Pulsed Electromagnetic Field Therapy Improves Tendon-to-Bone Healing in a Rat Rotator Cuff Repair Model

Jennica J Tucker[1]
James M. Cirone[1]
Tyler R. Morris[1]
Courtney A. Nuss[1]
Erik I. Waldorff[2]
Nianli Zhang[2]
James T. Ryaby[2]
Louis J. Soslowsky[1]

[1]McKay Orthopaedic Research Laboratory, Philadelphia, PA

[2]Orthofix Inc., Lewisville, TX

Introduction

Rotator cuff tears are common musculoskeletal injuries, which often require surgical intervention. Unfortunately, post-repair prognosis is poor, with surgical repairs that fail in up to 94% of cases.[1] In an effort to improve tendon-to-bone healing, non-invasive therapies have been utilized post-operatively including ultrasound and shock wave therapy. Of note, pulsed electromagnetic fields (PEMFs) have been shown to improve bone fracture healing,[2] but the effect on tendon-to-bone healing has not yet been elucidated. Therefore, the objective of this study was to investigate the effect of PEMF on rotator cuff healing using an established rat rotator cuff detachment and repair model.[3-8] We hypothesized that PEMF exposure post-repair would improve tendon-to-bone healing and joint function.

Methods

Sixty adult male Sprague-Dawley rats (400-450g) were used in this IACUC approved study. Animals received either: 1) acute injury and repair[4] followed by cage activity and PEMF (Physio-Stim®, Orthofix, Inc., Lewisville, TX; 3hrs daily) or 2) acute injury and repair[4] followed by cage activity only. Animals were sacrificed at 4, 8, and 16 weeks (n = 10 per group per time point). Additionally, throughout the experiment prior to sacrifice, all animals in the 16 week group underwent longitudinal in vivo ambulatory[9] and passive shoulder joint mechanics assessments.[10] At sacrifice, right shoulders (n = 7 per group per time point) were dissected and processed for histological analysis.[8,11,12] All contralateral limbs (n = 10 per group per time point) were frozen at −20°C and thawed for dissection prior to tendon cross-sectional area measures and mechanical testing.[4,12,13] Following mechanical testing, proximal humeri were subjected to μCT imaging and analysis (10.5 μm resolution). Statistical comparisons were made between the PEMF and non-PEMF groups at each time point. Mechanical testing, μCT, and collagen fiber organization comparisons were made using t-tests. Histological comparisons were made using Mann-Whitney U tests. Ambulatory assessment comparisons were made using a 2-way ANOVA with repeated measures on time with post-hoc tests at each time point. Multiple imputations were calculated for a repeated measures analysis for missing data (~10%). All significance was set at $p \leq 0.05$.

Results

At 4 weeks, the PEMF group had a significantly smaller tendon cross-sectional area compared to the non-PEMF group (Figure 1A), with no differences at 8 and 16 weeks. At 4 and 8 weeks, the PEMF group had a significantly increased tendon modulus (100% increased at 4 weeks, 60% at 8 weeks) compared to the non-PEMF group, with no differences detected at 16 weeks

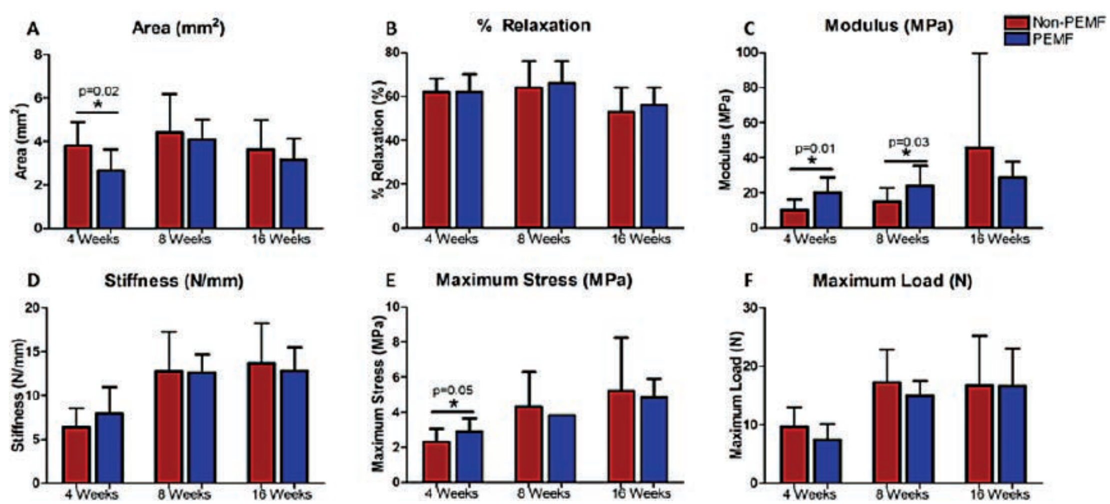

Figure 1. Tendon mechanical properties. (A) At 4 weeks, area was decreased in the PEMF group. (B) No differences were noted in % relaxation. (C) At 4 and 8 weeks, modulus was increased in the PEMF group. (D) No differences were noted in stiffness. (E) At 4 weeks, maximum stress was increased in the PEMF group. (F) No differences were noted in maximum load. Data as mean ± SD.

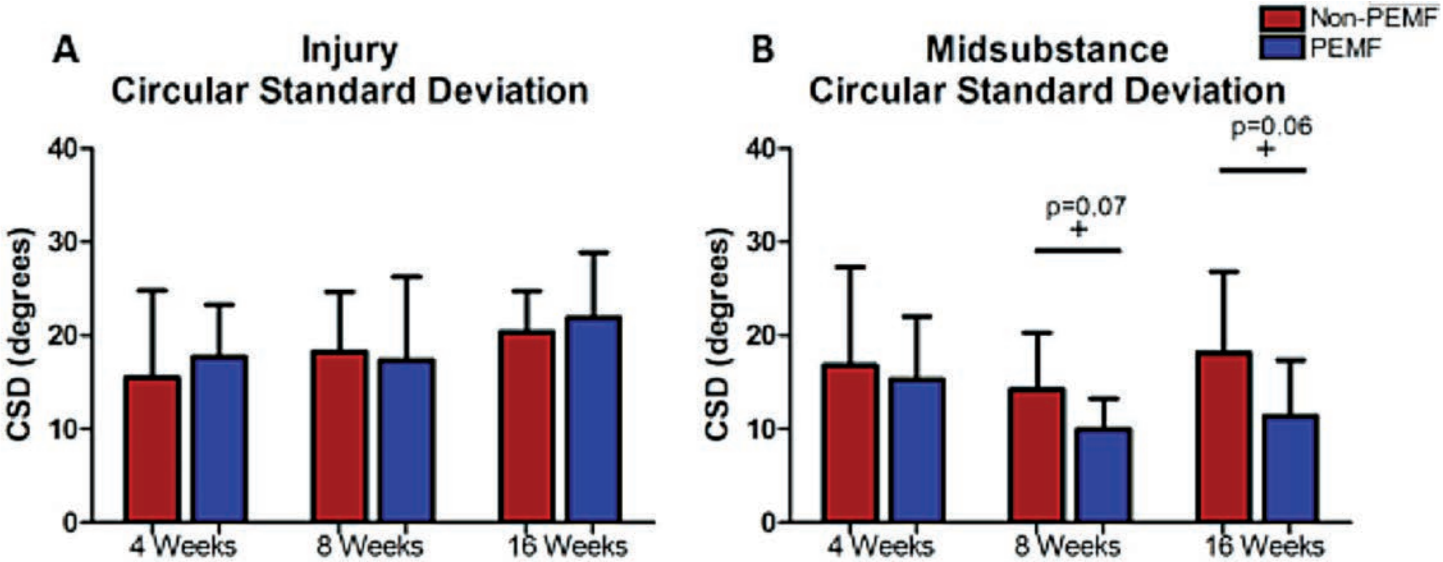

Figure 2. Collagen fiber alignment. (A) No differences were noted at the injury site. (B) At 8 and 16 weeks in the midsubstancethe PEMF group had a trend toward decreased CSD. Data as mean ± SD.

(Figure 1C). At 4 weeks, the PEMF group had significantly increased maximum stress compared to the non-PEMF group, with no differences at 8 and 16 weeks (Figure 1E). There were no differences in percent relaxation, stiffness, or maximum load at any time point (Figure 1B, D, F). For histology, at the injury site, no differences were detected in both cell shape and cellularity at any time point between groups (data not shown). Additionally, no differences were observed in collagen fiber organization at the injury site (Figure 2A). In the midsubstance at 8 weeks, the PEMF group had significantly more rounded cells (data not shown). For collagen fiber organization, the PEMF group had trends towards decreased circular standard deviation (CSD) at both 8 and 16 weeks (Fig. 2B). No differences were found in ambulatory assessment or passive joint mechanics (data not shown). For μCT analysis at 4 weeks, trabecular thickness was significantly decreased and connectivity density was significantly increased in the PEMF group (Figure 3E, H). At 8 weeks, no differences were observed in any parameter. At 16 weeks, the PEMF group had significantly increased bone volume fraction, trabecular thickness, and bone mineral density, and a trend toward increased bone mineral content (Figure 3).

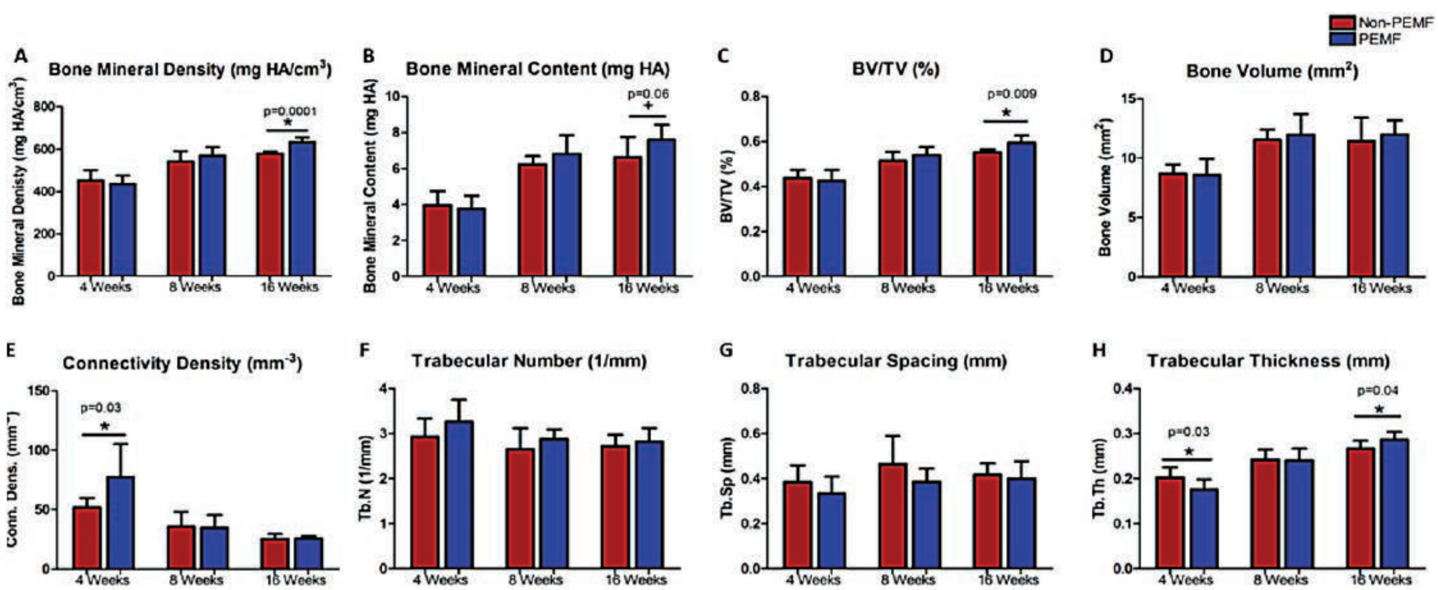

Figure 3. μCT analysis. (A) No differences were noted in bone mineral density at 4 and 8 weeks. At 16 weeks bone mineral density was increased in the PEMF group. (B) At 16 weeks bone mineral content trended toward increased in the PEMF group. (C) At 16 weeks bone volume fraction was increased in the PEMF group. (D) No differences were noted in bone volume. (E) At 4 weeks connectivity density was increased in the PEMF group. (F) No differences were noted in trabecular number. (G) No differences were noted in trabecular spacing. (H) At 4 weeks trabecular thickness was decreased in the PEMF group. At 16 weeks trabecular thickness was increased in the PEMF group. Data as mean ± SD.

Discussion

Overall, results suggest that PEMF has a positive effect on rat rotator cuff healing. Specifically, tendon mechanical properties were drastically improved in the PEMF group at both 4 and 8 weeks (100% and 60%, respectively) with a subsequent increase in bone properties at the tendon repair site. Histological analysis showed a more rounded cell shape in the PEMF group at 8 weeks in the midsubstance. This slight but significant finding might suggest inferior tissue, although this difference did not result in inferior mechanical properties. Additionally, collagen fiber organization in the midsubstance at 8 and 16 weeks showed the PEMF group trended toward decreased CSD, suggesting more organized tissue in the PEMF group, and perhaps later time points would further increase collagen organization. Overall, results demonstrate that PEMF improves tendon-to-bone healing in this animal model based on mechanical property measurements. Further studies can evaluate the mechanisms responsible for these changes.

Significance

PEMF provides a non-invasive way to improve tendon-to-bone healing in an acute rat supraspinatus detachment and repair model and shows potential for use in a clinical scenario of rotator cuff tendon to bone healing following rotator cuff repair.

Acknowledgements

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