Improved diagnostic accuracy in DCE MR-mammography by normalization of kinetic parameters following AIF deconvolution

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INTRODUCTION
Dynamic contrast enhanced MR-mammography (DCE-MRM) has emerged as a promising diagnostic tool for the assessment of breast cancer due to its ability to image tumor vascularity [1]. Accurate quantitative assessment of pharmacokinetic parameters related to the distribution of the contrast agent in the tumor requires knowledge of the arterial input function (AIF) obtained from an artery supplying the tumor region of interest [2]. Identification of the AIF in DCE-MRM is challenging due to limited spatial resolution combined with tissue motion during the dynamic scan. The purpose of this study was to propose a method for diminishing prospective error in the AIF by normalizing the pharmacokinetic parameters to breast parenchyma, which is assumed having normal vascularity, and to demonstrate the effect this approach can entail regarding the diagnostically performance of the pharmacokinetic model.

MATERIALS & METHODS
Thirty-nine patients with verified lesions underwent breast DCE-MRI. The study was approved by the regional ethics committee. The MR examination was performed 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 parameter quantification. 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, but for this study we specifically evaluated T1 related parameters. For each lesion a volume of interest (VOI) were manually drawn on the THRIVE images by a radiologist experienced in MR-mammography. From the first echo dynamic images, the permeability related kinetic parameter Ktrans [3] were extracted following deconvolution with the arterial input function (AIF) [4] obtained from the internal thoracic artery. Ktrans images were then overlaid on the THRIVE images making detailed Ktrans-values within the tumor available. The lesions 95th percentile Ktrans-value was then normalized to the mean Ktrans-value of the corresponding parenchyma, yielding the Ktrans ratio. Also, additional Ktrans values were estimated based on an idealized mono-exponential AIF for evaluating the need of an individual AIF. The post processing work was performed using the nICE software package (NordicNeuroLab, Bergen, Norway). Mann-Whitney U tests were used to evaluate the ability of each parameter to differentiate between malignant and benign lesions. Receiver operator characteristic (ROC) curve statistics were used to evaluate the diagnostically performance for the initial 95th percentile value and the normalized value respectively. The statistical analysis were executed using the statistical software package R (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS
Histology identified 21 lesions (54%) as malignant and 18 (46%) as benign. The initial 95th percentile Ktrans value did not show a significant correlation to malignancy (p>0.35), and displayed a poor diagnostic accuracy with an area under the ROC curve of 0.58. The normalized Ktrans value did however show a significant correlation to malignancy (p<0.001), and a good diagnostic accuracy with an area under the ROC curve of 0.81. The 95th percentile Ktrans values based on an idealized mono-exponential AIF did not show a significant correlation to malignancy (p>0.5), indicating the need for an individual AIF.

DISCUSSION & CONCLUSION
A quantitative acquisition of the pharmacokinetic parameters demands an accurate description of the AIF, which can only be achieved by applying a high temporal resolution sequence on the cost of the spatial resolution. As a result, the potentiality of AIF-error increases. Employing a normalization approach has shown a potential improvement in the diagnostically performance of the pharmacokinetic model, diminishing the prospective errors in the AIF.

REFERENCES

Figure 1: Box plot of the initial 95th percentile Ktrans value and normalized Ktrans ratio: Normalized values showing a significant higher performance in distinguishing malignant and benign lesions.