cancer detection by mammography is reduced[52]. The large magnitude of the apparently superior sensitivity for breast cancer of abMRI over mammography (additional cancer yield of 13.3/1000 - 31.4/1000) in these 3 studies increases the likelihood that the finding is real and suggests that abMRI is likely to perform better at diagnostic accuracy of breast cancer detection than mammography in a screening setting. However, none of these studies investigated the effect on clinical outcomes of changing screening modality from mammograms to abMRI, and this review has identified this gap in our current knowledge.

This systematic review was performed as a comprehensive database search to minimise publication bias and includes articles with a wide geographical distribution. A weakness of the review is that we took our data from published articles and did not attempt to contact the authors of articles to determine, for example, whether there was any overlap of data between articles. However, since our assessment of the level of current evidence is very low, it is unlikely that this assessment would have been altered if we had discovered further data overlap between any of our included studies.

Since this systematic review was performed, in November 2019, the results of a study comparing invasive cancer detection by abMRI directly with digital breast tomosynthesis in women with dense breasts have been published[53]. This prospective study, of 1444 comparison scans (abMRI and digital breast tomosynthesis) with randomised order of scan performance, included the FAST protocol in the abMRI studied and demonstrated a significantly higher rate of invasive breast cancer detection for abMRI (11.8/1000 abMRI and 4.8/1000 digital breast tomosynthesis, p = 0.002). These results are broadly in agreement with and provide some validity for the results of the current systematic review.

Further studies to validate the diagnostic accuracy comparisons suggested by the existing evidence. However, prior to any policy decisions being made about a potential change of screening modality to abMRI (either from fpMRI or from mammograms) the effect on clinical outcomes, cost effectiveness, acceptability and feasibility of any change will need to be determined within existing screening programmes. Only one study reported recall rates and biopsy rates for abMRI[50] and this leaves a crucial knowledge gap relating to workforce issues, feasibility and cost. Further research is needed to determine whether replacing either fpMRI or mammography with abMRI in a screening setting could improve clinical outcomes (such as achieving a reduction in interval cancer rates) for some women, and to determine which population of women it could benefit.

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## Key words

**Breast cancer, Screening, Breast MRI, Abbreviated MRI, FAST MRI**

## Figure legends

Figure 1: PRISMA flow chart illustrating the results of the literature search

Figure 2: Forest plot for sensitivity and specificity for abMRI (for each study that used fpMRI and histology of fpMRI positives as reference standard)

Figure 3: Forest plot for sensitivity and specificity for each study with follow-up for abMRI (A) and fpMRI (B)

## Table legends and footnotes

Table 1: Demographics and inclusion and exclusion criteria of 7 included full-text articles

Footnotes: *mean, **median, #any additional risk over population risk including dense breasts (23.7%)(defined as classified as 3 or 4 by 4th edition BIRADs criteria), and/or personal history (49.6%)

and/or family history (26.6%), ##level of risk not specified in article, ◊level of density not specified in article

## Table 2: Quality assessment for the 7 included full-text articles

Footnotes: *for FP positive cases, **for FP negative cases, #for AP positive cases, ##for AP negative cases

[1] reference standard read immediately following index test (readers were not blinded to index test when reading reference standard)

[2] reference standard read at least 1 month after index test and the order of the cases presented to the reader was randomised to minimise recall bias

[3] different reference standard applied to index tests that were concordant with reference standard to those that were discordant (because abMRI positives that were discordant with fpMRI were not biopsied)

## Table 3: Specifications of abbreviated protocols (AP) and of images available for AP interpretation

Footnotes: *Time from commencement of contrast injection to acquisition of first post contrast dynamic scan

519 Table 4: Diagnostic accuracy of abbreviated breast MRI (abMRI) with full protocol
520 (fpMRI) and histology of fpMRI positives as reference standard

521

522 Table 5: Diagnostic accuracy of abbreviated breast MRI (abMRI) with full protocol
523 (fpMRI) for studies with follow-up data

524

525 Table 6: GRADE quality assessment of the level of evidence provided about diagnostic
526 accuracy of abbreviated breast MRI (abMRI) versus full protocol (fpMRI), with
527 reference standard biopsy in test positives on either test and follow up to
528 symptomatic cancer detection

529 Footnotes: A full quality assessment would include a row for each of the patient-important outcomes
530 associated with each possible test result (TP, TN, FP, FN and inconclusive results) as well as test
531 complications and costs. We have presented a simplified summary of the quality and judgement on level
532 of evidence for the critical outcomes here.

533 [a] Judgement on level of evidence provided (High, Moderate, Low or Very Low) was defined along GRADE
534 guidelines specifically for Diagnostic Test Accuracy studies and does not imply the level of evidence
535 required to influence a change in practice, since diagnostic accuracy outcomes are only a surrogate for
536 patient outcomes

537 [1]Relatively short term (1-2 years) or no follow up data was included in the studies enabling only
538 comparison of abMRI deficiencies versus fpMRI with histology of fpMRI positives

539 [2]The terms high risk and dense breasts were not clearly defined (see Table 2)

Table 7: Time taken to acquire and to interpret abbreviated breast MRI (abMRI) and full protocol (fpMRI)

Table 8: Details of cancers found by abMRI

Table 8(a): Details of grade of cancer found by abMRI

Table 8(b): Details of stage of cancer found by abMRI

# Appendix legends

Appendix 1: An example of literature search conducted, with details

Figure 1



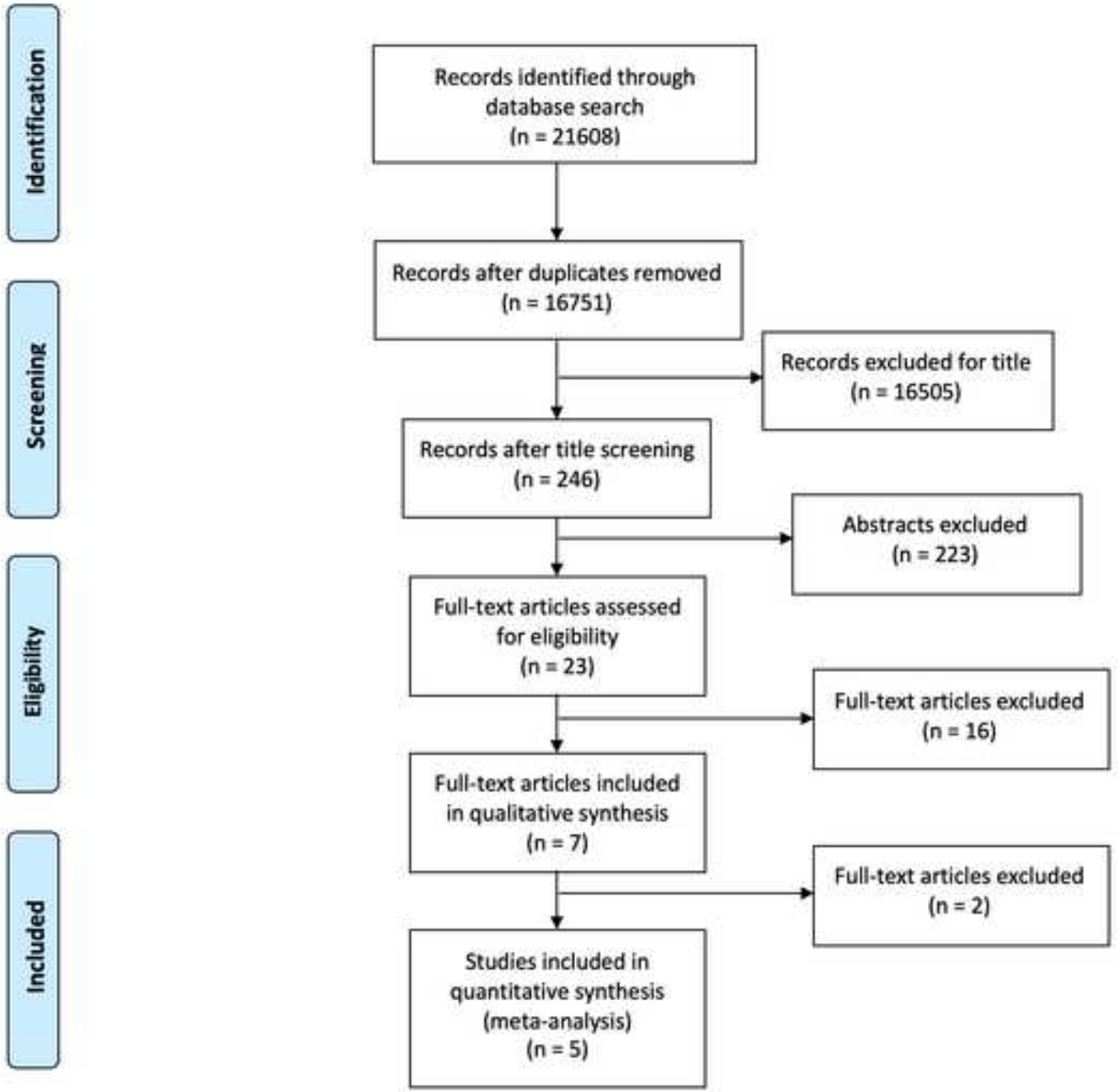


Figure 2: Forest plot for sensitivity and specificity for abMRI (for each study that used fpMRI and histology of fpMRI positives as reference standard)

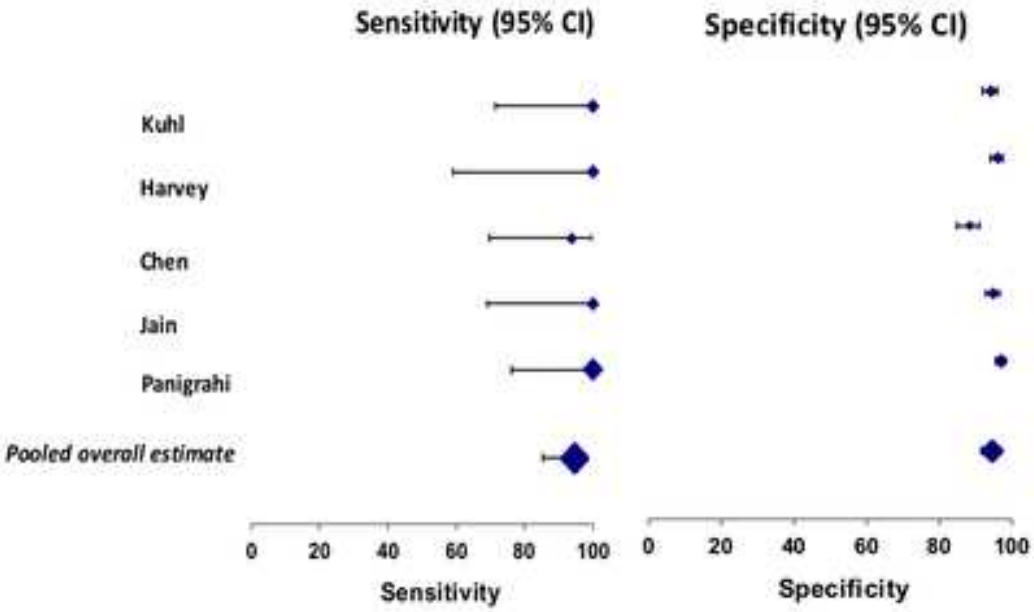
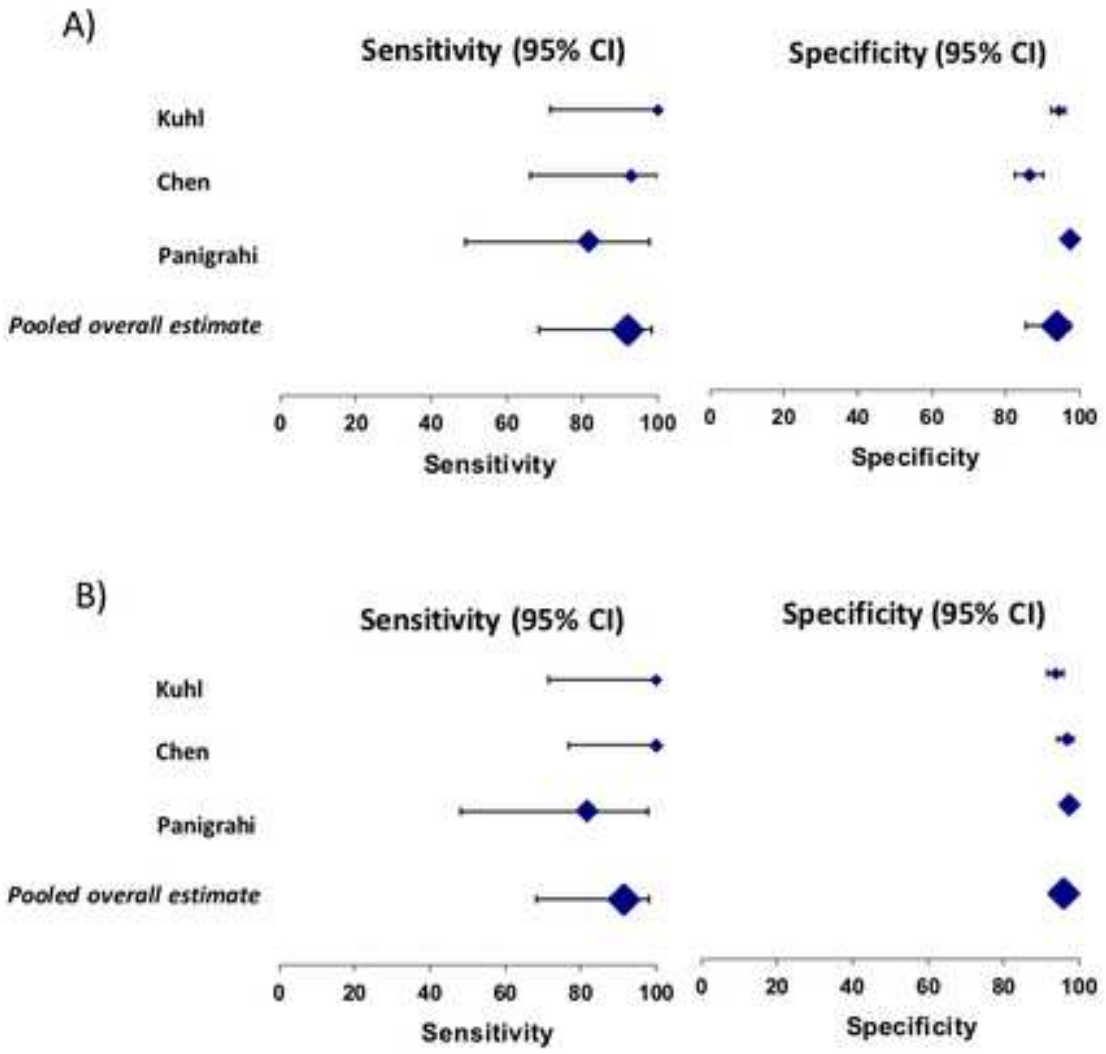


Figure 3: Forest plot for sensitivity and specificity for each study with follow-up for abMRI (A), and fpMRI (B)



## Table 1: Demographics and inclusion and exclusion criteria of 7 included full-text articles

| **Study** *(1st author and year)* | **Age (years)** | **Age range (years)** | **Inclusion criteria** | **Exclusion criteria** |
|---|---|---|---|---|
| **Kuhl 2014** | 54.2* | 25-73 | Negative mammogram<br>Above population risk[#] | If personal history of breast cancer, the affected breast was excluded |
| **Harvey 2015** | 53.2* | 24-81 | High risk[##] | |
| **Chen 2017 (a)** | 48.2* | 30-75 | Negative mammogram<br>Dense breasts[◊] | |
| **Chen 2017 (b)** | 49.3* | 30-71 | Negative mammogram<br>Dense breasts[◊] | Family history of breast cancer |
| **Jain 2017** | 44.3* | 21-74 | High risk[##] | |
| **Panigrahi 2017** | 53.1* | 19-86 | High risk[##]<br>Negative mammogram | |
| **Choi 2018** | 51** | 26-84 | Personal history of breast cancer | Indications other than screening/surveillance |

*mean, **median, [#]any additional risk over population risk including dense breasts (23.7%)(defined as classified as 3 or 4 by 4th edition BIRADs criteria), and/or personal history (49.6%) and/or family history (26.6%), [##]level of risk not specified in article, [◊]level of density not specified in article

## Table 2: Quality assessment that enabled inclusion for 7 full-text articles

| Study | Summary of CASP and BMJ critical appraisal toolkit assessments | | | | |
|---|---|---|---|---|---|
| | Validity | | | | Applicability |
| | Reference standard | Readers blinded to reference standard | Reference standard performed regardless of index test result | Validated in second group of patients | Screening context with consecutive cases |
| **Kuhl 2014** | FP MRI and histology* or 2 year follow up** | Yes[1] | Yes[3] | No | Yes |
| **Harvey 2016** | FP MRI and histology* | Yes[1] | Yes[3] | No | Yes |
| **Chen 2017 (a)** | FP MRI and histology* or 2 year follow up** | Yes[2] | Yes[3] | No | Yes |
| **Chen 2017 (b)** | FP MRI and histology* | Yes[2] | Yes[3] | No | Yes |
| **Jain 2017** | FP MRI and histology* | Yes[1] | Yes[3] | No | Yes |
| **Panigrahi 2017** | FP MRI (and histology* or 1 year follow up for a subset (651/1052)** | Yes[1] | Yes[3] | No | Yes |
| **Choi 2018** | Histology[#] or 1 year follow up[##] | Yes | Yes | No | Yes |

*for FP positive cases, **for FP negative cases, [#]for AP positive cases, [##]for AP negative cases

[1] reference standard read immediately following index test (readers were not blinded to index test when reading reference standard)

[2] reference standard read at least 1 month after index test and the order of the cases presented to the reader was randomised to minimise recall bias

[3] different reference standard applied to index tests that were concordant with reference standard to those that were discordant (because abMRI positives that were discordant with fpMRI were not biopsied)

Table 3: Specifications of abbreviated protocols (abMRI) and of images available for abMRI interpretation

| Study | abMRI read blinded to previous imaging | Tesla (T) | Orientation | Time* (seconds) | abMRI protocol 1 (images acquired and available for interpretation) | abMRI protocol 2 |
|---|---|---|---|---|---|---|
| **Kuhl 2014** | No | 1.5 | Axial | 0 | T1 without fat suppression: first post contrast dynamic subtracted (FAST), slices and MIP, and unsubtracted | none |
| **Harvey 2015** | Yes | Not stated | Axial | Not stated | T1 with fat suppression: FAST slices and MIP | none |
| **Chen 2017 (a)** | Yes | 3 | Axial | 0 | T1 with fat suppression: FAST slices and MIP | AP1 + diffusion weighted imaging (DWI) |
| **Chen 2017 (b)** | Yes | 3 | Axial | 0 | T1 with fat suppression : FAST slices and MIP, and unsubtracted | none |
| **Jain 2017** | Yes | 1.5 or 3 | Axial | 30 | T1 with fat suppression: FAST slices and MIP | none |
| **Panigrahi 2017** | Yes | 1.5 or 3 | Axial | Not stated | T1 with fat suppression: FAST slices and MIP, and unsubtracted | none |
| **Choi 2018** | No | 1.5 or 3 | Sagittal | 0 | T1 with fat suppression: FAST slices and MIP, and T2 sat suppressed (pre-contrast) | none |

*Time from commencement of contrast injection to acquisition of first post contrast dynamic scan

Table 4

Table 4: Diagnostic accuracy of abbreviated breast MRI (abMRI) with full protocol (fpMRI) and histology of fpMRI positives as reference standard

| | Total number of abMRI scans | Total number of cancer cases | True positives | False positives | True negatives | False negatives | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|---|---|---|---|
| **Kuhl 2014** | 606 | 11 | 11 | 34 | 561 | 0 | 100 | 94.3 | 24.4 | 100 |
| **Harvey 2015** | 568 | 7 | 7 | 22 | 539 | 0 | 100 | 96.1 | 24.1 | 100 |
| **Chen 2017 (b)** | 478 | 16 | 15 | 54 | 408 | 1 | 93.8 | 88.3 | 21.7 | 99.8 |
| **Jain 2017** | 591 | 10 | 10 | 29 | 552 | 0 | 100 | 95.0 | 25.6 | 100 |
| **Panigrahi 2017** | 1008 | 14 | 14 | 30 | 964 | 0 | 100 | 97.0 | 26.9 | 100 |

Table 5: Diagnostic accuracy of abbreviated breast MRI (abMRI) with full protocol (fpMRI) for studies with follow-up data

| | Total number of AP MRI scans | Total number of cancer cases | True positives | False positives | True negatives | False negatives | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|---|---|---|---|
| **abMRI** | | | | | | | | | | |
| **Kuhl 2014** | 606 | 11 | 11 | 34 | 561 | 0 | 100 | 94.3 | 24.4 | 100 |
| **Chen 2017 (a)** | 356 | 14 | 13 | 46 | 296 | 1 | 92.9 | 86.5 | 22.0 | 99.7 |
| **Panigrahi 2017** | 651 | 11 | 9 | 18 | 622 | 2 | 81.8 | 97.2 | 33.3 | 99.7 |
| **fpMRI** | | | | | | | | | | |
| **Kuhl 2014** | 606 | 11 | 11 | 36 | 559 | 0 | 100 | 93.9 | 23.4 | 100 |
| **Chen 2017 (a)** | 356 | 14 | 14 | 11 | 331 | 0 | 100 | 96.8 | 56.0 | 100 |
| **Panigrahi 2017** | 660 | 11 | 9 | 17 | 632 | 2 | 81.8 | 97.4 | 34.6 | 99.7 |

Table 6

Table 6: GRADE quality assessment of the level of evidence provided about diagnostic accuracy of abbreviated breast MRI (abMRI) versus full protocol (fpMRI), with reference standard biopsy in test positives on either test and follow up to symptomatic cancer detection

| | **Number of studies** (Number of abMRI scans) | **Design** | **Risk of bias** | **Indirectness of patients, intervention and comparator** | **Inconsistency** | **Imprecision** | **Quality of evidence** |
|---|---|---|---|---|---|---|---|
| **True positives (women with breast cancer)** | | | | | | | |
| **Factors affecting study quality** | 5 (3254) | Cross sectional<br>Short follow up[1] | 4/5 studies: Lack of clarity of definition of population[2]<br>Index tests not undertaken independently<br>Reference standard differed by index test (only fpMRI positive biopsied) | Different populations studied<br>Different abMRI protocols used | Mild heterogeneity of results | Very wide confidence intervals<br>Small numbers | No additional impairments to quality identified |
| **Judgement**[a] | N/A | Moderate[a] | Very Low[a] | Low[a] | Moderate[a] | Low[a] | High[a] |
| **False positives (women incorrectly classified as having breast cancer)** | | | | | | | |
| **Factors affecting study quality** | 5 (3254) | Cross sectional | 4/5 studies: Lack of clarity of definition of population[2]<br>Index tests not undertaken independently | Different populations studied<br>Different abMRI protocols used | Moderate heterogeneity of results | Small numbers | 1/5 studies excluded inconclusive results |
| **Judgement**[a] | N/A | High[a] | Low[a] | Low[a] | Low[a] | Moderate[a] | Moderate[a] |
| **True negatives (women without breast cancer) and False negatives (women incorrectly classified as not having breast cancer)** | | | | | | | |
| **Factors affecting study quality** | 5 (3254) | Cross sectional<br>Short follow up[1] | 4/5 studies: Lack of clarity of definition of population[2]<br>Index tests not undertaken independently<br>Reference standard differed by index test (only fpMRI positive biopsied) | Different populations studied<br>Different abMRI protocols used | Mild heterogeneity of results | Very wide confidence intervals<br>Very small numbers | No additional impairments to quality identified |
| **Judgement**[a] | N/A | Moderate[a] | Very Low[a] | Low[a] | Moderate[a] | Low[a] | High[a] |

A full quality assessment would include a row for each of the patient-important outcomes associated with each possible test result (TP, TN, FP, FN and inconclusive results) as well as test complications and costs. We have presented a simplified summary of the quality and judgement on level of evidence for the critical outcomes here.

[a] Judgement on level of evidence provided (High, Moderate, Low or Very Low) was defined along GRADE guidelines specifically for Diagnostic Test Accuracy studies and does not imply the level of evidence required to influence a change in practice, since diagnostic accuracy outcomes are only a surrogate for patient outcomes

[1]Relatively short term (1-2 years) or no follow up data was included in the studies enabling only comparison of abMRI deficiencies versus fpMRI with histology of fpMRI positives

[2]The terms high risk and dense breasts were not clearly defined (see Table 2)

Table 7: Time taken to acquire and to interpret abbreviated breast MRI (abMRI) and full protocol (fpMRI)

| Study | Time to acquire (seconds) | | Time to interpret (seconds) | |
|---|---|---|---|---|
| | abMRI | fpMRI | abMRI | fpMRI |
| **Kuhl** | 184 | 1024 | 28 | - |
| **Harvey** | 264 | 1392 | 93 | 386 |
| **Chen b** | - | - | 42 | 192 |
| **Jain** | - | - | - | - |
| **Panigrahi** | 180 | 1440 | 144 | 396 |
| **Choi** | 510 | N/A | - | N/A |

## Table 8: Details of cancers found by abMRI

### Table 8(a): Details of grade of cancer found by abMRI

| | Total number of cancer cases | Grade 1 invasive | Grade 2 invasive | Grade 3 invasive | Total invasive cancers as proportion of total cancers (%) | Low grade DCIS | Intermediate grade DCIS | High grade DCIS |
|---|---|---|---|---|---|---|---|---|
| **Kuhl 2014** | 11 | 0/7 | 3/7 | 4/7 | 7/11 (64) | 0/4 | 1/4 | 3/4 |
| **Harvey 2015** | 7 | 1/5 | 4/5 | 0/5 | 5/7 (71) | 1/2 | 0/2 | 1/2 |
| **Chen 2017 (a)** | 14 | 2/10 | 5/10 | 3/10 | 10/14 (71) | 0/4 | 1/4 | 3/4 |
| **Jain 2017** | 10 | - | - | - | 7/10 (70) | - | - | - |
| **Panigrahi 2017** | 14 | 1/12 | 7/12 | 4/12 | 12/14 ((86) | 1/2 | 0/2 | 1/2 |
| **Choi 2018** | 12 | - | - | - | 7/12 (58) | - | - | - |

### Table 8(b): Details of stage of cancer found by abMRI

| | Proportion of total cancers categorised by size | | | | | Proportion of cancer cases with lymph node positive at diagnosis | | | Proportion with distant metastases at diagnosis |
|---|---|---|---|---|---|---|---|---|---|
| | Tis | T1a | T1b | T1c | T2 or greater | N0 | N1 | N2 or N3 | M1 |
| **Kuhl 2014** | 4/11 | 3/11 | 2/11 | 2/11 | 0/11 | 11/11 | 0/11 | 0/11 | 0/11 |
| **Harvey 2015** | - | - | - | - | - | - | - | - | - |
| **Chen 2017 (a)** | 4/14 | 4/14 | 6/14 | 0/14 | 0/14 | 14/14 | 0/14 | 0/14 | 0/14 |
| **Jain 2017** | - | - | - | - | - | - | - | - | - |
| **Panigrahi 2017** | 2/14 | 1/14 | 6/14 | 5/14 | 0/14 | - | - | - | - |
| **Choi 2018** | 5/12 | 2/12 | 2/12 | 3/12 | 0/12 | 11/12 | 1/12 | 0/12 | 0/12 |

## Appendix 1: An example of literature search conducted, with details

**Date: 14th November 2019**
Database: Ovid MEDLINE(R)
Search Strategy:
---
1 exp Breast Neoplasms/
2 exp neoplasms/di
3 exp breast/
4 2 and 3
5 1 or 4
6 exp mass screening/
7 (screen$ or (routine$ adj3 (test$ or check$ or diagnos$ or detect$))).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
8 6 or 7
9 5 and 8
10 exp first post contrast subtracted/
11 exp maximum-intensity projection /
12 exp dynamic magnetic resonance/
13 11 or 12
14 10 and 13
15 exp Abbreviated Magnetic Resonance Imaging /
16 9 and 14
17 9 and 15
18 16 or 17
19 exp Shortened Magnetic Resonance Imaging/
20 5 and 19
21 8 and 20
22 exp dynamic contrast-enhanced MR imaging/
23 5 and 22
24 8 and 23
25 exp limited MRI/
26 5 and 25
27 8 and 26
28 exp Sequenc$ MRI
29 5 and 28
30 8 and 28

Declaration of interest form

**Declaration of interests**

☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☒The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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## Highlights

- Abbreviated breast MRI (abMRI) detects cancer in mammography negative cases
- Sensitivity and specificity of abMRI compared to full protocol MRI were both 95%
- Accuracy of abMRI and fpMRI may be similar but evidence quality is very low

Research is needed to compare outcomes from abMRI to those of standard screening