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### Facilitating cartilage volume measurement using MRI

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#### ABSTRACT

*Purpose:* To compare quantitative cartilage volume measurement (CVM) using different slice thicknesses. *Materials and methods:* Ten knees were scanned with a 1.5 T MRI (Sonata, Siemens, Erlangen, Germany) using a 3D gradient echo sequence (FLASH, fast low-angle shot). Cartilage volume of the medial and lateral tibial plateau was measured by two independent readers in 1.5 mm, 3.0 mm and 5.0 mm slices using the Argus® software application. Accuracy and time effectiveness served as control parameters.

*Results:* Determining cartilage volume, time for calculation diminished for the lateral tibial plateau from  $384.6 \pm 127.7$  s and  $379.1 \pm 117.6$  s to  $214.9 \pm 109.9$  s and  $213.9 \pm 102.2$  s to  $122.1 \pm 60.1$  s and  $126.8 \pm 56.2$  s and for the medial tibial plateau from  $465.0 \pm 147.7$  s and  $461.8 \pm 142.7$  s to  $214.0 \pm 67.9$  s and  $208.9 \pm 66.2$  s to  $132.6 \pm 41.5$  s and  $130.6 \pm 42.0$  s measuring 1.5 mm, 3 mm and 5 mm slices, respectively. No statistically significant difference between cartilage volume measurements was observed (p > 0.05) while very good inter-reader correlation was evaluated.

*Conclusion:* CVM using 1.5 mm slices provides no higher accuracy than cartilage volume measurement in 5 mm slices while an overall time saving up to 70% is possible.

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#### 1. Introduction

Osteoarthritis (OA) of the knee joint is a common cause of disability in people >65 years [1]. For the evaluation of the long term progression of OA conventional radiography is widely used in view of its cost effectiveness and availability. The main limitation is determined by the disability to directly visualize articular cartilage, the main pathological localization of OA [2].

Direct visualization of articular cartilage is provided by arthroscopy, a reliable and sensitive application to assess changes caused by osteoarthritis [3]. Since only cartilage surface is accessible for evaluation and moreover the invasive character of the procedure contradicts multiple evaluations of the same patient at regular intervals alternative modalities are developed consequently.

Cartilage sensitive MRI techniques have been shown to have a high correlation with arthroscopic grading scores. Due to missing side-effects MRI can be used as a non-invasive examination technique without limitations concerning the evaluation frequency [4–11]. In particular for the assessment of OA there has been increasing interest in the determination of knee cartilage volume for monitoring OA and evaluating therapeutic response [12–14].

Three-dimensional, post-processing techniques based on MRI data sets have proved their potential to reliably calculate cartilage volume. Since multiple intermediate steps and supplementary hard- and software components are necessary, introduction into daily clinical routine is still pending [15–17]. To improve the applicability of cartilage volume determination Maataoui et al. validated the Argus<sup>®</sup> evaluation software, which is normally used to assess functional data of the heart and great vessels, as an option for cartilage volume measurement [18]. They showed that the Argus® software enables the radiologist to measure cartilage volume even in high-grade degenerative knees in an experimental setup. Since the use of MRI in the management of OA is still controversial because MRI imaging is an expensive imaging modality, optimised (in particular faster) examination protocols are needed to make this promising modality routinely available to patients suffering from OA.

The intention of our study was to achieve a significant timesaving by measuring tibial cartilage volume using the MRI Argus<sup>®</sup> application in varying slice thicknesses.

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2

# **ARTICLE IN PRESS**

#### A. Maataoui et al. / European Journal of Radiology xxx (2009) xxx-xxx

#### 2. Materials and methods

Both knees of five healthy volunteers (age: 23–32; mean age: 27.5; two females and three males) were included in the study. The volunteers had no past history of joint disease or trauma in the examined joints. The study protocol was approved by the local ethic committee and written informed consent was obtained from all volunteers.

#### 2.1. Magnetic resonance imaging

Image acquisition was performed with a 1.5 T MR scanner (Magnetom Sonata, Siemens, Erlangen, Germany), using a standard circularly polarized transmit extremity coil. Coronal images were obtained using a 3D gradient echo sequence (FLASH, fast low-angle shot) with selective water excitation (TR = 19 ms; TE = 8.6 ms; FA =  $20^{\circ}$ ). Each of the knee joints underwent examination with section thicknesses varying from 1.5 mm to 3 mm to 5 mm, respectively. The in-plane resolution was 0.31 mm × 0.31 mm (field of view, 160 mm, matrix, 512 × 512 pixels).

#### 2.2. Measurement of cartilage volume with Argus®

Cicuttini et al. could show a strong correlation between femoral and tibial cartilage volume measured in both, the medial and lateral, tibiofemoral compartments of the knee [19]. The authors conclude that measurement of tibial cartilage volume alone is sufficient for evaluating cartilage volume in the tibiofemoral compartment, being the more reliable method due to the highly curved surface of the femur.

After initial blinding tibial cartilage volume was determined by two readers with more than 5 years of experience in musculoskeletal imaging. The readers were blinded to the results of the different slice thicknesses for each patient.

The MRI data were transferred to the Argus<sup>®</sup> software (Siemens Inc., Erlangen, Germany). In particular, the "heart function" tool was used for this study. By manually marking the contour in each relevant slice cartilage layers were assigned. Per addition of each single unit, cartilage volume for the medial and lateral tibial compartment of the knee joint was determined by the Argus<sup>®</sup> software. The intercondylar eminence separated both tibial plateaus and served as a landmark to circumscribe the cartilage covered plateaus. In summary the presented Argus<sup>®</sup> software was used as a segmentation tool. Similar segmentation software is available in all current MRI systems.

#### 2.3. Statistics

Statistical analysis was carried out using the BIAS software package (Epsilon publisher, Frankfurt a. M., Germany, http://www.bias-online.de) with the *t*-test and two-sided *t*-test. Data are presented as mean  $\pm$  standard error. A *p*-value less than 0.05 or a 95% confidence interval not including zero was regarded as statistically significant.

#### 3. Results (Table 1)

#### 3.1. Post-processing and expenditure of time

The acquisition of the coronal 3D MRI images (scan time) took 400 s, 207 s and 138 s for the 1.5 mm, 3 mm and 5 mm section thicknesses, respectively.

#### 3.1.1. First reader

For the lateral tibial plateau (LTP) determination of cartilage volume using the  $\text{Argus}^{\otimes}$  software took a mean time of  $384.6 \pm 127.7$  s

for the 1.5 mm section thickness. Measuring cartilage volume in the 3 mm and 5 mm slices a mean time of  $214.0 \pm 109.9$  s and  $122.1 \pm 60.1$  s was needed, respectively. Accordingly a time saving of 44.4% for the 3 mm slices and 68.3% for the 5 mm slices compared to the 1.5 mm slices was evaluated.

For the medial tibial plateau (MTP) determination of cartilage volume using the Argus<sup>®</sup> software took a mean time of  $465.0 \pm 147.7$  s for the 1.5 mm section thickness. Measuring cartilage volume in the 3 mm and 5 mm slices a mean time of  $214.0 \pm 67.9$  s and  $132.6 \pm 41.5$  s was needed, respectively. Accordingly a time saving of 54.0% for the 3 mm slices and 71.5% for the 5 mm slices was calculated.

#### 3.1.2. Second reader

For the lateral tibial plateau (LTP) determination of cartilage volume using the Argus<sup>®</sup> software took a mean time of  $379.1 \pm 117.6$  s for the 1.5 mm section thickness. Measuring cartilage volume in the 3 mm and 5 mm slices a mean time of  $213.9 \pm 102.2$  s and  $126.8 \pm 56.2$  s was needed, respectively. Accordingly a time saving of 43.6% for the 3 mm slices and 66.6% for the 5 mm slices compared to the 1.5 mm slices was evaluated.

For the medial tibial plateau (MTP) determination of cartilage volume using the Argus<sup>®</sup> software took a mean time of  $461.8 \pm 142.7$  s for the 1.5 mm section thickness. Measuring cartilage volume in the 3 mm and 5 mm slices a mean time of  $208.9 \pm 66.2$  s and  $130.6 \pm 42.0$  s was needed, respectively. Accordingly a time saving of 54.8% for the 3 mm slices and 71.9\% for the 5 mm slices was calculated.

#### 3.2. Tibial cartilage volume

#### 3.2.1. First reader

Cartilage volume as determined in the 1.5 mm slices varied for the lateral and medial tibial plateau between 1.6-4.1 ml and 1.1-3.3 ml, the mean volume being  $2.7 \pm 0.9$  ml and  $2.2 \pm 0.8$  ml, respectively.

Regarding the 3 mm and 5 mm slices for the LTP, a cartilage volume of 1.5–4.2 ml and 1.6–4.2 ml resulting in a mean cartilage volume of  $2.7 \pm 0.9$  ml and  $2.6 \pm 0.9$  ml was found. For the MTP, cartilage volume varied from 0.9 to 3.2 ml and 1.0 to 3.3 ml, resulting in a mean cartilage volume of  $2.1 \pm 0.8$  ml and  $2.3 \pm 0.8$  ml for the 3 mm and 5 mm sections, respectively.

#### 3.2.2. Second reader

Cartilage volume as determined in the 1.5 mm slices varied for the lateral and medial tibial plateau between 1.7-4.0 ml and 1.1-3.2 ml, the mean volume being  $2.6\pm0.8$  ml and  $2.2\pm0.7$  ml, respectively.

Regarding the 3 mm and 5 mm slices for the LTP, a cartilage volume of 1.4–4.2 ml and 1.3–4.3 ml resulting in a mean cartilage volume of  $2.6 \pm 0.9$  ml and  $2.6 \pm 0.9$  ml was found. For the MTP, cartilage volume varied from 1.1 to 3.1 ml and 1.0 to 3.3 ml, resulting in a mean cartilage volume of  $2.2 \pm 0.8$  ml and  $2.3 \pm 0.8$  ml for the 3 mm and 5 mm sections, respectively.

Using the *t*-test no significant difference between cartilage volume measurements in 1.5 mm slices compared to 3 mm and 5 mm slices was observed:

1. LTP [*p* = 0.73, CI: (-0.05; 0.09); *p* = 0.71, CI: (-0.08; 0.05)]; 2. MTP [*p* = 0.45, CI: (-0.13; 0.05); *p* = 0.06, CI: (-0.01; 0.06)].

#### 3.3. Inter-reader correlation

The results of both readers showed a very good correlation using the two-sided *t*-test with *p*-values of 0.83, 0.32 and 0.49 for LTP in 1.5 mm, 3.0 mm and 5.0 mm sections, respectively and *p*-values of

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Patient	LTP (ml) (1.5 mm)		Time (s) (1.5 mm)		LTP (ml) (3.0 mm)		Time (s) (3.0 mm)		LTP (ml) (5.0 mm)		Time (s) (5.0 mm)	
	R1	R2	R1	R2	R1	R2	R1	R2	R1	R2	R1	R2
1Right	4.1	4.0	670	656	4.2	4.2	472	448	4.2	4.3	256	240
1Left	4.0	3.7	420	403	4.0	3.9	325	330	4.0	3.9	180	192
2R	2.8	2.9	347	339	2.8	2.8	171	185	2.7	2.9	83	69
2L	2.3	2.1	399	360	2.2	2.2	140	154	2.4	2.2	81	89
3R	2.2	2.2	411	390	2.0	1.8	177	187	2.1	1.0	141	150
BL	1.6	1.7	250	271	1.5	1.4	111	103	1.6	1.3	64	70
4R	3.1	2.9	363	380	3.2	3.1	260	240	3.1	2.9	135	141
4L	2.8	2.9	230	241	3.0	2.8	171	165	2.5	2.6	62	80
5R	2.1	2.1	476	460	2.2	2.3	160	157	2.2	2.2	120	131
5L	1.7	1.9	280	291	1.7	1.9	153	170	1.7	1.8	99	106
Mean (SD)	2.7 (0.87)	2.6 (0.77)	384.6 (127.71)	379.1 (117.56)	2.7 (0.93)	2.6 (0.90)	214(109.94)	213.9 (102.17)	2.6 (0.89)	2.6 (0.93)	122.1 (60.13)	126.8 (56.21)
Patient	MTP (ml) (1.5 mm)		Time (s)		MTP (ml) (3 mm)		Time (s)		MTP (ml) (5 mm)		Time (s)	
	R1	R2	R1	R2	R1	R2	R1	R2	R1	R2	R1	R2
1Right	3.1	2.8	676	680	3.1	3.0	286	270	3.2	3.1	210	217
l Left	2.9	2.8	718	692	2.7	2.9	301	291	2.8	2.9	179	168
2R	1.9	2.1	434	440	1.8	1.9	202	200	1.9	2.1	85	78
2L	1.6	1.7	288	306	1.7	1.7	145	158	1.6	1.7	106	110
3R	0.9	1.2	448	392	0.9	1.1	210	194	1.0	1.2	123	120
BL	1.1	1.1	323	340	1.0	0.9	144	124	1.2	1.0	84	80
4R	3.3	3.0	584	600	3.2	3.1	276	252	3.3	3.3	170	162
4L	2.9	3.2	334	350	2.6	2.8	116	120	2.9	3.1	114	120
5R	2.1	2.0	425	432	2.2	2.1	280	300	2.3	2.2	135	129
5L	2.0	2.2	420	386	2.2	2.1	180	180	2.4	2.2	120	122
Mean (SD)	2.2 (0.84)	2.2 (0.74)	465.0 (147.65)	461.8 (142.70)	2.1 (0.80)	2.2 (0.78)	214(67.93)	208.9 (66.22)	2.3 (0.80)	2.3 (0.81)	132.6 (41.47)	130.6 (42.03)

 Table 1

 Cartilage volumes (in ml) of tibial plateaus (medial and lateral) and determination times for the two readers (R1: R2)

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A. Maataoui et al. / European Journal of Radiology xxx (2009) xxx-xxx

0.65, 0.57 and 0.68 for MTP in 1.5 mm, 3.0 mm and 5.0 mm sections, respectively.

#### 4. Discussion

Articular cartilage is well known to be the most important anatomical structure concerning osteoarthritis (OA). Since plain film radiography faces major restrictions in the evaluation of cartilage and arthroscopy represents an invasive alternative, there has been increasing interest in the use of MRI for the assessment of morphological changes of cartilage. The potential for MR imaging approach for knee OA is obvious: MR images enable the assessment of all the joint structures, including the menisci, synovial tissue, ligaments and in particular cartilage. Additionally MRI represents a nonradiant and non-invasive method providing a clear advantage over plain film radiography and arthroscopy.

Recently, the use of cartilage volume for the assessment of the clinical course of osteoarthritis (OA) has become more and more important. It has been shown that a loss rate at an average of 5% per year of knee cartilage volume can be proposed for patients suffering from OA [20]. For evaluation of therapeutic effects several techniques for determination of cartilage volume using MRI have been validated as accurate and reproducible methods [12–14]. Furthermore the decrease of cartilage volume showed a well correlation with the radiographic grading of OA [21].

To date, because of durable examination procedures MR imaging remains too expensive to be applied routinely in the assessment of OA. This is mainly due to cartilage volume assessment being performed in high resolution techniques using a 1.5 mm or 2 mm section thickness. Correspondingly, cartilage volume calculation still remains a time consuming procedure which makes it not possible to be introduced to the daily clinical routine. We in our study showed that by augmenting slice thickness to a maximum of 5 mm it is possible to reduce examination time by more than 65%.

Cartilage volume calculation using the Argus® software showed significant decrease of determination time by using 5 mm sections compared to 3 mm and 1.5 mm sections, respectively. Overall a time saving of 67.6% was achieved. These results allocate radiologists an application for fast and accurate cartilage volume determination. Furthermore evaluation of cartilage volume using the Argus® software application requires only little experience and practice by the investigator.

The presented study faces limitations. Firstly, the number of examined subjects is very less. Secondly, the knees examined showed no evidence of OA. Thus differentiation of cartilage from the surrounding tissue was easy to perform. Determination of cartilage volume in osteoarthritic knees, especially in late stages of the disease where spreading of fibroid tissue accompanies OA, is much more challenging and needs further investigation. Lastly, image quality decreased significantly with raising section thickness. While 3 mm slice thickness still allowed some differentiation of anatomical structures, 5 mm slices had no diagnostic value and are only suitable for determination of cartilage volume.

In summary the presented study indicates a possibility of fast and accurate cartilage volume determination by changing MRI scan parameters concerning section thickness.

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#### **Conflict of interest**

None.

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