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Review article

MRI of the breast

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Abstract. MRI of the breast is rapidly evolving as a sensitive technique for the detection and staging of breast cancer. It has considerable benefits but is time consuming and expensive. The benefits and limitations of this technique are presented.

The detection and diagnosis of breast cancer is an emotive issue and a test is required that is sensitive and specific for both the symptomatic and screened population. Mammography is at present the mainstay of diagnosis. However, even when performed optimally, the sensitivity of mammography is between 69% and 90% [1–5]. Although some mammographically occult lesions may be palpable, others will defy detection. Tumours may be missed because of poor mammographic technique or observer error, or the size and nature of the lesions relative to the surrounding breast tissue, which may obscure them. This is a particular problem in the dense breast, following surgery or radiotherapy, adjacent to implants or in the younger population. In addition, the specificity of mammography may be sacrificed to improve sensitivity, thus requiring increasing numbers of biopsies for indeterminate lesions. The reported specificity of mammography ranges from 10% to 40%. Up to 75% of mammographically demonstrated indeterminate or suspicious masses are benign at biopsy.

Ultrasound (US) is an excellent method for assessing palpable abnormalities, differentiating between cystic and solid lesions, and classifying solid masses. It also allows accurate needle placement for biopsy. The development of high frequency transducers has improved spatial resolution so that lesions less than 1 cm in size are now identified. However, US has limitations as a screening modality because microcalcification in ductal carcinoma *in situ* (DCIS) may not be identified. The false negative rate is very variable, ranging from 0.3% to 47% in some series. US is time consuming and it is difficult to ensure that the entire breast has been imaged [6–8]. The excellent soft tissue resolution combined with tomographic imaging to prevent tissue overlap and the lack of ionizing radiation makes MRI an attractive imaging modality. MRI has changed cancer detection and staging elsewhere in the body. This review will discuss the advantages and limitations of breast MRI.

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Technique

The initial experience with MRI was disappointing. Although cancers could readily be identified within fatty tissue, benign and malignant breast tissue could not be differentiated based on signal characteristics using T_1 weighted or T_2 weighted sequences [9, 10], and spatial resolution using the body coil was poor. Spatial resolution has improved considerably with the advent of surface coils. The use of intravenous gadolinium, which passes into the extravascular space and accumulates in tissues with rich vascularity, has increased both the sensitivity and specificity of the investigation. The rationale for the use of gadolinium is that most cancers markedly enhance. Carcinomas greater than 3 mm in size secrete angiogenic molecules leading to angioneogenesis, with recruitment of new vessels, arteriovenous shunting and perivascular cuffing. Other factors promoting enhancement in malignancy include expansion of the extracellular space, increased interstitial pressure and increased capillary permeability due to an abnormal basement membrane or the effect of cytokinins that promote vessel growth. This results in more rapid accumulation of gadolinium in cancers than in benign lesions, which have a more normal microvascularity [11, 12]. There is a correlation between neovascularity and tumour grade in breast cancer, a 40% increase in vessels on microscopy doubling the risk of metastases [13–16].

Most cancers show an early steep rise in enhancement within 5 min following injection of 0.1–0.2 mmol kg^{-1} of gadolinium, with a greater than 70% increase in signal intensity. The rate of enhancement correlates with the number of vessels in the pathological specimen [17, 18]. When assessing the degree of enhancement using a region of interest (ROI), it is important that it lies over the most enhancing region. The ROI should not include the entire lesion, as this will decrease the apparent degree of enhancement as lesions may enhance non-homogeneously and thus increase the false negative rate [19]. A semi-automated method of ROI selection has been developed by Mussurakis et al [20], who also suggest that selective sampling may not provide any diagnostic advantage over using lesion-encompassing ROIs that are easier to draw [21]. Rather than using a 70–100% increase in signal intensity, Hewang et al [22] suggested using normalized fat units (NU), comparing the enhancement of a lesion with that of fat, which does not enhance, with enhancement of above 300 NU being considered significant (Figure 1).

After the initial steep rise, enhancement reaches a plateau. This is followed by washout of the contrast agent over the next 5 min, which is more rapid in malignant than benign lesions [23–25]. Cancers can be differentiated from many benign lesions, which either do not enhance or show continued enhancement over time with delayed washout, probably related to poor vascularization [26] and microvascular distribution [27]. However, some cases of benign breast change enhance in a similar fashion to cancers and this appears to be related to the proliferating activity of the hyperplastic parenchymal cells [28]. In benign lesions that enhance, time/intensity curves cannot be used to differentiate benignity from malignancy [29] as there is overlap. It is important to image cancers early, as normal glandular breast tissue enhances relatively slowly over 10 min following the injection of iv gadolinium. As a result, enhancement of normal breast tissue may be the same as a malignant tumour and obscure a

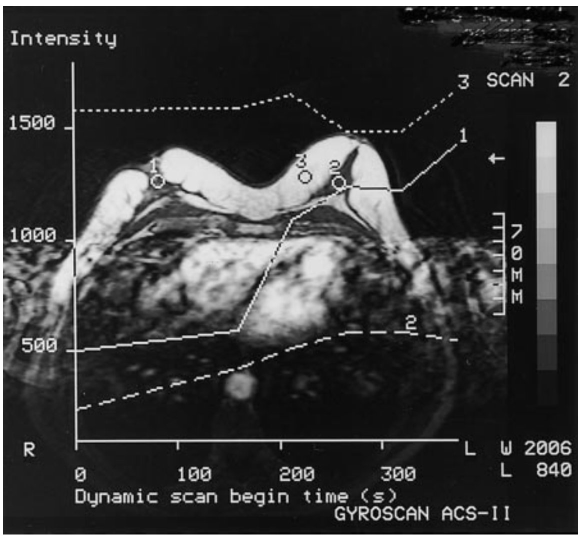


Figure 1. Recurrent invasive ductal carcinoma time/intensity curves. 1, invasive tumour; 2, normal breast tissue; 3, fat.

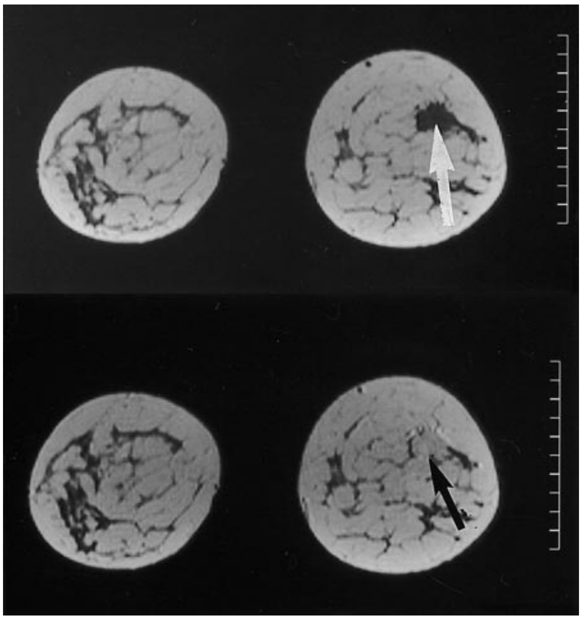
cancer. The pattern of enhancement is also helpful. Peripheral or rim enhancement occurs in invasive cancers, with linear enhancement in DCIS.

Imaging protocols

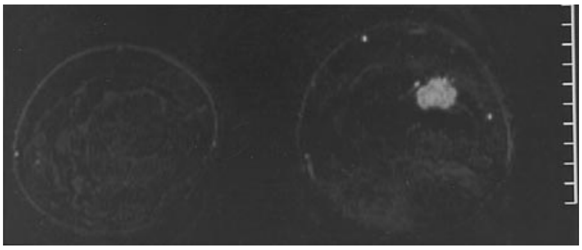
The protocol will vary, depending on the field strength of the magnet. Most centres use a dedicated breast coil that can receive in a single or double breast mode. The prone position will decrease the amount of respiratory motion artefact, and minimal compression applied within the coil will decrease motion artefact. The phase encoding direction should not pass anterior to posterior, but from left to right, to ensure that cardiac activity is not projected over the breast.

Two main techniques have been employed; either a high resolution 3D sequence or a dynamic 2D sequence with improved temporal resolution. To detect lesions less than 5 mm, high resolution using a 2–4 mm slice with no gaps is required with an in-plane resolution of 1 mm. This thin section, high resolution 3D acquisition will improve lesion detection and aid morphological assessment. The images are acquired before and after gadolinium injection. However, the acquisition time may be 5 min or more, particularly if fat suppression techniques are employed, and contrast agent dynamics cannot be assessed. Newer sequences allow thin section, high resolution imaging of the entire breast with better temporal resolution. Heywang-Kobrunner and Beck [23] employ a 3D FLASH (fast low angle shot) gradient echo sequence using a TR of 14 ms, TE of 6.7 ms and a flip angle of 35°. This allows the entire breast to be imaged using 2.5 mm slice thickness in 90 s. This sequence can be repeated before and five times after a bolus of gadolinium so that the rate and duration of enhancement can be assessed. Slowly enhancing tumours will also be detected. The 3D data set can be acquired in the coronal plane to decrease cardiac motion artefact, and reformatted in other projections for correlation with standard mammograms (Figure 2). This sequence allows a combination of high resolution and limited dynamic assessment and is used in many institutions.

An alternative method is to perform a 2D dynamic sequence with an acquisition time of between 2 s and 60 s, employing multiple acquisitions after a bolus of gadolinium to assess enhancement dynamics and construct detailed time/intensity curves. The limitation of this method is that spatial resolution, signal-to-noise ratio or the volume covered will be sacrificed for improved temporal resolution. An alternative method is to use a high temporal



(a)



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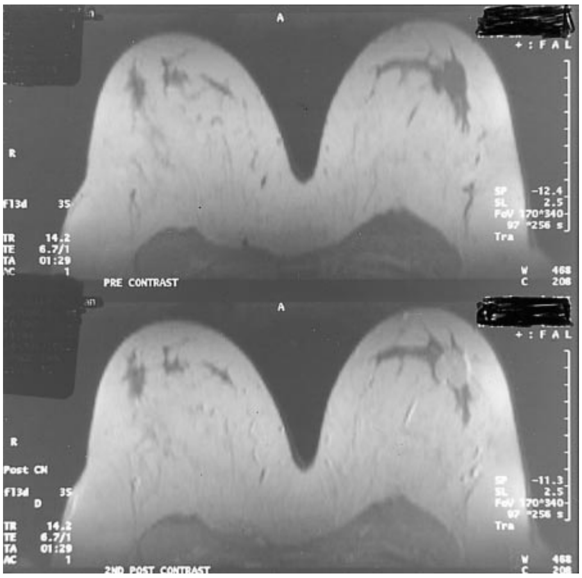


(c)

Figure 2. (a) Coronal T_1 weighted 3D FLASH sequence. Pre-contrast (white arrow) and post-contrast (black arrow) invasive cancer. (b) Subtraction image of tumour. (c) Axial reformat of coronal sequence, pre-contrast (upper) and post-contrast (lower). This compares favourably with the craniocaudad mammographic view.

resolution, lower spatial resolution scan through the entire breast, followed immediately by a slower high resolution 3D sequence [2]. In an attempt to combine sensitivity and specificity in one study, Boetes et al [30] suggested a 3D MP-RAGE sequence with a TR of 10 ms, TE 4 ms, TI 300 ms, an 8° flip angle and 1.4 mm slice thickness. This sequence is a 5 min acquisition performed prior to contrast. The optimal slice for the tumour is identified and a high specificity dynamic 2D sequence is performed using a single slice turbo FLASH sequence in the transverse plane, so that the aorta is included. This sequence uses a 10 mm slice thickness with a TR of 9 ms, TE 4 ms, TI 15 ms and 8° flip angle. 60 acquisitions, one every 2–3 s are obtained in total, and after the first four acquisitions a bolus of gadolinium (0.2 mmol kg^{-1}) is injected rapidly over 10 s followed by a chaser bolus of saline. The MP-RAGE sequence is repeated at the end of the sequence to ensure that no other enhancing lesions are present. Based on the turbo FLASH sequences, these authors stated that malignant lesions enhanced within 11.5 s of the aorta and enhanced from the periphery to the centre. They also tended to have poorly defined or spiculated margins and ring enhancement was an indication of malignancy. The increase in signal intensity between the pre- and post-contrast images was greater than 60%. Benign lesions enhanced 12 s or more after the aorta, from the centre to the periphery, were smooth or regular in outline and retained gadolinium longer.

Other techniques that have been described include images using pharmacokinetic parameters such as amplititude and rate of enhancement, which are colour coded on a pixel to pixel basis [21, 31, 32]. Daniel et al [33] found the exchange rate constant had the greatest ability to differentiate benign and malignant disease. The elimination rate constant and washout were the most specific parameters and exchange rate constant and washin were the most sensitive. Muller-Schimpfle et al [34] compared standard and pharmacokinetic analysis in the differentiation of benign and malignant lesions. Although both were discriminant, the pharmacokinetic analysis was time consuming and added no benefit in routine clinical diagnosis.

Kuhl et al [35] have investigated the use of T_2* perfusion imaging, with the early work giving good results in helping differentiate malignant from benign, rapidly enhancing lesions.

Fat suppression sequences will improve visualization and morphological assessment of enhancing lesions in the background of a fatty breast on T_1 weighted sequences [36]. The disadvantage of some of these techniques is the increase in the time of the acquisition, which makes them unsuitable for breast imaging. Chemical shift imaging adapted from the Dixon method may be used but is sensitive to field inhomogeneity, and the non-uniformity of the fat suppression over the entire field may be a problem. Harms et al [37] described a method of fat suppression using rotating delivery of excitation off resonance (RODEO), which is very successful and, with other techniques including a spectrally selective saturation pulse for fat, enables 3D acquisitions to be obtained within 5 min [38]. Fat suppression can also be obtained by subtraction of the pre-contrast from the first post-contrast image on a pixel to pixel basis to identify enhancing lesions [39]. The limitation of this method is decreased signal-to-noise ratio and potential patient movement. The subtracted images provide a quick method of identifying areas of enhancement. If this method is employed, it is important to always look back at the source images to confirm that apparent areas of enhancement are not artefactual as a result of patient movement.

Results

Wide reported variations in sensitivity and specificity are partly related to different techniques and field strengths of the magnets, but also to patient selection and even the dose of gadolinium. Heywang-Kobrunner et al [40] found that a dose of 0.16 mmol kg^{-1} gave better results with improved conspicuity of lesions compared with 0.1 mmol kg^{-1} of gadolinium, small foci of enhancement being seen only following the higher dose in some cases.

The amount and speed of enhancement, and the morphological appearances of the lesion have to be considered. Quantitative data alone cannot be used to separate benign from malignant lesions as there is some overlap. False positive enhancement will occur with fibrocystic disease, fibroadenomas, sclerosing adenosis, atypical hyperplasia, lobular carcinoma *in situ* and breast papillomas. All these conditions may exhibit enhancement patterns indistinguishable from cancer [22, 29, 37, 41, 42]. A pre-determined minimum threshold for enhancement is helpful and many authors choose a 70–100% increase in signal intensity, which produces a high sensitivity but low specificity as benign and malignant lesions may have similar values. Increasing the level of the threshold will increase the specificity but at the cost of decreased sensitivity. Similarly, the specificity will be increased if the speed of enhancement is used, as benign lesions tend to enhance more slowly than cancers although up to 10% of cancers will enhance slowly [23]. The most specific pattern of enhancement using time/intensity curves was studied by Kuhl et al [43] and appears to be the rapid rise of enhancement by more than 60% in the first minute followed by a rapid washout after 2–3 min (specificity 87%). Importantly, these authors suggested that time/intensity curves did not need to be reconstructed routinely if the lesion had morphological features of malignancy, although biopsy should be undertaken if the morphology suggested a benign or indeterminate lesion but the time/intensity curve showed rapid washout. However, the lack of rapid washout does not preclude malignancy. A benign time/intensity curve for an incidental, enhancing lesion can be used to preclude biopsy.

Using contrast enhanced 3D FLASH or MP-RAGE sequences, the reported sensitivity for the detection of cancers is between 85% and 100%, but specificity varies between 37% and 85% [5, 29, 39, 44, 45]. However, incorporating morphological information from the high resolution 3D images will improve the specificity [46]. Nunes et al developed an interpretation model [47] using a combination of morphological features and enhancement characteristics. The features that gave a high positive predictive value were MR visibility, enhancement degree and pattern, focal mass border characteristics and focal mass internal septations. The features that gave a high negative predictive value for malignancy were absence of MR abnormality, focal masses with smooth borders, masses with lobulated or irregular borders, non-enhancing internal septations and non-enhancing focal masses. Using these criteria, the sensitivity, specificity, accuracy, and positive and negative predictive value were 96%, 79%, 86%, 76% and 97%, respectively. Irregular or spiculate masses were malignant (positive predictive value, PPV 89%). These authors found that the addition of dynamic sequences did not add any additional diagnostic information (Figures 3 and 4).

Use of the dynamic sequences to look at enhancement patterns may also increase the specificity, Boetes et al [30] reporting a sensitivity of 95% and specificity of 86% for the detection of cancers. The main problem with their technique is that it is a single slice acquisition, so that the correct slice may not be selected if the lesion is not appreciated on the pre-contrast MP-RAGE image and is not palpable. This problem is overcome with the development of dynamic spiral MR when the entire breast can be covered in 12 sections every 8 s, with no signal from fat. The disadvantage is the 10 mm slice thickness and lack of morphological information [33]. However, Schorn et al [48] compared ultrafast dynamic imaging with a temporal resolution of 2 s with the standard dynamic sequence with a temporal resolution of 90 s. They were unable to differentiate enhancing benign from malignant lesions based on the time to enhancement, but were able to improve specificity by using morphological features and suggested that it is better to improve spatial resolution rather than temporal resolution.

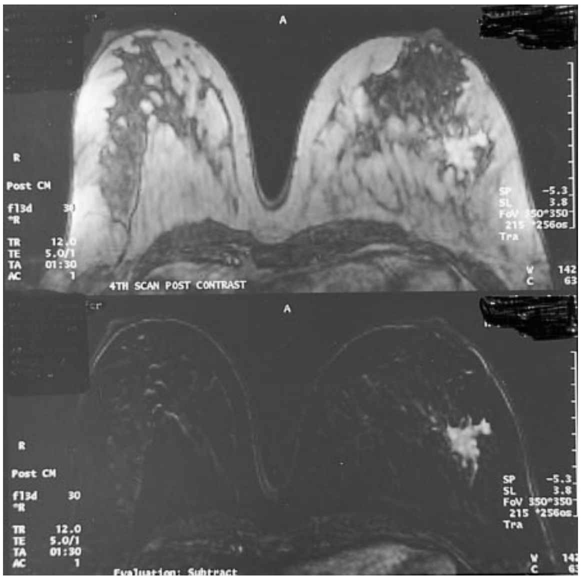


Figure 3. Post-contrast (upper) and subtracted (lower) image from a 3D T_1 weighted FLASH sequence clearly demonstrates the irregular spiculated outline of an invasive ductal cancer.

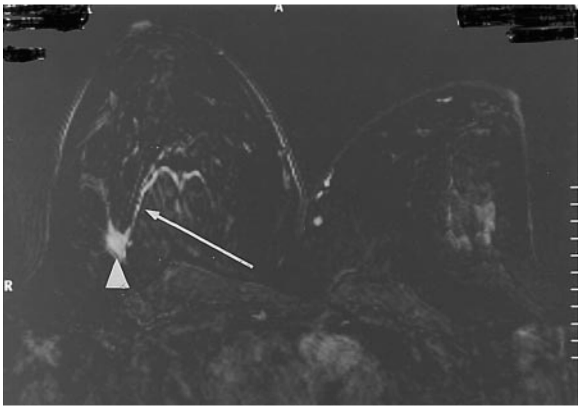


Figure 4. Subtracted image of an invasive ductal cancer (arrowhead) and linear enhancement in ductal carcinoma *in situ* (arrow).

Staging of breast cancer

Traditionally, breast cancer was treated with mastectomy, although equivalent long-term survival is obtained with breast-conserving surgery and radiotherapy [49, 50]. Recurrence following breast-conserving surgery ranges from 3–19%, compared with local recurrence after primary mastectomy of 2–9%. Whether a patient is suitable for breast-conserving surgery depends on the size of the mass, particularly in relation to the size of the breast, the presence of multifocal or multicentric disease, and involvement of the nipple. Multicentric disease occurs when tumour is present in multiple quadrants, whereas multifocal disease indicates multiple tumours in the same quadrant (Figure 5). Holland et al [51] identified additional foci of tumour in 63% of mastectomy specimens, with 43% more than 2 cm from the main tumour and which may therefore not be removed at the original breast-conserving surgery.

Several authors [37, 52, 53] have assessed the sensitivity of MRI for the detection of multicentric disease. A total of 153 cancers was evaluated and in 40 (25%) cases additional foci of tumour were found, of which MRI detected 98%. Of these additional tumours, 60% were more than 2 cm from the primary lesion. In a study by Orel et al 34% of patients had additional foci of

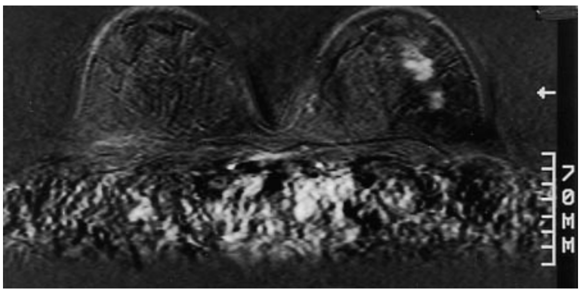


Figure 5. Multifocal tubular carcinoma (subtracted image).

tumour not seen on mammography and 20% had multifocal disease that altered the surgical approach. A disadvantage of using MR in assessing the extent of disease is that false positive MRI may lead to a larger excision than planned or unnecessary surgery. The ability to perform MR-guided biopsy would help overcome this problem [52].

Mammography, US and MRI were compared in multicentric disease by Kramer et al [54], who found the sensitivity for MRI was 89%, US 79%, mammography 66% and clinical palpation 47%. Although MRI was the most sensitive it was also the least specific modality.

MRI may also be helpful in identifying the extent of tumour, in particular involvement of the chest wall and nipple, which may alter surgical planning [55], and is better than US or mammography in determining the size of the tumour [53, 56]. Post-processing of the data to produce surface shaded reformats from the 3D images can aid surgical planning [57].

Breast-conserving surgery requires that the excision margins are clear of tumour, as incomplete excision is associated with a higher recurrence rate. In a study by Schmidt-Ullrich et al [58] inadequate excision margins were found in 32% of T1 and 49% of T2 tumours. There was residual tumour in 71% of tumours greater than 2 cm, requiring re-excision. The extent of residual disease following primary resection may be difficult to assess and MRI may be helpful in this respect. Orel et al [59] studied 47 patients after initial excision biopsy and prior to further surgery using MRI and mammography. The positive predictive value of MRI for residual disease was 82% and the negative predictive value was 61%. MRI also identified multifocal tumour and the proposed surgery was changed in 4 out of 14 patients. Although MRI was helpful in this group of patients, the high false negative rate of 25% means that a negative MRI cannot reliably predict the removal of all tumour. The cost of MRI may limit its use in this group of patients. However, it may be more cost effective to perform MRI rather than to undertake repeated excisions that may ultimately lead to a mastectomy if adequate margins cannot be obtained.

Nodal status and the grade of tumour is important information. Although invasive tumours tend to show more enhancement than non-invasive tumours, there does not appear to be a correlation between the degree of enhancement and the histological type, grading, nodal status or the results of immunohistochemistry [60]. Mussurakis et al [61] suggested that maximum enhancement ratios may be helpful in predicting nodal status but it is unlikely that this will obviate the need for nodal biopsy.

MRI is very sensitive in the detection of invasive cancer, although the reported sensitivity for MRI in the detection of DCIS ranges between 40–100% [19, 37, 62, 63], with MRI missing 6 out of 15 cases of DCIS in one series [52]. The enhancement patterns with DCIS are rather variable, with 20% showing little or no enhancement and 30% atypical enhancement [25, 39, 64]. The lack of contrast enhancement may be due to poor tumour vascularization, as the intraduct cells of the DCIS can be fed by diffusion from surrounding tissue and angiogenesis is not always necessary. The size and morphology of contrast enhanced lesions correlates with the size and density packing of ducts involved with DCIS [19]. The comedo subgroup, which is associated with tumour necrosis, showed greater enhancement (76%) compared with non-comedo carcinomas (50%) in Westerhof's series. No relationship was found between degree of enhancement and grade of tumour [64], which confirms the results of Boetes [65] who missed 4 out of 17 DCIS, three of which were non-comedo in type and demonstrated no pathological enhancement. Failure to identify the DCIS was not related to size, as one of the lesions missed was 90 mm. However, as typical malignant enhancement, including focal and ductal patterns of enhancement, may occur in 50% of DCIS, MRI may detect DCIS not visible by other methods [19, 63, 64, 66].

MRI cannot identify microcalcification, which is an important mammographic sign of DCIS. Several studies [64, 66, 67] have demonstrated that the enhancement patterns associated with mammographic microcalcification cannot be used to determine whether it is benign or malignant. In these circumstances the reported sensitivity is 45–82% and specificity 56–72% [64, 68]. MRI should therefore not be used to determine whether biopsy should be undertaken. Stereotactic biopsy is a more specific and less costly method of investigation than MRI for suspicious microcalcification and should be the investigation of choice.

MRI is also of value in identifying occult breast cancer in patients who present with metastases compatible with a breast primary but with no lesions identified on mammography [69, 70], and is more sensitive than mammography in these cases. In one study [69] on 12 patients, MRI identified the breast tumour in nine patients, with one false positive study.

Although MR is sensitive for cancer, false negatives will occur. Boetes et al [65], despite good technique, missed 6 out of 145 (4%) cancers. Four of these six tumours were DCIS, one was a small, 2 mm invasive carcinoma associated with DCIS, and one was a 4 cm invasive lobular carcinoma. Lobular carcinomas may have an infiltrative growth pattern, which may make it difficult to assess, and others [39] have also reported false negatives with this tumour type. Interestingly, all but one of the six false negative cases described by Boetes were suspicious on mammography, which remains the diagnostic test, with MRI better for assessing tumour size, additional lesions and tumour in dense breasts [53].

Recurrent carcinoma

Breast-conserving surgery is increasingly being used to treat breast cancer. The risk of local recurrence is 1–2% per year after treatment. Mammograms following breast-conserving surgery and radiotherapy may be difficult to interpret owing to distortion, scarring and calcification. Tumour recurrence may therefore be missed on mammography, palpation or US. MRI is a sensitive test, particularly in the dense distorted breast, and is better than palpation or mammography for detecting recurrence [71–73]. Mumtaz et al [74] found MRI had a 93% sensitivity and a specificity of 88%, while cytology had a sensitivity of only 79% owing to sampling error. The timing of the investigation is critical. Hewang-Kobrunner et al [75] identified 4 out of 11 recurrences, while 10 out of 18 single recurrent foci were only seen on the MRI based on focal enhancement. These authors suggested that MRI should not be used in the first 9 months after radiotherapy as there was marked generalized enhancement in the treated breast (Figure 6). From 9 to 18 months, the results should be treated with caution, but a negative examination is reassuring, and in the 25% of patients who continue to exhibit enhancement it could represent either tumour or post-radiation fibrosis. Radiation fibrosis should not enhance after 18 months (Figure 7) and MRI is then an accurate method for identifying tumour (Figure 8) and differentiating it from post-radiation fibrosis [44, 76]. MRI was useful after 6 months if the patient had had surgery but no radiotherapy [77]. Muuller [78] suggested that MRI was successful after 12 months in differentiating radiation change from tumour recurrence. Drew et al [79] reported MRI to be as sensitive as clinical examination combined with mammography for the detection of recurrence and showed the specificity for MR was much higher (93% compared with 67%).

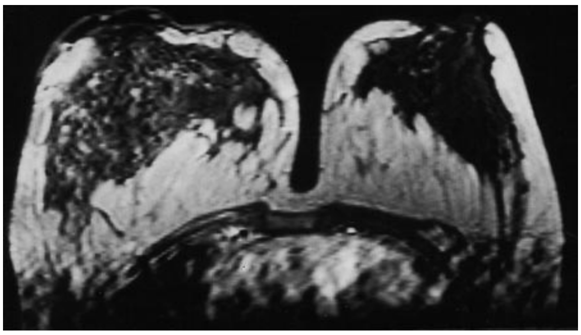


Figure 6. Post-enhancement T_1 weighted FLASH sequence showing diffuse enhancement of the right breast 6 months following radiotherapy.

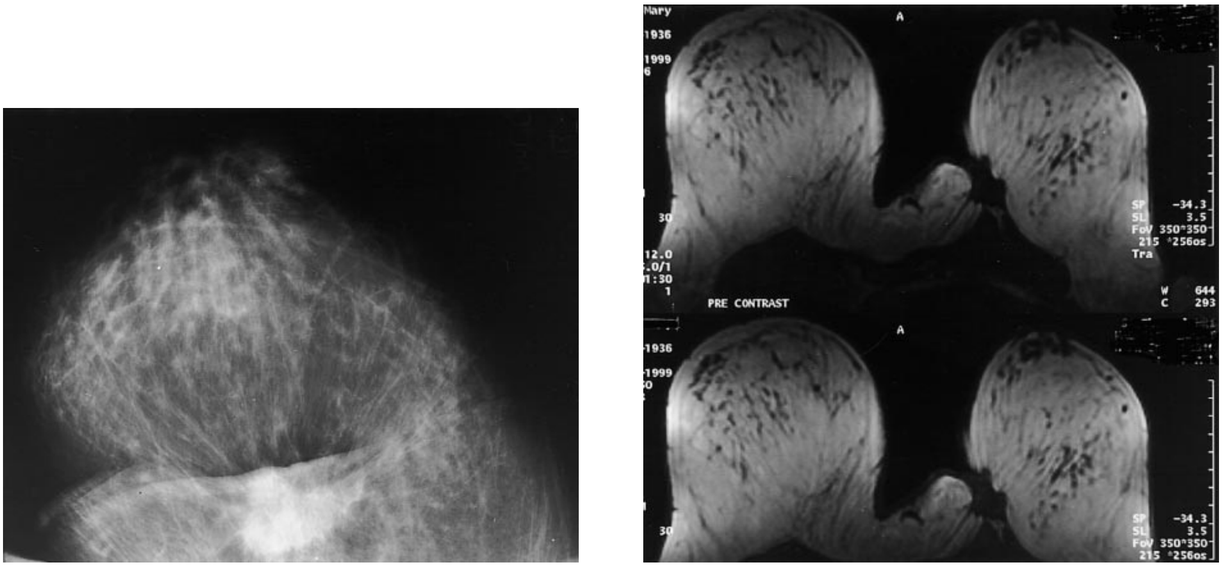
Apart from identifying recurrent tumour, a potential use for MRI is in assessing the response of breast cancer to chemotherapy. Rieber et al [80] studied a small group of patients, looking at the uptake curves before and after chemotherapy. In the patients who responded, the uptake curve became flatter after the first course with no uptake by the end of the fourth course. The non-responders did not demonstrate these findings. MRI can also identify residual tumour following chemotherapy, although it will miss isolated tumour cells leading to an underestimate of the extent of remaining tumour [80, 81].

Implants

Numerous types of breast implants are available and can be very well demonstrated on MRI [82–85]. MRI is the most reliable method of depicting the integrity of implants, followed by US and then mammography, which is the least sensitive [86]. Using selective chemical shift or phase selective techniques to separate fat/silicone and water, the MRI criteria for implant failure include a collapsed implant shell (linguine sign), foci of silicone outside the shell (teardrop sign) and extracapsular gel (Figure 9). It is important to remember that the sequences for assessing implant integrity do not utilize gadolinium and cannot therefore be used to exclude malignancy. A conventional gadolinium enhanced sequence must be obtained if malignancy is suspected. MRI is superior to palpation and mammography in identifying coincidental malignancy, and is particularly useful for identifying recurrence in patients following breast reconstruction [71] (Figure 10).

MR-guided biopsy

One of the major problems with breast MRI is the difficulty in localizing lesions that are detected by MRI but not identifiable on the mammogram. Some of these lesions will be seen on guided high resolution US but some will not. Various types of add-on devices have been produced in addition to using interventional magnets. The increasing use of MRI, particularly if used as a screening method, means more biopsies will be performed. For instance, Fischer et al [87] now perform MR-guided intervention in approximately 3–5% of all



(a) (b)

Figure 7. (a) Mammogram following breast conservation and radiotherapy with a mass suspicious for malignancy. (b) Pre-contrast (upper) and post-contrast (lower) 3D T_1 weighted sequence. No enhancement is seen. Fibrosis is demonstrated on biopsy.

patients undergoing MR mammography. This will be the stimulus for the development of localization devices to become commercially available. A great disadvantage of MRI localization is the inability to produce a specimen image and thus know if the lesion has been excised.

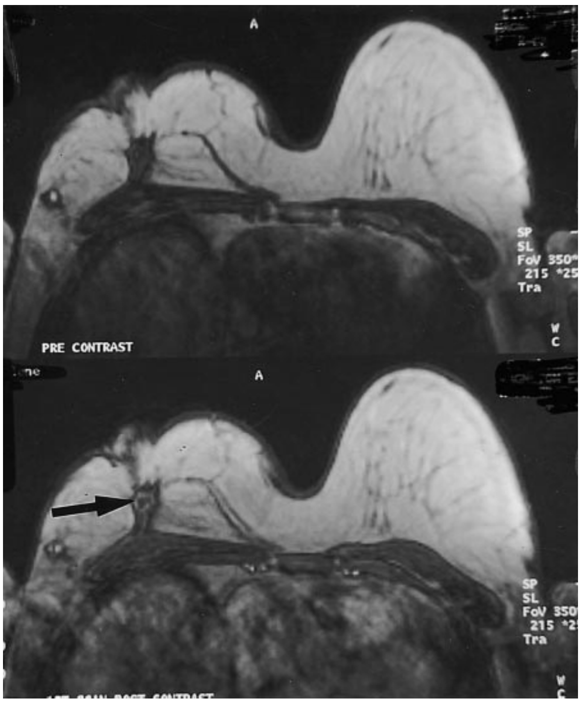


Figure 8. Pre-contrast (upper) and post-contrast (lower) MRI after breast conservation. Rim enhancement (arrow) suggesting malignancy. On biopsy, a granulomatous reaction to suture material is seen.

Limitations

There are several limitations to the use of MRI in the breast, which will particularly limit its use in the pre-menopausal group.

There are changes in the T_1 value of the breast tissue during the menstrual cycle. In the second half of the cycle, the stroma is loose and oedematous with dilatation of the lumen of the ducts owing to acinar sprouting and hormone-induced growth [88–90]. Normal breast tissue enhancement peaks one week prior to menstruation. Ideally, patients should be scanned between the 6th and 16th day of the cycle and not in the second half or proliferative phase as this increases the number of false positive scans. Patients with benign breast disease may have focal enhancement that may exceed that of malignancy and may also show diffuse fibroglandular enhancement. In one study, 80% of healthy pre-menopausal women had focal areas of enhancement that resolved during follow-up studies, with the degree of enhancement exceeding that of malignancy in 45% [91]. The nipple will also enhance in normal patients and the use of

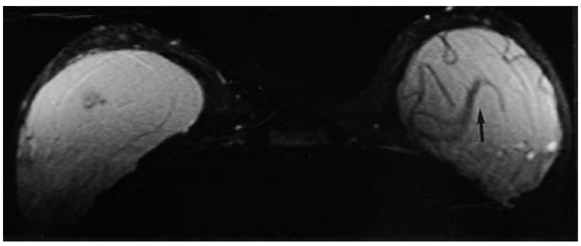
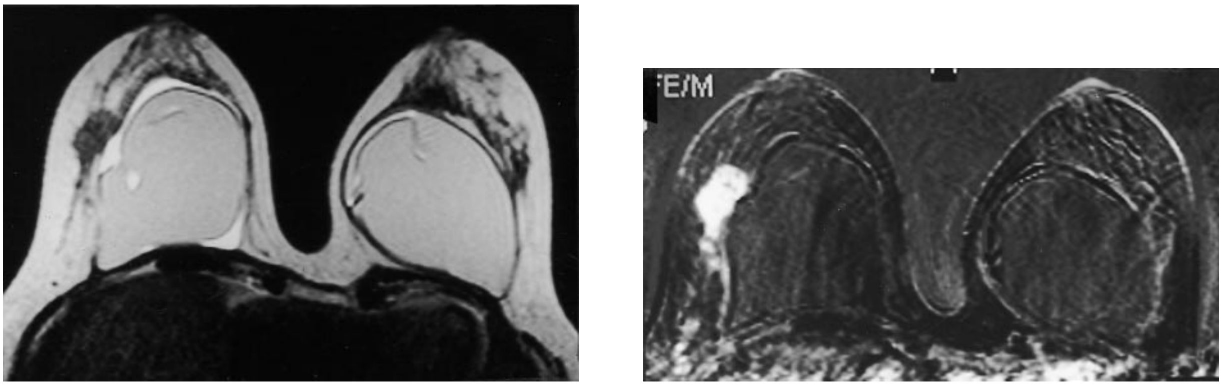


Figure 9. Axial image demonstrating silicone implant. Linguine sign (arrow) of intracapsular rupture is seen.



(a) (b)

Figure 10. (a) Pre-contrast and (b) subtraction image of invasive lobular cancer adjacent to an implant.

hormone replacement therapy will also alter the enhancement pattern in the breast. Lawrence [92] has discussed the likelihood of incidentally detected foci of enhancement on MRI being malignant in those patients who are not known to have breast cancer, with no known risk factors and normal clinical examination and mammography. The study was based on the published sensitivity and specificity of MRI in breast cancer and concluded that the lesions are unlikely to be malignant and immediate biopsy could be avoided. Rescanning at a different phase in another cycle will often resolve the problem.

Benign breast change and benign lesions may enhance in a similar manner to malignancy. Fibroadenomas are composed of fibrous stroma, proliferative ducts and acinar tissue and evolve from the proliferation of multiple lobules. They may be predominantly adenomatous, fibrous or myxoid. The internal septations identified on MRI may be related to the margins of the adjacent lobules. The enhancement pattern of fibroadenomas is variable. The myxoid variety enhances rapidly, similar to carcinoma (Figure 11); the adenomatous variety show variable patterns of enhancement; and the fibrous one does not enhance. Fibroadenomas in pre-menopausal women generally enhance more than in the post-menopausal group [93–95].

Phylloides tumours are more cellular than fibroadenomas and it is difficult to predict their biological behaviour. 16% of low grade tumours will recur after excision and 7% of high grade tumours will metastasize. They tend to enhance rapidly following iv gadolinium (Figure 12) and MRI cannot be used to predict behaviour. MRI cannot differentiate between inflammatory breast cancer and abscesses [96].

MRI may be useful following mammography when the diagnosis is uncertain, although if the lesion was easy to biopsy this would be more cost efficient. Kacl et al [1] found sensitivity and specificity for mammography of 82% and 64%, and for MRI 92% and 76%, respectively. Combining the two investigations increased the sensitivity to 95% but decreased the specificity to 52%. Similarly, Muller-Schimpfle et al found that the addition of MR to mammography and US increased the confidence level of observers in the diagnosis. The cost of increased sensitivity was a decrease in the specificity and accuracy, thus limiting its use in screening or the work-up of a suspicious lesion [97]. Sardanelli et al [98], in a small series combining MRI with mammography, found MRI correctly changed 12 false positive mammograms into true negatives and concluded that MRI was useful if the mammogram was indeterminate.

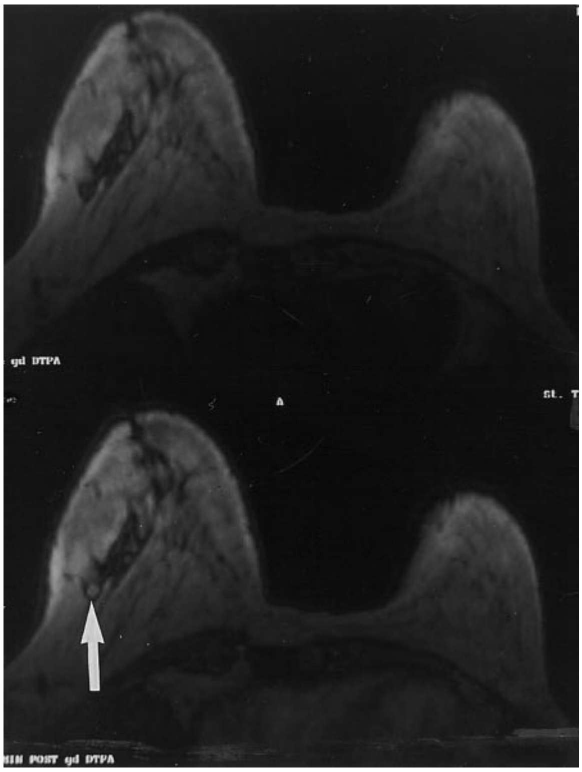


Figure 11. Pre-contrast (upper) and post-contrast (lower) T_1 weighted FLASH sequence. A rapidly enhancing fibroadenoma (arrow) is seen.

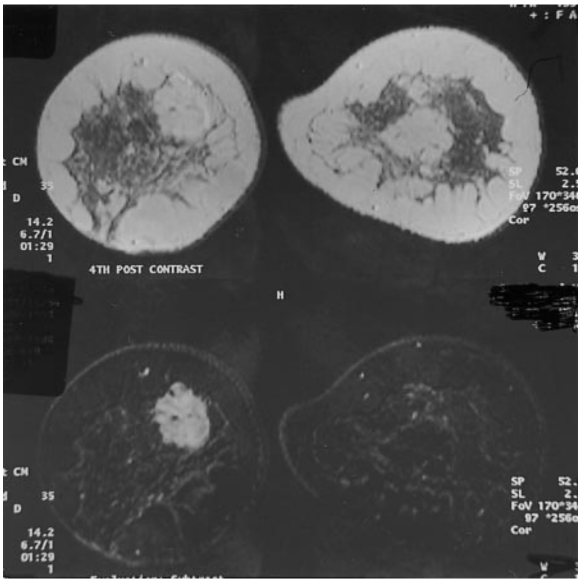


Figure 12. Post-contrast (upper) and subtraction (lower) image. A rapidly enhancing mass with spiculated margins is seen. Histology showed a low grade phylloides tumour.

Heywang-Kobrunner and Beck [23] have suggested several well reasoned indications and contraindications for MRI of the breast. They suggest that MRI should not be used in a population with a low prevalence of breast cancer, for example young patients with dense breasts who have no risk factors. In this group, breast cancer occurs in less than 1 in 10 000 and a high percentage (30%) will have enhancing foci in benign breast disease and MRI will not reliably differentiate benign from malignant change. Similarly, in a fatty breast, mammography is a very sensitive test and it is unlikely that MRI will have any benefit.

MRI is unhelpful, or other methods are more cost effective, in the differential diagnosis of microcalcification, where biopsy is the most appropriate investigation. In patients with no previous surgical history, trabecular distortion on a mammogram may represent a radial scar, DCIS or sclerosing adenosis. MRI cannot accurately differentiate between these lesions and should therefore not be used and biopsy undertaken instead.

Core biopsy has comparable sensitivity and a higher specificity than MRI at a lower cost and is therefore more cost effective than MRI for diagnosing mammographically detected lesions that are easily accessible. In this instance, MRI should be reserved for cases where biopsy is difficult or contraindicated, but MRI may be helpful in directing the biopsy to the area of greatest concern. There is on-going discussion as to whether MRI is of value in the screening of the young, high risk patient whose mammograms may be difficult to interpret. Risk of developing breast carcinoma for women carrying the BRCA1 or the BRCA2 genes is 51% by the age of 50 years, rising to 85% by the age of 70 years. Patients who carry the TP 53 gene have an 18 times greater risk over the general population of developing breast cancer by the age of 45 years. Mammography may be relatively insensitive in this group of patients who may have dense breasts, but the sensitivity and specificity of MRI in this group is not yet defined and is at present being investigated in a multicentre trial.

Conclusion

MRI of the breast is still under development. The indications, optimal imaging parameters and methods of interpretation have not yet been fully established [99–101]. MRI is a sensitive method for the detection of breast cancer but is expensive and time consuming. The lack of specificity will decrease its acceptability to clinicians and patients. It has proven advantages in the assessment of the extent of cancer and detection of recurrence, and may also be of value in the evaluation of response to therapy and in the use of an interventional magnet to develop MRI-directed interstitial hyperthermia as a treatment option [102].

At the present time it is an impractical tool for routine screening, but undoubtedly has a major role as an adjunct to mammography and US for specific problems.

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