Single Section versus Volumetric analysis of dGEMRIC scans in a Longitudinal Multicenter MultivendorTrial : The A9001140 Study

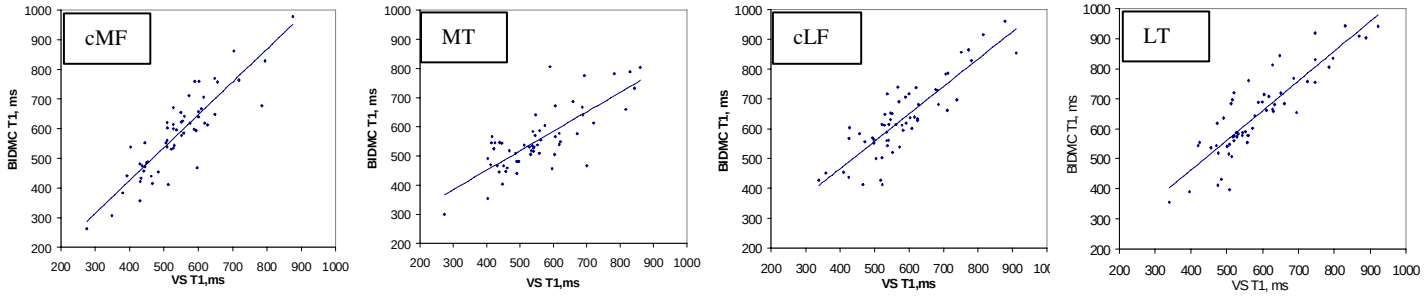
N. Krishnan[1], B. Wyman[2], R. Buck[3], M-P. Hellio[3], S. Totterman[4], J. Tamez[4], and D. Burstein[1]

[1]Radiology, Beth Israel Deaconess Medical Center, Boston, MA, United States, [2]Pfizer Global Research and Development, Groton, CT, United States, [3]Pfizer Global Research and Development, Ann Arbor, MI, United States, [4]VirtualScopics, Rochester, NY, United States

INTRODUCTION: delayed Gadolinium Enhanced MRI of Cartilage (dGEMRIC) has previously been applied *in vivo* under a number of conditions, and has demonstrated changes with physiologic and pathologic conditions or interventions [1-3]. With one exception [4] these dGEMRIC application studies were performed at 1.5T in a single center. The purpose of the current study was to analyze data from a longitudinal multicenter, multivendor trial at 3T. Within this analysis were three main goals: (1) To determine if analysis of a single section from each of the medial and lateral condyles would provide data comparable to analysis of the entire cartilage volume, (2) To analyze the cross-sectional characteristics of the dGEMRIC data, and (3) To demonstrate changes over a 6 month period in this cohort.

METHODS: A subset (n = 53, female) of the A9001140 observational MRI study data was selected for the dGEMRIC analysis. The control group (n=31), consisted of subjects with no radiographic OA (KLG 0), and an average BMI of 26±6.3. The OA group consisted of patients with radiographic OA, including KLG 2 (n=10) and KLG 3 (n=12) patients with an average BMI of 36±4.7. The 3D dGEMRIC imaging was done at 7 clinical sites with Siemens and GE scanners with standard dGEMRIC protocol. Subjects were injected with a double bolus of Gd-DTPA2- (Magnevist) and asked to walk for 10 minutes. After 59-110 minutes post injection thirty-two 3.0 mm sagittal slices were acquired using an inversion recovery spoiled gradient recalled echo (IR-SPGR) with 5 inversion times (TI=2100, 800, 400, 200 and 130 ms), TR=6.5ms (GE) or nominal (Siemens), TE = 2.7 ms, flip angle=15 degrees, field of view = 16 cm, matrix = 256x256, bandwidth=62.5 kHz. For single section analysis, T1 (Gd) maps were created using custom coded software (MRIMapper, copyright 2006 BIDMC) that employs automatic image registration of sequential TI delay images and a pixel-by-pixel 3-parameter fit. Images were interpolated to a 512 x 512 matrix before the fitting routine algorithm was applied. Two ROIs were evaluated per medial / lateral compartment (cMF/cLF), and (MT/LT). For the 3D analysis, cartilage masks for the medial and lateral weight-bearing femur (cMF, cLF) and medial and lateral tibia (MT, LT) were generated using proprietary software (VirtualScopics) from the IR-SPGR series. The 5 dGEMRIC T1 weighted image sets were coregistered using a targeted articulated algorithm (VirtualScopics). T1 values were calculated for each cartilage voxel using Levenberg-Marquardt fitting. Summary statistics for each cartilage region were computed for the central weight-bearing regions. Voxels outside the range (200ms <T1<1300ms) and those with a fitting error 2.5 times larger than signal noise were excluded. Statistical comparison between different KLG and between the two analysis techniques was done using a paired comparison t test.

RESULTS: (1) A comparison between the values obtained from the single section and 3D analyses are shown in Figure 1.Good correlations were found in all regions. (2) The baseline (BL) data are shown in Table 1. As in prior studies, the KLG0 population had significantly higher dGEMRIC Indices than KL3, and in some cases KL2. The statistics were similar whether single section or 3D analyses were performed. (3) A slight increase in the dGEMRIC Index was seen at 6 months compared to baseline in the KLG0 group, and for a single compartment in the KLG2 group. All compartments showed trends towards higher values at 6 months.



Below left: Single section analysis. Right: 3D analysis

	KLG 0		KLG 2		KLG 3	
	BL	**Δ 6M**	**BL**	**Δ 6M**	**BL**	**Δ 6M**
cMF	616	28 (±92)	592	-2 (±56)	459	41 (±78)
MT	584	64 (±113)**	509	82 (±90)*	497	29 (±103)
cLF	660	31 (±112)	615	5 (±48)	557	62 (±98)
LT	684	59 (±91)**	619	27 (±83)	576	-9 (±94)

	KLG 0		KLG 2		KLG 3	
	BL	**Δ 6M**	**BL**	**Δ 6M**	**BL**	**Δ 6M**
cMF	571	37 (±83)*	532	39(±35)**	454	21 (±87)
MT	582	59(±106)**	529	31 (±107)	466	53 ±109)
cLF	615	33 (±83)*	541	15 (±66)	514	21 (±98)
LT	620	58 (±79)**	542	30 (±66)	528	22 (±69)

DISCUSSION:

(1) The single section analysis and full 3D analysis compared favorably with each other. Although 3D acquisitions are advantageous due to the faster acquisition protocols and ease of positioning, analysis of the full data set may not be necessary for these types of epidemiological studies. Analysis of lesion changes over time, assessments of an individual such as in presurgical planning, and other applications might be better served with volumetric analysis.

(2) The cross sectional data from this multi-site, multi-vendor trial are comparable to prior analyses of single site, 1.5T data.

(3) The increase of the dGEMRIC Index over time in KLG0 subjects warrants further study. This increase was present in all seven of the imaging sites, minimizing the possibility of experimental error being the source. Possibilities for artifact considered but ruled out were; self-reported exercise levels, exercise due to seasonal weather changes, and pain levels effecting ability to exercise. The increase seen over the six months could reflect short term biological variation in dGEMRIC measures. This has not yet been characterized and may have impacted the data, although one would expect a random change from that source. Another source may have been some subtle change of behavior resulting from participation in a clinical trial. The measured increase (which was more apparent in the control cohort) may have masked any potential longitudinal decrease due to disease progression in the OA cohort. Analysis for the remainder of the subjects and timepoints is still pending and should add to our knowledge of this technique and provide information for planning further natural history and interventional trials.

REFERENCES:

1. Kim YJ et al. Journal of Bone & Joint Surgery 2003, 85(10):1987-92.
2. Williams A et al. Arthritis and Rheumatism, 2005, 52(11): 3528–3535.
3. Nojiri et al. Knee Surg Sports Traumatol Arthosc 2006, 14(8):718-23.
4. Young AA et al. Journal of Bone & Joint Surgery 2005, 87(12): 2763-7.