Characterization of Malignancy of Adnexal Lesions using ADC Entropy: Comparison with Mean ADC and Qualitative DWI Assessment

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Introduction: The accurate characterization of an adnexal mass as benign or malignant is crucial to avoid unnecessary surgery. While qualitative assessment of diffusion-weighted imaging (DWI) contributes to characterization of adnexal lesions (1-3), the role of mean apparent diffusion coefficient (ADC) values is controversial (1,4-5). Entropy, a texture-based measure of variation in the ADC histogram within a volume of tissue, has been shown to be of value in evaluation of liver fibrosis and multiple sclerosis (6-7). To our knowledge, no prior study has assessed the role of ADC entropy in the characterization of adnexal lesions. The purpose of this study is to assess the utility of ADC entropy in discrimination of benign and malignant adnexal lesions, using histopathology as the reference standard. Mean ADC and ADC entropy were compared with the qualitative visual assessment of adnexal lesions using conventional and DWI MR sequences.

Methods: 37 adult female patients (mean age 54±14 years) with an ovarian mass that was resected between June 2006 and January 2011 were included in this IRB approved study. Patients underwent 1.5 T pelvic MRI that included DWI with a b-value of 500 sec/mm^2 prior to resection. At histopathologic analysis, 9 masses were malignant and 28 were benign. Two radiologists (R1 with 2 years experience in Body MRI and R2 with 15 years experience in Women's Imaging) reviewed the MR examinations during two separate sessions (S1: conventional MRI without DWI, S2: both conventional MRI and DWI) and rated the adnexal lesions as benign or malignant based on a qualitative visual assessment. Readers were blinded to each other and to pathology results. A third radiologist (3 years experience in body MRI) drew ROIs on every slice that included the mass on the ADC map. The mean ADC and ADC entropy were computed using in-house developed software. Entropy was defined as $\sum(-p_i)\log(p_i)$, in which p_i represents the frequency of ADC values, i.e., the number of corresponding voxels normalized to the total number of lesion voxels (6-7). Mann-Whitney test and logistic regression for correlated data were used to compare the performance of mean ADC, ADC entropy, and the subjective interpretations of the two radiologists for distinguishing benign and malignant ovarian masses.

Table 1

Test	Accuracy	Sens.	Spec.	NPV	PPV
Mean ADC	57% (21/37)	56% (5/9)	57% (16/28)	80% (16/20)	29% (5/17)
ADC entropy	84% (31/37)	67% (6/9)	89% (25/28)	89% (25/28)	67% (6/9)
R1, Without DWI	73% (27/37)	67% (6/9)	75% (21/28)	88% (21/24)	46% (6/13)
R1, With DWI	81% (30/37)	67% (6/9)	86% (24/28)	89% (24/27)	60% (6/10)
R2, Without DWI	97% (36/37)	89% (8/9)	100% (28/28)	97% (28/29)	100% (8/8)
R2, With DWI	95% (35/37)	89% (8/9)	96% (27/28)	96% (27/28)	89% (8/9)

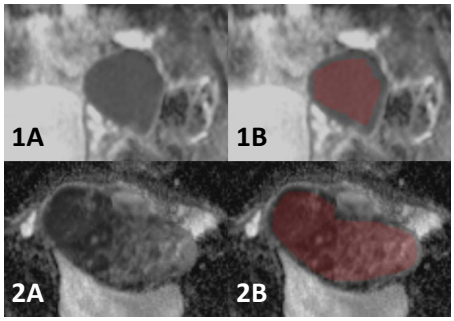

Fig 1: A) ADC map of right ovarian benign teratoma. B) Whole-lesion ROI yielded mean ADC of 0.66×10^{-3} mm^2/s and ADC entropy of 3.84.

Fig 2: A) ADC map of right ovarian malignant mixed Mullerian tumor. B) Whole-lesion ROI yielded mean ADC of 1.43×10^{-3} mm^2/s and ADC entropy of 5.46. Higher entropy in malignant lesion is consistent with results of our study.

Results: No statistically significant difference was observed in mean ADC between benign and malignant ovarian lesions (1.90±0.93 vs. 2.00±0.53 x10^{-3} mm^2/s respectively, p=0.768). ADC entropy was significantly higher in malignant than in benign lesions (4.94±0.40 vs. 4.54±0.44, respectively, p=0.009). Table 1 shows the diagnostic performance of mean and ADC entropy as well as of the two readers. ADC entropy, using a threshold of >4.92, demonstrated significantly higher accuracy for differentiation of benign and malignant lesions than did mean ADC (p=0.018). There was no significant difference in accuracy between ADC entropy and reader 1's qualitative assessments, with or without DWI (p≥0.20). The greater accuracy of reader 1's qualitative assessments when using DWI than conventional sequences alone was not statistically significant (p=0.172). Reader 2's qualitative assessments using conventional MRI alone achieved significantly higher accuracy than mean ADC, ADC entropy, and reader 1's qualitative assessments (p=0.003-0.039).

Conclusions: The observed lack of significant difference in mean ADC between benign and malignant ovarian lesions has been observed in previous studies (4,5). However, malignant ovarian lesions demonstrated significantly higher ADC entropy than benign lesions, most likely reflecting the sensitivity of entropy to both macroscopic and microscopic cellular changes (8). ADC entropy performed significantly better than mean ADC and comparable to the qualitative assessments of reader 1. Greatest performance was achieved by reader 2's qualitative assessments, reflective of this reader's experience in Women's Imaging. Inclusion of all lesion voxels within the ROIs allowed for measurement of entropy of ADC in a straightforward and objective manner. Therefore, ADC entropy may serve as a useful quantitative metric for ovarian lesion evaluation with potential to provide significantly greater accuracy than the more traditional metric of mean ADC. Our data suggests that the benefit of entropy measurement decreases with greater reader experience. Our findings require validating in a larger cohort.

References: [1] Nakayama T, et al. JMRI 2005;22:271-278 [2] Imaoka, I. et al. Radiographics 2006;26:1431-1448 [3] Bakir B, et al. Br J Radiol 2011;84:600-611 [4] Katayama M, et al. J Comput Assist Tomogr 2002;26:250-256 [5] Fujii S, et al. JMRI 2008;28:1149-1156 [6] Benedict RH, et al. Mult Scler 2007;13:722-730 [7] Fujimoto K, et al. Radiology 2011;258:739-748 [8] Tavazzi E, et al. Neuroimage 2007;36:746-754