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Atelocollagen-associated Autologous Chondrocyte Implantation for the Repair of Large Cartilage Defects of the Knee: Results at 3 to 7 Years

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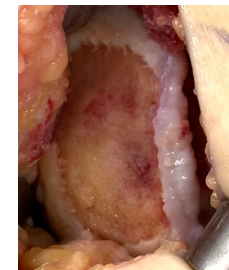
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COI disclosure

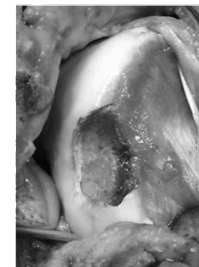
TAKUMA KAIBARA, M.D.

We have no financial conflicts to disclose

- Various surgical techniques for the cartilage lesions in the knee
 - ✓ Autologous chondrocyte implantation (ACI)
 - One of the best candidates for treating large cartilage defects
- Atelocollagen-associated ACI (**A-ACI**)
 - ✓ Utilizing atelocollagen as a matrix to culture the harvested chondrocytes in three dimensions [1]
 - ✓ Favorable clinical outcomes [2-4]
 - ✓ The only ACI covered by Japanese Health Insurance since 2013
- The indications of the **A-ACI**
 - ✓ Trauma or osteochondritis dissecans (OCD) for knee joints
 - ✓ Cartilage defect area $> 4 \text{ cm}^2$
- Previous studies on the **A-ACI** had included patients with off-label indications [2-4]
 - ✓ Osteoarthritis
 - ✓ Cartilage defect area $< 4 \text{ cm}^2$



20x30 mm



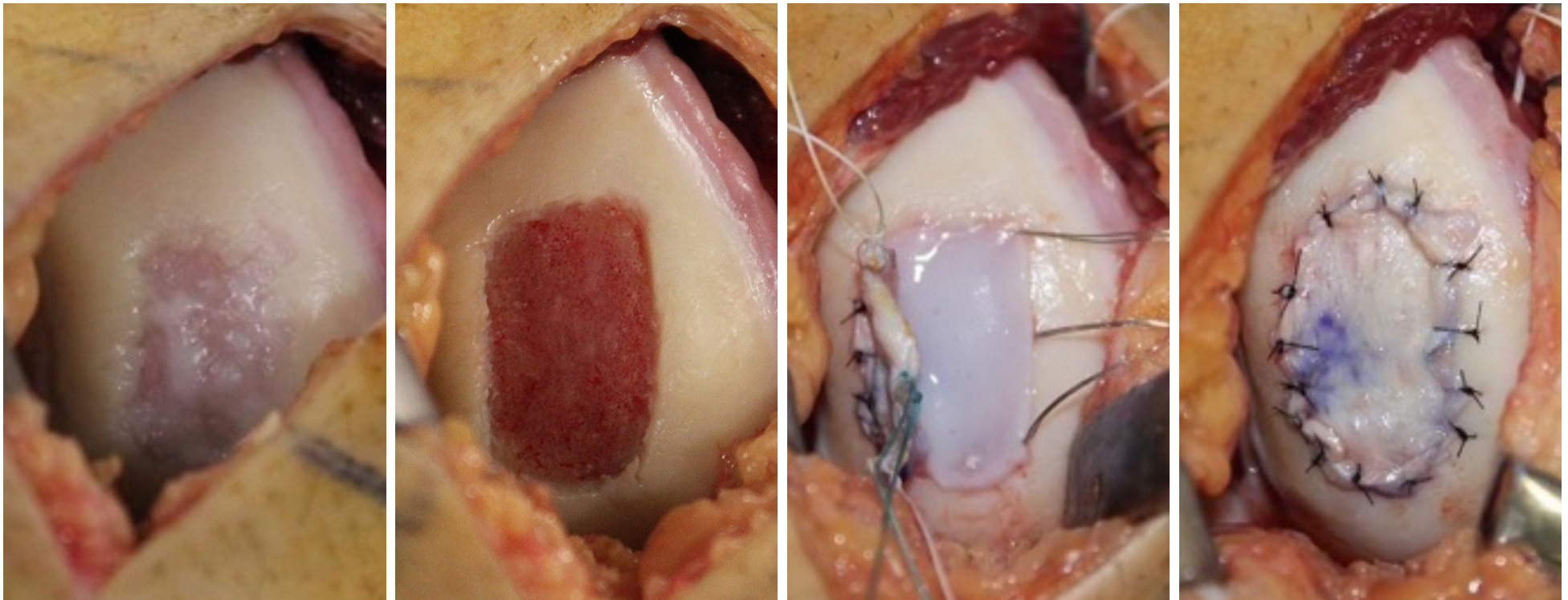
15x15 mm



10x20 mm

- Purpose

- ✓ To evaluate midterm clinical results after A-ACI for the treatment of large-sized and full-thickness cartilage defects of the knee

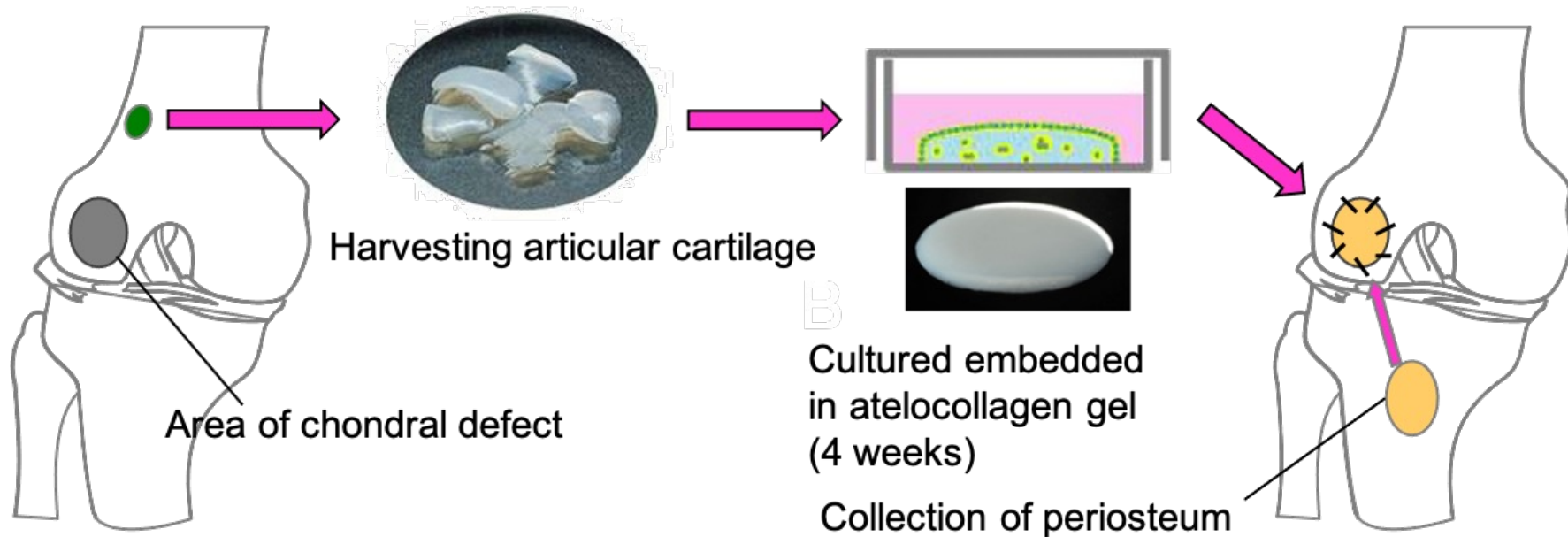


- 13 patients who underwent A-ACI (2014-2018)
 - ✓ Sex: 11 men, 2 women
 - ✓ Mean age: 34 (15-52) years
 - ✓ Causes of the cartilage defect
 - Trauma: 10 knees, OCD: 3 knees
 - ✓ Lesion site
 - MFC: 5 knees, LFC: 5 knees, Femoral trochlea: 5 knees
 - ✓ Mean lesion size: 5.3 (4.0-10.5) cm²
 - ✓ Mean F/U periods: 51 (36-84) months
- Clinical evaluation
 - ✓ Lysholm score, Knee injury and Osteoarthritis Outcome Score (KOOS)
- MRI evaluation
 - ✓ Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) 2.0
- Arthroscopic evaluation
 - ✓ Oswestry Arthroscopy Score (OAS), ICRS score
- Histological evaluation
 - ✓ H&E, Safranin-O
 - ✓ International Cartilage Repair Society (ICRS) II score

- Surgical procedure

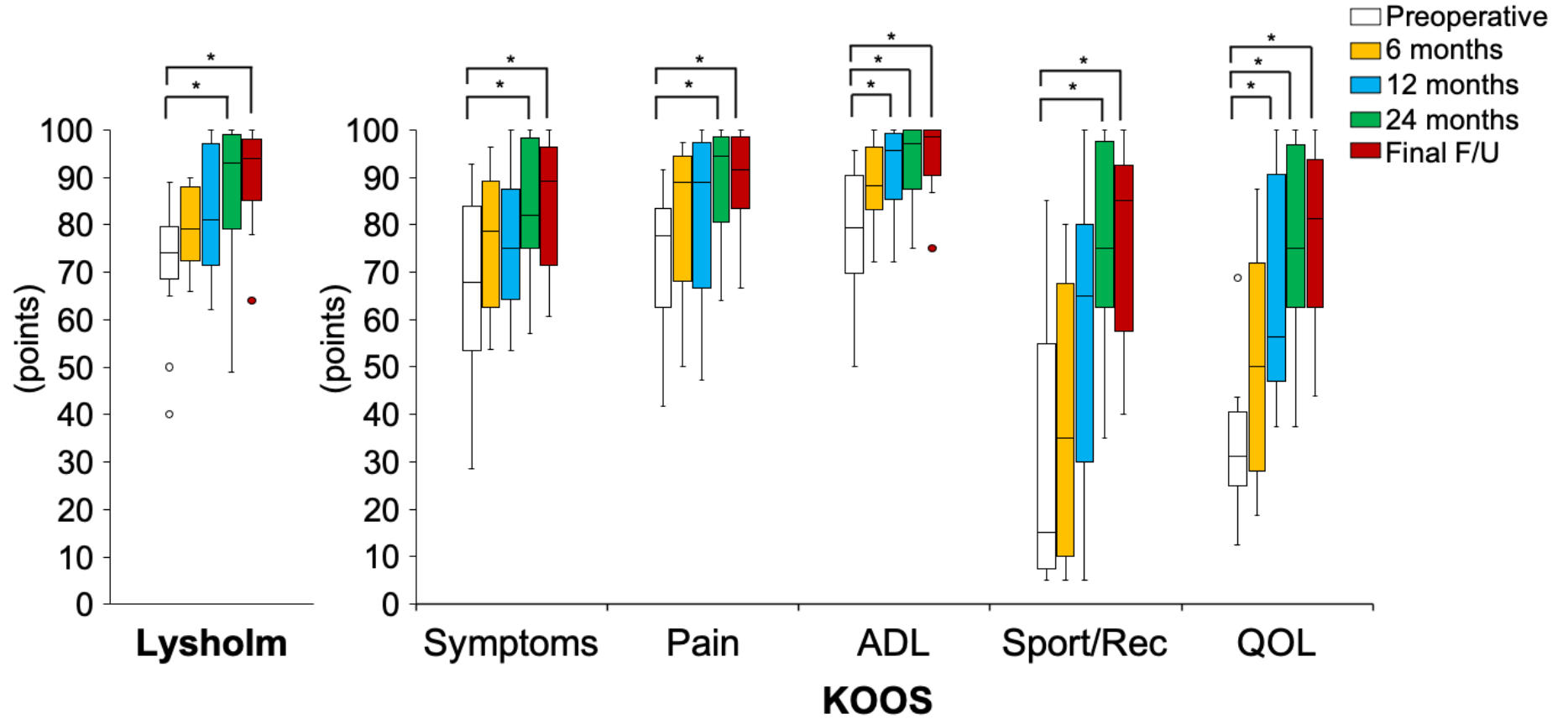
- ✓ Patients underwent a 2-stage process

- 1st step: Harvesting articular cartilage from a NWB area of the femur
 - The chondrocytes were cultured in an atelocollagen for 4 weeks
- 2nd step: Implantation of tissue-engineered cartilage into a cartilage defect and covering it with a periosteal flap



- Clinical outcomes

- ✓ Lysholm score, KOOS

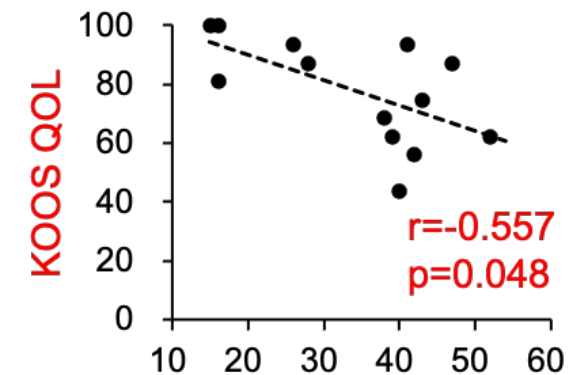
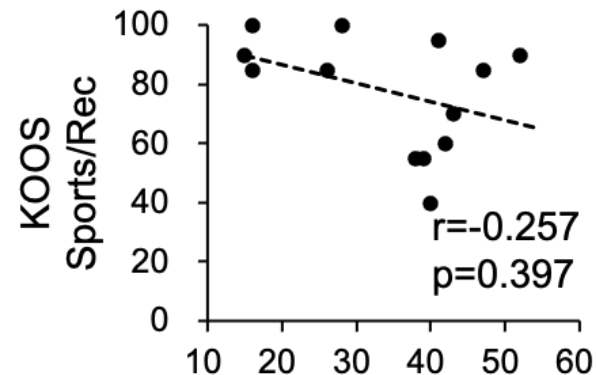
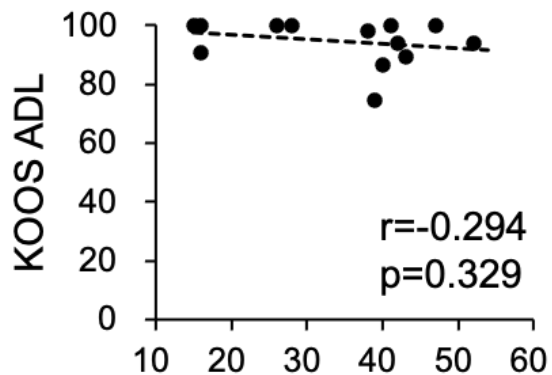
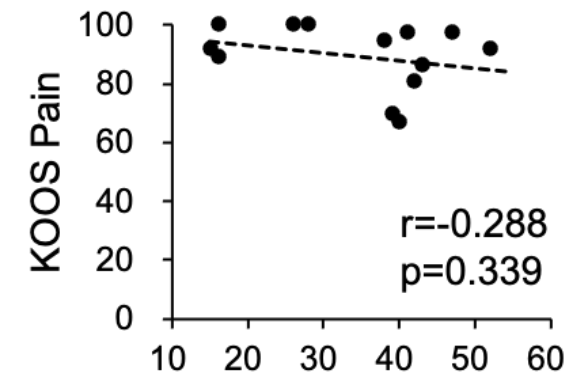
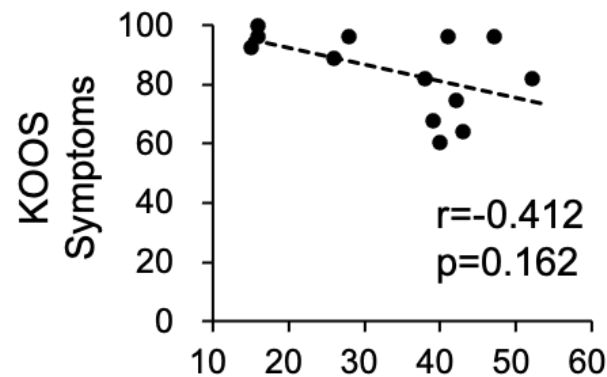
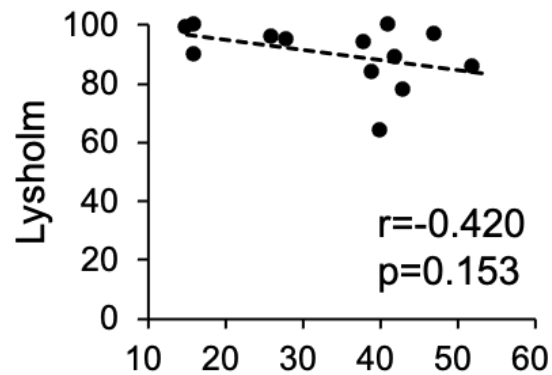


- ✓ Tegner activity scale

- Pre: 6.2 +/- 1.4 points

- Post: 5.7 +/- 1.5 points

- Correlation between demographic characteristics and clinical outcomes
 - ✓ Negative tendencies in correlation between age and clinical outcomes
 - ✓ A significant negative correlation between age and KOOS QOL subscale



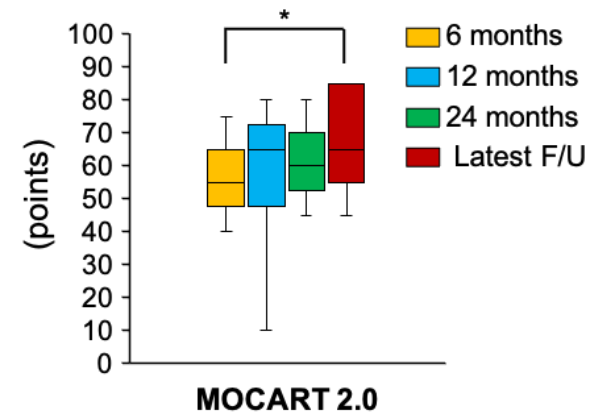
Age

- MRI evaluation

- ✓ MOCART 2.0

- The highest score at the mean latest follow-up of 38 months

- ✓ Hypertrophy: 4 grafts (27%)



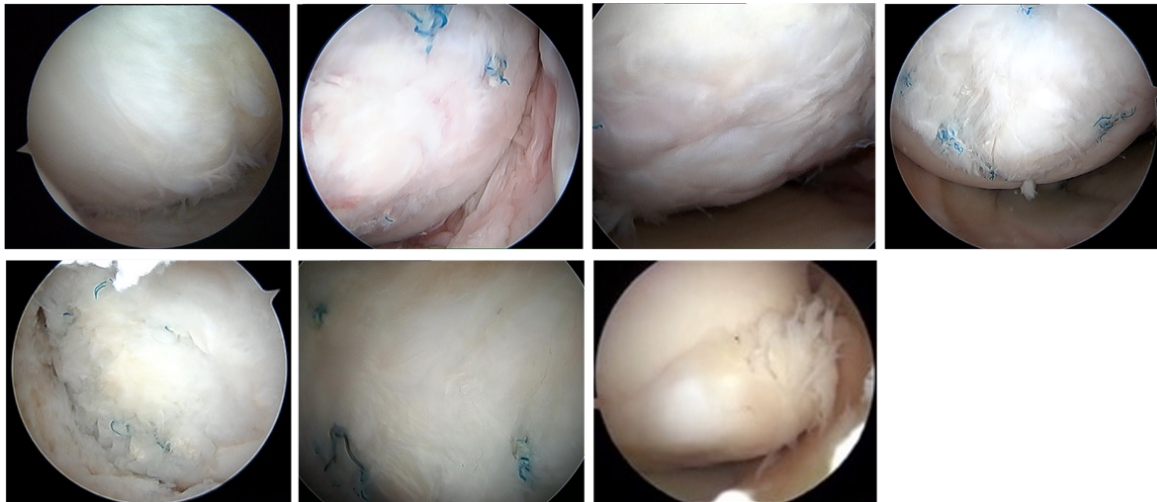
- Second-look arthroscopy (7/13 knees)

- ✓ At a mean of 22 (8-41) months after implantation

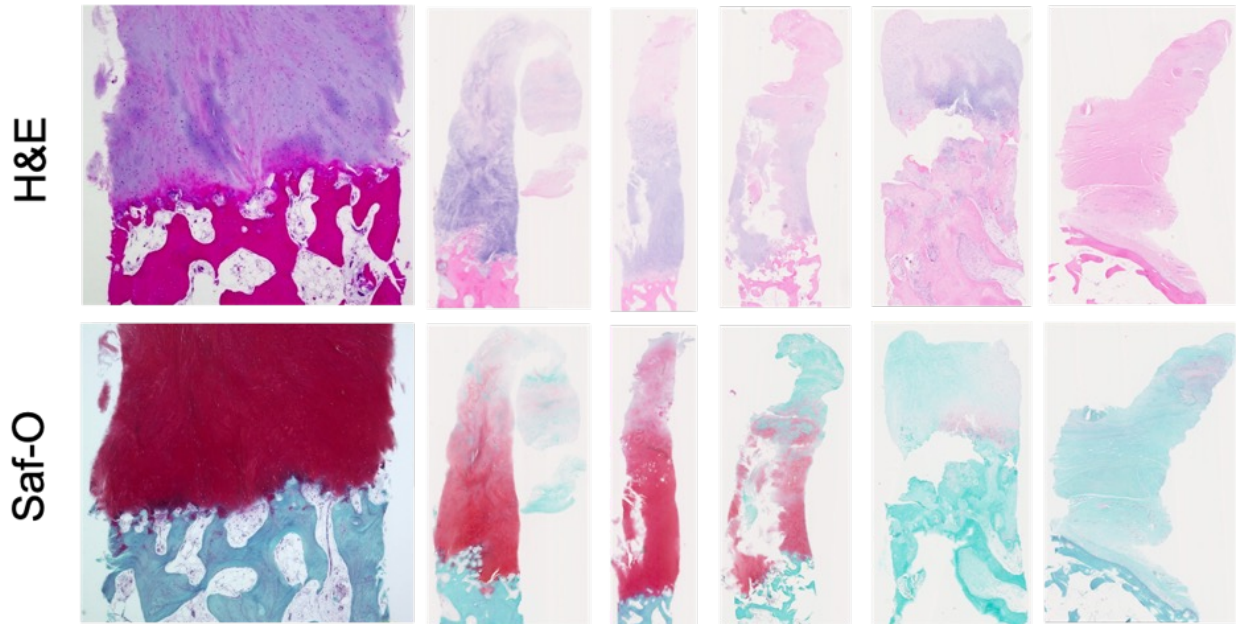
- ✓ OAS: 7.9 +/- 2.1 points

- ✓ ICRS: 10.1 +/- 3.6 points

- Normal: 3 knees ➤ Nearly normal: 3 knees ➤ Severely abnormal: 1 knee



- Histological evaluation (6/13 knees)
 - ✓ Cartilage-like tissues in 5 specimens
 - Safranin-O staining
 - Strong: 3 specimens
 - Partial: 2 specimens
 - ✓ Fibrous tissue with blood vessel: 1 specimen
 - ✓ ICRS II score
 - Overall assessment: 75 points at the median (10-90)

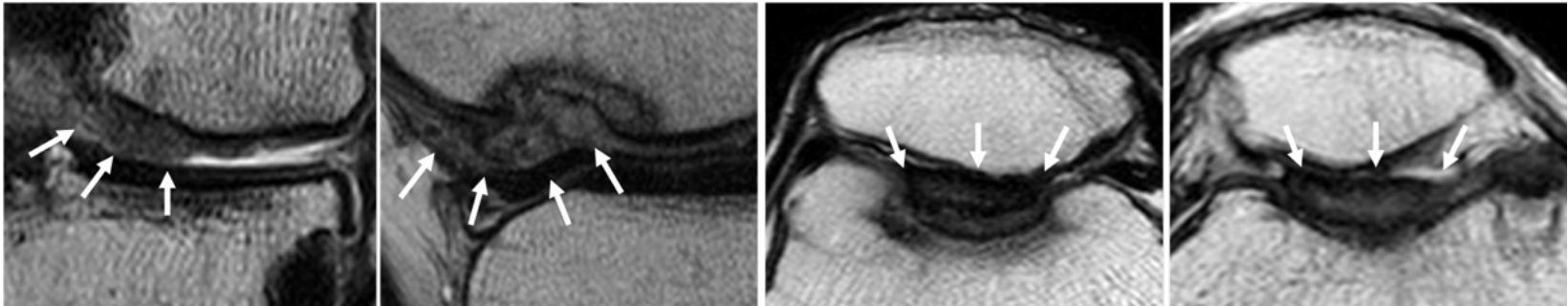


ICRS II Parameter	ICRS II score
	Median (range)
Tissue morphology	50 (15-70)
Matrix Staining	65 (10-90)
Cell Morphology	70 (5-80)
Chondrocyte clustering	100 (100)
Architecture of Surface	97.5 (70-100)
Basal Integration	90 (30-100)
Calcification Front/Tidemark	45 (0-60)
Subchondral Bone	95 (0-100)
Abnormalities	
Abnormal Calcification	100 (100)
Inflammation	100 (100)
Vascularization in Repair	100 (5-100)
Tissue	
Surface/Superficial Assessment	30 (10-90)
Mid//Deep Zone Assessment	50 (10-80)
Overall Assessment	75 (10-90)

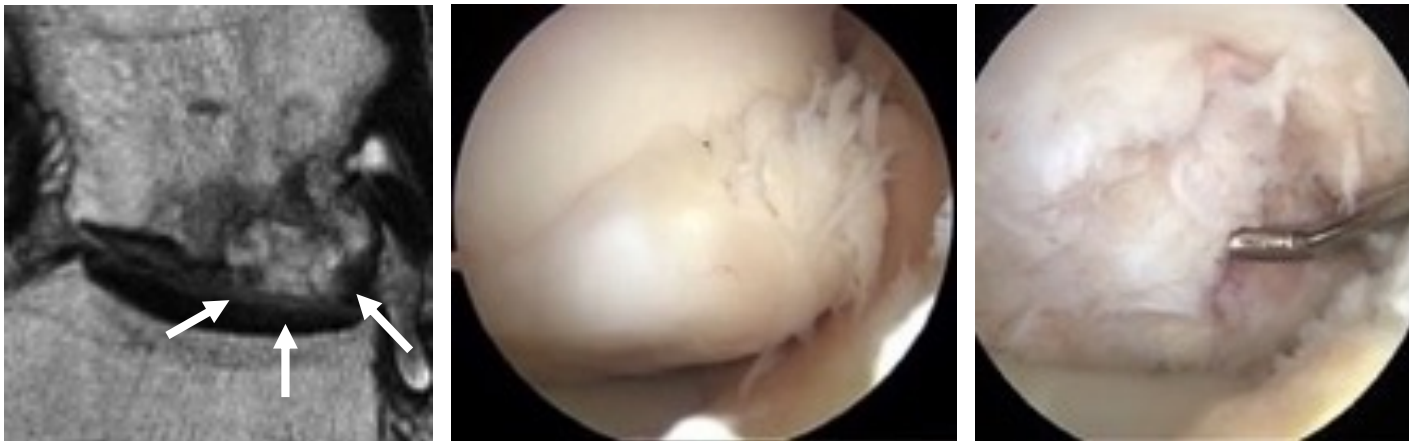
- Complications

- ✓ Revision arthroscopy: 5 patients (38%)

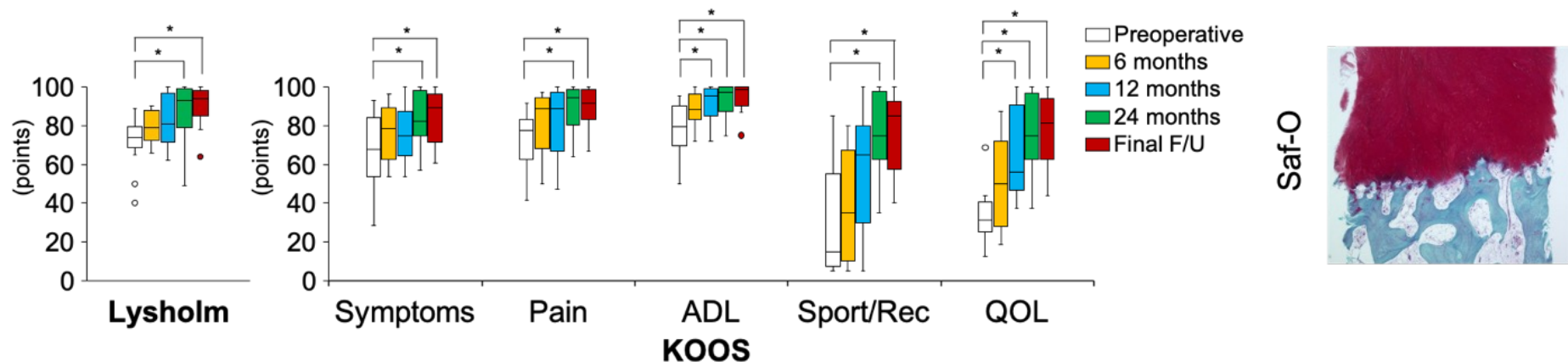
- Symptomatic graft hypertrophy: 4 knees



- Partial graft detachment: 1 knee



- The A-ACI for the treatment of large-sized and full-thickness cartilage defects of the knee in 15 lesions
 - ✓ A significant improvement of clinical scores @ a minimum 3-year f/u
 - ✓ A significant higher MOCART score @ the mean f/u of 38 months
 - ✓ “Normal” or “nearly normal” arthroscopic appearance
 - ✓ Cartilage-like tissue stained with safranin-O in 83% of specimens



- Transplanting chondrocytes embedded in a 3-dimensional atelocollagen gel matrix (A-ACI) promotes the restoration of the articular cartilage of the knee

- Complications

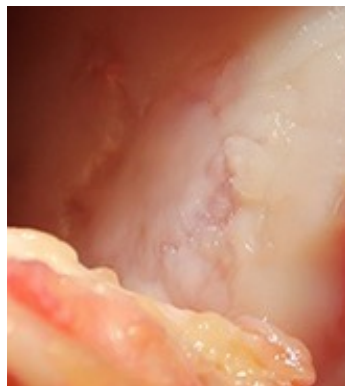
- ✓ Revision arthroscopy for symptomatic graft hypertrophy or partial graft detachment in 5 patients (38%)

- Rate of complications and failures after A-ACI: 11-30% [2-4]
- Graft hypertrophy after ACI: 9-40%
 - Higher risk in periosteum-covered ACI [6, 7]



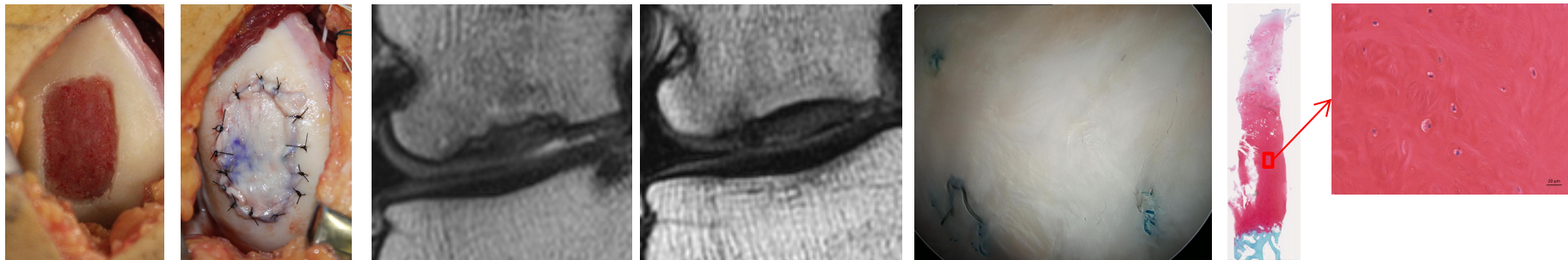
- ✓ The case with partial graft detachment

- Previous AOT for OCD
- Sclerotic subchondral bone bed
 - Inferior outcomes in ACI after a failed bone marrow stimulation compare to primary ACI because of altered subchondral bone bed [8, 9]



● Conclusion

A-ACI provided satisfactory clinical, radiological, and histological outcomes for the repair of large-sized cartilage defects of the knee @ a minimum follow-up period of 3 years



● References

- [1] Ochi et al. Artif Organs 2001
- [2] Tohyama et al. J Orthop Sci 2009
- [3] Adachi et al. Knee Surg Sports Traumatol Arthrosc 2014
- [4] Takazawa et al. J Orthop Sci 2012
- [5] Niethammer et al. Am J Sports Med 2018
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- [8] Minas et al. Am J Sports Med 2009
- [9] Pestka et al. Am J Sports Med 2012