Correlation of breast parenchymal enhancement in MRI and SUVmax in 18FDG breast PET-CT

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Aims and objectives

Breast cancer (BC) is the most common cancer in women, showing an increase in incidence but also a decrease in mortality due to improving therapeutic options and imaging techniques. Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) are essential tools in breast imaging, with MRI providing morphologic information, and $^{18}$Fluorodeoxyglucose-PET ($^{18}$FDG-PET) offering an insight into tumor glucose metabolism.

The diagnostic value of BC detection with MRI is dependent on the morphologic and kinetic data provided after intravenous administration of contrast agent, achieving a high sensitivity and moderate specificity in dynamic contrast-enhanced MRI (DCE-MRI). But it has been observed that not solely malign or benign lesions of the breast show enhancement. Breast parenchymal enhancement (BPE), also referred to as background enhancement, is a known phenomenon in DCE-MRI, showing nodular or diffuse enhancement of the fibroglandular parenchyma of the normal breast. It is regarded as a limiting factor on diagnostic accuracy, as the physiologic patterns of BPE may be mistaken for suspicious lesions and malignancies may be masked. A recent study by DeMartini et al. reveals that BPE does cause a higher rate of abnormal MRI interpretation, but sensitivity and specificity are not significantly different between patient groups with differing BPE [1]. It is considered to reflect tissue proliferative activity due to hormonal stimulation. Researchers found that it varies with the menstrual cycle in premenopausal women and increases in postmenopausal women treated with hormone replacement therapy [2-4]. Initial results even hint at BPE being a risk factor for BC [5]. Contradicting results regarding the relationship between BPE and breast density, a factor associated with higher breast cancer risk while limiting mammographic breast screening, exist.

$^{18}$FDG-PET of the breast is based on tracer uptake in suspicious lesions after intravenous administration of $^{18}$F-FDG and has a good sensitivity and limited specificity. It is regarded as a very effective imaging technique for the staging of BC patients, as nodal and distant metastases can be detected easily in one single examination. $^{18}$F-FDG is the mostly used tracer in PET-examinations, having no potential adverse effects and leading to small radiation exposure because of its small half-life period. Glucose is able to enter almost every cell, making the tumor visible as malignant lesions show a higher glucose metabolism than healthy breast tissue. Nevertheless, similar to BPE in DCE-MRI, in $^{18}$FDG PET-CT tracer uptake can also be seen in normal breast tissue and might have a negative effect on BC detection. Studies could demonstrate a positive association between $^{18}$F-FDG uptake and mammographic breast density in women with normal breast tissue [6]. $^{18}$F-FDG uptake is most commonly measured with maximum Standardized Up-take Values (SUVmax).
As to date there is no study investigating the correlation between these two factors, the aim of our study was to evaluate if BPE with DCE-MRI of the breast at 3T correlates with quantitative SUVmax in $^{18}$FDG breast PET-CT.
Methods and materials

130 patients between the age of 19 and 89 undergoing $^{18}$FDG PET-CT and 3T DCE-MRI of the breast due to BIRADS 4 or 5 imaging findings from 12/2009 to 02/2013 were included in this IRB approved prospective study. All patients had no previous treatment and no contraindications against MRI imaging and contrast agents. $^{18}$FDG PET-CT and DCE-MRI examinations were scheduled no longer than 3 days apart. Afterwards, all patients received biopsy and histopathological verification of the suspicious lesion.

MRI imaging was performed in the prone position using a 3T MRI with a four-channel breast coil, and a split dynamics protocol with high-spatial and high-temporal resolution (VIBE, TR/TE 3.61/1.4ms, 1.7mm isotropic and FLASH-3D TR/TE 877/3.82ms, 1mm isotropic). The MRI protocol included a contrast-enhanced 3D-T1-weighted sequence before and after application of a standard dose of 0.1 mmol/kg Gadoteratameglumine. Gd-DOTA was injected as a bolus using a power injector at 4 ml/s with a saline flush after injection. All premenopausal patients had their MRI planned between the 7th and 14th day of their menstrual cycle. Total MRI examination time was approximately 34 min.

In all patients, a prone PET-CT dataset over the breasts was acquired using a combined PET-CT in-line system, allowing the same patient geometry as with MRI. The prone position improves diagnostic accuracy in MRI as well as in PET-CT imaging due to a greater expansion of the breast, which is suspected to lead to higher SUVmax levels by researchers. Patients fasted 6 hours before the injection of approximately 300 MBq $^{18}$FDG, depending on the patient's weight. Blood glucose levels were <150mg/dl (8.3 mmol/l) at the time of tracer application. Scanning from the neck to upper abdominal region was started 45 min after injection. No contrast agent was injected for the CT scan, CT data was only used for attenuation correction. PET images were reconstructed using the TrueX algorithm.

BPE and breast parenchyma SUVmax of the normal contralateral breast, which was confirmed as healthy by experienced radiologists using PET-CT and MRI images, were recorded. BPE was qualitatively assessed by two independent readers and graded as none (# 25% enhancement of fibroglandular tissue), mild (25-50% enhancement), moderate (50-75% enhancement) and marked (#75% enhancement), based on pre-enhanced, initial contrast-enhanced, maximum enhanced and subtraction images. Reader 1 re-assessed all cases. For the assessment of parenchyma SUVmax, 3D regions of interest (ROIs) were manually drawn in the most enhancing part of the normal contralateral breast. ROIs were drawn in adequate distance to breast margins to avoid artifacts. In each ROI, SUVmax was calculated and corrected for the patient's weight.
Statistical analysis was carried out by a statistician using SPSS 19.0. Appropriate statistical tests (One Way ANOVA, Tukey's range test, Cohen's kappa coefficient) were used to assess correlation of BPE and SUVmax, as well as inter-rater and intra-rater agreement for BPE on DCE-MRI.
Results

There was no BPE in 58, mild in 54, moderate in 14 and marked in 4 patients. Due to the small sample size of marked BPE, moderate and marked BPE were considered together (n=18). SUVmax for patients with no BPE was 1.56 (SD 0.6), for mild BPE 1.9 (SD 0.6), for moderate/marked 2.3 (SD 0.6). SUVmax increased with BPE and there was a significant difference in SUVmax for patients with none and mild BPE (p=0.003) and none and moderate/marked BPE (p<0.01). There was no significant difference between mild and moderate/marked BPE (p=0.71). Inter-rater and intra-rater agreement for BPE was very good with a kappa value of 0.862 and 0.805 respectively.
Conclusion

The results of this study demonstrate that SUVmax on $^{18}$FDG PET-CT of normal breast parenchyma is positively correlated with BPE on DCE-MRI of the breast.

The data in our study is contrary to a study by Koo et al., who investigated the correlation of tracer uptake in $^{18}$F-FDG positron emission mammography ($^{18}$F-FDG PEM), BPE in DCE-MRI and mammographic breast density (grade 1-4), and suggest that $^{18}$F-FDG uptake of normal breast parenchyma does not increase with higher BPE [7]. Koo et al. also criticize the observer dependence of BPE measurement and mention the need for a more objective technique to quantify background enhancement of the breast. However, in this study there was very good inter-rater and intra-rater agreement for BPE.

As our study and the study by Koo et al. are contradicting and to our knowledge are the only existing studies on the correlation of BPE and SUVmax, further research on this topic is needed, especially as hybrid PET-MRI systems at 3T have been developed and tested. These systems provide simultaneous acquisition of morphologic, functional and metabolic information on malignancies, and are expected to offer an even better imaging technique for breast cancer patients.

A limitation of our study is the small number of patients with moderate and marked BPE as compared to none or mild BPE. Thus further study, preferably using simultaneous PET-MRI systems, with larger patient numbers are warranted to confirm those findings. Another limitation of this study is that BPE was assessed qualitatively and that SUVmax was measured by manually drawn ROIs. However it can be expected that the use of CAD systems, which are able to quantitatively assess BPE and SUVmax, can overcome this limitation.

In conclusion, in the current study SUVmax on $^{18}$FDG PET-CT of normal breast parenchyma is positively correlated with BPE on DCE-MRI of the breast. As higher SUVmax is expected in patients with moderate/marked BPE, a possible masking effect of lesions in such cases has to be considered with PET-MR imaging.
Fig. 1: DCE-MRI and 18FDG-PET-CT in the same patient: DCE-MRI shows mild BPE, 18FDG-PET-CT shows low breast background tracer uptake with SUVmax of 1.88.

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Fig. 2: DCE-MRI and 18FDG-PET-CT in the same patient: DCE-MRI shows moderate BPE, 18FDG-PET-CT shows medium breast background tracer uptake with SUVmax of 2.35.

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**Fig. 3:** DCE-MRI, 18FDG-PET-CT and 18FDG-PET in the same patient: DCE-MRI shows marked BPE. 18FDG-PET-CT and 18FDG-PET show high breast background tracer uptake with SUVmax of 2.78.

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References


