Cartilage T2 Mapping of Stickler Syndrome: An MR Image Marker for Type II Collagen Deficient Cartilage

T. J. Mosher[1,2], Y. Liu[1], S. A. Jimenez[3]

[1]Center for NMR Research, Radiology, Penn State Milton S. Hershey Medical Center, Hershey, PA, United States, [2]Orthopaedics and Rehabilitation, Penn State Milton S. Hershey Medical Center, Hershey, PA, United States, [3]Medicine, Division of Rheumatology, University Hospital, Thomas Jefferson University, Philadelphia, PA, United States

Introduction: Premature development of osteoarthritis (OA) has been associated with several mutations of the type II procollagen gene (COL2A1)(1). Collectively these are termed *Type II collagenopathies*. Stickler Syndrome, or hereditary arthro-ophthalmopathy is a rare autosomal dominant connective tissue dysplasia associated with several point mutations in the COL2A1 gene, and is characterized by blindness, hearing loss, and premature OA. This mutation of the COL2A1 gene leads to abnormally low type II collagen in the cartilage matrix, and provides a natural model to test the hypothesis that cartilage T2 mapping is a sensitive image marker for integrity of the type II collagen matrix.

Methods: T2 mapping was performed on 2 patients diagnosed with Stickler Syndrome: a 27 year old male with hearing loss and severe arthropathy, and a 55 year old female with primarily visual symptoms, and mild arthropathy. Quantitative cartilage T2 mapping was performed of both knees using a Bruker 3T MR spectrometer, a 24 cm gradient insert, and 15 cm linear Litz coil (Doty Scientific). Sagittal T2 maps of the femoral tibial joint were calculated from a 6 slice, 12 echo sequence with TR/TE = 1500/9-106 ms, 4 mm section thickness (ST), 384 x 384 matrix and a 12.75 cm field of view (FOV). Axial T2 maps of the patellofemoral joint were obtained from 5 sections with a 3 mm ST, 256 x 256 matrix, and a 14.00 cm FOV. Cartilage T2 profiles were generated using CCHIPs/IDL software and compared to T2 profiles (mean ± s.d.) from 8 young normal controls.

Results: Representative patellar T2 maps of a normal volunteer and a 27-year-old Stickler patient are shown in **Figure 1**. Unlike normal cartilage, the T2 map of the Stickler patient demonstrates diffusely elevated T2 with loss of normal spatial variation. Cartilage T2 profiles (**Figure 2**) demonstrate elevated cartilage T2 in both Stickler patients. For the Stickler patient with severe arthropathy, T2 profiles of weight-bearing femoral tibial cartilage demonstrates reversal of the normal spatial dependency in cartilage T2 with lower values observed near the articular surface.

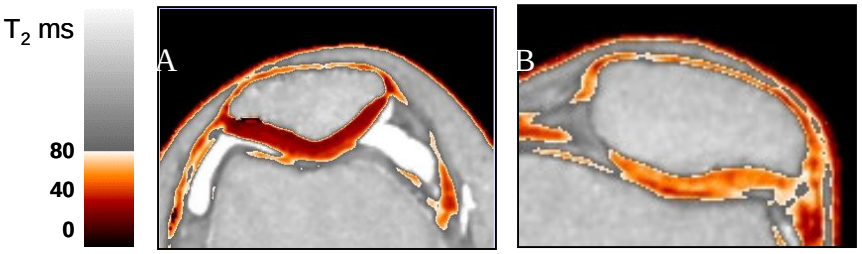

Figure 1: ***Patellar Cartilage T2 Map*** of **(A)** normal volunteer, and **(B)** 27 year-old male with Stickler syndrome. In contrast to normal cartilage, the T2 map of the Stickler patient demonstrates diffusely elevated cartilage T2 and loss of normal T2 spatial variation.

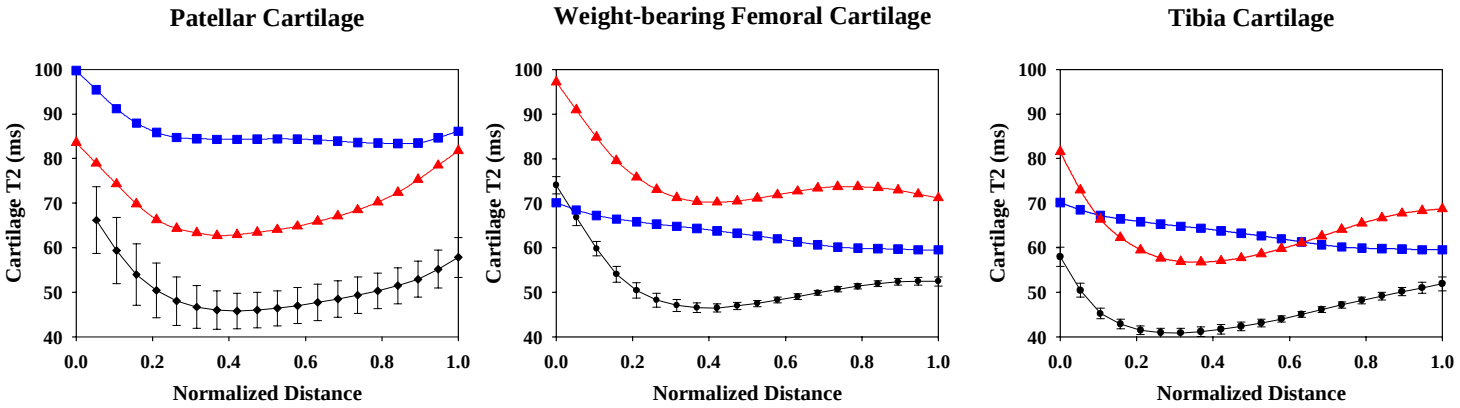

Figure 2: ***Cartilage T2 Profiles***: Mean T2 as a function of normalized distance from bone for (♦) normals (mean±s.d.), (■) male, and (▲) female Stickler patients in patellar, weight-bearing femoral, and tibial cartilage. Cartilage T2 is significantly elevated in patients with Stickler syndrome. For the male Stickler patient with severe arthropathy, the weight-bearing portion of the femoral tibial joint demonstrates a linear decrease in cartilage T2 toward the articular surface, rather than the increase seen in normal cartilage. Normal spatial variation in T2 is seen in the female Stickler patient.

Discussion: Abnormally elevated cartilage T2 observed in Stickler Syndrome is consistent with prior *ex vivo* studies correlating elevated T2 with loss of type II collagen (2). The pattern of T2 elevation differs between Stickler patients, and may reflect differences in expression of the underlying genetic mutations. In loaded femoral tibial cartilage of the Stickler patient with severe arthropathy, T2 decreases linearly toward the articular surface. We hypothesize this is due to lower water content near the surface of the more compressible collagen deficient cartilage. The spatial variation of the female Stickler patient suggests a more normal organization of the collagen matrix. The sensitivity of cartilage T2 mapping to alteration of the collagen matrix makes it a potential image marker to study the phenotypic expression of different genetic mutations of the COL2A1 gene.

References:

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