A novel strategy for repairing preganglionic cervical root avulsion in brachial plexus injury by sural nerve grafting

Clinical article

JAU-CHING WU, M.D.,1,2,5,6 WEN-CHENG HUANG, M.D.,1,2,5 MING-CHAO HUANG, M.D.,1,2,5 PH.D.2,5 YUN-AN TSAI, M.D.,2,3,5 YU-CHUN CHEN, M.D., M.SC.,2,4 YANG-HSIN SHIH, M.D.,1 AND HENRICH CHENG, M.D., PH.D.1,2,5,6

1Department of Neurosurgery, 2Neural Regeneration Laboratory, Neurological Institute, 3Department of Physical Medicine and Rehabilitation, and 4Department of Family Medicine, Taipei Veterans General Hospital, Taipei; 5School of Medicine and 4Institute of Pharmacology, National Yang-Ming University, Taipei, Taiwan

Object. In this study, the authors evaluated the efficacy of a new surgical strategy for reconnecting the injured brachial plexus with the spinal cord using fibrin glue containing acidic fibroblast growth factor as an adhesive and neurotrophic agent.

Methods. Eighteen patients with preganglionic brachial plexus injuries, each with varying degrees of upper limb dysfunction, underwent cervical laminectomy with or without sural nerve grafting. The treatment of each avulsed root varied according to the severity of the injury. Some patients also underwent a second-stage operation involving supraclavicular brachial plexus exploration for reconnection with the corresponding segment of cervical spinal cord at the trunk level. Muscle strength was graded both pre- and postoperatively with the British Medical Research Council scale, and the results were analyzed with the Friedman and Wilcoxon signed-rank tests.

Results. Muscle strength improvements were observed in 16 of the 18 patients after 24 months of follow-up. Significant improvements in mean muscle strength were observed in patients from all repair method groups at 12 and 24 months postoperatively (p < 0.05). Statistical significance was not reached in the groups with insufficient numbers of cases.

Conclusions. The authors’ new surgical strategy yielded clinical improvement in muscle strength after preganglionic brachial plexus injury, such that nerve regeneration may have taken place. Reconnection of the brachial plexus to the cervical spinal cord is possible. Functional motor recovery, observed through increases in Medical Research Council–rated muscle strength in the affected arm, is likewise possible. (DOI: 10.3171/2008.8.JNS08328)

Key Words • acidic fibroblast growth factor • preganglionic brachial plexus injury • sural nerve

PREGANGLIONIC BPI involves the very proximal portion of the brachial plexus at the junction of the central and peripheral nervous systems, which controls high-level neurological functions such as hand movements. The majority of brachial plexus palsies in adults are the result of traumatic injuries caused by high-energy forces such as motor vehicle accidents, whereas root avulsion accounts for most BPIs in adults. Brachial plexus injuries with root avulsions can have significant socioeconomic consequenc-

Abbreviations used in this paper: aFGF = acidic fibroblast growth factor; BPI = brachial plexus injury; EMG = electromyography; LIMOC = lateral interscalenic, multilevel, oblique corpectomy; MRC = Medical Research Council; NCS = nerve conduction studies; SCI = spinal cord injury.
repair of the brachial plexus carries considerable risks of complications involving the spinal cord. The complexity of the body’s anatomy at the cervical roots also obstructs surgical access. Neurosurgeons today are increasingly interested in addressing this problem, thereby making this study particularly timely.

Various recent animal studies have documented spinal nerve root implantation as a feasible repair method for cervical root avulsion. In 1995 Carlstedt et al. presented the case of a 25-year-old man with preganglionic BPI, who underwent treatment for direct reimplantation of his avulsed cervical roots. Electromyographic testing conducted 9 months after the surgery revealed voluntary activity in the proximal arm muscles. These findings were confirmed 1 year postoperatively, and at 3 years postoperatively the patient had recovered some voluntary muscle strength in the deltoids, biceps, and triceps muscles, with some co-contractions. This finding proved that regeneration did occur between the spinal cord and muscles, with some co-contractions. This finding proved that regeneration did occur between the spinal cord and muscles, with some co-contractions.

In 2003 Bertelli and Ghizoni achieved muscle reinnervation by grafting nerves directly into the spinal cord for connection with the distal nerves, in conjunction with extraplexal nerve transfer. This combination of intra- and extradural neurotization resulted in improvement in the proximal muscles of the arm.

In cases of root avulsion, performing repair procedures in which the spinal cord and the spinal nerve roots interconnect instead of bypassing the injured level may be of significant importance to functional recovery. In previous studies both in patients and animal models, we made modifications to the innovative surgical approaches described above but have retained the critical part: direct root implantation. Motor deficits caused by root avulsion in the brachial plexus can be ameliorated by this novel surgical strategy.

Methods

From 1999 to 2003, 18 patients in the Department of Neurosurgery at Taipei Veterans General Hospital who were undergoing treatment to reconnect the trunk portion of their brachial plexus with their spinal cord participated in this study. All patients underwent NCS and EMG for documentation of their preganglionic BPIs. Each avulsed root of the injured brachial plexus, from C-4 to T-1, was treated in 1 of 4 different ways based on the severity of the injury (summarized in Table 1).

The patients had an average age of 24.1 years (range 8–46 years) and all had sustained traumatic (not obstetric) brachial plexopathies. All but 3 patients were victims of motor vehicle accidents. Patients with combined cervical SCIs, moderate or severe head injuries, or other neuromuscular disorders affecting the limbs were excluded. All patients gave written informed consent for their participation in this study, and the study received approval from the Ethical Committee for Medical Research and the Department of Health at our institution.

Preoperative Diagnosis

All patients underwent NCS and EMG prior to surgery. If a patient joined the study immediately after injury, these examinations were intentionally delayed until 2 weeks after the injury. The delay enabled us to maximize the accuracy of NCS and EMG localization of the injury site. Patients with longstanding injuries were able to undergo NCS and EMG immediately.

For detailed evaluations of the injured plexus and the anatomical structures surrounding it, MR images were also obtained in all patients prior to any therapeutic intervention. A special MR imaging procedure combining coronal-oblique, 2-mm slicing with 3D fast imaging employing steady-state acquisition (FIESTA; GE) reconstructions was performed in each patient. The combination of electrophysiological and MR imaging studies allowed us to estimate the exact levels of preganglionic plexopathy before conducting any surgical procedures, thus allowing a more complete treatment plan. The final therapeutic procedures performed, however, depended on intraoperative findings at the roots.

The British MRC scale (0–5) was carefully used to grade the strength of the target muscles affected by the brachial plexopathies. We tested the following muscles in our patients: deltoid, biceps brachii, triceps brachii, extensor digitorum communis, flexor digitorum profundus, and abductor pollicis brevis. All muscle strength grading was performed and recorded by 2 experienced physical therapists under the supervision of a physical medicine and rehabilitation physician. All of the clinical and electrophysiological studies were conducted preoperatively and every 3 months postoperatively.

Surgical Techniques

The patients were placed prone on a standard operation table with head fixation in a Mayfield head-holder. Each patient underwent a total cervical laminectomy from C-4 to T-1 via a posterior neck midline approach. These laminectomies were extended by a partial facetectomy on the injured side of the brachial plexus to fully expose every root and provide adequate working space for the subsequent repair. A posterior midline opening of the dura mater at the exposed cervical segment was then made, enabling direct inspection of the roots. Injury severity in each root was classified according to the following categories: 1) partial or complete avulsion of the cervical roots, including ventral and dorsal roots, with remaining root stumps or rootlets; 2) complete avulsion of both ventral and dorsal roots without residual stumps; and 3) remainder and preserved connection to the spinal cord of the ventral and dorsal roots or rootlets despite atrophic changes or morphological abnormality of the ventral and dorsal roots or rootlets.

Microneurolysis was performed in every exposed root. The cervical roots with remaining root stumps or partially torn rootlets were directly reimplanted into the spinal cord via a small incision in the pia mater and the white matter at the ventral lateral aspect of the spinal cord, and then fixed with tissue glue containing aFGF and/or 10-0 nylon. Repair of the avulsed dorsal rootlets

J. C. Wu et al.
Direct repair of cervical root avulsion by sural nerve grafting

was similarly attempted by implanting them into the dorsal lateral sulcus.

To achieve tension-free anastomosis, it was necessary to perform sural nerve grafting in some patients. The graft served as a bridge between the spinal cord and the root stump, and preparations for sural nerve harvesting were made simultaneously with the laminectomies. Some specialists have argued that posterior laminectomies do not open adequate access to the ventral roots, but we made this access possible by dividing the denticulate ligaments that hold the spinal cord in position. The cornerstone of achieving optimal exposure of the ventrolateral side of the cervical spinal cord was the incision of the denticulate ligament, which released the spinal cord from its fixation in the dural sac. After releasing the spinal cord by cutting several denticulate ligaments at the appropriate site, the cord was mobilized slightly and pulled very gently so that ventrolateral implantation could be performed once microscopic illumination was adjusted.

Every effort was made to implant each avulsed ventral nerve root stump or graft ~ 2 mm into the ventral lateral side of the spinal cord. This implantation site was the nearest point to the motor neurons in the anterior horn with the smallest amount of white matter that could act as a barrier between the implanted cervical root or the nerve graft and the motor neurons.

The cervical roots in some patients were completely avulsed, and the stumps remained missing even after dissection around the surrounding muscles and the neural foramen was undertaken to locate them (Method 4, Table 1). In these cases we conducted a 2-stage operation. In the first stage, a sural nerve graft was harvested and one end was implanted into the ventral lateral aspect of the spinal cord (Fig. 1). The graft was fixed into the pia mater by 10-0 nylon sutures or fibrin glue alone. Acidic FGF was mixed with fibrin glue and then applied to the anastomotic site, forming a glue cast. The dura was then closed with sutures and sealed with fibrin glue. The other end of the sural nerve graft was protected with a small segment of Foley catheter and 1 or 2 hemoclips as radioopaque markers. The free end of the graft, protected by the Foley catheter, was then inserted carefully into the paraspinous muscles toward the anterior supraspinal region. This end with the Foley catheter was later dug out with or without fluoroscopic guidance. After the Foley catheter was removed, the nerve graft was anastomosed to its corresponding trunk via a small neurotomy (Fig. 2).

The second stage of the operation was typically performed several days after the first and with the patient positioned supine. The other end of the previously implanted sural nerve graft, which had been inserted into the paraspinous muscles under the protection of a segment of Foley catheter, was dissected away from the ventrolateral side of the neck. An epineuromyotomy was performed, followed by anastomosis to the corresponding trunk level of the brachial plexus using 10-0 nylon. Fibrin glue containing aFGF was then applied at the anastomotic site to form a glue cast.

The patients were asked to use an arm sling for at least 2 weeks postoperatively to avoid excessive traction on the shoulder region during daily activity.

<table>
<thead>
<tr>
<th>Repair Method</th>
<th>Nerve Root</th>
<th>Neurorhesis</th>
<th>Root Stump Reimplantation</th>
<th>Root Stump &amp; SNG Implantation</th>
<th>SNG Implantation &amp; Trunk Anastomosis (2 Stages)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-5</td>
<td>5</td>
<td>4</td>
<td>6</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>C-6</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>C-7</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>C-8</td>
<td>14</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>T-1</td>
<td>17</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

* SNG = sural nerve graft.

**Follow-Up Examination**

As with the preoperative procedures, the MRC scale was carefully used to assess the strength of the target muscles in the brachial plexus, including the deltoid, biceps brachii, triceps brachii, extensor digitorum communis, flexor digitorum profundus, and abductor pollicis brevis. All muscle strength grading was performed and recorded by the same people who performed the grading preoperatively. The patients were instructed to undergo clinical evaluation of muscle strength at least every 3 months in the first year and every 6 months thereafter.

**Statistical Analysis**

For each cervical root in the brachial plexus, the data were grouped according to repair method: neurorhesis, root stump reimplantation, root stump with sural nerve graft implantation, or sural nerve graft implantation with trunk anastomosis. Five key muscles were chosen as representative of the 5 cervical nerve root functions: deltoid for C-5, biceps brachii for C-6, triceps brachii for C-7, the extensor digitorum communis for C-8, and the abductor pollicis brevis for T-1. The mean MRC strength scores in these 5 key muscles were recorded preoperatively ($t_0$) and at 12 ($t_1$) and 24 months postoperatively ($t_2$). The scores were then processed with commercially available software (SPSS, Inc.) to generate descriptive statistics and contingency tables.

The Friedman test ($\alpha = 0.05$) was used to compare muscle strength at the 3 time points, whereas the Wilcoxon signed-rank test ($\alpha = 0.10$) was used to compare preoperative scores with those measured at 12 and 24 months postoperatively.

**Results**

The average time from injury to surgical repair was 178 days (range 28–601 days). The mean follow-up duration was 32.6 months (range 24–48 months; Table 2). Prior to surgical repair, 4 (22%) of the 18 patients had complete flail arm, 2 (11%) had little preservation of the deltoid muscle strength and near flail arm, and 12 (67%) had some preservation of lower trunk functioning (Table

J. Neurosurg. / Volume 110 / April 2009 777
3). The mean muscle strength scores in the key muscles assessed in the 18 patients increased significantly at 12 and 24 months postoperatively compared with the preoperative scores (Fig. 3 and Table 4). Improvements in MRC grades in all key muscles were observed at the end of this study (Table 2).

Within each repair method group, statistically significant increases were noted in mean MRC scores (Table 4). In the neurolysis group, the Wilcoxon signed-rank test demonstrated significant increases in mean muscle strength for muscles innervated by C-7, C-8, and T-1 roots at $t_1$ and $t_2$ compared with $t_0$. An overall comparison of $t_0$, $t_1$, and $t_2$ showed that there was also a significant increase in mean muscle strength. Strength improvement in muscles innervated by the C-5 and C-6 subgroups did not reach statistical significance because there were < 5 cases in these subgroups.

In the root stump reimplantation group, significant improvement in muscle strength at $t_1$ and $t_2$ compared with $t_0$ was observed at the C-6 nerve root. An overall comparison of $t_0$, $t_1$, and $t_2$ for the C-6 root also showed a significant increase in mean muscle strength. With respect to the C-5, C-7, and C-8 roots, there were < 5 cases of remarkable improvement. However, the mean muscle strength in these cases still followed an upward trend. The T-1 roots were not included in the root stump reimplantation repair group because none of them were found intraoperatively with their stump present.

In the group of patients who underwent root stump repair by sural nerve graft and implantation, the C-5 roots showed significant improvements at $t_1$ and $t_2$ compared with $t_0$. These comparisons also demonstrated significant improvement at C-5. However, the C-6 and C-7 roots were represented by < 5 cases and despite a clear trend toward increased muscle strength, statistical significance was not achieved. There were no C-8 or T-1 cases in this group.

In the patients who received sural nerve graft implantations and anterior trunk anastomosis in a 2-stage procedure, the C-5 and C-6 roots demonstrated significant improvement in mean muscle strength at $t_1$ and $t_2$ compared to $t_0$. These comparisons also demonstrated significant improvement at C-5. However, the C-7 root only demonstrated significant improvement at $t_2$. Overall comparisons within this group showed that significant increases occurred in muscle strength from $t_0$ to $t_1$ and $t_2$ in the C-5 and C-6 roots. Increases in strength in muscles innervated by the C-7 roots were obvious but did not reach statistical significance.
Direct repair of cervical root avulsion by sural nerve grafting

There were only 2 cases with C-8 and T-1 root involvement in this group, but there was a substantial increase in mean muscle strength as compared with t₀ (Table 4).

During the mean follow-up period of 32.6 months (range 24–48 months), no surgically related complication was observed in any patient. Although this relatively invasive repair procedure carried the risk of causing SCI, none of the patients presented with any deficits (not even transient) in their lower extremity motor functions after surgery. There no wound infections or CSF leaks either.

To preclude the development of a cervical kyphotic deformity in patients after wide multilevel laminectomies, internal fixation lateral mass screws were inserted in the last 4 patients in the study. No kyphotic deformity was observed in any patient during the follow-up period. However, the possibility of kyphosis remains an issue for future research, and a longer follow-up period would allow for more definite assessments.

**Discussion**

Comparison of Surgical Exposures and Site of Root Implantation With Other Reports

In 1995, Carlstedt et al.⁵ was the first to experiment with the reimplantation of cervical roots in human patients. In 2000, he and his colleagues⁴ published the largest clinical series of patients treated with reimplantation techniques. Although the results were not generally applicable clinically, they were promising, and this pioneering research paved the way for further investigation. We attempted the repair procedures in the present study according to the descriptions by Carlstedt et al., but found several disadvantages to their method, such as suboptimal exposure of multiple-level injuries of the cervical roots of the brachial plexus, particularly at the lower portion of the brachial plexus. The approach of Carlstedt and colleagues also led to excessive venous bleeding because of the quantity of venous plexus at this approach site. Having determined these drawbacks, we developed a new surgical approach that would allow us to avoid the venous plexus. We chose to expose the cervical roots through a laminectomy at the posterior midline, followed by an incision into the dura mater. Once the dura of the cervical spinal cord was incised and sutured aside, the dorsal roots were clearly accessible. However, the critical root was the avulsed ventral root. Therefore, the principle benefit of performing a wide laminectomy lay in gaining easy access to all affected cervical roots in the brachial plexus.

Axons will not regenerate if they are surrounded by too much myelin.⁷,38–41 We considered the ventrolateral sulcus to be the ideal intraspinal implantation site for repairing a ventral root avulsion because it was the closest to the gray matter and the path of the avulsed axons. The ventromedial region of the anterior horn of the gray matter is the point at which the greatest number of axiosensory fibers terminate. This approach provides an opportunity for functional recovery, and several studies have confirmed that motor function can be restored in cases with ventral root avulsion, even when there is a significant delay in repair.⁵,⁷,²₀,²³,²⁷,²⁸,²⁹,³⁷,³⁸,⁴₁,⁴₂ Even though this was the first report of using an avulsed ventral root for reimplantation, the outcomes of this study suggest that this approach is safe and effective. Furthermore, the outcomes of this study are consistent with previous studies that have reported the successful repair of a ventral root avulsion, demonstrating that the prognosis in cases of ventral root avulsion is significantly better than that of ventral root avulsion.

**TABLE 2: Improvement in MRC grades at the final evaluation compared with preoperative measures**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Deltoid</th>
<th>Biceps Brachii</th>
<th>Triceps Brachii</th>
<th>Extensor Digits communis</th>
<th>Abductor Pollicis Brevis</th>
<th>Flexor Digits Profundus</th>
<th>Length of FU (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+2</td>
<td>+4</td>
<td>+3</td>
<td>+3</td>
<td>+1</td>
<td>+1</td>
<td>42</td>
</tr>
<tr>
<td>2</td>
<td>+4</td>
<td>+3</td>
<td>+1</td>
<td>+4</td>
<td>+1</td>
<td>+1</td>
<td>42</td>
</tr>
<tr>
<td>3</td>
<td>+4</td>
<td>+1</td>
<td>0</td>
<td>0</td>
<td>+1</td>
<td>+1</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>+2</td>
<td>0</td>
<td>+1</td>
<td>+1</td>
<td>+3</td>
<td>+2</td>
<td>48</td>
</tr>
<tr>
<td>5</td>
<td>+1</td>
<td>+2</td>
<td>+1</td>
<td>+1</td>
<td>+1</td>
<td>+1</td>
<td>30</td>
</tr>
<tr>
<td>6</td>
<td>+2</td>
<td>+2</td>
<td>+1</td>
<td>+1</td>
<td>+1</td>
<td>+1</td>
<td>30</td>
</tr>
<tr>
<td>7</td>
<td>+2</td>
<td>+4</td>
<td>0</td>
<td>+2</td>
<td>0</td>
<td>+1</td>
<td>36</td>
</tr>
<tr>
<td>8</td>
<td>+3</td>
<td>+3</td>
<td>+1</td>
<td>+3</td>
<td>+1</td>
<td>0</td>
<td>36</td>
</tr>
<tr>
<td>9</td>
<td>+2</td>
<td>+2</td>
<td>+1</td>
<td>+2</td>
<td>0</td>
<td>0</td>
<td>36</td>
</tr>
<tr>
<td>10</td>
<td>+5</td>
<td>+3</td>
<td>+5</td>
<td>+5</td>
<td>+2</td>
<td>+2</td>
<td>42</td>
</tr>
<tr>
<td>11</td>
<td>+3</td>
<td>+3</td>
<td>+1</td>
<td>+2</td>
<td>+1</td>
<td>+1</td>
<td>27</td>
</tr>
<tr>
<td>12</td>
<td>+3</td>
<td>+2</td>
<td>+2</td>
<td>+2</td>
<td>+1</td>
<td>0</td>
<td>36</td>
</tr>
<tr>
<td>13</td>
<td>+4</td>
<td>+2</td>
<td>+3</td>
<td>+3</td>
<td>+1</td>
<td>+1</td>
<td>38</td>
</tr>
<tr>
<td>14</td>
<td>+2</td>
<td>+3</td>
<td>+1</td>
<td>+1</td>
<td>0</td>
<td>0</td>
<td>36</td>
</tr>
<tr>
<td>15</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>24</td>
</tr>
<tr>
<td>16</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>24</td>
</tr>
<tr>
<td>17</td>
<td>+1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>+2</td>
<td>24</td>
</tr>
<tr>
<td>18</td>
<td>+2</td>
<td>0</td>
<td>+1</td>
<td>0</td>
<td>+1</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>average</td>
<td>+2.33</td>
<td>+1.89</td>
<td>+1.28</td>
<td>+1.72</td>
<td>+0.89</td>
<td>+0.83</td>
<td>32.61</td>
</tr>
</tbody>
</table>

* Final muscle strength grades minus initial. Abbreviation: FU = follow-up.
TABLE 3: Summary of patient profile and muscle strength data

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Time to Op (days)</th>
<th>Deltoid (C-5)</th>
<th>Biceps Brachii (C-6)</th>
<th>Triceps Brachii (C-7)</th>
<th>Extensor Digitorum Communis (C-8)</th>
<th>Abductor Pollicis Brevis (T-1)</th>
<th>Flexor Digitorum Profundus (C-8)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>t₀  t₁  t₂  Imp</td>
<td>t₀  t₁  t₂  Imp</td>
<td>t₀  t₁  t₂  Imp</td>
<td>t₀  t₁  t₂  Imp</td>
<td>t₀  t₁  t₂  Imp</td>
<td>t₀  t₁  t₂  Imp</td>
</tr>
<tr>
<td>1</td>
<td>8</td>
<td>43</td>
<td>B 2 4 4 yes</td>
<td>D 0 2 3 yes</td>
<td>D 0 0 0</td>
<td>A 0 2 3 yes</td>
<td>A 0 1 1 yes</td>
<td>A 0 1 1 yes</td>
</tr>
<tr>
<td>2</td>
<td>27</td>
<td>28</td>
<td>D 0 4 4 yes</td>
<td>D 0 2 3 yes</td>
<td>B 4 5 5 yes</td>
<td>A 0 4 4 yes</td>
<td>A 4 5 5 yes</td>
<td>A 4 5 5 yes</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>69</td>
<td>B 0 4 4 yes</td>
<td>B 2 3 3 yes</td>
<td>B 5 5 5</td>
<td>A 5 5 5</td>
<td>A 4 5 5 yes</td>
<td>A 4 4 5 yes</td>
</tr>
<tr>
<td>4</td>
<td>23</td>
<td>31</td>
<td>D 0 2 2 yes</td>
<td>B 0 0 0</td>
<td>B 0 1 1 yes</td>
<td>A 0 1 1 yes</td>
<td>A 2 4 4 yes</td>
<td>A 2 2 4 yes</td>
</tr>
<tr>
<td>5</td>
<td>38</td>
<td>450</td>
<td>C 3 4 4 yes</td>
<td>C 1 3 3 yes</td>
<td>A 4 5 5 yes</td>
<td>A 4 5 5 yes</td>
<td>A 4 5 5 yes</td>
<td>A 4 5 5 yes</td>
</tr>
<tr>
<td>6</td>
<td>23</td>
<td>345</td>
<td>C 2 4 4 yes</td>
<td>B 0 2 2 yes</td>
<td>A 3 5 5 yes</td>
<td>A 4 5 5 yes</td>
<td>A 4 5 5 yes</td>
<td>A 4 5 5 yes</td>
</tr>
<tr>
<td>7</td>
<td>22</td>
<td>143</td>
<td>A 0 1 2 yes</td>
<td>D 0 3 4 yes</td>
<td>D 0 0 0</td>
<td>D 0 1 2 yes</td>
<td>A 0 0 0</td>
<td>D 0 1 1 yes</td>
</tr>
<tr>
<td>8</td>
<td>21</td>
<td>601</td>
<td>D 0 3 3 yes</td>
<td>D 0 3 3 yes</td>
<td>A 2 3 3 yes</td>
<td>A 0 3 3 yes</td>
<td>A 4 5 5 yes</td>
<td>A 4 4 4</td>
</tr>
<tr>
<td>9</td>
<td>18</td>
<td>160</td>
<td>D 0 2 2 yes</td>
<td>D 0 1 2 yes</td>
<td>B 0 0 1 yes</td>
<td>B 0 0 2 yes</td>
<td>A 0 0 0</td>
<td>B 0 0 0</td>
</tr>
<tr>
<td>10</td>
<td>24</td>
<td>38</td>
<td>B 0 4 4 yes</td>
<td>B 0 2 2 yes</td>
<td>A 0 4 4 yes</td>
<td>A 0 3 4 yes</td>
<td>A 3 5 5 yes</td>
<td>A 3 4 4</td>
</tr>
<tr>
<td>11</td>
<td>20</td>
<td>223</td>
<td>A 1 4 4 yes</td>
<td>B 0 1 3 yes</td>
<td>C 0 1 1 yes</td>
<td>D 0 2 2 yes</td>
<td>D 0 1 1 yes</td>
<td>D 0 1 1</td>
</tr>
<tr>
<td>12</td>
<td>21</td>
<td>210</td>
<td>C 0 3 3 yes</td>
<td>D 0 2 2 yes</td>
<td>D 1 3 3 yes</td>
<td>A 0 2 2 yes</td>
<td>A 2 4 4 yes</td>
<td>A 4 4 4</td>
</tr>
<tr>
<td>13</td>
<td>19</td>
<td>330</td>
<td>D 0 3 4 yes</td>
<td>D 0 0 0</td>
<td>D 0 0 3 yes</td>
<td>B 0 0 3 yes</td>
<td>A 3 3 4 yes</td>
<td>B 3 4 4</td>
</tr>
<tr>
<td>14</td>
<td>21</td>
<td>36</td>
<td>C 0 2 2 yes</td>
<td>A 0 3 3 yes</td>
<td>A 4 5 5 yes</td>
<td>A 4 5 5 yes</td>
<td>A 4 5 5 yes</td>
<td>A 5 5 5</td>
</tr>
<tr>
<td>15</td>
<td>40</td>
<td>171</td>
<td>B 0 0 0</td>
<td>D 0 0 0</td>
<td>D 0 0 0</td>
<td>A 0 0 0</td>
<td>A 1 1 1</td>
<td>A 3 3 3</td>
</tr>
<tr>
<td>16</td>
<td>22</td>
<td>150</td>
<td>C 0 0 0</td>
<td>D 0 0 0</td>
<td>C 0 0 0</td>
<td>A 0 0 0</td>
<td>A 0 0 0</td>
<td>A 0 0 0</td>
</tr>
<tr>
<td>17</td>
<td>20</td>
<td>33</td>
<td>C 0 0 1 yes</td>
<td>C 0 0 0</td>
<td>C 0 0 0</td>
<td>A 0 0 0</td>
<td>A 0 0 0</td>
<td>A 0 0 2</td>
</tr>
<tr>
<td>18</td>
<td>46</td>
<td>146</td>
<td>A 1 3 3 yes</td>
<td>D 0 0 0</td>
<td>D 4 5 5 yes</td>
<td>A 3 4 4 yes</td>
<td>A 5 5 5</td>
<td>A 4 5 5</td>
</tr>
</tbody>
</table>

* MRC muscle strength recorded at each time point are listed and an increase in the score is considered an improvement. Abbreviations: A = neurolysis; B = root stump reimplantation; C = root stump repair w/ sural nerve graft; D = 2-stage repair (sural nerve graft & trunk anastomosis); Imp = improvement; Op = operation; t₀ = preoperative examination; t₁ = 12 months postoperative examination; t₂ = 24 months postoperative examination.
Direct repair of cervical root avulsion by sural nerve grafting

Fig. 3. Graph of the mean muscle strengths of the 6 key muscles (deltoid, biceps, triceps, extensor digitorum communis, abductor pollicis brevis, and flexor digitorum profundus) in the 18 patients, recorded preoperatively and at 12 and 24 months postoperatively.

The 2 major benefits of our approach are that it offers full exposure of every cervical root in the brachial plexus and reconstruction of the nervous pathways similar to the patient's original state.

Surgical exploration and inspection of intradural segments of the brachial plexus may uncover different injuries than those shown on electrophysiological or neuroimaging assessments in the diagnosis of BPIs. This is not to say that surgical exploration and inspection should replace these processes; in fact, it is difficult to identify and access incomplete lesions intraoperatively without the aid of electrophysiological testing. Hems and colleagues found that isolated intradural damage is not immediately obvious or detectible on exploration. As such, EMG, MR imaging, and surgical exploration all have a role in the assessment of BPIs.

Our technique allows immediate discovery and repair of the completely injured root stump without hindering or affecting future repair procedures (such as would be true of nerve transfer, neurorization, or tendon transfer) because no rerouting of the nervous pathways takes place. Full inspection of the brachial plexus at the cervical root level after our surgical procedures also provides an opportunity to understand more about the mechanism of injury. In performing this procedure, we discovered that complete root avulsion injuries, whether or not the root stumps were found, were more common in the upper plexus. This finding may relate to the mechanism of injury, although further investigation is needed to verify this.

Because our technique involves multilevel cervical laminectomy combined with spinal cord manipulation, it definitely carries the risk of damaging previously intact motor functions, such as those of the lower limbs and the unaffacted arm. The key to minimizing such risks is to perform the delicate microsurgical techniques after the dural incision is made, and in resecting the dentate ligaments prior to mobilizing the spinal cord for repair. We also believe that watertight closure of the dural sac with or without graft duraplasty is helpful in decreasing the amount of CSF leakage, thus minimizing the risk of wound infection. For the most part, applying fibrin glue to the suture site of the dural closure is an effective sealant.

There is also the risk of future kyphotic deformity of the cervical spine because our patients were relatively young, with an accumulated risk that in the long-term would be high after undergoing a multilevel laminectomy and unilateral partial facetectomy. Although we did not observe such problems during the follow-up period, we began placing instrumentation in some of the patients later in the study to reduce the risk of kyphotic deformity.

Use of aFGF

Acidic FGF was first mentioned in 1990 as a possible growth factor in mammalian brains and spinal cords and was later shown to contribute to repair after SCI in mammals. Authors of some studies of axonal regeneration after SCI have incorporated aFGF research, using a slice culture model system. In this system, aFGF has been found to rescue neurons and promote axonal growth. In studies of SCI repair, some authors have reported promising results with the use of aFGF in BPI models, functional recovery was achieved in rats after repair of the transected left sixth and seventh cervical roots when aFGF was used. Peripheral nerve grafting and aFGF induced the regeneration of transected dorsal roots in adult mammals.
TABLE 4: Summary of results*

<table>
<thead>
<tr>
<th>Nerve Root</th>
<th>Neurolysis Mean Muscle Strength</th>
<th>Root Stump Reimplantation Mean Muscle Strength</th>
<th>Root Stump w/ SNG Implantation Mean Muscle Strength</th>
<th>SNG Implantation &amp; Trunk Anastomosis (2 stages) Mean Muscle Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t₀</td>
<td>t₁</td>
<td>t₂</td>
<td>p Value</td>
</tr>
<tr>
<td>C-5</td>
<td>0.7</td>
<td>2.7</td>
<td>3.0</td>
<td>NS</td>
</tr>
<tr>
<td>C-6</td>
<td>0.0</td>
<td>3.0</td>
<td>3.0</td>
<td>NS</td>
</tr>
<tr>
<td>C-7</td>
<td>2.6</td>
<td>4.4++</td>
<td>4.4++</td>
<td>0.012</td>
</tr>
<tr>
<td>C-8†</td>
<td>1.4</td>
<td>2.8+++</td>
<td>2.9+++</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T-1‡</td>
<td>2.4</td>
<td>3.1+++</td>
<td>3.2+++</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* The Friedman test (α = 0.05) was used to compare muscle strength at the 3 time points and the Wilcoxon signed-rank test (α = 0.10) was used to compare preoperative scores with those measured 12 and 24 months postoperatively. Significance levels for the Wilcoxon signed-rank test are expressed as: + < 0.10; ++ < 0.05; and +++ < 0.01. The C-8 and T-1 roots underwent considerably less repair than C-5, C-6, and C-7 roots. Abbreviations: NA = not applicable; NS = no significance (although improvement was observed, the sample size was < 5 patients); t₀ = preoperative examination; t₁ = 12-month postoperative examination; t₂ = 24-month postoperative examination.
† Root stump with sural nerve graft implantation was not performed on any C-8 roots.
‡ Root stump reimplantation and root stump with sural nerve graft implantation was not performed on any T-1 roots.

Influencing Regeneration

Individual Differences in Improvement and Factors Influencing Regeneration

Many variables must be considered in evaluating the effectiveness of a repair strategy for BPI. Some of these factors are predetermined, including the severity of the injury at various parts of the sophisticated nervous network and the regenerative ability of the individual patient, which, among other factors, might be age related. Other variables are controllable, such as the time between injury and repair, the quality of the surgical procedure, the comprehensiveness of rehabilitation, and the duration of follow-up. Given that it can be difficult to control all of these variables in a clinical setting, it is difficult to evaluate the results.

In the present study, we observed great differences in the degree of improvement between individual patients. The greatest improvement observed was in a young man (Case 10) who presented with no muscle strength in his deltoid, biceps, triceps, or extensor digitorum communis; his C-5 and C-6 roots were completely avulsed. We located the stumps and reimplanted them into his spinal cord. He had Grade 3 muscle strength in his biceps and Grade 5 in the other 5 key muscles at 30 months postoperatively. Three photographs taken of him at follow-up 42 months after the operation are shown in Fig. 4. The ratio of the compound motor neuron action potential of the muscles of his injured arm to his normal arm was (× 100 to yield a percentage): deltoid 18.6%, biceps 13.8%, and triceps 31.3%. These measurements were made at the same time the photographs were taken. In contrast, a patient with complete flail arm after injury showed no improvement in the key muscles 24 months postsurgery (Case 16). These were the most extreme examples among our patients.

In general our patients achieved modest improvements; the mean muscle strength scores in our 18 patients at 24 months postoperatively was 2.7 (compared with 1.3 preoperatively, p < 0.001). Further investigations are underway to analyze the significance of each factor that produced such varying results. Although our results are irregular and difficult to interpret definitively, overall we present an important, pioneering study with positive results.

It is well documented in the literature that surgical timing plays a key role in neuronal regeneration. Authors of previous studies both in animal models and in patients have demonstrated the importance of operating as early as possible after the injury. However, most of our
patients did not undergo surgery until > 3 months postinjury. In 11 patients, the repair took place > 140 days later. Despite this considerable loss of time, some improvements were noted in those who underwent repair surgery. For results to reflect the efficacy of this novel surgical procedure more accurately, operations in future research must be performed much earlier. As it is, not only are successful surgical outcomes less likely after a longer interval, they may present an inadequate picture of what this surgical procedure is really capable of achieving.

The regeneration of denervated muscles may be partially attributable to plasticity within the spinal cord\textsuperscript{18} or to the spontaneous recovery of partially torn roots, including roots documented on EMG as having been injured, but nevertheless visualized as morphologically intact intraoperatively.\textsuperscript{14} It is possible to document the regeneration of motor neurons using EMG. Discrepancies have been found, however, between clinical muscle strength recovery measurements and improvements on electrophysiological examinations. The MRC grading system sometimes shows less improvement than the corresponding EMG studies. We believe that this is because different functional types of neurons are attracted to the regrowth of axons on the implanted root, as judged by their position in the ventral horn. Thus, neurons that normally supply antagonistic muscles, such as the triceps muscle, contribute instead to the innervation of the biceps muscle. Functionally, this deficiency in directional specificity correlates both to spasticity and cocontractions among agonistic and antagonistic muscles.\textsuperscript{18} This deficiency may also contribute to the well-known difficulty in restoring patient dexterity.\textsuperscript{22}

Even taking these complicating factors into account, we have nevertheless demonstrated evidence of distal muscle group recovery, although the improvement was not as marked as in the proximal muscles. The unevenness of muscle regeneration between the dorsal and ventral roots may also be a reason that MRC grades showed less improvement in muscle strength than was seen on EMG studies. Therefore, given the evidence of muscle regeneration in our research, and given the factors that impede muscle regeneration and complicate surgical procedures, a longer follow-up period is mandatory in our patients to clarify whether muscle strength will continue to improve over a longer period of rehabilitation.

Some of the improvements in shoulder function in our patients may have resulted from compensation by the pectoralis muscles or other back muscles, or even from scapular rotation. Continuous rehabilitation will make these muscle groups even stronger. Rehabilitation has an important role to play as a factor in clinical performance and muscle regeneration.

The results of the present study are positive. Although they do not yet justify complete replacement of the current repair strategies, we have nevertheless delivered positive results that provide the basis for potential future repair techniques or other neurobiological strategies. More research should be undertaken with a focus on the underlying reasons for variations in muscle strength improvement in patients who undergo treatment with this technique. In general, more clinical studies are needed with regard to intradural repair.\textsuperscript{1}

\textbf{Conclusions}

In patients with preganglionic BPIs, surgical exposure of the avulsed cervical roots followed by direct re-implantation of the roots into the spinal cord or indirect implantation by inserting an autologous nerve graft via the ventral lateral aspect of the spinal cord at the injury site may be a viable alternative method to current repair.
strategies in the field of brachial plexus reconstruction. We have documented nerve regeneration in the present study through assessment of functional recovery and improvement in electrophysiological evaluations. Because our technique is still in the experimental stage, further investigation and validation are necessary to achieve general clinical acceptance and establish this procedure as a primary or as adjuvant part of BPI repair.

Disclosure
This work was supported by the Neural Regeneration Investigation Program of Taipei Veterans General Hospital (Grant # VGH 94-372, V95S6-001). This study and its authors have no relationship with, or have received any kind of financial support from, any commercial party. The authors also did not receive any commercial benefit ensuing from the results.

References
Direct repair of cervical root avulsion by sural nerve grafting

43. Tsai EC, Dalton PD, Shoichet MS, Tator CH: Matrix inclusion within synthetic hydrogel guidance channels improves specific supraspinal and local axonal regeneration after complete spinal cord transection. Biomaterials 27:519–533, 2006

Manuscript submitted April 18, 2008.
Accepted August 25, 2008.
Please include this information when citing this paper: published online January 2, 2009; DOI: 10.3171/2008.8.JNS08328.
This paper was presented at the Annual Meeting of the American Association of Neurological Surgeons, April 2007 in Washington, D.C.
Address correspondence to: Henrich Cheng, M.D., Ph.D., Neural Regeneration Laboratory, Department of Neurosurgery, Neurological Institute, Taipei Veterans General Hospital, Room 509, 17F, No. 201, Shih-Pai Road, Sec. 2 Peitou, Taipei 11217, Taiwan. email: hc_cheng@vghtpe.gov.tw.