Biomechanical and Histological Assessment of a Polyethylene Terephthalate Screw Retention Technology in an Ovine Metatarsal Fracture Model

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Abstract

Objective Screw loosening in fracture fixation poses a clinical risk which may lead to implant failure, particularly in poor bone quality. The objective of this study was to examine the effectiveness of a novel screw retention technology (SRT) for increased screw purchase in a large animal metatarsal fracture model.

Study Design This was a biomechanical, radiographic, and histological study utilizing an ovine metatarsal fracture model. Twenty-four sheep metatarsi underwent 3-mm ostectomies and were repaired with a nine-hole plate and 3.5-mm screws placed in oversized 3.5-mm holes to simulate worst case revision surgeries (i.e. no initial screw thread bone contact). Sheep were sacrificed at 3, 6 or 12 weeks ($n = 6$ each) post-operation. Post-sacrifice, each surgically implanted screw underwent either destructive mechanical testing or histomorphometric analyses.

Results Treated metatarsi showed improved screw retention and normal fracture healing. Significant improvement in breakout strength and pullout strength of screws treated with the SRT were found as a function of healing time. Histologically, bone ingrowth at the screw interface was also shown to significantly increase with healing time. Improvements in fracture healing, indicated by an increase in bone fraction and decrease in void space at the osteotomy, were also observed with healing time.

Conclusion The results demonstrate the effectiveness of the SRT as a method for improved screw retention in a rescue-screw type scenario.

Keywords
- screw loosening
- screw failure
- fracture healing
- ovine
- screw retention

Introduction

Screws are the most commonly used implant in orthopaedic surgery.[1] However, screws do not always operate effectively and may loosen leading to fracture non-union.[2,3] Screw failure is especially prevalent following procedures that treat patients with poor bone quality,[3–5] and is one of the primary causes of revision procedures for orthopaedic hardware.[4] These revision procedures typically require extensive pre-operative planning, the use of specialized implants and tools and mastery of technically challenging surgical techniques that dramatically raise health care costs.[6] There is a wide range of screw failure processes that can include screw backout, stripping, complete fracture or loosening due to

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infection.[3,7] Screw loosening is considered an unsolved issue and new techniques or devices that prevent loosening would represent a significant development for orthopaedic clinical practice.

To reduce the incidence of screw loosening, various groups have focused on improving screw/plate technologies,[8–11] among other approaches including bone cements, materials from the operating room and high friction surface coatings.[12–14] Many of these efforts are mechanical solutions implemented intraoperatively and carry additional sets of risks such as undue bone–implant pressure, compromised bone stability or increased bone removal. The most popular competing solutions are rescue screws (a screw with a larger diameter)[11] and locking plate systems (systems that lock the screw and plate together).[7,15] However, current solutions have not adequately addressed screw loosening by these hardware advancements.[7,13,14]

Accordingly, a novel rescue screw technology has been proposed that directly engineers the bone–screw interface (►**Fig. 1**). Succinctly, a unique bio-textile was fabricated into a braided sleeve; placed around the screw increasing the surface area of contact between the screw and the bone, thus enhancing screw engagement to prevent loosening.[16] The screw retention technology (SRT) studied here uses a cylindrical braided device composed of polyethylene terephthalate mono filaments; a member of the polyester family with no additives, it is not bioabsorbable.[16] Polyethylene terephthalate has previously demonstrated biocompatibility in many clinical applications, including cardiovascular grafts,[17] plastic surgery application,[18,19] artificial ligaments[20,21] and bone augmentation.[22]

In this application, the bio-textile interface provides a compliant layer between the screw and bone; mechanical loads are distributed to reduce the pressure-induced bone resorption that frequently occurs at the screw–bone interface.

The objective of this study was to investigate the *ex vivo* biomechanics and histological composition of ovine metatarsal fracture model treated with a fixation plate and the SRT. The post-implantation *ex vivo* breakout and pullout strength biomechanics were determined. In addition, the bone ingrowth adjacent to screws and callus healing was evaluated via histomorphometry.

Materials and Methods

This investigation was approved by the Institutional Animal Care and Use Committee (IACUC no. 16-6379). This study used 24 skeletally mature sheep that underwent a unilateral ostectomy and subsequent hardware implantation on their right metatarsus. Three time points at 3, 6 and 12 weeks postoperatively were used; six sheep were sacrificed at each of the three time points.

Sheep metatarsal bones underwent a 3 mm mid-diaphyseal transverse ostectomy that was stabilized with a 9-hole, 3.5 mm LC-DCP plate (DePuy Synthes; West Chester, Pennsylvania, United States) using seven proximally placed bicortical 3.5 mm cortical screws (DePuy Synthes; West Chester, Pennsylvania, United States) and two distally placed unicortical 4.0 mm cancellous screws (DePuy Synthes). To simulate a scenario requiring rescue screws, 3.5 mm pilot holes were drilled for the seven proximal bicortical screws and 4.0 mm pilot holes were created for each of the distal screws. This surgical model was utilized to induce the worst possible case of screw–bone engagement (e.g. no screw–bone engagement without SRT augmentation). The SRT device (OGmend Implant System; Woven Orthopedic Technologies, LLC Manchester, Connecticut, United States) was slid over the outer diameter of all screws.[16] The length of the SRT was matched to the length of the screw body and placed into the pilot hole using a stylus, leaving $\leq$ 1 mm portion of the device exposed. The exposed portion of the SRT implant was monitored to ensure the device did not migrate.

Terminal *in vivo* insertion torque (N-m) was measured during surgery using a torque sensing screwdriver (TAT300; Futek, Inc., Irvine, California, United States). Following healing,

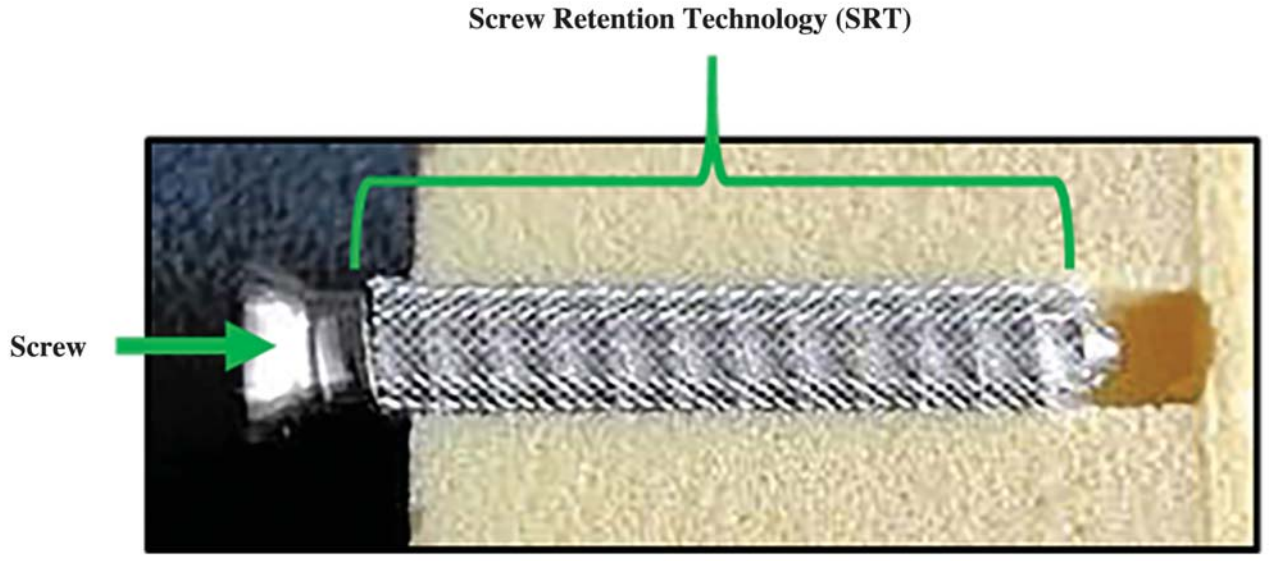

Fig. 1 Example image of a novel rescue screw retention technology designed to directly engineer the bone–screw interface. The implant comprises a unique bio-textile (i.e. a braided sleeve is placed around the screw).

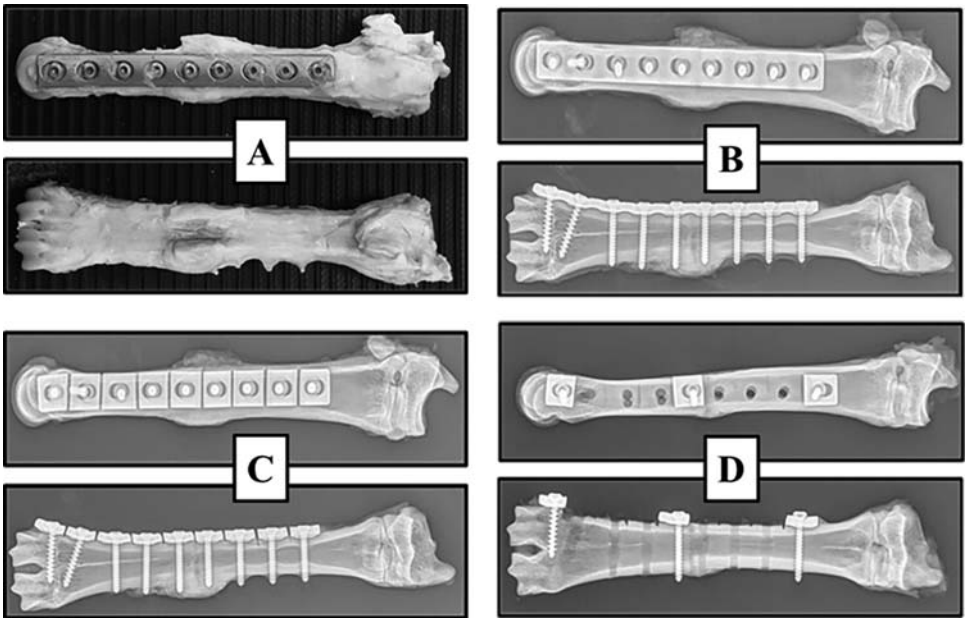

Fig. 2 Example images of metatarsals in the study, including (**A**) radiograph at time 0, (**B**) photograph following dissection, (**C**) radiograph prior to screw pullout showing cut plate and (**D**) radiograph following screw pullout showing remaining screws for histology.

euthanasia and gross dissection, freshly harvested metatarsal samples were prepared; extraneous soft-tissue was removed, taking great care not to damage the screw insertion, SRT implant, callus or ostectomy.

Following gross dissection, the bone samples were photographed and subject to biplanar digital radiography (►**Fig. 2A** and **2B**). Screw breakout torque (defined as the initial break-out moment [N-mm] required to loosen the screw) was also determined for $n = 3$ of 9 screws per sample by the digital torque sensing screwdriver.

Destructive screw pullout force was also determined for $n = 3$ of 9 screws per sample. Fracture fixation plates were cut using a rotary cutoff wheel to isolate each screw (►**Fig. 2C**). Care was taken to ensure that the isolation process did not detrimentally affect the adjacent screws; samples were irrigated with saline to minimize thermal effects. Metatarsi were then rigidly mounted into a testing system (Mini Bionix 858, MTS System, Eden Prairie, Minnesota, United States). The long axis of the screw was aligned collinearly with the actuator to ensure a normal vector pullout direction. Individual screw–plate constructs were quasi-statically withdrawn at a rate of 1 mm/s. Force (N) and displacement (mm) data were collected at 150 Hz. Construct stiffness (N/mm) and ultimate failure load (N) were calculated for samples allocated to pullout testing. A total of 18 screws were investigated each for breakout and pullout at each time point.

Histological analyses were conducted on the ostectomy fracture to demonstrate the quality of healing at the bone defect site, contributing six tissue samples per time point. Osteotomy site samples were processed using standard decalcified paraffin techniques and stained with haematoxylin and eosin.

The remaining three screws in each metatarsal (►**Fig. 2D**) were used for non-decalcified hard tissue histology, yielding a total of 18 screws for histological evaluation at each time point. Samples were processed using standard non-decalcified techniques.[16,23,24] Sections were taken along the long axis of the screw to display the implant and surrounding bone. Sections were stained with Sanderson's Rapid Bone, and then counterstained using Van Gieson's solution.

Images were acquired for the entire section using a microscope (AG Heinze; Lake Forest, California, United States) and digital camera (Diagnostic Instruments; Sterling, Heights, Michigan, United States). Image Pro software (Media Cybernetics, Silver Spring, Maryland, United States) was used for histomorphometric measurements.

The ostectomy region of interest (ROI) was set as the area from the proximal surgical osteotomy cut to the distal cut. The screw ROI was set as the length of screw within the bone with an area extending 300 µm towards the centreline of the screw and 300 µm into the native bone. The histomorphometric parameters measured within each ROI were percent bone area within the ROI (%), percent fibrous/soft tissue within the ROI (%), percent implant (as applicable for screw and SRT device) area within the ROI (%) and percent void area within the ROI (%).

Histology sections were also evaluated by a certified pathologist to document the cellular responses for each of the samples. The pathologist was blinded to the treatment group. The sections were qualitatively analysed according to cell type (i.e. polymorphonuclear, lymphocytes, plasma, macrophages, giant and osteoblastic cells) and implant responses (i.e. signs of bone remodelling, implant degradation and neovascularization).

Significance was determined using a standard one-way analysis of variance (ANOVA) test, where p-values less than 0.05 were considered to be significant (SigmaStat; Systat Software Inc., San Jose, California, United States). A *post-hoc* Student–Newman–Keuls multiple comparison analysis was performed to determine statistically relevant p-values. Significant differences are designated with similar letters. The statistical power for any comparison was above 0.80.

Results

Clinical assessment, as observed by two board certified veterinary surgeons (J.T.E and R.H.P.), of screw insertion in the oversized holes indicated that surgical screw insertion with SRT augmentation felt surgically tight and clinically acceptable during *in vivo* implantation. All animals survived to term and gross necropsy yielded no adverse findings. Post-sacrifice radiographs indicated normal osteotomy healing, no screw backout or plate migration. All biomechanical and histological tests were run to completion and no experimental issues were noted.

For cortical screw trajectories, the terminal insertion torque (mean ± one standard deviation) with the SRT augmentation was 0.34 ± 0.10 N-m, 0.43 ± 0.15 N-m and 0.37 ± 0.12 N-m for 3, 6 and 12-week groups respectively. Similarly, the terminal insertion torque for cancellous screws was 0.45 ± 0.20 N-m, 0.61 ± 0.27 N-m and 0.36 ± 0.17 N-m for 3, 6 and 12-week groups respectively. No significant difference in insertion torque was found between groups for either the cancellous or cortical screws.

Three-, 6- and 12-week group cortical screw breakouts exhibited mean torques of 0.07 ± 0.03 N-m, 0.14 ± 0.08 N-m and 0.15 ± 0.09 N-m, respectively. Despite no significant difference between the 6- and 12-week groups, both 6- and 12-week groups had significantly larger breakout torque magnitudes as compared with the 3-week group ($p < 0.01$).

Screw pullout force (N) and stiffness (N/mm) data are presented (►**Fig. 3**). The mode of failure was consistent across sacrifice time points with screws failing under straight axial displacement with mild/moderate bone avulsion. No micro-motion at the screw–plate interface was observed.

Cortical and cancellous pullout forces for screws with cortical trajectories are shown (►**Fig. 3A** and **3B**, respectively). Cortical screw pullout forces were significantly different, with pullout forces significantly increasing between all three sacrifice time points (all $p < 0.01$). Cancellous pullout forces also demonstrated significant increases in magnitude as a function of healing time ($p = 0.02$), with the lone exception that there was not a significant increase between the 6- and 12-week time points ($p = 0.06$).

The results of histomorphometric analyses for screw ROI and ostectomy ROI are shown in ►**Tables 1** and **2**, respectively). No statistical differences were calculated for total ROI areas across sacrifice time points (p-values of 0.93, 0.84 and 0.73 for the cortical screw, cancellous screw and osteotomy ROI respectively).

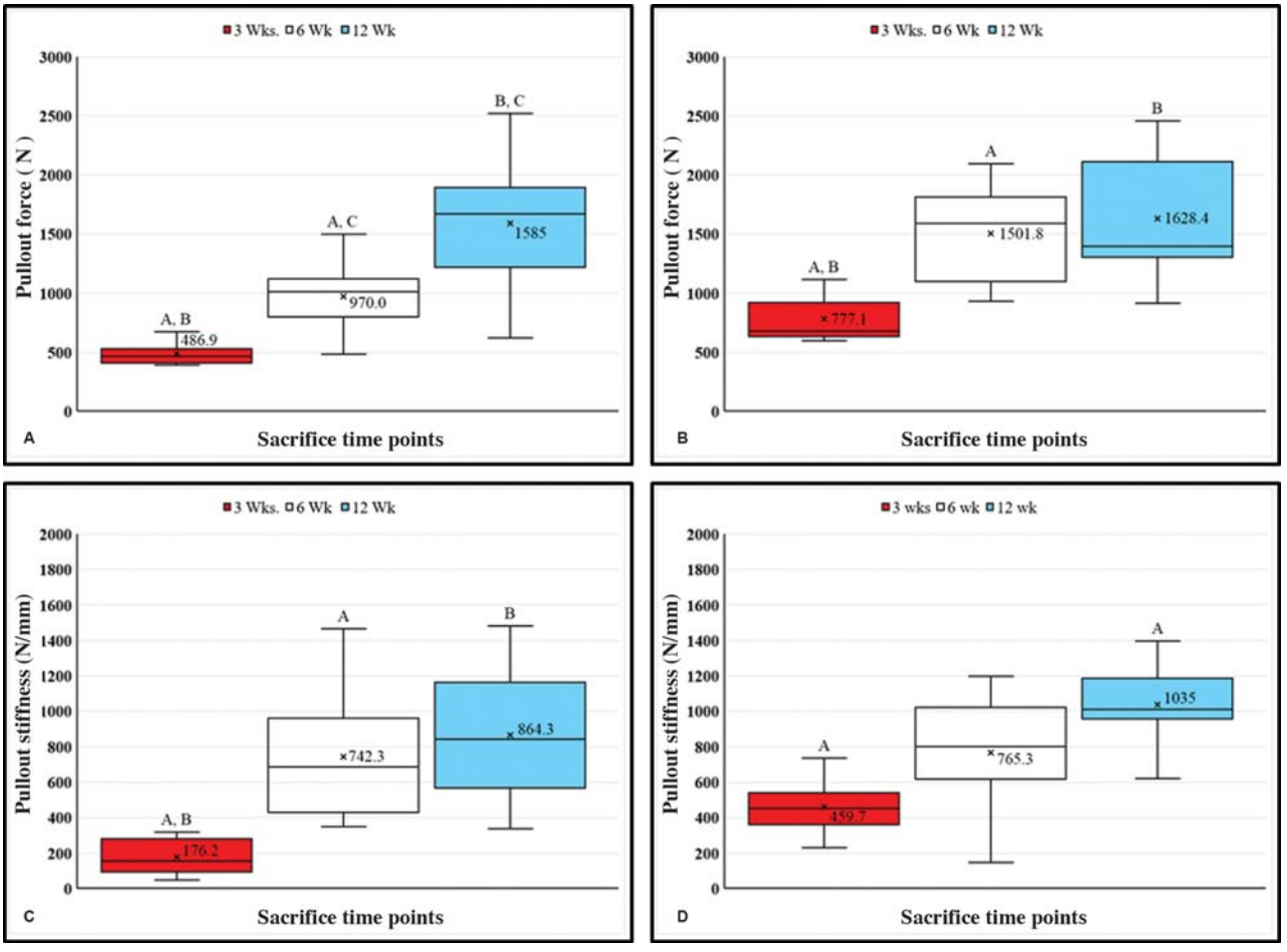

Fig. 3 Screw pullout data of metatarsals treated with screw retention technology after 3 , 6 and 12 weeks, showing (**A**) cortical screw pullout force (A, B, C: $p < 0.01$), (**B**) cancellous screw pullout force (A, B: $p = 0.02$), (**C**) cortical screw pullout stiffness (A, B: $p < 0.01$), and (**D**) cancellous screw pullout stiffness (A: $p = 0.01$).

Table 1 Histomorphometric data (mean ± standard deviation) for cortical and cancellous screw ROI

Constituents of interest	Cortical screws			Cancellous screws		
	3 Wk	6 Wk	12 Wk	3 Wk	6 Wk	12 Wk
% Bone	16.60 ± 3.70^{A}	17.90 ± 4.90^{B}	$21.5 \pm 5.40^{A,B}$	10.10 ± 4.30^{C}	14.80 ± 5.30^{D}	$17.90 \pm 6.60^{C,D}$
% Soft tissue	8.06 ± 4.13^{E}	8.88 ± 6.40^{F}	$5.42 \pm 3.32^{E,F}$	$12.8 \pm 4.70^{G,H}$	6.42 ± 2.80^{G}	7.74 ± 4.67^{H}
% Implant	3.35 ± 1.73	2.99 ± 1.53	3.04 ± 1.95	2.74 ± 1.14	2.18 ± 1.10	3.07 ± 1.35
% Screw	57.6 ± 7.20	53.7 ± 11.40	58.90 ± 5.90	47.10 ± 7.60	42.10 ± 14.90	43.40 ± 9.50
% Void space	14.40 ± 5.60^{I}	16.60 ± 6.90^{J}	$11.20 \pm 4.50^{I,J}$	27.20 ± 5.50	34.50 ± 17.70	27.80 ± 9.60

Abbreviation: ROI, region of interest.
Note: Significant differences are indicated by like letters (A, B, D, E, G, H, I, J: $p < 0.01$; C: $p < 0.04$; F: $p < 0.03$).

Table 2 Histomorphometric data for osteotomy ROI

Constituents of interest	3 Wk	6 Wk	12 Wk
% Bone	43.20 ± 12.80	46.70 ± 14.80	53.40 ± 9.70
% Soft tissue	13.00 ± 8.00	16.20 ± 12.80	14.00 ± 9.40
% Void space	43.70 ± 10.70	38.40 ± 14.30	32.60 ± 10.90

Abbreviation: ROI, region of interest.
Note: No significant differences were found.

Histopathology showed that the SRT sleeves were embedded within reactive fibrosis and associated with a rare population of lymphocytes and few macrophages. The SRT sleeve was observed to be embedded within the bone in most cases (►**Fig. 4**). Qualitative histopathology analysis indicated that there were no signs of abnormal gross cellular reactions (inflammation or infection) at the bone–screw–SRT interfaces or osteotomy sites. There were also no gross signs of device degradation or debris indicating the device maintained its structural integrity throughout the study.

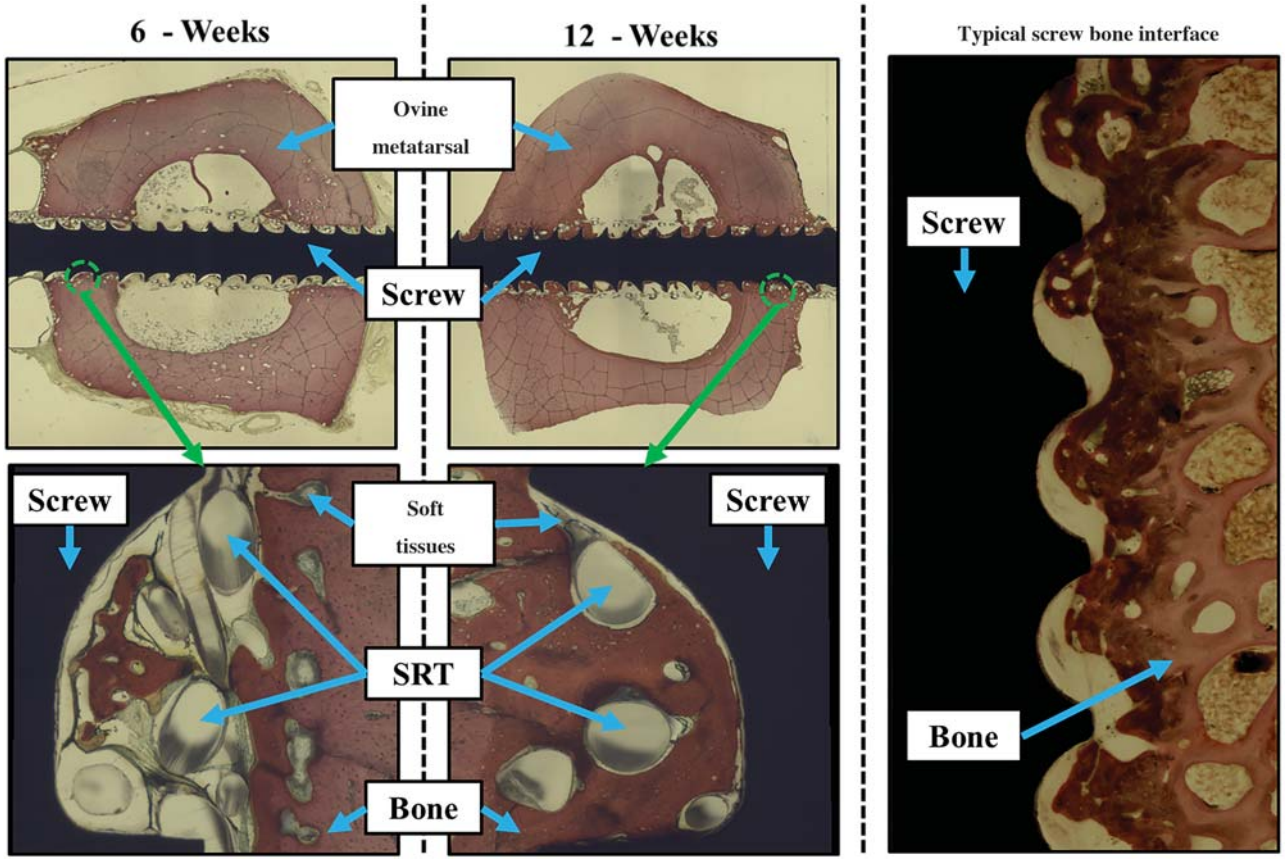

Fig. 4 (Top left and top middle) Example histologic images demonstrating the histomorphometric region of interest (i.e. the screw–bone interface) at 10x magnification at 6 and 12 weeks post-implantation. (Bottom left and bottom middle) Example images highlighting the implant, screw retention technology (SRT) device, bone and soft tissue at the screw–bone interface at 100x magnification at 6 and 12 weeks post-implantation. (*Right*) Example image (derived from an unrelated study; unpublished data) showing a typical control screw–bone interface in the ovine metatarsal at 12 weeks post-implantation.

Discussion

Pullout and breakout biomechanical testing exhibited consistent improvements in screw retention as a function of increased healing times. Histologically, increased bone fraction surrounding the cortical and cancellous screws consistent with improved screw retention was observed following healing. Increased bone fraction and decreased void fraction, as well as radiographic changes, were identified at the ostectomy indicating successful progression of osteotomy healing toward osseous union consistent with metatarsal osteotomy healing previously observed by our group utilizing standard screw–bone engagement models.[25–28]

Unfortunately, no previous studies in the literature were found on screw pullout and breakout in ovine metatarsals for direct comparison. However, sheep metatarsi are commonly used as an analogue for human tibia due to similarities in size and bone mineral density between the two bones.[25–27]

Matityahu and colleagues[29] evaluated the pullout strength of 3.5-mm self-tapping screws in a standard drill hole model using cadaveric diaphyseal tibiae. It was found that a single insertion, four insertions and five insertions yielded pullout strengths of 1710 ± 550 N, 1030 ± 543 N and 364 ± 209 N respectively. These findings are of a similar magnitude to the pullout strengths of the present study and indicate that, after 12 weeks of healing, the SRT provides similar screw retention to screws with one insertion and no over drilling. In addition, our data indicated that after 3 weeks of healing, the SRT provides greater screw retention than screws with five insertions and no overdrilling. Similarly, Oldakowska and colleagues[30] evaluated the pullout strength of 4 mm self-tapping screws in a standard drill hole model in cadaveric thoracic ovine bone. It was found that the screws exhibited a failure force of 695.0 ± 82.4 N, and a stiffness of 618.5 ± 114.1 N/mm. Again, these findings are of a similar magnitude to the pullout and stiffness data generated for this study, which utilized an overdrilled hole model, following 6 and 12 weeks of healing. The similarity between our data and these studies indicates that the SRT may allow relevant healing at the screw–bone interface in an overdrilled (i.e. rescue) screw scenario following healing.

Claes and colleagues[31] explored the tissue differentiation of ovine metatarsal ostectomies (2.1 mm) following 9 weeks of healing subject to the established method of external fixation. Despite discrepancies in healing times and fracture size, all values in the present study were within one standard deviation of all reported cortical and medullary tissue distributions for bone, soft tissue and connective tissue/void space. Indeed, even the 3-week time point in the present study observed similar ostectomy tissue differentiation to a smaller fracture after a longer healing duration. Similarly, Augat and colleagues[32] also investigated external fixation of 2.0 mm ovine metatarsal ostectomies. Following 9 weeks of healing, histological data at the ostectomy yielded similar composition of bone, soft tissue and connective tissue/void space to the present study. Histomorphometric data indicated the percent bone increased, the percent soft tissue did not increase and the percent implant remained constant; these trends likely resulted from normal bone remodelling, lack of excessive fibrotic reaction to the SRT and no degradation of the SRT. This increase in bone likely resulted in the observed increases in mechanical integrity. The congruence of the tissue differentiation with the discussed studies indicates that effective fracture healing was induced in the treated group of this study. Therefore, it appears that the SRT was essential at promoting the appropriate mechanical integrity to allow for fracture healing.

When complications occur, either intraoperatively or in revision procedures, surgeons must remove additional bone stock to replace the loose screws, thus limiting the ability of the surgeon to generate the necessary stability and reduction for fracture fixation. When orthopaedic screws require revision, surgeons use a variety of ad-*hoc* techniques including the use of larger and/or longer screws (i.e. rescue screw), inserting screws in a different trajectory/pilot hole, use of additional plates or augmenting the failed hole with bone void fillers or polymethyl methacrylate (i.e. bone cements) or with the Matchstick method.[33] Unfortunately, the use of a strip ('matchstick') of bone graft to act as a shim leads to asymmetric hoop stresses with force concentration at the strip of bone graft and increases the risk of screw hole wall fracture particularly with compromised (osteoporotic) bone quality. Cements also have several drawbacks. A major problem is the difficulty of precise placement and the prevention of inadvertent migration of the semi-liquid cement which could cause problems (i.e. mechanical impingement). In addition, the most commonly used orthopaedic cement, polymethyl methacrylate, in the process of *in situ* polymerization can cause local or systemic toxicity as in the case of monomer release. Also, there is the generation of high local temperatures as the cement exothermically polymerizes, with the potential for thermal injury to local structures. The main problem with repositioning approaches is the creation of stress risers with the empty screw holes weakening the underlying osseous structure; local anatomic considerations may also prevent plate repositioning. Therefore, there still exists a clinical need for a device which can prevent screw complications and revisions, and, if revision is required, provides a more robust stabilization augmentation in clinical surgery. The SRT device studied here does not suffer from these issues. The structure of the device maximizes screw bone engagement in a uniform circumferential fashion avoiding stress concentration. The SRT has no issues with either exothermic curing, or local toxicity as the material of the SRT has well-documented history of bio-compatibility. With the SRT, there is no need to leave a screw hole empty eliminating subsequent stress riser creation and obviating the need to reposition an orthopaedic plate or device.

The design of this study excluded an *in vivo* negative control group (i.e. overdrilled pilot hole with a standard screw). Subjectively, all screws in a negative control group were considered clinically unacceptable and unsafe for fracture repair in an *in vivo* setting by two board-certified veterinary surgeons. This was further validated by time-zero ramp to failure testing on cadaveric ovine metatarsal samples (data not shown); the measured failure load for a proposed negative control group was determined to be less than the estimated load on the treated limb at any time during *in vivo* healing. Accordingly, application of a negative control group in an *in*

vivo animal model would have been ill-advised, in-humane and against the spirit of IACUC guidelines. It was determined that any negative control group samples would suffer catastrophic failure upon standing and full-weight-bearing immediately following recovery from surgery. A positive control (i.e. a screw placed in the surgically standard hole or the use of some form of rescue screw) was deemed to be the most appropriate control for this model. However, as this study was an initial attempt to prove the efficacy of the SRT device a positive control arm of the study was not implemented. By comparing our results to data from previous studies,[29,30] that used the current standards of screw insertion, it appears that augmentation of an overdrilled hole with the SRT leads to similar levels of acute biomechanical stability following healing. This assertion is further strengthened by the fact that all fractures generated within this study had typical healing pathways leading towards clinically acceptable osseous union, which would be unlikely if the implanted hardware was not adequality stabilizing the fracture. A recent study examining the effectiveness of the SRT in an ovine spine model, in which a positive and negative control where possible, demonstrated that the SRT device does improve screw–bone purchase as compared with a negative control.[16] However, while the literature is replete with studies that have translated the general results of sheep orthopaedic models to human applications,[26,27,34,35] one should take caution when prescribing the absolute values of ovine-derived data to that of the human condition.

In conclusion, the novel SRT investigated in this studied showed improved screw retention in an *in vivo* ovine metatarsal model with oversized holes as healing time progressed, and that the biomechanical stability imparted by the SRT device was of the same order observed for standard screws implanted acutely. The biomechanical and histological results of this study demonstrate the SRT as an effective method for improved screw retention for mitigation of clinical screw failure in situations that might otherwise have clinically unsatisfactory fixation.

Author's Contributions

All authors drafted, revised and approved the submitted manuscript. Jeremiah Easley, Christian Puttlitz, Cecily Broomfield, Ross Palmer and Kirk C. McGilvray contributed to conception of study, study design, acquisition of data and data analysis and interpretation. Alexander Jones contributed to conception of study, study design, and data analysis and interpretation.

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Conflict of Interest

Dr Broomfield reports grants from Woven Orthopedic Technologies, Manchester, Connecticut, United States, during the conduct of the study. Dr Easley reports grants from Woven Orthopedic Technologies, Manchester, Connecticut, United States. Dr. Jones has a patent OGmend Implant System, Woven Orthopedic Technologies, LLC Manchester, Connecticut, United States. issued. Dr McGilvray reports grants from Woven Orthopedic Technologies, Manchester, Connecticut, United States, during the conduct of the study. Dr Palmer reports grants from Woven Orthopedic Technologies, Manchester, Connecticut, United States, during the conduct of the study. Dr Puttlitz reports grants from Woven Orthopedic Technologies, Manchester, Connecticut, United States, during the conduct of the study. The authors, Dr McGilvray, Dr Easley, Dr Puttlitz, Mrs Broomfield and Dr Palmer report no perceived or potential conflicts of interest that may have biased the work presented within this manuscript. Dr Jones holds the patent on the device described within this study.

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