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Chitosan-based Semi-permeable Nerve Conduits Support Periphereal Nerve Regeneration in Goats and Nonhuman Primates

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We have produced chitosan nerve guidance conduits with desirable mechanical properties and semi-permeable wall structure through a mold-casting/lyophilizing procedure. In previous in vivo studies, we found that transected sciatic nerve of rats was able to successflly regenerate through a chitosan nerve conduit across a 10 mm gap. In this study, goats and nonhuman primates were used as animal models to evaluate the effectiveness of the chitosan conduits in bridging longer peripheral nerve defects. The conduit was used for bridging common peroneal nerve across a 25 mm defect in 4 goats, which were used as an experimental group. Autograft group (n = 3) and a nongrafted group (n = 3) were used as control. Meanwhile, another two adult male *Mucaca fusciculuris* non-human primates were used to further elucidate the functionality of the conduits, one with a 15 mm common peroneal nerve defect, the other with a 20 mm tibial nerve defect, both bridged with appropriate sized chitosan conduits. All animals were monitored for changes in their appearance, gait and locomotion activities after surgery. Sixteen months post-operatively, functional reinnervation of motor and sensory nerves was investigated by electrophysiological examination including compound muscle action potential (CMAP) and somatosensory evoked potential (SEP). Histological assessment including light microscopy and transmission electron microscopy, and immunohistochemistry as well as morphometric analyses to regenerated nerves were utilized to investigate the nerve repair effects of the conduits.

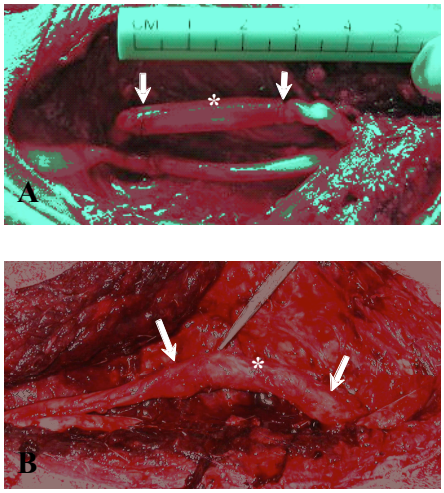

Figure 1 : (**A**) Intra-operative view immediately after implantation of the chitosan nerve guide conduit (asterisk) into a 25-mm goat common peroneal nerve defect. (**B**) Gross view of the regenerated nerve tissue (asterisk) 16 months after bridge implantation of the chitosan nerve conduits. The arrows indicate the proximal and the distal coaptations.

The results demonstrated that, in both the goat and monkey models, the injured nerve trunk had been reconstructed with restoration of nerve continuity and functional recovery, improving locomotion activities of the operated limb. This study confirms the feasibility of the chitosan nerve conduits for peripheral nerve regeneration in large animal models, which is the first report of long term *in vivo* evaluation of chitosan nerve conduits in goats and nonhuman primates and provides important data for further potential clinical research.

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