2

Laser nerve welding

Kun Hwang, MD, PhD,[1] and Sun Goo Kim, MD, PhD[2]
[1]*Inha University College of Medicine,* [2]*Gachon University Gil Hospital,*
Republic of Korea

1. Introduction

Microsurgial suture (Conventional microsurgical suture repair, CMSR) is the most commonly used method for anastomosis of severed peripheral nerves. Functional recovery after this type of repair is often inadequate, however, even though the peripheral nervous system has a remarkable ability to regenerate adequate sizes and numbers of axons. The most significant problems with microsuture repair are inherent in the technique: (1) surgery traumatizes the nerve by repeated introduction of a needle; (2) suture material at the anastomotic site presents a focus for scar and neuroma formation that may impede the growth of regenerating axons from the proximal segment into the proper distal segment endoneurial tubes and, ultimately, the neuromuscular junction; (3) microsurgical repair inevitably leaves small gaps that allow entry of fibroblasts and other scar tissue forming cells, permit regenerating axons to escape into an improper extraneural space, and promote loss of neurotrophic hormones that may be secreted locally to aid in the conduction of regenerating axons to their proper target; and (4) microsurgery is time-consuming and may be difficult to perform in restricted areas, particularly when supportive epineurial material is scarce. Also, especially in the head and neck region, there are often areas in which poor exposure or difficult surgical access precludes the placement of microsutures in nerve repair (Korff et al., 1992; Eppley et al., 1989; Huang et al., 1992).

A major focus of nerve repair research has been the development of procedures with which to avoid or minimize the use of sutures and prevent fibrous ingrowth at the repair site (Menovsky & Beek, 2001; Maragh et al., 1988). Several sutureless methods have been developed, although none of them has been demonstrated to be consistently superior to sutures.

Most importantly, sutureless methods must fulfill several criteria to have an advantage over suture repair. First, the procedure must result in a sufficient acute tensile strength. Second, it must not compress the nerve and must not involve increased severity of trauma compared with sutures. Third, the early and late tissue reaction of the nerve must be kept to a minimum and the axonal regeneration must not be impaired (Menovsky & Beek, 2001).

The laser was introduced in 1960s and is now widely used in medicine and surgery for the cutting, coagulation, and vaporization of various tissues. At low powers, thermal lasers, such as CO2, argon, and YAG, can be used to 'weld' tissue together by local protein coagulation. This property of the laser has been applied to nerve anastomosis as well as other tubular structures, such as vessel, bowl (Huang et al., 1992; Okada et al.,1987; Neblett et al., 1986). Laser nerve welding (LNW) has great potentials over conventional suture methods, such as a less trauma to tissue, less inflammatory reaction, and a faster surgical procedure (Menovsky et al., 1995). Thus, sutureless repair of peripheral nerves, by using lasers, has stimulated the interest of researchers.

2. General principle

Laser nerve welding had been investigated by several authors, since it offers a significant theoretical improvement to the problems just noted.

The mechanism of laser repair involves protein denaturation and subsequent fusion of the collagenous portion of the proximal and distal segment epineurium by low level thermal coagulation. Laser application has been shown to cause a change in collagen substructure with interdigitation of altered fibrils (Korff et al., 1992). Due to this mechanism, laser nerve welding provides significant theoretical advantages over conventional suturing methods, such as atraumatic nerve handling, avoidance of a foreign body reaction, a water tight seal of the epineurium with prevention of axonal escape and proliferation of connective tissue into the anastomosis, and a reduced operation time. There are several hypotheses to explain the improved results obtained with the laser. First, the irradiation of peripheral nerves with the CO2 laser does not result in severe inflammatory changes, nor does the nerve regeneration capacity seem limited by laser effects. The laser injury to the tissue heals very favorably, without excessive scar tissue or structural morphological alterations. The epineurium heals more favorably due to minimizing the foreign body reaction, and thus the axons are less blocked or misdirected at the repair site; consequently, the neural alignment is improved. Second, because of less instrumental manipulation of the nerve segments and avoidance of an excessive number of sutures, better axonal alignment of the nerve ends is achieved, and the cellular and fibroblastic reaction can be restricted to a minimum. Better alignment may also be achieved because the compressive forces and trauma to the epineurium resulting from sutures are reduced by simply using fewer of them. Intraneural scarring, which is mainly caused by collagen production by fibroblasts and Schwann cells inside the nerve, is less likely to be prevented by laser repair. Third, because of a ‘‘sealed’’ epineurium, the tendency of the regenerating proximal axons to sprout outside the nerve is suppressed, which leads to minimal neuroma formation and less scar tissue than in suture control groups. Also, ingrowth of fibrous scar tissue from outside the nerve is avoided. The epineurial seal is also postulated to provide a more favorable microenvironment for axonal growth by holding neurotrophic factors (Menovsky & Beek, 2001; Menovsky & Beek, 2003).

Laser nerve welding requires precise control of the thermal effects of the laser to permit welding of the epineurium without damage to the delicate underlying axons. This method became technically feasible with the development of the CO2 milliwatt laser, which can operate in power increments of 0.001 W while precise power stability is maintained (Huang et al., 1992). The first attempt at laser neurorrhaphy by Fischer et al. used a CO2 laser at relatively high powers (5 watts in 0.5 second pulses). As a result, dense carbonaceous deposits surrounded by a mild inflammatory reaction were found at the repair site (Fischer et al., 1985). No such carbon deposits were with the use of the CO2 milliwatt laser in the 120 to 150 mW range. This low thermal energy allows welding of superficial tissue without deep thermal penetration (Huang et al., 1992).

Many factors may influence the bonding strength of laser nerve welding, such as the amount of laser exposure, the amount of tissue available for fusion, and the technique that is used. Menovsky performed experimental studies for laser settings and end point determination which produce the greatest bonding strength (Menovsky et al., 1994). In laser welding procedure, the opposite nerve ends were closely approximated, and the epineurium of one of the nerve sections was pulled over the nerve end of the other nerve section and welded around its circumference with 2 to 3 laser pulses; the repair site is welded around its circumference with 5 to 8 laser pulses (Fig. 1) (Menovsky et al., 1994; Hwang et al., 2005).

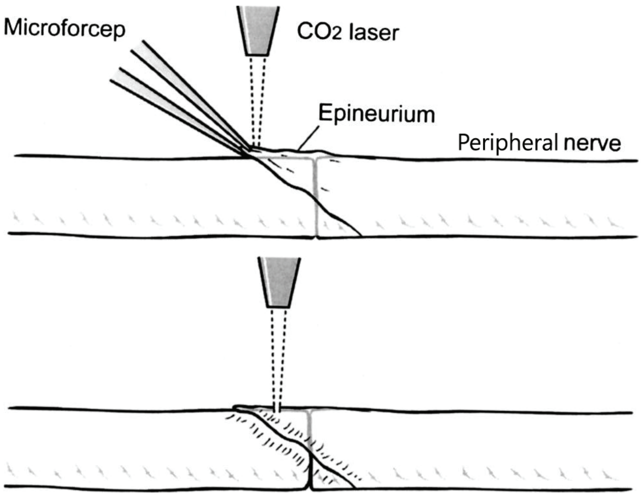

Fig. 1. The procedure of laser nerve welding. The epineurium of one of the nerve sections is pulled over the nerve end of the other nerve section and welded with 2 to 3 laser pulses; the repair site is welded around its circumference with 5 to 8 laser pulses. Reproduced with permission (Hwang et al., 2005).

Several technical points were essential for effective welding with the CO2 laser. Most importantly, bonding occurred only when the tissues were directly opposed with the epineurium overlying the repair site. Also, dry tissue surfaces were essential to obtain adequate welds. The dryer the tissue surface, the greater the effect of the laser on tissue. Welding of the overlying epineurium has the advantage that the two epineurium of the different nerve stump can be welded tightly without having tension on the repair site. This may be an advantage because tension on the repair site increases the amount of connective tissue that is formed and thus decreases regeneration (Menovsky et al., 1994).

The end point of the welding procedure was defined as the visible fusion of the epineurium, which was observed meticulously with a 40 fold magnification. And the visible effects of laser radiation on the epineurium were scored quantitatively with values varying from 0 to 6, where 0 indicated no visible effect, 1 drying of the epineurium, 2 shrinkage, 3 whitening, 4 caramelization (slightly browning), 5 carbonization, and 6 perforation of the epineurium (Menovsky et al., 1994). In experimental and clinical tissue welding, the endpoint of welding is normally based on visual changes of tissue. Drying and shrinkage, blanching, tanning, and browning of the tissue were indicated as the endpoints for proper welds (Maragh et al., 1988; Menovsky et al., 1994; Poppas et al., 1992). The results of one study show that the strongest welds were produced at powers and exposure times (100mW-1.0s) that gave whitening and a beginning of caramelization (beginning of browning) of the epineurium. The whitening is related to the denaturation of proteins. The use of higher powers and longer pulse durations gave rapid carbonization with weaker bonds. When the epineurium was perforated, the exposed fascicles reacted differently to the laser irradiation. Curling of the fascicles, creating small excavations without bonding of the tissue occurred. The difference in the reaction of epineurium and perineurium to laser radiation can be explained by the difference in composition. The epineurium is mainly composed of densely packed collagen bundles, while the perineurium is formed of several lamellae which consist of closely packed perineurial cells (Menovsky et al., 1994).

Comparable functional and morphometric data with much better results for the laser nerve welding than microsuture have been achieved by only few authors. This is probably due to the difference in the welding technique, taking into consideration the basic requirements of laser welding (Happak et al., 2000). The epineurial edges need to be approximated precisely by two forceps trying to avoid any air gap between the epineurium of the nerve stumps. Furthermore, laser welded nerve coaptations should be performed without tension, as it has been assumed for sutured nerve repair. The bonding effect of welded collagen fibers and other proteins was made responsible for a sufficient tensile strength of coaptations and anastomoses (Schober et al., 1986; Bass et al., 1992). Bass et al. have shown that the welding effect does not depend on the amount of collagen that has been welded, but on different molecular binding mechanisms (Bass et al., 1992).

Also noted were the thermal effects of LNW anastomosis on the underlying fascicular structures. The heat resulted in the deleterious effects of the destruction of myelin and loss of axons immediately adjacent to the anastomotic site. Some authors reported that irradiation of nerves with laser nerve energy does not appear to have any adverse effects on axonal regeneration. Morphometric analysis of myelinated axons around the repair site by Beggs et al. and Maragh et al. revealed no deleterious effects of the laser on the degree of retrograde axonal degeneration or regeneration as shown by the similar numbers and sizes of regenerated fibers present in the distal stump compared with suture repairs (Maragh et al., 1988; Beggs et al., 1986; Eppley et al., 1989).

If a CO2 laser is used for fusing the epineurium, a water tight seal can be established without damage to the underlying neural tissue. For welding of nerves, the CO2 laser should be used because the penetration depth of this laser is small compared to other lasers proposed for LNW and LANR (Nd:YAG laser, and the argon laser) (Schober et al., 1986; Campion et al., 1990).

The major advantages of laser welded nerve coaptation are, under optimal circumstances, the decreased surgical time, the extreme precision, the minor damage to the nerve tissue, and the prevention of foreign-body reactions (Happak et al., 2000; Balies et al., 1989). In contrast, the essential drawback of welding techniques is the initial low tensile strength after coaptation, which leads to a relatively high dehiscence rate, varying between 12 and 41% (Ochi et al., 1995). The clinical application of laser-assisted nerve repair has been limited by the risk of dehiscence in the postoperative period and the inability to achieve consistently successful laser welds (Korff et al., 1992; Maragh et al., 1988; Dubuisson & Kline, 1993). One study showed that the anastomotic strength of the laser weld has been found consistently inferior to that of microsuture repair for at least the first 4 days after surgery. The weak initial weld has caused unacceptable rates of dehiscence (Maragh et al., 1988). As reported by Maragh et al. in the rat sciatic nerve model, there was no significant difference in tensile strength of the laser repaired nerves and the suture repaired nerves at 8 days postoperatively. The critical period is clearly the first week before host-connective tissue elements add the necessary stability. To make laser repair an attractive alternative to suture repair, the tensile strength of the laser repaired nerve must be improved further (Korff et al., 1992).

To overcome this problem, one or more stay sutures for supporting the welds (called laser assisted nerve repair, LANR) or nerve grafts to reduce the tension at the repair site have been used (Fischer et al., 1985; Menovsky et al., 1994; Eppley et al., 1989). However, these adaptations impair the nerve regeneration. Grafting gives the additional complication of two repair sites, and sutures produce a foreign body reaction. Some authors performed a laser assisted nerve repair with the aid of stay sutures which were eventually removed (Fischer et al., 1985; Balies et al., 1989; Ochi et al., 1995; Benke et al., 1989). In 1988, Maragh et al. reported about CO2 laser welded nerve coaptations by using a circumferential epineurial technique. No sutures were used, and the dehiscence rate of the coaptations was 12% (Maragh et al., 1988). Nerve coaptations with the CO2 laser were only achieved without dehiscence when an additional bonding material was used. The coaptations were strengthened with peri-epineurial sheets (Korff et al., 1992; Kim & Kline, 1990), fibrin sheets (Ochi et al., 1995), or fibrin glue (Menovsky & de Vries, 1998).

Although the precise mechanism of nerve welding is not yet understood, tissue welding by the CO2 laser is probably caused by protein denaturation and fusion of collagen, and/or dehydration of the structural proteins (Menovsky et al., 1994; Dew, 1986; Fenner et al., 1992). As these proteins are believed to be the primary component of welding process, topically applied proteins (used as solders) may provide the necessary amount of proteins for welding and result in a greater bonding strength (Menovsky et al., 1994). Another significant development in laser welding is the use of protein solders as an adjunct to the welding process. These solders, which provide extra protein for the fusion process, are melted on the outer surface of the repair site to hold the tissue together, and result in stronger welds and theoretically less thermal damage to the tissue (Menovsky et al., 1994; Menovsky, 2000).

In general, the CO2 laser-repaired nerves appeared to heal with less cellular response and less scar tissue than the sutured nerves. Also, proliferation of the epi- and perineurium was significantly less than that of the CMSR nerves. The alignment of axons and intraneural scars was most favorable in the soldered nerves. The severe inflammatory reaction around the solder observed in the first week was absent, and instead, a well defined epi- and perineurium was present. Consequently, the regeneration in the distal nerve segment was most advanced in the soldered nerves. In this segment there were also fewer extraneural fibers compared to other repair groups (Menovsky & Beek, 2003). The addition of solder seems to result in even better histological results than the CO2 laser alone. In a rat sciatic nerve repair using the CO2 laser and a fibrin film, the repair site revealed a smooth continuity of nerve fibers at 8 weeks (Ochi et al., 1995).

Besides the use of protein solders, extra tissues for improving the bonding strength have been used. Kim and Kline used perineurial and epineurial tissue to serve as a supplement for the welding procedure, resulting in 100% bonding rate (Kim & Kline, 1990). Korff et al. used LNW in combination with subcutaneous tissue wrapped around the nerve (Korff et al., 1992).

On the other hand, Happak et al. suggested that a minimal amount of collagen and other proteins of the epineurium provides sufficient welding strength in case of an adequate laser irradiation being applied without additional bonding materials or stay suture. This has been documented by the lack of dehiscences of the coapted nerves after 6 months of regeneration in their study (Happak et al., 2000). And Hwang et al. performed facial nerve repair by laser nerve welding and microsurgical suture in rat model and they also reported that they did not perform supportive procedures to enhance the laser welding site and there was no dehiscence in any of the 12 rats (Hwang et al., 2005).

3. Experimental study

During the last decade laser has become an increasingly useful surgical tool, and laser welding repair of injured peripheral nerves has been investigated. Since first successful CO2 laser welded coaptations were published by Fischer et al. in 1985 (Fischer et al., 1985), several authors reported that laser nerve welding was at least equal or more successful to microsurgical suture in effectiveness in animal model of facial and sciatic nerve repairs.

3.1 Facial nerve repair and facial – hypoglossal nerve anastomosis

Eppley et al. performed an experimental study to evaluate the effectiveness of laser nerve welding versus conventional suture repair of facial nerve grafts in the rabbit (Eppley et al., 1989). A group of 10 animals underwent bilateral 1 cm facial nerve resections which were primarily repaired with the contralateral resected nerve in which the right side was anastomosed by suture (CMSR, interrupted epinueural 10-0 nylon sutures) and the left side by laser nerve welding (CO2 laser with 150mW, 300u spot size and 0.5s duration assisted by a single suture for traction and rotation). Postoperative assessment was carried out at 1 and 3 months and consisted of electrophysiological recording prior to sacrifice, which was compared to preoperative recordings of the same nerve, and was then followed by histological evaluation of the anastomosis and graft. Electrophysiologic assessment of function revealed no significant difference between the two techniques after 3 months follow up period. It resulted in similar conduction recording to CMSR after 3months and appeared to reduce the amount of axonal intermingling, although quantitative axonal assessment was not performed in this study. Histological differences were apparent between two groups. Unlike sutures, laser nerve welding provides a seal around the epineurium without the potential of the introduction of foreign material into the underlying structures. Theoritically, this seal may prevent axonal escape as well as proliferation of connective tissue into the anastomosis. The author’s findings indicate that less entrapment of axons occurred with laser nerve welding, presumably due to the fewer sutures required with this type of repair. However, both types of repair had evidence of axons outside the anastomosis, thus indicating that the laser nerve welding did not provide a watertight epineurial seal in the mW power levels used. Also noted was the thermal effect of laser nerve welding on the underlying fascicular structures. The heat resulted in the deleterious effects of the destruction of myelin and loss of axons immediately adjacent to the anastomotic site. While this appeared to be of little consequence in the 3 month specimens, this tissue destruction could lead to fibrous tissue formation which may be as detrimental to axonal regrowth as that induced by retained suture material. The effects of heat upon neural structures at 1 month were apparent but did not affect the longer term specimens.

The authors concluded that laser nerve welding may offer an alternative to conventional suturing or be useful when suturing is technically difficult due to access (with the intraoral repair of the lingual and mandibular nerves) or when lack of supportive neural structure exists (Eppley et al., 1989).

Hwang et al. performed facial nerve repair by laser nerve welding and microsurgical suture in rat model and evaluated nerve regeneration with an immunochemical detection of the retrograde nerve tracer cholera toxin B (Hwang et al., 2005). In the buccal branches of rat's facial nerves on the both sides were transected, and CO2 laser welding of the epineurium was performed on the right side and microsurgical suture technique was applied on the left side. For the laser nerve welding, the proximal and distal epineurium of the severed nerve ends were pulled together to meet the nerve ends of each other and welded at two directly opposite spots with 2 to 3 pulses of a CO2 laser (Wonderful CO2 Laser, Wonder Laser, Inc., Daejon, Korea) setting at 100mW continuous wave energy, 320 mm spot size, and 1 second duration time and the repair site is welded around its circumference with 5 to 8 laser pulses (Fig.1). In six rats Cholera Toxin B Subunit (CTb) was injected in the epineurium distal to the nerve anastomosis site at postoperative week 4 and 8 (Fig. 2).

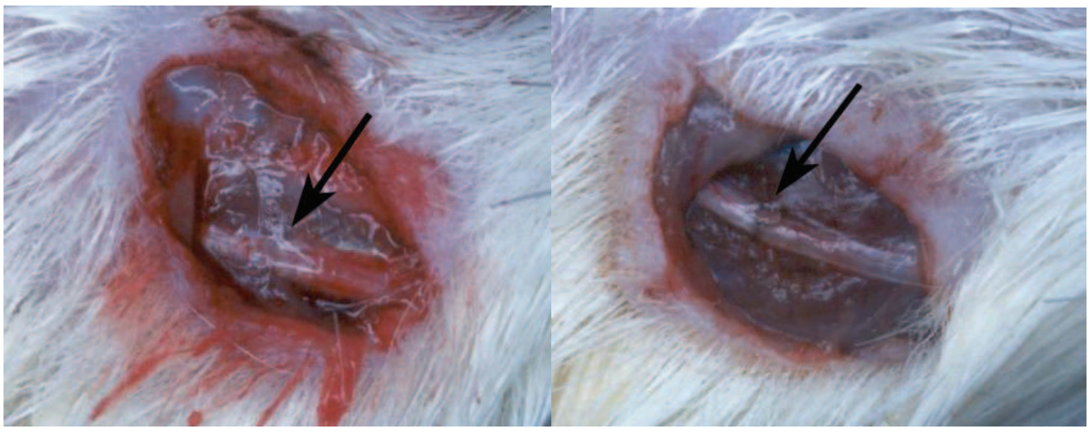

Fig. 2. Four-week postoperative photographs. (Left) Laser-assisted nerve anastomosis. Arrow indicates anastomosis site. (Right) Microsurgical suture anastomosis. Arrow indicates suture site. Reproduced with permission (Hwang et al., 2005).

Neurons of facial nuclei labeled positively by CTb were detected immunohistochemically, and the numbers were counted. CTb-positive neurons were seen significantly more in the group with laser welding than in the group with microsurgical suture in postoperative week, but there was not much difference in postoperative week 8. None of 12 rats showed dehiscence at the nerve anastomosis done by laser welding. This study showed that nerve regeneration is more apparent in the nerve repaired by laser welding than in that repaired by microsurgical suture. And this study showed that laser nerve welding affected regeneration of the repaired nerve equally to or more effectively than microsurgical suturing. Quantitative assessment was carried out with the immunohistochemical detection of the retrograde nerve tracer cholera toxin, which is one of the most widely used probes for studies of neuronal connectivity (Hwang et al., 2005).

The authors did not perform supportive procedures to enhance the laser welding site. There was no dehiscence in any of the 12 rats. This result indicates that the cranial nerves, including the facial nerve and other nerves in the head and neck, are not subjected to significant stretching or tension as occurs with peripheral nerves in the extremities, such as the sciatic nerve (Huang et al., 1992). Thus, dehiscence is expected low in the head and neck area.

Hypoglossal-facial anastomosis (HFA) is an alternative surgical measure of facial palsy as the facial nerve itself can not be restored. HFA is usually attempted in a delayed repair because it is difficult to suture directly a disrupted facial nerve in most clinical cases (Angelov & Gunkel, 1993; Chen & Hsu, 2000).

Hwang et al. performed another study to compare laser nerve welding to microsurgical suturing of hypoglossal-facial anastomosis (HFA), and a result of immediate to delayed repair, and to evaluate the effect of laser nerve welding on HFA for reanimation of facial palsy in animal model of rats (Hwang et al., 2006). The first group underwent immediate HFA by microsurgical suturing and the second group by CO2 laser welding. The right hypoglossal nerve was transected 1 mm proximal to the bifurcation of the medial and lateral branches. The right facial nerve was transected at near stylomastoid foramen, sparing the posterior auricular branch. Proximal stump of the hypoglossal nerve and distal stump of the facial nerve were approximated by laser nerve welding without additional stay suture in the first group and by microsurgical suturing with three sutures of 9-0 nylon in the second group. The third group underwent delayed HFA by microsurgical suturing, and the fourth group by laser nerve welding. The right facial nerve was transected at near stylomastoid foramen, sparing the posterior auricular branch. The proximal stump was left, but the distal stump was tagged with a 9-0 nylon stitch before closing the wound. Ten days later, the distal stump of the facial nerve was explored. The previous tagged suture was removed, and a 1-mm segment of the stump was cut. Ipsilateral hypoglossal nerve was exposed and transected proximally at the bifurcation of its medial and lateral branch. Intact proximal stump of the hypoglossal nerve was approximated to the predegenerated distal stump of the facial nerve by laser nerve welding in the third group and by microsurgical suturing in the fourth group.

In all rats of the four different treatment groups, cholera toxin B subunit (CTb) was injected in the epineurium distal to the anastomosis site on the postoperative 6th week. Neurons labeled CTb of hypoglossal nuclei were positive immunohistochemically, and the numbers were counted. There was no significant difference between immediate and delayed anastomosis in the laser welding group, but there was significance between immediate and delayed anastomosis in the microsurgical suturing group. No dehiscence in the laser welding site of nerve anastomosis was seen at the time of re-exploration for injection of CTb in all rats. This study showed that the regeneration of anastomosed hypoglossal-facial nerve was affected similarly by laser welding and microsurgical suturing, and more effective, especially in delayed repair.

And tensile strength of the anastomosis site is insecure in the laser welded nerve. The cranial nerves in the head and neck area are not so tense as peripheral nerves in the extremities. A dehiscence rate of the laser welded nerves in the head and neck area is expectedly quite low (Huang et al., 1992). In this study, no dehiscence in the laser welding site of the nerve anastomosis was seen at the time of re-exploration for injection of CTb in all 20 rats. These results were thought to show the possibility of successful application of laser nerve welding in clinical settings, especially of head and neck area (Hwang et al., 2006).

Hwang et al. performed additional study to compare laser nerve welding of hypoglossal-facial nerve to microsurgical suturing and a result of immediate and delayed repair, and to evaluate the effectiveness of laser nerve welding in reanimation of facial paralysis of the rabbit models (Hwang et al., 2008). The first group underwent immediate HFA by microsurgical suturing and the second group by CO2 laser welding. The third group underwent delayed HFA by microsurgical suturing, and the fourth group by laser nerve welding. In laser welding group, one stay-suture of 9–0 nylon was applied temporarily only in mild tensed gap of the severed nerves (Fig. 3 & 4).

In this study, in microsurgical suturing group, the mean number of labeled neurons in immediate HFA was significantly higher than in delayed HFA. The mean number of labeled neurons subjected to laser welding was higher than microsurgical suturing in the delayed HFA. In microsurgical suturing, axons may be caught up and displaced from their connections because of the passage and retention of sutures. And gaps persist in the epineurium between the sutures which can allow for connective tissue invasion or axonal extravasation (Eppley et al., 1989). In the delayed nerve repair, there were degeneration and weakness of epineural tissue and a lot of inflammation and scar tissues around the repair site. This result indicates that the sutures especially could be adverse to the regenerating axon with degeneration in a delayed nerve repair.

In laser welding group, the mean number of labeled neurons was all but same in the immediate and delayed HFAs. Laser welding provides strict thermal effect on the epineurium without adding any damage to the adjacent tissue like underlying axons. Unlike sutures, this provides a seal around the epineurium without any potential for the introduction of foreign material into the underlying fascicular structures and makes no mechanical damage to the degenerated epineural tissue in the delayed repair (Eppley et al., 1989). Therefore, the laser nerve welding may give a less trauma to the regenerated axon and the mean number of labeled neurons in the laser welding group was almost the same in the immediate and delayed HFAs in this study.

There was little difference of nerve regeneration between laser welding and microsurgical suturing in the immediate HFA. In the immediate repair group in which there is little inflammation and scar tissue, the method of neurorrhaphy may not affect the regeneration of anastomosed hypoglossal-facial nerve.

In this study, 1 epineurial stay-suture of 9–0 nylon was applied temporarily only in cases with mild tensed gap of the severed nerves. The stay-suture was used for approximation between both nerve ends and the repair sited was sealed circumferentially by laser nerve welding. No dehiscence was seen on the laser welding site of nerve anastomosis in all the rabbits.

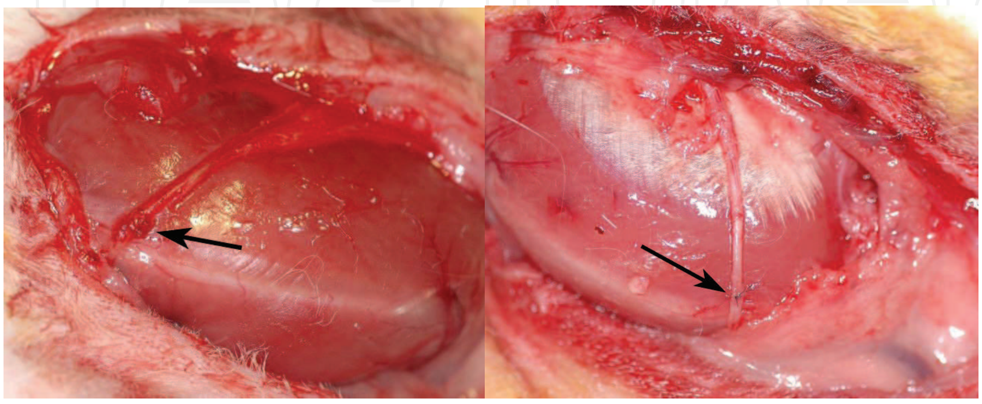

Fig. 3. Immediate postoperative photographs. (Left) Hypoglossal-facial nerve anastomosis (HFA) by laser nerve welding. Arrow indicates anastomosis site. (Right) HFA by microsurgical suturing.

Arrow indicates suture site. Reproduced with permission (Hwang et al., 2008).

This study showed that regeneration of the anastomosed hypoglossal-facial nerve was affected similarly by either laser welding or microsurgical suturing in immediate repair; however, the welding was more effective especially in delayed repair (Hwang et al., 2008).

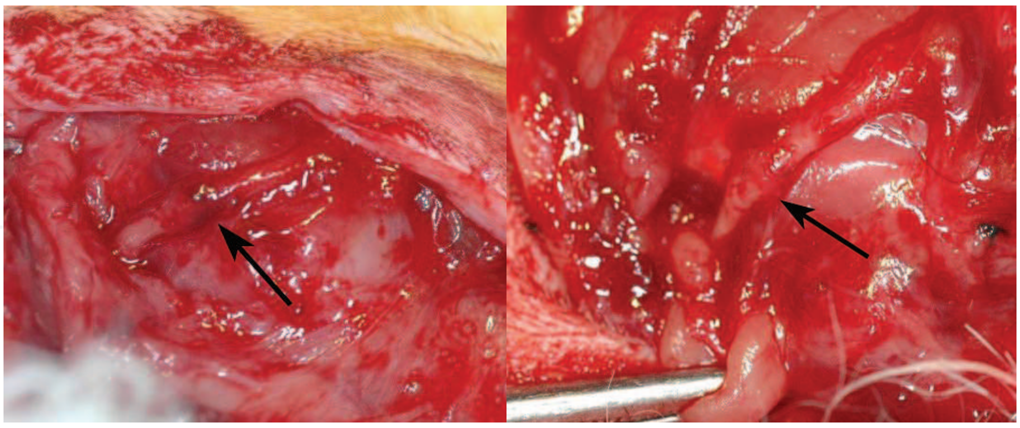

Fig. 4. Postoperative 6 weeks photographs. (Left) Hypo- glossal-facial nerve anastomosis (HFA) by laser nerve welding. Arrow indicates anastomosis site. (Right) HFA by microsurgical suturing. Arrow indicates suture site. Reproduced with permission (Hwang et al., 2008).

3.2 Sciatic nerve repair

Huang et al. performed a comparative study between microsuture and CO2 laser repair of transected sciatic nerves in rats (Huang et al., 1992). The left sciatic nerves of rats were transected and repaired by microsuture (six 10-0 nylon sutures) and laser nerve welding (CO2 laser with 120 to 150 mW power setting, 0.5 mm spot size, 30 to 60 sec duration time, and two epineurial sutures of 10-0 nylon as markers). No attempt was made postoperatively to immobilize the lower extremity of the animals. Nerve regeneration was measured in terms of morphology, electrophysiology, and function. For measurement of motor function of sciatic nerve, 'Sciatic function index's, reflecting footprint length and width, toe spread, and stride length, were measured preoperatively, then weekly for the first 2 months postoperatively, and then every other week until 4 months after nerve repair. At 4 months after repair, the mean nerve conduction velocity of repaired sciatic nerves was measured.

Functional recovery, as determined objectively using measurements of gait footprints, showed no difference between suture and laser repair. EMG and nerve conduction velocity were similar for the two repair methods. On histologic analysis, there was no difference in the size and number of regenerated axons. The laser repaired nerve demonstrated good axonal regeneration and no evidence of tissue charring or carbonaceous deposits. Good axonal regeneration was also found in microsuture repaired nerves. However, foreign body reactions were present surrounding the sutures and appeared to cause distortion of axon fibers and perineurial fibrosis around the suture granulomas. Laser nerve repair using epineurial welding and two anchoring sutures took approximately one-third less time than microsuture repair using six epineurial sutures. However, this study showed a 41% rate of nerve dehiscence in laser repair group, even with placement of two anchoring sutures, probably as a result of inadequate tensile strength of the anastomosis immediately postoperatively. The authors suggested that one possible solution of high dehiscence rate is to be temporarily immobilize the limb for 7 to 10 days postoperatively to allow adequate healing to occur before tension is allowed on the repaired nerve. However, laser nerve welding was faster and simpler than microsurgical suture repair and required less manipulation of the nerve.

This study showed laser repair of peripheral nerve is possible with results comparable to conventional microsurgical nerve repair and laser nerve repair may be effective alternative to microsurgical suture repair (Huang et al., 1992).

Happak reported an experimental study to obtain functional and morphologic informations by using a nerve coaptation technique by epineurial CO2 laser welding only (Happak et al., 2000). In this study, the sciatic nerves of 24 rats were transected and epineurially coapted with the CO2 laser at 60 mW, 135 um spot size or with microsuture as a control. Walking track analysis was carried out to evaluate the functional recovery, and the nerves were harvested for histology after 6 months of regeneration. None of the 24 nerves showed dehiscence of the coaptations, and all showed good nerve fiber regeneration. Better results were obtained for the functional evaluation of the sciatic function index ($P<0.02$) and the toe spread index ($P < 0.04$) from the laser nerve coaptations. Likewise, the morphologic evaluations of the fiber density ($P<0.04$) and area fraction ($P < 0.002$) were better in the laser group. The better functional and morphologic results of the LNC group might be explained by the avoidance of disturbing effects on nerve tissue and its regeneration due to laser welding. The thermal damage of the underlying nerve fascicles is described, as one concern, connected with the epineurial CO2 laser welding (Trickett et al., 1997; Lauto et al., 1997). In this study, the authors selected the lowest power setting, 60 mW, to prevent the nervous tissue from any possible damage. They have found no hard evidence of such damage, because no carbonization of the epineurium was visible under the microscope during the welding procedure. The CO2 laser parameters chosen for this procedure kept the absorption depth of the light at a minimum, and it seemed to prevent any immediate damage. CO2 laser irradiation of the epineurium does not impair the nervous tissue in contrast to the damage caused by sutures in the control group.

On gross morphology, the authors found neuromatous thickening, which was typical of the coaptation site in the microsuture group. The thickening of the coaptation site is described as the neuromatous regeneration of nerve fibers outside of the epineurium through the gaps between the sutures. Less neuromatous thickening was observed in the laser group, these findings are in accordance with the results of other authors (.Fischer et al., 1985; Ochi et al., 1995; Almquist et al., 1994). In their opinion, this is due to the water tight seal of the epineurium, which prevented the sprouting of nerve fibers outside the epineurial tube. In the laser group, these fibers remain extrafascicular within the epineurium of the distal nerves and, thus, may contribute to the better functional results as a higher number of nerve fibers reach the target organ.

And they conclude that a minimal amount of collagen and other proteins of the epineurium provide sufficient welding strength in case of an adequate laser irradiation being applied. This has been documented by the lack of dehiscences of the coapted nerves after 6 months of regeneration in this study. In this study, in the rat sciatic model, the laser nerve weldings are significantly better in several parameters than the sutured nerve repair (control) and CO2 laser welding may result in a better nerve regeneration with better functional outcome and may be a new approach for clinical trials. The results of this study could be to fulfill the aforementioned advantages by simply welding the epineurial edges of the transected sciatic nerve by using the CO2 laser, excluding additional aids (Happak et al., 2000).

3.3 Complementary methods using stay sutures, protein solders

Korff et al., attempted to improve on the laser welding technique by examining the effect of laser radiation on the compound action potential (CAP) of intact rat sciatic nerves (Korff et al., 1992). In the second phase of the study, a new technique to improve anastomotic strength was developed, S-Q weld, which involved harvesting a sheet of subcutaneous tissue from the experimental animal, wrapping it around the cut nerve ends, and lasering it to the epineurium. The final part of the study examined the long term effectiveness of the technique as compared to microsuture repair in the rat sciatic nerve model.

In S-Q weld procedure, the nerve ends were reapproximated and the subcutaneous tissue was wrapped around the nerve and spot welded to the epineurium using CO2 laser with 1.0 w, 0.05 s, 0.36mm spot size. Multiple pulses were applied to the S-Q sheath around a circumference of 180 degrees to allow adequate stump alignment.

CO2 laser produced almost no decrease in CAP transmission at 0.5 watts. However, this level of irradiation did not provide adequate bonding of subcutaneous tissue to nerve epineurium during S-Q welding. In this study, a higher power of 1.0 w was used, because it produced adequate bonding with minimal anticipated increase in damage to endoneural axons and support structures. The strength of the S-Q weld was considerably greater than that produced by laser welding alone. And the other phase of the study compared regeneration at 2 months in severed rat sciatic nerves repaired by either microsuture or S-Q weld. Analysis of the compound action potential values indicated that the number of regenerating fibers after laser repair was greater than that after suture repair, although a significant difference could not be demonstrated.

The S-Q weld technique uses host tissue, which is allographic, biocompatible, and readily available, to provide an instrument for sealing and binding severed nerve stumps. Using this approach, the laser energy is focused on the subcutaneous wrap at sites removed from the actual nerve juncture, where scarring and neuroma formation should be avoided. The tensile strength of the S-Q weld immediately after repair was far greater than the tensile strength without subcutaneous sheath. The strength of S-Q welded nerves was also inferior to the tensile strength of the acute suture repair, but the improvement over CO2 laser weld alone was substantial and would encourage further refinement of this procedure.

The authors concluded that laser nerve welding using the S-Q weld technique has several theoretical advantages over suture repair. The observed improvement in initial anastomotic strength over laser repair alone warrants the need for further investigation with different laser energies and other improvement in technique (Korff et al., 1992).

Menovsky et al. designed experimental study to investigate the in vitro bonding strength of nerves welded by a CO2 laser at different radiant exposures and exposure times. Laser nerve welding was performed at 15 different laser settings (power outputs of 50, 100 and 150 mW; pulse durations of 0.1, 0.5, 1.0, 2.0, and 3.0s) with a spot size of 320 um. The effect of different solders on the bonding strength was investigated and compared to conventional microsurgical suture repair, laser assisted nerve repair, and fibrin glue repair. As a solder, 5 and 20 % albumin solution, dried albumin solution, egg white, fibrinogen solution, fibrin glue, and red blood cells were used (Menovsky et al., 1994).

The strongest welds (associated with whitening and caramelization of tissue) were produced at 100 mW with pulses of 1.0 s and at 50 mW with pulses of 3 s. The use of a dried albumin solution as a solder at 100 mW with pulses of 1 s increased the bonding strength 9-fold as compared to LNW. However, positioning the nerves between cottons soaked in saline for 20 minutes (rehydration) resulted in a decrease of the bonding strength. Other solders did not increase the bonding strength in comparison to LNW. Understanding of the precise mechanism of the fusion process, however, might lead to an appropriate selection of the concentration and kind of proteins to be used as a solder. Although the bonding strength of LNW in combination with the use of 20% albumin solution and egg white as a solder was lower than in CMSR, improvement over LNW alone was substantial and encourages further in vivo research on the use of solders.

In this study, the bonding strength of LNW performed at optimal laser settings was significantly lower than in CMSR (bonding strength 2.4 +- 0.9 versus 29.6 +- 10.4 g). Comparison between the fibrin glue repair and LNW without solder showed no differences. For LANR using one 10-0 nylon stay suture, the bonding strength was about 20% that of the nerves sutured with four 10-0 nylon stay sutures and was independent of the laser settings used.

Despite the low bonding strength of LNW, it seems likely that the strength of the weld will increase in time in vivo studies (Menovsky et al., 1994; Richmond, 1986). The critical period for dehiscence is the first week postoperatively before the fibroblasts have formed a definite closure of the wound. Maragh et al. reported that LNW (90-95 mW, 200 um spot size, 0.2s exposure time) had a strength of 43.1 g at day 4 postoperatively. At day 8, LNW had a strength comparable to the epineurial suture control group (166.7 g) (Maragh et al., 1988). Thus, for 7 to 10 days postoperatively to allow adequate healing to occur before tension is allowed on the repaired nerve, additional complement such as temporary splint to limb could be one possible solution.

The substantial increase in bonding strength for some solders suggests that it is worthwhile to investigate the dehiscence rate and nerve regeneration of solder enhanced LNW in an in vivo study.

One possible source of complications with the use of solders in general could be the persistence of solder between the nerve ends. If this happens, the solder could block the sprouting axons and could induce scar tissue formation between the nerve ends. Therefore, it is preferable to weld the epineuria first and then to continue the procedure with solder. Also, premature absorption and disintegration of the solder is possible, which may result in early dehiscence of the union.

The authors demonstrated that (1) the operation time of LNW or LNW + solder is short compared to CMSR, (2) the strongest welds are associated with specific changes in tissue appearance, which can be used to determine the end point of the welding, (3) that LNW in combination with 20% albumin solution, dried albumin solution, and egg white as solders gives bonding strengths that may be sufficient for holding the nerve ends together in an in vivo study, and (4) that the strongest welds in LNW and LNW + solder were found at 100mW with pulses of 1.0 s and at 50 mW with pulses of 3.0s (Menovsky et al., 1994).

Menovsky et al. performed a study to evaluate CO2 laser–assisted nerve repair and compare it with nerve repair performed with fibrin glue or absorbable sutures (Menovsky & Beek, 2001). The sciatic nerves of rats were sharply transected and approximated using two 10-0 absorbable sutures and then fused by means of CO2 milliwatt laser welding (power 100 mW, exposure time 1 second per pulse, spot size 320um), with the addition of a protein solder (bovine albumin) to reinforce the repair site. The control groups consisted of rats in which the nerves were approximated with two 10-0 absorbable sutures and subsequently glued using a fibrin sealant (Tissucol), and rats in which the nerves were repaired using conventional microsurgical sutures (four to six 10-0 sutures in the perineurium or epineurium). Evaluation was performed 16 weeks postsurgery and included the toe-spreading test and light microscopy and morphometric assessment. The motor function of the nerves in all groups showed gradual improvement with time. At 16 weeks, the motor function was approximately 60% of the normal function, and there were no significant differences among the groups. On histological studies, all nerves revealed various degrees of axonal regeneration, with myelinated fibers in the distal nerve segments. There were slight differences in favor of the group treated with laser repair. There were no significant differences in the number, density, or diameter of the axons in the proximal or distal nerve segments among the three nerve repair groups, although there was a trend toward more and thicker myelinated axons in the distal segments of the laser-repaired nerves.

Soldering procedures rely on laser energy to produce fixation of the solder to the tissue (Menovsky et al., 1996; Menovsky et al., 1997). The protein behaves the same way in the welding process as does an inorganic solder used to join metal parts with the application of heat. In this way, a sleeve-type joint is formed by the solder, which is much stronger mechanically than a simple edge-to-edge joint. In addition to being mechanically stronger, laser soldering methods may be more technically forgiving than non soldering methods, because the solder may be able to bridge small gaps in coaptation that would otherwise produce a lead point for separation of the weld, and therefore it may reduce the need for stay sutures. Solder may also be beneficial in that it can protect the underlying tissue from the damaging thermal effects seen with non soldering methods.

It was found that CO2 laser–assisted nerve repair with soldering is at least equal to fibrin glue and suture repair in effectiveness in a rodent model of sciatic nerve repair (Menovsky & Beek, 2001).

The clinical application of laser assisted nerve repair (LANR) is limited by the high dehiscence rate and the inability of achieving consistent successful laser welds (Korff et al., 1992; Huang et al., 1992). So far, two sutures placed equidistantly are thought to be essential to facilitate the initial coaptation and subsequent handling of the nerve during LANR. In this case, an important issue is the choice of suture material which is used in combination with laser repair, and it is important to use sutures which cause the least tissue reaction. Menovsky et al. tried to find an optimal laser assisted technique which would result in the most favorable nerve healing, by choosing several suture materials and adding solder to the repair site. This study was designed to investigate regeneration of peripheral nerves repaired with a CO2 milliwatt laser in combination with three different suture materials and a bovine albumin protein solder (Menovsky & Beek, 2003).

In the laser repair group, the nerves ends were approximated with two stay sutures, including 10-0 nylon, 10-0 PGA, and 25-um-thick stainless steel. Thereafter, circumferential irradiation of the nerve with a CO2 milliwatt laser was performed at 100 mW, with pulses of 1.0 s and a spot size of 320 um. A total of 5-8 pulses were needed for each nerve, with a total irradiation time of 5-8 s. In the fourth subgroup of laser repair, the nerves were approximated with two 10-0 nylon stay sutures, and a protein solder consisting of bovine albumin powder dissolved in saline was applied to the repair site. The control group consisted of nerves repaired by conventional microsurgical suture repair (CMSR), using 4-6 10-0 nylon sutures.

Evaluation was performed at 1 and 6 weeks after surgery, and included qualitative and semiquantitative light microscopy. At sacrifice, no dehiscence was observed, and all nerves were in continuity. After 6 weeks, the nylon and stainless steel sutures were visibly detectable; the PGA sutures were not. LANR performed with a protein solder results in good early peripheral nerve regeneration, with an optimal alignment of nerve fibers and minimal connective tissue proliferation at the repair site. All three suture materials produced a foreign body reaction; the least severe was with polyglycolic acid sutures. CMSR resulted in more pronounced foreign-body granulomas at the repair site, with more connective-tissue proliferation and axonal misalignment. Furthermore, axonal regeneration in the distal nerve segment was better in the laser groups. Based on these results, CO2 laser-assisted nerve repair with soldering in combination with absorbable sutures has the potential of allowing healing to occur with the least foreign-body reaction at the repair site.

In this study, the authors concluded that LANR with the addition of a protein solder leads to optimal early histological results. Concerning the choice of suture material, PGA sutures can be used for LANR and have the potential of allowing healing to occur with the least foreign-body reaction at the repair site. In further experiments, the combination of PGA sutures and LANR using a solder may further improve the histological results (Menovsky & Beek, 2003).

4. Conclusion

Laser nerve welding of peripheral nerves may offer several advantages over conventional microsurgical suture repair, such as a less trauma to the tissue, less inflammatory reaction, a water tight seal of the epineurium and a faster surgical procedure (Menovsky et al., 1995).

Nevertheless, the clinical application of laser-assisted nerve repair has been limited by the risk of dehiscence in the postoperative period and the inability to achieve consistently successful laser welds (Korff et al., 1992; Maragh et al., 1988; Dubuisson & Kline, 1993).

In previous studies, the high risk of nerve dehiscence has been overcome by placing one or two stay sutures before laser welding (Fischer et al., 1985; Beggs et al., 1986) or, by the use of protein solders, which are melted onto the outer surface of the repair site, resulting in stronger welds (Menovsky et al., 1994). Besides the use of protein solders, extra tissues for improving the bonding strength have been used, which included perineurial and epineurial tissue as a supplement for the welding procedure (Kim & Kline, 1990), and LNW in combination with subcutaneous tissue wrapped around the nerve (Korff et al., 1992).

As reported in the rat sciatic nerve model, there was no significant difference in tensile strength of the laser repaired nerves and the suture repaired nerves at 8 days postoperatively (Maragh et al., 1988). The critical period is clearly the first week before host-connective tissue elements add the necessary stability. To make laser repair an attractive alternative to suture repair, the tensile strength of the laser repaired nerve must be improved further, especially during this period (Korff et al., 1992). In experimental studies, the bonding strength for LNW with additional aids, as stay suture, protein solder, subcutaneous tissue, was inferior to the tensile strength of the acute suture repair, but the substantial improvement over CO2 laser alone would encourage further refinement of this procedure.

However, some authors suggested that a minimal amount of collagen and other proteins of the epineurium provide sufficient welding strength in case of an adequate laser irradiation being applied without additional bonding materials or stay suture. This has been documented by the lack of dehiscences of the coapted nerves after 6 months of regeneration in their study (Happak et al., 2000). In some studies of facial nerve repair and facial-hypoglossal nerve anastomosis, no dehiscence in the laser welding site was seen. They did not perform supportive procedures to enhance the laser welding site (Hwang et al., 2005; Hwang et al., 2006). These results indicate that the cranial nerves, including the facial nerve and other nerves in the head and neck, are not subjected to significant stretching or tension as occurs with peripheral nerves in the extremities, such as the sciatic nerve (Huang et al., 1992). Thus, dehiscence is expected low in the head and neck area. And these studies showed that the regeneration of anastomosed nerve by laser nerve welding was affected more effectively especially in delayed repair. These results were thought to show the possibility of successful application of laser nerve welding in clinical settings, especially of head and neck area (Hwang et al., 2006).

Moreover, consistent achievement of successful laser nerve weld can be increased by careful selection of the laser parameters and technique and by the aforementioned use of additional aids.

Acknowledgments

This review is supported by a grant from INHA university.

5. References

Almquist, E.; Nachemson, A.; Auth, D.; Almquist, B. & Hall, S. (1984). Evaluation of the use of the argon laser in repairing rat and primates nerves. *J Hand Surg [Am]*, Vol.9, No.6, 792–799, 0363-5023

Angelov, D. & Gunkel, A. (1993). Recovery of original nerve supply after hypoglossal-facial anastomosis causes permanent motor hyperinnervation of the whisker-pad muscles in the rat. *J Comp Neurol*, Vol.338, No.2, 214-224, 0021-9967

Bailes, J.; Cozzens, J.; Hudson, A.; Kline, D.; Ciric, I.; Gianaris, P.; Bernstein, L. & Hunter, D. (1989). Laser-assisted nerve repair in primates. *J Neurosurg*, Vol.71, No.2, 266–272, 0022-3085

Bass, L.; Moazami, N.; Pocsidio, J.; Oz, M.; LoGerfo, P. & Treat, M. (1992). Changes in type I collagen following laser welding. *Lasers Surg Med*, Vol.12, No.5, 500–505, 0196-8092

Beggs, J.; Fischer, D. & Shetter, A. (1986). Comparative study of rat sciatic nerve microepinuerial anastomosis made with carbon dioxide lasers and suture techniques: Part 2. *Neurosurgery,* Vol.18, No.3, 266-269, 0148-396X

Benke, T.; Clark, J.; Wisoff, P.; Schneider, S.; Balasubramaniam, C.; Hawkins, H.; Laurent, J.; Perling, L. & Shehab ,A. (1989). Comparative study of suture and laser-assisted anastomosis in rat sciatic nerves. *Lasers Surg Med*, Vol. 9, No.6, 602–615, 0196-8092

Campion, E.; Bynum, D. & Powers, S. (1990). Repair of peripheral nerves with the argon laser. *J Bone Joint Surg* , Vol.72, No. 5, 715-723, 0021-9355

Chen, Y. & Hsu, C. (2000). Histologic rearrangement in the facial nerve and central nuclei following immediate and delayed hypoglossal facial nerve anastomosis. *Acta Otolaryngol* , Vol.120, No.4, 551-556, 0001-6489

Dew, D. (1986). Review and status on laser fusion. *Int Soc Opt Eng*, Vol. 712, No.2, 255-257, 0091-3286

Dubuisson, A. & Kline, D. (1993). Is laser repair effective for secondary repair of a focal lesion in continuity? *Microsurgery,* Vol.14, No.6, 398–403, 0738-1085

Eppley, B.; Kalenderian, E.; Winkelmann, T. & Delfino, J. (1989). Facial nerve graft repair: Suture versus laser assisted anastomosis. *Int J Oral Maxillofac Surg*, Vol.18, No.1, 50-54, 0901-5027

Fenner, J.; Martin, W.; Moseley, H. & Wheatley, D. (1992). Shear strength of tissue bonds as a function of bonding temperature: A proposed mechanism for laser assisted tissue welding. *Lasers Med Sci,* Vol.7, No.1, 39-43, 0268-8921

Fischer, D.; Beggs, J.; Kenshalo, D. & Shetter, A. (1985). Comparative study of microepineural anastomosis with the use of CO2 laser and suture technique in rat sciatic nerves. Part 1. *Neurosurgery*, Vol. 17, No.2, 300-307, 0148-396X

Happak, W.; Neumayer, C.; Holak, G.; Kuzbari, R.; Burggasser, G. & Gruber, H. (2000). Morphometric and Functional Results After CO2 Laser Welding of Nerve Coaptations. *Lasers Surg Med,* Vol.27, No.1, 66–72, 0196-8092

Huang, T.; Blanks, R.; Berns, M. & Crumley, R. (1992). Laser VS. suture nerve anastomosis. *OTOLARYNGOL HEAD NECK SURG*, Vol.107, No.1, 14-20, 0194-5998

Hwang, K.; Kim, S.; Kim, D. & Lee, C. (2005). Laser welding of rat's facial nerve. *J Craniofacial Surg,* Vol.16, No.6, 1102-1106, 1049-2275

Hwang, K.; Kim, S. & Kim, D. (2006). Facial-hypoglossal nerve anastomosis using laser nerve welding in the rats. *J Craniofacial Surg,* Vol.17, No.4, 687–691, 1049-2275

Hwang, K.; Kim, S. & Kim, D. (2008). Hypoglossal-Facial Nerve Anastomosis in the Rabbits Using Laser Welding. *Ann Plast Surg,* Vol. 61, No.4, 452–456, 0148-7043

Korff, M.; Bent, S.; Havig, M.; Schwaber, M.; Ossoff, R. & Zealear, D. (1992). An investigation of the potential for laser nerve welding. *Otolaryngol Head Neck Surg*, Vol. 106, No.4, 345-350, 0194-5998

Kim, D. & Kline, D. (1990). Peri-epineurial tissue to supplement laser welding of nerve. *Neurosurgery,* Vol.26, No.2, 211–216, 0148-396X

Lauto, A.; Trickett, R.; Malik, R.; Dawes, J. & Owen, E. (1997). Laser- activated solid protein bands for peripheral nerve repair: an vivo study. *Lasers Surg Med,* Vol.21, No.2, 134-141, 0196-8092

Maragh, H.; Hawn, R. & Gould, J. (1988). Is laser nerve repair comparable to microsuture coaptation? *J Reconstr Microsurg*, Vol. 4, No.3, 189–195, 0743-684X

Menovsky, T.; Beek, J. & van Gemert, M. (1994). CO2 laser nerve welding: optimal laser parameters and the use of solders in vitro. *Microsurgery,* Vol.15, No.1, 44-51, 0738-1085

Menovsky, T.; Beek, J. & Thomsen, S. (1995). Laser(-assisted) nerve repair. A review. *Neurosurg Rev,* Vol.18, No.4, 225–235, 0344-5607

Menovsky, T.; Beek, J. & van Gemert, M. (1996). Laser tissue welding of dura mater and peripheral nerves: a scanning electron microscopy study. *Lasers Surg Med*, Vol.19, No.2, 152–158, 0196-8092

Menovsky, T.; van der Bergh Weerman, M. & Beek, J. (1997). Transmission electron microscopy study of acute laser welds in dura mater and peripheral nerves. *Lasers Med Sci,* Vol.12, No.2, 131–136, 0268-8921

Menovsky, T. & de Vries, J.(1998). Use of fibrin glue to protect tissue during CO2 laser surgery. *Laryngoscope*, Vol.108, No.9, 1390–1393, 0023-852X

Menovsky, T. (2000). CO2 and Nd:YAG laser-assisted nerve repair: a study of bonding strength and thermal damage. *Acta Chir Plast* , Vol.42, No.1, 16-22, 0001-5423

Menovsky, T. & Beek, J. (2001). Laser, fibrin glue, or suture repair of peripheral nerves: a comparative functional, histological, and morphometric study in the rat sciatic nerve. *J Neurosurg*,Vol. 95, No.4, 694-699, 0022-3085

Menovsky, T. & Beek, J. (2003). Carbon dioxide laser-assisted nerve repair: effect of solder and suture material on nerve regeneration in rat sciatic nerve. *MICROSURGERY,* Vol.23, No.2, 109–116, 0738-1085

Neblett, C.; Morris, J. & Thomsen, S. (1986). Laser-assisted microsurgical anastomosis. *Neurosurgery,* Vol.19, No.6, 914-934, 0148-396X

Okada, M.; Shimizu, K.; Ikuta, H.; Horii, H. & Nakamura, K. (1987). An alternative method of vascular anastomosis by laser: experimental and clinical study. *Lasers Surg Med,* Vol.7, No.3, 240-248, 0196-8092

Ochi, M.; Osedo, M. & Ikuta, Y. (1995). Superior nerve anastomosis using a low-output CO2 laser on fibrin membrane. *Lasers Surg Med,* Vol.17, No.1, 64–73, 0196-8092

Poppas, D.; Rooke, C. & Schlossberg, S. (1992). Optimal parameters for CO2 laser reconstruction of urethral tissue using a protein solder. *J Urol,* Vol. 148, No.1, 220-224, 0022-5347

Richmond, I. (1986). The use of lasers in nerve repair, In: *Advanced Intraoperative Technologies in Neurosurgery,* Fasano VA (Ed.), 175-183, Springer Verlag, 0387818804, New York

Schober, R.; Ulrich, F.; Sander, T.; Du¨ rselen, H. & Hessel, S. (1986). Laser induced alteration of collagen substructure allows microsurgical tissue welding. *Science,* Vol.232, No.4756, 1421–1422, 0036-8075

Trickett, I.; Dawes, J.; Knowles, D.; Lanzetta, M. & Owen, E. (1997). In vitro laser nerve repair: protein solder strip irradiation or irradiation alone? *Int Surg,* Vol.82, No.1, 38-41, 0020-8868

Laser Welding

Edited by Xiaodong Na, Stone

ISBN 978-953-307-129-9
Hard cover, 240 pages
Publisher Sciyo

Published in print edition August, 2010

This book is entitled to laser welding processes. The objective is to introduce relatively established methodologies and techniques which have been studied, developed and applied either in industries or researches. State-of-the art developments aimed at improving or next generation technologies will be presented covering topics such as monitoring, modelling, control, and industrial application. This book is to provide effective solutions to various applications for field engineers and researchers who are interested in laser material processing.

Kun Hwang and SunGoo Kim (2010). Laser Nerve Welding, Laser Welding, Xiaodong Na, Stone (Ed.), ISBN: 978-953-307-129-9, InTech, Available from: http://www.intechopen.com/books/laser-welding/laser-nerve-welding-

INTECH
open science | open minds

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821