Contralateral C7 Transfer to Axillary and Median Nerves in Rats with Total Brachial Plexus Avulsion

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Research article

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Abstract

Background: Contralateral cervical 7 nerve (cC7) was used to repair two recipient nerves simultaneously for patients with total brachial plexus avulsion (TBPA). Objective: To evaluate the effect of cC7 transfer to axillary and median nerves in rats with TBPA.

Methods: Eighty S-D rats were divided into 4 groups averagely. Group A: cC7 → median nerve, Group B: cC7 → axillary nerve, Group C: cC7 → median and axillary nerves, Group D: TBPA without repair. The evaluation tools included behavioral test, electromyogram (EMG), cross-sectional area of muscle fiber, nerve fiber count and gene expression.

Results: The positive rates of EMG were 90% and 70% in Flexor Carpi Radialis (FCR) in Group A and C, while 70% and 60% in deltoid (DEL) In Group B and C. The difference of effective rates in grip or shoulder abduction between groups was not significant. The mean cross-sectional area of FCR in Group A or C was significantly larger than that in Group D. Either the number of median or axillary nerve fibers in Group A, B or C was statistically more than that in Group D. No matter for FCR or DEL, there were no significant differences of the ratios of relative expression of MAFBOX and MURF1 among these groups.

Conclusion: Compared with cC7 transfer to median nerve, cC7 transfer to both median and axillary nerves did not affect median nerve recovery and the deltoid muscle also could be restored. The recovery proportion of axillary nerve was less than that of median nerve.

Background

In recent years, nerve transfer was the main treatment of total brachial plexus avulsion (TBPA) and the functional improvements were mainly embodied in shoulder abduction and elbow flexion. However, the repairs of shoulder external rotation and hand function were not satisfactory.[17,22] According to the anatomy, the muscle fibers in the posterior part of deltoid muscle (DEL) innervated by the axillary nerve had the function of shoulder external rotation. Therefore, the repair of axillary nerve could improve the shoulder external rotation theoretically.

Contralateral cervical 7 nerve (cC7) transfer was usually used to repair the median nerve in the affected side, which was effective in restoring partial sensation of hand ,wrist and finger flexion without permanent sensory and motor damage to the healthy upper limb.[3,9] Because the number of myelinated nerve fibers of cC7 root was much more than that of any recipient nerve including radial nerve, median nerve or musculocutaneous nerve, some scholars tried to repair two recipient nerves simultaneously by cC7 transfer and found that both of the two recipient nerves had recoveries.[7,24,25,27] However, there was no report on the cC7 transfer to median and axillary nerves simultaneously. Therefore, we carried out an animal experimental research to study the effect of cC7 transfer to both median and axillary nerves in order to lay the animal experimental foundation for the further clinical application.

Methods

Animals and preparation before surgery

Animal handling and procedures in this study were in agreement with the guidelines of the Animal Care and Use Committee of Fudan University. Male Sprague-Dawley(S-D)rats (n = 80; weight, 200-250 g; age, 8 weeks) were kept in an environment with temperature of 20˚C and humidity of 50%. All the rats were supplied by the company (Shanghai Slake Laboratory Animals Company, Shanghai, China). The rats were maintained on a 12/12-h light/dark cycle and allowed free access to food and water. The animal use protocol was reviewed and approved by the Animal Ethics Committee Review Board of Fudan University.

Eighty rats were divided into 4 groups averagely.

Group A: Rats with TBPA and cC7 transfer to median nerve (cC7 — median nerve)

Group B: Rats with TBPA and cC7 transfer to axillary nerve (cC7 — axillary nerve)

Group C: Rats with TBPA and cC7 transfer to both median and axillary nerves (cC7 — median and axillary nerves)

Group D: Rats with TBPA without repair

The right side of each rat was selected as the injure side in all groups. Intraperitoneal injection of 1% pentobarbital sodium (1 ml/100 g body weight; Shanghai Reagent Company, Shanghai, China) was used before operation. After anesthesia, the rats were fixed and disinfected in supine position.

Surgical techniques

TBPA Rat model

A right supraclavicular incision was made. Part of sternocleidomastoid and anterior scalene muscles were cut off. C5 and C6 nerve roots were identified. Then the clavicle was pulled down to explore C7, C8 and T1. After the right brachial plexus was completely exposed, the C5-T1 nerve roots were pulled out to avulsion at foramen levels in the Group A, B, C and D.

The first stage of cC7 transfer

CC7 nerve transfers were performed after TBPA in Group A, B, and C. A longitudinal incision was made along the ulnar side of the right upper limb. The ulnar nerve was exposed from the wrist to the armpit. Then the ulnar nerve was cut off at wrist and separated from the wrist to the axilla. The superior ulnar collateral artery was reserved. A transverse incision was made on the left supraclavicular fossa. The cervical 7 nerve root was explored and separated from the intervertebral foramen to anterior and posterior divisions. 2% lidocaine (Shanghai Reagent Company, Shanghai, China) was used for nerve block before

the whole cC7 root was cut. The distal end of the right ulnar nerve was moved to the left supraclavicular fossa through the subcutaneous tunnel and sutured to the left whole cervical 7 nerve root.

The second stage of cC7 transfer

Eight weeks after the first stage of cC7 transfer, the rats in Group A, B and C underwent the second stage of cC7 transfer. The procedure of the second stage operation in each group was as follows.

Group A (cC7 — median nerve): A right longitudinal incision was made on the inner side of the upper arm. The ulnar and median nerves were identified at the turning point of ulnar nerve. (Fig. 1) Both of them were cut off. The proximal end of ulnar nerve was sutured to the distal end of median nerve without tension.

Group B (cC7 — axillary nerve): A Z shape incision was made in the right axilla. Axillary nerve was found on the anterior edge of the latissimus dorsi along the brachial plexus and ulnar nerve was exposed at the turning point. The axillary nerve was cut off at the level of the quadrilateral foramen and the ulnar nerve was cut in the armpit. (Fig. 2) Then the proximal end of ulnar nerve was sutured to the distal end of the whole axillary nerve without tension.

Group C (cC7 — median and axillary nerves): The right axillary Z shape incision was made to expose the ulnar nerve, median nerve and axillary nerve respectively. The axillary nerve was cut off at the level of the quadrilateral foramen. The ulnar and median nerves were isolated to enough length for suture in the armpit. Then they were cut off. The proximal end of ulnar nerve was sutured to the distal ends of the axillary and median nerves without tension at the same time. (Fig. 3)

In the experiment, the nerves were sutured with 11 − 0 nylon (Ethicon, Johnson & Johnson, New Brunswick, New Jersey) under 10 times microscope.

Evaluation methods

All the examinations and evaluations were carried out 12 weeks after the second stage of cC7 transfer. First, the behavioral tests were carried out. Then Electromyogram (EMG) examinations (Neuromatic 2000M electrophysiological apparatus, Dantec, Les Ulis, France) were made in the rats, which were anesthetized by intraperitoneal injection of 1% pentobarbital sodium. After EMG test, the median and axillary nerves were biopsied for nerve fibers count. Flexor Carpi Radialis (FCR) and deltoid (DEL) were biopsied for calculating the mean cross-sectional areas of muscle fibers. Gene expressions related to muscle atrophy were assayed by RT-qPCR (Agilent Technologies, Inc., Santa Clara, CA, USA).

Behavioral test

In Group A, the rats' upper limb grasping test were performed. The rat was put on the wire mesh and its paw would do the grasp action to catch the wire under normal circumstance. We divided grasp results into M0-M2. M0: no finger flexion was observed. M1: finger flexion was observed without grasp. M2: finger grasp was observed. We defined M1 and M2 as effective finger flexion recovery.

In Group B, water spray test was performed. The rat's nose was continuously sprayed with a syringe to observe whether it had shoulder abduction or not. We recorded the number of rats with shoulder abductions and calculated the effective rate.

The right upper limb grasping test and water spray test were carried out in Group C.

EMG examination

The rats were anesthetized with sodium pentobarbital injected intraperitoneally. The transverse incision of the neck was made to expose the bridging ulnar nerve. The stimulating electrode was put on the bridging ulnar nerve. The recording electrode was inserted into the target muscle. A current of 1 Hz, 0.5 mA was used for stimulating the nerve.

Group A: recording electrode was placed into the FCR.

Group B: recording electrode was placed into the DEL.

Group C: recording electrodes were placed into FCR and DEL.

The emergence of compound muscle action potential (CMAP) was regarded as a positive recovery of motor function.

Cross-sectional area of the muscle fiber

FCR and DEL were biopsied from the affected side in Group A and B, respectively. Both of the two muscles were obtained in Group C and D. All the muscles were fixed with 10% paraformaldehyde (Shanghai Reagent Company, Shanghai, China). Then they were fixed with paraffin (Shanghai Reagent Company, Shanghai, China) and stained with hematoxylin and eosin(HE)(Shanghai Reagent Company, Shanghai, China). The mean cross-sectional area of the muscle fiber was measured and calculated by Image J system (National Institutes of Health, USA).

Nerve fiber count

Median and axillary nerves were biopsied from the affected side in Group A and B, respectively. Both of the two nerves were obtained in Group C and D. All nerve dissections were near the entry points into target muscles. The samples were fixed with 25% glutaraldehyde (Shanghai Reagent Company, Shanghai, China) and paraffin-embedded for slices. Then they were stained with 5% toluidine blue (Shanghai Reagent Company, Shanghai, China). The average number of nerve fibers in unit area was measured and calculated by the Image J system.

Gene expressions related to skeletal muscle atrophy

As previous research reported[5], Muscle RING Finger 1(MuRF1)and Muscle Atrophy F-box □MAFbx□were the genes related to skeletal muscle atrophy. They were positively correlated with muscle atrophy. In Group A and B, the FCR and DEL were biopsied respectively, while both of the two muscles were biopsied in Group C and D. Muscle tissue samples were obtained and dissolved with TRIzol™ (1600 Faraday Ave,

Carlsbad CA92008 USA). Then DNA was separated, precipitated and extracted from the samples. The purity of purified DNA was determined. Expression of each gene was determined by RT-qPCR (Agilent Technologies, Inc., Santa Clara, CA, USA). The relative expression levels of the two genes were determined using the $2^{-\Delta\Delta Ct}$ method.

At the completion of the biopsy, each group was euthanized using CO2. The flow rate for CO2 euthanasia displaced 20% of the chamber volume/min according to the 2013 edition of the American Veterinary Medical Association Guidelines for the Euthanasia of Animals.

Date analysis

Comparisons of the effective and positive rates among different groups were performed using Fisher's exact test in behavioral test and EMG. One-way ANOVA (analysis of variance) was used for continuous variables comparisons in the aspects of cross-sectional area of the muscle fiber, nerve fiber count and gene expressions. The p-values were two-tailed and p-values < 0.05 were considered significant. All analyses were performed using Statistical Package for Social Sciences (SPSS, Chicago, IL, USA) 24.0 software.

Results

Two rats died after operations in Group C. We supplemented two rats into Group C and did the operations under the same conditions. Finally, no wound infection was found in any of the surviving rats.

Behavior test

According to the grasping test, 14 rats (70%) and 12 rats (60%) reached effective finger flexion recoveries in Group A and C respectively, while there was no significant difference between the two groups. For abduction recovery, we observed shoulder abduction in 12 rats in Group B and 8 rats in Group C. The effective rate in Group B (60%) was larger than that in Group C (40%). However, there was no statistical difference between the two groups. In the Group C, the effective rate of finger flexion recovery (60%) was larger than that of shoulder abduction recovery (40%), although there was no significant difference. The effective rate of finger flexion recovery in Group A (70%) was larger than that of shoulder abduction recovery in Group B (60%). (Table 1)

Table 1. The results of behavioral tests and EMG in Group A, B, C

Group	Finger flexion		Shoulder abduction		Effective Rate (%)	EMG (FCR)		EMG (DEL)		Positive Rate (%)
	(+)	(-)	(+)	(-)		(+)	(-)	(+)	(-)	
A	14	6	/	/	70%	18	2	/	/	90%
B	/	/	12	8	60%	/	/	14	6	70%
C (FCR)	12	8	/	/	60%	14	6	/	/	70%
C (DEL)	/	/	8	12	40%	/	/	12	8	60%

EMG examination

Table 1 showed the CMAP rates in FCR and DEL. CMAP in FCR could be recorded in 18 rats (90%) and 14 rats (70%) in Group A and C, respectively. There was no significant difference between the two groups. In DEL, CMAP could be recorded in 14 rats (70%) in Group B and 12 (60%) in Group C. No statistical difference existed between the two groups. In Group C, CMAP rate in FCR (70%) was larger than that in DEL (60%) without significant difference. In addition, CMAP rate in FCR in Group A (90%) was larger than that in DEL in Group B (70%), although there was no statistical difference.

Cross-sectional area of the muscle fiber

We evaluated the mean cross-sectional areas of FCR and DEL muscle fibers to represent the recoveries of median and axillary nerves respectively. (Figure 4) The average muscle fibers cross-sectional areas of FCR were 352.44±71.33μm² in Group A and 327.71±134.11μm² in Group C. There was no statistical difference between the two groups. Either the cross-sectional area in Group A or C was significantly larger than that in Group D (115.65±19.46μm²). The mean cross-sectional areas of DEL were 339.09±117.69μm², 332.75±111.54μm² and 261.61±37.78μm² in Group B, C, D, respectively. There was no statistical difference among the three groups. (Figure 5A)

Nerve fiber count

Figure 5B showed the differences in the number of nerve fibers in different groups. The numbers of median nerve fibers were 17.67±3.06/mm² in Group A and 13.33±3.06/mm² in Group C. There was no significant difference between the two groups. However, either the number in Group A or C was significantly more than that in Group D (7.00±2.00/mm²). The numbers of axillary nerve fibers were 13.00±2.00/mm², 11.33±3.21/mm² and 6.33±1.53/mm² in Group B, C and D, respectively. Either the number of axillary nerve fibers in Group B or C was significantly more than that in Group D, while there was no

statistical difference between Group B and C. In Group C, the number of median nerve fibers (13.33±3.06/mm□) was more than that of axillary nerve fibers (11.33±3.21/mm□) without significant difference. The number of median nerve fibers in Group A (17.67±3.06/mm□) was more than that of axillary nerve fibers in Group B (13.00±2.00/mm□) without significant difference. Figure 6 showed the different nerve fibers in different groups.

PCR for MAFBOX and MURF1

By qRT-PCR assay, the ratio of MAFBOX expression in FCR on affected side to contralateral side successively increased from Group A to C to D, but there were no significant differences of the ratios among the three groups. The trend for the ratio of MURF1 in FCR from Group A to C to D was the same with MAFBOX. (Figure 7a)

As for DEL, the ratios of MAFBOX and MURF1 also rose from Group B to C to D. The ratios in the three groups had no statistical differences between each other, no matter for MAFBOX or MURF1. (Figure 7b)

Discussion

Brachial plexus injury was one of the severe injuries to the upper limb. It was reported that 10–20% of peripheral nerve injuries were brachial plexus injuries,[16] especially the total brachial plexus root avulsion, which was difficult to repair. At present, nerve transfer is the primary method for total brachial plexus nerve root avulsion. It is widely accepted that the extraplexal nerve transfer is a feasible way for functional restoration of the affected limb,[19,22] which includes intercostal nerve transfer,[21] spinal accessory nerve transfer,[1] phrenic nerve transfer[10] and cC7 transfer[11]. In patients with total brachial plexus injury, cC7 transfer is usually used to repair the median nerve. Clinically, simultaneous repair of two recipient nerves by cC7 transfer has been reported to achieve a certain curative effect.[5] Although the spinal accessory nerve was often transferred to the suprascapular nerve for shoulder abduction reconstruction,[14] the recovery of shoulder abduction was not satisfying.[8] Recent studies showed that the repair of both axillary and suprascapular nerves could achieve effective shoulder abduction.[12] So this study was designed to explore the efficacy of cC7 in repairing the median and axillary nerves at the same time.

In the study, behavioral tests, EMG examination, mean muscle fiber cross-sectional area, nerve fiber count and gene expression related to muscle atrophy were used to demonstrate the efficacy of cC7 transfer. EMG and the number of nerve fibers represented nerve regeneration after nerve repair. The cross-sectional area of muscle fiber reflected the degree of muscle atrophy and regeneration. Based on previous studies, the expressions of MAFBOX and MURF1 were positively correlated with muscle atrophy.[6] All the results showed there were no significant differences in the efficiency of median nerve recovery between Group A and C, while both of the two Groups improved the median nerve regeneration, compared with Group D.

The above results indicated that cC7 transfer to both median and axillary nerves would not affect the recovery of median nerve, compared with cC7 transfer to median nerve alone. Anatomical reports showed 17000–40000 myelinated nerve fibers in cC7 nerve root[4]. The average number of myelinated nerve fibers was about 14800[20] in the median nerve, while it was 2704 in axillary nerve.[26] The number of nerve fibers in cC7 nerve root was more than that of any other recipient nerve and it had the capacity to provide enough dynamic nerve fibers to both of median and axillary nerves in theoretically, which was consistent with our results.

Many studies recommended the suprascapular and axillary nerves should be repaired simultaneously to obtain better shoulder joint function, because the repair of suprascapular nerve alone was not enough for the reconstruction of shoulder abduction.[12,15] In aspect of the number of axillary nerve fibers, the results in Group B and C were statistically better than that in Group D, while there was no statistical difference between Group B and C. The results of shoulder abduction and EMG also showed deltoid recovery in Group B and C, while no statistical difference existed between the two groups. All these results above indicated that the axillary nerve could be repaired no matter by cC7 transfer to axillary nerve alone or by cC7 transfer to axillary and median nerves.

As for the cross-sectional area of DEL fibers, although there were no statistical differences among Group B, C and D, the mean cross-sectional areas of DEL fibers decreased successively form Group B to C to D. The results demonstrated muscle atrophy was related to denervation and nerve transfer made innervation which could reduce the muscle atrophy. There was functional impairment in Group D compared with Group B and C, while no statistical demonstration was showed in muscle fiber count of DEL. Because the completion of an action requires sufficient muscle fibers for contraction, when there are not enough muscle fibers regeneration, the functional differences are revealed. But at the same time, in the aspect of cross-sectional area of the muscle fiber, statistics do not necessarily show differences in cross-sectional area. The cross-sectional area of DEL successively decreased from Group B to C to D, which coincided with the result of functional test. Another reason might be the time from operation to biopsy, which was not long enough to make the muscle completely atrophy in Group D. It induced no statistical differences of the cross-sectional area of DEL to occur among groups.

Bodine SC et al.[2] reported only a small subset of genes was universal in all atrophy models. Two of these genes encode ubiquitin ligases: Muscle RING Finger 1 (MuRF1) and Muscle Atrophy F-box (MAFbx). Overexpression of MAFbx in myotubes produced atrophy, whereas mice deficient in either MAFbx or MuRF1 were found to be resistant to atrophy. The models were the rats with denervation or immobilization or unweighting, which were a little different from our models. In our study, there were four groups, including one denervation group and three nerve regeneration groups. From our research, the negative data of MAFbx and MURF1 in DEL coincided with the result of the mean cross-sectional areas of DEL, while the data in gene expression in FCR was not so consistent with the mean cross-sectional areas of FCR. We know that muscle regeneration takes time. When innervation to the muscle occurred, the time course of inducing the change of MAFbx and MURF1 was unknown yet, which is an intriguing question. Maybe the time from operation to biopsy was not long enough to show the different change of MAFbx

and MURF1 between innervation and denervation groups. We think the innervation process with the gene regulation might not just be the opposite process of denervation and its correlation with these two genes needs a further study.

The proportion of the recovery of axillary nerve was less than that of median nerve in terms of behavior tests, EMG and the number of nerve fibers in the study. The main reason was the anatomy of axillary nerve, which passed through the quadrilateral foramen. This nerve was easily compressed in the quadrilateral foramen, especially during the process of nerve growth, which influenced the growth of the nerve fibers. In addition, the axillary nerve was smaller in diameter than the median nerve and most of the cC7 nerve fibers would grow into the median nerve.

Previous meta-analysis showed that the average effective rate of cC7 transfer to median nerve was 50%, which was close to our result (70%).[13] There were also some clinical and experimental reports of cC7 transfer to two recipient nerves simultaneously. Gao et al.[7] reported cC7 transfer to the median nerve and biceps branch or the median nerve and triceps branch. The recovery rate of motor function of median nerve was 68.2%, while those of biceps branch and triceps branch were 66.7% and 20%, respectively, which suggested that cC7 could achieve exact results by repairing two recipient nerves at the same time. Pan et al. reported an animal experiment of cC7 transfer to the median and musculocutaneous nerves. The target muscles innervated by the median and musculocutaneous nerves had regeneration,[18] but the details about the recovery rate of muscle strength were not reported. Chuang et al.[5] also found that cC7 could repair the median and musculocutaneous nerves at the same time. The recovery rates of finger and elbow flexion were 39% and 82.6%, respectively. Terzis et al.[23] repaired axillary nerve with hemi-cC7 nerve root and muscle strength of DEL achieved M3 or above was 20%. In our experiment research, the axillary nerve was repaired with the total root of cC7 and effective rate was 60% in rats. There were two probable reasons for the difference. One was the difference of nerve growth speed between human beings and rats. The other was the difference in the number of donor nerve fibers. There was no animal experimental report on cC7 transfer to both of the median and axillary nerves before.

There were some limitations in this study. First, there was a lack of a simple and accurate rat behavior test for shoulder external rotation. Secondly, the muscle tension measurement was an important method for judging the recovery of muscle function, while we did not use it in our experiment. Third, the number of samples in the research is small, which made the results not so convincing. Afterwards, we'll increase the number of animals in the future research. In both the functional tests and EMG results, we compared the percentages of effectiveness (positive) among groups. Due to the small number of samples, the statistical analysis seemed to lower the power of the test. The amplitude and latency of CMAP of the muscles could be used for evaluation. In the future research, we'll use amplitude and latency as indicators for nerve regeneration evaluation. In addition, there was a remodeling process of cortical plasticity after cC7 transfer and its mechanism would be the focus in the future research.

Conclusions

Compared with cC7 transfer to median nerve, cC7 transfer to both median and axillary nerves did not affect the recovery of the median nerve and the deltoid muscle could also be restored. In this animal experimental research, the proportion of the recovery of axillary nerve was less than that of median nerve.

Abbreviations

TBPA —-total brachial plexus avulsion

cC7—Contralateral cervical 7 nerve

S-D— Sprague-Dawley

EMG —electromyogram

FCR —Flexor Carpi Radialis

DEL —deltoid

CMAP —compound muscle action potential

HE —hematoxylin and eosin

ANOVA—analysis of variance

SPSS —Statistical Package for Social Sciences

MuRF1—Muscle RING Finger 1

MAFbx —Muscle Atrophy F-box

Declarations

Consent for publication

All authors have agreed to submit the manuscript to the journal “BMC Musculoskeletal Disorders” and consented it for publication.

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Fudan University.

Competing Interests

I, Jie Lao, M.D, Department of Hand surgery, Huashan Hospital, Fudan University, Shanghai, China, declare that we have no conflict of interest. We have no proprietary, financial, professional or other personal interest of any nature or kind in any product, service or company that could be construed as influencing the position presented in, or the review of, the manuscript entitled, “Contralateral C7 Transfer to Axillary and Median Nerves in Rats with Total Brachial Plexus Avulsion”.

Authors’ Contributions

All authors have made substantial contributions to the study: JL designed the study and made the final approval of the version to be submitted. YL drafted the article and revised it critically for important intellectual content. FX did the behavioral test, EMG examination and made date analysis. YZ did the experiment for cross-sectional area of the muscle fiber, nerve fiber count and gene expressions related to skeletal muscle atrophy. All Authors read and approved the manuscript.

References

1. Allieu Y, Privat JM, Bonnel F: Paralysis in root avulsion of the brachial plexus. Neurotization by the spinal accessory nerve. Clin Plast Surg 11:133-136, 1984
2. Bodine SC, Latres E, Baumhueter S, et al. Identification of ubiquitin ligases required for skeletal muscle atrophy. Science 294(5547):1704-1708, 2001
3. Chen L, Gu YD: An experimental study of contralateral C7 root transfer with vascularized nerve grafting to treat brachial plexus root avulsion. J Hand Surg Br 19:60-66, 1994
4. Chuang DC: Neurotization procedures for brachial plexus injuries. Hand Clin 11:633-645, 1995
5. Chuang DC, Hernon C: Minimum 4-year follow-up on contralateral C7 nerve transfers for brachial plexus injuries. J Hand Surg Am 37:270-276, 2012
6. de Palma L, Marinelli M, Pavan M, Orazi A: Ubiquitin ligases MuRF1 and MAFbx in human skeletal muscle atrophy. Joint Bone Spine 75:53-57, 2008
7. Gao K, Lao J, Zhao X, Gu Y: Outcome of contralateral C7 transfer to two recipient nerves in 22 patients with the total brachial plexus avulsion injury. Microsurgery 33:605-611, 2013
8. Gao KM, Hu JJ, Lao J, Zhao X: Evaluation of nerve transfer options for treating total brachial plexus avulsion injury: A retrospective study of 73 participants. Neural Regen Res 13:470-476, 2018
9. Gu YD, Chen DS, Zhang GM, Cheng XM, Xu JG, Zhang LY, et al: Long-term functional results of contralateral C7 transfer. J Reconstr Microsurg 14:57-59, 1998
10. Gu YD, Wu MM, Zhen YL, Zhao JA, Zhang GM, Chen DS, et al: Phrenic nerve transfer for brachial plexus motor neurotization. Microsurgery 10:287-289, 1989

11. Gu YD, Zhang GM, Chen DS, Yan JG, Cheng XM, Chen L: Seventh cervical nerve root transfer from the contralateral healthy side for treatment of brachial plexus root avulsion. J Hand Surg Br 17:518-521, 1992
12. Leechavengvongs S, Malungpaishorpe K, Uerpairojkit C, Ng CY, Witoonchart K: Nerve Transfers to Restore Shoulder Function. Hand Clin 32:153-164, 2016
13. Li WJ, He LY, Chen SL, Lyu YW, Wang SF, Yong Y, et al: Contralateral C7 Nerve Root Transfer for Function Recovery in Adults: A Meta-analysis. Chin Med J (Engl) 130:2960-2968, 2017
14. Malungpaishrope K, Leechavengvongs S, Witoonchart K, Uerpairojkit C, Boonyalapa A, Janesaksrisakul D: Simultaneous intercostal nerve transfers to deltoid and triceps muscle through the posterior approach. J Hand Surg Am 37:677-682, 2012
15. Merrell GA, Barrie KA, Katz DL, Wolfe SW: Results of nerve transfer techniques for restoration of shoulder and elbow function in the context of a meta-analysis of the English literature. J Hand Surg Am 26:303-314, 2001
16. Mumenthaler M: Some clinical aspects of peripheral nerve lesions. Eur Neurol 2:257-268, 1969
17. Narakas AO: The treatment of brachial plexus injuries. International Orthopaedics 9:29-36, 1985
18. Pan F, Wei HF, Chen L, Gu YD: Different functional reorganization of motor cortex after transfer of the contralateral C7 to different recipient nerves in young rats with total brachial plexus root avulsion. Neurosci Lett 531:188-192, 2012
19. Panagopoulos GN, Megaloikonomos PD, Mavrogenis AF: The Present and Future for Peripheral Nerve Regeneration. Orthopedics 40:e141-e156, 2017
20. Schreiber JJ, Byun DJ, Khair MM, Rosenblatt L, Lee SK, Wolfe SW: Optimal axon counts for brachial plexus nerve transfers to restore elbow flexion. Plast Reconstr Surg 135:135e-141e, 2015
21. Seddon HJ: Nerve grafting. J Bone Joint Surg Br 45:447-461, 1963
22. Songcharoen P: Management of brachial plexus injury in adults. Scand J Surg 97:317-323, 2008
23. Terzis JK, Kokkalis ZT: Selective contralateral c7 transfer in posttraumatic brachial plexus injuries: a report of 56 cases. Plast Reconstr Surg 123:927-938, 2009
24. Terzis JK, Kokkalis ZT, Kostopoulos E: Contralateral C7 transfer in adult plexopathies. Hand Clin 24:389-400, 2008
25. Wang SF, Li PC, Xue YH, Yiu HW, Li YC, Wang HH: Contralateral C7 nerve transfer with direct coaptation to restore lower trunk function after traumatic brachial plexus avulsion. J Bone Joint Surg Am 95:821-827, S1-S2, 2013
26. Witoonchart K, Leechavengvongs S, Uerpairojkit C, Thuvasethakul P, Wongnopsuwan V: Nerve transfer to deltoid muscle using the nerve to the long head of the triceps, part I: an anatomic feasibility study. J Hand Surg Am 28:628-632, 2003
27. Zou YW, Wang ZJ, Yu H: Treatment of brachial plexus injury with modified contralateral C7 transfer. Orthop Surg **2:14-18, 2010**

Figures

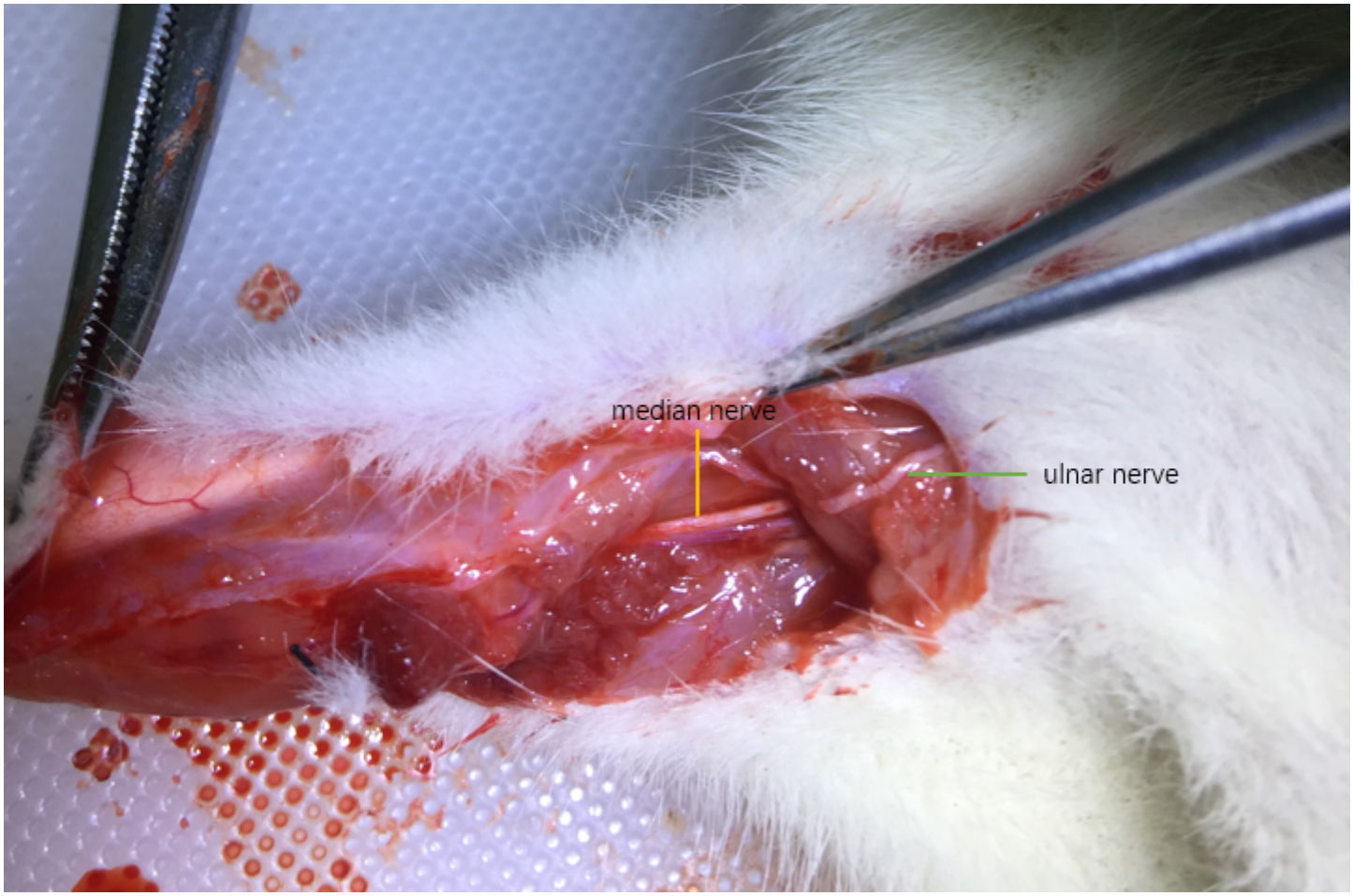

Figure 1

cC7 transfer to median nerve: The ulnar nerve and median nerve were identified at the turning point of ulnar nerve.

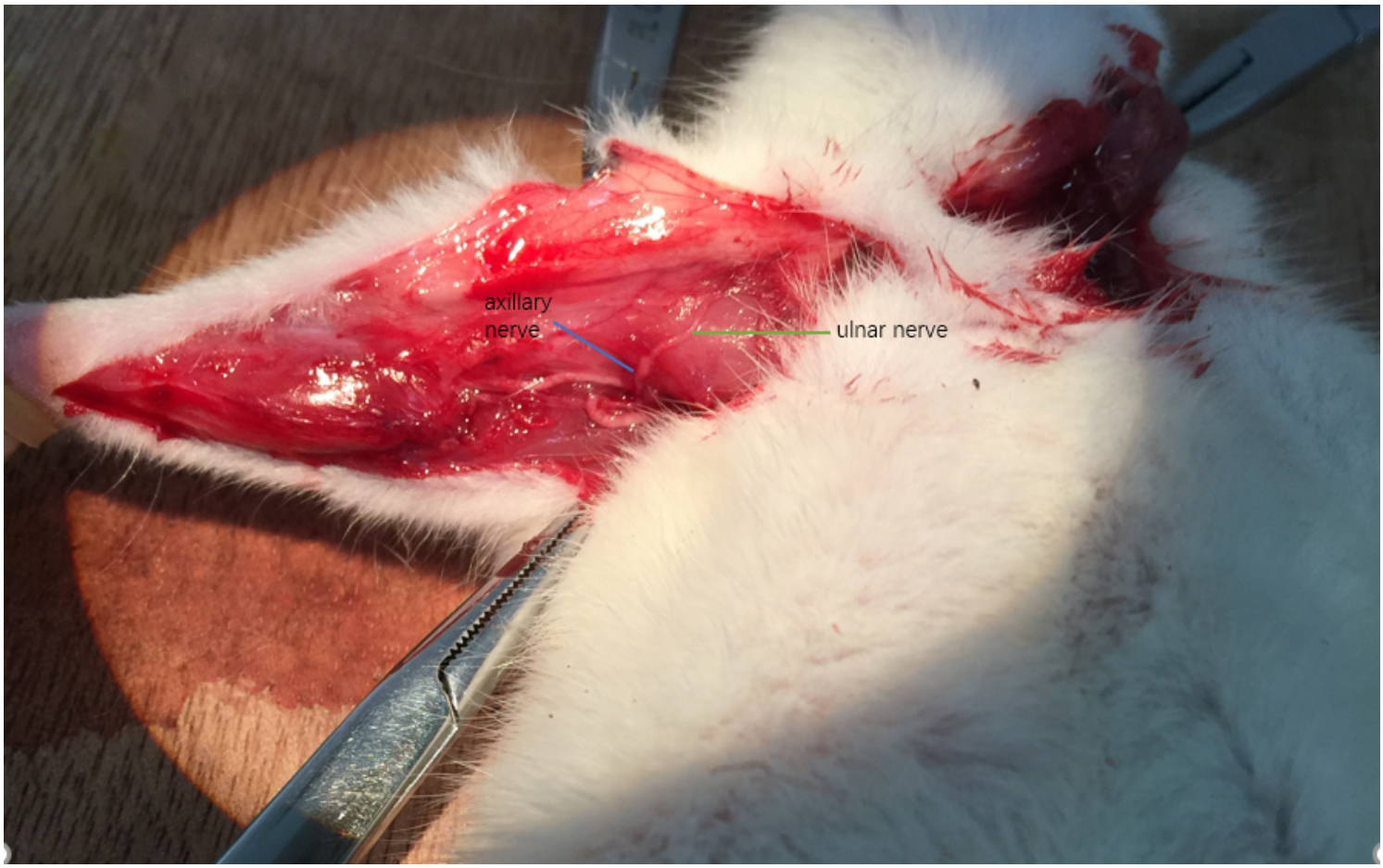

Figure 2

cC7 transfer to axillary nerve: The proximal end of ulnar nerve was sutured to the distal end of the whole axillary nerve without tension.

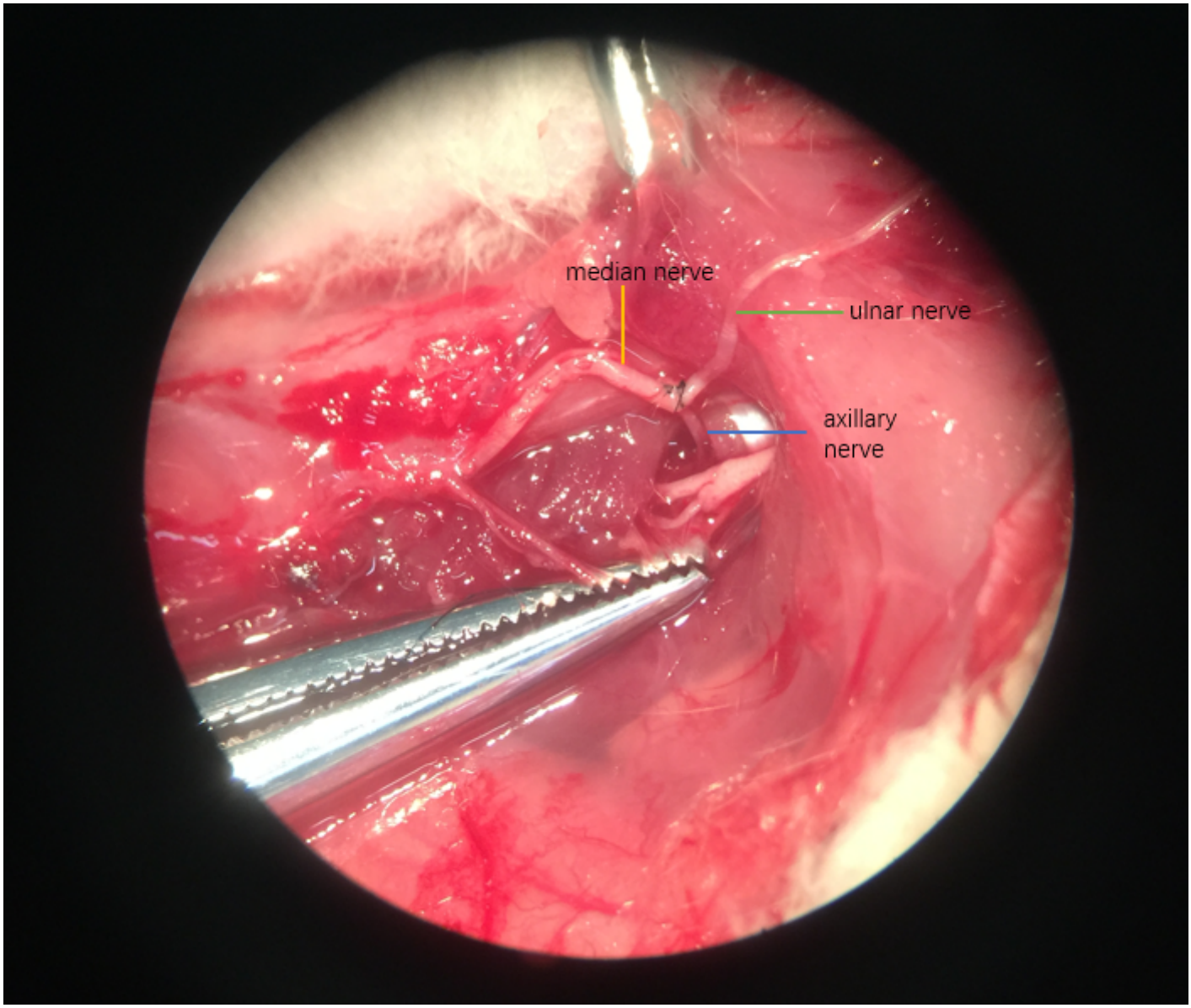

Figure 3

cC7 transfer to median and axillary nerves: Axillary nerve and median nerve were separated to enough length for suturing to the ulnar nerve without tension.

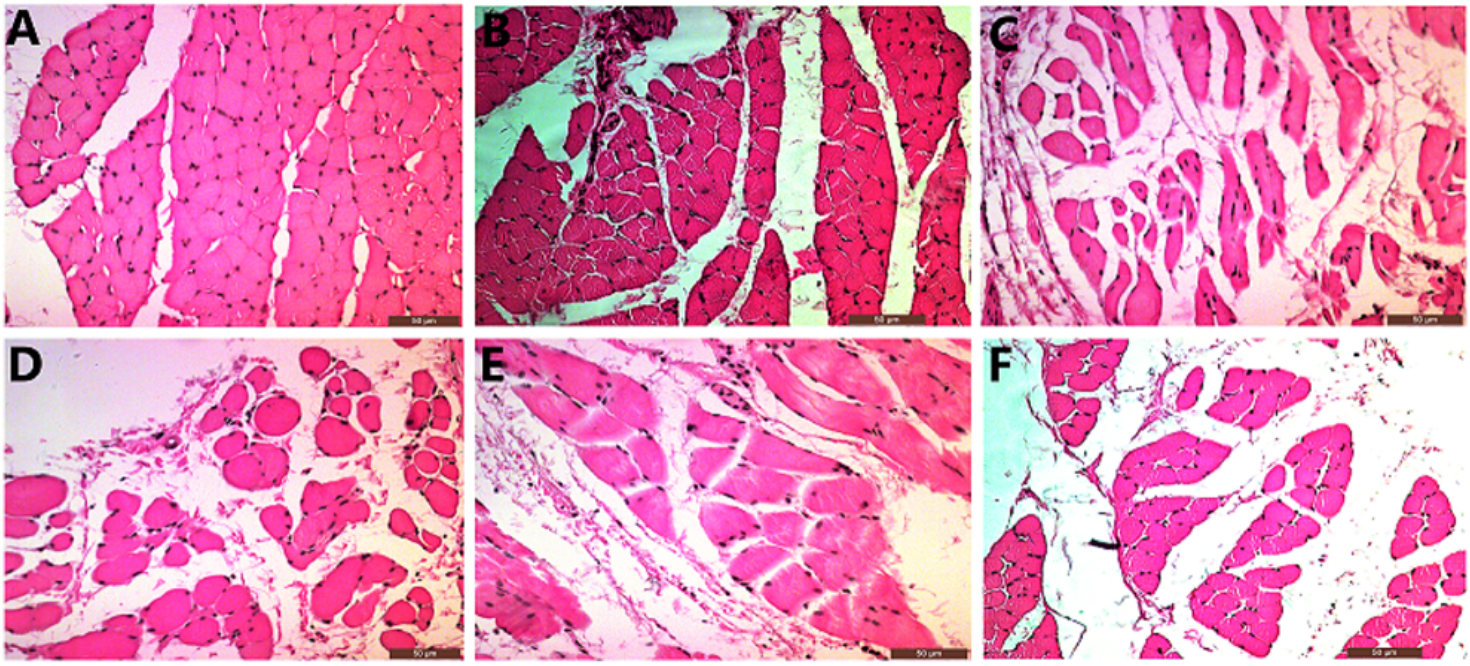

Figure 4

Figure 4.A— The cross-section of FCR muscle fibers in Group A Figure 4.B— The cross-section of FCR muscle fibers in Group C Figure 4.C— The cross-section of FCR muscle fibers in Group D Figure 4.D— The cross-section of DEL muscle fibers in Group B Figure 4.E— The cross-section of DEL muscle fibers in Group C Figure 4.F— The cross-section of DEL muscle fibers in Group D

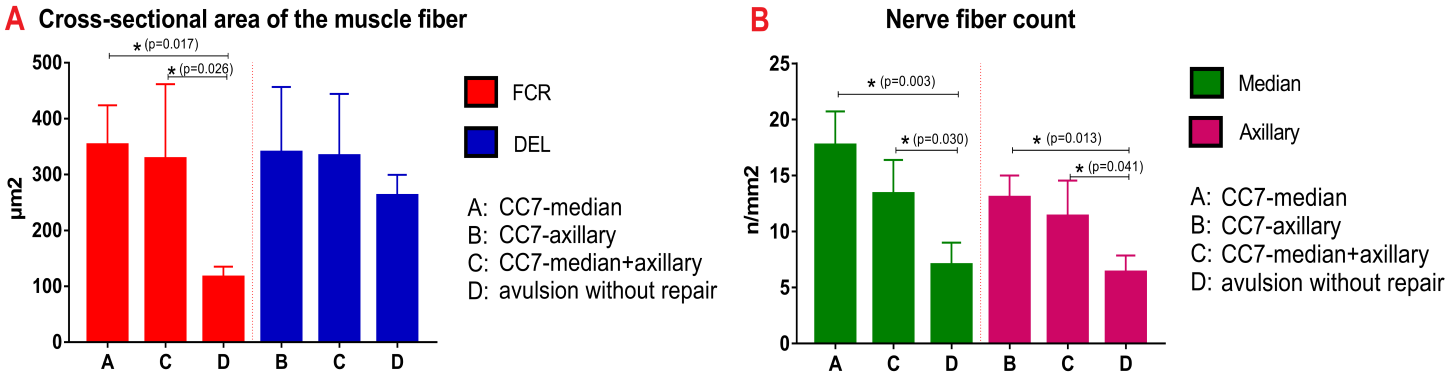

Figure 5

Figure 5.A— The mean cross-sectional areas of FCR and DEL muscle fibers in different groups Figure 5.B — The nerve fiber counts of median and axillary nerves in different groups

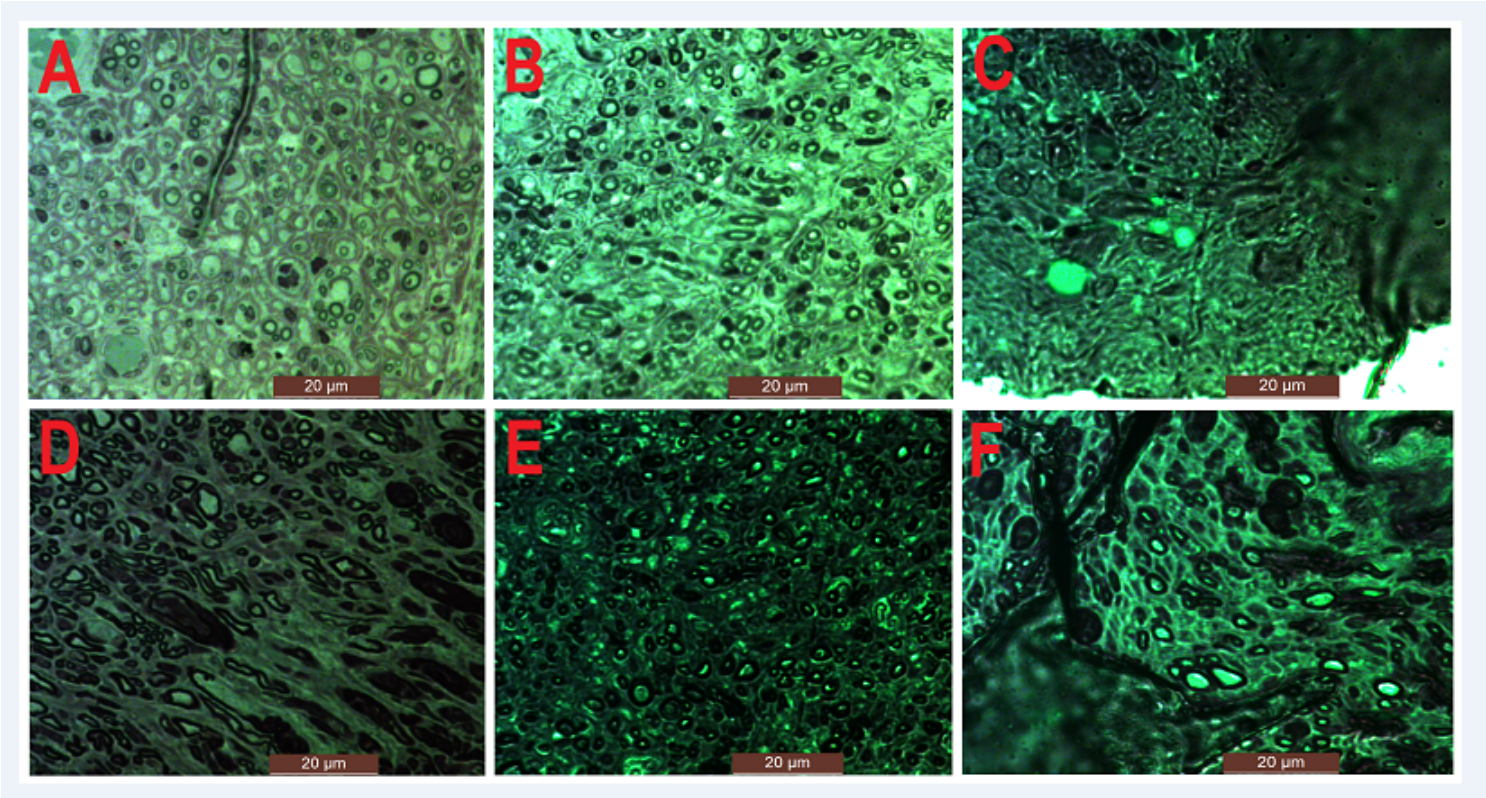

Figure 6

Figure 6.A— The nerve fibers of median nerve in Group A Figure 6.B— The nerve fibers of median nerve in Group C Figure 6.C— The nerve fibers of median nerve in Group D Figure 6.D— The nerve fibers of axillary nerve in Group B Figure 6.E— The nerve fibers of axillary nerve in Group C Figure 6.F— The nerve fibers of axillary nerve in Group D

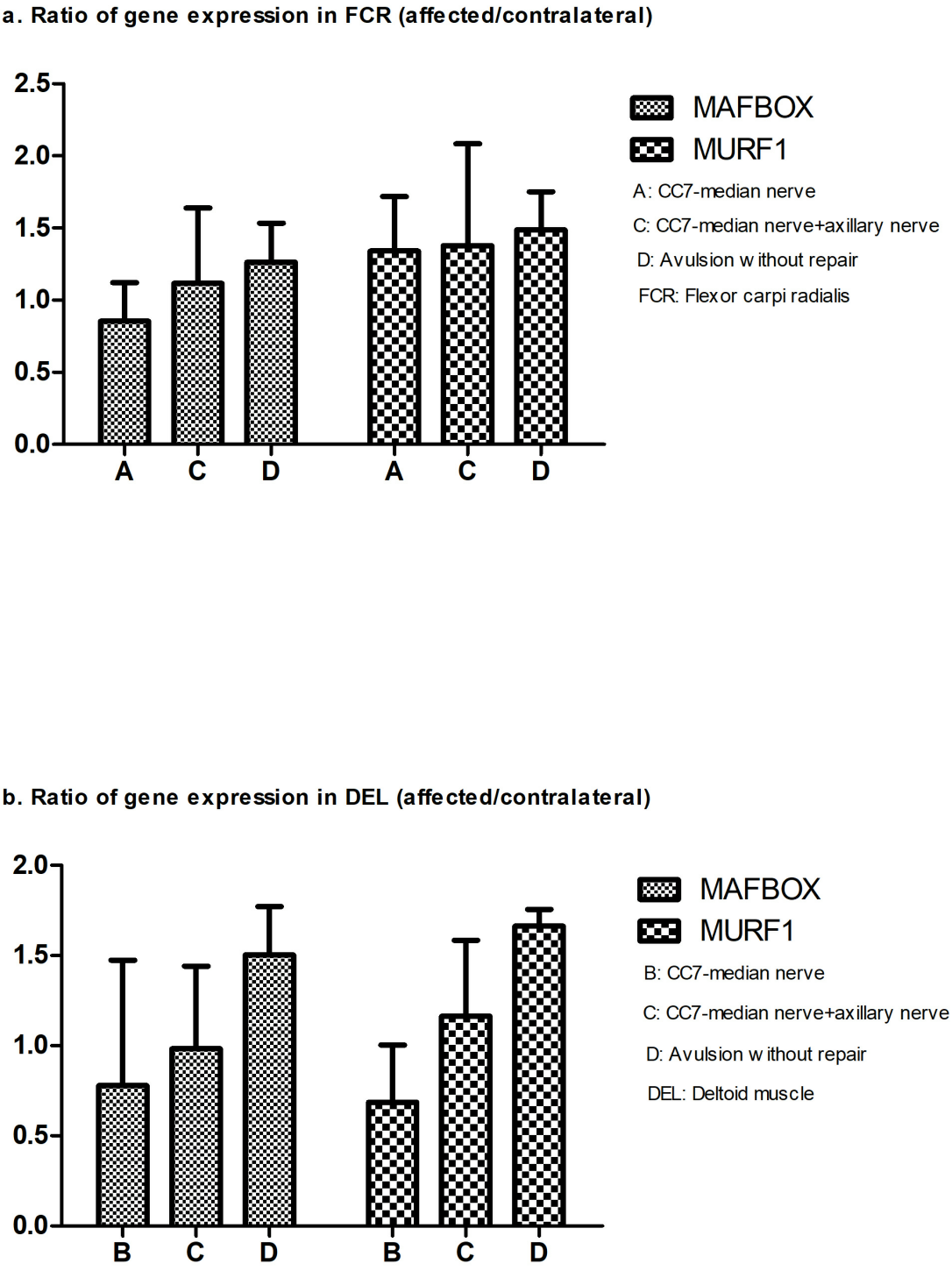

Figure 7

Figure 7.a — The ratios of gene expressions in FCR (affected/contralateral) in different groups Figure 7.b —The ratios of gene expressions in DEL (affected/contralateral) in different groups

Supplementary Files

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