Evaluation of the Ability of Delayed Gadolinium-Enhanced MRI (dGEMRIC) to Detect Change in Cartilage Characteristics among Individuals with Knee Osteoarthritis (OA) Receiving a Collagen Hydrolysate Formulation

N. Krishnan[1], T. McAlindon[2], M. Nuite[3], K. Carr[3], D. Burstein[1,4], L. Price[3], and K. Flechsenhar[5]

[1]Department of Radiology, Beth Israel Deaconess Medical Center, Boston, MA, United States, [2]Division of Rheumatology, Tufts Medical Center, Boston, MA, United States, [3]Tufts Medical Center, Boston, MA, United States, [4]Health Sciences and Technology, Harvard Medical School, Boston, MA, United States, [5]Research & Development, Gelita AG, Eberbach, Germany

INTRODUCTION: The aim of this pilot study was to determine if delayed Gadolinium Enhanced MRI of Cartilage (dGEMRIC) or T2-mapping could detect changes in knee hyaline cartilage among participants treated with collagen hydrolysate (Fortigel®) versus those treated with placebo. Proprietary collagen hydrolysate Fortigel® is a nutritional product produced by GELITA.

MATERIALS AND METHOD: A randomized, placebo-controlled, double-blind, 24-week clinical trial was conducted among 30 participants with symptomatic knee OA. Treatment assignment was according to a blocked randomization scheme, stratified by body mass index (BMI). Half of them received 10 grams collagen hydrolysate orally once per day. Fortigel® and placebo formulations were indistinguishable in appearance and flavor. Participants received clinical assessment every 8 weeks and dGEMRIC and T2 MRI scans were acquired at baseline, 24 and 48 weeks. The dGEMRIC imaging was performed using quad knee coil at 1.5T. Patients were injected with a double bolus of Gd-DTPA2- (Magnevist) and asked to walk for 10 minutes. After 90 minutes post injection thirty-two 3.0 mm sagittal slices were acquired using 3D IR-SPGR sequence with 5 inversion times (TI=1650,650,350,150,28ms), TR/TE=7.7/3.4ms, flip angle=20 degrees, FOV = 14cm, matrix = 512x512, bandwidth=62.5 kHz. The dGEMRIC index was calculated in 6 specified regions of interest in cartilage. The primary outcome of the trial was change in dGEMRIC index in the study knee hyaline cartilage. Secondary endpoints included change in cartilage mean T2 relaxation time, WOMAC scores, timed walk and chair stand tests. Tested for differences between groups using a Wilcoxon Rank Sum (non-parametric) test since there was evidence of a non-normality of distribution of study outcomes.

RESULTS: The assignment groups were balanced in most respects but the placebo group had slightly more functional limitation. During the first 24 weeks, the dGEMRIC indices in the medial and lateral tibial regions fell in the placebo group but increased in the treatment group (table 1). Significant trends were not seen for other regions of interest. The clinical indices broadly improved in both groups without any major differences between them (e.g. change in WOMAC pain at 24 weeks: -1.4 versus -1.5, p=ns). Analysis of the 48-week outcomes showed no further change.

Table 1: Change in dGEMRIC Index from baseline (median) at 24 weeks.

	Placebo group		CH group	
	24 weeks	48 weeks	24 weeks	48 weeks
Medial Tibia	**-38.0**	14.0	**28.0***	47.0
Lateral Tibia	**-30.5**	-1.0	**40.0***	28.0
Central Medial Femur	-33.5	-5.0	-18.0	17.0
Posterior Medial Femur	21.0	-6.0	26.0	15.0
Central Lateral Femur	22.5	2.0	-17.0	-6.0
PosteriorLateralFemur	26.0	19.0	36.0	32.0

*between group p-value <0.05

Fig 1: dGEMRIC image from a participant randomized to Placebo:

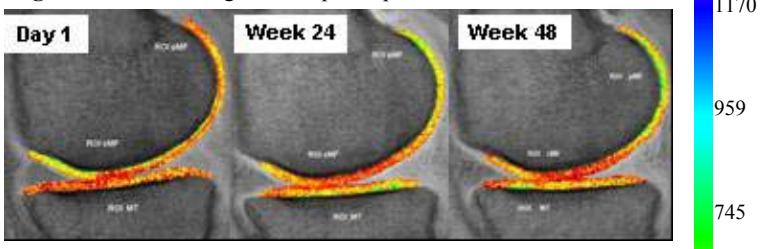
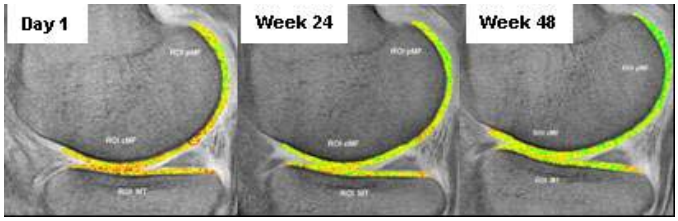


Fig 2: dGEMRIC image from a participant randomized to Fortigel®



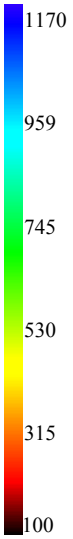
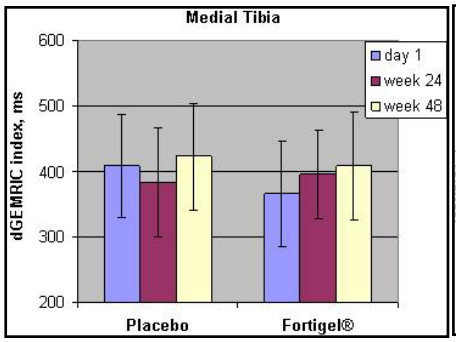
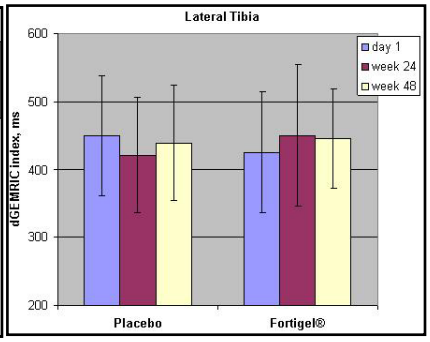


Fig 3: change in dGEMRIC index over time in Medial and lateral tibia section between Placebo and Fortigel® groups:





DISCUSSION: In summary, the dGEMRIC index was able to discriminate between treatment and placebo groups in the tibial regions. The sample size was small, so these data should be regarded as preliminary.