

## Cartilage repair update: Indications are being refined and the future is bright

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Cartilage is a highly structured tissue with low cellularity and virtually no reparative capabilities. As such, symptomatic cartilage defects require surgical intervention to heal. The field of cartilage repair remains one of the most active areas in orthopedics, both from a clinical and a research perspective.

Although several procedures are currently available to orthopedic surgeons to repair damaged cartilage, the indications and treatment algorithms continue to evolve as additional data become available. We have brought together several respected experts in this challenging area to share their thoughts and visions with us. Our questions to the experts aim to clarify several key points when selecting appropriate treatment options: Is there a role for prophylactic treatment of asymptomatic defects? Which factors influence treatment decisions? What is the role of articular comorbidities such as malalignment, instability and meniscal deficiency? and, What are the guidelines for return-to-activities?

Lastly, we asked our panel about their expectations regarding future developments for cartilage repair in the next 5 to 10 years. We hope that you will find this Round Table discussion helpful and will be able to incorporate some of these recommendations into your clinical practice.

**Andreas H. Gomoll, MD**  
Moderator

### Round Table Participants

#### Moderator



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**Andreas H. Gomoll, MD:** Is there a role for early or prophylactic treatment of the asymptomatic patient with an isolated full-thickness chondral defect or a recently meniscectomized knee?

**Brian J. Cole, MD, MBA:** The difficulty with this situation is that the natural history of most chondral and osteochondral pathology is largely unknown. I also believe that most incidental lesions can be observed with proper patient education as to the development of clinically relevant symptoms. There are patients, however, who present with a significant risk for pathology progression. For example, osteochondritis dissecans of the lateral femoral condyle can often involve a significant portion of the weightbearing area of the condyle and may be associated with cystic changes that often predictably become symptomatic with activities. These lesions might require early treatment due to their limited biomechanical integrity. Another example includes the relatively young active female who undergoes a subtotal lateral meniscectomy who also has physiologic valgus alignment. This clinical scenario has a significant risk for disease progression in the lateral compartment.

The threshold for early lateral meniscal allograft transplantation in this at-risk group is generally low and the first sign of effusions or radiographic change (X-ray and/or MRI) might lead to a recommendation for early lateral meniscal allograft transplantation. This might occur even without complaints of pain in the involved compartment.

**Jack Farr II, MD:** This is a challenging question. The treatment of true, absolutely asymptomatic chondral lesions remains controversial as current restorative techniques are not 100% efficacious, there is always the potential for complications with any surgery and the risk of progression is unknown. Thus, I would be hesitant to treat truly asymptomatic lesions.

On the other hand, I find that many of these “asymptomatic lesions” are mislabeled, as the patient often has limited his or her activity to avoid pain and/or effusions. In these patients, I would encourage a brief increase in activity to his or her desired level and at that point many patients indeed, have symptoms and would be treated.

**“In the future I look forward to genetic profiles to tell us the quality of the patient’s articular cartilage.”  
— Jack Farr II, MD**

In the young patient, if there are no symptoms even with an increased activity level, I would follow them closely both clinically and with MRI as I do not want lesion progression or “collateral damage,” especially in the malaligned, meniscal-deficient and/or unstable joint. This early intervention in the young is supported by the published work of Mithöfer et al who found earlier articular cartilage restoration intervention leads to better outcomes than delayed treatment.

In the future I look forward to genetic profiles to tell us the quality of the patient’s articular cartilage. At that time, patients at genetic high risk of chondrosis progression may benefit from “prophylactic” meniscal and/ articular cartilage restoration.

**Scott D. Gillogly, MD:** There is a very limited role in the adult. However, in the adolescent or young adult there is definitely a place for early treatment. Clear examples would be the valgus aligned knee following near-complete lateral meniscectomy, or a full-thickness chondral defect of the trochlea in a knee with a subluxing or dislocating patella.

**J. Richard Steadman, MD:** Full-thickness cartilage defects are encountered during arthroscopic surgery. With the availability of high-resolution MRI, it is uncommon not to have recognized the defects before the surgery. Several rules can be followed if a full-thickness defect is discovered incidentally.

**“Pain is the number one determinant for invoking treatment recommendations.”  
— Brian J. Cole, MD, MBA**

My first line procedure for these lesions is microfracture. The treatment protocol requires that the procedure and rehabilitation be done with a specific technique. If this has not been explained to the patient and the rehabilitation agreed to, then I would not do a microfracture. Debridement of unstable flaps is done, but treatment with microfracture is withheld until the patient has agreed to the full program in a second procedure. Another reason for delaying treatment is the possibility of malalignment which is a major

consideration prior to microfracture.

I have seen several patients who have had defects identified but not treated, and then over time they have progressed to lesions five to 10 times the size of the original defect. If the patient elects not to have the defect treated, the possibility of dramatically increasing the size of the defect must be considered, and this should be explained to the patient. If the defect is not treated, follow-up MRI can be done, but major damage or degeneration can occur between MRIs.

Degenerative defects where the cartilage surrounding the defect is thinned due to degenerative joint disease (DJD) are often observed. In these degenerative defects, meticulous attention should be paid to the joint environment during the surgery. For example, stiffness, decreased joint volume, synovitis, and decreased range of motion should be addressed.

Treatment of the knee after total or subtotal meniscectomy is evolving. I have been involved in a project in which collagen implants are inserted to replace the missing portion of meniscus. This procedure is promising, but currently it is not approved by the U.S. Food and Drug Administration. The use of the product in Europe has increased markedly and with noteworthy success.

**Gomoll:** What patient-specific or defect-specific factors are most important in determining treatment, and how do they influence your decision when choosing between marrow stimulation, osteochondral autografting, osteochondral allografting or autologous chondrocyte implantation?

**Cole:** Pain is the number one determinant for invoking treatment recommendations. Obviously, second to pain, activity limitations are often present. The mere presence of a chondral or osteochondral lesion, however, must be associated with clinically relevant symptoms before one should attribute the patient's problem to the cartilage defect.

Another important factor is the treatment history for that defect. First-line treatment recommendations will often include debridement, especially when symptoms are relatively short-lived and are largely mechanical in nature. Patient activity level and the severity of symptoms with the absence of any other intra-articular pathology might encourage the first-line use of marrow stimulation (eg, microfracture) in my practice for most lesions. This is especially true for out-of-season athletes who can afford the time required to maximize the benefit of this technique.

Chondral defects or shallow osteochondral defects of the femoral condyle when very small might easily be amenable to osteochondral autograft transplantation. My bias for recommending this technique includes defects of less than 10 mm to 12 mm so as to utilize one larger diameter plug to treat the entire lesion. Second-line treatment of most defects is often guided first by defect depth, with osteochondral lesions generally being treated with osteochondral allograft transplantation, especially in slightly older patients with defect depths of more than 6 mm to 8 mm. Larger chondral defects or shallow osteochondral defects, especially in younger patients who require second line treatment, are often treated with autologous chondrocyte implantation. Notably, this remains my preferred treatment option for the trochlea and patella.

**Farr:** Demand matching the patient and the knee is very important to achieve patient satisfaction. I will not repeat the many algorithms presented recently in the cartilage literature, but would point out that there appears to be some agreement among cartilage surgeons that younger patients are candidates for the procedure that offers the highest probability of hyaline-like cartilage without the same concerns for total (initial) cost or time with limited weightbearing and activity compared to the older patient.

**“Osteochondral autografts are most useful when the lesion can be treated with two or less plugs.”**  
— Scott D. Gillogly, MD

Along the same line of thought, older patients often cannot tolerate extended time to be off work and may not even elect for biologic options.

In terms of cartilage genetics, if the patient has what appears to be an early predisposition to osteoarthritis (OA), the use of his or her own poorly functioning cells seems less appealing. Additionally, when autologous pluripotential marrow cells are used there may likewise be an age factor to be considered. Kreuz and Steinwachs' recent study suggests suboptimal results for marrow stimulation in an older age group.

In regards to the knee specific factors you mentioned:

- In terms of size, larger defects are more often treated with cell therapy or osteochondral allograft (OCA) and smaller defects are often treated with debridement alone, marrow stimulation, autograft plugs with overlap between these extremes;
- In terms of location of defect, for large defects on the condyles I lean toward cell therapy or OCA while in the patellofemoral compartment as the lesions I see are typically large and not uncommonly bipolar, I use more cell therapy than OCA (my tibial experience is limited);
- When there is a lack of defect containment, cell therapy and OCA are viable, but autograft plugs and marrow stimulation are less appealing; and
- When there is a chondral defect with bone involvement, I use autograft bone graft plus cell therapy in the younger patient or OCA in larger deeper lesions especially in (relatively) older individuals.

**Gillogly:** With advancing age, over 40-45 years old, I would be more likely to treat any osteochondral lesion with OCA, whereas in the adolescent I would reserve that treatment as a salvage procedure. Osteochondral autografts are most useful when the lesion can be treated with two or less plugs (up to 11 mm). Containment, or lack thereof, is seldom a decision-forcing issue. Marrow stimulation seems most reasonable with smaller lesions on the condyles in healthy, compliant adult patients. I would otherwise favor autologous chondrocyte implantation (ACI) for any larger lesion, in any location, with chondral involvement. I would reserve bone grafting of osseous lesions prior to ACI for adolescents.

**Steadman:** My first treatment for chondral defects is microfracture. If the treatment is unsuccessful, my experience with other procedures is limited. If the procedure fails, reasons for failure are thoroughly explored. If a problem occurs during the recovery, repeat microfracture may be considered while correcting the problem. If the joint environment has stiffness, decreased volume, synovitis, and decreased range of motion, then these issues are addressed and corrected.

Axial alignment is very important in treatment of chondral defects, and if significant malalignment is present, osteotomy is recommended. All patients have an assessment of the mechanical axis to assist in the decision for treatment. Nonsurgical options are considered and initiated if alignment is not acceptable for cartilage defect treatment.

**Gomoll:** How do you factor in comorbidities such as meniscal deficiency, ligamentous instability, and tibio- or patellofemoral malalignment?

**Cole:** Correcting tibiofemoral alignment for femoral lesions and patellofemoral alignment for patellofemoral lesions remains the most critical determinant for a successful clinical outcome. Even minor degrees of physiologic varus or valgus are corrected to neutral when the defects being treated reside in the relevant compartment. Unlike in the osteoarthritic patient where overcorrection is recommended, I will typically try to bring the mechanical axis to the center of the knee, or possibly to the contra-lateral tibial eminence.

Lateral or central patellofemoral lesions are treated with concomitant tibial tuberosity anteromedialization (AMZ), which, when associated with patellar instability, generally achieves a tibial tuberosity to trochlear groove distance of about 12- to 15-mm while anteriorizing the tuberosity about 10 to 15 mm. Medial patellofemoral lesions are often treated with a modification of the AMZ which involves a vertical osteotomy from anterior to posterior that stops short of the posterior tibial cortex. The osteotomy is completed in the coronal plane from lateral to medial to “swing” the tibial eminence straight anterior to achieve a Maquet-type effect that does not require bone grafting. This avoids the inevitable increase in medial patellofemoral forces, which otherwise occurs with a traditional AMZ.

Regarding the meniscus in the same compartment as the defect, my threshold to recommend concomitant allograft meniscus transplantation is relatively low if the meniscus is compromised back to the periphery along even very short longitudinal distances, which renders it biomechanically non-functional. Similarly, if the ACL is non-functional, this is corrected at the time of cartilage treatment, or at the very least, prior to definitive articular cartilage and/or meniscal deficiency treatment.

**“I am a very strong proponent of the microfracture technique and of biological repair of articular cartilage.”— J. Richard Steadman, MD**

**Farr:** I feel it is important to optimize the environment for the cartilage implant. I attempt to treat all co-morbidities with the goal of normalization rather than marked overcorrection. For example, a varus knee is corrected to 1° to 2° of valgus, rather than the classic overcorrection of 3° to 5° for the treatment of medial compartment OA. I reconstruct ligaments and transplant menisci for the same reason.

Of particular interest to me is the patellofemoral compartment. It is not forgiving; you have one opportunity to “get it right.” As any surgery can lead to muscle debilitation and scar, preoperative planning is essential to allow all necessary “normalization surgeries” to be performed at the same time as the cartilage restoration. That is, the goal is one “big” surgery rather than a series of surgeries. This combined/concomitant approach will often include correction of medial surgery (repair, tightening or reconstruction of the medial patellofemoral ligament) lateral surgery (Biedert lateral lengthening or titrated lateral release), distal tibial tuberosity surgery (straight anteriorization or AMZ with or without proximalization or distalization) and rarely the trochlea (trochleoplasty).

I would agree with the comments on the Fulkerson AMZ. It has an important, if incompletely defined role (see the finite element analysis work of Cohen and Ateshian) in optimizing the contact area and forces at the patellofemoral compartment. It is thus important to keep abreast of the changing recommendations when addressing the tibial tuberosity (tibial tuberosity-trochlear groove distance and Caton ratio), noting normalization is the goal, not

overcorrection.

**Gillogly:** I recommend aggressive treatment of co-morbidities in almost all circumstances. Proper alignment of the tibio-femoral joint and patellofemoral joint is this highest priority. Ligament stabilization is the next concern and when performed concomitantly with cartilage restoration procedures, adds very little morbidity. In the meniscal deficient patient, I favor meniscal transplantation for those less than 30 years old and osteotomy in patients over 40 years, with individual decisions in those cases in between.

**Steadman:** I believe that it is important to treat co-morbidities concurrently with treating the chondral lesion. All of the co-morbidities influence the order in which I do the microfracture as part of a single procedure. Typically, I almost always perform other procedures first. For example, I would perform a meniscus repair first and then perform the microfracture. I want to minimize flow of the arthroscopic fluid as soon as possible after completion of the microfracture so that the marrow elements (stem cells and growth factors) are not diluted or washed away.

I feel strongly that correcting any axial malalignment is critical to the success of microfracture. I pay close attention to alignment and include osteotomy as a part of the treatment regimen if indicated. The question of whether osteotomy affects performance in the competitive athlete is unresolved; therefore, osteotomy is reserved until other options have been considered and tried.

These same co-morbidities influence my rehabilitation program and may alter my guidelines for return to full activities. If the rehabilitation requires immobilization, I would delay microfracture until the normal routine postoperative rehabilitation can be done.

**Gomoll:** What are your guidelines for return to activities including recreational and high-level athletic participation?

**Cole:** This is a tough question without a lot of supporting data other than our anecdotal findings. Our experience is that patients who achieve a successful clinical outcome at 2 years are very unlikely to present with recurrent symptoms before 5 to 10 years, independent of their activity level. If patients are indifferent relative to two different activities (ie, running vs. swimming) then I often encourage them to adopt the lower stress activity. Those who achieve a satisfactory clinical outcome and desire to return to high-level athletic participation are educated about activity-related graft issues, including the potential for premature breakdown and macroscopic failure. After performing nearly 1,000 transplants, I can recall few athletes in whom this has actually occurred. The most common scenario is that they simply cannot tolerate the highest level of activity and are forced to reduce their participation due to the inability to compete as opposed to the risk of re-injury.

**Farr:** Preoperatively, setting realistic goals is important. I believe some well-intended studies may create unrealistic optimism for some patients. That is, a high-level or professional athlete's outcome does not equal what most of our patients will experience.

The goal of cartilage restoration, in my mind, is to re-establish comfort with activities of daily living and hopefully prevent or slow the progression to degenerative arthritis – the ability to play sports is an extra. Fortunately, the outcomes for the younger patients with truly focal lesions are good. In these patients, the size of the lesion, the site, and the type of repair/restoration all come into play in the decision on when to return to play. I use the lessons we collectively have learned from ACL reconstructions to guide my recommendations: First, re-establish motion, proprioception and strength, and then allow a gradual increase in activity to a sports specific “functional progression”. If they have pain or swelling, they are not ready for their sport. The time to return to sport can vary from months for small osteochondral autografts to as long as 2 years for larger lesions treated with cell therapy — and many cannot return to sport.

**“Because of the rigors of the FDA, next generation technologies are likely to emerge around the 10-year time-frame.”**

**— Brian J. Cole, MD, MBA**

**Gillogly:** Return to sports activities varies depending on the confounding factors and repair techniques. Individual patient factors also influence the desire and pace to return. In general, osteochondral grafts may return in about 4 to 6 months, meniscal transplants and marrow stimulation repairs in about 6 months and ACL in about 9 to 12 months. Some concurrent procedures, such as osteotomies combined with cartilage repair, seem to slow recovery, adding approximately 25% more time. Also, some patients may take up to 18 months or even longer before returning to full activities.

**Steadman:** Return to activities is dependent on several factors, including lesion size, co-morbidities, patient age, size/body mass, expectations, and pre-injury activity level eg, recreational versus professional athlete.

Generally speaking, I do not let a patient return to full unrestricted activity for 6 months following microfracture. If the lesion was isolated and only 1 cm<sup>2</sup>, I might allow full activity somewhat sooner, perhaps as early as 4 months. If the lesion is very large, say over 10 cm<sup>2</sup>, I would bring that patient along slower with use of non-impact activities for 6 months, and then proceed with advanced rehabilitation as tolerated.

If there are co-morbidities such as ACL or meniscus injuries that require repair or reconstruction, I may extend that to 9 months. I am concerned that patients older than 50 years may heal a bit slower, and so I like to protect them longer. Large patients, especially professional athletes such as football linemen, put tremendous biomechanical stresses on their chondral surfaces. I would wait 9 months, and sometimes 12 months, before allowing them to return to full competitive action. I also go slower with large patients who are not competitive athletes.

**“Of particular interest to me is the patellofemoral compartment. It is not forgiving; you have one opportunity to “get it right.”**  
— Jack Farr II, MD

Regarding patient expectations, if a patient’s goal is to walk up and down stairs and grocery shop relatively pain-free, then I will return that patient to this activity level by 6 months. If the patient wants to play golf or tennis, or if they are competitive athletes at an elite level, I will assess them very carefully through use of a “sport” test (a functional test for strength and endurance) before allowing return to full activity. As noted already, I may prolong the rehabilitation of high-impact elite athletes, especially those with a large body mass.

**Gomoll:** What do you regard as the most promising emerging technologies in the next 5 to 10 years?

**Cole:** In the next 5 years, the regulatory process will permit the effective utilization of minimally manipulated human tissue such as juvenile or adult allograft tissue. Many of these technologies are undergoing clinical trials and post-market evaluation.

Other technologies such as biologically active scaffolds that might enhance the outcomes of traditional marrow stimulation techniques might also become available in this time-frame depending upon the regulatory requirements of the FDA. These are appealing as they are likely to be cost-effective alternatives that can be chosen at the time of surgery as off-the-shelf technology for point-of-care decision making.

Because of the rigors of the FDA, next-generation technologies are likely to emerge around the 10-year time-frame. These might include 2nd- and 3rd-generation cell-based technology that will be more predictable than ACI with less morbidity at the time of surgery and less likelihood of postoperative conditions that would otherwise require repeat surgery.

**Farr:** In the next 5 to 10 years, I look for a rapid articular cartilage specific genetic profile identification of the patient (or donors). With due respect to the company functionally profiling autograft cultures (ChondroCelect, Tigenix, Belgium), I am talking about the complete underlying genetic make-up of the patient or donor cartilage. Does the patient have “Grade A” articular cartilage that with small lesions or loss of meniscal function that will not result in arthritis later in life; “Grade C” that we as a society need to spend resources to restore the joint, as it will both avoid future surgery and save productive work function; or “Grade F” cartilage that is genetically doomed with any autologous dependent biologic approach?

In the latter case, society should avoid spending on autologous approaches and focus on allograft, xenograft or possibly “bridging” synthetic approaches such as hydrogels or other biocompatible polymers.

The next 5 years should see optimization of cell on/in scaffold therapy, growth and other cell modifying factors, single-stage cell therapy and allograft cell therapy. There are also implications for modifying the repair tissue of marrow stimulation (increasing hyaline nature of the repair). In 10 years, the merging of biologics with bio-synthetics may allow an early glimpse (the preclinical stage) of truly biologic unicompartamental, bi-compartmental and total knee arthroplasties.

**Gillogly:** Ideally, the enhancement of cell-based therapies with growth factors to stimulate and hasten various healing cascades. Realistically, I expect matrix ACI and arthroscopic or mini-open ACI.

**“ Return to sports activities varies depending on the confounding factors and repair techniques.”**  
— Scott D. Gillogly, MD

**Steadman:** I am a very strong proponent of the microfracture technique and of biological repair of articular cartilage. We have a strong research program which focuses on methods to enhance and improve microfracture. Studies with which we have been involved

already have led to publications dealing with the mechanical aspects of microfracture, the scientific basis for our rehabilitation program following microfracture, and most recently a preliminary study on enhancement with gene therapy.

Presently, we are actively pursuing studies using adult autologous stem cells, a possible adjunct to microfracture that we see as having exceptional potential.

In the next 5 to 10 years, we envision much more extensive work with gene therapy, especially if we are successful in our efforts to identify a safe vector that can carry more than one gene.

We also have a strong interest and enthusiasm for functional tissue engineering that might use a biological scaffold, perhaps collagen. While use of exogenous growth factors may also hold great promise, we believe that their potential application may be greatly curtailed in today's regulatory environment. Regardless, the future is bright for the biological treatment of joint injuries.

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#### **References:**

- Cohen ZA, Roglic H, Grelsamer RP, et al. Patellofemoral stresses during open and closed kinetic chain exercises. An analysis using computer simulation. *Am J Sports Med.* 2001;29(4):480-487.
- Mithöfer K, Minas T, Peterson L, et al. Functional outcome of knee articular cartilage repair in adolescent athletes. *Am J Sports Med.* 2005;33(8):1147-1153.
- Steinwachs MR, Gugli T, Kreuz PC. Marrow stimulation techniques. *Injury.* 2008;39 Suppl 1:S26-S31.