

MAGNETIC RESONANCE IMAGING FOR BREAST CANCER SCREENING, PRE-OPERATIVE ASSESSMENT, AND FOLLOW-UP

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The recommendations contained in this guideline are a consensus of the Alberta Provincial Breast Tumour Team and represent a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

BACKGROUND

Diagnostic imaging is now an essential part of breast cancer screening, assessment, and follow-up. Mammography has been the gold standard for screening and surveillance. Ultrasound is an accepted adjunct to mammography in the diagnostic work-up of suspicious lesions. Increasingly, magnetic resonance imaging (MRI) is also being used in the work-up and surveillance of breast cancer. Given the issues of accuracy, access and cost, the appropriate use of MRI in the context of breast cancer requires clarification and ongoing review.

GUIDELINE GOALS AND OBJECTIVES

To develop a consensus based guideline, structured on evidence from existing practice guidelines, for using magnetic resonance imaging within the context of breast cancer.

GUIDELINE QUESTIONS

1. Should MRI be used for breast cancer screening?
2. Should MRI be used for preoperative assessment of breast cancer?
3. Should MRI be used for the follow up of patients treated for breast cancer?
4. In which patients is the use of MRI appropriate?
5. Are there other considerations?

DEVELOPMENT PANEL

This guideline was reviewed and endorsed by the Alberta Provincial Breast Tumour Team. Members of the Alberta Provincial Breast Tumour Team include medical oncologists, radiation oncologists, surgical oncologists, nurses, pathologists, pharmacists, and radiologists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Breast Tumour Team and a Knowledge Management Specialist from the Guideline Utilization Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the [Guideline Utilization Resource Unit Handbook](#).

SEARCH STRATEGY

A systematic search for relevant, existing practice guidelines, systematic reviews, health technology assessments, meta-analyses, and randomized controlled trials was conducted of: MEDLINE, CINAHL, EMBASE, CancerLit, the Cochrane Library, and the National Guidelines Clearinghouse.

The search terms included “breast neoplasm” and “magnetic resonance imaging.” The search covered the period between 1965 and July 2010. A total of 95 articles were returned. The majority was review articles; there were seven clinical trials, nine meta-analyses, 12 comparative studies, and nine guidelines.

There is a paucity of data on many of the uses of MRI in the context of breast cancer. As such, the guideline developers have chosen to make provincial recommendations for use of MRI, by adapting from existing evidence-informed guidelines elsewhere. A recommendations matrix highlighting key guidance from nine existing guidelines on the use of MRI for breast cancer assessment, staging, and follow-up, is included in the Appendix.

RECOMMENDATIONS

Screening

The following sources were considered in developing the screening recommendations: the *Alberta Breast Cancer Screening Program*,¹ the *National Comprehensive Cancer Network*,^{2,3} the *National Institute for Health and Clinical Excellence*,⁴ *Cancer Care Ontario*,⁵ the *American Cancer Society*,⁶ and the *American College of Radiology*.⁷

Mammography is the recommended modality for screening breast cancer in the general population of asymptomatic women.^{8,9}

- The Alberta Breast Cancer Screening Program¹ recommends:
 - *Encouraging eligible women age 50 to 69 to have a screening mammogram every two years,*
 - *Advising them of their results, and*
 - *Reminding them if they are overdue for a repeat screening.*
 - *Women aged 40-49 and over 70 may be referred to the Program by a family physician.*

MRI should be used in addition to mammography, at an interval of every 12 months, for screening high-risk category patients; these include women who:^{2,3,4,7}

- Have known personal history of deleterious mutation(s) in either BRCA1, BRCA2, TP53 or PTEN.
- Have never been tested personally but have a first degree relative with known BRCA1, BRCA2, TP53 or PTEN.
- Have a personal lifetime risk of developing breast cancer of 20-25 percent or more according to models that are largely dependent on family history.
- Are under 50 years of age and have received radiation treatment to the chest between ages 10 and 30 (e.g. thoracic radiation therapy for Hodgkin's disease)

A more detailed guideline, *Risk Reduction and Surveillance Strategies for Individuals at High Genetic Risk for Breast and Ovarian Cancer*, developed by Alberta Health Services in 2008 is available at the following website: [http://www.calgaryhealthregion.ca/breasthealth/HBOCFullApril2008\[1\]\[2\]\[1\].pdf](http://www.calgaryhealthregion.ca/breasthealth/HBOCFullApril2008[1][2][1].pdf).¹⁰

There is **insufficient** evidence to recommend routine use of MRI screening in women who:^{5,6,7}

- Have a lifetime risk of breast cancer of 15–20 percent, as defined by models that are largely dependent on family history.
- Have only had lobular carcinoma in situ (LCIS) or atypical lobular hyperplasia (ALH).
- Have only had atypical ductal hyperplasia (ADH).
- Have heterogeneously or extremely dense breasts on mammography with no other risk features.
- Have personal history of breast cancer, but do not otherwise fit into the high-risk category as noted above.

Pre-operative Assessment

The following sources were considered in developing the pre-operative assessment recommendations: the *National Comprehensive Cancer Network*^{2,3} and *Cancer Care Ontario*.⁵

Pre-operative MRI may be considered in the following circumstances:

- Biopsy proven axillary nodal adenocarcinoma with no primary identified on mammography, ultrasound, and physical examination.

- Discordant clinical and mammogram/ultrasound findings.

Pre-operative MRI may be used in the following situations where the patient desires breast conserving surgery and:^{2,3,10}

- There is high risk for multifocal/multicentric disease.
- The extent of disease is unclear.

MRI may be used for breast cancer evaluation before, during and after neoadjuvant therapy to help evaluate response to systemic treatments.^{11,12}

- MRI may overestimate response to neoadjuvant chemotherapy and should not be used to plan post-chemotherapy breast conserving surgery.
- MRI accurately predicts lack of response to neoadjuvant chemotherapy and may be used to support a change in therapy.

Problem Solving

The following sources were considered in developing the recommendation on problem solving: the *National Institute for Health and Clinical Excellence*,⁴ the *BC Cancer Agency*,¹³ and the *Scottish Intercollegiate Guidelines Network*.¹⁴

MRI may be considered only after high quality mammogram and ultrasound have been carried out and the results are inconclusive or discordant. MRI **should not** be used in lieu of biopsy if more appropriate or in cases where clinical and radiological suspicion is low.

MRI is not recommended for the routine screening of patients with nipple discharge.

Follow-up

The following recommendation has been adapted from the *National Comprehensive Cancer Network*.^{2,3}

There is **insufficient** evidence to recommend MRI for follow-up screening of the ipsilateral and contralateral breast of women with prior breast cancer unless they are in the high-risk category, as per the recommendations in the section on *Screening*.

Operational Considerations

The following recommendations have been adapted from the *National Comprehensive Cancer Network*.^{2,3}

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.

Breast MRI examinations should be performed and interpreted by an experienced radiologist with training in breast MRI, working in concert with the multidisciplinary treatment team.

Patients meeting the criteria for MRI should be referred to a centre with an MRI machine that has been configured with a dedicated breast coil.

DISCUSSION

Screening

Several meta-analyses have examined the sensitivity and specificity rates of MRI. Warner, et al. (2008),¹⁵ conducted a meta-analysis of 11 prospective studies to compare the sensitivity and specificity of mammography alone, MRI alone, and mammography plus MRI in patients with known BRCA mutations and/or patients with various family history criteria but no known mutation (median age, 40-47 years). The analysis included 15,496 mammographies, 15,576 MRIs, and 6,781 mammography plus MRI screenings and revealed sensitivity and specificity rates of 39% and 95%, respectively, for mammography in BI-RADS 3+ patients (32% and 98.5%, respectively, in BI-RADS 4+ patients) versus 77% and 86%, respectively, for MRI in BI-RADS 3+ patients (75% and 96%, respectively, in BI-RADS 4+ patients). The combined (mammography plus MRI) rates were 94% and 77%, respectively, in BI-RADS 3+ patients (84% and 95%, respectively, in BI-RADS 4+ patients).

Another meta-analysis¹⁶ of nine prospective studies and one retrospective study evaluating the use of MRI for screening of women at high risk for breast cancer also showed sensitivity rates ranging from 71-100% for MRI. Thus, the mean positive predictive value of biopsies resulting from a positive MRI screen was 45% (range, 17-89%), which is close to or exceeds the 25-40% desirable positive biopsy rate range recommended by the ACR BI-RADS.¹⁷ MRI was also shown to detect unsuspected malignancies in the ipsilateral and contralateral breasts as well as malignancies in patients with metastatic axillary adenocarcinoma and unknown primary at rates of 15.9%, 4.4%, and 60.9%, respectively.

An analysis of the correlation between mammography and MRI in women at increased risk of developing breast cancer revealed correlation coefficients ranging from -0.38 to 0.18, among seven included studies. In all but one study, the 95% confidence interval for the correlation coefficient included 0.0, indicating no significant correlation;¹⁸ however, because the sensitivity of combined mammography and MRI is higher than each modality alone,¹⁵ MRI alone is not recommended for screening for high risk women and should always be used in conjunction with mammography. Using both tests for breast cancer screening is likely to improve the early detection of breast cancer in women at increased risk.¹⁸ Prior to partaking in a high risk screening program using MRI, patients should be made aware of the risk of false positives.

In women with newly diagnosed invasive breast cancer, there is insufficient evidence to recommend routine MRI unless there is a specific problem to be addressed. MRI has been used to screen for contralateral lesions. A systematic review and meta-analysis of 22 studies revealed a positive predictive value of 47.9% (95% CI, 31.8% to 64.6%) and a sensitivity (true positive to false positive ratio) of 0.92 (95% CI, 0.47 to 1.82) for MRI in this setting. However, caution is warranted before recommending that this group of women undergo routine contralateral MRI, as 35.1% of the MRI-detected cancers were ductal carcinoma in situ and the majority were stage pTis or pT1 and node negative; nevertheless, many women were reported as having undergone contralateral mastectomy.¹⁹ Women should be informed that MRI does not reliably distinguish benign from malignant findings and that they may be at risk of additional investigations or unnecessary surgery, as a result of the MRI findings.

Pre-Operative Assessment

Despite the high sensitivity rates reported for MRI, there is a need to reduce false positive rates in MRI detection. A meta-analysis²⁰ of 19 retrospective and prospective studies that examined MRI detection or accuracy in local staging (or in determining disease extent) in women with proven or suspected breast cancer (n = 2,610) showed that the diagnostic odds ratio (a measure of both sensitivity and specificity)

was 88%, while the area under the curve (a global measure of accuracy) was 96%. However, the positive predictive value (a ratio of true positive results to all positive results) was only 66% (95% CI, 52-77%). This resulted in a change in surgical management for patients with multifocal/multicentric histologically-proven cancer from wide local excision (WLE) to mastectomy of 8.1% (95% CI, 5.9-11.3%) and from WLE to more extensive surgery (i.e. wider/additional excision or mastectomy) of 11.3% (95% CI, 6.8-18.3%). In patients who did not have additional malignancy on histology (false positive detection), a change from WLE to mastectomy of 1.1% (95% CI, 0.3-3.6%) and from WLE to more extensive surgery of 5.5% (95% CI, 3.1-9.5%) was made.

A more recent comparative study by Pengel, et al. (2009)²¹ showed that in women with invasive breast cancer, the rate of incomplete tumour excisions in wide local excisions was not significantly different among 176 patients eligible for breast-conserving therapy (on the basis of conventional imaging and palpation only) versus 173 who had an additional preoperative MRI (19.4% vs. 13.8%, respectively; P = 0.17). The large COMICE trial²² showed that the addition of MRI to conventional assessment (e.g. mammography, ultrasound, and physical exam) was not significantly associated with a reduction in re-excision rates (odds ratio 0.96, 95% CI 0.75-1.24; p=0.77); however, breast cancer patients with all histologies were included in the analysis and other research has shown a decrease in excision rates.²³ The utility of MRI in this setting may be limited to patients with certain breast cancer subtypes; for example, Mann, et al. (2008) showed that in patients with invasive lobular carcinoma, the sensitivity of MRI was 93.3% and correlation with pathology ranged from 0.81 to 0.97; MRI resulted in a change in surgical management in 28.3% of cases.²⁴ In patients with occult breast cancer (i.e. no primary tumour identified on physical examination, mammography or ultrasound), MRI was shown to detect the tumour in more than two thirds of patients and provided the possibility of breast conserving surgery in one third of patients.²⁵ However, in patients with ipsilateral breast tumor recurrence, MRI evaluation in the planning of initial lumpectomies was not associated with improved local outcomes, as it did not influence the achievement of negative margins and was not associated with lower rates of re-excision (MRI: 11.8% versus no-MRI: 13.3%; P=0.50).²⁶ Until more conclusive data is available, surgical decisions should not be based solely on MRI findings.

MRI has demonstrated high specificity but a low sensitivity in assessing response to neoadjuvant chemotherapy.¹¹ MRI has been shown to accurately evaluate the size of non-responders to neoadjuvant chemotherapy ($r > 0.87$)^{22,27,28,29} Compared to ultrasound or physical exam, MRI was found to correlate most closely with pathologic tumour size ($r = 0.749$) in breast cancer patients ($n = 68$) who underwent MRI, ultrasound, and physical exam prior to the start of neoadjuvant chemotherapy and one week after completion of treatment.³⁰ However, five out of six smaller studies^{31,32,33,34,35,36} conducted in patients with locally advanced breast cancer have provided no clear evidence that MRI is advantageous over physical examination, for assessing tumour response. An ongoing study at the Cross Cancer Institute in Edmonton, Alberta is collecting data on the use of MRI in this setting and may be able to provide clarification once the data have been analyzed. In the mean time it is recommended that, although MRI may be used support a change in therapy upon detecting a non-response to neoadjuvant chemotherapy, it should not be used to plan post-chemotherapy breast conserving surgery.¹²

Problem Solving

Breast MRI is often used to further assess equivocal mammographic and ultrasound findings. The use of breast MRI in this mode, over guided biopsy or short term follow-up, often depends on the particular case, as well as the preferences of the radiologist, patient, primary physician, or surgeon. The use of breast MRI as a means for problem-solving has been supported in by several other organizations, including the National Institute for Health and Clinical Excellence,⁴ the BC Cancer Agency,¹³ and the Scottish

Intercollegiate Guidelines Network.¹⁴ These guidelines specifically recommend, however, that MRI be used to further assess inconclusive or discordant clinical and imaging findings, only after mammography and ultrasound have been carried out. Further, a recent retrospective study by Moy, et al. (2009)³⁷ showed that, in cases in which mammographic or sonographic findings are inconclusive, MRI performed for the indication of problem-solving (i.e. asymmetry and architectural distortion) had a sensitivity of 100% and compared with mammography had significantly higher specificity (91.7% vs. 80.7%, $p = 0.029$), positive predictive value (40% vs. 8.7%, $p = 0.032$), and overall accuracy (92.2% vs. 78.3%, $p = 0.0052$). The frequency of incidental lesions detected at MRI was high (15.7%), all of which were subsequently found to be benign; therefore, strict patient selection criteria should be employed.

Follow-up

MRI may be used to diagnose local relapses of breast cancer; however, the accuracy of MRI can be affected by inflammatory changes in the breast tissue operative bed after surgery, for up to 6 months, and after radiation therapy, for up to 24 months; it is generally after this time period that local tumour recurrence appears, making the timing of MRI important.³⁸ MRI may be used to identify and differentiate tumour recurrence from post-surgical or post-radiation scar when conventional imaging is indeterminate.³⁹ In a study of patients with suspected tumour recurrence after lumpectomy, with or without radiotherapy and chemotherapy, Lewis-Jones, et al. (1991) reported a sensitivity of 100% and a specificity of 94% for MRI in detecting new tumour versus post-treatment fibrosis.⁴⁰ However, a retrospective study (Gorechlad, et al. 2008⁴¹) in patients treated with breast-conserving therapy and followed for a median of 5.4 years showed that the recurrence rate (1.7% of patients, ipsilateral breast) and risk of contralateral disease (2.3% of patients) were both very low and the authors concluded that MRI screening would not have been cost-effective and was unlikely to have improved overall survival. Therefore, MRI is not recommended for the follow-up of women with prior breast cancer unless they are in the high-risk category.

Operational Considerations

The use of MRI should be limited to trained and experienced radiologists, as there is evidence of a learning curve, especially for ductal carcinoma in situ (DCIS).^{42,43} In general, the sensitivity of MRI increases with experience,⁴⁴ while the number of benign lesions investigated unnecessarily decreases with experience.⁴⁵ The American College of Radiology (ACR) has introduced a voluntary accreditation program⁴⁶ that evaluates the qualifications of personnel, the quality control program, MRI safety policies, and image quality specific to MRI. The program also defines the physician's and the medical physicist's qualifications (experience and education) and continuing medical education requirements in order to be accredited. The physician's responsibility includes reviewing all indications for the examination, specifying the pulse sequences to be performed, specifying the use and dosage of contrast agents, interpreting images, generating written reports, and assuring the quality of both the images and interpretations. The medical physicist must be familiar with the principles of MRI safety, the Food and Drug Administration's guidance for MRI diagnostic devices, and other regulations pertaining to the performance of the equipment being monitored; knowledgeable in the field of nuclear physics and MRI technology (e.g. function, clinical uses, performance specifications, calibration processes); and have an understanding of clinical imaging protocols and methods of their optimization.

The minimal technical requirements to adequately perform breast MRI include high spatial resolution with a breast coil on a high field magnet (minimum 1.5 T), with thin slices and high matrix (approximately 1 mm in-plane resolution). This will help to ensure better quality imaging and a higher signal-to noise ratio, which are imperative for MRI to be able to detect breast cancer. Annual evaluation of MRI equipment should be performed and should include the following tests: magnetic field homogeneity, slice position

accuracy, slice thickness accuracy, radiofrequency calibration for all coils, frequency and gain/ attenuator verification, image signal-to-noise ratio (SNR) for all coils, intensity uniformity for all volume coils, phase stability and image artifact assessment for all coils, and softcopy (monitor) fidelity. In addition, the safety standards (e.g. signage, access control, screening procedures, and cryogen safety) should be assessed annually.³² Facilities performing breast MRI should have the capacity to perform MRI-guided intervention or to create a referral arrangement with a cooperating facility that could provide the service.⁷ In Alberta, the current availability of MRI machines that have been configured with a dedicated breast coil may be limited to the larger centres.⁴⁷ Patients meeting the criteria for MRI should be referred to a centre with an MRI machine capable of performing breast MRI, if one is not available locally.

Cost-Effectiveness

The large COMICE trial⁴⁸ out of the UK showed that in women with biopsy-proven primary breast cancer who had undergone conventional assessment followed by MRI (1.5 T or 1.0 T) with a dedicated bilateral breast coil (n = 816), the re-excision rates were similar (odds ratio = 0.96, 95% CI 0.75-1.24, p = 0.7691) to those of women who had not undergone MRI (n = 807) and there were no significant differences in the proportion of patients receiving chemotherapy, radiotherapy or additional adjuvant therapies, local recurrence-free interval rates, quality of life measures, or economics. As such, the use of MRI in this setting may be limited in cost-effectiveness. However, preoperative biopsy of MRI-only-detected lesions (i.e. occult breast cancer) could minimize the incidence of inappropriate mastectomy, as MRI has been shown to provide the possibility of breast conserving surgery in as many as a third of patients with occult breast cancer.²⁵ Furthermore, MRI may be cost-effective in patients with invasive lobular carcinoma, in which a sensitivity of MRI of 93.3% has been demonstrated and resulted in a change in surgical management in 28.3% of cases.²⁴ More research is needed in order to identify the subtypes of breast cancer patients that may benefit most from MRI assessment, thereby maximizing the cost-effectiveness of this application.

Within Alberta Health Services, Cancer Care, access to MRI machines configured with a dedicated breast coil may be limited to the larger urban centres.⁵⁰ As such, patients presenting with indications for breast MRI, as outlined in the recommendations section, may require a referral to a larger centre if an MRI machine capable of imaging the breast is not available locally or if local expertise in breast MRI is limited. The cost of a typical MRI scan in 2004/2005 in Alberta was approximately \$500.⁴⁹ The number of additional MRI scans, as a result of this guideline, is expected to be minimal. In 2011, there are expected to be 2,090 new diagnoses of breast cancer.⁵⁰ Assuming conservatively that up to 15% of new breast cancer cases require MRI for the purposes of problem solving or pre-operative assessment, and that 1% of the population of women in Alberta fall into the high-risk category,⁵¹ an estimated 330 breast MRI scans will be performed annually, as a result of this guideline. This would result in a total cost per year of \$165,000. Other possible costs would include staffing and travel expenses for remote patients.

Safety in Pregnancy and Breast-Feeding

Contrast enhanced MRI, using Gadolinium-based contrast agent, is contraindicated during pregnancy, as there are no adequate and well-controlled studies of its use in pregnant women. However, in rare and extenuating circumstances, whereby the health of the mother and/or fetus would be significantly compromised without a contrast enhanced MRI, and after all other imaging options (i.e. ultrasound, CT, nuclear scintigraphy, fluoroscopy, etc.) have been exhausted, MRI with a Gadolinium-based contrast agent could be considered. Patients should be informed of the risks and benefits of the procedure.

GLOSSARY OF ABBREVIATIONS

Acronym	Description
ACR	American College of Radiology
ADH	atypical ductal hyperplasia
ALH	atypical lobular hyperplasia
AUC	area under the curve
CE	contrast enhanced
DCIS	ductal carcinoma in situ
DOR	diagnostic odds ratio
LCIS	lobular carcinoma in situ
MRI	magnetic resonance imaging
PPV	positive predictive value
SNR	signal-to-noise ratio
US	ultrasound
WLE	wide local excision
XRM	x-ray mammography

DISSEMINATION

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services website.
- Send an electronic notification of the new guideline to all members of Alberta Health Services, Cancer Care.

MAINTENANCE

A formal review of the guideline will be conducted at the Annual Provincial Meeting in 2012. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

CONFLICT OF INTEREST

Participation of members of the Alberta Provincial Breast Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. Alberta Health Services, Cancer Care recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Breast Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

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APPENDIX: RECOMMENDATIONS MATRIX

Guideline	Recommendations
Screening Guidance	
National Comprehensive Cancer Network (NCCN), 2009	<ul style="list-style-type: none"> • Current evidence does not support the routine use of breast MRI as a screening procedure, in average risk women. • Criteria for the use of breast MRI as an adjunct to mammography in high risk women include: <ul style="list-style-type: none"> • Have BRCA 1 or 2 mutation • Have a first degree relative with a BRCA 1 or 2 mutation and are untested • Have a lifetime risk of breast cancer of 20-25 percent or more as defined by models that are largely dependent on family history • Received radiation treatment to the chest between ages 10 and 30 (i.e. Hodgkin's disease) • Carry or have a first degree relative who carries a genetic mutation in the TP53 or PTEN genes (Li-Fraumeni syndrome and Cowden and Bannayan-Riley-Ruvalcaba syndromes) • May be used as screening of the contralateral breast at the time of initial diagnosis. There are no data that demonstrate that use of MRI to affect choice of local therapy improves outcome (local recurrence or survival).
National Institute for Health and Clinical Excellence (NICE), 2006	<ul style="list-style-type: none"> • On the basis of current evidence, MRI and ultrasound should not be used in routine surveillance practice but may have a role in problem-solving mammographically detected abnormalities. • Women who are known to have a genetic mutation should be offered annual MRI surveillance if they are: <ul style="list-style-type: none"> • BRCA1 and BRCA2 mutation carriers aged 30–49 years • TP53 mutation carriers aged 20 years or older • MRI surveillance should be offered annually when indicated: <ul style="list-style-type: none"> • From 30–39 years: to women at a 10-year risk of greater than 8% • From 40–49 years: to women at a 10-year risk of greater than 20%, or to women at a 10-year risk of greater than 12% where mammography has shown a dense breast pattern. • Women who have not been tested but have a high chance of carrying a BRCA1 or TP53 genetic mutation should be offered annual MRI surveillance from 30–49 years if they are at: <ul style="list-style-type: none"> • a 50% risk of carrying one of these mutations in a tested family, or • a 50% risk of carrying a BRCA1 or TP53 mutation in an untested or inconclusively tested family with at least a 60% chance of carrying a BRCA1 or TP53 mutation (that is, 30% risk of carrying a mutation themselves)
British Columbia Cancer Agency (BCCA), 2009	<ul style="list-style-type: none"> • Inappropriate use of breast MRI: <ul style="list-style-type: none"> • Screening the general population • Recommended Uses of Breast MRI for Cancer (highest level of evidence) <ul style="list-style-type: none"> • Screening of high risk patients – patients with hereditary cancer risk <ul style="list-style-type: none"> • In patients who have tested positive for mutations of the BRCA 1 and 2 genes, MRI has been shown to detect cancers before mammography, ultrasound, or examination. • The greater incidence of high grade invasive malignancies in this high risk group does provide the rationale for using MRI as a screening modality in this small group of women. • Currently this is done at annual intervals with mammography done annually 6 months apart from the MRI. • The duration of MRI screening is not yet known; it may be that it can be omitted from screening but evidence from one surveillance study suggests MRI screening is valuable in this group independent of age. • There is no evidence concerning the role of MRI in patients with biopsy proven ADH or LCIS.

Guideline	Recommendations
American Cancer Society (ACS), 2007	<ul style="list-style-type: none"> • Recommend Annual MRI Screening (based on nonrandomized screening trials and observational studies) <ul style="list-style-type: none"> • <i>BRCA</i> mutation • First-degree relative of <i>BRCA</i> carrier, but untested • Lifetime risk ~20–25% or greater, as defined by BRCAPRO or other models that are largely dependent on family history • Recommend Annual MRI Screening (based on expert consensus opinion) <ul style="list-style-type: none"> • Radiation to chest between age 10 and 30 years • Li-Fraumeni syndrome and first-degree relatives • Cowden and Bannayan-Riley-Ruvalcaba syndromes and first-degree relatives • Insufficient Evidence to Recommend for or Against MRI Screening <ul style="list-style-type: none"> • Lifetime risk 15–20%, as defined by BRCAPRO or other models that are largely dependent on family history • Lobular carcinoma in situ (LCIS) or atypical lobular hyperplasia (ALH) • Atypical ductal hyperplasia (ADH) • Heterogeneously or extremely dense breast on mammography • Women with a personal history of breast cancer, including ductal carcinoma in situ (DCIS) • Recommend Against MRI Screening (based on expert consensus opinion) <ul style="list-style-type: none"> • Women at < 15% lifetime risk
Europe Against Cancer Program (EACP), 2007	<ul style="list-style-type: none"> • Service screening should be offered as a public health policy directed to women age 50–69, employing two-yearly mammography. • Mammography remains the cornerstone of population based breast cancer screening.
Alberta Breast Cancer Screening Program, 2009	<ul style="list-style-type: none"> • You should have a screening mammogram if: <ul style="list-style-type: none"> • You have no breast problems (such as a new lump or bloody nipple discharge) • You have not had a mammogram within the last 12 months • You have no history of breast cancer • You do not have breast implants • Women ages 50 - 69 do not need a referral for a screening mammogram. • Women ages 40 - 49 who are advised by their health care provider to begin screening mammograms will only need a referral for the first mammogram. • Women over 69 years of age are welcome to continue in the program but should discuss the need for regular screening mammograms with their health care provider.
American College of Radiology, 2008	<ul style="list-style-type: none"> • Screening of high-risk patients – Recent clinical trials have demonstrated that breast MRI can significantly improve the detection of cancer that is otherwise clinically and mammographically occult. Patients should be referred for screening breast MRI, preferably after careful risk assessment, by personnel trained in the assessment of hereditary breast cancer or by their referring physician who has used a risk assessment model. Breast MRI may be indicated in the surveillance of women with more than a 20% lifetime risk of breast cancer (for example, individuals with genetic predisposition to breast cancer by either gene testing or family pedigree, or individuals with a history of mantle radiation for Hodgkin’s disease). Although there is no direct evidence that screening with MRI will reduce mortality, it is thought that early detection by using annual MRI as surveillance, in addition to mammography, may be useful. • Screening of the contralateral breast in patients with a new breast malignancy – MRI can detect occult malignancy in the contralateral breast in at least 3%-5% of breast cancer patients. • Breast augmentation - postoperative reconstruction and free injections – Breast MRI using contrast may be indicated in the evaluation of patients with silicone or saline implants and/or free injections with silicone, paraffin, or polyacrylamide gel in whom mammography is difficult. The integrity of silicone implants can be determined by noncontrast MRI.

Guideline	Recommendations
Pre-operative and Post-operative Assessment Guidance	
NCCN, 2009	<ul style="list-style-type: none"> • May be used to define extent of cancer or presence of multifocal or multicentric cancer in the ipsilateral breast. There are no data that demonstrate that use of MRI to affect choice of local therapy improves outcome (local recurrence or survival). • May be useful to detect additional disease in women with mammographically dense breast, but available data do not show differential detection rates by any subset by breast pattern (breast density) or disease type (i.e. DCIS, invasive ductal cancer, invasive lobular cancer). • May be useful for identifying primary cancer in women with axillary nodal adenocarcinoma or with Paget's disease of the nipple with breast primary not identified on mammography, ultrasound, or physical examination. • Falsely 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.
CCO, 2006	<ul style="list-style-type: none"> • Subsets of patients that may benefit from MRI include: <ul style="list-style-type: none"> • Women with clinically palpable and mammographically occult breast cancer • Women with metastatic adenocarcinoma to axillary lymph nodes, with an unknown primary • Extent of disease needs better delineation, e.g. women with lobular carcinoma • Patients who require re-excision because of positive surgical margins. • Patients with a high-risk of multifocal disease • Recurrent breast cancer may be difficult to fully assess on mammography due to scarring and inflammation of previous surgery or radiation, so consider if: <ul style="list-style-type: none"> • The patient is a candidate for repeat lumpectomy • Discordant clinical and imaging findings • Imaging findings unclear or uncertain
American College of Radiology, 2008	<ul style="list-style-type: none"> • Invasive carcinoma and ductal carcinoma in situ (DCIS) – Breast MRI may be useful to determine the extent of disease and the presence of multifocality and multicentricity in patients with invasive carcinoma and ductal carcinoma in situ (DCIS). MRI can detect occult disease up to 15%-30% of the time in the breast containing the index malignancy. MRI determines the extent of disease more accurately than standard mammography and physical examination in many patients. It remains to be conclusively shown that this alters recurrence rates relative to modern surgery, radiation, and systemic therapy. • Invasion deep to fascia – MRI evaluation of breast carcinoma prior to surgical treatment may be useful in both mastectomy and breast conservation candidates to define the relationship of the tumor to the fascia and its extension into pectoralis major, serratus anterior, and/or intercostal muscles. • Postlumpectomy with positive margins – Breast MRI may be used in the evaluation of residual disease in patients whose pathology specimens demonstrate close or positive margins for residual disease. • Lesion characterization – Breast MRI may be indicated when other imaging examinations, such as ultrasound and mammography, and physical examination are inconclusive for the presence of breast cancer, and biopsy could not be performed (e.g., possible distortion on only one mammographic view without a sonographic correlate). • Postoperative tissue reconstruction – Breast MRI may be useful in the evaluation of suspected cancer recurrence in patients with tissue transfer flaps (rectus, latissimus dorsi, and gluteal). • MRI-guided biopsy – MRI is indicated for guidance of interventional procedures such as vacuum assisted biopsy and preoperative wire localization for lesions that are occult on mammography or sonography and demonstrable only with MRI.

Guideline	Recommendations
BCCA, 2009	<ul style="list-style-type: none"> • Recommended Uses of Breast MRI for Cancer (highest level of evidence) <ul style="list-style-type: none"> • Evaluation of occult breast cancer <ul style="list-style-type: none"> • In patients with an occult primary presenting with axillary lymphadenopathy or Paget's disease, MRI has been shown to identify the primary in many patients, thus allowing for conservative surgery rather than mastectomy. • This is not indicated if mammography clearly shows a suspicious lesion. Trials are ongoing studying the impact of MRI on this group of patients. • Possible Uses of Breast MRI (clinical scenarios where other imaging modalities have not provided adequate assessment and where an MRI showing more disease may impact and/or change management) <ul style="list-style-type: none"> • Evaluation of local extent of breast cancer • Positive margins – post segmental resection • Post surgical scar vs. recurrent tumor • Problem mammogram • Inappropriate Use of Breast MRI <ul style="list-style-type: none"> • Differentiation of benign vs. malignant lesions
Assessment During Neoadjuvant Chemotherapy Guidance	
NCCN, 2009	<ul style="list-style-type: none"> • May be helpful for evaluation before and after neoadjuvant therapy to define extent of disease, response to treatment, and potential for breast conserving therapy.
BCCA, 2009	Possible Use of Breast MRI: <ul style="list-style-type: none"> • Response to chemotherapy (in a clinical trial setting only)
CCO, 2006	Response Assessment <ul style="list-style-type: none"> • MRI is recommended for indicated study • Women with locally advanced breast cancer may benefit from MRI: <ul style="list-style-type: none"> • MRI will determine whether the tumour is responding to chemotherapy • Mammogram, CT and US are not indicated • In metastatic breast cancer the tests that were abnormal at baseline including MRI could be repeated every 3-4 months
American College of Radiology, 2008	<ul style="list-style-type: none"> • Neoadjuvant chemotherapy – Breast MRI may be useful before, during, and/or after chemotherapy to evaluate treatment response and the extent of residual disease prior to surgical treatment. If used in this manner, a pretreatment MRI is highly recommended. MRI-compatible localization tissue markers placed prior to neoadjuvant chemotherapy may be helpful to indicate the location of the tumor in the event of complete response with no detectable residual tumor for resection.
Follow-up	
NCCN, 2009	<ul style="list-style-type: none"> • Utility in follow-up screening of ipsilateral and contralateral breast of women with prior breast cancer is not defined.
American College of Radiology, 2008	<ul style="list-style-type: none"> • Recurrence of breast cancer – Breast MRI may be useful in women with a prior history of breast cancer and suspicion of recurrence when clinical, mammographic, and/or sonographic findings are inconclusive. • Metastatic cancer when the primary is unknown and suspected to be of breast origin – MRI may be useful in patients presenting with metastatic disease and/or axillary adenopathy and no mammographic or physical findings of primary breast carcinoma. Breast MRI can sometimes locate the primary tumor and define the disease extent to facilitate treatment planning.
CCO, 2006	<ul style="list-style-type: none"> • MRI is not recommended; routine imaging should not be carried out to detect distant metastases.

Guideline	Recommendations
Operations Guidance	
Europe Against Cancer Program (EACP), 2007	<ul style="list-style-type: none"> • Breast cancer screening is a complex multidisciplinary undertaking, the objective of which is to reduce mortality and morbidity from the disease without adversely affecting the health status of participants. It requires trained, experienced professionals using up-to-date, specialized equipment. • Screening usually involves a healthy and asymptomatic population which requires adequate information presented in an appropriate and unbiased manner in order to allow a fully informed choice as to whether to attend or not. • All units carrying out screening, diagnosis or assessment must work to agreed protocols forming part of a local quality assurance (QA) manual, based on national or European documents containing accepted clinical standards and published values. They should work within a specialist framework, adhering to set performance indicators and targets. Variations of practices and health care environments throughout the member states must not interfere with the achievement of these. • A robust and reliable system of accreditation is required for screening and symptomatic units, so that women, purchasers and planners of health care services, can identify those breast clinics and units which are operating to a satisfactory standard. Any accreditation system should only recognize centres that employ sufficiently skilled and trained personnel. • All staff in a screening program should: <ul style="list-style-type: none"> • Hold professional qualifications as required in each member state. • Undertake specialist training. • Participate in continuing medical education and updates. • Take part in any recognized external quality assessment schemes. • Hold any necessary certificate of competence. • All units involved in screening, diagnostic or therapeutic activities must ensure the formation of proper multidisciplinary teamwork involving a full range of specially trained professionals including a radiologist, radiographer, pathologist, surgeon, nurse counselor and medical oncologist/radiotherapist. • All women requiring breast surgery or other treatment should have their clinical, imaging and pathology findings discussed and documented in regular preoperative and postoperative meetings of the full multidisciplinary team. • Quality assurance programs should be mandatory in order for breast cancer services to qualify for funding from health care providers. • Each screening unit should have a nominated lead professional in charge of overall performance, with the authority to suspend elements of the service if necessary in order to maintain standards and outcomes.
NCCN, 2009	Personnel, Facility, and Equipment: <ul style="list-style-type: none"> • Breast MRI examinations 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 center should have the ability to perform MRI guided needle sampling and/or wire localization of MRI detected findings.
American College of Radiology, 2008	<ul style="list-style-type: none"> • In addition, interpreting physicians should have knowledge and expertise in breast disease and breast imaging diagnosis. Facilities performing breast MRI should have the capacity to perform mammographic correlation, directed breast ultrasound, and MRI-guided intervention, or create a referral arrangement with a cooperating facility that could provide these services. Whenever possible the histopathology of the biopsy should be available to the interpreting physician as well as the physician performing the breast MRI procedure. • Appropriate emergency equipment with medications must be immediately available to treat adverse reactions associated with administered medications. The equipment and medications should be monitored for inventory and drug expiration dates on a regular basis. The equipment, medications, and other emergency support must be appropriate for the ages and sizes in the patient population.

Guideline	Recommendations
BCCA, 2009	Breast MRI should be used in a problem solving mode only after high quality mammography and ultrasound have been carried out. As well, it should be done by a radiologist with expertise in breast MRI, as these images require specialized knowledge for interpretation.
NICE, 2006	<ul style="list-style-type: none"> • At entry to MRI surveillance program, and at each subsequent change in the program, women should be provided with a plan which includes: <ul style="list-style-type: none"> • a clear description of methods and intervals, including risks and benefits • the reasons for any changes to the surveillance plan • sources of support and further information • MRI of both breasts should be performed to high quality standards ensuring both high temporal and spatial resolution. Dynamic sequences are recommended post contrast. They should be double-read where possible. • When mammography is recommended in women under 50, digital mammography should be used in preference to conventional mammography at centres where this is available to NHS Breast Screening standards. • Women who have been referred to a clinical genetics centre who are not known to have a genetic mutation should be offered an assessment of their 10-year breast cancer risk using a validated risk assessment tool to assess whether they are or will be eligible for MRI.
Other Guidance	
Scottish Intercollegiate Network (SIGN), 2005	MRI should be considered in specific clinical situations where other imaging modalities are not reliable, or have been inconclusive, and where there are indications that MRI is useful.