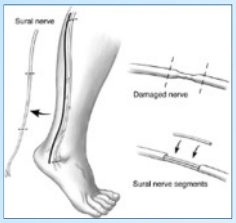
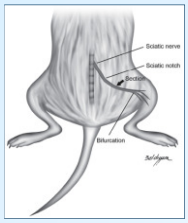
Extracorporeal shockwave therapy accelerates motor axon regeneration despite a phenotypically mismatched environment

David Hercher [1,2], Johannes Heinzel [1,2], Michaela Stainer [1,2], Rudolf Hopf [1,2], James Ferguson [1,2], Heinz Redl [1,2], Antal Nógrádi [1,2,3], Thomas Hausner [1,2,4]

[1] Ludwig Boltzmann Institut for Experimental and Clinical Traumatology, Vienna
[2] Austrian Cluster for Tissue Regeneration
[3] University of Széged, Department of Anatomy, Histology and Embryology, Hungary
[4] UKH Lorenz Böhler, Vienna



Clinical gold standard

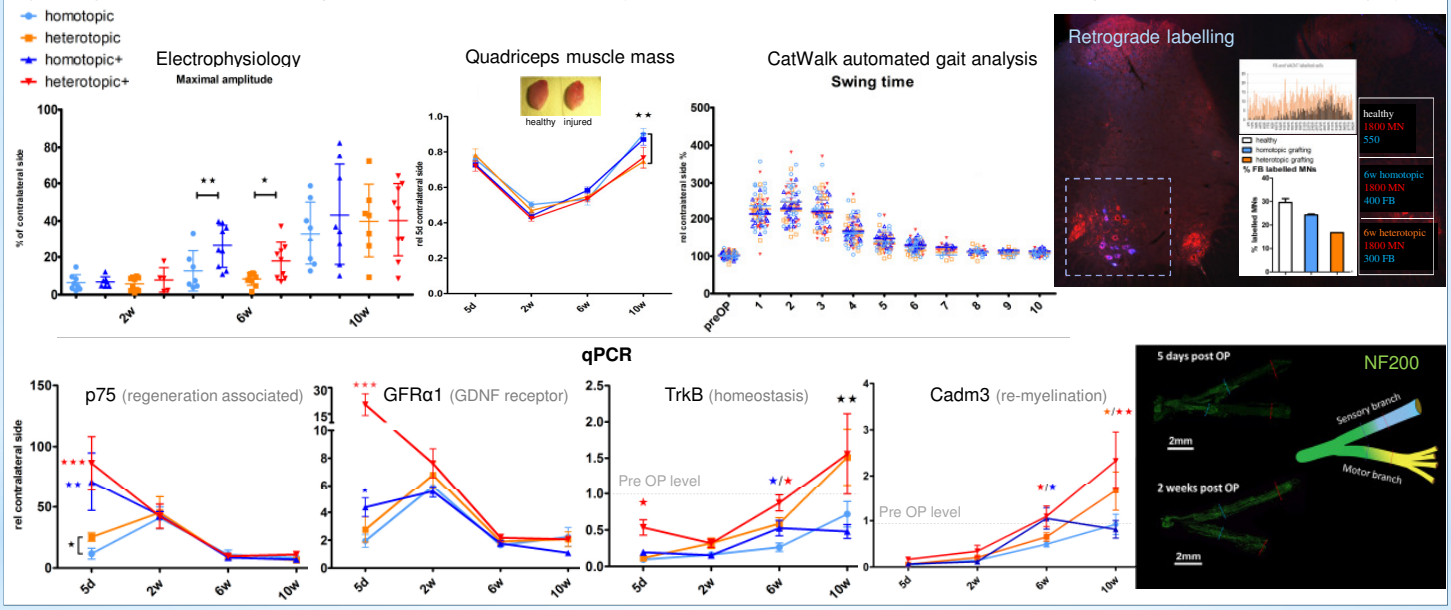


Experimental gold standard

Introduction: After peripheral nerve injury with segmental loss transplantation of an autologous nerve graft is necessary to restore continuity. Herefore a sensory nerve is harvested and used to bridge the existing gap in order to allow regeneration of axons and functional recovery. Most research groups use the sciatic nerve defect as an experimental model for autologous nerve transplantation, dismissing the influence of phenotypically different nerve grafts on regeneration. We thus hypothesize that this mismatch has a negative influence on motor axonal regeneration and that extracorporeal shockwave therapy (ESWT) can rectify this negative effect.

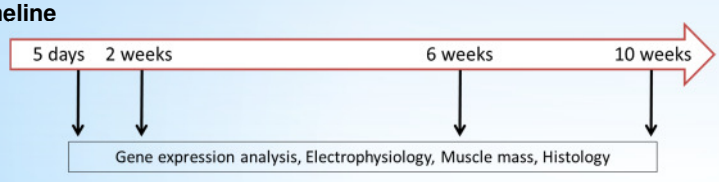
Aim: Our first aim was to establish and validate a **modified femoral nerve defect model,** reflecting the phenotypical difference of transplanted autologous nerve grafts in the clinic. Second, we evaluated **the influence of ESWT on regeneration** in this mismatched environment, as ESWT has been shown to be one of very few treatment options accelerating peripheral nerve regeneration.

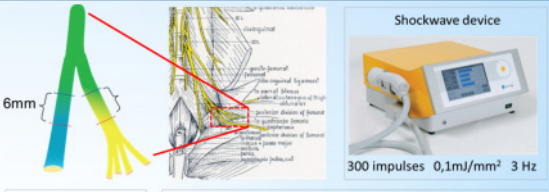
Results: Homotopic grafting resulted in faster regeneration of the target muscle than the heterotopic grafting. The use of ESWT resulted in an improved regenerative rate in both surgical groups. Motor nerves showed less than 50% expression of pro-regenerative markers (p75,GFRα1) in early stages of neuronal regeneration than sensory nerves. Furthermore, electrophysiological as well as histological evaluations indicated slower regeneration of motor axons in the heterotopic setting when compared to the homotopic grafting. ESWT increased expression of a marker for re-myelination (Cadm3) and homeostasis (TrkB) up to 100% 6 weeks after injury.

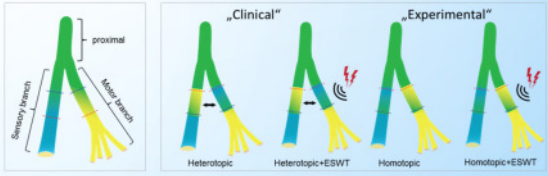


Conclusion: Regeneration is influenced by the use of a nerve graft derived from a sensory or a motor nerve. The use of a sensory graft results in inferior regeneration. This study shows that **ESWT is able to influence gene expression and accelerate peripheral nerve regeneration** in a successfully modified **femoral nerve model which reflects the clinical reality** after autologous nerve transplantation. Hereby, providing **support for the use of ESWT after surgical repair of peripheral nerve injuries**.

Timeline







Methods: Adult male Sprague Dawley rats were divided randomly in groups of at least 8 animals and underwent autologous nerve transplantation in an either homotopic or heterotopic fashion. Weekly functional analysis were performed using CatWalk automated gait analysis.
Data presented as mean ± SEM, 1-Way ANOVA ★ = p < 0,05 ★ ★ = p < 0,01 ★ ★ ★ = p < 0,001

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