# A Placental Membrane Allograft Nerve Wrap Accelerates Functional Recovery After Median Nerve Stretch Injury in Rats

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INTRODUCTION: Peripheral nerve stretch injuries are among the most devastating forms of nerve injury as outcomes remain poor and unpredictable. Newly developed nerve shield products could facilitate a pro-regenerative environment to improve functional recovery and rehabilitation. This study investigated the use of a placental membrane allograft nerve wrap for treating median nerve stretch injuries in a rat model. Specifically, we investigated a placental allograft wrap as a treatment for Epineuroclasis stretch injuries, which are characterized by disruption of the epineurium. We hypothesized that replacing the disrupted epineurium with an allograft composed of all intact layers of amniotic tissue would improve functional outcomes.

METHODS:

Upon IACUC approval, the median nerves of 14 rats were injured with six rats (12 nerves) receiving a treatment and eight rats (16 nerves) serving as untreated controls. Median nerves were surgically exposed and secured under two blunt metal pins 1 cm apart. A metal hook was attached to a load cell and raised from beneath the nerve at a speed of 0.2 mm/s until a drop in resistance force was observed on a load-time-curve, indicating epineurial disruption (Epineuroclasis). In the treatment group, a placental membrane allograft was wrapped around the median nerve at the site of epineurial disruption.

Pre-injury and at 1, 3, 6 and 9 weeks post-injury, grip strength was assessed by lifting each rat up by its tail while it grasped a bar fixed to a load-cell as an assessment of nerve function (grasping test).

Grip Strength data from each rat were normalized to the rat's respective pre-injury strength serving as a 100% baseline. The grip strength of the groups were compared using a two-way ANOVA with a multiple-comparisons model in GraphPad Prism. Full recovery was defined as statistically similar grip strength compared to pre-injury strength.

RESULTS:

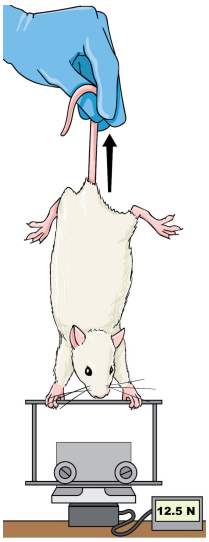
Rats treated with a placental membrane allograft demonstrated accelerated recovery of grip strength compared to rats without a treatment following Epineuroclasis nerve stretch injury. Rats in the treatment group demonstrated a significant reduction in grip strength at 1 and 3 weeks with mean values of 2% and 48% of pre-injury strength ($p<0.001$ each), but fully recovered nerve function at 6 weeks with a mean 100.8% and 104.5% of baseline strength at 6 and 9 weeks ($p>0.98$ each).

Untreated rats demonstrated incomplete recovery at 6 weeks, with grip strength reduced to 68.1% of baseline strength ($p=0.005$), and required a longer recovery period, regaining only 80.9% of baseline by 9 weeks ($p=0.14$).

Similarly, rats in the treatment group demonstrated a significantly greater percent-of-baseline grip strength at 6 weeks than untreated rats (100.8% versus 68.1%, $p=0.047$).

DISCUSSION AND CONCLUSION:

A placental membrane allograft wrap accelerates recovery after median nerve stretch injury in rats. The pro-regenerative benefit of this allograft is likely driven by its large reservoir of cytokines (e.g. VEGF, NGF), which promote Schwann-cell migration and extracellular matrix regeneration - functions normally facilitated by an intact epineurium. Since both groups in this study eventually regained pre-injury grip strength, future studies should investigate the use of placental allografts for non-recoverable nerve stretch injuries.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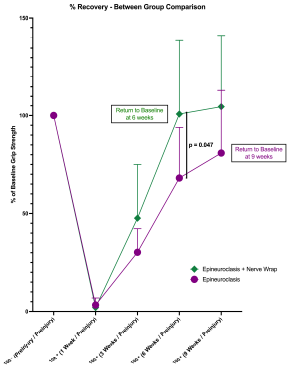
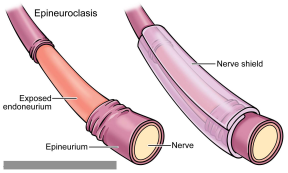

% Recovery - Between Group Comparison
% of Baseline Grip Strength
150
100
50
0
Return to Baseline at 6 weeks
p = 0.047
Return to Baseline at 9 weeks
Epineuroclasis + Nerve Wrap
Epineuroclasis


Epineuroclasis
Nerve shield
Exposed endoneurium
Epineurium
Nerve