Automated breast volume scanner (ABVS) compared to MRI in BRCA mutation gene carriers

Poster No.: C-2235
Congress: ECR 2015
Type: Scientific Exhibit
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Keywords: Breast, MR, Ultrasound, Equipment, Cancer
DOI: 10.1594/ecr2015/C-2235

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Aims and objectives

Of women diagnosed annually with breast cancer (87.4 /100000 in the Israeli Jewish population)\(^1\), only 5-10% are categorized as "inherited breast cancer", and up to 30% of these patients harbor either a \textit{BRCA1} (MIM 113705) or \textit{BRCA2} (MIM 600185) germline mutation. The lifetime risk for \textit{BRCA1} or \textit{BRCA2} female mutation carriers to develop breast cancer is significantly increased over that of the general population, and is estimated as high as 28-49% by age 50 years and 56-83% by age 80 years\(^2-4\). The imaging screening guidelines of high risk patients include annual mammography (MG) and annual breast MRI starting at age 25-30\(^5-8\). Since adjunct ultrasound US improves MG's sensitivity in women with dense breasts\(^9,10\) the practiced guidelines in our institute includes imaging every 6 months, alternating between MG, MRI and US.

In recent years, automated breast volumetric sonography (ABVS) was developed. The system utilizes a flat transducer promoted in a rectangular frame, which acquires 1mm thin consecutive axial slices. The patient lies in a supine position and the transducer is applied in three main views: antero-posterior (AP), lateral and medial, and additional superior and inferior view can be added if specifically required, for example in case of large breasts. This system provides consistent, reproducible, operator-independent ultrasound imaging of the entire breast\(^11\).

A study by Brem et al showed that addition of ABVS to screening MG in a women with dense breasts increased the cancer detection yield of clinically important cancers, 7.3 cancer per 1000 versus 5.4 cancers per 1000 women screened with MG alone\(^12\). Another study by Wang et al showed similar sensitivity (95.3% vs. 90.6%), specificity (80.5% vs. 82.5%), accuracy (85.8% vs. 85.3%), positive predictive value (73.0% vs. 74.0%), and negative predictive value (93.3% vs. 94.1%) compared to hand held US (HH-US)\(^13\). Zhang et al showed superior detection capabilities of ABVS over HH-US\(^14\).

Yet not all reports show these superior results. A smaller study by Jung Min Chang et al compared ABVS in 61 patients with HH-US in the ability to detect pathologies and reported detection of only 57.1-78.6% of the known cancers by ABVS, and a substantial number of false-positive results (8.3-20.8%) using ABVS in normal breasts\(^15\).

The purpose of this study was to compare between ABVS and breast MRI in the surveillance of Jewish female BRCA1/2 gene mutation carriers.
Methods and materials

This was a prospective study, in female Jewish Israeli BRCA1/2 mutation carriers, who underwent breast MRI and ABVS in a single follow up clinic in a tertiary medical center in Israel. Results of MRI and ABVS imaging, performed 6 months apart or less (#181 days interval), and relevant clinical data were reviewed. The BIRADS score results were divided into 3 groups according to subsequent expected management (normal study, probably benign study or suspicious findings): BIRADS 1 and 2, BIRADS 3, BIRADS 4 and 5 (respectively).

Statistics

The results obtained from the ABVS were compared with those of the MRI (as the gold standard). The data were analyzed using descriptive statistics. The software package SPSS Statistics was used for the statistical analysis.

McNemar’s test was done to determine whether the distribution of the BIRADS results of the two modalities ABVS and MRI are equal. In addition, classification of the concordance of the ABVS and MRI with the BIRADS was calculated based on Cohen's Kappa test. This test can provide a satisfactory estimation of the agreement between the two modalities. We used the magnitude guidelines published by Landis and Koch, who characterized the values of k < 0 for indicating no agreement, k 0-0.20 slight, k 0.21-0.40 fair, k 0.41-0.60 moderate, k 0.61-0.80 substantial, and k 0.81-1 as almost perfect agreement. Statistical significance was assumed at P< 0.05 for all tests.

Patients’ agreement

The study was approved by the Institutional Review Board and informed consent was obtained from all patients.
**Results**

Overall 68 women, 40 BRCA1 and 28 BRCA2 mutation carriers, ages 26-69 (mean 44.55±12.1), underwent 79 pairs of breast imaging by ABVS and MRI examinations. Table 1 presents the mutual distribution of the BIRADS results in the two modalities ABVS and MRI. Of these, 65 of 79 examination pairs had a concordant BIRADS score between modalities. In the remaining 14 pairs, 10 pairs were given a MRI higher BIRADS score, BIRADS 4, and 4 were given an ABVS higher BIRADS score, BIRADS 4. Biopsy results in the mismatching pairs when either examination scored BIRADS 4-5 are described in table 2, including time interval between examinations. Of the 13 lesions who underwent biopsy, 12 lesions were benign: Nine MRI lesions (average size 0.8cm not including 3.5cm non-mass enhancement) and 4 ABVS lesions (average size 0.775cm). Only one cancer was detected, a 0.8cm IDC (invasive ductal carcinoma) which was not detected in an ABVS performed 180 days prior to the MRI (figure 1).

The McNemar's test that was applied to determine whether the distribution of the BIRADS results of the two modalities ABVS and MRI are equal was found to be non-significant. A non significant result implies that marginal frequencies are homogeneous, namely that there is no significant difference between the ABVS and MRI distributions.

In addition, to estimate the agreement between the BIRADS classification of the two tested imaging modalities the Cohen's Kappa test, which analyses concordance for each BIRADS score group, was applied. We obtained a Cohen's Kappa value $k = 0.158$ (95% CI: -0.11 - 0.42) not significant ($p=0.052$) - an agreement that can be described using the Landis and Koch scale\textsuperscript{17} as only "slight agreement" between both modalities.

<table>
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<th>MRI BIRADS score</th>
<th>Total</th>
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<tr>
<td>63</td>
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<tr>
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<tr>
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<td>2</td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
<tr>
<td>4+5</td>
<td></td>
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<tr>
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</tr>
<tr>
<td>79</td>
<td></td>
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</tbody>
</table>

**Table 1:** Mutual distribution of the BIRADS results in the two modalities ABVS and MRI.
<table>
<thead>
<tr>
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<th>Examination (days)</th>
<th>Malignant (1)</th>
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<td>2</td>
</tr>
</tbody>
</table>

**Table 2**: Biopsy results in the BIRADS score 4-5 ABVS-MRI pairs.

*non mass enhancement

^a different benign lesion was reported in each modality
Fig. 1: MRI MIP reconstruction of a 59 year old BRCA 1 women, performed for high risk screening. Posterior to the nipple of the right breast there is a 0.8cm round enhancing lesion. This lesion was not seen in a 180 days prior ABVS.

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Fig. 2: The same patient as in figure 1, second look HH-US diagnosed a compatible lesion to the MRI lesion. A consequent ultrasound guided biopsy diagnosed it as invasive ductal carcinoma.

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**Fig. 3:** MRI MIP reconstructions of a 36 year old BRCA2 mutation carrier, performed for high risk screening. In the outer middle quadrant of the right breast there is a 0.7cm enhancing lesion. This lesion was not seen in a 25 days prior ABVS.

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Fig. 4: The same patient as in figure 3, second look HH-US diagnosed a compatible lesion to the MRI lesion. A consequent ultrasound guided biopsy diagnosed it as a Fibroadenoma.

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Conclusion

MRI shows higher sensitivity and specificity than MG alone or in combination with US in mutation carriers\(^\text{18}\). Previous reports have also shown ABVS to be a sensitive modality for breast evaluation\(^\text{12-14}\). The compared modalities are based on different physical principles for diagnosis. ABVS is an anatomic imaging modality and MRI is a functional imaging, based on contrast uptake of normal breast and pathological lesions. Regarding MRI as the gold standard, ABVS showed Cohen's Kappa value \(k = 0.158\), only "slight agreement", with MRI findings in BRCA 1/2 mutation carriers.

Most biopsies in this study (12 of 13, average size 0.79cm not including 3.5cm non-mass enhancement) were benign lesions. This high prevalence of benign biopsies was a common denominator for both modalities, but each modality identified different benign lesions, thus contributing to the lack of agreement.

Only one 0.8cm lesion was proved to be cancer, an IDC, discovered by MRI and not diagnosed in the ABVS performed 6 months prior to the MRI. This lesion was seen in second look hand held ultrasound, and consequently underwent biopsy using ultrasound guidance, raising the possibility that if the ABVS was performed simultaneously with MRI the lesion might have also been diagnosed by ABVS.

Breast cancer is more common in BRCA gene mutation carriers than in the general population by a factor of up to 7 fold, yet even in a group of cases at a substantially increased breast cancer risk, a large group of patients should be examined in order to evaluate and compare cancer detection rates between modalities.

These preliminary results that are based on a small group of healthy, high risk patients suggest that the diagnostic abilities of ABVS are inferior to MRI. Subsequent larger studies in ethnically distinct populations with longer follow up are needed to further evaluate ABVS ability in early detection of breast cancer.

Limitations

There are several limitations to this study:

- This is a small group of patients with limited spectrum of germline mutations all evaluated in a single medical center.
- In most cases ABVS and MRI were not performed on the same day, with an interval of up to 181 days apart, allowing for "interval tumor", a tumor detected in the period between annual breast imaging examinations, to appear.
• ABVS is a new technology, and the ABVS cases in this study were reported by several different radiologists with varied experience in ABVS reporting, so interobserver differences may have affected accuracy.
References

1. Israel National Cancer Registry. 2011.


