Influence of spatial heterogeneity on the diagnostic accuracy of DCE-MRI in breast tumor characterization

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INTRODUCTION – Dynamic contrast-enhanced MR imaging (DCE MRI) is a promising diagnostic tool for assessment of breast cancer [1]. When differentiating benign and malignant breast lesions, it is both diagnostically and with regard to therapy advantageous to know the tumor regions with the highest degree of malignancy [2]. Most breast lesions are heterogeneous in nature and may exhibit small regions of highly abnormal pharmacokinetic properties (hot-spots), which may be missed if only the mean or median properties of the entire tumor VOI are estimated. The purpose of the current study was thus to compare the diagnostic accuracy obtained using the VOI-50th percentile (median) versus VOI-95th percentile values for a defined set of pharmacokinetic parameters.

MATERIAL & METHODS – 39 patients with verified lesions (21 malignant and 18 benign) underwent breast DCE-MRI. The study had been approved by the regional ethics committee. The MR examination was preformed on a Philips Achieva (1,5 T) system with NOVA field gradients. The protocol consisted of both a high spatial resolution THRIVE sequence for tumor identification and a high temporal resolution sequence for kinetic and pharmacokinetic parameter extraction. The two sequences were run in an interleaved fashion during contrast enhancement. High temporal resolution images in the axial plane were created by a 3D T1 multi shot EPI sequence with two echoes. The sequence has the following key parameters: Repetition time = 42ms, first echo time = 5,5ms, second echo time= 23ms, flip angle = 28°, voxel size = 1,69*1,48*4mm^3, number of slices=30, time resolution = 2,8s/image volume, a PROSET fat suppression technique was applied along with a SENSE factor of 2,5. All together, 77 repetitions of the EPI sequence were performed. The sequence is capable of providing both T1 and T2* weighted information due to its double echo modus. From the first echo dynamic images, the permeability related kinetic parameters K^{trans} and k_{ep} [3] were extracted following deconvolution with the arterial input function (AIF) [4] obtained from the internal thoracic artery. The enhancement curves where also analyzed with regard to dynamic time parameters (i.e. time-to-peak (TTP), wash-in rate and wash-out rate). Finally, the peak absolute change in T2* relaxation rate was calculated on a pixel-by-pixel basis from the double echo data. The post processing work was performed using the nICE software package (NordicNeuroLab, Bergen, Norway). For each lesion a volume of interest (VOI) were manually drawn on the THRIVE images by a radiologist experienced in MR-mammography. The parametric VOI values were extracted by co-registering the parametric images with the high spatial image series, resulting in an image overlay. Mann-Whitney U tests were used to evaluate the ability of each parameter to differentiate between malignant and benign lesions. The data were then fitted with a logistic regression model, yielding the most explicative independent parameters. Receiver operator characteristic (ROC) curve statistics were used to evaluate the diagnostically performance of the VOI-50th model and VOI-95th-percentile model respectively. The statistical analyses where executed using the statistical software package R (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS – A significant higher diagnostic accuracy was obtained using the 95th percentile parametric values compared to the 50th percentile. Off the permeability related parameters, k_{ep} showed the significant ability for differentiating benign and malignant breast lesion, whereas K^{trans} added no significant diagnostic information. The most significant independent biomarkers, which consequently were included in the regression models, are listed in table 1 with its corresponding p-values. The 95th percentile regression model gives a significant improvement of distinguishing benign and malignant breast lesion (p=0). The area under the ROC curve was significantly higher using the 95th percentile regression model (0.90) compared to the 50th percentile regression model (0.79) as shown in figure 1.

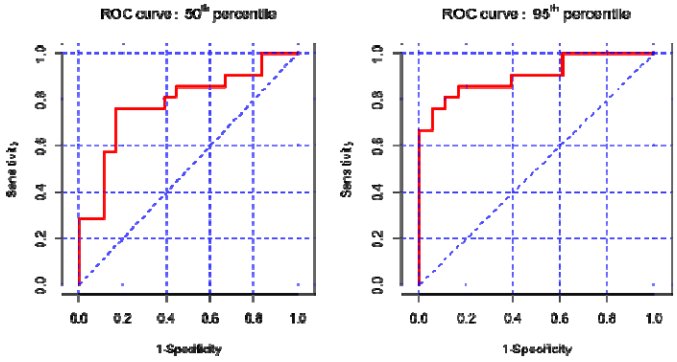

Figure 1: ROC curve for the 50th percentile regression model and the 95th percentile regression model respectively.

	K_{ep}	TTP	R2* $Peak_{enh}$
50th percentile	0,7277	0,0064	0,0007
95th percentile	0,0088	0,0011	0,0001

Table1: p-values of biomarkers estimated by the Mann-Whitney U test.

DISCUSION AND CONCLUSION – Due to the heterogeneous nature of breast lesions, the mean or median value of DCE derived kinetic parameters in a defined tumor VOI may reduce the diagnostic accuracy of the method. Our results suggest that a significant improvement in diagnostic accuracy can be obtained by identifying the 5% highest values of the kinetic parameters in the defined tumor VOI.

REFERENCE

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