ORTHO[PURE] XT

TRX Orthopaedics Limited

Pre-clinical evaluation of a novel decellularised ligament reconstruction solution

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Introduction

The OrthoPure® XT device is a porcine tendon graft which has been treated using a patented decellularisation processing technology (dCELL®) to remove all viable cells and native components which have the potential to elicit an immune response. This decellularisation technology gently cleanses the tissue whilst preserving the natural collagen architecture.

The OrthoPure® XT is an off-the-shelf device for knee ligament reconstruction that negates the need to take tissues from the patient, or to invest in complex and costly donor procurement processes. The result is a reduction in operative time, no donor site morbidity and associated muscle strength deficiencies for the patient, no specialist storage requirements and the flexibility to have the product ready to use off the shelf at any time.

The OrthoPure® XT device is a soft tissue graft that is specifically designed to be implanted using standard surgical techniques. It is compatible with standard instrumentation and with common soft tissue fixation devices for both femoral and tibial attachment. The handling properties are also comparable to commonly used soft tissue grafts (allograft or autograft).

Biomechanical properties

Tensile strength (N) of the OrthoPure® XT product range and commonly used allografts is presented in Figure 2.

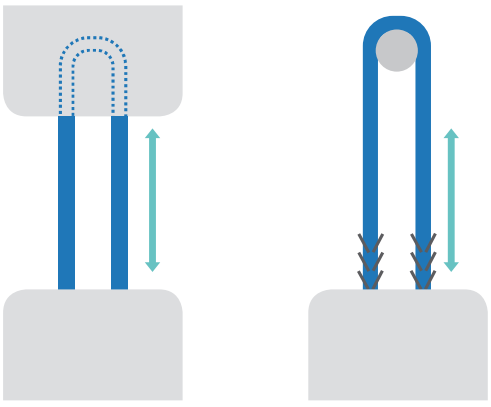

Figure 1. Illustration of biomechanical testing formats showing looped testing configurations.

Product size/allograft type	n	Mean tensile strength (N ± SD)
OrthoPure® XT Size 5	32	1816 (± 166)
OrthoPure® XT Size 6	30	2057 (± 251)
OrthoPure® XT Size 8	59	3559 (± 394)
OrthoPure® XT Size 10	37	5770 (± 698)
(a) 6 mm STG allograft[1]	11	2359 (± 474)
(b) 7 mm STG allograft[1]	11	3263 (± 677)
(c) 8 mm STG allograft[1]	11	3908 (± 556)
(d) 9 mm STG allograft[1]	11	4360 (± 606)

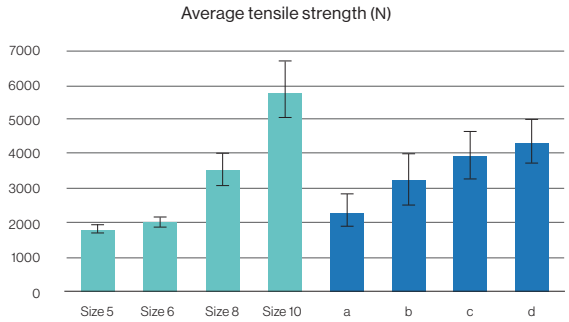

Figure 2. Biomechanical properties of OrthoPure® XT product range in comparison with commonly used allografts.

Allografts were combined semitendinosus and gracilis (STG). 1 to 3 tendons were placed together to create 1 sample construct representing the desired diameter. Allografts were disinfected using the Allowash® process (LifeNet Health, VA, non-irradiated). Allografts were tested in a looped configuration and cryogenically gripped at both ends (see Figure 1) using a screw-driven Instron® materials testing machine.

OrthoPure® XT products are derived from 1 (Size 5 and 6), 2 (Size 8) or 3 (Size 10) decellularised tendons, which were placed together and tested. Size 8 and 10 products were whipstitched at each free end prior to testing. OrthoPure® XT products were tested in a looped configuration folded over a pillion with free movement and cryogenically fixed at 1 end. OrthoPure® XT products were tested using an Instron® column mechanical test machine with measurements performed using BlueHill® software (Instron®).

In vivo performance

The in vivo performance of the OrthoPure® XT device has been assessed in a large animal study (sheep). Anterior cruciate ligament (ACL) reconstruction was performed in the stifle joint of skeletally mature sheep. The safety and performance of the OrthoPure® XT device material was compared to autologous tendon. Biomechanical and histopathological assessments were performed at 0, 3 and 6 months after implantation. OrthoPure® XT grafts were single stranded (not folded), measuring 3–6.5 mm (average 5.2 ± 0.6 mm). Autograft controls were folded over to form a 4–7 mm diameter graft (average 5.1 ± 0.4 mm). Grafts were measured using a sizing block. Fixation was achieved using MILAGRO® (DePuy Synthes) bioresorbable 7 mm (diameter) screws in the tibia and femur. 6 mm tunnels were drilled.

Fixation (maximum force at rupture immediately after surgery) was not significantly different for OrthoPure® XT and the autograft control.

Both grafts displayed multifocal calcification, ossification, Sharpey's fibre formation and screw osteointegration at the 3-month and 6-month time points.

Histopathological scoring was slightly lower for OrthoPure® XT, and a slightly higher inflammatory reaction was seen for OrthoPure® XT at 3 months, which is expected when comparing to autograft. The inflammatory reaction decreased to a comparable level by 6 months. Evaluation of the synovial fluid, organs, knee joints and draining lymph nodes showed no particle migration or adverse effects.

Both grafts displayed a reduction in biomechanical properties at 3 months, followed by an increase at 6 months. Biomechanical properties were lower for OrthoPure® XT at 3 months, but there was no statistically significant difference between the graft types at 6 months.

Graft	Time point (months)	n †	Mean tensile strength (N ± SD)	Mean stiffness (N/mm ± SD)
OrthoPure® XT	0	6	289.9 (± 109.7)	74.0 (± 23.3)
	3	4 (2)	57.1 (± 35.8)	20.8 (± 14.2)
	6	7 (2)	164.8 (± 111.2)	44.9 (± 31.8)
Autograft	0	6	391 (± 71.2)	70.5 (± 19.5)
	3	2 (4)	175.4 (± 13.6)	63.5 (± 10.5)
	6	6 (1)	305.9 (± 208.8)	58.1 (± 32.6)
Native ACL	N/A	13	1392.7 (± 279.5)	180.1 (± 33.4)

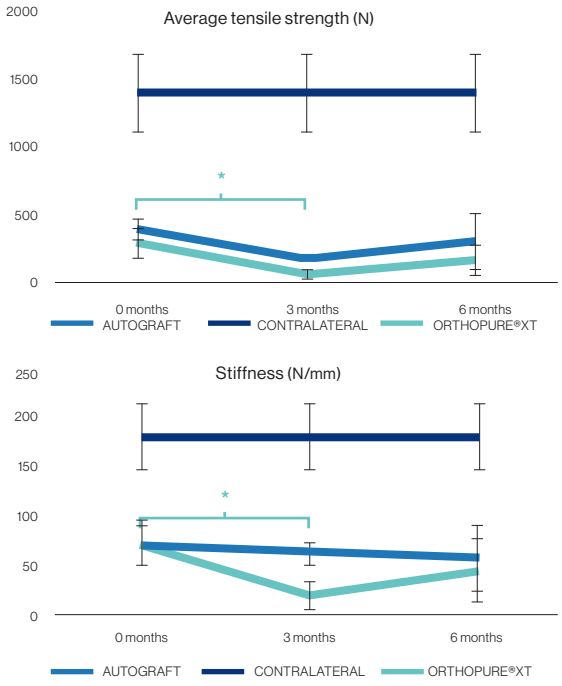

Figure 3. Biomechanical properties of OrthoPure® XT vs autograft and native ACL in a sheep model over 6 months.

Contralateral data = native ACL. Contralateral data not time point dependent and included for comparative purposes.

† Denotes number in brackets refers to number of graft breakages.

* Denotes statistical significance (OrthoPure® XT at 0 and 3 months).

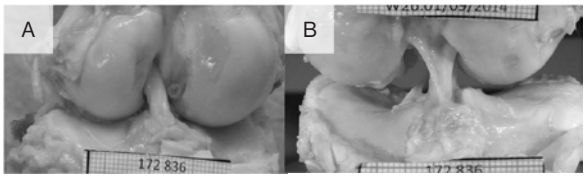

Figure 4. OrthoPure® XT (A) and autograft control (B) in sheep stifles at 6 months post implantation.

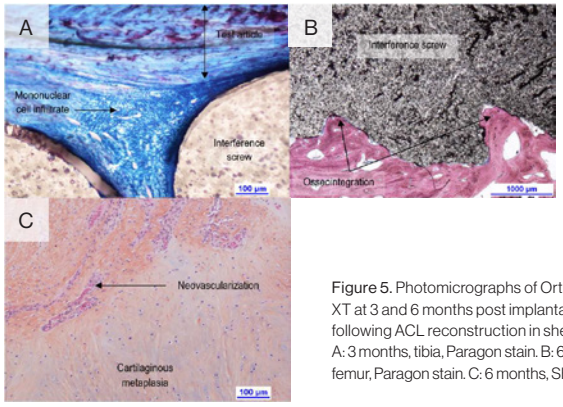

Figure 5. Photomicrographs of OrthoPure® XT at 3 and 6 months post implantation following ACL reconstruction in sheep. A: 3 months, tibia, Paragon stain. B: 6 months, femur, Paragon stain. C: 6 months, SHE stain.

Product information

Device size	Max strength	Indication
5	900 N	• Multi-ligament reconstruction Recommended for use in: Extra-articular ligament reconstruction
6	1200 N	• Multi-ligament reconstruction Recommended for use in: Extra-articular ligament reconstruction
8	3500 N	• Primary anterior cruciate ligament (ACL) reconstruction where autograft tissue is not suitable • Revision ACL reconstruction • Multi-ligament reconstruction Recommended for use in: Extra-articular ligament reconstruction
10	5700 N	• Multi-ligament reconstruction Recommended for use in: Posterior cruciate ligament (PCL) reconstruction

Device size	Catalogue number
5	2405XTS
6	2406XTS
8	2408XTD
10	2410XTT

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References

PUBLICATIONS: 1. BONIELLO, M. R., SCHWINGLER, P. M., BONNER, J. M., ROBINSON, S. P., COTTER, A., BONNER, K. F. IMPACT OF HAMSTRING GRAFT DIAMETER ON TENDON STRENGTH: A BIOMECHANICAL STUDY. ARTHROSCOPY: THE JOURNAL OF ARTHROSCOPIC AND RELATED SURGERY, 31 (2015), PP 1084–1090.

DATA REFERENCES: SIZE 5 & 6 TENSILE RAW DATA SIGNED 13 AUG 2020, SIZE 8 TENSILE DEV-STDY-229 V06, SIZE 10 TENSILE A03/0020/01, ANIMAL STUDY PRE-CLIN-36 V02.

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