## Diagnostic utility of breast MRI

There is broad published evidence suggesting that breast MR imaging is the imaging technique that offers highest sensitivity for diagnosing primary and recurrent breast cancer. Very much unlike mammography, the technique´s sensitivity is not impaired by dense breast tissue or by therapeutic interventions (postsurgical scars, radiotherapy-induced fibrosis). With current state-of-the-art MR scanners, sensitivity for invasive breast cancers is virtually 100%. A non-enhancing breast cancer is such a rare finding that it is still worth a case report. Sensitivity for intraductal cancer (DCIS) is lower, presumably owing to the inconsistent angiogenic activity of pre-invasive cancer that translates into a inconsistent enhancement pattern. Still, with adequate diagnostic criteria, sensitivity for DCIS will be about 90%. Current data suggests that regarding DCIS, breast MRI and mammography are complimentary: mammography helps detect the 10% of DCIS that do not enhance on MRI, and in turn, MRI helps detect additional DCIS that are mammographically occult owing to the absence of microcalcifications (8).

Specificity of breast MRI (or, specificity of any given breast imaging test) depends on the composition of the study cohort, of the imaging techniques and diagnostic guidelines that are used, and, most notably, on the expertise of the interpreting physician. Owing to the wealth of diagnostic information provided by breast MRI (tissue relaxation times, enhancement kinetics, cross-sectional morphology, and so forth), specificity is high in experienced hands; in our department, it is 86% in screening settings. This is substantially higher compared to the specificity of mammography, and again significantly higher than the specificity of high frequency breast ultrasound, with or without echo contrast agents. The downside to breast MRI is the fact that it is still the second most expensive breast imaging modality (after PET), that the scanner capacity for breast MRI is limited, and, most importantly, that there are only

few trained radiologists with expertise in breast MRI. Based on these facts, the following statements can be made regarding the clinical use of this technology (9):

## Current and emerging indications for using breast MRI in clinical practice

Given the superior sensitivity and overall diagnostic accuracy, the "added value" of breast MR in current clinical practice is to avoid unnecessary biopsies (and associated costs!) secondary to false-positive mammographic or sonographic diagnoses, and to improve the detection and staging of primary and recurrent breast cancer. The latter should translate into less invasive (and, thus, less expensive!) therapies, lower morbidity and, hopefully, improved survival. Currently, most of the indications in clinical settings suggest the use of breast MRI as a "second line" imaging modality, i.e. only after a suspicious or equivocal finding was made on a mammogram or breast ultrasound (11-17). Two different clinical scenarios are typical: In the setting of *equivocal or discordant* mammographic and/or sonographic and/or clinical findings, MRI can be used to decide upon whether or not a tissue diagnosis (biopsy) is actually necessary. In patients with mammographically or sonographically *suspicious or definitively malignant* lesions who, based on the mammographic and sonographic assessment, are candidates for breast conservation therapy, MRI is indicated to improve local staging: It is well established that in up to 26% of patients with a presumably solitary cancer, MRI detects additional, mammographically and sonographically occult cancers in the same or the contralateral breast. In about 16%, the multicentric or contralateral cancers detected by pre-operative MRI mandate an entire change of surgical or therapeutic approach. A recent large cohort follow-up study compared mid-term cancer recurrence rates after breast conservation therapy (including radiotherapy) in women who were staged with pre-operative breast MRI to the recurrence rates in women who were staged with mammography and high-frequency breast ultrasound alone. In women who were treated with compared to those treated without

MRI staging, recurrence rates were reduced from over 6% to under 1%. In addition, MRI is substantially superior compared to mammography or breast ultrasound regarding the assessment of disease extent: nipple invasion, chest wall invasion, multicentric cancer, and extensive intraductal component are all contra-indications for breast conservation and are all best visualized by MRI.

With increasing evidence regarding the superior diagnostic accuracy of MRI compared to conventional imaging methods, there are currently several international large-scale trials underway to evaluate the use of MRI as a *first line* imaging modality (18-22). This concept is increasingly supported because, in spite of the higher direct costs of MRI compared to conventional methods, it may not be sensible to have the less sensitive imaging methods (mammography, breast ultrasound) serve as gatekeeper for the method with higher sensitivity. This possible paradigm shift is in concordance with the concept to individualize screening efforts in that not all women are subjected to the same protocol (yearly mammographic screening starting age 40), but to tailor screening efforts to the individual risk profile, i.e. offering intensified screening protocols – possibly including MRI – to women who carry an increased risk. An increased risk for breast cancer harbor women who were already diagnosed with breast cancer (high risk of recurrent ipsilateral or synchronous or metachronous contralateral breast cancer), women with a history of borderline tissue diagnosis ("lobular carcinoma in-situ, LCIS", "atypical ductal hyperplasia, ADH" or "radial scars"), women with a strong family history for breast cancer (in particular early-onset breast cancer), and women with presumed or proven mutation in one of the breast cancer susceptibility genes (resulting in a condition called "hereditary" or "familial" breast cancer). The latter two groups are the so-called "high risk" subjects; for gene carriers, the individual lifetime risk is as high as 85%-90% (BRCA1-carriers). The first trial on using MRI screening in high risk women suggests that MRI helps *double* the number of cancers detected compared to conventional breast

imaging (sensitivity 100% by MRI compared to 44% for mammography and breast ultrasound), and with even increased PPV (64% compared to 34%). Further trials confirmed these encouraging results, consolidating MRI as the new “gold standard” for breast imaging.

For optimum clinical results, breast MRI should be performed with very high spatial and temporal resolution. There are a few emerging techniques that may help with this task: New image acquisition strategies (parallel imaging), High-field MRI (3T and higher) and new contrast agents (Gadomer) may improve our ability to meet these requirements.

*Parallel imaging* like “SENSE” (SENsitivity Encoding) is a new approach to MR image acquisition. The gain in image acquisition speed can be invested to improve spatial resolution at a given acquisition time, or to improve temoral resolution with high matrix imaging. While SENSE imaging is fully integrated into routine clinical practice for many body and MRA applications, its use in breast MR is lagging behind. The one reason for this is that owing to the reduced number of phase encoding steps, using SENSE will go along with an SNR reduction by about 30%. With the single-acquisition, high-matrix dynamic imaging technique that is required for breast MR, the resulting in borderline SNR. An ideal combination will be to do SENSE with *high field MR*. Magnets operating at 3T and higher become increasingly available in clinical settings. With the inherently increased SNR brought about by high field systems, SENSE can be used to acquire high-SNR, high spatial resolution images in a temporal resolution that ensures “arterial phase” lesion contrast. Another approach to solve the “temporal-versus-spatial dilemma” is to use contrast agents that are less rapidly diffusable compared to the small Gd chelates that are in use today. One of the promising candidates for this purpose is the blood pool agent *Gadomer*. Originally designed as new contrast agent for MR angiography (e.g., coronary angiography), it has been shown that it provides an “arterial phase” type of lesion-to-parenchma contrast not only for 2 minutes, but for a period of about 30 to 45 minutes. This would allow one to take time for very high spatial resolution imaging.

The resulting gadomer-enhanced MR images reveal cross-sectional views through breast cancers with unprecedented anatomic detail – it is to be expected that this will help further improve the PPV of breast MRI.

Owing to the wealth of diagnostic information provided by breast MRI (tissue relaxation times, enhancement kinetics, cross-sectional morphology), specificity is actually high (but, as always, this requires adequate expertise with the technique); in our department, it is 86% in screening settings. The downside to breast MRI is the fact that it is still the second most expensive breast imaging modality (after PET), that the scanner capacity for breast MRI is limited, and, most importantly, that there are not enough trained radiologists. Given the superior sensitivity and overall diagnostic accuracy, the "added value" of breast MR in current clinical practice is to improve the detection and staging of primary and recurrent breast cancer. The latter should translate into less invasive (and, thus, less expensive!) therapies, lower morbidity and, hopefully, improved survival.

## References:


1. Ries LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L, Edwards BK (eds). *SEER Cancer Statistics Review, 1973-1999*, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1973_1999/, 2002

2. Jackson VP Screening mammography: controversies and headlines. Radiology 2002 Nov;225(2):323-6

3. Smart CR, Hendrick RE, Rutledge JH III, et al. Benefit of mammography screening in women ages 40 to 49. Cancer 1195; 75:1619-26

4. Tabar L, Duffy S, Vitak B, et al. The natural history of breast carcinoma. What have we learned from screening? Cancer 1999; 86:449-62

5. Carney PA, Miglioretti DL, Yankaskas BC, Kerlikowske K, Rosenberg R, Rutter CM, Geller BM, Abraham LA, Taplin SH, Dignan M, Cutter G, Ballard-Barbash R Individual and combined effects of age, breast density, and hormone replacement therapy use on the accuracy of screening mammography. Ann Intern Med. 2003 Feb 4;138(3):I-28.

6. Stomper PC, Recht A, Berenberg AL. Mammographic detection of residual or residual or recurrent cancer in the irradiated breast. Am J Radiol 1987; 148: 39 – 43

7. Yasmeen S, Romano PS, Pettinger M, Chlebowski RT, Robbins JA, Lane DS, Hendrix SL. Frequency and predictive value of a mammographic recommendation for short-interval follow-up. J Natl Cancer Inst 2003 Mar 19;95(6):429-36

8. Kuhl CK. MRI of breast tumors. Review article. Eur Radiol 2000; 10: 46 – 58

9. Kuhl CK, Schild HH. Dynamic image interpretation of MRI of the breast. J Magn Reson Imaging 2000;12:965-974

10. Fischer U, Kopka L, Grabbe E. Breast carcinoma: effect of preoperative contrast-enhanced MR imaging on the therapeutic approach. Radiology 1999; 213: 881 – 888

11. Liberman L, Morris EA, Kim CM, Kaplan JB, Abramson AF, Menell JH, Van Zee KJ, Dershaw DD MR imaging findings in the contralateral breast of women with recently diagnosed breast cancer. AJR Am J Roentgenol 2003 Feb;180(2):333-41

12. Olson JA Jr, Morris EA, Van Zee KJ, Linehan DC, Borgen PI. Magnetic resonance imaging facilitates breast conservation for occult breast cancer. Ann Surg Oncol 2000 Jul;7(6):411-5

13. Morris EA, Schwartz LH, Drotman MB, Kim SJ, Tan LK, Liberman L, Abramson AF, Van Zee KJ, Dershaw DD. Evaluation of pectoralis major muscle in patients with posterior breast tumors on breast MR images: early experience. Radiology 2000 Jan;214(1):67-72

14. Morris EA, Schwartz LH, Dershaw DD, van Zee KJ, Abramson AF, Liberman L. MR imaging of the breast in patients with occult primary breast carcinoma. Radiology 1997 Nov;205(2):437-40

15. Lee SG, Orel SG, Woo IJ, Cruz-Jove E, Putt ME, Solin LJ, Czerniecki BJ, Schnall MD. MR imaging screening of the contralateral breast in patients with newly diagnosed breast cancer: preliminary results. Radiology 2003 Mar;226(3):773-8

16. Tillman GF, Orel SG, Schnall MD, Schultz DJ, Tan JE, Solin LJ. Effect of breast magnetic resonance imaging on the clinical management of women with early-stage breast carcinoma. J Clin Oncol 2002 Aug 15;20(16):3413-23

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

18. Harms SE. Integration of breast MRI in clinical trials. J Magn Reson Imaging 2001 Jun;13(6):830-6

19. Kuhl CK, Schmutzler R, Leutner C, Kempe A, Wardelmann E, Hocke A, Maringa M, Pfeifer U, Krebs D, Schild HH. Breast MR imaging screening in 192 women proved or suspected to be carriers of a breast cancer susceptibility gene: preliminary results. Radiology. 2000; 215(1):267-279

20. Cilotti A, Caligo MA, Cipollini G, Francesca D, Marini C, Moretti M, Roncella M, Bartolozzi C, Bevilacqua G. Breast MR imaging screening in eight women proved or suspected to be carriers of BRCA1&2 gene mutations. J Exp Clin Cancer Res 2002 Sep;21(3 Suppl):137-40

21. Podo F, Sardanelli F, Canese R, D'Agnolo G, Natali PG, Crecco M, Grandinetti ML. The Italian multi-centre project on evaluation of MRI and other imaging modalities in early detection of breast cancer in subjects at high genetic risk. J Exp Clin Cancer Res 2002 Sep;21(3 Suppl):115-24

22. Stoutjesdijk MJ, Boetes C, Jager GJ, Beex L, Bult P, Hendriks JH, Laheij RJ, Massuger L, van Die LE, Wobbes T, Barentsz JO. Magnetic resonance imaging and mammography in women with a hereditary risk of breast cancer. J Natl Cancer Inst. 2001 Nov 21;93(22):1754-5