Creation of an Ischemia/Fibrosis Limb Model and its Impact on Nerve Regeneration
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Introduction
Complex traumatic limb injury results in damage to nerve, muscle and other tissues. This creates a fibrotic and ischemic tissue bed that is hostile to nerve regeneration. To date most studies are conducted using a clean-cut nerve injury model in a non-compromised soft tissue environment. Which does not reflect the true clinical scenario. The aim of the study is to create a rat hindlimb soft tissue defect and fibrosis model and evaluate nerve regeneration in the scarred and ischemic environment.

Materials and Methods
Three surgical groups were designed with 6 female Lewis rats each. Double crush of the left sciatic nerve was done to all the animals to cause complete axotomy. Group A served as a control where soft tissue was intact. In group B the posterior thigh muscle groups were removed. In group C soft tissue fibrosis was induced by ligation of muscular vessels and caustic injury to the posterior thigh muscles. Nerve function was evaluated by nerve conduction study and walking track analysis pre-operatively and 2, 4, 6 weeks postoperatively. At the 6-week endpoint, histology of the posterior thigh muscles and neuromorphometric analysis of the mid-portion nerves were carried out.

Results
Gross observation at the endpoint showed that muscles in group C were thin and pale. Sciatic nerve was slightly fibrotic and less pliable. Epineurial vascularity was reduced. Nerves of groups A and B looked normal. Compound muscle action potential (CMAP) in group C was not recordable until 6 weeks and had much lower amplitude and longer latency, compared to CMAPs of groups A and B which were recordable at 4 weeks and similar. Foot eversion was seen following nerve injury as shown by the increased toe out angle (TOA). At 4 and 6 weeks postoperatively, recovery was observed in groups A and B as indicated by reduction in TOA. There was however no sign of recovery in group C. The posterior thigh muscles in Group C were atrophic and fibrotic as compared to control. Comparing to those of groups A and B, the neuromorphometric parameters of group C were inferior (Figure 1).

Discussion and Conclusions
This experiment demonstrated that 1) A fibrotic/ischemic nerve bed can be successfully created by ligation of nutrition vessels and caustic injury to the muscles; 2) Simple removal of muscles is not sufficient to generate unfavorable nerve bed; 3) Fibrotic and ischemic soft tissue environment leads to reduced vascularity of the nerve and consequently poorer nerve regeneration. The model will allow exploration of tissue engineering solutions to a complex, but common medical problem.

References

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