Non-Arthroplasty Options for Osteoarthritis of the Knee

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Disclosures

- Educational Support – Arthrex
- None related to this talk

Defining the Problem

- Osteoarthritis (OA)
  - Clinical syndrome of joint pain, swelling and stiffness
  - Characterized by gradual loss of articular cartilage, osteophyte formation, subchondral bone remodeling, and joint inflammation

Defining the Problem

- Osteoarthritis (OA)
  - Most common form of joint disease
  - 7.7 million ambulatory visits yearly
  - $3.4 to $13.2 Billion annual job-related costs
  - Among leading cause of disability worldwide
    - 10% of people over 55 yo with symptomatic knee OA
  - Correlation between severity of walking disability and risk of death (CV disease)

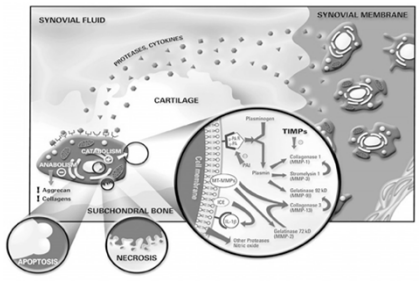
Why do people get OA?

- Trauma
- Gender (F > M)
- Race
- Age
- Occupation
- Obesity (3x increase in US since 1995)
  - Metabolic syndrome (Central obesity, dyslipidemia, HTN, elevated fasting glucose)
  - Altered metabolic profile = increased joint inflammation
- Genetic markers – Linked to Vit D receptor, estrogen receptor 1, IL-1, IL-4, BMP-2, BMP-5, matrilin-3

Other Factors

- Instability (Chronic ligament injury)
  - Shear stress on cartilage
- Muscle weakness
  - Stress and overload
- Malalignment
  - Overload
- All lead to abnormal stresses on the cartilage

Pathophysiology

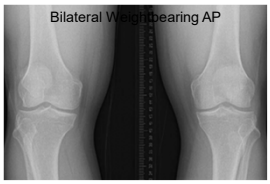


Pelletier, J., Martel-Pelletier, J. The Novartis-ILAR Rheumatology Prize 2001 Osteoarthritis: from molecule to man. *Arthritis Res Ther* **4,** 13 (2001). https://doi.org/10.1186/ar378

Patient presentation

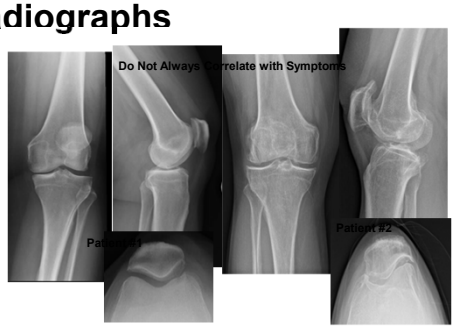
- Pain*
- Swelling
- Morning stiffness <30 min
- Worse with activities
- Mechanical symptoms
  - Catching, locking

Standard X-ray Series



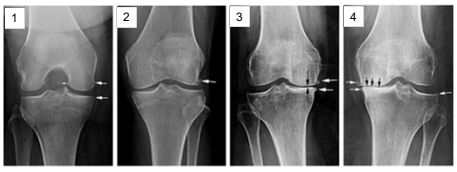
Standard X-ray Series

Radiographs



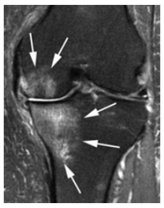
Radiographic Grading

- Kellgren-Lawrence Scale

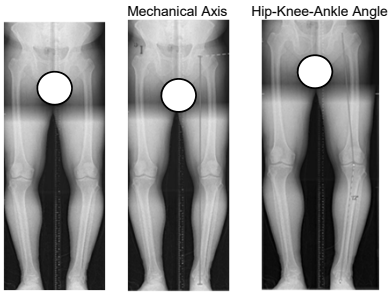


Magnetic Resonance Imaging (MRI)

- Not necessary
- Useful to rule out other pathology after failed conservative treatment
  - Meniscus
  - Ligament
  - Insufficiency fractures
- Surgical planning
  - Partial knee replacement
  - Osteotomy



Full Length Alignment Radiographs



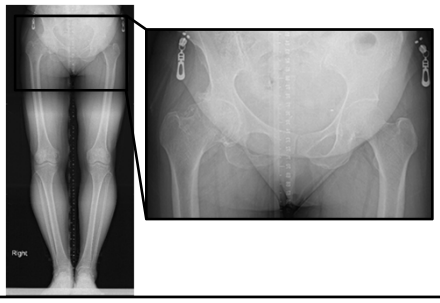
What is "Normal"?

Hip-Knee-Ankle Angle

- Bellemans, et al. Is Neutral Mechanical Alignment Normal for All patients? The Concept of Constitutional Varus. CORR 2012
- 500 knees in 250 healthy volunteers measured on full length weight bearing X-ray
  - Only 2% with neutral MA
  - **76% within 3°**
  - Males: 32% > 3° varus
  - Females: 17% > 3° varus
  - 2.4% >3° valgus

Full Length Alignment Radiographs

Full Length Alignment Radiographs



First Line Treatment Algorithm

- Self management – “Get moving”
- Physical therapy
- Weight loss
- Anti-inflammatory medications
  - Oral NSAIDs, COX-2 Inhibitors
  - Intra-articular steroids
- Unloader bracing

Self Management – “Home Exercise Program”

- Exercise*
  - Walking, stationary bike, water aerobics, elliptical
  - Underutilization due to fear of disease progression
  - Recommend 180 min/week

Physical Therapy

- Supervised exercise program
- Goals:
  - Preserve ROM
  - Correct gait impairment
  - Strengthening - Hip abductors, Quad, Hamstrings
- Severe OA
  - Aquatic PT
  - Land PT may worsen symptoms
- “Post-PT syndrome” → 6 weeks PT followed by...

Weight Loss

- **BMI 25 – 30**
  - Discussion of proper diet
- **BMI 30 - 35**
  - Consider nutritionist referral
- **BMI 35– 40**
  - Consider comprehensive weight management program
- **BMI >40**
  - Comprehensive weight management program referral prior to any surgery

Oral Medications

- Based on severity of symptoms
- Mild – Moderate
  - NSAIDs (Ibuprofen, Naprosyn)
  - Diclofenac
  - Meloxicam
  - COX-2 Inhibitors (Celebrex)
- Severe
  - Rarely Tramadol
  - Do NOT provide narcotic pain medications for OA pain

Topicals

- NSAIDs
  - Voltaren gel
- Compounded Creams
  - Mixture of medications
  - Can be $$$
- Capsaicin

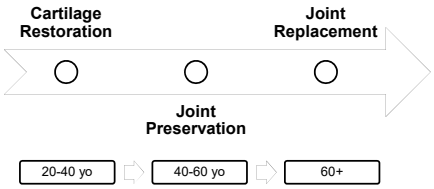
Unloader Brace

- Patients with **<u>isolated</u>** medial or lateral compartment OA
- Apply an external valgus (or varus) force, reducing the load in the medial/lateral compartment
- Improved joint proprioception can also help reduce pain

Intra-articular Injection Options

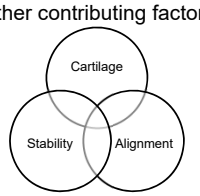
- Corticosteroids
- Hyaluronic Acid
- Orthobiologics:
  - Platelet Rich Plasma (PRP)
  - Adipose derived stromal cells
  - Bone marrow derived mesenchymal stem cells
  - Amniotic-derived therapies

Surgical Options in Knee OA



Cartilage Restoration in Knee OA

- Focal chondral defects (>2 cm^2)
  - Autologous chondrocyte implantation (MACI)
  - Osteochondral allograft transplant
- Correction of other contributing factors



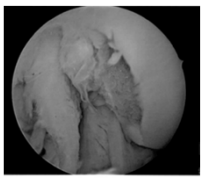
Autologous Chondrocyte Implantation

- ACI or MACI (Membrane)
  - Autologous cultured chondrocytes on porcine collagen membrane
- Goal: Form autologous "Hyaline-like" cartilage

Photo courtesy Dr. Tom Minas

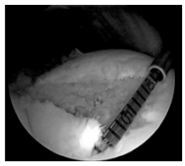
Autologous Chondrocyte Implantation

- Requires staged arthroscopic harvest from non-weight bearing area

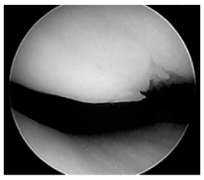
Autologous Chondrocyte Implantation

- Pros: Regeneration of autologous tissue
  - Can address larger and various sized defects
  - Multiple defects
- Cons: High costs
  - 2-stage procedure
  - Prolonged protection needed to allow maturation of chondrocytes

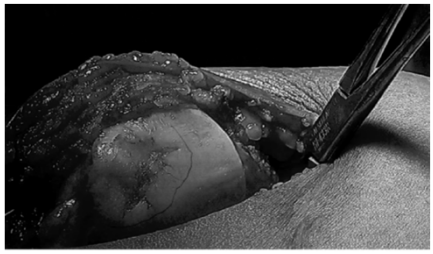


Case Example

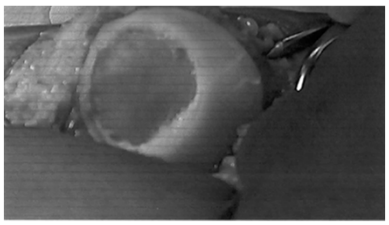
- 26 yo F persistent anterior knee pain
- Underwent previous arthroscopy → Partial thickness cartilage injury to patella
- 2 years of persistent pain
- Failed PT, NSAIDs, Nerve ablation, pain management



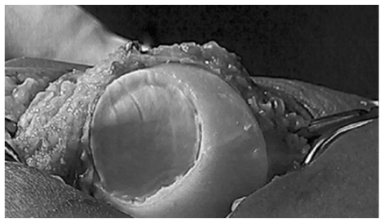
Patella cartilage defect



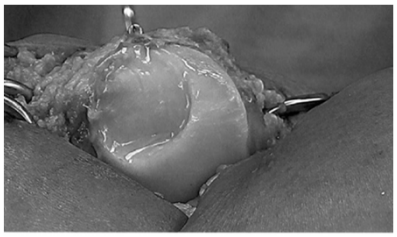
Cartilage defect after removal of damaged cartilage



After implantation of MACI

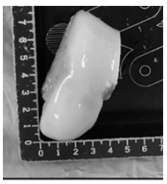


MACI sealed with fibrin glue



Osteochondral Allograft

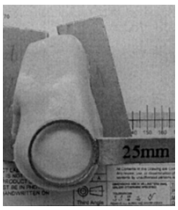
- Goal: Replace defect with live chondrocytes in mature matrix with underlying bone
- Fresh, refrigerated grafts
  - Retain chondrocyte viability



Allograft View 1

Osteochondral Allograft

- Performed as shell (dowel) or bulk grafts
- Match size and radius of curvature of the condyle
- Pros: Address large defects, correct bone loss, use in revision or failed ACI
- Cons: Limited availability, high costs, potential risk of infection
- “Catastrophic” failure



Osteochondral Allograft

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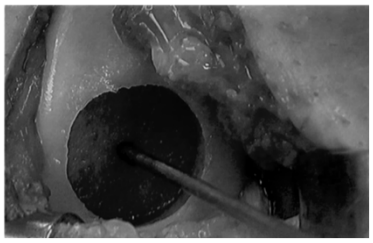
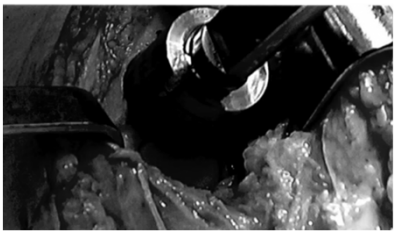
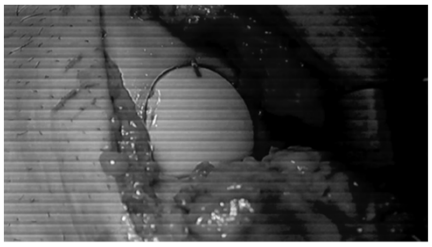


Osteochondral Allograft

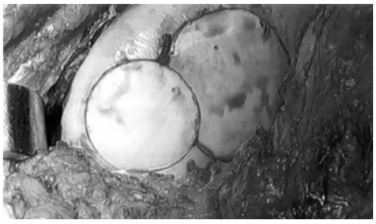


Osteochondral Allograft

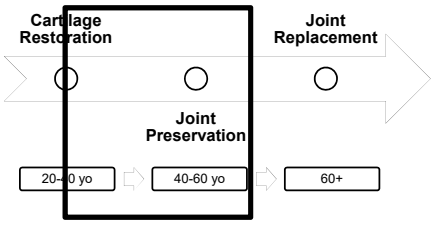


"Snowman" Technique

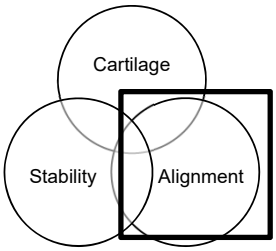
- Larger Defects



Surgical Options in Knee OA



Principles of Knee Joint Preservation



Lower Limb Malalignment

- Angular deformity in the lower limb
  - Abnormal distribution of weight bearing stresses
  - Accelerate wear in medial or lateral compartments
- Corrective osteotomy used to re-distribute forces evenly
  - Often combined with cartilage restoration to improve mechanical environment for biologic healing

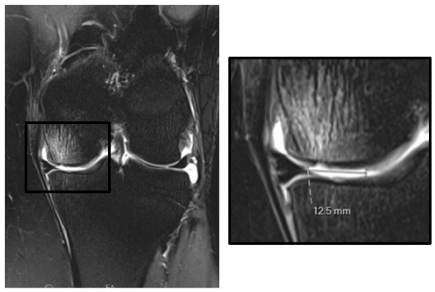
High Tibia Osteotomy Indications in Knee OA

	HTO	HTO vs. UKA	UKA
Age	<45	45-55	>55
OA Grade	KL 1-3	KL 4 → UKA	KL 3-4
Deformity	5 – 20° varus	>10° → HTO	≤10°
Activity	Any activity level		Low impact activities
Bottom line	More durable for laborer or runners – willing to tolerate some pain	Individualized discussion with patient	Better pain relief and functional outcomes

Case Example

- 45 yo F worsening medial joint line pain
- Recurrent knee effusion
- Steroid injection provided 1 month relief

- MRI
  - Full thickness cartilage defect
  - Subchondral edema



Full Length X-rays

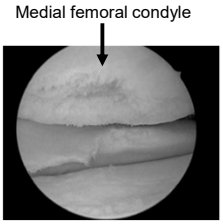
- Varus Malalignment
- Dx?

Full Length X-rays

- Varus Malalignment
- Dx?
  - Medial compartment overload

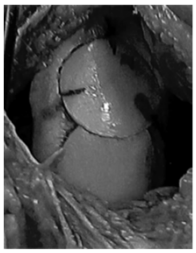
Treatment

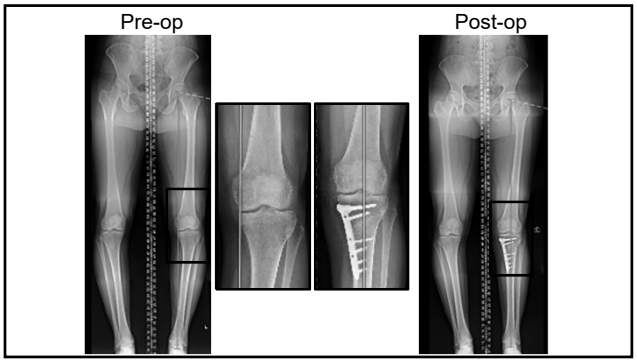
- Steroid injection
- Medial unloader brace
- Arthroscopic staging procedure
  - Chondroplasty, loose body removal



Second-Stage

- "Snowman" Osteochondral allograft
- Valgus producing high tibia osteotomy
  - Mechanical environment



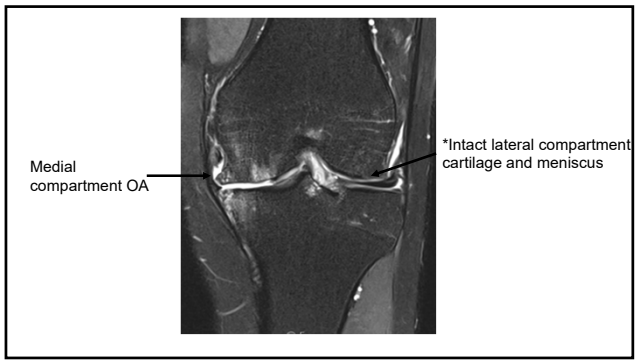


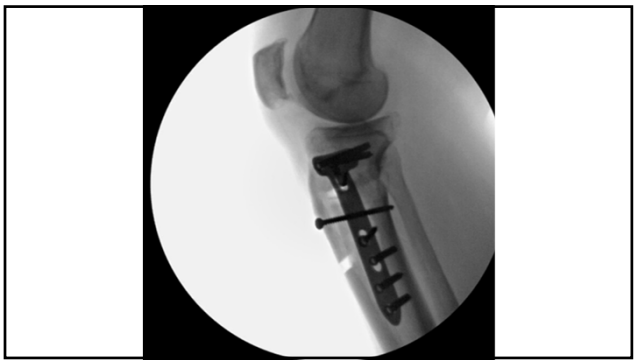
Case Example

- 44 M worsening bilateral knee pain
- Failed multiple conservative treatments
- Construction worker

Case Example

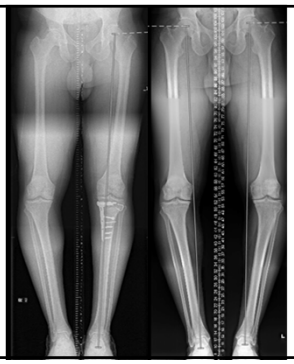
- Rosenberg View
- Kellgren Lawrence Grade 3


Medial
compartment OA
*Intact lateral compartment
cartilage and meniscus



Case Example

- 5 months post-op



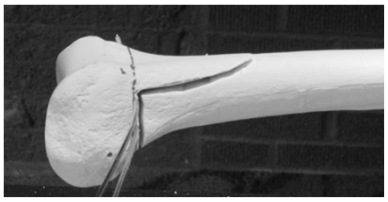
Valgus Malalignment

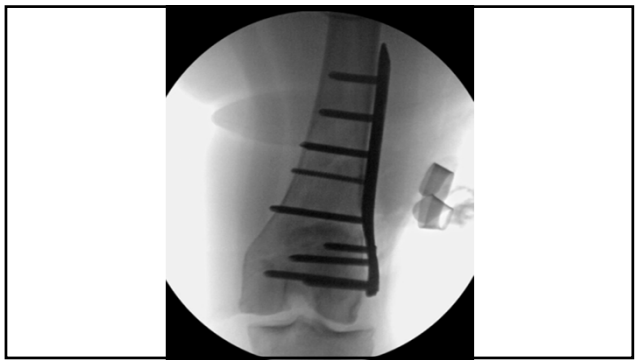
- 30 yo F
- Worsening pain
- Multiple knee arthroscopic surgeries
- Told that only option was TKA

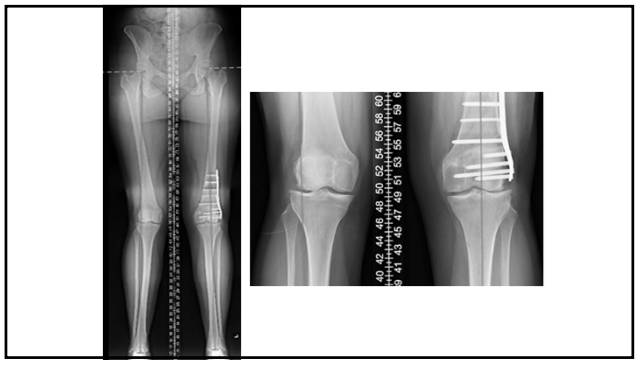
Distal Femur Osteotomy Templating

- 12° Valgus
- Calculated 14.8 mm correction

Distal Femur Osteotomy Biplanar Technique





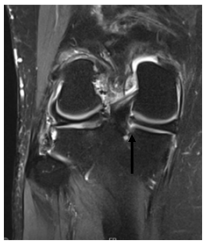


Osteotomy Outcomes in Knee OA

- High tibial osteotomy for varus knee OA
  - 10-year survivorship 74-95%
  - 15-year survivorship 67-90%
- Distal femur osteotomy for valgus knee OA
  - 10-year mean survivorship 80%

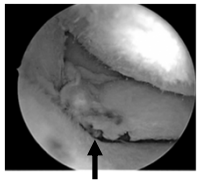
Medial Meniscus Posterior Root Tears

- "The Silent Epidemic" in joint preservation
- Often missed on MRI and arthroscopy
- Can lead to rapid OA
  - Inability to resist hoop stresses
  - Meniscal extrusion
  - Cartilage breakdown
  - Insufficiency fractures
- Early Dx important

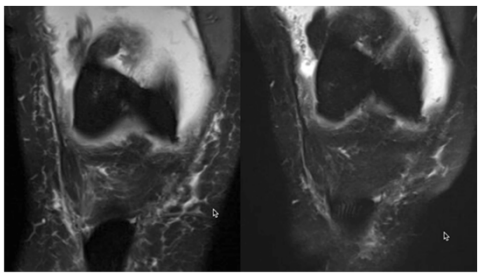


Diagnosis

- 40-60yo F
  - Posteromedial knee pain
  - BMI 30-40
- Minor trauma
  - i.e. Stepping off curb
  - Felt a "pop"
  - Sudden severe pain
- + Joint effusion, Medial joint line tenderness

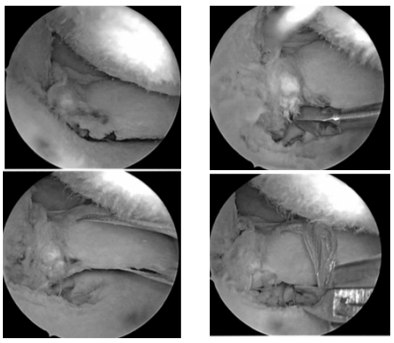


MRI: 7/26/19 10/27/2020



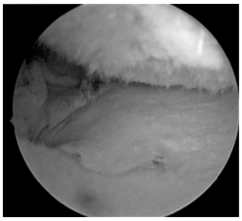
Treatment

- Historically, treated conservatively or with partial meniscectomy
- Improved surgical techniques → Transtibial meniscus root repair
- Goal: Restore hoop stresses to minimize OA
- Risk of progression to OA over 10 years
  - Conservative – 95.1%
  - Partial meniscectomy – 99.3%
  - Meniscus repair – 53% (Newer techniques lower)

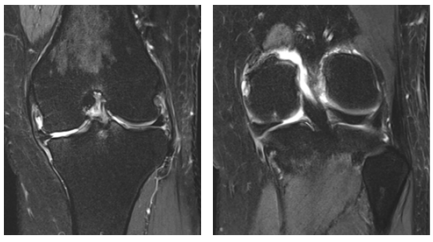


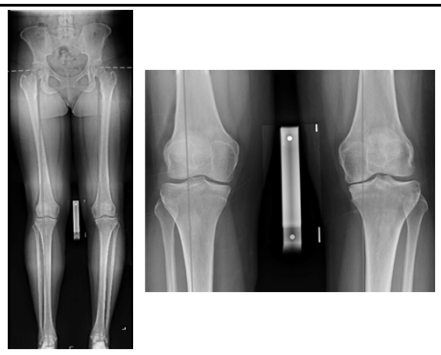
Meniscus Root Repair

- Post-op
  - 4 weeks of Non-weight bearing
  - 2 weeks of slow progression to WB
- 1 year in medial unloader brace to protect repair

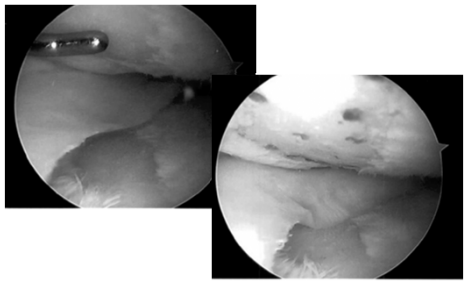


Case Example:
38yo F worsening medial joint pain

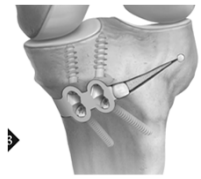




Meniscus root repair + Microfracture + PRP



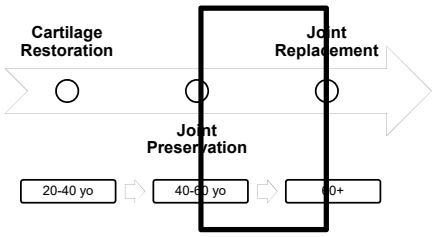
Arthrex iBalance HTO



10/22/2019

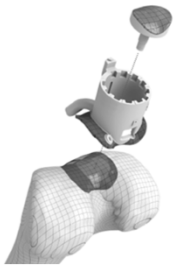
10/15/2020

Surgical Options in Knee OA

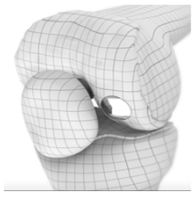


Emerging Surgical Techniques

- Episealer Implant
  - Patient-specific implant based on MRI
  - Remove damaged bone and cartilage
  - Replace with cobalt-chrome alloy
- US Clinical trial starting at OSU Spring 2021



Emerging Surgical Techniques

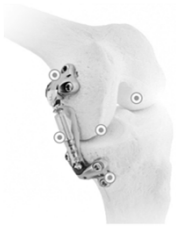


Emerging Surgical Techniques

- NuSurface
  - Polycarbonate-urethane meniscus replacement device
  - Used in patients after meniscectomy
  - Mimics function of normal meniscus and redistributes load transmission across joint
- Approved in Europe since 2008
- Ongoing FDA clinical trial
  - First device implanted at OSU

Emerging Surgical Techniques

- Moximed Atlas
  - Implantable joint unloader
- Ongoing US Clinical trial



Case Example: 58 yo M
- Years of worsening pain
- Previous conservative Tx
- Wants to get back to working out

Rosenberg View

Robotic-assisted Partial Knee Arthroplasty

Advantages of UKA

- Compared to TKA
  - Less blood loss
  - Less morbidity (smaller incision, less pain)
  - Shorter hospital stay
  - Faster recovery and rehab
  - Preservation of normal knee kinematics (ACL, PCL, lateral and PF joints)

Advantages of UKA

- Compared to HTO
  - Faster recovery and rehab
  - Higher initial success rates
  - Fewer short term complications
  - Longer durability
  - Easier to convert to TKA (Historically)

Intra-articular Injection Options

- Corticosteroids
- Hyaluronic Acid
- Orthobiologics:
  - Platelet Rich Plasma (PRP)
  - Adipose derived stromal cells
  - Bone marrow derived mesenchymal stem cells
  - Amniotic-derived therapies

Corticosteroids Efficacy

- Randomized controlled trials
  - Evidence that IA steroids are effective to reduce pain, but benefit over placebo is short-lived (4-6 weeks)
  - Inconsistent effects on functional outcomes
- Presence of an effusion is a good predictor for positive effect of Steroid (esp. with aspiration)

Corticosteroids Risks and Side Effects

- Steroid flare
  - May begin 6-12h post-injection, last 1-3 days
- Inconclusive evidence
  - Accelerated disease progression
  - Osteonecrosis
  - Insufficiency fractures

Steroid Injections – Bottom Line

- Consider in patients during "OA flare" with moderate to severe pain and large effusion
  - Short-term pain relief
- Minimum 3 months before repeat injection
- Counsel patients regarding no long-term benefit and risks of OA progression
  - Risk of disease progression may increase with repeated injections

Hyaluronic Acid

- HA is naturally occurring glycosaminoglycan and component of Synovial Fluid and Cartilage matrix
- Acts as viscous lubricant during slow joint movements and as elastic shock absorber during rapid joint movement
- Functions through anti-inflammatory, anabolic, analgesic, and chondroprotective mechanisms
- Harvested from Rooster combs or via bacterial fermentation

Hyaluronic Acid Efficacy

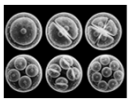
- Conflicting clinical data
- Meta-analyses
  - 2 concluded overall beneficial effect
  - 4 reported small benefit
  - 2 found no evidence to support use
- >50% studies industry funded → Risks of publication bias
- Adverse effects → transient local reaction 2-4% (higher rates with avian-based)

Hyaluronic Acid Bottom Line

- Intra-articular injection of HA is safe with low risk of local reaction
  - Recommend 15 minutes icing immediately after injection
- May provide pain reduction in mild OA for up to 6 months
- Cost-effectiveness is questionable, especially in patients with moderate-severe OA

Orthobiologics

- Platelet Rich Plasma (PRP)
- Adipose derived stromal cells
- Bone marrow derived mesenchymal stem cells



- Amniotic-based therapies

What is PRP?

- Autologous concentration of human platelets in a small volume of plasma produced from a patient's own centrifugated blood
- Concentrated platelets contain increased amounts of growth and differentiation factors
- At concentrations >1,000,000 per microliter → improvements in bone and soft tissue healing properties have been demonstrated

PRP in Knee OA

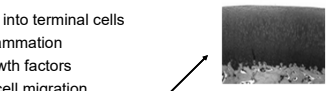
- Relatively safe procedure with minimal adverse effects (pain, effusion)
- Strong evidence that:
  - PRP may exert positive influence in patients with knee OA
  - RCTs demonstrate greater and longer efficacy for pain and function versus HA and placebo
  - Beneficial effect estimated to last up to 1 year with peak at 6 months
- Best results in younger patients with mild OA

Stem Cell-Based Therapies

- Knee OA
  - Limitation of cartilage is inability to heal or regenerate
  - After injury → Typically fibrocartilage forms and can more easily break down leading to OA
- Mesenchymal Stem Cells or Medicinal signaling cells (MSCs) may provide biologic machinery to organize the complex processes involved in the regenerative process

Stem Cell-Based Therapies

- Stem cells provide functions that can assist the healing:
  - Differentiate into terminal cells
  - Reduce inflammation
  - Secrete growth factors
  - Encourage cell migration
  - Coordinate tissue repair



Guided tissue regeneration

Regulate immune system to reduce inflammation

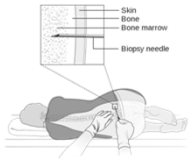
Stem Cells (MSCs)

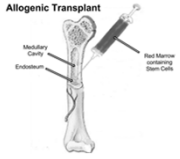
Challenges of Stem Cell-Based Therapies

- Efficient isolation and delivery
- Unclear optimal number of cells needed to achieve regeneration
- Regulatory restrictions by FDA
  - Cannot expand or manipulate MSCs outside of the body
  - Only allow simple mechanical preparation (Centrifugation)

Bone Marrow Derived Stem Cells

- Bone marrow aspirate concentrate (BMAC)
- Harvested from iliac crest, proximal tibia, or distal femur
- Centrifugation to concentrate MSCs
- Pros: Ease to harvest, large yield of cells
- Cons: Donor site pain, cost (procedure), effectiveness limited by patient health/age





Adipose Derived Stem Cells

- Lipoaspirate from abdomen
- Mechanical process to wash out the lipids be retain stromal vascular fraction that is rich in stem cells
- Pros: No significant decline of cell number with age, ease of harvest, large cell yield
- Cons: Morbidity, cost (procedure)

Stem Cells in Knee OA

- Promising pre-clinical data in animal studies
- Clinical studies report improvements in pain and function over baseline up to 2 years
  - Conclusions limited by small sample size, no control group, variable preparations and outcome measures
- Optimal cell dose and long-term durability unclear

Amniotic-Derived Therapies

- Amniotic Membrane
  - Extra-cellular matrix components
  - Multiple collagen types, fibronectin, laminins, aggrecan, hyaluronic acid
- Amniotic-derived stem cells
  - Human amnion epithelial cells (hAECs)
  - Human amnion mesenchymal stromal cells (hAMSCs)
- Amniotic Fluid
- Recovered during C-section from consenting, healthy, pre-screened donors

Amniotic-Derived Therapies

- **Bioactive characteristics**
  - Anti-microbial
  - Anti-tumorigenic
  - Anti-fibrotic
  - Anti-inflammatory
- **Clinical benefits**
  - Reduces pain and inflammation (ECM components)
  - Inhibits scarring (ECM components)
  - No immunogenicity (T cell suppression; monocyte inhibition)
  - Enhances wound healing (bioactive cytokines)

Amniotic-Derived Therapies

- Long history of safety and efficacy in preventing fibrosis and scarring in wound healing
- Promising pre-clinical evidence for efficacy in knee OA
- Single clinical trial (200 patients with knee OA) demonstrates safe and effective versus saline and HA

In Summary

- Get your patients moving → Exercise and weight loss are most important initial steps
- Consider Aquatic PT
- Several injectable options
  - OA Flare → Steroid
  - Mild OA → HA/Orthobiologics

In Summary