Costal chondrocyte-derived pellet-type autologous chondrocyte implantation versus microfracture for repair of articular cartilage defects

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Purpose

Limitation of 1st generation ACI

- Cell Source: <u>Articular Cartilage</u>
 - ✓ Only available to young patients
 - \checkmark Limitation of donor tissue
 - ✓ Donor site morbidity → post traumatic OA
- Limitation of <u>Cell Expansion</u>
 - ✓ Dedifferentiation: chondrocyte → fibroblast-like cell
 - ✓ Cell senescence
- Suspension-Type
 - ✓ Low mechanical property
 - \checkmark Long processing time
 - ✓ Periosteal flap: periosteum-related complications

Limitation of 2nd, 3rd generation ACI

- Cell Source: <u>Articular Cartilage</u>
- Limitation of <u>Cell Expansion</u>
- <u>Xenogeneic or synthetic polymer</u> based scaffold
 - ✓ Biocompatibility
 - ✓ Immune reaction/Inflammation
 - ✓ Intractable degradation rate
 - ✓ Harmful degradation products
 - ✓ Uneven cell distribution & attachment
 - ✓ Scaffold variability

To study the efficacy and safety results at 5 years after treatment with scaffold-free costal chondrocyte-derived pellet-type autologous chondrocytes implantation for repair of articular cartilage defects of the knee.

Methods & Materials

PHASE II (2013. 09 ~ 2017. 02) in Korea

- RCT, Active control (microfracture), Multi-Center, Open-Label
- 5 centers 30 patients (CartiLife, 20 vs Microfracture, 10)
- F/U at postoperative 24, 48 weeks
- Inclusion Criteria:
 - Male or female patients, age: between 19 and 65 years
 - Defect size: 2 to 10 cm2 on the unilateral knee cartilage (≤ 4 cm3 in volume)
 - Defect: isolated ICRS grade III or IV single defect chondral lesions
- Exclusion Criteria:
 - Any evidence of the following diseases in the target joint : inflammatory joint disease, gout, autoimmune mediated arthritis
 - Advanced osteoarthritis (OA) : kellgren and Lawrence grade ≥ 3
- Primary outcome : MOCART score (48 weeks) by MRI
- Secondary outcome : IKDC subjective, Lysholm, KOOS, VAS score



Methods & Materials

Manufacturing Process of CCP-ACI

- The chondrocytes from a patient's own costal cartilage
- Followed by expansion culture and 3D pellet culture
- The manufacturing process takes about 4–7 weeks



Implantation procedure of CCP-ACI

Characteristics of CCP-ACI

- Solid, smooth, and glossy white pellets with diameters of 1.1 to 1.8 mm
- Histological and immunohistologic characteristics of typical hyaline cartilage



white dot line, pellet surface

- Image: Provide rest of the second second
- 1. Debridement of the damaged cartilage (No marrow stimulation)
- 2. The pellets are then implanted into the defect. During this step, the pellets were transplanted to the level of the adjacent cartilage
- 3. Fibrin glue is applied to the surface to fix the pellets in the defect

Demographics

	CCP-ACI group	MFx group	<i>p</i> -valu
Patient, n	20	10	
Gender, male/female, n (%)	14 (70)/6 (30)	3 (30)/7 (70)	n.s
Age, y, mean ± SD	41.5 ± 13.0	47.2 ± 10.8	n.s
< 50, n (%)	11 (55)	6 (60)	
≥ 50, n (%)	9 (45)	4 (40)	
Lesion site			
Condyle, n (%)	9 (45)	7 (70)	n.s
Trochlear, n (%)	11 (55)	3 (30)	
Aetiology			
Trauma, n (%)	10 (50)	0 (0)	0.007
Osteoarthritis [§] , n (%)	7 (35)	4 (40)	
Others, n (%)	3 (15)	6 (60)	
Defect area, cm^2 , mean \pm SD	3.5 ± 1.4	2.5 ± 0.4	n.s
< 4 cm ² , n (%)	15 (75)	9 (90)	
\geq 4 cm ² , n (%)	5 (25)	1 (10)	
Defect depth, mm, mean ± SD	4.6 ± 1.7	3.2 ± 1.4	n.s
< 6 mm, n (%)	16 (80)	10 (100)	
\geq 6 mm, n (%)	4 (20)	0 (0)	
Defect volume, cm^3 , mean \pm SD	1.6 ± 0.8	0.8 ± 0.4	0.001
$< 2 \text{ cm}^3, \text{ n} (\%)$	14 (70)	10 (100)	
$> 2 \text{ cm}^3 \text{ n}(\%)$	6 (30)	0(0)	



Clinical scores & MOCART Score







MOCART scores at week 24 and 48 were significantly greater in the CCP-ACI group than the MFx group. At 24 and 48 weeks after surgery, the rates of complete defect repair and complete integration in the CCP-ACI group were significantly greater than those in the MFx group.



MOCART & Clinical Score (5 year follow-up data)





MOCART & Clinical Score (5 year follow-up data)





MOCART & Clinical Score (5 year follow-up data)





MR Images of the CCP-ACI group at 5-year FU



High-resolution MRI evaluation to evaluate structural improvements induced by CCP-ACI transplantation. Red arrow, cartilage defect; Yellow arrow, regenerative cartilage.



Solution

Treatment of cartilage defects with CCP-ACI yielded better clinical and radiologic outcome compared to microfracture at 5 years.



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