











# Quantitative Dual Contrast CT Technique for Evaluation of Articular Cartilage Properties

ABHISEK BHATTARAI <sup>1,2</sup> JUUSO T. J. HONKANEN <sup>3</sup> KATARIINA A. H. MYLLER <sup>1,2</sup>  
MITHILESH PRAKASH <sup>1,2</sup> MIITU KORHONEN <sup>1,2</sup> ANNINA E. A. SAUKKO <sup>1</sup> TUOMAS VIRÉN <sup>3</sup>  
ANTTI JOUKAINEN,<sup>4</sup> AMIT N. PATWA,<sup>5,6</sup> HEIKKI KRÖGER <sup>4</sup> MARK W. GRINSTAFF <sup>5</sup> JUKKA S. JURVELIN,<sup>1</sup>  
and JUHA TÖYRÄS <sup>1,2</sup>

<sup>1</sup>Department of Applied Physics, University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland; <sup>2</sup>Diagnostic Imaging Center, Kuopio University Hospital, P.O. Box 100, FI-70029 Kuopio, Finland; <sup>3</sup>Center of Oncology, Kuopio University Hospital, Kuopio, Finland; <sup>4</sup>Department of Orthopedics, Traumatology and Hand Surgery, Kuopio University Hospital, Kuopio, Finland; <sup>5</sup>Departments of Biomedical Engineering, Chemistry, and Medicine, Boston University, Boston, MA, USA; and <sup>6</sup>School of Liberal Studies and Education, Navrachana University, Vadodara, Gujarat, India

(Received 19 December 2017; accepted 21 March 2018)

Associate Editor Eric M. Darling oversaw the review of this article.

**Abstract**—Impact injuries of cartilage may initiate post-traumatic degeneration, making early detection of injury imperative for timely surgical or pharmaceutical interventions. Cationic (positively-charged) CT contrast agents detect loss of cartilage proteoglycans (PGs) more sensitively than anionic (negatively-charged) or non-ionic (non-charged, i.e., electrically neutral) agents. However, degeneration related loss of PGs and increase in water content have opposite effects on the diffusion of the cationic agent, lowering its sensitivity. In contrast to cationic agents, diffusion of non-ionic agents is governed only by steric hindrance and water content of cartilage. We hypothesize that sensitivity of an iodine(I)-based cationic agent may be enhanced by simultaneous use of a non-ionic gadolinium(Gd)-based agent. We introduce a quantitative dual energy CT technique (QDECT) for simultaneous quantification of two contrast agents in cartilage. We employ this technique to improve the sensitivity of cationic CA4+ ( $q = +4$ ) by normalizing its partition in cartilage with that of non-ionic gadoteridol. The technique was evaluated with measurements of contrast agent mixtures of known composition and human osteochondral samples ( $n = 57$ ) after immersion (72 h) in mixture of CA4+ and gadoteridol. Samples were arthroscopically graded and biomechanically tested prior to QDECT (50/100 kV). QDECT determined contrast agent mixture compositions correlated with the true compositions ( $R^2 = 0.99$ , average

error = 2.27%). Normalizing CA4+ partition in cartilage with that of gadoteridol improved correlation with equilibrium modulus (from  $\rho = 0.701$  to 0.795). To conclude, QDECT enables simultaneous quantification of I and Gd contrast agents improving diagnosis of cartilage integrity and biomechanical status.

**Keywords**—Biomechanics, Cartilage, Cationic contrast agent, Contrast enhanced computed tomography, Dual energy CT.

## INTRODUCTION

Mechanical impact injury of articular cartilage (e.g., fall or sports related accidents) often initiates cartilage degeneration and development of post-traumatic osteoarthritis (PTOA) due to the limited self-repair capability of the aneural and avascular cartilage tissue.<sup>28</sup> Using present diagnostic techniques, it has been challenging to detect tissue injury at its earliest stages. In contrast to primary osteoarthritis (OA), PTOA may be prevented with surgical or pharmaceutical interventions if detected early enough.<sup>2,6</sup> The first signs of cartilage injury include disruption of superficial collagen network, loss of proteoglycans (PGs), and increase in water content.<sup>5,12</sup> Symptoms experienced by a patient (e.g., pain and loss of mobility) arise only at later stages of disease progression, thus leaving clinicians with limited treatment options at the time of diagnosis. Hence, development of highly sensitive techniques, capable to detect lesions and earliest signs of post-traumatic degeneration in surrounding tissue, is

---

Address correspondence to Abhisek Bhattarai, Department of Applied Physics, University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland. Electronic mails: abhisek.bhattarai@uef.fi, juuso.honkanen@uef.fi, katarina.myller@uef.fi, mithilesh.prakash@uef.fi, miitu.korhonen@uef.fi, annina.saukko@uef.fi, tuomas.viren@kuh.fi, antti.joukainen@kuh.fi, anpatwa@gmail.com, heikki.kroger@kuh.fi, mgrin@bu.edu, jukka.jurvelin@uef.fi, juha.toyras@uef.fi