Repair of a Rotator Cuff Tendon Defect Using an Acellular Human Dermal Graft in a Large Primate Model

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Introduction: Injury of the shoulder rotator cuff is a common orthopedic condition which can result in disability and loss of work. Surgical repair can be complicated by the extent of tendon damage and frequency of reoccurrence. Complete reconstruction may not be possible due to tendon defects or loss of tendon integrity requiring replacement or augmentation with graft material. The use of certain xenografts for rotator cuff repair in human patients has resulted in inflammation of the shoulder, implicating an immunogenic response [1]. The purpose of this study was to evaluate an acellular dermal human graft for rotator tendon defect repair and augmentation in a large primate model which closely resembles the human shoulder anatomy, mechanics, and immunogenicity.

Materials and Methods: A primate rotator cuff injury model was developed under an IACUC-approved protocol and consisted of full thickness bilateral defects in the infraspinatus and subscapularis tendons. Ten adult female skeletally mature baboons (10.3 to 21.3 kg) were divided into two groups. In one group (n=5), the defects were repaired using a non-crosslinked human acellular dermis graft (GraftJacket® Regenerative Tissue Matrix, Wright Medical). In the other group (n=5) the defects were created, but no graft was applied. Surgical repair of the created defects in the infraspinatus and subscapularis tendons was performed under general inhalation anesthesia and a continuous infusion of morphine/ketamine. A full thickness rectangular defect (5mm wide X 7mm long) was made in the central body of each tendon using a template. The tendons were measured (infraciputus nominally 12mm X 12mm and subscapularis nominally 15mm X 15mm) and repaired using a patch of graft material cut to cover the tendon width and length and sutured with moderate and fine non absorbable polyester suture. At the bone insertion site, the patch was secured to the residual tendon and periosteum by suture placed through superficial bone tunnels. Postoperative analgesia was provided using buprenorphine twice a day for 5 days and Tramadol as needed. In all animals, the subscapularis tendon was used for histological study, and the infraspinatus tendon was used for mechanical testing (not reported here). The right and left shoulders were operated staged approximately 6 weeks apart. Thus, after euthanasia at 12 weeks, one 6-week and one 12-week shoulder was available from each animal. As indications of pain and function, the animals were assessed: (1) for grasping food, limb extension forward, limb extension to shoulder level, and limb extension overhead; (2) radiographically under sedation for changes to the gleno-humeral joint preoperatively, and at 6 and 12 weeks; and (3) by passive range of motion (ROM) measurements of the shoulder joint under sedation preoperatively, and at 0, 6 and 12 weeks postoperatively. Standard shoulder ROM measurements were recorded specifically for forward elevation, external rotation in abduction, internal rotation in abduction, external rotation limb at side, and internal rotation with limb behind back. After euthanasia, passive range of motion and gross appearance of the joint tissues were documented. The subscapularis tendon of each joint was studied histologically using sections stained with H and E, Masson’s trichrome and Verhoeff-van Gieson to determine healing of the model defect, incorporation of the graft material into the native tendon, and any immunogenic response to the implanted material. The Mann Whitney test was used to compare the ROM data between the groups.

Results: All incisions healed in a normal fashion with no drainage occurring at any time during the study. Postoperative minimal to mild incision erythema and swelling was completely resolved by 7 days. Clinical limb usage rated by the ability to grasp food with the manus was present in all limbs by the second day, reflecting limb neuromuscular function. Progressive improvement in limb function was noted in both groups with apparent normal clinical function present in all limbs at 6 weeks.

Willingness to extend the limb forward was present in all limbs by 2 weeks. Voluntary extension of the limb to shoulder level occurred in all limbs by 2 to 4 weeks. Voluntary extension of the limb to overhead occurred in all limbs by 4 to 6 weeks. At necropsy, all grafted tendons were intact. Grossly, grafted tendons were thickened by residual graft material and fibrinous tissue, and the defects were no longer present. In contrast, non-grafted tendons had normal to thinner dimensions, and the central defects were still visible grossly or covered only by a thin membrane. Radiographically, there were no differences between the groups. Only minimal to no changes were present around the fine bone tunnels in the greater tubercles. No changes in joint congruity were identified in any shoulder. All shoulders had a smooth ROM with no crepitation, enlargements or instability. ROM differences from preoperative values were seen in both groups with peak loss occurring at 6 weeks, returning toward, but not completely, to preoperative values at 12 weeks. At 6 weeks, these changes were most notable in loss of forward elevation (range, 5 to 60 degrees) and loss of external rotation in abduction (range, -10 to 20 degrees), but were not statistically significant between the groups. Histologically, in the grafted group, tendon continuity was re-established with incorporation of the graft into the substance of the tendon. The 6-week grafted specimens contained residual graft material (evident by staining of elastin fibers) which was incorporated into the native proximal and distal tendon with neo-vascularization, fibrosis, and a focal infiltrate of mono- and multi-nucleated cells which was in part a reaction to the sutures used for graft fixation. The 12-week grafted specimens were characterized by a greater degree of incorporation and remodeling with collagen fibers oriented in the long axis of the tendon and decreased cellular infiltrate compared to the 6-week specimens. The untreated tendon defects failed to heal after 6 or 12 weeks as evidenced by the remaining discontinuity in the tendon with proliferation of fibrous tissue only at the margins of the created defect.

Discussion: There was no impediment to wound healing from the acellular graft material. The created tendon defects resulted in substantial loss of nominally 30-50% of the tendon body and failed to heal without graft augmentation. Changes in shoulder function were transient and reversible with the decline in ROM returning toward normal values by 12 weeks. This time frame pattern of initial decrease and subsequent increase in ROM parallels that seen in clinical human rotator cuff repair recovery. Thus, this large primate rotator cuff defect model replicated well the human rotator cuff condition. There were no clinical signs of an immunogenic response to the xenograft material studied in this particular primate species. Active graft remodeling was still in progress at 12 weeks, but had diminished compared to 6 weeks. The acellular human dermal matrix was successful in restoring tendon integrity at defect sites and is supported by the favorable histological appearance.


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