Development of Osteochondral Treatment Using iPS Cell-Derived Cartilage Tissue + Artificial Bone Complex for Osteoarthritis of the Knee

Akihiko Ezaki[1)2)]、Teruya Ishibashi[3)]、Seira Sato[4)]、Tomoki Ohori[2)]、Akira Tsujii[5)]、Masashi Tamaki[3)]、Seiji Okada[2)]、Noriyuki Tsumaki[1)]

1）Laboratory of Tissue Biochemistry, Graduate School of Frontier Biosciences, Osaka University
2）Orthopedic Surgery Osaka University Graduate School of Medicine
3）Orthopaedic Biomaterial Science Osaka University Graduate School of Medicine
4） Sports Medical Science Osaka University Graduate School of Medicine
5） Sports Medical Biomechanics Osaka University Graduate School of Medicine

ISAKOS CONGRESS 2025
COI Disclosure Information

Presenter : Akihiko Ezaki

I have no financial relationships to disclosure.

Introduction

Current Treatments for Cartilage Injuries

	Microfracture (MF)	Mosaicplasty (OAT)	Autologous Chondrocyte Implantation (ACI)
Repair tissue	fibrocartilage	hyaline cartilage	fibrocartilage
Defect size	＜2cm²	＜4cm²	4cm²≦
Problems	Repair with fibrocartilage	Damage to normal tissue and size limitations	2 surgeries required

- Autologous osteochondral transplantation shows good outcomes

Nakagawa, Y, et al. Am. J. Sports Med. 2016

⇔Limitations：damage to healthy tissue and size limitations

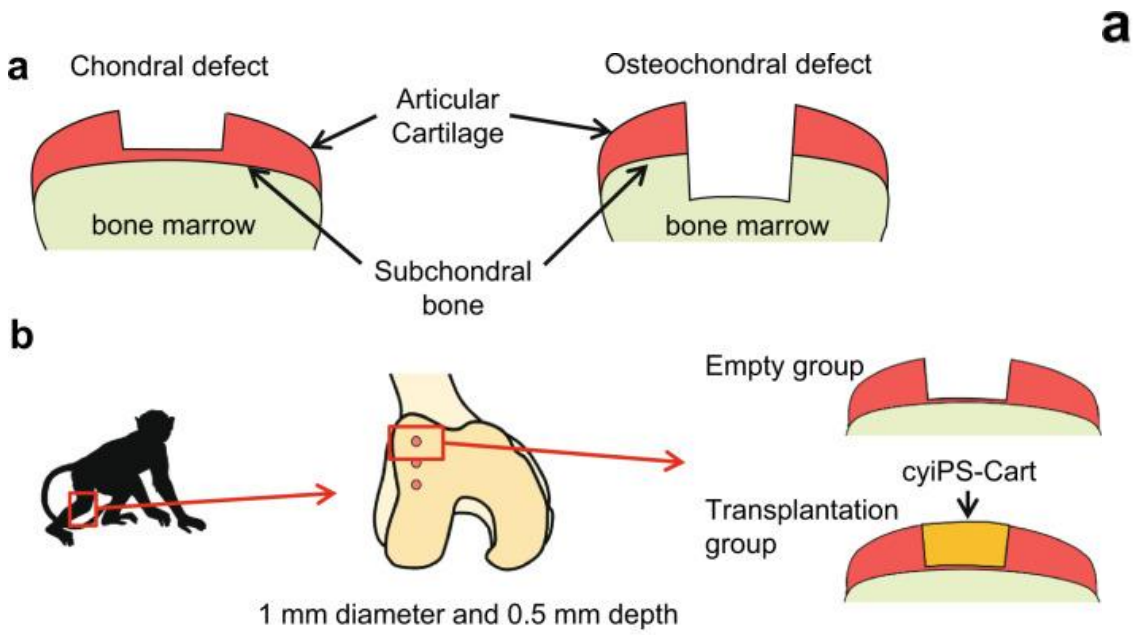
Hangody L, et al. JBJS. Am. 2003

- Treatment choice depends on defect size

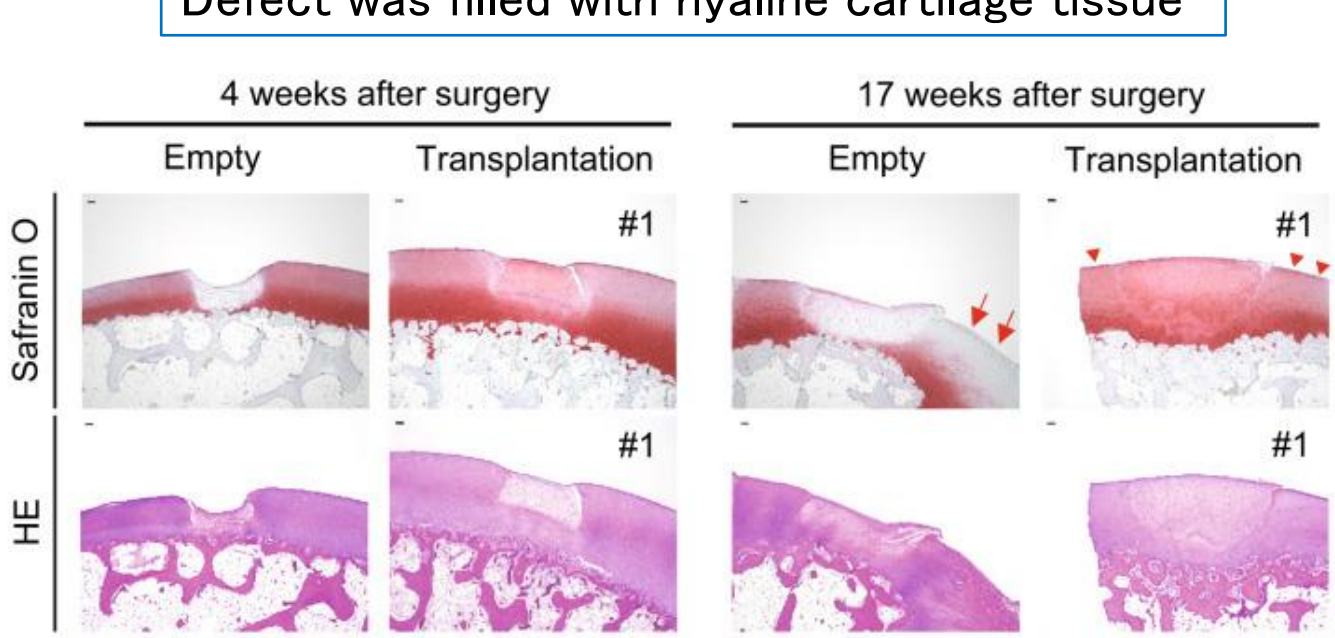
Hinckel BB, et al. Cartilage. 2021

Previous Studies

Cartilage Defect Model in Cynomolgus Monkeys
Allogeneic transplantation of iPS cell–derived cartilage tissue



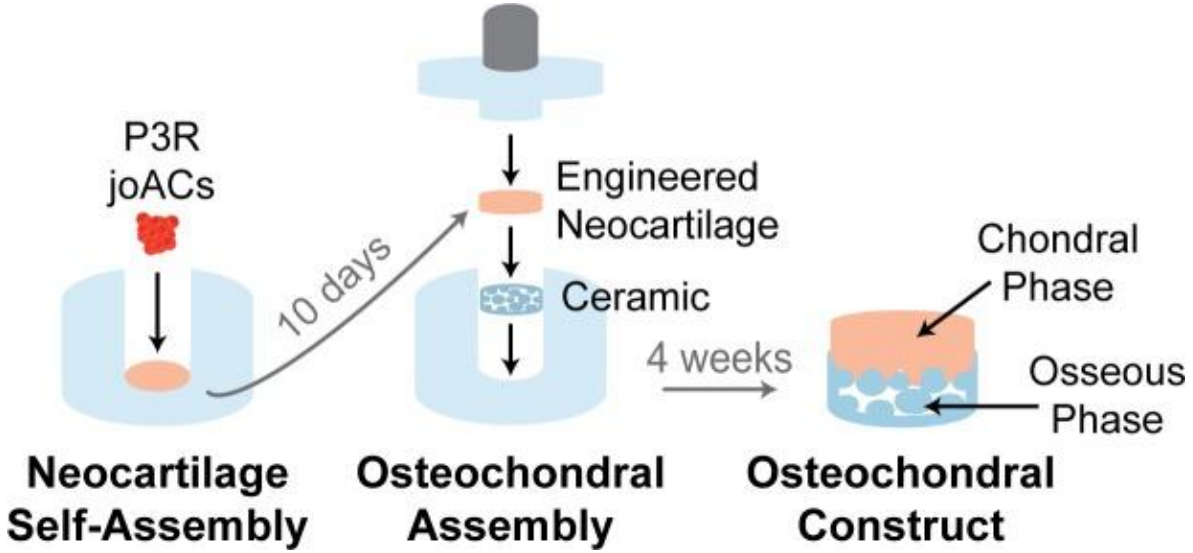
Defect was filled with hyaline cartilage tissue

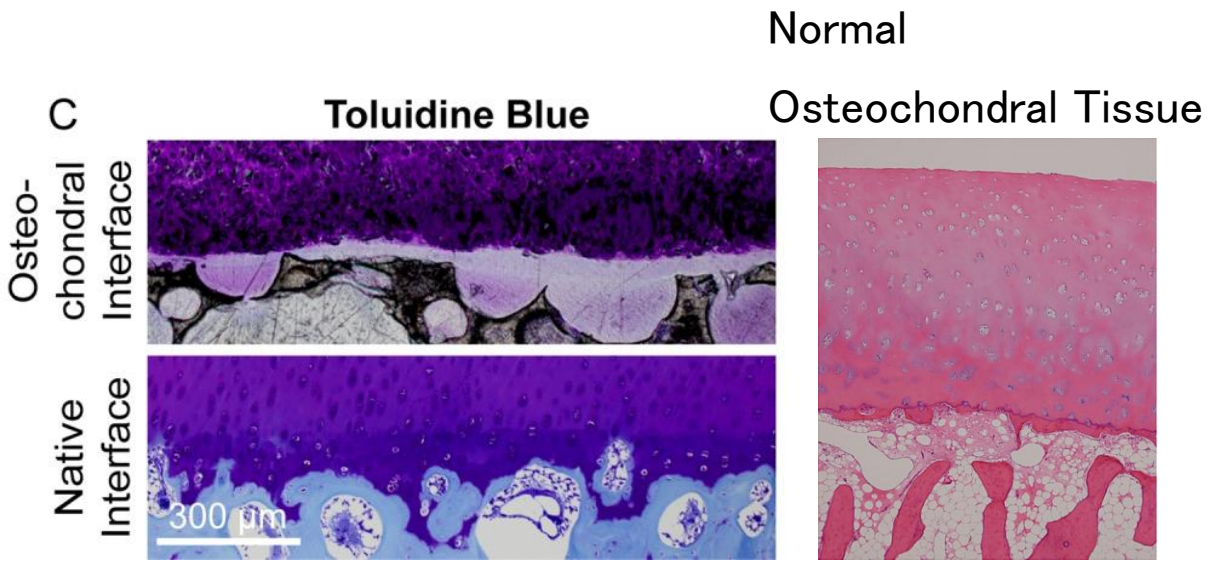


Abe K et al. Nature Communications 2023

Challenges:
fixation method and limited indications to cartilage defects

Past Reports





- Complex created using juvenile sheep chondrocytes on ceramics
- Poor tissue infiltration into ceramics → Incomplete complex

W Brown et al. PLoS One April 2018

- No reports on iPS cartilage + artificial bone complex

Potential treatment for advanced osteoarthritis (OA)

				
K-L Grade	Ⅰ	Ⅱ	Ⅲ	Ⅳ

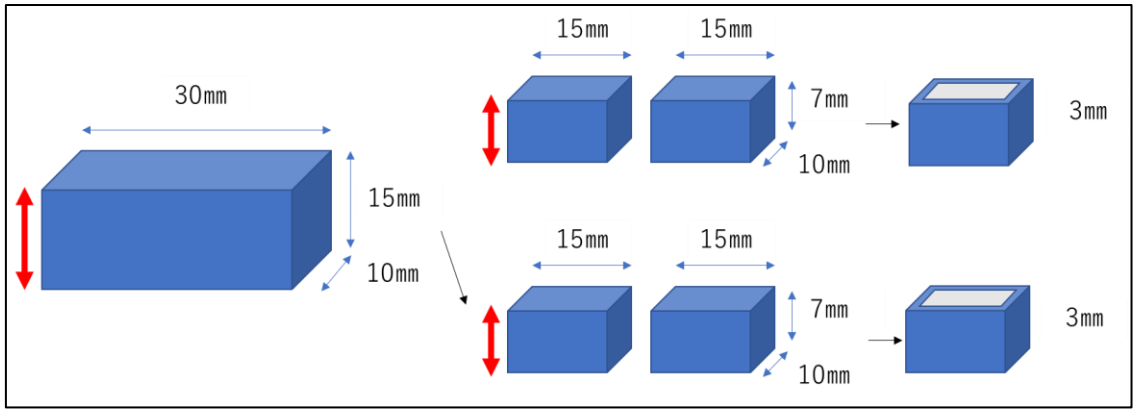
Knee osteotomy

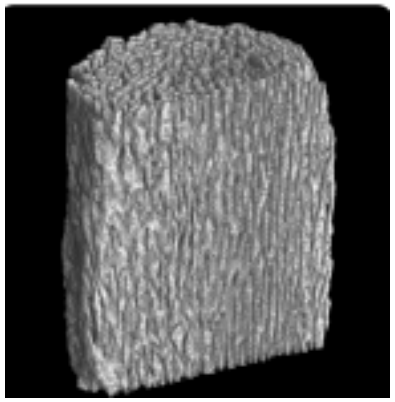
Total knee arthroplasty

iPS cell-derived cartilage tissue transplantation ?

iPS cartilage + artificial bone complex

Materials & Methods





artificial bone

37℃, 10 min

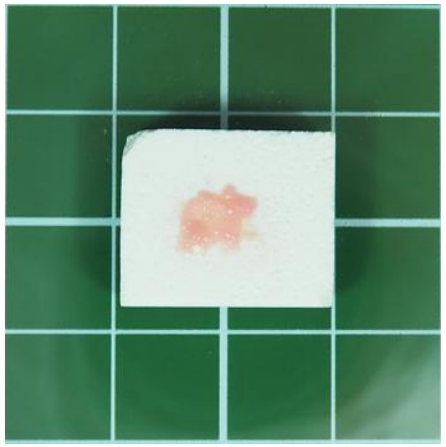
3–week differentiated particles grounded

Agitated culture

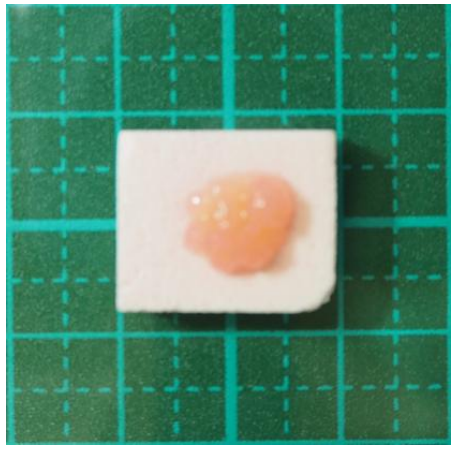
Assessment

- ✓ Evaluated differentiation period (3 vs. 7 weeks) and artificial bone materials
- ✓ Histological evaluation

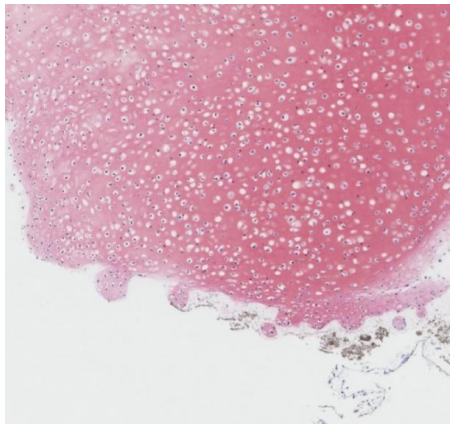
Results：Optimal Differentiation Period for Grounding



3-week differentiation

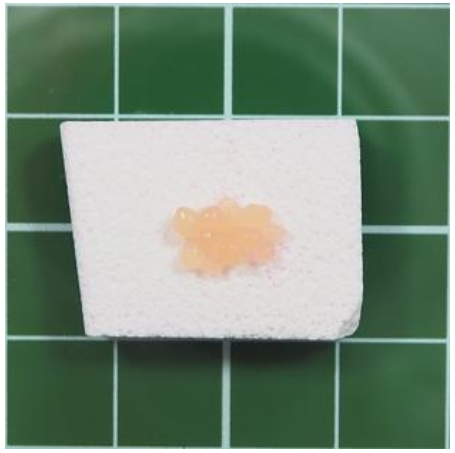


Stable



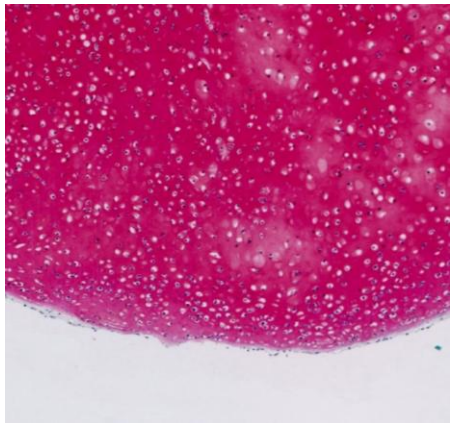
Saf-O

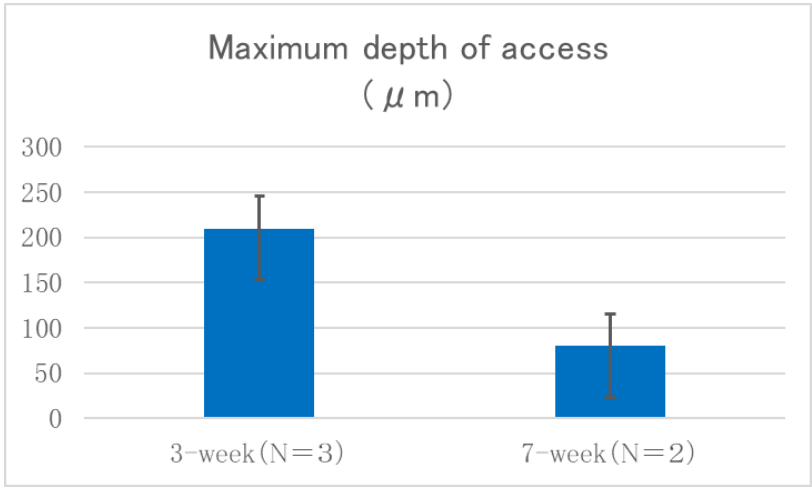
2 weeks later



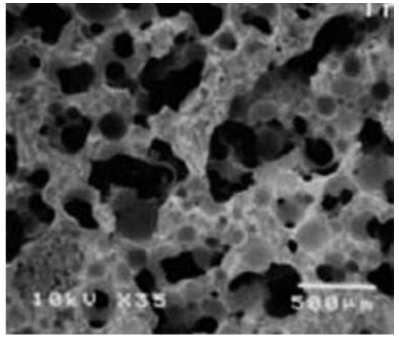
7-week differentiation

Partial adhesion





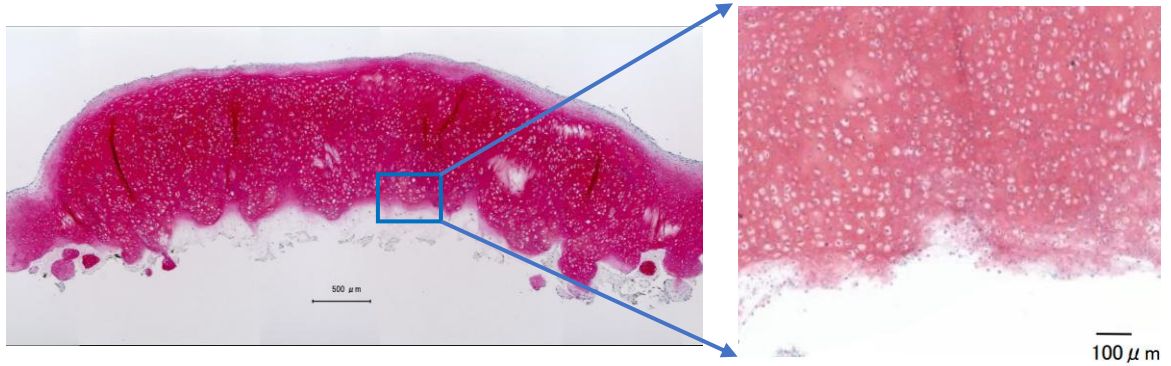
Results：Suitable Artificial Bone for Complex



Osferion

Porosity：60%

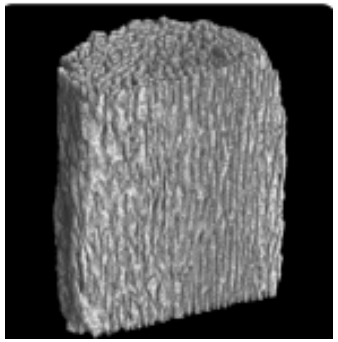
Randomly sized pores



3 weeks after differentiation

+17-weeks culture

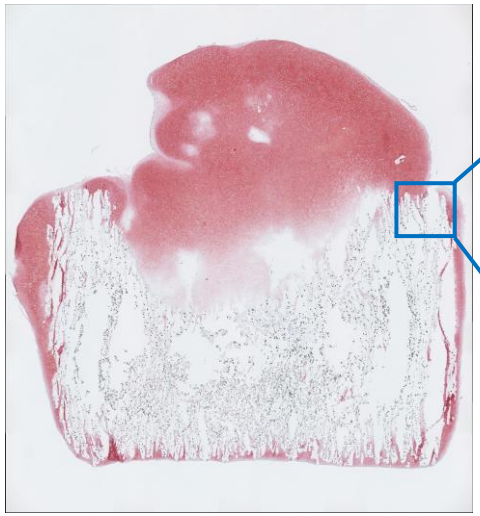
Saf-O

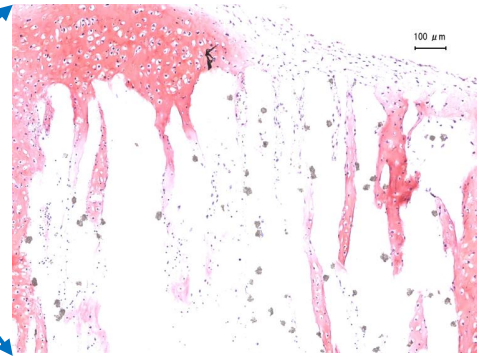


Affinos

Porosity：57%

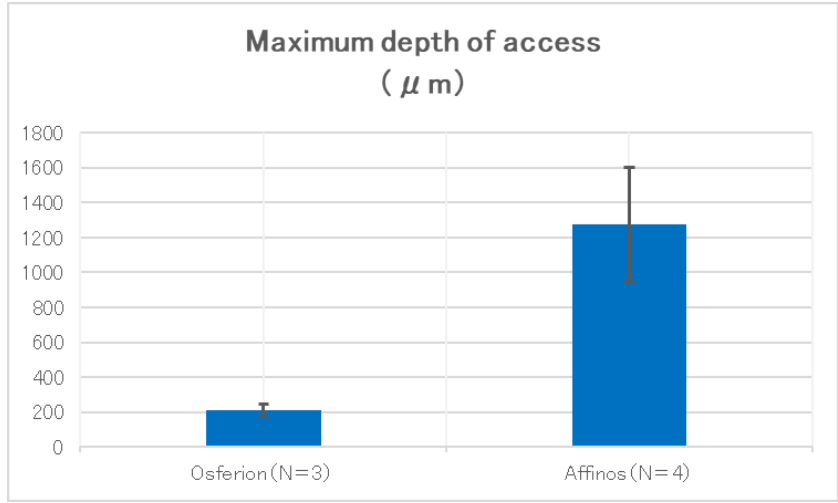
Vertical through-holes



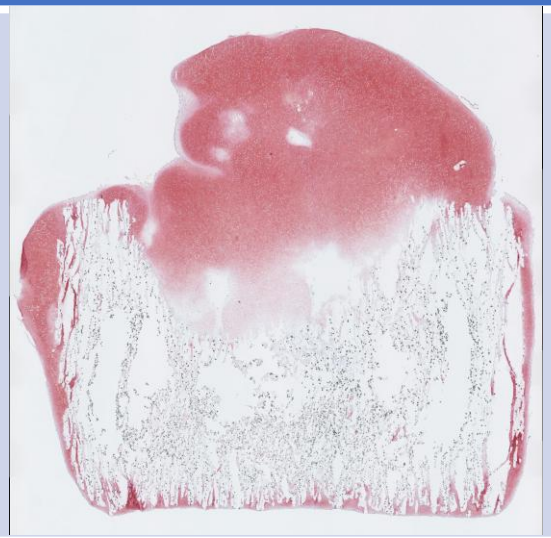


3 weeks after differentiation

+10-weeks culture



Results : Histology

Saf-O	COL1
	
COL2	**PRG4**
	

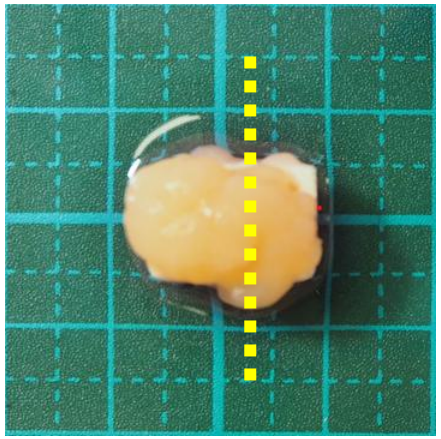
Stained on the surface

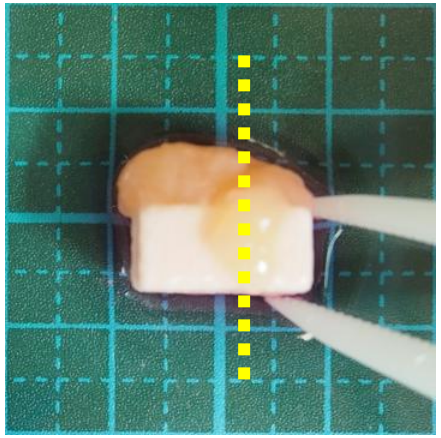
Stained throughout the tissue

Stained on a Cavity

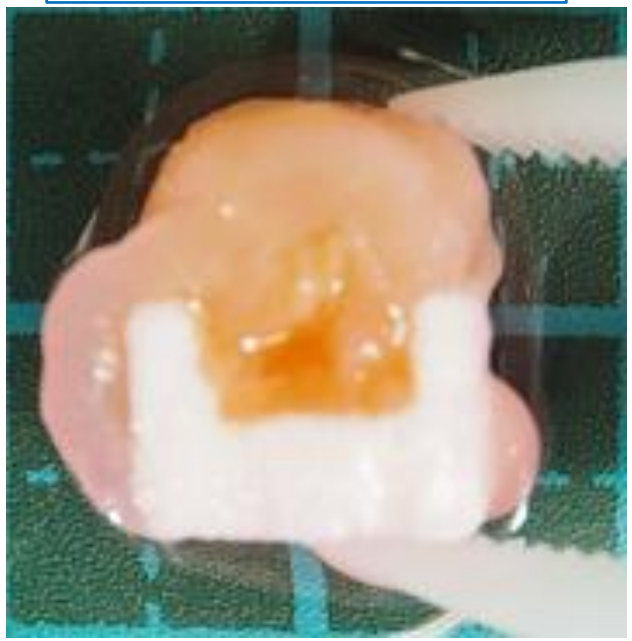
Challenge : Cavity formation in the central area

10-week culture



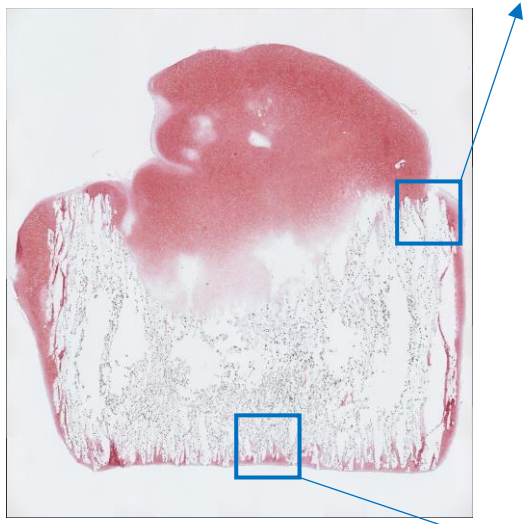


Tissue Cross Section

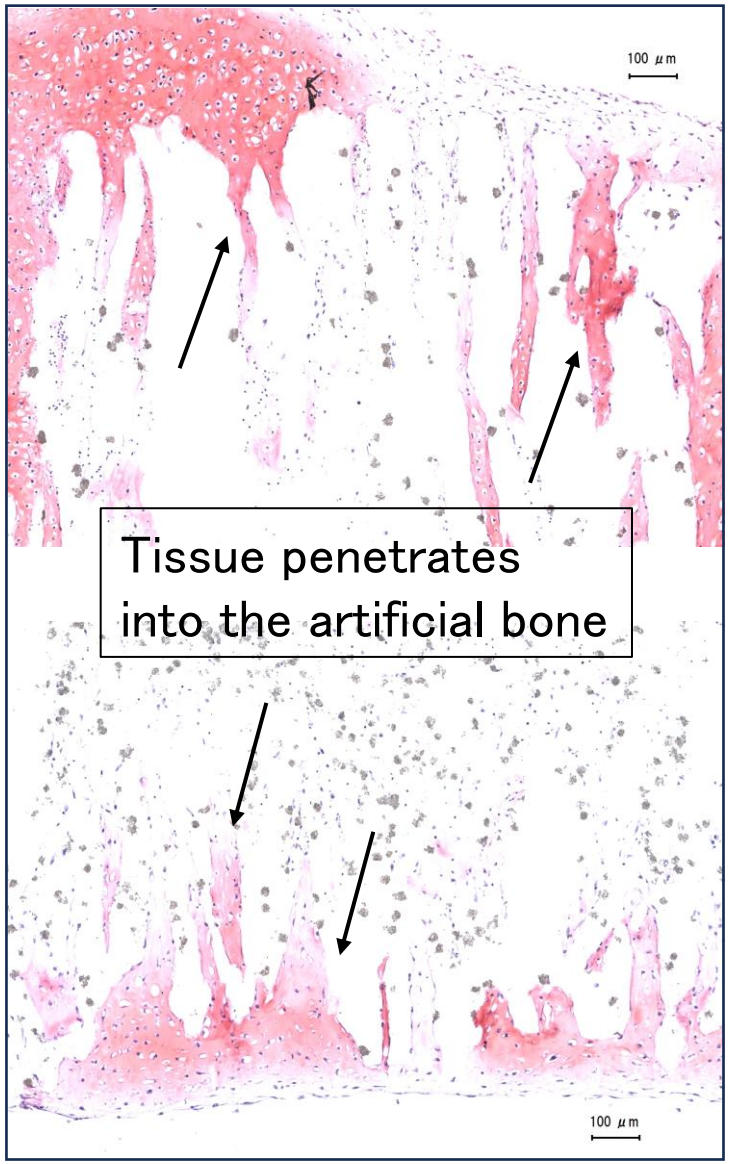


Particle shape remains in tissue center

Saf-O



- No penetration from the ground
- Penetration from the outer wall



Conclusion

- By co-culturing artificial bone and iPS cell-derived cartilage Particles, the tissue entered the artificial bone while maintaining the properties of cartilage tissue.
- Younger tissue at the week of differentiation grows better and penetrates deeper
- The interconnected pores in the artificial bone contributed to the deep penetration of the tissue

Reference

1. Yasuaki Nakagawa, Shogo Mukai, Hiromitsu Yabumoto, Eri Tarumi, Takashi Nakamura. Serial Changes of the Cartilage in Recipient Sites and Their Mirror Sites on Second-Look Imaging After Mosaicplasty. Am J Sports Med. 2016 May;44(5):1243-8. doi: 10.1177/0363546516634299. Epub 2016 Mar 28.PMID: 27022060
2. Hangody L, Füles P. Autologous osteochondral mosaicplasty for the treatment of full-thickness defects of weight-bearing joints: ten years of experimental and clinical experience. J Bone Joint Surg Am. 2003;85-A Suppl 2:25-32. doi: 10.2106/00004623-200300002-00004.PMID: 12721342
3. Hinckel BB, Thomas D, Vellios EE, Hancock KJ, Calcei JG, Sherman SL, Eliasberg CD, Fernandes TL, Farr J, Lattermann C, Gomoll AH. Algorithm for Treatment of Focal Cartilage Defects of the Knee: Classic and New Procedures. Cartilage. 2021 Dec;13(1_suppl):473S-495S. doi: 10.1177/1947603521993219. Epub 2021 Mar 20.PMID: 33745340
4. Abe K, Yamashita A, Morioka M, Horike N, Takei Y, Koyamatsu S, Okita K, Matsuda S, Tsumaki N. Engraftment of allogeneic iPS cell-derived cartilage organoid in a primate model of articular cartilage defect. Nat Commun. 2023 Feb 20;14(1):804. doi: 10.1038/s41467-023-36408-0.PMID: 36808132
5. Brown WE, Huey DJ, Hu JC, Athanasiou KA. Functional self-assembled neocartilage as part of a biphasic osteochondral construct. PLoS One. 2018 Apr 10;13(4):e0195261. doi: 10.1371/journal.pone.0195261. eCollection 2018.PMID: 29634740