Rotator cuff healing using demineralised bone fibers in an ovine infraspinatus tendon model

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Objectives

Rotator cuff tears are a common cause of shoulder pain and functional deficits. Although surgical repair is often able to restore function and resolve pain, high rates of postoperative structural failures are reported. A number of synthetic and biologic scaffolds have been used to augment/reinforce the primary tendon repair. The current study evaluated the use of human demineralised bone fibers (hDBF) formed into a patch providing a scaffold as well as a pool of inductive bone morphogenetic proteins known to facilitate healing. The in vivo response of human DBF Patches (hDBF-P) were evaluated as an Onlay over the infraspinatus tendon (IST) and at the IST-bone interface (enthesis) in an adult ovine model.

Methods

hDBF-P was manufactured from demineralized cortical bone and characterised using stereozoom (Figure 1A) and environment electron microscopy (Figure 1B). Osteoinductivity (OI) was evaluated in the standard nude rat intramuscular implantation (IM) model at 28 days using µCT and paraffin histology.

A bilateral infraspinatus tendon model was used to evaluate 4 groups at 6 and 12 weeks (n=3 per time point): Onlay control and hDBF-P Onlay; Enthesis repair control and hDBF treated. The Onlay model simulated a tendon injury by 4 longitudinal slits along the IST (Figure 2A) and lateral drill holes in the proximal humerus [1]. The hDBF-P was hydrated in saline and secured to the IST with interrupted 2-0 non-resorbable sutures (Figure 2B). On contralateral side, the central third of the IST was sharply dissected, the footprint burred, and 2 medial row anchors inserted. The sutures were passed through the IST in the enthesis repair control group. In the enthesis repair with hDBF-P the sutures were passed through the hDBF-P which was placed at the tendon bone interface followed by sutures through the IST (Figure 2C). Two lateral push lock anchors were used for a suture bridge (Figure 2D) in both repair groups. Endpoints included clinical recovery, macroscopic dissection, 3T MRI, radiographs, µCT and paraffin histology, H&E staining, and light microscopic evaluations to assess local cell and tissue responses and healing.

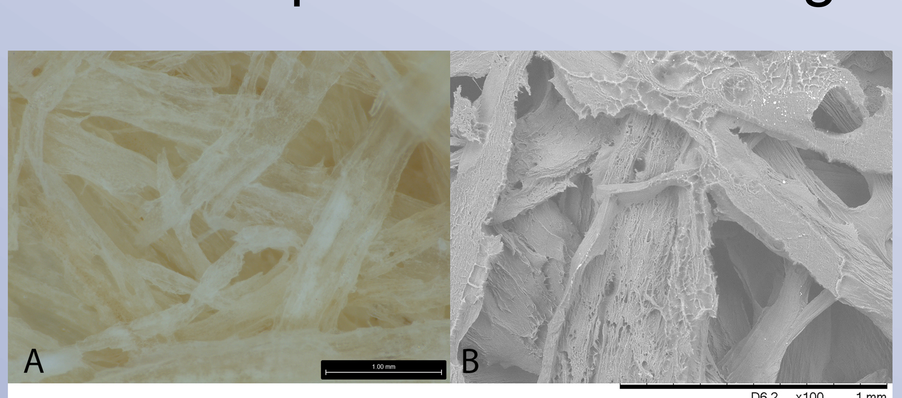

Figure 1: Demineralised bone fibers viewed under stereozoom microscope (A) and environmental scanning electron microscope (B) demonstrating the surface topography.

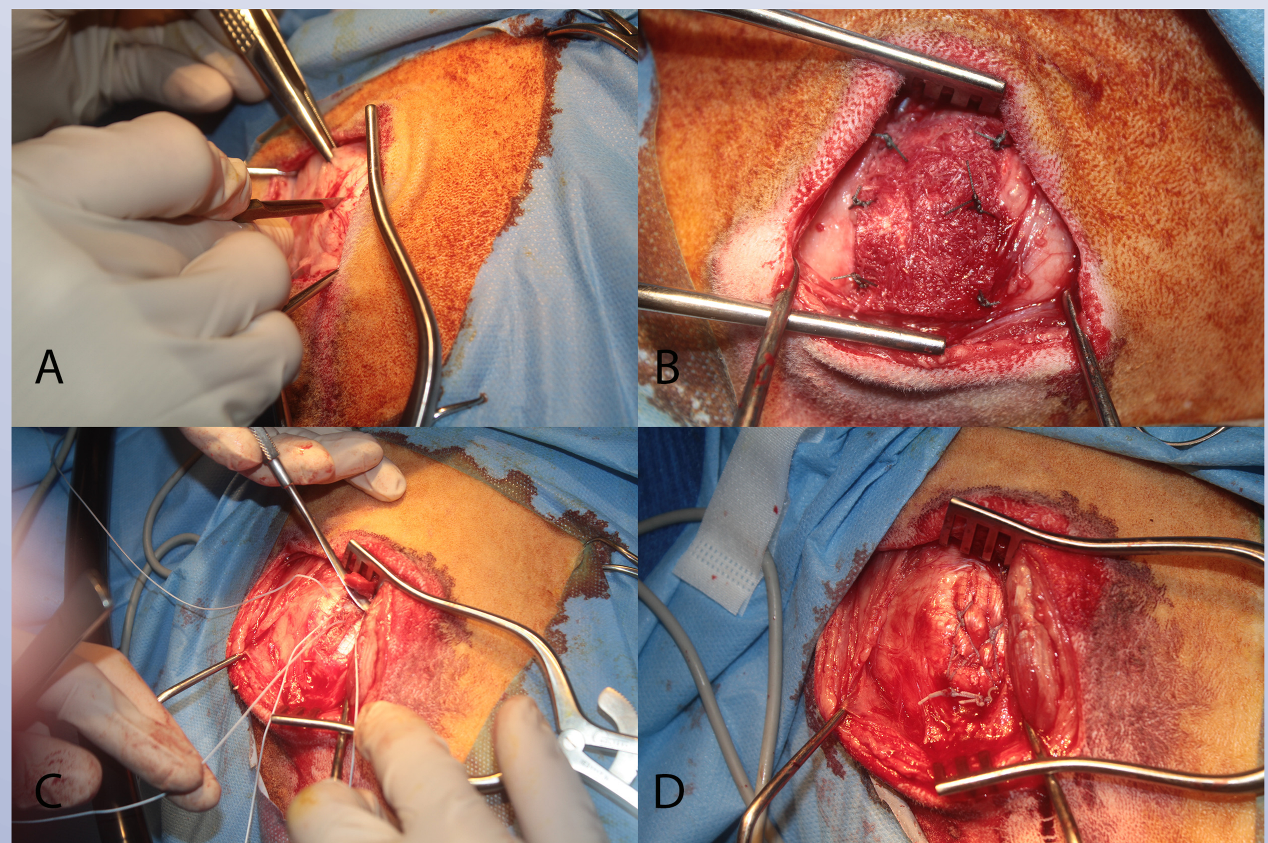

Figure 2: Surgery examples showing the slits placed into the tendon (A), hDBF Overlay on the infraspinatus tendon (B), hDBF at the tendon-bone interface (C) and final suture bridge construct (D).

Results

OI was confirmed on IM implantation (Figure 3). The sheep recovered uneventfully with no adverse events. MRI in the Onlay control group revealed little response or increase in tendon thickness. The Onlay hDBF-P treated demonstrated increased tendon thickness. Histology showed some initial inflammatory cells that decrease with time as the hDBF-P remodeled. MRI in the hDBF-P treated enthesis group supported increased activity at the bone interface at 6 and 12 weeks (Figure 4) compared to controls. 12 week histology with hDBF-P showed an active tendon-bone enthesis and Sharpey's fibers not seen in the control (Figure 5)

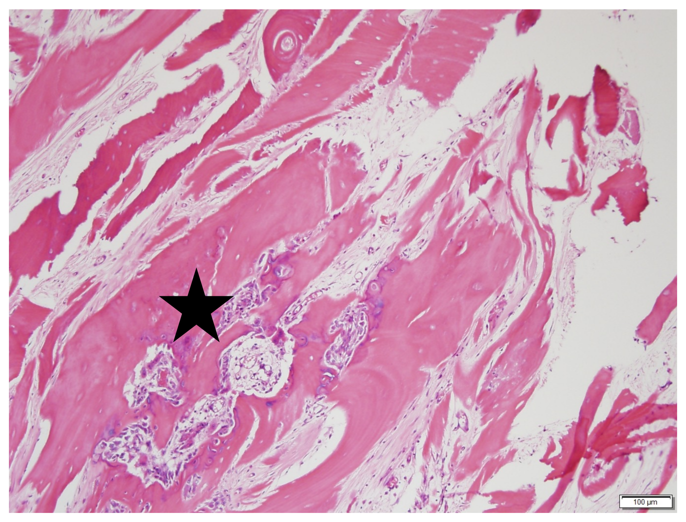

Figure 3: Osteoinductivity (★) was confirmed on histology for the hDBF-P implanted intramuscularly in nude rats at 28 days.

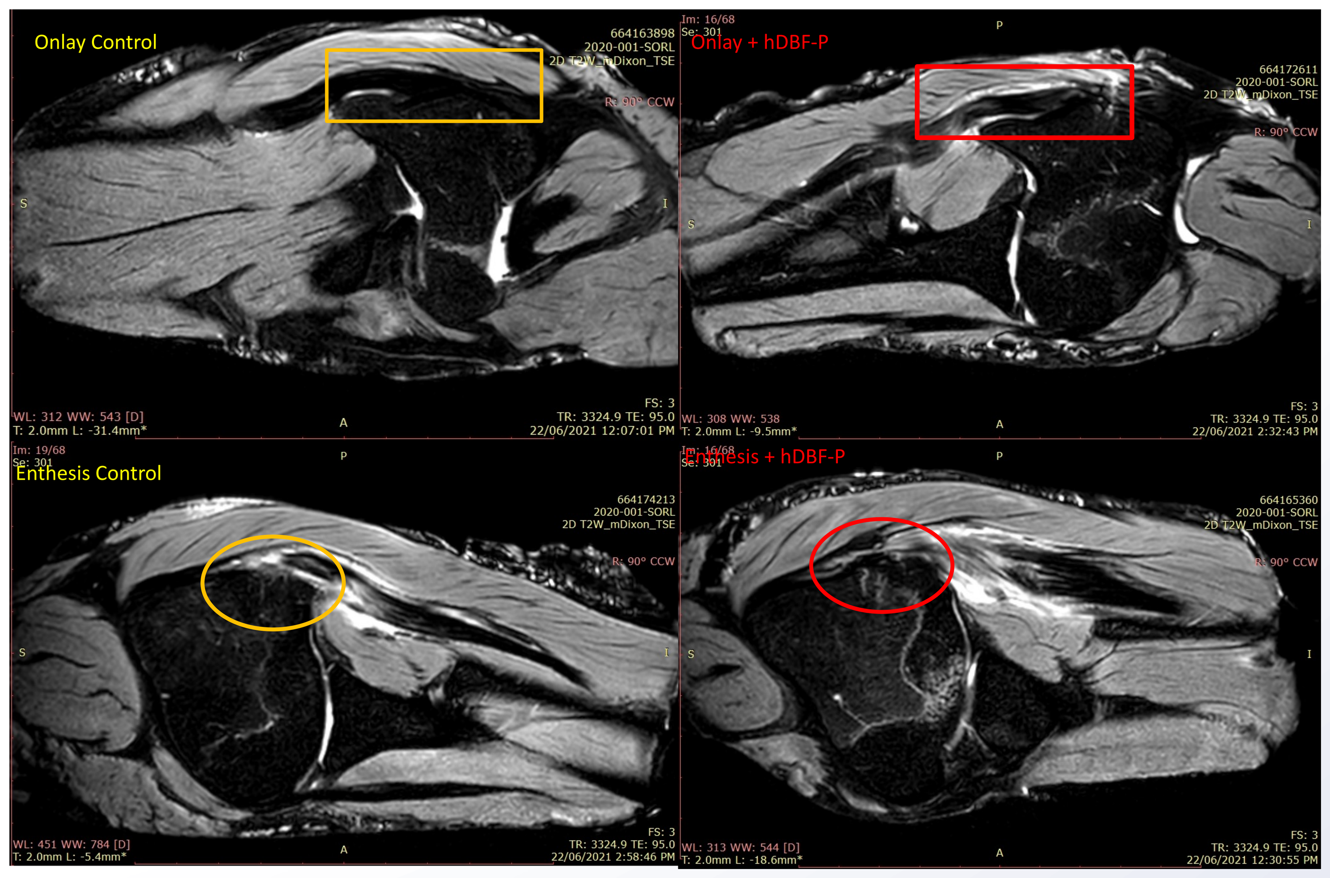

Figure 4: T2 MRI at 12 weeks for the Onlay Control, Onlay + hDBF-P, Enthesis Control and Enthesis + hDBF-P.

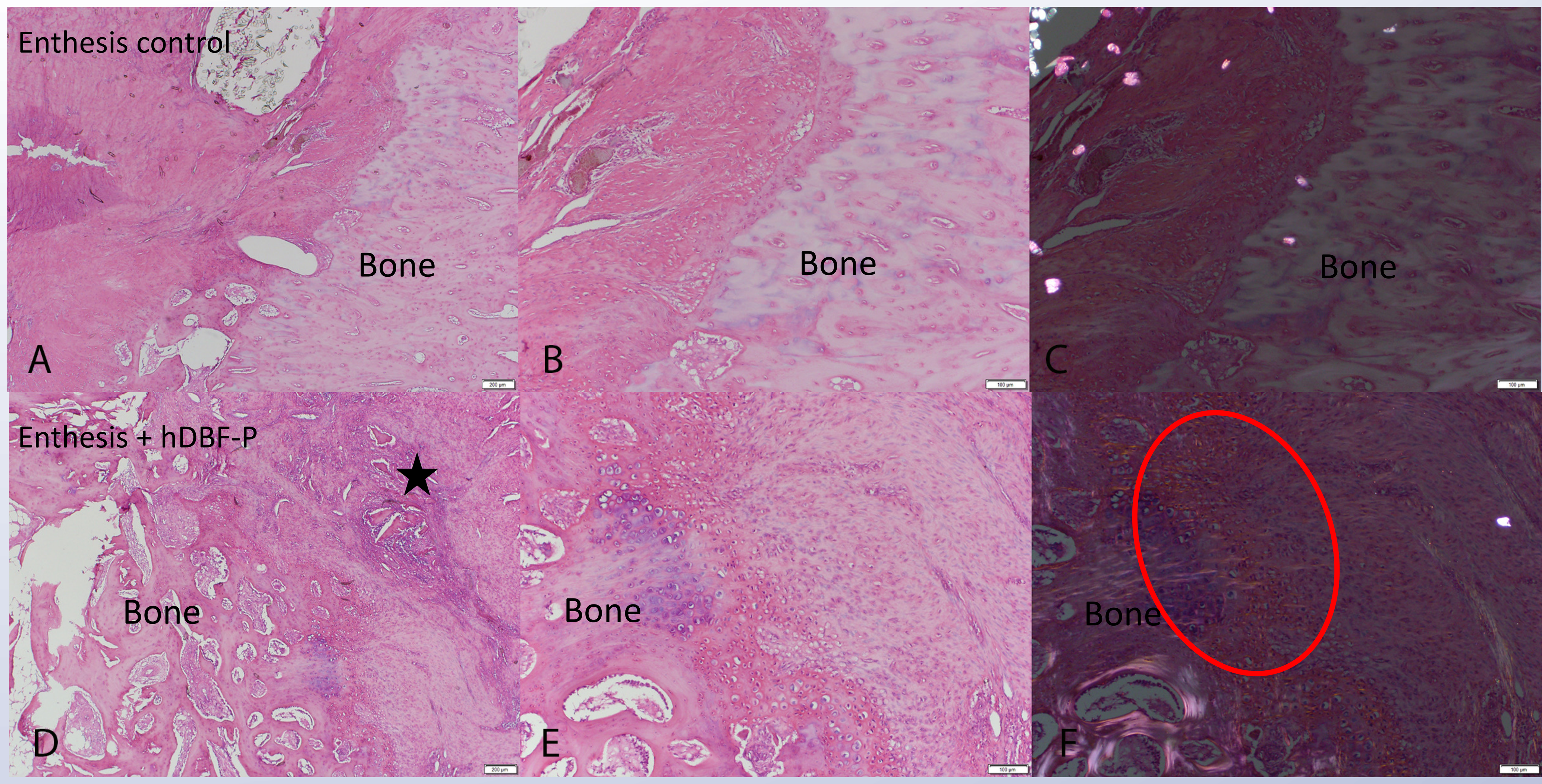

Figure 5: H&E histology at 12 weeks under normal light for the control (A,B) and hDBF-P (D,E) revealed an active interface with some residual hDBF-P (★) with reforming enthesis. Polarized light confirmed Sharpey's fibers with hDBF-P not present in the controls (F vs C).

Conclusion

hDBF-P is a collagen graft composed of demineralized bone fibers that have osteoconductive and osteoinductive potential. When formed into a patch, this implant provides a scaffold that can participate with the local biology. hDBF-P used as on-lay in a tendon injury model increased tendon thickness. hDBF-P when used at the interface between the tendon and bone facilitated enthesis reformation through its conductive and inductive potential as well as scaffold architecture. DBF patches represent an exciting allograft implant to address the clinical problems in rotator cuff surgery.