JBR–BTR, 2014, 97: 11-16.

CORRELATION OF MRI T2 MAPPING SEQUENCE WITH KNEE PAIN LOCATION IN YOUNG PATIENTS WITH NORMAL STANDARD MRI

R. Dautry[1], V. Bousson[2,3], J. Manelfe[1,3], A. Perozziello[4], P. Boyer[5], Ph. Loriaut[5], P. Koch[1], A. Silvestre[6], E. Schouman-Claeys[1,3], J.D. Laredo[2,3], B. Dallaudière[1,3,7]

Objective: **To assess the correlation of T2 mapping abnormalities to knee pain location, in young adults with normal standard knee MRI at 3.0 Tesla.**

Subjects and methods: **Twenty-three consecutive patients were included prospectively from September 2011 to April 2012. Inclusion criteria were age under 50 years old, knee pain without surgical history, and normal knee MRI at 3.0 Tesla (sagittal T1-weighted images, and sagittal, axial and coronal proton-density-weighted images with saturation of fat signal). Ten asymptomatic volunteers were also included as a control group. Patients and controls had a cartilage T2 mapping MRI sequence in addition to the standard MRI protocol. Two musculoskeletal radiologists, blinded to the patient/control condition and pain location, independently reviewed the T2 mapping images. T2 values below 40 ms were considered normal. They rated the number of hyaline cartilage lesions and their grade according to an ICRS-like score (inspired by the International Cartilage Research Society score) in each anatomical compartment (medial and lateral femoro-tibial and anterior patello-femoral joints). In addition, the T2 value of the largest lesion was measured. Patient's pain location was classified in the following categories: anterior, lateral, medial and global. T2 mapping findings were compared to pain location, and retrospectively to the initial standard sequences. Sensitivity and specificity were calculated for MRI with T2 mapping according to pain location for each reader. Kappa coefficient was calculated for inter-reader agreement. We used variance analysis in a linear regression to compare T2 values and ICRS-like classification in each compartment.**

Results: **Sensitivity of MRI with T2 mapping, according to the symptomatic compartment, was respectively: 78% and 87% for Reader 1 and Reader 2 and specificity was 70% for both readers. Kappa coefficient for T2 mapping abnormalities location and pain location was good, with a calculated value of 0.64. There was no significant correlation between ICRS-like classification and T2 values of lesions (p = 0.18).**

Conclusion: **Our results suggest that T2 mapping is an interesting MRI sequence for the exploration of young patients knee pain in case of normal MRI with a standard protocol, with a good correlation between pain location and focal prolongations of the cartilage T2 relaxation time.**

Key-words: Knee, MR – Knee, ligaments, menisci, and cartilage.

Isolated focal cartilaginous knee lesions are a frequent condition in young patients (1), can cause both pain (2) and functional impairment, and may lead to osteoarthritis.

MRI is the gold standard imaging technique for knee pain in young patients with normal radiographs, with high sensitivity and specificity for the detection of meniscal lesions, anterior cruciate ligament disruption, lesions of the tendons and bone marrow abnormalities. On the contrary its use for detection of chondral lesion is less widely accepted; although it is very accurate for deep chondral defects (accuracy superior to 90% for the grades III and IV of the ICRS classification (3)), it is much less sensitive for ICRS grades I and II lesions (4). This means that morphological MRI shows chondral damage at a stage when cartilage is already irreversibly lost.

CT-arthrography and MR-arthrography display better sensitivity and specificity than standard MRI for the detection and classification of low-grade chondral lesions (5), with the downside of intra-articular injection.

MRI T2 mapping of the cartilage is a non-invasive functional imaging technique delivering cartography of the T2 relaxation time of the cartilage without any contrast injection. It is sensitive to tissue anisotropy, and provides compositional information on the cartilage collagen network, water content and proteoglycans concentration (6). T2 mapping has been studied in both animal (7, 8) and human knee cartilage models, especially in the femoro-patellar joint (9). For knee osteoarthritis, it has been shown that T2 mapping is sensitive to T2 prolongation induced by cartilage degeneration (10), and that the cartilage T2 value increases with the severity of osteoarthritis (11). However, some results indicate that T2 values are not correlated with late, radiographic stages of osteoarthritis (12). In the early phase of osteoarthritis, elevated cartilage T2 values as well as cartilage damage have been shown to be associated with findings of pain (13).

It has also been hypothesized that a focal prolongation of the cartilage T2 value could be linked to focal cartilage damage, as foci of increased T2-weighted signal intensity are visible in such lesions on conventional T2 sequences (14).

To our knowledge, the value of T2 mapping for the detection of focal chondral lesions not visible on morphological MRI sequences has not yet been confirmed, and has neither been correlated with unexplained clinical symptoms.

The aim of our study was to assess the correlation of T2 mapping to knee pain location in young patients with a normal baseline standard knee MRI at 3.0 Tesla.

From: 1. Service de Radiologie, Hôpital Bichat - Claude Bernard, Paris, France, 2. Service de Radiologie Ostéo-articulaire, Hôpital Lariboisière, 3. Université Paris Diderot Paris - 7, 4. Unité de Recherche Clinique Hôpital Bichat - Claude Bernard, 5. Service de Chirurgie Orthopédique Hôpital Bichat - Claude Bernard, 6. Centre d'Imagerie Ostéo-articulaire, Clinique du Sport, Bordeaux-Mérignac, France, 7. Hôpital Bichat - Claude Bernard, Inserm U698, Paris, France.
Address for correspondence: Dr B. Dallaudière, M.D., Ph.D., Service de Radiologie, Bichat-Claude Bernard Hospital, 46, rue Henri Huchard, F-75018, Paris, France.
E-mail: benjamindallaudiere@gmail.com

Material and methods

Patients

All patients and controls were informed of the study procedure and gave their informed consent.

We conducted this prospective monocentric observational study from September 2011 to April 2012. Twenty-three consecutive ambulatory patients referred for an MRI examination at our institution were selected if they fulfilled the following criteria:

- Age over 20 years and below 50, in order to increase the probability of normal X-ray and normal knee MRI,
- Knee pain of at least one-month duration, without surgical knee history,
- Normal radiographs (standing antero-posterior view, Lyon - schuss view and femoro-patellar view).
- Normal conventional 3.0 Tesla MRI of the knee with sagittal T1-weighted images, and sagittal, axial and coronal proton-density-weighted (PDW) images with saturation of fat signal. All MRI were reviewed for ligaments, meniscus, enthesis, Hoffa fat, spongious bone and cartilage lesions. Cartilage lesion was defined either as a morphological irregularity of the cartilage, or as a signal abnormality on PDW images.

Exclusion criteria were abnormal radiographs, prior history of knee trauma or surgery, contra-indication to MRI.

Pain characteristics were recorded (duration of symptoms and location in medial, lateral or anterior compartment) at the time of the MRI examination.

The control group consisted of ten healthy volunteers (radiology technologists), selected using the same exclusion criteria. All MRI in the control group were performed with the same protocol as for the symptomatic group, and were normal.

Immediately following the acquisition of the conventional MRI sequences, patients and controls had a cartilage T2 mapping sequence on the patello-femoral and femorotibial joints.

Knee MRI technique

All MRI examinations were performed on a 3-Tesla MR scanner (*GE*® Healthcare MR 750) with a knee coil (8 elements, 8 channels). All exams were performed between 3.00 pm and 5.00 pm, with identical room temperature (18°C) to overcome diurnal and temperature linked variations of the cartilage T2 (15).

All patients rested for 40 minutes in supine position prior to MRI, to overcome variation linked to weight-loading of the knee (16).

During the MR-scan, patients were in supine position, feet first with full limb extension. The conventional MRI protocol included the following sequences:

- Sagittal T1- WI: TR = 588 ms, TE minimum, Nex = 1, FOV 16 cm, thickness 3 mm, spacing 0.5 mm; 24 slices, antero-posterior direction, duration 2 min 17 s
- Sagittal, coronal, and axial PDW sequences with fat-saturation:
- Sagittal PDW sequences: TR/TE: 2362/45 ms, Nex = 2, FOV 16 cm, 3 mm-thickness, 0.5 spacing, 24 slices, duration 3 min 14 s
- Coronal PDW sequences: TR/TE: 2000/45 ms, Nex = 2, FOV 16 cm, 3 mm-thickness, 0.5 spacing, 20 slices, duration 2 min 44 s
- Axial PDW: TR/TE: 2257/45 ms, Nex = 2, FOV 16 cm, 3 mm-thickness, 0.5 spacing, 24 slices, duration 3 min 05 s

A commercially available sagittal T2 mapping sequence (Cartigram, GE Healthcare, Waukeshaw, WI) was performed with the following parameters:

- Axial sequence for the patello-femoral joint: TR = 1000 ms, TE of 6.1, 14.1, 22.1, 30.1, 38.1, 46.1, 54.1 and 62.1 ms, Nex = 2, FOV 16 cm, 256 x 192 matrix, Slices = 9, thickness = 3 mm with 0.6 mm spacing, duration 5 min 09 s.
- Coronal sequence for the femorotibial joints: TR = 1000 ms, TE of 6.1, 14.1, 22.1, 30.1, 38.1, 46.1, 54.1 and 62.1 ms, Nex = 2, FOV 16 cm, 256 x 192 matrix, Slices = 9, thickness = 3 mm with 0.6 mm spacing, duration 5 min 09 s.

Image interpretation

T2 mapping sequences were qualitatively and quantitatively assessed on an ADW workstation with the "functool" software. All MRI images were anonymized.

Two musculoskeletal radiologists (BD with a 3 year experience and JM with a 2 year experience) analyzed the T2 mapping images independently, in random patient/control order, blinded to clinical data, and reported their results using a pre-written reading grid. In accordance with the literature (16, 17) and GE® healthcare engineer, and considering the clinical settings, the threshold for the normal T2 value was set at 40 ms. T2 mapping was considered positive for the presence of a chondral lesion when a prolongation of the T2 above 40 ms was demonstrated on at least two consecutive slices. T2 mapping images were viewed at two different windowing settings using color coding scales; the first with T2 values ranging from 0 to 39 ms, the second with values ranging from 40 to 160 ms. In each joint compartment, radiologists recorded the number of chondral lesions and T2-value of the largest chondral lesion using regions of interest having an area of at least 4 pixels. The largest lesion was graded according the depth of the T2 abnormality, using an ICRS-like classification (Grade 1: superficial lesions; Grade 2: lesions extending down to < 50% of cartilage depth; Grade 3: cartilage defects extending down > 50% of cartilage depth and down but not to the subchondral bone; Grade 4: lesions extending to the subchondral bone).

Once a T2 prolongation was detected, a comparison with the conventional MRI images (sagittal T1-weighted images and PDW with saturation of fat signal images) was performed by the 2 radiologists to retrospectively determine if T2 prolongations were linked to initially overlooked lesions in conventional MRI sequences.

Statistical methods

Statistical analysis was performed using the SAS/STAT® 9.2 software.

Sensitivity and specificity for the presence of chondral lesions were calculated for T2 mapping, according to pain location for each reader.

The kappa coefficient was used to estimate the inter-reader agreement according to pain location. A Wilcoxon test was also used to compare lesions distribution in each joint compartment for the MRI findings of each reader.

The association between the ICRS-like classification of lesions and the T2 value was tested using a regression model (linear regression).

A p value < 0.05 was considered as significant.

Results

Population

Twenty-three consecutive patients (symptomatic group: 16 men and

7 women), and 10 healthy volunteers (asymptomatic group 6 men and 4 women) were included in this study. The mean and median ages were 36.5 and 34 years (SD was 12.8 years). Eleven patients had anterior knee pain, 6 had medial pain, 1 had lateral pain and 5 had global knee pain. In patients with global knee pain, the three joint compartments were considered as symptomatic. The mean duration of knee pain was 39 days (SD 6.1 days).

In the 10 volunteers of the non-symptomatic control group, the mean and median ages were 33 and 34.5 years (SD was 10.1 years).

Lesion detection using T2 mapping and standard images

In the patient group, Reader 1 found T2 mapping focal abnormalities in the symptomatic compartments of 18 out 23 patients (13 out of 16 symptomatic anterior compartments, 8 out of 11 symptomatic medial compartments and 1 out of 6 symptomatic lateral compartment).

Reader 2 found T2 mapping focal abnormalities in the symptomatic compartments of 20 out 23 patients (16 out of 16 symptomatic anterior compartments, 8 out of 11 symptomatic medial compartments and 3 out of 6 symptomatic lateral compartments).

Figures 1 and 2 illustrate the aspect of the T2 mapping abnormalities in the patient group. Table I summarizes the T2 mapping findings in the symptomatic joint compartments of the patient group.

In the 10 volunteers of the control group, the two readers found the same T2 mapping focal abnormalities in 2 anterior compartments and 1 medial compartment. No T2 mapping abnormality was found in the lateral compartment. Table II summarizes the T2 mapping findings in the control group.

T2 mapping abnormalities and pain location

For Reader 1, sensitivity of the T2 mapping sequence in the patient group was 78%. For Reader 2 sensitivity of the T2 mapping sequence in the patient group was 87%. For both readers, specificity of T2 mapping in the control group was 70%.

Five T2 mapping lesions in 5 patients were retrospectively seen on conventional MR images. Figure 3 illustrates such a lesion on a patellar cartilage.

There were differences of interpretation between the two readers concerning the lateral and anterior compartment. This discrepancy may

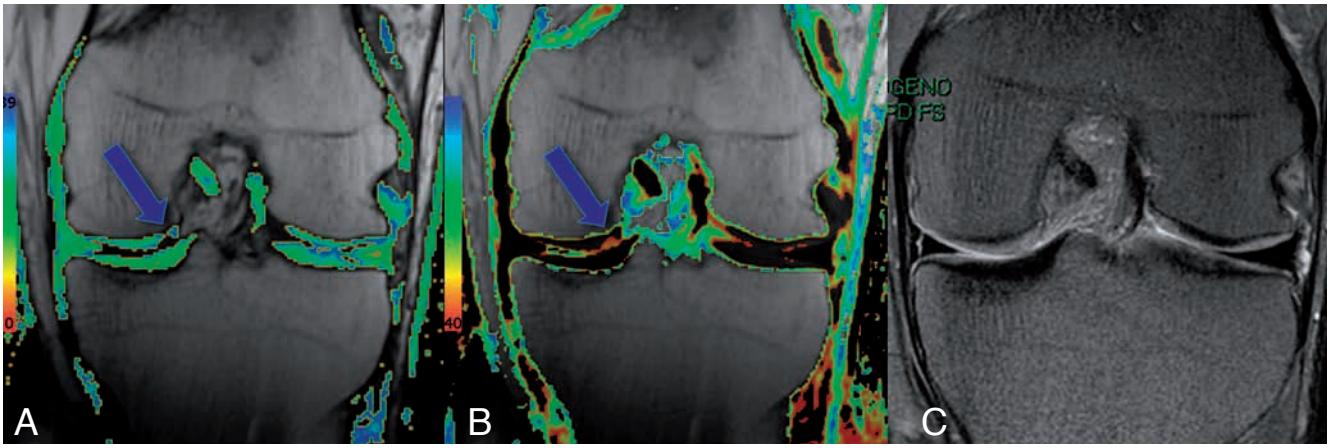

Fig. 1. — Medial cartilage abnormality (blue arrows) in a symptomatic medial compartment, visible as a focal prolongation of the T2 value on the coronal T2 maps (A: 0 ms ≤ T2 ≤ 39 ms; B: 40 ms ≤ T2) compared to the normal coronal PDW image (C).

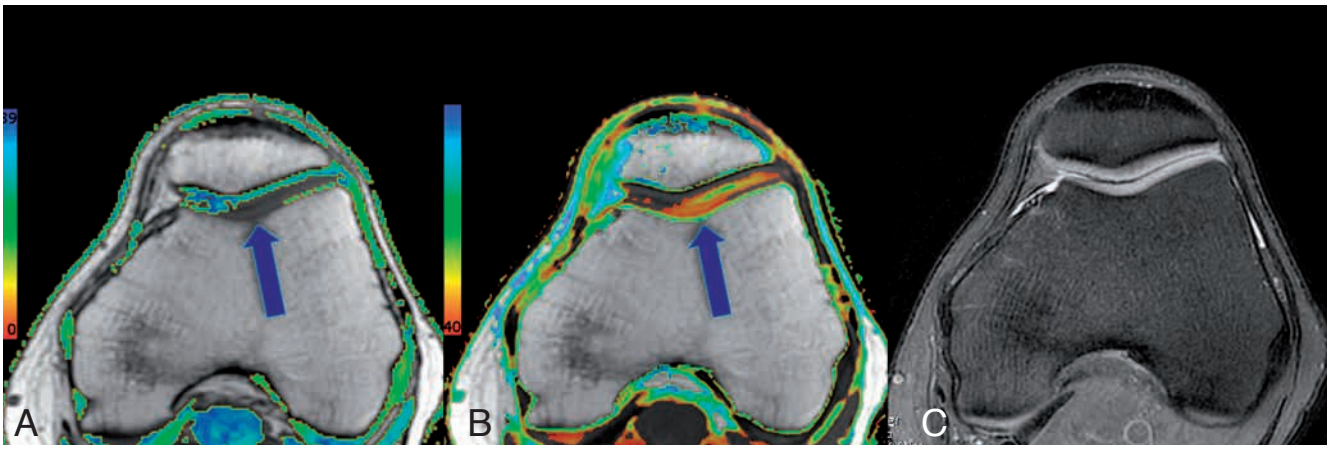

Fig. 2. — Anterior cartilage abnormality (blue arrows) in a symptomatic anterior compartment, visible as a focal prolongation of the T2 value on the axial T2 maps (A: 0 ms ≤ T2 ≤ 39 ms; B: 40 ms ≤ T2) compared to the normal axial PDW image (C).

Table I. — T2 mapping findings for Reader 1 (R1) and Reader 2 (R2) in the symptomatic joint compartments. No T2 mapping abnormality was found in the only patient with a lateral knee pain (not shown).

	11 patients with pain in anterior compartment		6 patients with pain in medial compartment		5 patients with global knee pain					
Reader	R1	R2	R1	R2	R1			R2		
Number of symptomatic compartments with T2 mapping lesions	9	11	5	4	4 Anterior	3 Medial	1 Lateral	5 Anterior	4 Medial	3 Lateral
Number of T2 mapping lesions	17	24	5	8	7	8	1	13	4	4
ICRS-like classification range	1-4	2-3	3-4	1-3	2-3	2-3	3	3	3	2-3
T2 value range (ms)	44-70	42-54	42-66	48-59	43-63	54-68	73	42-52	46-51	46-49

be explained by the frequent finding of an increased T2 value in the trochlear groove, and at the medial aspect of the lateral femoral condyle, that was sometime considered as a lesion. This was also found in some of our controls (Figure 4) and may be explained by a "magic angle" effect (18).

Inter-reader agreement

Common agreement for pathologic compartments in T2 mapping according to pain location was 0.64 (Kappa coefficient).

The Wilcoxon test for lesions distribution in knee joint compartments did not reveal a significant difference of lesions cartography for Reader 1 and 2 ($p = 0.37$).

T2 values and ICRS-like classification

There was no correlation between the T2 value and the ICRS-like classification of the lesions in all three joint compartments: medial ($p = 0.41$ for Reader 1, $p = 0.69$ for Reader 2), lateral ($p = 0.56$ for Reader 1, $p = 0.83$ for Reader 2) and anterior zone ($p = 0.11$ for Reader 1, $p = 0.19$ for Reader 2).

Discussion

Sensitivity and specificity of T2 mapping for the detection of focal T2 prolongations in the cartilage of the symptomatic compartments of the patients were excellent (sensitivity 78% and 87%, specificity 70% for both readers), with a substantial inter-reader agreement (kappa = 0.64). However, no significant correlation was found between the ICRS-like classification and T2 values of the lesions.

To our knowledge, this is the first study that prospectively analyzed the correlation between knee pain location and T2 mapping abnormalities at 3.0 Tesla in young adults with a normal conventional MRI.

T2 mapping is one of several MRI cartilage imaging techniques currently investigated, including T2* mapping, T1 rho mapping, dGEMRIC, sodium imaging and diffusion-weighted imaging (19). None of these techniques is used on a daily basis in clinical practice.

In our experience and according to the literature (10-12,19), T2 mapping is a sensitive technique for chondral lesions. However, it has several limitations. T2-value of the cartilage is dependent on field strength (17), moderately dependent on temperature (15) and more notably dependent on physical activity, weight-loading of the knee (16) and age (14). For these reasons, in the present study, MRI exams were performed on the same MRI device, during the same period of the day and after a 40 minutes resting time, while room temperature was kept constant at 18°C. Another limitation of the technique is that the T2 of the cartilage depends on the orientation of

Table II. — T2 mapping findings for Reader 1 (R1) and Reader 2 (R2) in the control group.

	Anterior compartment		Medial compartment		Lateral compartment	
Reader	R1	R2	R1	R2	R1	R2
Number of compartments with T2 mapping lesions	2	2	1	1	0	0
Number of T2 mapping lesions	2	2	2	2	0	0
ICRS-like classification range	1 to 2	2	2 to 3	2	…	…
T 2 value range (ms)	42-46	41-47	42-44	43-49	…	…

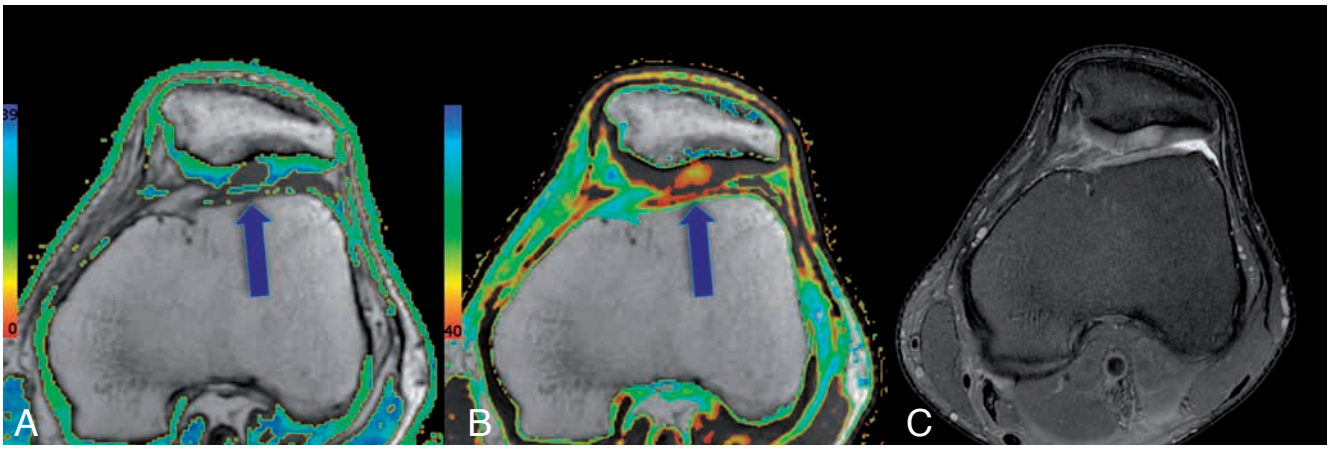

Fig. 3. — Anterior cartilage abnormality (blue arrows) in a symptomatic anterior compartment, visible as a focal prolongation of the T2 value on the axial T2 maps (A: 0 ms ≤ T2 ≤ 39 ms; B: 40 ms ≤ T2), and retrospectively visible on the axial PDW image (C) as an inconspicuous hypersignal.

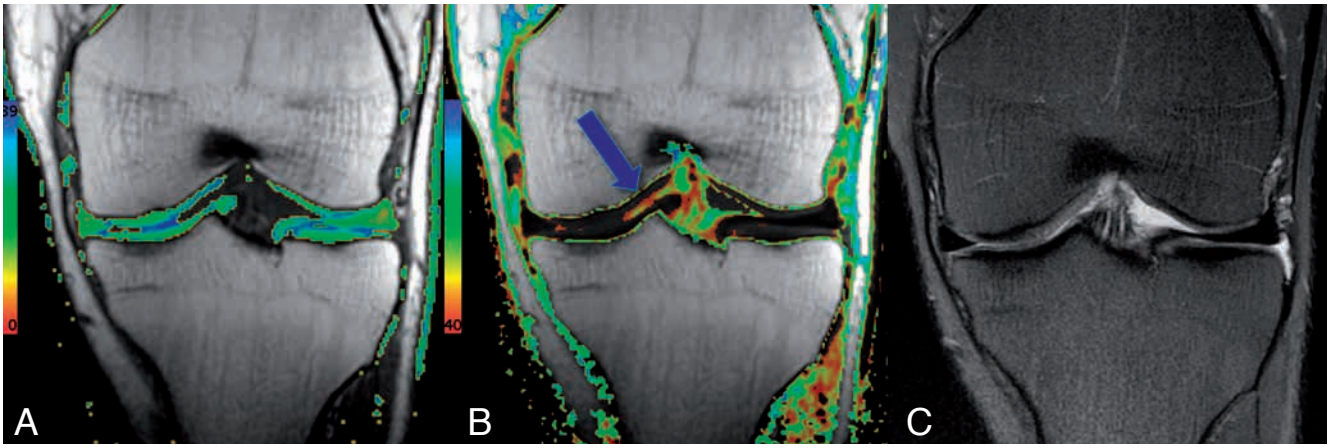

Fig. 4. — Superficial linear prolongation of the T2 value of the medial femoral cartilage (blue arrow) on the coronal T2 maps of an asymptomatic patient from the control group, interpretated as a "magic angle" effect (A: 0 ms ≤ T2 ≤ 39 ms; B: 40 ms ≤ T2) compared to the normal PDW image (C).

the collagen fibers. This "magic angle" effect, described by Mosher et al. (18), is at its maximum when the cartilage is oriented 55° to B_0, accounting for an increased T2 value in the trochlear groove, and at the medial aspect of the lateral femoral condyle, found in some patients as well as controls.

Our main results show that, as suggested by the literature (19), T2 mapping imaging may potentialize MRI ability to detect focal chondral lesions in the knee, when T2 mapping abnormalities are correlated to pain location. Although non-full thickness chondral defects are associated with knee pain (2) the mecanism is indirect and probably implies the release of cytokines and other signaling molecules from the cartilage (20). However, it has not been proven yet that isolated T2 mapping focal abnormalities without visible lesion on anatomical MRI are bound to turn into more severe chondral lesions.

At the minimum, the presence of a T2 mapping focal chondral abnormality, linked to pain location, should support a more precocious indication to CT-arthrography or MR-arthrography.

An interesting secondary result in the present study is that, in five patients, a lesion visible on the T2 mapping images in a painful joint compartment was retrospectively visible on the proton-density-weighted images with saturation of fat signal. These lesions were initially overlooked as they displayed inconspicuous hyper signal on proton-density weighted images. In these cases, T2 mapping improved the diagnostic performances of MRI.

Our study has some limitations. The number of patients included in our study is small, but it is to our best knowledge the only series correlating MRI T2 mapping to pain in patients with a normal conventional MRI protocol. It lacks the arthroscopic proof for the chondral defects. The body mass index of the patients and controls were not recorded, and cannot be matched. Location of the T2 prolongation was correlated to patient pain location, but we didn't study whether it was correlated to pain intensity and duration, or to knee articular function.

In conclusion, our results suggest that T2 mapping is an interesting MRI sequence for the exploration of young patients knee pain in case of normal MRI with a standard protocol, with a good correlation between pain location and focal prolongations

of the cartilage T2 relaxation time. It may improve the diagnostic accuracy of MRI for focal chondral lesions, and should help decide whether and MR-arthrography or CT-arthrography is necessary.

References

1. Widuchowski W., Widuchowski J., Trzaska T.: Articular cartilage defects: study of 25,124 knee arthroscopies. *Knee*, 2007, 14: 177-812.
2. Zhai G., Cicuttini F., Ding C., et al.: Correlates of knee pain in younger subjects. *Clin Rheumatol*, 2007; 26: 75-80.
3. Galea A., Giuffre B., Dimmick S., Coolican M.R.J., Parker D.A.: The accuracy of magnetic resonance imaging scanning and its influence on management decisions in knee surgery. *Arthroscopy*, 2009, 25: 473-480.
4. Figueroa D., Calvo R., Vaisman A., et al.: Knee Chondral Lesions: Incidence and Correlation Between Arthroscopic and Magnetic Resonance Findings. *Arthroscopy*, 2007, 23: 312-315.
5. Smith T.O., Drew B.T., Toms A.P., Donell S.T., Hing C.B.: Accuracy of magnetic resonance imaging, magnetic resonance arthrography and computed tomography for the detection of chondral lesions of the knee. *Knee Surg Sports Traumatol Arthrosc* 2012, 20: 2367-2379.
6. Watrin-Pinzano A., Ruaud J.-P., Olivier P., et al.: Effect of proteoglycan depletion on T2 mapping in rat patellar cartilage. *Radiology*, 2005, 234: 162-170.
7. Watrin A., Ruaud J.P.B., Olivier P.T.A., et al.: T2 Mapping of Rat Patellar Cartilage. *Radiology*, 2001, 219: 395-402.
8. Kim D.J., Suh J.-S., Jeong E.-K., Shin K.-H., Yang W.I. Correlation of laminated MR appearance of articular cartilage with histology, ascertained by artificial landmarks on the cartilage. *J Magn Reson Imaging*, 1999, 10: 57-64.
9. Frank L.R., Wong E.C., Luh W.-M., Ahn J.M., Resnick D.: Articular Cartilage in the Knee: Mapping of the Physiologic Parameters at MR Imaging with a Local Gradient Coil – Preliminary Results. *Radiology*, 1999, 210: 241-246.
10. Li X., Benjamin Ma C., Link T.M., et al.: In vivo T1 [rho] and T2 mapping of articular cartilage in osteoarthritis of the knee using 3 T MRI. *Osteoarthritis Cartilage*, 2007, 15: 789-797.
11. Dunn T.C., Lu Y., Jin H., Ries M.D., Majumdar S.: T2 Relaxation Time of Cartilage at MR Imaging: Comparison with Severity of Knee Osteoarthritis. *Radiology*, 2004, 232: 592-598.
12. Koff M.F., Amrami K.K., Kaufman K.R.: Clinical evaluation of T2 values of patellar cartilage in patients with osteoarthritis. *Osteoarthritis Cartilage*, 2007, 15: 198-204.
13. Baum T., Joseph G.B., Arulanandan A., et al.: Association of magnetic resonance imaging-based knee cartilage T2 measurements and focal knee lesions with knee pain: data from the Osteoarthritis Initiative. *Arthritis Care Res*, 2012, 64: 248-255.
14. Mosher T.J., Dardzinski B.J., Smith M.B.: Human articular cartilage: influence of aging and early symptomatic degeneration on the spatial variation of T2-preliminary findings at 3 T. *Radiology*, 2000, 214: 259-66.
15. Nelson T.R., Tung S.M.: Temperature dependence of proton relaxation times in vitro. *Magn Reson Imaging*, 1987, 5: 189-199.
16. Apprich S., Mamisch T.C., Welsch G.H., et al.: Quantitative T2 mapping of the patella at 3.0T is sensitive to early cartilage degeneration, but also to loading of the knee. *Eur J Radiol*, 2012, 81: 438-443.
17. Gold G.E., Han E., Stainsby J., et al.: Musculoskeletal MRI at 3.0 T: relaxation times and image contrast. *AJR*, 2004, 183: 343-351.
18. Mosher T.J., Smith H., Dardzinski B.J., Schmithorst V.J., Smith M.B.: MR imaging and T2 mapping of femoral cartilage: in vivo determination of the magic angle effect. *AJR Am J Roentgenol*, 2001, 177: 665-669.
19. Crema M.D., Roemer F.W., Marra M.D., et al.: Articular Cartilage in the Knee: Current MR Imaging Techniques and Applications in Clinical Practice and Research. *Radiographics*, 2011, 31: 37-61.
20. Dieppe P.A., Lohmander L.S.: Pathogenesis and management of pain in osteoarthritis. *The Lancet*, 2005, 365: 965-973.