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Evidence Summary 1-25

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Ontario Health (Cancer Care Ontario)

Preoperative Breast Magnetic Resonance Imaging

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You can access ES 1-25 via Guideline 1-25:
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Preoperative Breast MRI
Evidence Summary

THE PROGRAM IN EVIDENCE-BASED CARE

The Program in Evidence-Based Care (PEBC) is an initiative of the Ontario provincial cancer system, Ontario Health (Cancer Care Ontario) (OH (CCO)). The PEBC mandate is to improve the lives of Ontarians affected by cancer through the development, dissemination, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer control.

The PEBC is a provincial initiative of OH (CCO) supported by the Ontario Ministry of Health (OMH). All work produced by the PEBC is editorially independent from the OMH.

INTRODUCTION

In patients with newly diagnosed breast cancer, mammography is performed as a standard of practice. Ultrasound may be performed for evaluation of the abnormal screening or diagnostic mammogram as well as to facilitate image-guided biopsies necessary for a final diagnosis. Contrast-enhanced breast MRI (CE-MRI, often referred to as MRI) is one of the most sensitive, established, and widely used advanced imaging techniques. Its use after breast cancer diagnosis but before surgery to detect additional breast lesions or provide additional information on disease distribution or extent to guide surgery or systemic therapy is the topic of this review.

Sensitivity of breast MRI in detecting breast cancer is >90%, and sometimes reported as high as 97% to 100% (1-4) in studies of screening or for preoperative use after diagnosis. With MRI, results may be reported on a per lesion or per patient basis. Older studies (prior to 2000) suggested MRI had poor sensitivity for ductal carcinoma in situ (DCIS); however, with improvement in instrumentation, interpretation, and trial design, this is no longer the case (5-7). Specificity of MRI is generally >70%, and depends on study populations, technical methods, and criteria for interpretation; specificity of up to 97% has been reported (1). The benchmark for specificity in screening by MRI set in the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) Atlas (cited in (8)) is 85% to 90%. The high sensitivity of MRI is well established and therefore not an outcome of interest in this review. In cases of additional suspicious lesions detected by MRI, these should be confirmed or ruled out by biopsy unless correlation with other imaging allows definitive diagnosis, or if diagnosis of the specific lesion will not affect treatment.

The utilization of staging MRI is variable, depending on availability, surgeon's preference, and the practice environment. Use in Ontario increased from 3% in 2003 to 24% of breast cancer cases in 2012 (9). Use varied greatly among different health regions; rates for 2012 were 6-22%, while the two largest regions had rates of 43% and 64%. This study did not distinguish the reason for MRI use and likely included high-risk individuals and others for which there are specific indications not relevant to this review. While it is generally acknowledged that preoperative breast MRI will detect additional lesions, there is no consensus as to whether detecting these lesions improves patient outcomes. The Breast Cancer Advisory Committee of OH (CCO) along with the Cancer Imaging Program of OH (CCO) sponsored this document to provide guidance for the use of preoperative breast MRI in updating the Breast Cancer Disease Pathway.

This systematic review has been registered on the PROSPERO website (International prospective register of systematic reviews) with registration number CRD42019141365 (10).

RESEARCH QUESTION

In patients with newly diagnosed breast cancer, does additional information on extent of disease obtained by use of preoperative breast MRI after mammography and/or ultrasound (a) change the type or extent of surgery (breast conserving surgery [BCS], unilateral or bilateral mastectomy), type or extent of radiation therapy, or use of adjuvant therapy; (b) improve patient outcomes such as recurrence, disease- or event-free survival (DRD, EFS), distant metastasis-free survival (DMFS), overall survival (OS), rates of re-excision or re-operation, or quality of life?

A secondary objective of this review was to provide technical guidance on use of MRI by listing documents of possible relevance and summarizing some of the issues affecting imaging selection and performance

TARGET POPULATION

Patients diagnosed with breast cancer for which additional information on disease location or extent obtained prior to surgery may influence staging, treatment, or prognosis. Individuals at high risk[1] of breast cancer who have already had MRI as part of screening are not included in the current review.

INTENDED PURPOSE

The Breast Cancer Advisory Committee sponsored this document to provide guidance in updating the Breast Cancer Disease Pathway.

INTENDED USERS

1. The primary users will be members of the Breast Cancer Advisory Committee, OH (CCO) staff, and others involved in completion of the breast cancer pathway. The topic is also within the mandate of the Cancer Imaging Program of OH (CCO).
2. This review may also be of interest to general practitioners, radiologists, medical oncologists, surgical oncologists, and radiation oncologists.

METHODS

This evidence summary was developed by a Working Group consisting of four radiologists, two surgical oncologists, a medical oncologist, and a health research methodologist at the request of the Breast Cancer Advisory Committee of OH (CCO).

The Working Group was responsible for reviewing the identified evidence and drafting the summary. Conflict of interest declarations for all authors are summarized in Appendix A, and were managed in accordance with the *PEBC Conflict of Interest Policy*.

Literature Search

Embase, MEDLINE, and EBM Reviews (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews) were searched until July 3, 2019 and updated until

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[1] For high-risk individuals, use of MRI together with mammography is the standard of care for screening in Ontario as part of the Ontario Breast Screening Program (see https://www.cancercareontario.ca/en/guidelines-advice/cancer-continuum/screening/breast-cancer-high-risk-women). They define high risk as a personal or family history of a known gene mutation increasing the risk for breast cancer (e.g., BRCA1, BRCA2, TP53, PTEN, CDH1), personal or family history of breast or ovarian cancer and IBIS or BOADICEA score indicating ≥25% lifetime risk of breast cancer, or radiation therapy to the chest before age 30 at least eight years ago. Other jurisdictions may used different definitions of risk and eligibility for screening by MRI.

January 18, 2021 as indicated in Appendix B. Articles were included with terms for both breast cancer and MRI. The search strategy excluded case reports, comments, editorials, news, letters, and notes. As an earlier unpublished systematic review by PEBC (2) as well as several known reviews by others were not considered definitive, comprehensive, or of direct relevance, a search of primary studies was required; a search for additional systematic reviews therefore did not precede the main search. Duplicate publications were excluded. For purposes of this review duplicates included multiple citations of the same publication, articles in press or published as an abstract if there was a subsequent full publication, abstracts published from more than one conference or that were updated in other abstracts, reviews or guidelines that were subsequently updated, or reprints of a previously published article.

Guidelines and technical documents on MRI were located from the above databases, known guideline developer websites, suggestions by co-authors, and the earlier PEBC systematic review. For relevant guidelines identified, the organization websites were reviewed to ensure the most recent version was included. This search was updated in March 2021 (see Appendix B).

Study Selection Criteria and Process for Clinical Trials

Inclusion Criteria

Studies were included that met all the following criteria:

1. Included patients with newly diagnosed breast cancer evaluating use of breast MRI prior to surgery, or patients referred for biopsy due to suspicion of cancer (but not yet diagnosed with cancer).
2. Were either (a) a randomized controlled trial (RCT) of MRI versus no MRI (≥30 patients per group) or (b) a comparative study with ≥50 patients per group for the full study (≥25 patients per group for any subgroup analysis by patient or disease characteristics) comparing use of MRI versus no MRI in two or more groups with equivalent disease and patient characteristics or using methods to control potential confounders (such as multivariable analysis and/or propensity score matching). Within-group studies reporting a treatment plan before and after MRI for each patient were included in the initial screening.
3. Primary or secondary outcomes (or main outcomes in study design) included at least one of the following: recurrence; survival outcomes such as DFS, EFS, DMFS, or OS; rates of mastectomy, re-excision, or re-operation; adverse effects/morbidity due to surgery; or quality of life.

Exclusion Criteria

Studies of the following were excluded:

1. MRI as the initial screening or diagnostic test, or when no index cancer was previously identified (occult cancer).
2. MRI as a tool to monitor response to neoadjuvant treatment.
3. Studies reporting on performance characteristics of MRI (e.g., sensitivity, specificity) or detection rates of multicentric, multifocal, or contralateral cancer, but without outcomes listed in the inclusion criteria.

During initial screening, some non-randomized studies were retained where patient/disease characteristics were reported (see inclusion criteria 2) but it was unclear whether to judge the MRI and non-MRI groups as equivalent. Determination of equivalence required a thorough assessment of the studies and inclusion of relevant factors. As a minimum, studies should have

considered tumour size and lymph node status (stage) and patient age and/or menopausal status. Cancer subtype/histology such as DCIS, lobular carcinoma in situ (LCIS), invasive ductal cancer, or invasive lobular cancer (ILC) was considered important for outcomes of positive margins/reoperations and recurrence/survival (at least in situ vs. invasive). Receptor status for human epidermal growth factor receptor 2 (HER2), estrogen receptor (ER), and progesterone receptor (PR), systemic therapy, and radiotherapy use were also considered important for recurrence/survival outcomes. Breast density and high risk (hereditary) factors are known to affect cancer incidence and detection rates but were rarely reported and therefore were not criteria for accepting or rejecting studies.

A review of the titles and abstracts was done by one reviewer (GGF). For studies that warranted full-text review, the same author reviewed each study. In cases of uncertainty, co-authors were consulted.

Data Extraction, Assessment of Risk of Bias, and Trial Quality

Studies underwent data extraction by one author (GGF), with all extracted data and information audited subsequently by an independent auditor. Ratios, including odds or hazard ratios, were expressed with a ratio of <1.0 indicating that the experimental group (MRI use) had more favourable outcome than the control group. Favourable outcomes were considered to be lower mastectomy rates (more BCS); lower rates of positive margins, reoperations, or re-excisions; higher detection of synchronous contralateral breast cancer (CBC); lower rates of metachronous CBC; lower rates of recurrence (or specific type of recurrence), and higher overall survival. The risk of bias for randomized studies was assessed per outcome and per study by GGF using methods outlined in the Cochrane Handbook for Systematic Reviews of Interventions (11). The Cochrane risk-of-bias (RoB) tool (revised version RoB 2) for RCTs and ROBINS-I for non-RCTs are described in this handbook and other publications (12-14). Internal and external validity were also considered in assessing quality.

Synthesizing the Evidence

When clinically homogeneous results from two or more studies were available, a meta-analysis was conducted using Review Manager 5.4 software (RevMan) provided by the Cochrane Collaboration (15). The generic inverse variance model with random effects was used. While there is some debate as to whether odds ratio (OR) or relative risk is more meaningful and easier to interpret for clinical studies, multiple logistic regression calculates adjusted ORs (16-19). ORs and confidence intervals (CIs) were therefore the preferred statistic for meta-analysis. For RCTs or studies with matched/propensity-score matched groups, if ORs and CIs were not reported they were derived from event rates or p-value. For retrospective studies with multivariate analysis to adjust for confounding, only outcomes with adjusted ORs were reported.

Three sources of heterogeneity were explored for outcomes of mastectomy rates and positive margins: restriction of included patients to those determined to be BCS candidates (compared to including all patients diagnosed with breast cancer), stage/subtype of cancer, and trial design. The first two of these were also explored for reoperation, re-excision, and conversion mastectomy rates. For ease of presentation and to explore the effects of these factors, forest plots include all studies, with data in subgroups according to these criteria. Each line (study) in a forest plot has these three factors indicated. While the forest plots provide a concise pictorial representation of the included studies and outcomes, due to heterogeneity summary statistics (especially overall results for the full set of trials) should be interpreted with caution. It is acknowledged that such summary statistics are sometimes suppressed for this type of data; however, it was decided they had value in interpreting the results and variations observed.

Other Documents, Technical Requirements, and Other Issues

Guidelines, technical documents or practice parameters, and systematic reviews were screened for relevance; those published prior to 2014 were excluded. A few exceptions were made to this cut-off for key guidelines by major organizations still in use and widely cited in recent literature. For reviews and guidelines addressing the question of whether to use MRI prior to surgery, the same criteria as used for trials applied. In case of multiple reviews on the same topic, the most recent and comprehensive were preferred. During screening of primary studies, issues of particular relevance to breast imaging or MRI use were noted, with particular attention paid to issues that could affect MRI performance. These topics are crucial to breast imaging, but systematic reviews were not conducted for each of them as part of the current review.

RESULTS

The search in Embase, Medline, and EBM Reviews resulted in 27,745 citations; an additional 82 citations were added from other sources. A PRISMA diagram showing the search results is provided in Appendix C.

Within-Patient Studies: Treatment Plan Before and After MRI

Several studies were found that compared planned rates of BCS or mastectomy prior to MRI versus surgery planned or received in the same patients after MRI (20-124). Given the wide variations noted below, and lack of adherence to current or optimal methodology, data on changes in proportions of BCS versus mastectomy without long-term cancer-related outcomes appear to be of limited value. Prior to data extraction it was decided that these studies would be cited but no data reported and therefore only a brief description is provided. While data have not been extracted, citations of the 105 publications are provided and may be of interest to some readers.

Some studies used MRI in all patients seen, while others retrospectively studied a subgroup of patients that had MRI. Inclusion criteria varied among studies: all those for which BCS was planned or technically possible prior to MRI, all patients who had MRI, patients for whom there was diagnostic uncertainty or suspected multifocality/multicentricity, patients of specific stage (early, stage 0-2, locally advanced) or BI-RADS category (e.g., 1-2, 3, 3-4 4-5), or specific subtypes (e.g., lobular, DCIS). Some included patients with family history or genetic predisposition. Some excluded patients for whom mastectomy was planned; others included patients for which it was unclear whether BCS was feasible and additional information was sought. Studies that excluded patients for whom mastectomy was planned or recommended prior to MRI by design could only find an increase in mastectomy rates as they excluded patients for whom a downgrade from mastectomy to BCS based on MRI might occur.

Studies either used surgical plans from patient charts prior to MRI versus surgery actually received (which includes a portion of patients who choose mastectomy even when BCS is feasible or recommended), retrospective evaluation of traditional imaging and a decision of appropriate treatment versus actual surgery, or retrospective evaluation of traditional imaging and retrospective evaluation of MRI imaging with a decision of appropriate treatments before and after MRI. Most studies did not consider patient preferences or decision factors leading to final treatment.

How information about additional lesions detected on MRI was used also varied and may explain the wide variation in mastectomy rates and treatment changes among studies. Some modified treatment due to differences in apparent size of the primary lesion but only used follow-up for other lesions. Most common was biopsy of selected lesions, generally those detectable by second-look ultrasound, or those larger than a specified cut-off (e.g., 5 mm).

Few studies biopsied all lesions (or at least those that could potentially change treatment). Many studies did not mention how they assessed MRI-detected lesions, and a few indicated they did not have MRI-directed biopsy capability. Use of MRI-guided biopsy was rare. Change in treatment due to additional MRI-detected lesions without preoperative histological proof occurred in several studies and thus negative findings after surgery are not unexpected. Together, these limitations indicate changes in treatment without proof of histology, unknown specificity, and improper way to really assess impact of the modality.

Criteria of BCS varied among studies as well. Some had explicit criteria such that lesions had to be <3 cm or in only one quadrant to consider BCS and otherwise mastectomy was performed. Some presented results to patients and allowed them to decide whether to have biopsy or go straight to mastectomy. Oncoplastic surgery was not used in most studies.

Comparison of Groups of Patients with and without MRI

The second type of study design, and of primary interest for this review, consisted of comparisons of outcomes between groups of patients who had MRI and those who did not have MRI (9, 125-185). There are 53 included trials described in 62 publications. Studies reporting mastectomy or BCS rates are summarized in Table 1 (9, 125-154) and Table 2 (155-163). Studies with outcomes of positive excision margins or reoperation rates are reported in Table 3 (125-127, 129-133, 136, 139-143, 145, 146, 148-162, 164-171), and contralateral cancer and long-term outcomes of recurrence or survival are summarized in Table 4 (139, 148, 149, 153, 154, 157, 162, 165, 166, 170, 172-185). For ease of reading this section, the tables are included at the end of the review.

Studies included eight RCTs, two prospective cohort studies, and forty-three retrospective studies. Eighteen of the trials (including six of the RCTs) were limited to patients for whom BCS was the treatment plan determined prior to randomization and MRI use. The retrospective studies included eight with propensity-matched controls, one with matched controls, four with historical or equivalent controls, fifteen with multivariable/multivariate analysis of data from a single or small number of institutions, and fifteen using cancer registry data (all or several institutions in a geographic area) and multivariable/multivariate analysis. A series of forest plots created using RevMan (15) provide graphical summaries to aid in the interpretation of the tabulated results. These figures are inserted into the Results section where the corresponding outcomes are reported.

Risk of Bias and Quality of Evidence

Randomized Controlled Trials

Of the six RCTs that reported mastectomy rates, all had high risk of bias and low certainty of evidence for this outcome (see Appendix G). As described in more detail in the next sections, studies that restricted the patient population to only patients with a treatment plan of BCS have a high risk of bias for mastectomy rate outcomes, leading to an overestimation of the effect of MRI on increasing mastectomy rates. ICRIS (155), Turku University (162), BREAST-MRI (157), and COMICE trials (158) were RCTs conducted in patients preselected for BCS. The Alliance AO11104/ACRIN 6694 is an ongoing trial (no results reported yet) that will also only include BCS patients (170).

Other sources of bias apply to all outcomes. IRCIS had more patients with dense breasts and premenopausal status in the MRI arm, the BREAST-MRI trial was only reported as an abstract and had more premenopausal patients in the MRI arm, and the COMICE trial had more patients with multifocal and multicentric tumours in the MRI arm. The COMICE trial also had 53 patients in the MRI group who did not receive MRI compared to 9 in the non-MRI group who received MRI; results were not adjusted to account for this protocol violation. COMICE also categorized

initial mastectomy due to patient choice alone as reoperation, and those lost to follow-up as not having a primary endpoint event. The other two RCTs with mastectomy outcomes also had high risk of bias. POMB (130) randomized some patients only after multidisciplinary team discussion, groups had unequal baseline characteristics (prior to MRI, the suggested treatment was BCS in 153 vs. 132 patients), 10 patients without MRI were analyzed together with the MRI group, one out of three study sites did not perform MRI, and one site did not follow conventional MRI procedures. The MONET trial (132) randomized 463 patients with suspicious lesions (and conducted power calculations based on this) but only 149 had surgery and therefore the study was greatly underpowered; there are also concerns about the MRI technique as sensitivity was only 51% and prior to the start of the trial there were substantial problems that the investigators thought were resolved. The B-SMART trial (171) was terminated early, reported interim results only in an abstract, and gave no MRI details and is therefore also at high risk of bias.

Non-Randomized Studies

After review of the ROBINS-I questions (see Appendix G), it was determined that most either did not apply (Questions 1.3, 1.7, 1.8, treatment discontinuation and time-related confounding; Question 2.2 to 2.5, selection bias; Question 4, departure from interventions) or uniformly resulted in low to moderate risk of bias (Question 2.1, selection based on observations after intervention; Questions 3.2 and 3.3, classification bias; Question 6, measurement of outcomes; Question 7, selection of results). The exceptions were questions related to selection and appropriate adjustment for cofounders (Questions 1.4 and 1.5), details of the intervention (i.e., whether MRI procedures were conducted adequately and consistently and reported in sufficient detail, Question 3.1), and missing data (Question 5). As these items were among those extracted and reported in the data tables, a separate risk of bias assessment using the ROBINS-I tool was not conducted.

While well-conducted RCTs generally comprise the highest level of trial evidence, the RCTs in this review have limitations in design or conduct that affect the quality and generalizability of the evidence. Non-randomized studies may provide evidence of similar or greater levels of evidence than low-quality RCTs. Retrospective studies that were restricted to BCS candidates have the same bias as RCTs with this restriction and were judged as having serious or critical risk of bias for mastectomy outcomes. The evidence for mastectomy outcomes is of low quality in these studies. For other (non-mastectomy) outcomes the effect of restricting inclusion to BCS candidates is less clear, and these studies were evaluated with the other non-randomized trials.

Retrospectives studies are of variable risk of bias and quality, depending primarily on how well the patient and disease factors were matched in the MRI and non-MRI groups, or how adequate the correction for confounders was made in the multivariable analyses. The most rigorous studies controlled for many disease characteristics (size or stage, subtype or histology) and physical characteristics of patients (age, menopausal status, breast density); studies with obvious imbalance and failure to control for key factors have been excluded. However, the number of factors measured, reported, and corrected for varies widely; in general, those with more factors in the matching or multivariate analysis have less risk of bias. Provided they included the key factors, such studies have low risk of bias for confounding. Some studies decided to only include factors with significant correlation (e.g., $p<0.05$) in the multivariate analysis, and this is considered improper statistically; such studies were excluded or noted in the data tables and have high risk of bias. Due to the large number of trials, no attempt is made in this section to give a study-by-study evaluation, and the reader is referred to the data tables (see subsequent sections).

Most studies did not have data available as to why patients elected mastectomy. Some of the patient decision factors may include fear of any lesion (even if subsequently evaluated

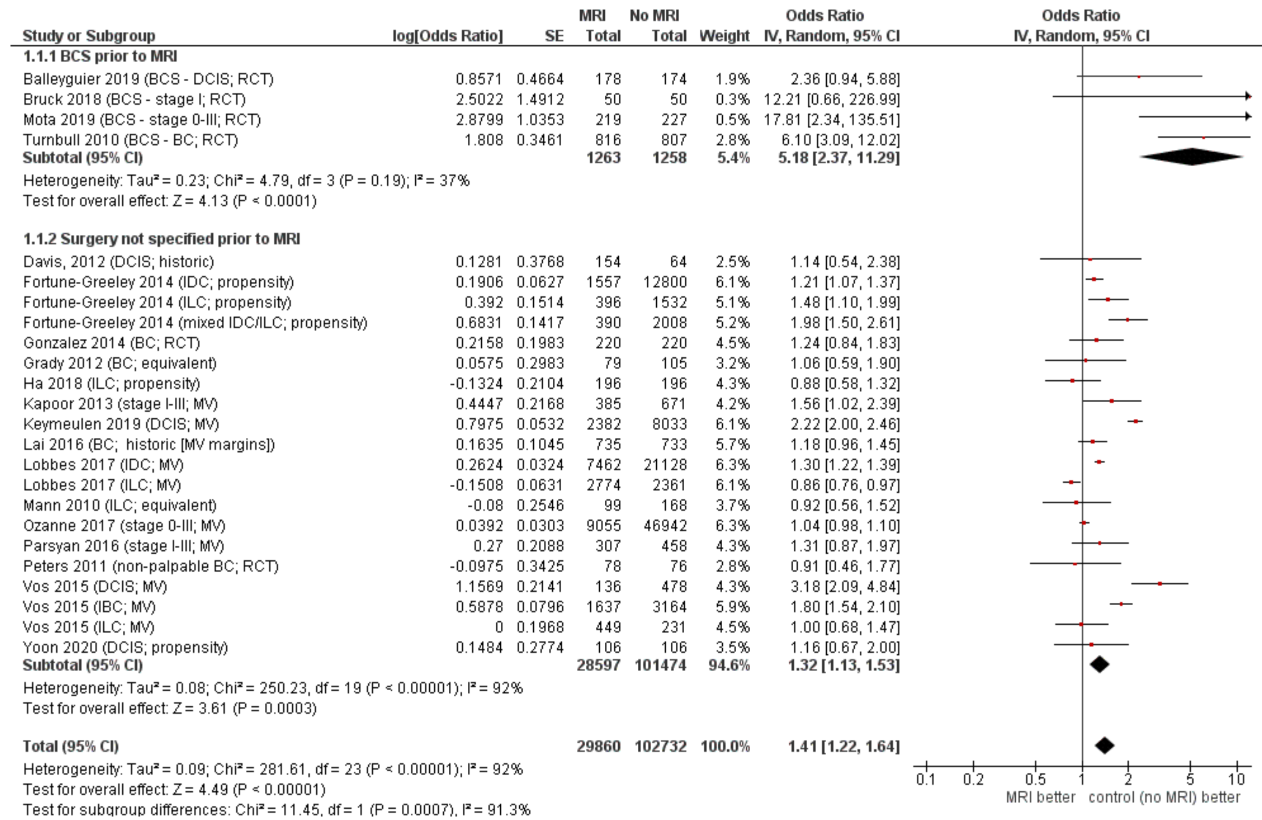
as benign), poor comprehension of risks, not wanting further biopsy, fear of recurrence, views on body image and sexuality, marital/relationship status, ethnicity, availability of reconstruction or oncoplastic procedures, attitudes and recommendations of surgeons, and institutional practice. Only in those studies with historic controls (125, 140, 141, 143) from the time period immediately before MRI was implemented are patient decision factors expected to be more similar in the MRI and non-MRI groups, although change in practice might still be an issue. One other study compared results for two surgeons in the same institution and with similar surgical practices (143). In this trial patient and disease characteristics appeared equivalent, although there could be unreported variations in patient or surgeon factors. . These studies are assessed as having low to moderate risk of bias. The remaining non-randomized trials have moderate to critical risk of bias for mastectomy outcomes.

Studies in which data were extracted from patient records in single or a small group of institutions tended to have better reporting of MRI and subsequent biopsy procedures and therefore generally had low risk of bias related to MRI techniques or reporting (with a few concerns noted in the data tables). Studies using registry data had inadequate documentation of MRI methodology and are considered to have serious risk of bias for all outcomes.

Mastectomy Rates

Trials reporting mastectomy or BCS rates in patients with or without preoperative MRI are summarized in Table 1 (9, 125-128, 130-154) and Table 2 (129, 155-163) and illustrated in Figures 1.1 to 1.7. Figures 1.1 to 1.4 present data on initial mastectomy rates, while Figures 1.5 to 1.7 look at final or overall mastectomy rates, including patients who had initial BCS but reoperation resulted in mastectomy. Table 1 includes 27 trials (31 publications) in which patients were determined prior to MRI to be suitable for surgical treatment(any type). Additional information from MRI could potentially result in more extensive surgery in those planning BCS or less extensive operation in those planning mastectomy. Table 2 includes five trials (nine publications) conducted only in patients for whom BCS was the treatment plan prior to MRI. As no patients identified as mastectomy candidates were included, it is impossible to downgrade treatment from mastectomy to BCS. Patients could only receive the same treatment as they would have without MRI (i.e., BCS) or more extensive treatment (mastectomy). This is clearly illustrated in Figure 1.1 in which the OR for initial mastectomy with versus without MRI is 5.18 in the studies of BCS patients only (as determined prior to MRI), and 1.41 in studies that did not restrict the study to BCS. This is especially important as four of the eight RCTs in this review (four out of six with mastectomy rate outcomes) were conducted only in patients identified for BCS.

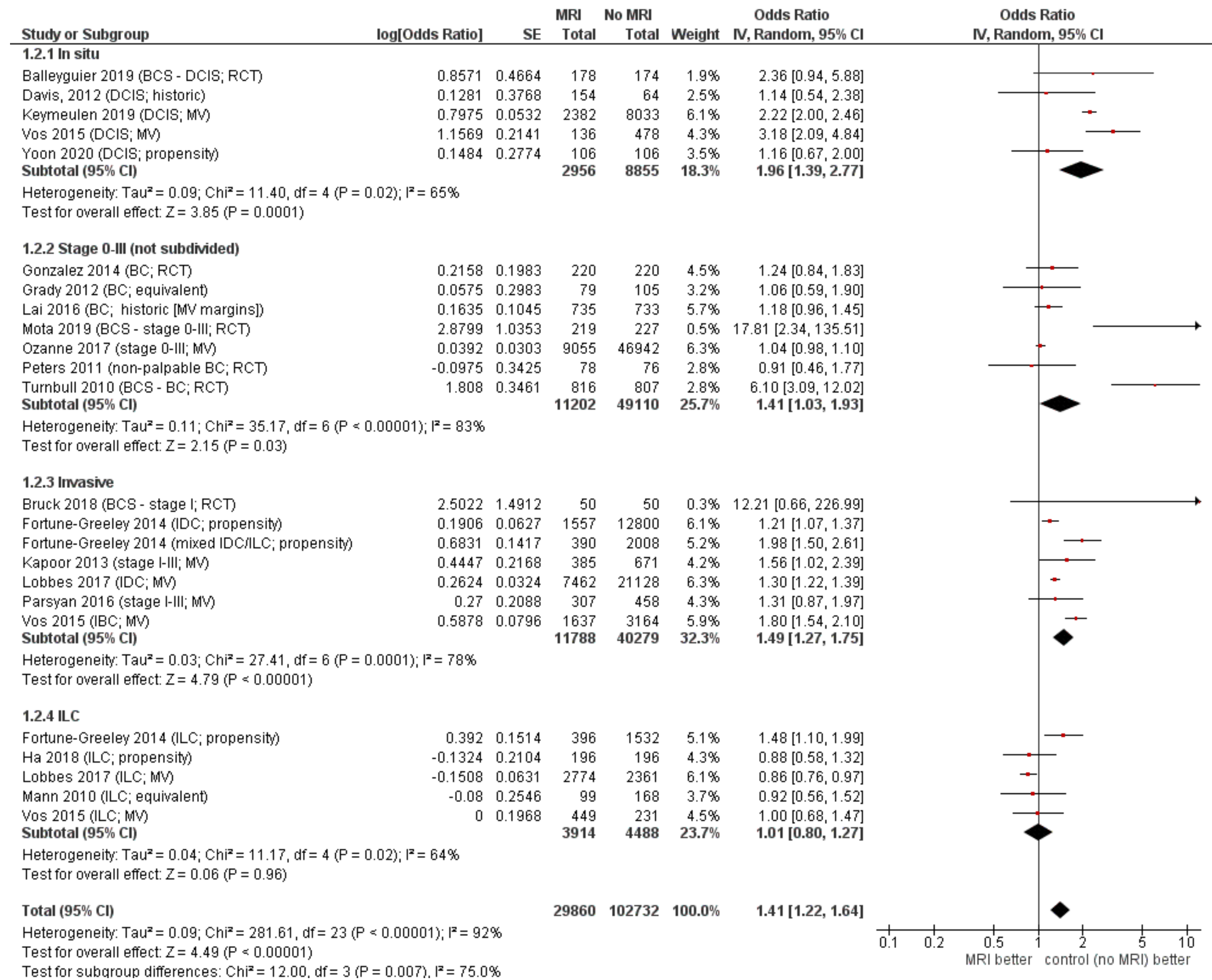
Figure 1.1. Initial mastectomy rate, by type of surgery determined prior to MRI



Study or Subgroup	log[Odds Ratio]	SE	MRI Total	No MRI Total	Weight	Odds Ratio IV, Random, 95% CI
1.1.1 BCS prior to MRI						
Balleyguier 2019 (BCS - DCIS; RCT)	0.8571	0.4664	178	174	1.9%	2.36 [0.94, 5.88]
Bruck 2018 (BCS - stage I; RCT)	2.5022	1.4912	50	50	0.3%	12.21 [0.66, 226.99]
Mota 2019 (BCS - stage 0-III; RCT)	2.8799	1.0353	219	227	0.5%	17.81 [2.34, 135.51]
Turnbull 2010 (BCS - BC; RCT)	1.808	0.3461	816	807	2.8%	6.10 [3.09, 12.02]
Subtotal (95% CI)			**1263**	**1258**	**5.4%**	**5.18 [2.37, 11.29]**
Heterogeneity: Tau² = 0.23; Chi² = 4.79, df = 3 (P = 0.19); I² = 37%						
Test for overall effect: Z = 4.13 (P < 0.0001)						
1.1.2 Surgery not specified prior to MRI						
Davis, 2012 (DCIS; historic)	0.1281	0.3768	154	64	2.5%	1.14 [0.54, 2.38]
Fortune-Greeley 2014 (IDC; propensity)	0.1906	0.0627	1557	12800	6.1%	1.21 [1.07, 1.37]
Fortune-Greeley 2014 (ILC; propensity)	0.392	0.1514	396	1532	5.1%	1.48 [1.10, 1.99]
Fortune-Greeley 2014 (mixed IDC/ILC; propensity)	0.6831	0.1417	390	2008	5.2%	1.98 [1.50, 2.61]
Gonzalez 2014 (BC; RCT)	0.2158	0.1983	220	220	4.5%	1.24 [0.84, 1.83]
Grady 2012 (BC; equivalent)	0.0575	0.2983	79	105	3.2%	1.06 [0.59, 1.90]
Ha 2018 (ILC; propensity)	-0.1324	0.2104	196	196	4.3%	0.88 [0.58, 1.32]
Kapoor 2013 (stage I-III; MV)	0.4447	0.2168	385	671	4.2%	1.56 [1.02, 2.39]
Keymeulen 2019 (DCIS; MV)	0.7975	0.0532	2382	8033	6.1%	2.22 [2.00, 2.46]
Lai 2016 (BC; historic [MV margins])	0.1635	0.1045	735	733	5.7%	1.18 [0.96, 1.45]
Lobbes 2017 (IDC; MV)	0.2624	0.0324	7462	21128	6.3%	1.30 [1.22, 1.39]
Lobbes 2017 (ILC; MV)	-0.1508	0.0631	2774	2361	6.1%	0.86 [0.76, 0.97]
Mann 2010 (ILC; equivalent)	-0.08	0.2546	99	168	3.7%	0.92 [0.56, 1.52]
Ozanne 2017 (stage 0-III; MV)	0.0392	0.0303	9055	46942	6.3%	1.04 [0.98, 1.10]
Parsyan 2016 (stage I-III; MV)	0.27	0.2088	307	458	4.3%	1.31 [0.87, 1.97]
Peters 2011 (non-palpable BC; RCT)	-0.0975	0.3425	78	76	2.8%	0.91 [0.46, 1.77]
Vos 2015 (DCIS; MV)	1.1569	0.2141	136	478	4.3%	3.18 [2.09, 4.84]
Vos 2015 (IBC; MV)	0.5878	0.0796	1637	3164	5.9%	1.80 [1.54, 2.10]
Vos 2015 (ILC; MV)	0	0.1968	449	231	4.5%	1.00 [0.68, 1.47]
Yoon 2020 (DCIS; propensity)	0.1484	0.2774	106	106	3.5%	1.16 [0.67, 2.00]
Subtotal (95% CI)			**28597**	**101474**	**94.6%**	**1.32 [1.13, 1.53]**
Heterogeneity: Tau² = 0.08; Chi² = 250.23, df = 19 (P < 0.00001); I² = 92%						
Test for overall effect: Z = 3.61 (P = 0.0003)						
Total (95% CI)			**29860**	**102732**	**100.0%**	**1.41 [1.22, 1.64]**
Heterogeneity: Tau² = 0.09; Chi² = 281.61, df = 23 (P < 0.00001); I² = 92%						
Test for overall effect: Z = 4.49 (P < 0.00001)						
Test for subgroup differences: Chi² = 11.45, df = 1 (P = 0.0007), I² = 91.3%						

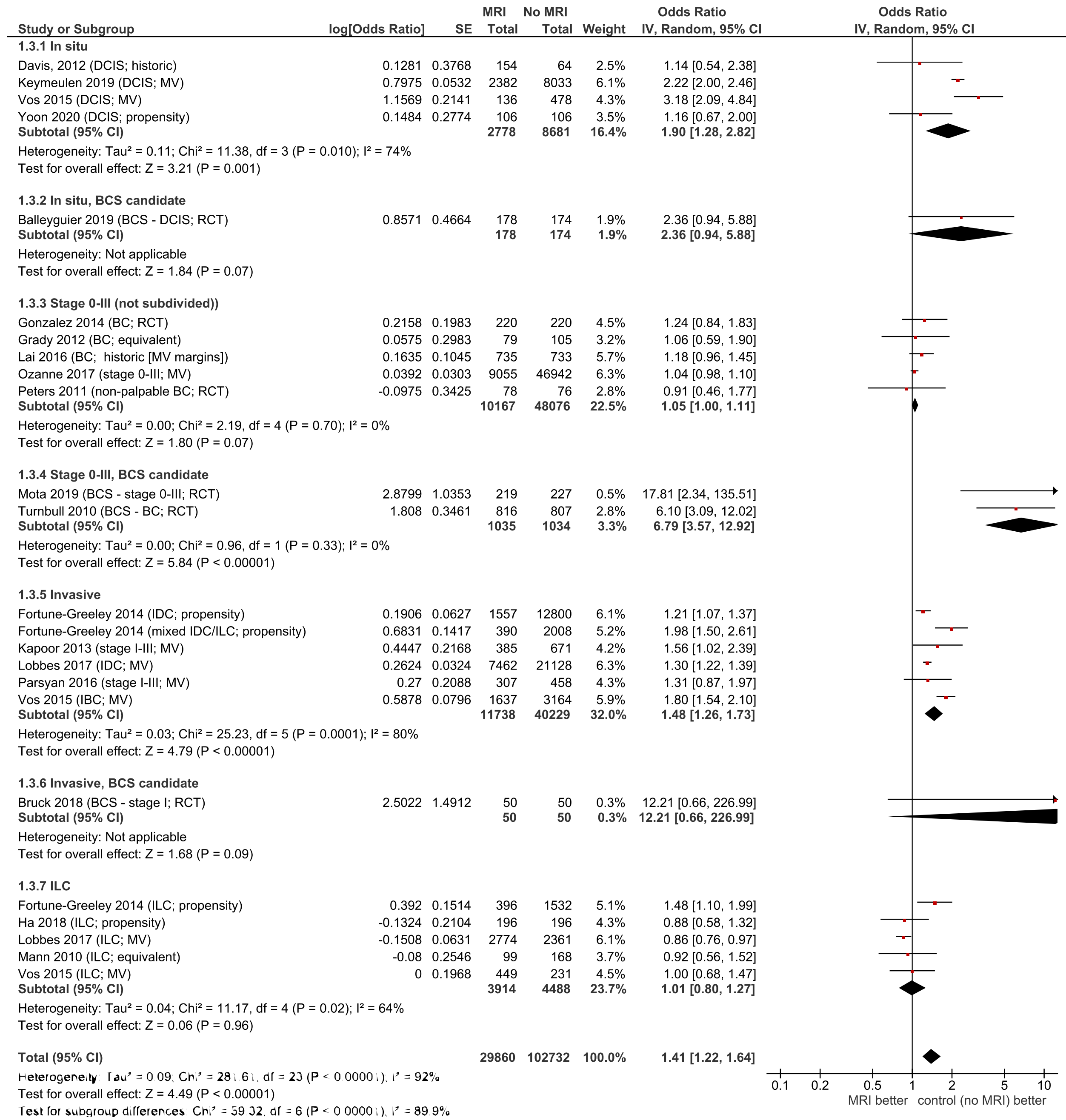
An odds ration of less than one indicates a lower rate of mastectomy in patients with preoperative MRI, while an odds ratio of greater than one indicates an increase in mastectomy rate. Subgroup 1.1.1 consists of studies in which prior to MRI patients were determined to be candidates for BCS; patients planning mastectomy were excluded. Subgroup 1.1.2 consists of studies where a decision about the type of surgery (either BCS or mastectomy) made prior to MRI did not determine inclusion in the study. Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

Figure 1.2. Initial mastectomy rate by subtype



An odds ration of less than one indicates a lower rate of mastectomy in patients with preoperative MRI, while an odds ratio of greater than one indicates an increase in mastectomy rate. Studies are displayed in subgroups according to type or stage of cancer. Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

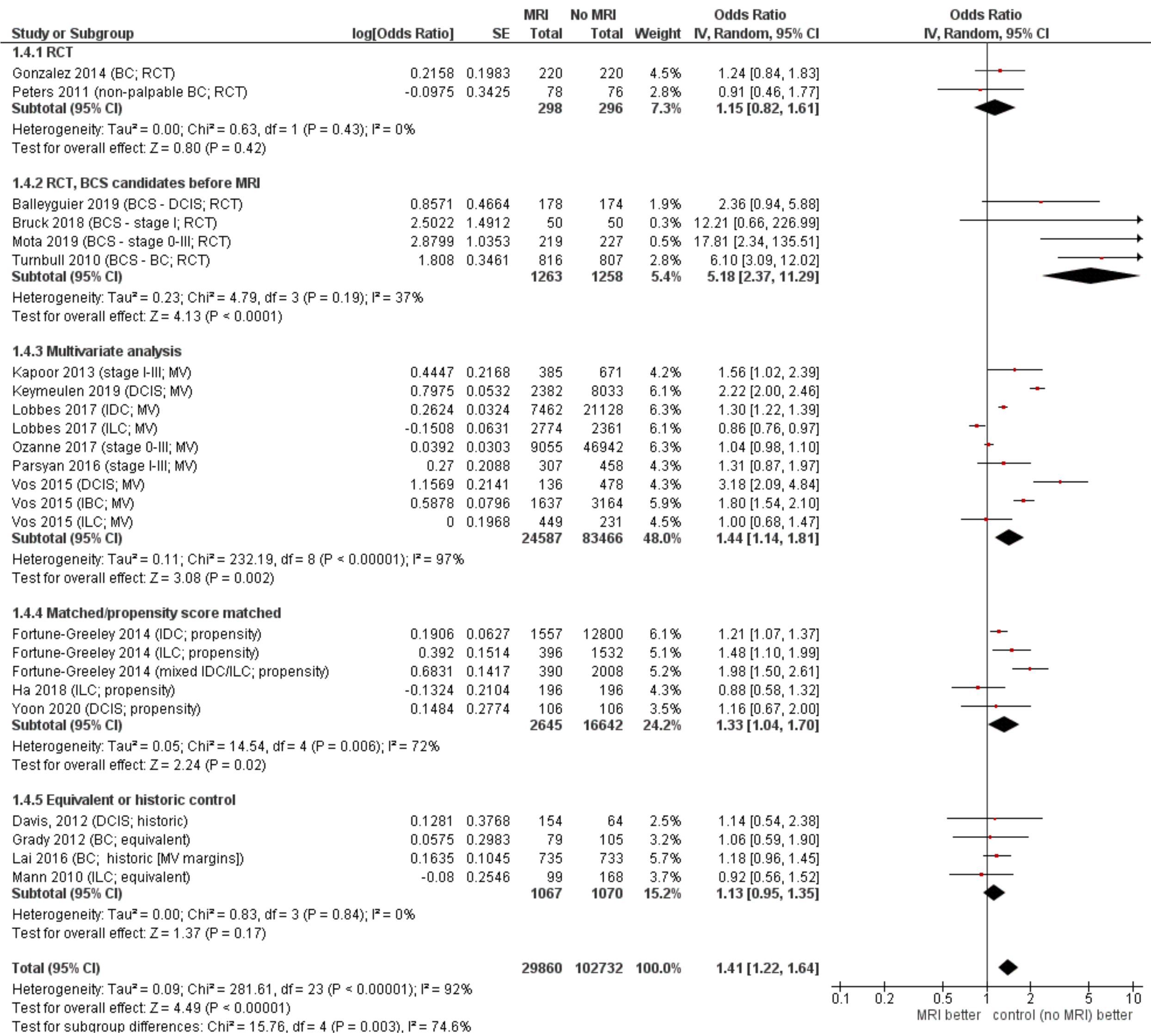
Figure 1.3. Initial mastectomy rate by subtype + BCS candidate prior to MRI



Study or Subgroup	log[Odds Ratio]	SE	MRI Total	No MRI Total	Weight	Odds Ratio IV, Random, 95% CI
1.3.1 In situ						
Davis, 2012 (DCIS; historic)	0.1281	0.3768	154	64	2.5%	1.14 [0.54, 2.38]
Keymeulen 2019 (DCIS; MV)	0.7975	0.0532	2382	8033	6.1%	2.22 [2.00, 2.46]
Vos 2015 (DCIS; MV)	1.1569	0.2141	136	478	4.3%	3.18 [2.09, 4.84]
Yoon 2020 (DCIS; propensity)	0.1484	0.2774	106	106	3.5%	1.16 [0.67, 2.00]
Subtotal (95% CI)			**2778**	**8681**	**16.4%**	**1.90 [1.28, 2.82]**
Heterogeneity: Tau^2 = 0.11; Chi^2 = 11.38, df = 3 (P = 0.010); I^2 = 74%						
Test for overall effect: Z = 3.21 (P = 0.001)						
1.3.2 In situ, BCS candidate						
Balleyguier 2019 (BCS - DCIS; RCT)	0.8571	0.4664	178	174	1.9%	2.36 [0.94, 5.88]
Subtotal (95% CI)			**178**	**174**	**1.9%**	**2.36 [0.94, 5.88]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.84 (P = 0.07)						
1.3.3 Stage 0-III (not subdivided))						
Gonzalez 2014 (BC; RCT)	0.2158	0.1983	220	220	4.5%	1.24 [0.84, 1.83]
Grady 2012 (BC; equivalent)	0.0575	0.2983	79	105	3.2%	1.06 [0.59, 1.90]
Lai 2016 (BC; historic [MV margins])	0.1635	0.1045	735	733	5.7%	1.18 [0.96, 1.45]
Ozanne 2017 (stage 0-III; MV)	0.0392	0.0303	9055	46942	6.3%	1.04 [0.98, 1.10]
Peters 2011 (non-palpable BC; RCT)	-0.0975	0.3425	78	76	2.8%	0.91 [0.46, 1.77]
Subtotal (95% CI)			**10167**	**48076**	**22.5%**	**1.05 [1.00, 1.11]**
Heterogeneity: Tau^2 = 0.00; Chi^2 = 2.19, df = 4 (P = 0.70); I^2 = 0%						
Test for overall effect: Z = 1.80 (P = 0.07)						
1.3.4 Stage 0-III, BCS candidate						
Mota 2019 (BCS - stage 0-III; RCT)	2.8799	1.0353	219	227	0.5%	17.81 [2.34, 135.51]
Turnbull 2010 (BCS - BC; RCT)	1.808	0.3461	816	807	2.8%	6.10 [3.09, 12.02]
Subtotal (95% CI)			**1035**	**1034**	**3.3%**	**6.79 [3.57, 12.92]**
Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.96, df = 1 (P = 0.33); I^2 = 0%						
Test for overall effect: Z = 5.84 (P < 0.00001)						
1.3.5 Invasive						
Fortune-Greeley 2014 (IDC; propensity)	0.1906	0.0627	1557	12800	6.1%	1.21 [1.07, 1.37]
Fortune-Greeley 2014 (mixed IDC/ILC; propensity)	0.6831	0.1417	390	2008	5.2%	1.98 [1.50, 2.61]
Kapoor 2013 (stage I-III; MV)	0.4447	0.2168	385	671	4.2%	1.56 [1.02, 2.39]
Lobbes 2017 (IDC; MV)	0.2624	0.0324	7462	21128	6.3%	1.30 [1.22, 1.39]
Parsyan 2016 (stage I-III; MV)	0.27	0.2088	307	458	4.3%	1.31 [0.87, 1.97]
Vos 2015 (IBC; MV)	0.5878	0.0796	1637	3164	5.9%	1.80 [1.54, 2.10]
Subtotal (95% CI)			**11738**	**40229**	**32.0%**	**1.48 [1.26, 1.73]**
Heterogeneity: Tau^2 = 0.03; Chi^2 = 25.23, df = 5 (P = 0.0001); I^2 = 80%						
Test for overall effect: Z = 4.79 (P < 0.00001)						
1.3.6 Invasive, BCS candidate						
Bruck 2018 (BCS - stage I; RCT)	2.5022	1.4912	50	50	0.3%	12.21 [0.66, 226.99]
Subtotal (95% CI)			**50**	**50**	**0.3%**	**12.21 [0.66, 226.99]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.68 (P = 0.09)						
1.3.7 ILC						
Fortune-Greeley 2014 (ILC; propensity)	0.392	0.1514	396	1532	5.1%	1.48 [1.10, 1.99]
Ha 2018 (ILC; propensity)	-0.1324	0.2104	196	196	4.3%	0.88 [0.58, 1.32]
Lobbes 2017 (ILC; MV)	-0.1508	0.0631	2774	2361	6.1%	0.86 [0.76, 0.97]
Mann 2010 (ILC; equivalent)	-0.08	0.2546	99	168	3.7%	0.92 [0.56, 1.52]
Vos 2015 (ILC; MV)	0	0.1968	449	231	4.5%	1.00 [0.68, 1.47]
Subtotal (95% CI)			**3914**	**4488**	**23.7%**	**1.01 [0.80, 1.27]**
Heterogeneity: Tau^2 = 0.04; Chi^2 = 11.17, df = 4 (P = 0.02); I^2 = 64%						
Test for overall effect: Z = 0.06 (P = 0.96)						
Total (95% CI)			**29860**	**102732**	**100.0%**	**1.41 [1.22, 1.64]**
Heterogeneity: Tau^2 = 0.09; Chi^2 = 281.61, df = 23 (P < 0.00001); I^2 = 92%						
Test for overall effect: Z = 4.49 (P < 0.00001)						
Test for subgroup differences: Chi^2 = 59.32, df = 6 (P < 0.00001), I^2 = 89.9%						

An odds ration of less than one indicates a lower rate of mastectomy in patients with preoperative MRI, while an odds ratio of greater than one indicates an increase in mastectomy rate. Studies are displayed in subgroups according to type or stage of cancer. Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

Figure 1.4. Initial mastectomy rate by trial type and BCS candidate



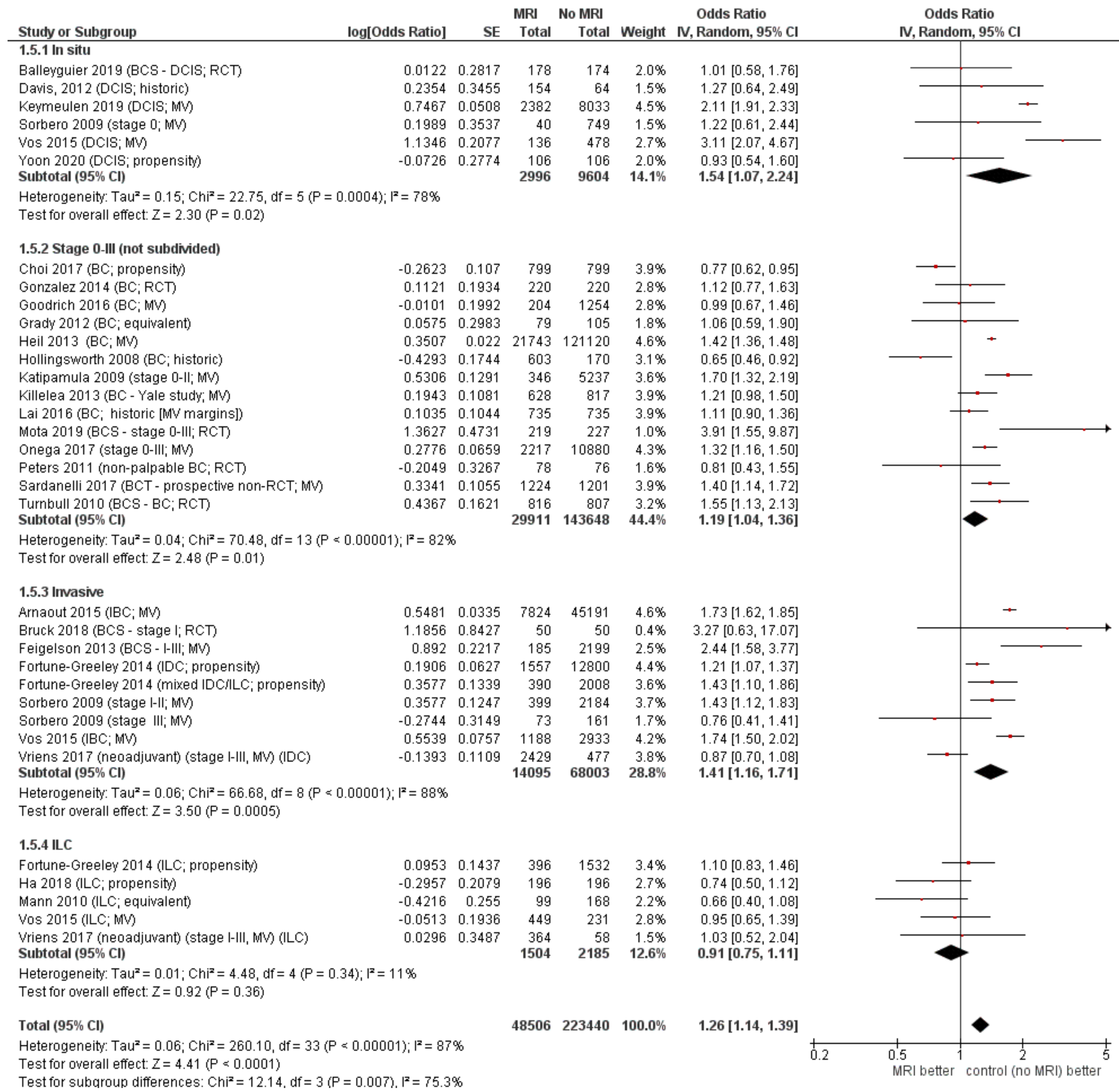
Study or Subgroup	log[Odds Ratio]	SE	MRI Total	No MRI Total	Weight	Odds Ratio IV, Random, 95% CI
1.4.1 RCT						
Gonzalez 2014 (BC; RCT)	0.2158	0.1983	220	220	4.5%	1.24 [0.84, 1.83]
Peters 2011 (non-palpable BC; RCT)	-0.0975	0.3425	78	76	2.8%	0.91 [0.46, 1.77]
Subtotal (95% CI)			**298**	**296**	**7.3%**	**1.15 [0.82, 1.61]**
Heterogeneity: Tau² = 0.00; Chi² = 0.63, df = 1 (P = 0.43); I² = 0%						
Test for overall effect: Z = 0.80 (P = 0.42)						
1.4.2 RCT, BCS candidates before MRI						
Balleyguier 2019 (BCS - DCIS; RCT)	0.8571	0.4664	178	174	1.9%	2.36 [0.94, 5.88]
Bruck 2018 (BCS - stage I; RCT)	2.5022	1.4912	50	50	0.3%	12.21 [0.66, 226.99]
Mota 2019 (BCS - stage 0-III; RCT)	2.8799	1.0353	219	227	0.5%	17.81 [2.34, 135.51]
Turnbull 2010 (BCS - BC; RCT)	1.808	0.3461	816	807	2.8%	6.10 [3.09, 12.02]
Subtotal (95% CI)			**1263**	**1258**	**5.4%**	**5.18 [2.37, 11.29]**
Heterogeneity: Tau² = 0.23; Chi² = 4.79, df = 3 (P = 0.19); I² = 37%						
Test for overall effect: Z = 4.13 (P < 0.0001)						
1.4.3 Multivariate analysis						
Kapoor 2013 (stage I-III; MV)	0.4447	0.2168	385	671	4.2%	1.56 [1.02, 2.39]
Keymeulen 2019 (DCIS; MV)	0.7975	0.0532	2382	8033	6.1%	2.22 [2.00, 2.46]
Lobbes 2017 (IDC; MV)	0.2624	0.0324	7462	21128	6.3%	1.30 [1.22, 1.39]
Lobbes 2017 (ILC; MV)	-0.1508	0.0631	2774	2361	6.1%	0.86 [0.76, 0.97]
Ozanne 2017 (stage 0-III; MV)	0.0392	0.0303	9055	46942	6.3%	1.04 [0.98, 1.10]
Parsyan 2016 (stage I-III; MV)	0.27	0.2088	307	458	4.3%	1.31 [0.87, 1.97]
Vos 2015 (DCIS; MV)	1.1569	0.2141	136	478	4.3%	3.18 [2.09, 4.84]
Vos 2015 (IBC; MV)	0.5878	0.0796	1637	3164	5.9%	1.80 [1.54, 2.10]
Vos 2015 (ILC; MV)	0	0.1968	449	231	4.5%	1.00 [0.68, 1.47]
Subtotal (95% CI)			**24587**	**83466**	**48.0%**	**1.44 [1.14, 1.81]**
Heterogeneity: Tau² = 0.11; Chi² = 232.19, df = 8 (P < 0.00001); I² = 97%						
Test for overall effect: Z = 3.08 (P = 0.002)						
1.4.4 Matched/propensity score matched						
Fortune-Greeley 2014 (IDC; propensity)	0.1906	0.0627	1557	12800	6.1%	1.21 [1.07, 1.37]
Fortune-Greeley 2014 (ILC; propensity)	0.392	0.1514	396	1532	5.1%	1.48 [1.10, 1.99]
Fortune-Greeley 2014 (mixed IDC/ILC; propensity)	0.6831	0.1417	390	2008	5.2%	1.98 [1.50, 2.61]
Ha 2018 (ILC; propensity)	-0.1324	0.2104	196	196	4.3%	0.88 [0.58, 1.32]
Yoon 2020 (DCIS; propensity)	0.1484	0.2774	106	106	3.5%	1.16 [0.67, 2.00]
Subtotal (95% CI)			**2645**	**16642**	**24.2%**	**1.33 [1.04, 1.70]**
Heterogeneity: Tau² = 0.05; Chi² = 14.54, df = 4 (P = 0.006); I² = 72%						
Test for overall effect: Z = 2.24 (P = 0.02)						
1.4.5 Equivalent or historic control						
Davis, 2012 (DCIS; historic)	0.1281	0.3768	154	64	2.5%	1.14 [0.54, 2.38]
Grady 2012 (BC; equivalent)	0.0575	0.2983	79	105	3.2%	1.06 [0.59, 1.90]
Lai 2016 (BC; historic [MV margins])	0.1635	0.1045	735	733	5.7%	1.18 [0.96, 1.45]
Mann 2010 (ILC; equivalent)	-0.08	0.2546	99	168	3.7%	0.92 [0.56, 1.52]
Subtotal (95% CI)			**1067**	**1070**	**15.2%**	**1.13 [0.95, 1.35]**
Heterogeneity: Tau² = 0.00; Chi² = 0.83, df = 3 (P = 0.84); I² = 0%						
Test for overall effect: Z = 1.37 (P = 0.17)						
Total (95% CI)			**29860**	**102732**	**100.0%**	**1.41 [1.22, 1.64]**
Heterogeneity: Tau² = 0.09; Chi² = 281.61, df = 23 (P < 0.00001); I² = 92%						
Test for overall effect: Z = 4.49 (P < 0.00001)						
Test for subgroup differences: Chi² = 15.76, df = 4 (P = 0.003), I² = 74.6%						

An odds ration of less than one indicates a lower rate of mastectomy in patients with preoperative MRI, while an odds ratio of greater than one indicates an increase in mastectomy rate. Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

Figure 1.2 groups the results according to subtype of cancer (in situ, in situ plus invasive, invasive, ILC). MRI appears to have no overall effect on mastectomy rates in ILC but increases rates in other subgroups. Figure 1.3 combines the analyses in Figures 1.1 and 1.2, and again suggests patients initially scheduled for BCS have higher rate of mastectomy after MRI, and the overall effect of MRI on ILC is neutral. Figure 1.4 looks at the effect of MRI on mastectomy rates, subdivided by trial type and whether BCS is the initial plan prior to MRI. Of the six RCTs, four were conducted in patients who were to have BCS, and these four trials found increased rates of mastectomy, as would be expected based on the patient selection. Only two RCTs involved a broader patient population; data are therefore limited but suggest MRI does not result in increased mastectomy rates. In studies with multivariate analysis or matching to control for confounders, the studies generally show a small increase in mastectomy rate (OR of 1.3 for studies not restricted to BCS candidates). However, due to the retrospective nature, these trials did not have information on the reason for receipt of MRI or surgical choice, and the increased mastectomy rate is likely due to residual confounding. In studies with equivalent or historic controls, MRI does not appear to influence mastectomy rates; this may be due to less selection bias and confounding than in the other retrospective studies where MRI and MRI groups had many differences and only some of the factors could be adjusted for.

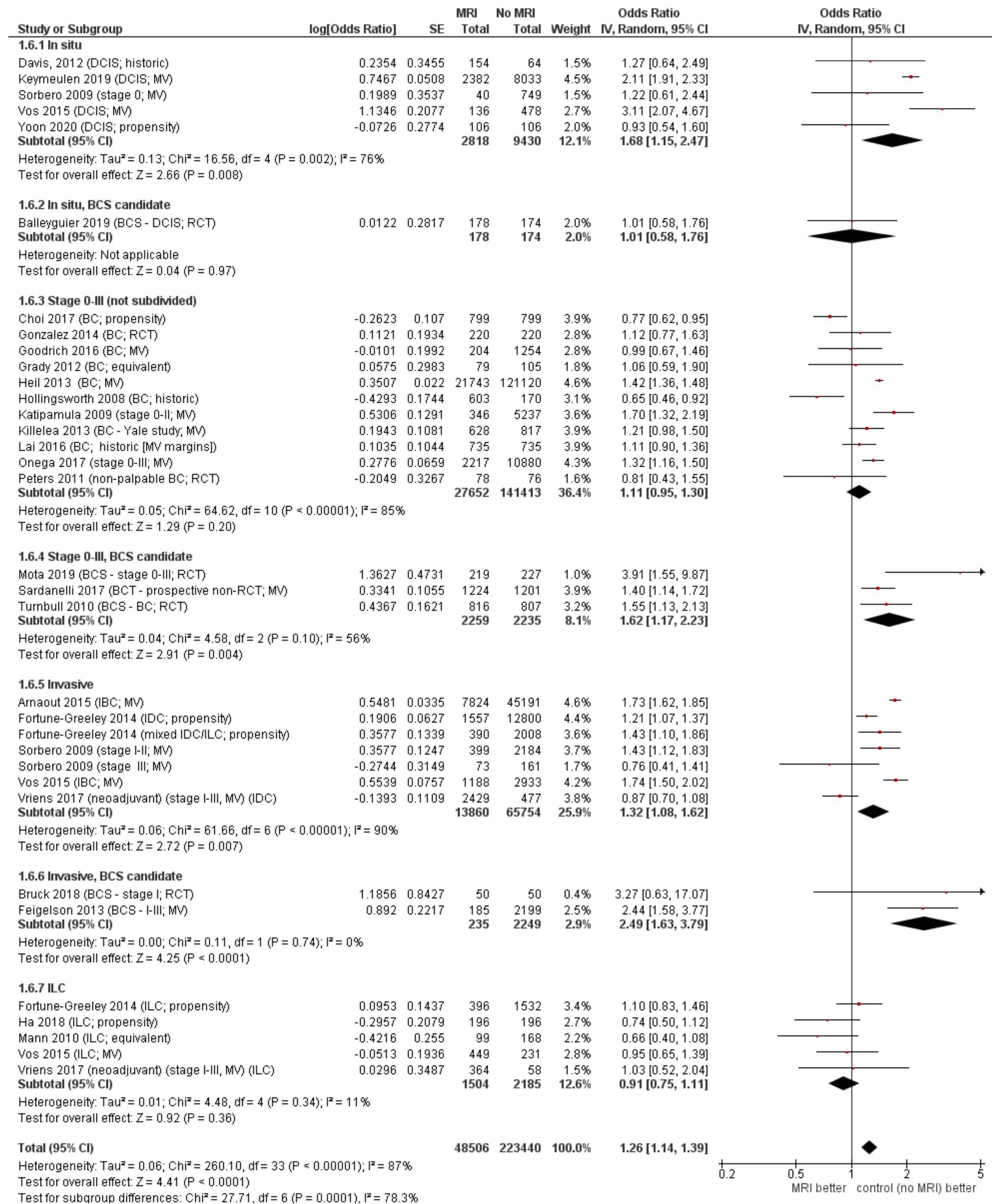
Figures 1.5 to 1.7 summarize final mastectomy rates and correspond to the initial mastectomy rates in Figures 1.2 to 1.4. While trends are similar, the ORs are lower for final mastectomy than for initial mastectomy for most of the subgroups analyzed, indicating that in patients without MRI there is more conversion from BCS to mastectomy than when MRI is initially performed. This effect is most evident in RCTs limited to patients whose treatment was determined to be BCS prior to MRI; the OR was 5.18 for initial mastectomy (Figure 1.4) and 1.72 for final mastectomy (Figure 1.7). Similar trends were found when dividing by cancer subtype (Figure 1.6). In trials not limited to predetermined BCS, results for initial and final mastectomy rates are similar.

Figure 1.5. Final (overall) mastectomy rate by subtype



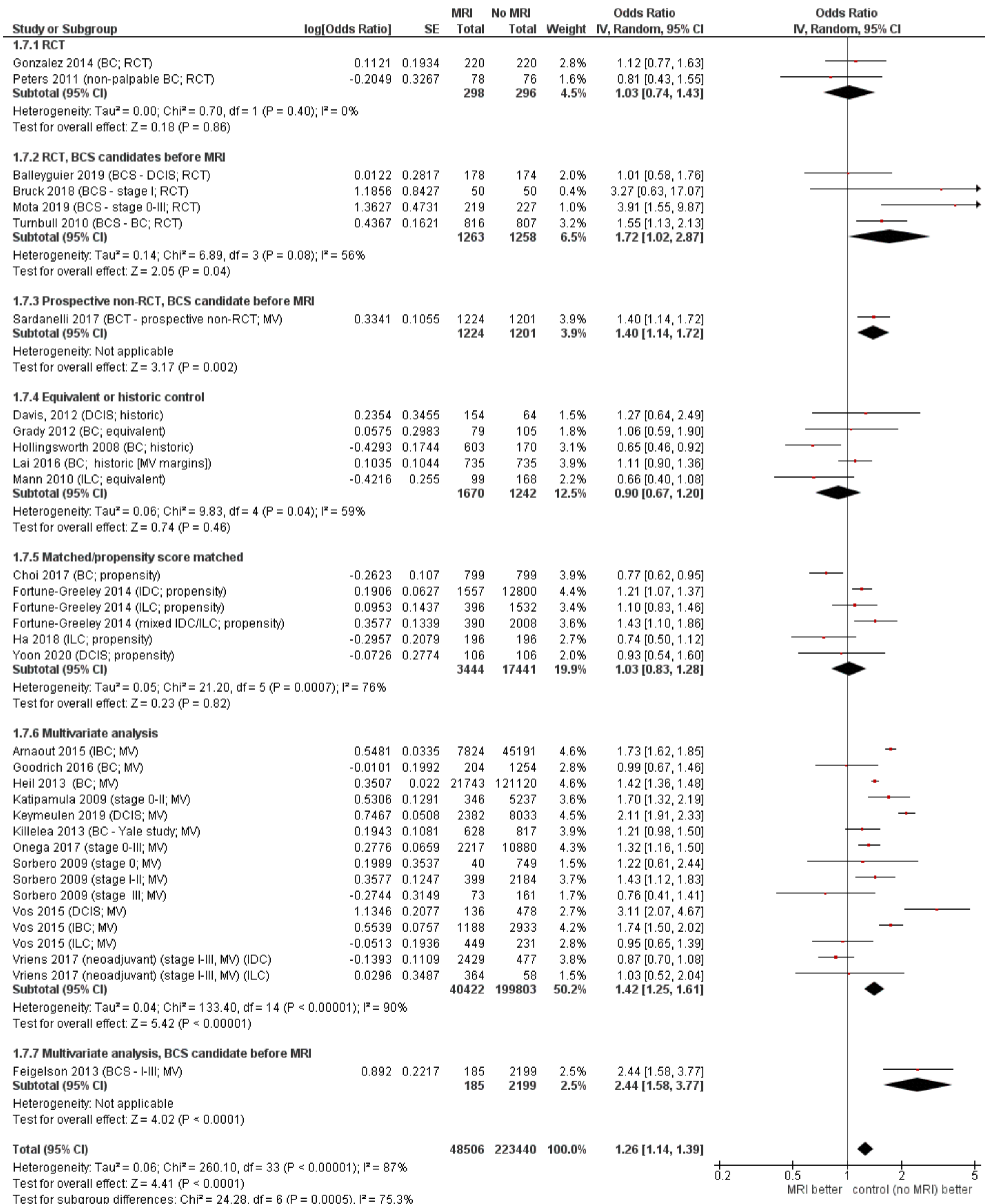
An odds ration of less than one indicates a lower rate of mastectomy in patients with preoperative MRI, while an odds ratio of greater than one indicates an increase in mastectomy rate. Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

Figure 1.6. Final (overall) mastectomy rate by subtype and BCS candidate prior to MRI



An odds ration of less than one indicates a lower rate of mastectomy in patients with preoperative MRI, while an odds ratio of greater than one indicates an increase in mastectomy rate. Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

Figure 1.7. Final (overall) mastectomy rate by trial type and BCS candidate



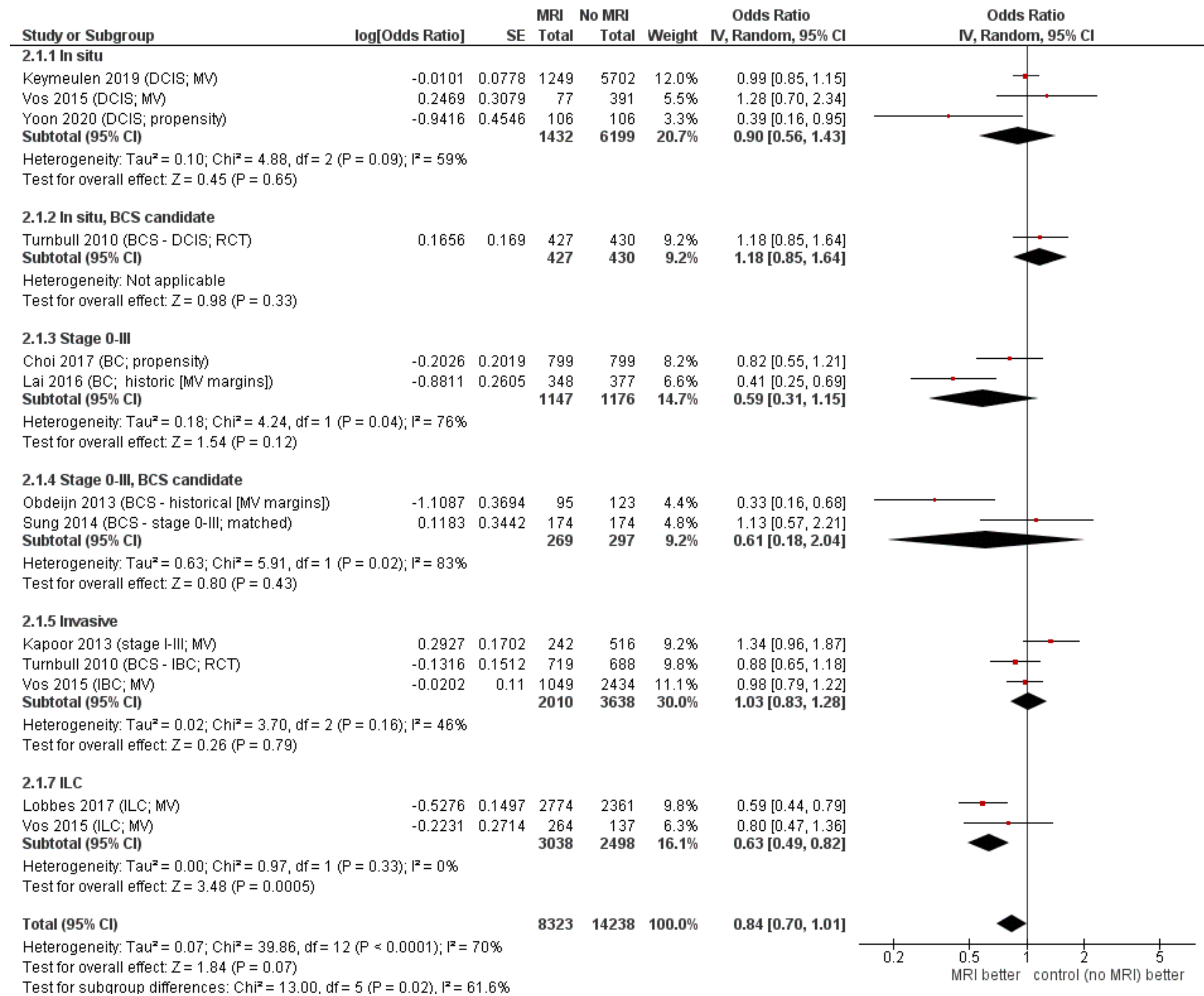
An odds ration of less than one indicates a lower rate of mastectomy in patients with preoperative MRI, while an odds ratio of greater than one indicates an increase in mastectomy rate. Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

Positive Margin and Reoperation Rates

Positive margins often result in reoperation, which may be re-excision or conversion to mastectomy. These outcomes from 31 trials in 39 publications (125-127, 129-133, 136, 139-143, 145, 146, 148-162, 164-171) are summarized in Table 3. Many of the trials only reported initial positive margin and reoperation rates in the patients who had BCS; a smaller portion of trials also reported positive margins rates in initial mastectomies. Figures 2.1 to 2.3 include 10 trials reporting positive margin rates with versus without MRI, according to various subgroups. The number of studies is small in each subgroup, limiting conclusions that can be made; however, MRI appears to decrease rates of positive margins (overall OR=0.84, 95% CI=0.70 to 1.01). It is noted that definitions of close or positive margins, and when these should result in reoperation varied among studies. Consensus guidelines for defining margins in BCS were developed by the Society of Surgical Oncology (SSO) and the American Society of Therapeutic Radiology and Oncology (ASTRO) for invasive cancer in 2014 (186, 187) and by SSO-ASTRO-ASCO for DCIS in 2016 (188, 189) and have been endorsed by several other groups (190). These guidelines define “no ink on tumour” as the standard for an adequate margin for patients with invasive cancer treated by BCS followed by whole breast radiotherapy and a 2 mm margin as the standard for an adequate margin in DCIS treated with whole breast radiotherapy. A meta-analysis found a decrease in reoperation rates after the publication of the SSO-ASTRO guideline (191) and more uniformity is expected in trials that use these definitions.

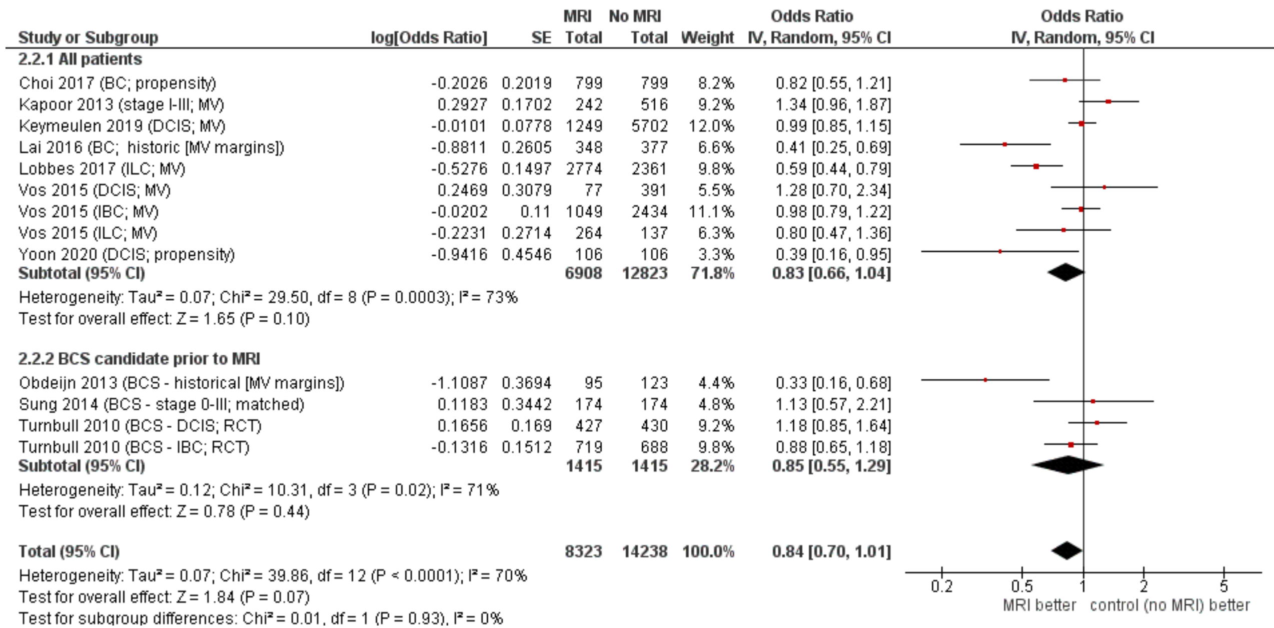
Figure 3.1 summarizes reoperations rates, with subgroups by cancer type and whether BCS was the treatment decision prior to MRI. MRI was found to reduce reoperation rates (OR=0.73, 95% CI=0.63 to 0.85). This applied to both the patients allocated BCS prior to MRI (OR=0.62, 95% CI=0.42 to 0.93) and in the other studies (OR=0.77, 95% CI=0.66 to 0.90). Figure 3.2 illustrates re-excision rates, according to the same subgroups as in Figure 3.1. The OR for re-excision is 0.81 (95% CI=0.64 to 1.03), showing a smaller effect of MRI on re-excision than on overall reoperations. Figure 3.3 indicates that MRI results in a larger and more consistent reduction in conversion mastectomy (mastectomy after initial BCS) (OR=0.67, 95% CI=0.50 to 0.90) than the reduction in re-excisions.

Figure 2.1. Positive margins by subtype + BCS candidate prior to MRI



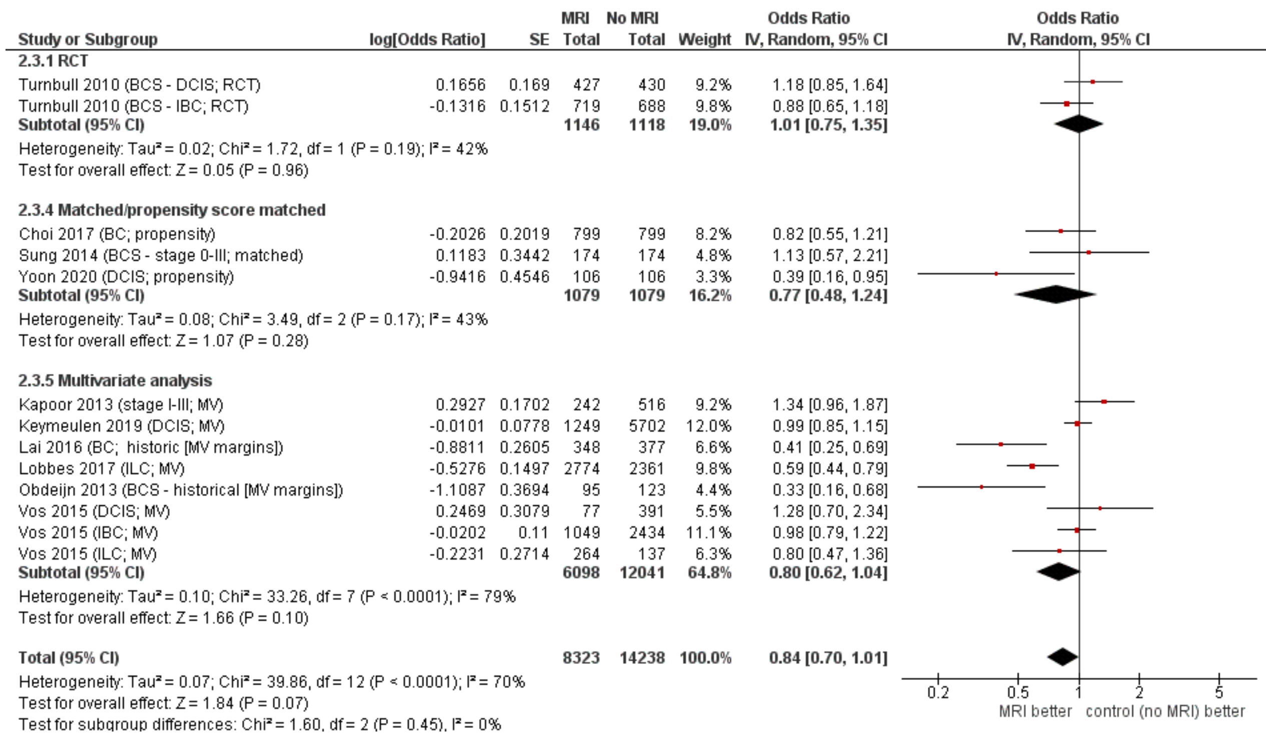
An odds ration of less than one indicates a lower rate positive margins after the first operation in patients with preoperative MRI, while an odds ratio of greater than one indicates a higher rate of positive margins. Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

Figure 2.2. Positive margins, all or BCS candidate



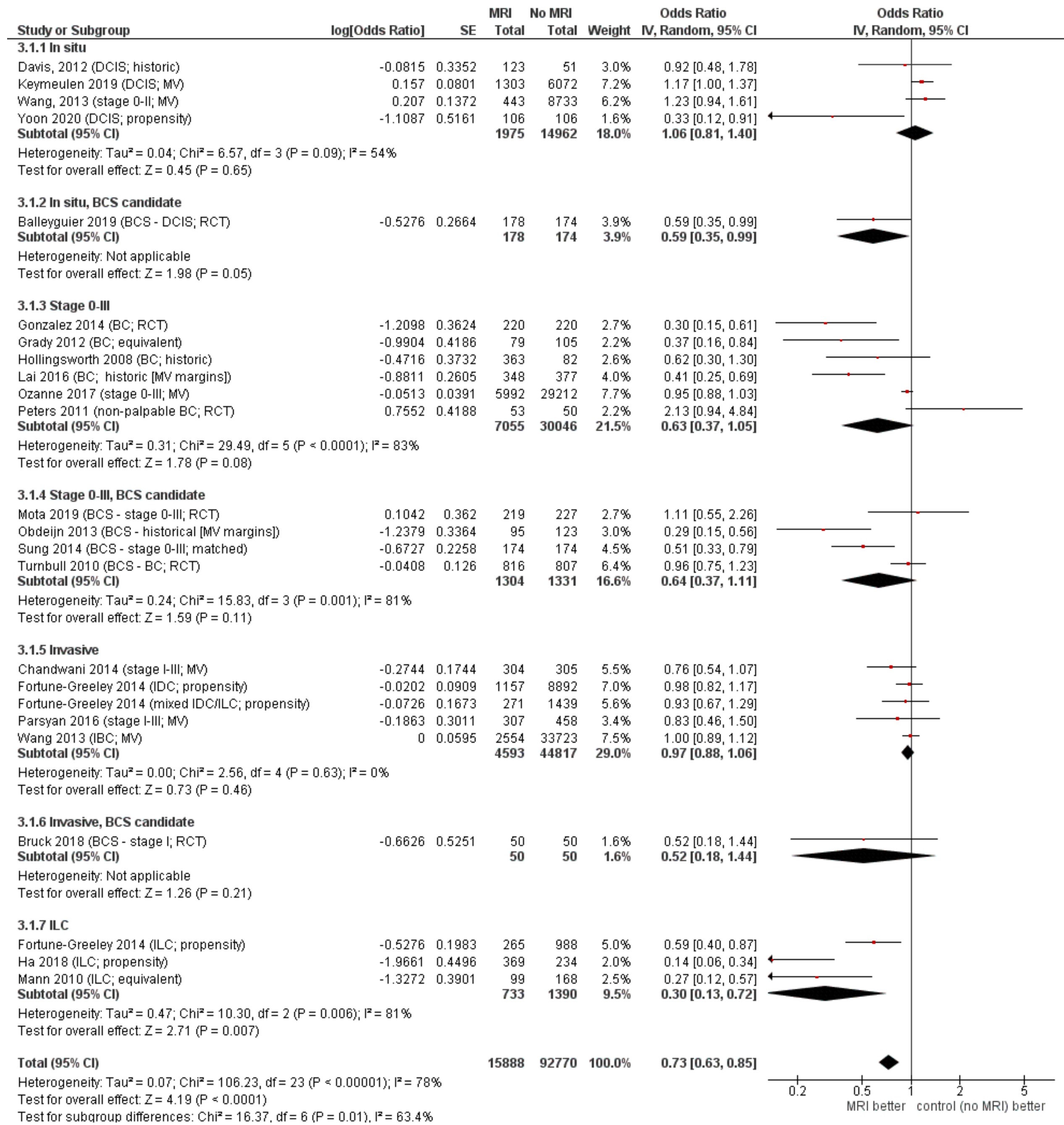
An odds ration of less than one indicates a lower rate positive margins after the first operation in patients with preoperative MRI, while an odds ratio of greater than one indicates a higher rate of positive margins. Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

Figure 2.3. Positive margins, by study type



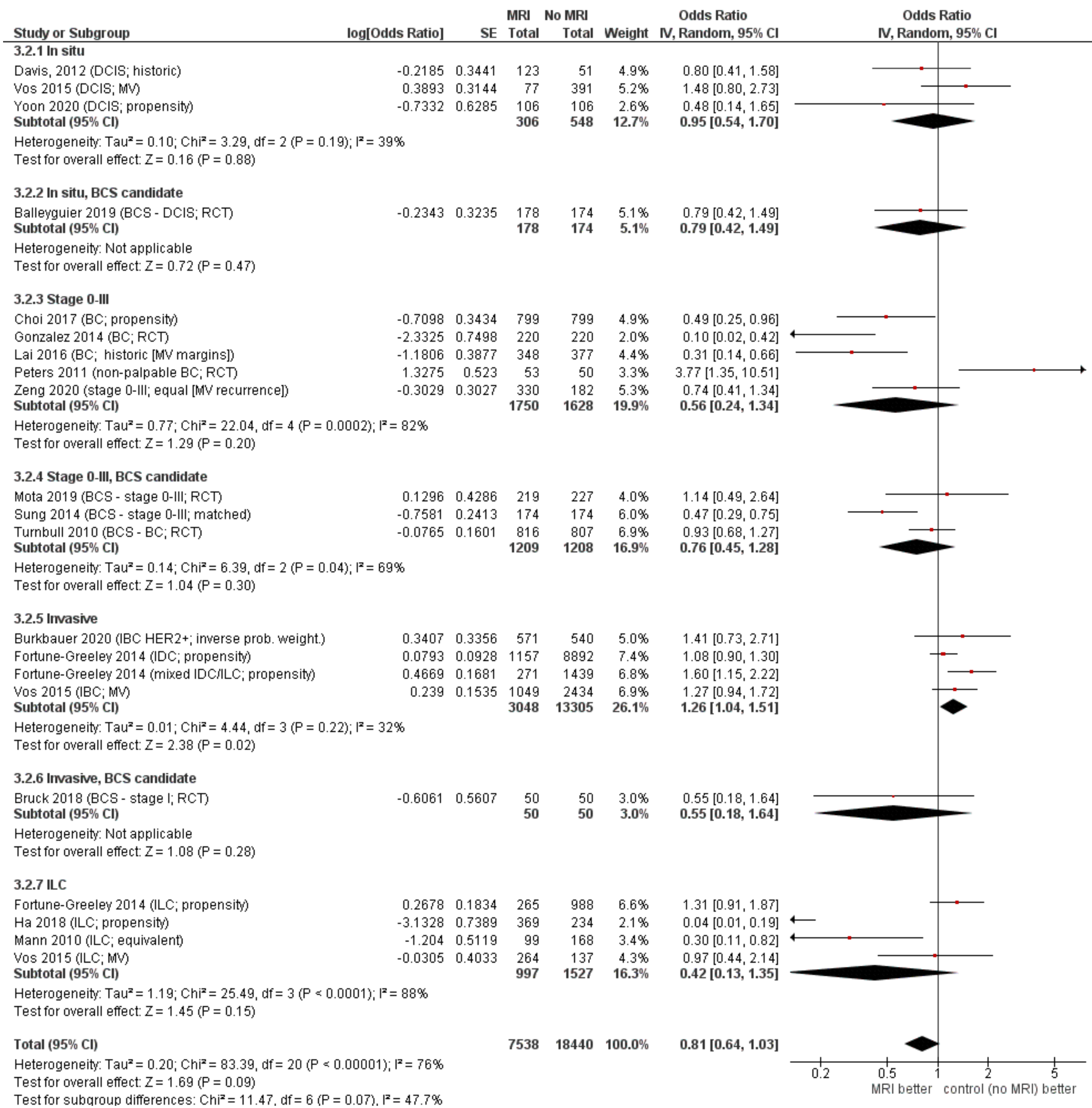
An odds ration of less than one indicates a lower rate positive margins after the first operation in patients with preoperative MRI, while an odds ratio of greater than one indicates a higher rate of positive margins. Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

Figure 3.1. Reoperations



Reoperations consist of both re-excisions and subsequent mastectomy following initial BCS. An odds ration of less than one indicates a lower rate reoperations in patients with preoperative MRI, while an odds ratio of greater than one indicates a higher rate of reoperations with MRI Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

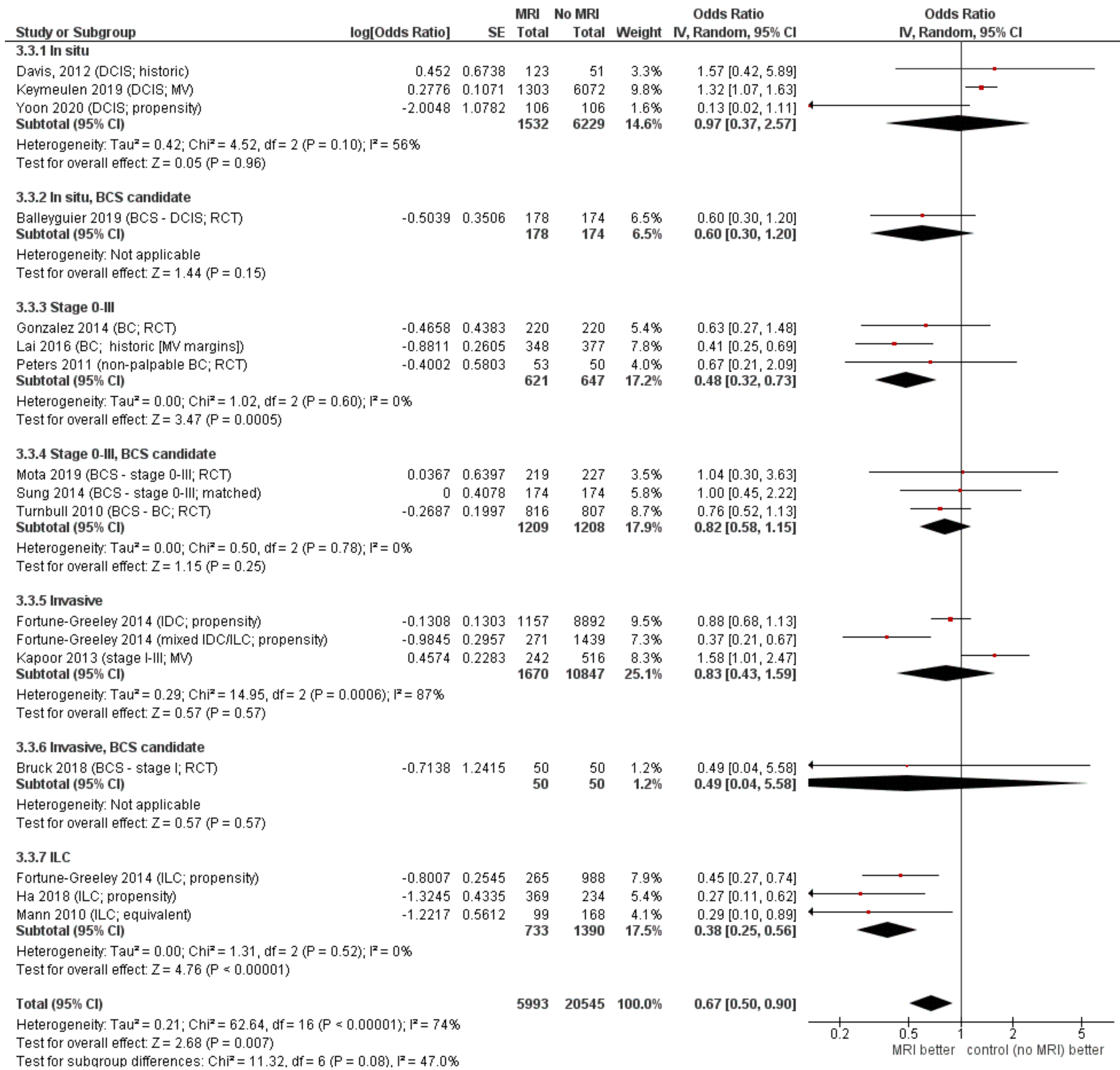
Figure 3.2. Re-excisions after the initial operation



Study or Subgroup	log[Odds Ratio]	SE	MRI Total	No MRI Total	Weight	Odds Ratio IV, Random, 95% CI
3.2.1 In situ						
Davis, 2012 (DCIS; historic)	-0.2185	0.3441	123	51	4.9%	0.80 [0.41, 1.58]
Vos 2015 (DCIS; MV)	0.3893	0.3144	77	391	5.2%	1.48 [0.80, 2.73]
Yoon 2020 (DCIS; propensity)	-0.7332	0.6285	106	106	2.6%	0.48 [0.14, 1.65]
Subtotal (95% CI)			**306**	**548**	**12.7%**	**0.95 [0.54, 1.70]**
Heterogeneity: Tau² = 0.10; Chi² = 3.29, df = 2 (P = 0.19); I² = 39%						
Test for overall effect: Z = 0.16 (P = 0.88)						
3.2.2 In situ, BCS candidate						
Balleyguier 2019 (BCS - DCIS; RCT)	-0.2343	0.3235	178	174	5.1%	0.79 [0.42, 1.49]
Subtotal (95% CI)			**178**	**174**	**5.1%**	**0.79 [0.42, 1.49]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.72 (P = 0.47)						
3.2.3 Stage 0-III						
Choi 2017 (BC; propensity)	-0.7098	0.3434	799	799	4.9%	0.49 [0.25, 0.96]
Gonzalez 2014 (BC; RCT)	-2.3325	0.7498	220	220	2.0%	0.10 [0.02, 0.42]
Lai 2016 (BC; historic [MV margins])	-1.1806	0.3877	348	377	4.4%	0.31 [0.14, 0.66]
Peters 2011 (non-palpable BC; RCT)	1.3275	0.523	53	50	3.3%	3.77 [1.35, 10.51]
Zeng 2020 (stage 0-III; equal [MV recurrence])	-0.3029	0.3027	330	182	5.3%	0.74 [0.41, 1.34]
Subtotal (95% CI)			**1750**	**1628**	**19.9%**	**0.56 [0.24, 1.34]**
Heterogeneity: Tau² = 0.77; Chi² = 22.04, df = 4 (P = 0.0002); I² = 82%						
Test for overall effect: Z = 1.29 (P = 0.20)						
3.2.4 Stage 0-III, BCS candidate						
Mota 2019 (BCS - stage 0-III; RCT)	0.1296	0.4286	219	227	4.0%	1.14 [0.49, 2.64]
Sung 2014 (BCS - stage 0-III; matched)	-0.7581	0.2413	174	174	6.0%	0.47 [0.29, 0.75]
Turnbull 2010 (BCS - BC; RCT)	-0.0765	0.1601	816	807	6.9%	0.93 [0.68, 1.27]
Subtotal (95% CI)			**1209**	**1208**	**16.9%**	**0.76 [0.45, 1.28]**
Heterogeneity: Tau² = 0.14; Chi² = 6.39, df = 2 (P = 0.04); I² = 69%						
Test for overall effect: Z = 1.04 (P = 0.30)						
3.2.5 Invasive						
Burkbauer 2020 (IBC HER2+; inverse prob. weight.)	0.3407	0.3356	571	540	5.0%	1.41 [0.73, 2.71]
Fortune-Greeley 2014 (IDC; propensity)	0.0793	0.0928	1157	8892	7.4%	1.08 [0.90, 1.30]
Fortune-Greeley 2014 (mixed IDC/ILC; propensity)	0.4669	0.1681	271	1439	6.8%	1.60 [1.15, 2.22]
Vos 2015 (IBC; MV)	0.239	0.1535	1049	2434	6.9%	1.27 [0.94, 1.72]
Subtotal (95% CI)			**3048**	**13305**	**26.1%**	**1.26 [1.04, 1.51]**
Heterogeneity: Tau² = 0.01; Chi² = 4.44, df = 3 (P = 0.22); I² = 32%						
Test for overall effect: Z = 2.38 (P = 0.02)						
3.2.6 Invasive, BCS candidate						
Bruck 2018 (BCS - stage I; RCT)	-0.6061	0.5607	50	50	3.0%	0.55 [0.18, 1.64]
Subtotal (95% CI)			**50**	**50**	**3.0%**	**0.55 [0.18, 1.64]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.08 (P = 0.28)						
3.2.7 ILC						
Fortune-Greeley 2014 (ILC; propensity)	0.2678	0.1834	265	988	6.6%	1.31 [0.91, 1.87]
Ha 2018 (ILC; propensity)	-3.1328	0.7389	369	234	2.1%	0.04 [0.01, 0.19]
Mann 2010 (ILC; equivalent)	-1.204	0.5119	99	168	3.4%	0.30 [0.11, 0.82]
Vos 2015 (ILC; MV)	-0.0305	0.4033	264	137	4.3%	0.97 [0.44, 2.14]
Subtotal (95% CI)			**997**	**1527**	**16.3%**	**0.42 [0.13, 1.35]**
Heterogeneity: Tau² = 1.19; Chi² = 25.49, df = 3 (P < 0.0001); I² = 88%						
Test for overall effect: Z = 1.45 (P = 0.15)						
Total (95% CI)			**7538**	**18440**	**100.0%**	**0.81 [0.64, 1.03]**
Heterogeneity: Tau² = 0.20; Chi² = 83.39, df = 20 (P < 0.00001); I² = 76%						
Test for overall effect: Z = 1.69 (P = 0.09)						
Test for subgroup differences: Chi² = 11.47, df = 6 (P = 0.07), I² = 47.7%						

An odds ration of less than one indicates a lower rate re-excisions in patients with preoperative MRI, while an odds ratio of greater than one indicates a higher rate of re-excisions with MRI Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

Figure 3.3. Conversion mastectomy



Conversion mastectomy occurs when patients had an initial BCS, but due to reasons such as positive margins or detection of additional tumours, a subsequent mastectomy was performed. An odds ration of less than one indicates a lower rate of conversion mastectomy in patients with preoperative MRI, while an odds ratio of greater than one indicates a higher rate of conversion mastectomy with MRI. Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

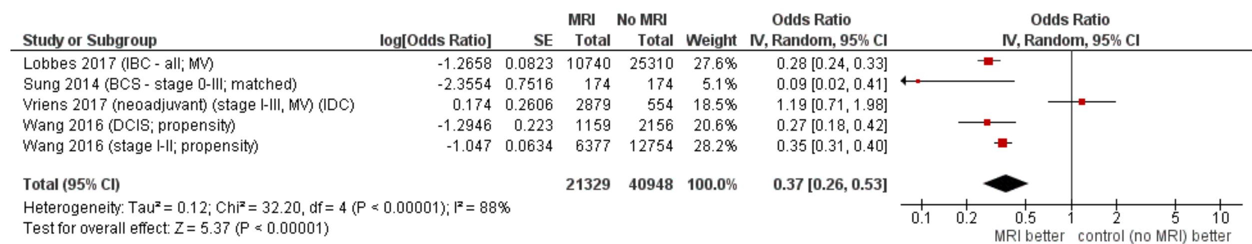
Contralateral Breast Cancer, Recurrence, and Survival Outcomes

Table 4 includes 22 trials in 24 publications (139, 148, 149, 153, 154, 157, 162, 165, 166, 170, 172-185) with outcomes of contralateral breast cancer (CBC), recurrence, or survival. CBC may be either synchronous (identified at the same time or sometimes defined as occurring within six months of the index cancer) or metachronous. Figure 4.1 illustrates that MRI increases detection of synchronous CBC (OR=0.37, 95% CI 0.26 to 0.53). Figure 4.2 shows that rates of metachronous breast cancer were lower with preoperative MRI overall (OR=0.78, 95% CI=0.56 to 1.08), although rates increased (but not significantly) in the two trials conducted in patients predetermined to be BCS candidates.

Measures of recurrence and survival varied greatly among studies (see Table 4 and Figures 5.1 to 5.7), so that only small numbers of studies reported on each outcome. Figure 5-1 indicates that MRI improves overall recurrence (OR=0.73, 95% CI=0.54 to 0.99). This result is based on six non-randomized studies. The study by Wang et al. (184) analyzed patients according to whether they received radiotherapy, and found MRI was of benefit in reducing recurrence in patients who did not have radiotherapy (OR=0.60, 95% CI=0.37 to 0.97) but had no effect on rates in those patients who had radiotherapy (OR=1.17, 95% CI=0.84 to 1.63). Other recurrence endpoints (Figures 5.2 to 5.5) together make up overall recurrence. Each of these outcomes are numerically better in the MRI groups, although they involve a relatively low number of trials and patients, and results are not statistically significant. ORs for distant recurrence, locoregional recurrence, local recurrence, and ipsilateral recurrence are 0.76 (95% CI=0.44 to 1.33), 0.90 (95% CI=0.44 to 1.84), 0.92 (95% CI=0.65 to 1.32), and 0.80 (95% CI=0.57 to 1.14).

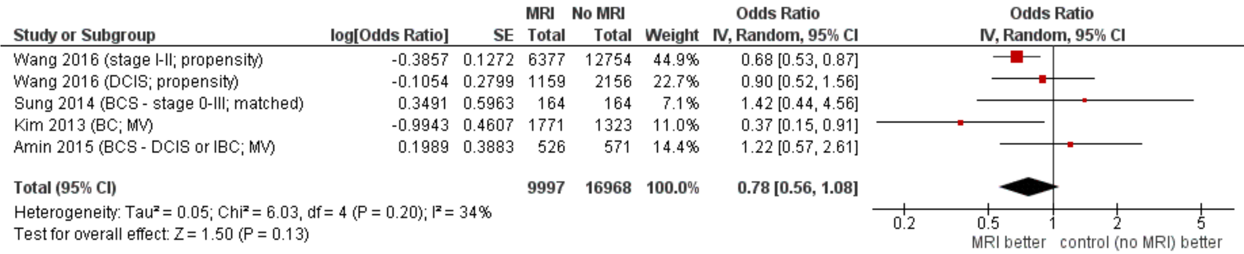
Figure 5.6 suggests that use of MRI is associated with longer recurrence-free survival (OR=0.76, 95% CI=0.53 to 1.09). The effect on overall survival is less clear (OR=0.91, 95% CI=0.75 to 1.11, p=0.36). The study by van Nijnatten et al., 2020 (179) found no effect for invasive cancer of no specific type (OR=0.96) and contributed 89.5% weight to the meta-analysis. Omitting this result, the benefit of MRI on overall survival appears greater (OR=0.60, 95% CI=0.33 to 1.09, p=0.10).

Figure 4.1. Synchronous Contralateral Breast Cancer



Synchronous CBC is detected at or around the same time as the index tumour, and therefore tumours in both breasts may be treated at the same time. An odds ration of less than one indicates a higher rate of detection of synchronous CBC in patients with preoperative MRI, while an odds ratio of greater than one indicates a lower rate of synchronous CBC with MRI Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

Figure 4. 2. Metachronous Contralateral Breast Cancer

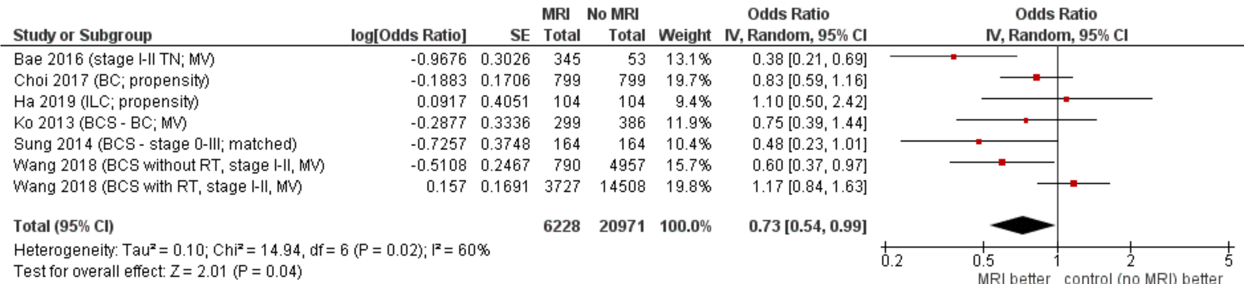


Study or Subgroup	log[Odds Ratio]	SE	MRI Total	No MRI Total	Weight	Odds Ratio IV, Random, 95% CI
Wang 2016 (stage I-II; propensity)	-0.3857	0.1272	6377	12754	44.9%	0.68 [0.53, 0.87]
Wang 2016 (DCIS; propensity)	-0.1054	0.2799	1159	2156	22.7%	0.90 [0.52, 1.56]
Sung 2014 (BCS - stage 0-III; matched)	0.3491	0.5963	164	164	7.1%	1.42 [0.44, 4.56]
Kim 2013 (BC; MV)	-0.9943	0.4607	1771	1323	11.0%	0.37 [0.15, 0.91]
Amin 2015 (BCS - DCIS or IBC; MV)	0.1989	0.3883	526	571	14.4%	1.22 [0.57, 2.61]
Total (95% CI)			**9997**	**16968**	**100.0%**	**0.78 [0.56, 1.08]**

Heterogeneity: Tau² = 0.05; Chi² = 6.03, df = 4 (P = 0.20); I² = 34%
Test for overall effect: Z = 1.50 (P = 0.13)

Metachronous CBC is detected later than the index tumour, and therefore will not be treated by surgery or RT at the same as the index tumour. It could have been present at the time of initial cancer treatment (but not detected) or developed later. An odds ration of less than one indicates a lower rate of metachronous CBC in patients with preoperative MRI, while an odds ratio of greater than one indicates a higher rate of metachronous CBC with MRI. Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

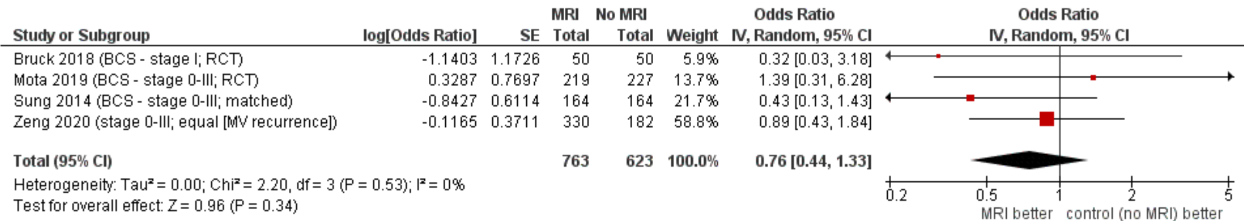
Figure 5.1. Any Recurrence



Study or Subgroup	log[Odds Ratio]	SE	MRI Total	No MRI Total	Weight	Odds Ratio IV, Random, 95% CI
Bae 2016 (stage I-II TN; MV)	-0.9676	0.3026	345	53	13.1%	0.38 [0.21, 0.69]
Choi 2017 (BC; propensity)	-0.1883	0.1706	799	799	19.7%	0.83 [0.59, 1.16]
Ha 2019 (ILC; propensity)	0.0917	0.4051	104	104	9.4%	1.10 [0.50, 2.42]
Ko 2013 (BCS - BC; MV)	-0.2877	0.3336	299	386	11.9%	0.75 [0.39, 1.44]
Sung 2014 (BCS - stage 0-III; matched)	-0.7257	0.3748	164	164	10.4%	0.48 [0.23, 1.01]
Wang 2018 (BCS without RT, stage I-II, MV)	-0.5108	0.2467	790	4957	15.7%	0.60 [0.37, 0.97]
Wang 2018 (BCS with RT, stage I-II, MV)	0.157	0.1691	3727	14508	19.8%	1.17 [0.84, 1.63]
Total (95% CI)			**6228**	**20971**	**100.0%**	**0.73 [0.54, 0.99]**

Heterogeneity: Tau² = 0.10; Chi² = 14.94, df = 6 (P = 0.02); I² = 60%
Test for overall effect: Z = 2.01 (P = 0.04)

Figure 5.2. Distant recurrence



Study or Subgroup	log[Odds Ratio]	SE	MRI Total	No MRI Total	Weight	Odds Ratio IV, Random, 95% CI
Bruck 2018 (BCS - stage I; RCT)	-1.1403	1.1726	50	50	5.9%	0.32 [0.03, 3.18]
Mota 2019 (BCS - stage 0-III; RCT)	0.3287	0.7697	219	227	13.7%	1.39 [0.31, 6.28]
Sung 2014 (BCS - stage 0-III; matched)	-0.8427	0.6114	164	164	21.7%	0.43 [0.13, 1.43]
Zeng 2020 (stage 0-III; equal [MV recurrence])	-0.1165	0.3711	330	182	58.8%	0.89 [0.43, 1.84]
Total (95% CI)			**763**	**623**	**100.0%**	**0.76 [0.44, 1.33]**

Heterogeneity: Tau² = 0.00; Chi² = 2.20, df = 3 (P = 0.53); I² = 0%
Test for overall effect: Z = 0.96 (P = 0.34)

Figure 5.3. Locoregional recurrence

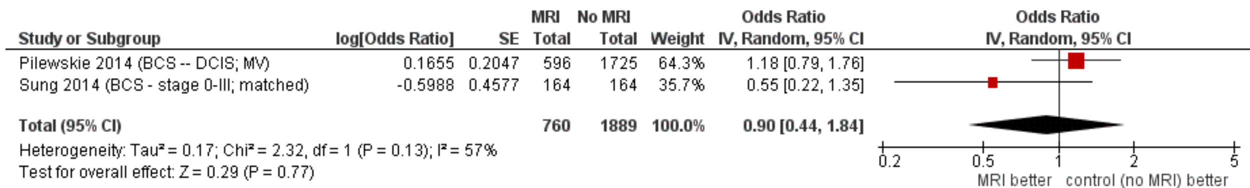


Figure 5.4. Local recurrence

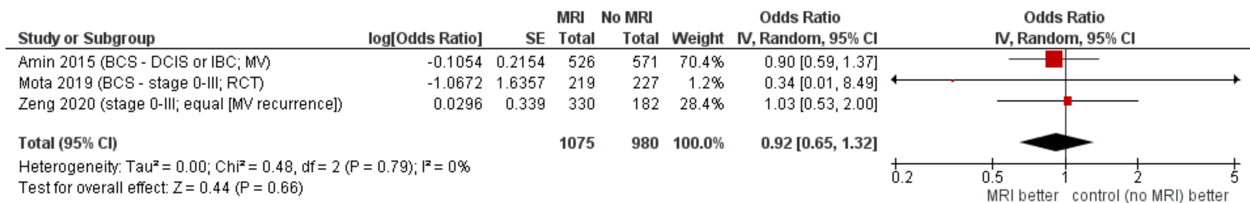


Figure 5.5. Ipsilateral recurrence

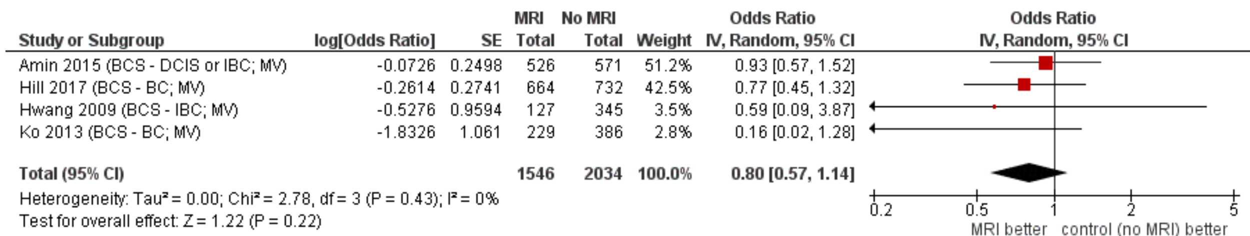


Figure 5.6. Recurrence-free survival (disease-free survival)

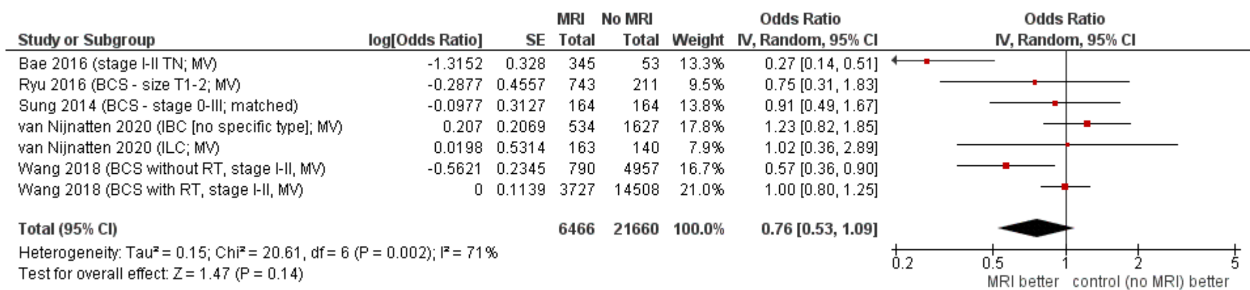
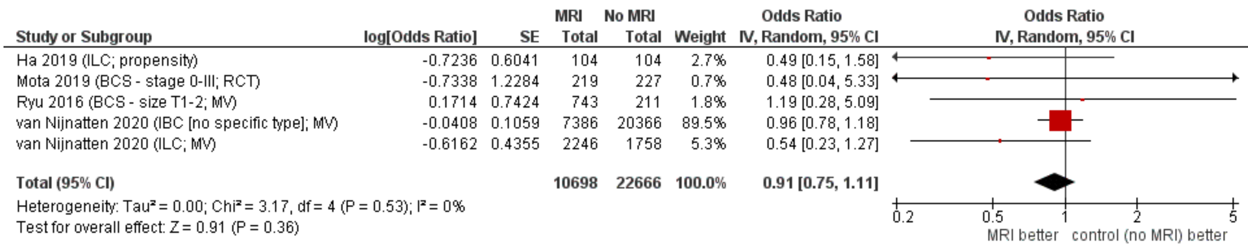


Figure 5.7. Overall survival



In Figures 5.1 to 5.7, an odds ratio less than one indicates a lower rate of recurrence or higher rate of survival in patients who had preoperative MRI. Designations in parentheses after study publication author and year are as follows: BCS, patients designated prior to MRI as candidates for BCS; subtype or stage of cancer (DCIS, ductal carcinoma in situ; BC, breast cancer, no other specification; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IBC, invasive breast cancer); trial design (RCT, randomized controlled trial; historic, historic control group without MRI; propensity, propensity score matching; equivalent, both MRI and non-MRI groups evaluated as equivalent; MV, multivariable or multivariate analysis).

Ongoing, Unpublished, or Incomplete Studies

Ongoing RCTs and prospective studies have been included in the data tables. RCTs include the ACRIN 6664/Alliance A011104 (170) and Breast-MRI (157) trials, and the B-SMART trial that was terminated but reported interim data (171). The MIPA trial (153, 154) is a large pragmatic prospective non-randomized trial that is also ongoing that may provide important long-term outcome data. The planned statistical analysis indicates that only variables significantly different between the two groups would be used as covariates; this is considered by the current authors to be inappropriate and suggests there may be high risk of bias.

Excluded Trials

Studies retained during the initial screening but excluded during data extraction primarily due to inadequate control for confounding factors or lack of outcomes of interest are summarized in Table 5 (4, 174, 192-213).

Other Systematic Reviews and Meta-Analyses

Nine systematic reviews or meta-analyses addressing MRI use in breast cancer, and four on other advanced imaging techniques are summarized in Appendix D. Two meta-analyses by Houssami et al. (214, 215) are frequently cited and address similar questions as the current review but based on more limited data. The first was an individual patient data meta-analysis for recurrence outcomes based on one RCT and three non-randomized studies (two of which did not meet the current review inclusion factors) (214). It concluded that there was no difference in 8-year local or distant recurrence-free survival. However, they only adjusted for potential confounding variables associated with recurrence at $p \le 0.01$ in univariate analysis; using such a low p value excludes many potentially relevant factors and is not a recommended statistical practice. Further, the crude rate of local recurrence was only 2%, and therefore much too low to expect any differences to be found. The more recent meta-analysis used study-level data from 3 RCTs and 19 comparative studies of invasive breast cancer (215). It did not use adjusted ORs for outcomes of interest in the current review (mastectomy, re-excision, reoperation, or positive margins) and found no evidence of effect of MRI. An increase in contralateral prophylactic mastectomy with MRI (based on adjusted ORs and three trials)

suggests the MRI and non-MRI group were not well matched and important factors influencing this outcome were not addressed.

The systematic review and meta-analysis by Di Leo et al. (216) supports the use of MRI in patients being considered for partial breast irradiation, and found MRI excluded 11% of patients initially eligible (range 6% to 25% in six studies of 3136 patients). The systematic review by Helme et al. (217) suggests a role for MRI in Paget's disease. Several guidelines recommend use of MRI in ILC, and this conclusion is supported by the data summarized in the Results section of the current meta-analysis. The review by Clauser et al. (218) suggests this conclusion regarding use of MRI in ILC may also apply to patients with atypical ductal hyperplasia and/or lobular neoplasia/LCIS as synchronous cancer rates in patients with these pathologic lesions are similar to those in patients traditionally classified as high-risk patients and for which MRI is routinely used.

Salmanoglu et al. (219) reviewed 143 papers on advanced imaging in breast cancer and notes that MRI is currently the most sensitive technique, with dedicated breast computed tomography (CT) an option when MRI is contraindicated. Use of contrast-enhanced CT is also supported by the review of Uhlig et al (220). Diffusion weighted Imaging (DWI) MRI studies were reviewed by Surov et al (221), and they recommended an apparent diffusion coefficient (ADC) threshold of 1.00×10^{-3} mm^2/s to distinguish malignant from benign lesions. Reviews suggest there may also be a role for breast-specific gamma imaging (222), proton magnetic resonance spectroscopy (223), and dedicated positron emission mammography (223). A brief summary of these modalities is given in Appendix F.

Guidelines and Technical Documents

Guidelines making recommendations on use of MRI in breast cancer or providing technical details or standards for imaging and are listed along with relevant recommendations in Appendix E. Of these publications, 19 were general guidelines on diagnosis or management of breast cancer containing one or more recommendations for MRI use (224-242), 10 were guidelines on use of MRI in breast cancer (243-252), and one focused on imaging during breast reconstruction (253). Twelve documents by the American College of Radiology (8, 254-264), and four by other groups (265-268) provide technical details or standards. There is some overlap between these groupings, as both rationale for use and technical details may be covered in the same document. It is noted that technical standards for MRI have been set by American College of Radiology Imaging Network (ACRIN) 6667 trial and the European Society of Breast Imaging (EUSOBI) (269), as well as the ACRIN 6698 trial for DWI (270). As per the scope of this review, technical documents have been listed but details were not generally extracted.

The various guidelines recommend breast MRI in several situations. Use for suspected occult primary breast cancer, evaluation of breast implants, high-risk screening, and evaluation of neoadjuvant chemotherapy response are standard indications but outside the scope of the current review. The evaluation of known or suspected multifocal or multicentric disease is an area where most guidelines agree that MRI is beneficial in deciding whether BCS is technically feasible, and if so, in guiding the procedure. MRI is also recommended in some guidelines for evaluation of the contralateral breast, prior to prophylactic mastectomy, Paget's disease of the nipple prior to BCS, discrepancy between imaging and clinical examination, indeterminant findings on mammography plus ultrasound especially if biopsy cannot be obtained, ILC with BCS, suspected involvement of the chest wall or pectoralis major muscle, evaluation of patients with dense breasts, patients eligible for partial breast irradiation, and evaluation of nipple discharge if other imaging is inconclusive or negative. CT or MRI angiography are recommended for preoperative planning prior to breast reconstruction with deep inferior epigastric perforator flaps or other oncoplastic surgery (253).

Other Considerations

While this document provides a systematic review of studies comparing patient outcomes with or without MRI, during the literature screening process it became apparent that there are several related issues to be considered. A brief overview of these issues is provided in the following subsections; a systematic review of these was not conducted.

Imaging

While the question asked is whether MRI should be used after diagnosis but before surgery, a broader question is whether additional imaging (subsequent to mammography and ultrasound) should be used, or even to replace mammography. Various advanced imaging techniques have been reviewed by Salmanoglu et al. (219) and described in the publications (271-293) summarized in Appendix F. It should be noted that several subtypes of MRI exist, at various stages of development and clinical usage, and the more common of these are also indicated (271-276). While all are within scope of this review, most studies comparing patient outcomes with and without MRI used CE-MRI. Some of the other MRI techniques have equivalent or better performance than CE-MRI and other advantages and need also be considered in any future discussion of MRI implementation. In particular, DWI provides additional information without the need for contrast agents and may be an option for patients with allergy or other contraindications to gadolinium contrast agents. Magnetic resonance spectroscopy (MRS) can also provide metabolic or functional information. The combination of CE-MRI, DWI, and MRS referred to as multiparametric MRI captures information beyond that of individual techniques and may reduce the need for biopsies. Accelerated and abbreviated MRI can shorten the image acquisition time to a few minutes, bringing down the cost substantially.

Contrast agents in general usage for CE-MRI are gadolinium-based and are summarized in Appendix F (154, 258, 294-309). Gadobenate dimeglumine (linear), gadobutrol (macrocyclic), and gadoterate meglumine (macrocylic) are the most commonly used in current practice. Gadoteridol is another macrocyclic agent used in brain and spinal MRI, but also approved for breast and other applications. Adverse effects including allergic reactions vary with the agent used. Nephrogenic systemic fibrosis has been observed mainly in patients with advanced renal failure (295); this appears more common with the linear agents gadopentetate dimeglumine, and gadodiamide, and use of these is not recommended in these patients (258, 310). Gadolinium deposition, especially after multiple MRIs, has been reported in the brain, although it is unknown whether this is harmful (307). The European Union has suspended use of all linear agents (except for liver or intra-articular use) due to this concern (311), although they are still used elsewhere. Guidelines such as The ACR Manual on Contrast Media (258) cover these topics in more detail.

Positioning During Imaging in Surgery

Breast MRI is usually performed in the prone position to overcome motion artifacts from respiration and provides the best position for signal, image quality, and definition, while surgery, ultrasound, and ultrasound-guided biopsy are conducted with the patient in the supine position (312-314). The breast tumours are deformed or displaced due to the change in patient position. The full MRI information is not adequately translated and it is difficult to accurately mark or determine the tumour location. This may be reflected in failure of MRI in some studies to reduce positive margins or need for re-excision. Supine positioning simplifies registration of images and aids **BCS** but appears to still be experimental. Joukainen et al. (313) found that for 27 lesions in 14 consecutive patients, compared to histology, prone MRI overestimated tumour size by 47.1% and supine MRI by 14.5%. The mean distance from the chest wall decreased by 69.4% and the nipple by 18.2%. Arıbal and Buğdaycı (314) found that supplementary abbreviated

supine MRI immediately after prone MRI detected 44 of 45 lesions initially found by prone MRI. Sakakibara et al. (315) compared patients with DCIS >2 cm diagnosed with vacuum-assisted core needle biopsy who had mammography plus prone MRI and conventional quadranectomy using hooked wires to those with patients who had mammography plus supine MRI-guided quadranectomy. The supine group had less additional intraoperative resection and lower rate of DCIS in a surgical margin. A study of 15 patients (316, 317) determined supine intraoperative MRI to be feasible and found changes in tumour volume and distance of the tumour from the chest wall and nipple compared to prone MRI. Barth et al. (318) conducted a randomized trial of 138 patients with non-palpable invasive cancers comparing preoperative supine MRI plus intraoperative optical scanning versus wire localized lumpectomy and found positive margins in 12% versus 23% (p=0.08), while mean specimen volumes were not different (74 mL vs. 70 mL, p=0.45). Information from supine MRI has been used to create 3-D printing surgical guides (319-321) and 3D models (322).

Breast Density

The Canadian National Breast Screening Study found a strong correlation between breast density and breast cancer risk (323). It is noted that the randomization process has been criticized and the results regarding use of mammography for screening are therefore controversial. A systematic review and meta-analysis (324) found breast density is one of the strongest risk factors for breast cancer. In the general population the relative risk of breast cancer on pre-diagnostic mammogram (compared to density of <5%) was 1.79 for density 5% to 24%; 2.11 for density of 25 to 49%, 2.92 for density of 50% to 74%, and 4.64 for density ≥75%.

Dense breasts are normal and common: 43.3% of women 40 to 74 years of age have heterogeneously or extremely dense breasts, and the incidence decreases with age, particularly around menopause (325). In dense breasts, mammography is not very sensitive, and ultrasound is often used, but may also not be sensitive. In a study of digital screening mammography of 365,426 women in centres of the Breast Cancer Surveillance Consortium (USA), the sensitivity of mammography in women aged 40 to 74 years decreases with increasing breast density (326). Ranges for sensitivity (depending on age group) were 81% to 93% for fatty breasts, 84% to 90% for breasts with scattered fibroglandular density, 69% to 81% for heterogeneously dense breasts and 57% to 71% for extremely dense breasts. Except in the extremely dense breasts, sensitivity in each group was lowest in the age subgroup aged 40 to 49 years. The Ottawa study of preoperative breast MRI in all consecutive patients found a significant correlation in findings affecting surgical management in women which increased with breast tissue density (327), Bishop et al. (328) reported sensitivities of 59% for mammography, 65% for ultrasound, and 97% for MRI. Vashi et al. (329) found no difference between the ability of MRI to detect additional lesions in dense versus non-dense breasts and concluded to use MRI in all patients to determine extent of disease. Gadobenate dimeglumine-enhanced MRI was significantly (p<0.02) superior to gadopentetate dimeglumine-enhanced MRI and mammography or ultrasound for malignant lesion detection, particularly in heterogeneously dense breasts (301). Density is greater in women with smaller breasts, younger age, or less than two pregnancies (330).

The Supplemental MRI Screening for Women with Extremely Dense Breast Tissue (DENSE trial, NCT01315015) (331) randomized 40,373 women with extremely dense breast tissue and normal screening mammography to either supplemental MRI or only mammography, and found MRI resulted in fewer interval cancers (thus, it found cancers earlier). Interval cancers were reduced by 50% in those offered MRI, and 80% in those who agreed to have an MRI (332, 333).

The GEMMA-1 and GEMMA-2 prospective trials studied women (n=906 total) with newly diagnosed and histologically proven breast cancer before surgery (306). They found CE-MRI more sensitive (80% to 89%) than unenhanced MRI alone (37% to 73%) or mammography (68% to 73%). Specificity of CE-MRI was 83% to 95%. Additional analysis by breast density (334) found

CE-MRI sensitivity was independent of breast density while sensitivity of x-ray mammography declined for index cancers (Gemma-1 83% to 83% MRI vs. 79% to 62% mammography as density increased; Gemma-2 91% to 91% MRI vs. 82% to 64% mammography). For additional cancers, MRI sensitivity increased with density (Gemma-1 50% to 73% vs. 34% to 20%; Gemma-2 57% to 81% vs. 24% to 25%). Elmi et al. (335) found that MRI detected more malignancy than mammography over all breast densities, and detected more than digital breast tomosynthesis in women with dense breasts.

Hormonal, Menstrual, or Menopausal Status

Background parenchymal enhancement in normal breast tissue varies with age, week of menstrual cycle, menopausal status, lactation, and use of exogenous hormones or endocrine therapy (336-338). It is sometimes recommended that non-urgent MRI in premenopausal women be conducted during the second week (days 7-15) of the menstrual cycle as background parenchymal enhancement is lower during this time. Using DWI-MRI, differences in ADC during the menstrual cycle are small and not statistically significant (339-341). ADC values are lower in postmenopausal compared to premenopausal women (340, 342, 343).

Screening

Riedl et al. (344) reported sensitivity of 90% with MRI, 37.5% with mammography, and 37.5% with ultrasound in screening high-risk women; 45% of cancers were detected only by MRI and there was no advantage to supplementing MRI with ultrasound or mammography. MRI is recommended in screening women at high risk of cancer (345). There is controversy as to whether MRI alone (without mammography or ultrasound) is sufficient for screening, and trials are ongoing. Conventionally, DCIS manifested as calcifications on mammography (especially BI-RADS 3) were detected more frequently with mammography than MRI and it was thought that such disease presentations were not detectable by MRI. With modern optimized techniques and improvements in interpretation, detection of DCIS is higher than in older studies and exceeds that of mammography or ultrasound (5). A high-risk breast screening study in Ontario reported on DCIS detection rates divided by periods before and after July 2001 to reflect advances in MRI methodology and expertise (6). In the early period there were 2 cases of DCIS (both not detected by MRI) out of 15 cases of cancer in 223 women. In the later period there were 10 cases of DCIS out of 29 cancers in 391 women; all of the DCIS cases were detected by MRI but only one by mammography. The largest and most often cited study was conducted Kuhl et al. in 7319 women, of whom 167 had both preoperative mammography and MRI and a final pathological diagnosis of DCIS (7). MRI was conducted for various reasons; 93 had an abnormal mammogram and 74 had normal mammogram (including screening in 29 women at average risk and 8 at increased familial risk). In patients with DCIS, sensitivity of mammography was 56% and MRI was 92% ($p<0.0001$); MRI sensitivity was greater in those with high-grade DCIS (98%) and intermediate grade DCIS (91%) than in low-grade DCIS (80%).

Occult Cancer

Occult breast cancer refers to cancer in axillary lymph nodes or metastasis to other locations with histology consistent with breast cancer but with no identified primary or index cancer detectable by physical examination and usual radiologic examination (breast ultrasound and mammography). MRI is often used in patients with occult breast cancer, although positron emission tomography (PET)-CT may also be used, especially to detect other sites of malignancy, or when the primary type is unknown (cancer of unknown primary) (346, 347). Small studies have found that non-treatment (observation) resulted in higher rates of local recurrence than radiotherapy or mastectomy (348, 349). This use of MRI is outside the scope of the current review.

Detection of Additional Ipsilateral Lesions

The recent study by Goodman et al. (350) looked for additional ipsilateral mammographically occult tumours that were more than 2 cm from the primary tumour and found 150 in 129 patients out of 667 consecutive patients with preoperative breast MRI. One additional tumour was found in 112 of 129 patients (86.8%)m, while 17 of 129 patients (13.2%) had two or more additional tumours. In 71 of 129 patients (55.0%) tumours were in different quadrants and in 58 of 129 patients (45%) tumours were found in the same quadrant as the original tumour but ≥2 cm away. In 20 of 129 patients (15.5%), the additional tumour was larger than the original/primary and in 26 of 129 patients (20.2%) the additional tumour was at least 1 cm.

Iacconi et al. (351) reported a retrospective review of 2021 patients who had biopsy after preoperative MRI. Of these, 285 (14%) had additional cancer detected by MRI. In 73 patients (3.6%) there were 87 cancers in different quadrants than the index cancer. In 17 of 73 patients (23%) the MRI-detected tumour was larger than the known index lesion, and in 18 of 73 patients (25%) the tumours were larger than 1 cm.

Contralateral Breast Cancer

Many studies have established that the rate of CBC in patients with breast cancer is higher than baseline rates for breast cancer in the general population. MRI may detect mammographically occult tumours in the contralateral breast that would not otherwise be treated by surgery or radiotherapy. There may be a significant effect on rates of subsequent operations and survival, especially for patients who do not have adjuvant therapy. A meta-analysis of 22 studies found the incremental cancer detection rate in the contralateral breast over conventional imaging to be 4.1% (352).

The following studies provide additional examples of utility of breast MRI in detection of contralateral cancer. In a study of 367 women with newly diagnosed breast cancer, there were 15 cancers (4.1%) in the contralateral breast, of which 14 (93%) were detected by MRI and one was detected by prophylactic mastectomy (353). In a study of 425 women with newly diagnosed cancer who underwent bilateral MRI, MRI found contralateral lesions requiring biopsy in 72 of 425 patients (17%); of these 16 of 72 patients (22%) had pathologically confirmed carcinoma, giving a rate of contralateral carcinoma detected by MRI of 3.8% overall, and 5.4% in those aged 70+ years (354). In a study of 103 women with newly diagnosed cancer, MRI lead to biopsy in 10% and found four cancers in the contralateral breast (4%), whereas mammography detected none (355). In the ACRIN 6667 trial (356-359), MRI detected malignant lesions in the contralateral breast in 30 of 969 patients. Patient factors and not breast MRI imaging were the main determinants in contralateral mastectomy. The incidence rate of contralateral cancer was 3.1%, and much higher than the 1% found by MRI in a study of high-risk patients. In 182 patients with newly diagnosed breast cancer after biopsy (360), CE-MRI detected suspicious lesions in the contralateral breast in 15 patients (8.2%), resulting in diagnosis of malignant results in 7 patients (3.8%). Of these there were four DCIS, two invasive ductal carcinomas with DCIS, and one invasive ductal carcinoma. Of the others, there were four fibrocystic changes, two atypical ductal hyperplasia, one atypical lobular hyperplasia and focal LCIS, and one ductal hyperplasia. Lai et al. (361) found preoperative MRI detected contralateral lesions in 70 of 735 (9.5%) patients with known unilateral breast cancer, with malignancy in 21 of 44 (47.7%) of those who had surgical interventions; of these there were 7 invasive ductal carcinoma, 1 mucinous carcinoma, and 13 DCIS. A study found MRI had a negative predictive value of 96.1% for synchronous contralateral cancer in 51 patients with a new diagnosis of invasive breast cancer or DCIS (362), suggesting it could be used to rule out the need for prophylactic contralateral mastectomy. In 35 patients with ILC, MRI detected contralateral lesions in 9

patients (24%), of which three (8%) were ILC and one was DCIS (363). In patients with invasive (ducto)lobular cancer, preoperative MRI detected clinically relevant findings (size discrepancy ≥5 mm or additional lesions) in 63% of patients, which on further workup included contralateral cancer in 9%, additional ipsilateral malignant foci in 18%, and more extensive disease in 20% (364).

Studies suggest that CBC, whether synchronous or metachronous, is usually a new or independent primary cancer instead of locoregional recurrence or metastasis (365, 366). A genetic analysis found that in 49 patients, only three sets of contralateral cancers were clonally related and consistent with metastasis, and an additional three sets had a solitary matching mutation (365). A study of based on the Netherlands Cancer Registry found a significant decrease from 2003 to 2008 for local recurrence (3.2% to 2.4%), regional recurrence (1.8% to 1.3%), and distant metastases (10.5% to 7.1%), but stable rates of CBC (3.1% to 2.8%, p=0.56) (366). Chemotherapy and hormonal therapy reduced the risk of recurrence and CBC, while tumour factors conferring risk for recurrence did not affect CBC rates.

Concordance or Correlation with Other Imaging or Biopsy

A study by Saunders et al. (367) found use of MRI avoided surgical excision in 68.9% of patients in which there was discordance between mammogram or ultrasound and benign core biopsy results. Lee et al. (283) found that for cases with discordance between MRI imaging and ultrasound-directed biopsy, 26% of presumed sonographic correlates localized to a site distinct from the MRI-detected lesion. Several studies suggest that when benign pathology is concordant to MRI imaging the false negative rate is around 2% to 5% (368-370). Even with MRI-guided biopsy, some lesions may be missed (369, 371).

MRI and Radiotherapy

MRI and/or CT are often used for radiotherapy treatment planning (372), and are often a requirement for partial breast irradiation protocols to determine patient eligibility (250). A systematic review and meta-analysis including six studies and 3136 patients, all of which used NSABP B-39 trial criteria, found MRI excluded 6% to 25% (pooled value 11%) of patients who had been deemed eligible for partial breast irradiation prior to MRI assessment (216). This represented 2% to 20% of all patients, and the authors concluded that MRI should be used in selection of patients for partial breast irradiation. Several studies reported on secondary cancers found by MRI that would not be removed by surgery or targeted in the radiotherapy field of partial breast irradiation (373-379). Kowalchik et al. (378) reported that of 566 women deemed eligible for partial breast irradiation according to NSABP B-39 inclusion criteria with physical examination, mammogram and/or ultrasound, MRI altered the recommendation for 141 patients (25%). There were 118 (21%) with additional ipsilateral cancer including 62 (11%) with more extensive disease, 64 (11%) with multicentric disease, and 28 (5%) contralateral cancer. A similar study (379) in patients with DCIS found 23 of 117 patients (20%) were ineligible for partial breast irradiation based on MRI results; 21 (18%) had additional ipsilateral cancer of which 5 (13%) had more extensive disease, 6 (5%) had multicentric disease, and 4 (4%) had cancer in the contralateral breast. MRI therefore changed treatment recommendations in 20% of patients.

Axilla/Axillary Staging

Several systematic reviews report on the use of MRI to detect axillary lymph node metastases, and thus possibly avoid sentinel lymph node biopsy or axillary lymph node dissection. Six reviews reported pooled sensitivities of 77% to 89%, and specificity of 82% to 93%. Some reviews did not specify the type of MRI (380, 381), while others included only DWI (382-384), either DWI or CE-MRI (DCE-MRI) (385, 386), or MRI + other techniques (387). DWI has

been reported to have higher sensitivity and specificity than conventional MRI (388). Dedicated axillary MRI may be more accurate than breast MRI (389). Kuckelman et al. (390) indicated that axillary specific protocols are not commonly used in the clinic. Superparamagnetic iron oxide (SPIO)-enhanced 3 T MRI was reported to have 100% sensitivity, 96% specificity and 97% accuracy for diagnosis of sentinel node metastases (391, 392), and is the basis of an ongoing trial (393). A study with ultrasmall SPIO reported 100% sensitivity, 98% specificity, and 98% accuracy on a node-by-node basis (394). SPIO has also been studied as a tracer for sentinel lymph node biopsy (395). MRI is able to detect involved internal mammary nodes (396-398). Use of MRI in radiotherapy planning can result in more precise targeting of lymph nodes (397, 399-404).

Standard versus Oncoplastic Surgery versus Mastectomy or Nipple-Sparing Mastectomy

Standard BCS may lead to fair to poor esthetic and functional results (405) and more complex oncoplastic surgery or mastectomy may be more appropriate if the optimal tumour-to-breast ratio for each quadrant is exceeded. Breast MRI or other advanced imaging (PET/CT) may be a prerequisite for extreme oncoplasty (BCS using oncoplastic techniques in patients for whom most physicians would not do so; generally >5 cm multifocal or multicentric tumours) (406).

MRI is frequently used prior to nipple-sparing mastectomy, especially in the case of centrally located tumours (407-411). Others suggest MRI does not improve detection of occult nipple-areola complex involvement (412). This may be at least in part due to non-optimal MRI technique and interpretation; Gao et al. (413) (plus commentary (414)) published a detailed analysis of normal nipple enhancement with breast MRI and radiologic-pathologic correlation and suggest that 2 cm is no longer the minimum tumour-to-nipple distance. Tumour-to-nipple distance of 1-2 cm is no longer a contraindication to nipple-sparing mastectomy (413, 415-419). Ponzone et al. found a distance of 5 mm allows optimal discrimination between positive and negative nipple-areola complex cases (420). A single abbreviated breast MRI scan was found by Liu et al. (421) to reduce the need for biopsy of the nipple-areolar complex in nipple-sparing mastectomy. DWI has also been found to predict nipple-areola complex invasion (422).

MRI used to characterize blood supply and innervation for autologous tissue flaps (423, 424) and other planning of nipple-sparing mastectomy may reduce rates of post-surgical complications including skin flap ischemia and nipple-areola complex necrosis (425-428).

Nipple Involvement or Discharge

Del Riego et al. (411) provide a pictorial review and diagnostic algorithm to evaluate benign and malignant diseases affecting the nipple-areolar complex, and indicate that this area has special anatomic and histologic characteristics, requires multimodal approach, and can present a challenge to radiologists. Reviews (429, 430) indicate that MRI had sensitivity superior to galactography for pathologic nipple discharge; while ductoscopy and MRI are both options, MRI has superior sensitivity and provides additional information (431). A network meta-analysis for diagnosis of pathologic nipple discharge (432) evaluates diagnostic efficacy of ultrasound, mammography, cytology, MRI, and ductoscopy. They found that MRI is the most sensitive for detecting malignancy (83%), followed by ductoscopy (58%), ultrasound (50%), cytology (38%), and mammography (22%). Specificity was highest for mammogram (93%), then ductoscopy (92%), cytology (90%), MRI (76%), and ultrasound (69%).

DISCUSSION AND CONCLUSIONS

MRI is one of the most sensitive imaging techniques in detecting breast tumours, with the potential to be highly specific. Performance depends on the equipment and MRI techniques used and expertise of those conducting the analysis. Guidance on performance of CE-MRI and

biopsies by the Canadian Association of Radiologists, American College of Radiology, EUSOBI, and others as listed in Appendix E of may be useful; however, these were not critically reviewed or compared in this evidence summary.

This systematic review compiled a comprehensive set of data from trials comparing patient outcomes with and without preoperative MRI. Data from RCT trials were of limited usefulness as all had some deficiencies and evidence was considered moderate to low quality. Non-randomized trials were determined to provide evidence of similar quality as RCTs. Due to absence of information suggesting one type of trial provided stronger evidence, limited data, and for ease of presentation, evidence from all trial types was combined, with data in some forest plots subdivided according to trial type. A strength of this approach is that a much larger number of trials informs the observations and conclusions.

The outcome of mastectomy rates (as opposed to BCS) is commonly reported but of limited use in determining whether MRI should be used. MRI's advantage is its greater sensitivity than mammography and ultrasound, and thus by definition should find more lesions. In some cases, their size, number, or position will make BCS difficult or impossible and in these patients the rate of mastectomy would increase. However, MRI can also rule out the presence of additional lesions or the extent of tumours and therefore confirm that BCS is technically feasible in cases that would otherwise have had mastectomy. With the ability to perform oncoplastic surgery and multiple lumpectomies, MRI could even decrease mastectomy rates. Several of the trials, including the majority of RCTs that measured mastectomy rates as an outcome, were conducted in a preselected patient population consisting only of those patients for whom BCS was to be performed. Due to this design, these studies could only result in an increase in mastectomy rate, and this is clearly seen in the figures in which studies are subgrouped by whether the patient population was limited to BCS candidates. The remaining studies found a much smaller or no effect of MRI on mastectomy rates, and trials in ILC suggest it may even decrease mastectomy rates. Even these results are of limited value, as non-technical factors appear to have a greater influence on the decision-making process, and mastectomy rates vary widely according to surgeon, institution, ethnic, and socioeconomic factors. Most of these are not collected or adjusted for in the retrospective studies. This is also exemplified by studies in which MRI found no lesions or lesions later determined by biopsy to be benign, yet mastectomy rates increased, and by non-zero initial mastectomy rates in patients selected for inclusion based on being suitable for BCS.

Several publications by Hollingsworth et al. at Mercy Hospital in Oklahoma are interesting (141, 142). This group uses MRI in all patients as part of the initial evaluation, instead of a final or tie-breaking add-on once a treatment decision has already been made. In this way they suggest patients and multidisciplinary teams see MRI as just one more piece of information, results are available prior to any decisions, staff have the required expertise in MRI use, and there was no net increase in mastectomy rates.

The second major limitation, to be expected in non-randomized studies, is that patients were selected to undergo MRI for specific reasons related to tumour characteristics or patient history and therefore MRI and non-MRI groups were non-equivalent. Due to the retrospective nature of using either patient records or cancer registries, much of the information related to decision-making was unavailable. The included studies used matching or multivariate analysis to try to control for confounding factors such as patient age or menopausal status (but frequently only in a dichotomous manner) and tumour characteristics such as size, stage, and histology. While a number of other patient, disease, and institutional factors are known to affect outcomes, such additional factors were often not reported or not used in adjusting for confounders. Various studies adjusted for 2 to more than 20 factors. Even in studies where data on potential confounders were available, statistical analysis was often insufficient. The most common example of this was restricting multivariate analysis to only those factors of

statistical significance in univariate analysis. In this way, even factors known to be important could be excluded either because the study was too small to reach statistical significance or factors have effect in a combined or interactive manner. A more appropriate and rigorous approach is to use all factors that have any possible influence on the outcome of interest (i.e., correlation not close to 1.0). Taking into account these factors, there was a wide range in quality of studies, and this can be observed by reviewing the information in the data tables. Even in the best studies there was often some imbalance between groups, and non-clinical factors that play a role in decision-making could not be accounted for.

While studies with historical controls are often considered as lower quality than those with matched cohorts or multivariate analysis, this may only be correct if all confounders can be accounted for in the later designs. Due to limitations mentioned, studies comparing consecutive patients after and immediately before implementation of MRI may provide higher quality of evidence. As illustrated in Figure 1.4, MRI had the lowest impact on mastectomy rates in these trials.

Other outcomes such as positive surgical margins, reoperations, recurrence, and survival, are less influenced by non-clinical (non-disease) factors, with margins and reoperations depending more on imaging, surgeon, and disease factors such as multifocality/multicentricity. Recurrence and survival are influenced by adjuvant treatments and disease characteristics. These outcomes are generally considered the more important to consider than mastectomy/BCS rates, although the relative importance is challenging to interpret, especially in non randomized designs. With OS >95% in several studies (see Table 4), an extremely large number of patients would be needed to measure a difference in survival due to MRI. Advances in systemic therapy and radiotherapy, and a growing number of effective later lines of therapy for recurrent disease make it very unlikely to be able to detect an effect of upfront MRI on these downstream outcomes. As indicated in Figure 5.7, no difference in OS was found. Recurrence outcomes are more sensitive, and Figure 5.1 shows a decrease in any recurrence in patients with MRI. More specific recurrence outcomes were reported by less studies, and while there was a trend for improvement with MRI these were not statistically significant.

The remaining outcomes, namely positive surgical margins, reoperations (including re-excisions and conversion to mastectomy) are those for which additional information obtained from imaging prior to surgery is likely to make the most difference. The imaging data can directly inform the surgeon and guide surgical planning. The data indicate MRI resulted in a reduction in positive margins for studies not restricted to BCS candidates (see Figure 2.2). Some of the variation may be because uniform definitions of positivity were not used. Reoperation rates were also reduced by preoperative MRI, as illustrated in Figure 3.1 (OR=0.73, 95% CI=0.63 to 0.85). While re-excisions were reduced (see Figure 3.2), there was a larger and more consistent reduction in conversion mastectomy (see Figure 3.3, OR=0.67, 95% CI=0.50 to 0.90). A study using the Alberta Cancer Registry found that 19% of patients with initial BCS had re-excision, and this varied significantly by geography and surgeon (433). Patients with or without re-excision had similar survival (all-cause and breast-cancer-specific).

Reoperation may delay adjuvant treatment, result in poorer cosmetic outcome, cause emotional distress, increase recovery times, and be a financial burden to the health care system and patients (434). Initial re-excision may lead to further re-excision and eventual mastectomy, or immediate conversion mastectomy instead of wider excision. The American Society of Breast Surgeons indicates that “a goal of breast cancer care is to minimize the number of operations a patient requires in order to optimize their oncologic outcomes and minimize their local recurrence” (435). Better information upfront could allow more BCS without conversion mastectomy, as well as mastectomy in a single operation for those patients whom BCS is technically or aesthetically inappropriate. When mastectomy is preplanned, there may be a wider range of reconstruction options including skin- and nipple-sparing procedures. It has

been proposed that the goal should be a single surgery (141, 142) and more than one re-excision should not be necessary for most patients. The United Kingdom National Health Service Breast Screening Programme target is that the reoperation rate for incomplete excision should not be more than 10% (158, 159). EUSOMA set a minimum standard (quality indicator) of 80% and target of 90% for proportion of patients with invasive cancer that should receive a single breast operation (excluding reconstruction); for DCIS standards were 70% and 90% (436). While this was achieved in some studies in the current review, such as the one by Hollingsworth (141, 142) in which rates dropped from 12% to 15% prior to MRI implementation to 9% afterwards, most did not. Some studies reported reoperation rates as high as 45%.

Some of the trials that reported increased rates of mastectomy with MRI did not confirm whether the additional lesions were benign or cancerous; it was later found that several mastectomies were unwarranted. Best practice, as indicated by the American College of Radiology and other guidelines (Appendix E), is that additional suspicious lesions be biopsied or otherwise confirmed if they could alter surgical procedures. Ideally, sites performing MRI should have the capacity for biopsy as familiarity with the complete process may result in better expertise in reading and interpreting MRI images as well as dedication to advances in the field (142). Some MRI facilities do not have this capacity and a compromise in many guidelines or regulations allows MRI to be conducted elsewhere, as long as there is a partnership or referral pattern to another facility for biopsy if needed. This can lead to delays in the diagnosis (437).

A common theme in many of the publications was the high rate of CBC detected by MRI but not mammography. A meta-analysis of 22 studies found the incremental CBC detection rate over conventional imaging to be 4.1% (352). This is much higher than the cancer rate of 1.4% in the High Risk Ontario Breast Screening Program (438). Some studies suggest most CBC are second primary cancers (365, 366). The mammographically occult cancer is sometimes larger or with worse prognosis than initial cancer detected and receiving treatment, but would not receive radiation treatment, which is considered as standard treatment after BCS. While chemotherapy or other systemic therapy may help with the CBC, not all patients receive systemic therapy, and that given may not be most appropriate for both the ipsilateral and contralateral tumours. Some have suggested that in cases where the contralateral tumour is larger or more advanced than the index tumour, failing to detect and treat the contralateral tumour could be considered inappropriate operation. As MRI is considered standard of care in screening high-risk patients, and patients diagnosed with breast cancer are at high risk of CBC, use of MRI can be considered for patients at high risk of CBC. This would allow treatment of both cancers in a single operation, followed by reconstruction and adjuvant therapy, instead of treating the contralateral cancer when detected symptomatically or at a subsequent screening when it is larger.

Mammographically occult ipsilateral lesions are larger than the index lesion in about 20% of cases (350, 351) and unless detected coincidentally during operation of the index tumour would be untreated surgically. While whole breast irradiation would provide some treatment, partial breast irradiation would be inadequate. The systematic review and meta-analysis by Di Leo et al. (216) supports the use of MRI in patients being considered for partial breast irradiation, and found MRI excluded 11% of patients initially eligible (range 6% to 25% in six studies of 3136 patients). Several guidelines recommend MRI in this situation.

Advances in CE-MRI, as well as in complementary techniques such as DWI-MRI and growing expertise of those interpreting output, have improved the sensitivity and specificity of MRI in detecting lesions and reduced the proportion of lesions that require biopsy. Accelerated or abbreviated MRI techniques may significantly reduce the acquisition time and related costs without sacrificing performance in most cases; this is a topic of recent and ongoing clinical trials. While MRI and mammography are generally used together, and in older studies MRI failed to detect calcifications, based on newer trials or modified procedures some researchers have

proposed that MRI could replace mammography altogether, eliminating radiation exposure and reducing cost (compared to mammography followed by MRI). A number of considerations such as positioning during MRI and how this translates to tumour position during surgery, tumour marking for biopsy and surgery, contrast agents to use, specific applications such as oncoplastic surgery and nipple-sparing mastectomy need to be considered. Other advanced imaging techniques (see Appendix F) may complement MRI or mammography when adapted to breast-specific imaging to increase sensitivity or for whole-body imaging for metastasis. Research and clinical adaptation for magnetic resonance spectroscopy and molecular breast imaging are less advanced than MRI and they are not widely available.

INTERNAL REVIEW

The evidence summary was reviewed by the PEBC Director. The Working Group was responsible for ensuring any necessary changes were made.

ACCEPTANCE BY SPONSORS

Concurrently with internal review, the report was presented to the Breast Cancer Advisory Committee and the Cancer Imaging Program of OH (CCO). The document was distributed to the sponsoring committees by email and was formally accepted.

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EVIDENCE TABLES

Table 1. Mastectomy rates - Patient population not defined by type of surgery planned before MRI.

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
In situ or DCIS								
Lebanon, NH 2007-2011	Davis, 2012 (125)	Retrospective chart review comparing those with and without MRI, n=154 + 64 No comparison of baseline characteristics; assumed similar due to before/after MRI implementation design	Newly diagnosed DCIS confirmed by fine-needle or core biopsy MRI not used for DCIS in 2007-2008; used in all pts in 2009-2011 Excluded pts diagnosed due to MRI in high-risk screening	1.5 T MRI, dedicated prone eight channel breast, gadopentetate dimeglumine (Magnevist; Bayer Health Care, Berlin, Germany) contrast	Initial mastectomy 20% vs. 19%, ns 12/44 mastectomies were in pts that were BCS candidates; 8/44 mastectomies due to additional MRI findings (4 had DCIS in contralateral breast of pt with invasive cancer and mastectomy was due to pt choice) Overall mastectomy 27.9% vs 23.4%, ns	Pt choice resulted in more mastectomy than MRI	R-MV	DCIS
Netherlands Cancer Registry 2011-2015	Keymeulen, 2019 (126)	Retrospective, MRI vs. no MRI; multivariable logistic regression analyses to adjust for incidence year, age, hospital type, DCIS grade, multifocality n=2,382 + 8,033 (n=1,303 + 6,072 with BCS)	Diagnosis of pure DCIS and treated with surgery, age <75 y Breast MRI used in pts with high-grade DCIS preferring BCS, unclear tumour size, or suspicion of microinvasion	Not reported	Mastectomy as first procedure 45.3% vs. 24.4%; OR=2.22, 95% CI=2.00-2.45, p<0.05 Secondary mastectomy after BCS 11.2% vs. 7.4%, OR=1.32, 95% CI=1.07-1.63, p<0.05 Final mastectomy 51.4% vs. 30.0%, OR=2.11, 95% CI=1.91-2.33, p<0.05	Differences in subgroups defined by age or grade were similar to that of the full study except for secondary mastectomy	R-MV-Reg	DCIS

[1] Only female patients unless indicated otherwise.
[2] When statistical adjustments are made to account for confounders, this applies to OR and p values; numbers or rates of events of are not adjusted. For studies with multivariate analysis, only those which adjusted for stage/size and age/menopausal status are included. Adjustment for high risk factors and lesion distribution such as multicentric or multifocal was desirable but not generally conducted.
[3] RCT, randomized controlled trial; P, Prospective non-randomized trial; R-PSM, retrospective with propensity score matching; R-MV, retrospective with multivariate analysis; R-MV-Reg, retrospective with multivariate analysis using registry data; R-EQ, retrospective using data from equivalent groups (e.g., historical controls)

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		Analyses were also stratified by age at diagnosis (less than 50 versus 50–74 y) and histological grade	MRI used more in younger pts, higher grade, multifocality					
University of Ulsan College of Medicine, Gangneung, Korea 2012-2016	Yoon, 2020 (127)	Retrospective, preoperative MRI vs. no MRI; propensity score matching using 18 confounding variates to create matched groups (included age, family and personal history, density, grade, tumour size, ER/PR/HER2 status) n=430 + 111 n=106 + 106 after propensity score matching	Consecutive pts with DCIS confirmed by US-guided CNB Excluded concurrent invasive carcinoma, no surgery, history of ipsilateral breast cancer	1.5 T MRI or 3.0 T MRI, prone position, dedicated 18-channel phased-array breast, gadoterate meglumine (Magnevist; Schering, Berlin, Germany and Uniray; Dongkook, Seoul) contrast	Initial mastectomy 37.7% vs. 34.0%, OR=1.16, 95% CI=0.68-1.98, p=0.59 Overall mastectomy 38.7% vs. 40.6%, OR=0.93, 95% CI=0.54-1.58, p=0.79	Patient and surgeon preference could not be controlled for	R-PSM	DCIS
Magee-Womens Hospital of the University of Pittsburgh Medical Center tumour registry and radiology databases	Sorbero, 2009 (128)	See: In situ and invasive						
Eindhoven Cancer Registry, The Netherlands 2011-2013	Vos, 2015 (129)	Retrospective, multivariable analysis Preoperative MRI vs. no MRI, multivariable binary logistic regression analyses adjusted factors with p<0.1 in univariable analysis; different set of factors used for each subgroup and outcome DCIS: n=136 + 478 (adjusted only for age)	IBC pT1-3 or pure DCIS Excluded neoadjuvant systemic therapy, stage T4, distant metastasis, unknown stage or T0, unknown surgery or margin status Contralateral breast cancer was analyzed as a new pt	Dynamic contrast-enhanced MRI was performed according to local protocol in each hospital No other details reported	Age-adjusted OR (95% CI) and p values DCIS • Mastectomy 43.4% vs. 18.2%, OR=3.44, 95% CI=2.28-5.20, p<0.001; adjusted OR=3.18, 95% CI=2.09-4.82, p<0.001 • Final mastectomy 48.5% s. 22.0%, OR=3.35, 95% CI=2.25-5.00, p<0.001; adjusted OR=3.11, 95% CI=2.07-4.66, p<0.001	No information on multifocality or multicentricity, indication for performing MRI, any changes in surgical plan Residual confounding may be present from factors not taken into consideration	R-MV-Reg	0-III (DCIS or IBC)

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		Subgroups of invasive cancer, high-grade DCIS, non-palpable invasive, age ≤40 y, lobular	MRI pts younger, more ILC (27.4% vs. 7.3%)		See later in table for invasive cancer results			
In situ and invasive								
POMB Breast units in 3 Swedish hospitals 2007-2011	Gonzalez, 2014 (130) Karlsson, 2019 (131)	Randomized prospective multicentre trial, preoperative MRI or no MRI n=220 + 220 [but 10 pts in MRI group did not receive MRI] Groups non-equivalent: suggested primary treatment (before MRI) was 17.7% vs 23.2% mastectomy, 10.9% vs. 13.6% neoadjuvant chemotherapy, 70% vs 60% BCS Some pts were randomized after MDT discussion “At pretreatment MDT, most patients’ participation in preoperative MRI of the breast (POMB) was known, but the allocated treatment arm was unknown in the vast majority of cases. It could not be ruled out that the unblinded and randomization design could have influenced the unbalanced planned treatment”	Women up to age 56 y with newly diagnosed IBC or non-invasive breast cancer; diagnosis confirmed with cytology or biopsy Demographic and clinical information collected retrospectively from pt records; stage, size, histology, ER/PR status, family history not reported	MRI at Sites A and C but not B Site A: 1.5 T MRI, prone position, 8-channel breast coil, Omniscan (GE Healthcare) gadolinium contrast Site C: 1.5T MRI, prone position, 4-channel breast coil, Dotarem (Guerbet) gadolinium contrast MRI-detected lesions biopsied if detectable by US. MRI-guided biopsy introduced in 2009 at one site, only used in 4 pts.	Initial mastectomy 39.1% vs. 34.1% [excluding neoadjuvant 31% vs. 27%] Overall mastectomy 43.2% vs. 40.5% Additional CBC found by MRI was 2.9% 13 incremental MRI findings were unverified as malignant or high-risk but treatment plan was changed anyway RCT authors concluded that approximately 15% of pts without MRI were denied adequate initial treatments with impacts on prognosis	Goal was to have ≥10 mm margins, but not touching inked surface for invasive carcinomas accepted; individual decision for DCIS Critique of trial by Brenner 2015 (439)	RCT	BC
Monet NCT00302120	Peters, 2011 (132) Peters, 2007 (133) [protocol]	Randomized before biopsy/diagnosis Routine care + preoperative MRI or routine care alone	Suspicious non-palpable breast lesions, BI-RADS 3-5 detected on mammography or breast US and referred for histological analysis	MRI at university hospital 3 T bilateral dynamic contrast enhanced (DCE) breast MRI prior to biopsy of suspicious	Initial mastectomy: 32.1% vs. 34.2%, p=0.776 Conversion of BCS to mastectomy 11.3% vs. 16.0%, p=0.489	Commentary on this article (440) indicated that sensitivity of 51% is well below 92% achievable in	RCT	BC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
4 hospitals in The Netherlands 2006-2008		(mammography, US, core needle biopsy) n=78 + 76 207 + 211 pts initially but only 74 + 75 pts had malignant lesions (78 + 76 breasts, 83 + 80 lesions) and underwent surgery Note: biopsy was after MRI Study designed to have sufficient power if 250 cancers with surgery in each group	Histological analysis from needle biopsy of in situ or invasive carcinoma to be included in study Excluded palpable lesions, breast surgery or RT within 9 months Approximately 50% of malignant lesions were DCIS and 50% invasive carcinoma for both MRI and control groups 60% of lesions had microcalcifications only compared to 25% described in the literature, possibly due to excluding palpable cancers	lesion, prone position, dedicated phased-array bilateral breast coil, Gadolinium-DTPA (Magnevist, Schering, Germany) contrast Additional lesions on MRI investigated with second-look US and sampled with US or MRI guidance 3 T MRI was relatively new, and they previously had substantial problems with fat suppression; they indicated image quality was at least comparable to 1.5 T in other systems	Final mastectomy rate 39.7% vs. 44.7% Only 47% of mammography lesions were detected on MRI; 96/120 were benign MRI detected 11 additional lesions of which 2 were malignant [this is indicated in text but missing in Figure 2]	some other studies, suggesting there may have been technical limitations with the MRI used; reoperation rate high		
Mayo Clinic, Rochester, MN 1997-2006	Katipamula, 2009 (134)	Retrospective study of pts in database; association of MRI with surgery type; preoperative MRI vs. no MRI n=337 + 5,068 (346 + 5,237 cancers) Logistic regression for association of breast MRI and surgical year on the type of surgery. Multiple logistic to adjust for age, TNM stage, histology, breast density, laterality, the presence of concurrent or prior CBC, and family history of breast cancer	Stage 0-II breast cancer with definitive surgical treatment 17% Stage 0, 49% stage I, 34% stage II	Not reported MRI recommended for biopsy-proven ILC, biopsy-proven IBC that was palpable but not visible by mammogram, axillary metastasis from presumed breast primary with negative mammogram and clinical breast exam, and problem-solving situations in the setting of biopsy-proven breast cancer. This guide was not followed by all clinicians	Mastectomy 54% vs. 36%, p<0.001 In multivariable model, MRI (OR=1.7, 95% CI=1.3-2.2, p<0.001) and surgical year independently predicated mastectomy	Without MRI, mastectomy rate was 45% in 1997, decreased to low of 29% in 2003, and then increased again to 41% in 2006. With MRI (2003 to 2006 only) mastectomy rate was relatively constant	R-MV	0-II

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Magee-Womens Hospital of the University of Pittsburgh Medical Center tumour registry and radiology databases 1998-2000 and 2003-2005	Sorbero, 2009 (128)	Retrospective, 2 time periods, effect of MRI on mastectomy; univariate and bivariate statistics; multiple logistic regression controlling for stage, family history, age, year of diagnosis, MRI uncommon during early period n=512 + 3,094 (early 1,863 pts, late 1,743 pts) Stage 0 (in situ) n=40 + 749 Stage I-II n=399 + 2184 Stage III n=73 + 161	Stage 0-III Excluded bilateral breast cancer	Not reported	CPM 9.2% vs. 4.7%, p<0.001 Mastectomy 38.5% vs. 27.5%, p<0.001 Multivariate analysis, CPM Stage 0: OR=0.64, 95% CI=0.15-2.78, p=0.55 Stage I-II: OR=2.04, 95% CI=1.32-3.16, p=0.001 Stage III: OR=0.81, 95% CI=0.30-2.16, p=0.68 Stage I-II, late period only: OR=1.45, 95% CI=0.88-2.39, p=0.15 Stage III, late period only: OR=0.87, 95% CI=0.26-2.88, p=0.82 Multivariate, mastectomy Stage 0: OR=1.22, 95% CI=0.61-2.43, p=0.57 Stage I-II: OR=1.43, 95% CI=1.12-1.83, p=0.005 Stage III: OR=0.76, 95% CI=0.41-1.41, p=0.38 Stage I-II, late period only: OR=1.14, 95% CI=0.85-1.51, p=0.38 Stage III, late period only, OR=1.15, 95% CI=0.58-2.30, p=0.69	Histology and BRCA status not included in models Significant for stage I-II overall, but not in later period	R-MV	0 I-II III 0-III
4 registries of BCSC (USA) 2010-2014	Onega, 2017 (135)	Retrospective, registry data, preoperative MRI vs. no MRI Multivariable logistic regression: adjusted for pt and tumour characteristics including age, race, urban/rural, family history, year of diagnosis mode	Non-metastatic unilateral breast cancer, stage 0-III, no personal history of breast cancer	Not reported	Unilateral mastectomy: 27.8% vs. 24.3%; OR=1.55, 95% CI=1.42-1.71; adjusted OR=1.32, 95% CI=1.16-1.50 Mastectomy + CPM: 14.5% vs. 7.8%; OR=1.64, 95% CI=1.40-1.91; adjusted OR= 1.32, 95% CI=1.05-1.65	Cannot determine whether association is due to MRI findings or to pt and/or provider preferences	R-MV-Reg	0-III

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		of detection, stage, histology, tumour size, grade ER/PR, nodal status, BCSC site n=2,217 + 10,880						
SEER-Medicare database 2005-2009	Ozanne, 2017 (136)	Retrospective, preoperative MRI vs. no MRI Unadjusted and multivariable logistic regression models n=9,055 + 46,942 Adjusted for age at diagnosis, race, SEER registry, marital status, median income, urban/rural status, Medicaid, previous other cancer, comorbidity index, year of diagnosis, histology, grade, stage, ER and nodal status, tumour size, teaching hospital, NCI cooperative oncology group member and hospital type	Stage 0-III breast cancer, BCS or mastectomy within 6 months of diagnosis, age ≥66 y Excluded prior history of breast cancer or diagnosed in a nursing home	Not reported	Mastectomy 33,8% vs. 37.8%, OR=0.84, 95% CI=0.80-0.88; adjusted OR=1.04, 95% CI=0.98-1.11 MRI increased over time, but not associated with increase in mastectomy		R-MV-Reg	0-III
4 registries of BCSC (USA) 2005-2009	Goodrich, 2016 (137)	Retrospective, MRI vs. no MRI Logistic regression to explore association between primary surgical treatment type and preoperative MRI n=204 + 1,254 • Interval cancer n=43 +161 • Screen-detected n=162 + 1,092 Adjusted for age, breast density, cancer type, tumour size, stage, grade, nodal status	Age ≥66 y, interval cancer (negative screening mammogram and subsequent breast cancer diagnosis within 365 days) or screen-detected breast cancer (positive screening mammogram) and primary surgery within 6 months of diagnosis	Not reported	Mastectomy 28.4% vs. 24.2%, adjusted OR=0.99, 95% CI=0.67-1.50 Interval cancer: 39.5% vs. 40.3% Screen-detected: 25.5% vs. 21.8%		R-MV-Reg	BC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Germany (>50% of West Germany cancer pts) 2006-2010	Heil, 2013 (138)	Mastectomy trends and predictive factors; retrospective multicentre unselected cohort, univariate and multivariate logistic regression analysis (age, stage, type [DCIS, IDC, ILC], nodal status, grade, receptor status, singe/multiple lesions, MRI, hospital type and cases) n=21,743 + 121,120	Surgical treatment for breast cancer, age 18 to 80 y Excluded distant metastasis, medical mastectomy	Not reported	Mastectomy 37.6% vs 31.9%, OR=1.29, 95% CI=1.25-1.33 univariate; OR=1.42, 95% CI=1.36-1.47 multivariate		R-MV-Reg	BC
University of Ulsan College of Medicine, Seoul, South Korea 2009-2010	Choi, 2017 (139)	Retrospective with propensity score matching those with MRI to those without based on 25 covariates n=828 + 1613; selected 799 matched pairs	Consecutive women with newly diagnosed breast cancer and curative surgery; excluded those with neoadjuvant chemotherapy or distant metastasis, bilateral breast cancer	1.5 T MRI, bilateral breast coil, Magnevist (Schering, Berlin, Germany) contrast Axial sequence for the evaluation of the supraclavicular and axillary lymph nodes	BCS 70.2% vs. 64.5%, p=0.016; mastectomy 29.8% vs. 35.5%, p=0.016		R-PSM	BC
Changhua Christian Hospital breast cancer database, Taiwan 2009-2013	Lai, 2016 (140)	Retrospective, preoperative MRI vs. no MRI Control group (no MRI) from Jan 2009-Dec 2010; MRI group starting Jan 2011 when coverage for MRI cost was implemented Multivariate analysis (propensity-score matching) to identify predisposing factors for margin involvement n=735 + 733	Primary operable breast cancer, mammography and sonography, surgery Excluded neoadjuvant chemotherapy Time periods chosen to minimize selection bias MRI group had less grade II and more grade III cancers but otherwise similar		Initial mastectomy 52.7% vs. 48.6%, p=0.13 Final mastectomy 52.9% vs. 50.5%		R-PSM	BC
Mercy Hospital, Oklahoma City 2003-2006	Hollingsworth, 2008 (141) Hollingsworth, 2015 (142)	Retrospective study of consecutive pts who all had MRI preoperatively; historical control comparison	Consecutive pts with newly diagnosed breast cancer, all underwent breast MRI	First 249 pts: 0.5 T breast-dedicated MRI with bilateral breast coil, gadolinium contrast	<u>2008 results</u> Mastectomy rate 39.8% initial and 41.1% final compared to 52% in the year prior to the study (without MRI)	<u>2008 results</u> 43 pts that had bilateral mastectomy did so for preventative	R-EQ	BC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Extended to 2014; controls 1996-2002		n=603 with MRI (141) n=2000 with MRI (142)	Excluded neoadjuvant chemotherapy or those without surgery after biopsy In 2008 publication: 388 invasive ductal carcinomas, 149 DCIS, 65 invasive lobular carcinoma, 1 malignant phyllodes tumour Historical controls 1996-2002 without MRI	Later pts: 1.5 T breast-dedicated MRI, both breasts, gadolinium contrast Image-guided biopsy included radiograph, US, or MRI guidance		reasons and unilateral BCS would have sufficed; excluding these, BCS rate was 65% The 7.7% multicentricity + 3.7% contralateral (11.4% combined) suggests MRI has major contribution, even if excluding role in evaluating the index lesion Expected that non-excised multicentric disease is significant at least for those considering APBI		
Single institution in USA 2004-2008	Grady, 2012 (143)	Retrospective review, after and before 2 surgeons started routinely using MRI; preoperative MRI vs. no MRI n=79 + 105 Groups equivalent in age, menopausal status, histology, pathologic stage, ER/PR status	Operative breast cancer diagnosed using core-needle biopsy One surgeon started use of MRI in late 2004, the other in late 2007	1.5 T MRI, prone position, 1.5 T 8-channel biopsy breast array coil, gadolinium (Magnevist – Bayer HealthCare Pharmaceuticals, Berkeley, CA) contrast Anatomic information for the breast and axilla	Mastectomy rate 48% vs. 47%		R-EQ	BC
Invasive								

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
National Comprehensive Cancer Network centres 2000-2009	Luis, 2015 (144) [abstract]	Prospective cohort, factors associated with mastectomy Multivariable logistic regression n=10,249 total (number with MRI not reported)	Stage I 23% mastectomy and 77% BCS as initial surgery; 8% converted to mastectomy	Not reported	Initial mastectomy 32% vs. 22%, OR=1.8 (95% CI=1.6-2.1), p<0.01	Age, BMI, comorbidity, income, centre, stage, tumour subtype, grade, histology, and preoperative MRI were associated with type of initial surgery	P	I
McGill University Health Centre 2006-2013	Parsyan, 2016 (145)	Retrospective from tumour registry, preoperative MRI or not Multivariate analysis controlling only for age; no difference in tumour size, histologic type, ER status grade, HER2 status; other factors not measured n=307 + 458	Stage I-III breast cancer, definitive surgical treatment Excluded neoadjuvant therapy, previous breast cancer in situ carcinoma, age < 30 y, history of Hodgkin's lymphoma, BRCA positive MRI group was younger (55.3 y vs. 66.3 y)	1.5 T MRI, bilateral, 8-channel breast phase array coil, gadolinium contrast	Adjusted for age: Initial mastectomy 20.5% vs. 17.2%, adjusted OR=1.31, 95% CI=0.87-1.97, p=0.200 Final mastectomy 23.5% vs. 19.0% Contralateral surgery 11.7% vs. 5.5%, adjusted OR=2.25, 95% CI=1.25-4.05, p=0.007		R-MV	I-III
Administrative data in Ontario 2003-2012	Arnaout, 2015 (9)	Population-based retrospective cohort Patterns of preoperative MRI use; MRI vs. no MRI n=7,824 + 45,191 Multivariate analysis found MRI associated with several outcomes Covariates in models: age, socioeconomic status, comorbidity, urban/non-urban, histologic type, year of diagnosis, stage, institution	Primary operable IBC and surgery within 3 months of diagnosis, excluded stage 0 or IV	Not reported No mention of whether MRI found additional lesions, or whether these were characterized.	Mastectomy: 36.8% vs. 29.8%, OR=1.37, 95% CI=1.30-1.44; adjusted OR=1.73, 95% CI=1.62-1.85 CPM: OR=1.45,95% CI=1.26-1.67; adjusted OR=1.48, 95% CI=1.23-1.77	Surgeon attributes, such as less experience, working in a teaching hospital, and performing more breast-related surgical procedures were associated with greater use of MRI	R-MV-Reg	IBC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		type, surgeon volume and experience						
Memorial Sloan-Kettering Cancer Center, New York, NY 2005-2007	Kapoor, 2013 (146)	Retrospective, evaluation relationship between breast density and BCS; adjusted for clinical and pathologic variables that were significant on univariate analysis using multivariate logistic regression (age, grade, multicentric/ focal, LVI, size, subtype, density) n=385 + 671	Stage I-III IBC, surgical treatment Excluded neoadjuvant chemotherapy, no mammogram, surgery at outside hospital, surgical diagnostic biopsy	Not reported	Initial mastectomy 37.1% vs. 23.1, OR=1.86, 95% CI=1.27-2.72, p=0.0014 univariate; OR=1.56, 95% CI=1.02-2.37, p=0.0381 multivariate Subgroup with initial BCS and positive margins: conversion to mastectomy 30.0% vs. 21.9%, OR=1.64, 95% CI=1.17-2.30, p=0.0039 univariate; OR=1.58, 95% CI=1.01-2.47, p=0.0458 Note: 24 additional pts with negative margins also converted to mastectomy but MRI status not reported; statistics for final mastectomy not reported	Breast density, young pt age, mammographically occult cancers, and the use of preoperative MRI are interrelated factors Patient participation in surgical decision making is strongly associated with mastectomy use	R-MV	I-III
SEER-Medicare database (USA) 2000-2009	Killelea, 2013 (147)	Retrospective cohort; preoperative MRI vs. no MRI; multivariable logistic regression n=7,333 + 65,128 Covariates of age, race, marital status, year of diagnosis, income, SEER region; stage, grade, tumour size, ER/PR status, number of positive lymph nodes	Medicare beneficiaries age ≥67 y diagnosed with stages I-III breast cancer and had surgery Excluded if previous breast cancer or if any other cancer within 2 y Majority had early-stage disease (56.1% stage I, 35.1% stage II; 60.8 % < 2.0 cm size); MRI used more in younger, white, higher median income, less comorbidity	Not reported Suggestion that non-biopsied findings on MRI may have increased CPM	Mastectomy 39.6% vs. 43.7%; OR=0.85, 95% CI=0.80-0.89, p<0.001; adjusted OR=1.21, 95% CI=1.14-1.28, p<0.001 In mastectomy group: • Bilateral cancer diagnosis 9.7% vs. 3.7%, p<0.001 • Bilateral mastectomy 12.5% vs. 4.1%, p<0.001; adjusted OR=1.98, 95% CI=1.72-2.29 • CPM 6.9% vs. 1.8%, adjusted OR=2.52, 95% CI=2.08-2.68 • Bilateral mastectomy for bilateral cancer, 5.6% vs. 2.3%, adjusted OR=2.20, 95% CI=1.81-2.68 Unilateral mastectomy for bilateral cancer 4.1% vs. 1.4%, adjusted OR=2.97, 95% CI=2.35-3.75	Does not address reason for high mastectomy rate in both groups, even in stage I disease Article suggests surgeon and pt preference may be large factors	R-MV-Reg	I-III

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Eindhoven Cancer Registry, The Netherlands 2011-2013	Vos, 2015 (129)	Retrospective, multivariable analysis Preoperative MRI vs. no MRI, multivariable binary logistic regression analyses adjusted factors with p<0.1 in univariable analysis; different set of factors used for each outcome Invasive: n=1,637 + 3,164 (including 449 + 231 ILC) Subgroups of invasive cancer, high-grade DCIS, non-palpable invasive, age ≤40 y, lobular	IBC pT1-3 or pure DCIS Excluded neoadjuvant systemic therapy, stage T4, distant metastasis, unknown stage or T0, unknown surgery or margin status Contralateral breast cancer was analyzed as a new pt MRI pts younger, more ILC (27.4% vs. 7.3%)	Dynamic contrast-enhanced MRI was performed according to local protocol in each hospital No other details reported	OR and 95% CI Invasive cancer (adjusted for age, palpability, histology, tumour size, grade, ER/PR and HER2 status, regional lymph node status): • Initial mastectomy 35.9% vs. 23.1%, OR=1.87, 95% CI=1.64-2.13, p<0.001; adjusted OR=1.80, 95% CI=1.54-2.09, p<0.001 • Final mastectomy 38.1% vs. 24.7%, OR=1.87, 95% CI=1.64-2.12, p<0.001; adjusted OR=1.74, 95% CI=1.50-2.03, p<0.001 ILC (adjusted for palpability, tumour size, grade, regional lymph node status): • Mastectomy 41.2% s. 40.7%, OR=1.02, 95% CI=0.74-1.41, p=0.898; adjusted OR=1.00, 95% CI=0.68-1.45, p=0.977 • Final mastectomy 44.1% vs. 44.6%, OR=0.98, 95% CI=0.71-1.35, p=0.903; adjusted OR=0.95, 95% CI=0.65-1.39, p=0.791 DCIS - see earlier in table	No information on multifocality or multicentricity, indication for performing MRI, any changes in surgical plan Residual confounding may be present from factors not taken into consideration	R-MV-Reg	0-III (DCIS or IBC)
Netherlands Cancer Registry 2011-2013	Vriens, 2017 (148)	Retrospective from registry Multivariable analysis n=2,879 + 554 (IDC n=2,429 + 477; ILC n=364 + 58) Adjusted for year of incidence, age, tumour size, nodal status,	Stage I-III IBC (cT1-3) and neoadjuvant therapy, age 18-70 y Excluded cT4 tumours	Not reported	Mastectomy as final surgical procedure • Overall OR=0.89, CI=0.73-1.09, p=0.27 • Subgroup of IDC OR=0.87, 95% CI=0.70-1.09, p=0.22 • Subgroup of ILC OR=1.03, 95% CI=0.52-2.06, p=0.93 • cT3 tumours OR=0.45, 95% CI=0.21-0.99	Family history information not available	R-MV-Reg	I-III

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		ER, PR, HER2 status, grade, multifocality			• cT1-2 tumours OR=0.95, 95% CI=0.75-1.20 Contralateral breast cancer by MRI prior to surgery OR=1.19, 95% CI=0.71-2.00, p=0.51			
Netherlands Cancer Registry 2011-2013	Lobbes, 2017 (149)	Retrospective population-based cohort study; MRI vs. no MRI Multivariable logistic regression analysis with covariates of year of diagnosis, age, clinical tumour size, nodal status, ER, PR, HER2 status, tumour grade, histological type, multifocality Analysis for full group and subgroups of ductal and lobular cancers n=10,740 + 25,310 Ductal: n=7,462 + 21,128 (26% MRI) Lobular: n=2,774 + 2,361 (54% MRI)	All Dutch pts with primary IBC (cT1-4N0-3M0) treated with primary surgery, Excluded distant metastases, DCIS, neoadjuvant therapy, unknown tumour localization Standard practice is mammography and/or US plus tissue sampling of lesions; discussion in tumour board determined whether MRI was performed Pts selected from cancer registry then hospital files reviewed Pts with MRI generally younger, ILC, multifocal cancer	Breast MRI protocols adhere to EUSOBI quality criteria. No other details reported	Multivariable analysis results Mastectomy • OR=1.22, 95% CI=1.15-1.29, p<0.001 • IDC OR=1.30, 95% CI=1.22-1.39, p<0.0001 • ILC OR=0.86, 95% CI=0.76-0.99, p=0.0303 Secondary mastectomy • OR=1.07, 95% CI=0.89-1.29, p=0.434 • IDC OR=1.23, 95% CI=1.00-1.53, p=0.054 • ILC OR=0.61, 95% CI=0.42-0.88, p=0.0088 Synchronous CBC (diagnosis at same time or within 3 months of first cancer diagnosis): OR=0.28, 95% CI=0.24-0.33, p<0.0001 • IDC OR=4.07, 95% CI=3.38-4.90, p<0.001 ILC OR=2.50, 95% CI=1.73-3.61, p<0.001	Limitations: breast size and density, tumour localization within the breast, pt breast cancer risk profile, and the initial surgical treatment plan based on mammographic and/or US findings) were not available Motivation for MRI unknown	R-MV-Reg	IBC, IDC, ILC
SEER-Medicare linked dataset 2004-2007	Fortune-Greeley, 2014 (150)	Retrospective, MRI vs. no MRI Propensity score methods (tumour grade, size, node positivity, ER/PR status, comorbidity, age, marital	IDC (n=14,357), ILC (n=1,928), mixed IDC/ILC (n=2,398); aged ≥66 y, stage I-IIB (AJCC 6th edition)	Not reported	Mastectomy as initial surgery • Overall: 27.4% vs. 30.5%; OR=1.33, 95% CI=1.19-1.48 • IDC: 25.6% vs. 30.5%, OR=1.21. 95% CI=1.07-1.38	Not able to balance pts on unobserved characteristics such as reason for MRI, MRI results,	R-PSM	IDC, ILC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		status, race, ethnicity, SEER region, education, financial status, facility, surgical volume) n=2,471 + 17,861 total n=1,557 + 12,800 IDC n=396 + 1,532 ILC n=390 + 2,008 mixed IDC/ILC	MRI more frequent in ILC or mixed IDC/ILC cancers Excluded neoadjuvant chemotherapy, tumours > 5 cm, second primary cancer within 12 months		• ILC: 33.1% vs. 35.5%, OR=1.48, 95% CI=1.10-2.00 • Mixed: 30.5% vs. 28.3%, OR=1.98, 95% CI=1.50-2.62 Final mastectomy (only or final surgery) • Overall: 31.8% vs. 36.0%: OR=1.20, 95% CI=1.08-1.33 • IDC: 30.1% vs. 35.3%, OR=1.21, 95% CI=1.07-1.37 • ILC: 37.9% vs. 45.0%, OR=1.10, 95% CI=0.83-1.47 • Mixed: 33.8% vs. 36.9%, OR=1.43, 95% CI=1.10-1.85	pt preference for mastectomy, multifocal disease, breast density, surgeon experience		
IDC								
SEER-Medicare linked dataset	Fortune-Greeley, 2014 (150)	See: Invasive section						
Netherlands Cancer Registry	Lobbes, 2017 (149)	See: Invasive section						
ILC								
Radboud University Nijmegen Medical Centre (RUNMC), The Netherlands, 1993-2005 The Netherlands Cancer Institute/Antoni van Leeuwenhoek	Mann, 2010 (151)	Retrospective study of pts in database, preoperative MRI vs. no MRI No multivariate analysis, but groups well matched except for age (mean 56 vs. 61 y) n=99 + 168	ILC Excluded history of cancer, prior breast surgery, neoadjuvant chemotherapy, or other non-surgical techniques, treated at another hospital	Various MRI systems, various field strengths ranging from 1.0 to 3.0 T, and various scan protocols. Prone position, dedicated bilateral breast coil, Gd-containing contrast agent Indications for MRI included accepted clinical indications, pt wish, and participation	All pts: • Initial mastectomy 45% vs. 46%, p=0.753 • Final mastectomy 48% vs. 59%, p=0.098	MRI reduced re-excision and final mastectomy	R-EQ	ILC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Hospital 1999-2005				in clinical studies that assessed: (1) the radiologic pathologic correlation of MR-visible tumours, (2) high-risk screening, (3) preoperative staging, and (4) new MRI sequences. Second look US or MRI-guided (excision) biopsy prior to adaptation of the surgical plan, other than for small extension to local excision				
Seoul, Korea 2005-2016	Ha, 2018 (152) Overlaps with pts in Ha, 2019 (185)	Retrospective, propensity score matching n=369 + 234, of which 196 pairs were matched using 17 variables	ILC diagnosed with biopsy or surgical excision Excluded neoadjuvant chemotherapy, stage IV, male, double primary, missing data on pt or tumour characteristics	1.5- or 3.0-T MRI, dedicated 18-channel phased-array breast coil, gadopentate dimeglumine (Magnevist; Schering, Berlin, Germany) or Gadoterate meglumine (Dotarem; Guerbet, Villapinte, France) contrast	Initial mastectomy 33.9% vs. 37.6%, p=0.397; after matching OR=0.876, 95% CI=0.580-1.323, p = 0.528 Final mastectomy 36.0% vs. 45.3%, OR=0.744, 95% CI=0.496-1.114, p=0.151		R-PSM	ILC
Netherlands Cancer Registry	Lobbes, 2017 (149)	See: Invasive section						
SEER-Medicare linked dataset	Fortune-Greeley, 2014 (150)	See: Invasive section						
Ongoing trials								
MIPA (27 centres, all except 2 in Europe)	Sardanelli, 2020 (153) [protocol]	Pragmatic observational non-randomized multicentre international prospective study	Consecutive pts with newly diagnosed breast cancer amenable to	The coordinating centre approved only MRI protocols following technical	Interim analysis of 2,425 pts:		P-ongoing	BC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
ISRCTN41143178 2013-2018 Enrollment complete, follow-up to end of 2023	Sardanelli, 2017 (154) [abstract, interim] ONGOING	for women offered MRI or not according to local practice n=1,224 + 1,201 Variables that will be shown to be significantly different between the two groups will be considered as covariates when the two groups will be compared in analyses. Target enrollment of 7,000 reached in 2018	upfront surgery, aged 18-80 y Excluded candidates for neoadjuvant therapy or with personal history or cancer or with evidence of metastases	recommendations issued by international societies such us the European Society of Breast Cancer Specialists (EUSOMA), the EUSOB, and the American College of Radiology. ≥1.5 T MRI, ≥4 channels of dedicated coils, gadolinium-based contrast agent	Mastectomy rate 21.0% vs. 16.0%, adjusted OR=1.4, 95% CI=1.3-1.6, p<0.001			

APBI, accelerated partial breast irradiation; BC, breast cancer; BCS, breast-conserving surgery; BCSC, breast cancer surveillance consortium; BI-RADS, Breast Imaging and Reporting and Data System; BMI, body mass index; CBC, contralateral breast cancer; CI, confidence interval; CNB, core-needle biopsy; CPM, contralateral prophylactic mastectomy; DCIS, ductal carcinoma in situ; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; IBC, invasive breast cancer; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; LVI, lymphovascular invasion; MDT, multidisciplinary team; MRI, magnetic resonance imaging; ns, not significant; OR, odds ratio; pt, patient; pts, patients; PR, progesterone receptor; RT, radiotherapy; SEER, Surveillance, Epidemiology, and End Results database; US, ultrasound

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Table 2. Mastectomy rates - Patients scheduled or evaluated as suitable for BCS prior to MRI.

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
DCIS								
IRCIS 10 hospitals in France NCT01112254 2010-2014	Balleyguier, 2019 (155) Kandel, 2020 (156) [costs]	RCT: superiority trial MRI vs. control arm (mammography and US) n=178 + 174 MRI group younger (median 56 vs 58 y) and more premenopausal (32% vs 27%), higher breast density	Age 18-80 with biopsy-proven limited DCIS, unifocal microcalcification cluster or mass <30 mm and scheduled for BCS Exclude bilateral lesions, history of breast cancer, high risk (BRCA1/2). Most had BI-RADS 4 lesions (82% vs. 83%)	Mostly 1.5 T MRI, 3 T MRI in 2 centres, with contrast agent For enhancement suggestive of a mass or multiple and large lesions (>3 cm from the initial lesion), second-look US or additional mammography with magnification views and biopsy, if indicated, with mammography, US, MRI, or computed tomography guidance	Mastectomy: initial surgery 9% vs. 4%, p=0.06; second surgery 9% vs. 13%; overall 18% vs. 17%, p=0.93	No significant difference in total cost between groups	RCT	DCIS
In situ or invasive								
BREAST-MRI ICESP, São Paulo, Brazil NCT02798796	Mota, 2019 (157) [Abstract]	RCT Stratified for mammary density n=219 + 227	Stage 0-III, candidate for BCS	1.5T MRI system Surgery was modified when MRI showed an increase of more than 50% of the tumour size	Mastectomy 5.9% vs. 0.5%; NSM 1.4% vs. 0 (total 7.3% vs 0.5%), p=0.001 BCS 76.7% vs. 99.5%; wide BCS 16% vs. 0%	Surgical change in 31.1% of those with MRI (49 pts ipsilateral; 13 contralateral, 6 both); conversion to	RCT	0-III

[1] Only female patients unless indicated otherwise.
[2] When statistical adjustments are made to account for confounders, this applies to OR and p values; numbers or rates of events of are not adjusted. For studies with multivariate analysis, only those which adjusted for stage/size and age/menopausal status are included. Adjustment for high risk factors and lesion distribution such as multicentric or multifocal was desirable but not generally conducted.
[3] RCT, randomized controlled trial; P, Prospective non-randomized trial; R-PSM, retrospective with propensity score matching; R-MV, retrospective with multivariate analysis; R-MV-Reg, retrospective with multivariate analysis using registry data; R-EQ, retrospective using data from equivalent groups (e.g., historical controls)

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
2014-2016					Subsequent mastectomy 2.3% vs. 2.2% Final mastectomy 9.6% vs. 2.6%	ipsilateral mastectomy in 19 pts		
COMICE ISRCTN 57474502 UK (45 centres) 2002-2007	Turnbull, 2010 (158, 159); Morris, 2010 (160); McMahon, 2013 (161)	RCT: Pragmatic trial MRI vs. further imaging, minimization factors were breast surgeon, age (<50 or ≥ 50), breast density group (1 vs. 2/3/4) n=816 + 807 randomized n=761 + 798 received correct test (MRI or not) Definitions were not standardized and varied by site: clear margins ranged from 0.5 to 5.0 mm for invasive disease and 1.0 to 10.0 mm for DCIS	Women aged ≥18 y with biopsy-proven primary breast cancer scheduled for WLE after triple assessment (clinical, radiological [mammogram and US] and cytology/biopsy); excluded neoadjuvant treatment or previous surgery 77% age ≥50 y; 70% postmenopausal	1.5 T MRI, dedicated bilateral breast-surface coils; a few scans at 1.0 T Gd-diethylenetriaminepenta-acetic acid contrast A second publication (159) indicates 1.5 T MRI required compromises in either the temporal or spatial resolution employed or to extent of the breast coverage obtained. In some centres fat-suppression was not available. MRI-directed biopsy was not available at the start of the trial and many women had mastectomy without pathological verification of disease (16/58, 27.6% of mastectomies in the MRI group) (159, 160)	Primary outcome was rate of repeat operation or further mastectomy within 6 months, or pathologically avoidable mastectomy Initial mastectomy 7.1% vs. 1.2%. Initial WLE 92% vs. 98%; Subsequent mastectomy: 5.9% vs. 7.6% Avoidable mastectomy 2% vs. 0.5% Overall justified mastectomy rate 11% vs. 9% About ¼ of mastectomies in the MRI were done without pathological verification and were later considered inappropriate	Investigators at one trial site (161) suggest that complicated cases, which benefited from MRI, were pre-selected out prior to randomization; mastectomy rate was 15.6% in COMICE pts and 42% in pts in the same time period not included in the trial. Lobular type was 13% in COMICE vs. 37%	RCT	BC
Invasive								
Turku University Hospital, Turku, Finland 2011-2013	Bruck, 2018 (162)	RCT Pre-operative MRI or not, n=100 (50+50) Based on palpation, mammography, or US	Age ≥35 y, newly diagnosed unilateral and clinically unifocal stage I invasive ductal carcinoma, ≤20 mm prior to MRI and with first plan being for BCS and SNB	1.5 T MRI, prone position, bilateral four-channel breast array coil, gadoteric acid (Dotarem, Guerbet, Roissy CdG Cedex, France) contrast agent	Mastectomy: initial rate 10% vs. 0%, p=0.022; final rate12% vs. 4%, p=0.140	Change in planned surgical management in 20% of pts with MRI Post-hoc power analysis: 24.5% power to detect difference in reoperation rate and 51.6% power for	RCT	I

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
			Excluded pts with breast parenchymal pattern DY	Imaging sequences also covered both axillary areas Second-look US for MRI-only lesions, US-guided core needle biopsy taken if possible, no MRI-guided biopsies were required		mastectomy; need 412 and 480 pts respectively to have 80% power Note: all MRI-detected lesions were visible on second-look US		
Breast Cancer Surgical Outcomes (BRCASO) database (4 institutions in USA) 2003-2008	Feigelson, 2013 (163)	Retrospective: multivariable regression Predictors of initial total mastectomy; prospective at 1 site and retrospective at the others; univariate analysis and random effects multivariable logistic regression models using variables significant at p≤0.05 (age, ethnicity, tumour size, grade) n=185 + 2,199	Incident cases of IBC, stage I-III, age >18 y, Excluded pts with clinical indications for mastectomy, stage 0 or IV, neoadjuvant therapy, inflammatory breast cancer, multifocal or multicentric, prior breast cancer, chest radiation, unknow preoperative malignant diagnosis	Not reported	Initial mastectomy 29.7% vs. 15.6%, OR=2.44, 95% CI=1.58-3.77, p<0.0001 • Subset <20 mm: 18.1% vs. 9.6%, OR=2.59, 95% CI=1.46-5.59, p<0.0025	Mastectomy rate varied by surgeon from <5% to > 50%	R-MV-Reg	I-III

BCS, breast-conserving surgery; BI-RADS, Breast Imaging and Reporting and Data System; CI, confidence interval; DCIS, ductal carcinoma in situ; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; IBC, invasive breast cancer; ILC, invasive lobular carcinoma; MRI, magnetic resonance imaging; ns, not significant; NSM, nipple-sparing mastectomy; OR, odds ratio; pt, patient; pts, patients; PR, progesterone receptor; SNB, sentinel node biopsy; US, ultrasound; WLE, wide local excision

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Table 3. Positive margins, reoperation, re-excision, and conversion to mastectomy.

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
In situ, DCIS								
Lebanon, NH 2007-2011	Davis, 2012 (125)	Retrospective chart review comparing those with and without MRI, n=154 + 64 No comparison of baseline characteristics; assumed similar due to before/after MRI implementation design	Newly diagnosed DCIS confirmed by fine-needle or core biopsy MRI not used for DCIS in 2007-2008; used in all pts in 2009-2011	1.5 T MRI, dedicated prone eight channel breast, gadopentetate dimeglumine (Magnevist; Bayer Health Care, Berlin, Germany) contrast	Re-excision rate 34.1% vs. 39.2%, p=0.52 Conversion to mastectomy due to positive margins 8.9% vs. 5.9%, p=1.0	Margins ≤1 mm were re-excised	R-MV	DCIS
Netherlands Cancer Registry 2011-2015	Keymeulen, 2019 (126)	Retrospective, MRI vs. no MRI; multivariable logistic regression analyses to adjust for incidence year, age, hospital type, DCIS grade, multifocality n=2,382 + 8,033 BCS: n=1,303 + 6,072 Analyses were stratified by age at diagnosis (less than 50 versus 50-74 y) and histological grade	Diagnosis of pure DCIS and treated with surgery, age <75 y Breast MRI in pts with high-grade DCIS preferring BCS, unclear tumour size, or suspicion of microinvasion MRI used more in younger pts, higher grade, multifocality	Not reported	Margin involvement in BCS: focal or more than focal (focal = 4 mm area of positive margins) 21.5% vs. 20.5%, OR=0.99, 95% CI=0.85-1.16 Secondary surgery after BCS 21.2% vs. 16.8%, OR=1.17, 95% CI=1.00-1.37, p<0.05 Secondary mastectomy after BCS 11.2% vs. 7.4%, OR=1.32, 95% CI=1.07-1.63, p<0.05	Differences in subgroups by age or grade were similar to that of the full study except for secondary mastectomy No information on reason for MRI, or on size of DCIS, pat or surgeon preference	R-MV-Reg	DCIS

[1] Only female patients unless indicated otherwise.
[2] When statistical adjustments are made to account for confounders, this applies to OR and p values; numbers or rates of events of are not adjusted. For studies with multivariate analysis, only those which adjusted for stage/size, age/menopausal status, and subtype/histology are included. Adjustment for lesion distribution such as multicentric or multifocal was desirable but not generally conducted.
[3] RCT, randomized controlled trial; P, Prospective non-randomized trial; R-PSM, retrospective with propensity score matching; R-MV, retrospective with multivariate analysis; R-MV-Reg, retrospective with multivariate analysis using registry data; R-EQ, retrospective using data from equivalent groups (e.g., historical controls)

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
University of Ulsan College of Medicine, Gangneung, Korea 2012-2016	Yoon, 2020 (127)	Retrospective, preoperative MRI vs. no MRI; propensity score matching using 18 confounding variates to create matched groups n=430 + 111 n=106 + 106 after propensity score matching	Consecutive pts with DCIS confirmed by US-guided CNB Excluded concurrent invasive carcinoma, no surgery, history of ipsilateral breast cancer	1.5 T MRI or 3.0 T MRI, prone position, dedicated 18-channel phased-array breast, gadoterate meglumine (Magnevist; Schering, Berlin, Germany and Uniray; Dongkook, Seoul) contrast	Positive resection margin 6.6% vs. 17.0%, OR=0.39, 95% CI=0.16-0.93, p=0.03 Repeat surgery (all pts) 4.7% vs. 14.2%, OR=0.33, 95% CI=0.12-0.92, p=0.03	Patient and surgeon preference could not be controlled for	R-PSM	DCIS
Eindhoven Cancer Registry, The Netherlands	Vos, 2015 (129)	See In situ or invasive						
SEER-Medicare database (USA)	Wang, 2013 (164)	See In situ or invasive section						
DCIS – BCS planned								
IRCIS 10 hospitals in France NCT01112254 2010-2014	Balleyguier, 2019 (155) Kandel, 2020 (156) [costs]	Prospective randomized superiority trial: MRI vs. control arm (mammography and US) n=178 + 174 MRI group younger (median 56 vs 58 y) and more premenopausal (32% vs 27%), higher breast density	Aged 18-80 y with biopsy-proven limited DCIS, unifocal microcalcification cluster or mass <30mm and scheduled for BCS Exclude bilateral lesions, history of breast cancer, high risk (BRCA1/2). Most had BI-RADS 4 lesions (82% vs. 83%)	Mostly 1.5 T MRI, 3 T MRI in 2 centres, with contrast agent For enhancement suggestive of a mass or multiple and large lesions (>3 cm from the initial lesion), second-look US or additional mammography with magnification views and biopsy, if indicated, with mammography, US, MRI, or computed tomography guidance	Additional excision in same (initial) surgery 54% vs. 51% Reintervention rate at 6 months: ITT analysis 20% vs. 27%, OR=0.68, 95% CI=0.41-1.1, p=0.13; Per protocol OR=0.59, 95% CI=0.35-1.0, p=0.05 Mastectomy: second surgery 9% vs. 13%	No significant difference in total cost between groups	RCT	DCIS
COMICE	Turnbull, 2010 (158, 159); Morris, 2010	See In situ or invasive – BCS section						

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
	(160); McMahon, 2013 (161)							
In situ or invasive								
POMB Breast units in 3 Swedish hospitals 2007-2011	Gonzalez, 2014 (130) Karlsson, 2019 (131)	Randomized prospective multicentre trial, preoperative MRI or no MRI n=220 + 220 Prior to MRI, higher rate of BCS planned in MRI group (70% vs. 60%)	Women up to age 56 y with newly diagnosed IBC or non-invasive breast cancer; diagnosis confirmed with cytology or biopsy Suggested primary treatment (before MRI) was 65% BCS, 20% mastectomy, 12% neoadjuvant chemotherapy, 3% further investigation	MRI at Sites A and C but not B Site A: 1.5 T MRI, prone position, 8-channel breast coil, Omniscan (GE Healthcare) gadolinium contrast Site C: 1.5T MRI, prone position, 4-channel breast coil, Dotarem (Guerbet) gadolinium contrast MRI-detected lesions biopsied if detectable by US. MRI-guided biopsy introduced in 2009 at one site, only used in 3 pts	Re-operation rate 5.0% vs. 15.0%, p<0.001 Re-excision 0.9% vs. 8.6% Conversion mastectomy: 4.1% vs. 6.4%	Goal was to have ≥10 mm margins, but not touching inked surface for invasive carcinomas accepted; individual decision for DCIS Critique of trial by Brenner 2015 (439)	RCT	BC
Monet NCT00302120 4 hospitals in The Netherlands 2006-2008	Peters, 2011 (132) Peters, 2007 (133) [protocol]	Randomized before biopsy/diagnosis Routine care + preoperative MRI or routine care alone (mammography, US, core needle biopsy) n=78 + 76 207 + 211 pts initially but only 74 + 75 pts had malignant	Suspicious non-palpable breast tumours, BI-RADS 3-5 detected on mammography or breast US at randomization. Histological analysis from needle biopsy of in situ or invasive carcinoma to be included in study	MRI at university hospital 3 T bilateral dynamic contrast enhanced (DCE) breast MRI prior to biopsy of suspicious lesion, prone position, dedicated phased-array bilateral breast coil, Gadolinium-DTPA (Magnevist, Schering, Germany) contrast	Re-excision or conversion of BCS to mastectomy combined 45.3% vs. 28.0%, p=0.069 Re-excisions in BCS 34.0% vs. 12.0%, p=0.008 Conversion of BCS to mastectomy 11.3% vs. 16.0%, p=0.489	Commentary on this article (440) indicated that sensitivity of 51% is well below 92% achievable in some other studies suggesting there may have been technical limitations with	RCT	BC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		lesions (78 + 76 breasts, 83 + 80 lesions) and underwent surgery Note: biopsy was after MRI Study designed to have sufficient power for primary outcome of re-operation if 250 cancers with surgery in each group	Excluded palpable lesions, breast surgery or RT within 9 months Approximately 50% of malignant lesions were DCIS and 50% invasive carcinoma for both MRI and control groups 60% of lesions had microcalcifications only, compared to 25% described in the literature, possibly due to excluding palpable cancers	Additional lesions on MRI investigated with second-look US and sampled with US or MRI guidance 3 T MRI was relatively new and previously had substantial problems with fat suppression; authors indicated image quality was at least comparable to 1.5 T in other systems		the MRI used; re-operation rate high Large proportion of false negative MRIs could have led to too little tissue being initially removed and therefore higher re-excision rates		
SEER-Medicare database (USA) 2002-2007	Wang, 2013 (164)	Retrospective, preoperative MRI vs. no MRI; multilevel logistic regression models, adjusted for pt and tumour characteristics n=2,554 + 33,723 IBC n=443 + 8733 in situ	Early-stage breast cancer, stage 0-II Excluded CPM or bilateral mastectomy, or contralateral recurrent breast cancer within 3 months	Not reported	Multiple surgeries (not adjusted) 25.6% vs. 20.5% overall; 25.1% vs. 20.9% IBC; 29.3% vs. 18.8% in situ Adjusted OR for multiple surgeries: IBC OR=1.00, 95% CI=0.89-1.11 in situ OR=1.23, 95% CI=0.94-1.59 Considerable geographic variation: rate of additional surgery varied from 10.1% in Iowa to 27.7% in San Jose Mastectomy results not adjusted: 37.4% vs. 31.7%, p<0.0001	Median OR for receiving multiple surgeries between 2 randomly chosen physicians is 2.02 for IBC and 2.11 for in situ cancer, indicating a large surgeon effect and lack of evidence-based criteria for re-excision	R-MV-Reg	0-II
Mercy Hospital, Oklahoma City 2003-2006 Extended to 2014	Hollingsworth, 2008 (141) Hollingsworth, 2015 (142)	Retrospective study of consecutive pts who all had MRI preoperatively; historical control comparison n=603 with MRI (141) n=2000 with MRI (142)	Consecutive pts with newly diagnosed breast cancer, all underwent breast MRI Excluded neoadjuvant chemotherapy or those	First 249 pts: 0.5 T breast-dedicated MRI with bilateral breast coil, gadolinium contrast Later pts: 1.5 T breast-dedicated MRI, both	<u>2008 results</u> Re-operation for positive margins 8.8% <u>2015 results</u> Re-excision rates 9% (range 8%-10%) with MRI vs 12% to 15% in years before MRI instituted	The 7.7% multicentricity + 3.7% contralateral (11.4% combined) suggests MRI has major contribution, even if excluding role in	R-EQ	**BC**

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Historical controls without MRI 1996-2002			without surgery after biopsy In 2008 publication: 388 invasive ductal carcinomas, 149 DCIS, 65 invasive lobular carcinoma, 1 malignant phyllodes tumour	breasts, gadolinium contrast Image-guided biopsy included radiograph, US, or MRI guidance	Of all pts with MRI, 91% had 1 surgical procedure and the rest (9%) had 2. No pts required >2 operations.	evaluating the index lesion		
Single institution in USA 2004-2008	Grady, 2012 (143)	Retrospective review, after and before 2 surgeons started routinely using MRI; preoperative MRI vs. no MRI n=79 + 105 Groups equivalent in age, menopausal status, histology, pathologic stage, ER/PR status	Operative breast cancer diagnosed using core-needle biopsy One surgeon started use of MRI in late 2004, the other in late 2007	1.5 T MRI, prone position, 1.5 T 8-channel biopsy breast array coil, gadolinium (Magnevist - Bayer HealthCare Pharmaceuticals, Berkeley, CA) contrast Anatomic information for the breast and axilla	Additional surgery to obtain clear margins 11% vs. 26%, p=0.04 Repeat axillary procedures 10% vs. 20%, p=0.05		R-EQ	BC
University of Ulsan College of Medicine, Seoul, South Korea 2009-2010	Choi, 2017 (139)	Retrospective with propensity score matching those with MRI to those without based on 25 covariates n=828 + 1613; selected 799 matched pairs	Consecutive women with newly diagnosed breast cancer and curative surgery; excluded those with neoadjuvant chemotherapy or distant metastasis, bilateral breast cancer	1.5 T MRI, bilateral breast coil, Magnevist (Schering, Berlin, Germany) contrast Axial sequence for the evaluation of the supraclavicular and axillary lymph nodes	Positive resection margins 6.0% vs. 7.3%, p=0.322 Re-excision rate 1.6% vs. 3.3%, p=0.035		R-PSM	BC
Changhua Christian Hospital Breast cancer database, Taiwan 2009-2013	Lai, 2016 (140)	Retrospective, preoperative MRI vs. no MRI Control group (no MRI) from Jan 2009-Dec 2010; MRI group starting Jan 2011 when coverage for MRI cost was implemented Multivariate analysis adjusted for biopsy method, MRI, and	Primary operable breast cancer, mammography and sonography, surgery Excluded neoadjuvant chemotherapy Time periods chosen to minimize selection bias MRI group had less grade II and more grade III		Positive margins 5.0% vs. 9.0%, p<0.01 Positive margins in BCS 6.6% vs. 14.6%, OR=0.42, 95% CI=0.72-2.63, p<0.01; multivariate OR=0.43, 95% CI=0.71-3.03, p<0.01 Positive margins in mastectomy 3.6% vs. 3.1%, p=0.84		R-PSM	BC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		multifocal/multicentric only for outcome of margin status in BCS Propensity-score matching appears insufficient as most parameters not equivalent after matching n=735 + 733 BCS subgroup n=348 + 377 Mastectomy subgroup n=387 + 356	cancers, more multifocal or multicentric cancer (14.3% vs 8.6%), more reconstruction (39.8% vs. 17.1%), more SLNB (58.0% vs. 38.5%)		Re-operation in BCS group 3.2% vs. 11.7%, p<0.01 Re-excision in BCS 2.6% vs. 8.0%, p=0.48 Conversion to mastectomy 0.6% vs 3.7%			
SEER-Medicare database 2005-2009	Ozanne, 2017 (136)	Retrospective, preoperative MRI vs. no MRI Unadjusted and multivariable logistic regression models n=9,055 + 46,942 Adjusted for age at diagnosis, race, SEER registry, marital status, median income, urban/rural status, Medicaid, previous other cancer, comorbidity index, year of diagnosis, histology, grade, stage, ER and nodal status, tumour size, teaching hospital, NCI cooperative oncology group member and hospital type	Stage 0-III breast cancer, BCS or mastectomy within 6 months of diagnosis, age ≥66 y Excluded prior history of breast cancer or diagnosed in a nursing home	Not reported	Re-operation after BCS: 21.3% vs. 20.5%, OR=1.05, 95% CI=0.98-1.12; adjusted OR=0.95, 95% CI=0.88-1.02		R-MV-Reg	0-III
Eindhoven Cancer Registry, The Netherlands 2011-2013	Vos, 2015 (129)	Retrospective, preoperative MRI vs. no MRI, multivariable binary logistic regression analyses adjusted factors with p<0.1 in univariable analysis; different set of factors used for each outcome	IBC pT1-3 or pure DCIS Excluded neoadjuvant systemic therapy, stage T4, distant metastasis, unknown stage or T0, unknown surgery or margin status	Dynamic contrast-enhanced MRI was performed according to local protocol in each hospital No other details reported	Adjusted OR (95% CI) and adjusted p values in pts with initial BCS All pts (adjusted for age and grade): • Positive margins in BCS 18.1% vs. 15.1%, OR=1.20, 95% CI=1.00-1.45, p=0.052	No information on multifocality or multicentricity, indication for performing MRI, any changes in surgical plan	R-MV-Reg	0-III (DCIS or IBC)

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		Invasive: n=1,637 + 3,164 (including 449 + 231 ILC) DCIS: n=150 + 563 Subgroups of invasive cancer, high-grade DCIS, non-palpable invasive, age ≤40 y, lobular	Contralateral breast cancer was analyzed as a new pt MRI pts younger, more ILC (27.4% vs. 7.3%)		• Re-excision in BCS 9.8% vs. 7.2%, OR=1.33, 95% CI=1.04-1.70, p=0.026 High-grade DCIS (grade 2-3; adjusted for age and grade): • Positive margins in BCS 23.4% vs. 18.4%, OR=1.35, 95% CI=0.75-2.43, p=0.314; adjusted OR=1.28, 95% CI=0.70-2.32, p=0.426 • Re-excision in BCS 20.8% vs. 15.1%, OR=1.48, 95% CI-0.80-2.73, p=0.216; adjusted OR=1.38, 95% CI=0.73-2.59, p=0.320 Invasive cancer (adjusted for age, palpability, histology, presence of DCIS component, tumour size, differentiation grade and regional lymph node status): • Positive margins in BCS 17.9% vs. 14.8%, OR=1.26, 95% CI=1.04-1.53, p=0.02; adjusted OR=0.98, 95% CI=0.79-1.22, p=0.882 • Re-excision in BCS 9.1% vs. 5.9%, OR=1.58, 95% CI=1.21-2.08, p=0.001; adjusted OR=1.27, 95% CI=0.94-1.72, p=0.125 ILC • Positive margins in BCS 24.6% vs. 27.0%, OR=0.88, 95% CI=0.55-1.41, p=0.603; adjusted OR=0.80, 95% CI=0.47-1.38, p=0.419 Re-excision in BCS 11.0% vs. 11.7%, OR=0.93, 95% CI=0.49-1.79, p=0.835;	Residual confounding may be present from factors not taken into consideration		

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
					adjusted OR=0.97, 95% CI=0.44-2.12, p=0.933			
In situ or invasive – BCS only								
BREAST-MRI ICESP, São Paulo, Brazil NCT02798796 2014-2016	Mota, 2019 (157) [Abstract]	Randomized, stratified for mammary density n=219 + 227	Stage 0-III, candidate for BCS	1.5T MRI system Surgery was modified when MRI showed an increase of more than 50% of the tumour size	Re-operation rate not different, 7.8% vs. 7.0%, p=0.95 Re-excision 5.5% vs. 4.8% Conversion to mastectomy 2.3% vs 2.2%	Surgical change in 31.1% of those with MRI (49 pts ipsilateral; 13 contralateral, 6 both); conversion to ipsilateral mastectomy in 19 pts	RCT	0-III
COMICE ISRCTN 57474502 UK (45 centres) 2002-2007	Turnbull, 2010 (158, 159); Morris, 2010 (160); McMahon, 2013 (161)	Pragmatic trial, randomized to MRI or no further imaging, minimization factors were breast surgeon, age (<50 or ≥ 50), breast density group (1 vs. 2/3/4) n=816 + 807 randomized n=761 + 798 received correct test (MRI or not) Invasive: n=719 + 688 with margin status results DCIS: n=427 + 430 with margin status results Definitions were not standardized and varied by site: clear margins ranged from 0.5 to 5.0 mm for invasive disease and 1.0 to 10.0 mm for DCIS	Women aged ≥18 y with biopsy-proven primary breast cancer scheduled for WLE after triple assessment (clinical, radiological [mammogram and US] and cytology/biopsy); excluded neoadjuvant treatment or previous surgery 77% age ≥50 y; 70% postmenopausal	1.5 T MRI, dedicated bilateral breast-surface coils; a few scans at 1.0 T Gd-diethylenetriaminepenta-acetic acid contrast A second publication (159) indicates 1.5 T MRI required compromises in either the temporal or spatial resolution employed or to extent of the breast coverage obtained. In some centres fat-suppression was not available. MRI-directed biopsy was not available at the start of the trial and many	Primary outcome was rate of repeat operation or further mastectomy within 6 months, or pathologically avoidable mastectomy Reoperation 16.3% vs. 18.7%, OR=0.96, 95% CI=0.75-1.24, p=0.77 Re-excision 10.4% vs. 11.2% Subsequent mastectomy 5.9% vs. 7.6% Positive margins for invasive tumours 14.3% vs. 15.9% Positive margins for DCIS: 22.0% vs. 19.3%; large amount of missing data for distance to margins (35%) and involved margins (22%)	Investigators at one trial site (161) suggest that complicated cases, which benefited from MRI, were pre-selected out prior to randomization; mastectomy rate was 15.6% in COMICE pts and 42% in pts in the same time period not included in the trial. Lobular type was 13% in COMICE vs. 37%	RCT	BC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
				women had mastectomy without pathological verification of disease (16/58, 27.6% of mastectomies in the MRI group) (159, 160)				
Memorial Sloan Kettering Cancer Center, New York 2000-2004	Sung, 2014 (165)	Retrospective institutional review, preoperative MRI vs. no MRI; MRI and control matched 1:1 by age (5 y increments), histopathologic features (DCIS, invasive ductal, invasive lobular, invasive mammary carcinoma), stage, surgeon for 85% of cases; 15% had broader age match and excluding surgeon matching n=174 + 174	Early stage (0-II) breast cancer undergoing BCS +RT Excluded if neoadjuvant therapy, mastectomy, distant metastases, or no RT MRI group more likely to have extremely dense breasts (28% vs. 6%, p<0.0001) and mammographically occult cancer (24% vs. 9%, p=0.0003) 10 pt pairs had intraoperative partial breast RT and were excluded from long-term outcome analysis; the rest had whole-breast RT with or without boost	1.5 T MRI, prone position, dedicated surface breast coil, gadopentetate dimeglumine (Magnevist, Berlex) contrast Suspicious lesions (mammography or MRI) remote from the index lesion potentially representing multifocal, multicentric, or contralateral were routinely sampled by either percutaneous or surgical biopsy	• Positive margins 11.5% vs 10.3% [positive margins 0% vs 1%; close margins (≤2 mm) 11% vs. 9%; p=0.29] • Reoperation 29.3% vs 44.8%, p=0.02 • Re-excision 21.8% vs. 37.4% • 1 excision 71% vs. 55%; 2 excisions 28% vs. 40%; 3 excisions 2% vs. 5%; 4 excisions 0% vs <1% • Subsequent mastectomy 7.5% vs. 7.5%		R-MC	0-II
Lynn Sage Comprehensive Breast Center at Northwestern Memorial Hospital, Chicago, Il	Zeng, 2020 (166)	Retrospective, preoperative MRI vs. no MRI Multivariable regression for recurrence outcomes only n=330 + 182 Two groups were well balanced for age, race, tumour size,	Primary stage 0-III breast cancer, BCT, tumour-free margins, age ≤50 y Excluded neoadjuvant therapy, RT use not ascertained, metastatic Cohort was derived from a gold-standard dataset	Not reported	Re-excision rates 8.8% vs. 11.5%, p=0.32	Reasons for pt acceptance of MRI were not recorded; most often declined for claustrophobia, fear of biopsies, cost	R-EQ	0-III

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
2006-2013		histology, grade, nodal and hormone receptor status	of 2045 pts; details are not provided					
Rotterdam, The Netherlands 2007-2010	Obdeijn, 2013 (167)	Consecutive pts with preoperative MRI, historical control group from 2005-2006 included all pts with BCS without MRI (21.2% DCIS, 78.8% invasive) n=140 + 132 lesions; 123 + 119 lesions n=95 + 123 for margins and reoperation (BCS pts only) Multiregression analysis was used to compare positive resection margins and re-operations, and included group and size of lesions	Diagnosis of either IBC (84.3%) or DCIS (15.7%) and eligible for BCS based on clinical examination and conventional imaging; final surgical plan included preoperative MRI information Mean size of both invasive malignancies and DCIS was significantly larger in the MRI group	1.5 T MRI, prone position, dedicated double breast coil, gadobutrol (Gadovist, Bayer Schering Pharma) contrast "Additional BI-RADS 3, 4, and 5 lesions found by MRI were investigated by second-look US or re-evaluation of the mammographic examination. In case an additional BI-RADS 3 lesion could be identified, fine-needle aspiration (FNA) or biopsy was performed, otherwise follow-up MRI was advised. In case of additional BI-RADS 4 or 5 lesions, FNA or biopsy was always performed. This was done under stereotactic, US, or MRI guidance."	Positive resection margins: • 15.8% vs. 29.3%, adjusted OR 0.33, 95% CI=0.16-0.69, p<0.01 Re-operations: • 18.9% vs. 37.4%, adjusted OR=0.29, 95% CI=0.15-0.58, p<0.01		R-EQ	0-III (DCIS or IBC)
Invasive								
Breast Cancer Treatment Disparity Study in New Jersey State Cancer Registry 2005-2010	Chandwani, 2014 (168)	Retrospective, preoperative MRI vs. no MRI Adjustment of re-operation and CPM outcomes for potential confounders using univariate and multivariate binomial regression	African American (n=289) and white (n=320) women with newly diagnosed early-stage (stage I, II, or T3N1M0) breast cancer and surgery, age ≤85 y		Re-operation 18.1% vs. 20.3%, RR=0.89, 95% CI=0.64-1.23, p=0.484; adjusted RR=0.76, 95% CI=0.54-1.08 Positive margins 12.5% vs 13.4%; close margins 15.5% vs. 12.1%; p=0.478, not adjusted		R-MV-Reg	I-II or T3N1

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		Adjusted for age, race, education, insurance, BMI, method of diagnosis, histology, multifocality or multicentricity, and surgical facility n=304 + 305 No adjustment for tumour grade, size, lymph node status; density not reported; only recorded whether tumour was ≤1 cm or >1 cm	MRI group was younger, higher education, more often white race, lower BMI, more private insurance, more family history; disease more often found by pt, more multifocal or multicentric disease, and more lymph node positive					
SEER-Medicare linked dataset 2004-2007	Fortune-Greeley, 2014 (150)	Retrospective, MRI vs. no MRI Propensity score methods (tumour grade, size, node positivity, ER/PR status, comorbidity, age, marital status, race, ethnicity, SEER region, education, financial status, facility, surgical volume) n=2,471 + 17,861 IDC (n=1,557 + 12,800), ILC (n=396 + 1,532), mixed IDC/ILC (n=390 + 2008)	aged ≥66 y, stage I-IIB (AJCC 6th edition) MRI more frequent in ILC or mixed IDC/ILC cancers Excluded neoadjuvant chemotherapy, tumours > 5 cm, second primary cancer within 12 months	Not reported	Reoperations • Overall: 21.0% vs. 20.6%: adjusted OR=0.89, 95% CI=0.77-1.02 • IDC: 19.2% vs. 19.1%, OR=0.98, 95% CI=0.82-1.15, p=0.96 • ILC: 25.3% vs. 29.1%, OR=0.59, 95% CI=0.40-0.86 • Mixed: 25.5% vs. 25.9%, OR=0.93, 95% CI=0.67-1.30	Not able to balance pts on unobserved characteristics such as reason for MRI, MRI results, pt preference for mastectomy, multifocal disease, breast density, surgeon experience For several outcomes, adjusted and non-adjusted data give opposing results	R-PSM	I-IIB
McGill University Health Centre 2006-2013	Parsyan, 2016 (145)	Retrospective from tumour registry, preoperative MRI or not Multivariate analysis controlling only for age; no difference in tumour size, histologic type, ER status grade, HER2 status; other factors not measured	Stage I-III breast cancer, definitive surgical treatment Excluded neoadjuvant therapy, previous breast cancer in situ carcinoma, age < 30 y, history of	1.5 T MRI, bilateral, 8-channel breast phase array coil, gadolinium contrast	Adjusted for age: Re-excision 7.5% vs. 8.7%, OR=0.86, 95% CI=0.52-1.40, p=0.540; adjusted OR=0.83, 95% CI=0.46-1.49, p=0.552		R-MV	I-III

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		n=307 + 458	Hodgkin's lymphoma, BRCA positive MRI group was younger (55.3 y vs. 66.3 y)					
Memorial Sloan-Kettering Cancer Center, New York, NY 2005-2007	Kapoor, 2013 (146)	Retrospective, evaluation relationship between breast density and BCS; adjusted for clinical and pathologic variables that were significant on univariate analysis using multivariate logistic regression (age, grade, multicentric/ focal, LVI, size, subtype, density) n=385 + 671	Stage I-III IBC, surgical treatment Excluded neoadjuvant chemotherapy, no mammogram, surgery at outside hospital, surgical diagnostic biopsy	Not reported	Positive margin after BCS 57.9% vs. 47.9%, OR=1.51, 95% CI=1.18-1.93, p=0.0010 univariate; OR=1.34, 95% CI=0.98-1.84, p=0.0703 multivariate Conversion to mastectomy after positive margins 30.0% vs. 21.9%, OR=1.64, 95% CI=1.17-2.30, p=0.0039 univariate; OR=1.58, 95% CI=1.01-2.47, p=0.0458	Breast density, young pt age, mammographically occult cancers, and the use of preoperative MRI are interrelated factors Patient participation in surgical decision making is strongly associated with mastectomy use	R-MV	I-III
Netherlands Cancer Registry 2011-2013	Vriens, 2017 (148)	Retrospective from registry Multivariable analysis n=2,879 + 554 Adjusted for year of incidence, age, tumour size, nodal status, ER, PR, HER2 status, grade, multifocality	Stage I-III IBC (cT1-3) and neoadjuvant therapy, age 18-70 y Excluded cT4 tumours	Not reported	Surgical margin involvement in BCS (more than focally positive, defined as positive over a length of >4 mm) 2.8% vs. 3.8%, OR=0.60, 95% CI=0.32-1.10, p=0.10; however also states 88 vs 15 pts (3.1% vs. 2.7% of all pts) and therefore impossible to get percentages stated for BCS subset. There must be errors in this paper and data for margins are unusable	Family history information not available	R-MV-Reg	I-III
Netherlands Cancer Registry 2011-2013	Lobbes, 2017 (149)	Retrospective population-based cohort study; MRI vs. no MRI Multivariable logistic regression analysis with covariates of year of diagnosis, age, clinical tumour size, nodal status, ER,	All Dutch pts with primary IBC (cT1-4N0-3M0) treated with primary surgery, Excluded distant metastases, DCIS, neoadjuvant therapy,	Breast MRI protocols adhere to EUSOBI quality criteria. No other details reported	Multivariable analysis results Positive margins after BCS (more than focally positive, defined as positive at inked margin over a length of >4 mm) • OR=0.84, 95% CI=0.73-0.97, p=0.015 • IDC 3.6% vs. 3.7%, OR=0.90, 95% CI=0.77-1.06, p=0.202	Limitations: breast size and density, tumour localization within the breast, pt breast cancer risk profile, and the initial surgical treatment plan	R-MV-Reg	IBC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		PR, HER2 status, tumour grade, histological type, multifocality Analysis for full group and subgroups of ductal and lobular cancers n=10,740 + 25,310 Ductal: n=7,462 + 21,128 (26% MRI) Lobular: n=2,774 + 2,361 (54% MRI)	unknown tumour localization Standard practice is mammography and/or US plus tissue sampling of lesions; discussion in tumour board determined whether MRI was performed Pts selected from cancer registry then hospital files reviewed Pts with MRI generally younger, ILC, multifocal cancer		• ILC 5.0% vs. 7.0%, OR=0.59, 95% CI=0.44-0.79, p=0.0003 Secondary mastectomy • OR=1.07, 95% CI=0.89-1.29, p=0.434 • IDC OR=1.23, 95% CI=1.00-1.53, p=0.054 • ILC OR=0.61, 95% CI=0.42-0.88, p=0.0088	based on mammographic and/or US findings) were not available Motivation for MRI unknown		
University of Pennsylvania 2009-2019	Burkbauer, 2020 (169) [abstract]	Retrospective, MRI vs. no MRI Inverse probability weighted analysis to control for baseline characteristics (age < 40 y, ILC, density, family history, prior RT, mutation carrier) n=571 + 540 n=311 + 368 with initial BCS No significant differences in race, socioeconomic status, ER/PR status, pathological stage	Invasive HER2+ breast cancer Excluded metastatic, neoadjuvant therapy, unknown stage, receptor status or surgery date MRI group younger	Not reported	Re-excision after BCS: crude rate 34.73% vs. 27.45%, p=0.04; adjusted p=0.31		R-MV	IBC HER2+
SEER-Medicare database (USA)	Wang, 2013 (164)	See in situ or invasive section						
Invasive - BCS								
Turku University	Bruck, 2018 (162)	Prospective randomized trial, pre-operative MRI or not, n=50 + 50	Age ≥35 y, newly diagnosed unilateral and clinically unifocal stage I invasive ductal	1.5 T MRI, prone position, bilateral four-channel breast array coil, gadoteric acid	Re-operation rate 14% vs. 24%, p=0.202		RCT	I

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Hospital, Turku, Finland 2011-2013		Diagnosis based on palpation, mammography, or US	carcinoma, ≤20 mm prior to MRI and with first plan being for BCS and SNB Excluded pts with breast parenchymal pattern DY	(Dotarem, Guerbet, Roissy CdG Cedex, France) contrast agent Imaging sequences also covered both axillary areas	All MRI-detected lesions were visible on second-look US, no MRI-guided biopsies were required			
COMICE	Turnbull, 2010 (158, 159); Morris, 2010 (160); McMahon, 2013 (161)	See: In situ or invasive – BCS only						
Eindhoven Cancer Registry, The Netherlands	Vos, 2015 (129)	See In situ or invasive						
IDC								
SEER-Medicare linked dataset	Fortune-Greeley, 2014 (150)	See Invasive section						
Netherlands Cancer Registry	Lobbes, 2017 (149)	See Invasive section						
ILC								
Radboud University Nijmegen Medical Centre (RUNMC), The Netherlands, 1993-2005 The Netherlands Cancer	Mann, 2010 (151)	Retrospective study of pts in database, preoperative MRI vs. no MRI No multivariate analysis Groups comparable for menopausal status, family history, tumour size, ER/PR status, in situ cancer	ILC Excluded history of cancer, prior breast surgery, neoadjuvant chemotherapy, or other non-surgical techniques, treated at another hospital Indications for MRI included accepted clinical	Various MRI systems, various field strengths ranging from 1.0 to 3.0 T, and various scan protocols. Prone position, dedicated bilateral breast coil, Gd-containing contrast agent	All pts: • Re-excision (primary endpoint) 5.1% vs. 14.9%, OR=0.30, 95% CI=0.11-0.82, p=0.014 • Conversion to mastectomy 4.0% vs. 12.5% Group with initial BCS (n=55 + 90) • Re-excision 9.1% vs. 26.7%, OR=0.27, 95% CI=0.10-0.77, p=0.010	MRI reduced re-excision and final mastectomy	R-EQ	ILC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Institute/Antoni van Leeuwenhoek Hospital 1999-2005		MRI group younger (mean 56 vs. 61 y; median 57 vs. 60 y) n=99 + 168	indications, pt wish, and participation in clinical studies that assessed: (1) the radiologic pathologic correlation of MR-visible tumours, (2) high-risk screening, (3) preoperative staging, and (4) new MRI sequences.	Second look US or MRI-guided (excision) biopsy prior to adaptation of the surgical plan, other than for small extension to local excision	• Conversion to mastectomy 7.3% vs 23.3%, p=0.013			
Seoul, Korea 2005-2016	Ha, 2018 (152) Overlaps with pts in Ha, 2019 (185)	Retrospective, propensity score matching n=369 + 234 of which 196 pairs were matched using 17 variables	ILC diagnosed with biopsy or surgical excision Excluded neoadjuvant chemotherapy, stage IV, male, double primary, missing data on pt or tumour characteristics	1.5- or 3.0-T MRI, dedicated 18-channel phased-array breast coil, gadopentate dimeglumine (Magnevist; Schering, Berlin, Germany) or Gadoterate meglumine (Dotarem; Guerbet, Villapinte, France) contrast	Reoperation 2.7% vs. 18.8%, p<0.001; after matching OR= 0.140, 95% CI=0.058-0.342, p <0.001		R-PSM	ILC
SEER-Medicare linked dataset	Fortune-Greeley, 2014 (150)	See Invasive section						
Netherlands Cancer Registry	Lobbes, 2017 (149)	See Invasive section						
Eindhoven Cancer Registry, The Netherlands	Vos, 2015 (129)	See In situ or invasive						
Ongoing Trials								
MIPA (27 centres, all except 2 in Europe)	Sardanelli, 2020 (153) [protocol] Sardanelli, 2017 (154)	Pragmatic observational non-randomized multicentre international prospective study for women offered MRI or not according to local practice	Consecutive pts with newly diagnosed breast cancer amenable to upfront surgery, aged 18-80 y	The coordinating centre approved only MRI protocols following technical recommendations issued by international	Re-operation rate for close or positive margins 8.3% vs. 13.4%, p<0.001		P-ongoing	BC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
ISRCTN4114317 8 2013-2018 Enrollment complete, follow-up to end of 2023	[abstract, interim] ONGOING	n=1,224 + 1,201 Variables that will be shown to be significantly different between the two groups will be considered as covariates when the two groups will be compared in analyses Target enrollment of 7,000 reached in 2018	Excluded candidates for neoadjuvant therapy or with personal history or cancer or with evidence of metastases	societies such us the European Society of Breast Cancer Specialists (EUSOMA), the EUSOB, and the American College of Radiology. ≥1.5 T MRI, ≥4 channels of dedicated coils, gadolinium-based contrast agent				
NCT01805076; Alliance AO11104; ACRIN 6694 2014-2020 plus follow-up Expected completion 2025	Bedrosian, 2011 (170) [Abstract] ONGOING	Randomized to standard of care with or without MRI Target n=556; actual n=317	Eligible for BCT by conventional criteria (clinical examination, mammography ± US) and ER- and PR- (ER-/PR-/HER2-or HER2+), Stage IA, IB, II. Excluded pts with multicentric or multifocal disease scheduled to undergo multiple lumpectomies	Not reported	Primary: LRR after BCS Secondary: re-operation rate, conversion to mastectomy, CBC rate, DFS, OS	Patients to be followed for 5 years from surgery	RCT-ongoing	I-II
B-SMART NCT00948285 Texas 2009-2011 at interim analysis; terminated 2019	Rahman, 2012 (171) [Abstract]	Prospective RCT, (mammogram / US) ± MRI prior to surgery Target n=400, Interim analysis with n=103 (91 analyzed) Final enrolment n=194; terminated 2019 due to low accrual	Newly diagnosed breast cancer, BCS candidate as assessed by surgeon after conventional imaging	Not reported	Margin revision rate Interim analysis: margin: 3.4 mm vs. 3.4 mm, p=0.99; re-excision rate 7.3% vs. 17%, p=0.21; margin volume 34 cm^3 vs. 17 cm^3, p=0.03	15 (35%) additional cancer by MRI; missed 2 (5%)	RCT	BC

ACRIN, American College of Radiology Imaging Network; BCS, breast-conserving surgery; BCT, breast-conserving therapy (BCS + RT); BI-RADS, Breast Imaging and Reporting and Data System; CBC, contralateral breast cancer; CI, confidence interval; CNB, core-needle biopsy; CPM, contralateral prophylactic mastectomy; DCIS, ductal carcinoma in situ; DFS, disease-free survival; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; IBC, invasive breast cancer; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; ITT, intent-to-treat; LRR,

loco-regional recurrence; LVI, lymphovascular invasion; MRI, magnetic resonance imaging; ns, not significant; OR, odds ratio; pt, patient; pts, patients; OS, overall survival; PR, progesterone receptor; RR, relative risk; RT, radiotherapy; SEER, Surveillance, Epidemiology, and End Results database; SLNB, sentinel lymph node biopsy; US, ultrasound; WLE, wide local excision

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Table 4. Contralateral breast cancer, recurrence, and survival.

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
DCIS – all surgeries								
SEER-Medicare dataset 2004-2009	Wang, 2016 (172)	Retrospective; MRI vs. no MRI; propensity score matching to adjust for baseline characteristics (age, comorbidity, income, stage, grade, size, histology, ER/PR status, and other factors) Relationship between MRI and CBC occurrences n=1,258 + 7,908 Matched: n=1,159 + 2,156	Women aged 67-94 y diagnosed with DCIS 2004-2009 and follow-up through 2011, and had surgery within 9 months of diagnosis MRI had to be in the period 90 days pre-diagnosis to date of surgery	Not reported	After propensity score matching: Synchronous CBC (< 6 months) 5.1% vs. 1.6% (from graph), 108.6 vs. 29.7 per 1000 person-years, HR=0.27, 95% CI 0.18-0.42, p<0.001. Subsequent CBC (≥6 months) with median 44 months follow-up 3.9% vs. 2.8% (from graph), 6.7 vs. 6.8 per 1000 person-years, HR=0.90, 95% CI=0.52-1.56, p=0.71	Units of cases per 1000 person-years makes comparison difficult	R-PSM	DCIS
DCIS – BCS only								
Memorial Sloan-Kettering Cancer Center (MSKCC) 1997-2010	Pilewskie, 2014 (173)	Retrospective, pts identified from database with MRI data from chart review; relationship between MRI and LRR examined using multivariable analysis (age, menopausal status, family history, mode of	Pure DCIS treated with BCS, with RT (61%) or without RT (39%); all had mammography, 26% had perioperative bilateral breast MRI (15% before biopsy, 66% after biopsy, and 19% after lumpectomy but before RT)	Bilateral. No other details reported	8-y LRR 14.6% vs. 10.2%, p=0.52; 5-y LRR 8.54% vs. 7.23%, p=0.52; adjusted HR=1.18, 95% CI=0.79-1.78, p=0.42 • No RT subgroup: 5-y LRR 13.2% vs. 10%, p=0.33; adjusted HR=1.36, 95% CI=0.78-2.39, p=0.28	RT and margin status had significant effect on LRR	R-MV	DCIS

[1] Only female patients unless indicated otherwise.

[2] When statistical adjustments were made to account for confounders, this applies to OR and p values; numbers or rates of events of are not adjusted. Stage/size, age/menopausal status, in situ/invasive proportion, HER2/ER/PR status, systemic therapy, and RT were considered to be potentially important cofounders.

[3] RCT, randomized controlled trial; P, Prospective non-randomized trial; R-PSM, retrospective with propensity score matching; R-MV, retrospective with multivariate analysis; R-MV-Reg, retrospective with multivariate analysis using registry data; R-EQ, retrospective using data from equivalent groups (e.g., historical controls)

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		presentation, margin status, number of excisions, adjuvant RT, adjuvant endocrine therapy, year of diagnosis) n=596 + 1,725	MRI group younger, more likely to be pre/perimenopausal, more family history of breast cancer, more clinical abnormalities, more postoperative RT, and adjuvant endocrine therapy		• RT subgroup: 5-y LRR 6.34% vs. 5.22%, p=0.54; adjusted HR=1.14, 95% CI=0.63-2.09, p=0.66 Metachronous CBC: 8-y CBC (not adjusted) 3.5% vs. 5.1%; 5-y CBC 3.5% vs. 3.5%, p=0.86 (p=0.87 no RT, p=0.73 RT)			
In situ or invasive – all surgeries								
University of Ulsan College of Medicine, Seoul, South Korea 2009-2010	Choi, 2017 (139)	Retrospective with propensity score matching those with MRI to those without based on 25 covariates n=828 + 1,613; selected 799 matched pairs	Consecutive women with newly diagnosed breast cancer and curative surgery; excluded those with neoadjuvant chemotherapy or distant metastasis, bilateral breast cancer	1.5 T MRI, bilateral breast coil, Magnevist (Schering, Berlin, Germany) contrast Axial sequence for the evaluation of the supraclavicular and axillary lymph nodes	Recurrence 8.8% vs. 10.4%, p=0.30 Death as first recurrence 2.6% vs. 3.3%, p=0.491		R-PSM	BC
Seoul National University College of Medicine, Korea 2004-2008	Kim, 2013 (174)	Retrospective, bilateral MRI 2007-2008 vs. unilateral MRI 2004-2006 Multivariate analysis using factors from univariate analysis with p<0.2 (index tumour size, lymph node status, ER status) n=1,771 bilateral MRI + 1,323 unilateral MRI	Surgery for breast cancer Excluded bilateral breast cancer identified by clinical symptoms or mammography prior to MRI, metastasis, missing follow-up to 12 months	Bilateral breast MRI replaced unilateral MRI in 2007 Bilateral: 1.5 T MRI, contrast-enhanced Details are likely the same as in Bae, 2016 (178)	CBC at preoperative evaluation: ultrasound/mammography 1.19% (21/1771) vs 1.36% (18/1323), p=0.62; by MRI 1.41% (25/1771) vs 0%, p<0.001; total 2.60% (46/1771) vs 1.36% (18/1332) Annual examination with mammography and bilateral whole-breast US Median follow-up 45 months vs. 65 months Metachronous CBC estimated at 45 months: 0.51% (9/1771) vs. 1.36% (18/1323), p=0.02; multivariate analysis: adjusted HR=0.37, 95% CI=0.15-0.92, p=0.03 Metachronous CBC at 24 months 1/1771 vs. 9/1323, p-0.04		R-MV	BC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Invasive or in situ – BCS only								
Enterprise Data Warehouse of Northwestern Medicine, Chicago, IL 2004-2010	Amin, 2015 (175) [abstract]	Retrospective, preoperative MRI vs. no MRI, multivariate analysis; adjusted for pt age, tumour size, nodal status, the presence of triple negative disease, and the use of radiotherapy and systemic therapy n=526 + 571	Invasive cancer or DCIS and BCS MRI pts were younger, more palpable tumours, more ILC, less DCIS, more node positive disease	Not reported	Mean follow-up 51.5 months vs. 59.4 months Events (local recurrence at > 6 months or new metachronous cancer in contralateral breast): 9.3% vs. 11.9%, adjusted HR=0.90, 95% CI=0.59-1.36, p=0.61 Ipsilateral events adjusted HR=0.93, 95% CI=0.57-1.51, p=0.76 Metachronous contralateral events adjusted HR=1.22, 95% CI=0.57-2.62, p=0.61		R-MV	0-III (DCIS or IBC)
Samsung Medical Center, Seoul, Korea 2005-2006	Ko, 2013 (176)	Retrospective, MRI vs. no MRI Multivariate Cox proportional hazards model used to assess the difference of total recurrence and IBTR, adjusting for treatment and tumour characteristics (grade, ER/PR status, tumour size; other factors not significantly different) n=310 + 475 Subset early stage with BCS and RT, similar characteristics except ER/PR status: n=229 + 386 Re-excision data not adjusted	Invasive or in situ breast carcinoma and BCS attempted MRI indications: 75% preoperative evaluation, 19% post-excisional biopsy, 5% neoadjuvant chemotherapy Recurrence outcomes limited to pts with unilateral early-stage breast cancer (T0-II) and BCS + RT	1.5 T MRI, prone position, bilateral, dedicated 2-channel breast coil, gadolinium contrast agent (Magnevist, Bayer Schering, Berlin, Germany) MRI-detected lesions biopsied by US or mammographic guidance; MRI-guided biopsy unavailable	Median follow-up 68 months; mammography and/or US every 6 months for first 3 y and then yearly thereafter Subset with unilateral early-stage cancer, BCS + RT: Recurrence 5.7% vs. 8.3%, p=0.264; adjusted HR= 0.75, 95% CI=0.39-1.45, p=0.385 IBTR 0.4% vs. 3.6%, p=0.013; adjusted HR=0.16, 95% CI=0.02-1.2, p=0.076 Metachronous CBC 2.2% vs. 1.3%, p=0.512 (not adjusted) 5-y IBTR-free survival: 99.5% vs. 96.7%, p=0.020 No difference in CBC-free survival (p=0.168), regional RFS (p=0.605), or total RFS (p=0.383) (not adjusted)		R-MV	BC
Dartmouth Hitchcock Medical Center,	Hill, 2017 (177)	Retrospective Univariate and multivariate analysis (age, ER/PR/HER2	All pts undergoing BCT Excluded pts with conversion from BCT to	Not reported	Median follow-up 76.7 months vs. 86.0 months	MRI associated with decrease in recurrence on	R-MV	BC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Lebanon, NH, USA 2000-2010		status, RT, endocrine therapy for IBC) n=664 + 732	mastectomy, without negative margins (cancer on ink of IBC or > 1 mm for DCIS) Starting 2005, MRI had been recommended for all IBC and was received by 86.8% of pts with IBC in 2006-2010 Starting 2008, MRI recommended for all DCIS and received by 79.9% in 2008-2010		IBTR at 8 y calculated using Kaplan-Meier estimates: All pts (DCIS + invasive): 4.0% vs. 8.0%, RR=0.6, 95% CI=0.36-0.98, p=0.04; multivariate RR=0.77, 95% CI=0.45-1.28, p=0.32	univariate but not multivariate analysis		
Memorial Sloan Kettering Cancer Center, New York 2000-2004	Sung, 2014 (165)	Retrospective institutional review, preoperative MRI vs. no MRI; MRI and control matched 1:1 by age (5 y increments), histopathologic features (DCIS, invasive ductal, invasive lobular, invasive mammary carcinoma), stage, surgeon for 85% of cases; 15% had broader age match and excluding surgeon matching n=174 + 174 n=164 + 164 in recurrence and survival analysis	Early stage (0-II) breast cancer undergoing BCS +RT Excluded if neoadjuvant therapy, mastectomy, distant metastases, or no RT MRI group more likely to have extremely dense breasts (28% vs. 6%, p<0.0001) and mammographically occult cancer (24% vs. 9%, p=0.0003) 10 pt pairs had intraoperative partial breast RT and were excluded from long-term outcome analysis; the rest had whole-breast RT with or without boost	1.5 T MRI, prone position, dedicated surface breast coil, gadopentetate dimeglumine (Magnevist, Berlex) contrast Suspicious lesions (mammography or MRI) remote from the index lesion potentially representing multifocal, multicentric, or contralateral were routinely sampled by either percutaneous or surgical biopsy	Contralateral cancer 6% at initial diagnosis (11% MRI vs. 1%) All pts had initial BCS • Synchronous contralateral 11% (19/174) vs. 1% (2/174) Median follow-up 8 y: • LRR 5% (8/164) vs. 9% (14/164), p=0.33 • New (metachronous) contralateral disease 4% (7/164) vs. 3% (5/164) • Distant metastasis 2% (4/164) vs. 5% (9/164) • DFS 88.4% (145/164) vs. 82.9% (136/164), from events table; 86.2% (141/164) vs. 84.6% (139/164) from graph, p=0.73		R-MC	0-II

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Lynn Sage Comprehensive Breast Center at Northwestern Memorial Hospital, Chicago, Il 2006-2013	Zeng, 2020 (166)	Retrospective, preoperative MRI vs. no MRI Multivariable regression adjusting for age, race/ethnicity, tumour size, tumour grade, lymph node status, ER status, HER2 status, P53 status, and systemic therapy status n=330 + 182 Two groups were well balanced	Primary stage 0-III breast cancer, BCT, tumour-free margins, age ≤50 y Excluded neoadjuvant therapy, RT use not ascertained, metastatic Cohort was derived from a gold-standard dataset of 2045 pts; details are not provided	Not reported	Average follow-up 5.8 y vs. 6.4 y Adjusted HRs Local recurrence 7.9% vs. 8.2%, HR=1.03, 95% CI=0.53-1.99, p=0.94 Distant recurrence 6.4% vs. 6.6%, HR=0.89, 95% CI=0.43-1.84, p=0.74 Subgroup age ≤40 y: local recurrence HR=1.82, 95% CI=0.43-7.76, p=0.42; distant recurrence HR=0.93, 95% CI=0.26-3.34, p=0.91	Tumor size, ER status, and nodal positivity were significantly associated with distant RFS Reasons for pt acceptance of MRI were not recorded; most often declined for claustrophobia, fear of biopsies, cost	R-MV	0-III
Invasive Cancer								
Seoul National University Hospital, Seoul, Korea 2003-2008	Bae, 2016 (178)	Retrospective review of database, MRI vs. no MRI Multivariate analysis (mammographic density, pt age, symptoms, family history of breast cancer, histologic tumour characteristics, tumour grade, tumour size, lymphovascular invasion, lymph node involvement, surgery type, margin status, and adjuvant treatment received). Variable in univariate analysis with p<0.2 were included in multivariate model n=345 + 53	Stage I or II triple-negative breast cancer, BCS or mastectomy Excluded if metastatic disease, neoadjuvant therapy, stage III, incomplete HER2 data 98.7% IDC	Preoperative MR imaging in pts with biopsy-confirmed breast cancer since 2003, and bilateral MR imaging has replaced unilateral MR imaging since 2007 1.5 T MRI, prone position, dedicated eight-channel breast coil, 2003-2006: unilateral, contrast-enhanced 2007-2008: bilateral, gadobenate dimeglumine (MultiHance; Bracco Imaging, Milan, Italy) contrast	Median 6.1 y follow-up Recurrence (LRR, contralateral cancer, or distant metastasis): univariate analysis 13.6% vs. 30.2%, HR=0.45, 95% CI=0.25-0.79, p=0.006; multivariate analysis: HR=0.38, 95% CI=0.21-0.67, p<0.001 RFS at 7 y 87% vs. 65% (from graph), adjusted p<0.001	Absence of MRI, dense breast tissue, family history, and LVI were independently associated with recurrence and RFS	R-MV	I-II, TN

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Netherlands Cancer Registry 2011-2013	Lobbes, 2017 (149)	Retrospective population-based cohort study; MRI vs. no MRI Multivariable logistic regression analysis with covariates of year of diagnosis, age, clinical tumour size, nodal status, ER, PR, HER2 status, tumour grade, histological type, multifocality Analysis for full group and subgroups of ductal and lobular cancers n=10,740 + 25,310 IDC: n=7,462 + 21,128 (26% MRI) ILC: n=2,774 + 2,361 (54% MRI)	All Dutch pts with primary IBC (cT1-4N0-3M0) treated with primary surgery, Excluded distant metastases, DCIS, neoadjuvant therapy, unknown tumour localization Standard practice is mammography and/or ultrasound plus tissue sampling of lesions; discussion in tumour board determined whether MRI was performed Pts selected from cancer registry then hospital files reviewed Pts with MRI generally younger, ILC, multifocal cancer	Breast MRI protocols adhere to EUSOBI quality criteria. No other details reported	Synchronous CBC (diagnosis at same time or within 3 months of first cancer diagnosis) 3.7% (399/10740) vs. 1.3% (336/25310), OR=0.28, 95% CI=0.24-0.33, p<0.0001 • IDC OR=4.07, 95% CI=3.38-4.90, p<0.001 • ILC OR=2.50, 95% CI=1.73-3.61, p<0.001	Limitations: breast density, tumour localization within the breast, pt breast cancer risk profile, and the initial surgical treatment plan based on mammographic and/or ultrasound findings) were not available Motivation for MRI unknown	R-MV-Reg	IBC
Netherlands Cancer Registry 2011-2013	Van Nijnatten, 2020 (179)	Retrospective, MRI vs. no MRI; stratified into histological subgroups (invasive of no special type, ILC). Possible confounders examined using univariable and multivariable Cox proportional hazard regression analysis; non-significant variables were excluded n=9,632 + 22,124 (all, OS)	IBC of no special type or ILC Exclude distant metastases at baseline, neoadjuvant treatment, pts without surgical treatment MRI indications: ILC, IBC with discrepancy in tumour assessment between physical examination and imaging if the pt preferred BCS,	Not reported	OS, mean follow-up 5.3 y for OS OS overall: 92.3% vs. 86.7%; multivariate analysis HR=0.91, 95% CI=0.74-1.11, p=0.35 OS, invasive no specific subtype: 92.3% (567/7,386) vs. 87.2% (2,615/20,366), HR=0.96, 95% CI=0.78-1.19, p=0.74 OS, ILC: 92.2% (176/2,246) vs. 81.6% (323/1,758), HR=0.54, 95% CI=0.23-1.24, p=0.15 DFS, mean follow-up of 4.6 y	Recurrence data only collected for pts diagnosed and treated in the first 3 months of 2012	R-MV-Reg	IBC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		• Invasive carcinoma no specific type n=7,386 + 20,366 • ILC n=2,246 + 1,758 DFS cohort n=697 + 1,767 • Invasive carcinoma no specific type n=534 + 1,627 ILC n=163 + 140			5-y DFS overall: 93.1% vs. 93.5%; multivariate analysis HR=1.16, 95% CI=0.81-1.67, p=0.42 DFS, invasive no specific subtype: 92.7% (39/534) vs. 93.7% (103/1,627), HR=1.23, 95% CI=0.82-1.83, p=0.32 DFS, ILC: 94.5% (9/163) vs. 92.1% (11/140), HR=1.02, 95% CI=0.36-2.94, p=0.96			
Netherlands Cancer Registry 2011-2013	Vriens, 2017 (148)	Retrospective from registry Multivariable analysis n=2,879 + 554 (IDC n=2,429 + 477; ILC n=364 + 58) Adjusted for year of incidence, age, tumour size, nodal status, ER, PR, HER2 status, grade, multifocality	Stage I-III IBC (cT1-3) and neoadjuvant therapy, age 18-70 y Excluded cT4 tumours	Not reported	Multivariate analysis results: Synchronous CBC within 3 months of primary diagnosis by use of MRI prior to chemotherapy OR=1.19, 95% CI=0.71-2.00, p=0.51	Family history information not available No mention of method of evaluating neoadjuvant response and whether this led to detection of contralateral cancer	R-MV-Reg	I-III
SEER-Medicare dataset 2004-2009	Wang, 2016 (180)	Retrospective; propensity score matching to adjust for baseline characteristics Relationship between MRI and CBC occurrences n=6,377 +32,594 Matched: n=6,377 + 12,754	Women aged 67-94 y diagnosed with stage I-II breast cancer 2004-2009 and follow-up through 2011, and had surgery within 9 months of diagnosis MRI had to be in the period 90 days pre-diagnosis to date of surgery Excluded synchronous stage IV CBC	Not reported	Median follow-up 43 months vs. 46 months CBC 7.0% vs. 3.8% (from graph), 18.9 vs. 9.2 per 1000 person-years, HR=2.01, 95% CI=1.81-2.23, p<0.001 Synchronous CBC 5.9% vs. 2.1%, 126.4 vs. 42.9 per 1000 person-years, HR=0.35, 95% CI=0.31-0.40, p<0.001 Subsequent CBC 1.1% vs. 1.7% (from graph), 3.3 vs. 4.5 per 1000 person-years, HR=0.68, 95% CI=0.53-0.86, p=0.002	Units of cases per 1000 person-years makes comparison difficult	R-PSM	I-II

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Invasive Cancer - BCS only								
Princess Margaret Hospital, Toronto 1999-2005 (95% were 2002-2005	Hwang, 2009 (181) Gervais, 2017 (182)	Retrospective, MRI vs. no MRI n=127 + 345 2009: Multivariate analysis to investigate association between MRI and ipsilateral recurrence 2017: Univariate analysis; stratified log-rank tests to adjust for treatment and tumour features one at a time (age, tumour size, triple negative status) for IBTR only Patients with MRI were younger, had more palpable lumps, had less favourable tumour characteristics, received more adjuvant chemotherapy Re-excision data not adjusted	Initial lumpectomy (BCS) for IBC (88% Invasive ductal ± DCIS) by a single surgeon; final pathologic negative margins (no tumour cells at inked margin), adjuvant RT Excluded pts with excisional biopsy at other institution, multiple synchronous lumpectomies on same breast, incomplete pathology reports or with positive margins on final specimen, mastectomy within 12 months of initial lumpectomy, or if no RT Allowed MRI that was performed prior to mammography MRI indications were younger age, dense breasts, hereditary breast cancer, radiology concerns from mammography or US	MRI details not reported Preoperative MRI was initially employed for younger pts, those with mammographically dense breast tissue opting for BCS, and those with palpable tumours that were not well seen on mammography. Over the trial it became quite routine except in older pts with mammographically fatty breasts	Median follow-up 54 months Crude IBTR 1.6% vs. 2.6%, actuarial 8-y IBTR 1.8% vs. 2.5%, p=0.67; adjusted HR=0.59, 95% CI=0.09-4.17, p=0.60 Median follow-up 97 months (85 months vs. 106 months) IBTR without distant metastases at 10 y: crude rate (not adjusted) 1.6% vs. 3.5%; Kaplan-Meir estimate 1.6% vs. 4.2%, p=0.37, HR=0.50, 95% CI=0.11-2.24 Publication indicates that there were "no differences in IBTR rate after adjusting for age, year of surgery, tumour size, adjuvant treatment" but did not report these results Median time to recurrence 26 months vs. 25 months High-risk subgroup (triple negative + HER2+): IBTR 3.3% vs. 11.8%, p=0.3 (adjusted data not reported) High-risk vs. non-high risk: With MRI, IBTR was 3.3% vs. 1.1%, p=0.44; without MRI IBTR was 11.8% vs. 1.8%, p=0.0002, suggesting MRI has benefit in high-risk pts		R-MV	IBC
Yonsei University Hospital, Seoul, Korea 2007-2010	Ryu, 2016 (183)	Retrospective, preoperative MRI vs. no MRI Cox proportional hazard model was used for both univariate and multivariate analyses; adjusted for age,	T1-2 breast cancer and BCT Excluded inflammatory breast cancer, phyllodes tumour, Paget's disease, neoadjuvant	3.0 T MRI, dedicated bilateral breast coils, dynamic contrast-enhanced MRI	Median follow-up 64.5 vs. 78.5 months 5-y LRRFS 99.7% vs. 99.0%, HR=1.055, 95% CI=0.270-4.124, p=0.938; adjusted HR=0.814, 95% CI=0.141-4.704, p=0.818		R-MV	I-II

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		stage, nodal status, ER status, grade n=743 +211	chemotherapy, distant metastasis, no RT		5-y RFS 95.7% vs. 97.0%, HR=0.775, 95% CI=0.364-1.650, p=0.508; adjusted HR=0.75, 95% CI=0.307-1.832, p=0.528 5-y OS 98.3% vs. 98.5%, HR=0.791, 95% CI=0.283-2.213, p=0.655; adjusted HR=1.187, 95% CI=0.277-5.087, p=0.818			
SEER-Medicare dataset, USA 2004-2010	Wang, 2018 (184)	Retrospective, preoperative MRI vs. no MRI; stratified groups by RT use Multivariable models were fitted to estimate HR for MRI use, adjusted for variables found to be associated with outcomes (p value < 0.20) in bivariate analyses n=4,691 + 19,688 No RT: n=790 + 4,957 Received RT: n=3,727 + 14,508 Adjusted for age, grade, tumour size, lymph node status, ER/PR status, chemotherapy, trastuzumab, RT, surgeon volume No difference is stage distribution so not used in adjustment	Stage I-II breast cancer and BCS, age 67-94 y; BCS within 9 months of cancer diagnosis Subsequent mastectomy defined as mastectomy >9 months after initial diagnosis MRI group more likely to be younger, white, married, higher income, fewer comorbidities, better disability index; more likely to receive RT, chemotherapy, and anti-HER2 therapy Groups similar in tumour stage	Not reported	Median follow-up 5.6 y Subsequent mastectomy at > 9 months after surgery as surrogate for recurrence: Treated recurrence 3.2 vs. 4.1 per 1000 person-years, HR=0.80, p=0.08; adjusted HR=0.92, 95% CI=0.70-1.19, p=0.51 Breast cancer mortality 5.3 vs. 8.7 per 1000 person-years, HR=0.62, p<0.001; adjusted HR=0.89, 95% CI=0.73-1.08, p=0.23 <u>Subgroup without RT</u>: • Treated recurrence 5.6 vs. 9.2 per 1000 person-years, HR=0.65, p=0.06; adjusted HR=0.60, 95% CI=0.37-0.98, p=0.04. • Breast cancer mortality 5.5 vs. 14.9 per 1000 person-years, HR=0.41, p<0.001; adjusted HR=0.57, 95% CI=0.36-0.92, p=0.02 <u>Subgroup with RT:</u> • Treated recurrence 2.8 vs. 2.8 per 1000 person-years, HR=1.03, p=0.84; adjusted HR=1.17, 95% CI=0.84-1.61, p=0.35 • Breast cancer mortality 5.2 vs. 7.1 per 1000 person-years, HR=0.74, p=0.004; adjusted HR=1.00, 95% CI=0.80-1.24, p=0.99	MRI improved survival and decreased subsequent mastectomy in pts who did not receive RT	R-MV-Reg	I-II

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
Invasive Ductal Carcinoma - BCS only								
Turku University Hospital, Turku, Finland 2011-2013	Bruck, 2018 (162)	Prospective randomized trial, pre-operative MRI or not, n=100 (50+50) Based on palpation, mammography, or US	Age ≥35 y, newly diagnosed unilateral and clinically unifocal stage I invasive ductal carcinoma, ≤20 mm prior to MRI and with first plan being for BCS and SNB Excluded pts with breast parenchymal pattern DY	1.5 T MRI, prone position, bilateral four-channel breast array coil, gadoteric acid (Dotarem, Guerbet, Roissy CdG Cedex, France) contrast agent Imaging sequences also covered both axillary areas Second-look US for MRI-only lesions, US-guided core needle biopsy taken if possible, no MRI-guided biopsies were required	Median follow-up 49 months: • Distant recurrence 0% vs. 6% • No local recurrence	Note: all MRI-detected lesions were visible on second-look US	RCT	I IDC
Invasive Lobular Carcinoma								
Seoul, Korea 2005-2012	Ha, 2019 (185) Overlaps with pts in Ha, 2018 (152) (mastectomy and reoperation results)	Retrospective. Groups with or without preoperative MRI, propensity score matching for 21 covariates (pt demographics, tumour characteristics, clinical features) Variables with a p<0.20 in the univariable analysis were entered as input variables for a multivariable Cox proportional hazards model using backward	Newly diagnosed ILC by biopsy or surgical excision; excluded neoadjuvant therapy, stage IV, incomplete pt or tumour data Annual follow-up by mammography and US	1.5 T or 3 T MRI, dedicated breast coil, Magnevist (Schering) or gadoterate meglumine (Dotarem) (Guerbet) contrast	Matched cohort analysis • Total recurrence 11.5% vs. 13.5%, HR=1.096, p=0.821 • OS 96.2% vs. 91.3%, HR=0.485, p=0.231 Inverse Probability Weighting Analysis • OS HR=0.353, p=0.078	Breast MRI protocols were non-uniform during the study period	R-PSM	ILC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
		elimination in unmatched data n=120 + 167 Before matching, the MRI group was younger, premenopausal, denser breast tissue, no hormone therapy Matched 104 pairs of pts						
Ongoing trials								
MIPA (27 centres, all except 2 in Europe) ISRCTN41143178 2013-2018 Enrollment complete, follow-up to end of 2023	Sardanelli, 2020 (153) [protocol] Sardanelli, 2017 (154) [abstract, interim] ONGOING	Pragmatic observational non-randomized multicentre international prospective study for women offered MRI or not according to local practice n=1,201 + 1,224 Variables that will be shown to be significantly different between the two groups will be considered as covariates when the two groups will be compared in analyses.	Consecutive pts with newly diagnosed breast cancer amenable to upfront surgery, aged 18-80 y Excluded candidates for neoadjuvant therapy or with personal history or cancer or with evidence of metastases	The coordinating centre approved only MRI protocols following technical recommendations issued by international societies such us the European Society of Breast Cancer Specialists (EUSOMA), the EUSOB, and the American College of Radiology. ≥1.5 T MRI, ≥4 channels of dedicated coils, gadolinium-based contrast agent	Ipsilateral recurrence, CBC, distant metastases at 5-y follow-up		P-ongoing	BC
NCT01805076; Alliance AO11104; ACRIN 6694 2014-2020 plus follow-up Expected	Bedrosian, 2011 (170) [Abstract] ONGOING	Randomized to standard of care with or without MRI Target n=556; actual n=317	Eligible for BCT by conventional criteria (clinical examination, mammography ± US) and ER- and PR- (ER-/PR-/HER2-or HER2+), Stage IA, IB, II. Excluded pts with multicentric or multifocal	Not reported	Primary: LRR after BCT Secondary: re-operation rate, conversion to mastectomy, CBC rate, DFS, OS	Patients to be followed for 5 years from surgery	RCT-ongoing	I-II

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes[2]	Other	Trial Type[3]	Stage / Histology
completion 2025			disease scheduled to undergo multiple lumpectomies					
BREAST-MRI ICESP, São Paulo, Brazil NCT02798796 2014-2016	Mota, 2019 (157) [Abstract] Interim analysis for recurrence; final results not available	Randomized, stratified for mammary density 219 + 227	Stage 0-III, candidate for BCS	1.5T MRI system	Follow-up 23.6 months (interim analysis; follow-up planned for 5 y; secondary outcomes) • local recurrence 0 vs. 0.4%, • distance recurrence 1.8% vs. 1.3% • breast cancer death 0% vs. 0.4% • any death 0.9% vs. 0.4%		RCT	0-III

ACRIN, American College of Radiology Imaging Network; BCS, breast-conserving surgery; BCT, breast-conserving therapy (BCS + RT); CBC, contralateral breast cancer; CI, confidence interval; DCIS, ductal carcinoma in situ; DFS, disease-free survival; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; IBTR, ipsilateral breast tumour recurrence; IBC, invasive breast cancer; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; LRR, loco-regional recurrence; LRRFS, locoregional recurrence-free survival; LVI, lymphovascular invasion; MRI, magnetic resonance imaging; ns, not significant; OR, odds ratio; OS, overall survival; pt, patient; pts, patients; PR, progesterone receptor; RFS, recurrence-free survival; RR, relative risk; RT, radiotherapy; SEER, Surveillance, Epidemiology, and End Results database; US, ultrasound

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Table 5. Excluded studies.

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes	Other	Trial Type[2]
Non-randomized prospective							P
University of Iowa Breast Molecular Epidemiology Resource	Xia, 2014 (192)	Prospective enrolment; univariate logistic regression and multivariate model to identify factors predicting CPM within 12 months of definitive mastectomy n=66 + 68 Adjusted for recommendation for MRI follow-up, age, whether the patient's youngest child was under the age of 6 y at diagnosis, BRCA testing, BRCA test result for those who received testing, family history, nodal status, history of benign biopsy findings, receptor status, body mass index, reconstruction performed Exclude: no adjustment for size, stage, histology; no data on mastectomy rates (only CPM)	Stage 0-III who had mastectomy for index cancer Excluded if bilateral cancer diagnosed prior to MRI	Not reported	CPM 51.5% vs. 27.9%, univariate OR=2.74, p=0.006; multivariate OR=1.27 (95% CI=0.328-4.893), p=0.732	Adjusted for recommendation for MRI follow-up, age, whether the patient's youngest child was under the age of 6 years at diagnosis, BRCA testing, BRCA test result for those who received testing, family history, nodal status, history of benign biopsy findings, receptor status, body mass index, reconstruction performed	P
Retrospective, historical							R-EQ

[1] Only female patients unless indicated otherwise.
[2] RCT, randomized controlled trial; P, Prospective non-randomized trial; R-PSM, retrospective with propensity score matching; R-MV, retrospective with multivariate analysis; R-MV-Reg, retrospective with multivariate analysis using registry data; R-EQ, retrospective using data from equivalent groups (e.g., historical controls)

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes	Other	Trial Type[2]
controls or equivalent groups							
Italy (single institution) 2006-2011	Petrillo, 2013 (193)	Retrospective, single institution database, consecutive pts (excluding neoadjuvant therapy); MRI vs. no MRI (conventional imaging = mammography and/or US) n=122 + 124 Exclude: not equivalent stage and multicentric or multifocal rate	Breast cancer, age <40 y Excluded neoadjuvant chemotherapy No differences between groups in age, pathologic subtype, tumour stage, receptor, nodal status (MRI group had slightly higher stage but not significant)	1.5 T MRI, prone position, bilateral synchronous dedicated 4-channel breast coil, gadobenate dimeglumine (MultiHance, Bracco, Milan, Italy) contrast Bi-RADS 4 or 5 lesions had needle biopsy or surgical excision; lesions only on MRI were sampled under US guidance if possible	Mastectomy rate (unilateral or bilateral) 53% vs. 37%, p=0.011 Unilateral mastectomy 51% vs. 37% Unilateral BCS 47% vs. 62% Unilateral BCS + unilateral mastectomy 2% vs. 0% Bilateral BCS 0% vs. 1% Planned mastectomy before MRI in the MRI group was 38% Multifocal, multicentric, synchronous, or bilateral cancers 27% vs. 8%, p<0.001; in the MRI subgroup, MRI detected 97% of these, while mammography detected 15% and ultrasound 45%	Article indicates “Mastectomy was considered appropriate when multicentric disease suspected at imaging was pathologically confirmed or when the ratio between the pathological extent of multifocal disease or large unifocal disease exceeded the limits for a conservative approach according to surgical guidelines”	R-EQ
Retrospective, matched cohorts							R-MC
Seoul National University Hospital 2004-2009	Yi, 2015 (194) Subset of pts in Kim, 2013 (174)	MRI vs. no MRI, matched according to age (<45 y, ≥45 y), histologic grade (I, II, III), nuclear grade (I, II, III), tumour size (≤20 mm, >20 mm), nodal status, stage (0 or I; II or III), hormone receptor status, Ki-67 status (>14% or ≤14%), molecular subtype, LVI	Newly diagnosed breast cancer, clinical breast examination, bilateral mammography, bilateral breast ultrasonography Excluded neoadjuvant chemotherapy, past	1.5 T MRI, dedicated breast coil, dynamic contrast enhanced MRI-guided biopsy used for lesions visible only by MRI	Unilateral period: mean follow-up 73.7 months: • Mastectomy 36.7% vs. 34.2%, p=0.441 • Re-excision after BCS 13.6% vs. 15.2%, p=0.691 • 5-y contralateral breast DFS 97.8% vs. 96.2% • Total recurrence 11.6% vs. 14.6%, HR=0.80, 95% CI=0.54-1.19, p=0.282 • LRR 1.4% vs. 4.0%, HR=0.33, 95% CI=0.12-0.91, p=0.032		R-MC

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes	Other	Trial Type[2]
		Unilateral MRI imaging 2004-2006, bilateral MRI imaging 2007-2009 371 pairs with unilateral imaging 97 pairs with bilateral imaging Exclude: serious concerns with matching procedure; started with controls and looked for cases to match (usually the reverse), major differences in pt characteristics between unilateral and bilateral period suggesting important factors not considered; age grouping for matching not appropriate and didn't consider menopausal status	breast cancer, metastatic disease, 3984 pts met criterial, 3440 had MRI and 544 not; 3094 previously reported in study of contralateral cancer using a historical controlled design (not comparison of MRI vs. no MRI)		• Contralateral metachronous breast cancer 3.2% vs. 4.6%, HR=0.75, 95% CI=0.36-1.57, p=0.440 • Distant recurrence 7.0% vs. 5.9%, HR=1.21,95% CI=0.68-2.14, p=0.515 Bilateral period: mean follow-up 65.3 months: • Mastectomy 32.0% vs. 34.0%, p=0.397 • Re-excision after BCS 15.2% vs. 17.2%, p=0.843 • 5-y contralateral breast DFS 99.0% vs. 80.4% • Total recurrence 8.3% vs. 32.0%, HR=0.15, 95% CI=0.07-0.32, p<0.001 • LRR 3.1% vs. 4.1%, HR=0.26, 95% CI=0.03-1.89, p=0.180 • Contralateral metachronous breast cancer 1.0% vs 21.7%, HR=0.03, 95% CI=0.004-0.21, p<0.001 Distant recurrence 4.1% vs 6.2%, HR=0.40, 95% CI=0.11-1.51, p=0.178		
Retrospective, multiple or multivariate regression							R-MV
Galway University Hospitals 2009-2017	Moloney, 2020 (195)	Retrospective from database; MRI vs. no MRI; adjusted for confounding using multivariable linear or logistic regression [factors not stated] n=70 + 148 Exclude: Only adjusted value for conversion mastectomy reported	Newly diagnosed symptomatic ILC, histologically proven, no prior surgery; surgical management anticipated as primary management Difference in age (mean 56.4 vs. 65.6 y), density (64.3% vs. 43.3% with high density); grade and	1.5 T MRI, 8-channel breast phase array breast coil, Gadoterate meglumine (Gd-DOTA) contrast	Most results were not adjusted for confounding Initial mastectomy 28.6% vs. 27.7%, p=0.894 Re-operation 27.1% vs. 16.9%, p=0.057 Re-excision of margins 5.7% vs. 6.8%, p=0.783 Mastectomy after BCS 21.4% vs. 10.1%, univariable analysis p=0.018, adjusted p=0.276 Overall mastectomy 50% vs. 37.8%, p=0.089	Mammographic breast density and reasons for MRI were recorded (90% to evaluate for multifocality/ multicentricity and bilaterality and assess suitability for BCS). MRI was frequently used in	R-MV

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes	Other	Trial Type[2]
			stage lower in MRI group			borderline BCS cases and posing an initial challenge in surgical planning	
Yale New Haven Breast Center 2004-2009	Killelea, 2013 (196)	Retrospective chart review, MRI vs. no MRI Multivariable logistic regression, calculated adjusted OR only for bilateral mastectomy n=628 + 817 Exclude: mastectomy results not adjusted; groups not equivalent	Newly diagnosed breast cancer MRI group younger (43% vs. 26% age < 50) Mostly stage 0 (25%), stage 1 (39%) or stage 2 (25%) Excluded pts without definitive surgery (neoadjuvant or metastases)	Not reported MRI at discretion of treating surgeon Targeted ultrasound with image-guided core biopsy was usually attempted before MRI-guided biopsy	• Unilateral mastectomy 23% vs. 26%, ns • Bilateral mastectomy 20% vs. 12%, p<0.005; adjusted OR=1.38, 95% CI=1.02-1.87, p=0.036 [adjusted for age, stage] Ipsilateral and bilateral mastectomy rates: • No MRI (n=817) 26%, 12% • Normal MRI (n=259) 17%, 16% • MRI with ipsilateral lesion (n=182) 34%, 15% • MRI with contralateral lesion (n=73) 21%, 26% • MRI with contralateral + ipsilateral lesions (n=114) 23%, 31% • Abnormal MRI and no biopsy (n=132) 35%, 26% • Abnormal MRI and benign biopsy (n=184) 21%, 13% • MRI + malignant ipsilateral biopsy (n=52) 38%, 27% • MRI + malignant contralateral biopsy (n=15) 0%, 67% MRI + malignant contralateral and ipsilateral biopsy (n=6) 0%, 100%	Normal MRI or MRI with benign biopsy had lower rate of mastectomy than without MRI (but ns)	R-MV
MARGINS trial and non-study control group The Netherlands Cancer Institute, Amsterdam,	Pengel, 2009 (197) Wintgens, 2014 (198) [abstract]	Non-randomized, MRI vs. no MRI Multivariate analysis using logistic regression (backward LR based on stepwise feature selection [f-to-entry: 0.05, f-to-remove: 0.10] to determine significant variables for incomplete surgery n=173 + 176	Consecutive pts with IBC and eligible for BCT Excluded neoadjuvant, DCIS Control group were those ineligible or refused participation in MARGINS trial; MRI	1.5 T MRI, prone position, dedicated double-breast array coil, Prohance (Bracco-Byk Gulden, Konstanz, Germany) contrast Second-look ultrasonography and FNA or biopsy if MRI lesions far from index lesion; if	Initial mastectomy in 9.2% vs 0% Incomplete excision (positive margins) 13.8% vs. 19.4%, p=0.1 overall; 1.6% vs. 8.1%, p=0.02, HR=0.18 for IDC involvement in IDC; 9.8% vs. 8.6% (ns) for in situ involvement in IDC; 23.1% vs. 19.2% for ILC involvement in ILC (ns); 3.8% vs. 11.5% for in situ involvement in ILC (ns) Re-excision 2.5% vs. 5.6%	Multivariate analysis results not shown; stated age, palpability, lymph node status, tumour size, grade were not significantly associated with incomplete surgical excision;	R-MV

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes	Other	Trial Type[2]
The Netherlands 2002-2004		Long-term follow-up n=158 + 149 Exclude: inadequate multivariable analysis and results not reported	group was from the MARGINS trial MRI group younger, more palpable tumours, larger, higher grade	pathology proof not obtained then BCT was advised along with follow-up MRI	Median follow-up 110 months [abstract report] Contralateral breast tumour 3.2% vs. 7.4% 10-y contralateral tumour-free interval probability 96% vs. 91% No difference in local recurrence-, local-regional recurrence- and distant metastasis-free interval Mastectomy after BCS 2.5% vs. 5.0%	MRI significant only for subgroup of IDC (HR=0.18, 95% CI=0.04-0.81, p=0.02)	
Mayo Clinic Arizona, Phoenix, AZ 2000-2008	Stucky, 2010 (199)	Retrospective Factors associated with CPM Predictors of CPM identified by multivariable regression analysis using variables with p<0.10 on univariate logistic regression analysis n=324 + 1,026 Exclude: no required outcomes	Pts in sentinel lymph node database, IBC, BCT or unilateral mastectomy or CPM Excluded surgery except CPM on contralateral breast; excluded bilateral cancer	Not reported	Unilateral mastectomy 34% vs. 17%, OR=1.654, 95% CI=0.972-2.813 CPM 17% vs. 4%, OR=2.358, 95% CI=1.378-4.037	One of the authors regularly used MRI to assess contralateral breast when CPM already decided on by pt	R-MV
University of Minnesota 2002-2009	Miller, 2012 (200)	Retrospective chart review of all cases by a single surgeon n=219 + 195 Multiple regression analysis adjusted for family history, tumour size, lymph node status, ER status, year of surgery, infiltrating lobular carcinoma: only for mastectomy outcome Exclude: age significantly associated with MRI use and strong predictor of mastectomy but not accounted for	Surgical treatment for breast cancer: biopsy-proven DCIS or stage I, II, or III Excluded stage IV, previous breast cancer, positive BRCA status, incidental detection with MRI MRI generally obtained for younger pts, with family history of breast cancer, or dense breasts; but also upon pt request or at other institutions	Not reported	Over time, MRI use increased from 9% to 75%, p<0.001; mastectomy rates increased 31% to 38%, p=0.06 at the study institution (not just for pts in this study) Overall (final) mastectomy 43% MRI vs. 28% no MRI, p=0.002; OR=1.8, 95% CI=1.1-3.2, P=0.03 Non-adjusted results Mastectomy rates •No MRI 28% •Negative MRI 39% •Positive MRI 51% ○ No biopsy 38% ○ Negative biopsy 31% ○ Positive biopsy (18/22) 82%	Breast density, pt age, HER2 status not adjusted for in regression analysis. Density was not measured; age significantly associated with MRI use and strong predictor of mastectomy but not accounted for Contribution of pt choice not mentioned but	R-MV

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes	Other	Trial Type[2]
					6 contralateral cancers detected by preoperative MRI, 2.7%; half of these had bilateral mastectomy and half had bilateral BCS Re-excisions 14% vs. 18%, p=0.34 IBTR 1.6% vs. 5.0%, p=0.13 Median follow-up 25 vs. 49 months after BCS	apparent from high rate of mastectomy	
Geisinger Medical Center, Danville, PA 2009-2013	Straus, 2015 (201) [abstract]	Retrospective, MRI vs. no MRI Bivariate and multivariate statistics n=150 + 252 Exclude: no information about of pt characteristics or confounders used in multivariate analysis; abstract only	Pts surgically treated for breast cancer MRI group younger (55.5 vs. 70 y, p<0.0001)	Not reported	Mastectomy 46.7% vs. 35.3%, p=0.0244; adjusted OR=1.28, 95% CI=0.80-2.05, p=0.30 BCS margin positivity 4% vs. 7.1%, p=0.1983; adjusted OR=0.36, 95% CI=0.10-1.36, p=0.13 BCS reoperation 8.7% vs. 10.7%, p=0.5071; adjusted OR=1.4, 95% CI=0.53-3.75, p=0.50		R-MV
Mayo Clinic Arizona 2001-2008	McGhan, 2010 (202)	Retrospective, preoperative MRI vs. no MRI n=70 + 108 Groups similar in tumour size; MRI group younger, more positive nodes Exclude: no multivariate analysis, different age distribution and stage	ILC on biopsy and final pathology Excluded neoadjuvant chemotherapy before MRI, excisional biopsy before MRI MRI at discretion of the treating surgeon	1.5 T MRI, prone position, dedicated breast coil, gadolinium contrast	BCS 52.78% vs. 66.97%, p=0.055 Mastectomy 31.94% vs. 23.85%, p=0.231 Bilateral mastectomy 13.89% vs. 7.34%, p=0.150 Local recurrence 1.39% vs. 0%, p=0.217 Distant recurrence 0% vs. 4.59%, p=0.065 Re-excision of margins 4.17% vs. 9.17%, p=0.202 Conversion to mastectomy 2.78% vs. 7.34%, p=0.189	Values not adjusted for possible confounding	R-MV
Province of Moderna Cancer Registry, Italy linked to MRI database of General	Cortesi, 2012 (203)	Retrospective, MRI vs. no MRI Univariate and multivariate analysis, taking into account tumour size, nodal status, grade, Ki67	Invasive and in situ breast cancer, follow-up until 2011 Exclude cases without surgery	Not reported	Pts treated with mastectomy: 5-y RFS 93.1% vs. 85.5%, p=0.2 Quadrantectomy (BCS) 51.8% vs. 39%, p<0.017; 13.8% converted to BCS due to MRI results		R-MV

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes	Other	Trial Type[2]
Hospital of Moderna 2000-2010		n=816 + 6,036 493 MRI were before surgery including 112 after neoadjuvant therapy Exclude: adjusted values not reported; 40% of MRI pts did not have MRI preoperatively and cannot tell if these are included in results numbers of pts in each group not reported			Pts treated with neoadjuvant chemotherapy and quadrantectomy: RFS 86.2% vs. 86% Pts treated with neoadjuvant chemotherapy and mastectomy 5-y RFS 80% vs. 59%, p=0.018		
Tianjin Cancer Hospital, Tianjin, China 2005-2018	Zhang, 2019 (204) [abstract]	Multivariate analysis of 5660 pts Exclude: abstract only, insufficient details	Planned for BCS	Not reported	Lower rate of positive margins, OR=0.775, p=0.001		R-MV
Mayo Clinic, Phoenix, AZ 2003-2008	Carpenter, 2009 (205)	Retrospective, MRI vs. no MRI Multivariate analysis n=232 + 582 Exclude: multivariate analysis to look for association, not to adjust results due to confounders; confounders used and adjusted values not reported	IBC treated by mastectomy or BCT; SLNB in all pts Excluded neoadjuvant therapy, history of treated breast cancer MRI used for occult primary, Paget's disease, discrepancy between imaging and physical examination, BRCA mutation, ILC with unclear imaging, hyperdense breast tissue, suspicion of multifocal or multicentric disease, positive margins after lumpectomy	1.5 T MRI, prone position, 8-channel breast coil, contrast agent (usually gadolinium) MRI-guided biopsy in prone position if lesions not by seen by ultrasound or mammography	Re-excision 8% vs. 10%, p=0.2386 Conversion to mastectomy 7% vs. 4%, p=0.3332 Local recurrence 0.8% vs. 1.0%, p=1.000 In multivariate analysis, the type of surgery was associated with MRI use, p=0.0040	Longer follow-up for recurrence is required	R-MV

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes	Other	Trial Type[2]
			MRI group younger, lower BMI, more genetic counselling and testing				
Enterprise Data Warehouse of Northwestern Medicine, Chicago, IL 2005-2015	Espino, 2017 (206) [abstract]	Retrospective, preoperative MRI vs. no MRI, multivariate analysis n=919 + 1,039 Exclude: Abstract only with no details of variables used	Invasive cancer or DCIS and mastectomy	Not reported	Mean follow-up 56 months vs. 57 months PMRT 51.8% vs. 48.2% Chest wall recurrence, 5-y rate 4.5% vs. 4.1%, p=0.041; adjusted HR=1.5, 95% CI=0.95-2.37, p=0.08 Distant recurrence 9.2% vs. 10%, p=0.78, adjusted HR=0.87, 95% CI=0.63-1.19, p=0.37		R-MV
Hospital of the University of Pennsylvania 1992-2001	Vapiwala, 2017 (207) Solin, 2008 (208) Weinstein, 2001 (209) Orel, 2001 (4) Nunes, 1997 (210)	Retrospective, preoperative breast MRI vs. no MRI n=215 + 540 Multivariate analysis to adjust for unbalance pt and tumour characteristics (factors used were not reported) used to estimate hazard ratios MRI at different points in management: 27% before cytology/ biopsy, 23% after biopsy but before excision, 50% after one or more excisions Exclude: only 50% of MRI was preoperative; adjustment factors not reported; tumour size unknown in 40% of pts	Unilateral DCIS or early-stage IBC (AJCC 5th edition stage 0, I, or II) who had BCS (+ ALN staging for invasive carcinoma) + RT (whole breast + boost); systemic therapy as clinically indicated. Mammography in all pts, correlation ultrasound as indicated. Breast MRI use started in early 1990s for some pts Excluded all pts with synchronous bilateral breast cancers by any means of detection MRI pts significantly younger; ≈40% in both groups had unknown clinical tumour size	Authors cited other papers for details, although there are some differences in methodology in them. 1.5 T MRI, prone position, specially designed breast multicoil array, gadopentetate dimeglumine (Magnevist; Berlex, Wayne, NJ) contrast (209) Prone position, 4-coil compression breast array, gadolinium chelate contrast. Only one breast can be imaged at a time. (4) Only one breast imaged at a time by MRI coil designed by one of the authors (210), imaging or results for the contralateral breast are not mentioned	Median 13.8 y follow-up Local failure 15-y 8% vs 8%, 10-y 4% vs. 4%, 5-y 2% vs. 2%; p=0.59; adjusted HR=0.98, 95% CI=0.52-1.87, p=0.96 15-y CBC 10% vs. 8%, 10-y CBC 7% vs 4%, 5-y CBC 6% vs. 2%, p=0.10; adjusted HR=1.36, 95% CI=0.76-2.44, p=0.31 15-y OS 77% vs. 71%, 10-y OS 82% vs. 81%, 5-y OS 92% vs. 92%, p=0.24 [adjusted value not reported] Freedom from distant metastases 15-y 86% vs. 90%, 10-y 87% vs 92%, 5-y 92% vs. 92%, p=0.08 [adjusted value not reported]	Low event rate in this group of pts with favourable prognosis limits ability to detect any true benefit of MRI. Would need RCT of 14,000 pts if baseline 10-y recurrence risk is 5% to detect a 20% benefit Only 50% of MRI were performed before initial surgical excision	R-MV

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes	Other	Trial Type[2]
				and may not have been conducted For pts who required MRI-guided wire localization of a suspicious lesion identified on MRI, a proprietary MRI needle localization system was used			
Department of Magnetic Resonance Imaging, Air Force General Hospital of People's Liberation Army, Beijing	Li, 2017 (211) [Chinese, only English abstract used]	MRI vs. no MRI Logistic regression model n=72 + 74 Exclude: unclear whether there is multivariate analysis due to language	Early non-mass breast carcinoma with ultrasonographic and mammographic examination; 30 invasive ductal carcinoma, 28 DCIS, 14 other breast carcinomas	[in Chinese]	Tumour-positive resection margins: invasive ductal carcinoma 23.3% (n=30 with MRI) vs. 40.0%, p=0.02; DCIS 21.4% (n=28 with MRI) vs. 26.9%, p=0.10; other breast carcinoma 14.3% (n=14 with MRI) vs. 38.9%, p=0.02		R-MV
USA [single institution but not specified] 2010-2013	So, 2018 (212)	Single institution retrospective study. MRI vs. no MRI Multivariate analysis adjusted for variables significant in bivariate analysis (size, surgeon specific practices) n=97 + 79 Exclude: groups not equivalent in age, race, density, grade, use of oncoplastic technique; size unknown in 30%	BCS for pure DCIS	Not reported	Stratified pts according to MRI status: re-excision rate 28.9% vs. 26.6%, p=0.87; adjusted OR=1.77, 95% CI=0.68-4.59, p=0.24 DCIS size and surgeon (A, B, C) were significant factors, p=0.005 and p=0.04, respectively and much larger effect than MRI	Surgeon factors including use of shave margins had more effect than MRI Size unknown in 30%	R-MV
Retrospective, multiple or multivariate regression, registry data							R-MV-Reg

Study name, location or group, time period of MRI	Author and source	Study design Number of patients (n) in MRI and non-MRI groups	Patient characteristics[1]	MRI details	Outcomes	Other	Trial Type[2]
6 BCSC registries sponsored by the National Cancer Institute, USA linked to Medicare or electronic health records 1998-2010 Follow-up until 2014	Onega, 2018 (213)	Retrospective, MRI vs. no MRI Multivariate analysis, adjusted for age, race, family history, density, education, comorbidity, histology, BCS/BCT/ mastectomy n=917 + 3,537 Exclude: Stage and size neither reported nor adjusted for	Non-metastatic breast cancer, stage I-III, age ≥66 y with BCS or mastectomy within 6 months of diagnosis MRI had to be within 30 days prior to 6 months after diagnosis and prior to surgery	Not reported	Median follow-up 4.6 y Mortality 10.9% vs. 18.1%, 24.90 vs. 38.41 per 1000 person-years, ns 5-y cumulative probably of death 0.12 vs. 0.17 All-cause mortality HR=0.67, 95% CI=0.54-0.82; adjusted HR=0.91, 95% CI=0.73-1.13		R-MV-Reg

ALN, axillary lymph node; BCS, breast-conserving surgery; BCSC, breast cancer surveillance consortium; BCT, breast-conserving therapy (BCS + RT); CBC, contralateral breast cancer; CI, confidence interval; CPM, contralateral prophylactic mastectomy; DCIS, ductal carcinoma in situ; DFS, disease-free survival; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; IBTR, ipsilateral breast tumour recurrence; IBC, invasive breast cancer; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; LRR, loco-regional recurrence; LVI, lymphovascular invasion; MRI, magnetic resonance imaging; ns, not significant; OR, odds ratio; OS, overall survival; pt, patient; pts, patients; PMRT, post-mastectomy radiotherapy; PR, progesterone receptor; RFS, recurrence-free survival; RT, radiotherapy; SLNB, sentinel lymph node biopsy; US, ultrasound

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REFERENCES

1. Mann RM, Kuhl CK, Moy L. Contrast-enhanced MRI for breast cancer screening. J Magn Reson Imaging. 2019;50(2):377-90.

2. Panu N, Lacchetti C, Spithoff K, Kellett S, Hamm C, and the Preoperative Breast MRI Expert Panel. The role of breast MRI in the preoperative staging of breast cancer. Program in Evidence-Based Care guideline No.: 27-1. Hamilton (ON): Program in Evidence-Based Care, McMaster University; 2015, May 29. [internal document, unpublished].

3. Schoub PK. Understanding indications and defining guidelines for breast magnetic resonance imaging. SA J Radiol. 2018;22(2):a1353 (12 pp).

4. Orel SG, Schnall MD. MR imaging of the breast for the detection, diagnosis, and staging of breast cancer. Radiology. 2001;220(1):13-30.

5. Lehman CD. Magnetic resonance imaging in the evaluation of ductal carcinoma in situ. J Natl Cancer Inst Monogr. 2010;2010(41):150-1.

6. Warner E, Causer PA, Wong JW, Wright FC, Jong RA, Hill KA, et al. Improvement in DCIS detection rates by MRI over time in a high-risk breast screening study. Breast J. 2011;17(1):9-17.

7. Kuhl CK, Schrading S, Bieling HB, Wardelmann E, Leutner CC, Koenig R, et al. MRI for diagnosis of pure ductal carcinoma in situ: A prospective observational study. Lancet. 2007;370(9586):485-92.

8. Covington MF, Young CA, Appleton CM. American College of Radiology accreditation, performance metrics, reimbursement, and economic considerations in breast MR Imaging. Magn Reson Imaging Clin N Am. 2018;26(2):303-14.

9. Arnaout A, Catley C, Booth CM, McInnes M, Graham I, Kumar V, et al. Use of preoperative magnetic resonance imaging for breast cancer: A Canadian population-based study. JAMA Oncol. 2015;1(9):1238-50.

10. Fletcher G, Muradali D, Eisen A, George R, Holloway C, Kulkarni S, et al. Preoperative breast MRI in average risk breast cancer patients. PROSPERO: International prospective register of systematic reviews CRD42019141365 [Internet]. York (UK): Centre for Reviews and Dissemination, University of York; 2019 Oct 2 [last modified 2021 Aug 9; cited 2021 Aug 9]. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019141365. 2019.

11. Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, et al. Cochrane handbook for systematic reviews of interventions version 6.1 [Internet]. London (UK): Cochrane; 2020 Sept [cited 2021 Aug 13]. Available from: https://training.cochrane.org/handbook.

12. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: A revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. [RoB 2 tool also available at: https://www.riskofbias.info/welcome/rob-2-0-tool].

13. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016;355:i4919 (7 pp).

14. Sterne J, Higgins J, Elers R, Reeves B, and the development group for ROBINS-I. Risk of bias in non-randomized studies of interventions (ROBINS-I): Detailed guidance [Internet]. Updated 2016 Oct 12. [cited 2021 Jul 16]. Available from: http://www.riskofbias.info

15. The Cochrane Collaboration. Review Manager (RevMan) [Computer program on internet]. Version 5.4. London (UK): Cochrane; 2020 [cited 2021 May 6]. Available from: https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman/revman-5-download.

16. McKenzie DP, Thomas C. Relative risks and odds ratios: Simple rules on when and how to use them. Eur J Clin Invest. 2020;50(8):e13249 (6 pp).

17. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA. 1998;280(19):1690-1.

18. Doi SA, Furuya-Kanamori L, Xu C, Lin L, Chivese T, Thalib L. Questionable utility of the relative risk in clinical research: A call for change to practice [in press]. Available online 2020 Nov 7 [cited 2021 Aug 7]. DOI: 10.1016/j.jclinepi.2020.08.019. J Clin Epidemiol.

19. Ranganathan P, Aggarwal R, Pramesh CS. Common pitfalls in statistical analysis: Odds versus risk. Perspect Clin Res. 2015;6(4):222-4.

20. Ali H, Hensley Alford S, Saltzgaber J, Jankowski M, Ruszkowski S, Zarbo A. The role of preoperative MRI in influencing the surgical decision making, a retrospective look at the experience of a large academic hospital in the face of a rising mastectomy rates [Abstract]. Breast. 2011;20(Suppl 1):S55.

21. Alsop SM, Kilgore LJ, Redick ML, Mammen JM, McGinness MK, Wagner JL, et al. High-risk lesions identified only by MRI core needle biopsy in newly diagnosed breast cancer patients: Incidence, upgrades to malignancy, and impact on surgical therapy [Abstract]. Ann Surg Oncol. 2014;21(Supp 2):20-1.

22. Amin AL, Sack S, Larson KE, Winblad O, Balanoff CR, Nazir N, et al. Does the addition of breast MRI add value to the diagnostic workup of invasive lobular carcinoma? J Surg Res. 2021;257:144-52.

23. An YY, Kim SH, Kang BJ. Characteristic features and usefulness of MRI in breast cancer in patients under 40 years old: Correlations with conventional imaging and prognostic factors. Breast Cancer. 2014;21(3):302-15.

24. Angarita FA, Acuna SA, Fonseca A, Crystal P, Escallon J. Impact of preoperative breast MRIs on timing of surgery and type of intervention in newly diagnosed breast cancer patients. Ann Surg Oncol. 2010;17(Suppl 3):273-9.

25. Antakia R, Penman D, Chadwick D, Holt S. MRI for breast lobular carcinoma [Abstract]. Eur J Surg Oncol. 2012;38(11):1130.

26. Arnal Burro A, Asensio Diaz E, Gonzalez Blanco I, Moreno Reviriego A, Martin Medrano E, Garcia Serna I, et al. Repercusion de la resonancia magnetica nuclear mamaria en el tratamiento final del cancer de mama [Spanish]. [Impact of breast magnetic resonance imaging on the final treatment of breast cancer]. Clin Invest Ginecol Obstet. 2017;44(2):61-5.

27. Arunan T, Bonomi R, Strukowska O, Betal D. The role of breast MRI in the surgical planning and management of invasive lobular carcinoma: A four-year retrospective study [Abstract]. Eur J Cancer. 2018;92(Suppl 3):S152.

28. Balasubramanian R, Rajendran I, Aref F, Vashisht R. Screen detected breast cancers - Is there a role for MRI? [Abstract]. Ann Oncol. 2010;21(Suppl 4):iv34, Abstract 49P.

29. Barchie MF, Clive KS, Tyler JA, Sutcliffe JB, Kirkpatrick AD, Bell LM, et al. Standardized pretreatment breast MRI—Accuracy and influence on mastectomy decisions. J Surg Oncol. 2011;104(7):741-5.

30. Barker SJ, Anderson E, Mullen R. Magnetic resonance imaging for invasive lobular carcinoma: Is it worth it? Gland Surg. 2019;8(3):237-41.

31. Bedrosian I, Mick R, Orel SG, Schnall M, Reynolds C, Spitz FR, et al. Changes in the surgical management of patients with breast carcinoma based on preoperative magnetic resonance imaging. Cancer. 2003;98(3):468-73.

32. Berg WA, Gutierrez L, NessAiver MS, Carter WB, Bhargavan M, Lewis RS, et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. Radiology. 2004;233(3):830-49.

33. Berg WA, Madsen KS, Schilling K, Tartar M, Pisano ED, Larsen LH, et al. Breast cancer: Comparative effectiveness of positron emission mammography and MR imaging in presurgical planning for the ipsilateral breast. Radiology. 2011;258(1):59-72.

34. Bernardi D, Ciatto S, Pellegrini M, Valentini M, Houssami N. EUSOMA criteria for performing pre-operative MRI staging in candidates for breast conserving surgery: Hype or helpful? Breast. 2012;21(3):406-8.

35. Biglia N, Bounous VE, Martincich L, Panuccio E, Liberale V, Ottino L, et al. Role of MRI (magnetic resonance imaging) versus conventional imaging for breast cancer presurgical staging in young women or with dense breast. Eur J Surg Oncol. 2011;37(3):199-204.

36. Bilimoria KY, Cambic A, Hansen NM, Bethke KP. Evaluating the impact of preoperative breast magnetic resonance imaging on the surgical management of newly diagnosed breast cancers. Arch Surg. 2007;142(5):441-5; discussion 5-7.

37. Blair S, McElroy M, Middleton MS, Comstock C, Wolfson T, Kamrava M, et al. The efficacy of breast MRI in predicting breast conservation therapy. J Surg Oncol. 2006;94(3):220-5.

38. Braun M, Polcher M, Schrading S, Zivanovic O, Kowalski T, Flucke U, et al. Influence of preoperative MRI on the surgical management of patients with operable breast cancer. Breast Cancer Res Treat. 2008;111(1):179-87.

39. Brennan ME, McKessar M, Snook K, Burgess I, Spillane AJ. Impact of selective use of breast MRI on surgical decision-making in women with newly diagnosed operable breast cancer. Breast. 2017;32:135-43.

40. Buxant F, Scuotto F, Hottat N, Noel JC, Simon P. Does preoperative magnetic resonance imaging modify breast cancer surgery? Acta Chir Belg. 2007;107(3):288-91.

41. Chung A, Saouaf R, Scharre K, Phillips E. The impact of MRI on the treatment of DCIS. Am Surg. 2005;71(9):705-10.

42. Ciocchetti JM, Joy N, Staller S, Warmack J, Mann A, Moore JT, et al. The effect of magnetic resonance imaging in the workup of breast cancer. Am J Surg. 2009;198(6):824-8.

43. Constantinidis F, Christodoulidis G, Spyridakis M, Pappi V, Dimas D, Moustaka A, et al. Impact of pre-operative breast magnetic resonance imaging upon surgical management of breast carcinoma [Abstract]. EJC Suppl. 2010;8(3):238.

44. Crowe JP, Patrick RJ, Rim A. The importance of preoperative breast MRI for patients newly diagnosed with breast cancer. Breast J. 2009;15(1):52-60.

45. Dao TN, Lamont JP, Knox SM. Clinical utility of breast magnetic resonance imaging in patients presenting with primary breast cancer. Baylor Univ Med Cent Proc. 2007;20(3):227-30.

46. De Felice C, Cipolla V, Stagnitti A, Marini A, Pasqualitto E, Meggiorini ML. The impact of presurgical magnetic resonance in early breast cancer: An observational study. Eur J Gynaecol Oncol. 2012;33(2):193-9.

47. Del Frate C, Borghese L, Cedolini C, Bestagno A, Puglisi F, Isola M, et al. Role of pre-surgical breast MRI in the management of invasive breast carcinoma. Breast. 2007;16(5):469-81.

48. Derpapas MK, Bright-Thomas RM, Mullan MH. The role of breast MRI in altering pre-planned surgical treatment in elderly women with lobular cancer thought to be suitable for breast conservative surgery [Abstract]. Eur J Surg Oncol. 2016;42(5):S21.

49. Destounis SV, Arieno AL, Morgan RC. Importance of presurgical breast MRI in patients 60 years of age and older. J Clin Imaging Sci. 2014;4(3):46 (5 pp).

50. Deurloo EE, Peterse JL, Rutgers EJ, Besnard AP, Muller SH, Gilhuijs KG. Additional breast lesions in patients eligible for breast-conserving therapy by MRI: Impact on preoperative management and potential benefit of computerised analysis. Eur J Cancer. 2005;41(10):1393-401.

51. Duygulu G, Oktay A, Bilgen IG, Kapkac M, Zekioglu O. The role of breast MRI in planning the surgical treatment of breast cancer. Diagn Interv Radiol. 2012;18(5):460-7.

52. Edwards C, Williams S, McSwain AP, Damle S, Rapelyea JA, Downs K, et al. Breast-specific gamma imaging influences surgical management in patients with breast cancer. Breast J. 2013;19(5):512-9.

53. El Sharouni MA, Postma EL, Menezes GL, van den Bosch MA, Pijnappel RM, Witkamp AJ, et al. High prevalence of MRI-detected contralateral and ipsilateral malignant findings in patients with invasive ductolobular breast cancer: Impact on surgical management. Clin Breast Cancer. 2016;16(4):269-75.

54. Elshof LE, Rutgers EJ, Deurloo EE, Loo CE, Wesseling J, Pengel KE, et al. A practical approach to manage additional lesions at preoperative breast MRI in patients eligible for breast conserving therapy: Results. Breast Cancer Res Treat. 2010;124(3):707-15.

55. Fan XC, Nemoto T, Blatto K, Mangiafesto E, Sundberg J, Chen A, et al. Impact of presurgical breast magnetic resonance imaging (MRI) on surgical planning - A retrospective analysis from a private radiology group. Breast J. 2013;19(2):134-41.

56. Fischer U, Kopka L, Grabbe E. Breast carcinoma: Effect of preoperative contrast-enhanced MR imaging on the therapeutic approach. Radiology. 1999;213(3):881-8.

57. Fischer U, Vosshenrich R, Probst A, Burchhardt H, Grabbe E. [Preoperative MR-mammography in diagnosed breast carcinoma. Useful information or useless extravagance?] [German]. Rofo. 1994;161(10):300-6.

58. França LKL, Bitencourt AGV, Makdissi FBA, Curi C, de Souza JA, Marques EF. Impact of breast magnetic resonance imaging on the locoregional staging and management of breast cancer. Radiol Bras. 2019;52(4):211-6.

59. Franca LKL, Bitencourt AGV, Paiva HLS, Silva CB, Pereira NP, Paludo J, et al. Role of magnetic resonance imaging in the planning of breast cancer treatment strategies: Comparison with conventional imaging techniques. Radiol Bras. 2017;50(2):76-81.

60. Furman B, Gardner MS, Romilly P, Clark J, Stowell N, Green B, et al. Effect of 0.5 tesla magnetic resonance imaging on the surgical management of breast cancer patients. Am J Surg. 2003;186(4):344-7.

61. Gatzemeier W, Liersch T, Stylianou A, Buttler A, Becker H, Fischer U. Präoperative MR-mammographie beim mammacarcinom. Einfluû auf die operative behandlung aus chirurgischer sicht [German]. [Preoperative MR mammography in breast carcinoma. Effect on operative treatment from the surgical viewpoint]. Chirurg. 1999;70(12):1460-8.

62. Gonzalez-Huebra I, Elizalde A, Garcia-Baizan A, Calvo M, Ezponda A, Martinez-Regueira F, et al. Is it worth to perform preoperative MRI for breast cancer after mammography, tomosynthesis and ultrasound? Magn Reson Imaging. 2019;57:317-22.

63. Grobmyer SR, Mortellaro VE, Marshall J, Higgs GM, Hochwald SN, Mendenhall NP, et al. Is there a role for routine use of MRI in selection of patients for breast-conserving cancer therapy? J Am Coll Surg. 2008;206(5):1045-50; discussion 50-2.

64. Gurdal SO, Ozcinar B, Kayahan M, Igci A, Tunaci M, Ozmen V, et al. Incremental value of magnetic resonance imaging for breast surgery planning. Surg Today. 2013;43(1):55-61.

65. Ha GW, Yi MS, Lee BK, Youn HJ, Jung SH. Clinical outcome of magnetic resonance imaging-detected additional lesions in breast cancer patients. J Breast Cancer. 2011;14(3):213-8.

66. Haragan A, Huws AM, Khawaja S, Gurung S, Muniweera N, Nadi K, et al. Invasive lobular carcinoma of the breast: A retrospective analysis of consecutive cases reviewing preoperative imaging assessment with sonography, digital breast tomosynthesis and MR [Abstract]. Eur J Surg Oncol. 2014;40(5):613-4.

67. He H, Plaxco JS, Wei W, Huo L, Candelaria RP, Kuerer HM, et al. Incremental cancer detection using breast ultrasonography versus breast magnetic resonance imaging in the evaluation of newly diagnosed breast cancer patients. Br J Radiol. 2016;89(1065):20160401 (10 pp).

68. Heil J, Buehler A, Golatta M, Rom J, Schipp A, Harcos A, et al. Do patients with invasive lobular breast cancer benefit in terms of adequate change in surgical therapy from a supplementary preoperative breast MRI? Ann Oncol. 2012;23(1):98-104.

69. Hlubocky J, Bhavnagri S, Swinford A, Mitri C, Rebner M, Pai V. Does the use of pretreatment MRI change the management of patients with newly diagnosed breast cancer? Breast J. 2018;24(3):309-13.

70. Hogan B, Al-Huneidi R, Holmes W, Dodwell D, Horgan K, Sharma N. Selective use of breast MR in all pathological subtypes has a high diagnostic yield [Abstract]. Eur J Surg Oncol. 2016;42(5):S40.

71. Jafferbhoy S, Tan Y, Chandarana M, Salehi-Bird S, Gunning E, Isa ZM, et al. Are lobular features on core biopsy an indication for pre-operative MRI? [Abstract]. Eur J Surg Oncol. 2018;44(6):908.

72. Jafferbhoy S, Tandon M, Kirby R, Narayanan S, Bajwa S, Salehi Bird S, et al. Selective use of MRI and impact on management in breast cancer [Abstract]. Cancer Res. 2017;77(4 Suppl 1):Abstract P3-02-10.

73. Jafferbhoy SF, Goussous G, Chandarana M, Salehi-Bird S, Mohd-Isa Z, Gunning E, et al. Impact of preoperative MRI in invasive ductal carcinoma with lobular features on core biopsy. Clin Breast Cancer. 2020;21(3):e194-e8.

74. Kilbas Z, Yildiz R, Ozturk E, Mentes MO, Gorgulu S. The impact of preoperative breast magnetic resonance imaging (MRI) on surgical planning of newly diagnosed breast cancer patients-analysis of 112 patients [Abstract]. Eur Surg Res. 2013;50(Suppl 1):114-5.

75. Kim EY, Youn I, Lee KH, Yun JS, Park YL, Park CH, et al. Diagnostic value of contrast-enhanced digital mammography versus contrast-enhanced magnetic resonance imaging for the preoperative evaluation of breast cancer. J Breast Cancer. 2018;21(4):453-62.

76. Kohara S, Ishigaki S, Satake H, Kawamura A, Kawai H, Kikumori T, et al. Background parenchymal enhancement in preoperative breast MRI. Nagoya J Med Sci. 2015;77(3):373-82.

77. Lafaye-Carre S, Collinet P, Vinatier D, Bendavid S, Place V, Pruvo JP, et al. Impact de l'IRM mammaire preoperatoire sur la prise en charge chirurgicale des cancers du sein: Experience de deux centres hospitaliers universitaires [French]. [Impact of preoperative breast magnetic resonance imaging on surgical management: Experience of two university hospitals]. Gynecol Obstet Fertil. 2014;42(10):686-91.

78. Lanitis S, Peristeraki S, Zafeiriadou V, Sourtse G, Ganis V, Nika F, et al. Breast MRI vs traditional triple assessment in the preoperative assessment of breast cancer patients. Does MRI affect correctly the decision about the extent of the surgery? A study based on the final histology specimen [Abstract]. Eur J Surg Oncol. 2019;45(2):e28-e9.

79. Law Y, Cheung PS, Lau S, Lo GG. Impact of magnetic resonance imaging on preoperative planning for breast cancer surgery. Hong Kong Med J. 2013;19(4):294-9.

80. Lee J, Jung JH, Kim WW, Hwang SO, Kim HJ, Park JY, et al. The role of preoperative breast magnetic resonance (MR) imaging for surgical decision in patients with triple-negative breast cancer. J Surg Oncol. 2016;113(1):12-6.

81. Liersch T, Langer C, Fischer U, Buttler A, Fuzesi L, Markus PM, et al. Praoperative magnet-resonanz-mammographie (MRM) beim mammakarzinom: Uberflussiger luxus oder relevante einflussgrose auf die OP-strategie? [German]. [Preoperative magnetic resonance mammography in breast cancer: Useless luxury or relevant factor influencing surgical strategy?] Viszeralchirurgie. 2002;37(2):106-15.

82. Lilly AJ, Johnson M, Kuzmiak CM, Ollila DW, O'Connor SM, Hertel JD, et al. MRI-guided core needle biopsy of the breast: Radiology-pathology correlation and impact on clinical management. Ann Diagn Pathol. 2020;48:151563 (6 pp).

83. Lim HI, Choi JH, Yang JH, Han BK, Lee JE, Lee SK, et al. Does pre-operative breast magnetic resonance imaging in addition to mammography and breast ultrasonography change the operative management of breast carcinoma? Breast Cancer Res Treat. 2010;119(1):163-7.

84. Majid F, Khan H, Goble E, Cox D, Alishah N, Bhatt R, et al. Utility of targeted ultrasound for MRI detected incidental enhancing lesions [Abstract]. Breast Cancer Res. 2017;19(Suppl 1):Article 116, p 8, Abstract PB.7.

85. Mameri CS, Kemp C, Goldman SM, Sobral LA, Ajzen S. Impact of breast MRI on surgical treatment, axillary approach, and systemic therapy for breast cancer. Breast J. 2008;14(3):236-44.

86. Mazilu L, Suceveanu AI, Tomescu D, Ciufu N, Baz R, Suceveanu AP, et al. Optimizing the indication for breast-conservative surgery (BCS) in patients with locally-advanced breast cancer. Chirurgia (Bucur). 2013;108(4):478-81.

87. Menes TS, Zissman S, Golan O, Sperber F, Klausner J, Schneebaum S. Yield of selective magnetic resonance imaging in preoperative workup of newly diagnosed breast cancer patients planned for breast conserving surgery. Am Surg. 2012;78(4):451-5.

88. Merrill AY, Renfroe S, Hill E, Henry-Tillman R, Ochoa D, Klimberg VS, et al. Breast MRI after neoadjuvant chemotherapy does not change clinical or surgical management and may be eliminated in patients desiring mastectomy [Abstract]. Ann Surg Oncol. 2018;25(1 Suppl 1):S96.

89. Messineo D, Izzo L, Pisanelli MC, Razionale F, Izzo S, Izzo P. The influence of preoperative MRI in early breast cancer: Gold standard. Ann Ital Chir. 2020;91(2):144-53.

90. Morais M, Pinho A, Magalhaes A, Costa S, Osorio F, Preto AS, et al. Breast MRI and invasive lobular carcinoma: An update [Abstract]. Eur J Surg Oncol. 2014;40(11):S85-S6.

91. Myers KS, Green LA, Lebron L, Morris EA. Imaging appearance and clinical impact of preoperative breast MRI in pregnancy-associated breast cancer. AJR Am J Roentgenol. 2017;209(3):W177-W83.

92. Myers KS, Kamel IR, Macura KJ. MRI-guided breast biopsy: Outcomes and effect on patient management. Clin Breast Cancer. 2015;15(2):143-52.

93. Nelson ME, Saouaf R, Noori SF, Chan JL, Varda MM, Mirzadehgan P, et al. Prevalence and histopathology of additional lesions found with MRI in breast cancer patients [Abstract]. Ann Surg Oncol. 2014;21(Suppl):85.

94. Obermeyer J, Wadhwani N, Bova D, Sarker S, Rychlik K, Salhadar A, et al. Magenetic resonance imaging of the breast: Radiologic-pathologic correlation [Abstract]. Lab Invest. 2009;89(Suppl):61A-2A, Abstract 266.

95. Orel SG, Schnall MD, Powell CM, Hochman MG, Solin LJ, Fowble BL, et al. Staging of suspected breast cancer: Effect of MR imaging and MR-guided biopsy. Radiology. 1995;196(1):115-22.

96. Parvaiz MA, Yang P, Razia E, Mascarenhas M, Deacon C, Matey P, et al. Breast MRI in invasive lobular carcinoma: A useful investigation in surgical planning? Breast J. 2016;22(2):143-50.

97. Pediconi F, Catalano C, Padula S, Roselli A, Moriconi E, Dominelli V, et al. Contrast-enhanced magnetic resonance mammography: Does it affect surgical decision-making in patients with breast cancer? Breast Cancer Res Treat. 2007;106(1):65-74.

98. Pediconi F, Catalano C, Roselli A, Dominelli V, Cagioli S, Karatasiou A, et al. The challenge of imaging dense breast parenchyma: Is magnetic resonance mammography the technique of choice? A comparative study with x-ray mammography and whole-breast ultrasound. Invest Radiol. 2009;44(7):412-21.

99. Pediconi F, Miglio E, Telesca M, Luciani ML, Kirchin MA, Passariello R, et al. Effect of preoperative breast magnetic resonance imaging on surgical decision making and cancer recurrence rates. Invest Radiol. 2012;47(2):128-35.

100. Perono Biacchiardi C, Brizzi D, Genta F, Zanon E, Camanni M, Deltetto F. Breast cancer preoperative staging: Does contrast-enhanced magnetic resonance mammography modify surgery? Int J Breast Cancer. 2011;2011:757234 (10 pp).

101. Pettit K, Swatske ME, Gao F, Salavaggione L, Gillanders WE, Aft RL, et al. The impact of breast MRI on surgical decision-making: Are patients at risk for mastectomy? J Surg Oncol. 2009;100(7):553-8.

102. Pilgrim S, Tanner J, Soonsein M, Foreman J, Britton P, Clayton G. Pre-operative MRI scanning changes surgical strategy in corebiopsy proven lobular breast cancer [Abstract]. Eur J Surg Oncol. 2013;39(5):516.

103. Pop CF, Stanciu-Pop C, Drisis S, Radermeker M, Vandemerckt C, Noterman D, et al. The impact of breast MRI workup on tumor size assessment and surgical planning in patients with early breast cancer. Breast J. 2018;24(6):927-33.

104. Rabasco P, Caivano R, Dinardo G, Gioioso M, Lotumolo A, Iannelli G, et al. Magnetic resonance imaging in the pre-surgical staging of breast cancer: Our experience. Cancer Invest. 2017;35(1):43-50.

105. Rabben T, Rodegerdts E, Bachmann H, Funder V. The impact of preoperative breast MRI in newly diagnosed breast cancer. A prospective study of treatment outcome in patients selected for breast-conserving surgery in a Norwegian multidisciplinary breast cancer clinic [Abstract]. Cancer Res. 2011;71(24 Suppl 3):Abstract P2-08-9.

106. Romanoff A, Schmidt H, McMurray M, Weltz C, Schwartzman M, Friedman K, et al. Who is ordering MRIs in newly diagnosed breast cancer patients? Am Surg. 2018;84(3):351-7.

107. Sanchez SA, Vozmediano MA, Ferrandez CS, Alvarez MG, Guerrero MB, Sanchez PM, et al. Influence of preoperative MRI in surgical management of breast carcinoma [Abstract]. Breast. 2011;20(Suppl 1):S36. Abstract P172.

108. Schelfout K, Van Goethem M, Kersschot E, Colpaert C, Schelfhout AM, Leyman P, et al. Contrast-enhanced MR imaging of breast lesions and effect on treatment. Eur J Surg Oncol. 2004;30(5):501-7.

109. Schell AM, Rosenkranz K, Lewis PJ. Role of breast MRI in the preoperative evaluation of patients with newly diagnosed breast cancer. AJR Am J Roentgenol. 2009;192(5):1438-44.

110. Schmidt H, Keleher A, Viola H, Zanieski G, Winterleitner S, Karp R. Utility of preoperative breast MRI for evaluation of DCIS [Abstract]. Ann Surg Oncol. 2012;19(2 Suppl 1):102-3.

111. Selvi V, Nori J, Meattini I, Francolini G, Morelli N, De Benedetto D, et al. Role of magnetic resonance imaging in the preoperative staging and work-up of patients affected by invasive lobular carcinoma or invasive ductolobular carcinoma [Erratum in 2018: 9056239]. Biomed Res Int. 2018;2018:1569060 (7 pp).

112. Siegmann KC, Baur A, Vogel U, Kraemer B, Hahn M, Claussen CD. Risk-benefit analysis of preoperative breast MRI in patients with primary breast cancer. Clin Radiol. 2009;64(4):403-13.

113. Tan JE, Orel SG, Schnall MD, Schultz DJ, Solin LJ. Role of magnetic resonance imaging and magnetic resonance imaging-guided surgery in the evaluation of patients with early-stage breast cancer for breast conservation treatment. Am J Clin Oncol. 1999;22(4):414-8.

114. Teller P, Jefford VJ, Gabram SG, Newell M, Carlson GW. The utility of breast MRI in the management of breast cancer. Breast J. 2010;16(4):394-403.

115. Tillman GF, Orel SG, Schnall MD, Schultz DJ, Tan JE, Solin LJ. Effect of breast magnetic resonance imaging on the clinical management of women with early-stage breast carcinoma. J Clin Oncol. 2002;20(16):3413-23.

116. Van Loevezijn A, Winter - Warnars GHAO, van der Noordaa MEM, Hernandez GS, de Bloeme C, van Duijnhoven FH, et al. Clinical impact of MRI-detected additional lesions in breast cancer patients treated with neoadjuvant systemic therapy at the Netherlands Cancer Institute [Abstract]. Eur J Surg Oncol. 2020;46(2):e23-e4.

117. Warnack E, Dhage S, Johnson E, Horowitz E, Joseph KA. The use of breast MRI for patients with preoperative breast cancer in an underserved population. J Surg Res. 2019;234:155-60.

118. Westerhof JP, Fischer U, Moritz JD, Oestmann JW. MR imaging of mammographically detected clustered microcalcifications: Is there any value? Radiology. 1998;207(3):675-81.

119. Wiener JI, Schilling KJ, Adami C, Obuchowski NA. Assessment of suspected breast cancer by MRI: A prospective clinical trial using a combined kinetic and morphologic analysis. AJR Am J Roentgenol. 2005;184(3):878-86.

120. Wong SM, Prakash I, Trabulsi N, Parsyan A, Moldoveanu D, Zhang D, et al. Evaluating the impact of breast density on preoperative MRI in invasive lobular carcinoma. J Am Coll Surg. 2018;226(5):925-32.

121. Xue C, MacFarlan J, Sareen P. Assessing the value of preoperative MRI in guiding diagnostic and surgical management of breast cancer patients [Abstract]. Eur J Surg Oncol. 2019;45(5):905, Abstract P075.

122. Yoshida M, Nakano S, Fujii K, Kousaka J, Shiomi Y, Tetsuka R, et al. The impact of preoperative real-time virtual sonography (RVS) in the surgical management of breast cancer: A single-institution review [Abstract]. Eur J Cancer. 2013;49(Suppl 2):S460-S1.

123. Yoshida M, Nakano S, Kousaka J, Mouri Y, Yorozuya K, Fujii K, et al. The impact of preoperative real-time virtual sonography (RVS) on surgical treatment of breast cancer [Abstract]. Eur J Cancer. 2012;48(Suppl 1):S168.

124. Zhang Y, Fukatsu H, Naganawa S, Satake H, Sato Y, Ohiwa M, et al. The role of contrast-enhanced MR mammography for determining candidates for breast conservation surgery. Breast Cancer. 2002;9(3):231-9.

125. Davis KL, Barth RJ, Jr., Gui J, Dann E, Eisenberg B, Rosenkranz K. Use of MRI in preoperative planning for women with newly diagnosed DCIS: Risk or benefit? Ann Surg Oncol. 2012;19(10):3270-4.

126. Keymeulen K, Geurts SME, Lobbes MBI, Heuts EM, Duijm LEM, Kooreman LFS, et al. Population-based study of the effect of preoperative breast MRI on the surgical management of ductal carcinoma in situ. Br J Surg. 2019;106(11):1488-94.

127. Yoon GY, Choi WJ, Kim HH, Cha JH, Shin HJ, Chae EY. Surgical outcomes for ductal carcinoma in situ: Impact of preoperative MRI. Radiology. 2020;295(2):296-303.

128. Sorbero ME, Dick AW, Beckjord EB, Ahrendt G. Diagnostic breast magnetic resonance imaging and contralateral prophylactic mastectomy. Ann Surg Oncol. 2009;16(6):1597-605.

129. Vos EL, Voogd AC, Verhoef C, Siesling S, Obdeijn IM, Koppert LB. Benefits of preoperative MRI in breast cancer surgery studied in a large population-based cancer registry. Br J Surg. 2015;102(13):1649-57.

130. Gonzalez V, Sandelin K, Karlsson A, Aberg W, Lofgren L, Iliescu G, et al. Preoperative MRI of the breast (POMB) influences primary treatment in breast cancer: A prospective, randomized, multicenter study. World J Surg. 2014;38(7):1685-93.

131. Karlsson A, Gonzalez V, Jaraj SJ, Bottai M, Sandelin K, Arver B, et al. The accuracy of incremental pre-operative breast MRI findings - Concordance with histopathology in the Swedish randomized multicenter POMB trial. Eur J Radiol. 2019;114:185-91.

132. Peters NH, van Esser S, van den Bosch MA, Storm RK, Plaisier PW, van Dalen T, et al. Preoperative MRI and surgical management in patients with nonpalpable breast cancer: The MONET - randomised controlled trial. Eur J Cancer. 2011;47(6):879-86.

133. Peters NHGM, Borel Rinkes IHM, Mali WPTM, van den Bosch MAAJ, Storm RK, Plaisier PW, et al. Breast MRI in nonpalpable breast lesions: A randomized trial with diagnostic and therapeutic outcome - MONET - study. Trials. 2007;8:40 (7 pp).

134. Katipamula R, Degnim AC, Hoskin T, Boughey JC, Loprinzi C, Grant CS, et al. Trends in mastectomy rates at the Mayo Clinic Rochester: Effect of surgical year and preoperative magnetic resonance imaging. J Clin Oncol. 2009;27(25):4082-8.

135. Onega T, Weiss JE, Goodrich ME, Zhu W, DeMartini WB, Kerlikowske K, et al. Relationship between preoperative breast MRI and surgical treatment of non-metastatic breast cancer. J Surg Oncol. 2017;116(8):1008-15.

136. Ozanne EM, Weiss JE, Onega T, DeMartini W, Kerlikowske K, Buist DS, et al. Locoregional treatment of breast cancer in women with and without preoperative magnetic resonance imaging. Am J Surg. 2017;213(1):132-9.e2.

137. Goodrich ME, Weiss J, Onega T, Balch SL, Buist DS, Kerlikowske K, et al. The role of preoperative magnetic resonance imaging in the assessment and surgical treatment of interval and screen-detected breast cancer in older women. Breast J. 2016;22(6):616-22.

138. Heil J, Rauch G, Szabo AZ, Garcia-Etienne CA, Golatta M, Domschke C, et al. Breast cancer mastectomy trends between 2006 and 2010: Association with magnetic resonance imaging, immediate breast reconstruction, and hospital volume. Ann Surg Oncol. 2013;20(12):3839-46.

139. Choi WJ, Cha JH, Kim HH, Shin HJ, Chae EY, Jung KH, et al. Long-term survival outcomes of primary breast cancer in women with or without preoperative magnetic resonance imaging: A matched cohort study. Clin Oncol (R Coll Radiol). 2017;29(10):653-61.

140. Lai HW, Chen CJ, Lin YJ, Chen SL, Wu HK, Wu YT, et al. Does breast magnetic resonance imaging combined with conventional imaging modalities decrease the rates of surgical margin involvement and reoperation? A case-control comparative analysis. Medicine. 2016;95(22):e3810 (11 pp).

141. Hollingsworth AB, Stough RG, O'Dell CA, Brekke CE. Breast magnetic resonance imaging for preoperative locoregional staging. Am J Surg. 2008;196(3):389-97.

142. Hollingsworth AB, Stough RG. Preoperative breast MRI: Barking up the wrong endpoints. Breast Dis. 2015;26(1):19-25.

143. Grady I, Gorsuch-Rafferty H, Hadley P. Preoperative staging with magnetic resonance imaging, with confirmatory biopsy, improves surgical outcomes in women with breast cancer without increasing rates of mastectomy. Breast J. 2012;18(3):214-8.

144. Luis IV, Hughes ME, Cronin A, Rugo HS, Edge SB, Moy B, et al. Variation in the use of mastectomy (MAST) in women with small node negative breast cancer (BC) treated at US academic institutions [Abstract]. Cancer Res. 2015;75(9 Suppl 1):Abstract P2-13-03.

145. Parsyan A, Moldoveanu D, Balram B, Wong S, Zhang DD, Svadzian A, et al. Influence of preoperative magnetic resonance imaging on the surgical management of breast cancer patients. Am J Surg. 2016;211(6):1089-94.

146. Kapoor NS, Eaton A, King TA, Patil S, Stempel M, Morris E, et al. Should breast density influence patient selection for breast-conserving surgery? Ann Surg Oncol. 2013;20(2):600-6.

147. Killelea BK, Long JB, Chagpar AB, Ma X, Soulos PR, Ross JS, et al. Trends and clinical implications of preoperative breast MRI in Medicare beneficiaries with breast cancer. Breast Cancer Res Treat. 2013;141(1):155-63.

148. Vriens IJH, Keymeulen K, Lobbes MBI, van Bommel ACM, Nieuwenhuijzen GAP, Smidt ML, et al. Breast magnetic resonance imaging use in patients undergoing neoadjuvant chemotherapy is associated with less mastectomies in large ductal cancers but not in lobular cancers. Eur J Cancer. 2017;81:74-80.

149. Lobbes MB, Vriens IJ, van Bommel AC, Nieuwenhuijzen GA, Smidt ML, Boersma LJ, et al. Breast MRI increases the number of mastectomies for ductal cancers, but decreases them for lobular cancers. Breast Cancer Res Treat. 2017;162(2):353-64.

150. Fortune-Greeley AK, Wheeler SB, Meyer AM, Reeder-Hayes KE, Biddle AK, Muss HB, et al. Preoperative breast MRI and surgical outcomes in elderly women with invasive ductal and lobular carcinoma: A population-based study. Breast Cancer Res Treat. 2014;143(1):203-12.

151. Mann RM, Loo CE, Wobbes T, Bult P, Barentsz JO, Gilhuijs KG, et al. The impact of preoperative breast MRI on the re-excision rate in invasive lobular carcinoma of the breast. Breast Cancer Res Treat. 2010;119(2):415-22.

152. Ha SM, Chae EY, Cha JH, Kim HH, Shin HJ, Choi WJ. Breast MR imaging before surgery: Outcomes in patients with invasive lobular carcinoma by using propensity score matching. Radiology. 2018;287(3):771-7.

153. Sardanelli F, Trimboli RM, Houssami N, Gilbert FJ, Helbich TH, Alvarez Benito M, et al. Solving the preoperative breast MRI conundrum: Design and protocol of the MIPA study. Eur Radiol. 2020;30:5427-36.

154. Sardanelli F. Preoperative breast MRI: First results from the MIPA study [Abstract]. Insights Imaging. 2017;8(Suppl 1):S491.

155. Balleyguier C, Dunant A, Ceugnart L, Kandel M, Chauvet MP, Cherel P, et al. Preoperative breast magnetic resonance imaging in women with local ductal carcinoma in situ to optimize surgical outcomes: Results from the randomized phase III Trial IRCIS. J Clin Oncol. 2019;37(11):885-92.

156. Kandel M, Dunant A, Balleyguier C, Bonastre J. Cost-effectiveness of preoperative magnetic resonance imaging to optimize surgery in ductal carcinoma in situ of the breast. Eur J Radiol. 2020;129:109058 (5 pp).

157. Mota BS, Reis YN, Doria MT, Ricci MD, Shimizu C, Ferreira V, et al. Brazilian randomized study: Impact of preoperative magnetic resonance in the evaluation for breast cancer conservative surgery (BREAST-MRI Trial) [Abstract]. Ann Oncol. 2019;30(Suppl 3):iii39-iii40.

158. Turnbull L, Brown S, Harvey I, Olivier C, Drew P, Napp V, et al. Comparative effectiveness of MRI in breast cancer (COMICE) trial: A randomised controlled trial. Lancet. 2010;375(9714):563-71.

159. Turnbull LW, Brown SR, Olivier C, Harvey I, Brown J, Drew P, et al. Multicentre randomised controlled trial examining the cost-effectiveness of contrast-enhanced high field magnetic resonance imaging in women with primary breast cancer scheduled for wide local excision (COMICE). Health Technol Assess. 2010;14(1):1-182.

160. Morris EA. Should we dispense with preoperative breast MRI? Lancet. 2010;375(9714):528-30.

161. McMahon MA, Sharma N, Shaaban A, Dall BJG. Did established clinical practice regarding MRI bias the COMICE trial? [Abstract]. Cancer Res. 2013;73(24 Suppl 1):Abstract P2-02-1.

162. Brück N, Koskivuo I, Bostrom P, Saunavaara J, Aaltonen R, Parkkola R. Preoperative magnetic resonance imaging in patients with stage I invasive ductal breast cancer: A prospective randomized study. Scand J Surg. 2018;107(1):14-22.

163. Feigelson HS, James TA, Single RM, Onitilo AA, Aiello Bowles EJ, Barney T, et al. Factors associated with the frequency of initial total mastectomy: Results of a multi-institutional study. J Am Coll Surg. 2013;216(5):966-75.

164. Wang SY, Kuntz KM, Tuttle TM, Jacobs DR, Jr., Kane RL, Virnig BA. The association of preoperative breast magnetic resonance imaging and multiple breast surgeries among older women with early stage breast cancer. Breast Cancer Res Treat. 2013;138(1):137-47.

165. Sung JS, Li J, Da Costa G, Patil S, Van Zee KJ, Dershaw DD, et al. Preoperative breast MRI for early-stage breast cancer: Effect on surgical and long-term outcomes. AJR Am J Roentgenol. 2014;202(6):1376-82.

166. Zeng Z, Amin A, Roy A, Pulliam NE, Karavites LC, Espino S, et al. Preoperative magnetic resonance imaging use and oncologic outcomes in premenopausal breast cancer patients. NPJ Breast Cancer. 2020;6:49 (8 pp).

167. Obdeijn IM, Tilanus-Linthorst MM, Spronk S, van Deurzen CH, de Monye C, Hunink MG, et al. Preoperative breast MRI can reduce the rate of tumor-positive resection margins and reoperations in patients undergoing breast-conserving surgery. AJR Am J Roentgenol. 2013;200(2):304-10.

168. Chandwani S, George PA, Azu M, Bandera EV, Ambrosone CB, Rhoads GG, et al. Role of preoperative magnetic resonance imaging in the surgical management of early-stage breast cancer. Ann Surg Oncol. 2014;21(11):3473-80.

169. Burkbauer L, Goldbach M, Malinovitch A, Keele L, Nazarian S, Tchou J. Does preoperative MRI improve surgical outcomes in HER2+ breast cancer? [Abstract]. Ann Surg Oncol. 2020;27(Suppl 2):S375-S6.

170. Bedrosian I, Suman VJ, Yao K, Shih YC, Yen TWF, Comstock C, et al. ACOSOG Z11101/ACRIN 6694: Effect of preoperative breast MRI on surgical outcomes, costs and quality of life of women with breast cancer [Abstract]. Cancer Res. 2011;71(24 Suppl):Abstract OT2-05-6.

171. Rahman RL, Khokhar MO, Day L, Larkin A, Quinlan R, Bavosi D, et al. Breast cancer staging with magnetic resonance for treatment planning (B-SMART)-a prospective randomized trial: Interim analysis [Abstract]. Ann Surg Oncol. 2012;19(2 Suppl 1):76.

172. Wang SY, Long JB, Killelea BK, Evans SB, Roberts KB, Silber A, et al. Preoperative breast magnetic resonance imaging and contralateral breast cancer occurrence among older women with ductal carcinoma in situ. Breast Cancer Res Treat. 2016;158(1):139-48.

173. Pilewskie M, Olcese C, Eaton A, Patil S, Morris E, Morrow M, et al. Perioperative breast MRI is not associated with lower locoregional recurrence rates in DCIS patients treated with or without radiation. Ann Surg Oncol. 2014;21(5):1552-60.

174. Kim JY, Cho N, Koo HR, Yi A, Kim WH, Lee SH, et al. Unilateral breast cancer: Screening of contralateral breast by using preoperative MR imaging reduces incidence of metachronous cancer. Radiology. 2013;267(1):57-66.

175. Amin AL, Helenowski IB, Kmiecik TE, Zaveri SR, Hansen NM, Bethke KP, et al. Effects of preoperative MRI on rate of ipsilateral and contralateral recurrence of breast cancer [Abstract]. Cancer Res. 2015;75(9 Suppl 1):Abstract P1-01-5.

176. Ko ES, Han BK, Kim RB, Ko EY, Shin JH, Nam SY, et al. Analysis of the effect of breast magnetic resonance imaging on the outcome in women undergoing breast conservation surgery with radiation therapy. J Surg Oncol. 2013;107(8):815-21.

177. Hill MV, Beeman JL, Jhala K, Holubar SD, Rosenkranz KM, Barth RJ, Jr. Relationship of breast MRI to recurrence rates in patients undergoing breast-conservation treatment. Breast Cancer Res Treat. 2017;163(3):615-22.

178. Bae MS, Moon HG, Han W, Noh DY, Ryu HS, Park IA, et al. Early stage triple-negative breast cancer: Imaging and clinical-pathologic factors associated with recurrence. Radiology. 2016;278(2):356-64.

179. van Nijnatten TJA, van Tiel LPT, Voogd AC, Groothuis-Oudshoorn CGM, Siesling S, Lobbes MBI. The effect of breast MRI on disease-free and overall survival in breast cancer patients: A retrospective population-based study. Breast Cancer Res Treat. 2020;184(3):951-63.

180. Wang SY, Long JB, Killelea BK, Evans SB, Roberts KB, Silber A, et al. Preoperative breast magnetic resonance imaging and contralateral breast cancer occurrence among older women with breast cancer. J Clin Oncol. 2016;34(4):321-8.

181. Hwang N, Schiller DE, Crystal P, Maki E, McCready DR. Magnetic resonance imaging in the planning of initial lumpectomy for invasive breast carcinoma: Its effect on ipsilateral

breast tumor recurrence after breast-conservation therapy. Ann Surg Oncol. 2009;16(11):3000-9.

182. Gervais MK, Maki E, Schiller DE, Crystal P, McCready DR. Preoperative MRI of the breast and ipsilateral breast tumor recurrence: Long-term follow up. J Surg Oncol. 2017;115(3):231-7.

183. Ryu J, Park HS, Kim S, Kim JY, Park S, Kim SI. Preoperative magnetic resonance imaging and survival outcomes in T1-2 breast cancer patients who receive breast-conserving therapy. J Breast Cancer. 2016;19(4):423-8.

184. Wang SY, Long JB, Killelea BK, Evans SB, Roberts KB, Silber AL, et al. Associations of preoperative breast magnetic resonance imaging with subsequent mastectomy and breast cancer mortality. Breast Cancer Res Treat. 2018;172(2):453-61.

185. Ha SM, Chae EY, Cha JH, Kim HH, Shin HJ, Choi WJ. Long-term survival outcomes in invasive lobular carcinoma patients with and without preoperative MR imaging: A matched cohort study. Eur Radiol. 2019;29(5):2526-34.

186. Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, et al. Society of Surgical Oncology-American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. Int J Radiat Oncol Biol Phys. 2014;88(3):553-64.

187. Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, et al. Society of Surgical Oncology–American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages i and ii invasive breast cancer. J Clin Oncol. 2014;32(14):1507-15.

188. Morrow M, Van Zee KJ, Solin LJ, Houssami N, Chavez-MacGregor M, Harris JR, et al. Society of Surgical Oncology-American Society for Radiation Oncology-American Society of Clinical Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in ductal carcinoma in situ. J Clin Oncol. 2016;34(33):4040-6.

189. Morrow M, Van Zee KJ, Solin LJ, Houssami N, Chavez-MacGregor M, Harris JR, et al. Society of Surgical Oncology-American Society for Radiation Oncology-American Society of Clinical Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in ductal carcinoma in situ. Pract Radiat Oncol. 2016;6(5):287-95.

190. Schnitt SJ, Moran MS, Giuliano AE. Lumpectomy margins for invasive breast cancer and ductal carcinoma in situ: Current guideline recommendations, their implications, and impact. J Clin Oncol. 2020;38(20):2240-5.

191. Marinovich ML, Noguchi N, Morrow M, Houssami N. Changes in reoperation after publication of consensus guidelines on margins for breast-conserving surgery: A systematic review and meta-analysis. JAMA Surgery. 2020;155(10):e203025-e.

192. Xia C, Schroeder MC, Weigel RJ, Sugg SL, Thomas A. Rate of contralateral prophylactic mastectomy is influenced by preoperative MRI recommendations. Ann Surg Oncol. 2014;21(13):4133-8.

193. Petrillo A, Porto A, Fusco R, Filice S, Vallone P, Rubulotta MR, et al. Surgical impact of preoperative breast MRI in women below 40 years of age. Breast Cancer Res Treat. 2013;140(3):527-33.

194. Yi A, Cho N, Yang KS, Han W, Noh DY, Moon WK. Breast cancer recurrence in patients with newly diagnosed breast cancer without and with preoperative MR imaging: A matched cohort study. Radiology. 2015;276(3):695-705.

195. Moloney BM, McAnena PF, Ryan EJ, Beirn EO, Waldron RM, Connell AO, et al. The impact of preoperative breast magnetic resonance imaging on surgical management in symptomatic patients with invasive lobular carcinoma. Breast Cancer. 2020;14:1178223420948477 (9 pp).

196. Killelea BK, Grube BJ, Rishi M, Philpotts L, Tran EJ, Lannin DR. Is the use of preoperative breast MRI predictive of mastectomy? World J Surg Oncol. 2013;11:154 (5 pp).

197. Pengel KE, Loo CE, Teertstra HJ, Muller SH, Wesseling J, Peterse JL, et al. The impact of preoperative MRI on breast-conserving surgery of invasive cancer: A comparative cohort study. Breast Cancer Res Treat. 2009;116(1):161-9.

198. Wintgens LIS, Pengel KE, Loo CE, Van Werkhoven E, Rutgers EJT, Gilhuijs KGA. An observational study to detect possible differences in long-term outcome due to preoperative breast MRI in patients treated with breast conserving therapy [Abstract]. Eur J Cancer. 2014;50(Suppl 2):S62.

199. Stucky CC, Gray RJ, Wasif N, Dueck AC, Pockaj BA. Increase in contralateral prophylactic mastectomy: Echoes of a bygone era? Surgical trends for unilateral breast cancer. Ann Surg Oncol. 2010;17(Suppl 3):330-7.

200. Miller BT, Abbott AM, Tuttle TM. The influence of preoperative MRI on breast cancer treatment. Ann Surg Oncol. 2012;19(2):536-40.

201. Strauss D, Shabahang MM, Kenny TC, Dove JT, Iqbal N, Hunsinger M, et al. Limited efficacy of preoperative magnetic resonance imaging in breast cancer patients [Abstract]. Ann Surg Oncol. 2015;22(1 Suppl):S67, Abstract P71.

202. McGhan LJ, Wasif N, Gray RJ, Giurescu ME, Pizzitola VJ, Lorans R, et al. Use of preoperative magnetic resonance imaging for invasive lobular cancer: Good, better, but maybe not the best? Ann Surg Oncol. 2010;17(Suppl 3):255-62.

203. Cortesi L, De Matteis E, Cirilli C, Filieri E, Pecchi A, Battista R, et al. MRI before initial surgery outside of clinical trials: The real world! Eur J Radiol. 2012;81(Suppl 1):S21-3.

204. Zhang J. Study on the socioeconomic and clinical factors affecting the proportion of breast conserving surgery in Chinese women breast cancer [Abstract]. Ann Oncol. 2019;30(Suppl 5):v78.

205. Carpenter SG, Stucky CC, Dueck AC, Grimsby G, Giurescu M, Apsey H, et al. Scientific Presentation Award: The impact of magnetic resonance imaging on surgical treatment of invasive breast cancer. Am J Surg. 2009;198(4):475-81.

206. Espino SG, Zeng Z, Roy A, Jiang H, Li X, Luo Y, et al. Breast cancer outcomes following MRI-based selection for mastectomy [Abstract]. Ann Surg Oncol. 2017;24(2 Suppl 1):124.

207. Vapiwala N, Hwang WT, Kushner CJ, Schnall MD, Freedman GM, Solin LJ. No impact of breast magnetic resonance imaging on 15-year outcomes in patients with ductal carcinoma in situ or early-stage invasive breast cancer managed with breast conservation therapy. Cancer. 2017;123(8):1324-32.

208. Solin LJ, Orel SG, Hwang WT, Harris EE, Schnall MD. Relationship of breast magnetic resonance imaging to outcome after breast-conservation treatment with radiation for women with early-stage invasive breast carcinoma or ductal carcinoma in situ. J Clin Oncol. 2008;26(3):386-91.

209. Weinstein SP, Orel SG, Heller R, Reynolds C, Czerniecki B, Solin LJ, et al. MR imaging of the breast in patients with invasive lobular carcinoma. AJR Am J Roentgenol. 2001;176(2):399-406.

210. Nunes LW, Schnall MD, Orel SG, Hochman MG, Langlotz CP, Reynolds CA, et al. Breast MR imaging: Interpretation model. Radiology. 1997;202(3):833-41.

211. Li XS, Song YL, Li DC, Zhu HX, Meng LM, Huang RR, et al. 术前MRI动态增强扫描可降低早期非肿块型乳腺癌保乳术切缘阳性率 [Chinese]. [Preoperative dynamic contrast-enhanced MRI can reduce the rate of tumor-positive resection margins after breast conserving surgery in patients with early non-mass breast carcinoma]. Zhonghua Zhong Liu Za Zhi. 2017;39(10):768-74.

212. So A, De La Cruz LM, Williams AD, Bahng J, Liao G, McDonald ES, et al. The impact of preoperative magnetic resonance imaging and lumpectomy cavity shavings on re-excision rate in pure ductal carcinoma in situ - A single institution's experience. J Surg Oncol. 2018;117(4):558-66.

213. Onega T, Zhu W, Weiss JE, Goodrich M, Tosteson ANA, DeMartini W, et al. Preoperative breast MRI and mortality in older women with breast cancer. Breast Cancer Res Treat. 2018;170(1):149-57.

214. Houssami N, Turner R, Macaskill P, Turnbull LW, McCready DR, Tuttle TM, et al. An individual person data meta-analysis of preoperative magnetic resonance imaging and breast cancer recurrence. J Clin Oncol. 2014;32(5):392-401.

215. Houssami N, Turner RM, Morrow M. Meta-analysis of pre-operative magnetic resonance imaging (MRI) and surgical treatment for breast cancer. Breast Cancer Res Treat. 2017;165(2):273-83.

216. Di Leo G, Trimboli RM, Benedek A, Jereczek-Fossa BA, Fossati P, Leonardi MC, et al. MR imaging for selection of patients for partial breast irradiation: A systematic review and meta-analysis. Radiology. 2015;277(3):716-26.

217. Helme S, Harvey K, Agrawal A. Breast-conserving surgery in patients with Paget's disease. Br J Surg. 2015;102(10):1167-74.

218. Clauser P, Marino MA, Baltzer PA, Bazzocchi M, Zuiani C. Management of atypical lobular hyperplasia, atypical ductal hyperplasia, and lobular carcinoma in situ. Expert Rev Anticancer Ther. 2016;16(3):335-46.

219. Salmanoglu E, Klinger K, Bhimani C, Sevrukov A, Thakur ML. Advanced approaches to imaging primary breast cancer: An update. Clin Transl Imaging. 2019;7(6):381-404.

220. Uhlig J, Uhlig A, Biggemann L, Fischer U, Lotz J, Wienbeck S. Diagnostic accuracy of cone-beam breast computed tomography: A systematic review and diagnostic meta-analysis. Eur Radiol. 2019;29(3):1194-202.

221. Surov A, Meyer HJ, Wienke A. Can apparent diffusion coefficient (ADC) distinguish breast cancer from benign breast findings? A meta-analysis based on 13 847 lesions. BMC Cancer. 2019;19(1):955 (14 pp).

222. Zhang A, Li P, Liu Q, Song S. Breast-specific gamma camera imaging with ^{99m}Tc-MIBI has better diagnostic performance than magnetic resonance imaging in breast cancer patients: A meta-analysis. Hell J Nucl Med. 2017;20(1):26-35.

223. Tan J, Xu L, Yao W, Wan Y, Zhou S, Xin SX. In vivo post-contrast 1H-MRS evaluation of malignant and benign breast lesions: A meta-analysis. Tumour Biol. 2015;36(1):345-52.

224. NICE: National Institute for Health Care Excellence. Early and locally advanced breast cancer: Diagnosis and management. NICE guideline NG101 [Internet]. London (UK): NICE; 2018 Jul 18 [cited 2021 Mar 26]. Available from: www.nice.org.uk/guidance/ng101.

225. Malaysian Health Technology Assessment Section (MaHTAS). Management of breast cancer (third edition). Clinical practice guidelines MOH/P/PAK/432.19(GU)-e [Internet]. Putrajaya (Malaysia): Ministry of Health Malaysia; 2019 [cited 2020 Mar 26]. Available from: https://www.moh.gov.my/moh/resources/Penerbitan/CPG/Kanser/Breast%20Cancer/CPG_Management_of_Breast_Cancer_(Third_Edition)_130720.pdf.

226. National Clinical Effectiveness Committee. An Roinn Slainte Department of Health. Diagnosis, staging and treatment of patients with breast cancer. National Clinical Guideline No. 7 [Internet]. Ireland: An Roinn Slainte Department of Health, 2015 Jun [cited 2021 Mar 26]. Available from: https://www.gov.ie/en/collection/6fb16f-diagnosis-staging-and-treatment-of-patients-with-breast-cancer/#.

227. The Royal College of Radiologists. Guidance on screening and symptomatic breast imaging. Fourth edition. Ref No. BFCR(19)9 [Internet]. London: The Royal College of Radiologists; 2019 [corrected 2019 Nov 29; cited 2021 Mar 26]. Available from:

https://www.rcr.ac.uk/publication/guidance-screening-and-symptomatic-breast-imaging-fourth-edition.

228. AWMF. Interdisziplinäre S3-leitlinie für die früherkennung, diagnostik, therapie und nachsorge des mammakarzinoms, langversion 4.3 – Februar 2020 AWMF-Registernummer: 032-045OL. [German]. [Interdisciplinary S3 guideline for the early detection, diagnosis, therapy and follow-up care of breast cancer, long version 4.3 - February 2020 AWMF registration number: 032-045OL] [Internet]. Duesseldorf (Germany): AWMF online: Das Portal der wissenschaftlichen Medizin; 2020 Feb [cited 2021 Mar 26]. Available from: https://www.awmf.org/leitlinien/detail/ll/032-045OL.html.

229. National Health Commission of The People's Republic of China. Chinese guidelines for diagnosis and treatment of breast cancer 2018 (English version). Chin J Cancer Res. 2019;31(2):259-77.

230. Rea D, Francis A, Hanby AM, Speirs V, Rakha E, Shaaban A, et al. Inflammatory breast cancer: Time to standardise diagnosis assessment and management, and for the joining of forces to facilitate effective research. Br J Cancer. 2015;112(9):1613-5.

231. Senkus E, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rutgers E, et al. Primary breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2015;26:v8-v30.

232. Cardoso F, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rubio IT, et al. Early breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2019;30(8):1194-220.

233. Bevers TB, Helvie M, Bonaccio E, Camp M, Chikarmane S, Conant EF, et al. NCCN clinical practice guidelines in oncology (NCCN guidelines)®. Breast cancer screening and diagnosis. Version 1.2020 [Internet]. Fort Washington (PA): National Comprehensive Cancer Network; 2020 Sept 17 [cited 2021 Feb 2]. Available from: https://www.nccn.org/professionals/physician_gls/default.aspx2020.

234. Gradishar WJ, Moran MS, Abraham J, Aft R, Agnese D, Allison KH, et al. NCCN clinical practice guidelines in oncology (NCCN guidelines)®. Breast cancer [Internet]. Version 1.2021. Fort Washington (PA): National Comprehensive Cancer Network; 2021 Jan 15 [cited 2021 Feb 2]. 240 p. Available from: https://www.nccn.org/professionals/physician_gls/default.aspx2021: Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp#site.

235. Ditsch N, Untch M, Thill M, Muller V, Janni W, Albert US, et al. AGO recommendations for the diagnosis and treatment of patients with early breast cancer: Update 2019. Breast Care. 2019;14(4):224-45.

236. Uematsu T, Nakashima K, Kikuchi M, Kubota K, Suzuki A, Nakano S, et al. The Japanese Breast Cancer Society clinical practice guidelines for breast cancer screening and diagnosis, 2018 Edition. Breast Cancer. 2020;27(1):17-24.

237. Wockel A, Festl J, Stuber T, Brust K, Stangl S, Heuschmann PU, et al. Interdisciplinary screening, diagnosis, therapy and follow-up of breast cancer. Guideline of the DGGG and the DKG (S3-Level, AWMF registry number 032/045OL, December 2017) - Part 1 with recommendations for the screening, diagnosis and therapy of breast cancer. Geburtshilfe Frauenheilkd. 2018;78(10):927-48.

238. American College of Radiology. ACR appropriateness criteria®. Breast imaging of pregnant and lactating women [Internet]. Reston (VA): American College of Radiology; cited 2020 Mar 16. Available from: https://acsearch.acr.org/list.

239. Galimberti V, Taffurelli M, Leonardi MC, Aristei C, Trentin C, Cassano E, et al. Surgical resection margins after breast-conserving surgery: Senonetwork recommendations. Tumori. 2016;2016(3):284-9.

240. Ueno NT, Espinosa Fernandez JR, Cristofanilli M, Overmoyer B, Rea D, Berdichevski F, et al. International consensus on the clinical management of inflammatory breast cancer from the Morgan Welch Inflammatory Breast Cancer Research Program 10th Anniversary Conference. J Cancer. 2018;9(8):1437-47.

241. Expert Panel on Breast Imaging, Lee SJ, Trikha S, Moy L, Baron P, diFlorio RM, et al. ACR appropriateness criteria. Evaluation of nipple discharge. J Am Coll Radiol. 2017;14(5S):S138-S53.

242. Paluch-Shimon S, Pagani O, Partridge AH, Abulkhair O, Cardoso MJ, Dent RA, et al. ESO-ESMO 3rd international consensus guidelines for breast cancer in young women (BCY3). Breast. 2017;35:203-17.

243. Institut national d'excellence en santé et en services sociaux (INESSS). Main indications for breast MRI in the context of investigation and planning of breast cancer treatment [Internet]. Québec (Québec): INESS; 2018 [cited 2021 Mar 26]. Available from: https://www.inesss.qc.ca/fileadmin/doc/INESSS/Rapports/Oncologie/IRM_sein/IRM_Cancer-du-sein_EN_VF.pdf

244. Eastern Health Breast Disease Site Group. Indications for use of breast magnetic resonance imaging [Internet]. St. John's (Nfld): Eastern Health; revised 2017 Aug 31 [cited 2021 Mar 26]. Available from: https://cancercare.easternhealth.ca/health-care-professionals/guidelines/breast-cancer/.

245. Blue Shield of California. 6.01.29 - Magnetic resonance imaging for detection and diagnosis of breast cancer [Internet]. Oakland (CA): Blue Shield of California; 2020 Nov 1 [cited 2021 Feb 9]. Available from: https://www.blueshieldca.com/bsca/bsc/public/common/PortalComponents/provider/StreamDocumentServlet?fileName=PRV_MRI_Breast.pdf.

246. The American Society of Breast Surgeons. Consensus guideline on diagnostic and screening magnetic resonance imaging of the breast [Internet]. Columbia, MD: The American Society of Breast Surgeons; 2017 Jun 22 [created 2018 Jun 21; modified 2019 Feb 18; cited 2020 Mar 19]. Available from: https://www.breastsurgeons.org/docs/statements/Consensus-Guideline-on-Diagnostic-and-Screening-Magnetic-Resonance-Imaging-of-the-Breast.pdf.

247. Appavoo S, Aldis A, Causer P, Crystal P, Kornecki A, Mundt Y, et al. CAR practice guidelines and technical standards for breast imaging and intervention [Internet]. Ottawa: Canadian Association of Radiologists; 2012 Sept 29 [modified 2016 Sept 17; cited 2020 Mar 17]. Available from: https://car.ca/book/breast-imaging-guidelines/.

248. Blue Cross Blue Shield Assocation. 6.01.45 - Computer-aided evaluation as an adjunct to magnetic resonance imaging of the breast [Internet]. Chicago (IL): Blue Cross and Blue Shield Association, Technology Evaluation Center; 2019 Oct [cited 2019 Oct 31]. Available from: https://www.evidencepositioningsystem.com/BCBSA/html/pol_6.01.45.html.

249. Blue Cross Blue Shield Association. 6.01.29 - Magnetic resonance imaging for detection and diagnosis of breast cancer [Internet]. Chicago (IL): Blue Cross and Blue Shield Association, Technology Evaluation Center; 2019 Oct [cited 2019 Oct 31]. Available from: https://www.evidencepositioningsystem.com/BCBSA/html/pol_6.01.29.html.

250. Sardanelli F, Boetes C, Borisch B, Decker T, Federico M, Gilbert FJ, et al. Magnetic resonance imaging of the breast: Recommendations from the EUSOMA working group. Eur J Cancer. 2010;46(8):1296-316.

251. Mann RM, Balleyguier C, Baltzer PA, Bick U, Colin C, Cornford E, et al. Breast MRI: EUSOBI recommendations for women's information. Eur Radiol. 2015;25(12):3669-78.

252. Mann RM, Kuhl CK, Kinkel K, Boetes C. Breast MRI: Guidelines from the European Society of Breast Imaging. Eur Radiol. 2008;18(7):1307-18.

253. Oliva IB, Day K, Dill KE, Hanley M, Ahmed O, Bennett SJ, et al. ACR appropriateness criteria® imaging of deep inferior epigastric arteries for surgical planning (breast reconstruction surgery). J Am Coll Radiol. 2017;14(11 Supplement):S456-S61.

254. American College of Radiology. Complete accreditation information: Breast MRI (Revised 12-12-19) [Internet]. Reston (VA): American College of Radiology; 2019 [revised 2020 Mar 31; cited 2021 Mar 23]. Available from: https://accreditationsupport.acr.org/support/solutions/articles/11000063266-complete-accreditation-information-breast-mri2020.

255. American College of Radiology. ACR appropriateness criteria®: Monitoring response to neoadjuvant systemic therapy for breast cancer [Internet]. Reston (VA): American College of Radiology; 2017 [created 2019 Dec 2; cited 2021 Mar 23]. Available from: https://acsearch.acr.org/list.

256. American College of Radiology Committee on Quality Assurance in Magnetic Resonance Imaging. Magnetic resonance imaging. Quality control manual, 2015 [Internet]. Reston (VA): American College of Radiology; 2016 May 10 [cited 2021 Mar 23]. Available from: https://www.acr.org/-/media/ACR/NOINDEX/QC-Manuals/MR_QCManual.pdf.

257. American College of Radiology Committee on MR Safety. ACR manual on MR safety. Version 1.0, 2020 [Internet]. Reston (VA): American College of Radiology; 2020 May 15

[cited 2021 Mar 23]. Available from: https://www.acr.org/Clinical-Resources/Radiology-Safety/MR-Safety2020.

258. American College of Radiology Committee on Drugs and Contrast Media. ACR manual on contrast media. 2021 [Internet]. Reston (VA): American College of Radiology; 2021 Feb 1 [cited 2021 Aug 13]. Available from: https://www.acr.org/Clinical-Resources/Contrast-Manual2021.

259. American College of Radiology. ACR practice parameter for the performance of magnetic resonance imaging-guided breast interventional procedures. Revised 2016 [Internet]. Reston (VA): American College of Radiology; 2016 [revised 2017 Oct 26; cited 2020 Mar 16]. Available from: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/MR-Guided-Breast.pdf?la=en.

260. American College of Radiology. ACR practice parameter for the performance of contrast-enhanced magnetic resonance imaging (MRI) of the breast. Revised 2018 [Internet]. Reston (VA): American College of Radiology; 2018 July 1[cited 2020 Mar 16]. Available from: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/MR-Contrast-Breast.pdf?la=en.

261. American College of Radiology. ACR BI-RADS atlas. Breast imaging reporting and data system. 5th ed. [Internet]. Reston (VA): American College of Radiology; 2013. Available from: https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Bi-Rads.

262. Amurao MR, Einstein SA, Panda A, Och JG, Pooley RA, Yanasak NE, et al. ACR–AAPM technical standard for diagnostic medical physics performance monitoring of magnetic resonance (MR) imaging equipment. Revised 2019 [Internet]. Reston (VA, USA): Americal College of Radiology; 2019 June 7 [cited 2019 Sep 20]. Available from: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/mr-equip.pdf?la=en.

263. DeMartini WB, Rahbar H. Breast magnetic resonance imaging technique at 1.5 T and 3 T: Requirements for quality imaging and American College of Radiology accreditation. Magn Reson Imaging Clin N Am. 2013;21(3):475-82.

264. Edwards SD, Lipson JA, Ikeda DM, Lee JM. Updates and revisions to the BI-RADS magnetic resonance imaging lexicon. Magn Reson Imaging Clin N Am. 2013;21(3):483-93.

265. Bick U, Trimboli RM, Athanasiou A, Balleyguier C, Baltzer PAT, Bernathova M, et al. Image-guided breast biopsy and localisation: Recommendations for information to women and referring physicians by the European Society of Breast Imaging. Insights Imaging. 2020;11(1):12 (8 pp).

266. Baltzer P, Mann RM, Iima M, Sigmund EE, Clauser P, Gilbert FJ, et al. Diffusion-weighted imaging of the breast-a consensus and mission statement from the EUSOBI International Breast Diffusion-Weighted Imaging working group. Eur Radiol. 2020;30(3):1436-50.

267. Heywang-Kobrunner SH, Sinnatamby R, Lebeau A, Lebrecht A, Britton PD, Schreer I, et al. Interdisciplinary consensus on the uses and technique of MR-guided vacuum-assisted

breast biopsy (VAB): Results of a European consensus meeting. Eur J Radiol. 2009;72(2):289-94.

268. Breast Imaging Working Group of the German Radiological Society. Updated recommendations for MRI of the breast. Rofo. 2014;186(5):482-3.

269. DeMartini WB, Ichikawa L, Yankaskas BC, Buist D, Kerlikowske K, Geller B, et al. Breast MRI in community practice: Equipment and imaging techniques at facilities in the Breast Cancer Surveillance Consortium. J Am Coll Radiol. 2010;7(11):878-84.

270. Rakow-Penner R, Murphy PM, Dale A, Ojeda-Fournier H. State of the art diffusion weighted imaging in the breast: Recommended protocol. Curr Radiol Rep. 2017;5(3):https://doi.org/10.1007/s40134-017-0195-y.

271. Sardanelli F, Carbonaro LA, Montemezzi S, Cavedon C, Trimboli RM. Clinical breast MR Using MRS or DWI: Who is the winner. Front Oncol. 2016;6(Oct):217 (8 pp).

272. Marshall HN, Plecha DM. Setting up an abbreviated breast MRI program: Our two-year implementation experience. J Breast Imaging. 2020;2(6):603-8.

273. Scoggins ME, Arun BK, Candelaria RP, Dryden MJ, Wei W, Son JB, et al. Should abbreviated breast MRI be compliant with American College of Radiology requirements for MRI accreditation? Magn Reson Imaging. 2020;72:87-94.

274. Mann RM, Mus RD, van Zelst J, Geppert C, Karssemeijer N, Platel B. A novel approach to contrast-enhanced breast magnetic resonance imaging for screening: High-resolution ultrafast dynamic imaging. Invest Radiol. 2014;49(9):579-85.

275. Belkić D, Belkić K. Review of recent applications of the conventional and derivative fast Padé transform for magnetic resonance spectroscopy. J Math Chem. 2019;57(2):385-464.

276. Marino MA, Helbich T, Baltzer P, Pinker-Domenig K. Multiparametric MRI of the breast: A review. J Magn Reson Imaging. 2018;47(2):301-15.

277. Lee SH, Jang MJ, Kim SM, Yun BL, Rim J, Chang JM, et al. Factors affecting breast cancer detectability on digital breast tomosynthesis and two-dimensional digital mammography in patients with dense breasts. Korean J Radiol. 2019;20(1):58-68.

278. Conant EF, Barlow WE, Herschorn SD, Weaver DL, Beaber EF, Tosteson ANA, et al. Association of digital breast tomosynthesis vs digital mammography with cancer detection and recall rates by age and breast density. JAMA Oncol. 2019;5(5):635-42.

279. Aase HS, Holen AS, Pedersen K, Houssami N, Haldorsen IS, Sebuodegard S, et al. A randomized controlled trial of digital breast tomosynthesis versus digital mammography in population-based screening in Bergen: Interim analysis of performance indicators from the To-Be trial. Eur Radiol. 2019;29(3):1175-86.

280. Hofvind S, Holen ÅS, Aase HS, Houssami N, Sebuødegård S, Moger TA, et al. Two-view digital breast tomosynthesis versus digital mammography in a population-based breast

cancer screening programme (To-Be): A randomised, controlled trial. Lancet Oncol. 2019;20(6):795-805.

281. Nam KJ, Han BK, Ko ES, Choi JS, Ko EY, Jeong DW, et al. Comparison of full-field digital mammography and digital breast tomosynthesis in ultrasonography-detected breast cancers. Breast. 2015;24(5):649-55.

282. Roganovic D, Djilas D, Vujnovic S, Pavic D, Stojanov D. Breast MRI, digital mammography and breast tomosynthesis: Comparison of three methods for early detection of breast cancer. Bosn J Basic Med Sci. 2015;15(4):64-8.

283. Lee AY, Nguyen VT, Arasu VA, Greenwood HI, Ray KM, Joe BN, et al. Sonographic-MRI correlation after percutaneous sampling of targeted breast ultrasound lesions: Initial experiences with limited-sequence unenhanced MRI for postprocedural clip localization. AJR Am J Roentgenol. 2018;210(4):927-34.

284. Sanchez-Jurado R, Ferrer Rebolleda J, Cozar Santiago M, Sanz Llorens R, Aguilar Barrios J, Blanco Perez E, et al. Prone versus supine breast F18-FDG PET acquisition in breast cancer [Abstract]. Eur J Nucl Med Mol Imaging. 2015;42(Suppl 1):S852.

285. Dominguez I, Herranz M, Teo SY, Brozos E, Rodriguez C, Chaal J, et al. Improving specificity and refining diagnostic accuracy of MRI in breast cancer with dedicated breast PET (dbPET) [Abstract]. Cancer Res. 2015;75(9 Suppl 1):Abstract P5-01-9.

286. Pinker-Domenig K, Bickel H, Bogner W, Gruber S, Magometschnigg HF, Bruck B, et al. Molecular imaging of breast tumor with PET-MRI at 3T obviates unnecessary breast biopsies [Abstract]. Mol Imaging Biol. 2012;14(2 Suppl 1):S2090.

287. Katja PD, Bickel H, Bogner W, Magometschnigg H, Gruber S, Dubsky PC, et al. Hybrid PET-MRI of the breast: A promising tool for the characterization of breast tumors [Abstract]. J Clin Oncol. 2012;30(15 Suppl 1):Abstract 10570.

288. Pujara AC, Kim E, Axelrod D, Melsaether AN. PET/MRI in breast cancer. J Magn Reson Imaging. 2019;49(2):328-42.

289. Fowler AM. Molecular imaging approaches for supplemental screening in women at increased breast cancer risk. J Nucl Med. 2016;57(5):661-2.

290. Ranzenberger LR, Booth KA. Mammoscintigraphy. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan [updated 2021 Jun 15; cited 2021 Aug 11]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559284/.

291. Adrada BE, Moseley T, Rauch GM. Molecular breast imaging: Role as a screening modality. Curr Breast Cancer Rep. 2016;8(4):230-5.

292. Brem RF, Ruda RC, Yang JL, Coffey CM, Rapelyea JA. Breast-specific gamma-imaging for the detection of mammographically occult breast cancer in women at increased risk. J Nucl Med. 2016;57(5):678-84.

293. Brem RF, Mehta AK, Rapelyea JA, Akin EA, Bazoberry AM, Velasco CD. Gamma imaging-guided minimally invasive breast biopsy: Initial clinical experience. AJR Am J Roentgenol. 2018;210(3):695-9.

294. Granata V, Cascella M, Fusco R, Dell'Aprovitola N, Catalano O, Filice S, et al. Immediate adverse reactions to gadolinium-based MR contrast media: A retrospective analysis on 10,608 examinations. Biomed Res Int. 2016;2016:3918292 (6 pp).

295. Mitsumori LM, Bhargava P, Essig M, Maki JH. Magnetic resonance imaging using gadolinium-based contrast agents. Top Magn Reson Imaging. 2014;23(1):51-69.

296. Elster AD. Questions and answers in MRI. Extracellular Gd agents [Internet]. St. Louis (MO): MRIquestions.com; 2019 [modified 2020 Feb 25; cited 2020 Mar 30]. Available from: http://mriquestions.com/so-many-gd-agents.html.

297. Pediconi F, Catalano C, Padula S, Roselli A, Dominelli V, Cagioli S, et al. Contrast-enhanced MR mammography: Improved lesion detection and differentiation with gadobenate dimeglumine. AJR Am J Roentgenol. 2008;191(5):1339-46.

298. Yang X, Liu G, Yu X, Zhang Q, Zhang W, Guo Y. [Controlled study of gadobenate dimeglumine versus gadopentetate in breast tumor MR dynamic enhancement scanning] [Chinese]. Zhonghua Yi Xue Za Zhi. 2015;95(25):2003-5.

299. Gilbert FJ, van den Bosch HC, Petrillo A, Siegmann K, Heverhagen JT, Panizza P, et al. Comparison of gadobenate dimeglumine-enhanced breast MRI and gadopentetate dimeglumine-enhanced breast MRI with mammography and ultrasound for the detection of breast cancer. J Magn Reson Imaging. 2014;39(5):1272-86.

300. Martincich L, Faivre-Pierret M, Zechmann CM, Corcione S, van den Bosch HC, Peng WJ, et al. Multicenter, double-blind, randomized, intraindividual crossover comparison of gadobenate dimeglumine and gadopentetate dimeglumine for Breast MR imaging (DETECT Trial). Radiology. 2011;258(2):396-408.

301. Zechmann C, Martincich L, Faivre-Pierret M, Corcione S, Van Den Bosch H, Gilbert F, et al. Does breast parenchyma density affect the detection of malignant lesions on gadobenate dimeglumine-enhanced MRI compared to gadopentetate dimeglumine-enhanced MRI, mammography, and ultrasound? [Abstract]. AJR Am J Roentgenol. 2012;198(5 Suppl 24):Abstract 198.

302. Clauser P, Helbich TH, Kapetas P, Pinker K, Bernathova M, Woitek R, et al. Breast lesion detection and characterization with contrast-enhanced magnetic resonance imaging: Prospective randomized intraindividual comparison of gadoterate meglumine (0.15 mmol/kg) and gadobenate dimeglumine (0.075 mmol/kg) at 3T. J Magn Reson Imaging. 2019;49(4):1157-65.

303. Pediconi F, Kubik-Huch R, Chilla B, Schwenke C, Kinkel K. Intra-individual randomised comparison of gadobutrol 1.0 M versus gadobenate dimeglumine 0.5 M in patients scheduled for preoperative breast MRI [Erratum in 23(8): 2100]. Eur Radiol. 2013;23(1):84-92.

304. Komura Y, Mogi T, Shimizu F, Yatabe K, Nedate J, Kanazawa H, et al. [Comparison of time-intensity curve with gadobenatedimeglumine and gadobutrol on multiphase contrast-enhanced breast MRI] [Japanese]. Nippon Hoshasen Gijutsu Gakkai Zasshi. 2018;74(4):368-74.

305. Fallenberg EM, Renz DM, Karle B, Schwenke C, Ingod-Heppner B, Reles A, et al. Intraindividual, randomized comparison of the macrocyclic contrast agents gadobutrol and gadoterate meglumine in breast magnetic resonance imaging. Eur Radiol. 2015;25(3):837-49.

306. Sardanelli F, Newstead GM, Putz B, Jirakova Trnkova Z, Trimboli RM, Abe H, et al. Gadobutrol-enhanced magnetic resonance imaging of the breast in the preoperative setting: Results of 2 prospective international multicenter phase III studies. Invest Radiol. 2016;51(7):454-61.

307. Seithe T, Braun J, Wolf M, Vahldiek J, Wolny D, Auer J, et al. Diagnostic efficacy and safety of gadoteric acid MR mammography in 1537 patients. Eur J Radiol. 2016;85(12):2281-7.

308. Rodriguez Nava G, Kesler A, Carrillo Martin I, Gonzalez-Estrada A. Gadolinium-induced anaphylaxis: Not all contrast agents are created equal [Abstract]. Ann Allergy Asthma Immunol. 2018;121(5 Suppl):S70-S1.

309. Rodriguez-Nava G, Kesler AM, Carrillo-Martin I, Gonzalez-Estrada A. Gadolinium-induced anaphylaxis with positive skin test results. Ann Allergy Asthma Immunol. 2019;122(6):654-5.

310. Schieda N, Maralani PJ, Hurrell C, Tsampalieros AK, Hiremath S. Updated clinical practice guideline on use of gadolinium-based contrast agents in kidney disease issued by the Canadian Association of Radiologists. Can Assoc Radiol J. 2019;70(3):226-32.

311. European Medicines Agency. EMA's final opinion confirms restrictions on use of linear gadolinium agents in body scans. EMA/625317/2017 [Internet]. Amsterdam: European Medicines Agency; 2017 Nov 23 [cited 2021 Aug 9]. Available from: https://www.ema.europa.eu/documents/referral/gadolinium-article-31-referral-emas-final-opinion-confirms-restrictions-use-linear-gadolinium-agents_en.pdf.

312. Siegler P, Ebrahimi M, Holloway CM, Thevathasan G, Plewes DB, Martel A. Supine breast MRI and assessment of future clinical applications. Eur J Radiol. 2012;81(Suppl 1):S153-5.

313. Joukainen S, Masarwah A, Kononen M, Husso M, Sutela A, Karja V, et al. Feasibility of mapping breast cancer with supine breast MRI in patients scheduled for oncoplastic surgery. Eur Radiol. 2019;29(3):1435-43.

314. Aribal E, Buğdaycı O. Supplementary abbreviated supine breast MRI following a standard prone breast MRI with single contrast administration: Is it effective in detecting the initial contrast-enhancing lesions? Diagn Interv Radiol. 2019;25:265-9.

315. Sakakibara M, Yokomizo J, Shiina N, Kazama T, Nakamura R, Fujimoto H, et al. MRI-guided quadrantectomy in patients with ductal carcinoma in situ detected preoperatively by mammographic calcifications. J Am Coll Surg. 2014;219(2):295-302.

316. Mallory MA, Sagara Y, Aydogan F, DeSantis S, Jayender J, Caragacianu D, et al. Feasibility of intraoperative breast MRI and the role of prone versus supine positioning in surgical planning for breast-conserving surgery. Breast J. 2017;23(6):713-7.

317. Gombos EC, Jayender J, Richman DM, Caragacianu DL, Mallory MA, Jolesz FA, et al. Intraoperative supine breast mr imaging to quantify tumor deformation and detection of residual breast cancer: Preliminary results. Radiology. 2016;281(3):720-9.

318. Barth RJ, Jr., Krishnaswamy V, Paulsen KD, Rooney TB, Wells WA, Angeles CV, et al. A randomized prospective trial of supine MRI-guided versus wire-localized lumpectomy for breast cancer. Ann Surg Oncol. 2019;26(10):3099-108.

319. Ko B, Lee SB, Lee JW, Kim HJ, Kim SB, Kim HH, et al. Fabrication and application of supine MRI-based 3D brest surgical guide for precise breast conserving surgery in breast cancer patients [Abstract]. J Clin Oncol. 2018;36(15 Suppl 1):Abstract e12612.

320. Ko B, Kim N, Seo J, Kim H, Gong G, Kim S, et al. Application of supine MRI-based 3D printing breast surgical guide for precision breast-conserving surgery [Abstract]. Cancer Res. 2018;79(4 Suppl 1).

321. Barth RJ, Jr., Krishnaswamy V, Paulsen KD, Rooney TB, Wells WA, Rizzo E, et al. A patient-specific 3D-printed form accurately transfers supine MRI-derived tumor localization information to guide breast-conserving surgery. Ann Surg Oncol. 2017;24(10):2950-6.

322. Byrd BK, Krishnaswamy V, Gui J, Rooney T, Zuurbier R, Rosenkranz K, et al. The shape of breast cancer. Breast Cancer Res Treat. 2020;183(2):403-10.

323. Boyd NF, Byng JW, Jong RA, Fishell EK, Little LE, Miller AB, et al. Quantitative classification of mammographic densities and breast cancer risk: Results from the Canadian National Breast Screening Study. J Natl Cancer Inst. 1995;87(9):670-5.

324. McCormack VA, dos Santos Silva I. Breast density and parenchymal patterns as markers of breast cancer risk: A meta-analysis. Cancer Epidemiol Biomarkers Prev. 2006;15(6):1159-69.

325. Sprague BL, Gangnon RE, Burt V, Trentham-Dietz A, Hampton JM, Wellman RD, et al. Prevalence of mammographically dense breasts in the United States. J Natl Cancer Inst. 2014;106(10):dju255 (6 pp).

326. Kerlikowske K, Zhu W, Tosteson AN, Sprague BL, Tice JA, Lehman CD, et al. Identifying women with dense breasts at high risk for interval cancer: A cohort study. Ann Intern Med. 2015;162(10):673-81.

327. Seely JM, Lamb L, Malik N, Lau J. The yield of pre-operative breast MRI in patients according to breast tissue density. Eur Radiol. 2016;26(9):3280-9.

328. Bishop J, Bassin L, Hall KC, Harris L, Mitchell S. Imaging modalities in screening of dense breasts: Is mammogram alone good enough? [Abstract]. Ann Surg Oncol. 2012;19(2 Suppl 1):27.

329. Vashi R, Butler R, Chen C, Philpotts L. Role of 3-T MRI in the evaluation of newly diagnosed breast cancer: Utility as a function of breast density [Abstract]. AJR Am J Roentgenol. 2012;198(5 Suppl 24):Abstract 199.

330. Stomper PC, D'Souza DJ, DiNitto PA, Arredondo MA. Analysis of parenchymal density on mammograms in 1353 women 25-79 years old. AJR Am J Roentgenol. 1996;167(5):1261-5.

331. Bakker MF, de Lange SV, Pijnappel RM, Mann RM, Peeters PHM, Monninkhof EM, et al. Supplemental MRI screening for women with extremely dense breast tissue. N Engl J Med. 2019;381(22):2091-102.

332. Klinkenbijl JHG, van Leeuwen E, Verkooijen HM. Wat zeggen de uitkomsten van de DENSE-studie? [Dutch]. [What do the results of the DENSE-trial tell?] [Commentary]. Ned Tijdschr Geneeskd. 2020;164(04):D4822.

333. Franz HBG. Profitieren frauen mit extrem dichtem brustgewebe von zusatzlicher MRT? [German]. [Do women with extremely dense breast tissue benefit from supplemental MRI?]. Geburtshilfe Frauenheilkd. 2020;80(5):460-2.

334. Barkhausen J, Bischof A, Haverstock D, Klemens M, Brueggenwerth G, Weber O, et al. Diagnostic efficacy of contrast-enhanced breast MRI versus X-ray mammography in women with different degrees of breast density. Acta Radiol. 2021;62(5):586-93.

335. Elmi A, Conant EF, Kozlov A, Young AJ, Long Q, Doot RK, et al. Preoperative breast MR imaging in newly diagnosed breast cancer: Comparison of outcomes based on mammographic modality, breast density and breast parenchymal enhancement. Clin Imaging. 2020;70:18-24.

336. Liao GJ, Henze Bancroft LC, Strigel RM, Chitalia RD, Kontos D, Moy L, et al. Background parenchymal enhancement on breast MRI: A comprehensive review. J Magn Reson Imaging. 2020;51(1):43-61.

337. Rella R, Bufi E, Belli P, Contegiacomo A, Giuliani M, Rosignuolo M, et al. Background parenchymal enhancement in breast magnetic resonance imaging: A review of current evidences and future trends. Diagn Interv Imaging. 2018;99(12):815-26.

338. Giess CS, Yeh ED, Raza S, Birdwell RL. Background parenchymal enhancement at breast MR imaging: Normal patterns, diagnostic challenges, and potential for false-positive and false-negative interpretation. Radiographics. 2014;34(1):234-47.

339. Al Rashidi N, Waiter G, Redpath T, Gilbert FJ. Assessment of the apparent diffusion coefficient (ADC) of normal breast tissue during the menstrual cycle at 3T using image segmentation. Eur J Radiol. 2012;81(Suppl 1):S1-3.

340. Kim JY, Suh HB, Kang HJ, Shin JK, Choo KS, Nam KJ, et al. Apparent diffusion coefficient of breast cancer and normal fibroglandular tissue in diffusion-weighted imaging: The effects of menstrual cycle and menopausal status. Breast Cancer Res Treat. 2016;157(1):31-40.

341. Partridge SC, McKinnon GC, Henry RG, Hylton NM. Menstrual cycle variation of apparent diffusion coefficients measured in the normal breast using MRI. J Magn Reson Imaging. 2001;14(4):433-8.

342. O'Flynn EA, Morgan VA, Giles SL, deSouza NM. Diffusion weighted imaging of the normal breast: Reproducibility of apparent diffusion coefficient measurements and variation with menstrual cycle and menopausal status. Eur Radiol. 2012;22(7):1512-8.

343. Shin S, Ko ES, Kim RB, Han BK, Nam SJ, Shin JH, et al. Effect of menstrual cycle and menopausal status on apparent diffusion coefficient values and detectability of invasive ductal carcinoma on diffusion-weighted MRI. Breast Cancer Res Treat. 2015;149(3):751-9.

344. Riedl CC, Luft N, Bernhart C, Weber M, Bernathova M, Tea MK, et al. Triple-modality screening trial for familial breast cancer underlines the importance of magnetic resonance imaging and questions the role of mammography and ultrasound regardless of patient mutation status, age, and breast density. J Clin Oncol. 2015;33(10):1128-35.

345. Warner E, Messersmith H, Causer P, Eisen A, Shumak R, Plewes D. Magnetic resonance imaging screening of women at high risk for breast cancer, version 3 [Internet]. Toronto (ON): Cancer Care Ontario; 2007; endorsed with data supplement 2012 Aug 3 and 2018 Jan 19 (Warner E, Agbassi C, reviewers); designated as requiring updating 2021 Jan. Program in Evidence-based Care Evidence-based Guideline No.: 15-11 Version 3. [last modified 2021 Mar 3; cited 2021 Oct 26]. Available from: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/2051.

346. Cetin Avci N, Hatipoglu F, Alacacioglu A, Bayar EE, Bural GG. FDG PET/CT and conventional imaging methods in cancer of unknown primary: An approach to overscanning. Nucl Med Mol Imaging (2010). 2018;52(6):438-44.

347. Makris A. Management and follow-up of patients presenting with breast cancer in axillary lymph nodes and occult breast primary [Abstract]. Breast Cancer Res Treat. 2018;167(1):318.

348. Foroudi F, Tiver KW. Occult breast carcinoma presenting as axillary metastases. Int J Radiat Oncol Biol Phys. 2000;47(1):143-7.

349. De Maat M, Bretveld R, Steevens J, Vissers Y, Hulsewe K. Treatment of the breast in occult breast cancer: Results of a prospective Dutch national cohort study with 5 years follow up [Abstract]. Cancer Res. 2016;76(4 Suppl 1):Abstract P2-12-07.

350. Goodman S, Mango V, Friedlander L, Desperito E, Wynn R, Ha R. Are mammographically occult additional tumors identified more than 2 cm away from the primary breast cancer on MRI clinically significant? Acad Radiol. 2019;26(4):502-7.

351. Iacconi C, Galman L, Zheng J, Sacchini V, Sutton EJ, Dershaw D, et al. Multicentric cancer detected at breast MR imaging and not at mammography: Important or not? Radiology. 2016;279(2):378-84.

352. Brennan ME, Houssami N, Lord S, Macaskill P, Irwig L, Dixon JM, et al. Magnetic resonance imaging screening of the contralateral breast in women with newly diagnosed breast cancer: Systematic review and meta-analysis of incremental cancer detection and impact on surgical management. J Clin Oncol. 2009;27(33):5640-9.

353. Berg WA, Madsen KS, Schilling K, Tartar M, Pisano ED, Larsen LH, et al. Comparative effectiveness of positron emission mammography and MRI in the contralateral breast of women with newly diagnosed breast cancer. AJR Am J Roentgenol. 2012;198(1):219-32.

354. Bernard Jr JR, Vallow LA, DePeri ER, McNeil RB, Feigel DG, Amar S, et al. In newly diagnosed breast cancer, screening MRI of the contralateral breast detects mammographically occult cancer, even in elderly women: The Mayo Clinic in Florida experience. Breast J. 2010;16(2):118-26.

355. Lehman CD, Blume JD, Thickman D, Bluemke DA, Pisano E, Kuhl C, et al. Added cancer yield of MRI in screening the contralateral breast of women recently diagnosed with breast cancer: Results from the International Breast Magnetic Resonance Consortium (IBMC) trial. J Surg Oncol. 2005;92(1):9-15; discussion -6.

356. Rahbar H, Hanna LG, Gatsonis C, Mahoney MC, Schnall MD, DeMartini WB, et al. Contralateral prophylactic mastectomy in the American College of Radiology Imaging Network 6667 trial: Effect of breast MR imaging assessments and patient characteristics. Radiology. 2014;273(1):53-60.

357. DeMartini WB, Hanna L, Gatsonis C, Mahoney MC, Lehman CD. Evaluation of tissue sampling methods used for MRI-detected contralateral breast lesions in the American College of Radiology Imaging Network 6667 trial. AJR Am J Roentgenol. 2012;199(3):W386-91.

358. Weinstein SP, Hanna LG, Gatsonis C, Schnall MD, Rosen MA, Lehman CD. Frequency of malignancy seen in probably benign lesions at contrast-enhanced breast MR imaging: Findings from ACRIN 6667. Radiology. 2010;255(3):731-7.

359. Lehman CD, Gatsonis C, Kuhl CK, Hendrick RE, Pisano ED, Hanna L, et al. MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. N Engl J Med. 2007;356(13):1295-303.

360. Lee SG, Orel SG, Woo IJ, Cruz-Jove E, Putt ME, Solin LJ, et al. MR imaging screening of the contralateral breast in patients with newly diagnosed breast cancer: Preliminary results. Radiology. 2003;226(3):773-8.

361. Lai HW, Hung WY, Lee CW, Wu HK, Chen ST, Chen DR, et al. Contralateral breast lesions detected by breast MRI study - An analysis of 735 Taiwanese women with primary operable breast cancer. Formos J Surg. 2017;50(5):175-80.

362. Bernard Jr JR, Vallow LA, McNeil RB, McLaughlin SA, Geiger XJ, Perez EA. In newly diagnosed breast cancer, is a contralateral prophylactic mastectomy necessary following a negative MRI? [Abstract]. J Clin Oncol. 2009;27(15 Suppl):627.

363. Pietrosanu R, Shah MA, Gay H, Heller S, Reddy M. Contrast-enhanced MRI in evaluating the contralateral breast for synchronous malignancy in patients with invasive lobular cancer [Abstract]. Breast Cancer Res. 2012;14(Suppl 1):P29.

364. Postma E, El Sharouni M, Van Den Bosch MA, Witkamp AJ, Verkooijen HM, Van Diest PJ. High prevalence of additional contralateral and ipsilateral malignant findings by MRI in patients with invasive (ducto)lobular breast cancers [Abstract]. Eur J Cancer. 2013;49(Suppl 2):S436-S7.

365. Begg CB, Ostrovnaya I, Geyer FC, Papanastasiou AD, Ng CKY, Sakr RA, et al. Contralateral breast cancers: Independent cancers or metastases? Int J Cancer. 2018;142(2):347-56.

366. Aalders KC, van Bommel ACM, van Dalen T, Sonke GS, van Diest PJ, Boersma LJ, et al. Contemporary risks of local and regional recurrence and contralateral breast cancer in patients treated for primary breast cancer. Eur J Cancer. 2016;63:118-26.

367. Sanders LM, El-Madany M, Persing A, Mehta A. Use of contrast-enhanced MRI in management of discordant core biopsy results. AJR Am J Roentgenol. 2019;212(5):1157-65.

368. Sasaki J, Kowzun M, Teng B, Potdevin L, Eladoumikdachi F, Kumar S. The utility of interval MRI after benign and concordant MRI-guided breast biopsy [Abstract]. Ann Surg Oncol. 2018;25(2 Suppl 1):281.

369. Lewin AA, Heller SL, Jaglan S, Elias K, Newburg A, Melsaether A, et al. Radiologic-pathologic discordance and outcome after MRI-guided vacuum-assisted biopsy. AJR Am J Roentgenol. 2017;208(1):W17-W22.

370. Li J, Dershaw DD, Lee CH, Kaplan J, Morris EA. MRI follow-up after concordant, histologically benign diagnosis of breast lesions sampled by MRI-guided biopsy. AJR Am J Roentgenol. 2009;193(3):850-5.

371. Bahrs SD, Hattermann V, Preibsch H, Hahn M, Staebler A, Claussen CD, et al. MR imaging-guided vacuum-assisted breast biopsy: Reduction of false-negative biopsies by short-term control MRI 24-48 h after biopsy. Clin Radiol. 2014;69(7):695-702.

372. Orecchia R. MRI for treatment planning: A necessity. Eur J Radiol. 2012;81 Suppl 1:S110-1.

373. Al-Hallaq HA, Mell LK, Bradley JA, Chen LF, Ali AN, Weichselbaum RR, et al. Magnetic resonance imaging identifies multifocal and multicentric disease in breast cancer patients who are eligible for partial breast irradiation. Cancer. 2008;113(9):2408-14.

374. Dorn PL, Al-Hallaq HA, Haq F, Goldberg M, Abe H, Hasan Y, et al. A prospective study of the utility of magnetic resonance imaging in determining candidacy for partial breast irradiation. Int J Radiat Oncol Biol Phys. 2013;85(3):615-22.

375. Godinez J, Gombos EC, Chikarmane SA, Griffin GK, Birdwell RL. Breast MRI in the evaluation of eligibility for accelerated partial breast irradiation. AJR Am J Roentgenol. 2008;191(1):272-7.

376. Horst KC, Fero KE, Ikeda DM, Daniel BL, Dirbas FM. Defining an optimal role for breast magnetic resonance imaging when evaluating patients otherwise eligible for accelerated partial breast irradiation. Radiother Oncol. 2013;108(2):220-5.

377. Tendulkar RD, Chellman-Jeffers M, Rybicki LA, Rim A, Kotwal A, Macklis R, et al. Preoperative breast magnetic resonance imaging in early breast cancer: Implications for partial breast irradiation. Cancer. 2009;115(8):1621-30.

378. Kowalchik KV, Vallow LA, McDonough M, Thomas CS, Heckman MG, Peterson JL, et al. Classification system for identifying women at risk for altered partial breast irradiation recommendations after breast magnetic resonance imaging. Int J Radiat Oncol Biol Phys. 2013;87(1):127-33.

379. Kowalchik KV, Vallow LA, McDonough M, Thomas CS, Heckman MG, Peterson JL, et al. The role of preoperative bilateral breast magnetic resonance imaging in patient selection for partial breast irradiation in ductal carcinoma in situ. Int J Surg Oncol. 2012;2012:206342 (6 pp).

380. Zhou P, Wei Y, Chen G, Guo L, Yan D, Wang Y. Axillary lymph node metastasis detection by magnetic resonance imaging in patients with breast cancer: A meta-analysis. Thorac Cancer. 2018;9(8):989-96.

381. Liang L, Ma LB, Wang LL, Xin WL, Zhu DM, Tian XX, et al. [MRI for assessment of axillary lymph node status in breast cancer: A meta analysis] [Chinese]. Chin J Med Imaging Technol. 2015;31(11):1701-6.

382. Liu HF, Liu YJ, Xu YS, Gao YL, Tian SS, Tian JH, et al. [Diagnostic value of diffusion weighted imaging sequence for assessing lymph node metastases in breast cancer: A meta-analysis] [Chinese]. Chin J Evid-Based Med. 2016;16(11):1276-83.

383. Xing H, Song CL, Li WJ. Meta analysis of lymph node metastasis of breast cancer patients: Clinical value of DWI and ADC value. Eur J Radiol. 2016;85(6):1132-7.

384. Sui WF, Chen X, Peng ZK, Ye J, Wu JT. The diagnosis of metastatic axillary lymph nodes of breast cancer by diffusion weighted imaging: A meta-analysis and systematic review. World J Surg Oncol. 2016;14:155 (11 pp).

385. Derwa S, Van Houtven L, Van Goethem M, Van Hal G, Tjalma WAA. The value of MRI in the detection of axillary lymph node metastases in breast cancer: A systematic review. Eur J Gynaecol Oncol. 2019;40(2):193-7.

386. Liang X, Yu J, Wen B, Xie J, Cai Q, Yang Q. MRI and FDG-PET/CT based assessment of axillary lymph node metastasis in early breast cancer: A meta-analysis. Clin Radiol. 2017;72(4):295-301.

387. Zhang R, Liu HF, Hu SS, Pei CX, Ma WT, Li JK, et al. [Diagnostic value of MRI combined with ultrasound for lymph node in breast cancer: A meta-analysis] [Chinese]. Chin J Evid-Based Med. 2016;16(12):1374-80.

388. Guvenc I, Whitman GJ, Liu P, Yalniz C, Ma J, Dogan BE. Diffusion-weighted MR imaging increases diagnostic accuracy of breast MR imaging for predicting axillary metastases in breast cancer patients. Breast J. 2019;25(1):47-55.

389. Kuijs VJ, Moossdorff M, Schipper RJ, Beets-Tan RG, Heuts EM, Keymeulen KB, et al. The role of MRI in axillary lymph node imaging in breast cancer patients: A systematic review. Insights Imaging. 2015;6(2):203-15.

390. Kuckelman J, Barron M, Bingham J, Mosier A, Sohn V. Pre-operative MRI exhibits limited utility in axillary staging for breast cancer. Cancer Treat Res Commun. 2017;12:49-52.

391. Motomura K, Hashizume S, Tabuchi Y, Koda M, Kawamoto S. SPIO 造影 MRI による正確なリンパ節転移診断 —センチネルリンパ節生検時代が終わる— [Japanese]. [Accurate diagnosis of lymph node metastasis by SPIO-enhanced MRI - The end of sentinel lymph node biopsy era]. Japan Society of Clinical Oncology. Abstract SY3-5. Cited 2020 Mar 11. Available from: http://archive.jsco.or.jp/detail.php?sess_id=14005.

392. Motomura K, Izumi T, Tateishi S, Tamaki Y, Ito Y, Horinouchi T, et al. Superparamagnetic iron oxide-enhanced MRI at 3 T for accurate axillary staging in breast cancer. Br J Surg. 2016;103(1):60-9.

393. Motomura K. Study of avoiding axillary surgery in patients with breast cancer by accurate diagnosis of sentinel node metastases using CT and MRI. Ongoing trial: JPRN-UMIN000027829 [Internet]; 2017 [cited 2020 Mar 11]. Protocol available at: http://apps.who.int/trialsearch/Trial2.aspx?TrialID=JPRN-UMIN000027829 and https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000031885. 2017.

394. Memarsadeghi M, Riedl CC, Kaneider A, Galid A, Rudas M, Matzek W, et al. Axillary lymph node metastases in patients with breast carcinomas: Assessment with nonenhanced versus USPIO-enhanced MR imaging. Radiology. 2006;241(2):367-77.

395. Karakatsanis A, Hersi AF, Abdsaleh S, Olofsson H, Pistiolis I, Esserman L, et al. Superparamagnetic iron oxide nanoparticles (SPIO): A sentinel node (SN) tracer with novel applications [Abstract]. Ann Surg Oncol. 2019;26(Suppl 1):S76.

396. Cheon H, Kim HJ, Lee SW, Kim DH, Lee CH, Cho SH, et al. Internal mammary node adenopathy on breast MRI and PET/CT for initial staging in patients with operable breast cancer: Prevalence and associated factors. Breast Cancer Res Treat. 2016;160(3):523-30.

397. Sachdev S, Goodman CR, Neuschler E, Kalakota K, Cutright D, Donnelly ED, et al. Radiotherapy of MRI-detected involved internal mammary lymph nodes in breast cancer. Radiat Oncol. 2017;12(1):199 (7 pp).

398. Lee HW, Kim SH. Breast magnetic resonance imaging for assessment of internal mammary lymph node status in breast cancer. J Breast Cancer. 2016;19(2):191-8.

399. van Heijst TCF, Eschbach-Zandbergen D, Hoekstra N, van Asselen B, Lagendijk JJW, Verkooijen HM, et al. Supine MRI for regional breast radiotherapy: Imaging axillary lymph nodes before and after sentinel-node biopsy. Phys Med Biol. 2017;62(16):6746-61.

400. Van Heijst T, Van Den Bongard HJGD, Hoekstra N, Philippens MEP, Eschbach D, Lagendijk JJW, et al. Lymph node MRI in regional breast radiotherapy leads to smaller target volumes and lower OAR dose [Abstract]. Radiother Oncol. 2017;123(Suppl 1):S146-S7.

401. Van Heijst T, Aalbers EM, Alberts E, Van Den Bongard HJGD, Lagendijk JJW, Van Asselen B, et al. MR imaging of internal mammary lymph nodes and organs at risk in supine breast radiotherapy [Abstract]. Radiother Oncol. 2017;123(Suppl 1):S933-S4.

402. Van Heijst TCF, Hoekstra N, Philippens MEP, Eschbach D, Lagendijk JJW, Van Den Bongard HJGD, et al. MRI-guided single-fraction boost delivery on individual axillary lymph nodes [Abstract]. Med Phys. 2016;43(6 part 32):3722.

403. van Heijst TC, van Asselen B, Pijnappel RM, Cloos-van Balen M, Lagendijk JJ, van den Bongard D, et al. MRI sequences for the detection of individual lymph nodes in regional breast radiotherapy planning. Br J Radiol. 2016;89(1063):20160072 (10 pp).

404. Van Heijst TCF, Van Den Bongard HJGD, Lagendijk JJW, Van Asselen B, Philippens MEP. MRI of individual axillary and periclavicular lymph nodes for MR-guided regional radiotherapy [Abstract]. Radiother Oncol. 2014;111(Suppl 1):S254-S5, Abstract EP-1717.

405. Pukancsik D, Kelemen P, Ujhelyi M, Kovacs E, Udvarhelyi N, Meszaros N, et al. Objective decision making between conventional and oncoplastic breast-conserving surgery or mastectomy: An aesthetic and functional prospective cohort study. Eur J Surg Oncol. 2017;43(2):303-10.

406. Silverstein MJ, Savalia N, Khan S, Ryan J. Extreme oncoplasty: Breast conservation for patients who need mastectomy. Breast J. 2015;21(1):52-9.

407. Tousimis E, Haslinger M. Overview of indications for nipple sparing mastectomy. Gland Surg. 2018;7(3):288-300.

408. Piato JR, de Andrade RD, Chala LF, de Barros N, Mano MS, Melitto AS, et al. MRI to predict nipple involvement in breast cancer patients. AJR Am J Roentgenol. 2016;206(5):1124-30.

409. Yamashita Y, Hayashi N, Nagura N, Kajiura Y, Yoshida A, Takei J, et al. Long-term oncologic safety of nipple-sparing mastectomy with immediate reconstruction [Abstract]. Cancer Res. 2019;79(4 Suppl 1).

410. Koike-Shimo A, Tsugawa K, Kawamoto H, Kanemaki Y, Maeda I. Oncologic outcome and technical consideration of nipple-sparing mastectomy in breast cancer: The St. Marianna experience with 384 patients [Abstract]. J Clin Oncol. 2014;32(15 Suppl 1):Abstract e12024.

411. del Riego J, Pitarch M, Codina C, Nebot L, Andreu FJ, Aparicio O, et al. Multimodality approach to the nipple-areolar complex: A pictorial review and diagnostic algorithm. Insights Imaging. 2020;11:89 (27 pp).

412. Krajewski AC, Boughey JC, Degnim AC, Jakub JW, Jacobson SR, Hoskin TL, et al. Expanded indications and improved outcomes for nipple-sparing mastectomy over time. Ann Surg Oncol. 2015;22(10):3317-23.

413. Gao Y, Brachtel EF, Hernandez O, Heller SL. An analysis of nipple enhancement at breast MRI with radiologic-pathologic correlation. Radiographics. 2019;39(1):10-27.

414. Cohen MA, Holbrook AI. Invited commentary on "An analysis of nipple enhancement at breast mri with radiologic-pathologic correlation". Radiographics. 2019;39(1):28-9.

415. Ryu JM, Nam SJ, Kim SW, Lee SK, Bae SY, Yi HW, et al. Feasibility of nipple-sparing mastectomy with immediate breast reconstruction in breast cancer patients with tumor-nipple distance less than 2.0 cm. World J Surg. 2016;40(8):2028-35.

416. Mariscotti G, Durando M, Houssami N, Berzovini CM, Esposito F, Fasciano M, et al. Preoperative MRI evaluation of lesion-nipple distance in breast cancer patients: Thresholds for predicting occult nipple-areola complex involvement. Clin Radiol. 2018;73(8):735-43.

417. Seki H, Sakurai T, Mizuno S, Tokuda T, Kaburagi T, Seki M, et al. A novel nipple-areola complex involvement predictive index for indicating nipple-sparing mastectomy in breast cancer patients. Breast Cancer. 2019;26:808-16.

418. Balci FL, Kara H, Dulgeroglu O, Uras C. Oncologic safety of nipple-sparing mastectomy in patients with short tumor-nipple distance. Breast J. 2019;25(4):612-8.

419. Frey JD, Salibian AA, Lee J, Harris K, Axelrod DM, Guth AA, et al. Oncologic trends, outcomes, and risk factors for locoregional recurrence: An analysis of tumor-to-nipple distance and critical factors in therapeutic nipple-sparing mastectomy. Plast Reconstr Surg. 2019;143(6):1575-85.

420. Ponzone R, Maggiorotto F, Carabalona S, Rivolin A, Pisacane A, Kubatzki F, et al. MRI and intraoperative pathology to predict nipple-areola complex (NAC) involvement in patients undergoing NAC-sparing mastectomy. Eur J Cancer. 2015;51(14):1882-9.

421. Liu Z, Li X, Feng B, Li C, Chen Y, Yi L, et al. MIP image derived from abbreviated breast MRI: Potential to reduce unnecessary sub-nipple biopsies during nipple-sparing mastectomy for breast cancer. Eur Radiol. 2021;27:3683-92.

422. Razek AKA, El-Adalany MA, El-Metwally D. Role of diffusion-weighted imaging in prediction of nipple-areolar complex invasion by breast cancer. Clin Imaging. 2021;69:45-9.

423. Pien IJ, Bahl M, Buretta KJ, Greenup RA, Ghate SV, Hollenbeck ST. Vascular patterns on preoperative breast MRI predict ischemia and necrosis after nipple-sparing mastectomy [Abstract]. J Am Coll Surg. 2015;221(4 Suppl 1):S120.

424. Edquilang J, Wu R, Momeni A, Mardi K. Outcomes after preservation of the internal mammary artery perforator in nipple-sparing mastectomy [Abstract]. Ann Surg Oncol. 2020;27(Suppl 2):S441-S2.

425. Amanti C, Vitale V, Lombardi A, Maggi S, Bersigotti L, Lazzarin G, et al. Importance of perforating vessels in nipple-sparing mastectomy: An anatomical description. Breast Cancer (Dove Med Press). 2015;7:179-81.

426. Colombo G, Garlaschi A, Stifanese R, Giunta G, Ruvolo V. Necrosis of the nipple-areola complex in breast reduction. Our personal way to solve problem. Ann Ital Chir. 2015;86(2):156-62.

427. Stolier AJ, Levine EA. Reducing the risk of nipple necrosis: Technical observations in 340 nipple-sparing mastectomies. Breast J. 2013;19(2):173-9.

428. Bahl M, Pien IJ, Buretta KJ, Hwang ES, Greenup RA, Ghate SV, et al. Can vascular patterns on preoperative magnetic resonance imaging help predict skin necrosis after nipple-sparing mastectomy? J Am Coll Surg. 2016;223(2):279-85.

429. Panzironi G, Pediconi F, Sardanelli F. Nipple discharge: The state of the art. BJR Open. 2019;1(1):20180016 (9 pp).

430. Berger N, Luparia A, Di Leo G, Carbonaro LA, Trimboli RM, Ambrogi F, et al. Diagnostic performance of MRI versus galactography in women with pathologic nipple discharge: A systematic review and meta-analysis. AJR Am J Roentgenol. 2017;209(2):465-71.

431. Gupta D, Mendelson EB, Karst I. Nipple discharge: Current clinical and imaging evaluation. AJR Am J Roentgenol. 2021;216:330-9.

432. Filipe MD, Patuleia SIS, de Jong VMT, Vriens MR, van Diest PJ, Witkamp AJ. Network meta-analysis for the diagnostic approach to pathologic nipple discharge. Clin Breast Cancer. 2020;20(6):e723-e48.

433. Fisher S, Yasui Y, Dabbs K, Winget M. Re-excision and survival following breast conserving surgery in early stage breast cancer patients: A population-based study. BMC Health Serv Res. 2018;18(1):94 (10 pp).

434. Jeevan R, Cromwell DA, Trivella M, Lawrence G, Kearins O, Pereira J, et al. Reoperation rates after breast conserving surgery for breast cancer among women in England: Retrospective study of hospital episode statistics. BMJ. 2012;345:e4505 (9 pp).

435. The American Society of Breast Surgeons. Quality measure: Return to the operating room for re-excision of previous microscopically negative margins in invasive breast cancer patients undergoing breast conserving therapy [Internet]. Columbia (MD): American Society of Breast Surgeons; 2020 [initially endorsed 2017 Oct 2; revised 2020 Sept 17; cited 2021 Jul 26]. Available from: https://www.breastsurgeons.org/resources/statements.

436. Biganzoli L, Marotti L, Hart CD, Cataliotti L, Cutuli B, Kühn T, et al. Quality indicators in breast cancer care: An update from the EUSOMA working group. Eur J Cancer. 2017;86:59-81.

437. Nessim C, Winocour J, Holloway DP, Saskin R, Holloway CM. Wait times for breast cancer surgery: Effect of magnetic resonance imaging and preoperative investigations on the diagnostic pathway. J Oncol Pract. 2015;11(2):e131-8.

438. Chiarelli AM, Blackmore KM, Muradali D, Done SJ, Majpruz V, Weerasinghe A, et al. Performance measures of magnetic resonance imaging plus mammography in the High Risk Ontario Breast Screening Program. J Natl Cancer Inst. 2020;112(2):136-44.

439. Brenner RJ. Preoperative MRI of the breast (POMB) influences primary treatment in breast cancer: A prospective, randomized, multicenter study: Gonzalez V, Sandelin K, Karlsson A, et al (Vastmanland County Hosp, Vasteras, Sweden; Karolinska Institutet, Stockholm, Sweden; Capio St Goran's Hosp, Stockholm, Sweden; et al) World J Surg 38: 1685-1693, 2014. Breast Dis. 2015;26(1):36-8.

440. Hollingsworth AB, Stough RG. Preoperative MRI and surgical management in patients with nonpalpable breast cancer: The MONET - Randomised controlled trial. Breast Dis. 2012;23(1):33-7.

441. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi: 10.1136/bmj.n71. See also: http://www.prisma-statement.org/.

442. Fancellu A, Turner RM, Dixon JM, Pinna A, Cottu P, Houssami N. Meta-analysis of the effect of preoperative breast MRI on the surgical management of ductal carcinoma in situ. Br J Surg. 2015;102(8):883-93.

443. Spick C, Baltzer PA. Diagnostic utility of second-look US for breast lesions identified at MR imaging: Systematic review and meta-analysis. Radiology. 2014;273(2):401-9.

444. Xu L. Reply to: "in vivo post-contrast 1H-MRS evaluation of malignant and benign breast lesions: A meta-analysis". Tumour Biol. 2015;36(9):6669-70.

445. Caldarella C, Treglia G, Giordano A. Diagnostic performance of dedicated positron emission mammography using fluorine-18-fluorodeoxyglucose in women with suspicious breast lesions: A meta-analysis. Clin Breast Cancer. 2014;14(4):241-8.

446. Wallis M, Tardivon A, Helbich T, Schreer I. Guidelines from the European Society of Breast Imaging for diagnostic interventional breast procedures. Eur Radiol. 2007;17(2):581-8.

447. Sheth D, Abe H. Abbreviated MRI and accelerated MRI for screening and diagnosis of breast cancer. Top Magn Reson Imaging. 2017;26(5):183-9.

448. Zhu X, Huang J-m, Zhang K, Xia L-j, Feng L, Yang P, et al. Diagnostic value of contrast-enhanced spectral mammography for screening breast cancer: Systematic review and meta-analysis. Clin Breast Cancer. 2018;18(5):e985-e95.

449. Tagliafico AS, Calabrese M, Mariscotti G, Durando M, Tosto S, Monetti F, et al. Adjunct screening with tomosynthesis or ultrasound in women with mammography-negative dense breasts: Interim report of a prospective comparative trial. J Clin Oncol. 2016;34(16):1882-8.

450. Comstock CE, Gatsonis C, Newstead GM, Snyder BS, Gareen IF, Bergin JT, et al. Comparison of abbreviated breast MRI vs digital breast tomosynthesis for breast cancer detection among women with dense breasts undergoing screening. JAMA. 2020;323(8):746-56.

451. Ribelles MJ, Rodriguez M, Sancho L, Guillen F, Pina LJ, Idoate M, et al. Fusion of prone FDG PET/CT and MRI improves staging of patients with breast cancer [Abstract]. Eur J Nucl Med Mol Imaging. 2015;42(Suppl 1):S249.

452. Tabouret-Viaud C, Loubeyre P, Guignard R, Garibotto V, Viallon M, Heinzer S, et al. Feasibility of simultaneous PET-MR imaging in breast cancer [Abstract]. Nuklearmedizin. 2012;51(3):A132.

453. Cowling T, Frey N. Macrocyclic and linear gadolinium based contrast agents for adults undergoing magnetic resonance imaging: A review of safety [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2019 Jun 6 [cited 2021 Aug 9]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK546000/.

454. Kanda T. The new restrictions on the use of linear gadolinium-based contrast agents in Japan. Magn Reson Med Sci. 2019;18(1):1-3.

455. Do C, DeAguero JL, Brearley A, Trejo X, Howard T, Escobar GP, et al. Gadolinium-based contrast agent use, their safety, and practice evolution. Kidney. 2020;1:561-8.

456. United States Food and Drug Administration. FDA Drug Safety Communication: FDA warns that gadolinium-based contrast agents (GBCAs) are retained in the body; requires new class warnings [Internet]. Silver Spring (MD, USA): Food and Drug Administration; 2018 May 16 update [cited 2021 Aug 9]. Available from: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-warns-gadolinium-based-contrast-agents-gbcas-are-retained-body.

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Appendix A. Affiliations and Conflict of Interest Declarations

Table A1. Members of the Breast MRI Working Group

Name	Affiliation	Declarations of interest
Derek Muradali	• Head, Division of Breast Imaging, University of Toronto • Associate Professor, St Michael's Hospital, Toronto • Radiologist-In-Chief, Ontario Breast Screening Program (until July 31, 2019)	none
Andrea Eisen	• Breast Disease Site Team Lead, Cancer Care Ontario • Medical Oncologist and Head Familial Cancer Program, Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto	none
Samantha Fienberg	• Clinical Lead for the Ontario Breast Screening Program (OBSP), Cancer Screening, Ontario Health (Cancer Care Ontario) effective January 10, 2020 • Assistant Clinical Professor Radiology, Faculty of Health Sciences, McMaster University • Radiologist, Grand River Hospital, Kitchener • Regional Breast Imaging Lead, Waterloo Wellington Regional Cancer Program	none
Glenn Fletcher	• Health Research Methodologist, Program in Evidence-Based Care, Department of Oncology, McMaster University	none
Ralph George	• Medical Director, CIBC Breast Centre, St. Michael's Hospital, Toronto • Associate Professor, Department of Surgery, University of Toronto	AbbVie: consultant and speaker on Hidradenitis suppurtiva (no conflict with this project); 2) Allergan: speakers fees (no conflict with this project); 3) Genetech: consultancy fees (no conflict with this project). Immode: equipment and training related to

		Hidradenitis suppurativa (no conflict with this project); Lutronic: equipment and training related to hidradenitis suppurativa treatment (no conflict with this project) Clinical trial grant for SHARPE: multinational study on Hidradenitis suppurativa treatment. Managerial responsibility for pay for consultation services for AbbVie; external expert for Hidradenits suppurativa. (also speakers fees, observership fees)
Claire Holloway	• Provincial Clinical Lead, Disease Pathway Management, Cancer Care Ontario • Associate Professor, Department of Surgery, University of Toronto	none
Supriya Kulkarni	• Assistant Professor, Medical Imaging, University of Toronto. • Department of Medical Imaging, Princess Margaret Hospital	none
Jean Seely	• Professor, Department of Radiology, University of Ottawa • Head, Breast Imaging Section, Department of Medical Imaging, The Ottawa Hospital • Regional Breast Imaging Lead, Ontario Breast Screening Program, Champlain LHIN, Cancer Care Ontario	Greater than $500 as Consultant to Hoffman Roche in 2018 in an advisory capacity. Site principal investigator for the TMIST (Tomosynthesis Mammography Intervention Screening Trial) in Ottawa, funded by National Cancer Institute, to the Canadian Clinical Trials Group

In accordance with the PEBC Conflict of Interest (COI) Policy, the evidence summary authors were asked to disclose potential conflicts of interest. The COI declared above did not disqualify any individuals from performing their designated role in the development of this evidence summary, in accordance with the PEBC COI Policy. To obtain a copy of the policy, please contact the PEBC office by email at ccopgi.mcmaster.ca.

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Appendix B. Literature Search Strategy

Initial Search July 3, 2019

Database(s): Embase 1974 to 2019 July 03, EBM Reviews - Cochrane Central Register of Controlled Trials June 2019, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to July 3, 2019, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to July 03, 2019

Search Strategy:

#	Searches	Results
1	exp breast neoplasms/ or exp mammography/ or (breast: or ductal carcinoma or lobular carcinoma or ductolubular carcinoma or LCIS or DCIS or mammograph: or mammogram: or mammary or nipple).ti.	1008653
2	exp magnetic resonance imaging/ or (magnetic resonance or MR imaging or MRI or MRI: or MRM or MR mammography or MR-mammography).ti,ab.	1656341
3	(breast MRI: or breast magnetic resonance imag: or (breast adj4 MRI)).mp.	8554
4	(1 and 2) or 3	36891
5	4 not (case reports or comment or editorial or historical article or letter or news or book or editorial or letter or note).pt.	32799
6	limit 5 to yr=2018-current	3955
7	limit 5 to yr=2016-2017	5444
8	limit 5 to yr=2014-2015	4529
9	limit 5 to yr=2012-2013	4530
10	limit 5 to yr=2009-2011	5169
11	limit 5 to yr=2003-2008	5092
12	5 not (6 or 7 or 8 or 9 or 10 or 11)	4081
13	remove duplicates from 6	2945
14	remove duplicates from 7	4064
15	remove duplicates from 8	3366
16	remove duplicates from 9	3500
17	remove duplicates from 10	3894
18	remove duplicates from 11	3598
19	remove duplicates from 12	2809
20	or/13-19	24175

June 15, 2020 search update

Database(s): Embase 1974 to 2020 June 12, OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present, EBM Reviews - Cochrane Central Register of Controlled Trials May 2020, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to June 11, 2020

Search Strategy:

#	Searches	Results
1	exp breast neoplasms/ or exp mammography/ or (breast: or ductal carcinoma or lobular carcinoma or ductolubular carcinoma or LCIS or DCIS or mammograph: or mammogram: or mammary or nipple).ti.	1068683
2	exp magnetic resonance imaging/ or (magnetic resonance or MR imaging or MRI or MRI: or MRM or MR mammography or MR-mammography).ti,ab.	1776719
3	(breast MRI: or breast magnetic resonance imag: or (breast adj4 MRI)).mp.	9343
4	(1 and 2) or 3	39907
5	4 not (case reports or comment or editorial or historical article or letter or news or book or editorial or letter or note).pt.	35484
6	5 and (2019: or 2020:).dd,ed,dp,em,dt,dc.	5690
7	limit 5 to yr=2019-current	3980
8	6 or 7	5784
9	remove duplicates from 8	4426

Of these, 2335 were already in original search and 29 were duplicates. Therefore, there were 2062 new citations in the June 2020 update.

Jan 18, 2021 search updates

Database: Embase <1974 to 2021 January 15>, OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present, EBM Reviews - Cochrane Central Register of Controlled Trials <December 2020>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to December 31, 2020>

Search Strategy:

#	Searches	Results
1	exp breast neoplasms/ or exp mammography/ or (breast: or ductal carcinoma or lobular carcinoma or ductolubular carcinoma or LCIS or DCIS or mammograph: or mammogram: or mammary or nipple).ti.	1111454
2	exp magnetic resonance imaging/ or (magnetic resonance or MR imaging or MRI or MRI: or MRM or MR mammography or MR-mammography).ti,ab.	1860031
3	(breast MRI: or breast magnetic resonance imag: or (breast adj4 MRI)).mp.	9910

4	(1 and 2) or 3	42118
5	4 not (case reports or comment or editorial or historical article or letter or news or book or editorial or letter or note).pt.	37515
6	5 and (2019: or 2020: or 2021:).dd,ed,dp,em,dt,dc.	8128
7	limit 5 to yr=2019-current	5974
8	Remove duplicates from 7	4368
9	6 not 7	2298
10	remove duplicates from 9	1956
11	8 or 10	6324

1466 of these were non-duplicate citations not found in previous searches

Search for Guidelines and Technical Standards, updated March 2021

- American College of Radiology (ACR): https://www.acr.org/Clinical-Resources
- Canadian Association of Radiologists https://car.ca/patient-care/practice-guidelines/
- Alberta Health Services https://www.albertahealthservices.ca/info/cancerguidelines.aspx.
- EUSOMA https://www.eusoma.org/recommendations/other%2dguidelines/1-149-1-.
- EUSOBI https://www.eusobi.org/breast-imaging-publications-and-guidelines/
- The American Society of Breast Surgeons https://www.breastsurgeons.org.
- GIN https://guidelines.ebmportal.com/guidelines-international-network
- Geneva Foundation for Medical Education and Research: https://www.gfmer.ch/guidelines/breast_diseases/Breast_imaging.htm
- CPAC Database: https://www.partnershipagainstcancer.ca/tools/cancer-guidelines-database/
- CMA Infobase: https://www.cma.ca/En/Pages/clinical-practice-guidelines.aspx
- NICE Evidence Search: https://www.evidence.nhs.uk/
- NICE (UK) – NICE Guidance https://www.nice.org.uk
- SIGN (UK) – SIGN Guidelines https://www.sign.ac.uk/
- ASCO (US) – ASCO Guidelines https://www.asco.org/research-guidelines/quality-guidelines/guidelines
- National Health and Medical Research Council – Australia Clinical Practice Guidelines Portal https://www.clinicalguidelines.gov.au/portal
- Cancer Council Australia – Cancer Guidelines Wiki https://wiki.cancer.org.au/australia/Guidelines
- ECRI GL Trust https://guidelines.ecri.org/

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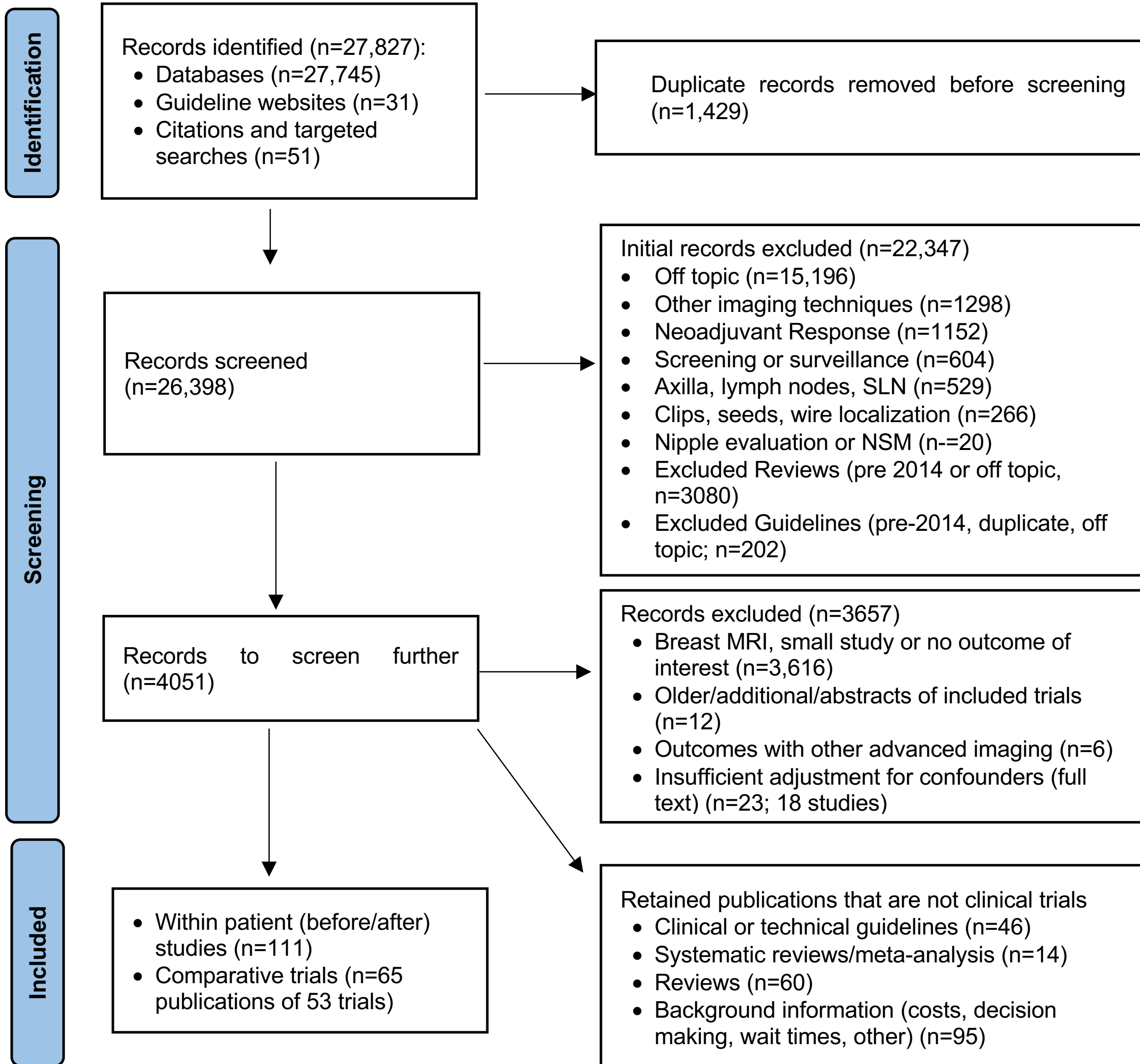
Appendix C. PRISMA Flow Diagram



Format adapted from: Page, 2021 (441)

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Appendix D. Systematic Reviews and Meta-analyses

Citation	Title	Method or topic	Results or conclusions
Systematic reviews or meta-analyses, MRI			
Surov, 2019 (221)	Can apparent diffusion coefficient (ADC) distinguish breast cancer from benign breast findings? A meta-analysis based on 13 847 lesions	Association of ADC and malignancy using DWI-MRI; included 123 publications of 13,847 lesions	ADC threshold of 1.00×10^{-3} was recommended
Salmanoglu, 2019 (219)	Advanced approaches to imaging primary breast cancer: An update	Imaging efficacy for breast cancer, 143 publications up to October 2018 Describe advantages and limitations to conventional and new imaging modalities	Mammography has low sensitivity in dense breasts and is often used together with US; addition of DBT or CESM can increase sensitivity Ultrasound is generally used to evaluate symptoms or together with other diagnostic imaging for biopsies; contrast-enhanced US may provide results more similar to MRI MRI has highest sensitivity; CT (especially dedicated breast CT) is an alternative when MRI is not suitable Other techniques are less common, and improvements are under investigation
Houssami, 2017 (215)	Meta-analysis of pre-operative magnetic resonance imaging (MRI) and surgical treatment for breast cancer	Study-level pooled analysis (meta-analysis) of 3 RCTs and 19 comparative studies on pre-operative MRI vs. no MRI for IBC; search up to December 2016	Did not use adjusted ORs for most analyses; used adjusted ORs for CPM analysis (3 studies) Limitation was heterogeneity between groups and across studies, only 3 studies were RCTs Primary analysis: increase in mastectomy, OR=1.39 (95% CI=1.23-1.57) Secondary analysis: increase in CPM; no statistical evidence of effect on re-excision, re-operation, or positive margins Subgroup analysis stratified by study-level median or mean age; subgroup analysis for ILC (3 studies) For ILC, mastectomy OR=1.00 (p=0.988); re-excision OR=0.65 (p=0.192)
Clauser, 2016 (218)	Management of atypical lobular hyperplasia, atypical ductal hyperplasia, and lobular carcinoma in situ	Atypical lobular hyperplasia and LCIS Management, search until August 2015: 102 studies including 4 with MRI	Cancer rate with MRI in pts with atypical ductal hyperplasia and/or lobular neoplasia/ LCIS (PPV approximately 20%) is similar to rate in high-risk pts and MRI may be useful
Helme, 2015 (217)	Breast-conserving surgery in patients with Paget's disease	Paget’s disease, search until August 2014 found 43 publications; 6 small studies used MRI	6 small studies used MRI and found it more sensitive than mammography. It is suggested that MRI has a role in patients with Paget’s disease, especially if BCS is desired or being considered

Fancellu, 2015 (442)	Meta-analysis of the effect of preoperative breast MRI on the surgical management of ductal carcinoma in situ	Preoperative MRI in DCIS, search until March 2014, 9 studies included (2 RCTs)	Most studies had small numbers of pts; no mention of using adjusted data from individual studies Two studies with combined total of 49 pts with MRI were the only ones with excess initial mastectomy rates with MRI; authors reported this to be significant (OR=1.72, p=0.012) No differences found for positive margins, reoperations, overall mastectomy rate
Di Leo, 2015 (216)	MR imaging for selection of patients for partial breast irradiation: A systematic review and meta-analysis	Eligibility for partial breast irradiation; search until July 2014, 6 studies included (3136 pts)	All studies applied NSABP B-39 criteria for partial breast irradiation MRI excluded 6% to 25% of pts initially eligible (pooled value 11%); MRI excluded 2% to 20% of all pts Analysis concludes MRI should be used to select pts for partial breast irradiation
Spick, 2014 (443)	Diagnostic utility of second-look US for breast lesions identified at MR imaging: Systematic review and meta-analysis	Ultrasound after MRI; review to January 2013. 17 studies	Ultrasound detection rate 22.6% to 82.1% in various studies for general lesions (overall 57.5%) Mass lesions and malignant lesions are more likely to show a correlate at second-look US Missing correlate does not exclude malignancy and MRI-guided biopsy is required
Houssami, 2014 (214) See Houssami, 2017 (215) for more recent meta-analysis of other outcomes	An individual person data meta-analysis of preoperative magnetic resonance imaging and breast cancer recurrence	Individual person meta-analysis, preoperative MRI vs. no MRI, search until January 2013, 4 studies with 3180 breasts in 3169 pts	Multivariable model was fitted to estimate the HR for MRI, adjusted for potential confounding variables found to be associated with recurrence (P ≤0.01) in univariable analyses Median follow-up 2.9 y, 64 local recurrences (crude rate 1.8% vs. 2.2%) and 93 distant recurrences 8-y local recurrence-free survival did not differ, 97% vs. 95%, p=0.87 by survival curve; HR=0.90, 95% CI=0.52-1.54, p=0.69 univariate; HR=0.88 (95% CI=0.52-1.51), p=0.65 in multivariate after adjusting for age, margin status, ER status, and tumour grade 8-y distant recurrence-free survival 89% vs. 93%, p=0.37 by survival curves; HR=1.28, 95% CI=0.83-1.97, p=0.27 univariate; adjusted HR=1.18 (95% CI=0.76-2.27), p=0.48 in multivariate after adjusting for age, pathologic tumour size, grade, nodal status, ER status, receipt of mastectomy, nonreceipt of systemic therapy
Systematic reviews, other advanced imaging			
Uhlig, 2019 (220)	Diagnostic accuracy of cone-beam breast computed tomography: a systematic review and diagnostic meta-analysis	Cone-beam breast computed tomography to discriminate benign vs. malignant breast lesions; included 6 studies	Non-contrast: pooled sensitivity 0.789 (95% CI=0.66–0.89) and pooled specificity 0.697 (95% CI=0.471–0.851 Contrast-enhanced: pooled sensitivity 0.899 (95% CI=0.785–0.956) and pooled specificity was 0.788 (95% CI: 0.709–0.85) CE results were comparable to breast MRI
Zhang, 2017 (222)	Breast-specific gamma camera imaging with 99mTc-MIBI has better diagnostic performance than magnetic resonance imaging in breast cancer patients: A meta-analysis	BSGI vs. MRI by meta-analysis; search until June 2016, 10 studies included	Pooled sensitivities of BSGI and MRI were 0.84 (95% CI, 0.79-0.88) and 0.89 (95% CI, 0.84-0.92) respectively, and the pooled specificities of BSGI and MRI were 0.82 (95% CI, 0.74-0.88) and 0.39 (95% CI, 0.30-0.49) respectively

Tan, 2015 (223); Xu, 2015 (444)	In vivo post-contrast 1H-MRS evaluation of malignant and benign breast lesions: A meta-analysis	Meta-analysis of in vivo postcontrast MRS, search until January 2014, 16 studies	Pooled sensitivity and specificity of post-contrast 1H-MRS were 74 % (95% CI=70%-77%) and 78% (95% CI=73%-82 %), respectively
Caldarella, 2014 (445)	Diagnostic performance of dedicated positron emission mammography using fluorine-18-fluorodeoxyglucose in women with suspicious breast lesions: A meta-analysis	Meta-analysis of PEM in suspicious breast lesions, search until February 2013, 8 studies included	Pooled sensitivity and specificity 85% (95% CI=83%-88%) and 79% (95% CI=74%-83%), respectively, on a per lesion-based analysis

ADC, apparent diffusion coefficient; BSGI, Breast-specific gamma imaging; CESM, contrast-enhanced spectral mammography; CPM, contralateral prophylactic mastectomy; CT, computed tomography; DBT, digital breast tomosynthesis; DWI, diffusion-weighted imaging; IBC, invasive breast cancer; ILC, invasive lobular cancer; MP-MRI, multiparametric MRI; MRI, magnetic resonance imaging; MRS, proton magnetic resonance spectroscopy; PEM, positron emission mammography; PET, positron emission tomography; US, ultrasonography

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Appendix E. Clinical Pratice Guidelines and Technical Documents

Organization	Citation	Title	Relevant recommendations[16]
MRI is the focus			
Blue Shield of California Blue Cross Blue Shield Association	Blue Shield of California, 2020 (245) Blue Cross Blue Shield Association, 2019 (249)	6.01.29 - Magnetic resonance imaging for detection and diagnosis of breast cancer	MRI for Detection Uses MRI of the breast for detection may be considered medically necessary for any of the following: I. Suspected occult breast primary tumour in patient with axillary nodal adenocarcinoma (i.e., negative mammography and physical exam) II. A new diagnosis of breast cancer to evaluate the contralateral breast with both of the following: A. Clinical exam is normal B. Mammographic findings are normal MRI for Treatment-Related Uses MRI of the breast for treatment-related issues may be considered medically necessary for any of the following: I. Preoperative tumour mapping of the involved (ipsilateral) breast to evaluate the presence of multicentric disease in patient with clinically localized breast cancer who are candidates for breast conservation therapy II. Presurgical planning in patient with locally advanced breast cancer (before and after completion of neoadjuvant chemotherapy) to permit tumour localization and characterization III. To determine the presence of pectoralis major muscle/chest wall invasion in patient with posteriorly located tumours IV. To evaluate a documented abnormality of the breast before obtaining an MRI-guided biopsy when there is documentation that other methods, such as palpation or US, are not able to localize the lesion for biopsy MRI of the breast is considered investigational for any of the following indications: I. Routine screening for an average risk patient II. Screening for breast cancer when the sensitivity of mammography (i.e., mammography using low-dose x-rays for imaging) is limited (i.e., dense breasts, breast implants, scarring after breast cancer treatment) III. The test is to diagnose low-suspicion findings on conventional testing that are not indicated for immediate biopsy and referral for short-interval follow-up IV. The test is to diagnose a suspicious breast lesion in order to avoid biopsy V. Determining the level of response during neoadjuvant chemotherapy in patients with locally advanced breast cancer

[16] **Due to nuances involved in wording of recommendations, information in this column is generally copied directly from the publications cited.**

			VI. Evaluating for residual tumour in patients with positive margins after initial lumpectomy or breast conservation surgery Cited from NCCN: Considerations for Performing Magnetic Resonance Imaging Breast magnetic resonance imaging (MRI) exams should be performed and interpreted by an expert breast imaging team working with the multidisciplinary oncology treatment team. Breast MRI exams require a dedicated breast coil and the use of contrast agents by radiologists familiar with the optimal timing sequences and other technical aspects of image interpretation. The breast MRI center also should have the ability to perform MRI-guided biopsy and/or wire localization of findings detected by MRI. Since these are standard, documentation is not needed for approval (unless something unusual is noted that is of concern). Considerations for Preoperative MRI Preoperative MRI in patients with localized disease results in higher rates of mastectomy and lower rates of breast-conserving therapy. There is uncertainty from the available evidence on whether outcomes are improved by changing to a more extensive operation. If biopsies are performed on all MRI-identified lesions, and if shared patient decision making is used for altering the surgical approach, then the probability of improved outcomes is increased.
Blue Cross Blue Shield Association	Blue Cross Blue Shield Association, 2019 (248)	6.01.45 - Computer-aided evaluation as an adjunct to magnetic resonance imaging of the breast	The use of computer-aided evaluation for interpretation of magnetic resonance imaging of the breast is considered investigational. The evidence is insufficient to determine the effects of the technology on health outcomes.
Institut national d'excellence en santé et en services sociaux (INESSS), Quebec	INESS, 2018 (243)	Main indications for breast MRI in the context of investigation and planning of breast cancer treatment	Breast MRI is recommended: • in case of axillary lymphadenopathy, which is most likely of breast origin, without a primary tumour detectable by clinical examination and conventional imaging (mammography plus breast ultrasonography). Level of evidence: low • amongst women with a high risk of breast cancer who opt for a prophylactic mastectomy. Level of evidence: low The need for an MRI should be discussed in a cancer diagnosis and treatment multidisciplinary team meeting: Preoperative breast MRI may be considered: • in cases of Paget's disease of the nipple when breast conserving surgery is desired and an associated tumour lesion could not be detected by clinical examination and conventional imaging (mammography plus breast ultrasonography). Level of evidence: expert opinion • for breast cancer patients who have a discrepancy between imaging and clinical examination. Level of evidence: expert opinion

			Preoperative breast MRI may be considered: • to clarify the extent of breast cancer when conventional imaging (mammography plus breast ultrasonography) detects multifocal involvement and breast conserving surgery is desired. Level of evidence: expert opinion • in cases of invasive lobular carcinoma when breast conserving surgery is considered. Level of evidence: low • when invasion of the pectoralis major muscle or chest wall is suspected on imaging or clinical examination. Level of evidence: low • to plan the type of surgery for patients who have achieved multifocal positive surgical margins following a lumpectomy. Level of evidence: expert opinion • for the selection of patients eligible for breast conserving surgery after neoadjuvant chemotherapy – but the systematic use is not indicated in these cases. Level of evidence: expert opinion
Eastern Health Breast Disease Site Group (Newfoundland & Labrador)	Eastern Health, 2017 (244)	Indications for use of breast magnetic resonance imaging	Breast MRI is indicated in the following circumstances: 1. Screening of high-risk individuals 2. Problem solving when mammographic, sonographic, or clinical findings are suspicious but inconclusive • Inconclusive findings of breast cancer - MRI imaging may be helpful for lesion identification when findings at physical examination and conventional imaging modalities are suggestive of breast cancer, but are inconclusive (11); • Pre-operative MRI - may be used in the following situations where the patient desires breast conserving surgery and: o there is a high risk for multifocal/multicentric disease; o the extent of the disease is unclear. 3. Assessment of positive margins following breast cancer surgery 4. Differentiation of post-surgical scarring from recurrent tumour 5. Search for source of primary malignancy when the breast is normal by conventional imaging in the presence of tumour positive axillary adenopathy 6. Assessment of response to neoadjuvant chemotherapy 7. Assessment of breast implant integrity
The American Society of Breast Surgeons (ASBrS)	The American Society of Breast Surgeons, 2017 (246)	Consensus Guideline on Diagnostic and Screening Magnetic Resonance Imaging of the Breast	1. The ASBrS does not recommend routine diagnostic MRI in newly diagnosed breast cancer patients except as part of a scientific study. 2. The ASBrS supports the use of MRI in the following situations: a. To search for occult breast cancer in patients with Paget's disease of the nipple or in patients with axillary node metastasis when clinical examination and conventional breast imaging fail to detect a primary breast cancer. b. For determining the extent of cancer or presence of multi-focal or multi-centric tumour or the presence of contralateral cancer, in patients with a proven breast cancer and associated clinical or conventional indeterminate imaging findings suspicious for malignancy. This may include patients with invasive lobular carcinoma or extremely dense breast tissue (limiting mammographic sensitivity), or when there are significant discrepancies in the estimated tumour size as measured on clinical exam, mammogram, and US. c. To aid the assessment for eligibility and response to neoadjuvant endocrine therapy or chemotherapy before, during, or after treatment. MRI can help identify those patients who are candidates for breast conservation, and assist in determining the extent of

			d. For the further evaluation of suspicious clinical or imaging findings that remain indeterminate after complete mammographic and sonographic evaluations. If lesions meet the criteria for biopsy by clinical examination or conventional imaging, then it may be preferable to perform minimally invasive needle biopsy, targeted by mammogram or US, rather than obtain an MRI. e. For evaluation of suspected breast implant rupture, especially in patients with silicone implants, if the MRI findings will aid the decision-making for implant removal or aid the diagnostic evaluation of indeterminate clinical or conventional imaging findings in patients with implants. The MRI protocol for detection of silicone leak is different from the protocol for detection of breast cancer. Thus, it is important to clearly define the purpose of the breast MRI if the concern is a silicone leak.
Canadian Association of Radiologists	Appavoo, 2016 (247)	CAR practice guidelines and technical standards for breast imaging and intervention	Indications a) Breast implants: to determine presence of silicone implant rupture or other complications b) Problem solving in the case of equivocal mammographic clinical and/or US findings. It should not replace the need for a biopsy. c) High risk screening: to screen women at high risk for breast cancer, with estimated lifetime risk of greater than 20–25%. This includes women who are BRCA 1 and 2 gene mutation carriers, women who received chest irradiation for treatment of another malignancy such as lymphoma between the ages of 10–30 years of age, PTEN Li-Fraumeni syndrome, Cowden syndrome, or Bannayan-Riley- Ruvalcaba syndrome, or one of these syndromes in first-degree relatives. Information on risk calculation is included in the Screening Mammography INDICATIONS section. d) Neo-adjuvant chemotherapy: to assess response to chemotherapy. e) Occult breast cancer: to determine the site of a primary carcinoma in a patient presenting with metastatic breast carcinoma such as axillary lymphadenopathy or other site of bony or body metastases when mammograms and breast US are negative. Also for patients with suspicious bloody or serous nipple discharge and negative mammograms and breast US. f) Peri-operative evaluation: to assess for residual disease. g) Pre-operative staging: to assess extent of disease in the affected breast and to screen for occult contralateral malignancy (expected in 3-6% of patients). Although the evidence for assessing extent of disease has shown that at least 16% of additional tumours are found in the affected breast, there is still insufficient evidence that it changes long-term patient outcome. h) Intervention: to guide an MRI interventional procedure such as biopsy or localization Biopsies MRI guided intervention is required when a lesion that looks suspicious on Breast MRI (BI-RADS® 4 or 5) does not have a sonographic correlate on MRI-directed US, or mammographic correlate. A suspicious lesion on MRI with no US or mammographic correlate requires tissue diagnosis. All centres providing Breast MRI service are required to provide MRI-guided biopsies, or to have an established referral pattern with a centre providing this service. Nipple Discharge Emerging evidence suggests that Breast MRI is a useful tool in the assessment of suspicious nipple discharge and may be performed in patients with negative mammograms and US, often demonstrating unexpected pathology. Additionally, MRI may be more widely accessible than galactography. NOTE: This guideline also includes sections on technical requirements for personnel, equipment, quality control, MRI protocols, biopsy performance

European Society of Breast Imaging (EUSOBI)	Mann, 2015 (251)	Breast MRI: EUSOBI recommendations for women's information	This document is written for the patients; further information is contained in the EUSOBI guideline (252) Indications for breast MRI Screening of women at high risk of breast cancer Preoperative staging of newly diagnosed breast cancer (ipsilateral and contralateral) Evaluation of the effect of neoadjuvant chemotherapy Evaluation of women with breast implants Occult primary breast carcinoma (search for breast cancer in patients with metastases and negative mammography and US) Suspected local recurrence Problem solving (equivocal findings at mammography/US) In premenopausal women, CE MRI is preferentially performed between days 7 and 14 of the menstrual cycle, when the background enhancement of the normal fibroglandular breast tissue is low, and hence abnormalities are better detected and false positives less frequent When the MRI-detected lesion is not detected with US and the indication for biopsy still stands, an MR-guided biopsy is indicated. In the case MR-guided biopsy cannot be performed (e.g., dedicated equipment not available; lesion site not accessible, such as those very close to the thoracic wall), computed tomography-guided biopsy or MR-guided presurgical localization may be performed. This guideline also provides technical details
European Society of Breast Imaging (EUSOBI)	Mann, 2008 (252)	Breast MRI: Guidelines from the European Society of Breast Imaging	The more recent version for women's information (251) is similar but less detailed Indications for Breast MRI Screening of women at high risk of breast cancer Inconclusive findings in conventional imaging Preoperative staging. Screening of the contralateral breast in patients with proven unilateral breast cancer; evaluation of cancer in patients with dense breasts or invasive lobular cancer The evaluation of therapy response in the neoadjuvant chemotherapy setting Unknown primary with diagnosed metastases in axillary lymph nodes, the supraclavicular lymph nodes, the bones, the liver, the brain, or the lungs Imaging of the breast after conservative therapy to evaluate residual disease, suspected recurrence, or screening Prosthesis imaging Before large adjustments to the surgical management are effectuated, histological analysis of MR-detected additional foci should be performed. Any site that performs breast MR examinations should either be able to perform MR-guided interventions in the breast or should be in close contact with a site that can perform these investigations for them.

European Society of Breast Cancer Specialists (EUSOMA)	Sardanelli, 2010 (250)	Magnetic resonance imaging of the breast: recommendations from the EUSOMA working group	A centre offering breast MRI should perform at least 150 examinations per year. If such a centre does not offer in-house breast MR-guided procedures, it should have an agreement with another institution which offers these procedures within an acceptable time interval. In order to reduce the risk of false positives, we recommend that premenopausal women undergo the examination ideally on day 6-13 of the menstrual cycle, even when oral contraception is used.15 In case of hormone replacement therapy, we recommend that MRI be performed at least 4 weeks after discontinuation of treatment.16 These schedule protocols can be waived in urgent cases Indications to preoperative MRI (1) Patients newly diagnosed with an invasive lobular cancer (LoE-2a, DoR-B). (2) Patients at high-risk for breast cancer (LoE-2b, DoR-B). (3) Patients under 60 years of age with discrepancy in size >1 cm between XRM and US with expected impact on treatment decision (LoE-2b, DoR-B). (4) Patients eligible for PBI on the basis of CBE and conventional imaging (LoE-3b, DoR-B). Other recommendations are: (5) Irrespective of whether the clinical team routinely uses preoperative MRI or not, women newly diagnosed with breast cancer should always be informed of the potential risks and benefits of preoperative MRI if this is under consideration prior to therapy (EPO). (6) Results of preoperative MRI should be interpreted taking into account CBE as well as XRM and US (whenever XRM and US are indicated); MRI findings with impact on patient treatment should be verified by percutaneous biopsy whenever possible (EPO). (7) Lesions visible on MRI alone require MR-guidance for needle biopsy with pathological assessment and, if needed, presurgical localization, implying the availability of specialized equipment and personnel15,17,80,81 (LoE-1a, DoR-A). (8) The total treatment delay due to preoperative MRI and possible workup should be no longer than 1 month (EPO). (9) Possible changes in therapeutic planning resulting from the findings of preoperative MRI should be decided by a multidisciplinary team composed by oncologists, pathologists, radiation oncologists, radiologists, and surgeons (EPO) Recommendations in neoadjuvant therapy (1) MRI does not have a role in the assessment of treatment options in patients with inoperable breast cancer at presentation (EPO). (2) Pretreatment breast MRI should be performed in patients with large potentially operable breast cancer before the first course of NAC, at the condition that performing MRI does not significantly postpone NAC initiation (LoE-1; DoR-A). (3) Post-NAC breast MRI should preferably be performed 2 weeks after the last NAC cycle and within 2 weeks before surgery (EPO); treatment delay due to preoperative MRI should not be larger than 1 month (as already stated at point 8 of Section 4.4, point 8). (4) Variations between pre- and post-NAC should be based on concomitant evaluation of both pre- and post-NAC MRI examinations; even very low enhancement located at the primary tumour site should be considered as a sign for residual disease (LoE-1, DoR-A). (5) Measurement of residual disease after NAC should be performed according to RECIST or WHO criteria; multifocal or multicentric disease should be evaluated by summing the largest diameter of the visible tumours165 (EPO). (6) Caution in interpreting MRI is recommended when patients are treated with taxane or bevacizumab containing regimens (EPO).

			(7) Presurgical issues such as verification of multifocal or multicentric disease etc. should be handled as explained in the paragraph on preoperative MRI; the ultimate surgical decision should be based on the relative volume of residual tumour compared to that of the affected breast and decided by a multidisciplinary team (EPO). (8) In poor responders to NAC, MRI generally confirms the results of clinical and conventional imaging evaluations and may, therefore, not be mandatory (EPO). Occult cancer (1) Breast MRI is indicated in presence of localized metastatic disease (typically, axillary lymphadenopathy) and negative CBE and conventional imaging (LoE-1b, DoR-A). (2) Breast MRI is not indicated when extensive metastatic disease exists and/or prognosis is poor, where knowledge of the site of the primary tumour is unlikely to influence the treatment options or the likely outcome (EPO). Nipple discharge (1) There is insufficient evidence of benefit to recommend the routine use of MRI in the clinical context of suspicious nipple discharge (EPO). (2) In countries where ductography is considered the routine test for suspicious nipple discharge, non-contrast T2-weighted and contrast-enhanced MRI can be considered if ductography fails for technical reasons or the patient refuses the procedure (LoE-3b, DoR-C). Inflammatory breast cancer (1) MRI should not be used for differential diagnosis of inflammatory breast cancers from acute mastitis before treatment (LoE-1b, DoR-A). (2) If after treatment of a presumed mastitis doubts remain about the presence of an underlying breast cancer, MRI can be considered (LoE-2b, DoR-C).
General breast cancer guideline, some MRI recommendations			
NCCN	Gradishar, 2021 (234)	NCCN clinical practice guidelines in oncology (NCCN guidelines)®. Breast cancer	• Breast MRI examinations are performed with IV contrast and should be performed and interpreted by an expert breast imaging team working in concert with the multidisciplinary treatment team. • Breast MRI examinations require a dedicated breast coil and breast imaging radiologists familiar with the optimal timing sequences and other technical details for image interpretation. The imaging centre should have the ability to perform MRI-guided needle sampling and/ or image-guided localization of MRI-detected findings • May be used for staging evaluation to define extent of cancer or presence of multifocal or multicentric cancer in the ipsilateral breast, or as screening of the contralateral breast cancer at time of initial diagnosis (category 2B). There are no high-level data to demonstrate that the use of MRI to facilitate local therapy decision making improves local recurrence or survival. • May be helpful for breast cancer evaluation before and after preoperative systemic therapy to define extent of disease, response to treatment, and potential for breast-conserving therapy.

			• May be useful in identifying otherwise clinically occult disease in patients presenting with axillary nodal metastases (cT0, cN+), with Paget disease, or with invasive lobular carcinoma poorly (or inadequately) defined on mammography, US, or physical examination. • False-positive findings on breast MRI are common. Surgical decisions should not be based solely on the MRI findings. Additional tissue sampling of areas of concern identified by breast MRI is recommended. • The utility of MRI in follow-up screening of patients with prior breast cancer is undefined. It should generally be considered only in those whose lifetime risk of a second primary breast cancer is >20% based on models largely dependent on family history, such as in those with the risk associated with inherited susceptibility to breast cancer.
NCCN	Bevers, 2020 (233)	NCCN clinical practice guidelines in oncology (NCCN guidelines)®. Breast cancer screening and diagnosis	MRI (optional) for nipple discharge with no palpable mass, age <30, Bi-RADS 1-3 Consider MRI for skin changes suspected as inflammatory breast cancer, Bi-RADS 1-3 or Bi-RADS 4-5 and benign on core needle biopsy MRI for axillary masses that are suspicious on mammogram + US and malignant on needle biopsy but with no breast mass
The Japanese Breast Cancer Society	Uematsu, 2020 (236)	The Japanese Breast Cancer Society Clinical Practice Guidelines for Breast Cancer Screening and Diagnosis, 2018 Edition	We advise using contrast-enhanced breast MRI in a diagnostic setting [SoR, 2; SoE, weak].
The Royal College of Radiologists, London	The Royal College of Radiologists, 2019 (227)	Guidance on screening and symptomatic breast imaging	MRI is indicated for staging of breast cancer: 1. If breast conservation is being considered and sizing is uncertain on clinical evaluation and conventional imaging (mammography and US) 2. If breast-conserving surgery is being considered for invasive cancer with a lobular component (invasive lobular carcinoma or mixed carcinomas with a lobular component)* 3. In mammographically occult tumours 4. Where there is suspicion of multifocal disease unconfirmed on conventional imaging 5. In the presence of malignant axillary node(s) with no primary tumour evident in the breast on conventional imaging 6. In Paget's disease of the nipple if breast conservation is being considered. *MRI to screen the contralateral breast in women with an invasive cancer with a lobular component is not recommended if mastectomy for the known cancer is planned (or has

			been performed). If gadolinium administration is contra-indicated, consider the combination of T2-weighted and diffusion-weighted imaging (DWI). Axillary US assesses nodal disease burden; documentation of the number of abnormal nodes demonstrated is good practice. The infraclavicular and supraclavicular fossae should also be scanned if there is a heavy nodal burden (>four obviously abnormal nodes). Core biopsy sampling is more sensitive than FNAC. Monitoring of response to neoadjuvant treatment: MRI is the most accurate imaging technique for baseline local staging and correlates best with pathological findings post-treatment. It is recommended at baseline and end of treatment to aid surgical planning. The use of an interim scan (after two or three cycles) aids prediction of response and will become of increasing importance in response-adapted therapy. Diffusion-weighted imaging (DWI) has the potential to be of use if protocols are standardized.
National Health Commission of The People's Republic of China	National Health Commission of The People's Republic of China, 2019 (229)	Chinese guidelines for diagnosis and treatment of breast cancer 2018 (English version)	Indications: 1) Unspecific results after mammography and breast US; 2) Preoperative staging and screening for contralateral tumours; 3) Evaluation of tumour response to neoadjuvant therapy; 4) Evaluation of the primary tumour in patients with suspected occult breast cancer; 5) Differential diagnosis between postoperative scar and cancer relapse; 6) Evaluation of residual disease in patients with positive margins after lumpectomy; 7) Evaluation of breast implants; 8) Screening in high-risk women; 9) Guided biopsy.
Malaysian Health Technology Assessment Section (MaHTAS)	Malaysian Health Technology Assessment Section (MaHTAS), 2019 (225)	Management of breast cancer, third edition	MRI may be considered in the following clinical situations in breast cancer: level III • invasive lobular cancer • LCIS • suspicion of multicentricity • genetic high risk • occult disease (T0 N+/M+ disease) - refer to Appendix 5 on TNM Classification • Paget's disease without routine radiological evidence of underlying tumour

			• breast implants/foreign bodies • diagnosis of recurrence in previous breast reconstruction • follow-up after neo-adjuvant therapy • dense breasts • pre-operative planning in breast-conserving surgery (BCS) Surgical decisions should not be based solely on the MRI findings. Additional tissue sampling of areas of concern identified by breast MRI is recommended.
ESMO	Cardoso, 2019 (232)	Early breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up	Imaging includes bilateral mammography and US of the breast and regional lymph nodes [8]. An MRI of the breast is not routinely recommended, but should be considered in cases of: • familial breast cancer associated with BRCA mutations [I, A]; • lobular cancers [I, A]; • dense breasts [II, B]; • suspicion of multifocality/multicentricity (particularly in lobular breast cancer) [I, A]; • large discrepancies between conventional imaging and clinical examination [III, B]; • before neoadjuvant systemic therapy, and to evaluate the response to this therapy [II, A]; and • when the findings of conventional imaging are inconclusive (such as a positive axillary lymph node status with an occult primary tumour in the breast) [III, A] [14]. • It may also be considered in case of breast implants Management of occult breast cancer: Routine diagnosis, apart from standard breast and axillary imaging, requires breast MRI and PET/CT (to exclude another primary tumour site). Neoadjuvant treatment: If BCS is anticipated, marking of the tumour site must be carried out [V, A] and pre- and post-treatment breast MRI should be carried out [II, A].
Breast Committee of the German Gynecological Oncology Group (Arbeitsgemeinschaft Gynäkologische Onkologie, AGO)	Ditsch, 2019 (235)	AGO recommendations for the diagnosis and treatment of patients with early breast cancer: Update 2019	MRI can be useful in high-risk patients and if clinical examination, mammography, US, and needle biopsy do not allow a definitive diagnosis (LoE 3b/GR B/ AGO+). Second-look US is recommended in cases of lesions detected by MRI only. MRI should not be used in general for preoperative staging purposes in the case of BCT. For some patients, e.g., with a reduced lesion detectability in mammography and US (detectability C–D), nipple involvement, lobular invasive cancer, suspicion of multilocular disease, and/or high risk, MRI can be considered (LoE 1b/GR B/AGO+/–) [32, 33]. The feasibility of performing MRI-guided vacuum-assisted biopsies is mandatory if suspicious lesions are detected by MRI of the breast. In axillary metastases of occult breast cancer, imaging should include mammography, US, and MRI.

German Society for Gynecology and Obstetrics (DGGG) and the German Cancer Society (DKG)	Wockel, 2018 (237) Updated version (German only), 2020 (228) [MRI recommendations unchanged]	Interdisciplinary screening, diagnosis, therapy and follow-up of breast cancer. Guideline of the DGGG and the DKG (S3-Level, AWMF REGISTRY NUMBER 032/045OL, December 2017) - Part 1 with recommendations for the screening, diagnosis and therapy of breast cancer	a) In a diagnostic setting, MRI with CM should be limited to those cases where a lesion cannot be adequately identified using conventional diagnostic methods (MG, US) or percutaneous biopsy. b) Carrying out MRI with CM prior to treatment to examine an already diagnosed breast cancer is only justified in specific exceptional cases. The decision that MRI with CM is indicated should be made during a multidisciplinary tumour conference. c) MRI with CM of the breast must only be carried out if an MRI-supported intervention can be carried out in the same centre or it is possible to access MRI-supported interventions, and the histological findings of the MRI intervention are presented to an interdisciplinary conference to document the outcome quality.
International conference at the Morgan Welch Inflammatory Breast Cancer Research Program of MD Anderson Cancer Center	Ueno, 2018 (240)	International consensus on the clinical management of inflammatory breast cancer from the Morgan Welch Inflammatory Breast Cancer Research Program 10th Anniversary Conference	MRI: For detecting a primary breast lesion (mass or non-mass enhancement), skin thickening, breast and chest wall edema, chest wall and nodal involvement and contralateral breast assessment. A proposed algorithm to be clinically validated in the future for clinical suspicion of IBC is breast MRI (to identify the primary breast lesion for US-guided biopsy and to detect skin lesions or skin enhancement suggesting tumour emboli in skin), US after MRI (to biopsy the most likely primary lesion detected on MRI and for locoregional nodal staging with possible nodal biopsy), PET/CT (for local and distant disease workup).
ACR	American College of Radiology, 2018 (238)	ACR appropriateness criteria. Breast imaging of pregnant and lactating women	Locoregional staging: It is well established that IV gadolinium chelates cross the placenta and enter the fetal circulation. Although there are no reported adverse fetal effects due to IV gadolinium in the pregnant mother, there is the potential for the dissociation of free toxic gadolinium ion with limited data in this patient population. Guidelines regarding gadolinium administration during pregnancy are outlined in detail in the ACR Manual on Contrast Media (258). Because of the concerns regarding gadolinium crossing the placenta and limited data regarding its safety in this setting, breast DCE-MRI is therefore not recommended in pregnant women. However, immediately following delivery or pregnancy termination, breast MRI is recommended for locoregional staging.
National Institute for Health Care Excellence (NICE)	NICE, 2018 (224)	Early and locally advanced breast cancer: Diagnosis and management. NICE guideline NG101	Do not routinely use MRI of the breast in the preoperative assessment of people with biopsy-proven invasive breast cancer or ductal carcinoma in situ (DCIS). [2009] 1.1.2 Offer MRI of the breast to people with invasive breast cancer: •if there is discrepancy regarding the extent of disease from clinical examination, mammography and US assessment for planning treatment •if breast density precludes accurate mammographic assessment •to assess the tumour size if breast-conserving surgery is being considered for invasive lobular cancer. [2009]

European School of Oncology (ESO) and the European Society of Medical Oncologists (ESMO); endorsed by the European Society of Breast Specialists (EUSOMA)	Paluch-Shimon, 2017 (242)	ESO-ESMO 3rd international consensus guidelines for breast cancer in young women (BCY3)	Diagnosis, imaging and staging in young women should follow standard algorithms consistent with older women. Additional consideration may be given to US and breast MRI in young women particular in the setting of very dense breast tissue or consideration of a genetic predisposition or other individuals at high risk (i.e., radiotherapy for childhood malignancy). (level of evidence IIC; Weak recommendation, low quality evidence) Timing of the menstrual cycle should be taken into account when planning and performing MRI (and mammography, if done) in order to optimize accuracy of imaging with optimal timing being in the first half of the menstrual cycle (day 7-10)
ACR	Expert Panel on Breast Imaging, 2017 (241)	ACR appropriateness criteria. Evaluation of nipple discharge	Although MRI or ductography is usually not appropriate as an initial examination, it may be useful when the initial standard imaging evaluation is negative. Contrast-enhanced breast MRI has high sensitivity for detecting benign papillary lesions as well as in situ and invasive carcinoma. Furthermore, MRI allows identification of index lesions in peripheral ducts that are beyond the area normally encompassed by terminal duct excision, ductogram, or targeted US
Focus on Controversial Areas Working Party of the Italian Senonetwork	Galimberti, 2016 (239)	Surgical resection margins after breast-conserving surgery: Senonetwork recommendations	Cites EUSOMA (250): Preoperative MRI is recommended in invasive lobular carcinoma, age <60 y with a difference in tumour size between mammography and US >1 cm and expected to impact treatment decision-making, or eligible for partial breast irradiation MRI should be used in cases meeting the EUSOMA criteria, or if there is an extensive intraductal component, or suspected multifocality
ESMO	Senkus, 2015 (231)	Primary breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up	An MRI of the breast is not routinely recommended, but should be considered in cases of familial breast cancer associated with BRCA mutations, breast implants, lobular cancers, suspicion of multifocality/multicentricity (particularly in lobular breast cancer), or large discrepancies between conventional imaging and clinical examination [III, B]. MRI may also be recommended before neoadjuvant chemotherapy, when evaluating the response to primary systemic therapy or when the findings of conventional imaging are inconclusive (such as a positive axillary lymph node status with an occult primary tumour in the breast) [III, A] Recommendations cite EUSOMA guideline (250)
U. K. Inflammatory Breast Cancer Working group	Rea, 2015 (230)	Inflammatory breast cancer: Time to standardize diagnosis assessment and management, and for the joining of forces to facilitate effective research	Staging and response assessment: We have recommended a combination of mammography and US as minimum requirements for radiological imaging of the breast. MRI is also recommended, as this is the most accurate technique for characterization and diagnosis of the primary lesion. In addition, it is accepted that in comparison with conventional imaging, MRI is the most accurate way of assessing both interim and final responses to treatment, which can help to guide therapy (for e.g., where breast conservation may be a possibility or to demonstrate persistent involvement of the chest wall musculature). Assessment of response to primary systemic chemotherapy should include a combination of physical examination and radiological assessment. MRI is recommended for baseline evaluation and response assessment
National Clinical Effectiveness Committee, Ireland	National Clinical Effectiveness Committee, 2015 (226)	Diagnosis, staging and treatment of patients with breast cancer	2.2.4.1 The routine use of MRI of the breast is not recommended in the preoperative assessment of patients with biopsy-proven invasive breast cancer or ductal carcinoma in situ. (B)

		National Clinical Guideline No. 7	2.2.4.2 Offer MRI of the breast to patients with invasive breast cancer, if there is discrepancy regarding the extent of disease from clinical examination, mammography and US assessment for planning treatment, or if breast density precludes accurate size assessment. (B) 2.2.4.3 In patients with invasive lobular cancer, MRI can be considered to assess tumour size, if breast conserving surgery is a treatment option. (C) 2.2.5.1 Breast MRI is indicated in the clinical setting of occult primary breast cancer (typically, axillary lymphadenopathy) and following negative clinical breast examination and negative conventional imaging. (B) 2.2.6.1 In the setting of negative conventional imaging, MRI can facilitate treatment planning for patients with Paget's disease. (C)
Surgical planning: reconstruction			
ACR	Oliva, 2017 (253)	ACR appropriateness criteria® imaging of deep inferior epigastric arteries for surgical planning (breast reconstruction surgery)	In preoperative planning before breast reconstruction using DIEP flap, CTA [CT angiography] of the abdomen and pelvis with IV contrast is the first-line imaging modality, and MRA [MR angiography] of the abdomen and pelvis without and with IV contrast is a reasonable alternative. CTA has effective radiation dose of 30-100 mSV, whereas MRI is 0 mSv
Technical standards and details			
ACR	American College of Radiology Committee on Drugs and Contrast Media, 2021 (258)	ACR manual on contrast media	
ACR	American College of Radiology Committee on MR Safety, 2020 (257)	ACR manual on MR safety. Version 1.0, 2020	
ACR	American College of Radiology, 2020 (254)	Complete accreditation information: Breast MRI	
ACR	Amurao, 2019 (262)	ACR–AAPM technical standard for diagnostic medical physics performance	

		monitoring of magnetic resonance (MR) imaging equipment	
ACR	Covington, 2018 (8)	American College of Radiology accreditation, performance metrics, reimbursement, and economic considerations in breast MR Imaging	
ACR	American College of Radiology, 2018 (260)	ACR practice parameter for the performance of contrast-enhanced magnetic resonance imaging (MRI) of the breast	
ACR	American College of Radiology, 2017 (255)	ACR appropriateness criteria®: Monitoring response to neoadjuvant systemic therapy for breast cancer	
ACR	American College of Radiology, 2016 (259)	ACR practice parameter for the performance of magnetic resonance imaging-guided breast interventional procedures	
ACR Committee on Quality Assurance in Magnetic Resonance Imaging	American College of Radiology Committee on Quality Assurance in Magnetic Resonance	Magnetic resonance imaging. Quality control manual, 2015	

	Imaging, 2015 (256)		
ACR	Edwards, 2013 (264)	Updates and revisions to the BI-RADS magnetic resonance imaging lexicon	
ACR	DeMartini, 2013 (263)	Breast magnetic resonance imaging technique at 1.5 T and 3 T: requirements for quality imaging and American College of Radiology accreditation	
ACR	American College of Radiology, 2013 (261)	ACR BI-RADS atlas. Breast imaging reporting and data system. 5th ed	
International Breast DWI working group, European Society of Breast Imaging (EUSOBI)	Baltzer, 2020 (266)	Diffusion-weighted imaging of the breast-a consensus and mission statement from the EUSOBI International Breast Diffusion-Weighted Imaging working group	Diffusion-weighted imaging The goals of the group are: • To promote the integration of DWI into clinical practice by issuing consensus statements and initiate collaborative research where appropriate • To define standards and provide practical guidance for clinical application of DWI • To develop a standardized and translatable multisite multivendor quality assurance protocol, especially for multisite research studies • To find consensus on optimal methods for image processing/analysis, visualization, and interpretation • To work collaboratively with system vendors to improve breast DWI sequences
European Society of Breast Imaging (EUSOBI)	Bick, 2020 (265)	Image-guided breast biopsy and localization: recommendations for information to women and referring physicians by the European Society of Breast Imaging	This is an update of the 2007 EUSOBI guideline (446) Image-guided breast biopsy techniques and imaging guidance MRI-guided VAB is a safe and accurate procedure that is mandatory when suspicious lesions are visible on MRI only

Breast Imaging Working Group of the German Radiological Society	Breast Imaging Working Group of the German Radiological Society, 2014 (268)	Updated recommendations for MRI of the breast	Recommendations describe the minimum requirements for acquiring high-quality MRI images of the breast
[European consensus conference, Germany, 2006]	Heywang-Kobrunner, 2009 (267)	Interdisciplinary consensus on the uses and technique of MR-guided vacuum-assisted breast biopsy (VAB): results of a European consensus meeting	Several consensus recommendations on MRI-guided vacuum-assisted breast biopsy

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Appendix F. Advanced Imaging and Contrast Agents

Types of MRI and Other Imaging

Contrast-enhanced MRI (CE-MRI), used together with unenhanced T2-weighted images, is the most widely used type of MRI, providing primarily morphological and some functional information about tumour perfusion and vascularity. Contrast agents, mainly gadolinium-based, are used; there is some concern about accumulation in the brain after multiple administrations, and allergy/sensitivity in a minority of patients. Nephrogenic systemic fibrosis (NSF) may occur in patients with acute kidney injury or severe chronic kidney disease (258).

Diffusion-weighted imaging (DWI) is based on a difference in diffusion of water molecules, and the apparent diffusion coefficient (ADC) is reported. Malignant tissue shows restricted diffusion and a lower ADC (271). Contrast agents are not required, although if DWI is conducted together with CE-MRI, the contrast agent does not negatively affect performance.

Accelerated MRI appears equivalent (not inferior) to MRI, with shorter machine time and interpretation time. Abbreviated and accelerated MRI allow shorter acquisition and interpretation times than standard MRI (272). The abbreviated MRI consists of a single early dynamic contrast-enhanced series, providing morphologic evaluation but not kinetic assessment (447). Studies have shown it comparable to the full protocol for cancer screening (273). Accelerated MRI (ultrafast MRI) acquires DCE-MRI images in a very short time and therefore provides kinetic assessment comparable to standard MRI. An example is time-resolved angiography with stochastic trajectories (TWIST) developed by Mann et al. (274). Applying accelerated MR techniques could enhance the diagnostic potential of abbreviated MRI while maintaining the short study time.

Magnetic resonance spectroscopy (most commonly proton MR spectroscopy [^{1}H-MRS or MRSI] evaluating the total choline peak [tCHO] as a biomarker of malignancy) may be useful but the field is not as advanced, and currently is not as good as MRI for small lesions (<1 cm). Advances in data management (e.g., use of derivative fast Padé transformation) as proposed by Belkic et al. (275) may resolve the tCHO components and discrimination of benign/malignant lesions. ^{31}P-MRSI and ^{23}Na-MRI are emerging.

Use of CE-MRI together with other functional imaging, especially DWI-MRI or ^{1}H-MRS is sometimes referred to as multiparametric MRI (mpMRI). This technique visualizes and quantifies the functional processes of cancer development and progression, improves diagnostic accuracy, and reduces need for biopsies (276).

Contrast-enhanced spectral mammography (CESM) or contrast-enhanced digital mammography appears an improvement on mammography, although with higher radiation exposure. It may be useful if there are contraindications to MRI or MRI is not available, and there may be differences in patient preferences. Test times are longer than conventional mammography and shorter than conventional MRI. As illustrated in the 2018 systematic review and meta-analysis by Zhu et al. (448), several studies have compared CESM to MRI.

Digital breast tomosynthesis (DBT; also referred to as tomosynthesis or 3-D mammography) may have better ability than conventional digital mammography to detect cancer but still has limitations. In a comparison of DBT and mammography in 300 breast cancers (288 in dense breasts), 13.3% were detected only by DBT, 63.7% with both DBT and digital mammography, and 23% not detected by either (277). The ASTOUND trial conducted adjunct screening with both DBT and ultrasound after negative screening mammography in 3,231 women with dense breasts (BI-RADS 3 or 4) (449). The supplemental screening found 24 additional malignancies, of which 12 were detected by both DBT and ultrasound, 1 only by DBT, and 11

only by ultrasound. The ACRIN EA1141 trial used both abbreviated breast MRI and DBT in 1444 women with dense breast undergoing screening and found MRI to be more sensitive (95.7% vs. 39.1%) based on a reference standard of biopsy and interval cancers within 13 months that identified 17 invasive cancers and 6 DCIS (450). MRI detected 17 invasive cancers and 5 DCIS while DBT detected 7 invasive cancers and 2 DCIS. If DBT is used in addition to 2-D mammography the radiation dose will be higher; however, it is possible to recreate the 2-D image from the 3-D one and then the overall radiation exposure may be the same or only slightly higher than 2-D mammography. The retrospective screening study by Conant et al. with 96,269 women (278) found DBT associated with increased specificity and cancer detection, especially in women aged 40-49. The randomized To-Be screening trial (n=28,749) is ongoing (279, 280) and so far has found equivalent radiation exposure and detection rates but lower recall and higher positive predictive value with tomosynthesis compared to digital mammography; data on interval cancers is planned but not yet available. The Tomosynthesis Mammographic Imaging Screening Trial (TMIST), funded by the National Cancer Institute is another randomized trial that is underway. In blinded evaluation of cases with cancer or suspicious lesions, more cancers were detectable with DBT than digital mammography (281, 282).

Ultrasound instead of mammogram is sometimes used in women age <40 with palpable lumps as it is more sensitive, less costly, more comfortable, and doesn't expose patients to ionizing radiation (as with mammography). Ultrasound directed biopsy after MRI is routine, however Lee et al. (283) found 26% of such biopsies were localized to a site distinct from the one identified on MRI. Other papers suggest that if MRI and biopsy are discordant, the reason may be that the lesion was not sampled (i.e., the wrong area was biopsied). The correlation between prone MRI and supine ultrasound may be challenging and clip placement directed by MRI following ultrasound biopsy should be encouraged to provide optimal MRI correlation.

PET/CT is less sensitive but more specific than MRI for detection of breast lesions. Integrated information from PET/MR improved detection compared to either technique alone. PET/CT can detect N3 lymph node disease and distant metastasis. A few studies with dedicated breast PET (MAMmography with Molecular Imaging [MAMMI] dedicated breast PET [dbPET]) found better sensitivity and suggest a combination with MRI may provide the best diagnostic performance. A comparison of PET/CT and MAMMI-PET [db-PET] (284) found prone imaging better than supine, and db-PET with better sensitivity (96.8%) and tumour size/quadrant diagnosis. Ribelles et al. (451) found PET/CT found more axillary and internal nodal disease and distant metastasis than MRI, and combined PET/CT + MRI better sensitivity, positive predictive value and negative predictive value than either alone. Dominguez et al. (285) also found dbPET had better specificity (93% dbPET vs. 54% MRI). Pinker-Domenig et al. (286) found dedicated PET/CT plus MRI had 100% sensitivity and 90% specificity; 90% of benign lesions did not need biopsy. Katja et al. (287) found similar results, and improved lymph node metastasis detection (87% vs. 70% with MRI alone). Hybrid PET-MR with dedicated breast coils allows better staging and shorter study time than doing PET/CT and MRI separately (452). Simultaneous PET and MRI is reviewed by Pujara et al., 2019 (288). PET-MRI has lower radiation exposure and better contrast but has a limited field of view compared to PET/CT. PET when performed on a dedicated breast PET machine is sometimes referred to as positron emission mammography (PEM).

Gamma imaging (scintimammography, molecular breast imaging) may be promising (289-293). It is not affected by breast density and can find a similar level of additional cancers as MRI but has worse positive predictive value than MRI. Radiation exposure is of concern and improvements to reduce this are being investigated.

Gadolinium Contrast Medium Selection and Adverse Effects

Various gadolinium-based contrast agents are used for CE-MRI (294-296), as summarized in the following table. Gadobenate dimeglumine has greater T1 relaxivity and provides more pronounced contrast enhancement at the same delivered dose as compared with other agents (295). Studies found it to have better sensitivity and specificity compared with gadopentate dimeglumine (297-301). Gadobutrol and gadoterate meglumine are the other forms generally used, although direct comparison is limited; a clinical trial of these two is ongoing (https://clinicaltrials.gov/show/nct03730051). One study using 3 T MRI found gadobenate dimeglumine better than gadoterate meglumine (302). Two small studies found gadobutrol noninferior to gadobenate for detection and sensitivity (303) and not different in the time-intensity curve (304). Comparison of gadobutrol and gadoterate meglumine found the former resulted in higher relative enhancement and less washout in malignant lesions (305). CE-MRI using gadobutrol has been evaluated in the multicentre prospective GEMMA1 and GEMMA 2 trials and found to provide high sensitivity and specificity (306), and was also used in 70% of patients in the MIPA trial (154).

Table F1. Gadolinium-Based Contrast Agents (258, 294-296, 311, 453-456)

Name	Chemical Abbreviation	Trademark	Type	Notes
Gadobutrol	Gd-BT-DO3A	Gadovist; Gadavist	Macrocyclic, non-ionic	Above average relaxivity
Gadoterate meglumine; Gadoteric acid	Gd-DOTA	Dotarem; Clariscan	Macrocyclic, ionic	
Gadoteridol	Gd-HP-DO3A	ProHance	Macrocyclic, non-ionic	Below average relaxivity
Gadobenate dimeglumine	Gd-BOPTA	MultiHance	Linear, ionic	Highest relaxivity; linear but similar NSF risk as macrocyclics; suspended in EU in 2017 except for liver
Gadopentetate dimeglumine	Gd-DTPA	Magnevist	Linear, ionic	Oldest agent, below average relaxivity; increased risk of NSF; use suspended in EU in 2017 except intra-articular; discontinued in USA
Gadoxetic acid disodium; Gadoxetate	Gd-EOB-DTPA	Primovist; Eovist	Linear, ionic	Designed for liver imaging; not used in breast imaging
Gadodiamide; Gadodiamide hydrate	Gd-DTPA-BMA	OmniScan	Linear, non-ionic	Low stability and increased NSF risk; use suspended in EU
Gadofosveset	Gd-DTPA-diphenyl cyclohexyl-phosphate	Ablavar; Vosovist	Linear, ionic	Production discontinued 2017
Gadoversetamide	Gd-DTPA-BMEA	OptiMARK	Linear, non-ionic	Production discontinued 2017; increased risk of NSF

Two studies reported acute adverse reactions in 0.3% of patients (294, 307). Reactions are generally allergic and may be more frequent in those with seasonal allergic rhinitis. Patients with allergy to one gadolinium-based agent may not exhibit allergy to a different one (294, 308, 309). NSF has been observed mainly in patients with advanced renal failure (295). The US FDA indicates gadolinium retention is highest with linear agents (especially gadodiamide and Gadoversetamide) and lowest with macrocyclic agents (456). The American College of Radiology (258) groups agents according to NSF potential, with the macrocyclic agents and gadobenate dimeglumine the lowest, gadoxetate disodium with limited data, and the other linear agents as having the most cases of NSF (258). The Canadian Association of Radiologists (310) refers to this in their updated guideline on use of gadolinium agents in patients with kidney disease (310). Gadolinium deposition, especially after multiple MRIs, has been reported in the brain, although it is unknown whether this is harmful (307). Use of linear contrast agents (except for specific applications) was suspended in the EU due to concerns of brain deposition (311) Guidelines such as The ACR Manual on Contrast Media (258) cover these topics in more detail.

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Appendix G. Risk of Bias Assessment

The risk of bias for randomized studies was assessed using the Cochrane Risk-of-Bias (RoB) tool (revised version RoB 2) (11, 12). An example of the evaluation for the outcome of mastectomy is indicate below. Assessment of other outcomes is summarized in the Results section.

Risk of Bias for RCTs, Mastectomy Outcome

Unique ID	Study ID	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall
1	IRCIS	MRI in BCS	no MRI	Mastectomy rate	NA	-	+	+	+	+	-
2	Turku	MRI in BCS	no MRI	Mastectomy rate	NA	-	+	+	+	+	-
3	Breast-MRI	MRI in BCS	no MRI	Mastectomy rate	NA	-	+	+	+	+	-
4	COMICE	MRI in BCS	no MRI	Mastectomy rate	NA	-	!	+	+	!	-
5	POMB	MRI	no MRI	Mastectomy rate	NA	-	-	+	+	+	-
6	Monet	MRI	no MRI	Mastectomy rate	NA	+	!	!	+	!	-

+ Low risk
! Some concerns
- High risk

D1 Randomisation process
D2 Deviations from the intended interventions
D3 Missing outcome data
D4 Measurement of the outcome
D5 Selection of the reported result

The risk of bias for non-randomized studies was assessed using ROBINS-I (13, 14). The table below is a generic evaluation for all included studies. Data that need to be evaluated individually are indicated and may be found in Tables 1-4.

Risk of Bias for Non-Randomized Studies.

1. Confounding	
1.1 Potential for Confounding	yes
1.2 Analysis based on splitting participants' follow-up time according to intervention received	no
1.3 Treatment discontinuation or switches affect outcome	n/a
Baseline Confounding (answer if no to 1.2)	
1.4 Appropriate analysis for confounding	To evaluate
1.5 Confounders measured validly and reliably	To evaluate
1.6 Controlled for post-intervention variables	n/a
Time-Related Confounding (answer if yes to 1.2 and 1.3)	
1.7 Controlled for confounding domains and time-varying confounding	n/a
1.8 Confounders measured validly and reliably	n/a
ROB confounding	low to serious
2. Selection Bias [applies only if participant selection based on characteristics observed after the intervention started]	
2.1 Selection of pts was based on observations after intervention	no
if 2.1 is yes	
2.2 Post-intervention variables associated with intervention	n/a
if 2.2 is yes	
2.3 Post-intervention variables influenced by outcome	n/a
If 2.1 is no	
2.4 Start of intervention and follow-up coincide	n/a
2.5 Appropriate adjustment for section bias	n/a
ROB selection	low
3. Classification Bias	
3.1 Intervention well defined	Yes except database studies
3.2 Information on intervention recorded at start of intervention	yes
3.3 Intervention Status unaffected by outcome risk	yes
ROB Measurement	low or moderate
4. Departure from Interventions	
Effect of Assignment	
4.1 Deviation in intervention is beyond usual practice	n/a
4.2 Were deviations unbalanced and likely to effect outcome	n/a
Effect of starting and adhering to intervention	

4.3 Balance in co-interventions (e.g., adjuvant therapy)	n/a
4.4 Was implementation failure minor	n/a
4.5 Low rate of switches to other interventions	n/a
4.6 Appropriate adjustment techniques to correct for issues	n/a
ROB Departure	low, n/a
5. Missing Data	
5.1 Outcome data for all/nearly all participants	To evaluate
5.2 Excluded due to missing data on intervention status	yes
5.3 Excluded due to other missing data (confounders)	To evaluate
5.4 Proportions and reasons for missing data similar	To evaluate
5.5 Appropriate statistics for missing data	To evaluate
ROB missing data	low to serious
6. Measurement of Outcomes	
6.1 Outcome measure objective	yes
6.2 Assessors aware of intervention	yes
6.3 Assessment methods comparable across groups	yes
6.4 Systematic errors in measurement of outcome	no
ROB Measurement	low
7. Selection of results to report	
7.1 Multiple outcome measurements within the outcome domain	no
7.2 Multiple analyses of intervention-outcome relationship	no
Effect likely to be reported for different subgroups	no
ROB Selection	low
OVERALL ROB	low to serious

Legend	
	Same for all studies
	To evaluate
	RoB rating