Pharmacokinetic analysis of DCE-MRI data from lumbar spine reveals pathologic changes in intervertebral disc endplates and subchondral bone

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Target Audience: This presentation is intended for clinicians and researchers who study spinal disc degeneration.

Introduction: The majority of chronic back pain is associated with degeneration of the intervertebral discs (IVD). Although it has been studied extensively, there is no consensus on the mechanisms of pathological degeneration or how it should be distinguished from the normal aging processes. One of the causes of degeneration is believed to be poor nutrient transport to the disc through the endplates (EP). EP is a thin layer of cartilage positioned between the vertebral body (VB) and nucleus pulposus (NP)[1]. It is known that calcified EP regions reduce transport of gas and solutes into the disc[2], which may initiate degeneration. In this study, Dynamic Contrast Enhanced MRI (DCE-MRI) was used to investigate the relation between IVD degeneration and aberrations in nutrient transport to the discs. A compartmental model with standard kinetic parameters was implemented to study perfusion in EPs and adjacent subchondral bone (SB) of the VBs. The ultimate goal is to understand how changes in fluid transport through the EPs contribute to the disc degeneration process.

Methods: This study was approved by the IRB and written consents were obtained from 26 adult participants (age: 21–57y; median: 37y) who took part in this study. DCE-MRI data were acquired in a 3T GE Discovery MR750 (Waukesha,WI USA) using a dual-echo FSPGR with Dixon's fat/water separation method. The parameters were: T_R=4.0ms, T_{E1}=1.1ms, T_{E2}=2.2ms, flip-angle=12°, FOV=31cm, acquisition matrix=310×300 (interpolated to 0.61mm in-plane resolution), 23 frames with 28s frame rate, 16-sagittal slices, 3mm thick. The contrast (Gd-DTPA 0.1 mmol/kg) was administered manually as a bolus via an antecubital vein at the end of the 2nd dynamic frame. A conventional T_2 weighted (T_2W) MRI was also acquired for grading of disc degeneration using Pfirrmann classification[3]. Two radiologists and a trained medical student graded each disc and the median value was used for analysis. The data was processed as shown in the pipeline illustrated in Fig. 1. Before the analysis, DCE-MRI image series were registered using 12-parameter affine transformation. Then, a trained operator manually drew regions of interest (ROI) on pre-contrast images of the DCE-MRI to segment the 10 EPs in the lumbar area and SBs adjacent to each endplate (Fig.2). Then, volume-averaged signal enhancement time course was calculated in each ROI. Assuming inter-subject variability of tissues' T_1 is minimal[1,4]; concentration of Gd-DPTA of each region was calculated[4]. Using a group-averaged arterial input function model, standardized DCE-MRI parameters K^{Trans} and k_{ep} were estimated[5]. Afterward, statistical analysis was performed using IBM SPSS v21 (Armonk, NY USA) to analyze the relation between disc degeneration and standardized DCE-MRI parameters, age and BMI. The statistical significance (alpha) level of 0.05 was used. Generalized Estimating Equations (GEE) procedure was employed to find ordinal logistic response between the measured parameters and disc degeneration level. Within-subject measurements are taken into account with the GEE procedure.

Results: A representative ROI selection and average enhancement curves from each ROI are shown in Fig. 2. GEE analysis revealed that age was a significant factor ($p<0.001$) in disc degeneration, which is in accord with earlier studies. BMI had some negative effect on disc degeneration but was not significant ($p=0.056$). After age effects were accounted for, K^{Trans} of caudal EPs and adjacent SB had positive associations with disc degeneration grade ($p=0.004$ and $p=0.003$, respectively). k_{ep} of cranial EP ($p=0.007$), caudal EP ($p<0.001$), and SB adjacent to caudal EP ($p<0.002$) had negative relationships with disc degeneration grade.

Discussion and Conclusion: Earlier ex vivo studies reported that dense regions of SB undergo structural changes as the disc degenerates[6]. Dramatic changes in porosity, pore diameter and trabecular thickness has been demonstrated in those studies. Increase in K^{Trans} could be an indication of such changes, since it is a measure of permeability, surface area and perfusion in tissues. Therefore, K^{Trans} could be a reliable measure of pathologic changes in EPs and adjacent SBs. Decrease in k_{ep} might also be expected. In resting position in the MRI, the osmotic swelling pressure draws fluids in, resulting in fast uptake of solutes, including contrast agent.[7] In this state, there is no noticeable outflow, hence only the Gd-DPTA that did not diffuse into the disc will slowly return to plasma. This would result in small k_{ep} values. As reported earlier,[6] increased degeneration leads to faster inflow to the discs. Thus, less Gd-DPTA will remain in the interstitial space of the SB, resulting in even lower k_{ep}. This might explain reduced k_{ep} with increasing degeneration.

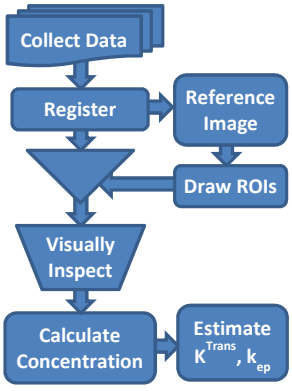

Fig. 1. Flow diagram of data processing pipeline

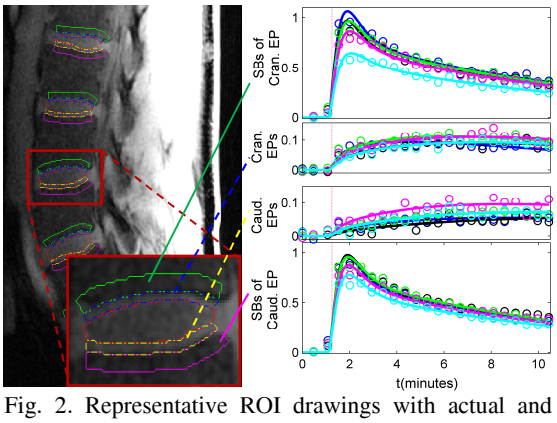

Fig. 2. Representative ROI drawings with actual and estimated enhancement curves in these ROI's.

References:

1. Moon SM, et al. *Eur. Spine J.* 2013; 22:1820–1828.
2. Jackson AR, et al. *Comput. Methods Biomech. Biomed. Engin.* 2011; 14:195–204.
3. Pfirrmann, CW, et al. *Spine* 2001; 26:1873–1878.
4. Rodriguez AG, et al. *J. Orthop. Res.* 2012; 30:280–287.
5. Tofts PS, et al. *J. Magn. Reson. Imaging* 1999; 10: 223–232.
6. Rajasekaran S, et al. *Spine* 2004; 29, 2654–2667.
7. Ayotte DC, et al. *J. Orthop. Res.* 2001; 19: 1073–1077