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Magnetic field therapy enhances muscle mitochondrial bioenergetics and attenuates systemic ceramide levels following ACL reconstruction: Southeast Asian randomized-controlled pilot trial

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Abstract

Background: Metabolic disruption commonly follows Anterior Cruciate Ligament Reconstruction (ACLR) surgery. Brief exposure to low amplitude and frequency pulsed electromagnetic fields (PEMFs) has been shown to promote *in vitro* and *in vivo* murine myogeneses via the activation of a calcium-mitochondrial axis conferring systemic metabolic adaptations. This randomized-controlled pilot trial sought to detect local changes in muscle structure and function using MRI, and systemic changes in metabolism using plasma biomarker analyses resulting from ACLR, with or without accompanying PEMF therapy.

Methods: 20 patients requiring ACLR were randomized into two groups either undergoing PEMF or sham exposure for 16 weeks following surgery. The operated thighs of 10 patients were exposed weekly to PEMFs (1 mT for 10 min) for 4 months following surgery. Another 10 patients were subjected to sham exposure and served as controls to allow assessment of the metabolic repercussions of ACLR and PEMF therapy. Blood samples were collected prior to surgery and at 16 weeks for plasma analyses. Magnetic resonance data were acquired at 1 and 16 weeks post-surgery using a Siemens 3T Tim Trio system. Phosphorus (^{31}P) Magnetic Resonance Spectroscopy (MRS) was utilized to monitor changes in high-energy phosphate metabolism (inorganic phosphate (P_i), adenosine triphosphate (ATP) and phosphocreatine (PCr)) as well as markers of membrane synthesis and breakdown (phosphomonoesters (PME) and phosphodiester (PDE)). Quantitative Magnetization Transfer (qMT) imaging was used to elucidate changes in the underlying tissue structure, with T1-weighted and 2-point Dixon imaging used to calculate muscle volumes and muscle fat content.

Results: Improvements in markers of high-energy phosphate metabolism including reductions in ΔP_i/ATP, P_i/PCr and (P_i + PCr)/ATP, and membrane kinetics, including reductions in PDE/ATP were detected in the PEMF-treated cohort relative to the control cohort at study termination. These were associated with reductions in the plasma levels of certain ceramides and lysophosphatidylcholine species. The plasma levels of biomarkers predictive of muscle regeneration and degeneration, including osteopontin and TNNT1, respectively, were improved, whilst changes in follistatin failed to achieve statistical significance. Liquid chromatography with tandem mass spectrometry revealed reductions in small molecule biomarkers of metabolic disruption, including cysteine, homocysteine, and methionine in the PEMF-treated cohort relative to the control cohort at study termination.

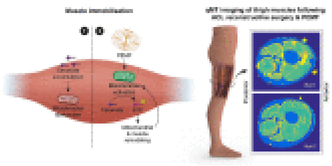
Differences in measurements of force, muscle and fat volumes did not achieve statistical significance between the cohorts after 16 weeks post-ACLR.

Conclusion: The detected changes suggest improvements in systemic metabolism in the post-surgical PEMF-treated cohort that accords with previous preclinical murine studies. PEMF-based therapies may potentially serve as a manner to ameliorate post-surgery metabolic disruptions and warrant future examination in more adequately powered clinical trials.

The translational potential of this article: Some degree of physical immobilisation must inevitably follow orthopaedic surgical intervention. The clinical paradox of such a scenario is that the regenerative potential of the muscle mitochondrial pool is silenced. The unmet need was hence a manner to maintain mitochondrial activation when movement is restricted and without producing potentially damaging mechanical stress. PEMF-based therapies may satisfy the requirement of non-invasively activating the requisite mitochondrial respiration when mobility is restricted for improved metabolic and regenerative recovery.

Keywords: Ceramides; Frailty biomarkers; Ligament reconstruction; Magnetic resonance; Metabolism; Mitochondria.

Figures



Graphical abstract

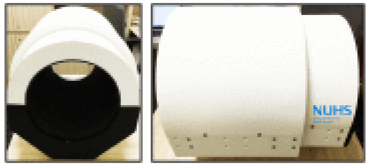


Fig. 1 PEMF prototype used in ACL-reconstructive…

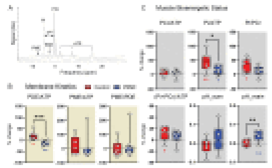


Fig. 2 ^{31} P MRS analysis of…

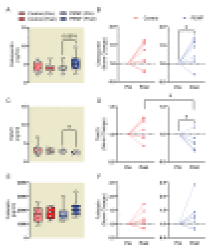


Fig. 3 Plasma biomarker analysis measured using…

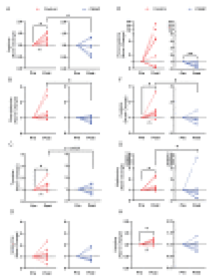


Fig. 4 Targeted metabolomics for small molecule…

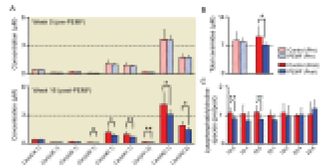


Fig. 5 Plasma ceramides levels. (A) Shows…

All figures (8)

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