Magnetic Resonance Imaging Role in Management of Breast Cancer

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Abstract

Background: Breast MRI is most often used in conjunction with other breast screening methods, such as mammography or ultrasound. Women with a breast cancer diagnosis often get a breast MRI to better understand the extent of their disease, identify any other tumors in the breast, and even detect tumors in the opposite breast. In addition to annual mammograms, some women at high risk for breast cancer should get a screening magnetic resonance imaging (MRI). Some magnetic resonance imaging (MRI) scans might produce false positive results, leading doctors to order unnecessary tests and biopsies. Breast MRI can help women who are very likely to develop breast cancer, but it is not often suggested for women who are just averagely at risk. Another red flag for breast cancer is the absence of micro-calcifications, which can be shown by a breast MRI.

Keywords: Magnetic Resonance Imaging, Breast Cancer

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Introduction:

The use of contrast-enhanced magnetic resonance imaging is based on neo angiogenesis. Tumour associated blood vessels have increased vascular permeability which is responsible for the uptake and washout of gadolinium after its administration. The morphology of the lesions, the enhancement and washout kinetics help distinguish breast cancers from benign lesions. The sensitivity of breast MRI is reported to be very high (over 90%) but the specificity is still low to moderate (72%) making the discrimination between benign and malignant lesions challenging.

Since 2000, breast MRI has been extensively used and has become an important modality in high risk screening, diagnosis, staging and follow up of breast cancer [Figure 1a]. Breast MRI has proven

value in high risk screening, evaluation of unknown primary, evaluating local extent of disease, multicentricity and bilaterally especially in dense breasts, differentiating a scar from local recurrence in women who had breast conserving surgery, evaluation of response to neoadjuvant chemotherapy and in evaluating the integrity of implants [Figure 1b]. However, breast MRI has its share of controversies.

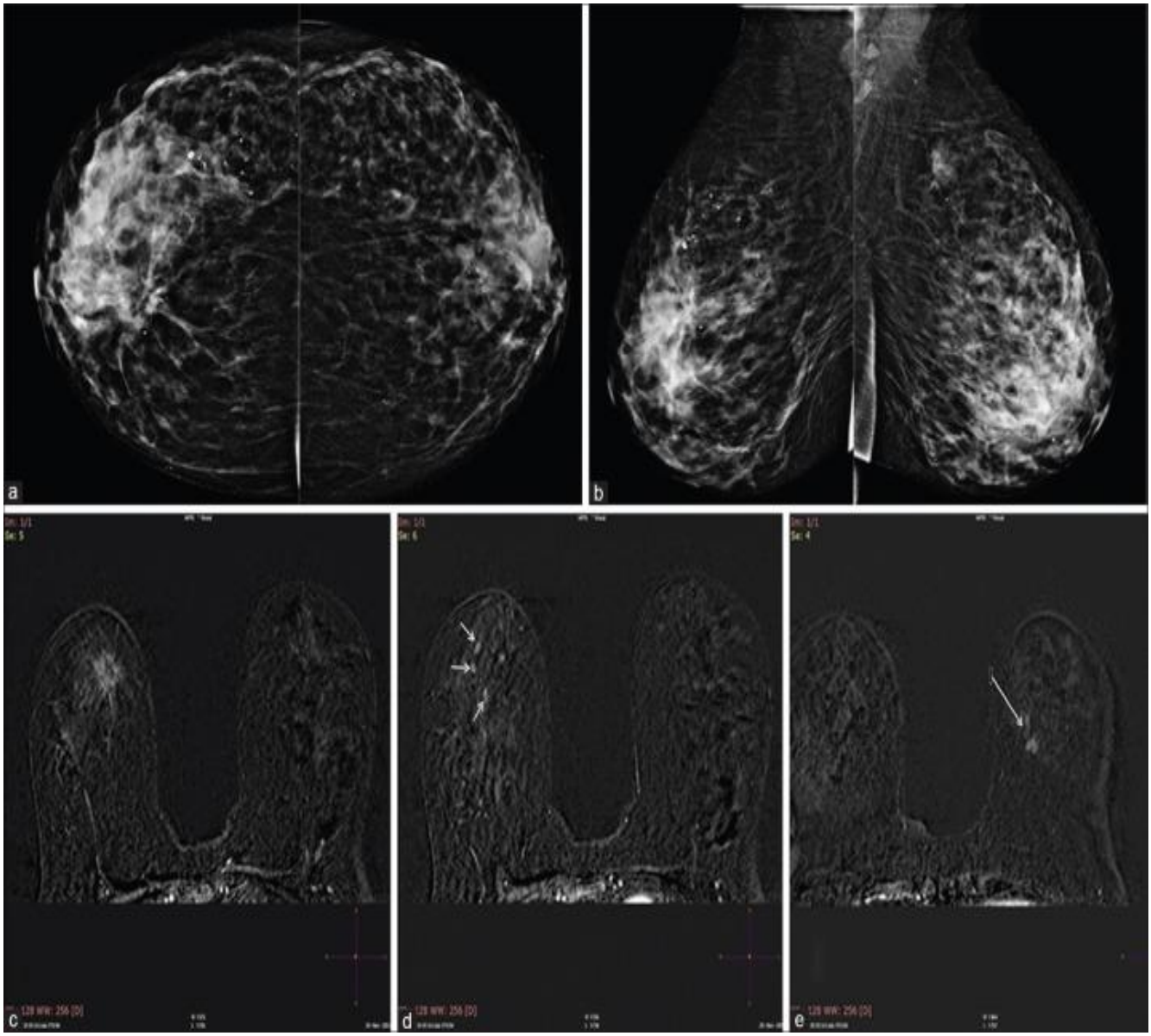

Figure 1

(a) Cranio-caudal view of both breasts. (b) Medio-lateral view of both breasts. Heterogeneously dense breast. Architectural distortion is seen in the right breast. There is focal asymmetry in the left breast upper outer quadrant seen in MLO view. (c) Postcontrast axial view showing a contrast enhancing spiculated lesion in the right breast corresponding to the mammographic image. HPE confirmed a tubular carcinoma. (d) In addition, there were other areas of contrast enhancement in the right

breast. Histopathology of these lesions confirmed an invasive lobular carcinoma. (e) The left breast enhancing lesion was reported to be an invasive ductal carcinoma

Hereditary mutations are thought to be responsible for about 5% of cancer cases. Among the many known and unknown mutations, the most prevalent ones are those affecting BRCA 1 and 2, but they can also affect P53, PTEN, CHEK2, ATM, and many more. Women treated with mantle radiation therapy (usually for Hodgkin's lymphoma) between the ages of 8 and 30 are another small but clinically relevant group at elevated risk of breast cancer.

There is less debate about high risk screening anymore. In their guidelines for high risk screening, the American Cancer Society, the European Society of Breast Cancer Specialists (EUSOMA), and the European Society of Breast Imaging (EUSOBI) have all included breast MRI. Mammography and breast ultrasound may no longer be necessary for high risk screening, according to the results of the EVA trial in Germany and the HIBCRIT-1 trial in Italy.1, 2

Women at average risk have not made MRI screening a priority owing to worries about the technology's lack of specificity, which could lead to unnecessary biopsies and wasted time and money. Mammography, due to its reduced sensitivity, is clearly not an option for women who have dense breasts. There are claims that mammography can detect less aggressive malignancies as well. By injecting contrast material (Gadolinium) into the bloodstream, breast MRI may identify higher-grade lesions more effectively than lower-grade ones, and it is not constrained by breast density. The new study by Christiane Kuhls did not find any interval malignancies, and MRI has a good negative predictive value, therefore a longer screening interval is possible. With a high negative predictive value in breast cancer screening, Christiane Kuhl's shortened MRI screening strategy promises to decrease study and interpretation time, cost, and overall screening time.the third For women at a moderate to medium risk of breast cancer, magnetic resonance imaging (MRI) may play an increasingly important role in screening.

Breast magnetic resonance imaging and DCIS

The appearance of microcalcifications on a mammogram is a common way to identify DCIS. After the tumor in the ducts and terminal ductal units develops too large for its blood supply, it calcifies, necrosise, and eventually expands. The calcifications are undetectable by MRI. On the other hand, the non-mass enhancement observed in DCIS is likely caused by gadolinium leaking into the ducts through the leaky basement, which is a result of protease activity produced by tumor cells. High grade lesions, which are more important from a clinical perspective, may be detectable by MRI. Although MRI can detect low-grade DCIS, the x-ray mammography can easily miss it. However, MRI can detect 10-15% of DCIS cases that do not calcify, which are overlooked by X-ray mammograms.

The usual manifestation of ductal or segmental distribution non-mass enhancement with a clumped or stippled morphological appearance is seen in approximately 70 to 80% of instances of

DCIS. Twenty to thirty percent of the time, you can notice several types of augmentation patterns, such a mass in a focused area, a regional dispersion, or a center. When it comes to diagnosing DCIS, the kinetics are less important because they are varied.

The function of breast MRI during preoperative assessment

Breast magnetic resonance imaging (MRI) before surgery for women who have just received a breast cancer diagnosis is a contentious topic with widely varying approaches. If you have lobular cancer or a thick breast, an MRI before surgery can help find multifocal or multicentric lesions and assess the opposite breast. In order to find studies that reported quantitative data on pre-operative MRI and surgical outcomes, a meta-analysis was conducted. The study comprised three randomized controlled trials and sixteen comparative studies. Recently diagnosed breast cancer patients are more likely to undergo ipsilateral or contralateral preventive mastectomy if magnetic resonance imaging (MRI) is performed prior to surgery, according to this analysis. As seen in Figure 1c1c-e.[4]

It is also believed that MRI provides a clearer picture of the tumor's size and extent, which aids in surgical planning. This has not materialized as anticipated, despite expectations that it would lower rates of re-excision, local recurrence, and overall survival. On the other hand, it causes more biopsies to be taken, which in turn causes patients to be anxious, which drives up the expense, which delays treatment, and could even lead to more mastectomy rates.

When it came to lowering rates of reexcision, the COMICE and MONET trials looked at the function of preoperative MRI. There were no statistically significant changes in the COMICE trial regarding the decrease of re-excision rates. Non-palpable lesions, whether benign or malignant, were the focus of the MONET trial, which assessed the value of preoperative magnetic resonance imaging (MRI). Patients with non-palpable breast cancer had an elevated re-excision rate when magnetic resonance imaging (MRI) was added to routine clinical care. Breast MRI should not be regularly used for preoperative work-up of patients with non-palpable breast malignancies, according to their recommendation.5,6

Much has been said about the margins being adequate, but there is a lot of diversity in how they are actually implemented. For invasive cancers, the 2014 SSO-ASTRO consensus guidelines state that there should be no ink on the tumor, while for ductal carcinoma in situ, 2 mm of margin is considered enough.[7] Since then, re-excision rates have dropped, suggesting that routine preoperative MRI is no longer necessary to achieve this goal.

Patients who can be appropriately assessed by mammography and ultrasound examination likely do not need pre-operative MRI on a routine basis. Women with thick breasts and individuals with lobular carcinoma may benefit greatly from it.

Assessment of responsiveness to neoadjuvant therapy using magnetic resonance imaging

Tumors can be effectively downstaged and brought within surgical reach with the use of neoadjuvant chemotherapy. When dealing with large operable lesions, neoadjuvant chemotherapy is being used more and more to save the breast. Numerous studies have demonstrated that MRI is superior to clinical assessment, mammography, and ultrasound for breast imaging, and that it also offers the best imaging association with disease.Eight and nine Breast MRI can help detect early non-responders to neoadjuvant chemotherapy, outline the residual tumor after NACT, and decide on the right amount of surgical excision by monitoring the response to the treatment.10, 11

A core biopsy is typically followed by the placement of a clip in the tumor's center, with more clips used to demarcate the lesion's extent. An MRI is done before NACT and compared to another MRI done after either one or two cycles of NACT. Using a mix of size and kinetic changes, non-responders can be quickly spotted on MRI. CAD tools that provide parametric color mapping and volumetric analysis make interpretation a breeze.

There is a correlation between contrast enhancement on MRI and viable tumors. On the other hand, quantifying the amount of enhancement may not always provide an appropriate estimate of tumor size, since it could lead to under- or overestimation. Tumor necrosis can cause granulation tissue and repair mechanisms, which can be overestimated if contrast is used too much. It is possible for chemotherapeutic drugs, such as taxanes, to have an anti-angiogenic effect without causing tumor necrosis, leading to an overestimation of the response to NACT due to a lack of enhancement. Possible remaining tumor nests dispersed over the original tumor expanse, requiring a mastectomy, are the cause of scattered focal foci of enhancement, which resemble Swiss cheese.

Patient handling

MRI of the breast is a study that requires the administration of a gadolinium-containing contrast agent during the study [1, 2]. Early studies have shown that breast MRI without contrast agent is not of diagnostic value [3, 4].

The uptake of contrast medium in breast tissue in premenopausal women is also dependent on the phase of the menstrual cycle. It is essential to perform breast MRI in the correct phase of the cycle as enhancing normal breast tissue may otherwise complicate the interpretation of the study. The optimal time in pre-menopausal women to perform a breast MRI is between the 5th and 12th day after the start of the menstrual cycle [5–7].

Placement of an intravenous cathether should be done before positioning the patient on the MR table. A long IV line avoids table and patient movement before the injection. The contrast agent should preferably be given by a power injector.

It is important to position the patient as comfortably as possible in order to avoid motion artifacts.

A dedicated bilateral breast coil is mandatory for this investigation, and the patient should be placed in the prone position with both breasts hanging in the coil loops. The breasts may be supported to further reduce motion artifacts, but should not be compressed.

The position of the breast should be checked before the start of the examination, both breasts must be placed as deeply as possible in the coils with the nipples pointing down. A larger breast coverage is usually obtained by placing both arms at the side of the body and not above the patient's head.

Virtually any MRI scanner can be used to perform contrast-enhanced breast MRI, as long as the system allows image acquisition at a sufficient spatial and temporal resolution (see below). However, scanning protocols need to be adapted to the scanners used, also because the relaxivity of the most commonly used contrast agents decreases at higher field strengths [8, 9]. Breast MRI at low and midfield strength (0.2 T, 0.5 T) depends heavily on parallel imaging to obtain a sufficient resolution. As this further decreases the signal-to-noise ratio (SNR), this is not optimal. In practice, most studies that employed low or midfield scanners did not obtain a sufficient spatial resolution [10, 11]. An increasing field strength (1.5 T, 3 T) allows a higher spatial resolution at a similar temporal resolution and consequently may increase diagnostic confidence [12]. A disadvantage is that, at higher field strengths (e.g. 3 T), inhomogeneity in the B1 field may cause reduced signal in parts of the image and thus less contrast enhancement, which in turn may cause false-negative image interpretation. Two-dimensional acquisitions are particularly sensitive to this effect and are therefore discouraged at 3 T [13].

Sequences

The conventional breast MRI investigation begins precontrast with either T2- or T1-weighted images.

The signal from the body coil can be used to evaluate the position and anatomy of the breasts. Furthermore, both axillae, the supraclavicular fossae, the chest wall and anterior mediastinum can be checked (e.g., for enlarged lymph nodes). However, this is not the purpose of a breast MRI, and this evaluation may also be omitted as there is no evidence of its diagnostic value.

Afterwards the signal from the dedicated double breast coil should be used.

T2-weighted fast spin echo images can be performed as a start.

In the T2-weighted images water-containing lesions or edematous lesions have an intense signal, and in this sequence small cysts and myxoid fibroadenomas are very well identified.

In most cases cancer does not yield a high signal on T2-weighted images; thus, these sequences can be useful in the differentiation between benign and malignant lesions. However, as most of these lesions can also be identified on T1-weighted images, there is no evidence as yet of added value of T2-weighted sequences in breast MRI [14, 15].

The most commonly used sequence in breast MRI is a T1-weighted, dynamic contrast enhanced acquisition. The sequence is called 'dynamic' because it is first performed before contrast administration and is repeated multiple times after contrast administration.

A T1-weighted 3D or 2D (multi-slice) spoiled gradient echo pulse sequence is obtained before contrast injection and then repeated as rapidly as possible for 5 to 7 min after a rapid intravenous bolus of a Gd-containing contrast agent. A 3D pulse sequence offers a stronger T1 contrast and enables thinner slices than 2D; in turn, a 2D sequence suffers less from motion and pulsation artifacts. Both sequences can be performed with and without fat-suppresion [16, 17].

The choice of the image orientation is important. For bilateral dynamic breast MRI, axial or coronal orientations are most frequently used. Coronal imaging has advantages in that it can reduce heart pulsation artifacts, but it is more susceptible to respirational motion and also to flow artifacts because vessels tend to travel perpendicular to the slice-encoding direction. Although bilateral sagittal imaging is possible today, it requires about double the number of slices required for the other orientations. As this hampers the spatio-temporal resolution, such an orientation is currently not feasible.

The optimal dose of the contrast medium is unknown and also depends on the contrast agent used. In literature, applied doses range roughly from 0.05 to 0.2 mmol/kg. One study showed some benefit of 0.16 mmol/kg gadopentetate dimeglumine over 0.1 mmol/kg [18]. However, a more recent evaluation did not find any improvement in diagnostic accuracy using 0.2 mmol/kg gadobenate dimeglumine over 0.1 mmol/kg of the same agent [19]. Consequently, a dose of 0.1 mmol/kg is probably sufficient.

Peak enhancement in the case of breast cancer occurs within the first 2 min after the injection of contrast medium. Therefore, relatively short data acquisition times, in the order of 60–120 s per volume acquisition, are necessary. This allows sampling of the time course of signal enhancement after contrast injection, which is useful because the highly vascularized tumor of the breast shows a faster contrast uptake than the surrounding tissue. More importantly, it enables a detailed analysis of morphologic details, because only in the very early post-contrast phase, the contrast between the cancer and the adjacent fibroglandular tissue is optimal. Tumors may lose signal (a phenomenon referred to as "wash out") as early as 2–3 min after contrast material injection, whereas the adjacent fibroglandular tissue can still exhibit substantial enhancement, resulting in little contrast between the cancer and the fibroglandular tissue. Long acquisition times will be associated with the risk of not resolving fine details of margins and internal architecture; this could have key importance for the differential diagnosis, and may even run the risk of missing cancers altogether because they are masked by adjacent breast tissue.

A dynamic sequence demands at least three time points to be measured, that is, one before the administration of contrast medium, one approximately 2 min later to capture the peak and one in the late phase to evaluate whether a lesion continues to enhance, shows a plateau or shows early

wash-out of the contrast agent (decrease of signal intensity) [20]. It is thus recommended to perform at least two measurements after the contrast medium has been given, but the optimal number of repetitions is unknown. However, the temporal resolution should not compromise the spatial resolution. It was shown that an increase in spatial resolution results in higher diagnostic confidence even when the temporal resolution is slightly sacrificed. [21].

The final spatial resolution of the images depends on different factors, especially the size of the imaging volume, defined by the field of view (FOV), the slice thickness and the acquisition matrix. Breast MRI should be capable of detecting all lesions larger than or equal to 5 mm. Therefore, the voxel size should be under 2.5 mm in any direction. Preferably, the in-plane resolution should be substantially higher as morphologic features needed for lesion characterization, such as margin appearance, can only be evaluated when the resolution is sufficiently high. Therefore, the in-plane resolution should be at least 1 mm^{-1} , in other words: pixel size (FOV/matrix) should not be greater than 1×1 mm, which requires a matrix of at least 300×300 in a 300-mm FOV.

Assessment of lesion morphology can be performed directly on the enhanced fat-suppressed images. However, as residual fat-signal (hyperintense at T1-weighted images) may cause difficulties in interpretation, the calculation of subtraction images from the pre- and post-contrast series is recommended [22, 23].

Subtraction suppresses the signal from bright fat because fatty tissue hardly enhances. When subtraction is performed, fat suppression in the acquisition is not needed and is even discouraged, because in the large fields of view that are usually required for axial and coronal imaging, homogenous fat suppression is difficult to obtain. This can be problematic since fat and water resonance frequencies are relatively close at 1.5 T—which implies that with less-than-optimal B0 homogeneity across the field of view, water (rather than fat) suppression can occur. Moreover, fat-suppression increases the noise in the image and usually also compromises spatio-temoral resolution.

Evaluation

Use of both detailed morphological information provided by high spatial resolution images and kinetic information (curve type) provided by at least two repetitions of the high spatial resolution sequence represents the latest trend in acquisition protocols and image interpretation to take into account the increasing importance of detailed morphological information without losing identification of washout enhancement curve types [24].

For the diagnostic interpretation the ACR breast imaging reporting and data system (BIRADS) for breast MRI illustrates many of the morphological findings seen on contrast-enhanced breast MRI. It also includes a lexicon that should be used for uniform reporting of the features seen on MRI [25].

Conclusion

MRI is superior to x-ray mammogram in high-risk breast cancer screening. In women with low to average risk of breast cancer, the role of MRI remains controversial. The use of pre-operative MRI continues to be controversial with wide variations in practice. In a neo-adjuvant setting, MRI breast is useful to identify the non-responders early. In those who respond to chemotherapy, it is helpful in planning conservation where feasible.

References:

1. Santoro F, Podo F, Sardanelli F. MRI screening of women with hereditary predisposition to breast cancer: Diagnostic performance and survival analysis. Breast Cancer Res Treat. 2014;147:685–7. [PubMed] [Google Scholar]

2. Kuhl C, Weigel S, Schrading S, Arand B, Bieling H, König R, et al. Prospective multicenter cohort study to refine management recommendations for women at elevated familial risk of breast cancer: The EVA trial. J Clin Oncol. 2010;28:1450–7. [PubMed] [Google Scholar]

3. Kuhl CK, Schrading S, Strobel K, Schild HH, Hilgers RD, Bieling HB, et al. Abbreviated breast magnetic resonance imaging (MRI): First postcontrast subtracted images and maximum-intensity projection-a novel approach to breast cancer screening with MRI. J Clin Oncol. 2014;32:2304–10. [PubMed] [Google Scholar]

4. 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;165:273–83. [PMC free article] [PubMed] [Google Scholar]

5. 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;375:563–71. [PubMed] [Google Scholar]

6. 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;47:879–86. [PubMed] [Google Scholar]

7. Harness JK, Giuliano AE, Pockaj BA, Downs-Kelly E. Margins: A status report from the annual meeting of the american society of breast surgeons. Ann Surg Oncol. 2014;21:3192–7. [PubMed] [Google Scholar]

8. Martincich L, Montemurro F, De Rosa G, Marra V, Ponzone R, Cirillo S, et al. Monitoring response to primary chemotherapy in breast cancer using dynamic contrast-enhanced magnetic resonance imaging. Breast Cancer Res Treat. 2004;83:67–76. [PubMed] [Google Scholar]

9. Rieber A, Brambs HJ, Gabelmann A, Heilmann V, Kreienberg R, Kühn T, et al. Breast MRI for monitoring response of primary breast cancer to neo-adjuvant chemotherapy. Eur Radiol. 2002;12:1711–9. [PubMed] [Google Scholar]

10. Stucky CC, McLaughlin SA, Dueck AC, Gray RJ, Giurescu ME, Carpenter SG, et al. Does magnetic resonance imaging accurately predict residual disease in breast cancer? Am J Surg. 2009;198:547–52. [PubMed] [Google Scholar]

11. Thibault F, Nos C, Meunier M, El Khoury C, Ollivier L, Sigal-Zafrani B, et al. MRI for surgical planning in patients with breast cancer who undergo preoperative chemotherapy. AJR Am J Roentgenol. 2004;183:1159–68. [PubMed] [Google Scholar]

12. Kuhl CK, Jost P, Morakkabati N, Zivanovic O, Schild HH, Gieseke J (2006) Contrast-enhanced MR imaging of the breast at 3.0 and 1.5 T in the same patients: initial experience. Radiology 239:666–676

13. Kuhl CK, Kooijman H, Gieseke J, Schild HH (2007) Effect of B1 inhomogeneity on breast MR imaging at 3.0 T. Radiology 244:929–930

14. Kelcz F (2006) Quantitative Assessment of T2 Imaging information in differential diagnosis of enhancing breast lesions. Eur Radiol 16(Suppl 5):E51–E53.

15. Kuhl CK, Klaschik S, Mielcarek P, Gieseke J, Wardelmann E, Schild HH (1999) Do T2-weighted pulse sequences help with the differential diagnosis of enhancing lesions in dynamic breast MRI? J Magn Reson Imaging 9:187–196.

16. Heiberg EV, Perman WH, Herrmann VM, Janney CG (1996) Dynamic sequential 3D gadolinium-enhanced MRI of the whole breast. Magn Reson Imaging 14:337–348.

17. Sardanelli F, Fausto A, Iozzelli A, Rescinito G, Calabrese M (2004) Dynamic breast magnetic resonance imaging. Effect of changing the region of interest on early enhancement using 2D and 3D techniques. J Comput Assist Tomogr 28:642–646.

18. Heywang-Kobrunner SH, Haustein J, Pohl C, Beck R, Lommatzsch B, Untch M, Nathrath WB (1994) Contrast-enhanced MR imaging of the breast: comparison of two different doses of gadopentetate dimeglumine. Radiology 191:639–646.

19. Knopp MV, Bourne MW, Sardanelli F, Wasser MN, Bonomo L, Boetes C, Muller-Schimpfle M, Hall-Craggs MA, Hamm B, Orlacchio A, Bartolozzi C, Kessler M, Fischer U, Schneider G, Oudkerk M, Teh WL, Gehl HB, Salerio I, Pirovano G, La NA, Kirchin MA, Spinazzi A (2003) Gadobenate dimeglumine-enhanced MRI of the breast: analysis of dose response and comparison with gadopentetate dimeglumine. AJR Am J Roentgenol 181:663–676.

20. Degani H, Gusis V, Weinstein D, Fields S, Strano S (1997) Mapping pathophysiological features of breast tumors by MRI at high spatial resolution. Nat Med 3:780–782.

21. Kuhl CK, Schild HH, Morakkabati N (2005) Dynamic bilateral contrast-enhanced MR imaging of the breast: trade-off between spatial and temporal resolution. Radiology 236:789–800.

22. Boetes C, Barentsz JO, Mus RD, Van Der Sluis RF, van Erning LJ, Hendriks JH, Holland R, Ruys SH (1994) MR characterization of suspicious breast lesions with a gadolinium-enhanced TurboFLASH subtraction technique. Radiology 193:777–781.

23. Flanagan FL, Murray JG, Gilligan P, Stack JP, Ennis JT (1995) Digital subtraction in Gd-DTPA enhanced imaging of the breast. Clin Radiol 50:848–854.

24. Schnall MD, Blume J, Bluemke DA, DeAngelis GA, DeBruhl N, Harms S, Heywang-Kobrunner SH, Hylton N, Kuhl CK, Pisano ED, Causer P, Schnitt SJ, Thickman D, Stelling CB, Weatherall PT, Lehman C, Gatsonis CA (2006) Diagnostic architectural and dynamic features at breast MR imaging: multicenter study. Radiology 238:42–53.

25. American College of Radiology (2003) BI-RADS(r) — MRI. BI-RADS (r) Atlas. 1 ed. Reston: American College of Radiology.