
EnFix® Implants for Enthesis Repair

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Unmet Clinical Need

There are 500,000 rotator cuff surgeries performed annually in the USA¹. Operative treatment is still far from perfect, with repair failure rates of 20% to 94% reported in the literature. Ratcliffe et al's² review of the literature reported failure rates for rotator cuff repair as assessed by MRI or ultrasound imaging. Their results are shown in Table 1 below. The cost of failed rotator cuff surgery in the USA was estimated to be over \$430m in 2022³. Longo et al⁴ in a systematic review and meta-analysis found that the radiographic re-tear rate was 15% at 3 months follow-up, 21% at 3–6 months follow-up, 16% at 6–12 months follow-up, 21% at 12–24 months follow-up, and 16% at follow-up longer than 24 months.

Tear Size	Failure Rate $\pm$ SD	Range
Small to Medium (1 – 3 cm)	22 $\pm$ 7%	10 – 40%
Large (3 – 5 cm)	46 $\pm$ 21%	10 – 95%
Massive (2 or more tendons)	58 $\pm$ 12%	37 – 76%

Table 1. Rotator Cuff Failure Rates from Ratcliffe et al².

In the uninjured state, the tendon-bone interface, or enthesis, has a fibrocartilage transitional region that exhibits gradations in cell phenotype, matrix composition, tissue organization, and mechanical properties. These natural gradations facilitate the effective transfer of load between two materials of greatly differing stiffness by reducing the potentially damaging stress concentrations that would otherwise arise at their interface. Numerous studies^{5,6,7,8} have shown that the enthesis has a poor healing potential and a weaker scar tissue generally forms. The resultant repair has a lower strength^{5,9}. Enhanced biologic repair at the interface between tendon and bone would be a major advance.

Over several decades, biologic tendon scaffolds derived from human and animal tissues have been generated, and synthetic scaffolds have been manufactured from absorbable and non-absorbable polymers to reinforce and replace tendons and ligaments. These patch products are placed on top of the tendon and do not seek to, nor do they accomplish, healing between the bone and the tendon which

then becomes the weak point of the construct leading to future failures.

Bone marrow aspirate has been investigated as a biological augmentation of rotator cuff repair. Snyder¹⁰ termed the phrase “crimson duvet” to describe the microfracture technique to access bone marrow elements. Toro et al¹¹ and, more recently, Hong et al¹² in randomized clinical studies failed to show benefit for bone marrow stimulation. Cole et al¹³ in a randomized study of the injection of bone marrow aspirate concentrate showed that it failed to improve treatment failure rates or patient reported outcomes.

The importance of enthesis repair was highlighted in a 2017 NIH / NIAMS hosted roundtable on Innovative Treatments for Enthesis Repair¹⁴. Preclinical research has investigated several strategies to generate an enhanced biologic repair including growth factors, demineralized bone matrix, tissue engineering, cell therapy, hyperbaric oxygen therapy, shockwave, and low intensity pulsed ultrasound. While some of these studies have shown promising results, the translational research requirements to commercialization have proven to be significant.

Demineralized Bone Matrix and Enthesis Repair

The seminal work of Marshall Urist's initial discovery of bone morphogenic proteins (BMPs) in 1965¹⁵ came from his observation that bone implants created from demineralized bone matrix (DBM) had the ability to induce the formation of new bone in experimental animals. He hypothesized that DBM contained a factor that could stimulate bone growth, and subsequent experiments led him to isolate and characterize the first BMPs. The various BMPs that have been identified reach beyond just bone and their physiologic roles impact the entire musculoskeletal system. These are tabulated in Table 2.¹⁶ Urist's discovery has had a significant impact in orthopedics and has led to the development of new treatments for bone and joint injuries and diseases. BMPs are used clinically in spinal fusion surgery and other orthopedic procedures to promote bone healing and regeneration. Allograft DBM has also been shown to be a potent biomaterial, with significant clinical usage as a bone void filler and graft material in spine surgery¹⁷.

BMP	Nomenclature	Main physiological roles
<i>Bone morphogenetic proteins</i>		
<u>BMP-2</u>	BMP-2a	Cartilage and bone morphogenesis/heart formation
BMP-3	Osteogenin	Negative regulator of bone morphogenesis
BMP-3b	GDF-10	Negative regulator of bone morphogenesis
<u>BMP-4</u>	BMP-2b	Cartilage and bone morphogenesis/kidney formation
BMP-5	–	Limb development/bone morphogenesis
<u>BMP-6</u>	Vrg1, Dvr6	Hypertrophy of cartilage/bone morphogenesis/oestrogen mediation
<u>BMP-7</u>	OP-1	Cartilage and bone morphogenesis/kidney formation
BMP-8	OP-2	Bone morphogenesis/spermatogenesis
<u>BMP-9</u>	GDF-2	Bone morphogenesis/development of cholinergic neurons/glucose metabolism
BMP-11	GDF-11	Axial skeleton patterning/eye development/pancreas development/kidney formation
<i>Cartilage-derived morphogenetic proteins</i>		
BMP-12	CDMP-3, GDF-7	Ligament and tendon development/development of sensory neurons
BMP-13	CDMP-2, GDF-6	Cartilage development and hypertrophy
BMP-14	CDMP-1, GDF-5	Chondrogenesis/angiogenesis
<i>Others</i>		
BMP-8b	OP-3	Spermatogenesis
BMP-10	–	Heart morphogenesis
BMP-15	GDF-9b	Ovary physiology
BMP-16	Nodal	Embryonic patterning
BMP-17	Lefty	Embryonic patterning
BMP-18	Lefty	Embryonic patterning

BMPs known to induce complete bone morphogenesis are underlined.

Table 2. BMPs in bone and their physiologic roles¹⁵.

There have been some studies of the effect of demineralized bone matrix products on enthesis repair reviewed by Hexter et al¹⁸ in 2017 and Villarreal-Espinosa et al¹⁹ in 2024. Sundar et al²⁰ produced strips of demineralized allogenic bone to use in a sheep model of tendon enthesis healing. Strips of DBM 15 x 30 x 2-3mm were interposed between tendon and bone and held in place using suture anchors. The treated group had fewer early failures than the control group, and histological analysis at 12 weeks demonstrated reformation of the enthesis in the DBM treated group but not in the control group. Smith et al²¹ studied rotator cuff healing in a dog model using a demineralized cancellous sponge loaded with PRP. They demonstrated improved histology, MRI scores, and repair strength at 12 weeks. Lovric et al²² showed that DBM powder introduced into the bone tunnel of an ACL repair in a rodent model demonstrated increased graft strength at 4 and 6 weeks. Heuberger et al²³ injected DBM powder into the tendon footprint of sheep and showed less scar tissue and a more physiologic enthesis morphology at 4 weeks.

The Solution

Tetrous® EnFix implants are the first-to-market, procedure-specific implants manufactured using patented Demineralized Bone Fiber (DBF) technology focused on enthesis healing initially in rotator cuff repair

surgery. Tetrous was spun out of TheraCell, a regenerative medicine company, in 2019 to further its patented DBF technology for application in sports medicine before TheraCell was sold to ISTO Biologics in April 2022.

The EnFix products are allogenic tissue products that conform to the Food and Drug Administration's (FDA) regulations governing human and cellular tissue-based products (HCT/P) according to 21 CFR Part 1271 and Section 361 of the PHS Act. The processes used to manufacture EnFix products were designed to cause minimal changes to the allograft tissue and to maintain the osteoinductive potential. The products are 100% cortical bone and contain no additives or excipients.

While DBM is a potent biomaterial, in its most used form as a powder its handling characteristics are lacking and moreover it lacks osteoconductivity. Excipients used to make DBM powder easier to handle are deficient in that they can contain up to 70% extraneous binding materials that have no beneficial value as biomaterials or to overcome the lack of osteoconductivity. Demineralized bone fiber technologies offered a means to improve osteoconductivity as superior putties but had no means to yield shaped allograft. Tetrous utilizes a highly differentiated and patented next-generation fiber technology approach that yields uniform long and strong fibers amenable to new bone-textile processes and overcomes many of the limitations of earlier manufacturing methodologies. This provides a means of producing procedure specific shaped products via methodologies such as the proprietary water-assisted injection molding (WAIM) while simultaneously yielding highly osteoinductive and osteoconductive properties. The technology also facilitates retention of the nanotopography of the collagen fibrils²⁴. DBF implants produced using this technology have been used in more than 150,000 spine procedures in the past 5 years, and in over 2,000 sports medicine procedures.

To exploit the technology in sports medicine, initially focusing on rotator cuff, two versions of the EnFix product have been produced, EnFix RC® and EnFix TAC®. The EnFix RC implant is designed to be used in conjunction with suture anchors. It is suture anchor agnostic and works well with most widely used threaded suture anchors of sizes 4.5mm - 6.5mm. The EnFix TAC implant is intended to be used independently of the suture anchor, being placed in the footprint between the medial and lateral anchor rows in a double row repair²⁵. This allows the increasingly popular all suture anchors to be used. A single row repair technique has also been developed.²⁶

The EnFix RC design rationale required use of DBF to provide optimal biologic performance while also making it easy for the surgeon to use with minimal disruption to the surgical technique. This was achieved by molding and manufacturing the DBF fibers into a "Top Hat" shape wherein the shaft of the implant is simply inserted into the awl hole used for suture anchor insertion using the introducer shown in Figure 2 below. This allows the implant to be held in place in the bone, as opposed to patch type product formats that the surgeon must sometimes literally chase around the joint. Additionally, placement into the bone cavity allows the fibers to access the marrow space allowing cells and other endogenous local factors to wick up from the subchondral bone to the top surface of the implant that sits at the interface between bone and tendon. The top of the implant is 8.5mm in diameter, allowing optimal spacing of suture anchors, and the peg portion is 14.5mm long.

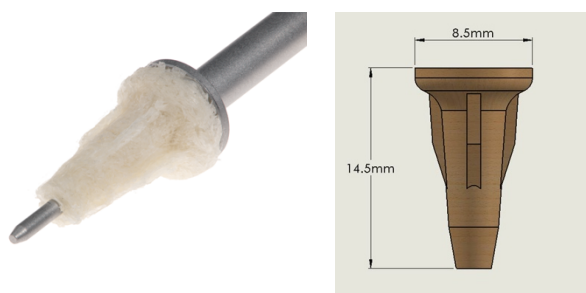


Figure 2. The EnFix RC implant

Use of EnFix RC does not require the surgeon to change their surgical technique and adds less than 2 minutes to the surgery time. The EnFix RC implant is placed into the awl hole created for the suture anchor and then held in place using the suture anchor, as shown in Figure 3. The implant is tapered with four ribs designed to resist rotation during suture anchor insertion. An additional benefit of the usage of the EnFix RC implant is that the peg portion of the implant enhances fixation of the suture anchor into bone, in the same manner as TheraCell's award winning Fibrant™ Anchor enhances pedicle screw fixation in compromised pedicle bone.

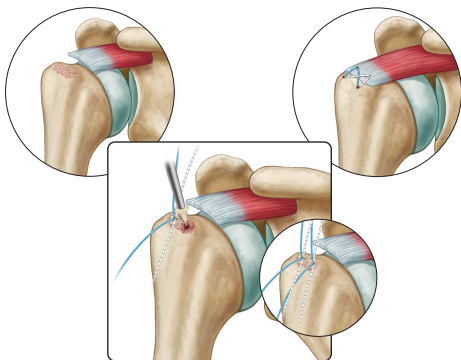


Figure 3. EnFix RC surgical placement

During the controlled launch of the EnFix RC product, two of the surgeons determined that placing the device between the medial and lateral anchor rows (rather than at the medial row) allowed more optimal placement of the device relative to where the enthesis regeneration was desired, while also allowing the placement to be independent of anchor type allowing use of all suture anchors. To optimize for this application, a new version of the EnFix device was developed with two formats; the TAC-O with an 8.5mm round top and the TAC-T with a 10mm x 4mm top. This affords the surgeon a choice of format to optimize placement based on the size of tear and the anatomy. Their dimensions and placement are shown in Figure 4 below.

The EnFix products are cannulated, allowing for easy introduction into the joint using the Introducer. The cannulation also allows blood and bone marrow elements from the subchondral bone to flow up into the healing site, providing a superior type of "crimson duvet"¹⁰ with a funnel from the subchondral space wherein the factors are absorbed in the implant's demineralized bone fibers and wicked up into the healing bone-tendon interface. The unique peg feature of both the RC and TAC products allows ease and speed of insertion without impacting the surgeon's repair technique.



Figure 4. EnFix TAC-O and TAC-T surgical placement between medial and lateral row anchors

Preclinical Studies

The EnFix technology has been evaluated in multiple bench-top, laboratory and preclinical studies.

Traditional demineralization techniques apply acid treatment after the fibers are cut from the mineralized bone, deleteriously etching the surface nanotopography (surface features) away. Tetrou's unique patented and proprietary process demineralizes the bone struts first and then cuts/cleaves fibers along the bone's long axis, thus maintaining their important nanotopography, and creating long and strong fibers. See Figure 5 below.

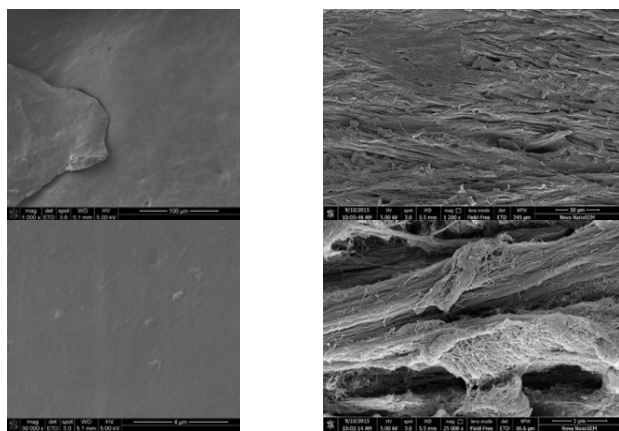


Figure 5. Conventional DBM / DBF surface topography, left panels, Tetrou's DBF right panels. Conventional DBM processing results in a smooth surface due to powdered bone being demineralized in acid, while Tetrou's DBF retains natural nanotopography as a result of demineralization prior to fiber cutting²³.

One design feature of the implant is the ability to allow cells and bone marrow to be wicked up and proliferate through the implant to the enthesis. Mercury Intrusion Porosimetry was used to characterize the implant and showed a porosity of 39% with an average pore size of 160 μm . In Figure 6, comparison is shown to two enthesis repair products that use electrospun fabrics. These materials have a very small pore size that is less than 10 microns and too small for cellular transport.

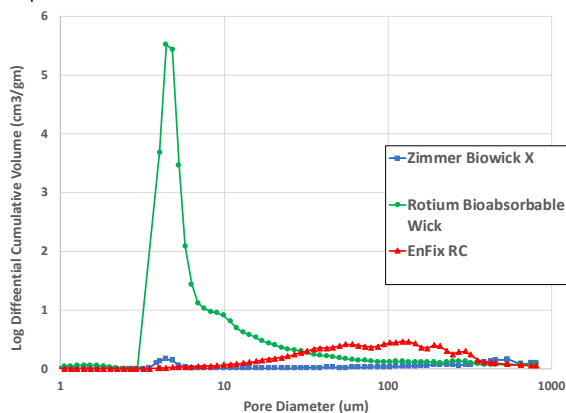


Figure 6. Pore diameter distribution for EnFix compared to competitor products²⁷.

Production of implants with intricate geometries required the development of a proprietary patented water assisted injection molding (WAIM) process that allows fibers to be suspended as a slurry and injected into shaped molds. A further process, designated Formlok™, causes the shape to be retained to control implant integrity even in a wet environment such as is experienced in arthroscopy. Figure 7 below shows the effect of water immersion on the integrity of the implant without Formlok versus with Formlok.

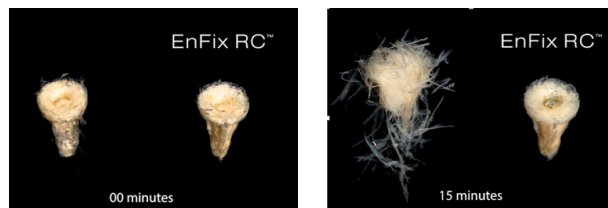


Figure 7. The implant on the left is untreated and loses shape rapidly on immersion in water. Implant to the right is Formlok™ treated²⁶.

As the only additive to the process is water, the manufacture of the DBF and the formed implants conforms with the requirements of minimal tissue manipulation as defined and regulated by the FDA.

While enhanced fixation is not the main purpose of the implant, evaluation of suture anchor fixation in the EnFix RC implant was performed in a laboratory model. Sawbones 10pcf cellular rigid polyurethane foam (Pacific Research Laboratories, WA, USA) is a well-accepted analog for osteopenic cancellous bone and is specified for screw testing in ASTM standards and FDA Guidance documents²⁸. A Mark 10 motorized test stand with a 1500N Force gauge was used for pull out testing with a pull out rate of 20mm/min. A Zimmer Biomet Quattro 5.5mm PEEK suture anchor was either placed directly into the Sawbones foam block or into an EnFix RC implant that was placed into the Sawbones foam block. The maximum pull out force data are shown in Figure 8 below, with standard deviation, n=5. The EnFix RC is shown to provide an improvement in fixation.

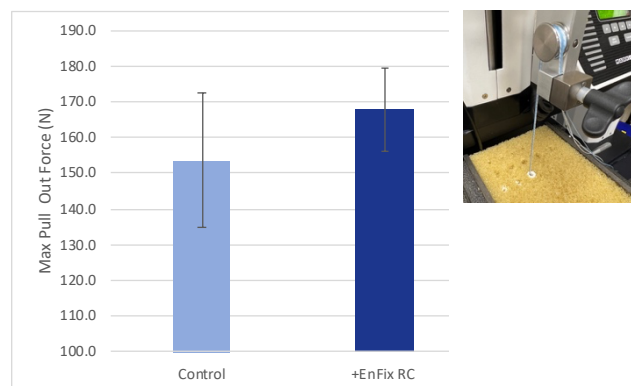


Figure 8. Photograph shows test set up for suture anchor pull out. Chart shows maximum pull out force observed²⁶.

DBF has become one of the most commonly used bone grafting materials and the ability of the Tetraous DBF to promote bone healing was evaluated in a critical sized distal femoral defect in a skeletally mature rabbit model. The results demonstrated rapid bone formation, growing from the outside of the defect toward the center at two weeks with complete remodeling of the DBF into bone seen at four weeks, as shown in Figure 9 below.

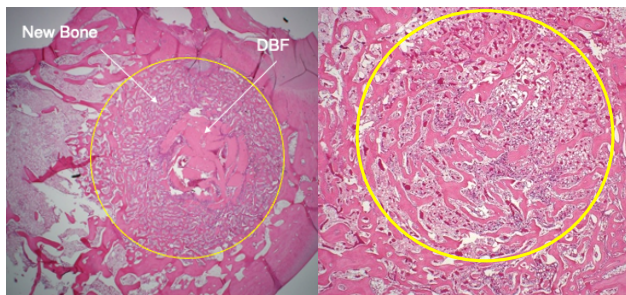


Figure 9. H&E stained histology shows rapid early woven bone formation at 2 weeks, left and 4 weeks, right.

In a sheep model of enthesis repair, presented as Poster # 105 at the 2023 AOSSM meeting²⁹, a DBF sheet was placed at the interface between tendon and bone. Histology (Figure 10) showed enthesis reformation at 12 weeks with Sharpey's Fibers in the treated group, but not the control.

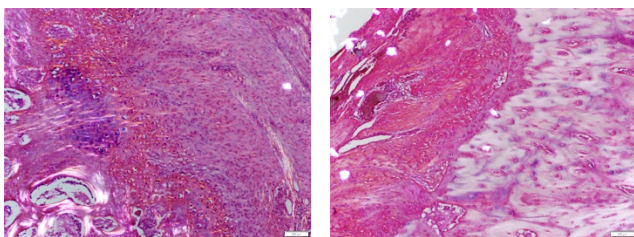


Figure 10. H&E histology at 12 weeks under polarized light confirmed Sharpey's fibers in the DBF treated group (left) not present in the controls (right).

In a separate study, 6.5mm diameter bone screws were placed into fiber sleeves mimicking the peg portion of the EnFix RC implant and placed into skeletally mature sheep distal femoral condyles. The study showed that new bone formation occurred around the screw facilitated by the DBF fibers. These data are shown in Figure 11 below. New bone formation can be seen at four weeks, with some residual DBF, while at 12 weeks all of the DBF has remodeled into new woven bone in the areas between the screw threads.

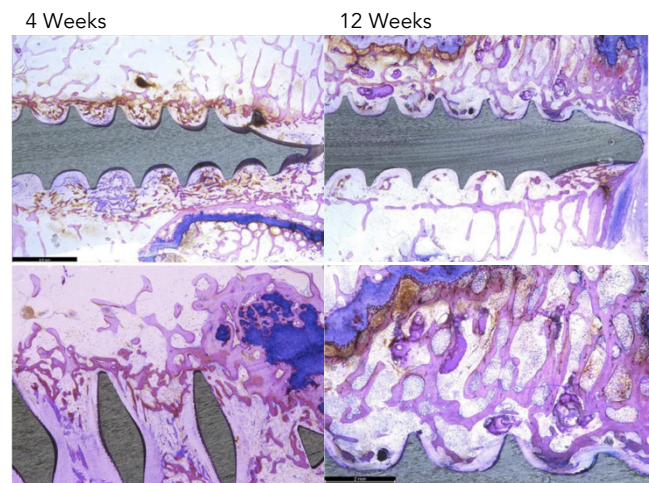


Figure 11. New bone formation around screw threads at 4 weeks (left) and 12 weeks (right)²⁶

A rabbit model of tendon repair was investigated using the infraspinatus tendon. Two bone tunnels were placed using a 1mm K-wire lateral and medial to the infraspinatus tendon insertion footprint. The infraspinatus tendon was sharply dissected from its insertion. Modified Kessler 3-0 sutures were placed through the tendon and then reattached by passing the two free ends of the suture through the bone tunnels using a straight mayo needle. In the treatment group an EnFix DBF sheet approximately 1mm thick and 5mm wide was placed in between the tendon and bone. In the control group the tendon was reattached without an EnFix implant.

Tensile testing of the repaired rotator cuffs was performed and the treated versus non treated repairs compared at 6 and 12 week timepoints. No. 1 Ethibond sutures were passed through the infraspinatus tendon, and interfaced to an MTS 858 Bionix Testing Machine (MTS, Eden Prairie, MN, USA). The humerus was secured in a jig. The infraspinatus tendon-humerus complex was positioned to allow tensile loading in the longitudinal direction of the infraspinatus tendon. The repair sutures were cut prior to mechanical testing in order to isolate the testing to the healing interface alone. Specimens were preconditioned for 5 cycles of loading and unloading with 5% strain of the initial length at a cross-head speed of 6 mm/min, and then loaded to failure at a speed of 6 mm/min. The results of this testing are shown in Figure 12 below. The cuff repairs deploying the DBF implant required greater force (21% at 6 weeks and 26% at 12 weeks) to detach the tendon from the bone than the control.

The results of the two preclinical rotator cuff studies demonstrate that the EnFix technology stimulates biological enthesis reformation and in turn yields better bone to tendon healing providing a biomechanically superior repair to the control scar tissue.

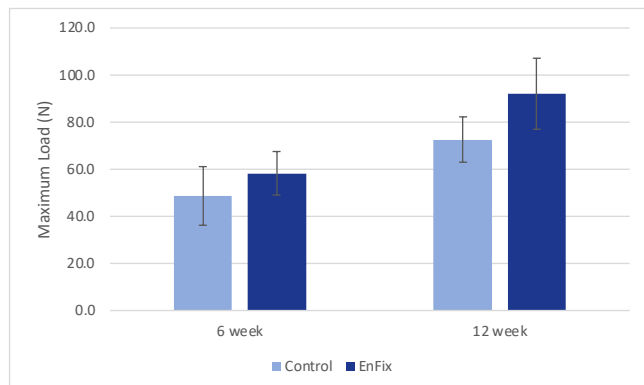


Figure 12. Maximum load of the infraspinatus tendon repair²⁶.

Commercial Status

The EnFix product portfolio was commercialized in Australia and the USA in July 2023 and has since expanded into New Zealand. As of May 2026, 100 surgeons are actively utilizing EnFix, with more than 2,000 procedures performed globally. Across this growing body of clinical use, consistent observations have emerged, including evidence of restored enthesis formation, accelerated biological healing, and reduced surgical failure rates.

The rotator cuff tendon entheses are just a few of the many entheses in the human body and surgeons using EnFix have identified a number of other areas where they can use EnFix RC and EnFix TAC to augment their repairs. EnFix has been used in proximal/distal biceps tenodesis, insertional Achilles tendinopathy, gluteus medius and proximal hamstring reattachment, lateral epicondyle repair, lateral extra articular tenodesis following ACL reconstruction and subscapularis repair during total shoulder arthroplasty. While surgeons have already used the EnFix RC and TAC products in knee indications, a product specifically designed for use in ACL reconstruction has recently been introduced in a controlled launch.

Clinical Results

EnFix devices have been used in cases ranging from primary repairs to complex revisions. Surgeons have been monitoring their patient outcomes and seeing positive benefits from their usage of EnFix.

A US surgeon has performed MRI assessment of repairs using the EnFix RC and EnFix TAC products on patients at 3 months and 6 months post op²⁶. A representative 6 Month

post-op MRI is provided in Figure 13. The MRI demonstrates excellent healing of the supraspinatus tendon repair at the greater tuberosity footprint with clear tendon-to-bone integration. High quality coverage of the greater tuberosity footprint by the repaired tendon, similar in morphology to a native tendon-bone interface, is clearly visible. The only evidence that a tear has been repaired, other than the bone anchors themselves, is a mild intermediate T2 signal in the tendon substance. The subtle T2 signal between the tendon and the adjacent footplate bone suggests a robust tendon-bone enthesis. The EnFix RC shows successful integration into the surrounding bone, with nearly no visible evidence of the EnFix RC such as marrow edema, cystic change or adverse localized soft tissue reaction. The PEEK suture anchor is well seated in the bone and is easily visible with no artifact obscuring the tendon insertion.



Figure 13. Example of MRI

An Australian surgeon did a retrospective review of his rotator cuff repairs pre and post availability of EnFix²⁶. Prior to EnFix usage his failure rate was 8.3%, while with EnFix (94 cases) his failure rate was 5.3% - a 36% reduction.

Another Australian surgeon has performed a review of prospectively collected data from patients who underwent arthroscopic rotator cuff repairs augmented with EnFix RC from August 2023 to October 2024³⁰. A matched control group based on age, sex, repaired tendons, tear characteristics, and follow-up period was selected from the database of patients who underwent rotator cuff repair without EnFix augmentation. Indications for the use of EnFix RC included large to massive rotator cuff tears, tears with poor tendon quality, and revision surgeries. Whenever appropriate, muscle slide and advancement with suprascapular nerve release were performed, especially for the large and massive retracted rotator cuff tears, to ensure tension-free repair.^{31,32} Standard double row repair technique was performed. For delaminated tears, separate repair of the deep and superficial layers was completed using the double layer Lasso loop technique.³³ Visual analogue scale (VAS) for pain, ASES, Constant score, active range of motion, and strength of lateral elevation were collected

preoperatively and at 6 and 12 months postoperatively using a data collection platform (Akunah PROMs, Brisbane, Australia) as part of standard clinical practice. Noncontrast MRI was obtained preoperatively for rotator cuff tear evaluation and at 6 months postoperatively for assessment of healing and enthesis reformation. These variables were then compared with the 6 and 12 month outcomes of the matched cohort who did not have EnFix augmentation with the repair.

A total of 32 patients from the augmented group and 32 patients from the matched control group with mean age of 55.4 years were included in the study. Both groups were comparable in terms of age, gender distribution, and preoperative tear characteristics due to the matching process. The majority of patients have at least two-tendon tears with Patte 2 to 3 retraction and low-grade fatty infiltration (Goutallier 0 to 2) with comparable distribution between the two groups.

The early clinical findings observed in the augmented group support the efficacy of the use of DBF in rotator cuff repairs. At 6 months postoperatively, the patients who had DBF had significantly higher raw PROMs scores and higher achievement rates for MCID and PASS. At 12 months, they persistently had significantly higher raw PROMs scores but the achievement rates for MCID and PASS were comparable with the control group. This indicates that at 6 months, the patients with DBF had better overall symptoms with greater clinically meaningful improvement and higher likelihood of acceptable symptoms. At 12 months the improvements were not clinically perceptible and were comparable with the control group. This plateauing of functional outcome scores and achievement of clinically relevant improvements at 6 months observed in patients with DBF could imply a temporal acceleration of the recovery trajectory compared to the control group. It has been reported in literature that the plateau of maximum recovery of pain and function after rotator cuff repair commonly occurs at 1 year postoperatively³⁴. Qualitative observation of the MRI scans of the patients in the augmented group showed more robust tendons, with obvious encroachment of tendon onto bone and bigger surface area of coverage on the footprint.

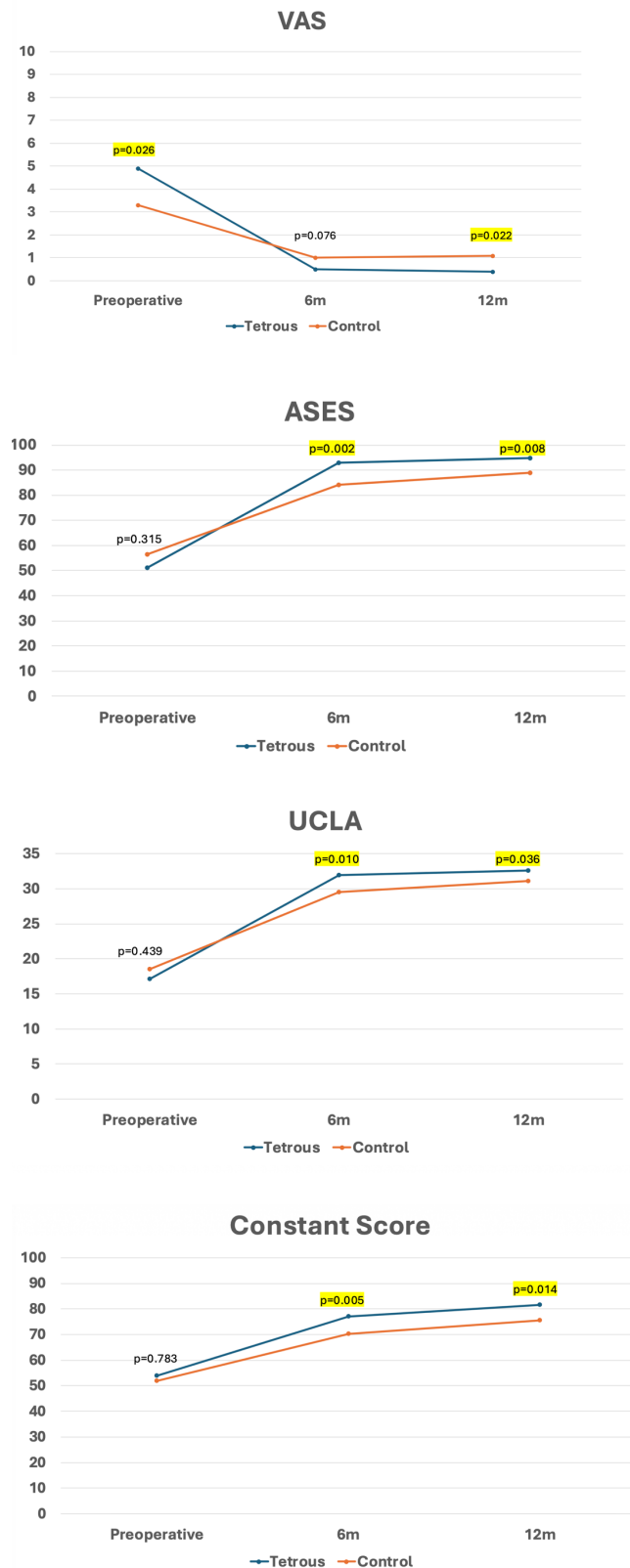


Figure 14. Patient Reported Outcomes at 12 months²⁹

Table 3 shows return to work data from this study. At six months postoperatively, 68.8% in the augmented group were able to return to sport completely, compared to only 33.3% in the control group.

		EnFix	Control	
Return to Work, n (%)				
6m	Unable	1 (3.1%)	3 (11.1%)	p=0.127
	Partial	10 (31.3%)	13 (48.1%)	
	Full	21 (65.6%)	11 (40.7%)	
12m	Unable	0 (0%)	1 (3.3%)	p=0.510
	Partial	6 (18.8%)	7 (23.3%)	
	Full	26 (81.3%)	22 (73.3%)	
Return to Sport, n (%)				
6m	Unable	1 (3.1%)	3 (11.1%)	p=0.023
	Partial	9 (28.1%)	15 (55.6%)	
	Full	22 (68.8%)	9 (33.3%)	
12m	Unable	0 (0%)	1 (3.3%)	p=0.135
	Partial	5 (15.6%)	10 (33.3%)	
	Full	27 (84.4%)	19 (63.3%)	

Table 3. Return to Work and Sports/Hobby

Ken Cutbush, a Brisbane surgeon, has recently presented preliminary data from his analysis of 135 patients treated with EnFix²⁶. Patient age was 59.5 +/- 9.3 years old, and gender was 104 males and 31 females. Concomitant biceps tenodesis was performed in 90 patients while 65 patients had subscapularis involvement.

All patients received MRIs at 6 weeks, 3 months and 6 months. Re-tears identified by MRI at 3 months follow up were determined from a cohort of 135 patients. Tears were classified using the Cofield system. The overall re-tear rate was 3.0% (4/135), or 5.2% (4/77) for large / massive tears. The re-tear rate as a function of tear size is given in Table 4 below. Closer examination of the re-tears showed that only 1 of 135 (0.74%) was a Cho type 1 tear, i.e. involved the enthesis, while the other 3 were Cho type 2, i.e. at the muscle – tendon junction.

Tear size	Re-tear rate
Medium	0% (0/58)
Large	2.3% (1/44)
Massive	9.1% (3/33)

Table 4. Re-tear rate according to tear size

On Going Clinical Studies

A multi-center prospective clinical study with 6 surgeons at 6 centers (in Australia and New Zealand) was initiated in May 2025 to further explore the benefits of EnFix across a broad group of surgeons, each using their own rotator cuff repair technique. Other clinical studies are also in progress in the USA and Australia studying other indications including rotator cuff and proximal hamstring repair.

Patents / Intellectual Property

The demineralized bone fiber technology incorporated into Tetrus products was originally developed by members of the Tetrus scientific team prior to the acquisition of TheraCell, Inc. by ISTO Biologics and is exclusively licensed to Tetrus for use in sports medicine applications. In addition to these exclusively licensed foundational technologies, Tetrus has independently developed a growing intellectual property portfolio, including multiple issued U.S. patents covering EnFix product designs, methods of manufacture, and methods of use. The granted U.S. patents applicable to the products are provided in Table 5 below. Additional patents have been issued internationally, and further patent applications have been filed in the United States and other jurisdictions to expand protection for rotator cuff repair and additional tendon-to-bone (enthesis) indications.

US Patents	
US 9,486,557	US 9,572,912
US 11,660,373	US 11,759,548
US 12,036,338	US 12,115,279
US 12,171,908	US 12,502,459
US 12,629,450	

Table 5. Tetrus Owned US Patents

EnFix®, EnFix RC®, EnFix TAC®, Tetrus® and “It’s All About the Enthesis”® are trademarks of Tetrus, Inc.

FormLok™ and Fibrant™ are trademarks of TheraCell, Inc.

Conclusions

The need for a means of improving the outcomes of rotator cuff repair is clearly demonstrated by the clinical data. This is a problem that all sports medicine practitioners acknowledge. Tetrus has focused on bone to tendon healing to transform the healing paradigm in sports medicine. The Tetrus technology addresses multiple anatomies with the entry into the market in rotator cuff repair. This represents an opportunity of over \$1B encompassing half a million cuff surgeries per year in the USA alone. Tetrus products apply in every one of these cases addressing the still unmet need to reduce the high surgical

failure rates. There are countless types of suture anchors, sutures and, recently, overlay tendon patches used in these surgeries, but none of these adequately address the reattachment of the tendon to the bone at the enthesis. Yet that is the persistent point of failure today. When one reattaches the tendon to the bone it generates scar tissue at the interface even if a tendon overlay patch is used.

Tetrous flipped the script, going between the bone and the tendon, triggering the bone to re-attach to the tendon. The demineralized cortical allograft when implanted into bone starts a process of endochondral ossification in the bone. This recapitulates embryonic development of bone to tendon attachment. The result, as demonstrated by multiple pre-clinical studies, is new healthy and strong tissue with continuity from the bone through the enthesis and into the tendon. Tetrous uses a novel next-generation demineralized bone fiber construct. These materials are a known potent orthobiologic material with significant usage in spinal fusion surgery. The product concept was borne out of a study of the literature on demineralized bone matrix materials for enthesis repair which was highly suggestive that DBM has efficacy for enthesis repair. Tetrous developed the EnFix family of products using unique patented methods to fabricate demineralized bone fiber into a consistent clinical product that can be easily introduced into the enthesis with minimal disruption of current surgical techniques. Extensive preclinical data and initial clinical data suggest that the EnFix products enable biological reformation of the enthesis,

generating a repair that is stronger than the scar tissue that results from current surgical techniques that do not use augmentation between the bone and tendon. With over 3,500 implants used in the first 34 months of clinical usage of the EnFix product and with multiple cases in other anatomies we believe that enthesis repair is now recognized as a need in sports medicine.

In summation, Nikhil Verma MD, Professor and Director, Sports Medicine and Shoulder, Midwest Orthopedics at Rush, Head Team Physician, Chicago White Sox said "Although advancements in rotator cuff technology have been made, limited changes in healing rates and time frames for recovery have been realized. The problem is biology. Current techniques are limited in regard to ease of use and widespread applicability. The Tetrous implant solves for these issues with a simple, reproducible technique designed to address the very foundation of tendon healing - enthesis regeneration."

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