

Effects of AIF selection and pharmacokinetic model selection on Discrimination of Chronic Infective from Chronic Inflammatory Knee Arthritis using DCE-MRI

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Introduction: Increased vascularity and cellular infiltration are typical characteristics of chronic inflammation in knee arthritis. Conventional MRI has a very limited role in discriminating infective from non-infective chronic inflammatory arthritis. DCE-MRI is an established method to measure tissue vascularity in tumors. Recent study has shown that DCE-MRI can be used to monitor inflammatory treatment response [2] in knee. Accuracy of DCE-MRI based quantitative analysis depends upon various factors such as selection of arterial input function (AIF), model used for pharmacokinetic analysis etc. There are many techniques are existed for DCE-MRI analysis. Objective of our study is to find out the most suitable technique for knee perfusion analysis so that we can discriminate chronic Infective from Chronic Inflammatory knee arthritis with a higher accuracy.

Materials and methods

MR Imaging: This study was performed on 46 patients who had inflammation in knee joint with age ranging from 18-65 years. All patients underwent DCE-MRI on a 3 Tesla scanner (Signa Hdxt, General electric, Milwaukee, USA), using a 8-channel knee coil after the approval from the institutional ethics committee. 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/10°/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 T₁₀. DTI and DCE data were processed by using JAVA based in-house developed soft-ware.

Post Processing: Voxel wise precontrast tissue parameter T₁₀ was calculated and used to converted the signal intensity time curve (S(t)) to the concentration time curve(C(t))[3]. A global AIF (C_g(t)) was estimated automatically from the voxels having properties early bolus arrival time, highest peak value, early time to peak etc[4]. Local AIF (C_l(t)) was also measured by : $C_l(t) = (1/k) \sum_{i=0}^n R_i C_g(t - i \cdot h) \cdot k = \sum_{i=0}^n R_i \dots (1)$, where h is the temporal resolution, and n is the duration of the first pass.

Both two and three compartmental model are used for pharmacokinetic analysis. Two compartmental model [6]: $C(t) = v_p C_p(t) + k^{tr} \int_0^t C_p(t) \exp(-k_{ep}(t-u)) du$.

Three compartmental model [5]: $C(t) = v_p C_p(t) + k^{tr} \int_0^t C_p(t) \exp(-k_{ep}(t-u)) du + \lambda^{tr} \int_0^t C_p(t)$. Where v_e is the volume of extracellular extravascular space (EES), v_p is

plasma space per unit volume of tissue, k^{tr} is the transfer rate constant (between plasma space and EES), $k_{ep} = k^{tr}/v_e$ and $C_p(t)$ is the AIF. The above two models were fitted to $C(t)$ in order to obtain the following parameters [k^{trans} , k_{ep} , v_p], [k^{trans} , k_{ep} , v_p , λ^{tr}] respectively. Cerebral blood volume (CBV) was calculated by finding area under calculated plasma concentration time curve of the tissue and normalized by that of AIF. Cerebral blood flow (CBF) was calculated by deconvolving AIF with $C(t)$. All the perfusion parameters estimated using both local AIF and global AIF. Discriminate function analysis were performed to classify subjects into tubercular and non-tubercular inflammation.

Results: Out of 46 patients ,32 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 14 cases were found to be non-infective inflammatory arthritis. Among five perfusion parameters (CBF, CBV, k_{ep} , v_p , v_e) considered for discriminant function analysis, except k_{ep} all are found to be significant discriminators between tubercular and non-tubercular inflammation. The overall model classified cases are shown in Table-1. A total of 93.5% cases were correctly classified using global AIF and two compartment model, 95.7% cases were correctly classified while using global AIF and three compartment model. Use of local AIF does not make any change in classification. A p-value ≤ 0.05 was considered as significant.

% of correctly classified cases	Two compartment	Three compartment
Global AIF	93.5%	95.7%
Local AIF	93.5%	95.7%

Table1: Showing % of correctly classified cases and discriminate functions.

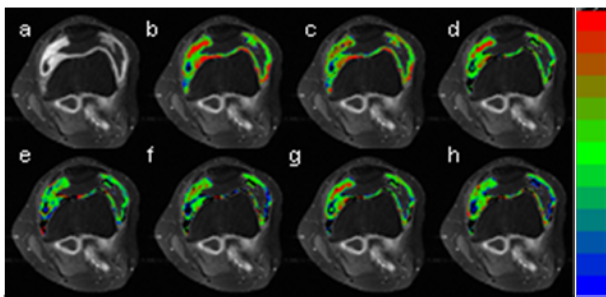


Figure2: Showing a) T₁ post contrast, b) CBF, c) CBV, d) k^{tr} , e) k_{ep} , f) v_p , g) v_e , h) λ^{tr} maps of a tuberculoma patient. All the color coded maps are overlaid on T1 postcontrast image.

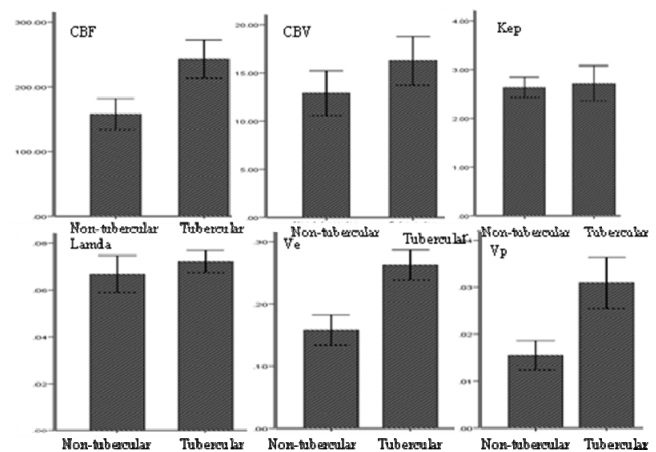


Figure1: Bar diagram showing values of perfusion metrics in tuberculoma and non-tuberculoma patients using global AIF with three compartmental model. Error bar represents mean \pm standard deviation.

Conclusion: Our result suggest that Global AIF and Local AIF does not effects the discrimination of tuberculoma from non-tuberculoma however using three compartment model instead of two compartment model significantly improves the discrimination.

References: [1] Stamp et. al. *Immunol Cell Biol* 2004; 82:1-9. [2] Boesen et al. *Arthritis*, doi:10.1155/2011/578252. [3] Singh et al. *JMRI* 2009;29:166-76. [4] Singh et al. *J Magn Reson Imaging* 2007;26:871-80. [5] Rathore et al. *ISMRM* 2011(Abtract no:539). [6] Ostergaard et al. *MRM*.1996;36:715-725. [7] Tofts et al. *MRM*. 1991;17:357-67.