



*Severance*



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# Particulated Costal Allograft with Microfracture Versus Microfracture Alone: a Multicenter, Prospective, Randomized, Participant- and Rater-blinded Study

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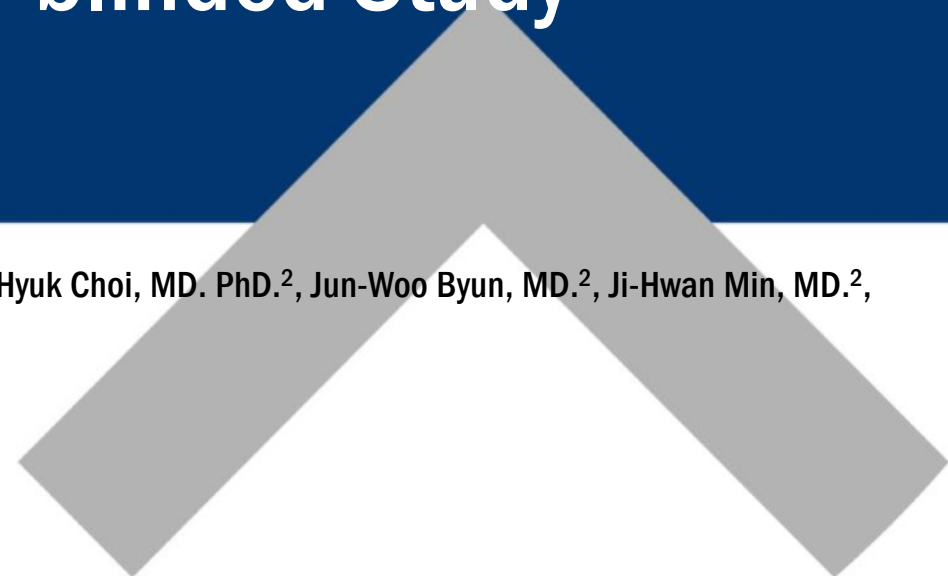
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# Disclosures

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# Introduction

- **Decellularized hyaline cartilage**
  - Potentially an **ideal scaffold** for cartilage regeneration
  - Resembles mechanical, biochemical, and structural properties of the native hyaline cartilage.
  - **Costal hyaline cartilage** could be another **emerging source of hyaline cartilage scaffold**
- **Necessity** of the study
  - **Only a few recent observational studies** reported favorable outcomes after microfracture with decellularized hyaline cartilage
  - Paucity of **high-quality randomized controlled clinical study**
  - No previously published work presenting the **result of the microfracture augmented with costal cartilage**
- The purpose of the study
  - **Compare the clinical efficacy and safety** between particulated costal allocartilage with microfracture and microfracture alone in treating knee cartilage defects.

# Hypothesis & Study design

- We hypothesized that
  - Combination of particulated costal allocartilage with microfracture would **result in superior cartilage repair quality** and **better clinical outcomes** compared to microfracture alone **at 48 weeks** post-operation for knee cartilage defects.
- **Multi-center, prospective, randomized,** and participant- and rater-blinded trial
- Conducted in four hospitals

## Inclusion/Exclusion

### Inclusion criteria

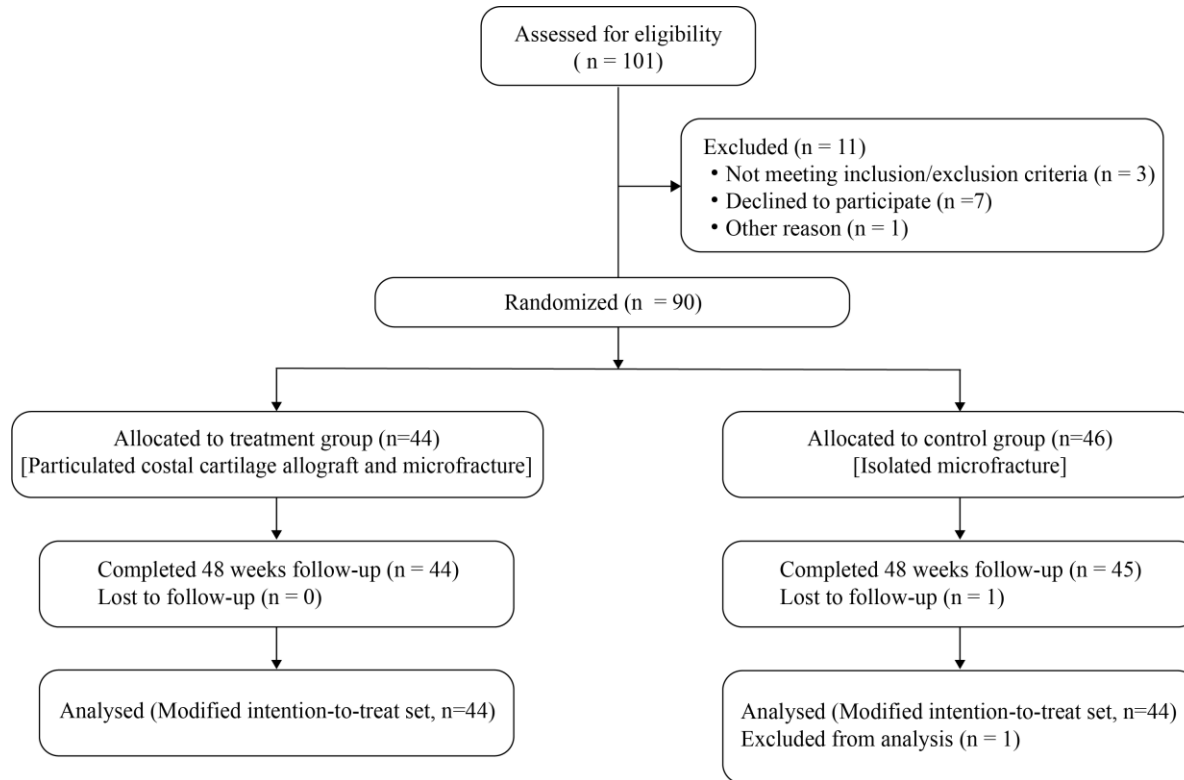
- 19 – 65 year of age
- Focal cartilage defects of less than 10cm<sup>2</sup> in size
- ICRS grade III or IV

### Exclusion criteria

- Cartilage surgery in the past 1 year
- BMI of 30 kg/m<sup>2</sup> or more
- Inflammatory arthritis
- Arthritis associated with autoimmune diseases
- Intra-articular injection in the past 3 months
- Systemic steroid medication in the past 1 month
- Pregnancy
- Systemic or localized infection.

# Study design

## Consort flow diagram



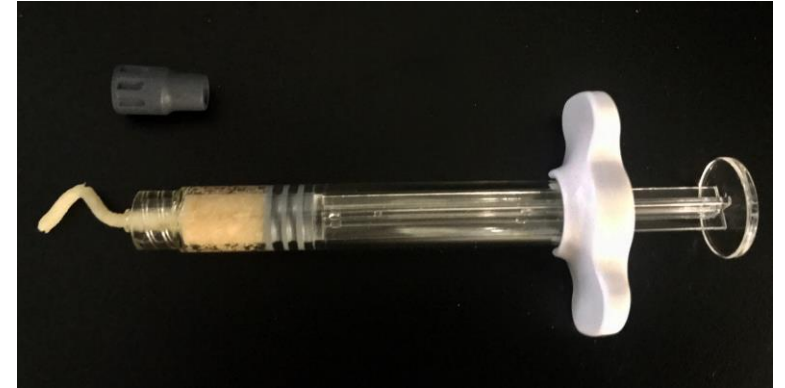
## Outcome Measures

- **MOCART score (MRI)**
- Patient-reported clinical outcomes:
  - VAS pain score**
  - IKDC subjective score**
  - KOOS**
- **Safety**

# Operative procedures

## ● Microfracture

- In either treatment and control group



## ● Augmented with Particulated costal allocartilage (Megacarti®) in treatment group

- A size of 200 to 1000  $\mu\text{m}$  and a weight of 1.5 g was prepared in a 3 cc prefilled syringe
  - **Viscous paste type** by adding a sodium hyaluronate cross-linked with sodium carboxymethyl cellulose
- 
- In case of varus malalignment of the affected lower extremity,
    - High tibial open wedge osteotomy (HTO) was additionally performed in either treatment and control group.

# Result – Baseline characteristics

Variable	Treatment group (n = 44)	Control group (n = 44)	P Value
<b>Age, years</b>	55.2 ± 9.2	53.2 ± 7.7	<b>.109</b>
<b>50 or less</b>	43.8 ± 9.0	43.6 ± 5.4	<b>.475</b>
<b>More than 50</b>	59.4 ± 4.4	57.3 ± 4.2	<b>.031</b>
<b>50 or less</b>	12 (27.3)	13 (29.5)	<b>.813</b>
<b>More than 50</b>	32 (72.7)	31 (70.5)	
<b>Sex</b>			<b>.496</b>
<b>Male</b>	13 (29.6)	16 (36.4)	
<b>Female</b>	31 (70.5)	28 (63.6)	
<b>Height, cm</b>	160.4 ± 7.9	164.1 ± 9.4	<b>.063</b>
<b>Weight, kg</b>	65.2 ± 9.6	69.0 ± 10.9	<b>.081</b>
<b>Body mass index, kg/m<sup>2</sup></b>	25.3 ± 2.7	25.6 ± 2.8	<b>.623</b>
<b>Current smoker</b>			<b>.110</b>
<b>Yes</b>	1 (2.3)	6 (13.6)	
<b>No</b>	43 (97.7)	38 (86.4)	
<b>Previous surgical history</b>			<b>.787</b>
<b>Yes</b>	9 (20.5)	8 (18.2)	
<b>No</b>	35 (79.5)	36 (81.8)	

Variable	Treatment group (n = 44)	Control group (n = 44)	P Value
<b>Affected Side</b>			<b>.831</b>
<b>Right</b>	23 (52.3)	22 (50.0)	
<b>Left</b>	21 (47.7)	22 (50.0)	
<b>Size of the defect, cm<sup>2</sup></b>	4.3 ± 2.6	4.0 ± 2.2	<b>.688</b>
<b>4 or less</b>	2.2 ± 1.1	2.1 ± 1.1	<b>.947</b>
<b>More than 4</b>	5.3 ± 1.3	5.9 ± 1.6	<b>.355</b>
<b>4 or less</b>	31 (70.5)	29 (65.9)	<b>.647</b>
<b>More than 4</b>	13 (29.5)	15 (34.1)	
<b>ICRS grade</b>			<b>.830</b>
<b>Grade III</b>	24 (54.5)	25 (56.8)	
<b>Grade IV</b>	20 (45.5)	19 (43.2)	
<b>Previous HTO</b>	2 (4.6)	0	<b>.494</b>
<b>Concurrent HTO</b>			<b>.669</b>
<b>Yes</b>	19 (43.2)	21 (47.7)	
<b>No</b>	25 (56.8)	23 (52.3)	
<b>Approach</b>			<b>.269</b>
<b>Mini-arthrotomy</b>	11 (25.0)	6 (13.6)	
<b>Arthroscopy</b>	33 (75.0)	38 (86.4)	

# Result – MRI outcomes at 48 weeks

Variables	Treatment group (n = 44)	Control group (n = 44)	p-value
<b>Total score</b>	56.0 ± 10.5	43.0 ± 17.4	<b>&lt;.001</b>
<b>1. Degree of defect repair and filling</b> of the defect score	13.5 ± 2.8	10.3 ± 5.0	<b>.004</b>
20: Complete (on a level with adjacent cartilage)	6 (6.8)	3 (3.4)	<b>&lt;.001</b>
15: Hypertrophy (over the level of the adjacent cartilage)	57 (64.8)	37 (42.1)	
10: >50% of the adjacent cartilage	18 (20.5)	16 (18.2)	
5: <50% of the adjacent cartilage	7 (8.0)	27 (30.7)	
0: Subchondral bone exposed (Complete delamination of dislocation and/or loose body)	0 (0)	5 (5.7)	
<b>2. Integration</b> to border zone score	11.5 ± 3.7	8.4 ± 4.8	<b>.001</b>
15: Complete (Complete integration with adjacent cartilage)	52 (59.1)	27 (30.7)	<b>&lt;.001</b>
10: Demarcating border visible (split-like)	13 (14.8)	22 (25.0)	
5: <50% of the length of the repair tissue	21 (23.9)	22 (25.0)	
0: >50% of the length of the repair tissue	2 (2.3)	17 (19.3)	
<b>3. Surface</b> of the repair tissue	5.3±2.4	3.8±2.4	<b>.005</b>
10: Surface intact (lamina splendens intact)	20 (22.7)	8 (9.1)	<b>.006</b>
5: <50% of repair tissue depth	53 (60.2)	50 (56.8)	
0: >50% of repair tissue depth of total degeneration	15 (17.1)	30 (34.1)	
<b>4. Structure</b> of the repair tissue	2.2 ± 1.5	1.3 ± 1.7	<b>.004</b>
5: Homogeneous	38 (43.2)	22 (25.02)	<b>.011</b>
0: Inhomogeneous or cleft formation	50 (56.8)	66 (75.0)	
<b>5. Signal intensity</b> of the repair tissue	4.8 ± 1.1	3.9 ± 2.1	.011
15: Normal (identical to adjacent cartilage)	1 (1.1)	1 (1.1)	<b>&lt;.001</b>
5: Nearly normal (slightly area or signal alteration)	82 (93.2)	65 (73.9)	
0: Abnormal (large area of signal alteration)	5 (5.7)	22 (25.0)	
<b>6. Subchondral lamina</b>	4.0 ± 1.6	3.0 ± 2.0	<b>.017</b>
5: Intact	70 (80.0)	53 (60.2)	<b>.005</b>
0: Not intact	18 (20.5)	35 (40.0)	
<b>7. Subchondral bone</b>	2.2 ± 1.8	1.6 ± 1.8	.095
5: Intact	39 (44.3)	28 (31.8)	<b>.088</b>
0: Edema, granulation tissue, cysts, sclerosis	49 (55.7)	60 (68.2)	
<b>8. Adhesions</b>	5.0±0.0	4.8±0.7	<b>.043</b>
5: No	88 (100.0)	84 (95.5)	.121
0: Yes	0 (0)	4 (4.6)	
<b>9. Effusion</b>	2.6 ± 2.3	2.2 ± 2.1	.346
5: No effusion	46 (52.3)	38 (43.2)	.227
0: Effusion	42 (47.7)	50 (56.8)	

Costal cartilage augmentation showed **significantly greater total MOCART scores at 48 weeks** ( P < .001).

Among 9 variables, **7 variables** were **significantly different** between the groups at 48 weeks.

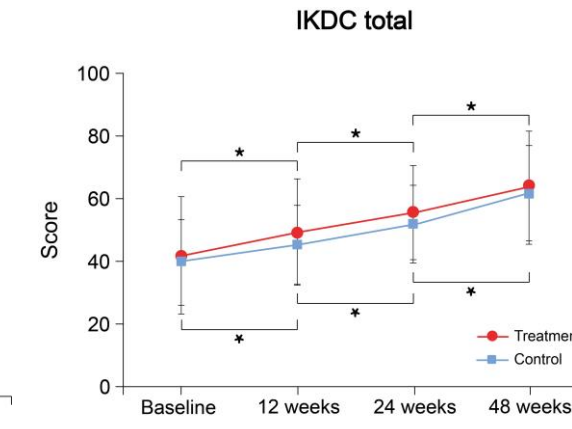
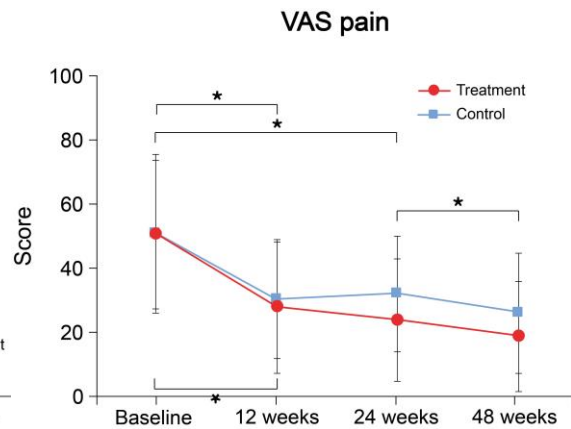
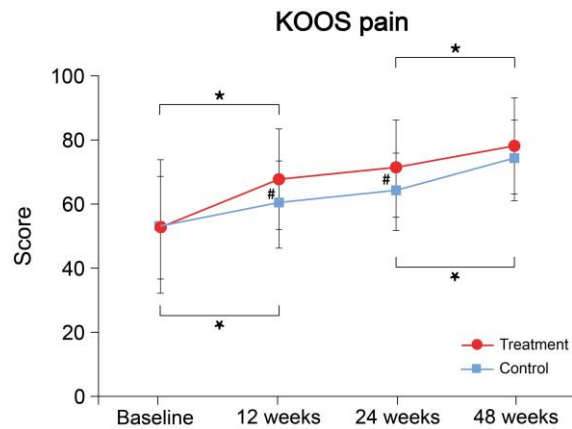
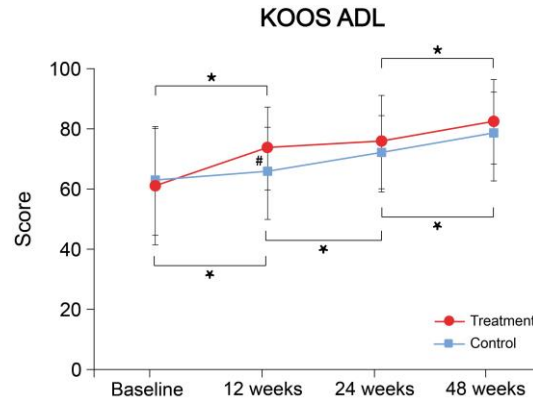
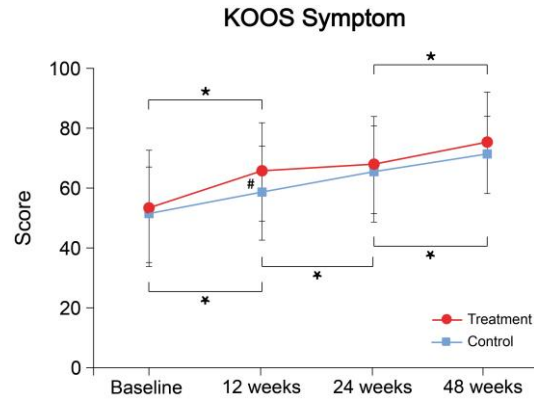
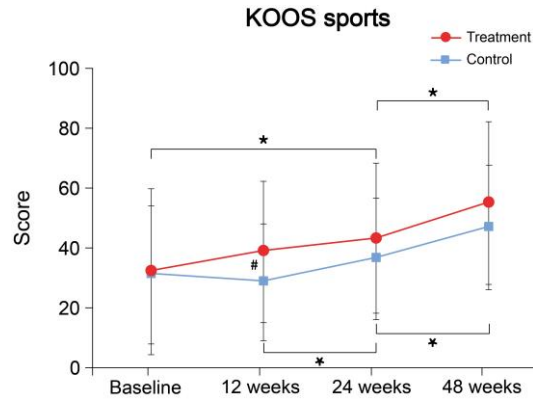
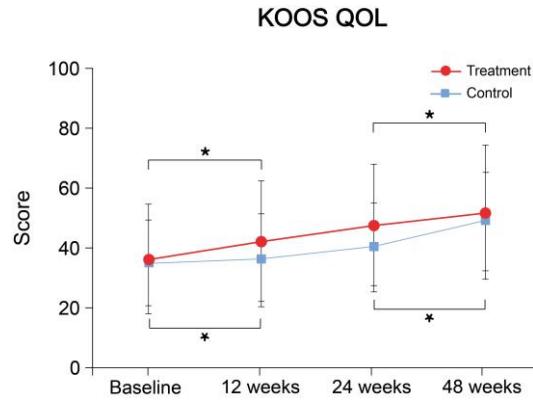


# Result – MRI outcomes of subgroup at 48 weeks

Variable	Treatment group	Control group	P Value
<b>Age, years</b>			
50 or less	61.7 ± 8.8	53.7 ± 9.7	.076
More than 50	53.8 ± 10.4	38.5 ± 18.0	< .001
<b>Size of the defect, cm<sup>2</sup></b>			
4 or less	58.5 ± 9.8	48.4 ± 16.1	.015
More than 4	50.0 ± 9.8	32.5 ± 15.3	.002
<b>ICRS grade</b>			
Grade III	58.0 ± 9.7	47.5 ± 17.3	.038
Grade IV	53.5 ± 11.0	37.0 ± 16.0	< .001
<b>Concurrent HTO</b>			
Yes	52.9 ± 9.5	35.7 ± 16.3	< .001
No	58.3 ± 10.8	49.6 ± 15.9	.075

**Costal cartilage augmentation showed significantly superior quality regardless of stratification according to size ( $\leq 4\text{cm}^2$ ,  $P = .015$ ;  $> 4\text{cm}^2$ ,  $P = .002$ ) and ICRS grade (grade III,  $P = .038$ ; grade IV,  $P < .001$ ) of the cartilage defects.**

# Result – Patient-reported functional outcomes



**Functional outcomes significantly improved over 48 weeks for both groups**

# Result – Patient-reported functional outcomes and safety outcomes

Variable	At preop			At 12 weeks			At 24 weeks			At 48 weeks		
	Treatment	Control	P Value	Treatment	Control	P Value	Treatment	Control	P Value	Treatment	Control	P Value
	group (n = 44)	group (n = 44)		group (n = 44)	group (n = 44)		group (n = 44)	group (n = 44)		group (n = 44)		
IKDC	41.8±18.6	39.7±13.6	<b>0.532</b>	49.4±16.9	45.1±12.6	<b>.181</b>	55.6±15.0	51.7±12.5	<b>.192</b>	64.0±17.5	61.1±15.7	<b>.356</b>
VAS pain	51.0±24.7	50.9±23.2	<b>0.812</b>	28.3±20.9	30.4±18.2	<b>.516</b>	24.1±19.1	32.3±18.2	<b>.012</b>	19.1±17.2	26.2±18.9	<b>.056</b>
<b>KOOS</b>												
Sports	32.3±27.6	31.4±23.0	<b>0.831</b>	38.9±23.5	28.6±19.5	<b>.029</b>	43.4±24.8	36.6±20.1	<b>.156</b>	55.1±27.0	46.8±20.7	<b>.052</b>
Symptom	53.1±19.5	51.0±15.9	<b>0.577</b>	65.5±16.5	58.3±15.9	<b>.039</b>	67.7±16.3	64.7±16.0	<b>.386</b>	75.1±16.9	71.0±13.0	<b>.202</b>
Pain	54.4±21.5	54.2±16.5	<b>0.964</b>	69.6±16.1	61.6±13.9	<b>.014</b>	72.9±15.5	65.5±12.5	<b>.005</b>	80.1±15.4	75.6±13.0	<b>.072</b>
ADL	61.4±19.9	62.4±17.8	<b>0.803</b>	73.7±13.9	65.5±15.4	<b>.010</b>	75.9±15.7	71.9±12.6	<b>.077</b>	82.6±14.1	78.3±14.3	<b>.085</b>
QOL	36.1±18.3	35.0±14.2	<b>0.913</b>	42.2±20.0	36.0±15.6	<b>.256</b>	47.6±20.3	40.2±14.9	<b>.055</b>	51.9±22.4	48.9±16.4	<b>.543</b>

**Better** some of the outcomes **at 12 and 24 weeks.**

**Comparable** outcomes **at 48 weeks.**

**No operation-related adverse event.**

# Conclusion

- **Particulated costal allograft with microfracture**

- Is a **safe and efficacious** surgical procedure for treating a cartilage defect of the knee joint.
- Resulted in **superior cartilage repair quality in terms of MRI evaluation** than microfracture alone at 48 weeks follow-up
- The **functional outcomes were favorable** for both treatments and **comparable** between the treatments at 48 weeks follow-up

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