Mapping Cartilage Degradation through Support Vector Machine Probabilistic Classification

P-C. Lin[1], O. Irrechukwu[1], and R. G. Spencer[1]
[1]National Institute on Aging, National Institutes of Health, Baltimore, MD, United States

Introduction The development of non-invasive MRI techniques for detection of early osteoarthritis and evaluation of therapeutic response to potential interventions has been a subject of intense interest. A major limitation with many current approaches is the fact that individual MRI parameters exhibit a great deal of overlap between experimental groups. Therefore, these parameters have limited sensitivity and specificity to cartilage pathology [1-2], In order to overcome these limitations, we are undertaking multiparametric aproaches to cartilage assessment, with both cluster analysis and support vector machine (SVM) analysis showing considerable promise [2-3]. In the present work, we have extended this by undertaking an SVM-based fuzzy classification approach to characterization of bovine nasal cartilage (BNC) samples subjected to pathomimetic degradation using trypsin and chondroitinase (Ch) AC [4]. The MRI parameters investigated included T_1, T_2, magnetization transfer rate (k_m) and apparent diffusion coefficient (ADC), with SVM analysis performed using pairs, triplets, and quadruplets of these parameters. Probabilistic maps resulting from the fuzzy cluster procedure represent maps of degradation, with values ranging from zero, for pixels with 0% probability of representing intact tissue, to unity, for pixels with 100% probability of representing intact tissue. These maps were compared to individual MRI parameter maps, and in particular, to maps generated by T_1, the single best univariate classifier [2, 5].

Materials and Methods *Sample Preparation:* BNC strips (4.0 cm x 0.5 cm x 0.3 cm) harvested from the nasal septa of 6 month-old calves were inserted into a 10-mm NMR tube and immersed to a depth of 1 cm in a 5 mg/ml trypsin or a 0.5 unit/ml Ch AC solution for 24 hours before being imaged. Through this, the tops of each strip were not exposed to the degradative enzymes, while the lower portions were immersed in the enzyme solution. Diffusion ensured monotonic, graded degradation that gradually decreased from the maximum. *MRI:* Imaging was performed using a 9.4T/105-mm Bruker DMX. T_2 maps were acquired using a 64-echo CPMG pulse sequence (TE/TR = 12.8 ms/ 5 s). T_1 maps were acquired using a progressive saturation sequence with TE = 12.8 ms and TR varying from 100 ms to 15 s in 12 steps. MT data were performed using the same sequence (TE/TR = 12.8 ms/ 5 s) preceded by a 6 kHz off-resonance saturation pulse incremented from 0.1 to 4.6 s in 8 steps. ADC was measured using a spin-echo sequence with a pair of gradient pulses with δ = 5 ms and Δ =12.5 ms, and diffusion gradient strength between 0 and 738 mT/m in 9 steps. Other parameters included NEX = 2, BW = 50 kHz, FOV = 4.0 × 1.5 cm, matrix size = 256 × 128 and slice thickness = 0.5 mm. For each pixel in the image plane, signal intensities were fit to appropriate three-parameter monoexponential functions to obtain T_1, T_2, MT rate (k_m) and ADC *Probabilistic Maps for Degree of Degradation:* For each enzymatic degradation category, image pixels from the top portion (no degradation; probability = 1) and the lower portion (severe degradation; probability = 0) were manually selected to create a training set for fuzzy classification analysis (see the indicated regions in Fig. 1). After establishing a separating hyperplane in a transformed feature space through the SVM algorithm, each image pixel was given a probabilistic assignment to the enzymatically degraded region of feature space. The assignement probabilities were based upon the sigmoidal distance between a pixel's transformed coordinate values and the separating hyperplane. A total of 11 different MR parameter combinations, consisting of all combinations of the four parameters investigated, were used to generate the probability maps as described above. Analyses were performed using in-house designed scripts written in Matlab 7.4 and the e1071 package, based on the libsvm library in R language [6].

Results As expected, MR parameters varied monotonically along the strip in correspondence with the known variation of enzymatic degradation along the BNC strips. The nondegraded top portion of the BNC strip shown in Fig. 2a, corresponding to region A in Fig. 1a, exhibited a T_1 of 1175 ± 78 ms, while the highly trypsin-degraded lower portion, corresponding to region B, exhibited a T_1 of 1400 ± 127 ms (Fig. 2a). The contrast in image 2a is relatively flat, reflecting the limited dynamic range of the T_1 measurement of degradation. Fig. 2b shows the probabilistic map constructed as described above from the (T_1, k_m) parameter pair. As seen, the results correspond to the T_1 map in Fig. 2a, but exhibit a markedly increased dynamic range. Similar results are shown in Fig. 3a, for which the non-degraded, upper tissue region, corresponding to region C in Fig. 1b, exhibited a T_1 of 1100 ± 135 ms, while the highly-Ch AC-degraded region, corresponding to region D, exhibited a T_1 of 1200 ± 140 ms. A degradation map constructed from (T_1, k_m) is shown in Fig. 3b. Again, the results are consistent with those in Fig. 3a, including demonstration of heterogeneous degradation in the immersed, lower, portion, of the sample, but show a much-increased dynamic range.

Discussion. Previous studies have demonstrated the limited ability of uniparametric MR characterization of cartilage to discriminate between control and degraded tissue. These limitations of univariate analysis highlight the fact that MR parameter values are poor indices of cartilage degradation. We have found substantial improvement in classification through adoption of multivariate SVM analysis [2, 5]. For this reason, we derived multivariate SVM-based probabilistic maps, as appropriate for the graded nature of cartilage degradation, to correlate to cartilage degradation and to define the local degree of partial degradation from MR measurements. As seen in Figs. 2 and 3, the probabilistic maps generated within the (T_1, k_m) parameter space exhibit particularly favorable classification properties and are able to delineate regions of enzymatic degradation, non-degradation and partial degradation in cartilage tissue with substantially more dynamic range than the best univariate classifier, T_1. Similar results were obtained with the parameter sets (k_m, ADC) and (T_1, k_m, ADC) (data not shown), which correspond to parameter sets also exhibiting excellent discriminant capabilties in multivariate analysis [2-3], Furthermore, the probabilistic classification maps delineated highly degraded regions as corresponding to the regions of BNC physically immersed in the enzyme solutions. These results, along with our previous findings that these parameter combinations show markedly improved binary classification characteristics, indicate that analysis in multidimensional feature space may emerge as an important and approach to cartilage matrix characterization. In conclusion, probabilistic degradation maps derived from combinations of MR parameters via the SVM algorithm may provide a substantial improvement over conventional univariate MR maps for defining the degradation in cartilage tissue.

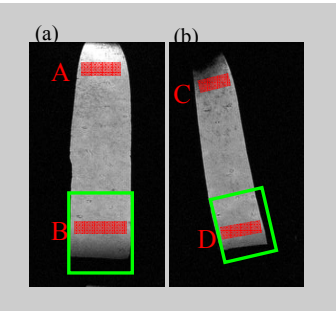

Fig. 1: T_2 images of (a) a BNC strip treated with trypsin; (b) a BNC strip treated with chondroitinase AC. Areas outlined by the green boxes are regions immersed in enzymatic solutions, while highlighted areas were selected as the training sets for SVM analysis.

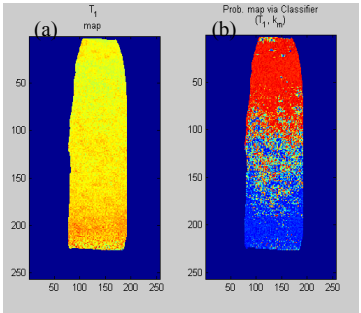

Fig. 2: A BNC strip imaged after immersion of the lower region in trypsin for 24 hrs. (a) T_1 map; colors in orange – long T_1; green – short T_1. (b) probabilistic map generated by the SVM algorithm in (T_1, k_m) space. Colors in (b): blue – degraded; red – nondegraded.

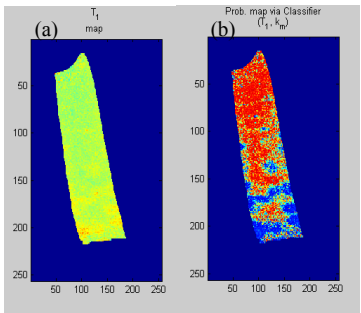

Fig. 3: A BNC strip imaged after immersion of the lower region in Ch AC for 48 hrs. (a) T_1 map; colors in orange – long T_1; green – short T_1. (b) probabilistic map generated by the SVM algorithm in (T_1, k_m) space. Colors in (b): blue – degraded; red – nondegraded.

References: 1. Laurent D, *et al.*, Magn. Reson. Imaging 19 (2001) 1279; **2.** Lin PC, *et al.*, J. Magn. Reson. 201 (2009) 61; **3.** Lin PC, *et al.*, ISMRM 2010; **4.** Hastie T, *et al.*, J Mach. Learn. Res. 5 (2004) 1391; **5.** Lin PC, *et al.,* Magn. Reson. Med. 62 (2009) 131; **6.** Dimitriadou E, *et al.*, Misc Functions of the Department of Statistics (e1071); 2009