<table>
<thead>
<tr>
<th>LAST TIME</th>
<th>NEW STUFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Bone</td>
<td>• Bone</td>
</tr>
<tr>
<td>– Structure</td>
<td>– Fracture healing</td>
</tr>
<tr>
<td>– Composition</td>
<td></td>
</tr>
<tr>
<td>– Composite nature</td>
<td>• Articular Cartilage</td>
</tr>
<tr>
<td>– Bone cells</td>
<td>– Histological appearance</td>
</tr>
<tr>
<td>– Bone formation</td>
<td>– Composition</td>
</tr>
<tr>
<td>– Growth in length</td>
<td>– Proteoglycan structure</td>
</tr>
<tr>
<td>– Biologic regulation of growth</td>
<td>– Cell shape</td>
</tr>
<tr>
<td>– Material properties</td>
<td>– Material properties</td>
</tr>
<tr>
<td>– Wolff’s law</td>
<td>– Biphasic theory</td>
</tr>
<tr>
<td></td>
<td>– Chondral defects</td>
</tr>
<tr>
<td></td>
<td>– Osteoarthritis</td>
</tr>
<tr>
<td></td>
<td>– Rheumatoid arthritis</td>
</tr>
<tr>
<td></td>
<td>LECTURE NOTES ON WEB:</td>
</tr>
<tr>
<td></td>
<td><a href="http://biomech.ame.arizona.edu/~weiss/">http://biomech.ame.arizona.edu/~weiss/</a></td>
</tr>
<tr>
<td></td>
<td>(look under “classes”)</td>
</tr>
<tr>
<td></td>
<td>username: bme511</td>
</tr>
<tr>
<td></td>
<td>password: ShowMeTheFiles</td>
</tr>
</tbody>
</table>

Fracture Healing

- **Primary fracture healing** - Occurs after fracture has been stabilized via internal fixation.
  - Bone union is achieved without any intermediate fibrous tissue or cartilage formation in the fracture gaps
  - Gradual disappearance of the fracture line and lack of external callus formation

- **Secondary fracture healing** - Occurs under relatively unstable conditions.
  - Prominent callus formation, followed by fibrocartilage formation and then endochondral ossification in the fracture area
Long Bone Healing by Callus Formation 
(Secondary Fracture Healing)

• Loss of mechanical integrity, ruptured blood vessels
  – leads to localized avascularity of fragment ends
• Interfragmentary stabilization by callus formation
• Restoration of continuity and bone union by intramembranous and endochondral ossification
• Substitution of avascular and necrotic areas by bone remodeling

Long Bone Healing by Callus Formation 
(cont’d)

• Callus formation is response of determined osteoprogenitor cells, principally in the periostium and endostium, to a number of activating factors released from freshly injured bone
  – Bone formation starts within a few days, depends mainly on the state of the blood supply
  – Woven bone is initially formed; Haversian remodeling starts after 3-4 weeks
  – More instability --> larger callus
Fracture Healing (cont’d)

- Bone formation depends on two fundamental prerequisites:
  - Ample blood supply - osteoblasts can function only in the neighborhood of capillaries
  - Mechanically solid surface for bone deposition - matrix deposition and mineralization occur only under mechanically stable conditions
A hypothesis for control of bone morphogenesis

Tissue Engineered Bone Matrix

Cortical Bone

Cancellous Bone
Articular Cartilage - Introduction

- Distributes load, minimizing peak stresses on subchondral bone
- Remarkable durability
- Provides low-friction bearing surface
- Low level of metabolic activity
- Lacks blood vessels, lymphatic vessels and nerves

Histological Appearance of Articular Cartilage

S - superficial zone; T - transitional zone; M - middle or deep zone; C - calcified cartilage.
Articular Cartilage - Composition

• Chondrocytes embedded in an abundant extracellular matrix
  – Cells are less than 10% of total tissue volume
• Matrix was thought to be homogeneous based on work of Virchow (1860) - “the intercellular matter is as clear as water…”. This led to name hyaline (Greek for hyalos, glass).
• Subsequent phase-contrast and electron microscope studies suggested that the matrix consisted almost entirely of a collagen fibril network

Articular Cartilage - Composition (Cont’d)

• Tissue fluid
  – ~60-80% of wet weight of cartilage
  – consists of water with dissolved gases, small proteins and metabolites
  – High water content makes essential contributions to material properties and participates in joint lubrication
  – Because tissue fluid is not contained within cellular membranes, volume, concentration, organization and behavior depend on interaction with structural matrix molecules
Articular Cartilage - Composition (cont’d)

• **Structural macromolecules**
  – Collagens
    • Principle collagen is type II (fiber forming) - accounts for 90-95% of total collagen
    • Other “minor” collagens - types IX, XI, V, VI
  – Proteoglycans
    • Form the major macromolecule of cartilage ground substance
    • Exist as individual monomers or aggregates
  – Noncollagenous Proteins
    • Consist primarily of protein and may have a small number of attached monosaccharides or oligosaccharides
    • Some of these molecules may help to organize and maintain the macromolecular structure of the matrix

Articular Cartilage - Composition (cont’d)

• **Chondrocytes** - maintain extracellular matrix
  – Surrounded with matrix - no cell-to-cell contacts
  – ER and golgi apparatus responsible for matrix synthesis
  – Extracellular matrix influences chondrocyte function
  – Matrix transmits mechanical signals to chondrocytes through changes in tension on the cell membrane or as an electromechanical transducer
  – During cartilage formation, chondrocytes proliferate rapidly and synthesize large volumes of matrix
  – With maturation, processes slow and cell density decreases
  – Under normal circumstances, chondrocytes rarely, if ever, divide. Cell density decreases with age.
Structure of a Proteoglycan Aggregate

Multiple monomers noncovalently associate with link proteins and a central hyaluronic acid filament to form an aggregate.

Electron Micrographs of Cartilage Proteoglycan Aggregate

A. Skeletally immature

B. Skeletally mature
Effect of Compressive Strain on Proteoglycan Aggregate

- Negative charges of GAG chains repel each other and bind water, expanding the domain of the proteoglycans. Pressure drives these charged chains closer together.

Change of Chondrocyte Shape with Depth

- Superficial zone
- Transitional zone
- Middle zone
- Superficial zone

(N-nucleus; G - glycogen granules; IF - intermediate filaments; MM - mineralized matrix; UN, unmineralized matrix.)
Split-line Pattern on Femoral Condyles

Cyclic Tensile Loading of Articular Cartilage

Figure 12.8:1 Stress response of bovine femoral articular cartilage subjected to cyclic stretching between $\lambda = 1.07-1.10$. Temp.: 37°C. Specimen immersed in saline. From Woo et al. (1979), by permission.
Figure 12.8: 2. The reduced relaxation function of articular cartilage at a lower stretch ($\lambda = 1.05$) and at higher stretches, $\lambda = 1.16$–1.29. From Woo et al. (1979), by permission.

Figure 12.8: 3. The experimental reduced relaxation function of articular cartilage compared with a theoretical expression given in Eq. (3) with the constants $c$, $\tau_1$, $\tau_2$ determined empirically. From Woo et al. (1979), by permission.
Matrix Deformation under Creep Loading

Fluid Motion under Stress Relaxation Loading
Modeling of Cartilage Mechanics

“To a modern worker, it appears that much of the work has to begin from the very beginning. To an analytical mechanist, the most serious frustration lies in the dearth of information about the material properties, i.e. the stress-strain-history laws of living tissues. Without the constitutive law, no analysis can be done. On the other hand, without the solution of boundary value problems the constitutive laws cannot be determined. Thus, we are in a situation in which serious analyses (usually quite difficult because of nonlinearity) have to be done for hypothetical materials, in the hope that experiments will yield the desired agreement. If no agreement is obtained, new analyses based on a different starting point would become necessary.”


Modeling of Cartilage Mechanics

• “The biphasic theory appears to provide the only consistent rheological model capable of describing most of the observed deformational behaviors of articular cartilage. The predominant mechanism responsible for the creep and stress relaxation is the diffusional drag of relative motion of the interstitial fluid with respect to the solid matrix.”

Biphasic Theory - Conservation of Mass

- Solid and fluid phases coexist
- Each phase is intrinsically incompressible
- Balance of mass leads to following continuity equation relating volume fractions of solid and fluid:

\[
\text{div}(\phi^s v^s + \phi^f v^f) = \nabla \cdot (\phi^s v^s + \phi^f v^f) = 0
\]

- \( \phi^s \) is solid phase volume fraction
- \( \phi^f \) is fluid phase volume fraction
- \( v^s \) is velocity of solid
- \( v^f \) is velocity of fluid

\[
\phi^s + \phi^f = 1
\]

Biphasic Theory - Equations of Equilibrium

- Start with momentum equation, add body force due to diffusive drag between solid and fluid and neglect inertial forces:

\[
\text{div}(\sigma^s) + \pi = 0 \\
\text{div}(\sigma^f) + \pi = 0
\]

- Here, \( \sigma^s \) and \( \sigma^f \) are the stress tensors acting on the solid and fluid phase, respectively.
- \( \pi \) is the diffusive drag from interaction between the phases:

\[
\pi = p\nabla \phi^f + K(v^f - v^s)
\]
**Biphasic Theory - Constitutive Equations for Solid and Fluid Phases**

- Solid phase is modeled as isotropic linear elastic:
  \[ \sigma^s = -\phi^s p I + \lambda_s \text{tr}(E) I + 2\mu_s E \]
- The fluid phase is assumed to be a compressible Newtonian fluid:
  \[ \sigma^f = -\phi^f p I - \frac{2}{3} \mu^f \text{div}(v^f) I + 2\mu^f V \]
- Here, \( V \) is the strain rate tensor. The fluid constitutive model is typically further simplified by the assumption of incompressibility and inviscid behavior at low shear rates:
  \[ \sigma^f = -\phi^f p I \]

**Steady State Uniaxial Filtration**

- Specimen is confined in radial \( r \)-direction and is supported at its surface \( z = h \) by a free-draining rigid-porous block.
- At \( z = h \), displacement \( u_z = 0 \).
- The pressure boundary conditions are \( P(z=0) = P_A \), \( P(z=h) = 0 \) \( \Rightarrow \)
  \[ \sigma_{zz}(0) = -P_A \]
- Volume flux \( Q \) of fluid per unit cross-sectional area must be constant at steady state through the thickness. From the momentum equation and the definition of the permeability, one obtains:
  \[ -k \frac{\partial p}{\partial z} = Q \]
- If \( k \) is constant, then the differential equation defines Darcy’s law for the hydraulic permeability:
  \[ k = Q \frac{h}{P_A} \]
- \( h \) is tissue thickness
- \( P_A \) is pressure drop
Confined Compression Creep

- Thin cylindrical plug is confined laterally by an impermeable-frictionless ring so that there is no radial displacement or fluid flow.
- Surface at $z = h$ is supported by rigid-impermeable plate.
- A step load $F_0 H(t)$ is applied to the axial direction ($H(t)$ is the Heaviside function). The governing equation for the solid matrix displacement is a diffusion-type equation given by:

$$H_A k \frac{\partial^2 u_z}{\partial z^2} = \frac{\partial u_z}{\partial t}$$

- Here, $H_A$ is the aggregate modulus, and $k$ is the apparent permeability

Chondral Defects

- Articular cartilage damage - exceedingly common problem affecting the joints of millions of people.
- When injury does not penetrate subchondral bone, outcome of biological healing is poor
- Young patients - treated using marrow-stimulation - subchondral drilling, microfracture, abrasion arthroplasty
  - Torn or compromised cartilage is removed to expose underlying bone
  - Rim of healthy cartilage is defined around the defect
  - Drilling, puncturing or abrading the underlying bone to stimulate an inflammatory response and/or generate a blood clot within the defect
Knee Anatomy, Anterior View

Knee Anatomy, Proximal Tibia
Human Knee Reconstructed From CT

Knee Articulation

0° flexion  45° flexion  90° flexion
Chondral Defects - Injury Mechanism

- Rotational force in direct trauma is the most common cause of injury to the articular cartilage
  - in adults, tidemark zone is weak link between overlying cartilage and subchondral bone --> shearing injuries most often produce a chondral injury rather than an osteochondral injury
- In most cases injury is in wt bearing regions of articular cartilage, and usually in the medial compartment (4 times more common than lateral injuries)

Chondral Defects - Types of Injuries

- mild lesion, w/ normal appearing cartilage, difficult to discern borders of lesion and normal surrounding cartilage;
- mild fibrillation, discoloration, cartilage softer than normal;
- linear crack: usually split thickness, and often encountered on lateral tibial plateau in assoc w/ anterior cruciate injuries;
- stellate: most common;
- diverging w/ central flaking of the cartilage;
- flap tear: the carilage is avulsed from the subchondral bone;
- crater: full thickness, in which subchondral bone is exposed;
- partial thickness w/ fibrillation;
- degrading lesion: cartilage is degenerative in nature and extends down to subchondral bone.
Treatment Options

- Abrasion
- Inlay Allograft
- Chondrocyte reimplantation (Genzyme)
- Microfracture

Effect of Defect Size

- Normal Condyle
- 1 cm lesion
- 2 cm lesion
Osteoarthritis - Pathology

- Gradual processes of destruction & regeneration
  - early in dz, articular cartilage loses its glistening appearance
  - later on surface layers flake off while deeper layers develop longitudinal fissures, process termed fibrillation
  - cartilage becomes thin and sometimes denuded
  - subchondral bone: - becomes thickened, sclerotic, & polished
  - subchondral bone displays thickened trabeculae, microfractures
  - tidemark is disrupted by vessels from the subchondral layer
  - osteophytes: - spurlike bony outgrowths covered by hyaline cartilage, may develop at margins of joint & progressively enlarge

Osteoarthritis - Histology

- Superficial zone demonstrates earliest changes
  - diminution of chondrocytes in superficial zones
- Cartilage matrix loses its ability to stain for proteoglycans with alcian blue or safranin-O
- Deeper chondrocytes demonstrate proliferation in clusters (brood capsules)
- Capillary buds penetrate the layer of calcified cartilage
- Split & reduplicating tidemark
- Synovium becomes hypertrophied and thrown into villose folds - may see infiltration with plasma cells, and lymphocytes
Osteoarthritis - Biomechanical Considerations

• the thick cartilaginous surfaces of the knee helps to spread out the joint reactive load over a wide area
• cam shape of the condyles maximizes the extensor lever arm
• in degenerative arthritis the quality of the articular cartilage is lost
• as wear occurs, the patello femoral joint is reduced to a cylindrical outline
• the mechanical outline is lost, but wear in the bone to bone contact area is reduced

Osteoarthritis - Treatment

• Nonoperative treatment:
  – NSAIDS
  – steroid injection
  – reduction of cartilage impact loading
  – cane
  – rubber heel wedges
  – wt loss;
• Operative treatment:
  – arthodesis (limited indications)
  – arthroscopy of osteoarthritic knee
  – high tibial osteotomy (HTO)
  – total knee arthroplasty (TKA)
Normal Knee Radiographs

Right knee, posterior view
Right knee, medial view

Osteoarthritis of the Knee

Left and Right knee, posterior view
Right knee, medial view
High Tibial Osteotomy (HTO)

Total Knee Replacement (TKR)
Rheumatoid Arthritis - Pathogenesis

- combination of genetic and environmental factors
  - important early event may result from interaction of antigen presenting macrophages w/ T cells (helper/inducer)
  - HLA-D allele DR4 is associated w/ RA patients
  - although clinical laboratories measure IgM, rheumatoid factor, other classes of RF have been described
  - inflammation in the joint cavity can be intense
    • the monocyte is most responsible for mediating tissue destruction
    • > one billion neutrophils enter moderate rheumatoid knee each day
    • leads to degradation of articular cartilage, menisci, and ligaments
  - Synovitis: in RA, normally delicate synovial membrane becomes infiltrated with macrophages, lymphocytes, plasma cells, and granulocytes - destructive potential

Rheumatoid Arthritis of Wrist

- Normal Wrist
- Wrist with RA
Carticel Package Insert

• CARTICEL®
  (autologous cultured chondrocytes) for Implantation

• DESCRIPTION
  • Autologous cultured chondrocytes, the Carticel® product, are derived from in vitro expansion of autologous
    chondrocytes harvested from a patient’s normal, femoral articular cartilage. Biopsies from a lesser-weight
    bearing area are the source of chondrocytes which are isolated, expanded through cell culture, and
    ultimately implanted into articular cartilage defects beneath an autologous periosteal flap. Each single use
    container of autologous cultured chondrocytes has approximately 12 million cells aseptically processed and
    suspended in 0.4 mL of sterile, buffered Dulbecco’s Modified Eagles Medium (DMEM). Prior to final
    packaging, cell viability is assessed to be at least 80%.

• CLINICAL PHARMACOLOGY
  • Studies have shown that implantation of the Carticel® product into the articular defect can result in the
    development of hyaline cartilage (see Clinical Experience). Hyaline cartilage consists of chondrocytes (< 5% total
    volume) and extracellular matrix (> 95% total volume). The matrix contains a variety of
    macromolecules, including type II collagen and proteoglycan. The structure of the matrix allows the
    cartilage to absorb shock and withstand shearing and compression forces. Normal hyaline cartilage also
    has an extremely low coefficient of friction at the articular surface. Damage to articular cartilage from acute
    or repetitive trauma often results in pain and disability. Parity because hyaline cartilage is avascular,
    spontaneous healing of large defects is not believed to occur in humans, though a variety of surgical
    procedures have been used in attempts to promote repair of cartilage. As cartilage heals after these
    procedures, fibrocartilage rather than hyaline cartilage is most commonly produced. Fibrocartilage has
    limited ability to withstand shock and shearing forces.

• CLINICAL EXPERIENCE
  • Clinical information regarding the use of autologous cultured chondrocytes is available from 2 sources: 1) a
    series of patients treated in Sweden, and 2) a U.S. patient registry. Patients in the Swedish series received
    an autologous cultured chondrocyte product which was produced slightly differently than Carticel®, the U.S.
    product.
  • The series consists of 153 consecutive patients who received autologous cultured chondrocyte
    implantations for various defects of the knee. Clinical follow-up ranged from 1 week to 94 months. Most
    patients had arthroscopic evaluation; a subset had biopsy and histological evaluations. Patients presented
    with cartilaginous defects of the femoral condyle, patella, tibia, a combination of these, or osteochondritis
    dissecans, with or without non-cartilaginous defects such as anterior cruciate ligament damage requiring
    repair.
  • Following autologous cultured chondrocyte implantation, patients were routinely followed for various
    durations. All patients were retrospectively classified as having one of the three clinical outcomes: resumed
    all activities, some improvement, or no improvement. Clinical outcomes were also reported for patient
    subgroups including: 1) those with femoral condyle lesions who had at least 18 months of follow-up, and 2)
    those who failed an earlier procedure. Most patients were also assessed for arthroscopic outcomes and
    some patients were assessed for histological outcomes.
  • Clinical Outcome - Patients with Femoral Condyle Lesions
    A total of 78 of 153 patients in the Swedish series had femoral condyle lesions with or without concurrent
    non-cartilaginous knee lesions. Patients had one or more defects ranging in size from <1-20 cm².
    Approximately 90% of the patients had defects of <10 cm². Clinical outcomes are shown below for 40
    patients who received autologous cultured chondrocytes and were evaluable after at least 18 months of
    follow-up (median = 25; range = 18-94 months). In this evaluation, 70% of the patients demonstrated some
    clinical benefit when compared to their pre-operative condition.
Carticel Package Insert

• INDICATIONS AND USAGE
  • Carticel® is indicated for the repair of symptomatic, cartilaginous defects of the femoral condyle (medial, lateral or trochlear), caused by acute or repetitive trauma, in patients who have had an inadequate response to a prior arthroscopic or other surgical repair procedure.
  • Carticel® is not indicated for the treatment of cartilage damage associated with osteoarthritis.
  • Carticel® should only be used in conjunction with debridement, placement of a periosteal flap and rehabilitation. The independent contributions of the autologous cultured chondrocytes and other components of the therapy to outcome are unknown. Data regarding functional outcomes beyond 3 years of autologous cultured chondrocyte treatment are limited.

• WARNINGS
  • This tissue is intended for autologous use and has not been tested for biohazards. Health providers should handle this product as if infectious agents are present.
  • Carticel® should not be used in patients with a known history of anaphylaxis to gentamicin. The biopsy medium used to transport the cartilage biopsies and the culture medium used during the first passage of cells contains DMEM with gentamicin. All subsequent processing is conducted aseptically and utilizes cell culture medium that does not contain gentamicin; however, trace quantities of gentamicin may still be present.
  • Carticel® should not be used in patients with known sensitivities to materials of bovine origin. The cell culture medium used during the culturing of the cells contains bovine serum. The medium used to package and transport the cells does not contain serum; however, trace quantities of bovine-derived proteins may still be present.

• PRECAUTIONS
  • General
    Implantation of the Carticel® product should be restricted to physicians who have completed Genzyme Tissue Repair's Surgeon Training Program.
  • Instability of the knee or abnormal weight-distribution within the joint may adversely affect the success of the procedure and should be corrected prior to Carticel® implantation. Abnormal varus loading of the medial compartment may jeopardize the implant. When treating trochlear defects, abnormal patellar tracking must be corrected, if possible.
  • Physical activity should be resumed according to the rehabilitation plan recommended by the physician. Vigorous activity may compromise the durability of clinical benefit from Carticel® (autologous cultured chondrocytes). Tissue hypertrophy was an observed adverse event in clinical studies (see Adverse Reactions). Patients who develop clinical signs of tissue hypertrophy should be evaluated with arthroscopy.
  • Both the long-term effect of cartilage harvesting on knee function and the long term safety of cartilage implantation are unknown.
  • The safety of the Carticel® product is unknown in patients with malignancy in the area of cartilage biopsy or implant. The potential exists for in vitro expansion and subsequent implantation of malignant or dysplastic cells present in biopsy tissue. In addition, implantation of normal autologous chondrocytes could potentially stimulate growth of malignant cells in the area of the implant, although there have been no reported incidents in humans.
  • The Carticel® product is shipped following a preliminary sterility test with a 48 hour incubation to determine absence of microbial growth. Final (14 day incubation) sterility test results are not available at the time of implantation.
  • Do Not Refrigerate, Freeze, or Incubate the Carticel® Shipping Container or its Contents. The Carticel® product consists of viable, autologous cells packaged and labeled for implantation within specified time limits. The Carticel® transport box should be held at room temperature and remain closed until the time of implantation to ensure proper storage conditions for the cells.
  • Do Not Sterilize. If the Vial is Damaged or Sterility has been Compromised, Do Not Use.
Carticel Package Insert

• Information for Patients
  Patients receiving autologous cultured chondrocytes for treatment of an articular cartilage defect should receive the following information and instructions. The rehabilitation protocol provided by the physician must be closely adhered to. Early motion is very important and should start with leg supported exercises gradually increasing the number of repetitions. If pain starts to develop as the next level of activity is increased, decrease activity to the former level until the pain resolves. If exercise causes pain and/or swelling, reduce the amount of physical activity. Swelling should be controlled using ice packs. When walking for the first 6 to 7 weeks, the treated knee should be supported with two crutches. The patient should attempt to walk with a normal gait, allowing a quarter of the body weight on the treated knee for the first 3 weeks, then gradually increasing the amount of weight. At anytime during the rehabilitation process or after, if sharp pain is experienced with locking or swelling, contact the physician for medical advice.

• Pediatric Use
  Safety and effectiveness of Carticel® in pediatric populations has not been established.

ADVERSE EVENTS

• General Adverse Events
  Any intra-operative and post-operative complication following knee arthrotomy may occur after autologous cultured chondrocyte implantation. Of 153 patients treated with autologous cultured chondrocyte implantation in Sweden, 34 (22%) patients had the following adverse events (other than hypertrophic tissue, see below): intra-articular adhesions, 8%; superficial wound infection, 3%; hypertrophic synovitis, 3%; post-operative hematoma, 2%; adhesions of the bursa suprapatellaris, 2%; and hypertrophic synovium, 1%. About 1% of patients developed severe adhesions resulting in "frozen knee" and requiring lysis. Adverse reactions noted at a level of less than 1% included keloid-like scar, pannus formation, significant swelling of the joint, pain with post-operative fever, and hematoma following arthroscopy.

• Tissue Hypertrophy
  Of 86 patients with a range of defects and at least 18 months of follow-up, 37 (43%) had hypertrophic tissue noted at follow-up arthroscopy. In those clinically evaluable patients with femoral condyle defects, 10 of 40 (25%) had some hypertrophic tissue noted at follow-up arthroscopy. The hypertrophic tissue ranged from a small amount of diffuse excess tissue at the implantation site, to a distinct ridge of tissue at the margin of the implant, to widespread excess tissue throughout the joint space. Some of these patients had clinical symptoms including painful crepitations or "catching." Symptoms generally resolved after arthroscopic resection of the hypertrophic tissue. Ten percent of patients with hypertrophy required additional treatment after hypertrophic tissue recurred following initial resection.

• Registry data on 891 patients who received implantation of autologous cultured chondrocytes were derived from voluntary reporting by surgeons and do not include those from routine arthroscopy; 131 patients had a follow up of at least 18 months. After correcting for differences in follow up time, cumulative rates of patients requiring additional operative procedures were calculated: 18% of all patients required an additional procedure within 18 months and 11% of all patients required (at a minimum) shaving, trimming, debridement, or chondroplasty.