

## Rehabilitation of Articular Lesions in the Athlete's Knee

Kevin E. Wilk, PT, DPT<sup>1</sup>

Kristin Briem, PT, MHSc<sup>2</sup>

Michael M. Reinold, PT, DPT, ATC, CSCS<sup>3</sup>

Kathleen M. Devine, PT, MPH<sup>4</sup>

Jeffrey R. Dugas, MD<sup>5</sup>

James R. Andrews, MD<sup>6</sup>

Articular cartilage lesions of the knee joint are common in patients of varying ages. Some articular cartilage lesions are focal lesions located on one aspect of the tibiofemoral or patellofemoral joint. Other lesions can be extremely large or involve multiple compartments of the knee joint and these are often referred to as osteoarthritis. There are numerous potential causes for the development of articular cartilage lesions: joint injury (trauma), biomechanics, genetics, activities, and biochemistry. Numerous factors also contribute to symptomatic episodes resulting from lesions to the articular cartilage: activities (sports and work), joint alignment, joint laxity, muscular weakness, genetics, dietary intake, and body mass index. Athletes appear to be more susceptible to developing articular cartilage lesions than other individuals. This is especially true with specific sports and subsequent to specific types of knee injuries. Injuries to the anterior cruciate ligament and/or menisci may increase the risk of developing an articular cartilage lesion. The treatment for an athletic patient with articular cartilage lesions is often difficult and met with limited success. In this article we will discuss several types of knee articular cartilage injuries such as focal lesions, advanced full-thickness lesions, and bone bruises. We will also discuss the risk factors for developing full-thickness articular cartilage lesions and osteoarthritis, and describe the clinical evaluation and nonoperative treatment strategies for these types of lesions in athletes. *J Orthop Sports Phys Ther* 2006;36(10):815-827. doi:10.2519/jospt.2006.2303

**Key Words:** chondral lesion, exercise, nonoperative treatment, nutrition, tibiofemoral joint

Articular cartilage degeneration of the knee joint, osteoarthritis (OA), often occurs in the middle- to later-aged individual who has often become sedentary as a consequence of the disease. Focal articular cartilage injury, however, typically affects young athletically active individuals in their middle 20s into their late 30s, and represents a significant clinical challenge for the physician and rehabilitation specialist. Often this type of patient is an active sports participant who routinely exercises

and may possess an active or strenuous work situation. In young, athletic patients the lesions are usually localized to 1 or possibly 2 compartments of the knee joint and represent a focal area that may vary in size from a relatively small (<2 cm<sup>2</sup>) to a larger lesion of 8 to 10 cm<sup>2</sup>. These lesions usually affect a weight-bearing portion of the joint or an area that receives significant loading when strenuous activities are performed.

The treatment plan for a young active patient with localized articular cartilage injury differs from that for an older patient with knee OA. Treating these 2 types of patients with the same rehabilitation plan is inappropriate because the pathology, activity levels, comorbidities, and patients' goals are tremendously different. Often our medical advice to the patient with OA is to "avoid performing weight-bearing exercise." Although the recommendation appears logical, it is not the most effective advice or best practice for the young athletic individual with a focal articular cartilage lesion. This type of patient is often highly motivated and desires an active lifestyle with exercise. We, as health care providers in the 21st century, must develop treatment strategies that effectively address and treat

<sup>1</sup> Vice President Education, Benchmark Medical Inc, Malvern, PA; Clinical Director, Champion Sports Medicine, Birmingham, AL; Director Rehabilitation Research, American Sports Medicine Institute, Birmingham, AL.

<sup>2</sup> Doctoral student, Biomechanics and Human Movement Sciences, University of Delaware, Newark, DE.

<sup>3</sup> Director of Rehabilitative Research, Massachusetts General Hospital Sports Medicine Center, Boston, MA; Assistant Athletic Trainer, Boston Red Sox Baseball Club, Boston, MA; Adjunct Faculty, Northeastern University, Boston, MA.

<sup>4</sup> Owner and Clinical Director, Advanced Health Systems, Sarasota, FL.

<sup>5</sup> Orthopaedic Surgeon, Alabama Orthopaedic and Sports Medicine, Birmingham, AL.

<sup>6</sup> Orthopaedic Surgeon, Alabama Orthopaedic and Sports Medicine, Birmingham, AL; Medical Director, American Sports Medicine Institute, Birmingham, AL.

Address correspondence to Kevin E Wilk, Champion Sports Medicine, 806 St Vincent's Dr, Suite 620, Birmingham, AL 35205. KWilkpt@hotmail.com.

the patients' unique injuries and facilitate return to desired activities.

Previous knee trauma is a clear risk factor for the development of knee OA. Commonly, we see middle-aged former competitive athletes with a diagnosis of knee OA that they believe originated from an "old injury back in high school or college." Perhaps better management at the time of the incident could have slowed down or prevented the progression of the lesion to its current state several years later. The authors of this paper classify articular cartilage lesions as any injury to the articular cartilage that causes softening, fissuring, and fibrillation of the articular cartilage. Furthermore, bone bruises and other abnormal findings on MRI or bone scans represent an alteration in the healthy state of the articular cartilage and should be treated as a risk factor for future potential articular cartilage degeneration. The authors believe that the early recognition of articular cartilage injuries and appropriate early intervention may decrease the severity and advancement of this type of lesion. The purpose of this paper is to thoroughly discuss risk factors, assessment, and nonoperative treatment options for various types of articular cartilage lesions in young athletically active individuals, in an endeavor to minimize their susceptibility to developing degenerative arthritis of the knee.

## REVIEW OF LITERATURE

### Types of Lesions

Chondral or osteochondral lesions are found in 61% to 66% of knees examined arthroscopically,<sup>3,17,37,98</sup> but are less frequently (54%) found in patients younger than 45 years of age.<sup>3</sup> Injury to the articular cartilage and subchondral bone can induce early changes of posttraumatic degenerative disease<sup>68</sup> and acute subchondral fractures have been shown to be a factor for future degenerative changes in animal studies of cartilage, even in the absence of any initial intra-articular damage.<sup>55</sup> Therefore, a geographic bone bruise is an important variable to include in the equation for risk of arthritis.<sup>43</sup> Chondral and osteochondral lesions are frequently associated with other intra-articular disorders.<sup>17</sup> The most commonly noted concomitant injuries are to the anterior cruciate ligament (ACL)<sup>3,37,75</sup> and menisci,<sup>37,98</sup> as well as patellar dislocations.<sup>3</sup> During 1000 consecutive arthroscopies, Hjelle et al<sup>37</sup> found focal chondral or osteochondral lesions in 19% of the knees examined (excluding chondromalacia), of which 80% were associated with concomitant ACL or meniscal injury. Isolated articular lesions do exist, although less frequent. Zamber et al<sup>98</sup> noted isolated articular cartilage lesions in 6.2% of 200 knee arthroscopies, and in a younger population, Thein and Eichenblat<sup>93</sup>

found a 3.5% incidence of articular lesions without concomitant injuries in 976 arthroscopic procedures.

### Effects of Specific Knee Injuries

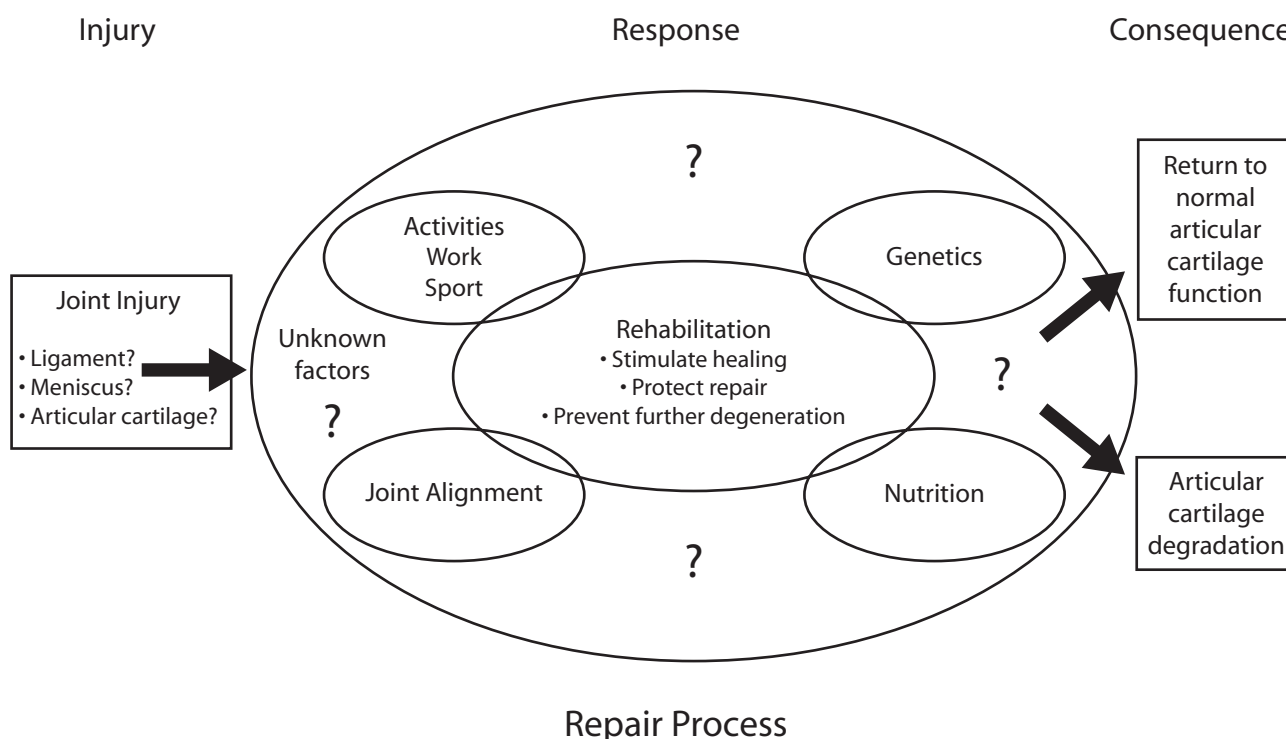
Although the etiology of posttraumatic knee OA is likely multifactorial,<sup>68</sup> numerous studies have documented that a significant knee injury in sports can markedly increase the risk of knee OA. This is especially true if the injury affects the articular cartilage, subchondral bone, or intra-articular structures.<sup>39</sup> The risk dramatically increases if the ACL and meniscus are damaged.<sup>54</sup>

One of the most significant primary functions of the meniscus is load transmission at the tibiofemoral articulation.<sup>1,2,31,67,84</sup> The majority of the load acting on the respective knee compartments is transmitted through the medial and lateral menisci.<sup>1,2,84,85</sup> The magnitude of load transmitted by the menisci varies based on the amount of knee flexion; with the knee in full extension approximately 50% of the compressive load is transmitted through the posterior horns of the menisci, while with the knee flexed to 90° the transmitted compressive loads increase to 85%. In addition, the lateral meniscus receives more compressive load than the medial meniscus. Following meniscal injury, especially when a meniscectomy is performed, the compressive forces increase as the average contact area decreases. These changes result in larger loads being directly applied to the articular cartilage, which may lead to cartilage degeneration.<sup>15,45</sup>

There is a controversy related to the relationship between the management of ACL injury and the development of OA. Daniel<sup>18</sup> reported a higher



**FIGURE 1.** MRI scan showing a bone bruise on the lateral femoral condyle. Note the depth of inflammation into the subchondral bone.



**FIGURE 2.** Factors possibly affecting outcomes following a joint or cartilage injury.

occurrence of OA in surgically treated, compared to conservatively treated, patients with an ACL injury; conversely, Lynch et al<sup>62</sup> and Sommerlath et al<sup>89</sup> reported a higher incidence in the ACL deficient knee (not reconstructed). Reportedly, 70% to 85% of all ACL injuries involve a concurrent bone bruise (Figure 1), an injury to the articular cartilage and subchondral bone<sup>30,34,43,44,90,91</sup> that must be returned to homeostasis.<sup>25</sup> Once an injury to the articular cartilage is sustained, a number of factors may determine whether the articular cartilage returns to its normal state or if the damage begins to progress to a softening of the articular cartilage and eventually full thickness lesions (Figure 2). Thus, we believe that the proper management of the osseous lesion may help prevent the future development of OA.

### Sport-Specific Injuries

Sports activities that appear to increase the risk of OA include those that demand high-intensity, direct joint impact as a result of contact with other participants, playing surfaces, or equipment.<sup>11</sup> Team sports, such as soccer,<sup>23,51</sup> Australian football,<sup>20</sup> hockey, and basketball<sup>51</sup> have been linked to a higher risk of knee disability. Running for fitness and exercise has become a popular activity in the United States. Several studies have examined distance running and shown that moderate regular running has low, if any risk of leading to knee OA.<sup>56,69</sup> No significant differences in incidence of OA have been found between runners and nonrunners based on radiographic evaluation,<sup>56,57</sup> or between long-distance runners and swim-

mers.<sup>88</sup> Kujala et al<sup>54</sup> compared the effects of long-term weight lifting to playing soccer and distance running. The incidence of knee OA was reportedly 31% in weight lifters, 29% in soccer players, and only 14% in runners. The authors concluded that soccer players and weight lifters are at increased risk for developing premature OA, in part explained by a history of knee injury for soccer players and increased body mass for weight lifters.

### Other Considerations

While assessing the patient and planning a rehabilitation program, factors other than type of lesion and concomitant injuries need to be taken into consideration, such as age, gender, body mass index (BMI), and time from initial injury. Older patients<sup>28,94</sup> and those who have long-term cruciate ligament deficiencies<sup>32,94</sup> are more likely to have more severe cartilage lesions. This has also been noted for young patients with a BMI of 25 or greater.<sup>28</sup> Zhai et al<sup>99</sup> report that chondral defects, osteophytes, and obesity are the main determinants of knee pain in younger subjects. Piasecki et al<sup>75</sup> suggest that gender specific differences in lower extremity alignment or injury mechanism could explain why female high school athletes with ACL injuries sustained fewer injuries to the medial compartment than males with the same injury.

### THE CLINICAL ASSESSMENT

The successful nonoperative treatment of articular cartilage lesions in an athlete's knee is based on a

careful and thorough history and clinical examination of the entire lower extremity. By identifying the injury mechanism, local contributing factors at the knee and associated lower extremity contributions, an accurate differential diagnosis may be established as well as a carefully planned rehabilitation program.

## History

The clinical examination should begin with a careful and thorough subjective history. A traumatic origin should be expected, although patients may not always remember sustaining an injury and some defects may be the result of repeated minor traumas.<sup>37,93</sup> Injuries are often sports or work related and noncontact in nature.<sup>42,93</sup> The history should include the patient's chief complaints, description and location of pain, and the nature of pain patterns (activities that aggravate and alleviate symptoms). Patients should also report swelling and dysfunction patterns based on time of day, activities, and the effects their exercise/sport participation has on their knee joint. Furthermore, any previous injuries and surgeries of their knee should be disclosed, as these may place the individual at a higher risk of developing knee OA.<sup>39,54</sup> The authors recommend obtaining medical records from previous surgeries and prior treatments. Lastly, patients should explain their former and present level of activity, and their functional goals.

## Physical Examination

By evaluating lower extremity alignment and function, one may attempt to determine whether the associated joints are contributing to the dysfunction at the knee joint. Thus, it is imperative that the clinical evaluation include not only the knee, but also the pelvis, hip, foot, and ankle. The presence of genu varum or genu valgus may lead to greater weight-bearing loads and is associated with increased risk of joint space narrowing in the medial or lateral compartment, respectively.<sup>92</sup> In addition, limb length, femoral anteversion, hip rotation flexibility, pelvis position, and foot alignment should be carefully evaluated. Furthermore, alterations in gait can have a significant effect on the knee joint.

Patients with articular cartilage lesions of the knee often exhibit joint line pain, swelling and diminished quadriceps muscle strength. Knee range of motion (ROM) is often altered, with the patient presenting with a lack of full knee extension, which may significantly affect the patient's gait mechanics. Limited knee flexion may be due to knee joint swelling or the development of osteophytes. Soft tissue flexibility, especially the hamstrings and hip flexors, must also be carefully assessed. Manual muscle testing to the entire lower extremity helps determine strength status and presence of pain. Isokinetic testing of the

knee extensors and flexors in active patients may be performed to determine torque-body weight ratios and unilateral muscle ratios. The clinician should also test the trunk (core) musculature to ensure that a lack of fitness in this region will not affect rehabilitation of the lower extremity. The patient's knee should be examined for integrity of the ligaments that may also contribute to symptoms. Often a computerized knee laxity test is performed (KT 2000) to determine objective ligamentous status and laxity.

## Imaging

The evaluation should include plain radiographs and possibly an MRI assessment. The plain radiographs should be carefully evaluated for bony abnormalities, osseous spurring, alignment abnormalities, etc. Risk factors for developing posttraumatic OA include malalignment, articular cartilage incongruity, and joint instability.<sup>11,12,40</sup> Articular cartilage incongruities greater than 3 mm significantly increase local contact stresses onto the articular surfaces.<sup>9,41</sup> These articular cartilage incongruities may develop secondary to fractures in the cartilage surfaces. More serious cartilage injuries are most commonly found at the medial femoral condyle and the patella.<sup>3,17,28,94</sup> An MRI may be useful to determine meniscus status, articular cartilage damage, bone bruises, and soft tissue lesions about the knee joint. Imaging of articular cartilage has been enhanced with the use of fast-spin-echo MRI that determines the location and extent of articular cartilage lesions more precisely.<sup>77</sup>

## Treatment Plan

Once the clinical examination is completed, a thorough and multiphased rehabilitation program must be outlined. In the opinion of the authors, compliance to the program is critical to obtaining a successful outcome. As compliance may be improved via patient education, the clinician must communicate to the patient information regarding the role of the rehabilitation program in preservation of articular cartilage. Interventions, such as physical activity, drugs or dietary factors, are aimed at reducing or reversing cartilage defects and may reduce the risk of subsequent knee OA.<sup>14</sup>

## THE REHABILITATION PROGRAM

The rehabilitation program of a young patient with an articular cartilage lesion of the knee joint is designed to reduce pain during exacerbating episodes and promote healing whenever possible. Function should be maximized by enhancing flexibility and lower extremity strength, while protecting against further articular cartilage degradation by correcting biomechanical factors. Furthermore, the patient



should be educated regarding desirable and undesirable activities. We recommend not rushing the patient back to sports that load the affected articular surfaces excessively when the joint has been injured or is in a painful episode. The rehabilitation team should design a rehabilitation program that regulates and gradually increases the exercise “dosage,” which refers to the type and intensity of the exercise, and the volume (number of repetitions). In the early stages following articular cartilage injury the exercise dosage should be low, with gradual increases as the patient improves. By recognizing the location and extent of the lesion an accurate and appropriate rehabilitation program can be developed, with respect to ROM, exercise dosage, joint loading, and functional activities (Table). For instance, patients with lesions contained to the patella or trochlea may be allowed to fully weight bear in a knee immobilizer, whereas lesions to the weight-bearing area of the medial femoral condyle may call for initially limiting a patient’s weight-bearing status. The location and extent of articular cartilage lesions can be accurately determined through fast-spin-echo MRI, as described by Potter et al.<sup>77</sup>

### The Acute Phase (Limited Joint Loading)

In the acute phase, the primary goals are to reduce pain and swelling, restore ROM/flexibility, improve muscular strength, enhance neuromuscular control, and normalize biomechanical forces through the lower extremity. Furthermore, the initial goal is to prevent the advancement of the lesion and promote articular cartilage healing. Both increases and decreases in knee cartilage defects are associated with changes in knee cartilage volume, which implies a potential for the reversal of knee cartilage loss.<sup>21</sup> Thus, controlling weight-bearing loads during all aspects of the rehabilitation program should be considered by the clinician, especially if the lesion is located on a weight-bearing portion of the knee joint.<sup>43,55,68</sup> We recommend developing a progressive weight-bearing program based on the extent and location of the lesion. Some patients may be placed on crutches for as short as 2 weeks and others as long as 8 weeks following an injury to the joint.

To reduce pain and possibly joint swelling, the authors recommend light motion, elevation, ice, compression, and activity modification. Physicians may recommend nonsteroidal anti-inflammatory medications (NSAIDs), possibly corticosteroid or other intra-articular injections, and acetaminophen for pain control. Although their use has risen, a growing concern is the evidence that NSAIDs may have a negative effect on cartilage metabolism. Ibuprofen and fenoprofen have been shown *in vitro* to reduce glycosaminoglycan synthesis in canine cartilage<sup>74</sup> and indomethacin was shown to speed the progression of OA in humans.<sup>79</sup> Agents such as COX-2 inhibitors

appear to cause significant side effects and the authors recommend careful consideration and exploration of the patients’ medical history before administering any anti-inflammatory agent.

ROM and stretching exercises are encouraged, with particular emphasis on knee extension and hamstring, calf flexibility, and hip rotation flexibility. Often, low-load, long-duration stretching is employed to obtain full knee extension (Figure 3).

Strengthening exercises are performed to improve quadriceps, hip, and trunk muscular strength. We think of the quadriceps as a shock absorber to the knee, which help dissipate ground reaction forces during ambulation and weight-bearing activities. Several longitudinal studies have reported that muscle weakness not only results from painful knee OA but is also a risk factor for structural damage to the joint,<sup>7,8,86</sup> and that quadriceps weakness has been shown to be a risk factor for developing knee OA.<sup>87</sup> Non-weight-bearing exercises are encouraged and, if the patellofemoral joint is involved, the ROM through which the exercises are performed is limited accordingly. Electrical muscle stimulation may be utilized to enhance the muscular contraction and facilitate muscular hypertrophy (Figure 4).

Rehabilitation drills focusing on proprioception and neuromuscular control are also performed in attempts to enhance dynamic joint stability and prevent knee-stiffening strategies. Childs et al<sup>13</sup> reported that subjects with OA exhibited a different lower extremity muscle-firing pattern than controls, exhibiting longer muscle activity of the quadriceps, hamstrings, tibialis anterior, and gastrocnemius during walking, and a stiffer knee during level walking and stair ambulation.

Exercises, such as aquatic exercise and cycling may be beneficial to gradually recondition the articular cartilage and provide the mechanical stimulus for articular cartilage healing, while minimizing joint compressive loads at the tibiofemoral joint. Morrison<sup>66</sup> has reported the tibiofemoral joint compressive loads to be 3.4 times body weight during level walking and up to 4.5 to 5.0 times body weight during ascending/descending stairs. In contrast, Ericson and Nisell<sup>27</sup> have reported tibiofemoral joint compressive forces to be 1.2 times body weight during stationary cycling. Aquatic exercises performed with the pool water up to the subject’s axilla will render approximately 25% to 30% of the patient’s body weight onto the lower extremity.<sup>35</sup> Progressing to shallower water levels increases the body weight forces (eg, to approximately 50% at waist level).

If clinical assessment reveals malalignment, such as genu varum and a varus thrust during ambulation, the patient may benefit from orthotics and/or lateral heel wedges.<sup>70</sup> Several studies have documented the efficacy of lateral heel wedges in reducing loading<sup>16</sup> and pain<sup>47,71,83</sup> in the medial compartment. Unloader

**TABLE.** Exercise examples and progression criteria for rehabilitation of articular lesions in the athlete's knee.

#### **The Acute Phase (Limited Joint Loading)**

Range of motion (ROM) and flexibility

- Restore full passive knee extension
  - Overpressure into extension
  - Hamstring stretches
  - Gastrocnemius stretches
- Gradually increase knee flexion
  - Active assisted ROM exercises
  - Quadriceps stretches
  - Passive ROM exercises

Strength

- Quad sets (electrical stimulation)
- Straight leg raises (use ankle weights when able)
- Initiate non-weight-bearing knee extensions 0°-90°\*
- 1/4 squats (partial weight bearing)\*
- Bicycle (high seat and low resistance)
- Hip abduction/adduction
- Core (trunk and hip) exercises

Modifications to limit loading

- Use of assistive device for ambulation
- Use of pool for exercise
- Heel wedges\*
- Knee braces
- Shoe insoles

Criteria for progressing to next phase

- Effusion 1+ or less
- Pain free gait without assistive device
- Full extension
- Flexion to 120°

#### **The Subacute Phase (Loading the Joint)**

ROM and flexibility

- Continue stretching exercises
  - Hamstrings and calf
  - Hip flexors, iliotibial band
  - Quadriceps\*

Progression for strength

- Quad sets
- 1/4 squats\*
- Wall squats\*
- Continue hip and core exercises

Endurance and fitness

- Bicycle (longer duration and resistance)
- Increase repetitions
- Pool program

Functional activities

- Walking program
- Golf
- No running

Criteria for progressing to next phase

- Effusion 1+ or less
- Full ROM
- No increase in pain or swelling after exercise

#### **The Advanced Phase (Progress Functional Activities)**

ROM and flexibility

- Continue stretches before/after exercise program

Progression for strength

- 1/2 squats
- Wall squats
- Lunges (front and back)\*
- Stepping drills (lateral and forward)
- Bicycle (increase duration and resistance)

Functional activities

- Small jumps
- Running (aquatic/elliptical)

TABLE (continued)

Criteria for progressing to next phase

- No effusion
- Full ROM
- Satisfactory muscle strength
- No increase in pain or swelling after exercise

Return-to-Activity Phase (Sport-Specific Activities)

Strength and flexibility

- Continue stretches before and after exercise program
- Continue progressing strength

Functional activities

- Running
  - Progress type of running (cutting, agility)
  - Progress intensity and duration of runs
- Jumping
- Sport-specific movements and drills

Gradual return to sport at preinjury levels

\* Denotes exercises or advice where special consideration must be given to the patellofemoral joint and may not be applicable.

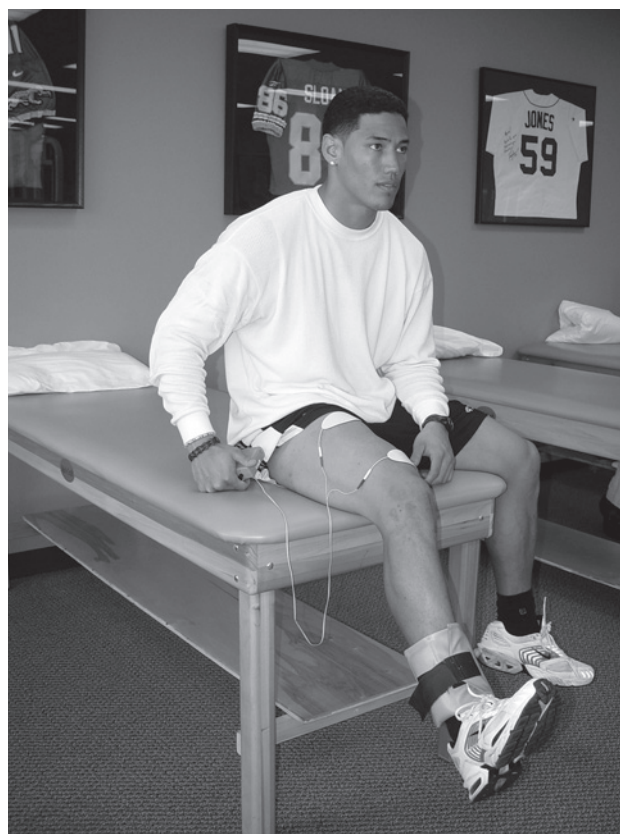


**FIGURE 3.** A low load over a long duration is applied to the knee to improve extension. This stretch would be utilized for 10 to 12 minutes, 3 to 4 times per day.

knee braces may also be of value in reducing pain, improving function, and reducing the varus moment.<sup>36,46,52,59</sup> Lindenfeld et al<sup>59</sup> reported a 48% reduction in pain, 79% improvement in function, and a 10% reduction in the adduction moment with the use of an OA unloader brace. Kirkley et al<sup>52</sup> reported on 119 patients who were randomly assigned to 1 of 3 groups: neoprene sleeve, unloader brace, or no brace (control group). After 6 months of activities, the unloader brace group exhibited significantly less pain and higher knee function compared to the other 2 groups. Thus, athletes with knee malalignments should be placed into a brace that unloads the compartment where the articular cartilage wear exists. The brace may be used temporarily during the initial phases of rehabilitation or long term.

Special consideration should be given to patients who exhibit a bone bruise on MRI. This represents

an injury to the articular cartilage and subchondral bone that must be protected. Subchondral fractures should be included in the equation for risk of arthritis,<sup>43</sup> even in the absence of any initial intra-articular damage.<sup>55</sup> Several authors<sup>30,34,43,44,82,90,91</sup> have reported a high incidence of bone bruises, ranging from 70% to 85% in patients who sustain a ACL injury. These patients may exhibit greater symptoms and worse function than those with isolated



**FIGURE 4.** Electrical muscle stimulation is applied to the quadriceps to enhance muscle contraction.

ACL injuries.<sup>44</sup> Dye et al<sup>26</sup> noted that a bone bruise alters the normal homeostasis of the knee joint. Dye and Chew<sup>25</sup> reported that 4 months following an ACL injury in a 32-year-old male, a bone bruise was present in 3 compartments of the knee joint, including the patellofemoral joint. A scan at 21 months revealed that the joint had returned to normal, indicating a return to osseous homeostasis. Patients with a bone bruise should remain on crutches longer to reduce compressive loads onto the knee joint and be treated with ice to reduce the inflammation of the osseous structures. We recommend the use of continuous cold, as icing times of 25 minutes have been reported to be more beneficial than shorter duration of icing in reducing soft tissue blood flow and skeletal metabolism.<sup>38</sup> Patients exhibiting a bone bruise are strongly advised not to progress their rehabilitation program to include high compressive loading until the bone bruise resolves.

### The Subacute Phase (Loading the Joint)

As objective and subjective gains are made, patients are progressed to phase 2 of the rehabilitation program. It is imperative to use clinical outcome tools to measure progress. During this phase the goals are to continue to enhance lower extremity flexibility/ROM, advance muscular strengthening program, and gradually increase weight-bearing forces through functional activities. The patient is progressed to weight-bearing exercises such as the leg press, squatting, and forward lunges. We often utilize a device that monitors weight-bearing percentages of body weight on each lower extremity and renders feedback to the patient regarding weight-bearing loads (Figure 5). Often exercises are performed in a limited ROM based on location of the lesion and symptoms.

In this phase we begin to load the injured area of the joint lightly and gradually increase the dosage with time. The progression is from low joint compression forces during exercises to moderate, with the primary focus of reconditioning the articular cartilage. Kessler et al<sup>50</sup> reported a change in volume and density in articular cartilage and the menisci in 48 runners as seen on 3-dimensional MRI. During this phase, the patient would be encouraged to perform the weight-bearing exercises in the brace, and/or with the orthoses in the shoes. Furthermore, the patient must continue to stretch and perform flexibility exercises. During this phase the patient generally performs weight-bearing exercises in a bilateral lower extremity posture to control body weight forces through the knee joint. In addition, hip rotation strengthening and balance drills on the tilt board and Biodex Stability System can be added. Exercises for



**FIGURE 5.** Weight-bearing exercises performed on a “balance trainer” device (UniCam Inc, Ramsey, NJ). Feedback regarding percent body weight on each lower extremity is provided.

the abdominal region and trunk stabilization exercises may continue to be implemented during this phase.

### The Advanced Exercise Phase (Progress Functional Activities)

During this period functional exercise drills are implemented, progressing from bilateral to unilateral weight-bearing exercises to increase the body weight forces onto the knee joint. The exercise dosage is gradually increased and is somewhat high, with resistance and joint loads approaching normal forces. Often these exercises are designed to be performed in a unilateral reciprocal manner to challenge both lower extremities. This phase includes exercises such as lateral and forward stepping drills, front and backward lunges, controlled plyometric drills on the leg press, and quick lateral lunges that can incorporate small jumps, if applicable to the athlete. These exercises can be performed on foam material surfaces (Figure 6) to reduce ground reaction forces while progressing the patient to more challenging exercise drills. Running is also initiated in the pool or on the elliptical device (Figure 7). The functional goal of this phase is to gradually increase the knee joint forces and monitor the patient’s response to these exercises.





**FIGURE 6.** Functional exercises: lateral lunges performed onto foam to stimulate proprioception and neuromuscular control while reducing ground reaction forces.

### The Return-to-Activity Phase (Sport-Specific Activities)

This fourth phase is initiated once the patient exhibits the following criteria: (1) full nonpainful knee ROM, (2) no effusion/pain, (3) satisfactory muscular strength, and (4) appropriate rehabilitation progression. During this phase, our goal is an asymptomatic knee. Sport-specific movements and drills are initiated, as are activities such as running and jumping, to gradually increase impact loading. The running program consists of a gradual progression in the type of running, intensity, and duration. As the athlete improves, the running program becomes more challenging.

During this demanding progression in functional ability, the athlete should continue strengthening and flexibility exercises. We recommend the patient perform running and sport-specific drills one day, and on alternating days perform strengthening exercises. As the patient improves and function returns without symptoms, gradual return to the desired sport may be approved by the medical team.

### Body Mass, Nutritional Supplements, and Viscosupplementation

There are several other concepts that may be beneficial to incorporate into the rehabilitation program. Obesity has been associated with the risk of developing both symptomatic and asymptomatic OA.<sup>29</sup> Recently, Mithoefer et al<sup>64</sup> reported a relationship between BMI and functional outcomes following tibiofemoral joint microfracture procedures. The authors stated patients with a lower BMI scored better for activities of daily living and the physical component of the Short Form-36. Furthermore, an active lifestyle is also critical. Exercise has been reported to have a protective effect on articular cartilage<sup>53,69,72</sup> and can significantly reduce pain.<sup>4,8,63</sup> Patients may complain of pain after exercise and consequently want to eliminate daily exercise from their life. Our role as rehabilitation specialists must be to find exercises and a level of exercise that the patient can perform without producing an exacerbation in symptoms.

The use of nutritional supplements may be beneficial in the reduction of knee pain and retardation of future articular cartilage degradation. Glucosamine and chondroitin, integral elements of the cartilaginous matrix, were recognized for their potential benefits as far back as 1969.<sup>97</sup> These supplements



**FIGURE 7.** Progressive loading program may include running on an elliptical trainer.

have been used extensively in Europe and Asia during the past 10 to 15 years for the treatment of OA. Public interest in the United States has increased in the past 10 years. Although a popular supplement, controversy exists regarding the mechanism of action, efficacy, and long-term effects. They are suggested to be chondroprotective agents with matrix modifying properties. Although substantiated evidence is still lacking, they appear to stimulate production of cartilaginous matrix and down regulate the production of proteolytic enzymes<sup>4,5,22,76</sup> and improve synovial fluid characteristics and anti-inflammatory properties.<sup>65,81</sup> Overall, results of glucosamine and chondroitin use in treating OA have been favorable. Studies have reported favorable treatment effects of glucosamine alone<sup>24,80,96</sup>; however, it appears that the body responds best when the 2 agents are taken together.<sup>10,19,58,60</sup> The current recommendation of accepted daily doses is 1500 mg of glucosamine and 1200 mg of chondroitin sulfate, but to discontinue the products use if symptoms do not improve within a few months.<sup>73</sup>

In the authors' opinion the management of mild to moderate OA should include intra-articular injections of a viscous material containing a high concentration of hyaluronic acid. This modality is termed viscosupplementation. Hyaluronic acid is a normal part of the collagen proteoglycan structure and therefore an important part of the normal collagen matrix of articular cartilage. Viscosupplementation involves a series of injections weekly over 3 to 5 weeks. At the time of the injection, any joint fluid in the joint is first removed to prevent dilution of the injected material. The patient is instructed to perform normal activities for the duration of the treatment. The benefit of viscosupplementation is pain relief that is thought to occur via increasing the viscosity of the joint fluid and providing needed nutrition to the articular cartilage.

Recent studies report effective pain relief in up to 75% of patients, with benefits lasting up to 1 year. Bellamy et al<sup>6</sup> reported in a meta-analysis comparing placebo, joint lavage, viscosupplementation, and corticosteroid injection treatment that viscosupplementation was more durable and more effective than the other treatments at 6 months following the treatment. Furthermore, Petrella<sup>74</sup> reported a reduction of knee pain and improved walking in patients following intra-articular injection therapy. Several investigators have reported similar results following viscosupplementation.<sup>33,61,95</sup>

The patient's psychological disposition may also significantly influence the ultimate outcome. Several studies have reported that patients with chronic knee OA who have a positive pain coping attitude exhibit higher functional levels and less pain complaints.<sup>48,49,78</sup>

## SUMMARY

The nonoperative treatment of articular cartilage lesions of the knee joint is a common and challenging task for the medical team. Knee articular cartilage lesions are especially challenging in the patient who desires an active athletic lifestyle. Athletes who have injured their knee appear to be more susceptible in developing tibiofemoral joint articular cartilage lesions and later OA, especially if the injury included the meniscus or ACL, or a bone bruise was present. Other factors that increase the risk of developing OA include malalignment, joint deformity, articular cartilage incongruities, high BMI, age, gender, quadriceps weakness, and nutrition. The rehabilitation specialist should recognize these risk factors and treat the patient appropriately. Bone bruises should be considered a serious injury and may progress to articular cartilage full-thickness lesions. The rehabilitation specialist should manage the patient with a multiphased approach, using sound mechanical principles and the available scientific evidence. During each phase of the rehabilitation program, specific goals must be determined and specific criteria accomplished prior to the progression to the next phase. The ultimate goal of the rehabilitation program is the long-term functional level of the patient. By approaching the patient with these treatment guidelines, the authors believe it will ensure the long-term optimal function of the knee joint.

## REFERENCES

1. Ahmed AM, Burke DL. In-vitro measurement of static pressure distribution in synovial joints--Part I: Tibial surface of the knee. *J Biomech Eng.* 1983;105:216-225.
2. Ahmed AM, Burke DL, Yu A. In-vitro measurement of static pressure distribution in synovial joints--Part II: Retropatellar surface. *J Biomech Eng.* 1983;105:226-236.
3. Aroen A, Loken S, Heir S, et al. Articular cartilage lesions in 993 consecutive knee arthroscopies. *Am J Sports Med.* 2004;32:211-215.
4. Bassleer C, Henrotin Y, Franchimont P. In-vitro evaluation of drugs proposed as chondroprotective agents. *Int J Tissue React.* 1992;14:231-241.
5. Bassleer CT, Combal JP, Bougaret S, Malaise M. Effects of chondroitin sulfate and interleukin-1 beta on human articular chondrocytes cultivated in clusters. *Osteoarthritis Cartilage.* 1998;6:196-204.
6. Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, Wells G. Viscosupplementation for the treatment of osteoarthritis of the knee. *Cochrane Database Syst Rev.* 2005;CD005321.
7. Brandt KD, Heilman DK, Slemenda C, et al. A comparison of lower extremity muscle strength, obesity, and depression scores in elderly subjects with knee pain with and without radiographic evidence of knee osteoarthritis. *J Rheumatol.* 2000;27:1937-1946.
8. Brandt KD, Heilman DK, Slemenda C, et al. Quadriceps strength in women with radiographically progressive

- osteoarthritis of the knee and those with stable radiographic changes. *J Rheumatol*. 1999;26:2431-2437.
9. Brown TD, Anderson DD, Nepola JV, Singerman RJ, Pedersen DR, Brand RA. Contact stress aberrations following imprecise reduction of simple tibial plateau fractures. *J Orthop Res*. 1988;6:851-862.
  10. Bruyere O, Honore A, Ethgen O, et al. Correlation between radiographic severity of knee osteoarthritis and future disease progression. Results from a 3-year prospective, placebo-controlled study evaluating the effect of glucosamine sulfate. *Osteoarthritis Cartilage*. 2003;11:1-5.
  11. Buckwalter JA, Lane NE. Athletics and osteoarthritis. *Am J Sports Med*. 1997;25:873-881.
  12. Buckwalter JA, Mankin HJ. Articular cartilage: degeneration and osteoarthritis, repair, regeneration, and transplantation. *J Bone Joint Surg*. 1997;79A:612-632.
  13. Childs JD, Sparto PJ, Fitzgerald GK, Bizzini M, Irrgang JJ. Alterations in lower extremity movement and muscle activation patterns in individuals with knee osteoarthritis. *Clin Biomech (Bristol, Avon)*. 2004;19:44-49.
  14. Cicuttini F, Ding C, Wluka A, Davis S, Ebeling PR, Jones G. Association of cartilage defects with loss of knee cartilage in healthy, middle-age adults: a prospective study. *Arthritis Rheum*. 2005;52:2033-2039.
  15. Cox JS, Cordell LD. The degenerative effects of medial meniscus tears in dogs' knees. *Clin Orthop Relat Res*. 1977;236-242.
  16. Crenshaw SJ, Pollo FE, Calton EF. Effects of lateral-wedged insoles on kinetics at the knee. *Clin Orthop Relat Res*. 2000;185-192.
  17. Curl WW, Krome J, Gordon ES, Rushing J, Smith BP, Poehling GG. Cartilage injuries: a review of 31,516 knee arthroscopies. *Arthroscopy*. 1997;13:456-460.
  18. Daniel DM, Stone ML, Dobson BE, Fithian DC, Rossman DJ, Kaufman KR. Fate of the ACL-injured patient. A prospective outcome study. *Am J Sports Med*. 1995;23:372-373.
  19. Das A, Jr., Hammad TA. Efficacy of a combination of FCHG49 glucosamine hydrochloride, TRH122 low molecular weight sodium chondroitin sulfate and manganese ascorbate in the management of knee osteoarthritis. *Osteoarthritis Cartilage*. 2000;8:343-350.
  20. Deacon A, Bennell K, Kiss ZS, Crossley K, Brukner P. Osteoarthritis of the knee in retired, elite Australian Rules footballers. *Med J Aust*. 1997;166:187-190.
  21. Ding C, Cicuttini F, Scott F, Boon C, Jones G. Association of prevalent and incident knee cartilage defects with loss of tibial and patellar cartilage: a longitudinal study. *Arthritis Rheum*. 2005;52:3918-3927.
  22. Dodge GR, Jimenez SA. Glucosamine sulfate modulates the levels of aggrecan and matrix metalloproteinase-3 synthesized by cultured human osteoarthritis articular chondrocytes. *Osteoarthritis Cartilage*. 2003;11:424-432.
  23. Drawer S, Fuller CW. Perceptions of retired professional soccer players about the provision of support services before and after retirement. *Br J Sports Med*. 2002;36:33-38.
  24. Drovanti A, Bignamini AA, Rovati AL. Therapeutic activity of oral glucosamine sulfate in osteoarthritis: a placebo-controlled double-blind investigation. *Clin Ther*. 1980;3:260-272.
  25. Dye SF, Chew MH. Restoration of osseous homeostasis after anterior cruciate ligament tear. *Am J Sports Med*. 1993;21:748-750.
  26. Dye SF, Wojtys EM, Fu FH, Fithian DC, Gillquist I. Factors contributing to function of the knee joint after injury or reconstruction of the anterior cruciate ligament. *Instr Course Lect*. 1999;48:185-198.
  27. Ericson MO, Nisell R. Tibiofemoral joint forces during ergometer cycling. *Am J Sports Med*. 1986;14:285-290.
  28. Eskelinen AP, Visuri T, Larni HM, Ritsila V. Primary cartilage lesions of the knee joint in young male adults. Overweight as a predisposing factor. An arthroscopic study. *Scand J Surg*. 2004;93:229-233.
  29. Felson DT, Anderson JJ, Naimark A, Walker AM, Meenan RF. Obesity and knee osteoarthritis. The Framingham Study. *Ann Intern Med*. 1988;109:18-24.
  30. Fowler PJ. Bone injuries associated with anterior cruciate ligament disruption. *Arthroscopy*. 1994;10:453-460.
  31. Fukubayashi T, Torzilli PA, Sherman MF, Warren RF. An in vitro biomechanical evaluation of anterior-posterior motion of the knee. Tibial displacement, rotation, and torque. *J Bone Joint Surg Am*. 1982;64:258-264.
  32. Geissler WB, Whipple TL. Intraarticular abnormalities in association with posterior cruciate ligament injuries. *Am J Sports Med*. 1993;21:846-849.
  33. Goldberg VM, Buckwalter JA. Hyaluronans in the treatment of osteoarthritis of the knee: evidence for disease-modifying activity. *Osteoarthritis Cartilage*. 2005;13:216-224.
  34. Graf BK, Cook DA, De Smet AA, Keene JS. "Bone bruises" on magnetic resonance imaging evaluation of anterior cruciate ligament injuries. *Am J Sports Med*. 1993;21:220-223.
  35. Harrison RA, Bulstrode SJ. Percentage of weight-bearing during partial immersion in the hydrotherapy pool. *Physiotherapy*. 1987;3:60-63.
  36. Hewett TE, Noyes FR, Barber-Westin SD, Heckmann TP. Decrease in knee joint pain and increase in function in patients with medial compartment arthrosis: a prospective analysis of valgus bracing. *Orthopedics*. 1998;21:131-138.
  37. Hjellev K, Solheim E, Strand T, Muri R, Brittberg M. Articular cartilage defects in 1,000 knee arthroscopies. *Arthroscopy*. 2002;18:730-734.
  38. Ho SS, Illgen RL, Meyer RW, Torok PJ, Cooper MD, Reider B. Comparison of various icing times in decreasing bone metabolism and blood flow in the knee. *Am J Sports Med*. 1995;23:74-76.
  39. Hoffman DF. Arthritis and exercise. *Prim Care*. 1993;20:895-910.
  40. Honkonen SE. Degenerative arthritis after tibial plateau fractures. *J Orthop Trauma*. 1995;9:273-277.
  41. Huber-Betzer H, Brown TD, Mattheck C. Some effects of global joint morphology on local stress aberrations near imprecisely reduced intra-articular fractures. *J Biomech*. 1990;23:811-822.
  42. Huegli RW, Moelleken SM, Stork A, et al. MR imaging of post-traumatic articular cartilage injuries confined to the femoral trochlea. Arthroscopic correlation and clinical significance. *Eur J Radiol*. 2005;53:90-95.
  43. Johnson DL, Bealle DP, Brand JC, Nyland J, Caborn DNM. The effect of a geographic lateral bone bruise on knee inflammation after acute anterior cruciate ligament rupture. *Am J Sports Med*. 2000;28:152-155.
  44. Johnson DL, William PU, Caborn DNM, Vanarthos WJ, Carlson CS. Articular cartilage changes seen with magnetic resonance imaging-detected bone bruises associated with acute anterior cruciate ligament rupture. *Am J Sports Med*. 1998;26:409-414.
  45. Jorgensen U, Sonne-Holm S, Lauridsen F, Rosenkint A. Long-term follow-up of meniscectomy in athletes. A prospective longitudinal study. *J Bone Joint Surg Br*. 1987;69:80-83.



46. Katsuragawa Y, Fukui N, Nakamura K. Change of bone mineral density with valgus knee bracing. *Int Orthop*. 1999;23:164-167.
47. Keating EM, Faris PM, Ritter MA, Kane J. Use of lateral heel and sole wedges in the treatment of medial osteoarthritis of the knee. *Orthop Rev*. 1993;22:921-924.
48. Keefe FJ, Caldwell DS, Queen K, et al. Osteoarthritic knee pain: a behavioral analysis. *Pain*. 1987;28:309-321.
49. Keefe FJ, Caldwell DS, Queen KT, et al. Pain coping strategies in osteoarthritis patients. *J Consult Clin Psychol*. 1987;55:208-212.
50. Kessler MA, Glaser C, Tittel S, Reiser M, Imhoff AB. Volume changes in the menisci and articular cartilage of runners: an in vivo investigation based on 3-D magnetic resonance imaging. *Am J Sports Med*. 2006;34:832-836.
51. Kettunen JA, Kujala UM, Kaprio J, Koskenvuo M, Sarna S. Lower-limb function among former elite male athletes. *Am J Sports Med*. 2001;29:2-8.
52. Kirkley A, Webster-Bogaert S, Litchfield R, et al. The effect of bracing on varus gonarthrosis. *J Bone Joint Surg Am*. 1999;81:539-548.
53. Kiviranta I, Tammi M, Jurvelin J, Saamanen AM, Helminen HJ. Moderate running exercise augments glycosaminoglycans and thickness of articular cartilage in the knee joint of young beagle dogs. *J Orthop Res*. 1988;6:188-195.
54. Kujala UM, Kettunen J, Paananen H, et al. Knee osteoarthritis in former runners, soccer players, weight lifters, and shooters. *Arthritis Rheum*. 1995;38:539-546.
55. Lahm A, Uhl M, Erggelet C, Haberstroh J, Mrosek E. Articular cartilage degeneration after acute subchondral bone damage: an experimental study in dogs with histopathological grading. *Acta Orthop Scand*. 2004;75:762-767.
56. Lane NE, Michel B, Bjorkengren A, et al. The risk of osteoarthritis with running and aging: a 5-year longitudinal study. *J Rheumatol*. 1993;20:461-468.
57. Lane NE, Oehlert JW, Bloch DA, Fries JF. The relationship of running to osteoarthritis of the knee and hip and bone mineral density of the lumbar spine: a 9 year longitudinal study. *J Rheumatol*. 1998;25:334-341.
58. Leffler CT, Philippi AF, Leffler SG, Mosure JC, Kim PD. Glucosamine, chondroitin, and manganese ascorbate for degenerative joint disease of the knee or low back: a randomized, double-blind, placebo-controlled pilot study. *Mil Med*. 1999;164:85-91.
59. Lindenfeld TN, Hewett TE, Andriacchi TP. Joint loading with valgus bracing in patients with varus gonarthrosis. *Clin Orthop Relat Res*. 1997;290-297.
60. Lippicello L, Woodward J, Karpman R, Hammad TA. Beneficial effects of cartilage disease-modifying agents tested in chondrocyte cultures and a rabbit instability model of osteoarthritis. *Arthritis Rheum*. 1994;42(Suppl):256.
61. Lo GH, LaValley M, McAlindon T, Felson DT. Intra-articular hyaluronic acid in treatment of knee osteoarthritis: a meta-analysis. *Jama*. 2003;290:3115-3121.
62. Lynch MA, Henning CE, Glick KR, Jr. Knee joint surface changes. Long-term follow-up meniscus tear treatment in stable anterior cruciate ligament reconstructions. *Clin Orthop Relat Res*. 1983;148-153.
63. Minor MA, Hewett JE, Webel RR, Anderson SK, Kay DR. Efficacy of physical conditioning exercise in patients with rheumatoid arthritis and osteoarthritis. *Arthritis Rheum*. 1989;32:1396-1405.
64. Mithoefer K, Williams RJ, 3rd, Warren RF, Wickiewicz TL, Marx RG. High-impact athletics after knee articular cartilage repair: a prospective evaluation of the microfracture technique. *Am J Sports Med*. 2006;34:1413-1418.
65. Morreale P, Manopulo R, Galati M, Boccanera L, Saponati G, Bocchi L. Comparison of the antiinflammatory efficacy of chondroitin sulfate and diclofenac sodium in patients with knee osteoarthritis. *J Rheumatol*. 1996;23:1385-1391.
66. Morrison JB. The mechanics of muscle function in locomotion. *J Biomech*. 1970;3:431-451.
67. Mow VC, Ratcliffe A, Chern KY, Kelly MA. Structure and function relationships of the menisci of the knee. In: Mow VC, Arnoczky SP, Jackson DW, eds. *Knee Meniscus: Basic and Basic Clinical Foundations*. New York, NY: Raven Press; 1992:37-58.
68. Nakamae A, Engebretsen L, Bahr R, Krosshaug T, Ochi M. Natural history of bone bruises after acute knee injury: clinical outcome and histopathological findings. *Knee Surg Sports Traumatol Arthrosc*. 2006;
69. Newton PM, Mow VC, Gardner TR, Buckwalter JA, Albright JP. Winner of the 1996 Cabaud Award. The effect of lifelong exercise on canine articular cartilage. *Am J Sports Med*. 1997;25:282-287.
70. Noyes FR, Schipplein OD, Andriacchi TP, Saddemi SR, Weise M. The anterior cruciate ligament-deficient knee with varus alignment. An analysis of gait adaptations and dynamic joint loadings. *Am J Sports Med*. 1992;20:707-716.
71. Ogata K, Yasunaga M, Nomiya H. The effect of wedged insoles on the thrust of osteoarthritic knees. *Int Orthop*. 1997;21:308-312.
72. Otterness IG, Eskra JD, Bliven ML, Shay AK, Pelletier JP, Milici AJ. Exercise protects against articular cartilage degeneration in the hamster. *Arthritis Rheum*. 1998;41:2068-2076.
73. Owens S, Wagner P, Vangsness CT, Jr. Recent advances in glucosamine and chondroitin supplementation. *J Knee Surg*. 2004;17:185-193.
74. Petrella RJ. Hyaluronic acid for the treatment of knee osteoarthritis: long-term outcomes from a naturalistic primary care experience. *Am J Phys Med Rehabil*. 2005;84:278-283; quiz 284, 293.
75. Piasecki DP, Spindler KP, Warren TA, Andrich JT, Parker RD. Intraarticular injuries associated with anterior cruciate ligament tear: findings at ligament reconstruction in high school and recreational athletes. An analysis of sex-based differences. *Am J Sports Med*. 2003;31:601-605.
76. Piperno M, Reboul P, Hellio Le Graverand MP, et al. Glucosamine sulfate modulates dysregulated activities of human osteoarthritic chondrocytes in vitro. *Osteoarthritis Cartilage*. 2000;8:207-212.
77. Potter HG, Linklater JM, Allen AA, Hannafin JA, Haas SB. Magnetic resonance imaging of articular cartilage in the knee. An evaluation with use of fast-spin-echo imaging. *J Bone Joint Surg Am*. 1998;80:1276-1284.
78. Rapp SR, Rejeski WJ, Miller ME. Physical function among older adults with knee pain: the role of pain coping skills. *Arthritis Care Res*. 2000;13:270-279.
79. Rashad S, Revell P, Hemingway A, Low F, Rainsford K, Walker F. Effect of non-steroidal anti-inflammatory drugs on the course of osteoarthritis. *Lancet*. 1989;2:519-522.
80. Reginster JY, Deroisy R, Rovati LC, et al. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. *Lancet*. 2001;357:251-256.



81. Ronca F, Palmieri L, Paniconi P, Ronca G. Anti-inflammatory activity of chondroitin sulfate. *Osteoarthritis Cartilage*. 1998;6 Suppl A:14-21.
82. Rosen MA, Jackson DW, Berger PE. Occult osseous lesions documented by magnetic resonance imaging associated with anterior cruciate ligament ruptures. *Arthroscopy*. 1991;7:45-51.
83. Sasaki T, Yasuda K. Clinical evaluation of the treatment of osteoarthritic knees using a newly designed wedged insole. *Clin Orthop Relat Res*. 1987;181-187.
84. Seedholm B. Transmission of the load in the knee with special reference to the role of the meniscus: part I. *Eng Med*. 1979;8:207-228.
85. Seedhom BB, Hargreaves DJ. Transmission of the load in the knee with special reference to the role of the menisci, part II. *Eng Med*. 1979;8:220-228.
86. Slemenda C, Brandt KD, Heilman DK, et al. Quadriceps weakness and osteoarthritis of the knee. *Ann Intern Med*. 1997;127:97-104.
87. Slemenda C, Heilman DK, Brandt KD, et al. Reduced quadriceps strength relative to body weight: a risk factor for knee osteoarthritis in women? *Arthritis Rheum*. 1998;41:1951-1959.
88. Sohn RS, Micheli LJ. The effect of running on the pathogenesis of osteoarthritis of the hips and knees. *Clin Orthop Relat Res*. 1985;106-109.
89. Sommerlath K, Odensten M, Lysholm J. The late course of acute partial anterior cruciate ligament tears. A nine to 15-year follow-up evaluation. *Clin Orthop Relat Res*. 1992;152-158.
90. Speer KP, Warren RF, Wickiewicz TL, Horowitz L, Henderson L. Observations on the injury mechanism of anterior cruciate ligament tears in skiers. *Am J Sports Med*. 1995;23:77-81.
91. Spindler KP, Schils JP, Bergfeld JA, et al. Prospective study of osseous, articular, and meniscal lesions in recent anterior cruciate ligament tears by magnetic resonance imaging and arthroscopy. *Am J Sports Med*. 1993;21:551-557.
92. Teichtahl AJ, Cicuttini FM, Janakiraman N, Davis SR, Wluka AE. Static knee alignment and its association with radiographic knee osteoarthritis. *Osteoarthritis Cartilage*. 2006;14:958-962.
93. Thein R, Eichenblat M. Concealed knee cartilage lesions: is arthroscopic probing therapeutic? *Am J Sports Med*. 1999;27:495-499.
94. Vasara AI, Jurvelin JS, Peterson L, Kiviranta I. Arthroscopic cartilage indentation and cartilage lesions of anterior cruciate ligament-deficient knees. *Am J Sports Med*. 2005;33:408-414.
95. Vaz AL. Double-blind clinical evaluation of the relative efficacy of ibuprofen and glucosamine sulfate in the management of osteoarthritis of the knee in outpatients. *Curr Med Res Opin*. 1982;8:145-149.
96. Vetter G. [Topical therapy of arthroses with glucosamines (Dona 200)]. *Munch Med Wochenschr*. 1969;111:1499-1502.
97. Wilk KE. Are there speed limits in rehabilitation? *J Orthop Sports Phys Ther*. 2005;3:50-51.
98. Zamber RW, Teitz CC, McGuire DA, Frost JD, Hermanson BK. Articular cartilage lesions of the knee. *Arthroscopy*. 1989;5:258-268.
99. Zhai G, Cicuttini F, Ding C, Scott F, Garnero P, Jones G. Correlates of knee pain in younger subjects. *Clin Rheumatol*. 2006;