ARTICULAR CARTILAGE: ADVANCES IN TREATMENT

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ARTICULAR CARTILAGE: ADVANCES IN TREATMENT

1. There have be no advances in treatment of articular cartilage

Thank you for coming!
“FDA APPROVED”

- Last device/intervention that was FDA approved was Genzyme/ACI (autologous chondrocyte implantation) back in 1997.
ADVANCEMENTS

- PRP – platelet rich plasma
- Stem Cells - MSC’s (mesenchymal stem cells)
  - Bone Marrow (BMAC – Bone Marrow Aspirate)
  - Fat cells/ Adipose cells
  - Amniotic tissue/ fluid
- The Regenokine Program
  - Interleukin 1 receptor antagonist / IL-1ra
- Biocartilage/ DeNovo
- MACI
ARTICULAR CARTILAGE: ADVANCEMENT IN MANAGEMENT

GOALS IN TREATMENT OF ATHLETES WITH ARTICULAR CARTILAGE RELATED PROBLEMS: (we already have procedures to “RESTORE” lost cartilage)

1. Decrease or eliminate Pain
2. Improve Function (Pain inhibition is a major component of function)

C. The “Ultimate” – Disease Modification
   -slowing down the rate of articular cartilage deterioration
   -stopping the process of cartilage deterioration
   -REVERSING the process – restoration of articular cartilage AND articular cartilage FUNCTION
WHAT IS CAUSING THE PAIN ???

- **THERE ARE NO NERVES IN ARTICULAR CARTILAGE**
- "**B.A.R.F.**" - Brainless Application of Radiologists Findings (also V.O.M.I.T.) Dr. Brian Cole

- NBA Combine – 50% of *asymptomatic* knee MRI abnormal – cartilage lesions
  - 7% had full thickness chondral defects

- Donald Shelbourne - ACL reconstruction long term follow-up
  - ACL and chondral lesions found at time of surgery
  - Majority had 10-15 years of asymptomatic chondral lesions
Arthroscopic Acetabular Labral Debridement in Patients Forty-five Years of Age or Older Has Minimal Benefit for Pain and Function

Gleddie Wilk, MD; Gerard March, MD; FRSCC; and Paul E. Beaulieu, MD; FRSCC

Introduction performed at the Division of Orthopaedic Surgery, The Ottawa Hospital, Ottawa, Ontario, Canada.

Background: Arthroscopy is being performed with increasing indications, commonly including symptomatic labral tears. The effect of various patient factors, including patient age, on clinical outcomes are not well understood. The purpose of the present study was to quantify the preoperative functional and quality-of-life outcomes after arthroscopic debridement of symptomatic acetabular labral tears in patients forty-five years of age or older.

Methods: Forty-one patients who were at least forty-five years of age with age, 52.7 years (range, 46.6 to 67.2) preoperatively were included in the study. Preoperative patient-reported outcome measures (Western Ontario and McMaster Universities Ossurieweak, 12-Item Short Form Health Survey SF [12]) and qualitative outcome measures (WOMAC and modified Harris hip score [mHHS]) and general health-related measures (Clavien Short Form Health Survey SF [12]) were collected preoperatively and postoperatively.

Results: The mean operation time was 17% (range, 20.2 to 90.1) at a mean of 21.3 months, and 66 of the seven preoperative patient-reported outcomes were statistically significant. The overall magnitude of change in pain was 17% (range, 20.2 to 90.1) at 21.3 months, and 66 of the seven preoperative patient-reported outcomes were statistically significant. The overall magnitude of change in function was 17% (range, 20.2 to 90.1) at 21.3 months, and 66 of the seven preoperative patient-reported outcomes were statistically significant. The overall magnitude of change in quality of life was 17% (range, 20.2 to 90.1) at 21.3 months, and 66 of the seven preoperative patient-reported outcomes were statistically significant. The overall magnitude of change in pain was 17% (range, 20.2 to 90.1) at 21.3 months, and 66 of the seven preoperative patient-reported outcomes were statistically significant. The overall magnitude of change in function was 17% (range, 20.2 to 90.1) at 21.3 months, and 66 of the seven preoperative patient-reported outcomes were statistically significant. The overall magnitude of change in quality of life was 17% (range, 20.2 to 90.1) at 21.3 months, and 66 of the seven preoperative patient-reported outcomes were statistically significant.
Hippocratic Oath: I will not treat a fever chart, nor the cancerous growth but instead the patient

“TREAT THE PLAYER - NOT THE MRI SCAN”
loose cartilage pieces

lateral patella

upper trochlea

cap/pec

inner trochlea

medial meniscus
COMPONENTS OF CARTILAGE:

Chondrocytes 10%
Collagen 10 - 30%
Water 60 - 80%
Proteoglycans/Aggrecan 5 – 15%
ARTICULAR CARTILAGE

Half Life of Aggrecans 20 years

Half Life of Collagen 100 years
CARTILAGE INJURY

- Compression
- Shear
- Oxygen tension; pH
- Growth factors and Cytokines
- Topography
  - Alignment
  - Stiffness
CYTOKINES/ INFLAMMATORY PATHWAY

“BAD GUYS”
- Interleukin 1 (IL-1)
- Tumor Necrosis Factor alpha (TNF-a)

“I PITY THE FOOL THAT PITIES THE FOOL”

“GOOD GUYS”
- Transforming Growth Factor beta (TGF-b)
- PDGF (Platelet Derived Growth Factor)
Study: Presence of bone marrow lesion may predict rate of radiographic change in knee joint space width.

Data from a multinational study published online in *The Journal of Rheumatology* suggest that the presence of bone marrow lesions (BMLs) on magnetic resonance imaging (MRI) scans of the knee may predict rate of radiographic change in joint space width. The researchers reviewed data on 176 participants in the placebo arm of the Strontium Ranelate Efficacy in Knee Osteoarthritis Trial. All participants were assessed via MRI at baseline and yearly for up to 3 years. The researchers found that 38.6 percent of participants were classified as BML-positive (BML ≥grade 2 at the tibiofemoral joint) at baseline. They found that patients who were BML-positive had a significantly higher rate of annualized change in joint space width; a relationship that remained robust after adjustment for age, sex, and baseline Kellgren-Lawrence grade.

Read more...
Read the abstract...
VISCO-SUPPLEMENTATION
(ARTICULAR CARTILAGE FUNCTION)

- Increase shock absorption/diminish stress transfer across area of damaged or diminished (NOT ABSENT) articular cartilage
- No significant effusion
- No mechanical symptoms
- Activity related pain, time on feet, end of day, workout days
VISCO-SUPPLEMENTATION

- "rooster comb": risk of pseudo-septic reaction
  - Synvisc, Hyalgan, Suppartz

- Synthetic
  - Orthovisc, Euflexxa

- In season strongly recommend use of synthetic only (we use Euflexxa)
Loose cartilage pieces

Lateral rotator

Upper trochlea

Lower trochlea

ACL / PCL

Before surgery
CHONDROPLASTY / LAVAGE

- Mechanical symptoms – catching, locking, instability, biting pain
- Recurrent/persistent effusion
  - Multiple loose bodies creating synovial inflammation
  - “Chemical” synovitis akin to intervertebral discs/neurogenic pain

- GOALS:
  - Flush irritating fragments visible down to microscopic
  - Stabilize lesions to decrease chance of additional fragmentation
  - Remove unstable, potentially painful flaps
Post-operative goals and return to play
  - Incision healing to prevent infection
  - NOT waiting for a healing response of treated tissue
  - Swelling control and maintain quad tone

**RTP:** variable-can be as little as 2 weeks
  - Depends on #3 above – swelling, quad inhibition
Microfracture

- Microfracture is Orthopedic Surgery version of Aspirin

- American Indians: Willow Bark Tea
- Hippocrates (Hippocratic Oath) 460 B.C.
  - White Willow bark tea
    - Salicin (acetylsalicylic acid)
    - Flavinoids
- Easy/ minimally invasive
- **Cheap** (*Cheap does NOT = NOT GOOD*)
MICROFRACTURE

- “Trauma” releases marrow stem cells from the trabeculae
- Blood clot is the matrix for cellular ingrowth
- At 6 weeks the micro-trabecular fractures have healed
  - 6 weeks non-weightbearing postulated to protect bony architecture (topography)
  - Not born out in studies (Timmerman et al)
  - CPM machine (synovial stimulation)
- Articular cartilage is only 10% cellular (?? Need to add extra cells post op)
- 8–15 weeks post op significant fibrous “tissue”
- 12 – 26 weeks - FIBROCARTILAGE
- REMODEL: 6 - 12 months
MICROFRACTURE / MARROW STIMULATION

- Immediate post-op to 6-8 weeks non-weightbearing vs protected weight bearing
- 8 weeks to 16 weeks generalized strengthening and non-impact cardio
- 16 weeks begin straight ahead running if swelling, muscle tone acceptable
- 5 months “functional rehab”

6 months – return to practice/participation
Success rate
- Literature generally a 75% success rate in patients 45 years and younger
- Maximum outcome may take 12-24 months (remodeling)

“Real Life Success Rate”??
- 1.5cm lesion in a 5’ 4” female soccer player vs 6’ 6” football lineman

General principles for Good Results with microfracture surgery:
- Symptoms less than 2 years
- Lesions smaller than 2cm squared
- 45 years old or younger
- BMI of < 30kg/m
Biocartilage
Minced allograft cartilage which may act as both a scaffold and provide the extra-cellular matrix (ECM) collagen for faster recovery time and better shock absorption capability

DeNovo – minced juvenile allograft articular cartilage
attached with fibrin glue
OATS - OSTEOCHONDRAL AUTOgraFT TRANSFER

- Dowel of bone and articular cartilage harvested from a non-weightbearing area of the knee (usually far anterior femoral cortex or lower trochlea)
- Chondral lesion is completely excised
- “plug” of bone and cartilage impacted into site – “press fit” no fixation devices needed
- Recommend 6 weeks of protected WB in order to prevent over-impaction (sinking) of plug
- CPM machine +/-
- Can be performed all arthroscopically or mini-open
- Can be performed with allograft fresh grafts for larger defects
O.A.T.S. — OSTEochondral AutoGraft TRANSFER

- Bone to bone healing – 6 weeks
- All components of normal articular hyaline cartilage present
- **Highest percentage of RTP** of all invasive cartilage procedures
  - “Accelerated rehab capability”
  - Better structural function
  - ?? Denervation procedure (a la Hamburg sports hernia clinic)
- One procedure – relatively low cost (sterile harvest/implant “kits”)

DOWNSIDES:

- Limited donor tissue available
- Questions regarding “topography” especially tibial plateau/ trochlea
LFC full ext.  LFC chordal def

Img size  donor site
Facility: PIPER
Surgeon: WASLEWSKI
ACI - AUTOLOGOUS CHONDROCYTE IMPLANTATION

- Better long term success rate than microfracture despite similar % of type II collagen
  - Longer rehabilitation and recovery time
- Two procedures approximately 3 - 6 weeks apart (harvest > re-implantation)
- Longer RTP recovery timeline which may = career ending procedure
- Cost
  - 2 procedures
  - Genzyme/ Carticel lab costs $10,300
- PROCEDURE OF CHOICE: Large lesion size, failed prior surgery
  - Best results when combined with osteotomy to change alignment axis
12-18 months RTP

- 0 – 6 weeks – free floating cells (water balloon stage)
- 6 – 12 weeks - matrix present -type II collagen and PG’s- (pudding stage)
- 12 – 26 weeks – attachment to bone and some architecture (jello stage)
- 26-39 weeks – maturation of ECM (putty stage)
- 39- 52 weeks (up to 18 months) remodeling stage (rubber stage)
ACI

- Protected WB for 8-12 weeks
- Running not allowed for minimum 6 months (de-weighted)
- Flat ground running at 8 months
- Functional rehabilitation 10-12 months

Return to practice at 12 months – 18 months
ARTICULAR CARTILAGE: ADVANCES IN MANAGEMENT

PRP

“Dream Saver” ...or Greed’s empty promise
Platelet rich plasma
- Autologous blood
- Signals for growth/differentiation/cellular production
- Preservatives or thrombin activator added?
- Leukocyte rich vs leukocyte poor
  - Leukocytes – white blood cells
    - Inflammatory/degradatory enzymes
    - IL-1 and IL-6 inflammation pathway signaling
- $\frac{1}{2}$ Life most factors in PRP is 2.5 hours
- Studies in tendinopathy equivocal
  - Spine fusion, rotator cuff repair show decrease in success rates
  - Shows some potential for improving outcomes administered post microfracture
PRP

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STEM CELLS / MSC’S

Main sources are bone marrow aspirates (BMA) and fat cells

- **Fat Harvest** – more cells but the cells are LESS CHONDROGENIC
  - FDA now says fat cells are “non-homologus” use in joints = FDA prohibited

- **BMA’s** – active MSC’s are firmly attached to trabecular bone NOT free floating
  - BMA is essentially an aspirate of venous blood which is mostly White Cells not MSC’s

- **Amniotic products** -
STEM CELLS/ MSC’S

- Need adequate amount of cells
- Need appropriate signaling factors – delivered at the appropriate time

- Think “10,000 kindergartners, the roofer, and the cement truck”
  or
  “Freedberg’s Roux”
- Need an adequate amount of cells
- Need appropriate signaling factors delivered at the appropriate times

Think "10,000 kindergartners, a roofer and the cement truck"
THE REGENOKINE PROGRAM

- AKA - The “Kobe Bryant Injections”
- Blocks the inflammatory pathway and blocks destructive signaling
- Interleukin 1 receptor antagonist
REGENOKINE PROGRAM
Dr. Peter Wehling  Dusseldorf Germany: ORTHOGEN AG

- Synthetic Interleukin 1 receptor antagonists exist:
  - Anakinra / Kinaret

- Naturally occurring/ generated products have markedly longer $\frac{1}{2}$ lives
  - Aggrecans 20 years vs hyaluronic acid 6-12 months
  - Dr Wehling’s results – improvement in symptoms and function for 2-5 years (Anakinra is usually administered monthly)

- **MAY BE DISEASE MODIFYING** (Deceleration of degenerative process)
  - Some players using this as a preventative treatment measure ie Kobe, Brandon Marshall
REGENOKINE

- 5-6 injections administered over a period of 1 – 3 weeks
- No restriction of activities during the injection process
- There does seem to be a systemic positive effect on other joints
- No adverse reactions locally nor systemic
- Use in Europe includes articular cartilage / joint problems; acute and chronic muscle and tendon injuries
- Goal is to have 20 centers across US to utilize this process

Regen AZ at the Arizona Sports Medicine Center is authorized by Dr Wehling to perform the Regenokine Program
REGENOKINE

- **DOWNSIDES**
  - # 1, 2 and 3 - **COST $$$$$$
    - $10,000 per treatment non-negotiable
    - Patented process/proprietary – fees set by Orthokine AG, Germany

Minimum of one week treatment time or spread over 3 weeks
REGENOKINE

- Experience at Regen AZ  - www.RegenAZ.com

- Early results excellent  - Brett Fischer P.T.

- No long term results as yet (every patient treated has been within the last one year)

TYPICAL PATIENTS FOR REGENOKINE PROGRAM

- End stage hip or knee DJD in young athletic patients wanting to avoid arthroplasty, inadequate improvement from steroids and oral medications

- Patients who feel they are too old for safe and successful total joint replacement

- Professional athletes with articular cartilage problems (only knees at this point) who have failed surgery, steroids, viscosupplementation
YOU THINK THE LESION IS THE PROBLEM

- NUTRITIONAL
- STRENGTH
- ALIGNMENT
- LOAD/OVERUSE
- MECHANICAL
Vitamin D - rickets

Elimination diets: low fat – fat soluble vitamins A, D, E, and K
  - Essential omega 3 FA’s – fatty acids (natural anti-inflammatory

RED – S syndrome: Relative Energy Deficiency Syndrome
  replaces the previous “Female Athletic Triad”
MECHANICAL

- LOOK CONTRALATERAL  !!!!!

- SOFT TISSUE
  - ACHILLES
  - HAMSTRING

- JOINT
  - CONTRACTURES
    - GIRD
    - HIPS – ESPECIALLY  I.R.  (FAI of the hip)
OPTIMIZATION OF NUTRITION IN SPORTS

- “Shock Absorption”
  - Glucosamine 1500mg/ day and Chondroitan Sulfate 1200-1500mg/day

- Metabolic
  - Metabolic activities of chondrocytes
  - Vitamin C - 1000mg/ day

- Inflammation
  - Essential omega -3 fatty acids
    - DHA
    - EPA
    - 1 gram/day - females; 2 gms per day - males
STRENGTH = SHOCK ABSORPTION

- Newton’s 3rd law: for every force delivered there is an equal but opposite force delivered
  - Major shock absorbers of the knee: quadriceps and gastroc
  - Shock absorption is directly proportional to the **CROSS SECTIONAL AREA** of the muscle
  - Eccentric load is what needs to be dissipated

- Quadriceps Inhibition
  - Pain inhibition
  - **Effusion** (chronic and acute)
ALIGNMENT

- May be physical/ ingrained
  - Leg length discrepancy
  - Varus/ valgus alignment

- Don’t forget **PROPRIOCESSION**
  - Weak Abductors = dynamic femoral anteversion at the PF joint

- Pelvic SI dysfunction
  - Contracted iliopsoas creates LLD
OVERLOAD/ OVERUSE

- Rest and Recovery
  - 7 day per week “training”

- WEIGHT
  - Biggest reason for failure of total joint replacement and microfracture

- Shoes
  - Mileage; inserts instead of flat insoles (lack of arch leads to internal tibial torsion)

- BRACING
  - Unloader bracing
THANK YOU

- www.azsportsmedicine.com
- Arizona Sports Medicine Center
  - (480) 558-3744
- www.RegenAZ.com