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Breast Imaging in Patients Aged 35−39 − Which Modality is Best?

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Background: In the last 12 months new best practice guidelines for the imaging of symptomatic breast problems in women aged 35−39 inclusive have been published.[1] These advocate that ultrasound scan (USS) should be adopted as the primary imaging modality in this age group and mammography (MMG) reserved for those with suspicious or atypical findings clinically and/or on imaging. This is a change in practice for many units including our own and we sought to investigate the adequacy of USS alone in our unit prior to introducing this change.

Materials and Methods: All new patients aged 35−39 years old attending breast clinic from January 2008 to December 2010 who had a radiological investigation were identified. Imaging results were cross referenced with histology to establish those diagnosed with cancer and to see how this was identified.

Results: 542 patients were identified. 15 (3%) were men and were excluded. 398 (73%) patients were investigated with MMG, 285 of these also had USS. 144 (27%) patients had USS only. 28 patients were diagnosed with breast cancer; all women with a mean age of 36.9 years.

17 cancers were investigated with both MMG and USS, but in all of these the USS was graded U3/4/5 using the breast imaging reporting and data system (BIRADS) classification. 1 cancer only had USS (U4/5) and 1 cancer was diagnosed on MMG only (although she had an informal unreported portable USS in clinic on which the cancer was seen).

There were no incidental findings of breast cancer on MMG. 2 patients had lesions graded benign by MMG but suspicious on USS: core biopsy of both lesions demonstrated malignancy.

In one patient a cancer was identified in the contralateral breast following prophylactic mastectomy which was not identified on MMG pre-operatively.

Conclusion: We found that USS in this group of patients was more sensitive for the identification of breast cancer than MMG. MMG alone here would have missed pathology in 3 patients. Thus MMG could be reserved for patients with uncertain or positive findings on USS and we have adjusted our guidelines accordingly.

References

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A Dedicated Breast PET-CT System for Metabolic Imaging of Breast Tumors

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Introduction: To demonstrate feasibility of a dedicated ^{18}FDG-PET-CT for metabolic imaging of breast lesions.

Material and Methods: 103 breast tumors in 93 patients classified by mammography or ultrasound as BIRADS 4 or 5 were included in this IRB approved prospective study. Patients fasted at least 6 h before injection of approximately 300–700 MBq 18F-FDG based on the patients weight. Scanning was started 45 min after injection. Blood glucose levels were <150 mg/dl (8.3 mmol/l). All patients were subjected to ^{18}FDG-PET-CT scanning using a combined PET-CT in-line system (Biograph, Siemens, Erlangen, Germany). PET data were acquired in the prone position similar to breast MRI to allow an optimal expansion of breast parenchyma. CT data was used for attenuation correction. PET scan was reconstructed applying a standard iterative algorithm [ordered-subset expectation maximization] into a 168×168 matrix. Dedicated breast ^{18}FDG-PET-CT was assessed for ^{18}FDG-avidity as well nodal status. Tumors within tissues of mild metabolic activity were classified as positive when 18F-FDG uptake > blood-pool activity. Tumors within tissues demonstrating moderate or high physiologic activity were considered positive if the activity was greater than the adjacent physiologic activity. All tumors were histopathologically verified.

Results: There were 33 benign and 70 malignant lesions. Mean histopathological tumor size was 28.8 mm (range 3−90 mm). ^{18}FDG-PET-CT demonstrated a sensitivity of 94%, a specificity of 82% and a diagnostic accuracy of 90%. PPV was 0.92 (CI: 0.83–0.96) and NPV was 0.87 (CI: 0.71–0.95). The 6 false positive tumors were juvenile fibroadenomas and one chronic abscess. The 4 false negative tumors were all smaller than 1cm associated with very high physiologic activity of the breast parenchyma.

Conclusion: Metabolic imaging of breast lesions with ^{18}FDG-PET-CT using a prone patient geometry is possible and allows a detection and assessment of breast tumors with a good sensitivity and specificity. False negative results seem to be influenced by tumor size (<1cm) and high physiologic background activity. Radiologist should be aware that lesions with high cellular density or inflammatory changes can mimic malignancy and lead to false-positive results in breast PET-CT.

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Pain in Stereotactic Breast Biopsy for Non-palpable Mammographic Lesions − Comparison of Two Biopsy Methods

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Background: Pain has been recognized as an important factor in the context of breast biopsy that affects both quality of life and patient compliance. The present study examines and compares pain during stereotactic breast biopsy for suspicious non-palpable mammographic lesions with two different biopsy methods.

Materials and Methods: In this study 181 consecutive women were included with mean age 51.57±9.02 years. The patients underwent a stereotactic breast biopsy for suspicious (BIRADS⩾4) non-palpable mammographic lesions, such as microcalcifications, solid lesions and asymmetric breast density. Biopsies were performed in a Fischer's Mammotest® stereotactic table, by the same surgical-radiologist team, using the Mammotome® large-core vacuum-assisted breast biopsy system or the radiofrequency-assisted intact-specimen Breast Lesion Excision System® (BLES). All procedures were performed under local anaesthesia, using the relevant for each method anaesthesia protocol. For the quantification of pain experience, the visual analogue scale (VAS) was used (0−10 scale,0 indicates 'no pain',10 indicates 'worst possible pain'). Immediately after the procedure, the patients were asked to retrospectively indicate the experienced pain, defined as the VAS score.

Results: In order to excise suspicious non-palpable mammographic lesions for pathologic diagnosis, we used large-core vacuum-assisted breast biopsy in 83 cases(Group A,patient age 49,9±8,5 years) and radiofrequency-assisted intact-specimen breast biopsy in 98 cases(Group B,patient age 52,9±9,22 years). The pain VAS score was 4,41±2,22 for Group A patients and 4,02±2,42 for Group B. Statistical analysis between groups showed no significant difference in the VAS score(p = 0,31, Mann-Whitney U test). Within-group analysis showed that the pain experience was not associated with the type of the lesion excised in both groups.

Conclusion: There is a broad spectrum of methods and devices available for the excision of suspicious non-palpable mammographic lesions in order to establish an accurate pathologic diagnosis. Although stereotactic breast biopsy is a relatively painful procedure, it has been suggested to be less painful than other methods of breast biopsy. According to our experience,there is no significant difference in pain experience between stereotactic large-core vacuum-assisted breast biopsy with the use of Mammotome® and radiofrequency-assisted intact-specimen breast biopsy with the use of BLES®.

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The Characteristics of Primary Breast Cancers with Non Mass like Enhancements in a Breast MRI

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Background: Breast MRI has been a popular method for patients in planning to breast conserving operations. The MR breast imaging reporting and data system (BI-RADS) lexicon of the American College of Radiology(ACR) includes a new lesion category defined as non-mass like enhacement(NME). The purpose of this study is to identify the incidence of this new entity, the correlation with breast cancer, and the impact on surgical treatment in primary breast cancers.

Methods: A retrospective review was performed for 133 patients with primary breast cancer evaluated with gadolinium enhanced MRI before surgical treatment. Detection of NME is made on contrast enhanced subtracted images. We categorized the MR-breast finding with 5 groups, such as, (1) group 1; solitary lesion, (2) group 2; another suspicious Cat 4a lesion in an ipsilateral breast, (3) group3; non mass-like enhancement with primary breast cancer. Before operations, we checked a lesion marking by a second-look ultrasonography, we took a excision for another lesions and definite cancer operations. If frozen biopsy of another lesions were found as a malignancy during breast conserving operations, wider excisions were performed. We compared MR-breast findings with clinicopathologic findings, such as, patient's age, histologic features,

hormone receptor status, lymphovascular invasion, her-2/neu status, p53 expression, histologic grade necrosis, and microcalcifications.

Results: 63 patients (47.4%) were found as solitary lesions. 30 patients (22.6%) were found at another suspicious lesions, NME were found at 40 patients (30.1%). NMEs have been found at younger patients (group 1: 53.7; group 2: 51.6; group 3: 46.1, p = 0.02), tumor sizes and specimen's sizes were not different among three groups, excistence of EIC, necrosis, calcification, lymph vascular invasion, hormone receptor status, histologic grade, her-2/neu status, lymph node status and p53 expressions were not correlated with NME. Histolgic features, such as ductal carcinoma with cribriform type and lobular carcinoma were more found at NME than other groups (p = 0.012) (Table 1). Group 2 were more taken mastectomy than other groups (p = 0.048)(Table 1). In breast conserving operations, the sizes of specimen were not different among three groups, but re-excision rates in NME were higher than other groups (group 1: 1.8%, group 2:9.5%, group: 20%).

Conclusions: NME has not been determined about an exact entity and the clinical significance. It was a small retrospective study, but it needs to get wider excision margins than non-NME contained breast cancers.

	Group 1	Group 2	Group 3	P-value
Age	53.6(±8.7)	51.6(±8.8)	46.1(±7.5)	**<0.001**
Tumor size	2.12(±1.3)	1.6(±1.1)	2.0(±2.0)	0.368
Specimen size	10.8(±3.4)	13.6(±4.8)	12.5(±5.6)	**0.021**
Specimen sized (BCS)	10.0(±2.2)	10.6(±1.7)	10.3(±3.4)	0.637
LN(−)	48	22	31	0.654
LN(+)	15	9	9	
ER(−)	29	12	19	0.806
ER(+)	34	18	21	
PR(−)	38	19	21	0.617
PR(+)	25	11	19	
Histology				**0.012**
DCIS/LCIS	5	4	13	
IDC	18	12	9	
ILC	0	1	0	
Others	3	0	0	
EIC(−)	53	22	28	0.21
EIC(+)	9	8	10	
LVI(−)	53	24	32	0.709
LVI(+)	9	6	8	
Necrosis(−)	35	21	24	0.458
Necrosis(+)	27	9	16	
Microcalcification(−)	40	24	17	0.752
Microcalcification(+)	22	16	13	
Operation				**0.049**
BCS	55	21	30	
MRM	8	9	10	
HG				0.499
low	24	13	12	
high	39	17	28	
p53(−)	42	24	25	0.272
p53(+)	21	6	15	
Her−2/neu(−)	49	22	25	0.244
Her−2/neu(+)	14	9	15	

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Role of Big Endothelin-1 in the Early Diagnosis of Lobular Neoplasia of the Breast

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Background: The endothelins and their receptors, collectively known as the endothelin system, exert important vasoactive properties while they are involved in various cellular processes including tissue differentiation, development, cell proliferation and hormone production. This network is often deregulated in human malignancy, contributing to mitogenesis, angiogenesis, invasion and metastasis, antiapoptosis and immune modulation. The tissue expression of endothelin-1 (ET-1) has been shown to increase during the progression of breast cancer, correlating with the acquisition of malignant potential. As far as its biological precursor Big ET-1 is concerned, clinical data suggest that it is a sensitive indicator of ET-1 activation. The aim of the present study is to investigate plasma ET-1 and Big ET-1 expression in patients with lobular neoplasia of the breast and their potential role in early diagnosis.

Materials and Methods: Peripheral blood samples were collected upon diagnostic biopsy of women with suspicious mammographic abnormalities BI-RADS ⩾4. Among them, 30 patients were diagnosed with lobular neoplasia (Mean age: 52.52±9.22 years) and 32 patients with benign breast lesions (Mean age: 55.68±11.32 years). Plasma ET-1 and Big ET-1 levels were quantitatively determined by enzyme-linked immunosorbent assay.

Results: Significantly higher plasma Big ET-1 levels were observed in patients with lobular neoplasia, compared to those with benign disease (0.72 and 0.33 fmol/ml, respectively, p < 0.0001). On the contrary, plasma ET-1 levels did not differ between the two patient groups (0.81 and 0.82 fmol/ml, respectively).

Table1: ET-1 and its biological precursor, Big ET-1, median plasma levels in patients with lobular neoplasia and benign lesions of the breast

	Lobular Neoplasia (N = 30)	Benign Disease (N = 32)	*p-value*
ET-1 (fmol/ml)	0.81	0.82	NS
Big ET-1 (fmol/ml)	0.72	0.33	<0.0001

Conclusions: Lobular neoplasia (LN) encompasses the entire spectrum of atypical epithelial proliferations in the terminal duct-lobular unit, including atypical lobular hyperplasia (ALH) and lobular carcinoma in situ (LCIS). LN is regarded as a risk factor for the subsequent development of invasive ductal or lobular carcinoma. To date, scarce data have been reported regarding circulating ET-1 and Big ET-1 levels in breast cancer while there are no studies specifically focusing on lobular neoplasia. This is an original observation of significantly higher plasma levels of Big ET-1 in patients with lobular neoplasia compared to benign breast disease, suggesting that Big ET-1 circulating expression may provide a promising biomarker for the early diagnosis of lobular neoplasia of the breast.

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Sonographic Features of BI-RADS(TM)-US 4 Breast Masses in Luminal, HER2 Overexpression and Triple Negative Phenotypes

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Background: The molecular dissimilarities between breast cancer types often lead to different clinical presentations and maybe correlate with some ultra sonographic (US) features. The purpose of this study was to assess the sonographic characteristics of BI-RADS®-US 4 breast masses in the Luminal, HER2 *overexpression* and Triple Negative phenotypes.

Methods: We consecutively examined a series of 335 women diagnosed as presenting BI-RADS®-US 4 breast masses between March 2009 and December 2010. All masses were biopsied and histological results were classified as malignant (n = 140, 42%) or benign (n = 195, 58%). Estrogen receptor (ER), progesterone receptor (PR) and Human Epidermal Growth Factor Receptor 2 (Her2) expression were assessed, using immunohistochemistry (IHC). For 8 (6%) cases, only ER and PR were evaluated. Lesions with complete IHC assessment were grouped into three phenotypic subtypes: Luminal (89 cases), Her2 overexpression (27 cases) and Triple Negative (16 cases). We then compared the sonographic features of the malignant lesions according to the phenotypic status of the masses. All calculations were performed with SPSS version 15 (SPSS Inc., Chicago IL). This study was approved by our institutional review board and all participants signed an informed consent form.

Results: The positive predictive values (PPV) for subcategories 4a, 4b and 4c of the 335 BI-RADS®-US 4 masses were 16%, 43% and 85%, respectively. Mucinous carcinomas were significantly associated with BI-RADS®-US 4a and 4b categories (p = 0.01). The Luminal phenotype was positively associated with the following sonographic features: spiculated margin (OR=6.4; 95% CI=1.8 to 23.6), indistinct margin (OR=17.2; 95% CI=1.8 to 23.6), echogenic halo (OR=3.8; 95% CI=1.05 to 13.6). The Luminal phenotype was negatively associated with enhancement (OR=0.3; 95% CI=0.15 to 0.76). Triple Negative phenotype was negatively associated with spiculated margin (OR=0.13; 95% CI=0.02 to 0.8) and shadowing (OR=0.02; 95% CI=0.01 to 0.47). The Her2 phenotype was not associated with any of the sonographic features.

Conclusion: Specific sonographic features may be positively related to the Luminal and Triple Negative phenotypes, but the BI-RADS®-US subcategories 4a, 4b and 4c were not associated with the molecular phenotypes of malignant breast masses.