Benign-Malignant lesion differentiation using functional ADC-thresholding – allowing expert radiologist interpretation – versus conventional thresholding based on ADC cut-off values

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Introduction - Diffusion-weighted imaging (DWI) may aid in the discrimination of benign from malignant (breast) lesions. Approaches to benefit from the information contained in the DWI dataset have mostly been based on trying to define a cut-off value for the lesion ADC. This may be limiting because of the relatively low SNR, the relatively high variability of lesion ADC - even within one hospital or patient population - and the limited potential of the results to be extrapolated to different field strengths, pulse-sequences or b-values.

Methods – Here we describe an approach in which the high CNR of DWI and the quantitative information of the ADC are presented to the radiologist in a "functionally-thresholded ADC (ftADC) map" (see Figs 1+2) that increases the conspicuity of lesions of interest, much like phase-images are used to increase vascular conspicuity in susceptibility-weighted imaging. Radiologists can "window-level" ftADC-maps at their discretion and diagnose a lesion as "ftADC-bright" without having to choose an ADC-threshold value; Similar to, for example, a cystic lesion being interpreted as "T2-bright" without using T2-cut-off values. We performed a retrospective, HIPAA-compliant, IRB-approved analysis of DW data sets of 103 consecutive women who underwent 1.5T MRI for the evaluation of breast cancer. Conventional ADC-thresholding was compared to ftADC-mapping and to dynamic contrast-enhanced (DCE) MRI, for all pathology-verified lesions.

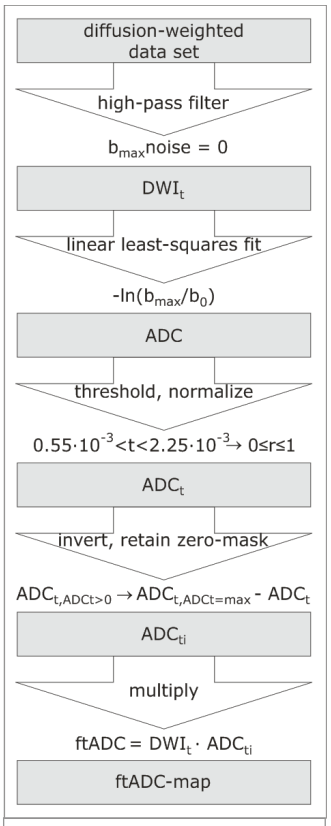

Fig 1. ftADC algorithm

Results - The results summarized in Table 1 confirm that lower ADCs are correlated with a higher chance of a malignant diagnosis, but that the discriminatory power of setting an ADC cut-off value – evaluated using ROC curves – is low. In addition, attempts to reduce variability by within-patient normalization of lesion ADC to muscle ADC are shown to be unsuccessful. The data in Table 2 shows the retrospective diagnosis-modifying effect of DWI and ftADC-mapping, based on 65 pathology-proven lesions in 49 patients. 5/6 lesions that were incorrectly down-staged by ftADC were BIRADS-6, known cancers, that were minimally enhancing on DCE-MRI, and were either in situ cancers (DCIS) post-biopsy (3/6), or DCIS (1/6) or invasive cancer (IDC; 1/6) after chemotherapy (2/6). If DCE-MRI is regarded the gold-standard, in 103 patients 1 minimally enhancing BIRADS-4 DCIS-lesion was missed, in a patient with a multicentric contralateral IDC. On the basis of ftADC-analysis, 9% of BIRADS-3 lesions and 16% of BIRADS-4 lesions could retrospectively be correctly down-staged

Table 1 – Classification accuracy of mean lesion ADC for benign and malignant breast lesions

	Lesion ADC (10^{-3} mm^2/s)	Muscle ADC (10^{-3} mm^2/s)	ADC Ratio (Lesion/Muscle)
Benign	2.18 ± 0.86	2.47 ± 0.38	0.95 ± 0.44
Malignant	1.82 ± 0.35	2.32 ± 0.26	0.79 ± 0.17
2-tailed sign[1]	.40	.23	.44
AUC[2]	0.679	0.487	.604
Benign	2.18 ± 0.86	2.47 ± 0.38	0.95 ± 0.44
Non-invasive	1.97 ± 0.51	2.25 ± 0.12	0.88 ± 0.22
Invasive	1.72 ± 0.17	2.37 ± 0.31	0.74 ± 0.11
2-tailed sign[3]	.11	.40	.12
AUC[4]	0.724	0.429	0.653

Values are mean ± SD, based on n = 22 biopsied or surgically resected malignant lesions and 7 biopsied benign lesions that were DWI-bright (i.e. possible malignant lesions)
[1] Independent samples Student's t-test
[2] Area under Receiver Operating Characteristics (ROC)-curve
[3] One-way ANOVA, showing post hoc p-value Benign vs Invasive
[3] Area under ROC-curve for discriminating Benign from Invasive

Conclusions - ftADC-mapping may improve lesion discrimination in (breast) MRI. In theory, after large-scale validation of the results, a significant number of patients could be down-staged from BIRADS-3 and possibly even from BIRADS-4, to a benign diagnosis, and thus be spared a biopsy.

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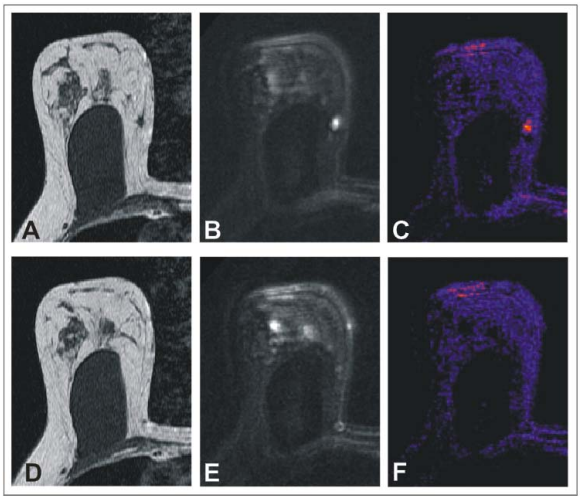

Fig 2. A+D Axial, pre-contrast T1W images; **B+E** DW-images; **C+F** corresponding ftADC maps. Note that only one of the DWI-bright lesions in (B+E) is visible on the ftADC map in (C). At subsequent lumpectomy the lesion in (B) was confirmed to be an invasive ductal carcinoma.

Table 2 - Diagnosis-modifying effect of ftADC-mapping in terms of up- or down- staging the DCE-MRI diagnosis[1]

	DWI alone	ftADC alone	ftADC [2] Clinical setting
Correctly up-staged	0 (0%)	0 (0%)	0 (0%)
Correctly down-staged - BIRADS 3	6 (9.2%)	6 (9.2%)	6 (9.2%)
Correctly down-staged - BIRADS 4+	13 (20.0%)	16 (24.6%)	16 (24.6%)
Incorrectly up-staged	3 (4.6%)	1 (1.5%)	0 (0.0%)
Incorrectly down-staged BIRADS 3	0 (0.0%)	0 (0.0%)	0 (0.0%)
Incorrectly down-staged BIRADS 4+	3 (4.6%) [3]	6 (9.2%)	1 (1.5%) [3]

[1]: The putative diagnosis-modifying effect was determined as follows:
Correct up-staging: PA proven malignant lesions that were BIRADS-2 (or BIRADS-1 for the whole breast) at DCE-MRI, and bright on DWI, or ftADC, respectively
Correct down-staging: PA proven benign lesions that were BIRADS-3 or higher at DCE-MRI, and negative on DWI, or ftADC, respectively
Incorrect up-staging: Follow-up or mastectomy proven benign lesions that were BIRADS-2 at DCE- MRI, and bright on DWI or ftADC, respectively
Incorrect down-staging: PA proven malignant lesions that were BIRADS-3 or higher at DCE-MRI and negative on DWI, or ftADC, respectively

[2]: Diagnosis-modifying effect based on combined analysis of the ftADC-maps and the T1- and T2-weighted sequences (preventing the incorrect upstaging of normal axillary lymph nodes); no contrast-enhanced sequences. Knowledge of the clinical setting prevents the incorrect down-staging of BIRADS-6 known cancers after chemo- or radiotherapy.

[3]: A minimally enhancing DCIS lesion in a patient with a BIRADS-6 multicentric IDC in the contralateral breast.