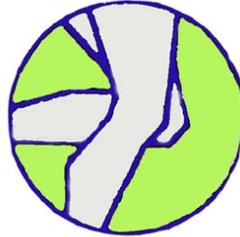


**Autologous Chondrocyte Implantation**  
**for full thickness cartilage defects of the knee**

**Tom Minas MD**  
**Brigham and Women's Hospital, Cartilage Repair Center**  
**850 Boylston Street, Suite 112, Chestnut Hill Ma 02467**  
**(617-732-9967 Fax (617) 732-9272**  
**Tim Bryant R.N., BSN (617) 732-9967 X 4**  
**[Cartilagerepaircenter.org](http://Cartilagerepaircenter.org) / [Tbryant@partners.org](mailto:Tbryant@partners.org)**



This handout is not intended as a substitute for professional medical care. Only your doctor can diagnose and treat a medical problem.

Articular cartilage covers the ends of bones at the joint surfaces. It is a smooth, glistening white, near frictionless, mechanically hard tissue, that lacks nerve endings, or a blood supply. If damaged, articular cartilage cannot regenerate or repair itself to its original form. It is meant to last a lifetime.

If articular cartilage is damaged through injury or cartilage loss from osteoarthritis at a young age, patients will usually experience pain if the area of damage is large. The bone underlying the articular cartilage is richly supplied with nerve endings and can become painful when exposed after the loss articular cartilage. The pain, as a result of cartilage loss, may limit activities of daily living, (ADL's), or recreational sports, and hence one's quality of life. The cartilage loss may also lead to damage to the opposite joint surface, eroding away the opposite cartilage surface producing osteoarthritis.

Repair of articular cartilage loss, is by surgical means only. Pharmaceutical means to date, such as shark cartilage, chondroitin Sulfate, glucosamine, or injectable visco-supplements – hyaluronic acid preparations, do not repair or regenerate cartilage. They may help with pain relief, or maintain cartilage health but even these observations have not been scientifically proven.

### ***Surgical Techniques for Cartilage Repair***

Arthroscopic debridement, (“clean-up” - removing loose fragments, or trimming sharp cartilage defect margins), is an arthroscopic technique aimed at relieving pain, without repair of the cartilage defect. This technique is useful if one has low physical demands on their knee, and when treating an area of damage that is small. Debridement allows improvement in pain, without a long rehabilitation and is minimally invasive, allowing a quick recovery. Arthroscopic repair of a cartilage defect by the body’s own marrow stem cells may be attempted arthroscopically. Marrow stem cells are those cells in the bone marrow space that have the capacity to become bone, cartilage, or fibrous tissue (scar tissue), or a mixture of all three. This involves minimally invasive arthroscopic techniques to penetrate the exposed bone under the area of cartilage loss by the use of a power drill, (sub-chondral drilling), a motorized burr, (abrasion arthroplasty technique), or a hand-held pick or awl, (microfracture technique). Reported success rates approach 60% return to sports and 75% of patients with pain relief with ADL’s. Success is more likely if the area of damage is a) small ( $< 3\text{cm}^2$  - the size of a nickel), b) of acute onset, (injury  $< 3$  months old), c) on a weight bearing surface, (femoral condyle), d) the patient is young, ( $< 40$  years old).

The rehabilitation after a marrow stimulation technique is strict; 6 weeks using a continuous passive motion machine (CPM machine), 3 months on crutches, and return to sports after 9 months, if successful. Approximately 75% of patients are improved, 15% are the same as before treatment, and the remaining 10% of patients claim they are worse than before treatment.

Osteochondral graft transfers (OATS) are new techniques that transfer healthy minor load bearing mature cartilage and bone dowels, to painful load bearing cartilage defects. The prime advantage is that transfer of normal mature tissue occurs to the area of damage. Osteochondral transfers can be performed as a single arthroscopic technique. Disadvantages include; technically a difficult operation that may have to be performed open, persistent early swelling, a slow time course to comfortable ADL’s, (6 months), and sports, (9 months). Osteochondral transfer should be performed only for small defects ( $< 1\text{-}2\text{ cm}^2$  – a dime-sized defect) so as to not create donor site pain (“Taking from Peter to pay Paul”).

### ***Autologous Chondrocyte Implantation (ACI) – Surgical Technique***

ACI was developed in Gothenburg, Sweden, by Lars Peterson MD, and co-workers. The first patients treated in Sweden in 1987 continue to function pain-free at this time. The first series of patients treated in the US was by, myself, and began in March 1995 and is to date the largest clinical series in the US.

The technique involves two surgical procedures that include an arthroscopy followed by an electively planned, open ACI knee procedure.

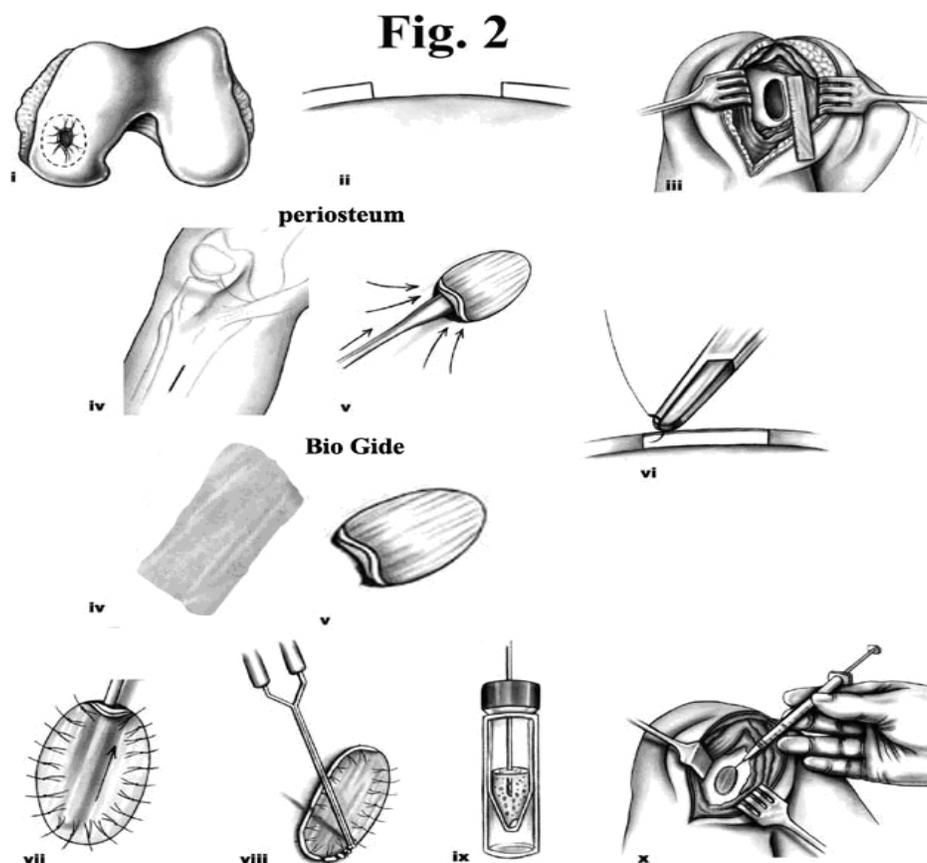
#### **Arthroscopy**

The first intervention is an outpatient, surgical, minimally invasive, arthroscopic assessment of the knee joint. If the area(s) of damage is localized rather than generalized (“like fixing potholes, rather than paving a road”) then the knee is suitable for cartilage repair by ACI and the defect area(s) is/are measured, so as to know how many vials of cells that need to be cultured. A biopsy of full thickness articular cartilage is taken for cartilage cell culturing. This is taken from a non-weight bearing area and is the size of a thumbnail clipping (about 1/8<sup>th</sup> of an inch wide by a 1/2 inch long) so as to not create a problem (see figures 1a, 1b). The cartilage is shipped, under sterile conditions, for commercial cell culturing, (Genzyme Biosurgery, Cambridge Ma). The cartilage biopsy is routinely cultured then cryo-preserved (frozen) with liquid nitrogen and may be stored for up to 18 months. Cryo-preservation allows time for insurance approval for ACI. Once approval is obtained, an elective surgical date is scheduled and then a date for cell thaw and culturing to the appropriate number of cell vials for surgery is then set. If the patient cancels surgery after the date of cell thawing and culturing begins then the patient is responsible for the cell culturing costs of (\$26,108 US).



***Open ACI Knee Surgery***

The open technique (see figure 2) involves an incision to open the joint and a second incision to harvest a thin 1-millimeter membrane covering the bone (periosteum) or a synthetic patch that as of June 2007 has been used with the consent of the patient. The name of the synthetic patch is Bio Gide and it is a highly purified collagen types I and III. The area of cartilage damage in the joint is identified and is cut away back to normal cartilage and bone bed. The defect is measured and templated with sterile tracing paper and placed over the bio-gide membrane and is cut to size and micro-sutured to the margins of the cartilage defect and sealed with commercially prepared fibrin glue to make the patched defect water-tight. The cartilage cells are then drawn up in their liquid culture medium with a needle and syringe and injected in an opening left for the cells. The opening is then sutured tight and sealed with fibrin glue. The transplanted area appears as a fragile blister on the end of the bone. The liquid cell suspension must grow inside the joint to form a hard cartilage tissue (a 9-12 month process, see figure 3). The joint is then closed and a soft dressing is applied, possibly with a drainage system in place to remove any excess blood. The procedure is complete.



## **Steps in ACI**

I - Outer bridge Grade IV medial femoral condyle (MFC) lesion with stellate fissuring. Dotted margins indicate extent of undermined chondral delamination. II - Radical debridement of damaged cartilage back to full thickness, healthy articular margins leaving subchondral bone intact debriding down to the cartilage tide mark. III - measuring length and width of chondral defect or alternatively accurate paper or aluminum template of defect if irregularly shaped. IV - Harvesting tibial periosteum on medial subcutaneous border of tibia distal to pes anserinus tendon insertion. OR IV – Bio-gide membrane is inspected and prepared to be measured and cut. . V - After sharp incision of the periosteum oversized in length and width by 2 mm to chondral defect careful subperiosteal dissection so as to not perforate periosteal cover. OR V – The bio-gide membrane is measured to match the defect and cut to size. VI - Micro suturing of bio-gide membrane flush to adjacent articular margin, and not overlapping, with 6-0 Vicryl cutting needle immersed in sterile glycerin or mineral oil to allow suture passage easily through periosteum and articular surface. VII- After circumferential suturing in an interrupted fashion of the bio-gide to chondral defect at 3 to 5 mm intervals. Superior opening is tested with a plastic catheter for saline water tightness. VIII - autologous or allogeneic fibrin glue sealant to margins to insure water-tight integrity of the bio-gide to native cartilage. IX - Gentle aspiration and mixing of cell pellet of 12 million cells in 0.4 cc's of culture media to a uniform mixture prior to injection under the bio-gide membrane. X - Suturing followed by sealant of injection port.

## ***Hospital Course***

### **Physician Rounds**

After your surgery, you will be seen by Dr. Minas' Orthopedic resident to assess your condition and monitor your recovery status. The Orthopedic resident is at all times in direct contact with Dr. Minas regarding your care and progress. Dr. Minas will typically visit Thursday mornings prior to 8:15 in the AM. This is not a set schedule but on average is the most likely time he will visit with you while you are in the hospital.

### Pain Management

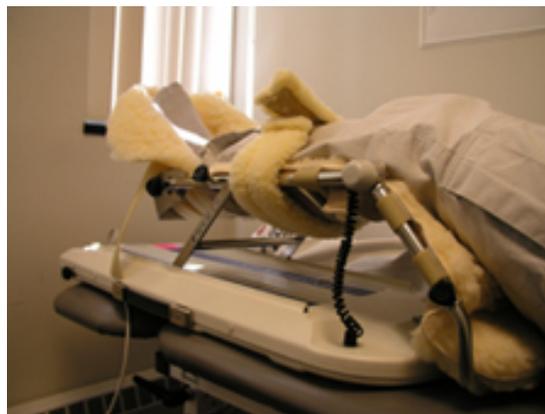
After surgery, pain is managed either by a PCA pump (Patient Controlled Analgesic pump usually containing a narcotic such as morphine) or a continuous epidural spinal catheter, which delivers a local anaesthetic around the spinal nerve roots often accompanied by a small dose of narcotic. The choice of anaesthetic depends on the extent of surgery required and patient preference (to be discussed with the anesthesiologist, either at the pre-op clinic visit or on the day of surgery). The PCA or Epidural is usually used for 48 hours after surgery, and then oral narcotics, Tylenol, and ice therapy (Cryo-cuff™) manage pain.

While in bed in the hospital, patients have a soft dressing on the knee, anti-thrombosis stockings (TEDS™ stockings), a cryo-cuff™, Velcro-strapped knee immobilizer, and drains. An intra-venous catheter administers fluids and antibiotics for 48 hours post-operatively, and a bladder catheter (Foley™), or urinary catheter is usually required. After 48 hours, all the tubes are removed, the dressing is changed, and the wounds are examined.

### Therapy

The day of surgery is confined to bed. Therapy begins the day after surgery. The principles of physical therapy are simple and commonsensical; 1) motion, 2) prevent ACI graft over-load and damage, and 3) encourage muscle tone.

To this end, a therapist experienced in managing patients undergoing ACI will meet and examine you the day after surgery. A specific ACI protocol will be ordered for your individual surgical reconstruction and taught to you. You will be placed on a CPM machine the day after surgery to allow the cartilage cells to attach to the defect surfaces before motion starts.



You will be sitting the day after surgery and the second day after surgery out of bed on crutches.

Discharge criteria for going home are based on: 1) safety, 2) good pain management on oral medications, 3) absence of fever, 4) a healthy appearing wound, 5) good mobility as determined by the therapist and nurses – ability to get in and out of bed, on and off the toilet, in and out of the shower and shower seat, 6) good walking with crutches or a walker, 7) ability to climb as many stairs as are required at home.

### ***Hospital Discharge Instructions***

You will be discharged home with a CPM machine arranged by the physical therapy department, your specific physical therapy exercises with do's and don'ts, crutches, and home therapy, and a Game Ready ice/compression sleeve, if approved by your insurance carrier.

If you have had an osteotomy with your ACI, you will also be on Coumadin for 3 weeks post-operatively with twice weekly blood draws via a visiting nurse or phlebotomist. The coumadin levels are monitored either by our anticoagulation service or your primary care physician, if the PCP. The anticoagulation nurse will only call if the dosage of coumadin needs to be changed. Local phlebotomists should call results directly to the anticoagulation nurse at (617)-732-8887 or toll free at (800)-262-0201 X 28887 and **not** Dr. Minas' office.

A One-week supply of pain medicine will be prescribed to you upon discharge from the hospital. If you are from New York State or Texas, post-operative pain management will need to be done by your referring surgeon or PCP. For other states Dr. Minas will manage your pain medicine needs. Narcotics such as Percocet, Oxycontin, Dilaudid, etc cannot be called in to a pharmacy. It is up to the patient to call the medication line at 617-732-9967 ext. 3 Monday thru Thursday, 3-4 days in advance of running out of medicine so a prescription can be mailed to you. A message should be left on voice mail with your name, date of surgery and dosage of the medicine so that a prescription may be mailed to your home. Please remember it is an institution policy that **only the patient or patients guardian**, if a minor, can call in for the refill.

The first week after surgery is the most painful, requiring narcotics on a 4-6 hour regular basis. After the first week, depending on a person's pain threshold, oral narcotics are usually required for 6-8 weeks after surgery, usually before physical therapy exercises and at bedtime. If osteotomy surgery is performed, then more frequent administration may be required. Anti-inflammatory agents (ibuprofen, aspirin, Aleve, Naprosyn, Vioxx, Celebrex, etc.) are not allowed for at least 6-9 months after surgery because of their adverse effect on cartilage growth.

You may shower, sitting in a shower seat, as soon as 4 days after surgery so long as there is no drainage from the incision or drain site. Your brace may be taken off for showering, sitting, or while in the CPM machine. It should be worn when walking or travelling. The steri-strips<sup>TM</sup> across the incision may be taken off 2 weeks after surgery.

If your wound should begin to drain, become red and hot to the touch, or you develop a fever, then you must call the office to discuss the problem and possibly be seen locally or in Boston.

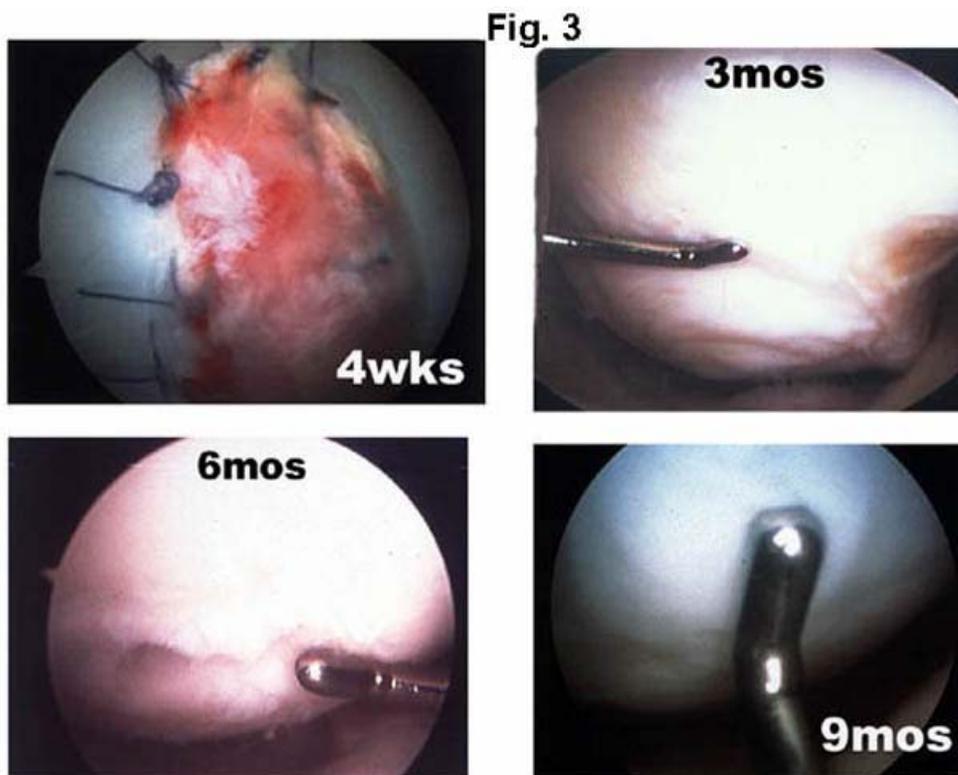
### ***Post-Operative Follow-Up and Rehabilitation***

The routine follow-up is at 6 weeks, 3 months, and 6 months, 1 year and yearly afterwards. There are 3 stages of rehabilitation which coincide with the clinic

visits; stage 1 – weeks 1-6, Stage 2 – weeks 7-12, and Stage 3 – weeks 13-26. These will be faxed to your therapist at the time of scheduled clinic visits, (and are not included here). Appendix 1 outlines the time course of ACI graft maturation, histology, and activities allowed. Rehabilitation after 26 weeks time is personal exercise training recommended by Dr. Minas unless the reconstruction is extensive or there have been complications during the recovery, requiring further supervised physical therapy. If osteotomy surgery or ligament reconstruction has also been performed X-rays are needed after surgery. Otherwise pre-operative films are needed and yearly films thereafter are needed to monitor for any progression to osteoarthritis.

### **Arthroscopy Photos At 4 Weeks, 3 Months, 6 Months, 9 Months**

Arthroscopic photographs demonstrating viscoelastic properties of autologous chondrocyte implantation grafts of medial femoral condyle in different patients at different stages of healing.



Four weeks; Absorbable 6.0 Vicryl sutures still present with complete fill of chondral defect with tissue soft and white.

Three months; Chondral defect completely filled with white, soft, jelly-like tissue which is not firmly attached to underlying subchondral bone and has a wave-like “consistency”.

Six months; “Putty-like” indentability of ACI graft which recoils within minutes of being indented.

Nine months; Graft is firm, hard and equal to viscoelasticity of adjacent host cartilage.

### ***Practical Tips***

- Practice crutch walking before surgery.
- Setup your home on one level.
- Prepare your meals the night before with assistance; it’s difficult to move around the kitchen with crutches.
- Obtain a shower seat and raised toilet seat.
- Shorts and side snap warm-up athletic pants are useful to leave the hospital, attend therapy, and MD office visits.
- Talk over arrangements of transportation needs with friends and family members.
- Absorbable (dissolving) sutures are use to close the skin. A cosmetic closure utilizing a monocryl stitch is used. Showering commences 4 days after surgery as long as there is no drainage. The Steri-strips should fall off on their own and can be taken off at 2 weeks after surgery.
- It is worthwhile to arrange to be on one level postoperatively and avoid stairs as much as possible to prevent the increased risk of fall or injury.
- Public transportation is difficult 4-6 weeks after surgery or until bone healing and surgical pain resolves.
- Shorts and side-snap athletic pants are useful for immediately postoperative due to ease of getting on and off over any braces or ice compression devices that may be use. They are also useful for office visits and x-rays postoperatively
- The outer aspect of the incision may remain numb for 6-12 months after surgery, this is normal after surgery (see risks).

- Keep the wound out of direct sunlight for 4 weeks after surgery and apply sun block 35 SPF or greater on the incision the first summer to prevent darkening of the final scar.

### ***Risks of Surgery***

There is no surgery that is guaranteed or without risk. ACI is reserved for the management of painful cartilage loss that limits activities of daily living. It is not meant to prevent osteoarthritis, although theoretically, repair may slow down or halt the progression of a defect to osteoarthritis. The goal of surgery, depending on the severity of cartilage loss, is to allow the patient to become comfortable with activities of daily living (ADL's). Sporting activities are also a possibility depending on the stage of disease at the onset of treatment.

The common risks associated with surgery are ACI graft overgrowth. The risk of overgrowth is 30% with periosteum and since the use of the Bio Gide Membrane has been all but diminished. ACI overgrowth causes painful catching of new onset. Frequently it will disappear altogether with further exercises, if not an MRI scan is recommended to document the ACI graft appearance prior to arthroscopy. This will also determine partial or complete graft failure prior to arthroscopy, so as to allow good surgical planning and allow realistic expectations. Arthroscopy resolves the catching and allows the grafts to heal without further delay in rehabilitation. It is rare, but possible for graft overgrowth to occur a second time.

Knee stiffness is another possible complication. Patients with multiple ACI grafts, prior history of knee stiffness after surgery, keloid scar formers, or ACI with tibial tubercle osteotomy are at risk. Treatment is arthroscopic release of scar tissue, manipulation under anesthesia, and CPM machine for 2 days in hospital with epidural catheter followed by home CPM for 3-6 weeks.

Failure of the treatment occurs 10-13% of the time, (87% of patients are improved). Failure means that there is no pain improvement from the pre-operative condition after 2 years. It may be due to the graft coming off the bone,

(usually as a result of a fall, overly aggressive rehabilitation, or too early a return to sports), or the graft forming fibrous tissue instead of cartilage. New sites of cartilage loss may account for a lack of pain relief, which is called progression of osteoarthritis. Rarely, the repair looks normal but the pain persists, and the reason for continued pain is unknown.

Numbness occurs routinely to the lateral, (outside portion), of the surgical incision due to cutting of the sensory nerves at surgery. Most of the sensation returns by 6-12 months but may be permanent.

Glucosamine/Chondroitin 1000mg for 6 months after the surgery is recommended. It is not proven to help definitively, but will not hurt, and some patients claim excellent improvement.

Recent Animal work demonstrated that external ultrasound can enhance cartilage healing early after surgery when used for 3 months. An Exogen Stimulator™ may enhance healing but is not usually covered by Insurance carriers.

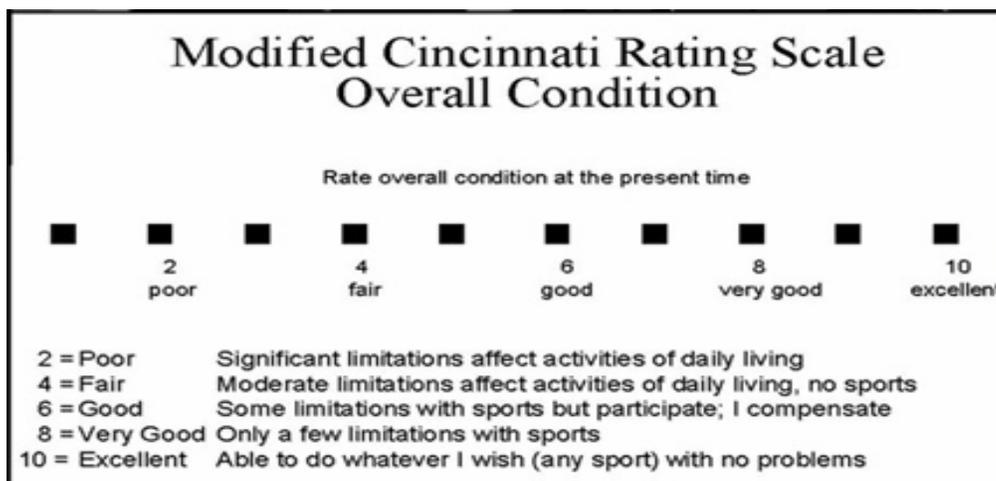
### ***Patient Outcomes***

The amount of clinical improvement is dependent on the stage of disease at the beginning of treatment. Three general categories of treatment have been used to classify patients, and capture the degree of improvement;

- Simple- a single weight bearing lesion in a healthy knee
- Complex- more than one lesion per knee, or requiring additional surgery, again in a non-arthritic knee
- Salvage- an arthritic knee by x-ray evaluation, or arthroscopic assessment, often involving 'kissing' ACI grafts

The results are based on patient reported clinical activity sports scores in the first 169 patients treated by Dr. Minas as of 11/99

The Cincinnati sports scale was used, which does not base itself on pain relief, just activity (see Figure 4).



The average areas resurfaced for these categories are;

- Simple=4 cm<sup>2</sup>(nickel-sized)
- Complex=7cm<sup>2</sup>(Fifty cent piece)
- Salvage=12cm<sup>2</sup>( about 2 fifty cent pieces)

Of the patients treated, 87% of patients improved, those who did not improve had graft failure, and were considered failures were;

- Simple-2/12
- Complex-8/86
- Salvage-12/71

Because of the few patients treated in the Simple category, and the 2 treatment failures, the results don't appear as good as they tend to be.

Cincinnati Knee scores by category of treatment;

- Simple - Preop 4, Postop 6
- Complex- Preop 4, Postop 8
- Salvage- Preop3, Postop 5, however the salvage patients have excellent pain relief, as measured by other outcome questionnaires.

Patients reported satisfaction improves on a yearly basis, as the knee function improves;

- Simple-60%
- Complex-80%
- Salvage-90%

Your individual situation and realistic expectations may be helped by speaking with Dr. Minas, Jeannette Vannan, or Tim Bryant RN. Please call 617-732-5322 to make an appointment.

## **Rehabilitation**

Weight-bearing status immediately following surgery can be found on stage 1 of your PT protocols found on your CD-ROM that is sent home with you from the hospital. Exercises after surgery include straight leg raises, quad sets, stationary biking, treadmill, elliptical trainer, and swimming. Outpatient physical can be utilized once the patient is no longer home bound and is safe to attend for modalities listed on the stage 1 protocol. Deep friction and massage of the quads and hamstring muscle is beneficial, as well as, iliotibial band (ITB) stretches. Mobilization of the patella and glides is recommended. A stationary bike in most cases can be used at around 4 weeks time post-operatively starting with the seat very high and with no resistance. If a full revolution cannot be made you can rock back and forth until the involved pedal makes it over the top. This cycling is done for 10 minutes, three times a day. Increase the flexion gradually by lowering the seat as tolerated every two to three days. The beginning restrictions are NO running, NO jumping, NO squatting, No leg presses and no progression of PT protocol unless cleared by Dr Minas.

### **Full extension is obtained by doing the following exercises:**

*Passive knee extension.*

- Sit in a chair and place your heel on the edge of a stool or chair.

*Relax the thigh muscles*

- Let the knee sag under its own weight until maximum extension is achieved.

*Heel Props*

- Place the heel on a rolled towel making sure the heel is propped high enough to lift the thigh off the table.
- Allow the leg to relax into extension 3 - 4 times a day for 10 - 15 minutes at a time. (See Figure 1)



Figure 1. Heel prop using a rolled towel.

#### *Prone hang exercise*

- Lie face down on a table with the legs hanging off the edge of the table and allow the legs to sag into full extension.



Figure 2. Prone Hang. Note the knee is off the edge of the table.

#### *Active-assisted extension*

- Performed by using the opposite leg and your quadriceps muscles to straighten the knee from the 90 degree position to 0 degrees. Hyperextension should be avoided during this exercise. See Figure 3:

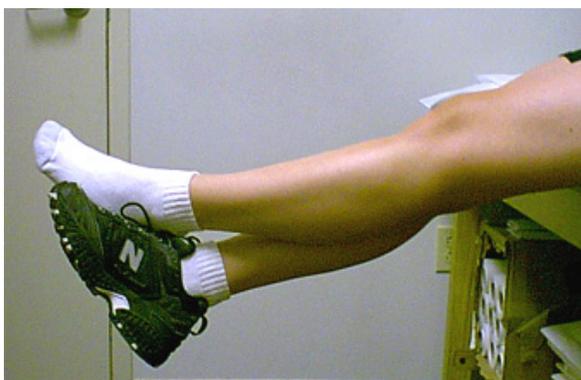


Figure 3. Use the non-injured leg to straighten the knee

**Bending (Flexion) is obtained by doing the following exercises:**

*Passive flexion (bending) of the knee to 90 degrees. (See Figure 4 below)*

- Sit on the edge of a bed or table and letting gravity gently bend the knee.
- The opposite leg is used to support and control the amount of bending.
- This exercise should be performed 4 to 6 times a day for 10 minutes. It is important to achieve at least 90 degrees of passive flexion by 5 - 7 days after surgery.



Figure 4. Passive Flexion allowing gravity to bend the knee to 90 degrees

**Wall slides are used to further increase bending.**

- Lie on the back with the involved foot on the wall and allow the foot to slide down the wall by bending the knee. Use other leg to apply pressure downward.



Figure 5. Wall Slide: Allow the knee to gently slide down

**Heel slides are used to gain final degrees of flexion.**

- Pull the heel toward the buttocks, flexing the knee. Hold for 5 seconds.
- Straighten the leg by sliding the heel downward and hold for 5 seconds.



Figure 6. Heel slide – leg is pulled toward the buttocks

- In later stages of rehabilitation, do heel slides by grasping the leg with both hands and pulling the heel toward the buttocks.



Figure 7. Heel slides in later stages of rehabilitation

## **Appendix**

### Time Course of ACI Graft Healing – Tissue Type, Appearance, Rehabilitation

#### Appendix 1

Time	0-6 Weeks	7-12 Weeks	>13Weeks-3 Years
Stage	I - Proliferation	II - Transition	III – Remodeling and Maturation
Histology	Rapid proliferation of spindle shaped cells with defect fill. Mostly type I collagen with early formation of colonies of chondrocytes forming Type II collagen	Matrix formation, mostly chondrocytes producing type II collagen and proteoglycans. Poor integration to underlying bone and cartilage.	Ongoing remodeling of matrix with reorganization and quantity of collagen type II, with integration to bone (arcades of Benninghoff), and adjacent host cartilage. Large chain aggregates of proteoglycans, with increased water content of cartilage.

Viscoelastic arthroscopic appearance	Filled, soft, white tissue	Jelly-like firmness, with “wave-like” motion when probed, not yet firm and integrated to underlying bone.	Firm “indentable”, but not “wave-like” when probed by 4-6 months after ACT. Graft whiter than host cartilage, may demonstrate periosteal hypertrophy (20%). Equal firmness to host cartilage 9-18 months after ACT.
Activity level	-CPM starts 6 hours after surgery for 6-8 hours/day x 6 weeks -Touch WB -Isometric muscle exercises and ROM	-Discontinue CPM -Active ROM -Partial graduated WB to full WB by 12 weeks -Functional muscle usage, stationary bicycle, treadmill	-Discontinue assistive devices 4-5 months post op if free of pain, catching, swelling -Distance walking, resistance walking -non-pivoting running 9-12 months -14-18 months pivoting allowed

Key	
CPM	Continuous Passive Motion
ROM	Range of Motion
WB	Weight Bearing

### ***Further Reading***

#### ***(References)***

#### ***ACI Treatment of Articular Cartilage Lesions***

##### Basic Science

- 1) Grande DA, Pitman MI, Peterson L, Menche D, Klein M: The repair of experimentally produced defects in rabbit cartilage by autologous chondrocyte transplantation. *J Orthop Res* 7:208-218, 1989.
- 2) Brittberg M, Nilsson A, Lindahl A, Ohlsson, C, Peterson L: Rabbit articular cartilage defects treated with autologous cultured chondrocytes. *Clin Orthop* 326:270-283, 1996.
- 3) Shortkroff, S, Barone, L., HSU, H-P., Wrenn, C, Gagne, T, CHI, T, Breinan, H, Minas, T, Sledge, CB, Tubo, R, and Spector, M. Healing of chondral and osteochondral defects in a canine model: The role of cultured chondrocytes in regeneration of articular cartilage. *Journal of Biomaterials & Research* 17:147-154, 1996.

4) Breinan, HA, Minas, T Hsu HP, Nehrer, S, Sledge CB, Spector, M: Effects of cultured autologous chondrocytes on chondral defects in a canine model. *JBJS, American* 79(10);1439-51, 1997.

5) Breinan, HA, Minas, T, Barone, L, et al.: Histological evaluation of the course of healing of canine articular cartilage defects treated with cultured autologous chondrocytes. *Tissue Engineering* 4:1, 1998.

6) Nehrer, S, Spector, M, Minas, T, Histological analysis of tissue after failed cartilage repair procedures. *Clin Ortho and Rel Res* 365: 149-162, 1999.

#### Epidemiology/Clinical Results/Economics:

1) Curl WW, Krome J, Gordon ES, Rushing J, Smith BP, Poehling GG, Cartilage injuries: A review of 31,516 knee arthroscopies. *Arthroscopy: The Journal of Arthroscopic and Related Surger* 1991; 13: 456-460.

2) Minas T, Nehrer S: Current concepts in the treatment of articular cartilage defects. *Orthopedics* 20:525-538, 1997.

3) Mandelbaum BR, Browne JE, Fu F, et al. articular cartilage lesions of the knee. *American Journal of Sports Medicine* 1998, 26:853-861.

4) Minas T. The role of cartilage repair techniques, including chondrocyte transplantation, in focal chondral knee damage. *AAOS Instructional Course Lectures* 1999; 48:629-643.

5) Noyes FR, Bassett RW, Grood ES, Butler DL. Arthroscopy in acute traumatic hemarthrosis of the knee. *The Journal of Bone and Joint Surgery* 1980: 62A:687-695.

#### Surgical Techniques/Rehabilitation:

1) Minas T, Peterson L: Chondrocyte transplantation. *Operative Techniques in Orthopaedics* 7(4): 323-333, 1997.

2) Minas T, Peterson L: Advanced techniques in autologous chondrocyte transplantation. *Clinics in Sports Medicine* 18(1): 13-44.

3) Gillogly S, Voight M, Blackburn B: Treatment of articular cartilage defects of the knee with autologous chondrocyte implantation. *JOSPT* 28(4); 241-251.

4) Peterson, L, Minas, T, Brittberg, M, Nilsson, A, Sjagren-Jasson, E, Lindahl, A: Two-to-9 year outcome after autologous chondrocyte Transplantation of the knee. *Clin Orthop and Rel Research* 374: 212-234 1999.

5) Minas, T, Peterson, L: Autologous chondrocyte transplantation. *Operative Techniques in Sports Medicine* 8(2): 144-157 2000.