

# Cartilage Restoration

## *Overview of Treatment Options*

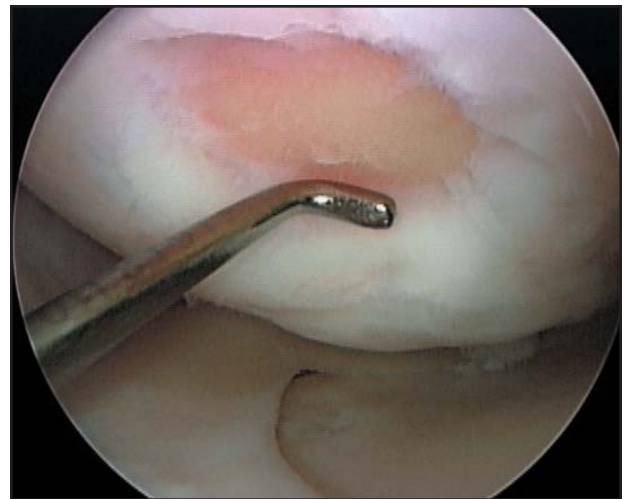
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### **INTRODUCTION**

In 1743, Hunter<sup>11</sup> described ulcerations of articular cartilage as problems that will not heal. The clinical consequences of articular cartilage knee defects are pain, swelling, mechanical symptoms, athletic and functional disability, and osteoarthritis (Figure 1). Full-thickness articular cartilage defects have a poor capacity to heal. The challenge to restore the articular cartilage surface is multidimensional, faced by basic scientists in the laboratory and orthopedic surgeons in the operating room. This article provides an overview of the contemporary treatment options available for the restoration of articular cartilage defects of the knee.

### **EVOLUTION OF CARTILAGE REPAIR OPTIONS**

Full-thickness articular cartilage injury incites a limited intrinsic healing response. This response begins with hematoma formation, stem cell migration, and vascular ingrowth.<sup>4</sup> This response usually produces type I collagen, resulting in fibrocartilage rather than the preferred hyaline cartilage that is produced by the chondrocyte.<sup>6</sup> This “repair cartilage” has diminished resilience and stiffness with poor wear characteristics. The first attempted articular cartilage repair techniques used procedures including lavage and debridement and drilling or microfracture to stimulate mesenchymal stem cell metaplasia to form fibrocartilage. Newer substitution replacement techniques use autograft or allograft to fill defects in articular cartilage. Most recently introduced technologies



**Figure 1.** Arthroscopic picture depicting a full-thickness, grade IV articular cartilage defect of the medial femoral condyle.

involve biologic replacement techniques using autologous chondrocyte cell culture technology.

#### ***Mesenchymal Stem Cell Stimulation***

***Abrasion Arthroplasty.*** Abrasion arthroplasty is performed using a shaver or burr to remove the superficial 1-2 mm of sclerotic subchondral bone to expose the underlying vascular subchondral plate.<sup>14</sup> The violation of the subchondral vasculature allows a clot to form within the defect that later develops into fibrocartilage. Jackson et al,<sup>13</sup> in 1988, and Jackson,<sup>12</sup> in 1991, demonstrated initial improvement with this technique but these results deteriorate over time.

***Microfracture.*** Microfracture involves penetrating the subchondral bone to expose the articular cartilage defect to pluripotent marrow stem cells (Figure 2). It is well

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**Figure 2.** Arthroscopic picture of the microfracture technique of a medial femoral condyle articular cartilage defect.

known that the mesenchymal stem cell derived from bone marrow can differentiate along a chondrogenic lineage.<sup>1,15</sup> Microfracture is favored over abrasion arthroplasty because it is less destructive to the subchondral bone and has a higher degree of controlled depth penetration. Microfracture has been shown to increase the tissue volume and percentage of type 2 collagen in filling defects when compared to untreated defects.<sup>5</sup>

### **Substitution Replacement Options**

Lexer<sup>16</sup> first introduced the repair of osteochondral defects by segmental replacement with fresh allografts in 1908. In a study of segmental allograft replacement for large traumatic articular cartilage defects, McDermott et al<sup>17</sup> reported good or excellent results in 75% and 64% of their patients at 5 and 10 years, respectively. Ghazavi et al<sup>7</sup> demonstrated 95% survival at 5 years, 71% at 10 years, and 66% at 20 years. Although these results have stood the test of time, the logistical problems of tissue procurement by using fresh, unirradiated osteochondral grafts combined with the potential for disease transmission have limited the widespread application of these techniques.

Autograft substitution replacements have become popular for the management of articular cartilage defects. Initially studied in a dog model, Hangody<sup>9</sup> reported on osteochondral plug repair of articular cartilage defects. He demonstrated survival of the osteohyaline plug while the interstices filled with fibrocartilage. The advantage of autograft replacement solves the logistical problems inherent within the use of allografts. However, autograft replacement cannot be used for large defects and is associated with donor-site morbidity. Autograft replacement may also

result in abnormal stress-strain distributions in articular cartilage.<sup>19</sup>

### **Cell/Biologic Replacement Options**

In 1989 using a rabbit model, Grande et al<sup>8</sup> demonstrated a more complete repair of articular defects when periosteal transplants were supplemented with cultured chondrocytes. The rationale for this procedure is based on the ability of normal articular chondrocytes to dedifferentiate in monolayer culture and undergo proliferative expansion.<sup>2</sup> This expansion provides a large number of cells that can be transferred into a large articular cartilage defect; the cells are contained by a periosteal flap where they differentiate and make hyaline-like cartilage.

In 2002, Peterson et al<sup>18</sup> evaluated the biomechanics and long-term durability of autologous chondrocyte implantation. Using an electromechanical indentation probe during second-look arthroscopies, the authors demonstrated stiffness measurements of  $\geq 90\%$  when compared to adjacent normal articular cartilage. Briggs et al<sup>3</sup> demonstrated histologically in 14 of 14 patients the potential to express both type IIa and type IIb collagen and observed regenerated hyaline cartilage in 8 of 14 patients.

Reoperation after autologous chondrocyte implantation is indicated when mechanical symptoms develop. The most common reason for the development of these symptoms is periosteal hypertrophy.<sup>10</sup> Henderson et al<sup>10</sup> reoperated on 22 of 135 patients treated with autologous chondrocyte implantation for knee pain or mechanical symptoms at a mean 10.5 months postoperatively. Of the 31 grafted lesions, 30 had normal or near normal visual repair scores and biopsy showed good integration with subchondral bone and at the marginal interface.

## **CLINICAL MANAGEMENT**

The most important issue in the management of articular cartilage defects requires a comprehensive and systematic means of assessment. As a consequence, the clinician must define, characterize, and classify local, regional and systemic, medical, and family history factors that may influence the progression, degeneration, or regeneration of the defect.

### **Local and Regional Factors**

To ensure uniform standards of evaluating articular cartilage repair, a universally accepted classification system is necessary. The International Cartilage Repair Society (ICRS) has developed a comprehensive method of documentation and classification.<sup>20</sup> The following variables are included in the standards.

1. Etiology. Is the defect acute or chronic? This may be a difficult differentiation as many injuries are acute on chronic.

2. Defect thickness. What is the thickness or depth of the defect as defined by the ICRS grade? Penetration of the tidemark and/or the presence of subchondral cysts can affect the functional articular cartilage unit.
3. Lesion size. A probe accurately measures size in centimeters squared during arthroscopy. Defects  $<2 \text{ cm}^2$  have different treatment options than defects  $>2 \text{ cm}^2$ .
4. Degree of containment. Is the defect contained or uncontained? Is the surrounding articular cartilage healthy or degenerative? As the degree of containment decreases, consequent loss of joint space is seen on radiographs.
5. Location. Is the defect in the weight-bearing region of the knee? Is it monopolar or bipolar?
6. Ligamentous integrity. Are the cruciate ligaments intact, partially torn, or completely torn? Is there residual instability or has the knee been reconstructed?
7. Meniscal integrity. Are the menisci intact? If not, has a partial, subtotal, or complete meniscectomy been performed? Has meniscal repair or transplantation been performed?
8. Alignment. Is the alignment normal, varus, or valgus? Is patellofemoral malalignment present? Has an osteotomy or realignment procedure been performed?
9. Previous management. If a prior cartilage restorative procedure has been performed, was the subchondral plate violated?
10. Radiological assessment. Weight-bearing anteroposterior or flexed posteroanterior views, lateral views, and patellofemoral views are necessary for the evaluation of joint space narrowing and subchondral cyst formation.
11. Magnetic resonance imaging (MRI) Assessment. New MRI sequences allow for the pre- and postoperative evaluation of defects and articular cartilage repairs. Bone bruising, osteochondritis dissecans, and avascular necrosis can also be evaluated.
12. General medical, systemic, and family history issues. Is a rheumatologic history present? Are endocrine-related factors present? Is a family history of osteoarthritis or cartilage disorders present?

### **THE CLINICAL ALGORITHM**

After completion of the comprehensive assessment described above, patients can then be stratified using a clinical algorithm. A comprehensive algorithm has been developed for the management of articular cartilage defects. The algorithm defines 10 patient-directed situations based on lesion size, depth, and associated issues such as alignment, ligament, and meniscal integrity. Each situation considers the problem category, therapeutic options, and current unresolved issues.

#### **Situation 1**

*Problem.* Meniscus tears and partial-thickness articular cartilage defect. (This is the most common condition the orthopedic surgeon sees in practice.)

*Treatment Options.* Arthroscopic debridement and partial meniscectomy followed by rehabilitation physical and conditioning therapy.

*Unresolved Issues.* Role of radiofrequency probes. Do they cause chondrocyte death or decrease regenerative and more degenerative or avascular consequences (bipolar, monopolar)? Why and when to use glucosamine and chondroitin sulfate and viscosupplementation?

#### **Situation 2**

*Problem.* Femoral articular cartilage defects  $<1 \text{ cm}^2$ .

*Treatment Options.* Debridement, microfracture, and osteochondral grafting.

*Unresolved Issues.* Do small defects heal sufficiently with mesenchymal stem-cell stimulation techniques such as microfracture in the short- and long-term?

#### **Situation 3**

*Problem.* Femoral articular cartilage defects including osteochondritis dissecans size 1-2  $\text{cm}^2$ .

*Therapeutic Primary Options.* Debridement, microfracture, osteochondral grafting, and autologous chondrocyte implantation.

*Therapeutic Secondary Options.* Osteochondral grafting and autologous chondrocyte implantation.

*Unresolved Issues.* Is a mesenchymal stem-cell stimulation technique an acceptable primary option?

#### **Situation 4**

*Problem.* Femoral articular cartilage defects including osteochondritis dissecans  $>2 \text{ cm}^2$ .

*Therapeutic Primary Options.* Autologous chondrocyte implantation, fresh allograft.

*Therapeutic Secondary Options.* Autologous chondrocyte implantation, fresh allograft.

*Unresolved Issues.* What is the optimal and maximal size of lesion that osteochondral autografts can be applied?

#### **Situation 5**

*Problem.* Complex femoral articular defects with malalignment, ligament, and meniscal deficiency.

*Therapeutic Primary Options.* Osteotomy, meniscal repair or allograft, cruciate reconstruction, autologous chondrocyte implantation, fresh allograft, or osteochondral autograft, depending on size.

*Unresolved Issues.* How to optimally stage procedures so that the index postoperative protocol does not compromise integrity of the secondary or tertiary procedures. Which meniscus allograft, osteotomy, or ligament reconstruction procedure can be used?

**Situation 6**

*Problem.* Patellar, trochlear, or both articular cartilage defects with no malalignment or instability.

*Therapeutic Primary Options.* Physical and conditioning therapy including taping, bracing, and pelvic stabilization.

*Therapeutic Secondary Options.* Arthroscopy and lateral release, therapeutic tertiary options, autologous chondrocyte implantation plus anteromedialization or patellofemoral realignment osteotomy.

*Unresolved Issues.* What are the definitive indications for arthroscopic lateral release? Does viscosupplementation have a role early in management of patellofemoral chondromalacia syndrome?

**Situation 7**

*Problem.* Patellar and trochlear articular cartilage defects with significant malalignment or instability.

*Therapeutic Primary Options.* Physical and conditioning therapy including taping, bracing, and pelvic stabilization.

*Therapeutic Secondary Options.* Autologous chondrocyte implantation plus anteromedialization or patellofemoral realignment osteotomy.

*Unresolved Issues.* Is the role of osteotomy beneficial early on to disease modifying such that it will prevent osteoarthritis of the patellofemoral joint?

**Situation 8**

*Problem.* Tibial articular cartilage defects—no significant malalignment or instability.

*Therapeutic Options.* Osteotomy as required in relation to the degree of malalignment in combination with microfracture or autologous chondrocyte implantation, depending on the size of the lesion.

*Unresolved Issues.* Successful access may require release of collateral ligaments and detached meniscus insertions. Concomitant procedures protocols should not conflict with postoperative rehabilitative protocol.

**Situation 9**

*Problem.* Significant chondropenia and early osteoarthritis (global grade III/IV articular cartilage defects in the 30- to 60-year-old patient with degenerative meniscal tears).

*Therapeutic Options.* Nonsteroidal anti-inflammatory medications/COX-2 inhibitors; hyaluronic acid; glucosamine/chondroitin sulfate; bike for exercise; unloading braces; arthroscopy for mechanical symptoms, loose bodies, and meniscal tears; osteotomy selectively as required in relation to the degree of malalignment, joint-space narrowing, or both.

*Unresolved Issues.* Is there a role for biological resur-

facing procedures concomitant with realignment procedures?

**Situation 10**

*Problem.* Degenerative meniscal tears and global grade IV defects (late osteoarthritis).

*Therapeutic Options.* Nonsteroidal anti-inflammatory medications/COX-2 inhibitors; hyaluronic acid; glucosamine/chondroitin sulfate; bike for exercise; unloading braces; arthroscopy for mechanical symptoms, loose bodies, and meniscal tears; osteotomy selectively as required in relation to the degree of malalignment, joint-space narrowing, or both; and total knee arthroplasty.

*Unresolved Issues.* What is the role of arthroscopy in late osteoarthritis other than alleviation of mechanical symptoms?

**FUTURE CHALLENGES**

The challenges of articular cartilage repair and restoration continue despite recent advances. Marrow stimulation techniques, substitution replacement options, and biologic replacement options each have a role in the treatment algorithm of articular cartilage defects. Yet no single treatment option can reestablish the hyaline cartilage seen in normal articular cartilage. The goal, then, is to develop new technologies and disease-modifying interventions that protect and preserve the joint over time by maintaining biochemical, biomechanical, and cellular integrity. Until these technologies exist, collaboration between the basic scientist and clinician will continue to advance our current technologies in an effort to restore the violated articular cartilage surface.

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