통증 및 근골격재활
발표일시 및 장소 : **10 월 27 일(토) 14:30-14:40 Room B(5F)**

OP1-3-4

Hybrid regenerative effects of 3D bioprinting with stem cell in rotator cuff tear in rabbit model

Sang Chul Lee[2], Dong Rak Kwon[1*†], Gi Young Park[1], Yong Suk Moon[3], Jinah Jang[4], In Ho Woo[1]

Daegu Catholic University Medical Center, Department of Rehabilitation Medicine[1], Severance Hospital, Department of Rehabilitation Medicine[2], Daegu Catholic University Medical Center, Department of Anatomy[3], Others, POSTECH, Department of Creative IT Engineering and IBIO[4]

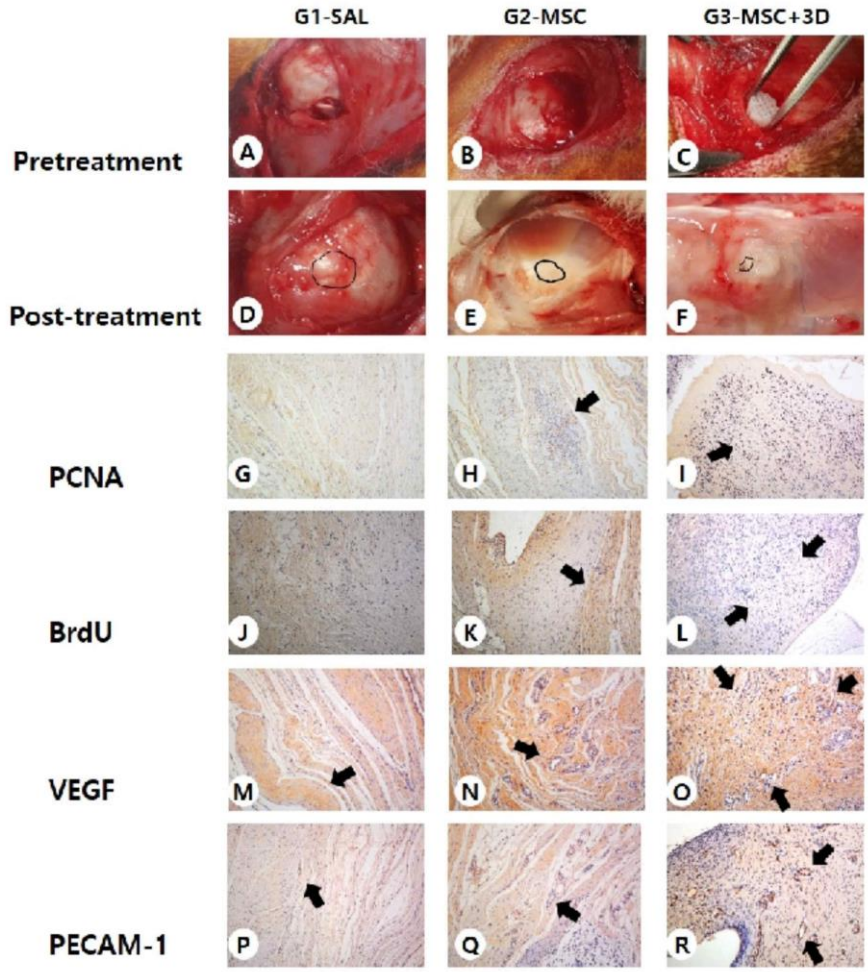
Objective
The aim of this study was to compare the regenerative effects of implantation with three-dimensional bioprinting of multilayered construct containing umbilical cord blood (UCB)-derived mesenchymal stem cell (MSC) and ultrasound (US)-guided injection with human umbilical cord blood-derived mesenchymal stem cells (UCB-MSCs).

Methods
Rabbits (n=18) were allocated into 3 groups. After a 5-mm sized full-thickness rotator cuff tendon tear (FTRCTT) just proximal to the insertion site on the supraspinatus tendon was created by excision, the wound was immediately closed by subcutaneous and skin sutures. Two injections (0.2 mL normal saline, G1-SAL; 0.2 mL UCB-MSCs, G2-MSC) were performed into FTRCTT under US guidance. 3D construct containing UCB-derived MSC was implanted into the FTRCTT (0.2mL UCB-MSCs+3D construct, G3-MSC+3D). Gross morphologic changes and histologic examination were performed on all rabbits after sacrifice. Motion analysis was also performed.

Results
The gross morphologic mean tendon tear size in G3-MSC+3D and G2-MSC was significant smaller than that of G1-SAL ($p<.05$). There was no significant difference in tendon tear size between G2-MSC and G3-MSC+3D. However there were differences in the degree of tendon recovery among three groups ($p<.05$). Complete healing(CH) was observed in two rabbits (33%) and partial thickness tear(PTT) was observed in four rabbits (67%) in G3-MSC+3D, CH was observed in one rabbit (16.7%), PTT was observed in three rabbits (50%) in G2-MSC. In G1-SAL, FTT was observed in every rabbits. In G3-MSC+3D, regenerative activity, angiogenesis, walking distance, fast walking time, mean walking speed were greater than in the other two groups on histological examination and motion analysis.

Conclusions

Three dimensional bioprinting of multilayered construct implantation with mesenchymal stem cell treatment was more effective than ultrasound guided injection in gross morphological, histological and motion analysis in a rabbit model of traumatic FTRCTT.



Gross morphological (A–F) findings of the supraspinatus tendons in G1-SAL, G2-MSC, and G3-MSC+3D. (A-C) Pre-treatment images; (D-F) Post-treatment images. Immunohistochemical (G-R) findings of the supraspinatus tendons in G1-SAL, G2-MSC, and G3-MSC+3D. (G-L) Numerous PCNA and BrdU stained cells (black arrow, X200) were observed in regenerated tendon fibers in G2-MSC, and G3-MSC+3D. Few PCNA stained cells were observed in G1-SAL. (M-R) Numerous VEGF-positive cells and PECAM-1 positive microvascular densities (black arrows, X200) were observed in G2-MSC, and G3-MSC+3D. Few VEGF-positive cells and PECAM-1 positive microvascular densities were observed in group G1-SAL.

Abbreviations are MSC : Mesenchymal stem cell; PCNA: proliferating cell nuclear antigen; BrdU : 5-bromo-2'-deoxyuridine; VEGF : vascular endothelial growth factor; and PECAM : platelet endothelial cell adhesion molecule.

Gross morphological and immunohistochemical findings

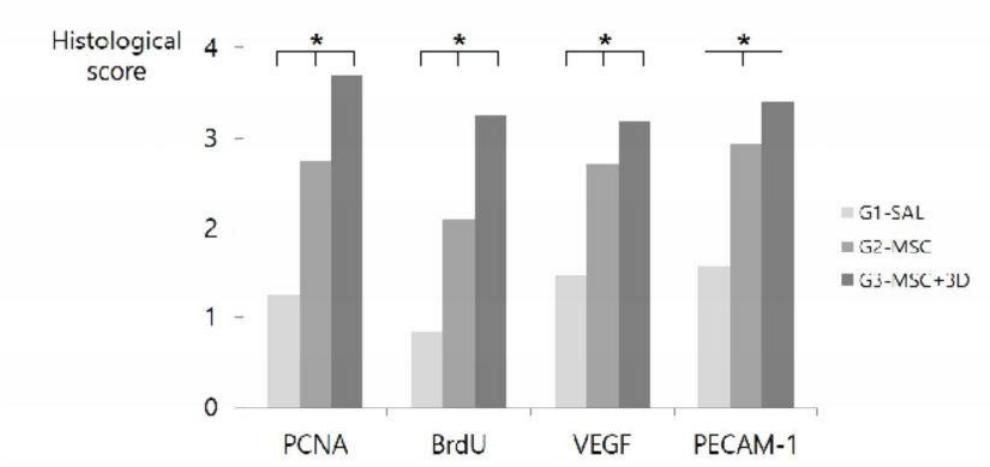


Fig. 2. Semiquantitative score of histological findings, immunoreactivity of stain.

The proportion of PCNA-, BrdU-, VEGF-, and PECAM-1-positive cells were scored as detailed in Materials and Methods.

*P < .05 one-way ANOVA, Turkey's post hoc test among group.

Abbreviations are MSC : Mesenchymal stem cell; PCNA: proliferating cell nuclear antigen; VEGF : vascular endothelial growth factor; and PECAM : platelet endothelial cell adhesion molecule.

	Groups (Injection regimens)		
	G1-SAL (n=6)	G2-MSC (n=6)	G3-MSC+3D (n=6)
Gross			
Tear size	14.75±3.13	4.98±4.1*	2.88±1.75†
Histological score			
PCNA	1.25±1.05	2.74±0.97*	3.69±0.76†‡
BrdU	0.84±0.89	2.1±1.02*	3.25±1.06†‡
VEGF	1.47±0.18	2.72±0.79*	3.19±0.75†‡
PECAM-1	1.56±0.95	2.94±0.9*	3.4±0.87†‡
Motion analysis			
Walking distance(cm)	4852.75±137.27	6343.63±213.57*	7291.83±433.74†‡
Fast walking time(%)	5.62±1.42	10.04±2.35*	14.06±1.79†‡
Mean walking speed(cm/sec)	6.3±0.57	9.63±1.79*	13.68±2.47†‡

Values are mean±SD.

The proportion of positive cells of PCNA, VEGF, PECAM-1 was scored as 0 = no cells stained positive, 1 = between 1% and 10%, 2 = between 11% and 33%, 3 = between 34% and 66%, and 4 = between 67% and 100%.

PCNA, proliferating cell nuclear antigen; BrdU : 5-bromo-2'-deoxyuridine; VEGF, Vascular endothelial growth factor; PECAM-1, Platelet endothelial cell adhesion molecule.

*) $p < .05$ one-way ANOVA, Tukey's post hoc test between group 1 and 2

†) $p < .05$ one-way ANOVA, Tukey's post hoc test between group 1 and 3.

‡) $p < .05$ one-way ANOVA, Tukey's post hoc test between group 2 and 3.

Semiquantitative score of gross morphologic, histological findings, immunoreactivity of stain and motion analysis according to treatment groups at 4 weeks after injection.