Age-related quantitative MRI changes in healthy cartilage: Preliminary results

Jean Christophe Goebel a, Astrid Watrin-Pinzano a, Isabelle Bettembourg-Brault b, Freddy Odille c, Jacques Felblinger c, Isabelle Chary-Valckenaire a,b, Patrick Netter a, Alain Blum a,d, Pierre Gillet a,b,* and Damien Loeuille a,b

a Department of Pharmacology, Faculté de Médecine, UMR 7561 CNRS University Nancy I, Avenue de la Forêt de Haye, 54505 Vandoeuvre lès Nancy, France
b Clinique Rhumatologique (Pr Jacques Pourel), Chu Nancy brabois, 54511 Vandoeuvre cedex, France
c Imagerie Adaptative Diagnostique et Interventionnelle (Pr. Jacques Felblinger), Chu de Nancy Brabois, Tour Drouet 4ème étage, 54511 Vandoeuvre lès Nancy cedex, France
d Service de Radiologie Guilloz (Pr. Alain Blum), Chu de Nancy, Hôpital Central, CO 34, 54000 Nancy cedex, France

Abstract. Objectives: As the early form of OA is characterized by elevated water content in the cartilage tissue, the purpose of this study was to verify in vivo if age-related changes in patellar cartilage in healthy volunteers can be detected using quantitative MRI with T2 mapping and volume measurement MRI methods. Design: Thirty healthy volunteers of various classes of age (18 to 65 years old) were enrolled in this study. MR images of the patellar cartilage were acquired at 1.5T. Patellar cartilage volume and T2 maps were determined. Results: Despite non-significance, there was a trend in reducing cartilage volume with ageing (r: −0.25). In contrast global T2 slightly increased with ageing (r: 0.46). BMI (r: 0.51) and bone volume (r: 0.69) are well correlated to cartilage volume. Conclusion. Age-related physiologic changes in the water content of patellar cartilage can be detected using MRI. The proposed T2-mapping method, coupled with other non-invasive MR cartilage imaging techniques, could aid in the early diagnosis of OA.

Keywords: Cartilage, MRI, T2 map, volume, patella, age-related changes

1. Introduction

Magnetic Resonance Imaging (MRI) of articular cartilage has attracted intense interest and been the subject of numerous research studies over the past 10 years [13]. There are several reasons: the essential role articular cartilage plays in the function of the diarthrodial joints of the body, the high prevalence of degeneration and traumatic injury of articular cartilage, and the recent development of new surgical procedures that hold the promise of forming repair tissue that is hyaline or hyaline-like cartilage. In fact, MRI is the optimal diagnostic method for non-invasive evaluation of chondral lesions.

Because MRI can directly visualize articular cartilage, it is likely to be a useful modality in the study of cartilage ageing and osteoarthritis (OA). Current clinical MRI techniques demonstrate joint anatomy, and can be used to determine morphologic parameters such as cartilage volume, thickness, and presence

*Address for correspondence: Pierre Gillet. E-mail: Pierre.Gillet@medecine.uhp-nancy.fr.
of focal, superficial cartilage lesions. More recently techniques have been described for generating spatially localized quantitative maps of MRI relaxation times of cartilage. Such MRI parametric mapping techniques have the potential to identify and localize specific biochemical and structural changes within the extracellular cartilage matrix [7].

Some new quantitative MR imaging techniques [4], such as cartilage T2 mapping [8] and volume assessment [3] demonstrate sensitivity to age- and OA-related biochemical and structural changes in the extracellular cartilage matrix and thus have the potential to serve as image markers of OA versus physiologic senescence [11,15]. The purpose of the study is thus to determine if an age-dependent variation in patellar cartilage T2 and patellar cartilage volume occurs in asymptomatic volunteers.

2. Patients and methods

2.1. Recruitment of volunteers

Thirty healthy volunteers (11 females and 19 males) were screened to exclude those with a known contraindication for MRI: pacemaker, cerebral aneurysm clip, cochlear implant, presence of metal/shrapnel in strategic locations, such as in the eye, claustrophobia, and inability to cooperate with study requirements and give informed consent. Healthy adults over the age of 18 years were included in the study if (1) they had no history of pain or traumatic injury of the studied knee and (2) if the studied knee has a normal pattern on a preliminary MRI (Spin Echo T2 weighted sequence (T2wSE)). The studied population was stratified by age into 5 cohorts: (A) 18–25 years ($n = 6$), (B) 26–35 years ($n = 7$), (C) 36–45 years ($n = 7$), (D) 46–55 years ($n = 5$) and 56–65 years ($n = 5$). Additional demographic data collected at time of the MRI study included height and weight. Body mass index (BMI) was calculated by dividing the subject’s weight in kilograms by the square of the height in meters. The study design was approved by the Institutional Review Board of University Hospital Center of Nancy.

2.2. MR protocol

The patella was examined in the axial plane with a 1.5 T whole body magnetic resonance unit (Signa Advantage HiSpeed GE Medical Systems, Milwaukee, WI) using a commercial coil dedicated to the knee. The following sequences and parameters were used:

**T2 map.** A four echo T2w SE imaging with TR (repetition time) constant at 3500 msec with four different TE (echo time, 16, 32, 48 and 64 msec); field of view 16 $\times$ 16 cm; acquisition matrix 256 $\times$ 192 pixels; resolution 0.47 $\times$ 0.47 mm; slice thickness 5 mm; spacing between slices 0.5 mm; 48 adjoining slices, number of excitation: 1; acquisition time: 25 minutes. T2 values were calculated from the four echoes by using a non-linear least squares curve fitting on a pixel by pixel basis assuming a monoexponential T2 decay. Obtained T2 values (global T2) were the averaged T2 data over the entire patellar cartilage thickness.

**Volume assessment.** A T1 weighted fat suppressed 3D gradient recall acquisition was performed with the following parameters: flip angle 15 degrees; TR 17.7 msec; TE 6.5 ms; FOV 12 $\times$ 12 cm; matrix acquisition 320 $\times$ 320 matrix; acquisition time 10 min; number of excitation: 1.5. Axial images were obtained at a partition thickness of 2 mm (60 adjoining slices). Patellar cartilage and bone volumes were determined by image processing after semi-automatic segmentation on an independent workstation using the software program Osirix [14].

Global and regional T2 values as well as volume were then studied, the whole patellar cartilage being digitally divided in 8 Regions Of Interest (ROIs): medial and lateral facets of the patella being equally subdivided into 4 parts in the axial direction.
Summary of the parameters studied, by age group cohort. Results are expressed as mean ± s.e.m.

<table>
<thead>
<tr>
<th>Group</th>
<th>BMI (g) ± s.e.m.</th>
<th>Bone (ml) ± s.e.m.</th>
<th>Cartilage (ml) ± s.e.m.</th>
<th>Global T2 cartilage (msec) ± s.e.m.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (18–25 years)</td>
<td>24.4 ± 1.23</td>
<td>20.6 ± 1.70</td>
<td>3.7 ± 0.34</td>
<td>27.9 ± 0.66</td>
</tr>
<tr>
<td>B (26–35 years)</td>
<td>25.1 ± 2.16</td>
<td>16.8 ± 1.52</td>
<td>3.4 ± 0.38</td>
<td>30.2 ± 0.80</td>
</tr>
<tr>
<td>C (36–45 years)</td>
<td>22.7 ± 0.98</td>
<td>15.3 ± 0.71</td>
<td>3.0 ± 0.26</td>
<td>27.2 ± 0.98</td>
</tr>
<tr>
<td>D (46–55 years)</td>
<td>23.2 ± 1.23</td>
<td>17.7 ± 3.16</td>
<td>3.2 ± 0.40</td>
<td>30.5 ± 1.81</td>
</tr>
<tr>
<td>E (56–65 years)</td>
<td>25.9 ± 1.79</td>
<td>17.4 ± 0.88</td>
<td>2.9 ± 0.13</td>
<td>31.9 ± 0.92</td>
</tr>
</tbody>
</table>

3. Results

No clear difference was observed between groups in terms of BMI and bone volume (Table 1). Despite non-significance, there was a trend in reducing cartilage volume with ageing ($r$: −0.25). In contrast, global T2 slightly increased with ageing ($r$: 0.46). BMI ($r$: 0.51) and bone volume ($r$: 0.69) are well correlated to cartilage volume.

ROIs study confirmed that cartilage volume was more abundant in the center of the patella especially in the lateral part. In this particular area, age-related T2 variation was more pronounced. In contrast it remained only a non-significant trend in age-related volume decrease.

4. Discussion

Our study reveals age-dependent changes in T2 relaxation time of patellar cartilage in healthy asymptomatic volunteers, like previously demonstrated by Mosher et al. [9,10]. In contrast, no concomitant significant variation in cartilage volume was depicted. The T2 relaxation time of articular cartilage is a function of the water content of the tissue [6]. To measure the T2 relaxation time with a high degree of accuracy, care must be taken with the MR technique. Typically, a multi-echo, spin-echo acquisition is used and signal levels are fitted to one degree or more decaying exponential, depending upon whether it is felt that there is more than one distribution of T2 within the sample.

The T2 relaxation time of articular cartilage characterizes the interactions of cartilage fluid (protons) with the solid matrix (collagen and proteoglycan [16]). In this tissue, there are several distinct “pools” of water molecules: the molecules associated with the collagen fibrils, the molecules hydrogen-bonded to proteoglycans by means of electrostatic attraction, and free water molecules. Only this last pool is responsible for the cartilage signal intensity.

During MRI T2-mapping, an image of the T2 relaxation times is then generated (Fig. 1), either with a color map or gray scale representing the relaxation times (see extensive review in [8]). Several investigators have measured in clinics the spatial distribution of T2 relaxation times within cartilage. In humans, ageing appears to be associated with a symptomatic increase in T2 relaxation times in the transitional zone of patellar cartilage [9]. Additionally, focal increases in T2 relaxation times within cartilage have been associated with matrix damage, particularly loss of collagen matrix [5]. Concerning our study, we can postulate that the age-related changes in T2 are related to “physiological” senescence denaturation process of the extracellular matrix and not to OA, even asymptomatic, because a normal MRI of the knee (T2wSE) was required to be included in the study.

Finally, in healthy asymptomatic volunteers, age-related T2 increase seems more sensible and site-depandent than cartilage volume decrease. It probably reflects asymptomatic early degeneration in articular cartilage, e.g. changes in water, proteoglycan and collagen contents before a “volumic” impact (i.e.
cartilage loss). In addition to cartilage volume assessment [1–3,12], in vivo cartilage T2 mapping can improve detection of cartilage ageing [10] and evaluation of new structure modifying pharmaceuticals and cartilage engineering.

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References


