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Comparison of quantitative imaging of cartilage for osteoarthritis: T2, T1ρ, dGEMRIC and contrast-enhanced computed tomography☆

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Abstract

Evaluation of glycosaminoglycan (GAG) concentration in articular cartilage is of particular interest to the study of degenerative joint diseases such as osteoarthritis (OA). Noninvasive imaging techniques such as magnetic resonance imaging (MRI) and computed tomography (CT) have demonstrated the potential to assess biochemical markers of cartilage integrity such as GAG content; however, many imaging techniques are available and the optimization of particular techniques in the diagnosis of joint disease remains an active area of research. In order to highlight the differences between these various approaches, this work compares MRI (T1, T2 and T1ρ) and contrast-enhanced CT in human articular cartilage, in both the presence and absence of gadolinium-based contrast agent. Pre- and postcontrast T2 values were found to be similar on a regional level and correlated with each other. As expected, T1 values were shortened significantly on both a global and a spatial basis in the presence of gadolinium (Gd); similar results were found for T1ρ. T2 values were found to correlate mildly with postcontrast T1, T1(Gd) and with precontrast T1ρ values. In addition, contrast-enhanced CT values correlated with both precontrast T1ρ and T1(Gd) more strongly than with precontrast T2. Finally, T1(Gd) and precontrast T1ρ were found to be moderately correlated with CT data. However, T1(Gd) and precontrast T1ρ were found to be almost completely uncorrelated. Together, these results indicate that T1ρ, T2 and contrast-enhanced techniques may provide complementary information about the molecular environment in cartilage during the evolution of OA.

Keywords: Cartilage; T2; T1rho; dGEMRIC; Contrast-enhanced CT; Osteoarthritis; MRI

1. Introduction

Osteoarthritis (OA) is a chronic degenerative disease characterized primarily by the loss of articular cartilage. Loss of articular cartilage may lead to inflammation, pain and associated pathology such as the growth of new vasculature, osteophyte development and joint space narrowing. Traditionally, OA has been diagnosed by these secondary indicators of cartilage loss via radiographic examination [1], in which a planar X-ray is used to assess the presence or absence of osteophytes and the width of the joint space; determination of pathology is based on indirect measures of surrounding anatomical structures [2]. Although this is an effective approach, radiographs tend to be limited to the detection of OA only at later stages of disease progression because they lack the ability to directly image soft tissues [3].

In addition, radiographs are relatively insensitive to biochemical changes, which are essential for early diagnosis and treatment of many pathologies. For example, in OA the early stages of cartilage degeneration are often marked by the loss of the proteoglycan components of the cartilage matrix [4]. Unlike collagen, which is uncharged, proteoglycans exhibit a net negative charge in solution. This fixed charge density attracts sodium and other small positive ions. These small ions in turn pull additional water into the cartilage matrix via osmosis and create a positive pressure within the tissue that helps articular cartilage to resist compressive loading forces encountered during normal activities such as walking and running. Disruption of proteoglycans may lead

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initially to swelling via increased osmotic pressure followed by the eventual loss of cartilage volume which accompanies the corresponding loss of particulates composed of degraded proteoglycan. As such, proteoglycan depletion and the concomitant degradation of the cartilage matrix have been hypothesized as one of the initiating events of the pathologic process leading to OA [5,6].

This awareness of biochemical correlates of pathology has spurred an increasing interest in employing the capabilities of magnetic resonance imaging (MRI) in the assessment of biochemical changes in the hopes of early diagnosis and treatment of diseases such as OA. MRI has all of the distinct advantages conferred from being a non-invasive assessment technique; moreover, it can assess cartilage morphology directly and has shown promise for the detection of soft tissue changes. For example, lesions found in T2-weighted images and T2 maps have been correlated with degradations of cartilage matrix (i.e., fibrillation, clefts) [7], T1ρ relaxation times with proteoglycan degradation [8] and T1 values using delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) with proteoglycan content of cartilage [9,10]. MRI has also been used to study the sodium content of cartilage directly by using new techniques to image sodium ions [11–13]. Each of these techniques offers a unique glimpse of the pathological processes encountered during the development of OA.

T2 imaging studies are of interest to OA because T2 is sensitive to tissue hydration. Early degradative changes in the extracellular matrix (ECM) affect tissue hydration not only by increasing the overall water content via osmosis but also by increasing the mobility of water. T2 has been found to be inversely correlated with both cartilage volume and thickness [14,15], and focal areas of increased T2 levels have been found to correspond to cartilage lesions upon arthroscopic evaluation [16,17]. In addition, early osteoarthritic changes in T2 have been linked to changes in collagen content [18–20]. However, T2 is not correlated with proteoglycan loss in the literature.

T1ρ describes longitudinal relaxation in the rotating frame. Because T1ρ measurements can probe very low frequency interactions, they are especially suited to probing spin-lattice energy exchange between water and large molecules such as those which comprise the ECM in articular cartilage. Disruption of this matrix, specifically disruption of the proteoglycan content of the matrix, leads to an increase in water molecule motion and hence to an increase in measured T1ρ [8,21,22]. In addition, proteoglycans are known to be major players responsible for the physical resilience of articular cartilage, and their loss has been correlated with a loss of mechanical integrity within articular tissue. Moreover, because proteoglycan loss is thought to precede the development of symptomatic OA, there is an interest in T1ρ as a noninvasive method for early assessment of disease development [23].

In contrast, T1 dGEMRIC studies have shown that proteoglycan content may be more directly inferred from the presence or absence of contrast agent accumulation within the cartilage [6,9,10,24]. In dGEMRIC studies, charged contrast agent such as gadopentate (Gd-DTPA2-) is injected intravenously into a patient and allowed to diffuse into articular cartilage over at least 2 h [25]. Because the gadopentate molecule exhibits a net negative charge, it is repulsed by the similarly negative fixed charge density due to proteoglycans within the cartilage matrix [26]. Damage to the matrix and the corresponding loss of proteoglycan component may be inferred from imaging data indicating an increased concentration of contrast agent within focal areas of articular cartilage. dGEMRIC methods are appealing for assessment of biological changes in OA due to this sensitivity to proteoglycan content.

In addition, contrast-enhanced computed tomography (CT) has also been proposed as an alternative to dGEMRIC [27]. In a similar manner to dGEMRIC imaging, CT employs a charged contrast agent and sodium imaging uses the sodium ions to identify focal areas of proteoglycan loss. However, because detection of contrast agent is accomplished directly via measurements of increased X-ray attenuation, these methods require increased amounts of contrast agent to be injected into the patient prior to imaging and hence an increased risk of complications related to contrast administration. Despite this limitation, CT methods are attractive because the imaging procedure is quick and can produce images with high-resolution and isotropic voxel dimensions.

In the wake of the development of new imaging methods for assessment of cartilage biochemistry, there is a need for a careful, systematic comparison of the proposed imaging parameters to assess the ability of each to assess pathology and progression of OA. Moreover, the relationships between each of these parameters have not been completely characterized; as such it is unknown which of the various imaging methods available might be complementary and hence could provide a better overall picture of OA pathology. The purpose of this study was to compare MRI (T1, T2 and T1ρ) and contrast-enhanced CT in human articular cartilage, in both the presence and absence of gadolinium-based contrast agent.

2. Methods

2.1. Specimen preparation

Sixteen human osteochondral specimens were used in this study; four were obtained from OA patients undergoing total knee arthroplasties and 12 were harvested from cadavers obtained from the National Disease Research Institute (NDRI). Specimens were stored at −80°C until use; when needed, specimens were allowed to equilibrate overnight in an isotonic saline bath at 4°C. Baseline MRI data were obtained for T1, T2 and T1ρ. Specimens were then soaked overnight at 4°C in an isotonic saline solution containing