Preliminary results using a split dynamic time series for DCE MR-mammography

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INTRODUCTION – MR-mammography is now the recommended method for evaluating women with high risk for breast cancer [1]. Further, it has been advised that MR of the controlateral breast in patients already diagnosed with breast malignancy should be performed [2]. Dynamic contrast-enhanced MRI (DCE-MRI) based on the acquisition of T1-weighted high spatial resolution images is the preferred method [3]. These images are most commonly evaluated by studying the shape of the tumor signal intensity curve [4].
However, there is still a need to increase breast MRI specificity [5]. This is especially true for differential diagnosis of fibroadenomas, which can present with DCE curves similar to those of malignant lesions.
Within the context of the current subject our research group proposed a method where two dynamic pulse sequences are applied in an interleaved fashion during the injection of a single dose of an intravenous contrast agent. One that is used with very high temporal resolution while the other procures detailed spatial information.
The purpose of this work is to present the preliminary results utilizing the signal intensity time information acquired from the high temporal resolution sequence.

MATERIAL & METHODS – 41 patients with verified lesions, 22 malignant (invasive ductal carcinomas (19), invasive lubular carcinomas (1), mucinous carcinomas (2)) and 19 benign tumors (fibroadenomas (14), papillomas (3), benign phylloides (1), tubular adenomas (1)) underwent breast DCE-MRI. The study was approved by the regional ethics committee. A dedicated 7 channel breast coil with parallel imaging capabilities was applied. All images were scanned as axial slices. The protocol consisted of both a high spatial resolution THRIVE sequence for tumor identification and a high temporal resolution sequence for parameter quantification. The two sequences were run in an interleaved fashion during contrast enhancement (MultiHance 0,2 mmol/kg body weight , Milan, Italy). High temporal resolution images were created by a 3D T1 multi shot EPI sequence with two echoes. The sequence has the following key parameters: Repetition time = 42ms, echo times = 5,5ms/23ms, flip angle = 28°, voxel size = 1,69*1,48*4mm^3, number of slices=30, time resolution = 2,8s/image volume with a total of 77 dynamic series acquired. A PROSET fat suppression technique was applied along with a SENSE factor of 2,5. The purpose of the EPI sequence was to provide both dynamic T1 and T2* information.
The signal-intensity-time curves were subjected to the corresponding arterial input function (AIF) and fitted to a two-compartment tracer kinetic model yielding the kinetic parameters, K^{trans}, K_{ep}, V_e and V_p. These parameters were than normalized to breast parenchyma, reducing the prospective error in the AIF and yielding the kinetic ratio between the normal tissue and cancer tissue. The qualitative dynamic curve parameters, wash in and wash out slope, area under the curve (AUC), time to peak enhancement (TTP) and peak enhancement were estimated in relative units. The transverse relaxation rate, R2*, was calculated on a pixel-by-pixel basis by assuming a mono-exponential dependence of signal change on echo time and parametric images representing the peak change in R2* were generated. The dynamic and pharmacokinetic parameters were extracted from the data set using the nICE software package (NordicNeuroLab, Bergen, Norway). For each lesion a volume of interest (VOI) were manually drawn by an experienced radiologist.
Mann-Whitney U test were used to evaluate the significance of the different parameters respectively. The data were then fitted with a logistic regression model, including the three most significant independent parameters. Receiver operator characteristic (ROC) curve statistics were used to evaluate the diagnostically performance of the logistic regression model. The statistical analyses where executed using the statistical software package R (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS – By investigating the VOI 95th percentile values we established the normalized K^{trans}-ratio ($p<0.001$), TTP ($p<0.002$) and R2* peak enhancement ($p<0.001$) as the most significant independent parameters (table 1). These biomarkers were included in the logistic regression model. For all lesions evaluated our method gave a sensitivity of 95% and a specificity number of 89%. The receiver operator characteristic curve statistics showed an area under the ROC curve of 0,96. We correctly characterized all the invasive ductal carcinomas (19) and the fibroadenomas (14).

	Normalized K^{trans}	Normalized K_{ep}	Normalized V_e	Normalized V_p	Wash in	Wash out	AUC	TTP	$Peak_{enh}$	R2* $Peak_{enh}$
p-value	0,0006	0,049	0,112	0,0051	0,114	0,01	0,217	0,0011	0,073	0,0001
Sensitivity (%)	71	62	62	57	68	72	50	77	68	81
Specificity (%)	83	56	56	83	58	84	68	74	68	79
AUROC	0,81	0,69	0,65	0,76	0,65	0,73	0,61	0,79	0,67	0,85

Table 1: Statistical values for the biomarkers evaluated.

DISCUSION & CONCLUSION – As shown, the high temporal resolution sequence generates numerous biomarkers that provide valuable information when differentiating benign and malignant breast lesions. By investigating the VOI 95th percentile values we established the three most significant biomarkers, which then successively distinguished all invasive ductal carcinomas form the fibroadenomas but not all the more rare tumors. When reflecting on the result it is important to consider the possibility of over adjustment when including several parameters in the model. However, this study was based on the dynamic and pharmacokinetic parameters alone. The method offers additional morphologic information through the high spatial resolution THRIVE sequence which was not evaluated in this study.

REFERENCES
[1] Saslow et al. *Am Cancer Journal for Clin* 2007: **57**(2): 75-89. [2] Lehman et al *N Engl J Med* 2007 **356**(13): 1295-1303. [3] Orel et al. *Radiology* 2001:**220**: 13-30. [4] Daniel et al. *Radiology* 1998:**209**: 499-509. [5] Blumke et al. J*AMA* 2004:**292**(22):2735-42.