I. INTRODUCTION
A. In 1743, Hunter stated that “From Hippocrates down to the present age, we shall find that an ulcerated cartilage is universally allowed to be very troublesome disease; that amidst a cure with more difficulty than a carious bone; and that, when destroyed it is never recovered.
B. In 1851, Paget said “There are, I believe, no instances in which a lost portion of cartilage has been restored, or a wounded portion repaired, with new and well formed permanent cartilage, in the human subject.”
C. Since then, numerous studies have confirmed that articular cartilage has limited capacity for spontaneous repair, except for formation of fibrous or fibrocartilaginous tissue, and its unique mechanical functions are never re-established spontaneously after a significant injury.
D. Articular cartilage is a unique tissue with no vascular nerve or lymphatic supply
1. This is why articular cartilage does not heal
2. No inflammatory response to tissue damage unless subchondral bone affected
3. Subsequently, no macrophage to phagocytose and remove damaged tissue
   a. no migration of cells with repair capacity into damaged area
E. The chondrocyte itself, encapsulated in its own matrix, is incapable of migrating and repopulating the damaged area
F. Chondral injuries penetrating subchondral bone
1. Will not heal
2. May progress into osteoarthritis over time
G. Osteochondral injuries penetrating subchondral bone into the trabecular bone
1. Cause inflammatory repair tissue
2. Fill lesion with fibrocartilage produced by mesenchymal stem cells or fibroblasts
H. PRIMARY PROBLEM
1. Fibrocartilage repair has not been shown to withstand mechanical wear over time
2. Fibrocartilage might degenerate and the lesion progress into osteoarthritis

II. Optimal Healing of Articular Cartilage
A. Regeneration with tissue identical to hyaline cartilage
1. Presently, this is not possible
2. Fibrocartilage forms instead
B. Repaired tissue should be able to fill and seal off defective area with good adhesion to the subchondral bone and complete integration to the surrounding cartilage
1. Repaired tissue must withstand mechanical wear over time
C. Articular cartilage functional unit includes:
   1. Different layers of cartilage
   2. Subchondral bone
   3. Trabecular bone
D. Techniques affecting subchondral bone plate may lead to stiffening of subchondral and trabecular bone

III. Classification of Chondral Lesions
A. International Cartilage Repair Society (ICRS) and Outerbridge Classification
   1. Grade 0 – Normal
   2. Grade 1 – Softening and/or superficial fissures and cracks
   3. Grade 2 – Injury involving transitional zone and extending down to less than 50% of cartilage depth
4. Grade 3 – Injury involving deep/radial zone extending greater than 50% of cartilage depth, and down to, but not through, the subchondral bone
5. Grade 4 – Subchondral bone exposed; osteochondral injuries with lesion extending through the subchondral bone plate or deeper defects down into the trabecular bone

B. Chondral delamination
C. Osteochondral lesion
   1. Fracture
   2. Osteochondritis dissecans
   3. Avascular necrosis

IV. Treatment Alternatives
A. Joint lavage
   1. Lavages catabolic cytokines
   2. No hyaline regeneration
   3. Variable short term results
B. Debridement
   1. Removes mechanical symptoms with loose flaps or loose bodies and degenerating cartilage
   2. Also removes synovitis and osteophytes which interfere with joint function
   3. Symptom relief initially is good, but results gradually decline over time
C. Marrow stimulation techniques introducing mesenchymal stem cells and fibroblasts from subchondral and trabecular bone
   1. Abrasion arthroplasty
      a. variable fill with fibrocartilage
      b. aggressive treatment can hasten degenerative changes
   2. Drilling – transmalleolar or transtalar
      a. fibrocartilage repair tissue
      b. question of increased stability of repaired tissue
      c. effects subchondral and trabecular bone plate
      d. avoid thermal necrosis
   3. Microfracture
      a. fibrocartilage repair tissue
      b. no thermal necrosis
      c. preserve subchondral bone plate but may increase stiffness long term
      d. no long term results
D. Osteochondral autograft plugs (OATS)
   1. “Robs Peter to pay Paul”
   2. Question of long term problems with femoral plug holes and subsequent pain
   3. Size limitations for autograft transplantation
   4. Advantage of single setting procedure
   5. Scranton et al. (2005) did 50 patients and showed significant improvement, with 90% good/excellent. The Karlsson scores increased from 24 to 83 points
E. Osteochondral allografts
   1. Chu (1999) reported 55 knees with average follow-up of 75 months
   2. Overall success for Chu was 76%
   3. Gross (2001) did 9 patients; 6 patients remain in situ with mean survival 11 years. 3 cases required fusion
   4. Bugbee et al. (2010) reported on 12 ankles
      a. Mean follow-up 38 months
      b. Average previous surgery 1.8
      c. Graft survival 83%
      d. Mean OMAS improved from 28 to 71
   5. Kelikian et al. (2011) did allografts on 38 patients
a. Mean follow-up 38 months  
b. Graft survival 89%  
c. AOFAS score went from 52 to 79

V. Autologous Chondrocyte Implantation  
A. Definition – implantation of in vitro cultured autologous chondrocytes using a periosteal tissue or membrane cover after expansion of isolated chondrocytes  
B. Smith (1965) was successful in isolating and growing chondrocytes in culture for the first time in rabbits  
C. Popularized by Dr. Lars Peterson et al. in Gothenburg, Sweden  
1. Animal models, 1984  
2. Human trials first done, 1987  
3. Cultured chondrocytes placed in defect under sutured periosteal graft  
4. Pre-chondrocyte cells attached to subchondral bone and repopulate defect  
5. Biopsies show progression from unorganized to well organized mature, hyaline-like cartilage  
6. Tissue typing shows type II articular cartilage  
D. ACI – Generations  
1. Generation 1 – Carticel suspended under periosteal flap or membrane  
2. Generation 2 – Carticel inserted under a tissue patch or onto a carrier scaffold  
3. Generation 3 – Carrier-free, immature cartilage tissue  
1. 23 patients, age 14-48 years old  
2. FT articular defects: 1.6 to 6.5 cm²  
3. Mean follow-up = 39 months  
4. 14 of 16 femoral lesions had G/E results at 2 years  
5. Second look arthroscopies show gradual return to firmness equal to surrounding cartilage  
F. Peterson et al. (AJSM 2010)  
1. Long term follow-up study done with 224 of 341 patients responding to questionnaire  
2. Mean size of cartilage lesion = 5.3 cm²  
3. Mean follow-up 12.8 years  
4. 92% satisfied and would do it again  
5. Lysholm 60 to 69  
6. Tegner 7.2 to 8.2  
7. Brittberg-Peterson 59 to 41  
G. Pros vs. Cons of ACI  
1. Pros  
   a. Autogenous tissue  
   b. Hyaline-like tissue  
   c. No donor site morbidity  
   d. Can treat larger lesions  
   e. More extensive follow-up  
2. Cons  
   a. Technically difficult: periosteum  
   b. Staged, arthrotomy required  
   c. High cost (reimbursable?)  
   d. Bone loss needs staged grafting or “sandwich procedure”  
   e. Extended recovery

VI. Indications for ACI in the Ankle  
A. Indications  
1. Patients aged 15 to 55
2. Focal defect > 1 cm²
3. Unipolar (only talus affected)
4. Contained
5. Edge loading
6. Failed previous surgery
7. Large lesions with extensive subchondral cystic changes

B. Relative Indications
   1. Multifocal unipolar lesions
   2. Uncontained lesions

VII. Contraindications for ACI in the Ankle
A. Relative
   1. Kissing (bipolar) lesions
   2. No previous surgery
   3. Early degenerative changes
B. Absolute
   1. Osteoarthritis
   2. Uncorrected malalignment
   3. Uncorrected instability

VIII. Preoperative Assessment
A. Patient factors
   1. Age – physiologic not chronologic
   2. Weight
   3. Activity level
   4. Family history of arthritis
   5. Medications, i.e., corticosteroids, NSAIDs
   6. Social history, smoking, ETOH
B. Joint Factors
   1. Subacute versus chronic
   2. Size – most patients have lesions approximately >2 cm x 1 cm
   3. Location in the talus
   4. Joint stability
   5. Limb alignment
   6. Previous surgeries such as subchondral bone stimulating types
C. Careful Preoperative Evaluation
   1. Physical exam determines that lesion is symptomatic and the cause of the patient’s pain
   2. Evaluation with weight bearing x-rays
   3. Evaluation with MRI/CT scans

IX. Surgical Procedure for ACI – Step 1
A. Biopsy procedure
   1. Chondral biopsy 200-300 mg
   2. Biopsy done in intercondylar notch of the knee arthroscopically
B. Simultaneous ankle arthroscopy
   1. More carefully assess lesion
   2. Treat associated problems that are not accessible by malleolar osteotomy
C. Tissue culture procedure
   1. Cartilage tissue sent for culture
   2. Enzymatic digestion
   3. Cultivation leading to tenfold increase in chondrocytes
   4. 14 to 12 days, sterile, antibiotics
5. 10 to 12 million cells available for transplant (.3 to .4 cc volume)

X. Surgical Technique – Step 2
A. Medial or lateral malleolar osteotomy performed under fluoroscopic control
   1. Medial osteotomy must extend central enough to access larger lesions and permit suturing
   2. Lateral osteotomy must be performed at syndesmosis with release of the anterior
talofibular and calcaneofibular ligaments and posterior reflection of fibula
   3. Pre-drill medial or lateral malleolus prior to osteotomy
B. Defect preparation
   1. Vertically incise and circumscribe the defect; remove all damaged cartilage from
subchondral bone
   2. Include all pathologic areas in defect excision
   3. Use sharp ring curette to make 90-degree angles and sharp walls between defect and
healthy cartilage
   4. Base of defect must be debrided from all fibrous and cartilage remnants; debride defect
down to calcified cartilage layer without penetrating bone
   5. Remove all fibrous tissue
C. Periosteum harvest
   1. Periosteum can be harvested 4 to 6 cm proximal to the ankle in the distal tibia, through the
same incision used for medial or lateral arthrotomy
   2. Additional periosteum can be harvested distal to the pes anserinus and proximal anterior
tibia through separate incision
   3. Use a ruler to accurately measure dimensions of defect and template from sterile foil to get
exact geometric fit
   4. Keep periosteum moist at all times to reduce shrinkage
   5. Add 1 to 2 mm to the periphery of the template prior to taking periosteal graft
D. Key is to mark non-cambium layer of periosteum
E. Periosteum fixation
   1. Place periosteum in the defect in proper orientation
   2. Place periosteum in the defect with the cambium layer down (facing towards subchondral
bone)
   3. Anchor periosteum at four corners of the defect using 5.0 or 6.0 Vicryl suture on a cutting
needle
   4. Do not allow patch to overlap cartilage – trim periosteum for optimal fit
   5. Continue to place interrupted sutures in periosteal patch and leave one small area for
cellous insertion
   6. When suture fixation is complete, test for water tightness
   7. If no cartilage rim is available, suture the periosteum to the synovial membrane or ligament,
or use suture anchors
F. Bioguide
   1. Absorbable porcine bilayer collagen I/III membrane has been used in knee and ankle ACI in
place of periosteum
   2. Has a rough and smooth layer
   3. Made by the same company as Chondro-gide and very similar
G. Application of fibrin glue
   1. Apply fibrin glue circumferentially along the periosteum-cartilage margin or at suture rifts
   2. Insert catheter with saline under periosteum to look for leaks
   3. Suction out saline to empty defect
H. Cell aspiration
   1. Aspirate vial contents, except for the cell pellet, slowly; slowly expel medium back in the
vial. This will break up cell pellet and resuspend the cells in the medium
2. Aspirate all contents of the vial into the syringe, being extremely careful

I. Cell implantation
1. Insert soft catheter tip through the opening of the periosteum; advance catheter to the most posterior aspect of the defect
2. Slowly inject cells while moving the catheter tip side-to-side and withdrawing proximally
3. Complete implantation by enclosing the remaining opening in the periosteum with additional sutures and fibrin glue

J. Wound closure
1. Re-insert pre-drilled guide pins and insert appropriate length screws in the medial malleolus
2. Insert lag screws in fibula, then appropriate size plate and screws
3. The patient goes into short leg cast in neutral position

XI. Surgical Technique with “Sandwich Procedure”
A. Same as above
B. Done for large cystic lesions >6 mm deep
1. Best measured on CT scan in the coronal and axial planes with sagittal reconstructions
C. Osteochondral lesion is excised and the entire cyst is curetted out
1. After cyst is removed, multiple holes are made in the base to facilitate bleeding
2. Bone graft obtained from the proximal or distal tibia, depending on the size of the cyst
D. Periosteum harvested as noted above or use BioGide used
1. Periosteum or BioGide is sewn over the bone graft site with the cambium side up
2. Periosteum or BioGide should be flush with the base of the lesion
3. Fibrin glue is used to seal the periosteum or BioGide further
4. Tourniquet is released and hemostasis obtained
E. Second periosteal flap is sutured at the level of the adjacent healthy articular cartilage with the cambium layer down
1. Fibrin glue used to seal the entire periosteum or BioGide membrane, with a hole left to inject the cells
F. Chondrocytes injected between the two periosteal or BioGide flaps, i.e., “sandwich procedure”
1. Hole in periosteum is sutured and additional fibrin glue used to seal the entire defect
G. Closure as above

XII. Postoperative Care
A. Early phase, day 1 to week 8
1. At one week, the patient's cast is removed and the wound is checked
2. The patient goes into removable CAM walker and TED stocking
3. The patient starts applying partial weight bearing (15-20 kg or 30-40 pounds)
4. The patient starts active range of motion in dorsi and plantar flexion, and CPM can be used on occasion
5. Isometric muscle strengthening or dorsi and plantar flexors can begin
B. Transition phase, 8 to 12 weeks
1. Increase weight bearing to full weight bearing
2. Try to achieve full range of motion
3. Increase muscle strengthening and functional training
C. Mid Phase, 3 through 5 months
1. Full weight bearing with faster speeds of walking; no running
2. Continue bicycling
3. Maintain active and passive range of motion and increase strengthening
4. Increase functional training
D. Final phase, 6 through 12 months
1. Full weight bearing, start light jogging on treadmill and doing interval work
2. Maintain full range of motion
3. Advance strengthening to Phase III and IV activities
4. Increase functional training, including jumping and landing, running in circles, and cutting

E. Time line for activities
   1. Low impact activities start at 4 to 6 months; ice skating, rollerblading, cross country skiing, cycling
   2. Repetitive impact activities start at 6 to 8 months; jogging, running, aerobic classes
   3. High level activities at 10 to 12 months; tennis, basketball

XIII. Results of ACI – First Generation (ACI-P)
A. Giannini et al. (2001)
   1. 8 patients with ACI of talus; mean follow-up of 26 months
   2. Second look arthroscopy at 12 months with biopsy
   3. All patients – pain, swelling, crepitation considerably reduced; AOFAS score improving from 32 to 91/100
   4. Second look arthroscopy showed regenerated areas of cartilage
   5. Histology showed all grafts retained cartilage that was normal in terms of thickness, chondrocyte viability and staining for type 2 cartilage
B. Peterson (2003)
   1. 14 patients
   2. Mean age 28 (18-42)
   3. All patients failed one prior surgery
   4. Defects mean size 1.7 cm²
   5. Mean follow-up of 28 months
   6. 11 of 14 good/excellent, 2 poor, 1 lost to follow-up
C. Whittaker et al. (2005)
   1. 10 patients
   2. Mean follow-up 23 months
   3. Mazur score increased 23 points
   4. Increased donor site morbidity
   5. “Second looks” were done on 9 patients and showed filled defects and stable cartilage
   6. Biopsies showed mostly fibrocartilage with some hyaline cartilage
D. Baums et al. (2006)
   1. 12 patients
   2. Mean follow-up 63 months
   3. Hannover score increased from 40 to 86 points
   4. AOFAS increased 45 points
   5. Patients involved in competitive sports were able to return to their full activity level
E. Ferkel (2011)
   1. 32 patients done; the first 11 patients have been reviewed and published in AJSM
   2. Current study: Follow-up on 29 of 32 (91%)
   3. Average age: 34 (18-54)
   4. Average follow-up: 70 months (24-129)
   5. 9 “sandwich” procedures done, with bone grafting of large cystic underlying defect and use of two periosteal grafts back to back
   6. 2nd look arthroscopy on 90% of patients (26/29)
   7. Results: Excellent: 8; Good: 15; Fair: 5; Poor: 1
   8. Entire paper presented at AAOS 2011
XIV. ACI Periosteal Problems
   A. First Generation ACI complications include:
      1. Periosteal hypertrophy
      2. Delamination
      3. Graft failure
   B. USFDA estimated 3.8 complication rate in knees
      1. 18% graft hypertrophy
   C. Type I/III bilayer porcine collagen membranes (BioGide) available in United States to be used in place of periosteum
      1. Gomoll et al. compared subsequent surgeries with periosteum versus collagen membrane
      2. Results similar except hypertrophy related surgery: 52% with periosteum and 3.4% with collagen membrane

XV. Second Generation ACI
   A. A variety of scaffolds being used in Europe, implanted either through a small arthrotomy or arthroscopically.
      1. Used as a patch and cells inserted underneath
      2. Cells seeded onto the scaffold membrane
   B. Collagen-covered autologous chondrocyte implantation (CACI or ACI-C)
      1. Absorbable porcine bilayer collagen I/III membrane
      2. Chondro-Gide membrane with one compact and one porous surface
      3. Gooding found no difference in results between periosteum and membrane cover in knees with CACI
   C. Hyalograft C
      1. Benzyl ester of Hyaluronic acid
      2. Bioabsorbs in 3 months
      3. Marcacci et al. presented 175 patients with grafts in the knee with 46 month mean follow-up. Results were 93% improvement at ICRS 2006
      4. Giannini et al. (2008) – 46 patients in ankle
         a. Mean age 32; follow-up 3 years
         b. Preop 57; postop 90 mean AOFAS score
         c. Biopsies collagen type II
   D. Membrane/matrix autologous chondrocyte implantation (MACI)
      1. Highly purified type I/III collagen membrane
      2. Guillen and Abelow presented first 50 cases (42 knees; 8 ankles)
      3. 8 ankles (ages 22-46)
      4. Large full thickness cartilage lesions of the talus (2-6 cm)
      5. 5/6 good & excellent results with follow-up 4 months-2 1/2 years
      6. Giza et al. did MACI on 10 patients; AOFAS 61 to 73

XVI. Third generation ACI
   A. Use carrier-free, immature cartilage tissue
   B. Lack of carrier scaffold
   C. Avoids carrier integration, degradation and biocompatibility complications
   D. Jubel et al. used an alginate matrix to produce cell-rich chondrocyte disc in MFC of 48 sheep
   E. Chondral defects treated with De Novo cartilage transplantation showed qualitatively better micro and macroscopic regeneration than those with periosteal flaps alone
      1. Fair and Yao reported early good results in the knee
      2. Adams et al. reported particulated juvenile articular cartilage transplant for OLT with early good results
XVII. **Recommended reading on current and future innovations on ACI and treatment of osteochondral lesions of the talus**
A. Safran, Kim and Zaffagnini in JAAOS, 2008
B. Mitchell, Giza, Sullivan in JAAOS, 2009
C. Getgood, Brooks, Fortier, Rushton in JBJS (Br) 2009
D. Gikas, Bayliss, Bentley, Briggs in JBJS (Br) 2009
E. O’Loughlin, Heyworth, Kennedy in AJSM 2009
F. Ferkel, Scranton, Stone, van Dijk et al. Instructional Course Lectures, vol. 59 2010
G. McGahan, Pinney in FAI 2010
H. Easley, Latt, Santangelo et al in JAAOS 2010
I. Harris, Siston, Pan, Flanigan in JBJS 2010

XVIII. **Is there a critical defect size for poor outcome?**
A. Chuckpaiwong et al. (2008) did debridement and microfracture on 105 patients with mean follow-up of 32 months.
   1. Lesions smaller than 15 mm, no failures
   2. Lesions great than 15 mm, one patient successful
   3. Factors affecting negative outcome: increasing age, higher BMI, trauma history and presence of osteophytes
B. Guo et al. (2010) treated 43 patients arthroscopically with mean age of 32 years
   1. AOFAS 70 to 90; 81% good/excellent
   2. Strong correlation with size of lesion (<10 mm) and successful outcome
C. Choi et al (2009) found initial defect size is important prognostic factor for OLT and can serve as a basis for preop surgical decisions
   1. OLT defect of 150 mm² or greater as calculated from MRI has a high correlation of having a poor clinical outcome
   2. OLT defect of <150 mm² has a high correlation of a good clinical outcome

XIX. **Summary**
A. Zengerink et al. has nicely summarized when to use which treatment for OLT (see Table 1)

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Type 1: asymptomatic lesions</td>
<td>Conservative</td>
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<tr>
<td>Type 2: symptomatic lesions ≤ 10 mm</td>
<td>Debridement and drilling/microfracturing</td>
</tr>
<tr>
<td>Type 3: symptomatic lesions 11-14 mm</td>
<td>Consider debridement &amp; drilling, fixation, an osteochondral graft or ACI</td>
</tr>
<tr>
<td>Type 4: symptomatic lesions ≥ 15 mm</td>
<td>Consider fixation, graft or ACI</td>
</tr>
<tr>
<td>Type 5: large talar cystic lesions</td>
<td>Consider retrograde drilling + bone grafting, or ACI with sandwich procedure, osteochondral transplant</td>
</tr>
<tr>
<td>Type 6: secondary lesions</td>
<td>Consider osteochondral transplant</td>
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</tbody>
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For types 4 through 6, debridement and bone marrow stimulation can always be considered a treatment option.


**References**


