The Effect of PRP with Gelatin Hydrogel Sheets on Rotator Cuff Repair

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Introduction: For the better clinical results after rotator cuff repair, it is important to promote the remodeling of humeral tendon-to-bone insertion. Plate rich plasma (PRP) is rich in various growth factors thought to be important for tissue healing. PRP injection to the humeral tendon-to-bone insertion may promote repair of tendon-to-bone insertion. However, clinical trials have failed to demonstrate convincing evidence that PRP improves rotator cuff healing in humans. It is thought that one of the reasons for this is difficulty in keeping the effective concentration at the tendon-to-bone insertion. Gelatin hydrogel sheets (GHS) have been used for the sustained release of growth factor, to keep local concentration. The purpose of this study is to analyze the curative effect of PRP with GHS on rotator cuff repair.

Methods: PRP was prepared from allogeneic blood of rats according to a published protocol (1) before surgery. Twelve-week-old Sprague-Dawley (SD) wild type male rats of the same strain (n=18) were used. The animals were housed in our institution's animal facility in accordance with the policies and procedures set out in the Guide for the Care and Use of Laboratory Animals by the National Institutes of Health. Bilateral supraspinatus tendons were transected and sutured at the insertion on the greater tuberosity by the Mason-Allen technique.

We evaluated the effect of PRP with GHS on rotator cuff repair. Phosphate buffered saline (PBS) or PRP was injected into subacromial bursa (PBS group, PRP group), PBS or PRP with GHS was set on the tendon-to-bone insertion (PBS+GHS group,PRP+GHS group) (Fig.1). At 2, 4, and 8 weeks after surgery, the rats were sacrificed and harvested from their shoulders (n=3). Heterotopic ossification was evaluated by micro computed tomography (μCT) (micro focus 2D/3D, ScanXmate-E090S40, Comscantecno Co., Ltd., Kanagawa, Japan). Sections were stained with hematoxylin and eosin, safranin O for light microscopic examination. Tissue repair was evaluated by the tendon-to-bone maturing score reported by Ide et al. They evaluated histologic parameters including cellularity, vascularity, proportion of fibers oriented parallel, proportion of fibers of large diameter, continuity, bone ingrowth, fibrocartilage cells, and tidemark. The first two parameters were classified into Marked, Moderate, Mild, Minimal and the last six parameters were classified into 25%>, 25-50%, 50-75%, 75 %< as compared to control (unoperated) group. They were scored each 1, 2, 3, 4 points. A perfect score in this scoring system is 32 points. Statistical analysis by three-way factorial analysis of variance using Kruskal Wallis rank was performed. All values were expressed as mean ± standard deviation.

Results: Heterotopic ossification was not observed by μCT in any groups. Cellularity was gradually reduced in all groups. Many inflammatory, mesenchymal cells and vessels were observed in PRP group
and PRP+GHS group at the tendon-to-bone insertion at 2 weeks after surgery. Cartilage formation in all groups and the columnar arrangement of chondrocytes in PRP+GHS group were observed at 8 weeks after surgery. There were no significant differences between any groups in the tendon-to-bone maturing score, however, it was almost same in PBS group (19.0±4.6), PRP group (18.3±1.5) and PBS+GHS group (16.3±4.7) and was the highest in PRP+GHS group (21.7±3.1) at 8 weeks after surgery (Table.1).

**Discussion:** PRP is a source of autologous growth factors, including platelet-derived growth factor, vascular endothelial growth factor, epidermal growth factor, and transforming growth factor-β. But it is difficult to maintain the local concentration of growth factors. Maintenance of therapeutic concentrations of growth factors typically requires the administration of large amounts of growth factors and frequent injections. Therefore, administration of such large amounts of growth factors can have unexpected side effects. In this study, heterotopic ossification was not observed by μCT in PRP+GHS group. This suggests that sustain release of PRP using GHS may be safe in shoulder joint. Tendon-to-bone insertion consists of tendon, fibrocartilage, and bone. PRP stimulates tenocyte proliferation, collagen synthesis, chondrocyte proliferation and proteoglycan synthesis. Rotator cuff repair at 8 weeks after surgery in PRP group was almost the same as in PBS group and, rotator cuff repair at 8 weeks after surgery in PRP+GHS group was more obvious than in PRP group especially about tendon and fibrocartilage. Thus, PRP with GHS may promote rotator cuff repair safely.

**Significance:** GHS including PRP may promote rotator cuff repair and shorten duration of rehabilitation after surgery.

![Fig. 1](image)

A: acromion  
G: gelatin hydrogel sheet 
H: humerus  
R: rotator cuff
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<th>Time after surgery</th>
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<tr>
<td></td>
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<td>PBS group</td>
<td>PRP group</td>
<td>PBS+GHS group</td>
<td>PRP+GHS group</td>
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<tr>
<td>2 weeks</td>
<td>15 ± 1</td>
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<td>4 weeks</td>
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<td>13.3 ± 2.5</td>
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<td>8 weeks</td>
<td>19 ± 4.6</td>
<td>18.3 ± 1.5</td>
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