Randomized Trial of Surveillance with Abbreviated MRI in Breast Cancer Survivors – Does it impact patient anxiety and cancer detection rate?

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Abstract

Purpose: Abbreviated breast MRI substantially reduces the image acquisition and reading times and has been reported to have similar diagnostic accuracy as a full diagnostic protocol but has not been evaluated prospectively with respect to impact on patient anxiety in breast cancer survivors and cancer outcomes.

Methods: This prospective controlled trial of parallel design was performed at an academic center on women with a personal history of breast cancer who were randomized into two groups: surveillance with MG or MG plus A-MRI. Primary outcome was anxiety compared between the two and measured by four validated questionnaires at three different time-points during the study. Other parameters including the CDR, abnormal interpretation rate (AIR), and positive predictive value for biopsy (PPV3) were compared between modalities of MG and A-MRI. Tissue diagnoses or 1 year of follow-up were used to establish the reference standard. Linear mixed models were used to analyze anxiety and Fisher’s exact test to compare imaging outcomes.

Results: 198 patients were allocated to either MG alone (94) or A-MRI plus MG (104). Anxiety scores in all questionnaires were similarly elevated in both groups (50.99 +/- 4.6 with MG vs 51.73 +/- 2.56 with MRI, p>0.05) and did not change over time. MRI detected 5 invasive cancers and 1 DCIS, and MG detected 1 DCIS. MRI had higher incremental CDR (48/1000 (5/104) vs MG 5/1000 (1/198, p=0.01)) and higher AIR 25% (26/104) vs MG 4.5% (9/198, p=0.00001), with no difference in PPV3: MRI 28.6% (6/21) vs MG 16.7% (1/6, p=0.557).

Conclusion:

Compared to mammography alone, A-MRI had significantly higher incremental cancer detection in breast cancer survivors. Despite a higher rate of recalls and biopsies, A-MRI had no adverse impact on anxiety.

Introduction

Women with a prior history of breast cancer (PHBC) often have a high level of anxiety related to breast cancer surveillance[1]. Their actual recurrence rates are estimated in the order of 1~5% per year[2, 3], and can be as high as 11% at 5 years and 20% at 10 years after completion of adjuvant chemotherapy[4, 5]. Early detection decreases mortality for women with breast cancer[6~8]. In women with PHBC, the survival benefit is improved if new or recurrent breast cancer is found on surveillance mammography instead of physical examination[9]. However, mammography has been shown to be less sensitive in women with PHBC, with sensitivity of 65.4% compared with 76.5% in women with no PHBC[10]. Breast MRI is the most sensitive test for detecting breast cancer[11]. Breast MRI is currently recommended for women with personal history of breast cancer and dense tissue or those diagnosed by age 50, as per American College of Radiology (ACR) guidelines[12]. High MRI costs associated with a lack of sites that offer high-level breast MRI limit clinical access to screening MRIs[4]. Compliance with MRI screening has been shown to be low, in the order of 25%[13]. Abbreviated breast MRI (A-MRI), which substantially reduces the image acquisition and reading time, has been reported to have similar diagnostic accuracy as a full diagnostic protocol[4, 14~18]. Currently, A-MRI has not been adopted as the standard for screening for breast cancer and more studies are required to evaluate outcomes.

Prior studies demonstrated that supplementary MRI surveillance in women at high risk of breast cancer does not impact anxiety, cancer-specific distress or health-related quality of life[1, 19]. This is the first study to our knowledge to evaluate the psychological effect of adding abbreviated MRI to mammography surveillance in women with PHBC.

The primary purpose of the study was to determine if A-MRI in addition to mammography impacted patient anxiety and, secondarily, if it improved cancer detection rate in breast cancer survivors.

Materials And Methods

Study subjects

This prospective randomized controlled trial of parallel design was performed at a large tertiary care academic medical center and was approved by the hospital's institutional review board (https://clinicaltrials.gov/ct2/show/NCT02244593). The patients' oncologists or surgeons obtained written informed consent. Recruitment began 2/1/2015 and was completed on 4/30/2019. Patients were followed for a minimum of 12 months.

The eligibility criteria included: (a) female patients 18 years or older; (b) personal history of breast carcinoma (including DCIS and invasive ductal or lobular carcinoma); (c) prior unilateral mastectomy or breast conservation surgery; (d) treatment for breast cancer completed;
and (e) no symptoms of breast cancer. Patients were excluded if they were considered high-risk (lifetime risk ≥ 25%) [20], were unable to undergo an MRI due to either physical or mental issues (i.e.: severe claustrophobia, allergy to gadolinium, severe renal failure), had bilateral mastectomies, were pregnant or breastfeeding, or had undergone a breast MRI within the last 6 months. Regular surveillance imaging consisted of annual surveillance mammography, irrespective of breast tissue density. All patients had undergone prior mammographic imaging, and some (< 50%) had undergone prior breast MRI imaging.

Eligible patients were randomized in a 1:1 allocation ratio to one of the two arms of the study: 1) surveillance with MG or 2) MG plus A-MRI, with use of permuted blocks of variable length (2, 4, and 6) to ensure that recruiting physicians remained unaware of the randomization. Researchers or study participants were not blinded to their allocation.

**Imaging Technique and Interpretation**

All mammographic examinations were performed using a full-field digital technique (Hologic, Bedford, MA, USA) in accordance with national guidelines. Standard two-dimensional craniocaudal (CC) and mediolateral oblique (MLO) views were obtained.

All abbreviated dynamic contrast material-enhanced breast MRIs were performed with one 3T system (Magnetom TrioTim Syngo, Siemens). The standardized protocol consisted of 8-channel breast coil (Sentinelle Medical Inc.), T1 localizer, T1 dynamic contrast-enhanced fat-suppressed with one precontrast and one 2 min postcontrast (3D transverse, phase encoding direction right to left, phase resolution of 60%, phase partial Fourier 6/8, no interpolation, FA 10 degrees, TR 4.07 msec and TE 1.96 msec, no IR, NEX 1, Voxel size: 1x1x1 mm, acceleration factor 4, no interpolation, base resolution 448,1:01 min, slice thickness 1 mm). Post-processing axial subtracted sequences and axial and sagittal maximum intensity projection were generated of the subtracted images. No T2-weighted sequences were obtained. For all examinations, gadolinium contrast material (Gadovist) was power injected (0.1 mmol/kg at 2mL/s) followed by a 20mL saline flush. The entire protocol took 3 minutes.

Surveillance MG and A-MRI were reviewed by one of two breast radiologists independently (8 and 20 years of experience) using ACR Breast Imaging-Reporting Data System (BI-RADS) lexicon [21]. For patients in the A-MRI group, mammography and A-MRI studies were usually performed on the same day. Radiologists were not blinded but reported each modality separately according to the imaging modality findings, with the mammograms interpreted first. Based on the imaging findings, additional mammographic images, including diagnostic tomosynthesis, or targeted ultrasound were requested at the discretion of the interpreting radiologist. Findings and management were communicated to the patient by telephone by the reporting radiologist. Subsequent imaging was performed on separate visits, within 3 weeks of the MG or MR. Histologic samples for pathologic diagnosis were obtained under ultrasound (14G, 5–6 cores), stereotactic (10G, 6–12 cores) or MRI (10G, 6–12 cores) guidance.

**Anxiety Measures**

Patients in both groups were asked to fill out four validated self-report questionnaires that measure anxiety level and overall health (22–24). Penn State Worry Questionnaire (PSWQ) [22] is a 16-item self-report questionnaire which measures frequency and intensity of worry symptoms. Items are rated on a 5-point scale, with total scores ranging from 16–80. A score between 16–39 indicates low worry, 40–59 moderate worry and 60–80 high worry. The Breast Cancer Worry Scale (BCWS) [23], is a 3-item scale which measures frequency of breast cancer worry and the impact of worrying on mood and ability to perform daily activities. Higher scores indicate greater cancer worry. The State-Trait Anxiety Inventory (STAI) [24], is a 40-item scale that includes 20 items that assess state anxiety (S-Anxiety) (i.e., how the person feels at this moment) and 20-items that assess trait anxiety (T-Anxiety) (i.e., how the personal generally feels). Items are rated on a 1 to 4 scale. The range of scores for each subscale is 20–80, with cut-off scores of ≥ 32.2 and ≥ 31.8 indicating elevated levels of state and trait anxiety, respectively. Both STAI subscales have solid psychometric properties and are sensitive to assessment of longitudinal change. The Health Status Questionnaire 12 (HSQ-12) assesses the impact of health on social, emotional and physical functioning over the past four weeks. Depending on the item, questions are rated of a 3-point, 5-point and 6-point scale, with higher scores indicating poorer health status. The questionnaires were completed upon enrolment during consultation (T0), upon receipt of the MG and/or MRI results (T1), and then 6 months later (T3). T3 questionnaires were mailed to patients and returned to the study coordination center.

**Data Collection and Statistical Analysis**

Medical records were reviewed to determine patient age, family history of breast and/or ovarian cancer in a first-degree relative, surgery modality, initial breast tumor stage (TNM), histology, hormone receptor status, months since diagnosis of breast cancer and breast density. Results were compared between the two groups. For malignant or atypical/high-risk lesions, surgical pathologic results were
reviewed when available. Imaging follow-up for all patients with benign imaging or pathology was documented with the date of the most recent negative mammogram.

The anxiety measures were analyzed using SPSS Statistics version 25. Analysis was based on intent-to-treat (ITT) principles. Data were analyzed using linear mixed models, with Intervention (Mammogram only versus Mammogram plus fast MRI), time of assessment (T1, T2, T3), and Intervention by Time interaction as fixed factors. Models were estimated using Restricted Maximum Likelihood (REML) with an unstructured covariance structure to account for correlations among repeated measures over time. A significant Time by Intervention interaction would suggest that changes in measures over time were different between the interventions; significant interactions were further analyzed with pairwise least square mean comparisons. Data from missing questionnaires were not imputed because our analytical strategy using REML allowed the estimation of reliable parameters without the need for imputation of the data under an assumption of missing at random (MAR)[22]. Descriptive statistics were calculated using a spreadsheet software program (Excel, Version 2013, Microsoft). Screening outcomes were compared between groups using Fisher's exact test. Sample size calculation was based on primary outcome the STAI. There is no generally accepted minimal clinically important difference for the STAI, and a 4-point difference was selected to be a minimal clinically important difference, as it would correspond to a complete difference in one of the 40 items. In order to have 80% power to detect a 4-point difference between the groups, we planned 134 patients per group. Recruitment stopped early due to differences in cancer detection rates. Results were considered significant if p < 0.05.

Imaging modalities (MG, A-MRI), and BI-RADS final assessment categories for each modality were noted. Imaging findings and outcomes were documented for all BI-RADS 3, 4 and 5 lesions, including suspicious extra-mammary findings. Results were compared between MG and A-MRI. A screening examination was considered as positive when additional diagnostic imaging was recommended prior to the next routine screening examination and included BI-RADS 0, 3, 4 and 5. True positive findings were defined as a cancer diagnosis within 12 months of a positive screening examination. Imaging studies were considered false negatives if there was a tissue diagnosis of cancer within 12 months of a negative study. The following performance metrics were calculated for each modality: CDR, AIR, biopsy rate, positive predictive value for biopsy recommendations (PPV2), positive predictive value for biopsies performed (PPV3), sensitivity and specificity.

Results

A total of 202 of 1000 patients fulfilled the eligibility criteria (Fig. 1). At enrollment, 94 were randomized to group 1 and 108 to group 2. Of these, four patients from group 2 were excluded because they withdrew from the study before undergoing MRI for different reasons: two patients developed breast cancer metastases, one patient developed sepsis and her doctor decided to postpone contrast injection and one patient opted to withdraw from the study. Accordingly, the study population consisted of 198 patients: 47.5% (94/198) randomized to regular surveillance with MG (group 1) and 52.5% (104/198) to surveillance with MG and A-MRI (group 2). Among the 104 patients from group 2, 82.7% (86/104) patients had both imaging exams the same day and 17.3% (18/104) patients on different days (average 33.2 days (range: 1-147)).

Patients' demographics

Patients’ demographics are presented in Table 1. Mean age was 59 years (range 35–80) for group 1 and 58.2 years (range 38–83) for group 2. No clinically important differences in age, family history of breast and/or ovarian cancer, surgery modality, months since diagnosis, breast density, initial tumor histology, stage, or hormone receptor status were noted between the two groups, although a non significant higher number of patient with triple negative cancers was observed in the MRI group.

Results regarding anxiety

Mean scores and standard deviations for self-report measures are displayed in Table 2. The intervention groups did not differ significantly on any of the baseline self-report measures. Linear mixed models revealed no significant Time main effects or Time x Intervention interactions for the worry measures PSWQ (p = .14 and p = .57, respectively) and BCWQ (p = .73 and p = .48, respectively). Analysis of the STAI revealed that the Time main effect and Time x Intervention interaction were not significant for trait anxiety (p = .51 and p = .20, respectively). In contrast, there was a significant time main effect (p < .001) and Time x Intervention interaction (p = .022) for state anxiety. Post hoc tests revealed that for both groups, state anxiety scores decreased from Time 1 to Time 2 (ps < .001) but increased from Time 2 to Time 3 (ps < .001). Between group differences were found at T2, with participants in the fast MRI condition reporting lower levels of state anxiety than those in the mammogram condition (estimated mean difference = 2.6 [95% CI, .13–4.19], p = .037), but was less than a 4 point difference. There was a significant Time main effect for self-report health status (p = .008), but the Time x Intervention interaction was not statistically significant (p = .10).
Findings according to imaging modality

Outcomes according to imaging modality are presented in Table 3. Among the 302 imaging examinations performed (198 mammograms and 104 A-MRI), 9 mammograms and 29 A-MRI were interpreted as abnormal (17%) (Fig. 2). Four patients had abnormal mammography and A-MRI findings, three for the same abnormality.

Mammography

There were 198 mammographic examinations performed: 94 for group 1 and 104 for group 2; 95.5% (189/198) were negative or benign (BI-RADS 1 and 2), 4.5% (9/198) were recalled (BI-RADS 0) and 3.0% (6/198) presented findings suspicious for malignancy (BI-RADS 4) and underwent biopsy. One cancer was detected (Table 4) and no high-risk lesions were identified.

MRI

There were 104 A-MRI studies performed in the second group of patients (A-MRI plus MG) and none in group 1 (MG only). 72.1% (75/104) were negative or benign (BI-RADS 1 and 2); 27.9% (29/104) were abnormal including extra-mammary findings, of which 19.2% (20/104) had suspicious breast lesions (BI-RADS 4 or 5); and 18.2% (19/104) underwent breast biopsy. One breast mass detected by A-MRI was not seen at the time of MRI-guided biopsy and showed stability on 6-month follow-up MRI. Five breast cancers were detected in 5 patients, 4 invasive carcinomas and one DCIS (Table 4), all only detected with A-MRI, 2 of which were in patients with original triple negative breast cancer (Fig. 2). Three patients had suspicious extra mammary findings: one lung mass seen in the right middle lobe on the A-MRI, and two bone lesions seen in the sternum and manubrium, respectively. The lung mass was confirmed to be a metastatic carcinoma from breast primary on CT guided transthoracic lung biopsy, the manubrial lesion was confirmed to be a hemangioma on bone scan and the sternal lesion was confirmed to be a hibernoma on CT guided biopsy. Of the MRI detected breast cancers, none was identified on mammography, even in retrospect. No high-risk lesions were detected.

The mammographic CDR of 5/1000 (1/98) was significantly lower than the CDR of 58/1000 (6/104, p = 0.003) for A-MRI including the extramammary findings, and CDR of 48/1000 (5/104, p = 0.0109) for MRI including the breast findings only. The diagnostic indicators for both modalities are presented in Table 5. Sensitivity for MG 14.2% (1/6)) was lower than A-MRI 100% (5/5)(p < 0.004); specicity for MG 95.8% (183/191) higher than MRI 76.5% (78/99) (p < 0.00001) and PPV3 for MG 16.7% (1/6) was lower than MRI 28.6% (5/19) (p = 0.55).

Necessity for full diagnostic or repeat MRI

Three patients required further investigation requiring diagnostic full MRI based on the radiologist's uncertainty of the findings seen on the A-MRI: 1 had a mass which was benign on assessment (fat necrosis) determined by the full protocol, one was a BI-RADS 3 lesion which showed stability on 12 month follow-up and one had BI-RADS 4B lesion that led to a benign MRI-guided biopsy of Pseudoangiomatous hyperplasia. A fourth patient had motion artifact and required a repeat abbreviated MRI that was normal and of high technical quality.

Follow-up

All 191 patients with benign imaging or pathology results underwent clinical and imaging follow-up at the same center, for an average 24 months (10–56 months). There were no cancers found retrospectively as false negatives on follow-up. 1.57% (3/191) had breast cancer on follow-up, all from group 1. Of the 3 cancers diagnosed on subsequent surveillance imaging, two were diagnosed at 26 & 27 months with MG (DCIS and invasive ductal carcinoma (IDC), T1N0M0) and one was diagnosed at 50 months on MRI IDC, T2N0M0). Two were new cancers in the contralateral breast and one DCIS was in the ipsilateral breast; no cancer was seen retrospectively on initial MG and/or MRI. Of the remaining 188 patients with no cancer diagnosed on follow-up, 98.9 % (186/188) had follow up of 12 months or longer and 1.06 % (2/188) had follow-up of shorter than 12 months. There were no patients lost to follow-up.

Discussion

This prospective randomized controlled trial showed that abbreviated breast MRI was superior to mammography in the detection of cancer in 198 breast cancer survivors; almost 10 times more cancers were detected with breast MRI than MG (48 (5/104) vs 5/1000 (1/198), p = 0.01). Despite higher rates of biopsies and abnormal interpretations, breast MRI was not associated with an increase in anxiety, with average anxiety scores of STAI of 50.99+/-.4.6 with MG vs 51.73+/-.2.56 with MRI, p > 0.05, 6 months after the study. Anxiety was moderately high in all patients and did not change, whether patients underwent surveillance with MG alone or MG plus A-MRI. Although a reassuring effect from undergoing A-MRI was not observed, there was no detrimental effect.
Our results support other studies on the impact of breast MRI on anxiety. The Dutch MRI screening (MRISC) study of patients at high risk for breast cancer found that the addition of breast MRI did not affect quality of life or anxiety[19]. In a more recent prospective non-randomized multicentre study, 1561 women at intermediate and high breast cancer risk were noted to have similar moderate distress levels, and there were no more harmful psychological effects observed between standard MG plus ultrasound as compared with the addition of MRI to standard imaging[23].

A significantly higher cancer detection rate was noted in the patients who underwent A-MRI as compared with mammography, despite similar demographics. Our study demonstrated A-MRI had a sensitivity of 100% and CDR 48/1000 as compared to mammography’s sensitivity of 14.2% and CDR 5/1000. The abnormal interpretation and biopsy rates were significantly higher for A-MRI than mammography, 25% and 18.3% for A-MRI and 4.5% and 3% for MG, respectively. PPV3 was higher with A-MRI than MG, 26.3% vs 16.7%, although this difference did not reach statistical significance. When extra-mammary findings were included, A-MRI offered the benefit of detecting an incidental lung metastasis.

There have been multiple studies of abbreviated MRI since Dr. Kuhl published her landmark study of abbreviated MRI [4, 14–18, 24–26]. In a similar study of 725 breast cancer survivors, Choi et al found 12 cancers using A-MRI, for a CDR 15 per 1000 [25], with comparable sensitivity 100% and specificity 89.2%. The results of A-MRI in our study were comparable to reported sensitivities (86–100%) and specificities (45–95.3%). However, our specificity of 76.5% was lower than the ACR benchmark for screening breast MRI 85–90%[21]. PPV3 26.3% was in the reported range for A-MRI (9.2–70.2%) and met the ACR benchmark of 20–50%[21]. In 2020, Park et al retrospectively compared abbreviated to full MRI in 1200 breast cancer survivors, 656 with A-MRI vs 656 patients with full protocol and found no significant differences in sensitivity (70% vs 100%), specificity (98% vs 96.9%), Negative predictive values (99.5 and 100%) and PPV (35% vs 23%) (all p > 0.05)[27].

We recognize some limitations of our study. Patients were recruited by their oncologists or treating surgeons, which could have introduced a bias in patient selection. This may have partly explained the high cancer detection rate in the MRI group. Nonetheless, the fact that randomization was blinded mitigated any potential bias of intervention arm selection and there were no clinical differences between the MRI and mammography groups. Because of the high cancer detection rates and minimal effect on anxiety in the MRI group we stopped the clinical trial early. Additionally, some patients could have developed breast cancer after the follow up period, which might have been missed with mammography. Given that the majority patients were followed for over 24 months, this is less likely. Another limitation is that the radiologists were not blinded to the allocation arm, which could have influenced their reporting of the mammogram, if they knew that an MRI would be done. However, given similar recall rates for mammography within both groups, this is unlikely to have been present. The high biopsy rate in the MRI group may be perceived as a limitation, but this was related to the high CDR with an acceptable PPV3. However, more research is required to find ways to further reduce the rate of false positives. There is likely a learning curve with A-MRI and the addition of T2 sequences may help to improve PPV3 without significant time cost[15]. We have subsequently adapted an abbreviated protocol to include T2 sequence and two more post contrast sequences to improve the specificity of MRI[28]. Another limitation is that assessment of anxiety was based on self-report questionnaires and limited by the time points in which it is measured. A more objective measure would be to evaluate adherence to follow-up rounds of screening, which may address poor compliance with MRI screening[13]. This is recommended for future study. Also, our study lacked the sample size and enough long-term follow-up to be able to say whether the earlier detection in the A-MRI group led to any difference in survival.

**Conclusions**

The addition of abbreviated breast MRI to surveillance mammography did not impact patient anxiety in breast cancer survivors, regardless of the significantly higher recall and biopsy rates. MRI showed significantly higher cancer detection rate compared to mammography alone, which is consistent with recent recommendations. Although further study with larger cohorts is warranted, an abbreviated protocol may be considered for surveillance in this population.

**Abbreviations**

1. Abbreviated breast magnetic resonance imaging (A-MRI)
2. Mammography (MG)
3. Cancer detection rate (CDR)
4. Ductal carcinoma in situ (DCIS)
5. Invasive ductal carcinoma (IDC)
6. Prior (personal) history of breast cancer (PHBC)
7. Breast Imaging-Reporting Data System (BI-RADS)
8. Cancer detection rate (CDR)
9. Abnormal interpretation rate (AIR)
10. Positive predictive value (PPV)

Declarations

Availability of data and material (data transparency) https://clinicaltrials.gov/ct2/show/NCT02244593

Code availability (software application or custom code) NA

Authors' contributions: available on request

Ethics approval (include appropriate approvals or waivers) REB approval by the Ottawa Hospital Research institute Ethics Board

Consent to participate (include appropriate statements) Yes

Consent for publication (include appropriate statements) Yes

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Tables
|                                | Group 1-MG (n = 94) | Group 2- A-MRI + MG (n = 104) | p value |
|--------------------------------|---------------------|-------------------------------|---------|
| **Age (years)**                |                     |                               |         |
| Mean                           | 59.0                | 58.2                          | 0.44    |
| Median                         | 58.5                | 58                            |         |
| Range                          | 35–80               | 38–83                         |         |
| **Family history breast and/ or ovarian cancer** |                     |                               |         |
| Yes                            | 26                  | 32                            | 0.63    |
| No                             | 68                  | 71                            | 0.53    |
| Unknown                        | 0                   | 1                             | 0.34    |
| **Surgery modality**           |                     |                               |         |
| Lumpectomy                     | 52                  | 69                            | 0.11    |
| Mastectomy                     | 42                  | 35*                           | 0.11    |
| **Months since diagnosis**     |                     |                               |         |
| <24                            | 42                  | 44                            | 0.73    |
| 24 < x < 60                    | 37                  | 39                            | 0.79    |
| 60 ≤ x ≤ 120                   | 13                  | 14                            | 0.94    |
| >120                           | 2                   | 6                             | 0.19    |
| Unknown                        | 0                   | 1                             | 0.34    |
| **Breast density**             |                     |                               |         |
| ACR A                          | 4                   | 7                             | 0.45    |
| ACR B                          | 45                  | 46                            | 0.61    |
| ACR C                          | 44                  | 45                            | 0.50    |
| ACR D                          | 1                   | 6                             | 0.73    |
| **Tumor histology**            |                     |                               |         |
| DCIS                           | 2                   | 7                             | 0.12    |
| IDC                            | 84                  | 89                            | 0.31    |
| ILC                            | 6                   | 8                             | 0.74    |
| Mucinous                       | 1                   | 0                             | NA      |
| Unknown                        | 1                   | 0                             | NA      |
| **Tumor stage of initial invasive cancer** |                     |                               |         |
| T1                             | 51                  | 44                            | 0.19    |
| T2                             | 27                  | 38                            | 0.14    |
| T3                             | 5                   | 8                             | 0.43    |
| T4                             | 8                   | 5                             | 0.35    |
| NA                             | 1                   | 2                             | 0.59    |
| N0,NX                          | 51                  | 54                            | 0.92    |
Table 2
Mean (SD) scores for self-report measures

| Outcome | Time 1         | Time 2         | Time 3         |
|---------|----------------|----------------|----------------|
| PSWQ    |                |                |                |
| Mammogram | 40.23 ± 13.6  | 39.52 ± 13.5   | 38.98 ± 14.2   |
| Fast MRI | 42.20 ± 13.4  | 41.08 ± 14.5   | 44.51 ± 14.9   |
| BCWS    |                |                |                |
| Mammogram | 6.87 ± 2.3    | 6.93 ± 2.4     | 6.44 ± 2.1     |
| Fast MRI | 6.73 ± 2.2    | 6.55 ± 2.3     | 6.39 ± 2.1     |
| STAI-State Anxiety | | | |
| Mammogram | 51.50 ± 2.6   | 51.55 ± 2.8    | 51.79 ± 2.5    |
| Fast MRI | 51.61 ± 2.5   | 51.20 ± 2.4    | 50.94 ± 2.5    |
| STAI-Trait Anxiety | | | |
| Mammogram | 51.85 ± 2.8   | 45.14 ± 5.6*   | 50.99 ± 4.6    |
| Fast MRI | 51.07 ± 2.9   | 42.88 ± 6.3    | 51.73 ± 2.56   |
| HSQ     |                |                |                |
| Mammogram | 29.99 ± 4.8   | 30.94 ± 4.1    | 31.12 ± 5.4    |
| Fast MRI | 30.5 ± 5.0    | 31.21 ± 5.4    | 30.50 ± 4.27   |

Note: Analysis is based on the intent-to-treat sample. Observed means are unadjusted. PSWQ= Penn State Worry Questionnaire; BCWS= Breast Cancer Worry Scale; STAI=State Trait Anxiety Inventory; HSQ=Health Status Questionnaire

*p<.05 Mammogram vs Fast MRI
Table 3

| Main imaging findings, BI-RADS category and outcomes according to imaging modality |
|---------------------------------|-----------------|-----------------|
|                                 | Mammography (n = 198) | A-MRI (n = 104)  | p value     |
| Normal                          | 189 (95.5)        | 75 (72.1)       | 0.00001     |
| Abnormal interpretation rate    | 9 (4.5%)          | 29 (27.9)       | 0.00001     |
| Mass                            | 1/9              | 15/29           |             |
| Calcifications                  | 6/9              | 0               |             |
| Asymmetry                       | 2/9              | 0               |             |
| Non mass enhancement            | 0                | 9/29            |             |
| Mass/non mass enhancement       | 0                | 1/29            |             |
| Extra-mammary finding*         | 0                | 3/29            |             |
| Motion artifact                 | 0                | 1/29            |             |
| BI-RADS category after work-up/ full MRI diagnostic protocol | 0.84 |             |             |
| 2                               | 2/9 (22.2%)       | 2/29 (6.9%)     |             |
| 3                               | 1/9 (11.1%)       | 4/29 (13.8%)    |             |
| 4A                              | 3/9 (33.3%)       | 10/29 (34.5%)   |             |
| 4B                              | 3/9 (33.3%)       | 8/29 (27.6%)    |             |
| 5                               | 0 (0%)            | 2/29 (6.9%)     |             |
| N/A (extra-mammary findings)    | 0 (0%)            | 3/29 (10.3%)    |             |
| Outcome (abnormal)              | 0.49             |                 |             |
| Work-up (> benign)              | 2/9 (22.2%)       | 2/29 (6.9%)     |             |
| Stable on follow-up             | 1/9 (11.1%)       | 6/29 (20.7%)    |             |
| Biopsied                        | 6/9 (66.7%) (6/198 = 3.0%) | 21/29 (72.4%) (21/104 = 20.2%) |             |
| Benign                          | 5/6 (83.3%)       | 15/21 (71.4%)   | 0.99        |
| Atypical/high risk              | 0 (0%)            | 0 (0%)          |             |
| Malignant                       | 1/6 (16.7%)       | 6/21 (28.6%)    |             |

Note: Unless otherwise indicated, data are numbers of patients and data in parentheses are percentages.

* 1 suspicious A-MRI finding was less conspicuous the day of the biopsy, for which follow-up was performed and showed stability.

** Extra-mammary lesions: 2 benign sternal masses (1 biopsied and 1 stable on follow-up) and 1 malignant lung mass (biopsied)
**Table 4**  
Surveillance detected cancer characteristics on MG and MRI

| ID | Age | Breast density (ACR BI-RADS) | Months since dx | Group | Abnormality | Detected by BI-RADS | Histology | TNM | ER | PR | HER |
|----|-----|-----------------------------|-----------------|-------|-------------|---------------------|-----------|-----|----|----|-----|
| 1  | 58  | C                           | 25              | 1     | Ca+         | MG only             | DCIS, intermediate nuclear grade Initial ca: IDC, ER-Her+ | -   |
| 2  | 80  | B                           | 216             | 2     | Mass        | A-MRI only          | DCIS, high nuclear grade Initial ca: DCIS | -   |
| 3  | 45  | C                           | 37              | 2     | Mass        | A-MRI only          | IDC, grade 2/3 Initial ca: IDC, ER+ Her- | T1c N0 M0 + + - |
| 4  | 67  | C                           | 144             | 2     | NME         | A-MRI only          | Microinvasive lobular carcinoma, Pleomorphic lobular carcinoma in situ Initial cancer: IDC, TN | T1miN0 M0 |
| 5  | 38  | C                           | 7               | 2     | Mass        | A-MRI only          | IDC, grade 3/3 Initial ca: IDC, ER+ Her+ | T3 N2 M0 - - + |
| 6  | 73  | C                           | 120             | 2     | Mass        | A-MRI only          | IDC, grade 2/3, DCIS Initial Ca: IDC, TN | T2 Nx + - - |
| 7  | 58  | B                           | 33              | 2     | Mass (lung) | A-MRI only          | Adenocarcinoma metastasis,consistent with breast cancer Initial ca: IDC, ER+ Her- | - + + - |

DCIS: ductal carcinoma in situ

IDC: invasive ductal carcinoma

TN: triple negative

ER: estrogen receptor

Her: Herceptin receptor

NME: nonmass enhancement

NA: not applicable
|                          | Mammography | A-MRI* | P value* | A-MRI** | P value** |
|--------------------------|-------------|--------|----------|----------|-----------|
| False negative           | 6           | 0      |          | 0        |           |
| True negative            | 183         | 75     | 78       |          |           |
| False positive           | 8           | 23     | 21       |          |           |
| True positive            | 1           | 6      | 5        |          |           |
| Recall rate              | 9/198 (4.5%)| 29/104 (27.9%) | 0.00001 | 25/104 (25%) | < 0.00001 |
| Biopsy rate              | 6/198 (3.0%)| 21/104 (20.2%) | 0.00001 | 19/104 (18.3%) | < 0.00001 |
| CDR                      | 1/198 (5/1000) | 6/104 (58/1000) | 0.003  | 5/104 (48/1000) | 0.0109 |
| PPV2 (recommended)       | 1/6 (16.7%) | 6/22 (27.3%) | 0.59   | 5/20 (25%) | 0.59     |
| PPV3 (performed)         | 1/6 (16.7%) | 6/21 (28.6%) | 0.55   | 5/19 (26.3%) | 0.557 |
| Sensitivity (%) (CI)     | 1/7 (14.2%, 0.36–57.8) | 6/6 (100%) | 0.004  | 5/5 (100%) | 0.004   |
| Specificity (%) (CI)     | 183/191 (95.8%, 91.9–98) | 75/98 (76.5%, 66.9–84.5) | 0.00001 | 78/99 (78.8%) | 0.00001 |

CI: 95% confidence intervals

A-MRI: Abbreviated breast MRI

CDR: Cancer detection rate (per 1000 women)

PPV2: positive predictive value for biopsies recommended

PPV3: positive predictive value for biopsies performed

CI: confidence interval

*including extra-mammary findings, **excluding extra-mammary findings

Figures
Figure 1
Flow Diagram.
67-year-old female had a history of a T2N0M0 triple negative invasive ductal carcinoma treated with right mastectomy 12 years earlier. a. Mediolateral (MLO) and b. Craniocaudal (CC) left surveillance mammograms show heterogeneously dense breast tissue (BI-RADS C) with unremarkable findings, unchanged from prior mammograms (not shown). c. Axial 3D Maximum Intensity Projection (MIP) image at 2 min post contrast performed after mammograms shows right mastectomy with no chest wall abnormalities and an irregular 4.5 cm enhancing mass in the medial left breast (circle) reported as BI-RADS 4B. The second circumscribed mass in the lateral breast (arrow) corresponded with a known benign fibroadenoma. d. Axial 2 min post contrast subtracted image demonstrates the spiculated enhancing mass in the upper medial quadrant of the left breast. e. Axial contrast enhanced image during MRI-guided biopsy shows the tip of the biopsy needle within the centre of the enhancing mass (circle), diagnosing pleomorphic lobular carcinoma in situ, subsequently confirmed at surgical excision to be invasive lobular carcinoma.