Anatomical and histomorphometric observations on the transfer of the anterior interosseous nerve to the deep branch of the ulnar nerve

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Abstract
This study focuses on the anatomical and histomorphometric features of the transfer of the anterior interosseous nerve to the deep motor branch of the ulnar nerve. The transfer was carried out in 15 cadaver specimens and is described using relevant anatomical landmarks. Nerve samples of donor and target nerves were histomorphometrically analysed and compared. The superficial and the deep ulnar branches had to be separated from each other for a length of 67 mm (SD 12; range 50–85) to reach the site of coaptation. We identified a suitable site for coaptation lying proximal to the pronator quadratus muscle, 202 mm (SD 15; range 185–230) distal to the medial epicondyle of the humerus. The features of the anterior interosseous nerve included a smaller nerve diameter, smaller cross-sectional area of fascicles, fewer fascicles and axons, but a similar axon density. The histomorphometric inferiority of the anterior interosseous nerve raises a question about whether it should be transferred only to selected parts of the deep motor branch of the ulnar nerve.

Level III

Keywords
Ulnar nerve paresis, reinnervation, extraanatomic, axon count, peripheral nerve repair, microsurgery

Introduction
Major nerve injuries and the associated loss of sensory and motor functions severely affect the patient’s quality of life. In the upper extremity, the ulnar nerve is the most commonly injured nerve (Kouyoumdjian, 2006). Recovery after ulnar nerve injuries is poorer with longer nerve defects and in more proximal injuries (Merle et al., 1986; Vastamäki et al., 1993). Because of the poor outcomes of proximal ulnar nerve repair, nerve transfers were introduced (Estrella and Mella, 2013; Harris, 1921; Jobe and Wright, 1998; Mackinnon and Novak, 1999). Nerve transfers involve the loss of an uninjured donor nerve, which is transferred and sutured to the distal stump of the injured target nerve (Mackinnon and Colbert, 2008). Nerve transfers are generally indicated in cases in which the time for regeneration through direct nerve repair is too long or recovery is impossible. Other reasons include a proximal nerve stump that is unavailable or inadequate and the avoidance of surgery in scarred tissue beds.

Wang and Zhu (1997) described the transfer of the anterior interosseous nerve (AIN) to the deep branch of the ulnar nerve (DBUN) to regain intrinsic hand muscle function. Battiston and Lanzetta (1999) described the reconstruction of the motor and sensory parts of the ulnar nerve. This study presents anatomical data on this nerve transfer

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and compares the histomorphometric characteristics of the two nerves.

**Methods**

**Anatomical dissection**

Anatomical measurements were made on 15 fresh cadaver upper limbs. The AIN was identified and transected proximal to the pronator quadratus (PQ) muscle. It was separated from the surrounding tissues in the proximal direction for a length of approximately 3–4 cm and transferred to the ulnar border of the PQ. The DBUN was identified within Guyon’s canal and dissected from the fascicles of the superficial branch of the ulnar nerve to the level of the AIN. There, the nerves were coapted and the distances to relevant anatomical landmarks the medial epicondyle, the pisiform, and the dorsal cutaneous branch of the ulnar nerve (DCBUN) – were recorded (Figure 1).

**Histomorphometric analysis**

Nerve samples were excised from 14 fresh specimens at the level of the coaptation and fixed at 4 °C in 2.5% glutaraldehyde with 0.1 M sodium cacodylate buffer for 60 min [pH 7.4; Science Services, Munich, Germany]. After postfixation in 2% aqueous osmium tetroxide, specimens were dehydrated in an ascending alcohol series (30%–100%) and propylene oxide (Science Services, Munich, Germany). Samples were embedded in epoxy resin (Merck, Darmstadt, Germany) preserving their orientation and cured for 24 h at 60 °C. Semithin transverse sections (1 µm) were obtained with an ultramicrotome (Reichert Technologies, Munich, Germany), stained for 1 min with 1% toluidine blue (Sigma-Aldrich, Taufkirchen, Germany), and scanned at a 20× magnification with a Mirax Scanner (Carl Zeiss, Jena, Germany). The nerve diameter, fascicle number, and cross-sectional area of the individual fascicles were measured at 200× magnification (Figure 2[A] and [D]). Cross-sectional areas were measured using specialized software (Pannoramic Viewer 1.15; 3DHISTECH, Budapest, Hungary). The total areas of fascicles were calculated as the sum of the cross-sectional surfaces of all fascicles. Myelinated axons were counted semi-automatically at 600× magnification [ImageJ, version 1.42; NIH, Bethesda, MD, USA] (Figure 2[B], [C], [E], and [F]). The low cut-off value for inclusion of axons was set at 4 µm. Axon density was calculated as the ratio of axon number and fascicle area. Donor-to-target ratios of the means were calculated for all parameters. Donor-to-target axon ratios were calculated for each specimen.

Statistical analysis was done using a two-tailed t-test with p ≤ 0.05 being considered as significant. All data are given as the mean and standard deviation (SD), along with the range when appropriate.

**Results**

**Anatomical dissection**

The AIN and the DBUN were identified in all specimens without any anatomical variations. After dissection, the AIN could be transferred towards the proximal and ulnar border of the PQ without loss of relevant length. The retrograde interfascicular neurolysis of the superficial and deep ulnar branch starting at their division at the pisiform never reached the takeoff of the DCBUN, which could be preserved in all cases. After neurolysis of the DBUN and nerve mobilization, a tension-free coaptation was possible at the proximal and ulnar border of the PQ in every specimen. Results of the anatomical measurements for the location of the coaptation, the neurolysis distance, and the takeoff of the DCBUN are shown in Figure 3. Nerve diameters are shown in Figure 4(A).

**Histomorphometry**

The comparison of donor-to-target nerves revealed that the AIN had a significantly smaller diameter, smaller fascicular cross-sectional area, fewer fascicles and axons, and a smaller axon density. Histomorphometric results are given in Figure 4 and Table 1. Individual donor-to-target axon count ratios for each specimen are depicted in Figure 5.

**Discussion**

One major factor for success in treating peripheral nerve injuries is the length of time between axotomy and reinnervation (Brown et al., 2009a). Nerve transfers increase the chance for successful reinnervation by shortening both the regeneration time and distance.
In the treatment of facial paralysis and brachial plexus injuries, nerve transfers are well-established procedures (Battiston et al., 2009; Flores, 2013; Klebuc, 2011; Kozin, 2008; Terzis and Barmpitsioti, 2012). In all specimens, the AIN could be transferred to the proximal and ulnar border of the PQ without loss of relevant length. Mobilization of the AIN did not interfere with its branches to the long flexors. The sensory DCBUN could be preserved in all cases (Figure 3). Loss of sensation could thus be avoided, keeping the nerve available as a donor for sensory transfers (Bedeschi et al., 1984; Brown et al., 2009b).

The proximity to target muscles is also a factor for success in nerve repair because denervated muscles

**Figure 2.** Semithin sections of the AIN (A), (B), (C) and the DBUN (D), (E), (F) from the coaptation site. Calibration bars represent 200 µm (A) and (D) and 50 µm (B), (C), (E), and (F).

**Figure 3.** Black dots highlight the location of nerve dissection. The courses of the AIN and DBUN before their transposition are shown in grey. Interrupted lines illustrate their positions after the transfer. The location of the coaptation is depicted by the red dot. For reasons of clarity the median nerve is shown just to the level shortly beyond the takeoff of the AIN. The pronator quadratus muscle is highlighted in brown, the pisiform in grey.

AIN: anterior interosseous nerve; DBUN: deep branch of the ulnar nerve; DCBUN: dorsal cutaneous branch of the ulnar nerve; SBUN: superficial branch of the ulnar nerve.
The speed of nerve regeneration is usually given by rule of thumb as 1 mm of nerve regeneration per day. We found the coaptation point to lie 202 mm (SD 15; range 185–230) distal to the medial epicondyle (Figure 3). This allows an estimation of the gains in reinnervation time and distance by this nerve transfer. For ulnar nerve injuries at the elbow level, the reinnervation distance is cut by more than half and the reinnervation time gained can be estimated to be 6.5 months. Our measurements also allow an estimate of the time span from surgery until the regaining of muscle function. A reinnervation time of about 100 days can be estimated, taking into account the distance from the point of coaptation to the target muscles. These time spans should be considered with regard to the limited window of time for nerve transfers. Our measurements are in line with other studies and equally valid for the end-to-side variant of this transfer (Barbour et al., 2012; Doyle and Botte, 2003; Robert et al., 2011; Tubbs et al., 2006). There is a variable number of interchanging nerve fibres between the DBUN and superficial branch of the ulnar nerve, which may be cut if they are small (Brown et al., 2009b). Our anatomical results present the AIN as a
suitable donor for the DBUN and should be of help in planning this procedure.

Comparisons between donor and target nerves by their histomorphometric characteristics are commonly accepted methods for estimating the results of nerve transfers (Boutros et al., 1999; Rodriguez et al., 2011). Our comparison revealed the AIN to be significantly smaller in all histomorphometric aspects (Table 1). However, nerve transfers with a donor that is smaller than the target nerve can be successful. Axons in the proximal stump can undergo collateral sprouting that increases the number of axons by 3–4 times (Jiang et al., 2007). Experiments with different donor-to-target axon ratios in rabbits have shown useful motor recovery beginning at a 1:3 ratio (Lutz et al., 2000). Based on these studies, the average axon ratio of 1:4.8 in the current study can be regarded as low. Although the absolute numbers of semi-automatic axon counts vary between studies owing to inclusion criteria, axon ratios are comparable (Raimondo et al., 2009). We calculated axon ratios for this nerve transfer from the axon numbers in other studies (Table 2). Interestingly, two studies used DBUN samples from the level of the pisiform (Üstün et al., 2001; Wang and Zhu, 1997). The two other studies did not state the location where the samples were collected (Brown et al., 2009b; Novak and Mackinnon, 2002). In contrast, we analysed the nerves directly at the site of coaptation.

The majority of specimens had donor-to-target axon ratios of 1:4 and 1:5, which can be considered to be close to the commonly accepted threshold of 1:3. Clinical reports of satisfactory outcomes could indicate that the poorer axon ratios are adequate for this particular nerve transfer (Battiston and Lanzetta, 1999; Brown et al., 2009b; Mackinnon and Novak, 1999; Wang and Zhu, 1997).

Two specimens presented with very poor donor-to-target axon ratios of approximately 1:13 (Figure 5). Sporadically occurring poor axon ratios might explain cases with a poor clinical outcome (Wang and Zhu, 1997). The poor ratio could be addressed by transferring the AIN to selected DBUN fascicles that are expected to be most helpful for hand function in the individual patient.

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