**Master of Medicine**

# The effect of FK506 (Tacrolimus) loaded with collagen membrane and fibrin glue on promotion of nerve regeneration in a rat sciatic nerve traction injury model

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# The effect of FK506 (Tacrolimus) loaded with collagen membrane and fibrin glue on promotion of nerve regeneration in a rat sciatic nerve traction injury model

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**English abstract**

# The effect of FK506 (Tacrolimus) loaded with collagen membrane and fibrin glue on promotion of nerve regeneration in a rat sciatic nerve traction injury model

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**Introduction**

In oral and maxillofacial surgery, peripheral nerve injury is one of the most common injuries that is likely to happen. The purpose of this study was to evaluate the effect of FK506 loaded with collagen membrane and fibrin glue to promote nerve regeneration after traction nerve injury in a rat model.

**Material & Methods**

Thirty male Sprague-Dawley rats were divided into three groups. Group A (n=10) were sham group which included exposure of the sciatic nerve without any injury. Group B (n=10) and C (n=10) underwent traction nerve injury of 200 g for one minute. In group C, the injured nerve was covered with collagen membrane soaked with FK506 (0.5 mg/0.1 ml) and fibrin glue. Functional analysis and microscopic evaluation were performed at 2 and 4 weeks after injury.

**Results**

The sciatic function index (SFI) was -5.78±3.07 for group A, -20.69±5.22 for group B, and -12.01±4.20 for group C, respectively in 2 week after injury. The SFI was -5.58±2.45 for group A, -19.69±4.81 for group B, and -11.95±1.94 for group C at 4 weeks. In both periods, significant differences were observed among each groups ($p<0.017$). Histomorphometric evaluation demonstrated improved nerve regeneration in group C compared to group B. However there were no statistical differences in axonal density among three groups ($p<0.017$).

**Conclusion**

Localized FK506 with collagen membrane and fibrin glue could promote axonal regeneration in traction nerve injury of a rat model.

Keywords: sciatic nerve, traction injury, nerve regeneration, FK506, collagen, fibrin glue

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# Introduction

Peripheral nerve injuries (PNI) might occur during operation and could lead to loss of function or cause chronic pain.[1)] Stretch-related injuries (traction), laceration, and compression are the three basic types of PNI.[2)] In oral and maxillofacial surgeries, traction nerve injury (TNI) is one of the most common traumatic injuries that is likely to happen. Injuries of this type can be seen in third molar extraction, orthognathic surgery, fracture reduction, parotidectomy, temporomandibular joint surgery, oral cancer surgery, and free flap reconstruction.[3-8)] Most TNIs result in transient dysfunction, however, some might develop as permanent anesthesia, paresthesia, or motor function loss. Therefore, it is essential to establish clinically applicable techniques for treating TNIs.

There have been many attempts to treat PNI. Several methods have been proposed such as conduits (e.g. autogenous, non-degradable, or degradable materials)[9-11)], cell-based therapy (e.g. Schwann cells, olfactory ensheathing cells, bone marrow derived mesenchymal stem cells, and pluripotent stem cells)[12-15)], and growth factors (e.g. nerve growth factor, neurotrophin-3, and basic fibroblast growth factor).[16-18)] Although these developments showed promising results, clinical limitations exist including cost, ethical, and preparation time limitations.

The immunosuppressant drug FK506 (Tacrolimus) is a medication preventing allograft rejection which is crucial for organ transplantation. FK506 has similar effects of cyclosporine A (CsA) as inhibiting the transcription of early T-cell activation genes, apparently by modulating the activity of transcriptional regulators.[19)] Another characteristic of FK506 is neuro-regenerative effect. Gold et al.[20)] first reported that FK506 promotes nerve growth *in vivo* in a crush nerve hind limb model in rats. *In vitro*, FK506 promotes neurite outgrowth by increasing sensitivity to nerve growth factor.[21)] Several studies suggested that systemic administration of FK506 increases nerve regeneration in a dose-dependent manner in rat's PNI.[22, 23)] Others reported significant results with topical application but with lesser systemic toxicity. Diaz et al.[24)] showed the facial nerve regeneration by applying FK506 topically when they used entubulation neurorrhaphy in a rabbit model. Yeh et al.[25)] demonstrated

similar results on facial nerve crush injury in rat model. Tajdaran et al.[26] reported enhanced axon regeneration in rats with different type of local delivery system. However, there was no study about the effect of FK506 on traction nerve injuries.

The purpose of our study is to verify the neurotrophic effect of localized FK506 in TNI of a rat model. Assessment of nerve regeneration was based on functional analysis and histomorphometric examination at 2 and 4 week interval after surgery.

# Materials and Methods

This experiment was approved by the ethics committee on experimental use of animals of the Asan Medical Center Animal Research Committee (2021-11-210).

**1. Preparation of FK506 (Tacrolimus)**

FK506 (F4679, Sigma-aldrich, St. Louis, USA) was used in this study. This product was supplied by powder, 5 mg in glass bottle. The powder was dissolved with 1ml of normal saline (20 ml, Choongwae Pharm, Korea) before application. The concentration of FK506 (0.5 mg/0.1 ml) was selected based on the previous published studies.[26, 27] Collagen membrane (OSSGUIDE®, Bioland Co., Cheongju, Korea, 5 mm x 5 mm x 0.5 mm) was used and cut into 10 pieces. Each pieces were prepared with 5 mm x 5 mm x 0.5 mm. The membranes (n=10) were hydrated with 0.1ml of FK506 solution (0.5 mg/0.1 ml). (Fig. 1)

**2. Surgical procedures**

Thirty male Sprague-Dawley (SD) rats weighing 250 gram were used for this study. Rats were divided into three groups (n=10 for each group). Animals were anesthetized by intra-peritoneal administration of 30 mg/kg of Alfaxan (Jurox, Rutherford, Australia) and 10 mg/kg of Rompun (Bayer, Leverkusen, Germany). After routine povidone iodine (Betadine™, Choongwae Pharm, Korea)

preparation of the operative field on the left thigh, all the limbs of the rat were fixed at the experimental plate with plaster. The left sciatic nerve was exposed through a 1.5 cm straight skin incision at the posterior surface of the upper thigh. After intermuscular fascial dissection, about 10mm segment of the sciatic nerve was isolated and dissected from the adjacent tissue and muscle clearly.

Group A underwent sham operation with no injury on the sciatic nerve. Group B and C underwent traction injury of 200 g for one minute. Before traction injury, both ends of the tension site equivalent to 10 mm were marked with indelible pencil. The final tension force and the sciatic nerve length was measured to compare the amount of change after the traction injury. In Group C, collagen membrane loaded with FK506 was used to cover the dissected nerve. Fibrin glue (Beriplast P, CSL Behring, Germany) was loaded after this application. The skin was closed with 4-0 Vicryl™ (Ethicon, UK) by layered suture technique. Antibiotic (Amoxicillin™ 150 mg/kg SC, Il Sung Pharm, Korea) and analgesic (Ketorolac™ 2 mg/kg SC, Dong Kook Pharm, Korea) were injected intramuscularly after operation every 24 hour for one week. The surgical procedure was identical to all animals. (Fig. 2) The food and water were supplied ad libitum.

**3. Functional analysis**

Function of the sciatic nerve was evaluated 2 and 4 weeks after the operation. At each week, randomly selected five rats in each groups were tested. For evaluation, walking track analysis and sciatic function index (SFI) value was calculated. By walking on a corridor, footprints were recorded on a white paper. The following parameters were measured from the footprints: (1) distance from the heel to the top of the third toe (Print Length; PL), (2) distance between the first and the fifth toe (Toe Spreading; TS) and (3) distance from the second to the fourth toe (Intermediary Toe Spreading; IT). These measures were taken both from the experimental sides (EPL, ETS, EIT) and from the non-operated side (NPL, NTS. and NIT). As the figures are measured, SFI was calculated by the following formula derived by Bain et al.[28] An SFI -100 indicates total impairment, such as result from a complete transaction of the sciatic nerve, whereas an SFI 0 is considered a normal function. (Fig. 3

and 4)

SFI formula

SFI = (-38.3xPLF) + (109.5xTSF) + (13.3xITF) - 8.8

PLF = $\frac{\text{EPL} - \text{NPL}}{\text{NPL}}$ ; TSF = $\frac{\text{ETS} - \text{NTS}}{\text{NTS}}$ ; ITF = $\frac{\text{EIT} - \text{NIT}}{\text{NIT}}$

**4. Histomorphometric examination**

Shortly after the functional analysis, five randomly selected rats in each group were euthanized with $CO_2$ and the sciatic nerve segments were harvested. The samples from each rats were fixed in 10% neutral formalin for 24 hours. After fixation, they were embedded in paraffin, sectioned at 5 μm in thickness with cross-sectionally and longitudinally. Then, they were stained with hematoxylin and eosin (H&E) and toluidine blue. Cross-sectional tissues (n=4 for each group) were observed at a magnification of x40 with light microscope. Longitudinally sectioned tissues (n=1 for each group) were examined with x10 magnification. Toluidine blue stained cross-sectional cuts were selected and examined under the light microscope. The total axon number and axonal density (axon number/$mm^2$) were counted in the endoneurial areas using a randomized counting frame. (Fig. 5 and 6)

**5. Statistical analysis**

Experimental data (SFI and axonal density) were expressed as mean ± standard deviation. In this study, all measurements were based on independent multiple groups. The Kruskal-Wallis test was used to compare mean values of the three groups, and $p<0.05$ was considered statistically significant. The Mann-Whitney test was used to compare the mean values of the groups two by two, and $p<0.017$ (0.05/3: Bonferroni correction) was considered statistically significant. All statistical calculations were carried out using SPSS software (ver. 23.0, SPSS, Inc., Chicago, IL, USA).

# Results

**1. Nerve elongation and decrease of tension force during injury**

The elongation of sciatic nerve and tension force change at the start and end point of the injury were measured during traction nerve injury (Table 1). The marked nerve length, which was initially 10 mm, was increased to 11.9±0.7 mm (range 11-13 mm) after injury. The ratio of elongation was 18.5±6.7 %. The tension force decreased from 200 g to an average of 181.3±5.1 g (range 175-190 g) in one minute. The sciatic nerve rupture or discontinuity was not occured during experiment.

**2. Sole examination**

All feet were inspected for signs of self-mutilation or injury before walking track analysis. During the observation period, no corresponding manifestations were found in all animals (Fig. 3).

**3. SFI**

The SFI was -5.78±3.07 for group A, -20.69±5.22 for group B, and -12.01±4.20 for group C respectively in 2 weeks after surgery. After 4 weeks, the SFI was -5.58±2.45 for group A, -19.69±4.81 for group B, and -12.01±4.20 for group C (Table 2 and Fig. 7). In both periods, statistically significant differences were observed among group A vs B, B vs C, and A vs C ($P<0.017$) (Table 3).

**4. Histologic analysis**

In cross-sectioned microphotographs, homogenous thickness and distribution of nerve fiber (axons) was observed in group A at 2 and 4 weeks after operation. In group B, irregularly spread nerve fibers and dead space between axons were observed at 2 and 4 weeks after operation. In group C, the separation between fibers was seen at 2 weeks after operation. However, it decreased at 4 weeks after surgery (Fig. 8).

In longitudinal sections, clearly stained myelin sheaths of group A were observed during 2

and 4 week period. In group B, nerve fibers with curling and vacuolization were observed during the same period. In group C, tortuous fiber tracts and vacuolization were seen at 2 weeks after operation. However, these findings were reduced during 4 weeks (Fig. 9).

In cross-sectioned image of toluidine blue staining, axons number and axonal density were measured (Fig. 10). At both weeks, the axonal density in group B was lower than in other groups. In both periods no significant differences were observed among group A vs B, B vs C, and A vs C ($p<0.017$) (Table 4).

# Discussion

In this study, we sought to determine whether local FK506 delivery with collagen membrane and fibrin glue could improve nerve regeneration following nerve traction injury. Through an experiment of a rat model, we analyzed the influence of FK506 using gait analysis and histologic findings. As a result, it was observed that local delivery of FK506 achieved nerve regeneration outcomes.

Characterizing the thresholds for nerve damage under stretch is a compelling area in clinical and experimental applications. Several studies indicate the minimum threshold for nerve stretch prior to functional deficit to be between 5% and 10%. Jou et al.[29] demonstrated that rat femoral lengthening above 8% caused deficits in the sciatic nerve. Rickett et al.[30] reported that after 10% stretch, significant value of compound action potential amplitude decreased, indicating excess of peripheral nerve's mechanical tolerance. For disruption of the rat sciatic nerve, Spiegel et al.[31] described the mean amount of 626 g traction force. Fowler et al.[32] experimented 50 g of traction force continuing for five minutes showing significant functional deficit. For this reason, the selected 200 g traction and one minute of time in this study were significantly enough for functional deficit. Also, the mean amount of elongation rate (18.5%) jumped over the threshold reported from previous studies.

The SFI which was previously composed of four values (striding ability, the length of the

footprint, spreading of the first and fifth toes, and spreading of the second and fourth toes) is considered a good assessment tool for overall nerve function in rat.[33] De Medinaceli et al.[34] described each of the components as equal importance. However, the index has changed its formula by several researchers.[28, 35] The striding ability was excluded and remaining components were given different weights according to their own statistical analysis. According to the index introduced by Bain et al.[28], which was used in our study, it compares the values in normal gait and after complete transection of the sciatic nerve. In our experiment, the index of FK506 group showed statistically different from other groups after 2 and 4 weeks indicating the neurotrophic property. Although the SFI is an important measure for the recovery of the sciatic nerve function, comparison with other measures such as histomorphometry or electrophysiology should be performed to compensate for its limitations.[36]

The prognosis of peripheral nerve repair depends on the extent of injury. Through several decades, injury grading systems have been developed that brings correlation of the microscopic changes occurring after nerve injury and patient symptoms. Classifications of Seddon[37] and Sunderland[38] are probably the most widely accepted ones. Seddon categorized the three types of injury as neurapraxia, axonotmesis, and neruotmesis.[37] Sunderland's classification further grades the three injury types described by Seddon into five categories according to severity.[38] Traction nerve injury usually results in first or second degree injury according to Sunderland's classification. Correspondingly in our experiment, the traction induced axonal injury while the connective tissue layers were preserved indicating a second degree injury. Separation and discontinuity of neighboring cells increased without perineural severance in injury group. There was no significant difference among each groups in axonal density in statistical analysis, but some degree of nerve regeneration was seen in histomorphometric examination. Histologically, the degree of nerve damage was decreased at 4 weeks compared to 2 weeks in group B and C. In addition, at 4 weeks, group C showed improved recovery than the injured group. Therefore, peripheral nerve injury caused by traction shows subsequent nerve regeneration, and it could be considered that FK506 might help to promote

this process.

It has been showed that FK506 increases nerve regeneration by increasing the rate of axonal regeneration.[20] However, unlike immunosuppressive mechanism, the exact mechanism of FK506's neuro-regenerative effect remains unclear.[39] Several studies have demonstrated that FK506 activity is mediated by a family of proteins termed FK506-binding proteins (FKBP); the 12 kDA receptor, FKBP-12.[40-42] Researchers have showed that FKBP not only exists in T-cells but also in neuronal tissue[43] and increases after axotomy. The complex of FK506 and FKBP-12 inhibits the calcium activated phosphatase, calcineurin, increasing phosphorylated levels of calcineurin substrates with growth associated protein-43 (GAP-43).[44] GAP-43, a calcineurin substrate in neurons, plays an important role in axon elongation[45] and growth cone formation[46]. Hence, FK506 could increase nerve regeneration by increasing phosphorylation of GAP-43 in advance of inhibiting calcineurin.[21] FKBP-52, also known as FKBP-59 or heat shock protein 56, was introduced as neurotrophic properties of FK506 by Gold et al.[47] It is a component of mature steroid receptor complexes[48] which associates with microtubules in the cytoplasm and nucleus[49], and plays an important role in cytoplasmic-nuclear shuttling of steroid receptors[50], which is decisive for neuronal growth. The present study showed clinical treatment potential of local FK506 in peripheral nerve injury, however, detecting the molecular mechanisms of neurotrophic property remains to be investigated.

Most of the studies investigating the nerve regeneration effect of FK506 were systemic administration, but there is less known about localized delivery of FK506 to nerve injuries.[20, 23, 39, 51, 52] In recent years, a few studies have reported the neuro-regenerative effect of local delivered FK506. All studies have been concerned about the substances to control the emission of FK506. Azizi et al.[53] demonstrated the improvement of functional and morphometric recovery of rat sciatic nerve by loading FK506 in a vein graft. Mekaj et al.[54] applied FK506 with wrapping absorbable gelatin sponge to a rabbit sciatic transection. Davis and his colleagues used poly(L-lactide-ε-caprolactone) nerve wraps[55] and micro-patterned poly(lactic-co-glycolic acid) (PLGA) films[56] to deliver FK506 locally. However, each study had limitations for clinical use such as donor site morbidity, fast biodegradability,

and high cost.

Among many biodegradable materials, collagen is favorable as a drug carrier. Highly purified type I collagen is processed into a tubular matrix with adequate mechanical strength and controlled permeability. OSSGUIDE®, collagen membrane we used, is high purified type I collagen derived from porcine tissue and cross-linked membrane. The cross-linking process enhances the tensile strength of collagen and extends degradation time.[57] This property is maintained *in vivo* for a long time during the healing period, which differentiates it from non-cross linked membranes. This characteristic was shown in our experiment, which was found that the collagen membrane slowly biodegraded but still remaining when the nerve tissue was harvested after 2 and 4 weeks. Also, the semipermeable property of collagen conduits has advantage of allowing diffusion of neurotrophic factors from the external environment into the repair site.[58]

Several experimental studies of topical administration of FK506 after peripheral nerve injury have reported various doses. In vitro, up to 0.25 mg showed good results at the site of rat sciatic nerve crush model.[47] In a rabbit model, Diaz et al.[24] suggested 10 ng/ml on the basis of comparison with previous study[59] on corneal endothelium. Tajdaran et al.[26] demonstrated the concentration of 200 μg based on the previous studies[27, 60] which used similar local dose of CsA. Taken together, the variety of dosage ranges in topical administration was associated with drug's persistence.

Likewise, the particle form of FK506 may also affect continuity of the drug's effect. Tajdaran et al[26] reported the effect of local delivery of FK506 incorporated in the fibrin glue by comparing forms of solubilized, particulate, and PLGA microsphere (MS) encapsulated FK506. All three forms were effective, but the particulate form and the MS encapsulated form showed superior axon regeneration. However, rather than their types, this experiment revealed the effectiveness of the fibrin glue-based delivery system over any conduit-based delivery *in vivo*.

Fibrin glue, which has been used in the surgical field for decades, has advantage of being clinically easy to use. In addition, there is no need for a secondary surgery for the removal of the delivery system as it has the characteristics of biodegradability and biocompatibility. Moreover,

Sameem et al.[61] reported that fibrin glue showed quicker and easier modality to use than microsuture repair for peripheral nerve injury.

When all of these are taken into account, we used the 0.5 mg of solubilized form of FK506 with collagen membrane and fibrin glue. This method had advantages in persistency, clinical reproducibility, manipulability, and achieved meaningful results.

FK506 has been reported of its serious side effects related to dosing including nephrotoxicity, hyperglycemia, and central nervous system toxicity.[62] Major side effect of FK506 is body weight loss accompanied by diarrhea.[20] Other symptoms include tremor, paresthesia, pain, and seizures. In our study, there were no clinical symptoms of body weight loss or self-mutilation. However, detailed toxicological evaluation should be further studied to ensure no systemic toxicity could occur following the local administration of FK506.

In this study, we showed the beneficial effects of the local FK506 on nerve regeneration following traction nerve injury. In addition, collagen was found to play an important role as a permeable membrane while being safely maintained for a long period of time *in vivo*. As FK506 was used in solubilized form, fibrin glue also appeared to help persistence and sustained local release. These results appeared without any serious side effects. However the molecular mechanisms of FK506 remain to be investigated in further study.

# Conclusion

Localized FK506 with collagen membrane and fibrin glue could promote axonal regeneration in traction nerve injury of a rat model.

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# List of tables

**Table 1. Measurement of nerve elongation and tension force change after tension injury**

| | Nerve length change | | | Tension force change | | |
|---|---|---|---|---|---|---|
| | Original(mm) | After(mm) | Ratio(%) | Initial(g) | Final(g) | Ratio(%) |
| 1 | 10 | 11.5 | 15 | 200 | 180 | 10 |
| 2 | 10 | 12 | 20 | 200 | 180 | 10 |
| 3 | 10 | 12 | 20 | 200 | 190 | 5 |
| 4 | 10 | 12.5 | 25 | 200 | 180 | 10 |
| 5 | 10 | 11.5 | 15 | 200 | 180 | 10 |
| 6 | 10 | 12 | 20 | 200 | 190 | 5 |
| 7 | 10 | 13 | 30 | 200 | 180 | 10 |
| 8 | 10 | 13 | 30 | 200 | 175 | 12.5 |
| 9 | 10 | 12.5 | 25 | 200 | 180 | 10 |
| 10 | 10 | 12 | 20 | 200 | 175 | 12.5 |
| 11 | 10 | 11.5 | 15 | 200 | 180 | 10 |
| 12 | 10 | 12 | 20 | 200 | 175 | 12.5 |
| 13 | 10 | 11 | 10 | 200 | 180 | 10 |
| 14 | 10 | 11.5 | 15 | 200 | 175 | 12.5 |
| 15 | 10 | 11 | 10 | 200 | 190 | 5 |
| 16 | 10 | 13 | 30 | 200 | 180 | 10 |
| 17 | 10 | 11 | 10 | 200 | 190 | 5 |
| 18 | 10 | 11 | 10 | 200 | 185 | 7.5 |
| 19 | 10 | 11.5 | 15 | 200 | 180 | 10 |
| 20 | 10 | 11.5 | 15 | 200 | 180 | 10 |
| AV | 10 | 11.9 | 18.5 | 200 | 181.3 | 9.4 |
| SD | 0 | 0.7 | 6.7 | 0 | 5.1 | 2.5 |

Original: original exposed nerve length, After: nerve length after tension injury, Initial: initial tension force, Final: tension at the time of tension removal

**Table 2. Sciatic function index**

| | Group A | | Group B | | Group C | |
|---|---|---|---|---|---|---|
| | 2w | 4w | 2w | 4w | 2w | 4w |
| 1 | -9.9 | -8.0 | -15.1 | -29.6 | -7.6 | -13.2 |
| 2 | -9.0 | -4.6 | -19.0 | -18.3 | -13.2 | -13.0 |
| 3 | -1.2 | -7.0 | -21.3 | -19.7 | -13.2 | -9.6 |
| 4 | -8.8 | -5.7 | -18.7 | -17.9 | -17.7 | -12.4 |
| 5 | -8.8 | -7.6 | -18.9 | -15.1 | -15.8 | -11.9 |
| 6 | -9.2 | -7.5 | -25.4 | -21.1 | -11.1 | -13.9 |
| 7 | -6.8 | -8.0 | -15.5 | -17.6 | -15.6 | -13.8 |
| 8 | -9.9 | -8.6 | -16.3 | -16.4 | -14.5 | -9.0 |
| 9 | -8.3 | -4.2 | -13.7 | -17.7 | -14.7 | -6.9 |
| 10 | -9.0 | -8.4 | -24.9 | -15.3 | -8.1 | -14.8 |
| 11 | -7.2 | -7.2 | -24.3 | -17.8 | -3.8 | -13.6 |
| 12 | -8.0 | -8.5 | -17.5 | -15.7 | -6.9 | -9.8 |
| 13 | -6.1 | -7.9 | -17.4 | -19.4 | -13.3 | -10.9 |
| 14 | -7.1 | -7.3 | -17.6 | -19.7 | -13.7 | -11.8 |
| 15 | -4.5 | -7.7 | -16.4 | -17.6 | -18.5 | -9.5 |
| 16 | -1.7 | -6.5 | -30.7 | -21.7 | -15.8 | -13.7 |
| 17 | -8.0 | -5.3 | -24.4 | -19.7 | -12.2 | -11.3 |
| 18 | -0.4 | -5.0 | -20.9 | -24.9 | -15.0 | -12.2 |
| 19 | -6.4 | -2.1 | -14.0 | -17.3 | -14.6 | -12.2 |
| 20 | -8.5 | -7.4 | -30.5 | -16.8 | -14.2 | -13.2 |
| 21 | -4.6 | -3.3 | -24.8 | -24.7 | -7.9 | -13.0 |
| 22 | -7.8 | -4.2 | -17.3 | -15.4 | -3.9 | -11.5 |
| 23 | -1.5 | -8.1 | -25.4 | -25.6 | -8.1 | -12.4 |
| 24 | -4.8 | -8.3 | -14.4 | -24.6 | -3.8 | -11.9 |
| 25 | -5.7 | -5.9 | -26.3 | -24.1 | -6.9 | -13.9 |
| 26 | -6.8 | -5.8 | -19.2 | -32.4 | -13.3 | -13.7 |
| 27 | -8.4 | -0.3 | -21.8 | -16.9 | -13.7 | -9.4 |
| 28 | -6.8 | -6.5 | -24.6 | -15.7 | -18.5 | -8.2 |
| 29 | -1.2 | -1.0 | -24.1 | -15.1 | -15.8 | -15.0 |
| 30 | -7.4 | -2.7 | -32.4 | -15.9 | -12.2 | -13.6 |
| 31 | -0.3 | -6.2 | -16.9 | -22.2 | -15.0 | -9.8 |
| 32 | -0.6 | -5.7 | -15.7 | -17.9 | -11.1 | -10.9 |
| 33 | -2.5 | -0.9 | -15.1 | -20.0 | -15.6 | -11.8 |
| 34 | -4.5 | -0.4 | -24.4 | -28.4 | -14.5 | -10.0 |
| 35 | -1.7 | -1.5 | -20.9 | -11.7 | -14.7 | -16.3 |
| 36 | -8.0 | -4.8 | -14.0 | -13.7 | -8.1 | -11.3 |
| 37 | -0.4 | -5.7 | -30.5 | -17.1 | -3.8 | -12.1 |
| 38 | -6.4 | -6.8 | -24.8 | -13.7 | -6.9 | -12.2 |
| 39 | -8.5 | -3.9 | -17.3 | -27.1 | -13.3 | -12.6 |
| 40 | -4.6 | -6.8 | -15.5 | -26.2 | -13.7 | -11.7 |
| AV | -5.8 | -5.6 | -20.7 | -19.7 | -12.0 | -11.9 |
| SD | 3.1 | 2.4 | 5.2 | 4.8 | 4.2 | 1.9 |

**Table 3. Statistical analysis of sciatic nerve function index**

| Group (2weeks) | p-value |
|---|---|
| Group A vs Group B | 0.001 |
| Group B vs Group C | 0.001 |
| Group A vs Group C | 0.001 |
| | |
| Group (4weeks) | |
| Group A vs Group B | 0.001 |
| Group B vs Group C | 0.001 |
| Group A vs Group C | 0.001 |

p<0.0167 (0.05/3: Bonferroni correction) was considered statistically significant

**Table 4. Total number of axons and axonal density**

| Group(2weeks) | Cell count | Area($mm^2$) | Axonal density (axon/$mm^2$) |
|---|---|---|---|
| A | 1954.25±47.61 | 0.51 | 3862.51±304.15 |
| B | 1510.75±43.44 | 0.50 | 3022.41±51.92 |
| C | 1742.75±46.11 | 0.49 | 3539.57±115.16 |
| p-value between the groups | | A and B | 0.029 |
| | | B and C | 0.029 |
| | | A and C | 0.057 |
| | | | |
| Group(4weeks) | | | |
| A | 1921.75±25.06 | 0.51 | 3805.87±32.52 |
| B | 1503.25±21.17 | 0.50 | 3037.84±58.44 |
| C | 1741.75±36.18 | 0.50 | 3520.14±103.24 |
| p-value between the groups | | A and B | 0.029 |
| | | B and C | 0.029 |
| | | A and C | 0.029 |

p<0.0167 (0.05/3: Bonferroni correction) was considered statistically significant

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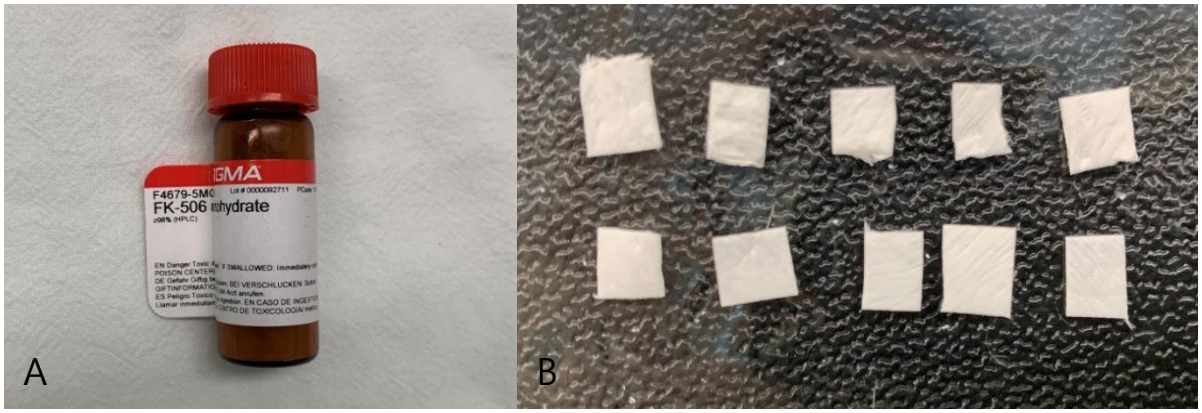


Figure 1. Preparation of FK506. (A) FK506 monohydrate. (B) Collagen membrane loaded with FK506.

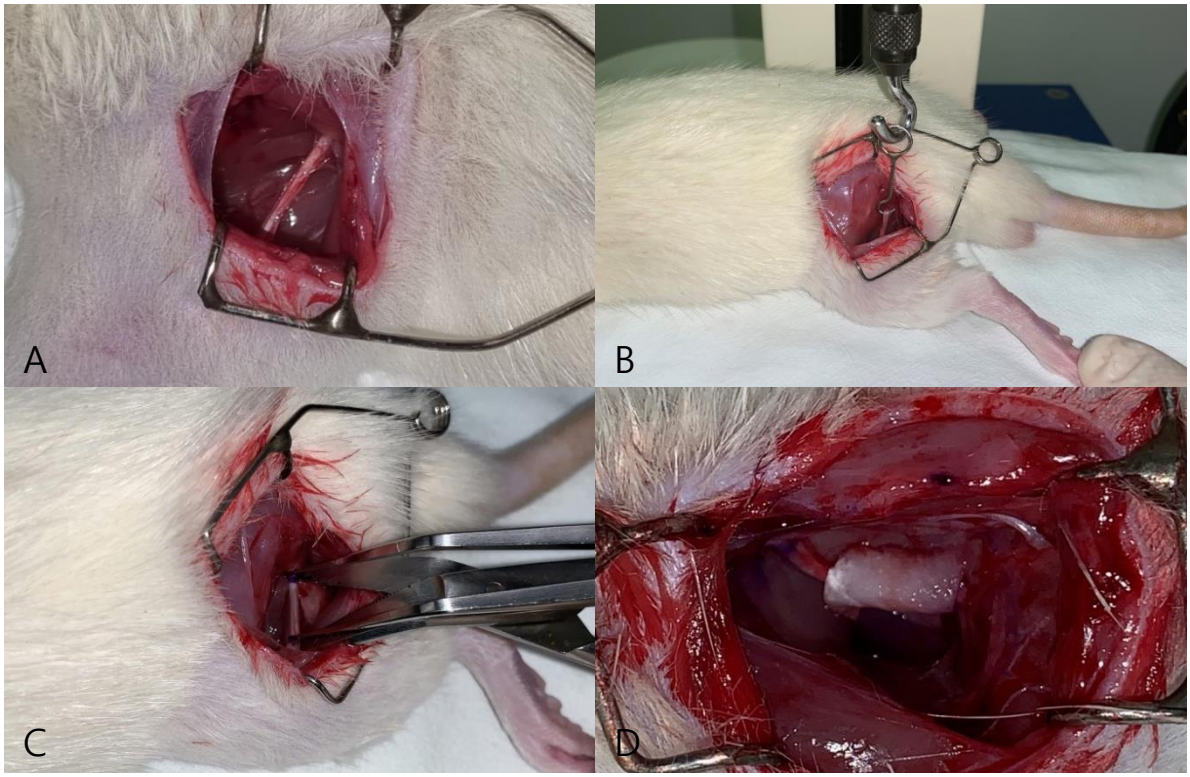


Figure 2. Surgical procedures. (A) Exposure of sciatic nerve of a rat. (B) Precise traction injury performed in the left sciatic nerve of the rat. (C) Measurement of the elongated sciatic nerve after traction injury. (D) Application of FK506 loaded with collagen membrane and fibrin glue on the injured sciatic nerve of a rat.

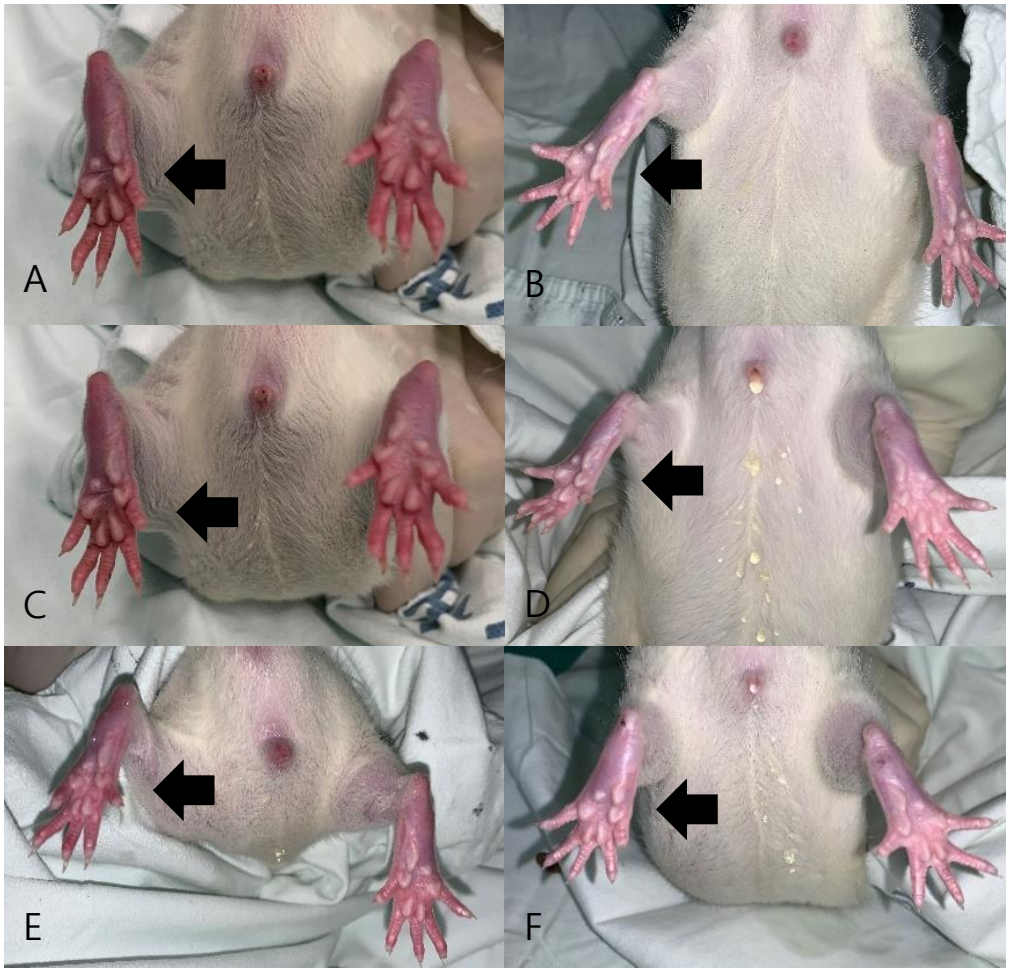


Figure 3. Photographs of the sole. (A) Representative in group A at 2 weeks. (B) Representative in group A at 4 weeks. (C) Representative in group B at 2 weeks. (D) Representative in group B at 4 weeks. (E) Representative in group C at 2 weeks. (F) Representative in group C at 4 weeks. In figure A and B, it appears that both feet are spread evenly (arrow). In figure C and D, the left foot appears to be crooked compared to the right foot (arrow). In figure E, left foot appears to be crooked compared to the right foot, however, in figure F, the left foot appears to have recovered slightly (arrow).

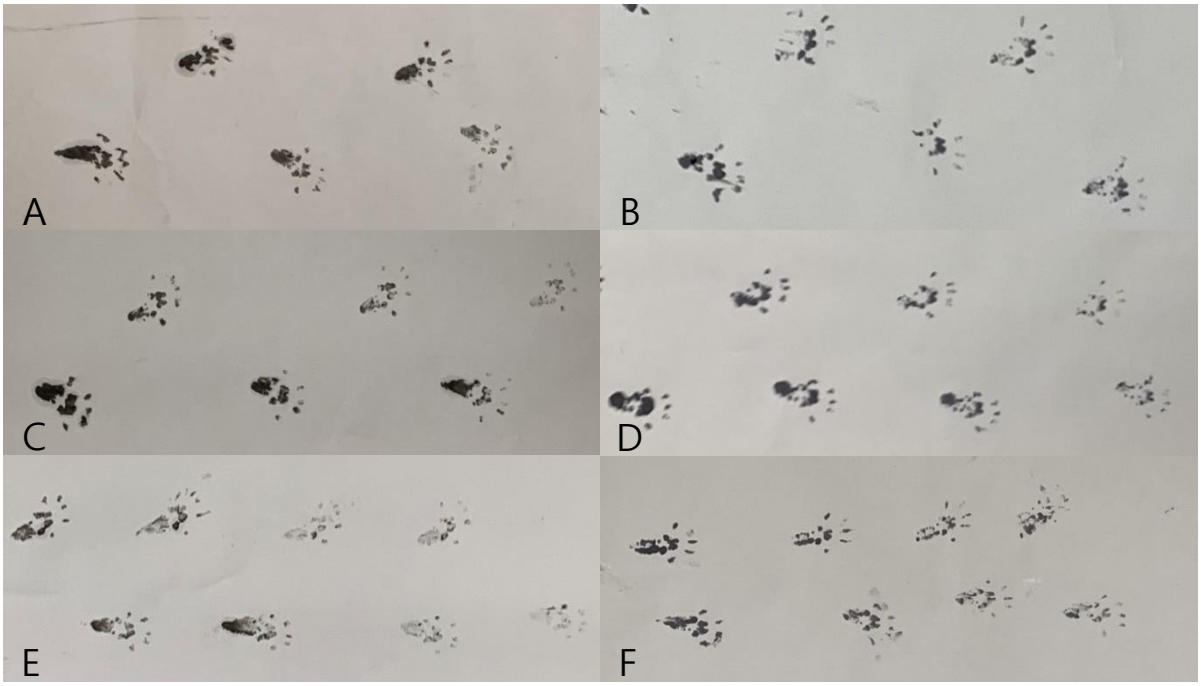


Figure 4. Walking track analysis. A. Foot prints of the group A at 2 weeks. B. Foot prints of the group A at 4 weeks. C. Foot prints of the group B at 2 weeks. D. Foot prints of the group B at 4 weeks. E. Foot prints of the group C at 2 weeks. F. Foot prints of the group C at 4 weeks.

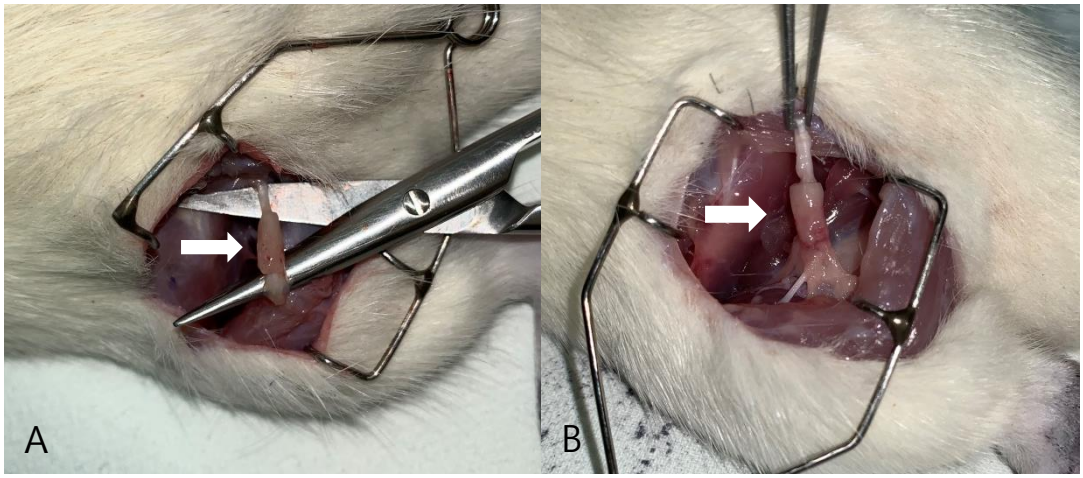


Figure 5. Harvesting the sciatic nerve. (A) Representative sciatic nerve of group C at 2 weeks. (B) Representative sciatic nerve of group C at 4 weeks. It is observed that the collagen membrane is maintained at both periods (arrow).

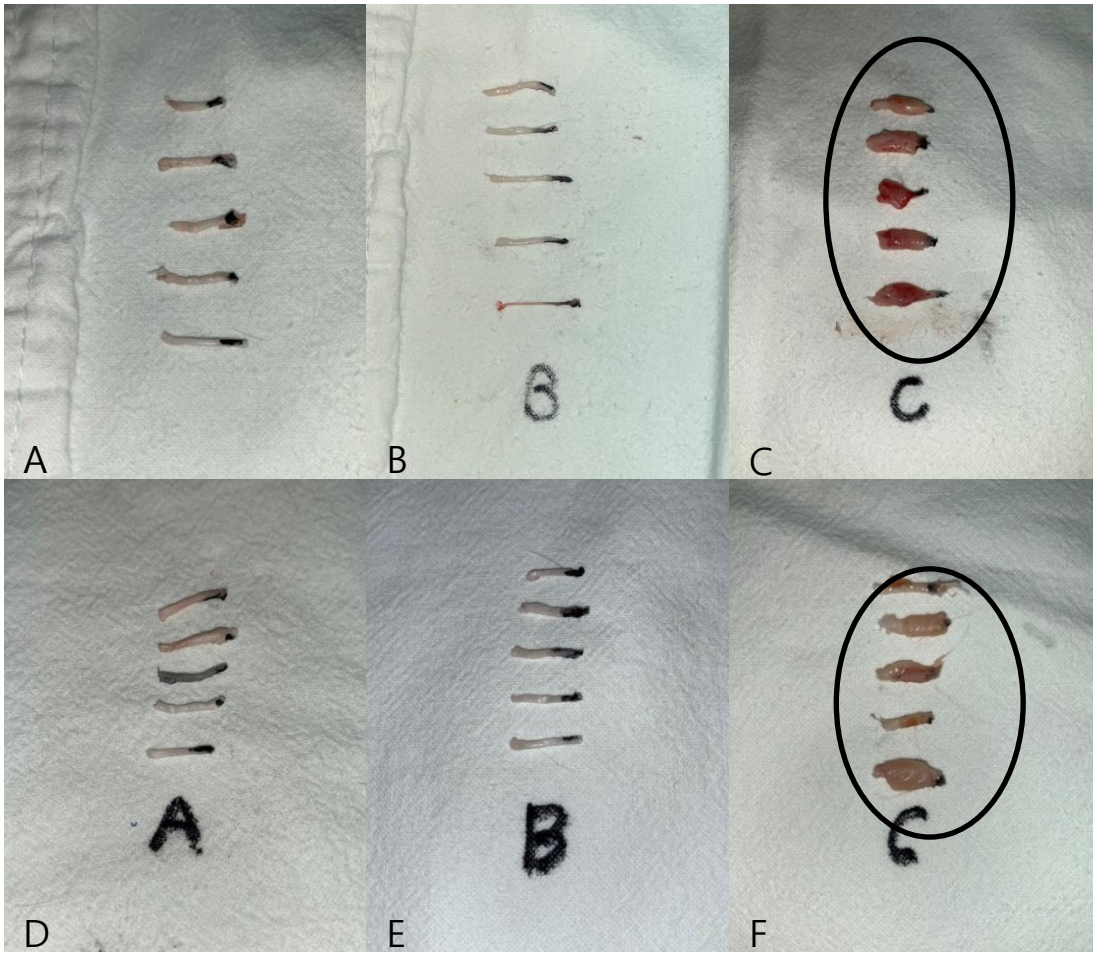


Figure 6. Sciatic nerve segments. All tissues were harvested 10 mm in length and the proximal area was marked with black ink. (A) Nerve segments of group A at 2 weeks. (B) Nerve segments of group A at 4 weeks. (C) Nerve segments of group B at 2 weeks. (D) Nerve segments of group B at 4 weeks (E) Nerve segments of group C at 2 weeks. (F) Nerve segments of group C at 4 weeks. In figure C and F, It is observed that the collagen membrane is maintained at both periods (circle).

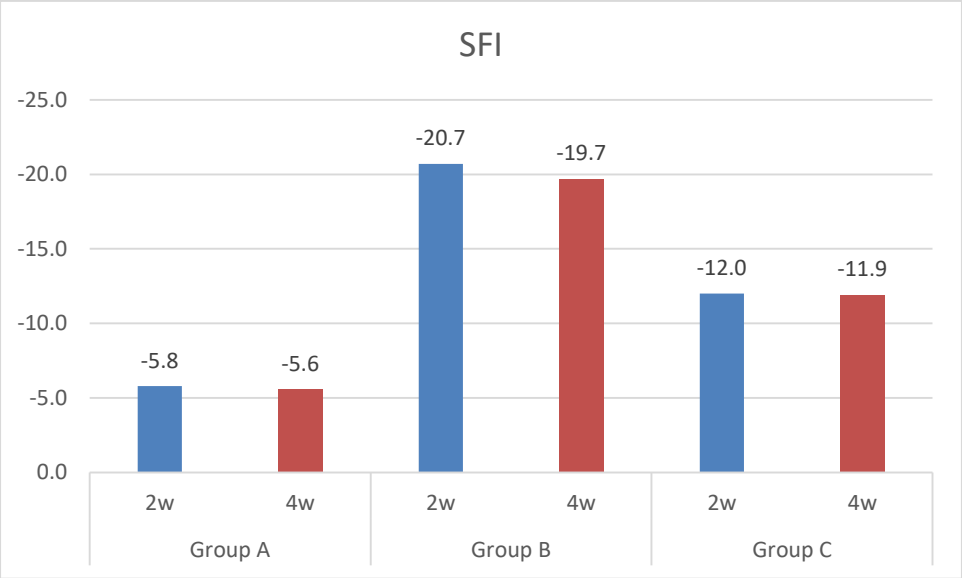


Figure 7. The mean value of Sciatic Functional Index in three groups.

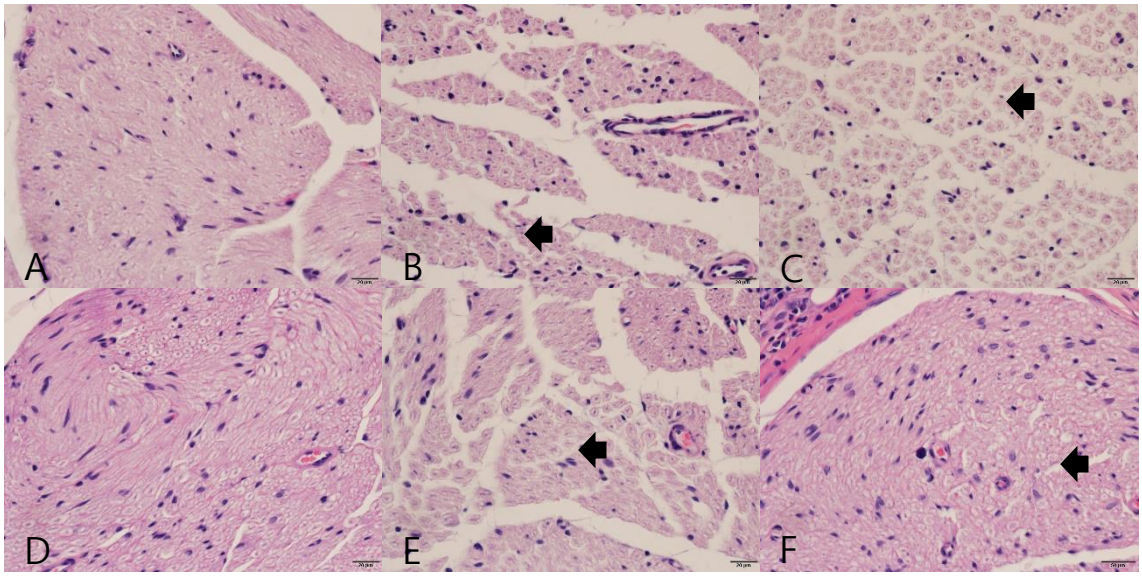


Figure 8. Cross-sectional photography of the sciatic nerve. (A) Group A at 2 weeks. It shows homogenous thickness and distribution of nerve fibers. (B) Group B at 2 weeks. Dead spaces between fibers are observed (arrow). (C) Group C at 2 weeks. Separations between fibers are seen (arrow). (D) Group A at 4 weeks. No significant difference between the result of 2 weeks. (E) Group B at 4 weeks. Dead spaces between fibers are still observed (arrow). (F) Group C at 4 weeks. Separations between fibers are decreased, showing relatively homogeneous density compared with the result of 2 weeks after surgery (arrow). (Hematoxylin and eosin staining, x40 magnification)

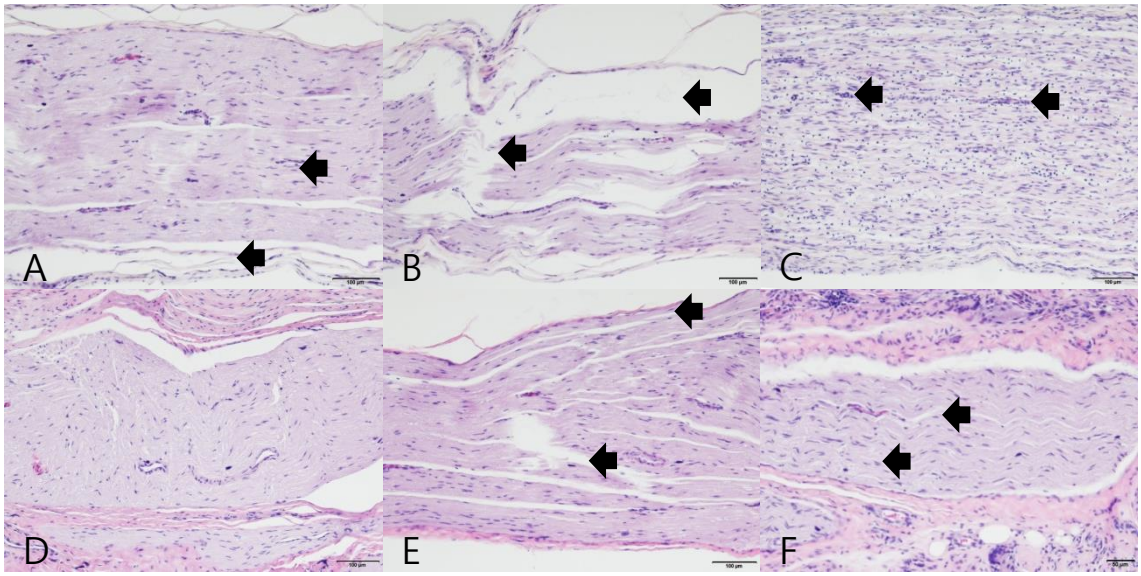


Figure 9. Longitudinal photography of the sciatic nerve. (A) Group A at 2 weeks. It shows orderly arranged fibers and intact epineurium (arrows). (B) Group B at 2 weeks. Edema and severance are seen (arrows). (C) Group C at 2 weeks. Arrows show misarranged fibers with lymphocyte infiltration. (D) Group A at 4 weeks. No significant difference is seen between 2 weeks. (E) Group B at 4 weeks. Edema and rupture which have been seen previously have decreased (arrows). Well-defined curling and vacuolization are observed. (F) Group C at 4 weeks. Orderly arranged fibers showing slight axonal swelling (arrows). (Hematoxylin and eosin staining, x10 magnification)

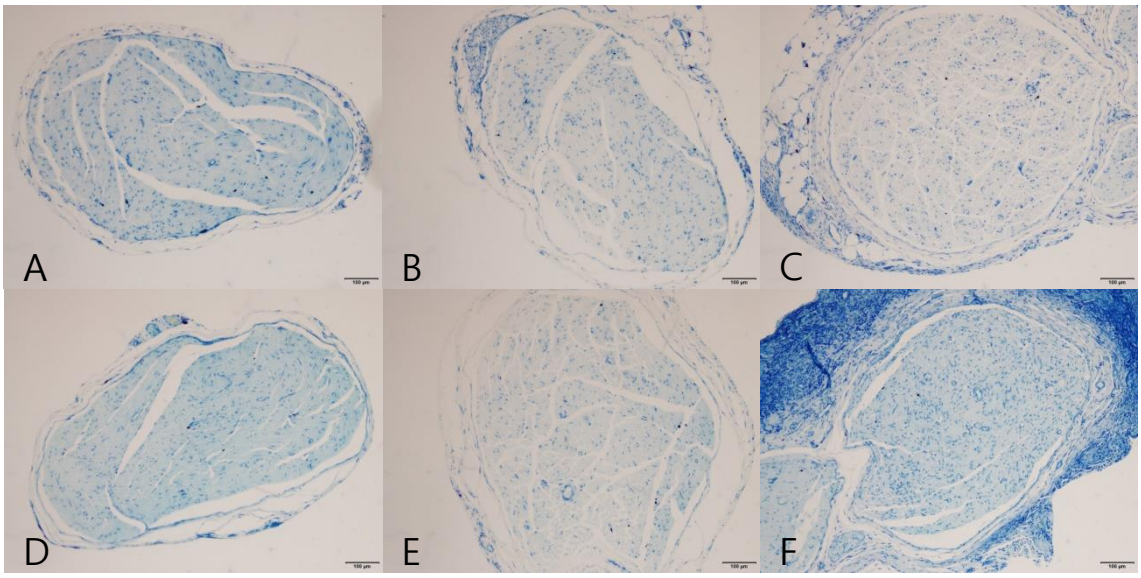


Figure 10. Cross-sectional photography of the sciatic nerve in toluidine blue. (A) Group A at 2 weeks. (B) Group B at 2 weeks. (C) Group C at 2 weeks. (D) Group A at 4 weeks. (E) Group B at 4 weeks. (F) Group C at 4 weeks. (Toluidine blue staining, x10 magnification)

# Appendix

**Appendix 1. Sciatic function index in group A (post 2weeks)**

| | EPL | ETS | EIT | NPL | NTS | NIT | PLF | TSF | ITF | SFI |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 34.1 | 21.1 | 13.2 | 36.2 | 21.5 | 14.6 | -0.1 | 0.0 | -0.1 | -9.9 |
| 2 | 34.2 | 20.9 | 11.5 | 35.0 | 21.0 | 12.0 | 0.0 | 0.0 | 0.0 | -9.0 |
| 3 | 34.3 | 23.2 | 13.0 | 35.0 | 22.0 | 12.2 | 0.0 | 0.1 | 0.1 | -1.2 |
| 4 | 35.6 | 20.2 | 11.6 | 35.0 | 20.0 | 12.0 | 0.0 | 0.0 | 0.0 | -8.8 |
| 5 | 33.1 | 20.1 | 11.5 | 34.0 | 20.0 | 13.0 | 0.0 | 0.0 | -0.1 | -8.8 |
| 6 | 33.3 | 23.5 | 12.0 | 35.0 | 24.0 | 12.0 | 0.0 | 0.0 | 0.0 | -9.2 |
| 7 | 33.4 | 22.1 | 10.0 | 37.0 | 22.0 | 12.0 | -0.1 | 0.0 | -0.2 | -6.8 |
| 8 | 35.9 | 22.0 | 14.0 | 32.0 | 21.0 | 16.0 | 0.1 | 0.0 | -0.1 | -9.9 |
| 9 | 32.0 | 21.4 | 14.2 | 35.0 | 22.0 | 14.0 | -0.1 | 0.0 | 0.0 | -8.3 |
| 10 | 33.2 | 19.8 | 13.0 | 34.0 | 20.0 | 13.0 | 0.0 | 0.0 | 0.0 | -9.0 |
| 11 | 32.2 | 22.8 | 12.0 | 35.5 | 23.0 | 13.0 | -0.1 | 0.0 | -0.1 | -7.2 |
| 12 | 36.3 | 22.1 | 14.0 | 35.0 | 22.0 | 12.4 | 0.0 | 0.0 | 0.1 | -8.0 |
| 13 | 34.0 | 21.3 | 12.0 | 35.0 | 21.0 | 12.0 | 0.0 | 0.0 | 0.0 | -6.1 |
| 14 | 34.2 | 23.0 | 12.0 | 37.8 | 23.0 | 14.0 | -0.1 | 0.0 | -0.1 | -7.1 |
| 15 | 34.3 | 22.3 | 14.8 | 35.1 | 21.9 | 13.4 | 0.0 | 0.0 | 0.1 | -4.5 |
| 16 | 37.9 | 24.5 | 14.0 | 36.6 | 23.0 | 12.7 | 0.0 | 0.1 | 0.1 | -1.7 |
| 17 | 36.8 | 24.3 | 13.2 | 37.9 | 24.3 | 13.5 | 0.0 | 0.0 | 0.0 | -8.0 |
| 18 | 34.2 | 22.4 | 14.1 | 36.6 | 21.4 | 13.3 | -0.1 | 0.0 | 0.1 | -0.4 |
| 19 | 34.0 | 26.0 | 13.4 | 37.2 | 26.2 | 13.5 | -0.1 | 0.0 | 0.0 | -6.4 |
| 20 | 36.7 | 24.0 | 12.6 | 36.0 | 23.5 | 14.0 | 0.0 | 0.0 | -0.1 | -8.5 |
| 21 | 37.0 | 24.0 | 12.9 | 37.8 | 22.9 | 15.0 | 0.0 | 0.0 | -0.1 | -4.6 |
| 22 | 34.2 | 24.7 | 13.5 | 38.6 | 25.0 | 16.0 | -0.1 | 0.0 | -0.2 | -7.8 |
| 23 | 35.4 | 25.5 | 14.6 | 37.4 | 24.3 | 14.8 | -0.1 | 0.0 | 0.0 | -1.5 |
| 24 | 33.9 | 24.5 | 13.2 | 38.5 | 24.2 | 15.4 | -0.1 | 0.0 | -0.1 | -4.8 |
| 25 | 37.4 | 23.5 | 12.2 | 37.6 | 22.7 | 13.2 | 0.0 | 0.0 | -0.1 | -5.7 |
| 26 | 37.8 | 23.8 | 13.7 | 38.1 | 23.7 | 12.5 | 0.0 | 0.0 | 0.1 | -6.8 |
| 27 | 34.1 | 25.7 | 13.4 | 35.4 | 25.9 | 13.6 | 0.0 | 0.0 | 0.0 | -8.4 |
| 28 | 35.9 | 24.5 | 14.3 | 37.3 | 24.7 | 12.9 | 0.0 | 0.0 | 0.1 | -6.8 |
| 29 | 37.1 | 24.5 | 15.5 | 37.1 | 23.2 | 14.0 | 0.0 | 0.1 | 0.1 | -1.2 |
| 30 | 37.2 | 24.6 | 14.2 | 38.2 | 24.4 | 14.8 | 0.0 | 0.0 | 0.0 | -7.4 |
| 31 | 35.9 | 23.7 | 12.4 | 37.7 | 22.4 | 12.1 | 0.0 | 0.1 | 0.0 | -0.3 |
| 32 | 36.5 | 24.4 | 14.9 | 37.6 | 23.0 | 14.4 | 0.0 | 0.1 | 0.0 | -0.6 |
| 33 | 36.0 | 22.6 | 14.3 | 37.1 | 21.5 | 14.8 | 0.0 | 0.1 | 0.0 | -2.5 |
| 34 | 34.3 | 22.3 | 14.8 | 35.1 | 21.9 | 13.4 | 0.0 | 0.0 | 0.1 | -4.5 |
| 35 | 37.9 | 24.5 | 14.0 | 36.6 | 23.0 | 12.7 | 0.0 | 0.1 | 0.1 | -1.7 |
| 36 | 36.8 | 24.3 | 13.2 | 37.9 | 24.3 | 13.5 | 0.0 | 0.0 | 0.0 | -8.0 |
| 37 | 34.2 | 22.4 | 14.1 | 36.6 | 21.4 | 13.3 | -0.1 | 0.0 | 0.1 | -0.4 |
| 38 | 34.0 | 26.0 | 13.4 | 37.2 | 26.2 | 13.5 | -0.1 | 0.0 | 0.0 | -6.4 |
| 39 | 36.7 | 24.0 | 12.6 | 36.0 | 23.5 | 14.0 | 0.0 | 0.0 | -0.1 | -8.5 |
| 40 | 37.0 | 24.0 | 12.9 | 37.8 | 22.9 | 15.0 | 0.0 | 0.0 | -0.1 | -4.6 |
| AV | 35.2 | 23.3 | 13.3 | 36.4 | 22.8 | 13.5 | 0.0 | 0.0 | 0.0 | -5.8 |
| SD | 1.6 | 1.6 | 1.1 | 1.5 | 1.6 | 1.1 | 0.0 | 0.0 | 0.1 | 3.1 |

**Appendix 2. Sciatic function index in group A (post 4weeks)**

| | EPL | ETS | EIT | NPL | NTS | NIT | PLF | TSF | ITF | SFI |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 34.2 | 22.2 | 12.1 | 34.1 | 22.0 | 12.2 | 0.0 | 0.0 | 0.0 | -8.0 |
| 2 | 34.9 | 22.5 | 11.5 | 34.1 | 21.5 | 11.5 | 0.0 | 0.0 | 0.0 | -4.6 |
| 3 | 33.1 | 20.6 | 15.1 | 36.0 | 21.0 | 14.2 | -0.1 | 0.0 | 0.1 | -7.0 |
| 4 | 34.2 | 20.4 | 15.0 | 35.0 | 20.0 | 15.0 | 0.0 | 0.0 | 0.0 | -5.7 |
| 5 | 33.0 | 22.0 | 13.0 | 35.0 | 22.0 | 14.0 | -0.1 | 0.0 | -0.1 | -7.6 |
| 6 | 32.0 | 23.0 | 13.0 | 34.0 | 23.0 | 14.0 | -0.1 | 0.0 | -0.1 | -7.5 |
| 7 | 36.0 | 24.1 | 12.8 | 36.1 | 23.9 | 13.0 | 0.0 | 0.0 | 0.0 | -8.0 |
| 8 | 35.9 | 23.7 | 11.8 | 35.0 | 23.4 | 12.0 | 0.0 | 0.0 | 0.0 | -8.6 |
| 9 | 34.5 | 20.3 | 13.0 | 35.0 | 20.0 | 11.0 | 0.0 | 0.0 | 0.2 | -4.2 |
| 10 | 34.6 | 21.1 | 11.5 | 35.0 | 21.0 | 12.0 | 0.0 | 0.0 | 0.0 | -8.4 |
| 11 | 36.0 | 24.3 | 14.0 | 36.2 | 24.1 | 13.5 | 0.0 | 0.0 | 0.0 | -7.2 |
| 12 | 35.4 | 24.3 | 13.5 | 36.0 | 24.4 | 13.4 | 0.0 | 0.0 | 0.0 | -8.5 |
| 13 | 35.0 | 22.2 | 14.0 | 34.0 | 21.8 | 14.0 | 0.0 | 0.0 | 0.0 | -7.9 |
| 14 | 33.0 | 22.0 | 14.0 | 33.0 | 21.7 | 14.0 | 0.0 | 0.0 | 0.0 | -7.3 |
| 15 | 34.9 | 27.1 | 15.6 | 35.1 | 26.8 | 16.0 | 0.0 | 0.0 | 0.0 | -7.7 |
| 16 | 35.5 | 24.6 | 14.5 | 36.1 | 24.2 | 14.7 | 0.0 | 0.0 | 0.0 | -6.5 |
| 17 | 37.6 | 25.2 | 17.0 | 37.7 | 25.0 | 14.3 | 0.0 | 0.0 | 0.2 | -5.3 |
| 18 | 32.2 | 26.9 | 16.4 | 35.0 | 27.1 | 14.7 | -0.1 | 0.0 | 0.1 | -5.0 |
| 19 | 36.8 | 27.7 | 17.1 | 35.8 | 26.0 | 16.4 | 0.0 | 0.1 | 0.0 | -2.1 |
| 20 | 33.2 | 25.4 | 14.3 | 35.4 | 25.5 | 14.9 | -0.1 | 0.0 | 0.0 | -7.4 |
| 21 | 36.9 | 25.2 | 14.3 | 38.2 | 24.0 | 15.8 | 0.0 | 0.1 | -0.1 | -3.3 |
| 22 | 35.2 | 24.4 | 15.6 | 36.0 | 23.6 | 15.6 | 0.0 | 0.0 | 0.0 | -4.2 |
| 23 | 35.7 | 26.8 | 15.5 | 35.6 | 26.5 | 16.0 | 0.0 | 0.0 | 0.0 | -8.1 |
| 24 | 37.7 | 27.4 | 16.9 | 37.2 | 27.1 | 17.1 | 0.0 | 0.0 | 0.0 | -8.3 |
| 25 | 37.9 | 25.4 | 17.1 | 37.1 | 25.1 | 14.3 | 0.0 | 0.0 | 0.2 | -5.9 |
| 26 | 35.0 | 27.8 | 16.5 | 36.7 | 27.7 | 15.5 | 0.0 | 0.0 | 0.1 | -5.8 |
| 27 | 37.3 | 27.7 | 17.4 | 37.6 | 25.9 | 16.7 | 0.0 | 0.1 | 0.0 | -0.3 |
| 28 | 34.7 | 26.8 | 13.9 | 34.9 | 26.3 | 13.9 | 0.0 | 0.0 | 0.0 | -6.5 |
| 29 | 36.8 | 23.5 | 14.3 | 37.8 | 22.3 | 13.4 | 0.0 | 0.1 | 0.1 | -1.0 |
| 30 | 35.8 | 25.7 | 15.7 | 36.3 | 24.5 | 15.4 | 0.0 | 0.0 | 0.0 | -2.7 |
| 31 | 35.0 | 24.8 | 15.4 | 35.8 | 24.5 | 15.0 | 0.0 | 0.0 | 0.0 | -6.2 |
| 32 | 38.2 | 25.3 | 17.8 | 38.0 | 25.3 | 14.3 | 0.0 | 0.0 | 0.2 | -5.7 |
| 33 | 37.3 | 27.1 | 17.0 | 37.9 | 25.5 | 16.5 | 0.0 | 0.1 | 0.0 | -0.9 |
| 34 | 37.0 | 23.8 | 14.0 | 38.5 | 22.0 | 16.6 | 0.0 | 0.1 | -0.2 | -0.4 |
| 35 | 35.4 | 25.5 | 14.6 | 37.4 | 24.3 | 14.8 | -0.1 | 0.0 | 0.0 | -1.5 |
| 36 | 33.9 | 24.5 | 13.2 | 38.5 | 24.2 | 15.4 | -0.1 | 0.0 | -0.1 | -4.8 |
| 37 | 37.4 | 23.5 | 12.2 | 37.6 | 22.7 | 13.2 | 0.0 | 0.0 | -0.1 | -5.7 |
| 38 | 37.8 | 23.8 | 13.7 | 38.1 | 23.7 | 12.5 | 0.0 | 0.0 | 0.1 | -6.8 |
| 39 | 34.1 | 24.7 | 13.4 | 35.4 | 23.9 | 13.6 | 0.0 | 0.0 | 0.0 | -3.9 |
| 40 | 35.9 | 24.5 | 14.3 | 37.3 | 24.7 | 12.9 | 0.0 | 0.0 | 0.1 | -6.8 |
| AV | 35.4 | 24.4 | 14.6 | 36.1 | 24.0 | 14.3 | 0.0 | 0.0 | 0.0 | -5.6 |
| SD | 1.6 | 2.1 | 1.7 | 1.4 | 2.0 | 1.5 | 0.0 | 0.0 | 0.1 | 2.4 |

**Appendix 3. Sciatic function index in group B (post 2weeks)**

| | EPL | ETS | EIT | NPL | NTS | NIT | PLF | TSF | ITF | SFI |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 33.1 | 19.6 | 12.2 | 35.0 | 20.8 | 14.5 | -0.1 | -0.1 | -0.2 | -15.1 |
| 2 | 32.3 | 19.2 | 14.4 | 34.3 | 21.8 | 13.8 | -0.1 | -0.1 | 0.0 | -19.0 |
| 3 | 32.8 | 22.5 | 14.4 | 31.0 | 24.5 | 16.0 | 0.1 | -0.1 | -0.1 | -21.3 |
| 4 | 33.5 | 19.0 | 9.0 | 36.3 | 21.0 | 11.0 | -0.1 | -0.1 | -0.2 | -18.7 |
| 5 | 33.0 | 20.0 | 9.2 | 35.0 | 22.0 | 11.2 | -0.1 | -0.1 | -0.2 | -18.9 |
| 6 | 36.0 | 19.0 | 11.8 | 33.4 | 21.0 | 15.5 | 0.1 | -0.1 | -0.2 | -25.4 |
| 7 | 35.0 | 22.0 | 11.0 | 36.0 | 23.0 | 14.2 | 0.0 | 0.0 | -0.2 | -15.5 |
| 8 | 36.7 | 21.9 | 11.1 | 34.4 | 22.7 | 12.1 | 0.1 | 0.0 | -0.1 | -16.3 |
| 9 | 34.7 | 21.3 | 11.4 | 33.3 | 21.7 | 12.6 | 0.0 | 0.0 | -0.1 | -13.7 |
| 10 | 36.1 | 21.5 | 12.6 | 34.6 | 24.4 | 14.1 | 0.0 | -0.1 | -0.1 | -24.9 |
| 11 | 36.3 | 22.0 | 12.3 | 33.0 | 24.0 | 15.2 | 0.1 | -0.1 | -0.2 | -24.3 |
| 12 | 34.8 | 21.5 | 11.5 | 33.6 | 22.8 | 12.5 | 0.0 | -0.1 | -0.1 | -17.5 |
| 13 | 37.6 | 22.3 | 12.3 | 36.7 | 23.5 | 14.6 | 0.0 | -0.1 | -0.2 | -17.4 |
| 14 | 39.1 | 22.1 | 11.1 | 38.3 | 23.4 | 13.0 | 0.0 | -0.1 | -0.1 | -17.6 |
| 15 | 35.2 | 21.9 | 11.2 | 33.2 | 22.7 | 12.6 | 0.1 | 0.0 | -0.1 | -16.4 |
| 16 | 36.5 | 20.9 | 12.2 | 33.1 | 24.3 | 15.3 | 0.1 | -0.1 | -0.2 | -30.7 |
| 17 | 36.8 | 21.8 | 12.4 | 34.7 | 24.4 | 14.1 | 0.1 | -0.1 | -0.1 | -24.4 |
| 18 | 34.9 | 19.8 | 11.1 | 32.7 | 21.6 | 11.4 | 0.1 | -0.1 | 0.0 | -20.9 |
| 19 | 35.9 | 21.9 | 11.5 | 34.6 | 22.2 | 13.9 | 0.0 | 0.0 | -0.2 | -14.0 |
| 20 | 37.8 | 23.2 | 12.4 | 33.6 | 26.8 | 14.8 | 0.1 | -0.1 | -0.2 | -30.5 |
| 21 | 37.7 | 22.1 | 12.8 | 35.0 | 24.8 | 14.0 | 0.1 | -0.1 | -0.1 | -24.8 |
| 22 | 34.8 | 21.6 | 11.3 | 33.5 | 23.0 | 11.6 | 0.0 | -0.1 | 0.0 | -17.3 |
| 23 | 35.8 | 19.2 | 10.9 | 33.6 | 21.9 | 11.4 | 0.1 | -0.1 | 0.0 | -25.4 |
| 24 | 39.6 | 22.0 | 12.2 | 39.0 | 22.9 | 12.9 | 0.0 | 0.0 | -0.1 | -14.4 |
| 25 | 36.8 | 21.6 | 12.6 | 33.2 | 24.0 | 15.3 | 0.1 | -0.1 | -0.2 | -26.3 |
| 26 | 36.3 | 21.4 | 11.1 | 33.9 | 22.8 | 12.0 | 0.1 | -0.1 | -0.1 | -19.2 |
| 27 | 37.9 | 21.3 | 12.2 | 36.2 | 23.7 | 12.3 | 0.0 | -0.1 | 0.0 | -21.8 |
| 28 | 35.5 | 22.8 | 14.9 | 33.2 | 25.9 | 15.0 | 0.1 | -0.1 | 0.0 | -24.6 |
| 29 | 38.8 | 22.9 | 14.5 | 35.0 | 25.3 | 15.4 | 0.1 | -0.1 | -0.1 | -24.1 |
| 30 | 37.9 | 20.5 | 13.2 | 35.5 | 24.9 | 15.1 | 0.1 | -0.2 | -0.1 | -32.4 |
| 31 | 37.3 | 22.0 | 11.0 | 36.7 | 23.4 | 11.8 | 0.0 | -0.1 | -0.1 | -16.9 |
| 32 | 39.6 | 26.1 | 15.8 | 39.2 | 27.4 | 17.5 | 0.0 | 0.0 | -0.1 | -15.7 |
| 33 | 34.9 | 25.8 | 15.3 | 33.9 | 27.0 | 15.7 | 0.0 | 0.0 | 0.0 | -15.1 |
| 34 | 36.8 | 21.8 | 12.4 | 34.7 | 24.4 | 14.1 | 0.1 | -0.1 | -0.1 | -24.4 |
| 35 | 34.9 | 19.8 | 11.1 | 32.7 | 21.6 | 11.4 | 0.1 | -0.1 | 0.0 | -20.9 |
| 36 | 35.9 | 21.9 | 11.5 | 34.6 | 22.2 | 13.9 | 0.0 | 0.0 | -0.2 | -14.0 |
| 37 | 37.8 | 23.2 | 12.4 | 33.6 | 26.8 | 14.8 | 0.1 | -0.1 | -0.2 | -30.5 |
| 38 | 37.7 | 22.1 | 12.8 | 35.0 | 24.8 | 14.0 | 0.1 | -0.1 | -0.1 | -24.8 |
| 39 | 34.8 | 21.6 | 11.3 | 33.5 | 23.0 | 11.6 | 0.0 | -0.1 | 0.0 | -17.3 |
| 40 | 35.0 | 22.0 | 11.0 | 36.0 | 23.0 | 14.2 | 0.0 | 0.0 | -0.2 | -15.5 |
| AV | 36.1 | 21.6 | 12.1 | 34.6 | 23.5 | 13.7 | 0.0 | -0.1 | -0.1 | -20.7 |
| SD | 1.8 | 1.5 | 1.5 | 1.7 | 1.7 | 1.6 | 0.0 | 0.0 | 0.1 | 5.2 |

**Appendix 4. Sciatic function index in group B (post 4weeks)**

| | EPL | ETS | EIT | NPL | NTS | NIT | PLF | TSF | ITF | SFI |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 35.0 | 20.5 | 10.5 | 36.0 | 24.5 | 15.0 | 0.0 | -0.2 | -0.3 | -29.6 |
| 2 | 35.1 | 19.0 | 11.0 | 36.0 | 21.0 | 11.0 | 0.0 | -0.1 | 0.0 | -18.3 |
| 3 | 34.2 | 20.0 | 11.2 | 35.0 | 22.0 | 13.0 | 0.0 | -0.1 | -0.1 | -19.7 |
| 4 | 34.0 | 19.5 | 12.0 | 36.0 | 21.5 | 13.0 | -0.1 | -0.1 | -0.1 | -17.9 |
| 5 | 35.9 | 22.0 | 11.5 | 38.1 | 23.5 | 13.0 | -0.1 | -0.1 | -0.1 | -15.1 |
| 6 | 33.7 | 20.8 | 14.8 | 35.0 | 24.1 | 13.5 | 0.0 | -0.1 | 0.1 | -21.1 |
| 7 | 33.0 | 22.4 | 14.6 | 33.0 | 24.5 | 14.0 | 0.0 | -0.1 | 0.0 | -17.6 |
| 8 | 33.8 | 24.5 | 13.5 | 34.2 | 26.0 | 15.5 | 0.0 | -0.1 | -0.1 | -16.4 |
| 9 | 31.8 | 23.5 | 14.0 | 34.0 | 26.0 | 15.0 | -0.1 | -0.1 | -0.1 | -17.7 |
| 10 | 35.0 | 23.5 | 12.0 | 36.0 | 25.0 | 13.0 | 0.0 | -0.1 | -0.1 | -15.3 |
| 11 | 33.2 | 24.0 | 12.0 | 34.0 | 26.0 | 13.5 | 0.0 | -0.1 | -0.1 | -17.8 |
| 12 | 34.0 | 20.0 | 14.0 | 34.0 | 21.0 | 16.0 | 0.0 | 0.0 | -0.1 | -15.7 |
| 13 | 35.0 | 22.0 | 12.5 | 36.0 | 24.5 | 13.0 | 0.0 | -0.1 | 0.0 | -19.4 |
| 14 | 34.5 | 21.8 | 13.0 | 36.0 | 24.0 | 16.0 | 0.0 | -0.1 | -0.2 | -19.7 |
| 15 | 35.0 | 23.0 | 15.0 | 35.0 | 25.0 | 15.0 | 0.0 | -0.1 | 0.0 | -17.6 |
| 16 | 34.8 | 21.0 | 11.5 | 37.0 | 24.0 | 13.0 | -0.1 | -0.1 | -0.1 | -21.7 |
| 17 | 35.0 | 20.0 | 13.0 | 35.0 | 22.0 | 14.0 | 0.0 | -0.1 | -0.1 | -19.7 |
| 18 | 35.2 | 21.0 | 14.5 | 37.0 | 25.0 | 15.0 | 0.0 | -0.2 | 0.0 | -24.9 |
| 19 | 34.0 | 22.0 | 13.5 | 35.4 | 24.0 | 14.5 | 0.0 | -0.1 | -0.1 | -17.3 |
| 20 | 38.9 | 24.2 | 13.0 | 35.4 | 24.6 | 15.9 | 0.1 | 0.0 | -0.2 | -16.8 |
| 21 | 37.6 | 22.2 | 13.1 | 35.3 | 25.2 | 13.5 | 0.1 | -0.1 | 0.0 | -24.7 |
| 22 | 38.3 | 23.3 | 11.6 | 38.2 | 24.4 | 13.2 | 0.0 | 0.0 | -0.1 | -15.4 |
| 23 | 36.9 | 23.4 | 14.0 | 34.8 | 26.6 | 15.5 | 0.1 | -0.1 | -0.1 | -25.6 |
| 24 | 35.5 | 22.8 | 14.9 | 33.2 | 25.9 | 15.0 | 0.1 | -0.1 | 0.0 | -24.6 |
| 25 | 38.8 | 22.9 | 14.5 | 35.0 | 25.3 | 15.4 | 0.1 | -0.1 | -0.1 | -24.1 |
| 26 | 37.9 | 20.5 | 13.2 | 35.5 | 24.9 | 15.1 | 0.1 | -0.2 | -0.1 | -32.4 |
| 27 | 37.3 | 22.0 | 11.0 | 36.7 | 23.4 | 11.8 | 0.0 | -0.1 | -0.1 | -16.9 |
| 28 | 39.6 | 26.1 | 15.8 | 39.2 | 27.4 | 17.5 | 0.0 | 0.0 | -0.1 | -15.7 |
| 29 | 34.9 | 25.8 | 15.3 | 33.9 | 27.0 | 15.7 | 0.0 | 0.0 | 0.0 | -15.1 |
| 30 | 39.2 | 24.2 | 13.5 | 35.7 | 24.4 | 16.5 | 0.1 | 0.0 | -0.2 | -15.9 |
| 31 | 37.0 | 22.5 | 13.4 | 35.2 | 25.0 | 13.9 | 0.1 | -0.1 | 0.0 | -22.2 |
| 32 | 38.4 | 23.3 | 12.2 | 37.5 | 24.9 | 13.3 | 0.0 | -0.1 | -0.1 | -17.9 |
| 33 | 35.3 | 23.1 | 14.2 | 34.4 | 25.3 | 15.0 | 0.0 | -0.1 | -0.1 | -20.0 |
| 34 | 38.1 | 20.3 | 13.2 | 37.3 | 24.1 | 14.9 | 0.0 | -0.2 | -0.1 | -28.4 |
| 35 | 36.5 | 22.3 | 11.3 | 36.4 | 22.7 | 12.1 | 0.0 | 0.0 | -0.1 | -11.7 |
| 36 | 38.3 | 26.2 | 16.2 | 38.2 | 27.4 | 16.2 | 0.0 | 0.0 | 0.0 | -13.7 |
| 37 | 34.8 | 25.4 | 15.1 | 34.0 | 27.1 | 15.7 | 0.0 | -0.1 | 0.0 | -17.1 |
| 38 | 38.3 | 26.2 | 16.2 | 38.2 | 27.4 | 16.2 | 0.0 | 0.0 | 0.0 | -13.7 |
| 39 | 38.1 | 20.9 | 13.2 | 37.9 | 24.6 | 15.0 | 0.0 | -0.2 | -0.1 | -27.1 |
| 40 | 37.7 | 22.2 | 13.1 | 35.6 | 25.6 | 13.7 | 0.1 | -0.1 | 0.0 | -26.2 |
| AV | 36.0 | 22.5 | 13.3 | 35.8 | 24.7 | 14.4 | 0.0 | -0.1 | -0.1 | -19.7 |
| SD | 2.0 | 1.9 | 1.5 | 1.5 | 1.7 | 1.4 | 0.0 | 0.0 | 0.1 | 4.8 |

**Appendix 5. Sciatic function index in group C (post 2weeks)**

| | EPL | ETS | EIT | NPL | NTS | NIT | PLF | TSF | ITF | SFI |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 37.1 | 24.1 | 17.0 | 36.0 | 24.2 | 14.0 | 0.0 | 0.0 | 0.2 | -7.6 |
| 2 | 36.1 | 22.2 | 14.0 | 36.0 | 23.1 | 14.0 | 0.0 | 0.0 | 0.0 | -13.2 |
| 3 | 35.2 | 20.1 | 13.0 | 35.0 | 20.9 | 13.0 | 0.0 | 0.0 | 0.0 | -13.2 |
| 4 | 37.0 | 20.3 | 13.0 | 37.0 | 22.1 | 13.0 | 0.0 | -0.1 | 0.0 | -17.7 |
| 5 | 33.4 | 20.8 | 11.0 | 36.0 | 22.7 | 11.5 | -0.1 | -0.1 | 0.0 | -15.8 |
| 6 | 35.1 | 20.6 | 11.0 | 35.0 | 20.8 | 12.0 | 0.0 | 0.0 | -0.1 | -11.1 |
| 7 | 34.3 | 22.0 | 11.0 | 35.0 | 23.0 | 14.0 | 0.0 | 0.0 | -0.2 | -15.6 |
| 8 | 35.1 | 23.0 | 12.0 | 35.0 | 24.0 | 13.0 | 0.0 | 0.0 | -0.1 | -14.5 |
| 9 | 35.2 | 23.0 | 15.0 | 34.0 | 24.0 | 15.0 | 0.0 | 0.0 | 0.0 | -14.7 |
| 10 | 37.3 | 24.0 | 14.0 | 38.0 | 24.0 | 14.0 | 0.0 | 0.0 | 0.0 | -8.1 |
| 11 | 37.5 | 23.0 | 13.0 | 36.5 | 22.0 | 12.0 | 0.0 | 0.0 | 0.1 | -3.8 |
| 12 | 36.9 | 24.0 | 17.0 | 36.0 | 24.0 | 14.0 | 0.0 | 0.0 | 0.2 | -6.9 |
| 13 | 35.8 | 22.0 | 14.0 | 36.0 | 23.0 | 14.0 | 0.0 | 0.0 | 0.0 | -13.3 |
| 14 | 34.7 | 20.0 | 13.0 | 35.0 | 21.0 | 13.0 | 0.0 | 0.0 | 0.0 | -13.7 |
| 15 | 36.8 | 20.0 | 13.0 | 37.0 | 22.0 | 13.0 | 0.0 | -0.1 | 0.0 | -18.5 |
| 16 | 33.1 | 21.0 | 11.0 | 36.0 | 23.0 | 11.5 | -0.1 | -0.1 | 0.0 | -15.8 |
| 17 | 35.2 | 20.6 | 11.0 | 35.0 | 21.0 | 12.0 | 0.0 | 0.0 | -0.1 | -12.2 |
| 18 | 33.7 | 22.0 | 11.0 | 35.0 | 23.0 | 14.0 | 0.0 | 0.0 | -0.2 | -15.0 |
| 19 | 35.2 | 23.0 | 12.0 | 35.0 | 24.0 | 13.0 | 0.0 | 0.0 | -0.1 | -14.6 |
| 20 | 34.7 | 23.0 | 15.0 | 34.0 | 24.0 | 15.0 | 0.0 | 0.0 | 0.0 | -14.2 |
| 21 | 37.1 | 24.0 | 14.0 | 38.0 | 24.0 | 14.0 | 0.0 | 0.0 | 0.0 | -7.9 |
| 22 | 37.6 | 23.0 | 13.0 | 36.5 | 22.0 | 12.0 | 0.0 | 0.0 | 0.1 | -3.9 |
| 23 | 37.3 | 24.0 | 14.0 | 38.0 | 24.0 | 14.0 | 0.0 | 0.0 | 0.0 | -8.1 |
| 24 | 37.5 | 23.0 | 13.0 | 36.5 | 22.0 | 12.0 | 0.0 | 0.0 | 0.1 | -3.8 |
| 25 | 36.9 | 24.0 | 17.0 | 36.0 | 24.0 | 14.0 | 0.0 | 0.0 | 0.2 | -6.9 |
| 26 | 35.8 | 22.0 | 14.0 | 36.0 | 23.0 | 14.0 | 0.0 | 0.0 | 0.0 | -13.3 |
| 27 | 34.7 | 20.0 | 13.0 | 35.0 | 21.0 | 13.0 | 0.0 | 0.0 | 0.0 | -13.7 |
| 28 | 36.8 | 20.0 | 13.0 | 37.0 | 22.0 | 13.0 | 0.0 | -0.1 | 0.0 | -18.5 |
| 29 | 33.1 | 21.0 | 11.0 | 36.0 | 23.0 | 11.5 | -0.1 | -0.1 | 0.0 | -15.8 |
| 30 | 35.2 | 20.6 | 11.0 | 35.0 | 21.0 | 12.0 | 0.0 | 0.0 | -0.1 | -12.2 |
| 31 | 33.7 | 22.0 | 11.0 | 35.0 | 23.0 | 14.0 | 0.0 | 0.0 | -0.2 | -15.0 |
| 32 | 35.1 | 20.6 | 11.0 | 35.0 | 20.8 | 12.0 | 0.0 | 0.0 | -0.1 | -11.1 |
| 33 | 34.3 | 22.0 | 11.0 | 35.0 | 23.0 | 14.0 | 0.0 | 0.0 | -0.2 | -15.6 |
| 34 | 35.1 | 23.0 | 12.0 | 35.0 | 24.0 | 13.0 | 0.0 | 0.0 | -0.1 | -14.5 |
| 35 | 35.2 | 23.0 | 15.0 | 34.0 | 24.0 | 15.0 | 0.0 | 0.0 | 0.0 | -14.7 |
| 36 | 37.3 | 24.0 | 14.0 | 38.0 | 24.0 | 14.0 | 0.0 | 0.0 | 0.0 | -8.1 |
| 37 | 37.5 | 23.0 | 13.0 | 36.5 | 22.0 | 12.0 | 0.0 | 0.0 | 0.1 | -3.8 |
| 38 | 36.9 | 24.0 | 17.0 | 36.0 | 24.0 | 14.0 | 0.0 | 0.0 | 0.2 | -6.9 |
| 39 | 35.8 | 22.0 | 14.0 | 36.0 | 23.0 | 14.0 | 0.0 | 0.0 | 0.0 | -13.3 |
| 40 | 34.7 | 20.0 | 13.0 | 35.0 | 21.0 | 13.0 | 0.0 | 0.0 | 0.0 | -13.7 |
| AV | 35.7 | 22.1 | 13.1 | 35.8 | 22.8 | 13.2 | 0.0 | 0.0 | 0.0 | -12.0 |
| SD | 1.4 | 1.4 | 1.8 | 1.1 | 1.2 | 1.0 | 0.0 | 0.0 | 0.1 | 4.2 |

**Appendix 6. Sciatic function index in group C (post 4weeks)**

| | EPL | ETS | EIT | NPL | NTS | NIT | PLF | TSF | ITF | SFI |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 35.4 | 23.1 | 13.2 | 36.4 | 24.1 | 14.2 | 0.0 | 0.0 | -0.1 | -13.2 |
| 2 | 35.1 | 22.1 | 13.5 | 36.0 | 22.9 | 15.0 | 0.0 | 0.0 | -0.1 | -13.0 |
| 3 | 37.9 | 23.4 | 11.1 | 40.0 | 23.8 | 12.0 | -0.1 | 0.0 | -0.1 | -9.6 |
| 4 | 36.2 | 23.2 | 13.2 | 37.0 | 24.1 | 13.5 | 0.0 | 0.0 | 0.0 | -12.4 |
| 5 | 35.8 | 22.0 | 13.5 | 37.0 | 22.8 | 14.0 | 0.0 | 0.0 | 0.0 | -11.9 |
| 6 | 38.1 | 21.5 | 11.4 | 38.0 | 22.5 | 11.5 | 0.0 | 0.0 | 0.0 | -13.9 |
| 7 | 35.2 | 24.5 | 14.0 | 35.0 | 25.5 | 14.5 | 0.0 | 0.0 | 0.0 | -13.8 |
| 8 | 35.3 | 24.5 | 14.0 | 37.2 | 25.0 | 14.0 | -0.1 | 0.0 | 0.0 | -9.0 |
| 9 | 34.5 | 22.2 | 15.0 | 35.3 | 22.0 | 15.0 | 0.0 | 0.0 | 0.0 | -6.9 |
| 10 | 35.2 | 23.5 | 15.0 | 36.0 | 25.0 | 15.3 | 0.0 | -0.1 | 0.0 | -14.8 |
| 11 | 35.9 | 22.8 | 16.0 | 37.0 | 24.1 | 16.0 | 0.0 | -0.1 | 0.0 | -13.6 |
| 12 | 36.1 | 21.5 | 14.0 | 36.5 | 22.0 | 13.0 | 0.0 | 0.0 | 0.1 | -9.8 |
| 13 | 35.2 | 23.0 | 12.0 | 35.0 | 23.0 | 14.0 | 0.0 | 0.0 | -0.1 | -10.9 |
| 14 | 34.7 | 21.3 | 12.0 | 37.0 | 22.0 | 14.0 | -0.1 | 0.0 | -0.1 | -11.8 |
| 15 | 36.2 | 21.0 | 12.5 | 36.0 | 21.0 | 13.0 | 0.0 | 0.0 | 0.0 | -9.5 |
| 16 | 35.8 | 20.5 | 12.0 | 36.0 | 21.3 | 13.0 | 0.0 | 0.0 | -0.1 | -13.7 |
| 17 | 37.1 | 20.2 | 11.5 | 36.0 | 20.0 | 14.0 | 0.0 | 0.0 | -0.2 | -11.3 |
| 18 | 36.3 | 20.6 | 11.2 | 37.0 | 21.2 | 12.1 | 0.0 | 0.0 | -0.1 | -12.2 |
| 19 | 35.8 | 20.4 | 11.5 | 36.5 | 21.2 | 11.5 | 0.0 | 0.0 | 0.0 | -12.2 |
| 20 | 35.4 | 23.1 | 13.2 | 36.4 | 24.1 | 14.2 | 0.0 | 0.0 | -0.1 | -13.2 |
| 21 | 35.1 | 22.1 | 13.5 | 36.0 | 22.9 | 15.0 | 0.0 | 0.0 | -0.1 | -13.0 |
| 22 | 37.9 | 23.4 | 11.1 | 38.0 | 23.8 | 12.0 | 0.0 | 0.0 | -0.1 | -11.5 |
| 23 | 36.2 | 23.2 | 13.2 | 37.0 | 24.1 | 13.5 | 0.0 | 0.0 | 0.0 | -12.4 |
| 24 | 35.8 | 22.0 | 13.5 | 37.0 | 22.8 | 14.0 | 0.0 | 0.0 | 0.0 | -11.9 |
| 25 | 38.1 | 21.5 | 11.4 | 38.0 | 22.5 | 11.5 | 0.0 | 0.0 | 0.0 | -13.9 |
| 26 | 35.2 | 24.5 | 14.1 | 35.0 | 25.5 | 14.5 | 0.0 | 0.0 | 0.0 | -13.7 |
| 27 | 35.3 | 24.5 | 13.8 | 37.2 | 25.0 | 14.2 | -0.1 | 0.0 | 0.0 | -9.4 |
| 28 | 34.5 | 22.0 | 15.0 | 35.3 | 22.0 | 15.3 | 0.0 | 0.0 | 0.0 | -8.2 |
| 29 | 35.2 | 23.5 | 14.8 | 36.0 | 25.0 | 15.3 | 0.0 | -0.1 | 0.0 | -15.0 |
| 30 | 35.9 | 22.8 | 16.0 | 37.0 | 24.1 | 16.0 | 0.0 | -0.1 | 0.0 | -13.6 |
| 31 | 36.1 | 21.5 | 14.0 | 36.5 | 22.0 | 13.0 | 0.0 | 0.0 | 0.1 | -9.8 |
| 32 | 35.2 | 23.0 | 12.0 | 35.0 | 23.0 | 14.0 | 0.0 | 0.0 | -0.1 | -10.9 |
| 33 | 34.7 | 21.3 | 12.0 | 37.0 | 22.0 | 14.0 | -0.1 | 0.0 | -0.1 | -11.8 |
| 34 | 36.2 | 21.1 | 12.5 | 36.0 | 21.2 | 13.0 | 0.0 | 0.0 | 0.0 | -10.0 |
| 35 | 35.8 | 20.0 | 12.0 | 36.0 | 21.3 | 13.0 | 0.0 | -0.1 | -0.1 | -16.3 |
| 36 | 37.1 | 20.2 | 11.5 | 36.0 | 20.0 | 14.0 | 0.0 | 0.0 | -0.2 | -11.3 |
| 37 | 36.3 | 20.6 | 11.2 | 37.0 | 21.2 | 12.0 | 0.0 | 0.0 | -0.1 | -12.1 |
| 38 | 35.8 | 20.4 | 11.5 | 36.5 | 21.2 | 11.5 | 0.0 | 0.0 | 0.0 | -12.2 |
| 39 | 36.2 | 23.2 | 13.2 | 36.8 | 24.1 | 13.5 | 0.0 | 0.0 | 0.0 | -12.6 |
| 40 | 35.8 | 22.0 | 13.5 | 37.2 | 22.8 | 14.0 | 0.0 | 0.0 | 0.0 | -11.7 |
| AV | 35.9 | 22.2 | 13.0 | 36.5 | 22.9 | 13.7 | 0.0 | 0.0 | 0.0 | -11.9 |
| SD | 0.9 | 1.3 | 1.4 | 1.0 | 1.5 | 1.2 | 0.0 | 0.0 | 0.1 | 1.9 |

국문 요약

# 백서 좌골신경 모델에서 견인 손상 이후 콜라겐 막과 섬유소 접착제에 함유된 FK506(Tacrolimus)이 신경재생촉진에 미치는 영향

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**개요**

구강악안면외과 수술에서 말초신경 손상은 가장 흔하게 일어날 수 있는 손상들 중에 하나다. 이 연구의 목적은 백서 좌골신경 모델에서 견인 신경 손상 후 신경 재생을 촉진하기 위한 콜라겐 막과 섬유소 접착제에 함유된 FK506 의 효과를 평가하는 것이다.

**재료 및 방법**

30 마리의 수컷 백서를 세 그룹으로 나누었다. 그룹 A (n=10)는 좌골 신경의 손상 없이 노출을 시행하였다. 그룹 B (n=10)와 그룹 C (n=10)는 1 분 동안 200g 의 견인 신경 손상을 시행하였다. 그룹 C 에서, FK506 (0.5 mg/0.1 ml)을 적신 콜라겐 막과 섬유소 접착제로 손상된 신경을 덮었다. 수술 후 2, 4 주차에 기능 분석과 현미경적 평가를 시행하였다.

**결과**

수술 2 주 후 좌골 신경 기능 지수(SFI)는 각각 A 군은 -5.78±3.07, B 군은 -20.69±5.22, 그리고 C 군은 -12.01±4.20 였다. 4 주 후 SFI 는 A 군은 -5.58±2.45, B 군은 -19.69±4.81, 그리고 C 군은 -11.95±1.94 였다. 두 기간 모두 각군 간에 유의한 차이가 관찰되었다 ($p<0.017$). 조직형태학적 평가에서는 그룹 B 보다 그룹 C 가 더 큰 신경 재생을 보였다. 하지만 세 그룹간에 축삭 밀도의 통계적 차이가 없었다 ($p<0.017$).

**결론**

콜라겐 막과 섬유소 접착제에 함유된 FK506 은 백서 모델의 견인 신경 손상에서 축삭 재생을 촉진할 수 있다.

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중심어: 좌골신경, 견인손상, 신경재생, FK506, 콜라겐, 섬유소 접착제