

# Preliminary Evaluation of Potential Disease Modification by Hylan G-F 20 (Synvisc®) Using dGEMRIC

P. Prasad<sup>1</sup>, W. Li<sup>1</sup>, T. Schnitzer<sup>2</sup>, N. Krishnan<sup>3</sup>, and D. Burstein<sup>3</sup>

<sup>1</sup>NorthShore University HealthSystem, Evanston, IL, United States, <sup>2</sup>Feinberg School of Medicine, Northwestern University, Chicago, IL, United States, <sup>3</sup>Radiology, Beth Israel Deaconess Medical Center, Boston, MA, United States

## INTRODUCTION

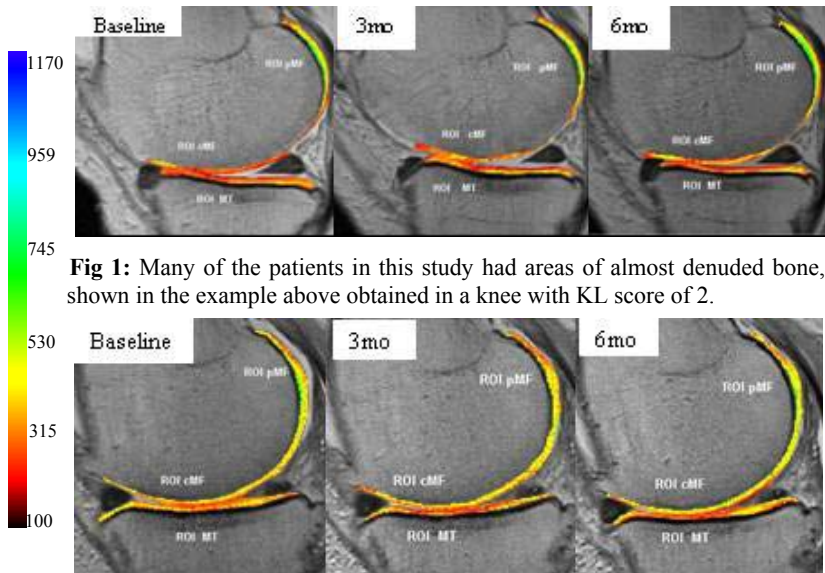
Treatment of osteoarthritis (OA) continues to be primarily based on symptom modification. The concept of disease modification for OA has been proposed and potential drugs are in the pipeline. Hylan G-F 20 (Synvisc) is an FDA-approved hyaluronate derivative which is administered by injection into osteoarthritic joints for treating pain associated with osteoarthritis. The present study was designed to determine if dGEMRIC imaging could detect cartilage changes over time in patients being treated with Hylan G-F 20 therapy.

## MATERIALS AND METHOD

**MR Scanner and Sequences:** The study was performed on a 32-channel 1.5 T MR system (Magnetom Avanto, Siemens, Erlangen, Germany) using a commercial transmit/receive extremity knee coil. 2D IR-TSE sequence (TR/TE=2200/13ms, TI=1680, 650, 350, 150, 50 ms, matrix size=384x384, slice thickness=3mm, FOV = 16cm) was used to acquire data in one central slice in the medial and lateral condyles. **Subjects:** This was an open-label, single-blind (dGEMRIC data was analyzed blinded to study group allocation), exploratory study of patients having knee OA with stable, moderate levels of pain appropriate for management by intra-articular injection with Hylan G-F 20. Patients meeting inclusion/exclusion criteria were randomly assigned to either active (intra-articular injection with Hylan G-F 20) or control (continued usual care consisting of maintenance of existing oral and/or physical therapy) groups in a 2:1 ratio. Patients treated with Hylan G-F 20 received the standard clinical dosage (3 injections, 1 week apart). Patients entered into the active arm of this trial underwent knee MRI (with dGEMRIC) prior to initiation of Hylan G-F 20 therapy and then at 3 months and 6 months post-treatment. Controls had knee MRI examinations with dGEMRIC performed at baseline, 3 and 6 months but did not have knee arthrocentesis performed. Thirty subjects (20 active, 10 control) were enrolled; one in the active group did not complete the trial. Most knees included had a KL score of 2 or 3, considered to be mild and moderate OA in current clinical practice. **Data Analysis:** For each subject, T1(Gd) values were reported from ROIs defined in the central femoral and tibial regions of the medial and lateral condyles (cMF, MT, cLF, LT).

## RESULTS

Example images over time are given in Figures 1 and 2. The dGEMRIC indices are given in Table 1.



**Fig 1:** Many of the patients in this study had areas of almost denuded bone, as shown in the example above obtained in a knee with KL score of 2.

Active arm (n=19)	Baseline	3-Month	6-Month
cMF	394±92	399±78	391±68
MT	401±92	370±66	371±69
cLF	444±96	448±79	451±82
LT	418±70	402±66	392±76
Control arm (n=10)			
cMF	455±75	456±77	466±100
MT	417±76	401±68	434±46
cLF	487±66	483±66	497±81
LT	429±86	458±108	461±89

**Fig 2:** Image showing little change in dGEMRIC over 6-mo in the active arm obtained in a representative knee with KL score of 2.

## DISCUSSION

There was overall little change in the mean dGEMRIC or pain indices in either the active or control group. A recent pre-clinical study reported intervention with G-F 20 showed improved proteoglycan levels [*Am J Sports Med.* 2009 Aug 31.]. However, a key factor in the preclinical study was that G-F20 was administered *early* after knee injury. We hypothesize that the lack of response in the current study may be related to the fact that the subjects included in the study had relatively advanced stage of disease with respect to cartilage integrity even though efforts were specifically made to enroll patients with mild symptoms and radiographic changes. Thus, while KL=2 is generally considered to be mild OA clinically, cartilage imaging has shown extensive changes including full thickness loss of cartilage. Such a hypothesis is consistent with previous observations of disease modifying activity in humans with sodium hyaluronate where a response was observed *only* in the radiologically milder disease group [*Int J Clin Pract.* 2003; 57(6):467-74].

There are a number of possible reasons for the lack of an observed effect in the current study: (i) The study may not have been adequately powered to detect an effect, (ii) G-F 20 may not be effective as a disease modifying agent in patients with this level of disease, (iii) the time course may be too short to detect such an effect. Recommendations based on these results include: (i) Utilizing the current results for power calculations of future studies. The stability of the control group can be determined from the current study; however, the level of possible change (improvement) with G-F 20 is still unknown. (ii) evaluating effects of administering G-F 20 at earlier stages of OA. Alternatively, subjects with acute ligament or meniscal tears may be a better population to evaluate G-F 20 and other potential disease modifying drugs. With the ability to detect and monitor early cartilage degeneration, the design of trials also need to change especially with respect to subject selection.