# Effects of Pulsed Electromagnetic Field Therapy at Different Frequencies and Durations on Rotator Cuff Tendon-to-Bone Healing in a Rat Model

Julianne Huegel, PhD[1]
Daniel Choi, BS[1]
Courtney Nuss[1]
Molly Minnig[1]
Jennica Tucker, BS[1]
Cody Hillin, MD[1]
Andrew Kuntz, MD[1]
Erik Waldorff, PhD[2]
Nianli Zhang[2]
James Ryaby[2]
Louis Soslowsky, PhD[1]

[1]McKay Orthopaedic Research Laboratory, Philadelphia, PA

[2]Orthofix Inc., Lewisville, TX

## Introduction

Rotator cuff tears affect millions of individuals each year, often requiring surgical intervention. Although advancements in surgical methods and rehabilitation protocols have improved clinical results, rotator cuff repair failure is common[1]. To further improve surgical outcomes, various non-invasive therapeutics have been utilized post-operatively[2,3]. We have previously shown that pulsed electromagnetic field (PEMF) therapy improved tendon-to-bone healing in terms of tendon modulus in a rat rotator cuff model[4]. While it is known that several cell and tissue responses, including osteogenic differentiation of stem cells, are frequency dependent, the effect of frequency has not yet been evaluated in this system[5,6]. Therefore, the objective of this study was to determine the influence of both PEMF frequency and exposure time on rotator cuff healing. We hypothesized that a PEMF signal with a higher fundamental frequency and for a longer duration would lead to further improvements in mechanical properties.

## Materials and Methods

210 (including 60 from[4]) adult male Sprague-Dawley rats (400-450 g) were used in an IACUC approved protocol. Animals underwent acute supraspinatus injury and repair[7] followed by either Physio-Stim® PEMF (PS, Orthofix, Inc.) or High Frequency PEMF (HF, similar to PS but with a higher fundamental frequency) for 1, 3, or 6 hours daily. Control animals did not receive PEMF therapy (non-PEMF). Animals were sacrificed at 4, 8, or 16 weeks (n = 10 per group per time point). At sacrifice, right shoulders (n = 7 per group per time point) were dissected and processed for histological analysis, including quantification of fiber alignment circular standard deviation as a measure of collagen organization[8-10]. Left 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[7,10,11]. Statistical comparisons were made between control animals and all treatment groups at each time point. Mechanical testing and collagen fiber organization comparisons were made using one-way ANOVAs with post-hoc tests. Histological comparisons were made using Mann-Whitney U tests. Significance was set at $p<0.05$.

## Results

### *Mechanical properties*

Improvements in mechanical properties were identified for all treatment modalities when compared to non-treated animals (Figure 1A, B). Specifically, one hour of PS treatment led to increased tendon stiffness at all time points, as well as an increase in modulus at 4 weeks. One hour of HF treatment increased stiffness and modulus at 8 weeks. Animals treated with three hours of PS had a decreased cross sectional area (not shown), increased max stress (not shown), and increased stiffness at 4 weeks, as well as increased modulus at 4 and 8 weeks. Three hours of HF PEMF led to increased max load at 4 weeks (not shown), and increased stiffness at 4 and 8 weeks. Treatment with six hours of PS increased modulus substantially at 4 weeks, and increased stiffness and modulus at 8 weeks. Cross-sectional area was also reduced at 4 weeks, but increased at 16 weeks (not shown). The final treatment regimen, 6 hours of HF PEMF, resulted in significant mechanical improvements; including increased stiffness at all time points and a three-fold increase in tendon modulus 8 weeks after repair. Tendon cross sectional area was increased at 16 weeks (not shown). No differences were noted in percent relaxation in any group.

### *Histological observations*

No differences were measured in tendon cell shape or cell density in any treatment group when compared to controls. Collagen organization showed improvements at the tendon insertion at 16 weeks in animals treated with 3 hours of HF PEMF (Figure 2A). This group also showed improved alignment at 8 weeks in the tendon midsubstance (Figure 2B). Additional improvements were identified for 1 hour HF PEMF and 6 hours of PS at 16 weeks in the midsubstance (Figure 2B). Importantly, no adverse effects were identified in any mechanical or histological property.

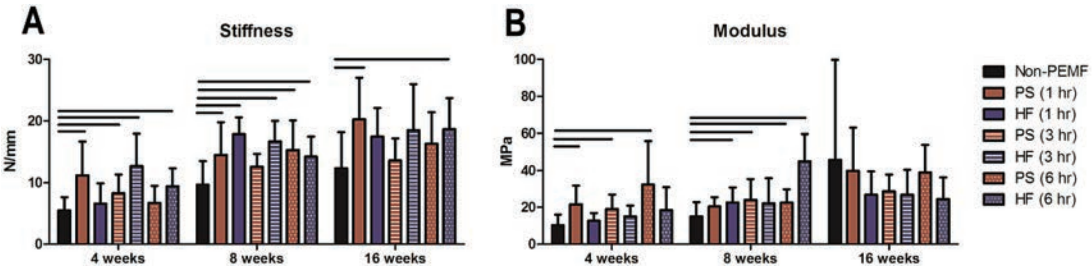


**Figure 1.** Tendon mechanical properties. **(A)** Tendon stiffness was increased in all groups receiving PEMF treatment, regardless of modality, when compared to non-PEMF controls. **(B)** Modulus was improved in all groups except HF (3 hr) at 4 and/or 8 weeks. By 16 weeks, properties were similar between control and treatment groups. Data displayed as mean ± SD. Bars indicate $p < 0.05$.

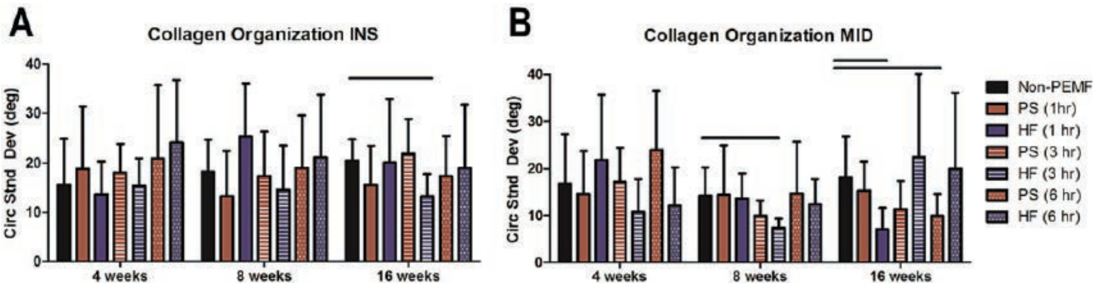


**Figure 2.** Collagen fiber alignment. **(A)** At 16 weeks, collagen alignment was improved at the injury site (insertion) in animals treated with HF (3 hr). **(B)** Collagen alignment was similarly improved for HF (3 hr) at 8 weeks in the midsubstance. Improvements were also seen at 16 weeks in groups treated with HF (1 hr) and PS (6 hr). Data displayed as mean ± SD. Bars indicate $p < 0.05$.

## Discussion

Overall, results suggest that PEMF has a positive effect on rat rotator cuff healing for pulse frequency or treatment duration tested in this study. Tendon mechanical properties, including tendon stiffness and modulus, were significantly improved with all six treatment modalities compared with control. Additionally, collagen fiber organization was improved after treatments, suggesting more organized tissue in PEMF-treated tissues, consistent with the improved mechanical strength seen in treated groups. We suspect that PEMF treatment may increase tendon cell metabolism, which then in turn increases both collagen production and matrix remodeling. These proposed changes are supported by our findings of improved mechanical properties and improved collagen alignment. Our previous work indicates that PEMF treatment does not alter joint function[4]; in conjunction with these current findings, these animal studies promote the evaluation of PEMF to improve rotator cuff healing in the clinical setting.

## Conclusions

Non-invasive PEMF therapy improves tendon-to-bone healing in an acute rat supraspinatus detachment and repair model, supporting investigation of this treatment in a clinical scenario of post-operative rotator cuff healing.

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