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Disclosures

I have the following potential conflicts of interest:

Consulting payments/royalties and research support directly related to products discussed:

- Vericel - consultant

FDA-status of devices discussed:

Many of the applications presented are considered off-label

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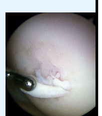
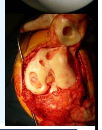
Hospital for Special Surgery
Weill Cornell Medical School

Surface Options for Articular Cartilage Reconstruction:
Established and Emerging





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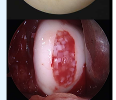
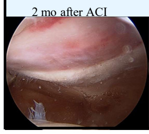
Surface treatment

Generally: maturation of a reparative tissue over time

- Microfracture (plus)
- Particulated juvenile cartilage allograft (PJAC)
- Autologous chondrocyte implantation (MACI)
- Perforated cartilage allograft
- Particulated cartilage autograft
- Bone marrow aspirate concentrate (BMAC)
- Stem cell implantation



2 mo after ACI



10 mo after ACI

24 mo after ACI

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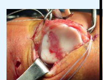
Microfracture plus

Microfracture – why “plus”

- Concerns over tissue quality with regular MFx
- Augment to bone marrow stimulation
- Mechanically stabilize clot, provide more favorable environment for cell differentiation, ?expand indications
  - Micronized cartilage ECM
  - Mix with PRP or BMAC, provides matrix, ?growth factors
  - **Results**:
    - Pre-clinical data in horses
    - No clinical data but registry data in progress



BioCartilage Improves Cartilage Repair Compared With Microfracture Alone in an Equine Model of Full-Thickness Cartilage Loss
Lisa A. Fortier, Hannah S. Chapman, Sarah L. Pownder, Brandon L. Roller, Jessica A. Cross, James L. Cook and Brian J. Cole
Am J Sports Med 2016 44: 2366 originally published online June 13, 2016
DOI: 10.1177/0363546516648644

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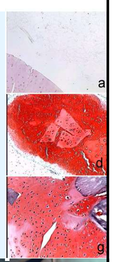
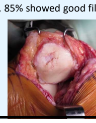
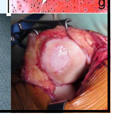
PJAC

Particulated juvenile allograft cartilage

- Hyaline cartilage, morcellized into <1 mm cubes
  - “Cell delivery vehicle”, different from OCA
  - Cell-based surface repair like MFx or ACI
  - **Results**:
    - **Tompkins - Arthroscopy 2013**
      15 knees in 13 patients 73% normal or nearly normal ICRS MRI
    - **Farr et al - AJSM 2014**
      25 patients with minimum 2 y post op; majority improved @ f/u
    - **Grawe et al - Cartilage 2017 (HSS group)**
      45 patients with patellar defects, 85% showed good fill at 12 months







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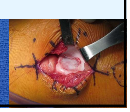
MACI

Autologous chondrocyte implantation

- 2-stage procedure: biopsy and implantation
- Autologous chondrocyte culture
  - Periosteum patch ‘97 → collagen patch ‘06 → MACI ’17
  - **Results**:
    - **Minas – CORR 2014**
      210 patients with ACI, min 10y (ave 12y), ave age 36yrs, ave defect size 8.4cm2
      75% with intact grafts, 25% revised: 10% with arthroplasty, 15% with cartilage





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PCA

Perforated cartilage allograft

- Allograft cartilage disc with microscopic subchondral bone
  - Perforated to allow cell proliferation and subchondral integration
  - Flexible – can conform to complex PF anatomy
  - Different from osteochondral allograft, but closer than JPAC
  - Most of the graft remains structurally intact
  - Implanted on an abraded/microfractured bed
  - **Results**:
    - None clinical

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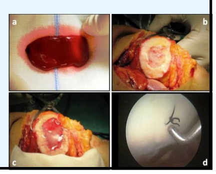
BMAC

Bone marrow aspirate concentrate

- Several providers of aspiration equipment/centrifuges
  - Aspirate from iliac crest, distal femur, prox. tibia
  - Centrifuge to decrease WBC and increase stem cell concentration
  - Implant clot under collagen membrane (off label)
  - **Results**:
    - **Gobbi - AJSM 2014**
      25 patients, ave defect size 8.3cm2
      Complete filling in 80% of patients



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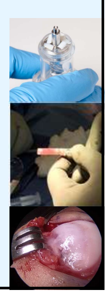
Particulated cartilage autograft

Particulated cartilage autograft

- Harvest autologous cartilage (scope or open)
  - Morselize (scalpel or dedicated device)
  - (Mix with BMAC and clot)
  - Implant with fibrin glue
  - **Results**:
    - **Cole et al. - AJSM 2011**
      29 patients RCT MFx vs CAIS
      Significantly better outcomes with CAIS
    - **Christensen and Lind - Cartilage 2015**
      Case series of 8 patients treated with cartilage autograft and bone grafting
      Clinical improvement and defect filling



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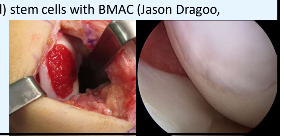
On the horizon

Cell based therapies

- Next generation autologous chondrocyte implants
  - Currently 2 Phase 3 trials on-going in US (Histogenics and Aesculap)
  - Stronger membranes, more mature tissue with possible faster rehab
  - Expected availability '19-'20
- Stem cell related technology
  - Cultured umbilical cord stem cells (Medipost, Phase 2 trial, concluded)
  - Peripheral blood derived MSCs (Adam Anz, Phase 2 trial, recruiting)
  - Single-step adipose-derived (fat pad) stem cells with BMAC (Jason Dragoo, Phase 3 trial, recruiting)



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Summary

- Surface treatments are viable options for cartilage repair
- FDA rules on when clinical trial required changed last year:
  - Only MACI and OCA definitely follow new rules
  - Might see several products disappear over next 3 years
- When to use:
  - Largely intact bone
  - MACI and JPAC with supporting clinical data:
    - MACI for larger defects
    - JPAC for small to medium sized defects
  - Micronized and perforated cartilage grafts interesting options, but clinical outcomes TBD

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Thanks very much!

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