# T1ρ Voxel Based Relaxometry for the Local Evaluation of the Knee Cartilage

Valentina Pedoia[1], Favian Su[1], Deepak Kumar[1], Richard Souza[1], Benjamin Ma[1], Xiaojuan Li[1], and Sharmila Majumdar[1]
[1]*UCSF, San Francisco, California, United States*

**INTRODUCTION:** Anterior cruciate ligament (ACL) rupture is a common and severe knee injury and it has been shown to be a risk factor for the development of early osteoarthritis (OA)[1]. $T_{1\rho}$ cartilage imaging provides information associated with cartilage matrix changes and enables the possibility of early stage cartilage degeneration detection[2]. The task of the MRI quantitative assessment of degenerative change is usually addressed through ROI-based approaches[3]. In this class of techniques compartments of the cartilage are segmented; and each ROI is described by the average of the $T_{1\rho}$ values. Segmentation is often performed manually or semi-automatically, introducing user variation in addition to an *extensive* use of human resource and time. Previous studies showed that spatially assessing MR images of the knee cartilage relaxation times using laminar and texture analyses could lead to better and probably earlier identification of cartilage matrix abnormalities[4]. Voxel Based Relaxometry (VBR) is a technique that could potentially be used for investigating local cartilage microstructural composition differences between 2 populations in a fully automatic way. A previous study, looking at the T2 relaxation in the brain in epileptic patients, showed that VBR is more sensitive to the common ROI-based approaches providing additional information for the clinical interpretation of the results[5]. In this study we demonstrate the feasibility of the use of this technique in the comparison of the spatial distribution of $T_{1\rho}$ after ACL reconstruction and in subjects with Osteoarthritis.

**METHODS:** *Subjects:* Two different datasets are considered in the study. *ACL dataset:* Injured knee was scanned using a 3 Tesla MRI scanner (GE Healthcare, Milwaukee, WI, USA) with an 8-channel phased array knee coil (Invivo, Orlando, FL, USA) for 20 patients with ACL injuries prior to surgical reconstruction and 1 year after reconstruction (age = 31.2 ± 8.7 years, BMI = 24.2 ± 3.2 kg/m$^2$). 15 controls with no history of knee injuries underwent MR imaging at baseline and 12 months later (age = 31.7 ± 4.6 years, BMI = 23.7 ± 4.8 kg/m$^2$). *OA dataset* includes 20 Osteoarthritic patients (age = 55.9 ± 9.7 years, BMI = 25.4 ± 3.1 kg/m$^2$ Kellgren–Lawrence (KL) scoring: 1.95) and 15 matched age controls (age = 47.7 ± 10.1 years, BMI = 26.6 ± 2.87 kg/m$^2$ Kellgren–Lawrence (KL) scoring<=1).
*Imaging Protocol:* The *ACL dataset* MRI protocol included quantitative $T_{1\rho}$: TSL = 0/10/40/80 ms, spin-lock frequency = 500 Hz slice thickness 4 mm, field of view of 14 cm, 256 × 128 matrix size. For the *OA dataset,* the only difference was that $T_{1\rho}$ sequence included 8 TSL: 0/2/4/8/12/ 20/40/80 ms.
*Image Processing:* All the images in both datasets were morphed to the space of a reference chosen through an iterative process aimed to minimize the global registration error. Tibial and Femoral cartilage was segmented semi automatically on this reference. Four compartments were considered: medial femoral condyle (MFC), medial tibia (MT), lateral femoral condyle (LFC) and lateral tibia (LT). Intensity based multi-resolution pyramidal approach was applied to accomplish the registration task basing our strategy on the elastix ITK library[6,7]. B-spline transformation was used for the morphing and Advance Matteus Mutual Information image similarity metric as a figure of merit of the transformation was iteratively optimized[7]. This process was performed on the first TSL and the transformation obtained was applied on all the later TSLs images. Morphed $T_{1\rho}$ map was computed through a 2 parameter exponential fitting. The reference ROIs were applied on the morphed images, setting a fully automatic atlas-based segmentation. Mean values in each ROI were computed and compared with those obtained through a classical semi-automatic ROI-based method. Coefficient of Variation (CV) was considered as the evaluation metric of the algorithm performance. Furthermore, the two groups *Controls/Cases* of each dataset were considered to be the Atlas of the $T_{1\rho}$ spatial distribution and used to analyze group differences at the voxel level. Unpaired t-tests provided the p-values for each voxel which were then comprised a volumetric Statistical Parametric Map (SPM); $p < 0.05$ was considered as level of significance.

**Table1**:Fully Automatic ROI-based analysis. In the table the average Coefficient of Variations (CV) between Automatic and semi Automatic segmentation for each compartments and datasets are reported

| Datasets | LFC: mean (sd) | CV | MFC: mean (sd) | CV | LT: mean (sd) | CV | MT: mean (sd) | CV |
|---|---|---|---|---|---|---|---|---|
| OA | 43.3 (6.1) | 6.30% | 42.3 (3.8) | 6.30% | 39.4 (5.3) | 4.20% | 41.2 (6.8) | 6.60% |
| Control | 39.4 (4.1) | 4.80% | 38.5 (4.1) | 4.80% | 36.4 (4.1) | 4.30% | 36.9 (3.0) | 4.60% |
| P-value | * 0.002 | | * 0.001 | | Ns | | * 0.033 | |
| ACL baseline | 40.5 (5.8) | 6.20% | 38.92 (4.46) | 5.90% | 38.36(4.45) | 7.24% | 37.42(4.41) | 6.90% |
| Control | 41.2 (4.3) | 3.20% | 40.3 (3.5) | 2.90% | 35.5 (4.8) | 4.69% | 34.9 (3.8) | 5.20% |
| p- value | NS | | NS | | NS | | NS | |
| ACL 1 Year | 40.6 (3.8) | 5.60% | 40.3 (2.8) | 6.50% | 36.6 (4.3) | 6.90% | 37.4 (4.4) | 8.70% |
| Control | 39.83 (4.3) | 4.80% | 39.5 3.5() | 3.20% | 35.47 (4.8) | 3,9% | 34.6 (3.8) | 6.40% |
| p- value | NS | | NS | | NS | | NS | |

**RESULTS:** Table 1 shows the mean and standard deviation (sd) of $T_{1\rho}$ in the four cartilage compartments computed with computed with fully automatic atlas-based segmentation in both the datasets and the CV obtained comparing automatic and semiautomatic with manual correction approaches. The Average CV is equal to 5.4 %. Better performances were observed in the control group CV 4.5% then both Osteoarthritis and ACL groups CV 5.9% and 6.7%. Figure 1 shows the SPM obtained when the OA patients are compared with the matched controls. Significant local $T_{1\rho}$ elevation was observed in both media and lateral central tibia. Despite the global MFC and LFC $T_{1\rho}$ elevation was observed to be significant by the ROI-based method; subtle local elevations were observed in these compartments. Figure 2 shows the comparison between *OA* and *ACL datasets.* Focal elevation in the posterior LT was observed in the in ACL group at baseline; at 1 year $T_{1\rho}$ values in this area are still higher in ACL vs controls but the differences are not significant, suggesting a partial recover. However, posterior LFC is significant higher at 1 both baseline and 1 year. Different patterns were observed in the *OA dataset* in the lateral side: most of the local elevation is in central LT. Subtle elevations were found in the medial side in the ACL group at baseline. However, strongly significant elevation in the $T_{1\rho}$ in the superficial MFC was seen 1 year after reconstruction, and a similar pattern was observed for the *OA dataset.*

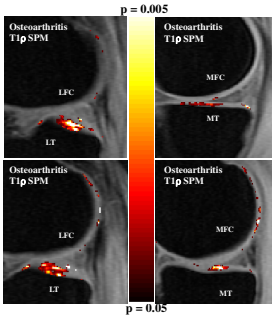


**Figure 1:** Statistical Parametric Map obtained comparing 20 Osteoarthritis patient and 15 Controls

**DISCUSSION and CONCLUSION:** VBR may potentially have the ability to compare different groups analyzing cartilage degeneration at the local level showing features hidden by the averaging of the ROI-based method, similar to the elevation of the posterior lateral tibia after ACL injury already observed through the use of sub compartments and laminar analysis[2]. On the other hand, diffuse elevations or focal lesions which show no specific common pattern amongst patients may not be detected as significant by the VBR but better shown by the ROI-based method as observed for the MFC and LFC in the *OA dataset* suggesting that a combined used of the two methods can provide the best analysis. The algorithm proposed in this study for the knee cartilage VBR showed the capability to detect specific local patterns of $T_{1\rho}$ increase that maybe potentially useful for a more accurate analysis and disease phenotyping. The morphing of the images in a unique space allows for a fully-automatic cartilage segmentation providing a why for a combined use of ROI-based and Voxel-based analysis. Segmentation performances could be improved by the use of multi-atlas and multispectral approaches.

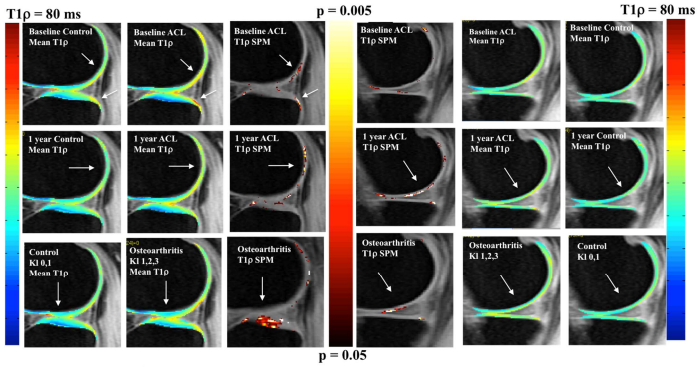


**Figure 2:** Comparison between the SPMs obtained comparing 20 ACL patient and 15 matched controls before the reconstruction (first row), 12 month after the reconstruction (second row) and the SPMs obtained comparing 20 osteoarthritis patient patient and 15 matched controls (third row)

**REFERENCES:** [1] Louboutin H at el. The Knee; 2009 16(4), [2] Li at el. Radiology 2011:258(2), [3] Li at el. Osteoarthritis and Cartilage, 2007 15(7); [4] Carballido-Gamio J at el. Med Phys. 2009;36(9) [5] Pell GS at el Neuroimage 21(2) [6] S. Klein IEEE Trans on Med. Ima., 29(1) 2010 [7] D.P. Shamonin at el. , Frontiers in Neuroinformatics, 7(50) 2014.