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Angaben zur Veröffentlichung / Publication details:

Vogt, Stephan, and Andreas B. Imhoff. 2006. "Injuries to the articular cartilage." *European Journal of Trauma* 32 (4): 325–31. <https://doi.org/10.1007/s00068-006-6096-z>.

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Injuries to the Articular Cartilage

Stephan Vogt, Andreas B. Imhoff¹

Abstract

Injuries to articular cartilage are commonly encountered in orthopedic sports medicine. These lesions can lead to sport invalidity and premature osteoarthritis. The management of chondral and osteochondral lesions represents a challenge to clinicians and scientists. The aim of the therapy has to be the recurrence to former sport levels and the prevention of early osteoarthritis. Today there are different concepts of treatment. One therapy principle is the recruitment of mesenchymal stem cells. These procedures lead at best to fibrocartilaginous repair tissue that is functionally inferior to normal hyaline cartilage. Another group of procedures is the transplantation of autologous osteochondral grafts, which provide repair with a hyaline cartilage matrix and show good clinical medium-term results. But osteochondral grafts are limited and there is a potential donor-site morbidity. Finally, the transplantation of autologous chondrocytes is used. However, this kind of transplantation repairs the chondral injury only by fibrocartilaginous repair tissue, too. Therefore, new techniques for the treatment of articular cartilage injuries have to be established. The most promising field today is the combination of tissue-engineering and gene therapeutic methods for the treatment of the chondral and osteochondral lesions.

Key Words

Chondral/osteochondral lesion/injury ·
Osteochondral transplantation · Mesenchymal stem
cells · Autologous chondrocyte transplantation ·
Tissue engineering · Gene therapy

Introduction

Chondral and osteochondral injuries are commonly encountered in orthopedic sports medicine [1]. These lesions can lead to sport invalidity, to premature osteoarthritis and may cause a decrease in the quality of life with long-term costs of health care. Hyaline cartilage in adults does not have a blood, lymphatic or nerve supply and the chondrocytes are incorporated into their extracellular matrix with limited metabolism activity. The potential for healing is therefore very low. Only in the cases of minor chondral damage with minimal loss of matrix components, the chondrocytes are able to synthesize new proteoglycans and to restore the cartilage [2]. The underlying vascularized subchondral area is involved in the healing of cartilage defects. A repair process can be initiated from the subchondral tissue and the blood by mesenchymal stem cells, which migrate into the defect. However, this repair tissue is connective tissue or at best fibrocartilaginous tissue and undergoes relatively fast degeneration processes and fails to function as hyaline cartilage [3]. The management of chondral and osteochondral lesions represents a challenge to clinicians and scientists [4, 5]. The aim of the therapy has to be the recurrence to former sport levels and the prevention of early osteoarthritis.

Current Concepts of Treatment

Recruitment of Mesenchymal Stem Cells

Based on knowledge of the pathophysiology of articular cartilage, many clinicians have attempted to improve healing by drilling [6], abrasion [7] or microfracturing [8] of the subchondral bone. The aim of these techniques is the recruitment of mesenchymal stem cells from the subchondral area to stimulate the formation of cartilage repair tissue. However, this fibrocartilaginous repair tissue contains a high proportion of fibrous elements

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Received: May 3, 2006; revision accepted: July 13, 2006.

and is functionally inferior to normal hyaline cartilage. With these techniques symptoms can be improved only temporarily. The long-term function of the joint is not enhanced [9]. Therefore, this treatment can be recommended only as a timesaving procedure.

Osteochondral Autologous Transplantation (e.g. OATS™)

The transplantation of autologous osteochondral grafts has shown promising results in the treatment of circumscribed cartilage lesions [10–15]. Therefore, autologous cylindrical osteochondral grafts are taken from the minimal weight-bearing periphery of the lateral or medial femoral condyle at the level of the patellofemoral joint and are transplanted to prepared defect sites on the weight-bearing surfaces. Compared with the outcome of subchondral bone penetration, osteochondral grafts provide repair with a fully formed articular cartilage matrix and viable chondrocytes potentially capable of maintaining the hyaline matrix [2, 16]. Reports of recent clinical studies indicate that these techniques can restore the articular surface of the joint. In limited cases, a morbidity of the donor site in the knee is described [17]. Therefore, our group introduced a new technique to prevent the donor-site morbidity in the cases of harvesting more or/and larger grafts. After harvesting of the osteochondral cylinder, a periosteal flap is prepared which is fixed direct above the defect. The defect is filled by a spongiosaplasty from the distal femur, and the periosteal flap is stitched over the defect (Figure 1).

Osteochondral Transplantation on Various Joints

Talus. The osteochondral autologous transplantation method on the talus is used in traumatic and non-traumatic osteochondral defects of the talus, age greater than

16 years and less than 50 years, orthograde weight bearing, stable ligaments of the ankle joint, and absence of severe knee pain or injury in the past [18, 19]. Open autologous osteochondral transplantation is performed by either anteromedial or anterolateral arthrotomy or lateral or medial malleolar osteotomy. Depending on the size of the defect, grafts are implanted using a maximum of three cylinders (Figure 2). In most cases, a medial malleolar osteotomy is used with osteosynthesis by malleolar screws. The postoperative regimen involves free range of motion for dorsalextension and plantarflexion without supination and pronation. Weight bearing is forbidden for 6 weeks. Radiographs are taken on postoperative day 1, 6 weeks and 6 months later, after surgery. If screws are used they will be explanted after healing of the malleolar osteotomy. Figure 3 shows the successful integration of such grafts 6 months after surgery.

Elbow. Avascular necrosis and chondral/osteochondral defects in the elbow joint remain challenging for proper treatment. Mostly the radio-humeral joint is affected. M. Panner as juvenile avascular osteonecrosis of the capitellum humeri [20] is distinguished from osteochondral lesions (OCL) and osteochondrosis dissecans (OCD) in adolescence affecting the capitellum [21], the trochlea [22] or the radial head.

A lateral approach with longitudinal incision from the lateral epicondyle along the radial head and the anconeus muscle is chosen. The fascia is split between the anconeus and extensor carpi ulnaris muscle. The joint capsule is exposed and then longitudinally incised anteriorly to the radial head. The annular ligament should be preserved. Now the humero-radial joint is well exposed, and by moving the joint in extension/flexion as well as rotation, a

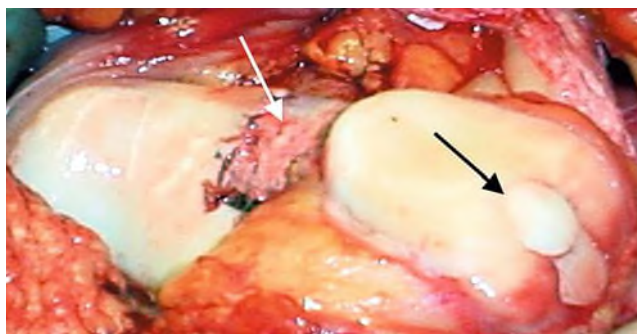


Figure 1. Covering the donor-site defect by a retro periosteal flap (white arrow) to prevent morbidity in the cases of harvesting more and/or larger grafts. Osteochondral grafts in the patella (black arrow).

Figure 2. Reconstruction of the medial talus shoulder with autologous osteochondral cylindrical grafts.



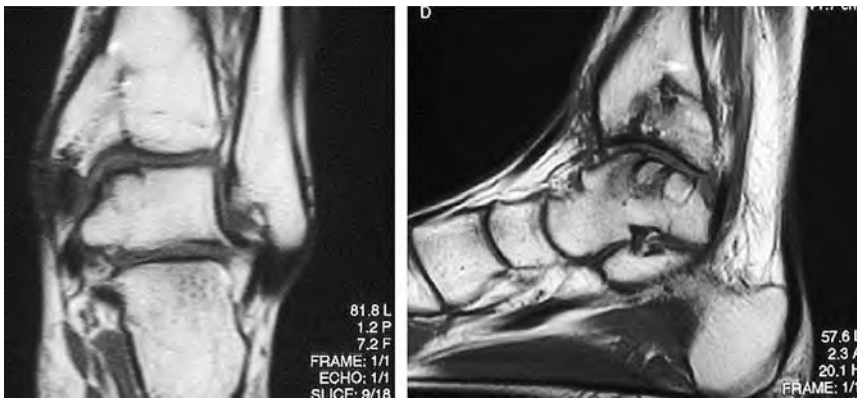


Figure 3. MRI with i.v.-Gd-DPTA 6 months postoperative showing a good integration and vitality of the transplanted osteochondral cylinders.

thorough inspection is possible. Usually, the defect in the capitulum is well exposed in full extension. The postoperative regimen involves free range of motion, especially full flexion and extension for 2 weeks passively, and then active free range of motion is allowed, non-weight bearing or lifting of heavy loads for 6 weeks for the elbow and weight bearing as tolerated for the knee. Radiographs are taken on postoperative day 1, 6 weeks and 6 months after surgery, MRI optional 8–12 weeks after surgery.

Retrograde Osteochondral Autologous Transplantation. Retrograde transplantation of osteochondral autografts on the tibial plateau can be done arthroscopically or by an open technique dependent on the defect [23]. With the arthroscope in the anterolateral portal, the ACL drill guide is passed through the anteromedial portal and positioned over the center of the defect (Figure 4). An anterolateral or anteromedial arthrotomy is performed to approach the lesion and introduce the drill guide for open procedures. Subsequent steps are performed in an analogous fashion.

A cortical window is removed from the tibia. A guide pin is placed and overreamed with the OATS chisel to obtain a bony cylinder. A cannulated reamer is then used to ream the remaining distance into the joint to remove the damaged subchondral and chondral tissue. A diagonal cartilage bone cylinder with the angle corresponding to the angle of the drill guide is harvested. The graft is inserted into the tibial tunnel in a retrograde fashion, and the remaining bony defect in the tibial tunnel is filled with the bony cylinder from the tibia. A diagonally cut bioabsorbable interference screw is inserted to prevent migration of the cylinder. The cortical block is then reinserted in the bony window and closed with the periosteum. The articular

surface of the cylinder should be congruent with the surface of the tibial plateau. Postoperatively, non-weight bearing is advised for 6 weeks with free range of motion. Postoperative MRIs showed vital cylinders, healing of the implanted plug, and a congruent chondral surface.

Transplantation of retrograde autografts on the distal tibia is possible too. An anterior or posterior incision is used to access the ankle joint line under protection of the tendons, vessels and nerves. The ACL drill guide is positioned at the

center of the defect. Under protection of the talus with a metal ruler, a guide pin is inserted through the cortical window and overreamed with the OATS instrument under radiographic control. The osteochondral donor plug is harvested from the knee in the described technique. The subsequent steps are performed in an analogous fashion as described above. The postoperative regimen involves free range of motion for dorsalextension and plantarflexion without supination and pronation. Weight bearing is forbidden for 6 weeks. Radiographs are taken on postoperative day 1, 6 weeks and 6 months after surgery [23]. Postoperative MRIs are done to show the vitality of the grafts and a congruent chondral surface.

Knee, Mega-OATS™. The Mega-OATS technique is a procedure merged of the press-fit idea of OATS and the transfer of the posterior femoral condyle [11, 12, 24].

The autologous posterior femoral condyle transfer was introduced in 1990 by the senior author as an

Figure 4. The ACL drill guide (Arthrex) positioned in the center of the defect (open procedure).



alternative procedure to arthroplasty, which was enhanced to the Mega-OATS technique, implementing the Mega-OATS workstation as a positioning device in 1999. As there are encouraging good results after osteochondral transplantations with single and multiple small OATS cylinders in the weight-bearing zone of the femoral condyle up to 2×2 cm defect size, there was a need for a technique, which could be applied in the case of larger lesions. Therefore, the indication is focused on lesions of osteochondritis dissecans (OCD), focal osteonecrosis and grade IV cartilage lesions, which exceed the maximum size for treatment with the standard OATS technique [12]. The presumed advantage of covering the lesion with hyaline autologous cartilage and replacing necrotic bone areas is achieved by the loss of the posterior femoral condyle, which makes clear that Mega-OATS is a salvage procedure.

Surgery starts with a central longitudinal cut. The next step is an anteromedial or anterolateral arthrotomy for exposure of the defect area. Before harvesting the posterior femoral condyle for transplantation, it is recommended to mark and exactly measure the defect in its diameter and depth (Figure 5). In about 130° flexion of the knee, the ipsilateral femoral condyle to the lesion is harvested by a chisel osteotomy. The ideal osteotomy follows the line of the posterior femoral corticalis. This procedure normally allows the harvesting of a graft up to 35 mm in diameter and up to 20 mm thickness in adults. The free graft now has to be prepared in a special workstation (Arthrex Inc., Naples, USA). The graft has a 0.3 mm larger diameter than the initially prepared graft's bed for press fit fixation. A sta-

ble anchorage of the graft requires a minimum of 270° bone support around the cylinder (Figure 6) in other cases a fixation with a minifragment screw is necessary. This requires an arthroscopic screw removal after 6 weeks. The regime after surgery requires 6 weeks non-weight bearing with crutches and limited flexion to 90° . We recommend continuous passive motion on a motor splint during this time. After this period, an increasing load with 20 kg per week up to the patient's body weight and progressive range of motion follows. Figure 7 shows the successful integration of such a graft 58 months after surgery.

Autologous Chondrocyte Transplantation

The autologous chondrocyte transplantation (ACT) was introduced to the therapy of the joint cartilage damage in the middle of the last decade [25]. This technique uses isolated chondrocytes, which are obtained from a cartilage biopsy by enzymatic digestion. These cells are proliferated under cell culture conditions. Important for this technique is the existence of intact subchondral bone (Figure 8). If the subchondral bone is affected this defect must be treated by spongiosaplasty before. This situation is however clearly more unfavorable. At this time, there are three competitive therapeutic procedures:

1. The transplantation of autologous chondrocytes in a suspension (ACT, ACI)
2. The matrix-associated autologous chondrocytes transplantation (MACT, MACI)
3. The matrix-associated microfracturing.

In the original technique of Brittberg et al. [25], the autologous chondrocytes are injected under aperi-



Figure 5. Marked osteochondritis dissecans lesion in the left medial femoral condyle.

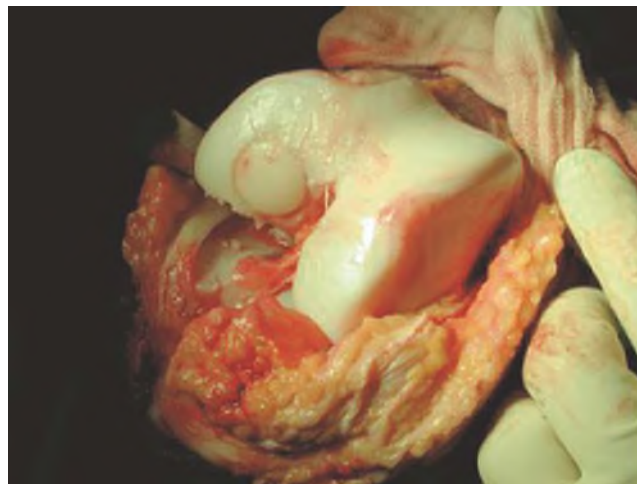


Figure 6. Intraoperative situs with press-fit implanted Mega-OATS graft.

Figure 7. MRI 58 months after Mega-OATS transplantation.



osteal flap. This is the classical non-matrix associated chondrocytes transplantation. Today new techniques of cell culture and modern materials permit the implantation of chondrocytes in or on absorbable three-dimensional scaffolds/matrices. They build the large group of the matrix-associated chondrocytes transplantations (Figure 9). The use of such scaffolds/matrices makes a more constant cell distribution in the defect possible and simplifies the procedure. A suture for transplant fixation is not absolutely necessary. The scaffolds/matrices shall dissolve after a defined time and assist the growth and differentiation of the repair tissue. At present, different absorbable materials are used in clinical application.

1. Collagenes of animal origin (collagen I and III) as fleece, gel and membrane
2. Hyaluronan and determined polymers (e.g. PLA, PGLA) as fleece.

The fixation of the implant is dependent on the biomechanical characteristics of the implant and the size and/or localization of the defect. Gels or certain membranes can be inserted into the defect and be fixed there without further adjustment by adhesive strengths. Alternatively, laminar or punctual attaching with fibrin glue or the fixation at the surrounding cartilage with sutures is possible. A transosseous anchorage reaches the highest initial biomechanical stability. This is necessary by stronger bleeding from the defect or with a defect at the edge with high shear loads. The use of biomechanically stable scaffolds/matrices makes the arthroscopic implantation possible. A special kind of this principle is the matrix-coupled microfracturing. In this case, the procedure of the microfracturing is combined with a collagen matrix. The mesenchymal stem cells should migrate into the defect and differentiate to chondrocytes with the help of the matrix. The advantage of this procedure is the cost reduction and the gain of time with only one operation. So far there is no study until now which show a significant advantage of one of these procedures. Although there is so far no histological proof on healing of the chondral defect with hyaline cartilage [26] the clinical results are partially encouraging.

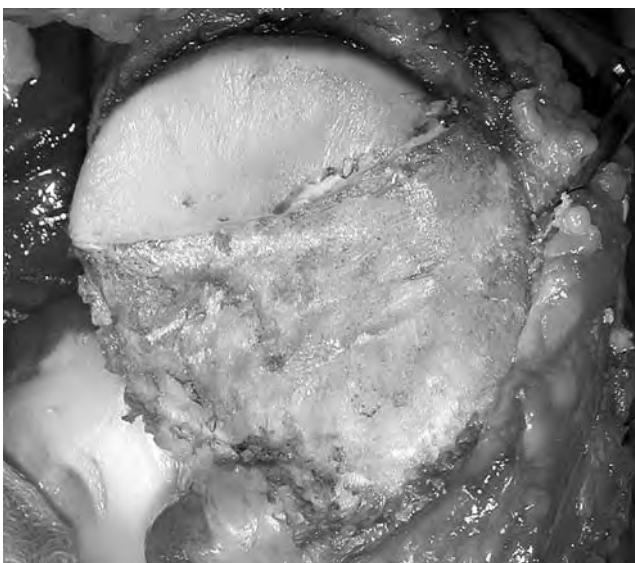


Figure 8. Cartilage lesion grade IV with intact subchondral bone. Intraoperative situs after debridement.

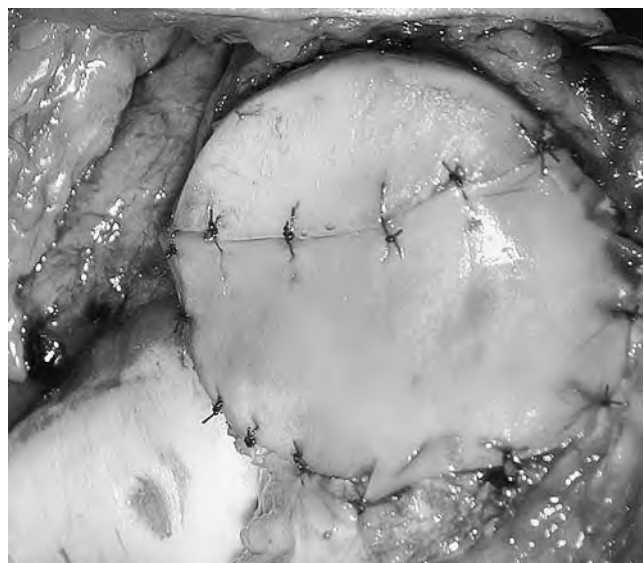


Figure 9. MACI implantation into the defect area. Fixation with transcartilaginous sutures (5-o Vicryl).

Future Concepts of Treatment

The use of growth factors together with tissue-engineering methods is an attractive extension for the future treatment of the chondral and osteochondral lesion [27]. These growth factors belong to the large group of cytokines and can be produced by mesenchymal stem cells immigrating into the defect, by chondrocytes and inflammatory cells. These factors stimulate the cell growth, the cell proliferation, the differentiation and the matrix synthesis [28]. Studies showed that these factors increased the metabolism of chondrocytes and promoted the healing of cartilage defects [28, 29]. An important group of cytokines is the transforming growth factor (TGF- β) family with the bone morphogenetic proteins (BMPs). BMP-2 leads for example to an increase in proliferation of immigrating cells and differentiation of these to chondroblasts and osteoblasts and an increase of the histological ICRS scores of cartilage regeneration in an animal trial [28, 30]. A sufficient production of the growth factor only in the defect area without influencing the surrounding tissue is important. Therefore, gene therapeutic procedures are suited best and a gene transfer of the "therapeutic gene" into cells of the defect is necessary. Different transfer systems are available at this time. The DNA of the "therapeutic gene" must move into the cytoplasm and/or in the cell nucleus via cell membranes (celltransduction). Carrier molecules that mediate this transfer process are named vectors. Fundamentally one distinguishes two main groups; the non-viral (plasmids) and the viral vectors. The non-viral vectors possess a slight toxicity, are simply applicable and do not show oncogenous potential. The disadvantages exist in the slighter transduction rate and stability of the transfer. Viral transfer systems are for example retroviral, adenoviral and lentiviral vectors with different operating mechanisms. In summary, the advantage in contrast to non-viral systems is that the gene transfer is more stable and efficient. The disadvantages are especially for retroviral vectors the oncogenous potential. Newer vector systems are controllable [31] and the probability of an insertional mutagenesis with a high tumor risk is unlikely [32]. After successful studies in animal models, these vector systems could become interesting for the therapy of OCL in humans.

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