Knee Surg Sports Traumatol Arthrosc (2010) 18:463–471
DOI 10.1007/s00167-010-1053-0

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Epidemiology and imaging of the subchondral bone in articular cartilage repair

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Received: 19 December 2009 / Accepted: 8 January 2010 / Published online: 11 February 2010

Abstract Articular cartilage and the subchondral bone act as a functional unit. Following trauma, osteochondritis dissecans, osteonecrosis or osteoarthritis, this intimate connection may become disrupted. Osteochondral defects—the type of defects that extend into the subchondral bone—account for about 5% of all articular cartilage lesions. They are very often caused by trauma, in about one-third of the cases by osteoarthritis and rarely by osteochondritis dissecans. Osteochondral defects are predominantly located on the medial femoral condyle and also on the patella. Frequently, they are associated with lesions of the menisci or the anterior cruciate ligament. Because of the close relationship between the articular cartilage and the subchondral bone, imaging of cartilage defects or cartilage repair should also focus on the subchondral bone. Magnetic resonance imaging is currently considered to be the key modality for the evaluation of cartilage and underlying subchondral bone. However, the choice of imaging technique also depends on the nature of the disease that caused the subchondral bone lesion. For example, radiography is still the golden standard for imaging features of osteoarthritis. Bone scintigraphy is one of the most valuable techniques for early diagnosis of spontaneous osteonecrosis about the knee. A CT scan is a useful technique to rule out a possible depression of the subchondral bone plate, whereas a CT arthrography is highly accurate to evaluate the stability of the osteochondral fragment in osteochondritis dissecans. Particularly for the problem of subchondral bone lesions, image evaluation methods need to be refined for adequate and reproducible analysis. This article highlights recent studies on the epidemiology and imaging of the subchondral bone, with an emphasis on magnetic resonance imaging.

Keywords Subchondral bone · Subchondral bone plate · Radiography · MRI · CT · Bone scintigraphy

Presented at the Conference "The subcondral bone in articular cartilage repair", October 8–10, 2009, Mondorf-les Bains, Luxembourg.

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Introduction

The capacity of osteochondral defects to heal is limited, and their treatment remains a challenge. For example, it has been suggested that the failure of subchondral bone restoration or maintenance contributes to the failure of cartilage-forming transplants [35, 36]. In osteoarthritis, the subchondral plate and subchondral cancellous bone contribute greatly to the initiation of osteoarthritis and its progression because increased subchondral bone density results in overloading of and damage to the articular cartilage [39]. In a focal full-thickness cartilage lesion, the subchondral plate is exposed to elements of the synovial

fluid (enzymes and cytokines). Therefore, protecting the subchondral bone plate be from the joint fluid may be a prerequisite for an optimal repair process. However, few epidemiological data exists regarding the epidemiology of defects extending into the subchondral bone, in particular as they relate to diseases such as traumatic osteochondral defects, osteochondritis dissecans, osteonecrosis and osteoarthritis.

Imaging of the subchondral bone needs to fit into the concept of the functional cartilage–subchondral bone unit as articular cartilage, and bone health appears to be tightly associated [21]. Ample evidence is found for bone changes during progression of osteoarthritis (OA), including, but not limited to, increased turnover in the subchondral bone, thinning of the trabecular structure, osteophytes, bone marrow lesions and sclerosis of the subchondral bone plate. In addition, a range of investigations has described secondary positive effects on cartilage health when bone resorption was suppressed, or deterioration of the cartilage when resorption is increased [22]. Other studies show improvement in bone homeostasis following autologous chondrocyte implantation [19]. However, different studies have not been able so far to answer the primary initiating event in osteoarthritis: does increased bone metabolism initiate cartilage destruction or vice versa? [1, 3, 9, 15, 26, 43, 44]. Hence, imaging methods that are accurate for the study of cartilage lesions and cartilage loss also need to provide information on the subchondral bone and marrow changes.

This article highlights recent studies on the epidemiology and imaging of the subchondral bone, with an emphasis on magnetic resonance imaging.

Subchondral bone lesions—locations, prevalence and prognosis

Chondral or osteochondral injuries are difficult to diagnose because there is no consistent or linear correlation between clinical presentations on the one hand, and the local gross and microscopic aspect of the lesion on the other hand [48]. Consequently, when treating a patient suffering from chondral injuries of the knee, a global and personalized evaluation, as well as thorough investigations, are necessary before deciding on a treatment.

Location of osteochondral lesions

The preferential site for focal chondral or osteochondral lesions was the medial femoral condyle (58%) in a study encompassing a 1,000 knee arthroscopies [20]. The remaining lesions were situated on the patella (11%), the lateral tibia (11%), the lateral femoral condyle (9%), the trochlea (6%) and the medial tibia (5%). Those findings are consistent with the observations made by Curl et al. [12], who showed that the most common locations for full-thickness chondral lesions with exposed bone (grade IV lesions based on a modified Outerbridge scale) were the medial femoral condyle (about 32% of patients), the patella (about 21% of patients) and lateral femoral condyle (about 20% of patients). Less than 5% of all patients had grade IV lesions in the medial and lateral tibial plateau.

Size and numbers of the lesions

Regarding the size of the lesion, the mean chondral or osteochondral defect area was 2.1 cm^2 (range, 0.5–12; SD, 1.5) [20]. Of all chondral or osteochondral defects, 88% were less than 4 cm^2 (19% of the defects were less than 1 cm^2; 26% ranged from 1 to 2 cm^2; 42% ranged from 2 to 4 cm^2; and 12% were more than 4 cm^2). An average of 2.7 lesions per knee was reported by Curl et al. [12]. According to Hjelle et al. [20], when narrowing down those lesions to focal chondral lesions only (as opposed to osteoarthritis, chondromalacia patella osteochondritis dissecans) 80% of the injuries were unique, 12% were double and 8% were triple.

Arthroscopic aspect of articular cartilage defects

Curl et al. [12] qualified the arthroscopic aspect of chondral lesions, using a modified Outerbridge classification. In this classification, Grade I lesions represented softening of the articular cartilage, Grade II lesions exhibited fibrillation or superficial fissures of the cartilage, in Grade III lesions there was deep fissuring of the cartilage without exposed bone while in grade IV lesions the subchondral bone was exposed. Such grade IV lesions accounted for 19% of all lesions. Grade III lesions of the patella were, however, the most common (41%), followed by grade II (28%) and grade I lesions (10%). Interestingly, 55% of all articular cartilage defects were full-thickness chondral (ICRS grade III), and only 5% ($n = 10$) were osteochondral (ICRS grade IV), using the ICRS classification [20]. ICRS grade I lesions occurred in 14% of patients, and 26% of the main focal defects were ICRS grade II.

Prevalence

It is difficult, if not impossible, to establish who, in the general population, suffers from chondral lesions of the knee. An unknown number of people who sustain articular surface injuries will never develop symptoms or seek medical treatment. Consequently, epidemiologic studies of cartilage defects are conducted for patients with symptomatic knees requiring arthroscopy, which entails a considerable bias. In a study of 200 arthroscopies performed

on symptomatic patients, Zamber et al. [48] found that 62% of them presented with at least one cartilage lesion. The retrospective study by Curl et al. [12] reviewed 31,516 knee arthroscopies. Chondral lesions were found in 63% arthroscopies. The prospective study of 1,000 arthroscopies of the knee conducted by Hjelle et al. [20] has also considerably contributed to mapping the chondral pathology of the knee. In the collective of 1,000 patients requiring knee arthroscopy for various reasons 61% of them revealed chondral or osteochondral lesions, of which 44% were osteoarthritis, 28% focal chondral lesions, 23% chondromalacia patella, 2% osteochondritis dissecans and 3% others. Curl et al. [12] identified 1% lesions caused by osteochondritis dissecans, 1% by articular fractures, 10% by grade I chondromalacia, 28% by grade II chondromalacia, 41% by grade III chondromalacia, and 19% by full-thickness defects with exposed subchondral bone. Grade III lesions (partial thickness chondral lesions with deep fissures) were the most common lesions in patients over 30 years of age. Focal chondral or osteochondral lesions were found in 19% of the arthroscopies. Levy et al. [27] have described an increasing frequency of chondral injuries in collegiate and professional players, suggesting that athletes practicing activities involving repetitive joint impact, pivoting movements and rapid deceleration motions, were a target population for surgical procedure [32, 33].

Patient age

Zamber et al. reported that 76% of patients suffering from chondral lesions were older than 30 years [34, 48]. According to Curl et al. [12], the average age of the patients with lesions was 43 years, predominantly in male patients (62 vs. 38% for female patients). Overall, the majority (72%) of grade IV lesions were found in patients over 40 years of age. Patients under 40 years of age with grade IV lesions accounted for 5% of all arthroscopies.

Concomitant lesions

Although isolated chondral lesions can occur, with a reported prevalence of approximately 4%, chondral and osteochondral injuries are generally associated with other intraarticular abnormalities, such as ligamentous and meniscal injuries, synovitis and less commonly pathology of synovial plica or a corpus liberum [20]. When arthroscopically reviewing focal chondral or osteochondral lesions of the knee, Hjelle et al. [20] found concomitant meniscal lesions in 42% of the cases. Curl et al. [12] found that medial meniscus injury was the most common associated lesion after 30 years of age. Medial meniscus injuries were more common in male than in female patients. Lateral meniscal injuries were more frequent in younger males than females, with an inversion of this tendency after woman reached the age of 50. Casscells [8] states that torn menisci and cartilage defects are concomitant but unrelated findings after he conducted a retrospective study on 350 knees after arthrotomy and menisectomies as well as a cadaver and arthroscopic study [7]. Other authors like Noble et al. [37] corroborate this opinion. However, there has been evidence of a positive correlation between the delay of meniscal surgery after injury and the severity of cartilage disease in the knee [13].

ACL lesions were concomitant to focal chondral or osteochondral defects in 26% of the knees reviewed by Hjelle et al. [20]. ACL tear is the most frequently associated injury for young patients [12]. About 40% of the patients under the age of 30 who suffer from chondral injuries have associated ACL tears [12]. The prevalence decreases with age (some 30% in the third decade, approximately 10% in the fifth decade). Casscells [8] has also reported on the strong prevalence of chondral lesions in knees suffering from ACL tears. Hjelle et al. [20] report both menisci and ACL tear association with chondral focal lesions in 12% of the cases. Focal chondral or osteochondral defects were found in 19% of the patients [20]. In these patients, 61% related their current knee problem to a previous trauma, and a concomitant meniscal or anterior cruciate ligament injury was found in 42 and 26%, respectively.

Clinical imaging of the subchondral bone

The subchondral bone cannot readily be evaluated during arthroscopy. However, knowledge of the subchondral bone state in the diagnostic phase is important since it might change a chosen treatment strategy. Evaluation of the subchondral bone state after cartilage (with or without subchondral bone) repair will not only give information about eventual complications, but will also have a prognostic value for long-term graft survival, since ACI repair tends to give improvement of bone homeostasis [19]. For this evaluation, different imaging techniques are available. In the next paragraphs we will give a short overview of each technique, with special attention to MRI, since MRI is actually considered the most accurate method for the evaluation of cartilage and underlying subchondral bone.

Radiography

Radiography still is the golden standard for imaging features of osteoarthritis and is widely used as an outcome measurement in multi-center clinical trials. Objective assessment, however, of osteoarthritis features such as joint

space narrowing, subchondral sclerosis and osteophyte formation is highly important. Therefore, radiographic acquisition needs to be standardized: apart from a standard lateral knee view, a postero-anterior, weight-bearing, fixed-flexion radiography with 10 degrees caudal beam angulation needs to be acquired [18, 24]. Usually, evaluation is performed using Kellgren and Lawrence scale [23]. Additional evaluation for central or intralesional osteophyte formation (Fig. 1) might seem appropriate, since it usually reflects a long-standing osteochondral defect [29]. Albeit the standard for evaluation of osteoarthritis, routine radiography is well known to have a low sensitivity for early osteoarthritis changes.

Bone scintigraphy

Radiopharmaceuticals that are available for clinical imaging target secondary features of osteoarthritis associated with articular cartilage damage and act primarily on bone turnover changes seen with osteophyte formation, subchondral bone sclerosis and subchondral cyst formation [30]. Bone scintigraphy using diphosphonate derivatives radiolabeled with Tc-99 m target the bone response that results from the abnormal biomechanics of joint motion when the articular cartilage is damaged and has therefore a high sensitivity in detecting bone reaction to the pathology of osteoarthritis [30]. It is therefore not surprising that bone scans show abnormal uptake before the detection of abnormal morphology in routine radiography. In clinical practice, bone scintigraphy is often used in patients with established osteoarthritis features for its predictive power, since a negative bone scan might provide some reassurance that disease is unlikely to progress in the next 5 years [15] In a comparative trial in a patient population with chronic knee pain, a good agreement was found between increased bone uptake and MR-detected subchondral lesions. However, the agreement between increased bone uptake and osteophytes or cartilage defects was poor as well as the agreement between the grade of bone uptake and the grade of the MR findings [5].

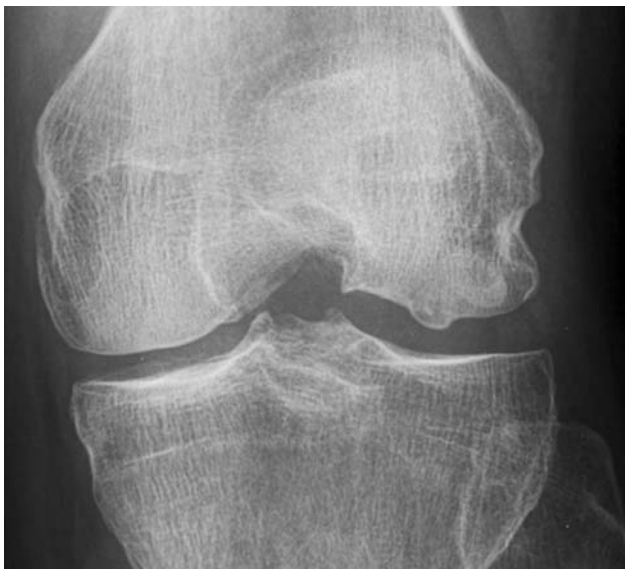

Fig. 1 Radiograph of the left knee with a central osteophyte in the lateral femoral condyle

Bone scintigraphy is considered one of the most valuable techniques for early diagnosis of spontaneous osteonecrosis about the knee. The diagnostic sensitivity may be further improved with SPECT (single photon emission CT), although MRI appears to be even more sensitive. There is still some debate about the most sensitive technique, since MR imaging abnormalities related to osteonecrosis depend on alterations in the fat cells which are somehow resistant to ischemia (up to 5 days survival after the insult). In daily clinical practice where a patient examination is often delayed due to limited availability of either scintigraphy or MRI, this debate might seem purely academical. Depending on the stage of the disease, bone scintigraphy shows a cold (early phase of blood supply interruption) or hot (reparative processes in the surrounding bone) lesion.

Computed tomography

Both CT and CT arthrography can show subchondral bone changes, such as subchondral bone sclerosis and osteophytes. Both techniques can show central osteophytes, associated with more severe changes of osteoarthritis than marginal osteophytes [29]. CT arthrography, performed after direct intraarticular injection of iodine contrast, is the most accurate method for the evaluation of cartilage thickness and cartilage defects (Fig. 2); thanks to its high spatial resolution and high contrast ratio [17]. However, purely intrachondral lesions, without communication with the surface cannot be detected [41]. In patients who have metallic hardware near the joint, post-operative evaluation using CT or CT arthrography might be preferable to MR imaging since metallic artifacts usually remain mild on new generation CT scanners [38, 47]. The subchondral bone plate is seen on CT as a homogeneous dense subchondral line. There is a sharp delineation with the overlying cartilage although it is not clear whether this border is formed either by the calcified zone of the cartilage or by the subchondral bone plate itself due to limitations in spatial resolution. Further investigation using micro-CT might therefore be warranted. The borders between the subchondral bone plate, the underlying subarticular spongiosa and the subchondral bone marrow are more difficult to define due to broad transition areas between these anatomical zones.

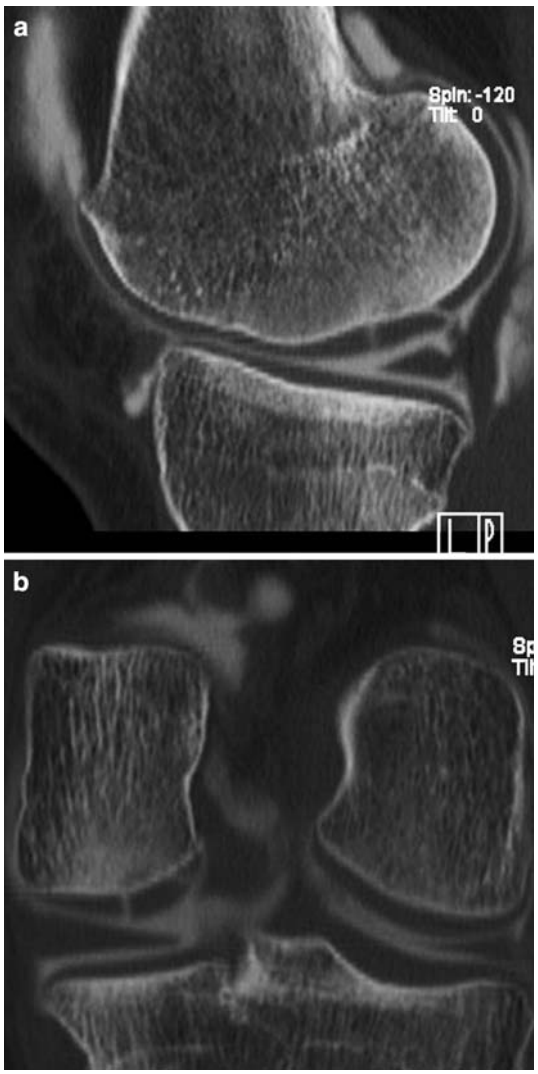

Fig. 2 CT arthrography of the right knee with sagittal (**a**) and coronal (**b**) reconstruction, showing two small full-thickness cartilage fissures in the lateral femoral condyle. An underlying area of subchondral bone sclerosis can be seen

CT scan is a valuable technique to evaluate suspected spontaneous osteonecrosis about the knee (differentiation with adult onset osteochondritis dissecans; eventual depression of the subchondral bone plate and appearance of intraarticular loose bodies). CT arthrography is highly accurate to evaluate the stability of the osteochondral fragment in osteochondritis dissecans. Major drawback for CT is the exposition of the patient to ionizing radiation and the need for invasive intraarticular punction to perform a CT arthrography examination.

Magnetic resonance imaging

Magnetic resonance imaging is actually considered the most accurate method for the evaluation of cartilage and subchondral bone. MR imaging of the cartilage and the subchondral bone should be performed under optimized technical circumstances to obtain high-resolution images with an optimal signal-to-noise ratio. Therefore, imaging should be done on high-performance MR systems (a high field strength system with high gradient amplitudes, high gradient slew rates and high RF receiver bandwidths), optimal coil selection is needed (multi-channel quadrature receive-only coil and/or phased array technology coil) as well as optimization of image sequences parameters. Cartilage-specific sequences, such as intermediate-weighted FSE and especially T2-weighted FSE with fat saturation are ideally to detect non-cystic bone marrow lesions in their maximum extend [49]. Gradient-recalled echo-type sequences with robust water excitation are insensitive to diffuse marrow abnormalities because of trabecular magnetic susceptibility, but are very sensitive in delineating subchondral cysts [16]. Additionally, for correct assessment of sclerotic lesions, a non-fat-saturated T1-weighted sequence is required. It is important to have these 4 basic sequences as they serve for optimal cartilage and subchondral bone scoring [42]. Moreover, these sequences can readily be applied on every MRI system which make them ideally for long-term patient follow-up in multi-center trials. Susceptibility artifacts are an important issue in postoperative patients because of the metallic debris left behind by the use of surgical instrumentation. This has proven to be a particular problem with allograft osteochondral transplantation and autologous chondrocyte implantation [2]. Unfortunately, these artifacts are enforced in higher field systems (3Tesla) and may possibly disable correct image interpretation.

Several additional MRI sequences can be performed for further evaluation of cartilage and subchondral bone. They often tend to be technically more challenging to perform, and some are not readily available for routine clinical use. Dynamic contrast-enhanced MRI can be performed to evaluate subchondral bone perfusion [1, 26]. Time-intensity curves suggest outflow obstruction as an underlying mechanism to bone remodeling and cartilage breakdown in osteoarthritis. The same injected contrast material can eventually be used for subsequent indirect MR arthrography, which has proven to be an accurate monitoring tool in the follow-up of scaffold implants with high correlation to histological findings [45]. Additional in vivo biochemical imaging such as dGEMRIC, T2 mapping and diffusing-weighted imaging make functional analysis of cartilage possible [4, 46].

A baseline MRI examination in a patient with clinical suspicion of a cartilage or osteochondral defect should be able to give—apart from an overall knee joint evaluation—a detailed description of the cartilage or osteochondral defect. Furthermore, appropriate radiological differentiation should

be provided on the visualized subchondral bone marrow lesions. Ideally, a definite appellation of the subchondral bone lesion can be done. Without being exhaustive, traumatic bone marrow lesions should be further differentiated for bone bruises, subchondral impaction, osteochondral/subchondral/chondral fractures, insufficiency/stress fractures or overuse lesions; non-traumatic bone marrow lesions should be further differentiated for avascular necrosis, spontaneous osteonecrosis of the knee, osteoarthritis-associated bone marrow lesions, transient bone marrow edema syndrome, osteochondritis dissecans, inflammatory bone marrow lesions [42]. Main challenge, however, for the radiologist, is to provide a distinction between self-resolving lesions from those that may evolve to epiphyseal collapse and joint impairment [25, 40].

Image evaluation

The adequate assessment of cartilage repair tissue on MRI has led to the definition of pertinent variables for the description of articular cartilage repair tissue after different repair techniques (MOCART: Magnetic resonance Observation of Cartilage Repair Tissue) as described by Marlovits et al. [28]. Modifications toward the relative value of some variables are appropriate since some variables seem more important then others [14]. Additional modifications regarding the subchondral bone marrow and the subchondral bone plate evaluation are needed. The original MOCART scoring system evaluates the subchondral bone either as intact (attributed score = 1) or not intact (attributed score = 0) meaning edema, granulation tissue, cysts or sclerosis. It seems appropriate to differentiate pure bone marrow edema-like signal from associated subchondral cysts since emerging evidence shows that subchondral cysts develop in preexisting regions of subchondral bone marrow edema-like signal [6, 10, 11]. Evolution toward subchondral bone cyst development over time might therefore be a bad sign for long-term survival of the repair tissue (Fig. 3). The original MOCART scoring system also lacks evaluation of the level of the subchondral bone plate. This is important, however, as either flattening or depression of the osseous articular surface (subchondral bone attrition) or elevation of the osseous articular surface (central or intralesional osteophyte) both alter local biomechanics of the overlying repair tissue and will eventually lead to premature graft failure [31, 44]. Bony overgrowth into the former defect is a frequent finding following microfracture [31]. This event may promote the development of intralesional osteophytes (Fig. 4), due to endochondral bone formation instead of articular cartilage formation, which in turn are associated with degeneration of overlying cartilage repair tissue due to the altered mechanical properties.

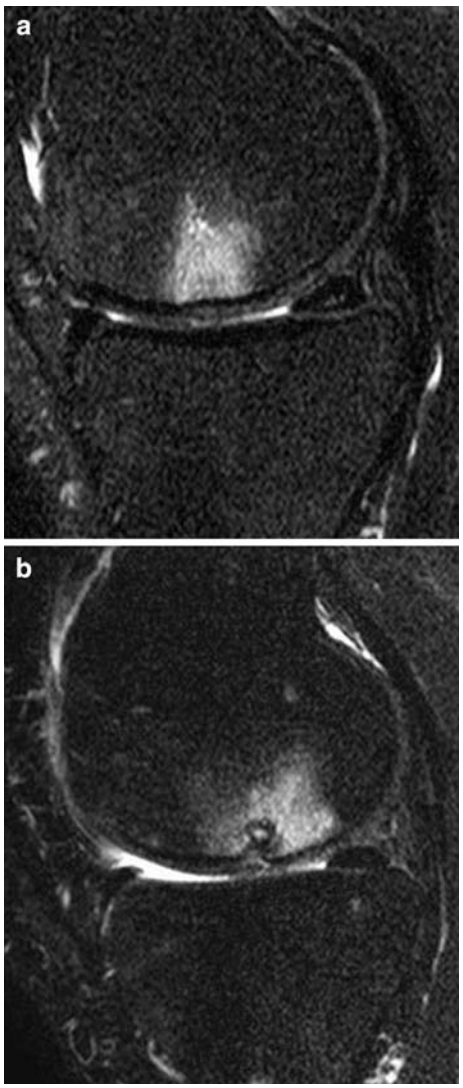

Fig. 3 Sagittal T2-weighted images with fat saturation in the post-operative follow-up, 12 months (**a**) and 24 months (**b**) after microfracture, showing subchondral cyst development in the central part of the bone marrow edema-like signal area with concomitant defect in the overlying graft tissue

In the original MOCART scoring system, the term "bone marrow edema" is used to describe ill-defined subchondral areas of high signal intensity on T2 or intermediate-weighted fat-suppressed FSE images [49]. In recent years, the more general term "bone marrow lesion" has become standard usage, since histologically, non-characteristic abnormalities are found in areas of edema-like signal changes in conjunction with osteoarthritis or cartilage damage [43]. These include bone marrow necrosis, bone marrow fibrosis and trabecular abnormalities but very little bone marrow edema [49]. Thus, the term bone marrow "edema" is not appropriate.

In the post-operative evaluation after cartilage or osteochondral repair, it is important to differentiate non-cystic

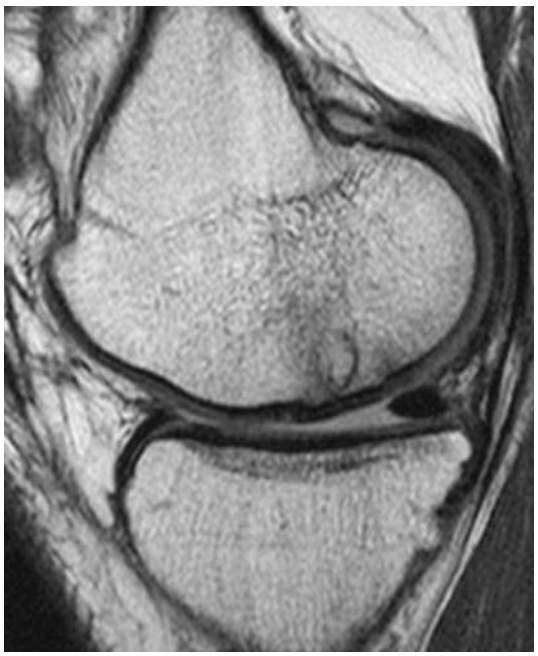

Fig. 4 Sagittal intermediate-weighted image (non-fat saturated) in a patient 24 months after microfracture showing upward migration of the subchondral bone plate (central osteophyte) underneath the area of repair

from cystic bone marrow lesions and to look for areas of subchondral bone sclerosis since these findings are associated with a higher degree of premature graft failure. More additional modifications of the original MOCART scoring system probably will emerge from new surgical techniques which attempt integrated cartilage–subchondral bone repair (e.g. bio-resorbable cartilage-bone scaffolds). The post-operative evaluation of patients after cartilage or cartilage–subchondral bone repair with MRI not only should focus on the repair tissue itself (modified MOCART scoring system), but should also look for complications related to the repair tissue or the performed surgical procedure. Finally, it should be possible to provide an impression on overall joint homeostasis.

Conclusion

The treatment of osteochondral lesion continues to remain a challenge. Epidemiological studies need to provide more data on osteochondral defects that are caused by trauma, osteochondritis dissecans, osteonecrosis and osteoarthritis. They also will need to provide more data on the potential impact of these different diseases on the outcome of surgical treatment. In addition, the causal relationship between cartilage injuries of the knee and associated lesions, such as ACL tears, on the natural history of osteochondral defects needs to be addressed in future studies.

In the diagnostic work-up of patients with clinical suspicion for a cartilage or osteochondral defect, apart from standard radiographs, an MRI examination should be performed. Before performing a cartilage or osteochondral repair procedure, additional scintigraphy seems indicated for its high predictive power for osteoarthritis progression. CT arthrography will add additional information regarding the exact morphology of the cartilage or osteochondral defect and might reveal small additional cartilage lesions which were unclear on the performed MRI examination. In the post-operative follow-up, regular and long-lasting evaluation of the repair tissue with standard radiography and MRI are required, since it is well known that the repair tissue exhibits ongoing maturation and differentiation even beyond 2 years after surgery. It might be worthwhile to streamline the post-operative imaging points (e.g. 6 months, 1, 2, 3 and 5 year), as well as to streamline image evaluation methods (i.e. modified MOCART scoring system) in order to obtain comparable data sets.

Improvements in imaging techniques will not only enable us to better identify patients with chondral or osteochondral defects without the need for arthroscopy, but also aid in the non-invasive evaluation of structural parameters of the cartilaginous repair tissue following reconstructive surgery.

Acknowledgments We thank Elke Dooley for help with the manuscript preparation. Supported in part by the Deutsche Forschungsgemeinschaft (DFG) and the Fonds National de la Recherche (FNR).

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