Sports Medicine Center
AT THE ORTHOPAEDIC GROUP, P.C.

Articular Cartilage Injury

Matrix Autologous Chondrocyte Implantation

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cular Cartilage

- primarily hyaline cartilage
- highly specialized connective tissue made up of type II collagen
- provides smooth low friction surface for articulation and transmission of loads
- no blood vessels or nerves

Rodeo et al Sports Health 2009 Nov;1(6)461-68

Articular Cartilage injury

- articular cartilage has limited healing abilities for cartilage injury that does not penetrate the subchondral bone
  - it lacks a direct blood supply and relies on its nutrients via diffusion of interstitial fluid
  - subchondral penetration allows for fibrin clot formation, vascular ingrowth and fibrocartilage formation (type I collagen) "scar cartilage."

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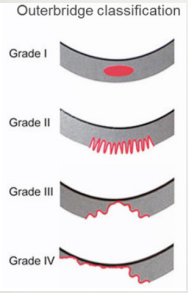
Outerbridge Classification of Articular Cartilage Injury



Table

ICRS grading Score[7]

Grade	Properties
1	Superficial lesions, fissures, cracks, and indentations
2	Fraying, lesions extending down to <50% of cartilage depth
3	Partial loss of cartilage thickness, cartilage defects extending down >50% of cartilage depth as well as down to calcified layer
4	Complete loss of cartilage thickness, bone only

Articular Cartilage Injury Natural Progression

- Progression of injury depends on many factors: size, location, BMI, age, joint stability, limb alignment, activity status, etc.
- Treatment also depends on many of the factors above.

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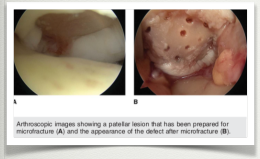
Treatment Options

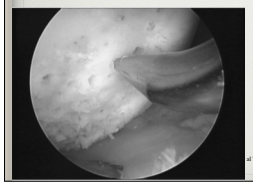
- Microfracture/ Marrow stimulation techniques
- Osteochondral Autograft/Allograft Transport Surgery (OATS)
- Matrix Autologous Chondrocyte Implantation (MACI)
- Others: Denova Cartilage, PRP, Stem cells

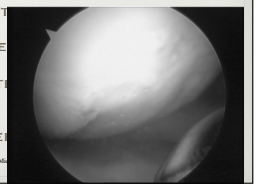
Microfracture



Arthroscopic images showing a patellar lesion that has been prepared for microfracture (**A**) and the appearance of the defect after microfracture (**B**).

- Technique of marrow stimulation (stem cells) producing fibrocartilage (Type I collagen)
  - Hyaline cartilage is Type II
- Defects <2cm2
- Less act
- Postope
- Short t
  good
- Long te





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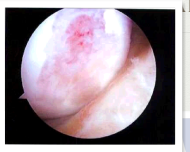
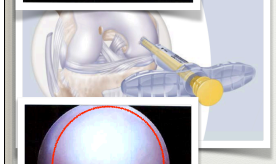
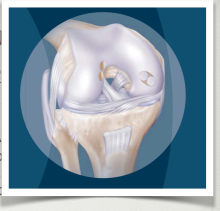






- Transpla
  osteocho
  a Low we
  region to
- Can be performed first line or for failed marrow stimulation procedure
- Recommended in <2cm2 in higher demand pts
- Single plug is preferred
- Multiple plugs (mosaicplasty) can cause "cobblestone feel"

- 2018 J. Farr, A. H. Gomoll (eds.), *Cartilage Restoration* Cole et al. Ch 5

ACI vs MACI Procedures

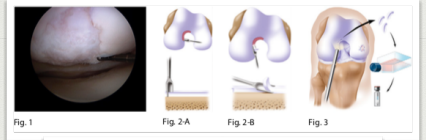


Fig. 1 Fig. 2-A Fig. 2-B Fig. 3

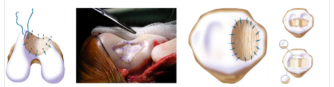
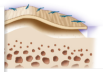


Fig. 9-A Fig. 9-B Fig. 10-A Fig. 10-B



Minas et al. JBJS ESS

Bartlett et all Bone J

Indications for Autologous Chondrocyte implantation

- injuries considered for treatment
  - full thickness lesions (Grade III or IV)
  - >2cm squared on femur, trochlea or patella
  - 13-55 yo
  - compliant pt

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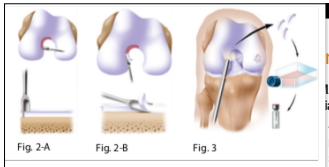
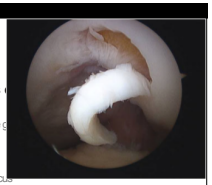
CONTRAINDICATIONS

- >50% loss of cartilage thickness (JSN/OA)
- Inflammatory joint disease
- smoking
- BMI>35kg/m2
- chronic narcotic uses

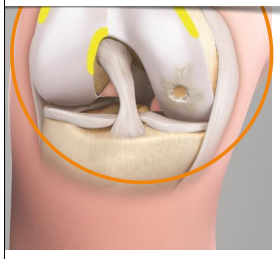




rocess

ACI eligibility is
ia arthroscopy[1]

At least 1 Outerbridge g
Defect ≥2 cm²
Stable knee
Intact or partial meniscus
(≥50% of functional meniscus remaining)



II **Cartilage tissue collected[2]**
200-300 mg healthy cartilage tissue collected from non–load-bearing area of the knee
Recommended sites include: Lateral intercondylar notch and superior medial or lateral trochlear ridge

III **Biopsy tissue is packed and shipped to Vericel using supplied transport kit**

[1]Saris D, et al. *Am J Sports Med.* 2014;42(6):1384-1394. [2]MACI Surgical Manual. Vericel Corporation 2016.

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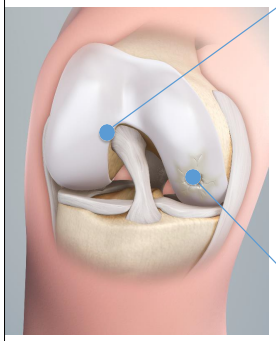
maci

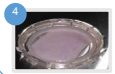
MACI Overview



1. Defect assessment and cartilage biopsy

2. Cells are isolated and expanded (~4 weeks)

3. Cells are seeded on a collagen membrane (2-4 days)



4. Chondrocyte viability and screening assays

5. Cell-seeded membrane is implanted via an arthrotomy with fibrin sealant

Average time from biopsy to implantation is 6 weeks

Brittberg M, et al. *Am J Sports Med*. 2010;38(6):1259-1271.

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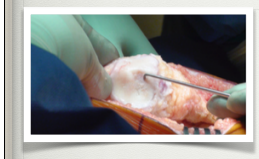
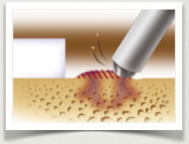
MACI Procedure





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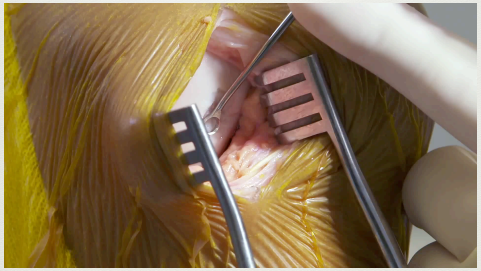
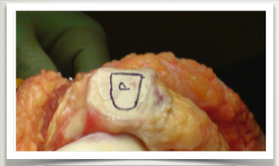
Debridement of Lesion



MACI Procedure



- After defect is appropriately derided the template is sized and shaped to match the defect.

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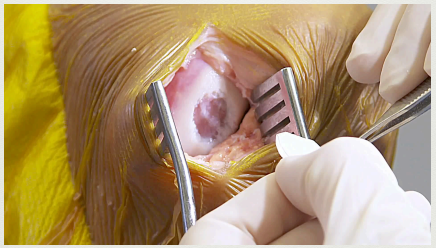
Template

MACI Procedure

- Fibrin is placed in the defect
- The membrane is then placed with the cells facing the bone bed and sealed with the fibrin glue

Implantation



Key Features of MACI

At the time of implantation, **viable cells are distributed** throughout the MACI implant[1]

Cells seeded on the MACI implant **attach to fibers and re-differentiate to their chondrocytic phenotype**[2]

The use of a smaller arthrotomy with fibrin glue enables **less invasive and shorter** implantation surgeries (as compared to second-generation ACI)[3]

Following implantation, cultured chondrocytes migrate through the **fibrin glue, which promotes cell proliferation**[2,4]

- Cartilage repair tissue has been observed by 21 days post-surgery[2]
- By 6-8 months, **chondrocytes produce extracellular matrix; graft begins to firm**

An **enhanced rehabilitation program** has been used with MACI[5]

Patients can return to full weight bearing at 8 weeks post-surgery, compared with 11 weeks in a traditional rehabilitation program

[1]Gigante A, et al. *Knee Surg Sports Traumatol Arthrosc.* 2007;15(1):88-92. [2]Zheng MH, et al. *Tissue Eng.* 2007;13(4):737-746. [3]Brittberg M. *Am J Sports Med.* 2010;38(6):1259-1271. [4]Kiriiak Y, et al. *Int J Mol Med.* 2006; 17:551-558.
[5]Ebert JR, et al. *Cartilage.* 2010;1(3):180-187.

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Rehabilitation Overview

Continuous Passive Motion	Begin 12-24 hours after surgery, continue for 6 hours per day for 6 weeks
Weight Bearing	Gradual progression from touchdown for 2 weeks to full weight at 8 weeks, as tolerated by the patient
Range of Motion	0°-90° for first week; increase by 10° per week to 135° Stationary bike at 4 weeks
Strengthening	Quadriceps strength is restored initially followed by CORE lower extremities Elliptical trainer at 2-3 months
Impact Loading	Low impact 5-6 months; jogging 6-7 months Return to sports at 12-18 months
Special Considerations	Trochlea implants: no open chain or shear loading for first 3 months Combined procedures (eg, ACL repair): follow ACI rehab first

Data on File. Vericel Corporation.

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Phases 1-3:
Implantation and Protection

WEEKS	PHASE	GOALS	CRITERIA
0-1	1	Maintain joint mobility and muscle tone without placing stress on the implant area	Patient must be proficient in home exercise program and functional activities
2-3	2	Pain-free, full passive knee extension, limited weight bearing	Have pain-free active knee flexion to 125° and pain-free gait using 1 or 2 crutches, depending on weight- bearing status
4-6	3	More ROM activities, more strengthening exercises, and greater weight bearing	Weight bearing should progress to 60% with a tibiofemoral graft and to full weight bearing with a patellofemoral graft once cleared by the orthopaedic specialist

Ebert JR, et al. MACI Rehabilitation Manual. Vericel Corporation. 2016.

Post-Operative Timeline:
Phase 1 / Week 1

	Weight-Bearing Status	Ambulatory Aids	Knee Bracing	Knee ROM
TF Joint	≤20% BW	2 crutches used at all times	0-2 weeks Lock at zero during weight-bearing activities **0˚-30˚**	Passive and active ROM from **0˚-30˚**
PF Joint	20%-30% BW	2 crutches used at all times	Locked at full knee extension Phase 1 exercises	Passive and active ROM from **0˚-20˚**

BW, body weight; PF, patellofemoral; ROM, range of motion; TF, tibiofemoral

Ebert JR, et al. MACI Rehabilitation Manual. Vericel Corporation. 2016.

Phase 1: Post-Surgery (Week 0-1)
Rehabilitation Plan (start on post-operative Day 1)

Pain Control
- Provide appropriate analgesics for pain control

Exercises
- Start 0°-30° CPM of knee flexion
  12-24 hours post-surgery for at least 1 hour each day
- For first 3 weeks, wear ROM control brace
  Set at 0°-30° of knee flexion
- Apply cryotherapy
  20 minutes of ice, at least 3 times per day
- Perform active flexion ankle exercises
- Encourage contraction of quadriceps, hamstrings, and gluteal muscles

Reminders
- Ensure proper breathing techniques during exercise
- Offer information on proper ambulation with crutches, bed transfers, and stairs
- Provide written and verbal instruction on performing daily living activities while limiting weight bearing on knee implant

CPM, continuous passive motion

Ebert JR, et al. MACI Rehabilitation Manual. Vericel Corporation. 2016.

PHASES 1-3 Implantation and Protection | PHASE 4 | PHASE 5 | PHASES 6-7

Post-Operative Timeline: Phase 2 / Weeks 2-3

	Weight-Bearing Status	Ambulatory Aids	Knee Bracing	Knee ROM
TF Joint	**30% BW** (Week 3)	2 crutches used at all times	**0˚-30˚** (Weeks 1-2) to **0˚-30˚** (Weeks 1-2)	Passive and active ROM from: **0˚-30˚** (Week 2) to **90˚** (Week 3)
PF Joint	**50% BW** (Week 3)	2 crutches used at all times	Lock brace at full knee extension	Active ROM from: **0˚-30˚** (Week 2) to **60˚** (Week 3)

Clinic and Adjunct Modalities:
- Perform clearance and lymphatic massage as needed to assist with edema; perform cryotherapy, compression, and elevation to assist with edema

Ebert JR, et al. MACI Rehabilitation Manual. Vericel Corporation. 2016.

PHASES 1-3 Implantation and Protection | PHASE 4 | PHASE 5 | PHASES 6-7

Phase 2: Post-Surgery (Weeks 2-3)

Rehabilitation Plan (by post-surgery Week 3)

Along with the weight bearing, ambulatory aids, knee ROM, and knee bracing exercises, patients should include:

ROM and flexibility exercises
- Use CPM at end of session for 20-30 minutes
- Passive and active heel slides
- Passive knee extension
- Slight patellar mobilization in all directions

Strengthening exercises
- Contraction and co-contraction of quadriceps
- Contractions of hamstrings, adductor, calf, and gluteal muscles
- Straight-leg-raise activities

Hydrotherapy exercises (If available to the patient After 3 weeks/incision healed)
- Deep water walking and calf raises
- Straight-leg hip movements
- Passive knee flexion
- Hamstring and calf stretching

Ebert JR, et al. MACI Rehabilitation Manual. Vericel Corporation. 2016.

PHASES 1-3 Implantation and Protection | PHASE 4 | PHASE 5 | PHASES 6-7

Post-Operative Timeline: Phase 3 / Weeks 4-6

	Weight-Bearing Status	Ambulatory Aids	Knee Bracing	Knee ROM
TF Joint	**40%-60% BW** (Weeks 4-6)	1-2 crutches	**0˚-60˚** (Week 4) to **Full flexion** (Week 6)	Active ROM from: **0˚-110˚** (Week 4) to **125˚** (Week 6)
PF Joint	**75%-full BW** (Week 6)	1-2 crutches (Weeks 4-5); 1 crutch as required beginning (Week 6)	Use brace as required (Week 6) Clinic and adjunct modalities	Active ROM from: **0˚-90˚** (Week 4) to **125˚** (Week 6)

Clinic and Adjunct Modalities:
- Perform clearance and lymphatic massage as required; perform cryotherapy, compression, and elevation as required

Ebert JR, et al. MACI Rehabilitation Manual. Vericel Corporation. 2016.

PHASES 1-3 | PHASE 4 Transition and Proliferation | PHASE 5 | PHASES 6-7

Post-Operative Timeline:
Phase 4 / Weeks 7-12

	Weight-Bearing Status	Ambulatory Aids	Knee Bracing	Knee ROM
TF Joint	**80%** (Week 7) to **Full BW** (Weeks 8-10)	1 crutch as needed in outdoor/unfamiliar	Discontinue after 6 weeks if no extensor lag with SLR	Progress to full active ROM: (Weeks 7-8)
PF Joint	**Full BW** as tolerated	No crutches	NO brace	Progress to full active ROM: (Weeks 7-8)

Begin proprioception exercises after full BW is achieved

PHASES 1-3 | PHASE 4 | PHASE 5 Remodeling | PHASES 6-7

Post-Operative Timeline:
Phase 5 / (Months 3-6)

	Weight-Bearing Status	Ambulatory Aids	Knee Bracing	Knee ROM
TF Joint	**Full WB** as tolerated	No crutches	NO brace	Full and pain-free active ROM
PF Joint	**Full WB** as tolerated	No crutches	NO brace	Full and pain-free active ROM

PHASES 1-3 | PHASE 4 | PHASE 5 | PHASES 6-7 Maturation

Maturation Phases 6-7

WEEKS	PHASE	GOALS	CRITERIA
27-36 (6-9 Mo)	**6** Maturation	Increase difficulty of exercises Return to low-impact recreational activities Be able to walk more than 5 km Light jogging	
37-52 (9-12 Mo)	**7** Return to sports	Resume all normal functionality Return to low-compression recreational activities Running/pivotal activities	Clearance by physician Graft able to withstand the specific demands of activities as evaluated by functional tests

Results

Long-Term Clinical and MRI Results of Matrix-Assisted Autologous Chondrocyte Implantation for Articular Cartilage Defects of the Knee

Peter Cornelius Kreuz[1,*], Richard Horst Kalkreuth[1,*], Philipp Niemeyer[2], Markus Uhl[3], and Christoph Erggelet[4]

Indications, Techniques, Outcomes for Matrix Induced Autologous Chondrocyte Implantation (MACI)

Brandon J. Erickson MD , Sabrina M. Strickland MD , Andreas H. Gomoll MD

Autologous Chondrocyte Implantation for Bipolar Chondral Lesions in the Tibiofemoral Compartment

Takahiro Ogura,*[,1] MD, Tim Bryant,* BSN, RN, Brian A. Mosier,*[,1] MD, and Tom Minas,*[,§] MD, MS
Investigation performed at the Cartilage Repair Center, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA

Patellofemoral Cartilage Restoration: Indications, Techniques, and Outcomes of Autologous Chondrocytes Implantation, Matrix-Induced Chondrocyte Implantation, and Particulated Juvenile Allograft Cartilage

Betina B. Hinckel, MD, PhD[1] Andreas H. Gomoll, MD[2]

[1]Missouri Orthopaedic Institute, University of Missouri, Columbia, Missouri. [2]Cartilage Repair Center, Brigham and Women's Hospital, Boston, Massachusetts.

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Articular Cartilage Treatment Studies

Table 1

Summary of Level I and II Prospective Randomized Trials on the Surgical Management of Articular Cartilage Defects

Study	Technique (No. of Subjects)	Patient Characteristics	Lesion Characteristics	Follow-up	Outcomes
Bentley et al[17]	ACI (58) vs mosaicplasty (42)	Mean age, 31.3 yr (range, 18 to 49 yr) Mean duration of symptoms, 7.2 yr Mean prior surgeries, excluding arthroscopy, 1.5	Avg size, 4.66 cm² Posttraumatic defect in 66%, osteochondritis dissecans in 19% Location: MFC, 53%; patella, 25%; LFC, 18%; trochlea, 3%; LTP, 1%	Mean, 19 mo (range, 12 to 31 mo) Follow-up arthroscopy in 37 knees treated with ACI, and in 23 treated with mosaicplasty	Modified Cincinnati and Hospital for Special Surgery scores demonstrated good to excellent results with ACI and mosaicplasty at 1 yr (98% vs 68%; $P = 0.277$) Arthroscopy at 1 yr demonstrated good to excellent ICRS results in 82% of patients treated with ACI versus 34% treated with mosaicplasty ($P = 0.01$)
Horas et al[18]	ACI (20) vs open OAT (20)	Mean age, 31.4 yr (ACI), 34.5 yr (OAT) Preoperative symptoms not listed Avg number of prior surgeries, 0.3	Avg size, 3.75 cm² Chondral defects only Location: MFC, 80%; LFC, 17.5%; MFC + patella, 2.5%	24 mo Follow-up arthroscopy was performed in 39% within 2 yr	Lysholm score indicated faster recovery for OAT at 6, 12, and 24 mo ($P < 0.02$) Meyers and Tegner activity scores demonstrated equal improvement with each procedure Arthroscopic findings: fibrocartilage = limited hyaline-like cartilage (ACI); hyaline cartilage = fibrous tissue at gaps (OAT)
Knutsen and colleagues[19,20]	ACI (40) vs microfracture (40)	Mean age, 32.2 yr (range, 18 to 45 yr) Mean duration of preoperative symptoms, 3 yr 95% of patients had had prior surgery (avg 1.6 surgeries for ACI group, and avg 1.4 surgeries for microfracture group)	Lesion size not listed Posttraumatic defect in 65%, osteochondritis dissecans in 35% Location: MFC, 89%; LFC, 11%	2 and 5 yr Radiographs Follow-up arthroscopic biopsy was done at 2 yr	No difference in improvement at 2 or 5 years according to ICRS, Tegner, Lysholm, and SF-36 mental component scores; ACI group showed greater improvement on the SF-36 physical component at 5 yr but not at 2 yr 34% of patients demonstrated signs of OA at 5 yr, and 24% had reduced joint space (<4 mm) Nine failures were reported in each group at 5 yr (23% total) No difference was noted in histologic results
Gudas et al[21]	Arthroscopic OAT (28) vs microfracture (29) in athletes	Mean age, 24.3 yr (range, 15 to 40 yr) Mean duration of preoperative symptoms, 1.8 yr No patient had had prior surgery Isolated, unilateral injuries only included No associated ligamentous injury	Avg lesion size, 2.8 cm² Posttraumatic defect in 56%, osteochondritis dissecans in 44% Location: MFC, 84%; LFC, 16%	Avg 37.1 mo (range, 36 to 39 mo) At 1 yr, follow-up arthroscopy was done in 93%, and biopsy in 46%	HSS and ICRS scores demonstrated good to excellent results in 96% after OAT versus in 52% after microfracture ($P < 0.001$) A better histologic grade was noted following OAT ($P < 0.05$)
Saris et al[22]	CCI (57) vs microfracture (61)	Age range, 18 to 50 yr Mean duration of preoperative symptoms: 1.57 yr (microfracture), 1.49 yr (CCI) Prior surgery in 82%	Mean defect size of 2.4 cm² for microfracture vs 2.6 cm² for CCI	6, 12, and 18 mo Follow-up arthroscopic biopsy performed 1 yr postoperatively	KOOS score demonstrated no difference in improvement between both groups at 6, 12, and 18 mo Biopsy demonstrated improved structural regeneration after CCI compared with microfracture ($P = 0.003$)

ACI = autologous chondrocyte implantation, CCI = characterized chondrocyte implantation, HSS = Hospital for Special Surgery, ICRS = International Cartilage Research Society, KOOS = Knee Injury and Osteoarthritis Outcome Score, LFC = lateral femoral condyle, LTP = lateral tibial plateau, MFC = medial femoral condyle, OA = osteoarthritis, OAT = osteochondral autograft transplantation, SF-36 = Medical Outcomes Study 36-Item Short Form

Table 1 (continued)

Summary of Level I and II Prospective Randomized Trials on the Surgical Management of Articular Cartilage Defects

ACI = autologous chondrocyte implantation, CCI = characterized chondrocyte implantation, HSS = Hospital for Special Surgery, ICRS = International Cartilage Research Society, KOOS = Knee Injury and Osteoarthritis Outcome Score, LFC = lateral femoral condyle, LTP = lateral tibial plateau, MFC = medial femoral condyle, OA = osteoarthritis, OAT = osteochondral autograft transplantation, SF-36 = Medical Outcomes Study 36-Item Short Form

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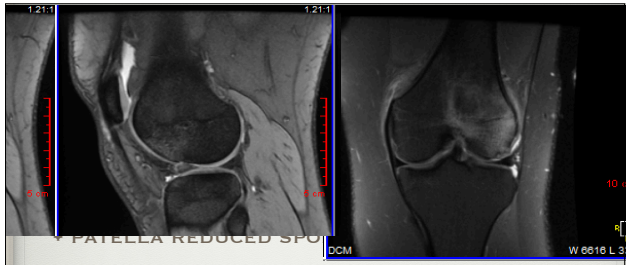


+ PATELLA REDUCED SPO

+ PT IS DEALING WITH PF INSTABILITY, SWELLING AND PAIN

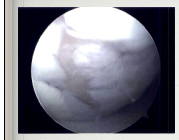
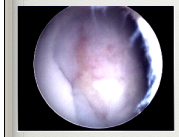
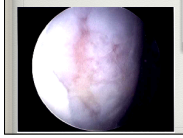
+ X-RAYS NORMAL

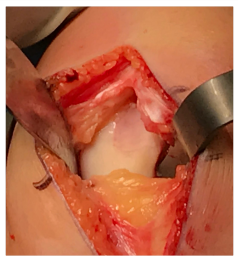
+ MRI- 12X10 MM OCD

Case example

- decision was to proceed with surgery
- discussed option with Pt and his mother
- Surgical options
  - Matrix Autologous Chondrocyte Implantation vs OATS
  - MPFL reconstruction
- Time of surgery defect noted to be larger than 1.2x1.0 cm
  - ACI harvest performed

Treatment



Conclusion

- Treatment of articular cartilage injury depends on many factors
- for larger defects MACI is an excellent option with good overall outcome in active pts
- can be used as a primary procedure or when other cartilage restoration procedures have failed
- two stage procedure
- Rehabilitation and recovery is a long process and compliance is very important