DTI and DCE perfusion MRI Metrics Discriminate Chronic Infective from Chronic Inflammatory Knee Arthritis

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Introduction:

Chronic inflammation in knee arthritis is characterized by cellular infiltration and increased vascularity. The accumulated inflammatory cells secrete lots of proinflammatory cytokines and various enzymes like matrix metalloproteinases (MMPs) leading to joint effusion, cartilage damage and bone erosions[1]. Conventional MRI has a very limited role in discriminating infective from non-infective chronic inflammatory arthritis. Synovial histology and culture are the only means to differentiate between these two entities. It is not always possible to perform biopsy in every patient with synovitis and a non invasive biomarker is needed to differentiate chronic inflammation from chronic infection. We hypothesize that diffusion tensor imaging (DTI) derived metrics (FA and MD) and dynamic contrast enhanced (DCE) perfusion parameters like blood flow (BF) and volume (BV) correlate with the degree of inflammation in synovium and vary with the intensity of the inflammation. Thus increased inflammation in infection should lead to greater variation in DTI and perfusion parameters that should be able to discriminate chronic inflammatory from chronic infective synovitis.

Materials and methods

MR Imaging: This study was performed on 73 patients who had inflammation in knee joint with age ranging from 18-65 years Conventional (T2, T1 pre and post contrast with fat saturation) as well as DT and DCE-MRI were performed on a 3T MR scanner (Signa Hdxt, General electric, Milwaukee, USA), using a 8-channel knee coil after the approval from the institutional ethics committee. DTI data were acquired using a single-shot echo-planar dual spin-echo sequence with ramp sampling with 10 uniformly distributed directions. The acquisition parameters were: TR=10sec/TE=100ms/slice no.=28/thickness=3mm/interslice gap=0/FOV=240mm/image matrix=256×256 (following zero-filling)/NEX=2/diffusion weighting b-factor=1000 s mm^{-2}. DCE-MRI was performed using a three dimensional spoiled gradient recalled echo (3D-SPGR) sequence [TR/TE/flip angle/ number of excitation(NEX)/slice thickness/ field of view (FOV)/matrix size=5.1ms/2.1ms/10º/0.7/3mm/240×240mm/256×256, number of phases=40]. At the sixth acquisition, Gd-DTPA-BMA (Omniscan, GE Healthcare, USA) was administered intravenously through a power injector at 5ml/sec, followed by 30ml saline flush. A series of 1120 images in 40 time points for 28 slices were acquired (Temporal resolution: 7.85sec). Prior to 3D SPGR, T1-weighted, FSE (TR/TE/NEX/slice-thickness/FOV/matrix size=360 ms/9.5 ms/ 1/3 mm/240×240 mm/256×256 mm), and fast double spin echo proton density (PD) weighted and T2-weighted (TR/TE1/TE2/NEX/slice-thickness/FOV/matrix size=3500 ms/25 ms/85 ms/ 1/3/240×240 mm/256×256 mm) imaging were performed for the same slice position to quantify voxel wise the pre-contrast tissue longitudinal relaxation time T_{10}. DTI and DCE data were processed by using JAVA based in-house developed soft-ware[2,3]. The DTI and DCE metrics were quantified from the segmented synovium based on post contrast enhancement.

***Statistical analysis*:** Descriptive statistics, Box-plot with Tukey's hinges were produced for all DTI and perfusion parameters. The mean difference between the two groups was compared using Student's –t-test for independent samples. To classify subjects into tubercular and non-tubercular inflammation, two-group discriminant function analysis (DFA) with stepwise inclusion of variables was performed.

Result

Out of 73 patients (age 18-75yrs, 51M), 15 were detected to have tuberculosis (Mycobacterium tuberculosis positive on culture of synovial fluid 2, synovial membrane 1, acid fast bacilli staining with epithelioid cell granulomas 4), while rest of 58 cases were found to be non-infective inflammatory arthritis. On Student's t-test, except k^{trans}, all the parameters were significantly different for both the groups (Table1). It was found that ADC and k^{trans} values for both the groups were completely overlapping while BV and FA were almost distinct (Figure). Among the four variables (FA, ADC, BV and k^{trans}) considered for the discriminant analysis, DCE derived BV and DTI derived FA values were found to be significant discriminators between tubercular and non-tubercular inflammation with canonical correlation of 0.851. The linear discriminant score to classify cases for each case is obtained by using the expression: D = 34.27FA+0.203BV-8.831. This discriminant function was tested for misclassification and fitness of the model to the actual data. The function classified 93.3% of tubercular arthritis correctly while 100% of non-tubercular arthritis correctly. The overall model classified 98.6% cases correctly (Table2).

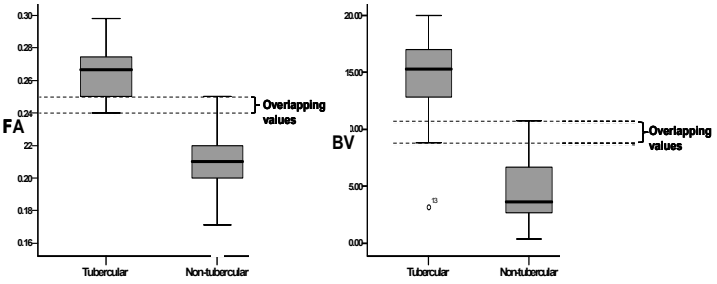

Fig 1*: Showing the average and range of FA and BV values in tubercular and non-tubercular arthritis. The overlapping range is shown as dotted lines where FA and BV values may not be able to discriminate tubercular and non-tubercular arthritis.*

Table.1*: Descriptive statistics for DTI and perfusion parameters in tubercular and non-tubercular synovitis*

DTI and Perfusion Parameters	Mean±SD		Statistical significance
	Tubercular Synovitis	Non-tubercular Synovitis	
FA	0.26±0.02	0.20±0.02	**<0.001**
ADC($\times 10^{-3}$ mm^2sec^{-1})	1.23±0.39	1.7±0.5	**<0.001**
BV (ml/100gm)	14.35±4.21	4.57±2.77	**<0.001**
BF(ml/100gm/min)	155.7±29.5	94.9±34.5	**<0.001**
$\mathbf{k^{trans}}$ (Min^{-1})	0.54±0.35	0.35±0.27	**0.06**

Pathology		Predicted Group Membership		Total cases
		Tubercular	Non-tubercular	
Original Count	Tubercular	14 (93.3%)	1 (6.66%)	15 (20.55%)
	Non-tubercular	0 (0%)	58 (100%)	58 (79.45%)
Total		14 (19.18%)	59 (80.82%)	73 (100%)

Table.2*: Classification of cases into tubercular and non-tubercular arthritis*

Discussion

In this study by combining DCE-MRI with DTI metrics, we were able to correctly classify a total of 98.6% of original grouped cases into tubercular and non-tubercular knee arthritis with very narrow range of overlapping values (Fig1). Inflammation is presented with pathological features such as activation of synovium with discharge of pro-inflammatory cytokines into the synovial fluid as well as increased vascularity due to neoangiogenesis. Aggregation of the inflammatory cells due to adhesion molecules has been shown to increase FA in brain abscess cavity[4], whereas high relative cerebral blood volume values have been shown to be associated with infective lesions like brain tuberculomas. The increased FA and BV in tubercular arthritis may have resulted from increased infiltration of various inflammatory cells, facilitated by different cytokines and chemokines. We conclude that the DTI and DCE-MRI are sensitive enough to differentiate chronic infective from chronic inflammatory arthritis. Hence, these imaging tools can be used as a non-invasive tool eliminating the need of biopsy to make a confirmatory diagnosis and may also be used as marker for treatment response in these patients.

References: 1) Stamp LK et. al.Immunol Cell Biol 2004; 82:1-9. 2) Purwar A, et al. Proceedings of ESMRMB, 2006, 21-23, Abstract #644. 3) Singh et al. *J Magn Reson Imaging* 2007;26 :871-80. 4) Gupta RK et al. AJNR 2008; 29:326-32.