The role of using multimodal imaging for diagnosing malebreast cancer: new challenges and new diagnostic tools

Poster No.: C-1301
Congress: ECR 2018
Type: Scientific Exhibit
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Keywords: Breast, Oncology, Elastography, Mammography, MR, Diagnostic procedure, Cancer
DOI: 10.1594/ecr2018/C-1301

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Aims and objectives

Breast cancers are quite rare in men and are found in approximately 1% of cases. Nevertheless, breast cancer is the second most frequent pathology in men after gynecomastia. Because of its rarity, our data of breast cancer in men is very limited and derives largely from case reports and female patients (1-3). Gynecomastia, the most common breast lesion in men, is very similar to other nodular diseases. In addition, breast malignancies in men mostly occur at the subareolar plan of the breast as localized, painful masses (4-6). For this reason, the malignancy should be recognized and examined thoroughly in the initial stage. A delay in diagnosis and treatment leads to the progression of the disease and decreases survival rates (7-9). Elastography is a non-invasive method of measuring the hardness of a tissue and has been a useful method in radiology practices recently (10). By measuring the tissue strain induced by hand-free compression, tissue hardness is estimated, analogous to clinical palpation. Elastography has been concluded to be useful for differentiating malignant from benign masses in female patients (11-13). Recently, the most commonly used elastographic techniques have been strain elastography and share wave elastography. Strain elastography analyzes the deformation of tissue induced by manual compression and the information is encoded in a color scale result from the tissue displacement (14-17). However, there is currently no study using the elastography technique for elastographic findings in male breast cancers.

Our study is an initial one and a pioneer study in this respect. The purpose of this study is to evaluate the contribution of imaging modalities for male breast cancer and the initial clinical experience of elastography in the male breast cancer.
**Methods and materials**

**Patient population:** This study took place at our institution in Istanbul from 2011 to 2017, and was approved by the Human Subjects Institutional Review Board. Informed written consent was obtained from all the patients before any interventional procedures. In this study, 14 men who had malign breast lesions were included in the study. Benign lesions and suspicious lesions which were verified to be histopathologically benign were excluded. The patients who had breast mass but declined core-needle biopsies were also excluded from the study.

**Data acquisition:** Mammography (MG), Ultrasonography (US) with real-time strain elastography (RTE) and Magnetic Resonance Imaging (MRI) were performed. MG (IMS Giotto Digital Radiography and Tomosynthesis, Bologna, Italy) was primarily performed for the appropriate patients. Where the breast of the patient was too small for the device to compress automatically, MG shooting could not be achieved. US and RTE (Hitachi Medco's Digital Ultra Sound Examination Device, HI-VISION Avius, Tokyo, Japan) were performed for all patients using the 6-13 Mhz probe after MG whenever possible. Otherwise, performing US was the first imaging method. The elastography index (EI) and the scoring (ES) were obtained. The elastography scoring system, based on the Ueno system suggested by Itoh et al. (4), assigns a score from 1 to 5: according to the Tsukuba elasticity score, 1 shows a tri-stratified pattern and the lesion is entirely green; score 2 shows a mainly elastic lesion with a mosaic pattern; score 3 is a mainly elastic lesion, but with some stiff areas, is peripheral blue; score 4 shows that most of the lesion is nondeformable and entirely blue; score 5 shows a nondeformable lesion surrounded by stiff tissue and surrounded by a blue margin around the lesion. If a lesion is classified from 1 to 3, it is considered benign; 4 or 5 is considered malignant. EI was calculated automatically by the device. The ROI was placed to contain the maximum area of the solid mass. According to the research by Itoh et al., the cut-off value is accepted as 4.2. With freehand compression, if the elasticity of lesion values was unstable, no elastography was done for certain cases. Breast MRI was performed at 1.5 Tesla (Achieva Philips, The Netherlands) while the patients were placed in prone position. Dynamic contrast-enhanced imaging was performed, and subtraction images were obtained for each contrast-enhanced series by subtraction of the non-enhanced series from the enhanced series. Diffusion MRI was obtained by following main sequences and ADC was calculated by the device automatically. The patients who had claustrophobia, renal dysfunction and were not able to use contrast agents did not undergo MRI.

**Data analysis:** Based on the US, MG and MRI findings, the lesions were classified into the final BI-RADS category according to the American College of Radiology BI-RADS lexicon, without knowledge of the final pathologic diagnosis. US and RTE, MRI reports and biopsy applications were analyzed by a single consultant radiologist.
(T.I., seven years of experience in breast radiology). All patients underwent core-needle biopsies using 16-gauge automatic needles under sonographic guidance and were verified histopathologically.
Results

Because of histopathology, a total of 16 malignant breast lesions were diagnosed (the mean size was 24.29±12.51 mm) on 14 men. The mean age was 62.21±11.00 years (age range, 39-75 years). 14 of the 16 solid breast lesions were invasive ductal carcinomas (IDC), 1 was papillary carcinoma (PC) and 1 was ductal carcinoma in situ (DCIS). One patient had bilateral breast cancer: the right breast was IDC and the left breast was PC, and also had a primary risk factor (Figure 1). His daughter was undergoing breast cancer chemotherapy at the same time. Another patient had multicentric breast cancer (Figure 2a, b). He had been diagnosed with gynecomastia in both breasts. Another patient had Paget's disease. The remaining 11 patients had no risk factor for breast cancer or no history of taking estrogen, irradiation, or any other disease.

Out of 14 patients, 5 patients (35.72%) were assessed as BI-RADS 4 and 9 (64.28%) as BI-RADS 5 by MG, US, RTE, and MRI findings.

MG was obtained from 7 patients, 7 patients had unilateral, nodular breast masses; 2 patients had microcalcifications and macrocalcifications; 6 patients had skin changes such as edema, nipple retraction, ulceration, and skin thickening; 7 patients already had positive axillary nodes (Figure 3a, b, c).

The conventional US was obtained from all patients and RTE was performed on only 9 patients; ES had 2 false negatives, although the EI of 2 patients were malignant. The EI showed 1 false negative result. The elastography's performance combined with the conventional US had no false negative result (Figure 4).

MRI in selected patients (n=11) had no false negative.
**Fig. 1:** 73-year-old male patient with family history of breast cancer, who had bilateral breast cancer, invasive ductal carcinoma in the right breast, papillary carcinoma in the left breast: MRI, axial contrast-enhanced subtraction image shows bilateral breast masses, spiculated and irregular shaped mass in the right breast; lobulated mass with positive skin invasion in the left breast.

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Fig. 2: Multicentric invasive ductal carcinoma in the left breast of a 39-year-old male patient, a) Maximum intensity projection shows that there are 2 irregular-shaped masses with axillary lymph nodes. b) the elastogram demonstrates Tsukuba ES 4, EI 7,80 according to Ueno classification.

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**Fig. 3:** 59-year-old male patient with invasive ductal carcinoma a) right MLO mammogram shows a mass at the subareolar plan with axillary nodes b) Tsukuba ES 3, elastography index 4.85 according to Ueno classification system c) maximum intensity image shows the irregular shaped mass and multiple axillary lymph nodes in the right breast.

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Fig. 4: 62-year-old male patient with invasive ductal carcinoma; the lesion appears morphologically malignant with irregular-shaped and posterior attenuation in B mode. The elastogram shows Tsukuba ES 4, EI 12.00 according to Ueno classification system.

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Conclusion

Radiologic imaging played an essential role in diagnosing male breast cancer. Using the combinations of imaging methods improves diagnostic performance. Elastography combined with conventional ultrasound can provide specific benefits and information on breast malignancy in men, as well as better characterization when diagnosing breast masses.
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