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Background

Hyaluronic Acid (HA) viscosupplementation is usually employed for conservative management of early knee osteoarthritis (OA). To date a reproducible and effective method to evaluate HA effects on articular cartilage still remains to develop. To detect articular cartilage loss or damage, a Magnetic Resonance Imaging (MRI) of the knee can be performed. Because of the small thickness of articular cartilage and long acquisition time necessary to obtain high resolution images, the use of the ultra high field (UHF) magnets can be advantageous. So the employment of a 7 Tesla (T) magnet represents a possibility to study in vivo articular cartilage. The highest resolution of 7T imaging could allow to detect morphological data, such as initial and limited cartilaginous defects, but also and above all the structural alterations with greater accuracy and shorter acquisition times than the lower magnets field. Fig 1.

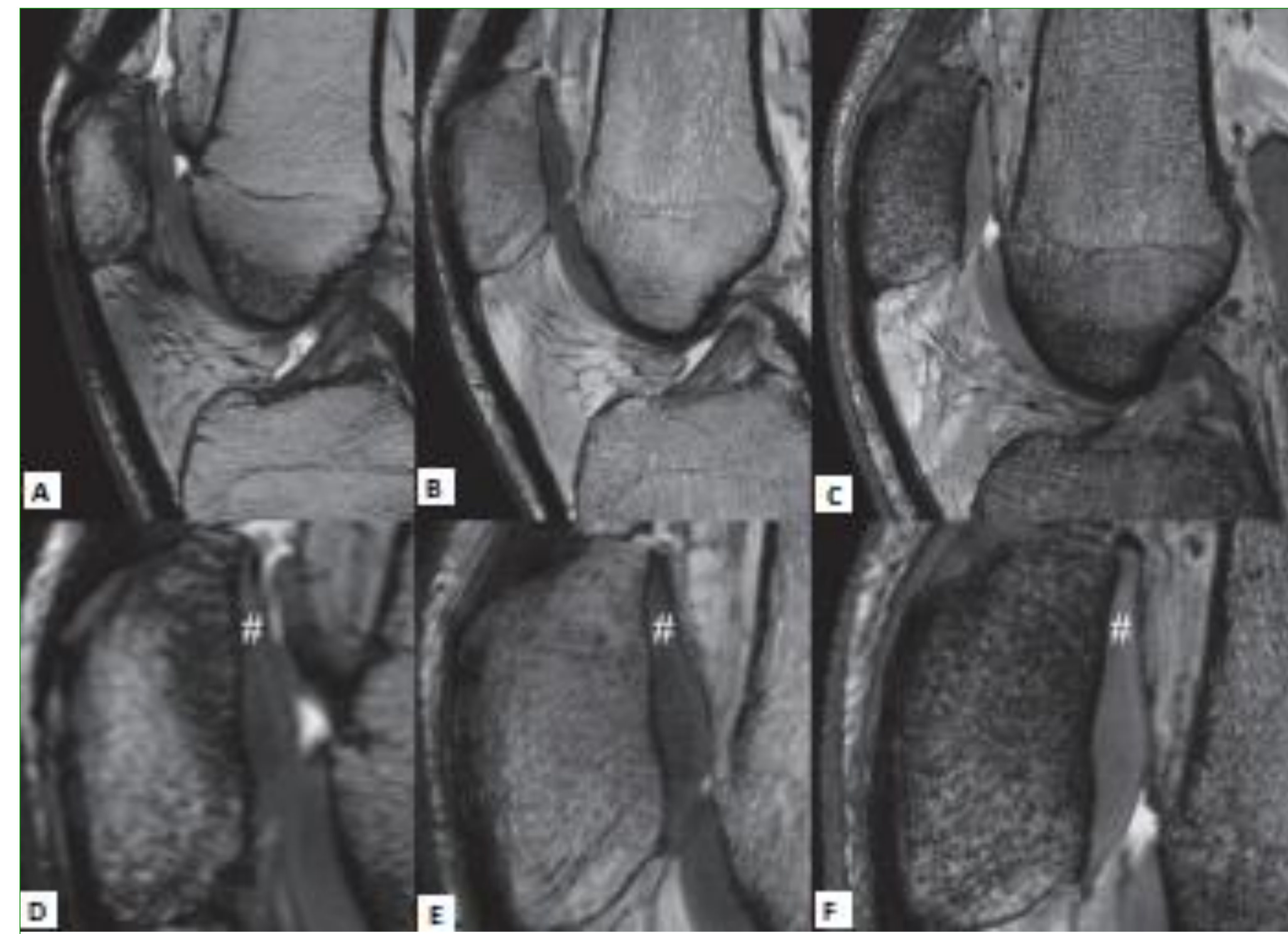


Fig.1. Images A-C show medium field MRI 1.5 T (A), high field MRI 3 T (B), and UHF-MRI 7 T (C) of the knee cartilage in the same 31-year-old male. Comparing the images acquired at increasing field strength, we can observe an improvement in spatial resolution and image detail. Images D-F focus on the patellar cartilage (#) and show a better definition of the borders and a higher spatial resolution obtained at 7 T, with a pixel size of 130 micron (F), in comparison with 1.5 T (D) and 3 T MRI (E).

Objectives

The purpose of this study is to evaluate the efficacy of a new HA-based product - Hymovis® - in the management of early OA of the knee and its effect on patients symptoms and articular cartilage.

Design and methods

14 patients (20 knees), 7 males and 7 females, were prospectively enrolled in the present study and treated by 2 consecutive injections of Hymovis at one week interval, from 2017 April the 1st to 2018 May the 31st and received target knee MRI 3 times during this study. All MRI procedures were obtained with an UHF up to 7T and all Patients were clinically evaluated 5 times during the follow-up, from Visit(V)0 to V4. Knee MRIs were performed at V1, before the first HA injection; at V3, after 45 days from the second HA injection; and at V4, after 180 days from the second HA injection. Clinical evaluations consisted of WOMAC index recorded at V1 and V4, and VAS recorded at V0,V1, V3 and V4. Main inclusion criteria were: age between 40 and 80 years old, BMI<40, symptomatic and radiological knee OA (K&L grade II or III) and mean knee pain at rest > 40 mm (VAS).

Results

We report good clinical outcomes with statically significant reduction in symptoms with an increased knee and global activity functions. The total WOMAC score decreased from 30.8 ± 14.2 at V1 to 12.1 ± 7.7 at V4 ($p<0,001$), while mean VAS values decreased from 60.8 ± 12.0 at V0 to 15.1 ± 14.9 at V4 ($p<0.001$). To date we just report preliminary results related to MRI acquisitions.

We recorded an increasing in cartilage volume and thickness in the most of the patients with fibrous tissue formation in some cartilage defects, but we didn't found MRI signals clearly referable to cartilage regeneration. Fig. 2 and 3

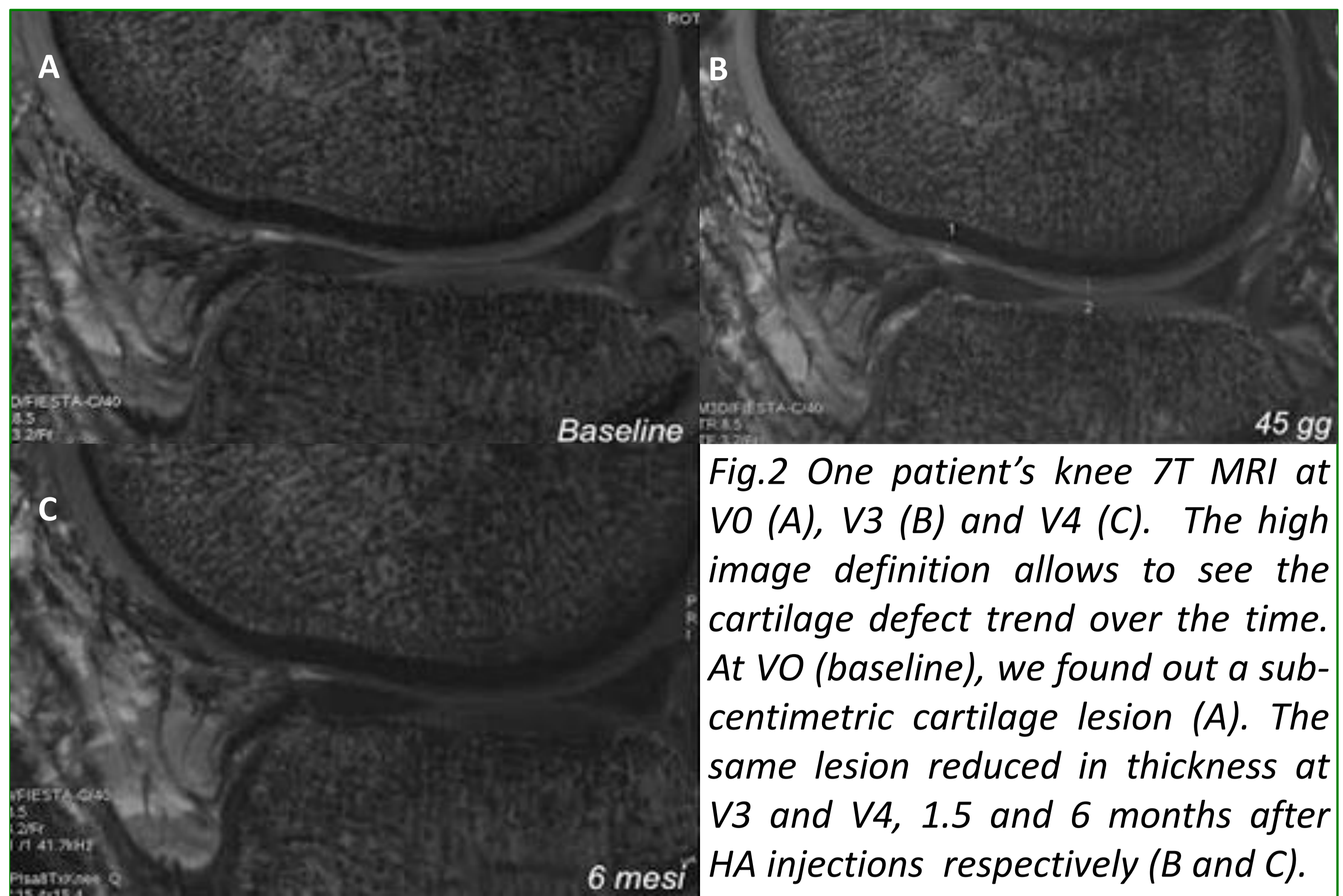


Fig.2 One patient's knee 7T MRI at V0 (A), V3 (B) and V4 (C). The high image definition allows to see the cartilage defect trend over the time. At V0 (baseline), we found out a sub-centimetric cartilage lesion (A). The same lesion reduced in thickness at V3 and V4, 1.5 and 6 months after HA injections respectively (B and C).

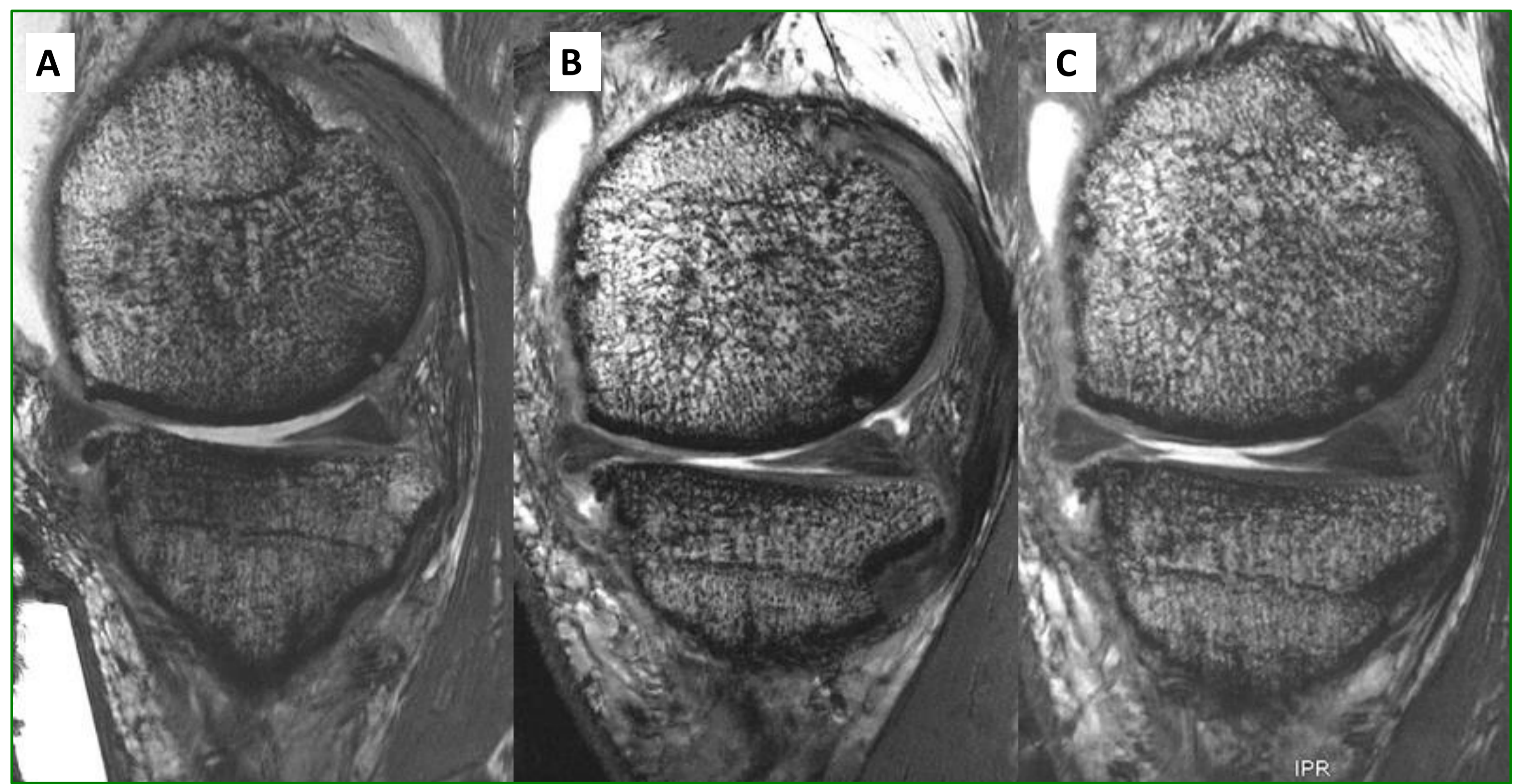


Fig.3. 7T MRI of the knee showing cartilage thickness increase over the time: at V0 (A), V3 (B) and V4 (C).

Discussion

Several reports focused on the viscosupplementation clinical efficacy and on the use of high-field MRI to detect cartilage defects are available in the literature. However, to date, we didn't found any study estimating the effectiveness of HA viscosupplementation on the cartilage structure. In our work the use of a 7T magnet allowed us to evaluate the cartilaginous structure before and after using HA viscosupplementation.

Conclusion

Hymovis showed good clinical outcomes and the preliminary MRI results reported confirm the possibility to employ 7T magnets to evaluate early changes in cartilage structure in vivo, even if the use of HA viscosupplementation doesn't seem to modify cartilage morphology over the time. Statically significant reduction in symptoms and significant improvement in global activity functions were confirmed.

References

1. Benazzo F, Perticarini L, Padolino A, Castelli A, Gifuni P, Lovato M, Manzini C, Giordan N. A multi-centre, open label, long-term follow-up study to evaluate the benefits of a new viscoelastic hydrogel (Hymovis®) in the treatment of knee osteoarthritis. *Eur Rev Med Pharmacol Sci.* 2016 Mar;20(5):959-68.
2. Zorzi C, Rigotti S, Screpis D, Giordan N, Piovan G. A new hydrogel for the conservative treatment of meniscal lesions: a randomized controlled study. *Joints.* 2016 Jan 28;3(3):136-45.
3. Friebe B, Richter M, Penzlin S, Stärke C, Kropf S, Lohmann C, Fischbach F, Speck O. Assessment of Low-Grade Meniscal and Cartilage Damage of the Knee at 7 T: A Comparison to 3 T Imaging With Arthroscopic Correlation. *InvestRadiol.* 2018 Jul;53(7):390-396.
4. Huang GS, Lee HS, Chou MC, Shih YY, Tsai PH, Lin MH, Lin CY, Lee CH, Chung HW. Quantitative MR T2 measurement of articular cartilage to assess the treatment effect of intra-articular hyaluronic acid injection on experimental osteoarthritis induced by ACLX. *Osteoarthritis Cartilage.* 2010 Jan;18(1):54-60.
5. Aringhieri G, Vitali S, Rossi P, Caramella D. The new frontier of imaging: the micron. *Clin Exp Rheumatol.* 2018 Jan-Feb;36(1):169.