Pattern Recognition Classification of Weighted MR Images of OARSI Scored Human Articular Cartilage at 3T

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Introduction: Noninvasive MRI approaches for early detection of osteoarthritis (OA) and for monitoring the response to therapy are still under development, and have been the subject of intense activity. One factor limiting progress in this area is the fact that individual MR parameters overlap substantially between different degrees of cartilage degradation. As previously demonstrated, this overlap results in limited classification accuracy between controls and pathomimetically degraded cartilage, as well as between histologically normal human articular cartilage explants and those with cartilage matrix loss[1,2]. In both of these tissue models, multiparametric analysis resulted in improved discrimination capability[1,3,4]. We now build on this through use of an alternative multivariate classification approach using an established pattern recognition algorithm, *weighted neighbor distance* using *compound hierarchy* of *algorithms representing morphology (wndchrm),* which detects subtle differences in textures and intensity patterns between images through examination of multiple image transforms (features), including Zernike, Chebyshev-Fourier, and Haralick[5,6]. *Wndchrm* has already been applied to predict the longitudinal development of knee OA defined by Kellgren-Lawrence grade in radiographic images[7]. In the present work, human articular cartilage explants imaged at clinical field strength (3T) and physiological temperature (37 °C) were first classified by OARSI histological grade. *Wndchrm* was then used to classify the explants using individual MR outcome measures, consisting of image intensities derived from T_1, T_2, T_2^*, ADC and MT weighted images. A number of weightings were explored, including several corresponding to the OA Initiative (OAI)[8].

Methods: *Sample Preparation*: Human tissue was obtained from knee joints in an IRB-approved protocol from subjects undergoing elective arthroplasty or from tissue banks. Two adjacent osteochondral plugs (6 mm dia, n = 38 pairs) were harvested from standardized sites within the femur, flash frozen, and stored at -80°C until analyzed; one of the plugs was histologically scored by two independent observers for OA severity using the OARSI scoring system while its paired plug was imaged[9]. The thawed plugs were inserted into a susceptibility-matched ULTEM sample holder containing Fluorinert® FC-77 (Sigma-Aldrich, St. Louis, MO). *MRI Measurements*: Imaging was performed using a 3T Philips Achieva System equipped with an 8 channel SENSE knee coil at a sample temperature of 37.0 ± 0.1 ºC. *T_1 measurements:* A 2D Look-Locker sequence with EPI readout (TE = 5 ms, TR = 6s, td = 50 ms, FA = 14°, ETL = 80, EPI factor = 3) was used to acquire two 4 mm thick slices with BW = 17.5 kHz, FOV = 75 × 44.5 mm (vertical × horizontal), MTX = 120 × 66 pixels, and NSA = 2. *T_2 measurements:* A 3D multi-echo spin echo sequence (TE = 12 ms, TR = 767 ms, ETL = 30) was used with BW = 28.2 kHz, FOV = 75 × 45 × 23 mm, MTX = 188 × 78 × 7 pixels, and NSA = 1. *T_2^* measurements:* A 2D gradient echo sequence (TE1 = 1.5 ms, ΔTE = 4.2 ms, TR = 2 s, FA = 25°, ETL = 30) was used to acquire two 3.5 mm thick slices with BW = 98.9 kHz , FOV =75 x 45 mm, MTX = 152 × 73 pixels, and NSA = 2. *ADC measurements:* A 2D spin echo sequence with EPI readout (TE = 62 ms, TR = 2 s, EPI factor = 3) was used to acquire two 4 mm thick slices with b-values of 0, 333, 666, 1000, 1333, 1666, and 2000 s/mm^2, Δ = 25.3 ms, δ= 12.4 ms, BW = 12 kHz, FOV = 75 × 43.75 mm, MTX = 96 × 43 pixels, and NSA = 1. *MT measurements:* A 2D FFE (fast field echo) sequence (TE = 2.4 ms, TR = 517 ms, FA = 25°) preceded by two 50 ms sinc-shaped presaturation pulses with 1 kHz offset and B_1 = 2.15 μT was used with two 5 mm slices, BW = 98.9 kHz, FOV = 75 × 45 mm, MTX = 152 × 73 pixels, and NSA = 2. *T_1 (as per the OAI) measurements:* A 3D FFE sequence (TE = 7.57 ms, TR = 20 ms, FA = 13°, partial Fourier factor = 0.75) was used with BW = 31.1 kHz, FOV = 75 × 45 × 24 mm, MTX = 240 × 144 × 16 pixels, and NSA = 1. *T_2 (OAI) measurements:* A 2D multi-slice multi-echo turbo spin echo sequence (TE = 10 ms, TR = 2700 ms, ETL = 7) was used to acquire two 3 mm thick slices with BW = 59.8 kHz, FOV = 75 × 45 mm (vertical × horizontal), MTX = 240 × 101 pixels, and NSA = 1. *ROI selection*: Rectangular regions of interest (ROI) centered on the full cartilage cross-sectional area and excluding subchondral bone were drawn using ImageJ software (NIH, Bethesda, MD). *Classification analysis*: OARSI histological grades of OA severity (ranging from 0 to 6) were used to define two cartilage groups: normal (< 2.5, n = 26) and matrix-degraded (≥ 2.5, n = 12). This cutoff value was selected prior to the analysis and corresponds roughly to a transition between near-normal and substantially degraded. *Wndchrm* was used to extract image content features from the raw image, image transforms and compound image transforms[5]. A Fischer score was computed for each feature (n = 2919). Because not all features are equally informative and many represent noise, only the top 15% were used for classification and similarity measurement as per convention[5]. Each ROI from the MR-weighted images was individually classified as normal or matrix-degraded using a unique feature set. Classification sensitivity and specificity were determined using a modified leave-one-out analysis. *Wndchrm* results were reported as sensitivity (proportion of true positives), specificity (proportion of true negatives), and accuracy (proportion of correctly classified samples).

Results: Table 1 shows the *wndchrm* classification results for T_1W, T_2W, T_2*W, ADCW and MTW. Of these, T_1W and MTW were the best classifiers, with accuracies above 0.84. Table 2 shows the *wndchrm* test set classification results for the T_1W and T_2W weightings corresponding to those used in the OAI. These weightings produced reasonably high accuracies of 0.76 or greater.

Table 1. *Wndchrm* test set sensitivity, specificity, and accuracy for conventional MR modality weightings.

MR Modality	Weighting	Sensitivity	Specificity	Accuracy
T_1W	TI = 931 ms	0.97 ± 0.01	0.79 ± 0.02	0.85 ± 0.01
T_2W	TE = 48 ms	0.79 ± 0.01	0.87 ± 0.02	0.80 ± 0.01
T_2*W	TE = 31.25 ms	0.97 ± 0.01	0.76 ± 0.02	0.83 ± 0.01
ADCW	b = 666	0.82 ± 0.01	0.86 ± 0.02	0.80 ± 0.02
MTW	T_{Sat} = 150 ms	0.91 ± 0.02	0.81 ± 0.02	0.84 ± 0.01

Table 2. *Wndchrm* test set sensitivity, specificity, and accuracy for OAI MR modality weightings.

MR Modality	Weighting	Sensitivity	Specificity	Accuracy
T_1W	TI = 7.57 ms	0.86 ± 0.02	0.73 ± 0.02	0.77 ± 0.01
T_2W	TE = 20 ms	0.87 ± 0.02	0.74 ± 0.02	0.78 ± 0.01
	TE = 30 ms	0.94 ± 0.01	0.70 ± 0.02	0.78 ± 0.01
	TE = 40 ms	0.95 ± 0.01	0.72 ± 0.02	0.79 ± 0.01
	TE = 50 ms	0.88 ± 0.02	0.72 ± 0.02	0.77 ± 0.01
	TE = 60 ms	0.93 ± 0.02	0.71 ± 0.02	0.78 ± 0.01
	TE = 70 ms	0.96 ± 0.01	0.67 ± 0.02	0.76 ± 0.01

Discussion: Our results indicate the potential for feature-analysis algorithms such as *wndchrm* to successfully classify MR parameter weighted images. In all but two MR modality weightings, sensitivity was higher than specificity indicating that *wndchrm* features were better at classifying matrix-degraded than normal ROIs. Additionally, the classification was successful in spite of the relatively small sample size, as indicated by the small standard deviations of the validation set sensitivities, specificities, and accuracies. Having demonstrated the potential for success of *wndchrm* in the setting of binary classification, this work can be extended to account for the continuous nature of cartilage degradation. The availability of OARSI graded data will permit us to train a multivariate linear regression model with computed image feature values, leading to a synthetic OA severity score based on image transforms. This score will be evaluated through its correlation with OARSI histological grade.

Conclusions: *Wndchrm* results in substantially higher classification performance than conventional univariate analysis of MR parameters for human articular cartilage plugs imaged at 3T [1]. These initial results represent a promising step towards clinical detection and classification of cartilage matrix degradation during early stages of OA using conventional MR contrast weightings.

References: 1) Lukas VA, et al. ISMRM Annual Meeting 2013. 2) Lin PC, et al. Magn Reson Med 2009; 62(5):1311–1318. 3) Lin PC, et al. J Magn Reson 2009; 201(1):61-71. 4) Lin PC, et al. Magn Reson Med 2012; 67(6):1815-1826. 5) Shamir L, et al. Source Code Biol Med 2008; 3:13. 6) Shamir L, et al. PLoS Comp Biol 2010; 6(11). 7) Shamir L, et al. Osteoarthritis Cartilage 2009; 17(10):1307-1312. 8) OAI Protocol; Appendix F 2006. 9) Pritzker KP, et al. Osteoarthritis Cartilage 2006; 14(1):13-29.