Evidence-based Rating: B

Personal Rating: 3

Correlation between 3 T apparent diffusion coefficient values and grading of invasive breast carcinoma

Diffusion-weighted-imaging (DWI) is provided in all clinical MR scanners, and it can be easily incorporated into a breast MRI examination protocol. The DWI sequence takes a very short imaging time, yet it can provide unique information related to cellular density that are not revealed in other sequences. Typically two diffusion-weighted images with a low b (b=0 or 50 s/mm^2) and a high b (800 to 1,000 s/mm^2) values are acquired, which can then be used to derive the apparent diffusion coefficient (ADC). Although DWI can be easily prescribed, the major limitation for its wide clinical use is the low signal-to-noise ratio (SNR) and the severe image distortion artifact. In recent years, with the more frequent use of 3.0 Tesla scanner for breast imaging and the advancement in MR imaging technology, the SNR and image quality for breast DWI is greatly improved, and many studies have evaluated the capability of DWI for characterization of breast lesions.

It was consistently reported that the ADC value is related to cellular density, and that may be used for differential diagnosis. As the cellular density increases, more restricted diffusion would lead to a higher signal intensity on DWI and a lower derived ADC value. On average, ADC values decrease with the aggressiveness of disease; from the highest to lowest: normal tissue, benign tumor, in-situ cancer, and invasive cancer. ADC was further correlated with established prognostic factors, such as tumor size, grade, lymph node status and molecular

biomarkers (estrogen receptor ER, progesterone receptor PR, HER-2, and Ki-67) to determine its prognostic value. ADC was also used in therapy monitoring and prediction. The change in ADC at early times after neoadjuvant chemotherapy has also been shown to be associated with treatment outcome, again based on evaluating the changes in cellular density after the drugs are administered.

In this article, Cipolla and colleagues performed a retrospective review based on pre-surgical MRI done for local staging purposes. Cases that included both DCE-MRI and DWI done at 3T were identified, and a total of 96 lesions (from 92 patients) that were proven to be invasive cancer and with all 4 molecular biomarkers (ER, PR, HER2, and Ki67) available were included in the analysis. The region of interest (ROI) was manually placed on ADC maps, by using both DCE-MRI and DWI as references to locate solid portion of the lesion that showed strong contrast enhancements on DCE subtraction images and had a high signal intensity on DWI. Although ADC maps are noisy, placing ROI directly on ADC maps is better than using DCE subtraction images (may have registration error due to image distortion) or using DWI images (may be mis-led by necrotic tissues that show a high signal intensity of DWI). The histopathological grade was determined according to the Nottingham Grading System (NGS) by evaluating tubule formation, pleomorphism, and mitotic count, with the total score of 3–5 as Grade-1, scores of 6 and 7 as Grade-2, and scores of 8 and 9 as Grade-3.

The results showed a higher ADC in G1 tumors (median 1.16×10^{-3} mm^2/s; range 0.89–2.24) than in G3 tumors (median 1.03×10^{-3} mm2/s; range of 0.45–1.77), with p=0.037. The mean ADC of all lesions was $1.09 \pm 0.29 \times 10^{-3}$ mm^2 /s. Although the difference between G1 and G3 reached statistical significance, it was only marginally lower than the threshold of p=0.05. In the analysis of molecular biomarkers, G1 tumors were smaller (84.4% < 2 cm) and more likely to have

positive ER (100%), positive PR (93.7%), negative HER2 (100%), and low Ki67 <14% (81.3%) compared to G3 Tumors that were larger (32.5% < 2 cm) and less likely to have positive ER (60%), positive PR (55%), negative HER2 (65%), and low Ki67 <14% (12.5%). These results are consistent with the knowledge that hormonal receptor (ER/PR) positive tumors are less aggressive than hormonal receptor negative tumors, HER-2 negative tumors (except triple negative) are less aggressive than HER-2 positive tumors, and low Ki-67 tumors are less aggressive than high Ki-67 tumors. The authors did not specifically compare the ADC values in different molecular sub-type groups. All ten triple negative cancer were G3, and their median ADC was $1.22 \pm 0.37 \times 10^{-3}$ mm^2 /s, which was higher than the whole group mean of $1.09 \pm 0.29 \times 10^{-3}$ mm^2 /s, but it was not significantly different compared to any other group. The authors did not discuss why some triple negative cancers have a relatively high ADC value.

Although ADC values show a significant difference between G1 and G3, the difference is very small, so the results presented in this work do not provide a strong evidence to support the prognostic value of ADC. Similarly, for most ADC studies published in the literature, very often it was shown that a significant difference was found between benign and malignant, between in-situ and invasive, and between low-grade and high-grade cancers, yet the difference was small and had substantial overlap between groups. For diagnosis of prostate cancer, the value of DWI and ADC is well-established – this may be partly because of the difficulty of using anatomic T1- and T2- weighted and contrast-enhanced MRI for diagnosis of prostate lesions. In contrast, for diagnoses of breast cancer, DCE-MRI with a high spatial resolution to real anatomic details of detected lesion is known to perform very well for an accurate diagnosis, and the clinical value of the low-spatial-resolution DWI will be very difficult to prove. Nonetheless, with the continuing improvement in MR imaging technology, particularly with a better coil design for parallel

imaging and better field homogeneity, the quality of DWI may be further improved, and that will help researchers in the breast imaging community to investigate the clinical role of ADC and establish its diagnostic value and prognostic value in the management of breast diseases.

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References

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