

## Zimmer® Collagen Repair Patch for Rotator Cuff Tendon Repair

Jian Q. Yao, PhD, Zimmer, Inc.

Cheryl R. Blanchard, PhD, Zimmer, Inc.

Steve Bloor, PhD, Tissue Science Laboratories, plc.

### I. Background

*Function of Rotator Cuff:* The rotator cuff is made up of four muscles of the shoulder complex: the supraspinatus, infraspinatus, teres minor and subscapularis (Post et al 1998). These muscles all originate from the scapula and connect with either the greater or the lesser tuberosity of the humerus via the respective tendons. These muscle/tendon assemblies actively control the kinematics of the shoulder, as well as provide passive restraints to prevent dislocation of the shoulder complex.

*Clinical Needs for Reinforcement Patches:* Unfortunately, rotator cuff tendon injuries occur frequently as a result of either trauma or degeneration. The most commonly injured rotator cuff tendon is the supraspinatus (Gschwend et al 1988). Subacromial impingement of the supraspinatus tendon is thought to be related to its tearing. Rotator cuff damage can also be due to degeneration and it afflicts patients with pain and instability of the shoulder. While rotator cuff damage is common, rotator cuff tears often do not heal spontaneously. Without a prompt and effective surgical treatment, it may progress further and result in the complete tear of the affected cuff tendon. Therefore, surgical repair of rotator cuff tears is now one of the most commonly performed orthopaedic procedures. In the United States alone, 250,000 rotator cuff tendon injuries are repaired annually (Medical Data International 2000; Millennium Research Group 2002). However, these surgeries have had limited success. As much as 30% of cases require subsequent revision surgeries due to re-tear (Bishop et al 2003). The re-tear may be due to either suture pull-out of the frayed tendon before biological healing becomes adequate or non-healing of the tendon/bone junction. Consequently, there have been considerable efforts to devise ways to mechanically augment the repair with reinforcement patches to reduce tension along the suture line, which may assist in the healing of the tendon/bone junction.

*Desirable Properties of Reinforcement Patches:* For a reinforcement patch to be efficacious in assisting the tendon repair, it needs to have a number of properties:

- It must provide effective tension relief to the primary repair along the suture line for a sufficiently long duration to allow timely healing of the tendon/bone junction. This requires that reinforcement patches should have appropriate mechanical properties (load to failure, stiffness). If load to failure is too low, the patch will rupture. If the patch is too compliant, i.e. if its stiffness is too low, it loses load-sharing capacity;
- It needs to be able to integrate with surrounding native tissues;
- It has to be conducive to the healing process of the tendon and the re-establishment of the tendon/bone junction;
- It needs to be biocompatible, sterile and not lead to inflammation of surrounding tissues.

While existing reinforcement patches have some of these required features, they remain lacking in some of the above required properties.

## II. Zimmer Collagen Repair Patch

In partnership with Tissue Science Laboratories, plc (Aldershot, England), Zimmer has developed a reinforcement patch for rotator cuff repair. This patch is made of a chemically crosslinked, acellular collagen/elastin material derived from porcine dermis (Fig.1). In this article, key properties of this new product, known as the *Zimmer* Collagen Repair Patch, will be described based on a series of *in-vitro* and *in-vivo* evaluations. Where appropriate, comparison will be made between this material and other materials which are used for rotator cuff repair reinforcement.



Fig.1 *Zimmer* Collagen Repair Patch (5 cm x 10 cm x 1.5 cm)

Important features of the *Zimmer* Collagen Repair Patch include:

- The *Zimmer* Collagen Repair Patch is made of processed, acellular porcine dermal tissue. It retains the natural three-dimensional collagen/elastin structure of dermis (in contrast to the weak structure of collagen sheets made of re-constituted collagen).
- It is chemically crosslinked, and thus is resistant to enzymatic degradation. The patch has a long residence time after implantation, and hence provides a durable reinforcement.
- It can be stored at room temperature.
- It has a long shelf-life (3 years).
- It is depleted of cellular debris during the chemical washing process, which minimizes potential cell-mediated responses commonly associated with allogeneic or xenogeneic cells.
- It is mechanically strong, stiff and durable, hence appropriate as a reinforcement patch (see data below).
- It can be easily handled (is easily trimmable and does not curl up during suturing).
- It is easily sutured.
- It is conducive to fibroblast infiltration and integrates well with surrounding connective tissues (see below).

### III. In vitro evaluation

Tensile tests demonstrated that *Zimmer* Collagen Repair Patches have higher tensile failure loads than commercially available SIS (small intestine submucosa) patches (Fig.2).

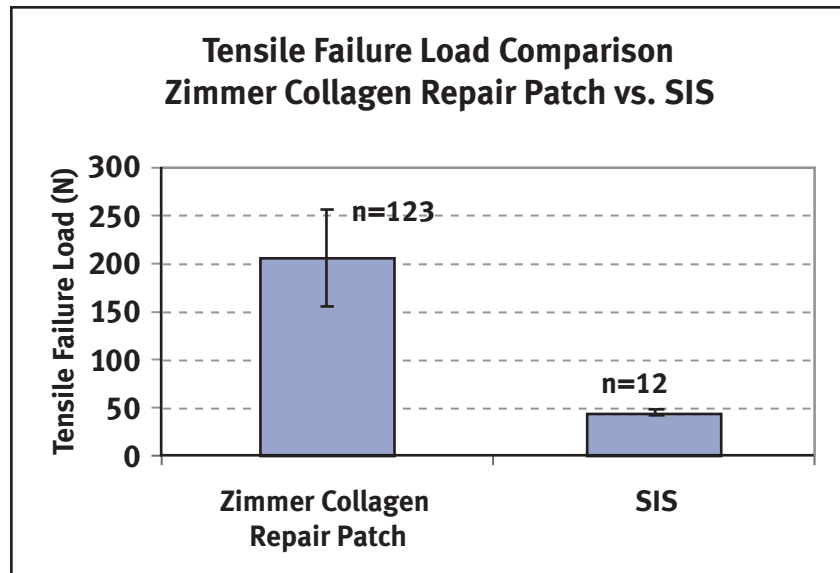


Fig.2 Tensile failure load comparisons (data on file)

### IV. In vivo evaluation in an ovine model: a 24-week follow-up study of Zimmer Collagen Repair Patches for rotator cuff tendon repair

*This study was conducted at Purdue University, West Lafayette, Indiana in collaboration with D. van Sickle (PhD, DVM, Emeritus Professor, Purdue University) and G. Bruer (PhD, DVM, Associate Professor, Purdue University), and G. Nicholson (MD, Assistant Professor of Orthopaedic Surgery, Rush University, Chicago, IL).*

**Study Objectives:** The study was designed to evaluate the *Zimmer* Collagen Repair Patch in an *in vivo* model (sheep) in comparison with the standard of care (suture repair alone) and a commercially available patch product made out of SIS. Ovine infraspinatus tendon was utilized for the repair model, as it has similar dimensions as human supraspinatus tendon.

Specifically, the study intended to answer the following questions: What is the product's inflammatory response in a tendinous environment; what are its short and long term mechanical properties; and does the product have any inductive or conductive potential for regeneration of neotendinous tissue? The animal study protocol was approved by the Institutional Animal Care and Utilization Committee of Purdue University. An orthopedic surgeon with extensive surgical experience of rotator cuff tendon repair was involved in the development of the animal model and surgical technique.

*Materials and Methods:* The animal study involved 2 groups of eight adult non-pregnant cross-bred ewes weighing 180-240 pounds; one group was designated as a nine-week follow-up group, the other as a twenty-four-week follow-up group. Aseptic bilateral surgeries were performed on each of the 16 ewes by the same board certified veterinary surgeon. Fresh T-shaped tears were created with a scalpel. The torn tendon was then sutured to the humeral bone through bone tunnels. A reinforcement patch was then sutured to the tendon close to the muscle-tendon junction and to the bone through the bone tunnels. The surgical treatment was alternated so no pair of shoulders had the same treatment. Within each follow-up group (8 sheep), 5 shoulders were treated with suture repair alone, 6 with *Zimmer* Collagen Repair Patch reinforcement and 5 with SIS reinforcement. Bone tunnels were prepared for fixation of tendons and patches to the bone (Fig.3).

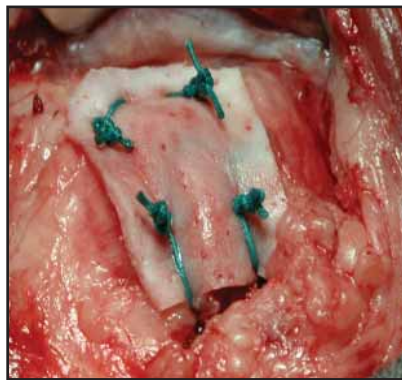


Fig.3 Surgical technique

Fibrinogen measurements (a measure of inflammatory response) were made preop and at various time points postop (3, 6, 9, 12, 20 and 24 weeks). At the time of euthanasia (9 or 24 weeks post-op), the shoulders for histology were isolated, sparing the infraspinatus tendon area, and placed in fixative. Immediately after necropsy, those shoulders for biomechanical testing were prepared and placed in a cooler on ice packs. These were usually tested within two hours after necropsy, placed back in the cooler, and delivered to the histology laboratory where they were placed in fixative.

In addition to the soft tissue histology, the gross specimens (which included bone, cartilage, muscle and tendon) were cut and processed for plastic embedded undecalcified slides of the tendon-bone composite. These slides provided histology data around and along the implants as well as in the bone and tissue adjacent to the implant.

*Results:* Since different treatments were applied to contralateral joints in the same animal (e.g. some animals had *Zimmer* Collagen Repair Patch reinforced repair in one shoulder and SIS in the contralateral shoulder), fibrinogen analysis was performed on selected sub-groups of animals without co-implantation of *Zimmer* Collagen Repair Patches and SIS patches. At 3 weeks postop, animals repaired using SIS showed significantly elevated plasma fibrinogen levels ( $p=0.019$ ) (Fig.4a), whereas, the *Zimmer*

Collagen Repair Patch group showed no significant elevation of fibrinogen (Fig.4b). Subsequently, i.e. at 6, 9, 12, 24 weeks postop, the fibrinogen levels were not statistically significantly different from the pre-op baseline levels for any group of animals.

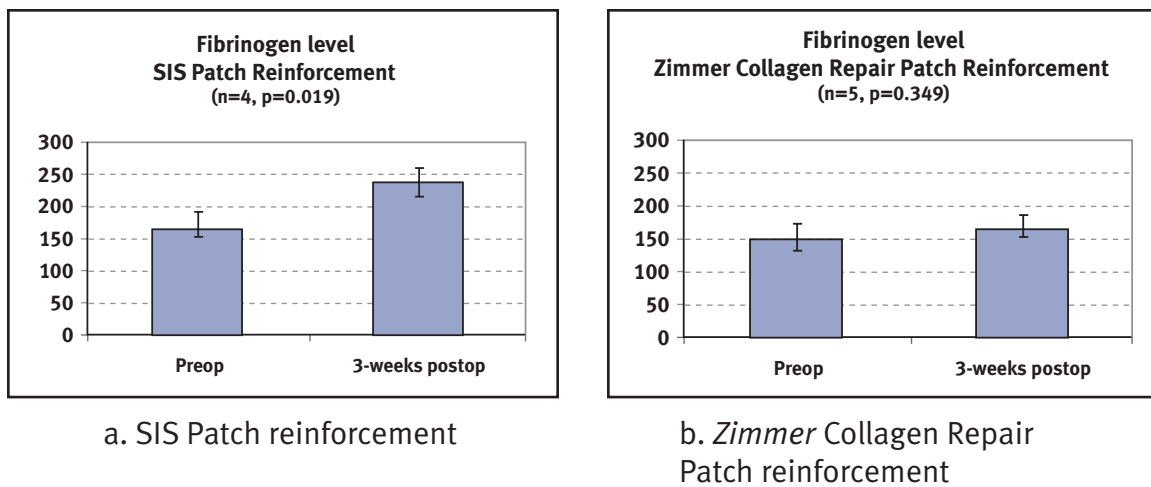


Fig.4 Fibrinogen comparisons preop and 3-weeks postop (data on file)

Biomechanically, at nine weeks, the average failure load for the *Zimmer* Collagen Repair Patch reinforced tendons was  $182 \pm 63$  pounds, for SIS,  $137 \pm 16$  pounds, and for suture,  $201 \pm 60$  pounds. Furthermore, at 9 weeks, when within-subject comparison was made, it was found that the *Zimmer* Collagen Repair Patch reinforcement led to higher failure loads than either suture repair alone or SIS reinforcement (n=4).

By 24 weeks, the suture only tendon repair had an average peak load of  $331 \pm 55$  pounds, SIS was  $340 \pm 33$  pounds and the *Zimmer* Collagen Repair Patch was  $316 \pm 97$  pounds. However, the differences were not statistically significant.

Histologically, at nine weeks, a total of six tendons were studied; 3 non-tested for histology and 3 tested specimens (all undecalcified and embedded in plastic). At twenty-four weeks a total of 16 tendons were studied: 3 intact for histology and thirteen tested specimens (fourteen specimens in plastic, portions of five specimens in paraffin).

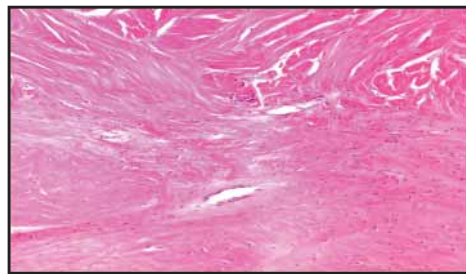
At nine weeks postop, macrophages and fibroblasts were seen on the surface of the *Zimmer* Collagen Repair Patch. In comparing the tissue response to the three tendon treatments at nine weeks, SIS produced the most diverse tissue response ranging from loose connective tissue to osteogenesis. The rate and maturity of genesis of bone/ tendon reinsertion was not as mature in the SIS as in the suture-only repair. At 9 weeks, the majority of SIS patches appeared to have resorbed. The *Zimmer* Collagen Repair Patches were intact, but not fully integrated with surrounding tendon tissues yet.

By twenty-four weeks, the cellular reaction around the *Zimmer* Collagen Repair Patch reinforced tendon had changed dramatically. The encompassing layer of inflammatory cells was largely absent or present only in foci. In all samples, the surrounding connective

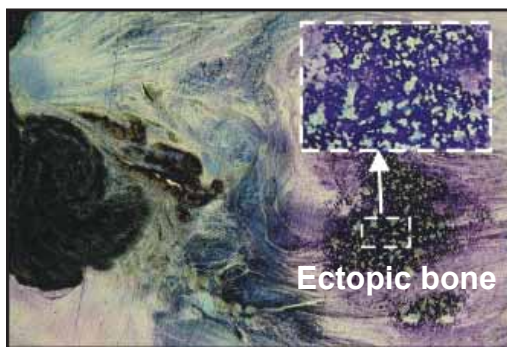
tissue was interdigitating with the *Zimmer* Collagen Repair Patch as well as concurrent vascular and fibroblastic invasions (seen as purple spots in Fig.5a). While the *Zimmer* Collagen Repair Patch provided a strong stable environment for connective tissue and vascular invasion as well as reinforcement for the tendon, it also was flexible enough to experience the biomechanical forces around or through it, allowing tissue expression to occur to provide stiffness (evidenced by fibrocartilage formation within the *Zimmer* Collagen Repair Patch matrix).

Within the vicinity of SIS, at twenty-four weeks, diverse types of tissue were evident but with more of an osteogenic response than at nine weeks. Ectopic bone formation was seen, which can serve to weaken the tendon repair (Fig.5b).

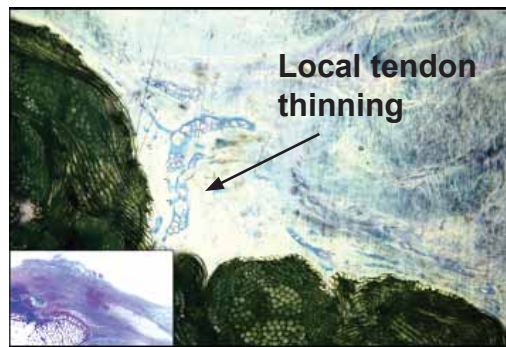
Surprisingly, necrosis and rarefaction of surrounding tissue matrix was observed around the non-resorbable suture in some shoulders repaired with suture alone (without any patch reinforcement) (Fig. 5c).



(a) Zimmer Collagen Repair Patch reinforced repair



(b) SIS reinforced repair



(c) suture repair alone

Fig.5 Typical histology at 24 weeks post-op (data on file)

**Discussion:** This study is based on an acute injury model. Suture alone repair led to satisfactory healing. Clinically, when chronic injuries to the rotator cuff tendon occur, suture alone repair does not produce consistent, satisfactory results (as much as a 30-40% re-tear rate is reported (Bishop et al 2003)).

*Summary:* In this acute injury model, it was observed that:

- At 3 weeks postop, fibrinogen levels were elevated (indicative of inflammation) for animals implanted with SIS patches, but not so for animals implanted with *Zimmer* Collagen Repair Patches.
- No increase in the fibrinogen level over the baseline was observed at 6, 9, 12, 20 and 24 weeks postop for any groups.
- At 9 weeks, the majority of SIS patches appeared to have resorbed. *Zimmer* Collagen Repair Patches were intact, but not fully integrated with surrounding tendon tissues yet.
- At 24 weeks, *Zimmer* Collagen Repair Patches were integrated with surrounding tendon tissues. Ectopic bone formation was observed in some tendons repaired with SIS patches. Surprisingly, necrosis and rarefaction of surrounding tissue matrix was observed around the non-resorbable suture in the shoulders repaired with suture alone (without any patch reinforcement).

## **V. References**

Bishop et al (2003) American Association of Orthopaedic Sports Medicine, June 2003, Diego, CA.

Gschwend, N., Ivosevic-Radovanovic, D. and Patte, D. (1988) Rotator cuff tear - relationship between clinical and anatomopathological findings. Arch. Orthop. Traum. Surg., 107:7-15.

Medical Data International (2000) Market and Technology Reports: US Market for Orthopedic Biomaterials, #RP-591149 (available at Zimmer Business Intelligence Unit).

Millennium Research Group (2002) US markets for arthroscopy 2002. Toronto, ON. (available at Zimmer Business Intelligence Unit).

Post, M., Flatow, E.L., Bigliani, L.U. and Pollock, R.G. (1998) The shoulder: operative technique. Williams & Wilkins, Baltimore, Maryland.

