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As our understanding of the underlying pathophysiological changes grows, osteoarthritis (OA) has become a disease of the osteochondral unit and entire joint, rather than a disorder limited to the articular cartilage [1]. Current data suggest that OA could be initiated through activation of the secondary center of ossification with thickening of the subchondral bone and corresponding thinning of the overlying cartilage [2, 3]; a similar mechanism is potentially at work after marrow stimulation [4, 5]. While the significance of these findings has not been conclusively proven, changes in the subchondral bone are regarded as a potential explanation for the deterioration and failure of microfracture; the regenerated tissue overlies a thickened, prominent, and stiff subchondral plate, a potential factor predisposing it to degeneration [6–8]. As mentioned previously, similar changes are found in OA and chronic chondral defects, which have demonstrated worse outcomes with cartilage repair procedures [9]. It can be theorized that the altered subchon-

dral plate is responsible for the worse outcomes both in chronic defects as well as in those lesions treated with marrow-stimulation techniques (MST). Interestingly, osteochondritis dissecans (OCD) lesions, by definition associated with altered subchondral bone, have shown success rates after autologous chondrocyte implantation (ACI) similar to those for the treatment of conventional focal chondral defects [10, 11].

Cartilage micro-architecture varies substantially from the articular surface to the subchondral bone, being divided into four distinct zones: superficial, transitional, deep, and calcified. The deepest layer, the zone of calcified cartilage, separates hyaline cartilage from subchondral bone and is characterized by small rounded chondrocytes distributed in an extra-cellular matrix encrusted with apatitic salts. Histologically, the calcified cartilage zone may be distinguished from the deep zone by the tide-mark, which appears as a bluish line with hematoxylin eosin staining.

Lamellar bone is found throughout the mature skeleton in both trabecular and cortical bone, regardless of whether the bone was formed by intramembranous or endochondral ossification. Bone is a very dynamic and well-organized tissue, and trauma to cortical, trabecular, or subchondral bone may activate a reparative process [12]. One theory of OA suggests that microfractures from subclinical, chronic repetitive micro-trauma to the subchondral bone or calcified cartilage may trigger reactivation of the secondary centers of ossification, resulting in thickening

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of the subchondral plate and calcified cartilage, with advancement of the tidemark and corresponding thinning of the overlying cartilage [3]. This thinner layer of viscoelastic cartilage overlies a thickened and stiffened subchondral plate; finite element analyses suggest that the subchondral stiffening causes elevated shear stresses in the deep cartilage layers [13, 14].

Recently, there has been an increasing interest in potential parallels between the above mentioned theory on the etiology of OA and the influence of subchondral bone changes on subsequent cartilage repair. As our understanding of the underlying pathophysiological changes grows, it is becoming apparent that cartilage lesions need to be evaluated as an integral part of the entire osteochondral unit, rather than a disorder limited to the articular surface; without support from an intact subchondral bed, any surface treatment is likely to fail [15]. In addition to the repetitive microtrauma seen with chronic defects, subchondral bone may be affected primarily or secondarily in many diseases of the articular cartilage. Both OCD and spontaneous osteonecrosis start in the subchondral bone and progressively affect the articular cartilage, while traumatic osteochondral fractures concomitantly affect both articular cartilage and subchondral bone. In addition, iatrogenic intervention may also lead to permanent changes in the subchondral bone, for example, after the microfracture procedure.

Imaging

Besides concrete structural changes in the subchondral bone, Magnetic resonance imaging (MRI) evaluation has demonstrated traumatic and degenerative changes manifested by an increase in the bone marrow signal intensity on fat-saturated T2-weighted images. These hyper-intense abnormalities may be an expression of a number of noncharacteristic histological abnormalities that include bone marrow necrosis, bone marrow fibrosis, and trabecular abnormalities [16–18]. Bone marrow edema has been associated with severity and progression of OA [19]. Subchondral edema is a non-specific reaction of the bone to

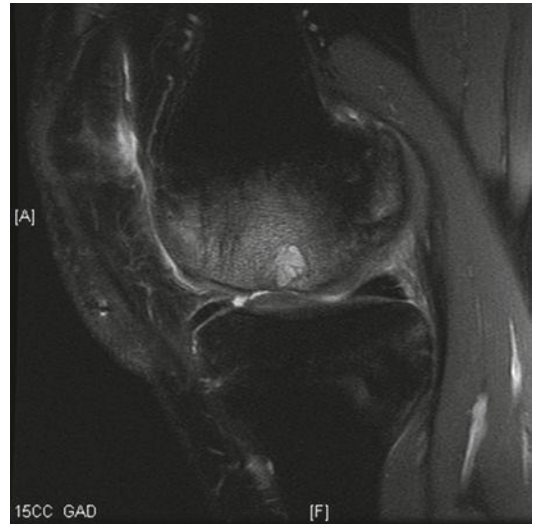


Fig. 2.1 Magnetic resonance imaging (MRI) (*sagittal cut*; proton density, fat suppressed sequence with intravenous Gadolinium contrast) of the medial femoral condyle after failed microfracture showing a large subchondral cyst with extensive subchondral edema

trauma, both acute and chronic microtrauma from overload. Commonly seen after anterior cruciate ligament (ACL) tears and patellar dislocation, in up to 90% of patients [20, 21] traumatic edema resolves in the majority of patients within 1 year [22]. Niemeyer demonstrated significantly worse functional outcomes after ACI in patients with severe preoperative subchondral edema [23].

The MRI assessment of the subchondral bone should include evaluation of the bone marrow signal intensity, the subchondral lamina, the presence of intralesional osteophytes, granulation tissue or sclerosis, and the presence of cysts (Fig. 2.1) [24–26].

The superior sensitivity of MRI for fluid signal is helpful to detect evidence of bone marrow edema; this signal at times can drown out finer anatomic detail. This can be overcome by the use of less fluid-sensitive signals such as Proton Density (PD), but the overall spatial resolution of MRI is inadequate to assess trabecular structure changes, lesser amounts of subchondral plate thickening, or the presence of smaller subchondral cysts. Generally speaking, whenever the subchondral bone is the focus of one's attention, consideration should be given to computed to-

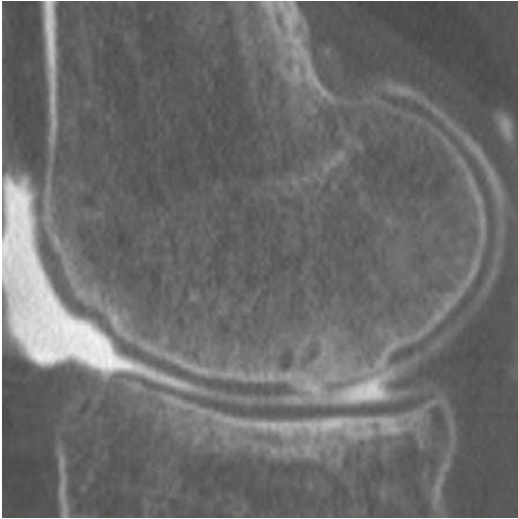


Fig. 2.2 Computed tomography (CT) arthrogram (*sagittal cut*) of the medial femoral condyle after failed microfracture showing a large intralesional osteophyte covered with only a thin fibrous layer

mography (CT) as the imaging modality of choice due to its superior resolution and insensitivity to fluid signal. While isolated CT does not depict articular cartilage very well, in combination with a contrast arthrogram, excellent visualization of the articular surface can be achieved (Fig. 2.2). In many complex situations, both an MRI and CT arthrogram may be desirable, the former to assess subchondral edema and potential qualitative changes in the articular cartilage through cartilage-sensitive sequences; the latter for structural changes in the subchondral bone. Further detail on these imaging modalities will be discussed in Chap. 3.

Subchondral Changes After Surgical Intervention

Marrow stimulation includes the original techniques of subchondral drilling [27] and abrasion arthroplasty [28], as well as the more recently developed microfracture procedure [29]. All three attempt to affect filling of a chondral defect with reparative tissue resulting from stimulation of the subchondral bone at the bottom of the defect. Blood and mesenchymal cells from the underly-

ing bone marrow form a clot in the defect that over time differentiates into a fibrocartilaginous repair tissue [29]. Animal models have demonstrated significant changes in the subchondral bone after marrow stimulation; Buschmann et al. investigated differences between microfracture and drilling in a rabbit model, showing better repair tissue and bone healing with the latter, although both result in bone alterations [30–32]. Another group examined subchondral drilling for cartilage repair in a sheep model, which resulted in the formation of subchondral cysts in 63% and intralesional osteophytes in 26% of cases. In addition, bone mineral density was lowered significantly [33]. These findings were supported by another animal study that also demonstrated a high incidence of subchondral bone cysts after microfracture [34]. Several clinical studies have demonstrated a 27–33% incidence of thickening of the subchondral plate and intralesional osteophytes after treatment with the microfracture procedure [4, 5, 35]. These findings are similar to those seen in chronic defects, which have yielded lower success rates after any type of cartilage repair, including ACI [9]; this has prompted concerns that treatment with MST could negatively impact later cartilage repair procedures. Better understanding of technical details to minimize the subchondral bone unit dysfunction after bone marrow stimulation should be pursued (Fig. 2.3). Currently, complete removal of all calcified cartilage is advised to obtain better defect filling with repair tissue [36]. Animal studies demonstrated that failure to completely remove the calcified cartilage layer leads to poor healing of the defect. However, Frisbie et al. observed significantly more new bone formation in defects in which the calcified cartilage had been removed at the time of surgery (26.5 vs. 3.7%), while the overall incidence of subchondral cysts after microfracture was not affected by removal or preservation of the calcified zone [34].

Other cartilage repair procedures besides marrow stimulation also impact the subchondral bone. Osteochondral autograft transfer and allograft transplantation both replace the entire osteochondral unit, but changes in the subchondral bone are commonly observed. Specifically, cysts

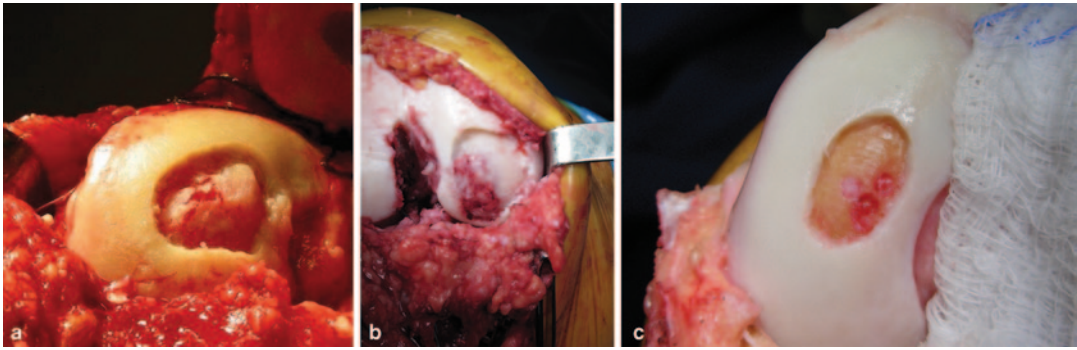


Fig. 2.3 Examples of subchondral changes after failed marrow stimulation techniques (MST), all after debridement for revision cartilage repair with ACI. **a** A large intralesional osteophyte of the medial femoral condyle; **b** diffusely abnormal subchondral plate in the inferolateral aspect of this cartilage defect; the superomedial aspect appears normal. **c** Largely intact subchondral plate with the exception of several drill-holes that have not filled in

can form especially when there is a mismatch in the level of the tide mark between graft and host [37]. Also, one major failure mechanism for osteochondral allografts is the collapse of the transplanted subchondral bone, resulting in an osteochondral defect not unlike an OCD lesion [38].

Even ACI, as an isolated surface treatment, has a chance to result in bone marrow changes. Specifically, the subchondral plate can thicken, become irregular or form intralesional osteophytes, most likely due to trauma created when debriding the layer of calcified cartilage. A recent randomized trial comparing ACI and microfracture demonstrated subchondral plate changes in approximately 25% of ACI patients at 3 years after surgery, compared with 50% of patients treated with microfracture [39].

Effects on Subsequent Cartilage Repair

Conventional wisdom holds that the results of other cartilage repair procedures are not negatively influenced by previous treatment, especially with marrow stimulation such as microfracture, which has been termed a “non-bridge-burning” procedure. While several studies failed to detect any detrimental effects of prior treatment with microfracture, two recent publications were designed to specifically investigate this question. Both found substantial increases in failure rates

of ACI when patients had previously undergone attempts at cartilage repair with bone marrow stimulation techniques. In comparison to patients who had only undergone debridement and/or chondroplasty, marrow stimulation increased failure rates between 3- and 7-fold [40, 41]. No studies have specifically investigated the effects of prior treatment with osteochondral auto- or allograft on ACI, but any changes in the subchondral bone have the potential to negatively affect subsequent treatment with ACI.

The effects of prior marrow stimulation on subsequent cartilage repair other than ACI are varied and controversial. While no study has investigated this issue specifically for osteochondral autograft transfer or allograft transplantation, conceptually, no effects would be expected since the entire osteochondral unit is being replaced.

Treatment Options

Additional research is needed to identify the exact cause of failure, for example the increased mechanical stiffness of the subchondral plate, and how to address potential causes. Furthermore, subchondral changes are common, even without prior treatment. For example, chronic defects are often associated with subchondral edema and mild thickening of the subchondral plate. It would therefore be important to determine whether there is a threshold for these findings,



Fig. 2.4 The large intralesional osteophyte from Fig. 2.3a is shown after removal using a micro-burr. The defect now has a clear base for ACI implantation

where mild changes are found not to influence subsequent ACI, while more severe changes will increase failure rates to unacceptable levels, and treatment with allograft should be recommended instead.

If treatment with ACI is performed, an abnormally thickened subchondral plate or intralesional osteophyte should be treated with a micro-burr under constant irrigation to avoid thermal necrosis of the bone. The sclerotic portion of the plate should be carefully removed in layers, being mindful not to break into the subchondral bone itself to avoid undue bleeding (Fig. 2.4). In general, this sclerotic bone is avascular and no significant bleeding occurs. In the rare event that bleeding becomes an issue, fibrin glue can be pre-clotted on the surgeon's glove and then pressed into the defect, closing off any vascular channels.

Conclusion

Cartilage disease is not an entity solely limited to the articular surface, and successful management requires careful assessment of the entire osteochondral unit. Current research does not provide conclusive information of whether there is a threshold, beyond which isolated surface treat-

ment is inadequate, and an osteochondral procedure is needed. Extensive subchondral edema of the majority of the ipsilateral condyle has been shown to increase failure rate of ACI; intralesional osteophytes and a thickened subchondral plate can be addressed with micro-burring prior to ACI in hopes of decreasing the stiffness, although at this point the long-term effects of this intervention are not known.

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