Clinica Ortopedica e Traumatologica

Università degli Studi di Pavia

Policlinico San Matteo, Pavia

Direttore: Prof. Francesco Benazzo

Fondazione IRCCS Policlinico San Matteo

Update on chondral grafts and scaffold

F. Benazzo

7th Advanced Course on Knee Surgery
14th to 18th January 2018
Val d'Isère - France

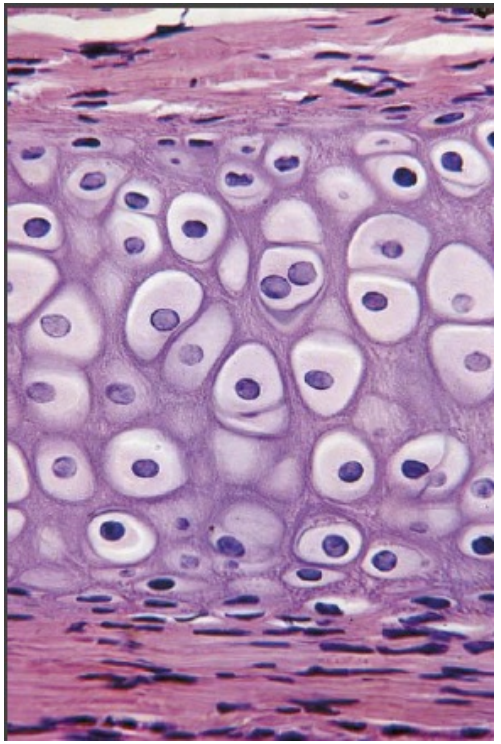
KNEE OSTEOCHONDRAL LESIONS

Limited intrinsic capacity for

spontaneus healing due to

avascular and hypocellular

nature of articular cartilage



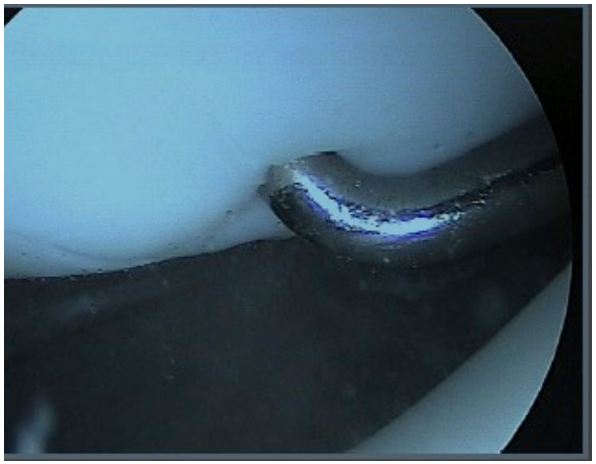
Pain, loss of function and

long-term complication (osteoarthritis)

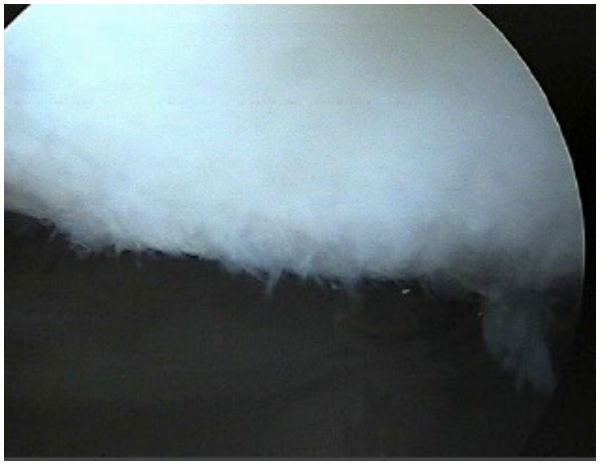
Gomoll AH, Wound Repair Regen, 2014

OUTERBRIDGE'S CLASSIFICATION

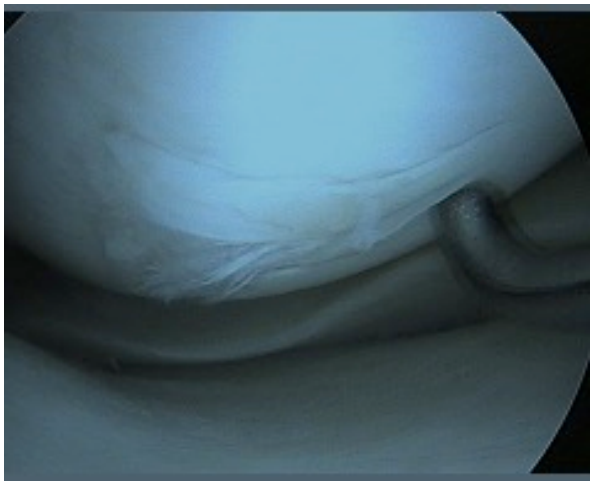
GRADE I



GRADE II



GRADE III



GRADE IV

Outerbridge RE, J.Bone Joint Surg, 1961

KNEE OSTEOCHONDRAL LESIONS

- ***CONSERVATIVE TREATMENT***

ARTHROSCOPIC LAVAGE AND DEBRIDEMENT

PALLIATIVE

DEGENERATIVE

- ***SURGICAL TREATMENT***

REPARATIVE — **MICROFRACTURES**

FOCAL

REPLACEMENT — **AUTO/ALLOGRAFTS**

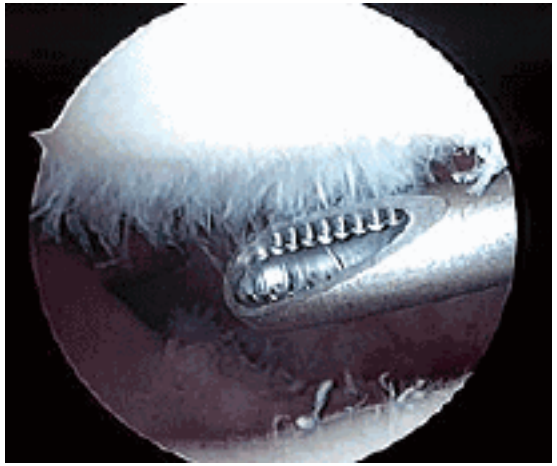
REGENERATIVE — **SCAFFOLDS**
ACI
CELLS

KNEE OSTEOCHONDRAL LESIONS

ARTHROSCOPIC LAVAGE AND DEBRIDEMENT

Remove infiammatory mediators and

unstable cartilage fragments



Clinical improvements in 80% of

patients at 3.5 years but facilitate

degenerative changes

Jackson RW, J Bone Joint Surg, 1998

KNEE OSTEOCHONDRAL LESIONS

MICROFRACTURES

Unstable or full-thickness (Outerbridge grade III-IV)

focal chondral defects

Does not cause damage to other normal regions,

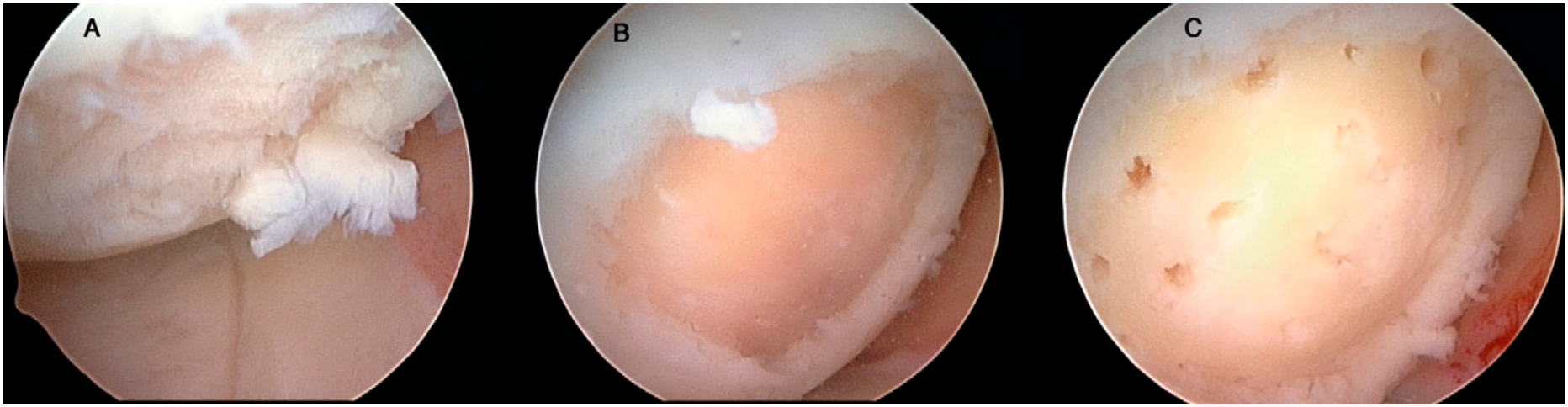
Easy to perform and economical

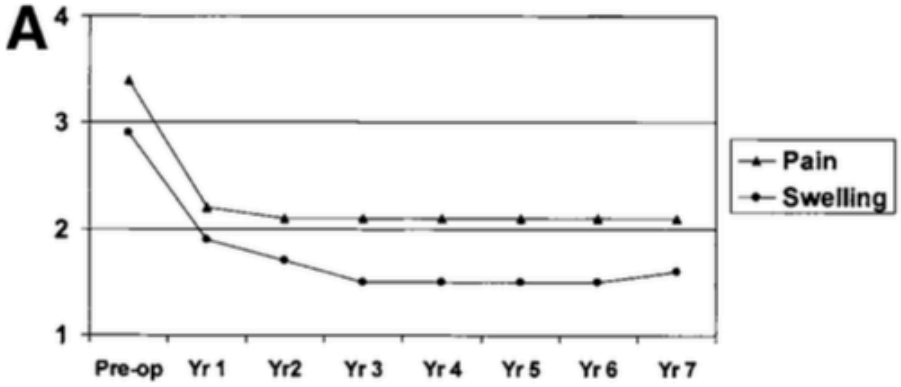
Mesenchymal stem cells differentiate mostly

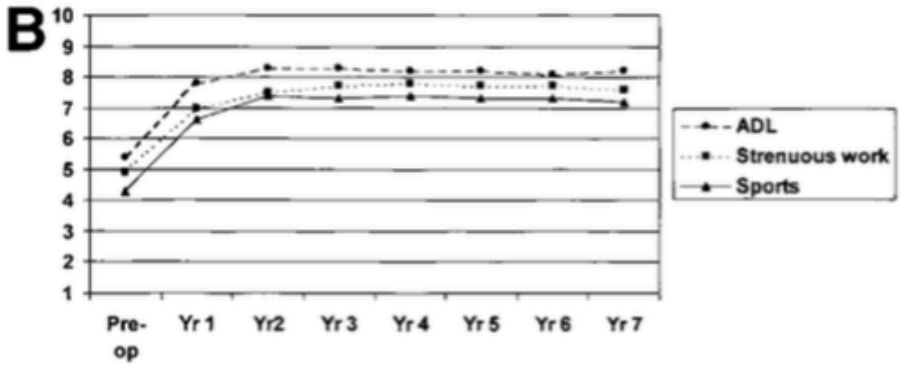
into fibrocartilagine cells

Lesions larger than 4 cm^2 respond worse

MICROFRACTURES







Steadman JR, Sports Med Arthrosc, 2003

OSTEOCHONDRAL AUTOGRAFT TRANSPLANTATION

Symptomatic anterior cartilage defect

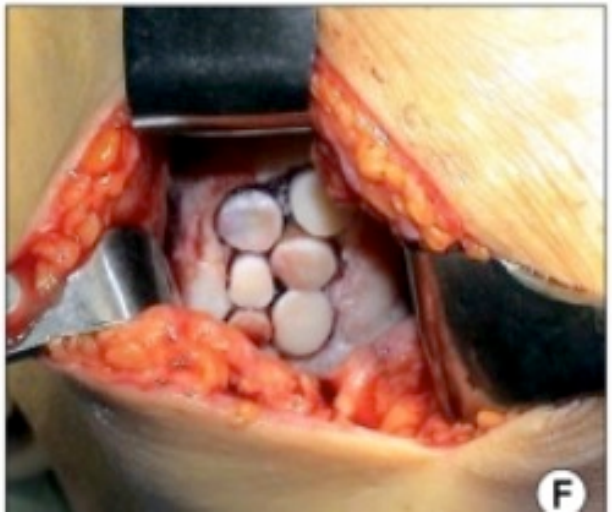
(1-4 cm^2, Outerbridge stage III o IV) in younger patients

One stage procedure, can be performed arthroscopically

for small lesions, earlier rehabilitation, the lesion is covered by hyaline cartilage, few complications

Cannot be applied for large lesions

OSTEOCHONDRAL AUTOGRAFT TRANSPLANTATION



Effective in 76-93% of the patients in achieving clinical improvement with high complication/reoperation rates in patients with large-sized lesions

Jakob RP, Clin Orthop Relat Res, 2002

OSTEOCHONDRAL ALLOGRAFT TRANSPLANTATION

Large lesion >10 cm^2 in traumatic osteoarthritis

Difficulty of obtaining grafts in a timely manner, high cost, and the possibility of immune reaction and disease transmission

OSTEOCHONDRAL ALLOGRAFT TRANSPLANTATION

- Fresh allograft

- *Cryopreserved frozen allograft*
- *Fresh frozen allograft*

Successfull outcome in 85% of

the cases at 7,5 years after surgery

Ghazavi MT, J Bone Joint Surg Br, 1997

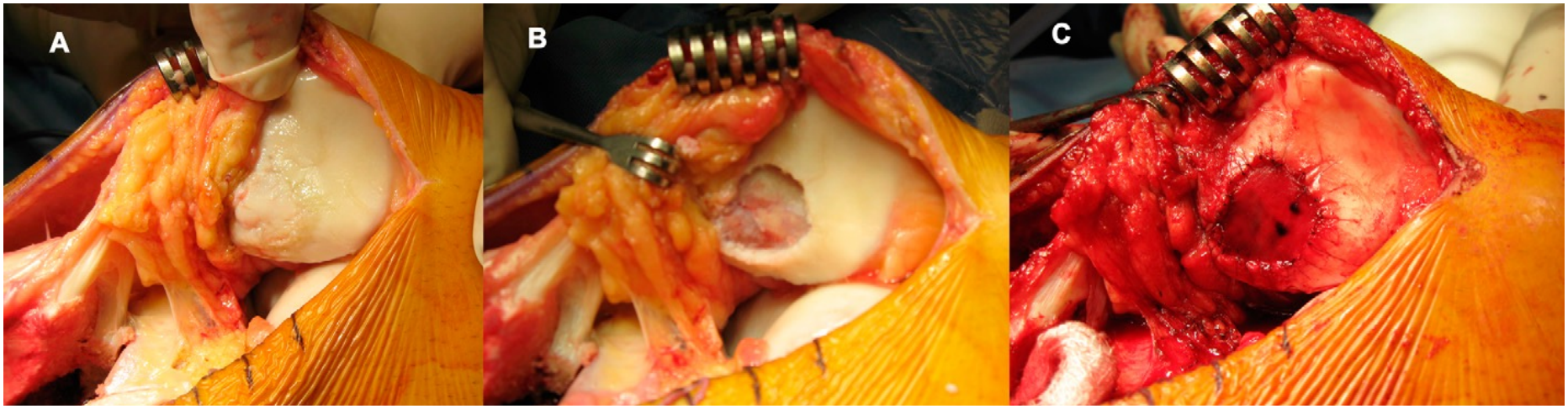
AUTOLOGOUS CHONDROCYTE IMPLANTATION (ACI)

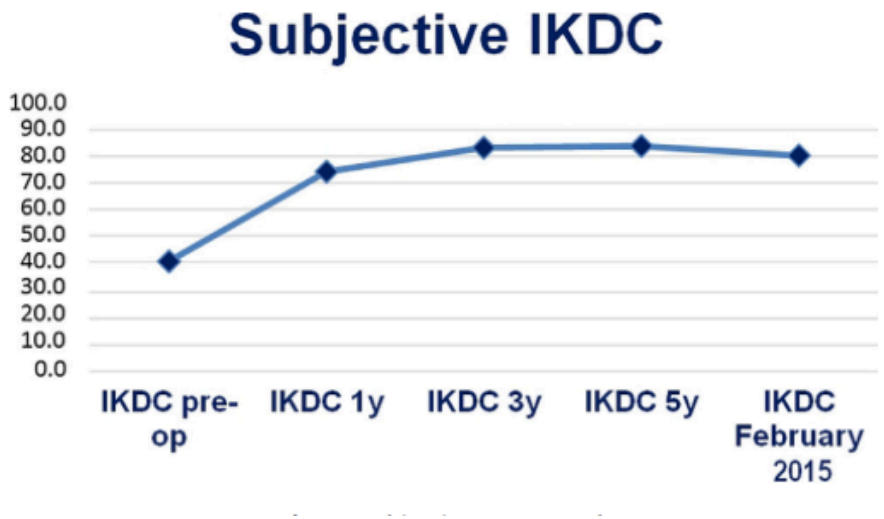
Younger active patients with an isolated traumatic femoral chondral lesion (2-10 cm^2, Outerbridge grade III-IV)

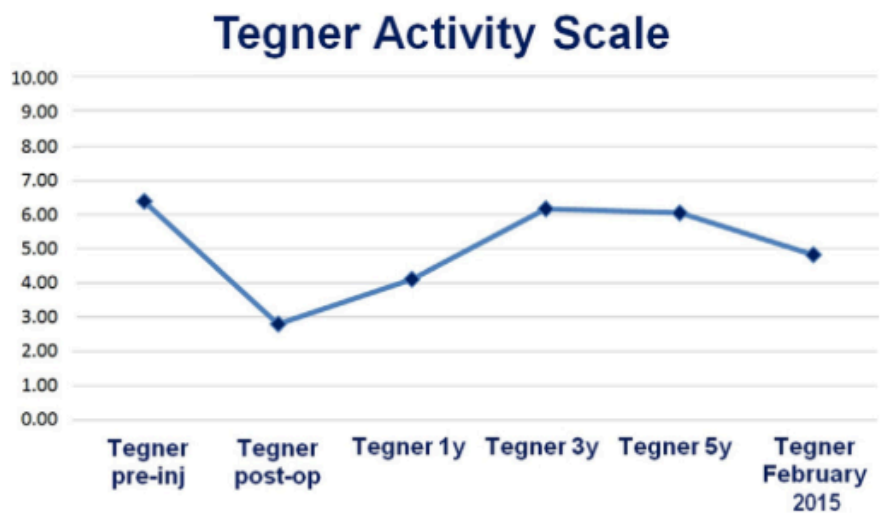
Can be performed on larger lesions, no donor site discomfort or complication and easy to perform

Require joint excision (I generation), two separate steps and long rehabilitation period

OSTEOCHONDRAL AUTOGRAFT TRANSPLANTATION







Berruto M, Injury, 2017

SCAFFOLDS

	SCAFFOLD	KEY POINTS		PECULIARITY	INDICATIONS	ADVANTAGES	DISADVANTAGES
TWO-STEP	HYALOGRAFT C	Hyaluronic acid benzilic ester membrane	+ Autologous cultured chondrocytes	Arthroscopic implantation possible	Post-traumatic or microtraumatic cartilage defects Osteochondral defects (combined with autologous bone graft or bone substitutes)	Good medium term clinical and MRI results Autologous tissue	Two surgical steps Extensive cell manipulation High costs Minimum donor site morbidity
	MACI	Porcine collagen type I/III membrane					
	BIOSEED C	Fibrin, polydioxanone, PGA - PLA membrane					
	NOVOCART	Collagen - chondroitin sulfate membrane		Biphasic matrix - pores: even chondrocytes distribution			
	CARTIPATCH	Agarose – alginate hydrogel gel		Perfect fit of the gel scaffold squeezed into the defect			
	ATELOCOLLAGEN	Atelocollagen gel		Removed animal antigenic telopeptides of collagen-I			
	CHONDRON	Fibrin gel		Easier attachment and even distribution of chondrocytes			
	NEOCART	Collagen type I membrane		Bioreactor based manufacturing			
	CARES	Collagen type I hydrogel		Custom made manifacture			
ONE-STEP	AMIC	Porcine collagen type I/III membrane	+ Bone marrow stimulation / AMIC Plus: +PRP	Arthroscopic implantation possible	Post-traumatic or microtraumatic cartilage defects	One surgical step Off-the-shelf No donor site morbidity Lower cost	No clinical experience over two years of follow-up Unclear mechanism of cartilage regeneration
	CHONDROTISSUE	Fibrin, PGA - PLA, polydioxanone membrane	+ Bone marrow stimulation				
	CAIS	PCL - PGA foam reinforced with PDO mesh	+ Minced autologous cartilage	Minimum donor site morbidity Not in the market			
	ALGINATE BEADS	Alginate gel	+ Allogenic cultured chondrocytes	Periosteal flap needed Overcome interpatient chondrocyte variability			
	HYALOFAST	Hyaluronic acid benzilic ester membrane	+ Bone marrow concentrate + PRP	Arthroscopic implantation possible Necessity of bone marrow	Post-traumatic or microtraumatic chondral or osteochondral defects		
	TRUFIT	PGA calcium solfate plug	Osteochondral biphasic structure	Arthroscopic implantation possible Long maturation time	Small chondral or osteochondral defects		
	MAIOREGEN	Nanostructured collagen-hydroxyapatite scaffold		Flexible osteochondral scaffold	Extensive chondral or osteochondral defects		

SCAFFOLDS

Pros:

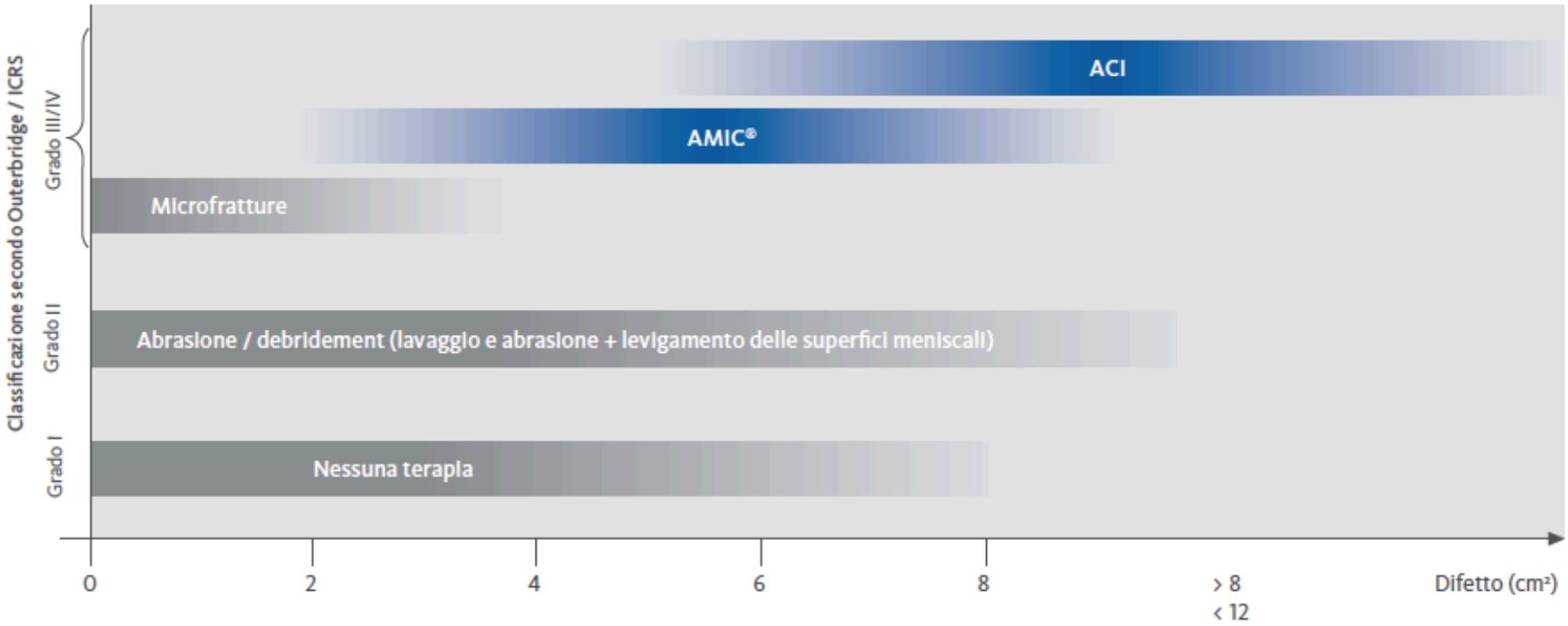
- Single step procedure
- No site morbidity
- Easy and ready to use
- Conforms to any lesion shape
- Arthroscopic (?)

Cons:

- Costs
- No EBM (lack of double blinds, long term studies)
- Mini (?) open

	SCAFFOLD	KEY POINTS		PECULIARITY	INDICATIONS	ADVANTAGES	DISADVANTAGES
TWO-STEP	HYALOGRAFT C	Hyaluronic acid benzilic ester membrane	+ Autologous cultured chondrocytes	Arthroscopic implantation possible	Post-traumatic or microtraumatic cartilage defects Osteochondral defects (combined with autologous bone graft or bone substitutes)	Good medium term clinical and MRI results Autologous tissue	Two surgical steps Extensive cell manipulation High costs Minimum donor site morbidity
	MACI	Porcine collagen type I/III membrane					
	BIOSEED C	Fibrin, polydioxanone, PGA - PLA membrane					
	NOVOCART	Collagen - chondroitin sulfate membrane		Biphasic matrix - pores: even chondrocytes distribution			
	CARTIPATCH	Agarose – alginate hydrogel gel		Perfect fit of the gel scaffold squeezed into the defect			
	ATELOCOLLAGEN	Atelocollagen gel		Removed animal antigenic telopeptides of collagen-I			
	CHONDRON	Fibrin gel		Easier attachment and even distribution of chondrocytes			
	NEOCART	Collagen type I membrane		Bioreactor based manufacturing			
	CARES	Collagen type I hydrogel		Custom made manifacture			
ONE-STEP	AMIC	Porcine collagen type I/III membrane	+ Bone marrow stimulation / AMIC Plus: +PRP	Arthroscopic implantation possible	Post-traumatic or microtraumatic cartilage defects	One surgical step Off-the-shelf No donor site morbidity Lower cost	No clinical experience over two years of follow-up Unclear mechanism of cartilage regeneration
	CHONDROTISSUE	Fibrin, PGA - PLA, polydioxanone membrane	+ Bone marrow stimulation				
	CAIS	PCL - PGA foam reinforced with PDO mesh	+ Minced autologous cartilage	Minimum donor site morbidity Not in the market			
	ALGINATE BEADS	Alginate gel	+ Allogenic cultured chondrocytes	Periosteal flap needed Overcome interpatient chondrocyte variability			
	HYALOFAST	Hyaluronic acid benzilic ester membrane	+ Bone marrow concentrate + PRP	Arthroscopic implantation possible Necessity of bone marrow	Post-traumatic or microtraumatic chondral or osteochondral defects		
	TRUFIT	PGA calcium solfate plug	Osteochondral biphasic structure	Arthroscopic implantation possible Long maturation time	Small chondral or osteochondral defects		
	MAIOREGEN	Nanostructured collagen-hydroxyapatite scaffold		Flexible osteochondral scaffold	Extensive chondral or osteochondral defects		

AMIC

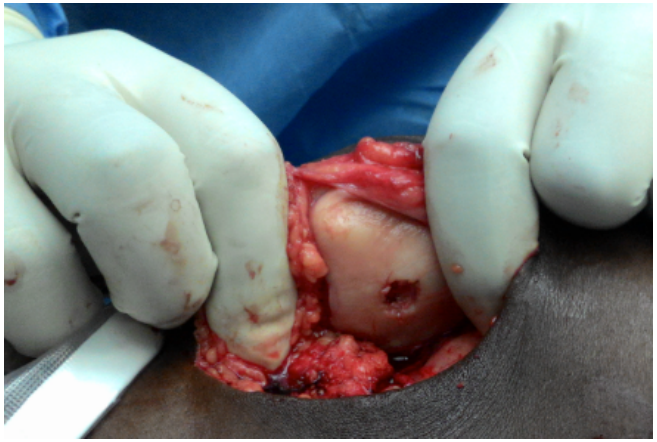


Focal chondral defects 2-8 cm^2 (Outerbridge III-IV)

One step technique, improvement of clinical results

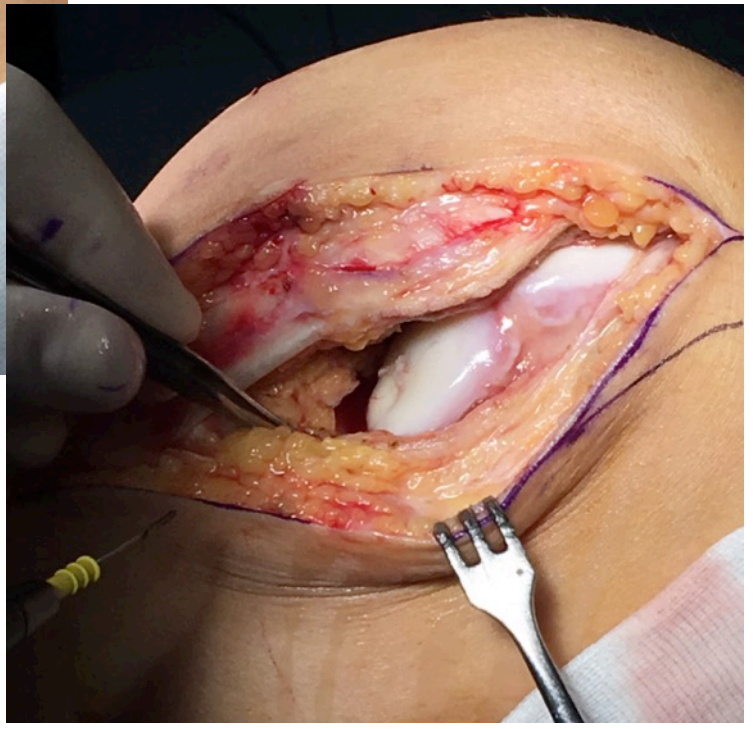
…patellofemoral joint?

- 11%-37% of cases
- “kissing-lesions” problems
- Treatment of malalignment or associated patellar instability

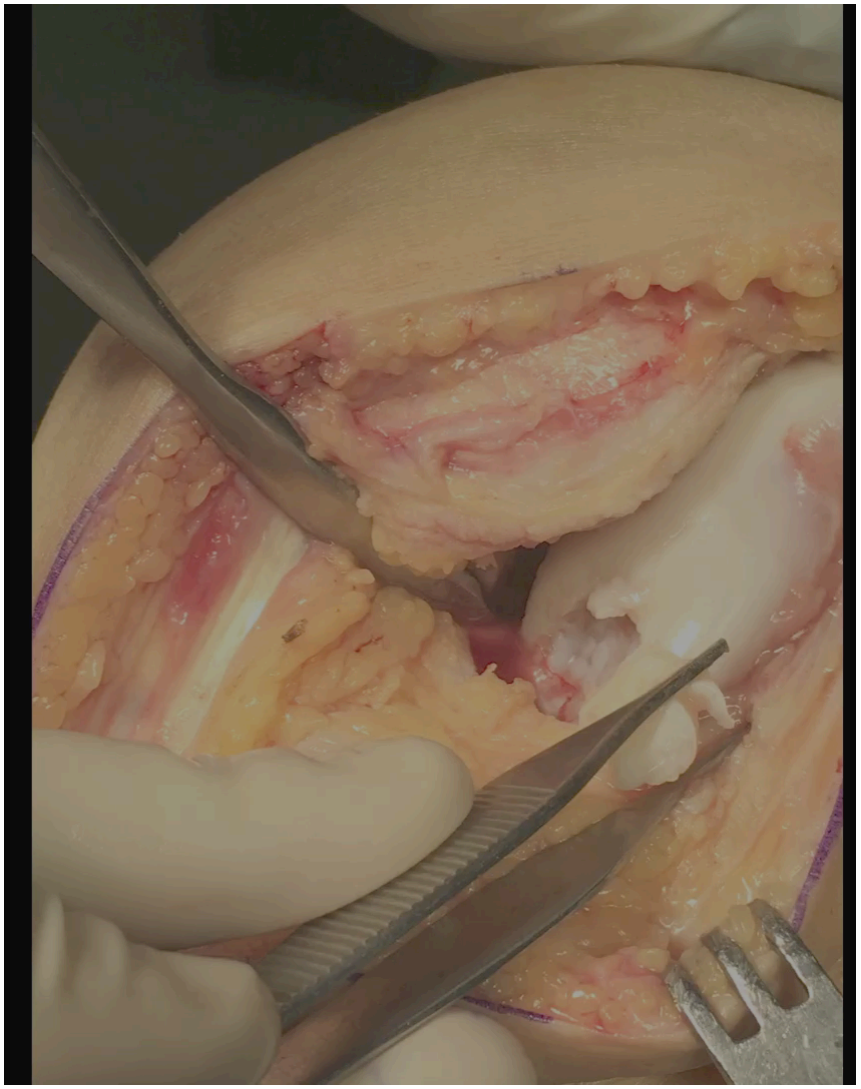


Widuchowski W, The Knee, 2007

AMIC



Preparation of the lesion



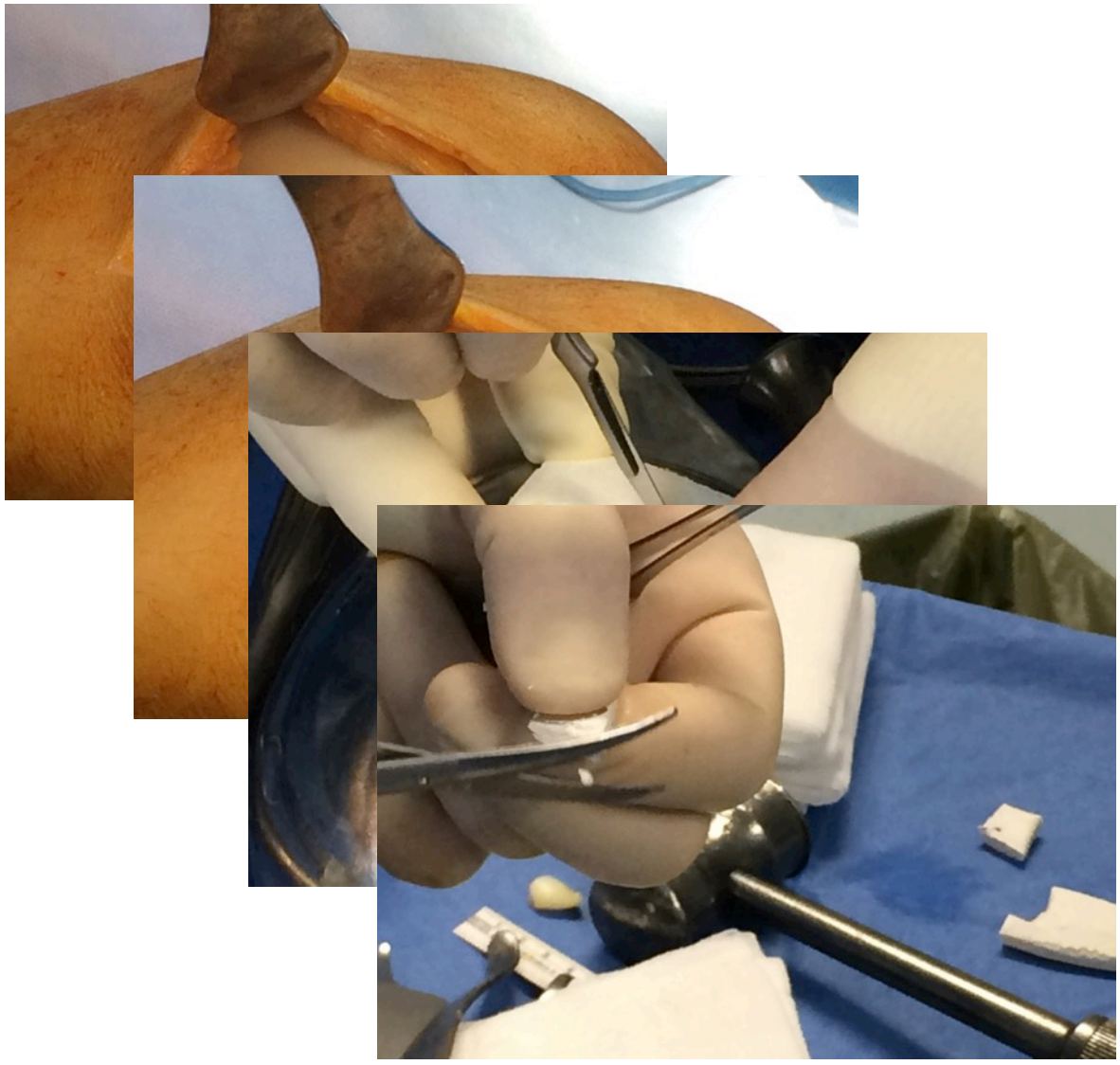
Application of AMIC

BIOSCAFFOLD

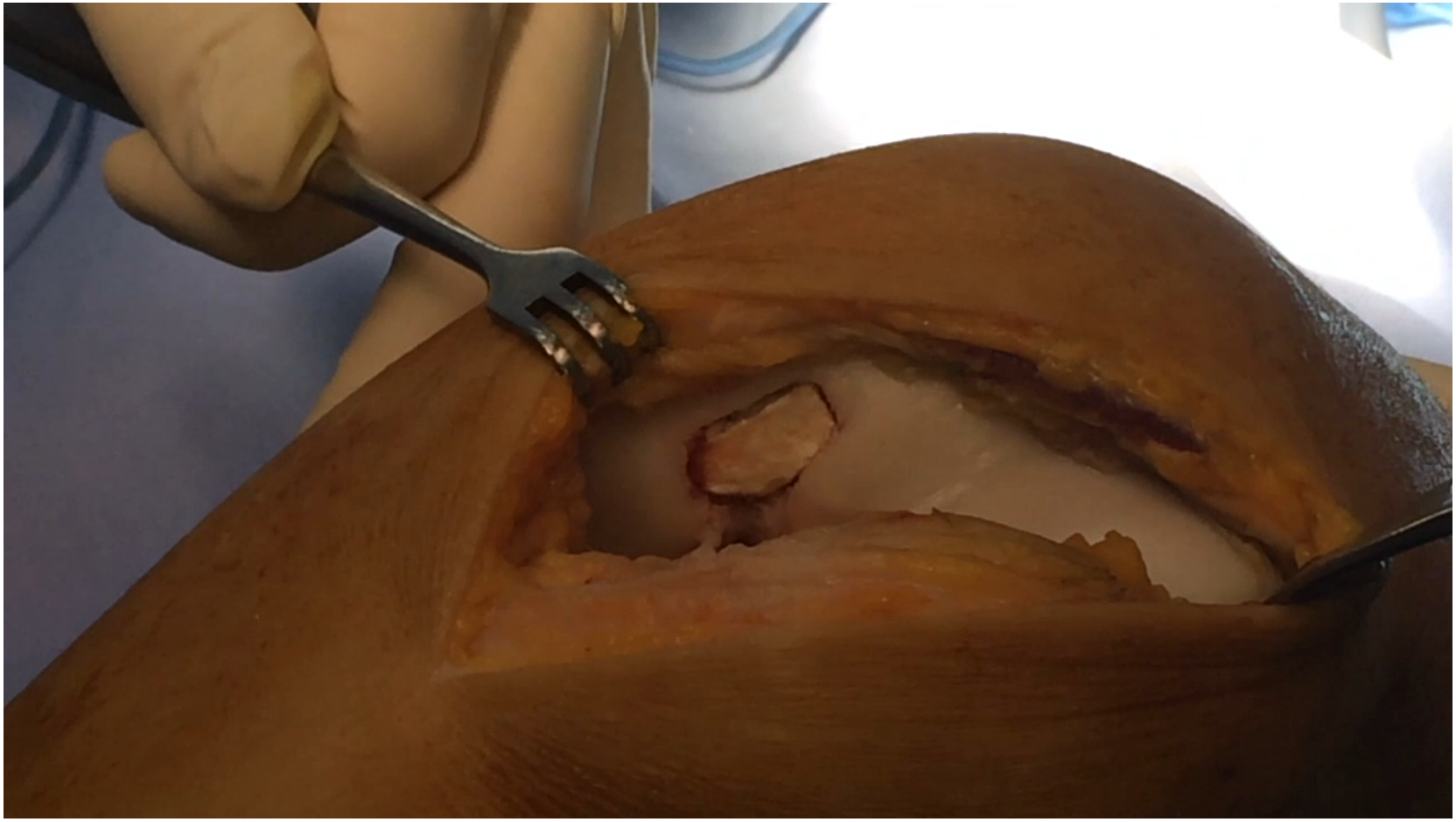
It is easily prepared by mixing a buffer, a chitosan solution and the patient's whole blood to create a liquid bioscaffold.

Very promising but early results

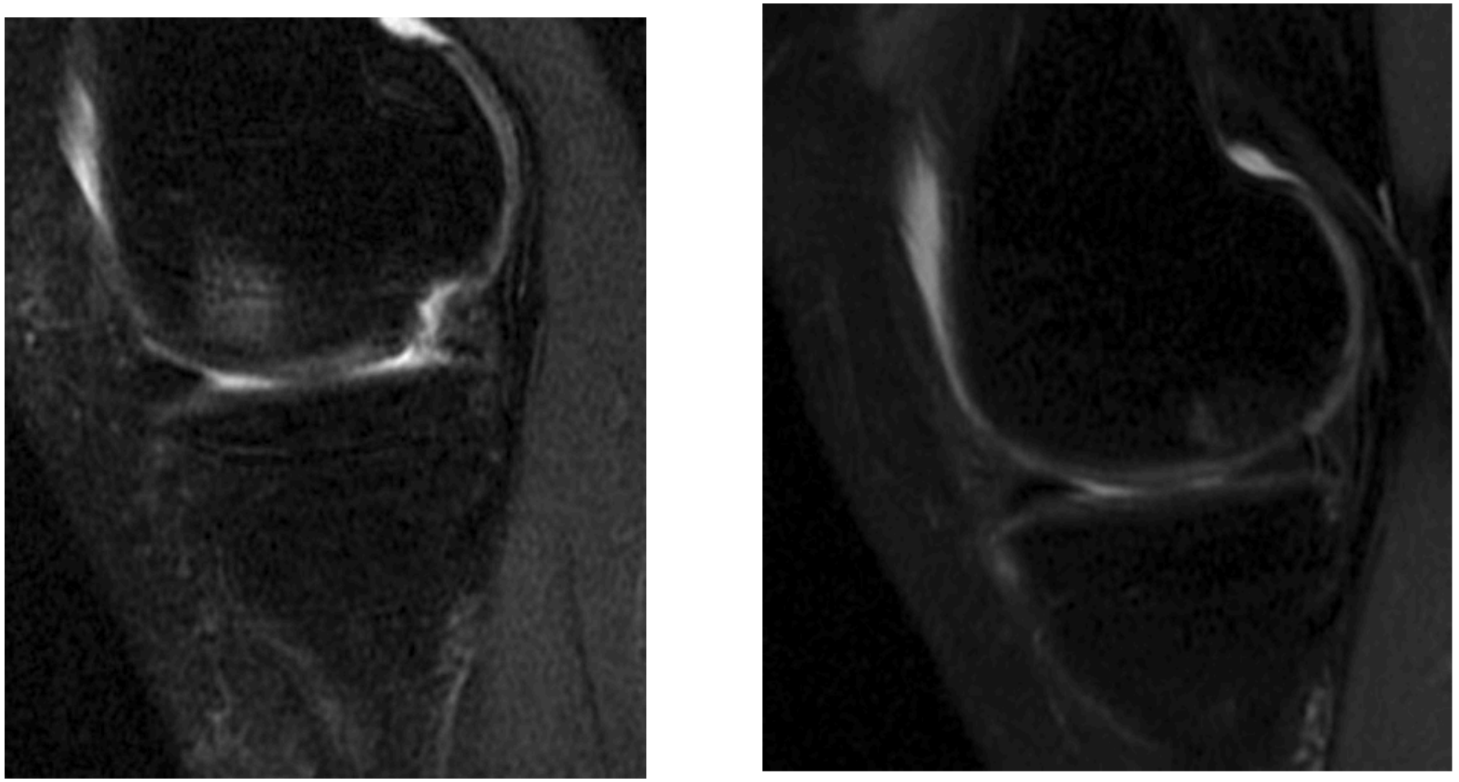
MAIOREGEN



MAIOREGEN



MESENCHYMAL STEM CELLS

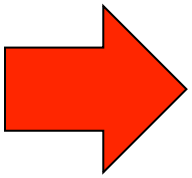


3 years of FU, improvement of clinical result,

comparable to those achieved with ACI

Buda R, Muscoloskelet Surg, 2013

MESENCHYMAL STEM CELLS



Necessary to clarify:

1. Potential risk of in MSCs use

2. The proper cell dosage to be administered

3. The effect of therapeutic agents

(growth, transcription or signallling factors)

Filardo G, Knee Surg Sports Traumatol Arthrosc, 2013

SUMMARIZING…..

- Articular cartilage is a nearly frictionless system with unique biomechanical properties with a bad intrinsic reparative process

- The management of articular cartilage lesions is complex and multifactorial

SUMMARIZING…..

1-2 cm^2:	Low activity	debridment
	High activity	MF/OAT
2-4 cm^2:	Low activity	Debridment/MF
	High activity	ACI/OAT/Regenerative
4-10 cm^2:	Low activity	Debridment
	High activity	ACI/Regenerative
>10 cm^2:	Osteochondral allograft	

TAKE HOME MESSAGES

- Micro-fracture and osteochondral autograft transplantation can provide a faster clinical and functional results
- Regenerative treatments represent a promising modern new approach
- Stem cells and tissue engineering can be the future?

In any case we need more data

KNEE OSTEOCHONDRAL LESION

CONSERVATIVE TREATMENT

Mild pain or when the risk of surgey is greater than beneficts

- Non steroid anti infiammatory drugs (NSAIDs)
- intra articular injection of steroid or hyaluronic acid
- physical treatment

KNEE OSTEOCHONDRAL LESION

CONSERVATIVE TREATMENT

In 14 years of FU patients had good

or excellent clinical results,

but radiographic examination revealed

abnormal findings in >50% of patients

Messner K, Acta Orthop Scan, 1996