Clinical Evaluation of the
Rotation Medical Bioinductive Implant

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Background

A study of the Rotation Medical Bioinductive Implant in sheep demonstrated that the device had the ability to induce the formation of new tendinous tissue consisting of well-organized collagen with fibers oriented in the direction of the load.[1] The device did not elicit an inflammatory response or foreign body reaction and was completely absorbed within 6 months after implantation. The new tissue induced by the device was well-integrated with the underlying rotator cuff tendon and demonstrated a fibrocartilagenous transition zone at its insertion into bone. The increased thickness of the tendon (approximately 2.5 mm of new tissue) was stable throughout the 12-month follow-up of the study. These results suggest that use of the device to induce new tendinous tissue may be effective for preventing the propagation of partial-thickness tears of the supraspinatus tendon in humans by decreasing intra-tendinous strain, which may also create an environment more conducive for tendon healing. In addition, adding tendon thickness following the repair of full-thickness tears may lead to a reduction in re-tear rates.

Based on the consistent tissue induction observed in sheep using the Rotation Medical Bioinductive Implant, a clinical trial was conducted in Australia to demonstrate tissue induction in humans. Surgeries were performed at five hospitals in the North Sydney area: Royal North Shore Hospital, North Shore Private Hospital, Ryde Hospital, Macquarie University Hospital, and Sydney Adventist Hospital. Magnetic Resonance Imaging (MRI) was performed at two institutions: Royal North Shore Hospital and Macquarie University Hospital. All MR images were read by a single musculoskeletal radiologist, Dr. Luke Deady, who was blinded to the clinical outcomes.

Materials and Methods

Study Enrollment

Patients requiring surgical treatment of supraspinatus tendon pathology were asked to participate in a prospective, multi-center, non-randomized trial designed to assess tissue induction associated with the Rotation Medical Bioinductive Implant. The trial was approved by the Ethics Committees of the hospitals and all patients signed informed consent. The inclusion criteria specified patients aged 40-65 with chronic shoulder pain of over 3 months duration who were resistant to conservative treatment and had not had a steroid injection within the last 4 weeks. Exclusion criteria included instability of or previous rotator cuff surgery on the index shoulder, insulin-dependent diabetes, heavy smokers (more than a pack a day), and patients with a known hypersensitivity to bovine-derived materials.

Twenty-four patients with partial- or full-thickness tears of the supraspinatus tendon underwent arthroscopic subacromial decompression (ASD) followed by implantation of the Rotation Medical Bioinductive Implant. A traditional rotator cuff repair was performed in 9 of the patients prior to implantation of the device, while the other 15 patients had the device implanted without traditional cuff repair. Thirteen of the patients with partial-thickness tears met criteria that enabled MRI comparison of the preoperative tendon thickness to the postoperative thickness, and 10 of these patients also met criteria that enabled MRI comparison of the preoperative tear size to the postoperative tear size. In addition, 6 patients with partial-thickness tears of the supraspinatus tendon underwent ASD without repair, but did not receive the device.

The mean age of the patients that had the device implanted was 55.4 years (range 41-67). There were 15 males and 9 females, with the device implanted in 7 left shoulders and 17 right shoulders. The partial-thickness tears were distributed about equally between intermediate- and high-grade tears, with one low-grade tear; while the full-thickness tears in the repair group were all intermediate-grade. The procedure was performed arthroscopically in 14 patients and a mini-open procedure was performed in 10 patients. The median time for implantation of the device was 15 minutes. The 6 patients that did not receive the implant all had low-grade partial-thickness tears.

Radiological Analysis and Clinical Assessment

MR scans were performed preoperatively and at 3, 6, 12, and 24 months postoperatively. The technique for performing the scans was similar to standard scans performed to assess rotator cuff pathology, with two exceptions: First, the coronal scan was done in an orientation that was oblique to the actual coronal plane such that the plane of the scan was approximately orthogonal to the plane of the supraspinatus tendon and the scan was aligned in the direction of the length of the supraspinatus tendon. This “double-oblique” coronal scan enabled a more representative measurement of the true thickness of the supraspinatus tendon. Second, care was taken to position the patient for the scans as reproducibly as possible at each follow-up to enable better longitudinal thickness comparisons. MR images were also obtained in the standard sagittal and axial planes. All scans were done on 3 Tesla MRI machines using 2 mm slices, with proton density (PD) and T2 weighted scans, both with and without fat saturation (fat sat). All of the MR measurements were performed using the PD fat sat images.

Detailed diagnostic MR observations were made regarding the pathology of the tendon and tear size, as well as general observations of the overall pathology of the shoulder. For patients that did not undergo a cuff repair procedure, the thickness of the supraspinatus tendon was measured in the area of the tear preoperatively and a careful effort was made to measure the thicknesses of the tendon and the induced tissue in the same area for each follow-up scan. For patients that did undergo a cuff repair procedure, the preoperative tendon thickness was not measured; in these patients the postoperative thickness was measured at the approximate midline of the repair, again carefully making the measurement in the same area for each follow-up scan. In most cases the new tissue was well-integrated with and indistinguishable from the underlying tendon, therefore, a single measurement was made of the combined thickness of the tendon and the induced tissue. For tears that were not repaired, the amount of fill in of the tear, or progression of the tear, was assessed. For tears that were repaired, the postoperative scans were evaluated for evidence of re-tears, and the medial-lateral length of the footprint was measured at 24 months and compared to the estimated preoperative length of the footprint. In addition, maturation and integration of the induced tissue was assessed, the quality of the underlying tendon was assessed, and observations were made regarding evidence of bursitis, capsulitis, etc.

Clinical assessments included use of both the Constant-Murley shoulder score and the American Shoulder and Elbow Society (ASES) shoulder scale, which were administered preoperatively and at 3, 6, 12, and 24 months postoperatively. These validated shoulder-specific assessments include functional parameters and pain assessment. In addition, the SF-36 quality-of-life assessment was administered at the same preoperative and follow-up times. All clinical data, as well as operative data, were recorded on case report forms and entered into a central database.

Surgical Procedures

The surgical procedures were performed in either the lateral decubitus or beach chair position under general anesthesia. A posterolateral portal was used for the arthroscope to enable the anterior edge of the supraspinatus tendon to be readily viewed in the subacromial space. The arthroscope was initially inserted into the intra-articular space to assess the rotator cuff tendons and the condition of the glenohumeral joint. Two Rotation Medical tendon markers were inserted along the biceps tendon to mark the anterior edge of the supraspinatus tendon prior to biceps tendon tenodesis or tenotomy if indicated. Also if indicated, minor fraying of the labrum was debrided. The arthroscope was then positioned in the subacromial space and a thorough bursectomy was performed to enable visualization of the tendon markers and to remove the tissue from the bursal surface of the supraspinatus tendon. In addition, the soft tissue was removed from the bone lateral to the insertion of the supraspinatus tendon to enable clear visualization of the lateral edge of the footprint. An acromioplasty was performed in all patients and the tendon was debrided if indicated. Also if indicated, the coracoacromial ligament was released.

Implantation of the device on the bursal surface of the supraspinatus tendon was performed either arthroscopically (n=14) or using a mini-open approach (n=10). The arthroscopic procedure utilized a set of instruments developed by Rotation Medical, Inc., which enabled delivery of the device into the subacromial space and fixation to the tendon with PLA staples (a polylactic acid copolymer designed to completely absorb in approximately one year) and to bone with non-absorbable PEEK staples (polyetheretherketone). The mini-open procedure utilized the same instruments for tendon and bone fixation, but did not require use of the arthroscopic delivery instrument. A device size was selected that covered almost the entire width of the supraspinatus tendon, with a 20x25 mm device implanted in 20 patients and a 25x30 mm device implanted in 4 patients. After hydration the device was approximately 2 mm thick. The anterior edge of the device was aligned with the anterior edge of the supraspinatus tendon, using the tendon markers as a guide, and the lateral end of the device overlapped onto bone 5 mm beyond the lateral edge of the supraspinatus footprint. Generally, seven tendon staples were placed around the perimeter of the device – three at the medial end and two at the anterior and posterior sides – and two bone staples were placed at the lateral end of the device. Standard methods were used for closure.

Postoperative care

The use of the device did not require any significant changes to the routine postoperative protocol. For patients that did not undergo traditional cuff repair, i.e., ASD only with or without the device, patients discarded the sling when comfortable (maximum of 2 weeks) and progressed as tolerated from passive to active-assisted to active motion. Active motion was allowed with forward flexion limited to 100° for the first 4 weeks, and no resistance exercises were allowed for 6 weeks. After 6 weeks there were no restrictions on the use of the arm. For patients that underwent traditional cuff repair, with the device implanted over the repair, there were no changes to the routine postoperative protocol. Repair patients

were in a sling for 6 weeks and then progressed from passive through active range-of-motion as tolerated, with no resistance exercises allowed until after 12 weeks.

Statistical analysis

Differences in tendon thickness over time were analyzed using a repeated measures ANOVA and changes in clinical scores were assessed using the Friedman two-way ANOVA for non-parametric data. Differences between individual time periods were evaluated using post-hoc analyses and statistical significance was considered at $p < 0.05$.

Results

No significant adverse events occurred during surgery and all patients recovered from surgery without any unanticipated complications in the early postoperative period. Occasionally, there were some range-of-motion limitations in the early postoperative period, which is not uncommon following rotator cuff surgery. One patient was lost to follow-up at 24 months.

Radiological Findings

All 13 of the patients with partial-thickness tears, who had the device implanted and met the criteria for comparing the preoperative and postoperative tendon thicknesses, showed an increase in the thickness of the tendon that was consistent with the observations in the sheep study. At 3 months after surgery there was a distinct layer of new tissue on the bursal surface of the tendon that had a mean thickness of 2.2 mm. At both 6 and 12 months after surgery the mean increase in tendon thickness was 2.4 mm, which is a 64% increase in the thickness of tendon. At 24 months the new tissue appeared to have remodeled and consolidated, with the increase in the mean tendon thickness going down slightly to 1.8 mm (49% greater than the preoperative thickness). The layer of new tendinous tissue was stable throughout the 24-month follow-up of this study and was well-integrated with the underlying tendon and bone. The induced tissue gradually became more mature such that the new tissue had the radiological appearance of organized tendinous tissue, with the rate of maturation varying from patient-to-patient. The increase in mean tendon thickness compared to preoperative tendon thickness was highly statistically significant ($p < 0.0001$) at all follow-up times.

In addition, 10 of the above 13 patients with partial-thickness tears met criteria for comparing the preoperative and postoperative size of the defect. None of the MR images showed any progression or propagation of the partial-thickness tears. On the contrary, the preoperative defects consistently filled in with new tissue. In 7 of these 10 patients, the defects (1 bursal-sided, 2 articular-sided, and 4 intra-substance) were completely filled in with new tissue by 12 months, such that the partial-thickness tears appeared to be healed. In the other 3 patients, the defects (1 bursal-sided, 1 articular-sided, and 1 intra-substance) were substantially filled in by 12 months. At 24 months the 7 defects that were filled in completely at 12 months remained healed, while the 3 defects that were not filled in completely at 12 months showed some additional, but not complete healing. Furthermore, there were 3 patients for which the preoperative MR scans did not allow the amount of fill in of the defect to be quantified; however, in these patients the postoperative quality of the tendons appeared to be improved and no defect was apparent by MRI at 12 or 24 months.

In contrast, of the 6 patients with partial-thickness tears that did not have the device implanted, there was no induction of new tendinous tissue and no filling in of the tears.

Of the 9 patients that underwent cuff repair prior to implantation of the device, it was not possible to measure a meaningful preoperative baseline tendon thickness; therefore, an increase in thickness compared to the preoperative thickness was not calculated. However, the MR images at 3 months after surgery generally showed a distinct layer of new tissue on the bursal surface of the repaired tendon that was similar in thickness and appearance to that observed in the partial-thickness tear patients at 3 months. In the repair patients where the new tissue could be distinguished from the underlying tendon at 3 months, the mean thickness of the layer of new tissue was 2.4 mm; in comparison the mean thickness of the layer of new tissue in the partial-thickness tear patients was 2.2 mm at 3 months. In addition, the combined thickness of the repaired tendon and the induced tissue was similar to total thickness of tendon and new tissue in the partial-thickness tear patients. Therefore, it was concluded that an equivalent thickness of new tissue was induced in the repair patients as was measured in the partial-thickness tear patients. In addition, the MR images showed consistently that the footprint was fully restored in the repair patients. In 6 of the repair patients for which the preoperative length of the footprint could be measured, the mean length of the footprint preoperatively was 16.0 mm compared to 16.9 mm at 24 months. In all 9 of the repair patients, at 24 months follow-up there was no MRI evidence of re-tears.

There were 2 other patients that had the device implanted without cuff repair. These patients did not meet the criteria for comparing the postoperative measurements to the preoperative measurements. However, analysis of their MR images, as described in the preceding paragraph for the repair patients, indicated that new tendinous tissue was also induced in these patients, resulting in an increase in the thickness of the tendons and a filling in of the defects.

Clinical Outcomes

The clinical outcomes were similar in all of the patients, therefore, a summary of the combined data for all of the patients that had the device implanted is as follows: The mean pain scores showed steady improvement throughout the 24-month follow-up period (preoperative (n=24): Constant=8.0, ASES=5.3; 24 months (n=23): Constant=1.8, ASES=1.3). Similarly, the mean overall scores showed steady improvement (preoperative (n=24): Constant=55.3, ASES=46.2; 24 months (n=23): Constant=80.1, ASES=85.6). The mean Constant and ASES scores at 24 months were significantly improved compared to the preoperative scores ($p < 0.05$). The improvements in the Constant and ASES pain and overall scores observed in this trial are comparable to the published literature. The mean SF-36 scores also showed improvement over the 24-month follow-up period (preoperative (n=24): physical=41.4, mental=48.4; 24 months (n=23): physical=49.8, mental=49.9); the improvement in the physical score was statistically significant ($p < 0.05$), but the change in the mental score was not statistically significant.

Complications

Two patients had issues that were not believed to be related to the device. One patient with significant preoperative biceps tendinitis (who did not have his biceps released at time of surgery) reported postoperative pain, which resolved at 14 months when the long head of the biceps spontaneously ruptured. Preoperatively, this patient had a very large, near full-thickness, bursal-sided tear that was not repaired. Tissue induction and defect filling in this patient were not compromised by his biceps problem.

Another patient experienced a return to pain at 12 months after surgery that was associated with significant bursitis; therefore, an arthroscopic clean-up procedure was performed to debride the bursa. Cultures and histology showed no evidence of infection and no unanticipated reaction associated with

the device. This patient's pain immediately improved after recovery from the clean-up procedure. An MRI performed 6 months following the clean-up procedure showed complete resolution of the bursitis. Preoperatively, this patient had a large, near full-thickness, articular-sided tear that was not repaired. At 12 months the defect was completely filled in with new tissue and her MRI at 18 months showed that the thickness of the tendon was 66% greater than the preoperative thickness. Tissue induction and tendon healing in this patient were not compromised by her bursitis problem.

Discussion

Induction of new tendinous tissue was observed in all patients that had the device implanted. In 13 patients with partial-thickness tears, the mean increase in tendon thickness at 6 and 12 months was 2.4 mm (64% greater than the preoperative thickness), which is equivalent to the 2.5 mm increase in thickness observed in sheep. At 24 months some remodeling and consolidation of the new tissue resulted in a mean increase in tendon thickness of 1.8 mm (49% greater than the preoperative thickness). In addition, there was a consistent filling in of the partial-thickness defects. In contrast, there was no induction of new tendinous tissue or filling in of the defects in the patients that did not have the device implanted.

The increase in tendon thickness in patients that had a cuff repair prior to implantation of the device was similar to the increase in the partial-thickness tear patients. The repaired tendons appeared to have full restoration of the footprint and there were no re-tears.

The new tissue in all of the patients that had the device implanted appeared by MRI to be well-integrated with the host tissues and to show progressive maturation, which varied from patient-to-patient. The tissue maturation observed radiologically appears to correlate with histological collagen fiber alignment observed in sheep. There were no complications that were related to the device. All of the patients that had the device implanted have done well clinically, with statistically significant improvements in the mean Constant and ASES scores.

Conclusions

The Rotation Medical Bioinductive Implant consistently induced the formation of new tendinous tissue in a clinical trial involving 24 patients. The new tissue was well-integrated with the host tissues and showed progressive maturation. The MRI observations were consistent with the histological results from prior sheep studies. In addition, in all of the patients with partial-thickness tears there was filling in of the tear, rather than tear progression, and in all of the patients that had repair procedures there was full restoration of the footprint and no re-tears.

Reference

1. Van Kampen, CL, SP Arnoczky, PJ Parks et al., 2013. Tissue-engineered augmentation of a rotator cuff tendon using a reconstituted collagen scaffold. A histological evaluation in sheep. *Muscles, Ligaments, Tendons J* 3:229-235.