The Effects of Intraoperative Electrical Stimulation on Nerve Regeneration Across Nerve Isografts

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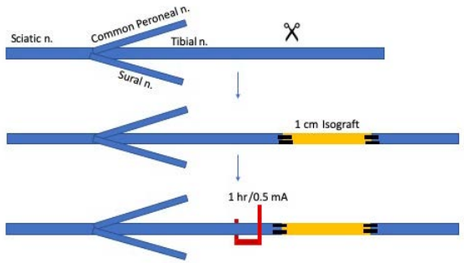
Introduction

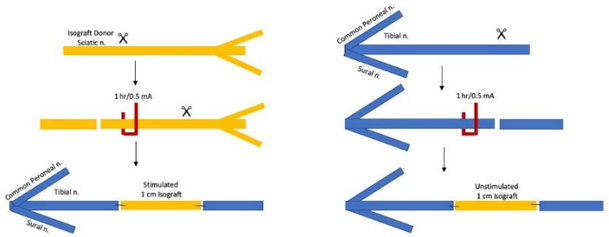
- Despite their regenerative ability, peripheral nerve injuries in humans typically result in minimal functional recovery and debilitating morbidity.
- Brief electrical stimulation (Estim) has demonstrated positive outcomes on nerve regeneration after injury.
- Using a rat tibial nerve isograft model, we explored the effects of Estim on axon regeneration and functional recovery across nerve isografts.
- We also aimed to parse where Estim functions to improve peripheral nerve regeneration: the neuronal cell-body, the non-neuronal cells of the isograft, or some combination of both.

Methods

- One (1) cm isografts were inserted between cut tibial nerve ends and stimulated proximally for 1 hr at 0.5 mA.

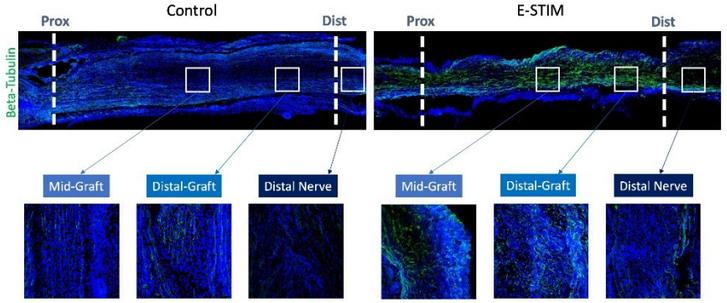


- Axon regeneration and cell populations were quantified using immunofluorescence; Recovery via walking track and grid walk analysis.
- To determine which cells are affected by Estim to improve regeneration, the donor isograft or the recipient nerve were independently stimulated prior to grafting.



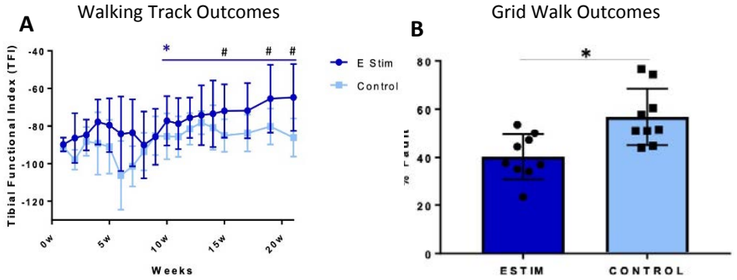
Results

Estim Increases Early Axon Regeneration



ß-III-tubulin (axons) quantification revealed axon regeneration at POD 14 was greater between the EStim vs Control groups.

Estim Improves Long-Term Functional Recovery



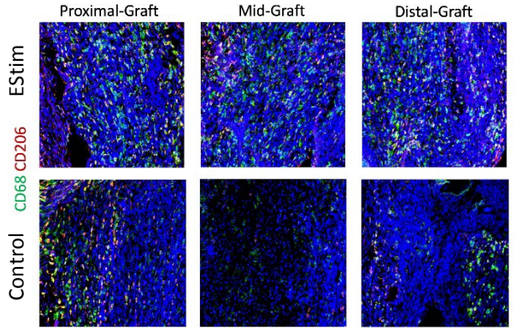
#p<0.05 for difference b/w Estim vs Control
* p<0.05 for difference b/w EStim wk 10-21 vs EStim wk 1

* p<0.05 for difference b/w Estim vs Control

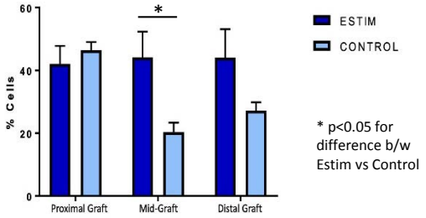
(**A**) TFI improved by 15 weeks comparing Estim vs Control groups.
(**B**) Fewer foot faults occurred at 21 weeks for Estim vs Control groups.

Results

Estim Affects Macrophage Accumulation

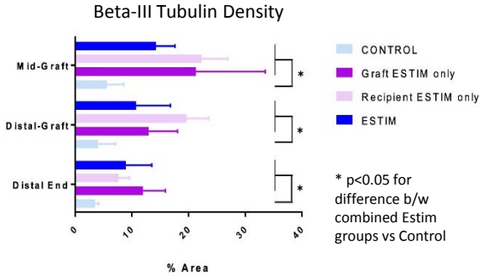


CD68+ cell quantities (Macrophages) within the isografts were greater within the mid-graft in EStim vs Control at POD 14.



* p<0.05 for difference b/w Estim vs Control

Estim of Isografts Alone Promotes Axon Growth



* p<0.05 for difference b/w combined Estim groups vs Control

There was an increase in β-III-Tubulin density in the pooled average of the BES conditions as compared to the Control.

Conclusions

Estim promotes regeneration likely via effects to the neuron and its axons, but also via non-neuronal cells within an isograft. These effects improve axon regeneration and functional recovery across short (1 cm) isografts.