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Orthopedic Advances in Knee Replacements

Biologic knee repair may soon replace harsher artificial joint replacements.

By Kevin R. Stone, MD

Arthritis patients used to have two choices. They could live with pain, tempered by dangerous levels of anti-inflammatory drugs. Or they could wait until the pain became unbearable, eventually undergoing artificial joint replacement.

Luckily, kinder treatments are on the horizon. At the Stone Clinic, we focus on biologic—not bionic—alternatives. Supplements and exercise are a first line of defense. But when more invasive methods are necessary, we perform surgery using a paste grafting method to regrow articular cartilage, combined with allograft meniscus replacement.

This procedure—known as biologic knee replacement—is still in its infancy. Nevertheless, we have seen promising results and have helped many patients return to their pre-injury status.

#### Arthritis Etiology

Osteo and traumatic arthritis are considered degenerative joint diseases. These are not considered inflammatory, as is rheumatoid arthritis. The damage to the joints can be genetic (osteoarthritis) or caused by misalignment or injury. Loss of the knee's shock absorber, called the meniscus cartilage, is a frequent precursor to traumatic arthritis. In addition, tears of the cruciate ligament or medial collateral ligament also can cause knee instability and abnormal mechanics, leading to early wear and tear.

In most cases, the damage in the joint is due primarily to a loss of the articular cartilage covering of the end of the bones. When the cartilage wears off, bone grinds against bone, resulting in small fragments of cartilage scattered around the joint. The fragments irritate the joint and produce swelling. The knee fluid, called synovial fluid, contains enzymes, known as inflammatory cytokines, which accelerate the breakdown of cartilage and cause pain.

Most often, surgeons replace the knee with an artificial one. Joint replacements are effective at removing the pain; in experienced hands, a success rate of more than 90 percent is reported at 10 years. But this approach has limitations. Patients lose range of motion and cannot perform impact sports.

When the artificial implants fail, usually because the cement-fixed components loosen, the revisions are more difficult, with worse outcomes. A major complication of revisions is the considerable bone loss that occurs during removal of the old cemented implants. Survival and success rates of the revision devices are significantly lower than those for the primary total knee replacement. Pain, loss of motion and restricted activities are the primary complaints.

#### A Nonoperative Approach

Most patients with arthritis benefit from nonoperative methods of joint mobilization and core strengthening. Exercise programs that strengthen the whole body, focusing on the extremities and the core can help diminish the symptoms of OA by strengthening the muscles around the joint. Despite having severe arthritis, many people can delay surgical intervention for years, if they combine strengthening and joint mobilization with a nutrition program to optimize their weight.

In addition, newer generations of drugs and supplements treat the disease of arthritis, not just the symptoms. Glucosamine (minimum of 1,500 mg daily) stimulates cartilage repair, inhibits cartilage breakdown, builds the natural lubricant of the knee (called hyaluronan) and helps hydrate all tissues. An NIH prospective blinded trial (the GAIT study) of glucosamine showed equal effectiveness in pain control to an expensive prescription drug (Celebrex) in patients with moderate to severe arthritis. In those with mild changes, there were no measurable effects.

Glucosamine also may be a natural performance enhancer, promoting faster recovery after intense exercise, with less pain and stiffness. Although glucosamine comes in pills or liquid formulas, we have found the liquid form provides the most efficient

method of absorption into the body, and compliance is better among patients.

We also use hyaluronan, a lubricant that is normally found in joints. As we age, we produce less natural joint lubricant. Injections of hyaluronan can lubricate the joint, but pain relief is not long-lasting. However, the injections appear to stimulate the joint-lining cells to produce more natural lubricant, inhibit the enzymes that cause the breakdown of cartilage and keep the active joints healthy and moving smoothly.

When pain management is needed, we prefer to use natural anti-inflammatory medications, such as glucosamine, and newer pain management programs that carry few side effects. These programs include soft-tissue massage, ice massage, electrical stimulation, ultrasound, acupuncture and exercise modifications in combination or individually. Although these measures are helpful, they often only extend the time before more invasive measures are required.

### **Biologic Joint Replacement**

It is far less invasive to do a biologic joint replacement than an artificial joint replacement. Unfortunately, many physicians still think cartilage cannot be repaired. They believe if there is bone-on-bone, artificial joint replacement is the only next step. However, cartilage can be stimulated to produce fibrocartilage repair tissues. Even though these tissues may not have the durability or conformity of normal cartilage, the repair tissue can provide excellent pain relief. If the meniscus is missing, we combine this approach with a minimally invasive meniscus replacement. The two procedures together are known as biologic joint replacement.

Certain candidates are ideal for this procedure. They have localized pain, with cartilage loss in one side of the joint. They also have a strong desire to remain active. We have extended these criteria to patients with more global arthritis when their sporting desires are high and their understanding of the goals of the procedures are clear.

### **Regrowing Articular Cartilage**

Many scientists are working on methods to stimulate articular cartilage repair. Most of the procedures are designed for isolated chondral defects—not osteoarthritis. However, innovations in the field support the basic premise that cartilage repair is possible.

The most common procedure is called microfracture. This involves making holes with a surgical awl into the arthritic bone to stimulate fibrocartilage repair. With mosaicplasty, the surgeon takes plugs of cartilage and bone from an unaffected part of the knee and transplants it to the site of cartilage damage.

Autologous cartilage implants (also called Carticel) takes cartilage cells from the knee in a two-step procedure. First, the cartilage is harvested arthroscopically. The harvested cartilage cells are then grown in culture for several weeks. Next, the physician places the cultured cartilage cells back in the knee, covered with a periosteal flap in open surgery. The procedures are designed to treat focal damage to the articular cartilage surface. While they do not grow normal cartilage, the procedures demonstrate that cartilage cells can grow, dispelling the old concept that cartilage could not be repaired.

In 1991, we designed another procedure, known as articular cartilage paste grafting, to regrow normal cartilage. Currently, this is the only arthroscopic cartilage repair procedure indicated for severely arthritic patients. It is not an experimental treatment and is supported by published, peer-reviewed, long-term studies.

Paste grafting is a single-step, arthroscopic, outpatient procedure. We use the patient's own healthy cartilage, bone and stem cells harvested from the intercondylar notch in the nonweight-bearing area of the femur. The tissue is removed and pounded into a paste in the operating room. We use this paste to repair damaged, arthritic areas of the joint.

In recent cell culture studies of the paste, these undifferentiated cells become chondrogenic when placed in the appropriate media and environment. Paste grafting works for several reasons. New blood supply is brought to the dead arthritic area through fracturing of the surface with an awl. The marrow cells released from the fracture holes and the stem cells contained within the mixture of bone and hyaline cartilage paste differentiate into chondrocytes post-implantation. And the paste, when impacted into the fractured surface, provides a matrix for new cartilage regeneration.

An anabolic, cartilage-friendly environment is created by the new fracture, as opposed to the hostile environment of a degrading arthritic knee. In this environment, cartilage and bone precursor cells produce growth factors that aid the repair process. Additional growth factor injections are under evaluation, which we expect will play an integral role in the biologic joint repair process.

Patients who have had paste grafting for arthritic knees experience pain relief and improved function not just in the first two to

five years of follow-up, but also in the nine to 12 years of follow-up.<sup>1</sup>

In unpublished data, Polish researchers Jaroszewski, Kruczynski and Trzeciak conducted a controlled study to investigate and compare the articular cartilage paste grafting technique to a modified microfracture technique. Full-thickness articular cartilage defects (penetrating through the bone underneath the articular cartilage) were created in the knees of 41 rabbits. Cartilage defects were treated with articular cartilage paste grafting, a modified paste graft technique with periosteal coverage or were left untreated postmicrofracture (control group).

The paste graft treatment group without periosteal coverage demonstrated the best results with the fastest defect filling. In addition, there was more advanced articular surface continuity and defect fill. The results of this study are extremely encouraging and support articular cartilage paste grafting for treating severely arthritic cartilage defects.

### **Meniscus Replacement**

The meniscus is the fibrous shock absorber of the knee. When torn, this tissue is often partially removed. The loss of meniscus tissue leads to force concentration, rather than force dispersion, on the tibial plateau. Consequently, early wearing away of the articular cartilage surface down to the bone occurs. Replacing the meniscus with a cadaveric meniscus tissue can restore some of the meniscus protection, diminish pain and increase function for arthritic patients.<sup>2</sup>

When combined with cartilage replacement procedures, the new meniscus absorbs the force and protects the repaired cartilage surface. Combining meniscus replacement with articular cartilage repair is a biologic version of a joint replacement. Joint surfaces are replaced by natural tissue rather than metal and plastic. Fortunately, the biologic procedure can be performed as an outpatient arthroscopic procedure. The patient has to use crutches for a month and follow a defined rehabilitation program. Long-term outcomes for each of these procedures have been reported in peer-reviewed journals.<sup>2</sup> Outcomes for the combined procedures in comparison to artificial joint replacement are part of a prospective trial now planned at the Stone Clinic.

We believe these results will expand the indications for cartilage repair surgery and delay artificial joint replacement surgery for many people suffering from arthritis. However, delaying artificial joint replacement is not always an option, and for some, total joint replacement may be the preferred treatment.

### **The Future**

Biologic joint replacement is in its early stages. The current efforts at tissue regeneration with or without meniscus replacement will be rapidly replaced by preformed, preloaded matrices of collagen or collagen-like materials, with cells primed to make an extracellular matrix. These off-the-shelf implants will be arthroscopically inserted and applicable to a wider variety of arthritic joints than the current techniques. Each of these advances—cell optimization, matrix selection and growth factors—are in active development around the world.

For example, we are working on a new cartilage replacement technique that will resurface the joint with young, healthy tissue harvested from animals. This shell of articular cartilage is treated to remove the antigens (immune system stimulators) and then repopulated with new cells.

The Stone Research Foundation is now raising funds for these studies, and cell graft optimization studies are under way. These studies are in the preclinical phase and will not see clinical application for several years. However, if joints with only moderate arthritis can be treated biologically without artificial joint replacement, then we hope the developments of tomorrow will be available to patients.

For a list of references, go to [www.advancweb.com/healthyaging](http://www.advancweb.com/healthyaging) and click on the references toolbar.

*Kevin R. Stone, MD, is a physician and surgeon at the Stone Clinic in San Francisco. The Stone Clinic is internationally recognized for the treatment of athletic injuries and arthritis. The Stone Clinic shares its developments with the medical community at seminars around the world. The results of these efforts are published in peer-reviewed journals and can be found online at [www.stoneclinic.com](http://www.stoneclinic.com).*

*Disclosure: Dr. Stone, indicates that he is the orthopedic surgeon at the Stone Clinic, the Stone Research Foundation, and founder of Joint Juice Inc. and CrossCart Inc.*