

Osteoarthritis and Cartilage



Advanced hip osteoarthritis: magnetic resonance imaging aspects and histopathology correlations

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SUMMARY

Objectives: To correlate magnetic resonance imaging (MRI) aspects of the femoral head with histological findings in advanced hip osteoarthritis (OA), with special emphasis on bone marrow edema (BME).

Methods: MRI was performed in patients with advanced hip OA scheduled for hip arthroplasty. Coronal T1-, fat-suppressed T2-, T1 with gadolinium intravenous injection sequences were obtained on a 1.5 T MR-scanner within 1 month before surgery.

Coronal MR images corresponding to the ligamentum teres plane were analyzed by two independent readers blinded to histological data. Normal bone marrow, subchondral cyst, subchondral fracture, edema-like, necrosis-like, and necrosis MR patterns were reported on a synthesis scheme. After surgery, the femoral heads specimens were cut through the ligamentum teres plane and histologically analyzed for correlations.

Results: Twenty-three femoral heads were analyzed (female 56.5%, mean age 64.5 years). Edema-like MR pattern was correlated with histological (H) edema (Kappa (K): 0.77). Necrosis-like MR pattern was correlated with H fibrosis (K: 0.49) and with H necrosis (K: 0.24). Cyst MR pattern was correlated with H bone cysts (K: 0.58). Necrosis MR pattern corresponded to a mixture of histological lesions. Sensitivity and specificity of MRI varied from 26% to 80% and from 86% to 95% respectively.

Conclusion: In advanced hip OA, the so-called “BME” MR lesion corresponds to a combination of edema, fibrosis, and necrosis at histopathology. When the classical “BME” is more specifically separated into edema-like and necrosis-like MR patterns, MR Imaging and histological findings show substantial agreement, with edema-like MR pattern mainly corresponding to histological edema.

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Introduction

Osteoarthritis (OA) is a heterogeneous and multifactorial disease characterized by progressive loss of hyaline articular cartilage and development of altered joint congruency, subchondral sclerosis, intraosseous cysts, and osteophytes. Hip OA is an incapacitating disease and a major public health problem^{1,2}. Today there are over 200,000 total hip replacements performed per year in the United States¹.

Magnetic Resonance imaging (MRI) increases the possibilities in hip and knee OA research and offers insights into the pathogenesis of the disease. Indeed, MRI is commonly used to visualize articular cartilage and other joint structures such as subchondral bone and synovium that are now recognized as parts of the disease process.

Among these lesions, the so-called “bone marrow edema” (BME) is a MRI-determined abnormality, appearing as an ill-defined area with low signal intensity on T1-weighted spin-echo (SE) sequences, and high signal intensity on T2-weighted fat-suppressed SE sequences or short TI inversion recovery (STIR) images³. The prognosis role of BME has been emphasized in the recent literature, especially for knee OA, in which correlations with severity of radiographic grading and pain or OA progression have been documented^{4–7}.

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Table 1

MRI descriptions: low and high signal intensity is established in comparison to normal fatty marrow

Lesion	Description	Diagnosis
1		Normal hematopoietic marrow
2		Normal fatty marrow
3	Ill-defined, low signal intensity on T1-weighted images and high signal intensity on T2 fat-suppressed images. Complete homogenization after gadolinium intravenous injection	Edema-like ¹¹
4	Well defined, low signal intensity on T1-weighted images and high signal intensity on T2 fat-suppressed images. Incomplete homogenization after gadolinium intravenous injection	Necrosis-like ¹¹
5	Low intensity signal on T1- and T2 fat-suppressed images. Variable after gadolinium intravenous injection	Sclerosis ⁸
6	Well defined, low signal on T1- and T2 fat-suppressed images. No enhancement after gadolinium intravenous injection	Necrosis ⁸
7	Minor deformity of the subchondral bone plate and presence of a low signal intensity line (perpendicular to the trabecular network and parallel to the subchondral bone plate) more visible on T1- and T2 fat-suppressed images, with BME in periphery	Subchondral fracture ⁸
8	Well defined, round, homogeneous with low signal intensity on T1-weighted images and with pronounced hyperintensity on T2 fat-suppressed images. Linear intensification in suburb after gadolinium intravenous injection	Cystic bone marrow ¹¹

The term BME has been used in association with a wide spectrum of pathological conditions, including transient osteoporosis of the hip, post-traumatic contusion, insufficiency fractures, osteonecrosis of the femoral head, rapidly destructive OA, and arthritis⁸. Two studies on knee OA have suggested that areas of BME were in fact not only correlated with histological BME but also with areas of bone marrow necrosis and fibrous tissue^{9,10}. Thus, the terms “BME pattern”, “BME-like changes”, or even “subchondral bone marrow lesions” have been proposed as more advisable^{9,11}. Finally, it was recently proposed that BME observed at MRI should be separated more specifically into edema-like and necrosis-like patterns¹¹.

Contrasting with knee OA, very few data are available on bone marrow MR features in hip OA and on the histopathological significance of BME in this particular joint. One recent study only found that the BME pattern corresponds to a mixture of histological lesions including edema, necrosis, and fibrosis lesions¹².

The aim of this study was to correlate MRI patterns and histological findings in hip OA, with special emphasis on BME.

Methods

From September to December 2007, a prospective study was designed to evaluate MRI findings and their correlations with histology in hip OA. Because pathological specimens can be obtained only at the time of joint replacement, the study concerned only the femoral heads of advanced hip OA.

Patient selection

All patients with advanced hip OA scheduled to undergo surgical hip replacements in our Orthopedic Department were eligible. Exclusion criteria were declining participation to the study, contraindications for

MRI, rapidly destructive hip OA¹³, and OA secondary to specific diseases (Paget's disease, avascular necrosis or rheumatoid arthritis) or severe dysplasia¹⁴. Informed consent was obtained.

MRI

All patients underwent hip MRI within 1 month before surgery. The MRI exams were performed with a 1.5 T MR scanner (*Philips Intera*). Images were obtained in the coronal plane using T1 SE (time to echo (TE)/time to repetition (TR) 18/500 ms); fast spin-echo (FSE) T2-weighted with fat saturation (TR range/TE range, 3000–6000/60–75, echo-train length (ETL) of 8); T1 SE with gadolinium injection sequences, (slice thickness 3 mm, and matrix 512 × 204). The femoral heads only were analyzed because it was not possible to obtain suitable material for histopathology from acetabulum. In addition, the study focused on the coronal slice corresponding to the femoral head fovea, which allowed direct topographic correlation with the corresponding sample at histopathology.

MRI examinations were analyzed independently by two readers (two staff radiologists with 5 years and more than 15 of experience in musculoskeletal MR imaging) blinded to histopathological data. Eight different elemental MR lesions were described in keeping with published MR descriptions (Table 1). For categorization, we used the distinction of BME changes between *edema-like* and *necrosis-like*¹¹. An *edema-like* pattern corresponded to an ill-defined area, with low signal intensity on T1-weighted images, high signal intensity on T2 fat-suppressed images, and complete homogenization after gadolinium intravenous injection. A *necrosis-like* pattern corresponded to a well-defined area, with low signal intensity on T1-weighted images, high signal intensity on T2 fat-suppressed images, and incomplete and inhomogeneous enhancement after gadolinium intravenous injection.

Discrepancies between the two radiologists were resolved by consensus.

The tight ball and socket constitution of the hip joint made it difficult to distinguish, without prior intra-articular contrast injection, the acetabular cartilage from the adjacent femoral cartilage under limited image resolution. So, cartilage abnormalities were not analyzed.

For each femoral head, MRI lesions observed on the ligamentum teres section were drawn on a synthesis scheme (Fig. 1)⁹.

Histopathology

After total hip arthroplasty the femoral heads were instantly fixed in a 4% neutral buffered formalin solution and then cut into 1-mm-thick coronal slices. The slices were photographed and then decalcified with a rapid decalcifier (RDO, prepared in our laboratory). After decalcification, the slices were cut into five or six samples, depending on the femoral head size, and the location of the samples was recorded on a scheme (Fig. 1). Each sample was processed into paraffin wax, cut into 4- μ m-thick slices and stained with hematoxylin and eosin. Finally, the analyzed area corresponded to a 4 μ m coronal section crossing the ligamentum teres plane.

Histopathological analysis was performed by a pathologist experienced with bone diseases and OA who was blinded to MRI data. Every anatomical zone was precisely described according to the classification in Table II. The lesions on each slide were rated according to a semi-quantitative method. For each slide, the pathologist selected the predominant histological lesion(s) (Table II).

Correlation MRI/histology

Histopathological and imaging analyses were performed independently and in a blinded manner. Comparison between the

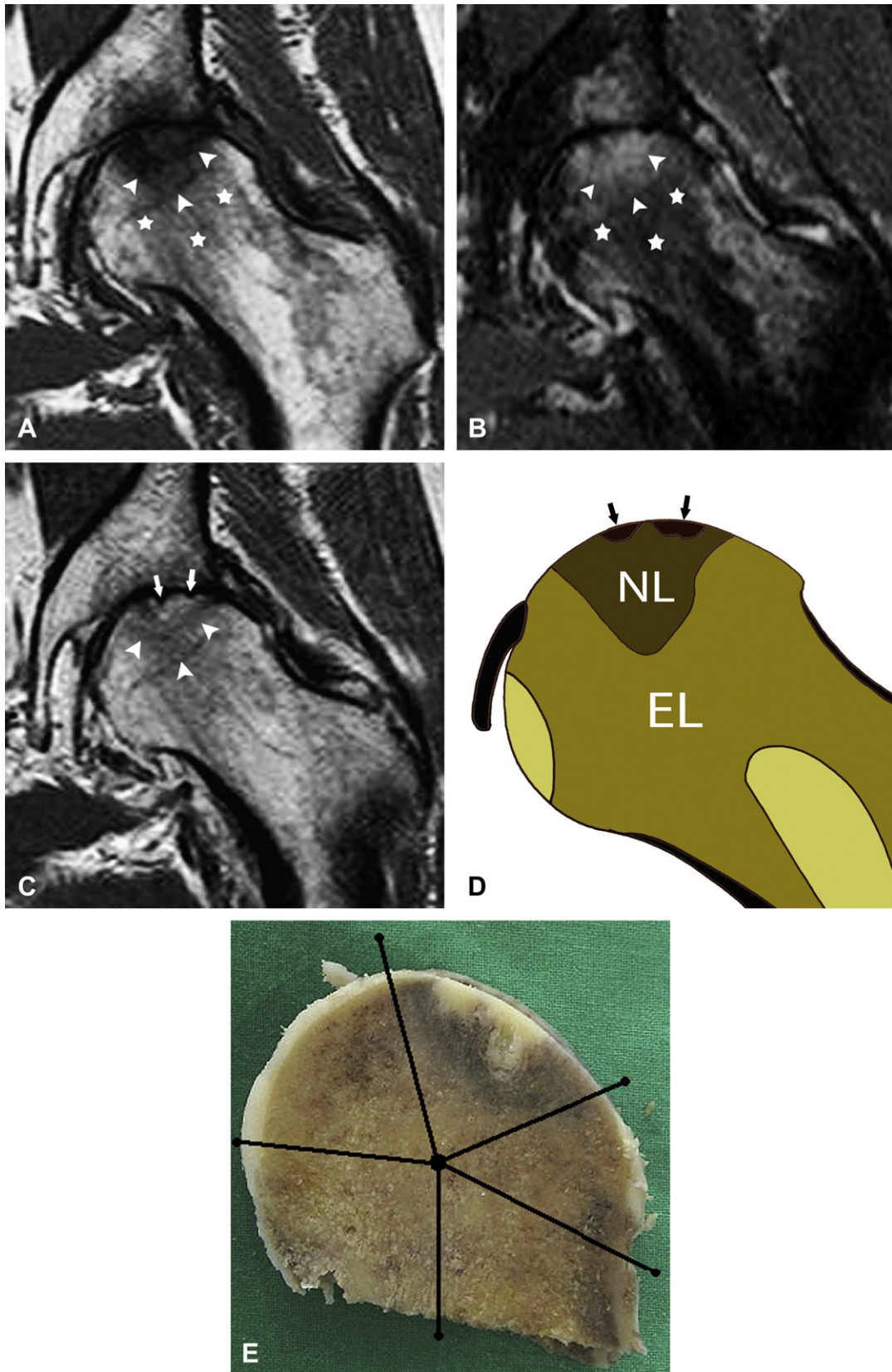


Fig. 1. Coronal T1 SE-weighted (A) and FS T2 FSE-weighted (B) MR images through the femoral head fovea showing the edema-like (stars) and necrosis-like (arrowheads) MR patterns. Coronal T1 SE-weighted MR section after gadolinium intravenous injection (C) exhibiting the incomplete enhancement of the necrosis-like lesion (arrowheads) and the homogenization of the edema-like lesion. The necrosis MR pattern displays no enhancement (arrows). Schematic drawing obtained (D) showing the edema-like pattern (EL), the necrosis-like pattern (NL) and the necrosis pattern (arrows). (E) The photographed slice of the femoral head.

Table II
Histological descriptions

Lesion	Description	Diagnosis
1		Normal hematopoietic marrow
2		Normal fatty marrow
3	Accumulation of eosinophilic extracellular fluid into intertrabecular spaces (pale pink), swollen fat cells and incipient disintegration of fat cells	BME
4		Bone marrow fibrosis
4'	Replacement of fatty marrow with collagenous fibers +/- vessels (orange)	Bone marrow fibrosis and vessels
5	Accumulation of eosinophilic material, (pink), with loss of nuclei	Bone marrow necrosis
6	Discontinuity into intertrabecular spaces	Subchondral fracture
7	Mucinous cavities (blue-shaded) without cover	Pseudocysts

photograph of the histological area and of the selected MR image ensured that the same section was analyzed by both methods. For each area of the femoral heads, the predominant histological lesion (s) identified by the pathologist and the MRI patterns noted on the scheme were established, so that the correlations could be calculated in the same area (Fig. 2). Histological findings were considered as the gold standard.

Statistical analysis

Continuous variables were described by their median and range, and qualitative variable by their count and proportion. Characteristics of the included and excluded patients were compared by Chi-squared test or by Fisher's exact test for qualitative variables (characteristics of the population) and by Mann–Whitney *U* test for quantitative variables. The inter-rater agreement for MRI was measured using the Kappa (*K*) coefficient. The reliability of MRI in accurately identifying the histological lesions was also assessed using *K* statistic, with its 95% confidence intervals (CI), and was interpreted as follows: 0.00 = poor agreement, 0.00–0.20 = slight agreement, 0.21–0.40 = fair agreement, 0.41–0.60 = moderate agreement, 0.61–0.80 = substantial agreement, 0.81–1.00 = almost perfect agreement¹⁵. For each histological elemental lesion, the diagnostic performances of MRI were quantified by the sensitivity (*Se*) (true positives/(true positives + false negatives) × 100), the specificity (*Spe*) (true negatives/(true negatives + false positives) × 100) and positive (true positives/(true positives + false positives) × 100) and negative (true negatives/(true negatives + false negatives) × 100) predictive values (PPV and NPV) with their 95% CI. All statistical tests were two-tail sided, and *P* values of less than 0.05 were considered significant. Analyses were performed with R software (version 2.7).

Results

Population

Thirty-one consecutive patients (31 hips) undergoing arthroplasty for hip OA were included prospectively during a period of 4 months (19 women and 12 men; age range 23–87.2 years; mean 63.9 years).

Of the 31 hips, eight were excluded because of the poor quality of the histopathological specimen (one case), artefact movements at MRI examination (six patients), and lack of gadolinium injection because of hypersensitivity (one case), leaving 23 femoral heads suitable for analyses.

Demographics and clinical parameters of included and excluded patients did not differ (Table III).

MRI findings (Table IV)

The inter-rater agreement for MRI was good (*K*: 0.97).

The lesions most frequently observed were edema-like and necrosis-like, found in 100% (23/23) and 73.9% (17/23) of patients respectively. Cystic lesions and necrosis were present in 56.5% (13/23) and 34.8% (8/23) of the femoral heads, respectively. We found no subchondral fractures in our population.

Edema-like and necrosis-like lesions presented a close topographic relation, with an edema-like lesion consistently found at the periphery of necrosis-like lesions. Isolated necrosis-like patterns, i.e., not associated with edema-like, were not observed.

Correlation between MRI and histological findings (Tables V–VII)

The best correlations were between edema-like at MRI and histological BME (*K*: 0.77; CI 95%: 0.61–0.91). Necrosis-like was correlated with histological bone marrow fibrosis (*K*: 0.49; CI 95%: 0.28–0.69) and to a lesser degree with bone marrow necrosis (*K*: 0.24; CI 95%: 0.01–0.47). MRI cystic bone marrow was correlated with histological pseudocysts (*K*: 0.58; CI 95%: 0.32–0.78). MRI necrosis was weakly correlated with histological bone marrow necrosis (*K*: 0.28; CI 95%: 0.03–0.52) and corresponded mainly to a mix of histological lesions. Normal hematopoietic and fatty marrow at MRI corresponded to histological normal bone tissue (*K*: 0.9; CI 95%: 0.73–1). MRI specificity was much better than sensitivity for any elemental bone marrow lesion. Sensitivity and specificity of MRI varied from 26% to 80% and from 86% to 95%, respectively.

Discussion

Hip OA is an incapacitating disease and a major public health problem^{1,2}. The aim of this study was to correlate MR patterns and histological findings found in hip OA, with special emphasis on BME.

Interestingly, our data showed a substantial agreement between MRI and histological findings for edema-like pattern and histological BME.

Other diseases and OA in other body parts seem to behave somewhat differently. For example, in rheumatoid arthritis, BME changes would correspond to regions of inflammation, being variously associated with invading pannus, lymphocytic aggregates, and increased vascularity^{16,17}. In avascular necrosis, BME change would correspond essentially to zones of necrosis, reorganization, or scar tissue fibrosis of the subchondral bone¹⁸.

For knee OA, MRI BME seemed to correspond to a mix of histological lesions except edema^{9,10}. Two studies compared MRI patterns and histopathology in tibial plateaus of knees with severe OA undergoing total joint replacement^{9,10}. Zanetti *et al.* described six MRI patterns; marrow edema found at histology represented a small percentage of tissue and was present in equal proportions in each of the MRI zones. The MRI edema-like pattern was composed mainly of normal tissue (fatty bone marrow, normal trabeculae, and blood vessels).

Yet, in hip OA our results show that the edema-like MR pattern mainly corresponds to histological edema and to a lesser degree to vascular fibrosis, and that the necrosis-like MR pattern corresponded mainly to marrow necrosis combined with fibrosis. If we had included both edema-like and necrosis-like lesions together, we would probably have obtained a histological mixture of fibrosis, edema, and necrosis, as reported in previously published studies^{9,10}.

This distinction is crucial for elucidating the pathophysiology of "BME". These two MR lesions were the most frequently encountered in our study. Furthermore there was a very close topographic

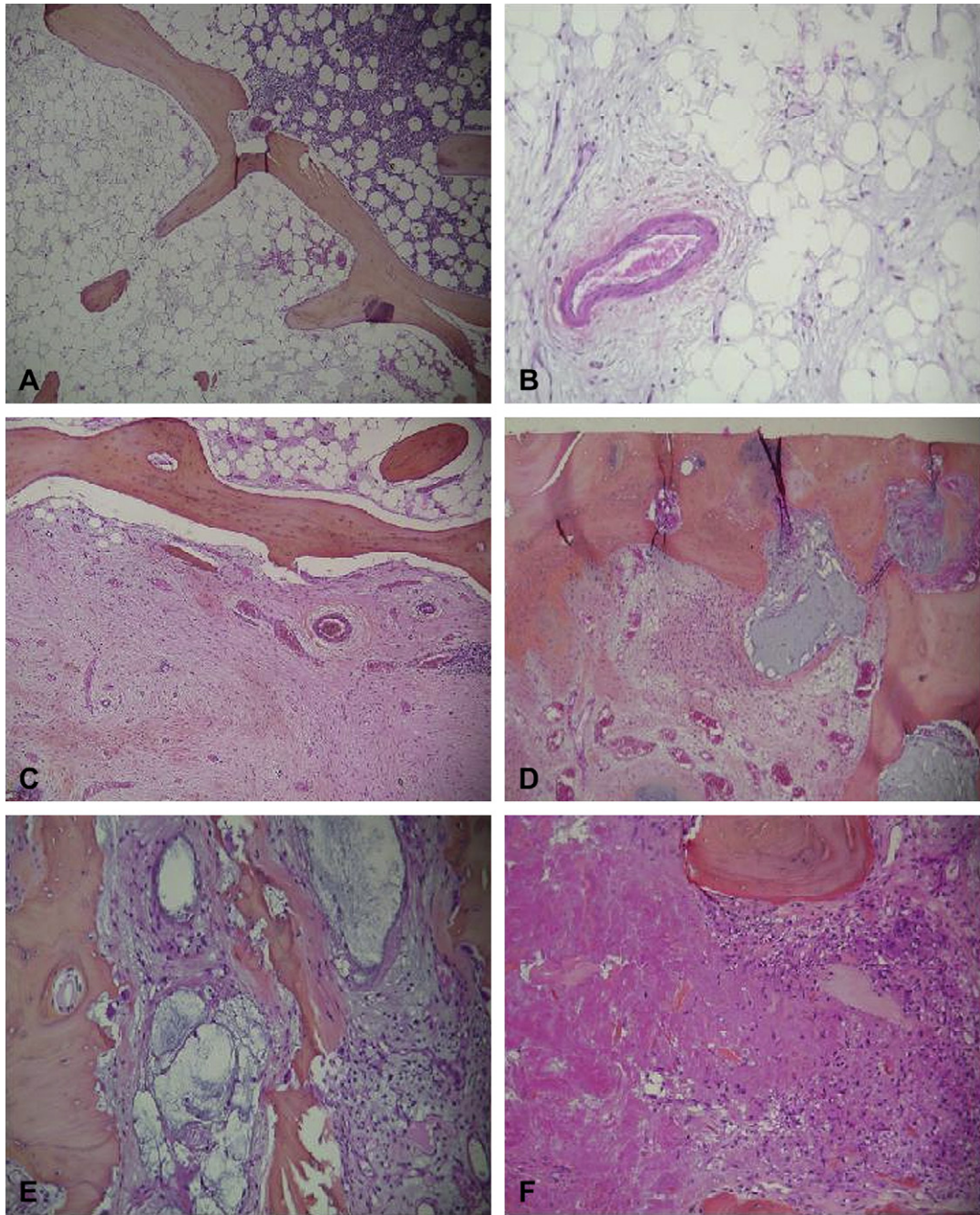


Fig. 2. (A) BME in the intertrabecular space below normal hematopoietic marrow (HES $\times 10$); (B) BME: faint eosinophilic material between adipocytes and around a vessel (HES $\times 20$); (C) fibrous replacement of fatty marrow (HES $\times 10$); (D) subchondral fibrous intertrabecular spaces with pseudocysts and numerous ectatic vessels (HES $\times 10$); (E) pseudocysts with central basophilic material and necrotic bone trabecula at higher magnification (HES $\times 20$); (F) eosinophilic necrotic material in the intertrabecular space (HES $\times 20$).

Table III
Characteristics of the population

Population	Included patients	Excluded patients	P
Men n (%)	10 (43.5)	2 (25)	0.43
Women n (%)	13 (56.5)	6 (75)	0.43
Mean age (years)	64.5	62.4	0.84
Symptoms evolution (month)	28	22.2	<0.001
Delay MRI/surgery (days)	6.9	10.2	0.25

Table IV
MRI observation

MRI observation	Number of patients (total = 23)	%
Normal H. marrow	12	52.2
Normal F. marrow	23	100
Edema-like	23	100
Necrosis-like	17	73.9
Sclerosis	0	0
Necrosis	8	34.8
Subchondral fracture	0	0
Cystic bone marrow	13	56.5

Table V
Indicators of diagnostic performance (95% CI) of the edema-like lesion according to histological findings

Histological lesion	Se	Sp	PPV	NPV	K
Normal H. marrow	0.08 (0.01–0.35)	0.74 (0.64–0.82)	0.04 (0.00–0.21)	0.84 (0.74–0.91)	–0.12 (–0.23 to 0.03)
Normal F. marrow	0.04 (0.00–0.22)	0.70 (0.59–0.79)	0.04 (0.00–0.20)	0.72 (0.60–0.81)	–0.24 (–0.35 to –0.11)
BME	0.80 (0.60–0.91)	0.95 (0.88–0.98)	0.86 (0.67–0.95)	0.93 (0.84–0.96)	0.77 (0.61–0.91)
Bone marrow fibrosis	0.26 (0.12–0.46)	0.76 (0.65–0.84)	0.26 (0.12–0.46)	0.76 (0.65–0.84)	0.02 (–0.17 to 0.22)
Bone marrow fibrosis and vessels	0.69 (0.42–0.87)	0.82 (0.73–0.89)	0.39 (0.22–0.59)	0.94 (0.86–0.97)	0.39 (0.16–0.60)
Bone marrow necrosis	0.05 (0.01–0.24)	0.71 (0.60–0.80)	0.04 (0.01–0.20)	0.75 (0.30–0.83)	–0.21 (–0.32 to –0.08)
Subchondral fracture	NA	NA	NA	NA	NA
Pseudocysts	0 (0.00–0.20)	0.71 (0.60–0.80)	0 (0.00–0.14)	0.79 (0.68–0.86)	–0.23 (–0.31 to –0.14)

Abbreviations: HM: Hematopoietic marrow, FM: Fatty marrow, Se: Sensitivity, Sp: Specificity, PPV: Positive predictive value, NPV: Negative predictive value, NA: Non available.

Table VI
Indicators of diagnostic performance (95% CI) of the necrosis-like lesion according to histological findings

Histological lesion	Se	Sp	PPV	NPV	K
Normal H. marrow	0 (0.00–0.24)	0.79 (0.69–0.86)	0 (0.00–0.18)	0.84 (0.74–0.90)	–0.17 (–0.23 to –0.10)
Normal F. marrow	0 (0.00–0.15)	0.77 (0.66–0.85)	0 (0.00–0.18)	0.73 (0.62–0.81)	–0.24 (–0.31 to –0.15)
BME	0.16 (0.06–0.34)	0.81 (0.70–0.88)	0.23 (0.09–0.47)	0.73 (0.62–0.81)	–0.02 (–0.20 to 0.17)
Bone marrow fibrosis	0.52 (0.32–0.70)	0.93 (0.84–0.96)	0.70 (0.46–0.86)	0.85 (0.76–0.91)	0.49 (0.28–0.69)
Bone marrow fibrosis and vessels	0.30 (0.12–0.57)	0.84 (0.74–0.90)	0.23 (0.09–0.47)	0.88 (0.79–0.93)	0.13 (–0.08 to 0.36)
Bone marrow necrosis	0.36 (0.19–0.58)	0.86 (0.77–0.92)	0.41 (0.21–0.63)	0.84 (0.75–0.90)	0.24 (0.01–0.47)
Subchondral fracture	NA	NA	NA	NA	NA
Pseudocysts	0.13 (0.03–0.37)	0.81 (0.71–0.88)	0.11 (0.03–0.34)	0.83 (0.73–0.89)	–0.05 (–0.19 to 0.12)

Table VII
Indicators of diagnostic performance (95% CI) of the other MR lesion according to histological findings

MRI/histology	Se	Spe	PPV	NPN	K
HM/HM	0.91 (0.64–0.98)	0.98 (0.93–0.99)	0.91 (0.64–0.98)	0.98 (0.93–0.99)	0.90 (0.73–1.00)
FM/FM	0.95 (0.77–0.99)	0.97 (0.90–0.99)	0.90 (0.72–0.97)	0.98 (0.92–0.99)	0.90 (0.79–1.00)
Necrosis/Bone marrow necrosis	0.26 (0.11–0.48)	0.96 (0.89–0.98)	0.62 (0.30–0.86)	0.83 (0.74–0.90)	0.28 (0.03–0.52)
Cystic bone marrow/pseudocysts	0.6 (0.35–0.80)	0.95 (0.87–0.98)	0.69 (0.42–0.87)	0.92 (0.84–0.96)	0.58 (0.32–0.78)

association between them. The disposition of edema-like at the periphery of necrosis-like and the absence of necrosis-like without associated edema-like suggest that the edema-like lesion could precede the necrosis-like lesion. The edema-like pattern would represent a less severe lesion, that could be reversible. Thus, this could explain why some subchondral bone marrow lesions become larger and are associated with structural progression whereas a smaller proportion of these lesions can reverse^{19,20}.

In our study, MRI specificity was better than sensitivity to detect any histological elemental lesion. This suggests a threshold phenomenon for MRI detection of BME-like changes, i.e., histological changes must be substantial to be depicted by MRI. This has already been pointed out in other processes such as rheumatoid arthritis or ankylosing spondylitis^{18,21}.

Some limitations inherent to the materials and methods used in this study should be discussed. First, because of the need to obtain gross anatomical material, our study was limited to hip OA advanced enough to justify total hip replacement. For the same reason, it was limited to femoral heads, because en bloc resection of the acetabulum is not technically feasible. However, the MRI lesions we observed on acetabuli were not significantly different from those observed on femoral heads (data not shown). This study concerned a limited number of cases, but it is in the range found in the literature on this topic. Finally, distinguishing edema-like and necrosis-like patterns are not always easy and require sometimes a complete MRI protocol including gadolinium injection. So it is probably not realistic to apply this in routine clinical practice.

The strengths of our study are as follows. Femoral heads can be properly resected as a whole and provide much better anatomical material than knee pieces. Also, a major difficulty in MRI–histological correlations is to ensure that the areas analyzed by both

methods are actually the same. Otherwise, the observed associations remain too crude to allow suitable conclusions. We believe this goal was achieved in this study.

Evidence is mounting that MRI patterns corresponding to so-called BME have great importance whatever the pathology, mechanical or inflammatory, and may be considered as crucial prognosis factors^{4,5,16,18,22}. In knee OA, such MRI patterns are generally associated with clinically and radiologically poor prognosis, but in some cases they are also found in apparently normal subjects and can reverse^{19,20}. Nevertheless, very few data are available on OA to characterize the underlying histological processes. We chose to specifically separate “bone marrow edema pattern” into edema-like and necrosis-like lesions, the former corresponded to histological BME, and the latter to bone marrow fibrosis and necrosis. Our data showed a good correlation between edema-like MRI patterns and histopathological BME. We hypothesize that the edema-like lesion represents a potentially reversible stage preceding the more advanced and pejorative necrosis-like lesion. Our conclusions need to be confirmed by further histological and clinical studies.

Contributions

All authors have made substantial contributions to this work, especially for the conception and design, drafting and final approval. Jean-Noël Argenson provided femoral heads, Corinne Bouvier and André Maues de Paula performed Histopathological analysis and Roch Giorgi did the statistical analysis. Hélène Leydet-Quilici (helene.leydet@mail.ap-hm.fr) takes responsibility for the integrity of the work as a whole, from inception to finished article.

Conflict of interest

All authors have no conflict of interest.

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