[SY12] JSMRM–KSMRM Joint Symposium

SY12-01

IVIM and non-Gaussian diffusion MRI of the breast

Mami Iima

Department of Diagnostic Imaging and Nuclear Medicine, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Diffusion MR imaging has become an important clinical imaging modality in the breast imaging, for the detection of lesions and metastases, as well as therapy monitoring. Some studies have shown that pretreatment ADC or early changes in tumor ADC has the potential to be a useful biomarker for predicting a response to breast cancer therapy. However, cell density is not the only histological indicator which sets tumor grade. Necrotic or cystic tumor components, which show high ADC, could reduce the association between ADC and cell density. Diffusion Tensor Imaging has revealed that diffusion could sometimes be anisotropic in the breast, but mechanisms for this anisotropy are controversial. Non-Gaussian diffusion has the potential to extract more microstructural information than the ADC, as a high degree diffusion weighting (high b values) increases the effect of obstacles to free diffusion present in tissues, notably cell membranes. Indeed, the "kurtosis" which reflects diffusion non-gaussianity is high in malignant lesions compared to benign lesions. Still, a particularly challenging problem for breast diffusion MRI is the detection of the non-mass enhancing lesions seen on contrast-enhanced MRI, such as with DCIS. On the other hand, tissue perfusion which is also available from diffusion MRI images (IVIM effect) gives information on the blood fraction which appears correlated with vessel density. The IVIM fraction is usually high in malignant lesions, but there seems to be a large overlap with benign lesions. Combination of non-Gaussian diffusion and IVIM parameters appears to boost diagnosis accuracy. Still, the results have been sometimes inconsistent in the literature partly due to differences in study design (choice of b values and acquisition methods, data analysis approaches, differences in patient population), and the standardization of acquisition protocols and models used for quantitative DWI analysis is need to be addressed for diffusion MR imaging to become a clinically useful biomarker.

In future, statistical methods taking into account diffusion MRI parameters together with other biological data, such as genomic signatures (radiogenomics), might also give clues on the risk of tumor recurrence and response to therapy for each individual patient. However, investigations on the relationship between the IVIM/diffusion parameters and the underlying tissue structure at microscopic level, as well as changes induced by therapy, must be pursued using animal models, MRI of specimens at ultra-high resolution and validation with histology. Reliability and reproducibility of diffusion MRI results must also be assessed to facilitate monitoring disease progression or response to therapy in individual patients.

Keywords : IVIM, Non-Gaussian diffusion MRI, Breast

Clinical application of ultrafast DCE-MRI in breast cancer

Naoko Mori

Diagnostic Radiology, Tohoku University Graduate School of Medicine, Sendai, Japan

Kinetic analysis of dynamic contrast-enhanced (DCE) MRI covering the whole breast with high-spatial-resolution images (generally 60-90 seconds) has been found useful in distinguishing between benign and malignant lesions, and this method has been employed in the BI-RADS MRI lexicon as standard DCE-MRI. Recently, an approach using high-temporal-resolution (3-10 seconds) with or without k-space acquisition strategies has been developed as a ultrafast DCE-MRI. It uses higher sensitivity encoding (SENSE) acceleration factors and generates images that are of high temporal resolution covering the whole breast. This method is considered more reliable for quantitative analysis of the enhancement rate or increasing rate of signal intensity in whole tumoral area in very early post-contrast phases of DCE-MRI. The kinetic assessment of the ultrafast DCE-MRI was shown to be comparable to the standard kinetic assessment obtained from the combination of early and delayed phases of standard DCE-MRI for distinguishing between benign and malignant lesions. In my talk, I am planning to talk about ultrafast DCE-MRI research and how to use the sequence in clinical setting.

Keywords : Breast cancer, Dynamic contrast-enhanced MRI

Interpretation of breast MRI: based on BI-RADS descriptors and previous literature.

Youichi Machida

[1]Radiology, Kameda Medical Center, Kamogawa City, Chiba, Japan, [2]Radiology, Kameda Kyobashi Clinic, Chuo City, Tokyo, Japan

While recent studies have shown the potential of newer image analysis using quantitative imaging or artificial intelligence, qualitative descriptors remain the basics of interpretation of breast MRI.

Breast Imaging – Reporting and Data System (BI-RADS) suggests that breast imaging interpretation should be based on categorization according to estimated positive predictive value (PPV) of malignancy. Radiologists should keep in mind reproducibility as well as PPV of each BI-RADS lexicon in order to categorize breast lesions properly. Combination of two or more findings could also be useful for better interpretation; combination of benign-looking shape and kinetics would be sign of benignity, while suspicious distribution and internal enhancement patterns would be keys in assessing the PPV of non-mass enhancement.

Nowadays, more and more patients are interested in not only oncologic but also plastic success in breast surgery, and opt for nipple-preseving operation. Breast MRI is also useful for selecting good candidates for nipple sparing mastectomy.
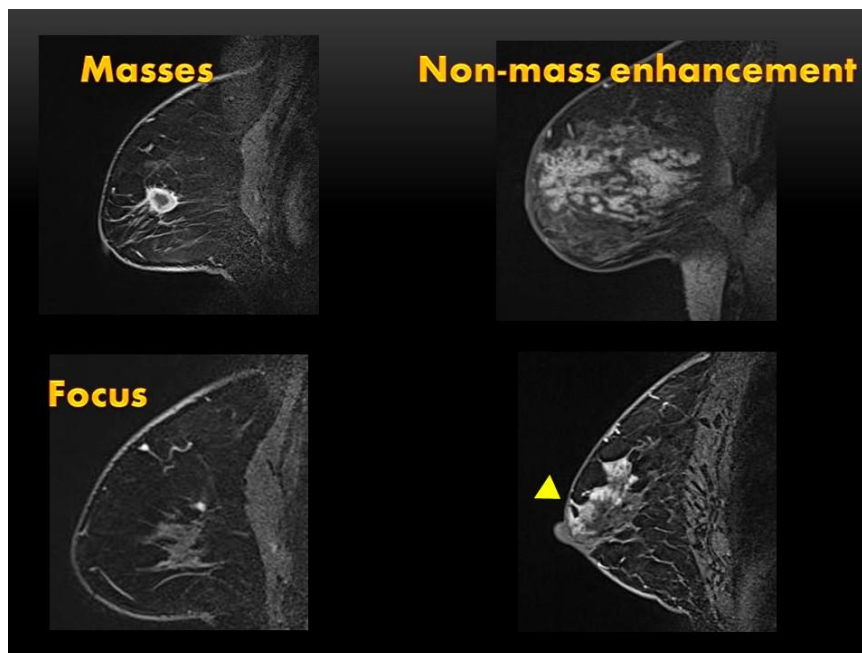

Figure 1. Findings for breast cancer diagnosis and nipple-areolar complex preservation will be talked in this presentation.

Keywords : Breast, MRI, BI-RADS, Nipple-sparing mastectomy

Breast DWI for Screening

Woo Jung Choi

Department of Radiology and Research Institute of Radiology, Asan Medical Center, Seoul, Korea

Diffusion weighted imaging

Diffusion weighted imaging (DWI) is a non-invasive technique that makes use of MR imaging to visualize the degree of water molecule diffusion in a defined voxel by means of the application of motion probing gradients.

Diffusion is quantified by measuring what is known as the apparent diffusion coefficient (ADC) value in square millimeters per second, which defines the average area covered by a molecule per unit time. The ADC value can be calculated by assessing the signal attenuation that occurs at DWI performed at different b values.

Potential benefits include improved differentiation of benign and malignant breast lesions, assessment and prediction of therapeutic efficacy, and non-contrast detection of breast cancer.

Non-contrast MR screening

While DCE MRI is highly sensitive for the identification of breast cancers, most women do not have access to this exam due to high cost. In addition, gadolinium-based contrast agents used for breast DCE MRI can sometimes cause life-threatening complications. Early investigations showed many mammographically and clinically occult breast cancers are visible on DWI and exhibit low ADC values. In addition, non-contrast DWI provided higher accuracy for detection of breast malignancies than screening mammography. The study investigating the performance of DWI to detect mammographically occult breast cancers specifically in women with dense breasts showed that DWI has the potential to identify as many as 8 additional cancers over mammography per 1000 women screened, with reasonable specificity and positive predictive value.

Table 1. Results of prior studies of non-contrast MRI *(Baltzer et al. Invest Radiol 2018;53:229-235*

Author	Cancer prevalence	Field Strength	NC-MRI technique	Study population	Sensitivity	Specificity
Baltzer, 2010	66.6%	1.5T	ssEPI, T2-TSE	Consecutive BIRADS 4 & 5 masses	94%	85%
Yabuuchi, 2011	66.6%	1.5T	ssEPI, T2-STIR, SPAIR	Mixed: asymptomatic cancers & control group	50%	95%
Wu, 2013	44.6%	3T	ssEPI, T2-TSE	Suspicious lesions ≤ 2 cm	86-93%	81-94%
Trimboli, 2014	31.9%	1.5T	EPI, T1-GE, T2-STIR	Mixed: 46% preop. Staging	78%	87%
Telegrafo, 2015	62.6%	1.5T	DWIBS, STIR, T2-TSE	Mixed: BIRADS 4 & 5 lesions; positive family Hx and dense breast	94%	58%
Bickelhaupt, 2016	48.0%	1.5T	DWIBS MIP, T2-TSE, SPAIR	Screening detected BIRADS 4 & 5 lesions	92%	96%
Belli, 2016	44.6%	1.5T	ssEPI, STIR	Mixed; cancer or equivocal finding cases	79%	97%
Shin, 2016	82.9%	3T	rsEPI, T1-VIBE	Biopsy-proven malignant masses	92%	86%
McDonald, 2016	25.3%	1.5T, 3T	ssEPI, T2-FSE, T1-GRE	Case-control: 50% malignant, 50% healthy; all with dense breasts	42%	90%
Baltzer, 2018	59.3%	3T	rsEPI	BIRADS 4 & 5 lesions after conventional workup	91%	71-75%

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Breast DWI for lymph node

Su Hyun Lee

Radiology, Seoul National University Hospital, Seoul, Korea

The accurate evaluation of axillary lymph node status is crucial in deciding the treatment plan and predicting the long-term survival in breast cancer patients. Surgical staging with axillary lymph node dissection (ALND) or sentinel lymph node biopsy (SLNB) with or without subsequent ALND is a current standard of care. However, up to 70% of clinically node-negative patients are found to be free of metastatic disease. Although less invasive compared to ALND, the SLNB is still associated with non-negligible morbidity such as lymphedema, pain, paresthesia. Therefore, non-invasive imaging with high negative predictive value could replace SLNB, eliminating its morbidity risk. Ultrasound, computed tomography, and magnetic resonance imaging (MRI) with or without gadolinium contrast medium have been proposed to evaluate the presence of axillary lymph node metastases based on the size and morphology of axillary lymph nodes. MRI has several advantages over other imaging modalities such as the lack of ionizing radiation or less intra- and inter-observer variation.

Diffusion-weighted imaging (DWI) measure intercellular water motion and obtains the apparent diffusion coefficient (ADC), which can quantify the diffusion of water molecules. A recent meta-analysis showed that the mean ADC value of metastatic ALNs was lower than that of the benign ones and ADC can differentiate metastatic and non-metastatic lymph node with a pooled sensitivity of 89% and specificity of 83%. A study of reproducibility and reliability of DWI for detecting metastatic axillary lymph nodes showed good interobserver and intraobserver agreement. However, DWI has still issues for limited spatial resolution and vulnerability to artifacts, and the ADC values used in DWI are dependent on the scanner and *b*-values. Clinical usefulness of DWI in addition to conventional MRI such as noncontrast T1-weighted or T2-weighted imaging is controversial. The use of a dedicated axillary protocol or a lymph node-specific MR contrast may further improve the diagnostic accuracy of DWI for detection of axillary lymph node metastasis.

In summary, DWI is a promising method to differentiate metastatic from nonmetastatic axillary lymph nodes. However, current evidence is based on single center studies with heterogeneous study designs and limited population. Further larger studies are needed to evaluate the clinical usefulness of DWI for detection of axillary lymph node metastasis.

Keywords : Diffusion-weighted imaging; axillary lymph node; staging

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Breast DWI for treatment monitoring

Youngjean Park

Radiology, Yonsei University College of Medicine, Seoul, Korea

Diffusion-weighted imaging (DWI) is a functional imaging technique that measures the molecular diffusion of water through tissue, which is impacted by tissue characteristics such as tissue microstructure, membrane integrity and cell density. In the context of treating known breast cancer, DWI has the potential to help monitor and even predict response to neoadjuvant chemotherapy. Cytotoxic effects of chemotherapy cause cell lysis, apoptosis and necrosis, which result in a less restrictive environment for water to diffuse. Thus, DWI may allow earlier and more accurate evaluation of treatment response by reflecting changes in tumor cellularity and membrane integrity leading to increased water diffusion and ADC values [1,2].

Several studies have reported that early changes in tumor ADC after the first cycle of chemotherapy can significantly differentiate responders from nonresponders [3-5]. In addition, ADC values have been shown to be predictive of clinical response [5,6]. Furthermore, the utility of DWI to predict pathological complete response (pCR) has also been investigated by several groups. In a recent meta-analysis, the pooled sensitivity and specificity of DWI for detecting pCR was 0.93 and 0.85, respectively, across eight studies with 539 total patients [7]. In the very recently published results of the ACRIN 6698 multicenter trial, the percentage change in tumor ADC (ΔADC) at midtreatment (12 weeks after start of treatment) was moderately predictive of pCR, and a model combining tumor subtype and midtreatment ΔADC improved predictive performance (AUC = 0.72; 95% CI: 0.61, 0.83) over ΔADC alone (AUC = 0.57, 95% CI: 0.44, 070) [8].

In this talk, previous and updated literature regarding breast DWI for monitoring and predicting treatment response to neoadjuvant chemotherapy will be reviewed.

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Keywords : Diffusion-weighted imaging, Breast, Neoadjuvant chemotherapy