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ORIGINAL ARTICLE
Peripheral Nerve

Histologic Comparison of the Fascicular Area of Processed Nerve Allograft Versus Cabled Sural Nerve Autograft

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Background: The use of multiple cables of sural nerve autograft is common for peripheral nerve reconstruction when injured nerve caliber exceeds the nerve graft caliber. Although the optimal matching of neural to nonneural elements and its association with functional outcomes are unknown, it is reasonable to consider maximizing the neural tissue structure available for nerve regeneration. No prior studies have compared directly the cross-sectional fascicular area between cabled nerve autografts and size-selected nerve allografts. This study evaluated the cross-sectional fascicular area between native nerve stumps and two reconstructive nerve grafting methods: cabled sural nerve autograft (CSNA) and processed nerve allograft (PNA).

Methods: CSNA from matched cadaveric specimens and PNA were used to reconstruct nerve defects in the median and ulnar nerves of six pairs of cadaveric specimens. Nerve reconstructions were done by fellowship-trained hand surgeons. The total nerve area, fascicular area, and nonfascicular area were measured histologically.

Results: The CSNA grafts had significantly less fascicular area than PNA and caliber-matched native nerve. The PNA grafts had a significantly higher percent fascicular area compared with the intercalary CNSA graft.

Conclusions: Fascicular area was significantly greater in PNA versus CSNA. The PNA consistently demonstrated a match in fascicular area closer to the native nerve stumps than CSNA, where CSNA had significantly smaller fascicular area compared with native nerve stumps. *(Plast Reconstr Surg Glob Open 2023; 11:e5201; doi: 10.1097/GOX.0000000000005201; Published online 17 August 2023.)*

INTRODUCTION

Nerve autografts are the historical standard for bridging peripheral nerve defects.[1] Common nerve autograft sources include sural, medial, and lateral antebrachial cutaneous, and posterior and anterior interosseous nerves; however, the sural nerve is the most commonly harvested nerve autograft.[1–3] Although good outcomes of nerve autografts have been reported, drawbacks include anatomical variations, inconsistent outcomes,[4,5] and donor-site morbidity.[6] Anatomical variations in autografts include sural nerve diameter (ranging[7] from 2.0 to 4.0 mm), branching patterns,[8] and the number of fascicles (ranging[7] from nine to 14 fascicles). Inconsistent outcomes of nerve autografts have been described, with between 35.7%[4] and 83% of patients[5] regaining meaningful motor function.

Nerve reconstruction with processed nerve allograft (PNA) may reduce total surgical time and donor-site morbidities associated with autograft harvest, with reported meaningful sensory and motor outcomes equivalent to nerve autograft.[9] PNA may be prepared fresh, frozen, or decellularized through chemical processing; however, limitations exist with each of these preparation methods, including the need for immunosuppression.[10] Currently available off-the-shelf PNAs in the United States undergo processing to remove cellular debris, myelin, diffusible and membranous nerve fractions, and axonal growth inhibitors.[11–13] The remaining

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components of PNA include structural and functional proteins (including laminin), which are beneficial for nerve regeneration.[14] Preclinical studies indicated that the lack of Schwann cells and endothelial lined blood vessels in PNAs limit the optimal length and diameter of nerve gap reconstruction.[15,16]

Autograft, PNA, and cabled isograft effectiveness have been evaluated in preclinical studies. A 2008 study by Whitlock et al found that isografts and PNA were equivalent in short gap nerve reconstruction; however, isografts showed better outcomes than PNA in long gap nerve reconstruction.[17] Tang et al reported that caliber-matched PNA and reversed autograft had similar functional recovery, but PNA provided superior functional recovery compared with a cabled autograft.[18] In 2019, Tang et al reported similar outcomes in caliber-matched PNA, reversed autograft, and cabled autograft and suggested that outcomes may be impacted by caliber-matching the nerve graft with the native nerve stump.[19] A clinical study meta-analysis by Lans et al reported that there were no significant meaningful recovery differences between autograft and allograft nerve reconstructions across both short and long nerve gaps.[9]

During caliber-matching, the structure of the native nerve and nerve graft has been considered important in peripheral nerve reconstruction, and the cross-sectional fascicular area may have a greater influence on functional outcomes.[19] Myelinated and unmyelinated fiber counts, fascicular area, and cross-sectional nerve area have been evaluated to understand the impact of fascicular area and nerve caliber on peripheral nerve repair.[20–22] Intrafascicular components, such as laminin, support and guide neurite extension[23,24]; therefore, optimal nerve regeneration may be influenced by maximizing the fascicular area matching of the reconstructed nerve defect and nerve graft, compared with nonneural connective tissue that may not support nerve regeneration.[1,25,26]

Quantifying laminin within the fascicles using immunohistochemistry may serve as a surrogate estimate of functional regenerative area. We hypothesized that when using PNA or cabled sural nerve autograft (CSNA) that are caliber-matched to cadaveric native nerve during simulated peripheral nerve reconstruction, PNA will have a fascicular area that more-closely matches the native nerve fascicular area compared with CSNA based on the introduction of greater nonneural connective tissues within the nerve repair site. Also, we hypothesized that PNA would have a higher density of fascicular area compared with a CSNA.

MATERIALS AND METHODS

Nerve Graft Sources

Matched sural nerve autograft or PNA (Avance Nerve Graft, Axogen Corporation, Alachua, Fla.) were used for the reconstruction of nerve defects in fresh cadaveric upper extremity specimens. Sural nerve autografts were obtained from six matched fresh lower extremity cadaveric specimens (n = 6; three female and three male specimens).

Takeaways

Question: Are there cross-sectional fascicular area differences between cabled sural nerve autograft (CSNA) and processed nerve allograft (PNA) of similar caliber?

Findings: The PNA group had a significantly higher percent fascicular area compared with the intercalary CSNA group. The CSNA group had significantly less fascicular area than PNA and caliber-matched native nerve.

Meaning: A smaller fascicular area may limit the ability of regenerating axons to extend through the nerve graft to the distal target, which may inhibit axonal outgrowth.

The entire sural nerve was harvested, including the lateral branch. The sural nerve was divided into segments as required for reconstructing the upper extremity nerve defect, each measuring 18–25 mm in length; the diameter of the nerve segments was not measured. The harvested sural nerve was cabled with two or three individual sural nerve segments to form the CSNA, as determined appropriate by the surgeon. Each PNA segment was handled per manufacturer's instructions. The harvest location of these PNAs was unknown, as this commercially available product does not specify anatomical location of the nerve allograft segments. Using a standard surgical ruler, the PNA diameter was measured to ensure that PNA diameters were within a range of 3–5 mm, and PNAs were divided into shorter segments measuring 18–25 mm in length.

Nerve Defect Reconstruction

Six matched pairs of upper extremity cadaveric specimens (n = 12 arms; three pairs of female and three pairs of male specimens) were donor-matched to lower extremity specimens used for sural nerve autograft harvest, thus simulating sural nerve autograft reconstruction. Upper extremity specimens were positioned with the joints in full extension, ensuring clinical recommendations for minimizing repair site tension were considered. Nerve defects were created in the left and right forearm of each upper extremity specimen by transecting the ulnar and median nerves approximately 30 ± 10 mm proximal to the wrist crease. A 10 mm segment was removed from each nerve proximal to the transection, creating a defect of approximately 20 mm after natural retraction of the nerve.

Nerve defects were reconstructed by attending surgeons trained in autograft nerve harvest, cabled nerve graft preparation, and peripheral nerve reconstruction. Both median and ulnar nerve defects were reconstructed with either donor-matched CSNA or PNA; these nerve grafts were referred to collectively as nerve graft segments. The nerve graft segments were assigned randomly to either the ulnar or the median nerve defects. Forty-eight nerves were reconstructed with nerve grafts: 12 median nerves with CSNA, 12 ulnar nerves with CSNA, 12 median nerves with PNA, and 12 ulnar nerves with PNA.

Each nerve graft segment and native nerve stump (ulnar or median nerve) was measured using a standard operative ruler. The CSNA was visually caliber-matched for diameter to the native nerve stump by surgeons

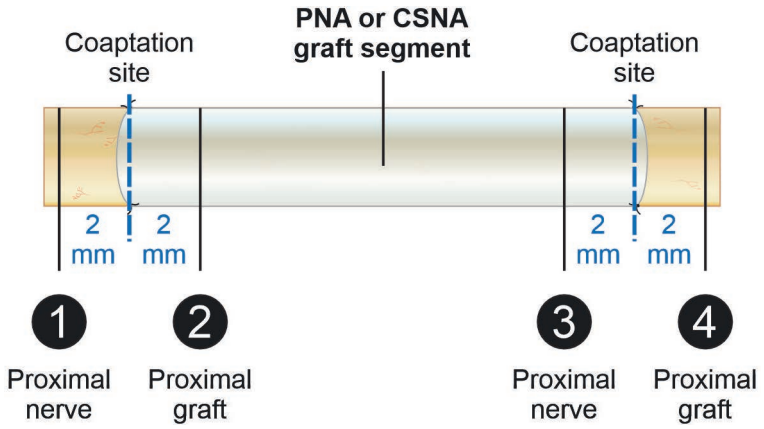


Fig. 1. Location of nerve graft segment histology sections for nerve reconstructions performed with CSNA and PNA. All histology section sites were consistent across groups.

performing each nerve reconstruction. Each cable segment of CSNA was added to the nerve reconstruction individually and was coapted with a minimum of two sutures at each repair site. Additional sural nerve segments were added to optimize caliber-matching to the native nerve stump as determined by the surgeon. Each CSNA reconstruction used two or three sural nerve autograft segments. PNA reconstruction involved selection of a single caliber-matched allograft approximating the injured nerve stump diameter as measured with a standard operative ruler. The PNA segment was sutured in place using a minimum of three sutures at each coaptation site.

Histology Specimen Preparation and Analysis

Histology specimens were explanted immediately after simulated surgical reconstruction and included the nerve graft segment (CSNA or PNA) and an approximately 10–20 mm portion of the proximal and distal native nerve stump. Histology specimens were fixed with 10% neutral buffered formalin for a minimum of 48 hours and embedded in paraffin (Premier Laboratory, Longmont, Colo.). Sections of 5-μm thickness were obtained at four locations: (1) proximal native nerve stump 2 mm proximal to the coaptation site, (2) proximal nerve graft segment 2 mm distal to the coaptation site, (3) distal nerve graft segment 2 mm proximal to the coaptation site, and (4) distal native nerve stump 2 mm distal to the coaptation site (Fig. 1). Histology sections were stained with rabbit polyclonal antibody to laminin 111 at a 1:7125 dilution of the stock solution (Cat# RPCA-Laminin, EnCor Biotechnology, Inc. Gainesville, Fla.).

Stained histology sections were scanned using Aperio ScanScope AT2 and Scanner Console v 102.0.7.5 (Leica Biosystems Division of Leica Microsystems Inc., Buffalo Grove, Ill.). Scanned images of the histological sections were evaluated and traced manually with ImageJ (National Institutes of Health, Bethesda, Maryland). Total nerve area was traced by following the epineurial layer surrounding each nerve histology section image. The epineurium traced in the CSNA group excluded inter-graft white space and adipose tissue, as histology sections may exhibit shrinkage and histology artifacts due to processing. Measurements were obtained for each of the four sections collected from the 12 histology specimens (total nerve area, fascicular area, and nonfascicular area) (Fig. 2) and were calibrated through the Aperio ScanScope Scanner.

Statistical Analysis

A *t* test was used to determine statistical differences in the following measurements: (1) total nerve area of the native nerve versus nerve graft segments and (2) fascicular area of the native nerve versus nerve graft segments. These data were grouped by nerve type and graft type: median native nerve versus CSNA, ulnar native nerve versus CSNA, median native nerve versus PNA, and ulnar native nerve versus PNA. Results were reported for mean, SD, and 95% confidence interval. A *P* value of less than 0.05 was considered statistically significant.

To ensure that the nerve graft segments were caliber-matched appropriately, the total nerve area measurements of native nerve versus nerve graft segment were compared. Collected measurements for total nerve area were used to calculate the ratio of native nerve area to nerve graft segment [nerve area ratio (%) = (total area of native nerve/total area of nerve graft segment) × 100]. The nerve area ratio and total area of native nerve versus nerve graft segment were used to evaluate group differences for caliber-matching between native nerve and nerve graft segment. Collected measurements for total nerve area, fascicular area, and nonfascicular area were used to calculate the percent fascicular area [%FA = (fascicular area/total nerve area) × 100] and percent nonfascicular area [%nFA = (nonfascicular area/total nerve area) × 100]. The percent fascicular area and percent nonfascicular area were used to determine differences among all groups in this study, using normalized data. A one-way ANOVA with Tukey test was used to evaluate differences in the following measurements: nerve area ratio, percent fascicular area, and percent nonfascicular area. Results were reported for mean, SD, and 95% confidence interval. A *P* value of less than 0.05 was considered statistically significant.

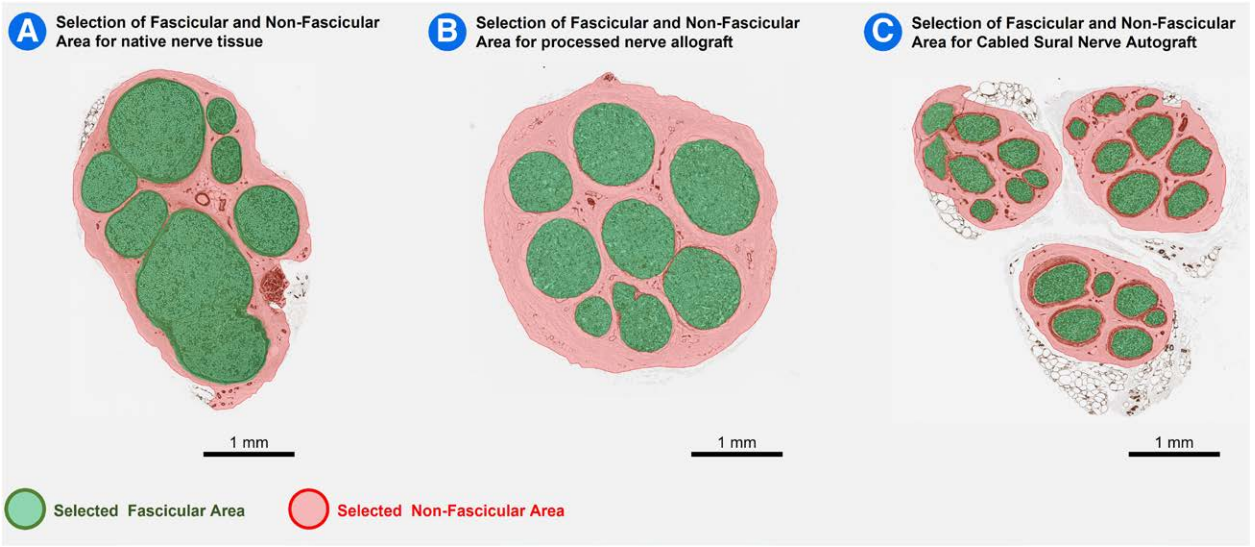


Fig. 2. The fascicular area (green) and nonfascicular area (red) are selected. The representative images for selection of fascicular and nonfascicular area for (A) native nerve tissue, (B) PNA, and (C) CSNA are shown. Total nerve area included both fascicular and nonfascicular area.

RESULTS

There were no significant differences between the total nerve area of native nerve and implanted graft segments. Also, there were no significant differences in nerve area ratio between native nerve groups compared with repair-matched nerve graft segment groups for CSNA or PNA in median or ulnar nerve reconstructions. These results confirmed that nerve graft segments were not significantly oversized or undersized, where the overall mean ± SD of the nerve graft area to native nerve area was 94 ± 33% (95% CI 85–104%; Table 1). Differences were noted, however, when evaluating the fascicular area and percent fascicular area of the native nerve compared with the nerve graft segments. The fascicular area was similar in the PNA versus median native nerve (Fig. 3A), significantly higher in the PNA versus ulnar native nerve (Fig. 3B), significantly lower in the CSNA versus median native nerve (Fig. 3C), and significantly lower in the CSNA versus ulnar native nerve (Fig. 3D).

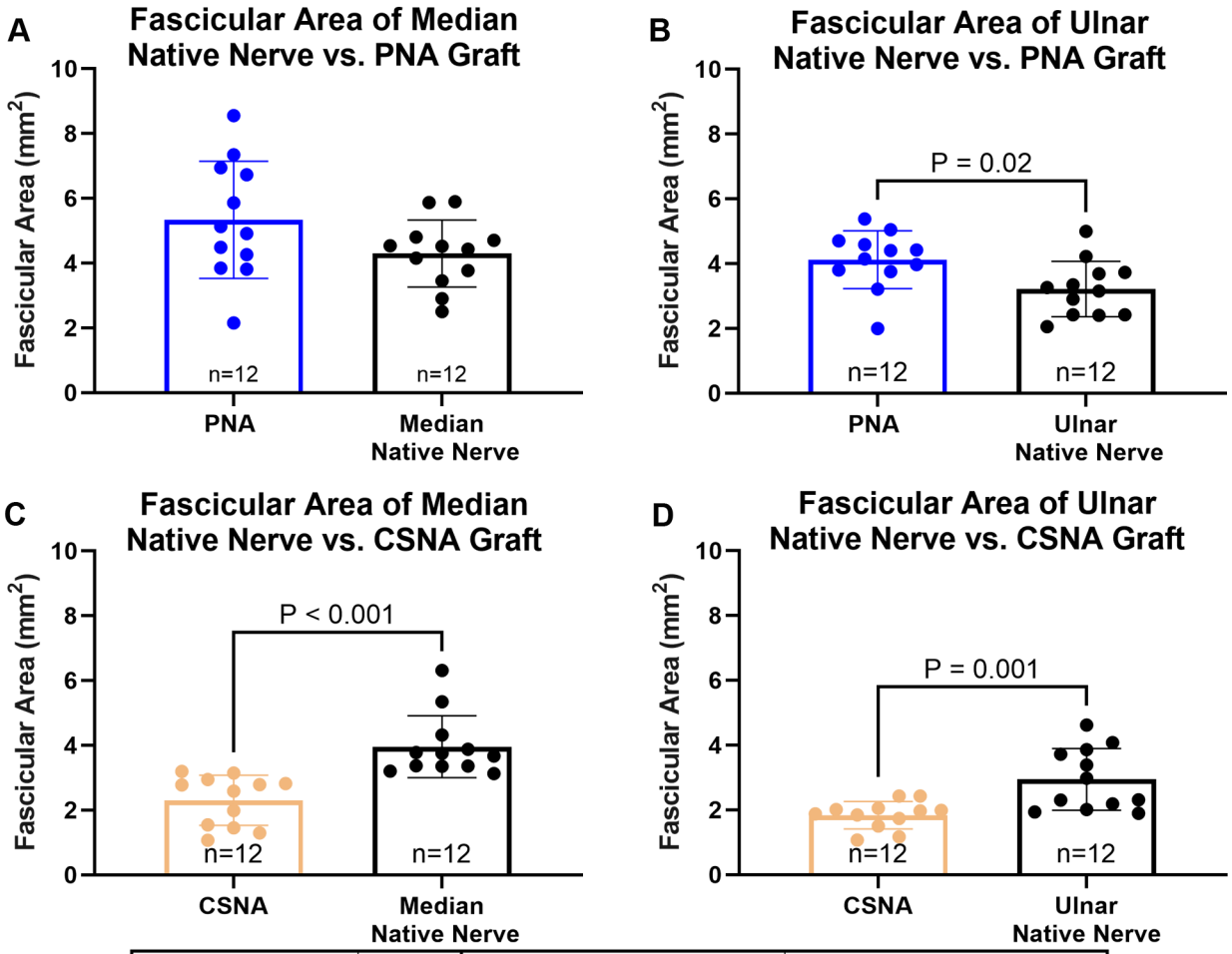
There were no significant differences between the percent fascicular area of PNA used for the median nerve versus ulnar nerve reconstruction groups (Fig. 4). Similarly, there were no significant differences in percent fascicular area between CSNA used for the median nerve versus the ulnar nerve reconstruction groups. However, percent fascicular area of PNA groups for both median and ulnar nerve reconstructions was significantly higher than the percent fascicular area of CSNA groups for both median and ulnar nerve reconstructions. This lower percent fascicular area noted in the CSNA group was consistent in the individual grafts of the CSNA group as well, with the average percent fascicular area of the single sural nerve grafts sutured to the median nerve measuring 27±6.6% (95% CI 23%–31%) and sutured to the ulnar nerve measuring 26±5.0% (95% CI 23%–29%).

The percent nonfascicular area showed an inverse relationship to the percent fascicular area measurements. There were no significant differences between the percent nonfascicular area of PNA used for the median nerve versus ulnar nerve reconstruction groups (Fig. 5). Furthermore, there were no significant differences in percent nonfascicular area between CSNA used

Table 1. Ratio of Native Nerve to Nerve Graft Segment Area, Expressed in Percentages

			Ratio of Native Nerve to Nerve Graft Segment Area (%)	
Nerve Graft Segment Used for Repair	**Nerve**	**Coaptation Site**	**Mean ± SD**	**95% CI**
CSNA	Median	Proximal (n = 6)	93.2 ± 36.2	55–131
		Distal (n = 6)	67.8 ± 16.3	51–85
	Ulnar	Proximal (n = 6)	112.0 ± 42.0	68–156
		Distal (n = 6)	85.2 ± 38.6	45–126
PNA	Median	Proximal (n = 6)	90.2 ± 29.9	59–122
		Distal (n = 6)	82.2 ± 20.4	61–104
	Ulnar	Proximal (n = 6)	124.0 ± 23.7	99–149
		Distal (n = 6)	100.0 ± 29.4	69–131
Overall			94.4 ± 32.9	85–104

No significant differences were noted between groups, $P = 0.082$.



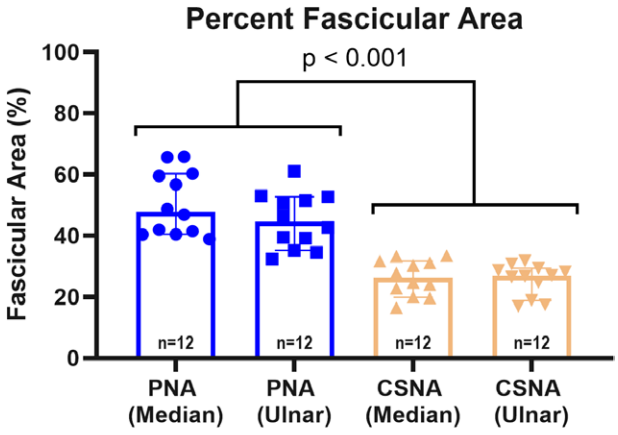
Nerve graft segment used for reconstruction	Nerve	Intercalary Nerve Graft (mm^2)		Native Nerve (mm^2)	
		Mean ± SD	95% CI	Mean ± SD	95% CI
PNA	Median	5.3 ± 1.8	4.2 - 6.5	4.3 ± 1.0	3.6 - 5.0
	Ulnar	4.1 ± 0.89	3.6 - 4.7	3.2 ± 0.86	2.7 - 3.8
CSNA	Median	2.3 ± 0.78	1.8 - 2.8	4.0 ± 0.96	3.3 - 4.6
	Ulnar	1.8 ± 0.42	1.6 - 2.1	2.9 ± 0.96	2.3 – 3.6

Fig. 3. Fascicular area of nerve graft segments are compared between groups. Fascicular area of nerve graft segments was (A) similar in processed nerve allograft vs. median native nerve, $p = 0.1$; (B) significantly higher in processed nerve allograft vs. ulnar native nerve, $p = 0.02$; (C) significantly lower in cabled sural nerve autograft vs. median native nerve, $p < 0.001$; and (D) significantly lower in cabled sural nerve autograft vs. ulnar native nerve, $p = 0.001$.

for the median nerve versus the ulnar nerve reconstruction groups. However, percent nonfascicular area of CSNA groups for both median and ulnar nerve reconstructions were significantly higher than the percent nonfascicular area of PNA groups for both median and ulnar reconstructions.

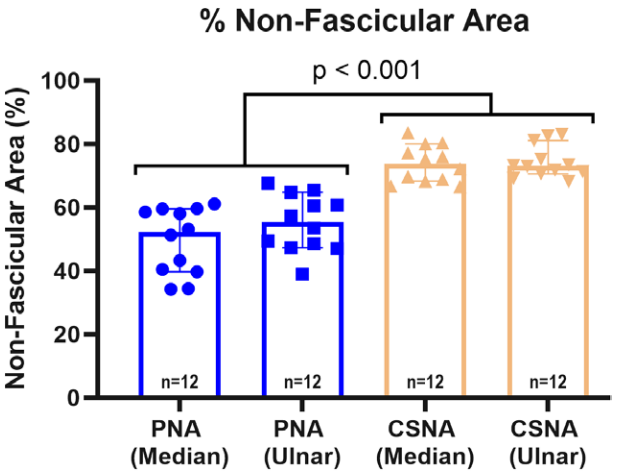
DISCUSSION

This histological study evaluated the absolute value and percentage of fascicular area as proxy measurements for the potential functional regenerative area of PNA or CSNA caliber-matched reconstructions of median and ulnar nerve defects in surgically reconstructed cadaveric specimens. The caliber-matched PNA groups showed a similar or significantly larger fascicular area compared with native nerves, in theory; this may be favorable when performing peripheral nerve reconstruction using nerve grafts. Interestingly, the caliber-matched CSNA groups showed a significantly smaller fascicular area compared with native nerves. In theory, this may be less favorable when performing peripheral nerve reconstruction using



Nerve graft segment used for repair	Nerve	Percent fascicular area (%)	
		Mean ± SD	95% CI
PNA	Median	51 ± 10	44 - 57
	Ulnar	45 ± 9	39 - 51
CSNA	Median	26 ± 6	23 - 30
	Ulnar	26 ± 5	22 - 29

Fig. 4. The percent fascicular area showed significant differences attributable to graft type, $P < 0.001$. PNA (Median) represents PNA used for median nerve reconstruction; PNA (Ulnar) represents PNA used for ulnar nerve reconstruction; CSNA (Median) represents CSNA used for median nerve reconstruction; CSNA (Ulnar) represents CSNA used for ulnar nerve reconstruction.



Nerve graft segment used for repair	Nerve	Percent non-fascicular area (%)	
		Mean ± SD	95% CI
PNA	Median	49 ± 10	43 - 56
	Ulnar	55 ± 9	49 - 61
CSNA	Median	74 ± 6	70 - 77
	Ulnar	74 ± 5	71 - 78

Fig. 5. The percent nonfascicular area showed significant differences attributable to graft type, $P < 0.001$. PNA (Median) represents PNA used for median nerve reconstruction; PNA (Ulnar) represents PNA used for ulnar nerve reconstruction; CSNA (Median) represents CSNA used for median nerve reconstruction; CSNA (Ulnar) represents CSNA used for ulnar nerve reconstruction.

nerve grafts. Using a nerve graft with a smaller fascicular area than the repaired native nerve stump reduces the potential functional regenerative area in the nerve graft compared with the native nerve. This may restrict the potential number of axons regenerating across an injured nerve segment based on a finite quantity of endoneurial tubes in the regenerative area, thereby limiting the number of axons capable of reaching the distal sensory or motor target.

Inter-group comparisons of the nerve graft segments proved that the regenerative area of the PNA groups (both median and ulnar nerve reconstructions) was significantly larger than that of the CSNA groups. The smaller percent fascicular area in the CSNA groups was attributed to the introduction of increased connective tissue, or nonfascicular tissue associated with nerve grafts used to reapproximate the cross-sectional area of the injured nerve. This study provides evidence that cabled sural nerve grafts have a lower fascicular cross-sectional area than the evaluated larger caliber nerves. Additional studies evaluating fascicular area in nerves at various anatomical locations with varying calibers may be beneficial.

This study was limited to the evaluation of cadaveric tissues through histological characterization; therefore, a correlation between nerve graft fascicular area and functional outcomes was not assessed. Functional outcomes of peripheral nerve reconstruction using an autograft or allograft have been reported to be dependent on the success of Schwann migration and vascular support for appropriate axon regeneration.[16,27]

The decellularization process used to prevent immune rejection of the nerve allograft removes Schwann cells and the endothelial lining of blood vessels. The use of nerve allografts in small diameter short gap nerve reconstruction has been reported to be as effective as nerve allografts; however, a reduced efficacy has been noted in large diameter long neve allografts compared with isografts in animal studies.[28] The reduced efficacy of nerve allograft has been attributed to Schwann senescence in long gap nerve allografts and scant vascularization in large diameter nerve grafts.[16,27] These preclinical results may not be apparent clinically, as a meta-analysis published recently concluded that there were no significant meaningful recovery differences between autograft and allograft nerve reconstructions across short and long nerve gaps.[9,10] Although our current study did not investigate functional outcomes, future studies should consider the influence of fascicular area on functional outcomes. Although it is currently unknown if the differences in the regenerative area noted in this study lead to meaningful differences in clinical outcomes, previous basic scientific studies indicate that the available neural tissue (fascicular area) in the intercalary graft segment may influence potential nerve regeneration and distal reanimation.[18]

Following peripheral nerve transection and reconstruction, axons extend from the proximal stump to the distal stump to re-establish function in the end organ.[1] Endoneurial

tubes located within the nerve fascicle (ie, regenerative fascicular area) provide a path for axonal regeneration across the native nerve defect through an intercalary graft to the distal end organ.[1] If the nerve graft has less regenerative fascicular area than the proximal native nerve stump, such as in the CSNA groups in this study, potential axonal regeneration may be diminished due to a reduced number of available endoneurial tubes. As the fascicles contain neurite-promoting molecules, such as laminin, fibronectin, and type IV collagen,[23,24] a larger regenerative fascicular area may optimize conditions for neurite extension through a nerve graft after peripheral nerve reconstruction. This study investigated CSNA versus nerve allograft; however, the results of this study may also aid in decision-making when considering options for cabled nerve autograft. This study suggests that selecting fewer large-caliber cabled nerve autografts rather than more small-caliber nerve autografts may provide more potentially regenerative area.

These observations are supported by in vivo studies, where PNA had similar functional recovery compared with reversed autograft, but superior recovery compared with cabled nerve autograft.[18] Additionally, Slutsky discussed the importance of matching both the caliber of the nerve graft and the number of fascicles.[1] This concept of matching regenerative fascicular area is slightly different than simply matching the nerve caliber and number of fascicles, where the area of the fascicles is unknown. Using a graft with similar caliber and fascicles may provide an optimal regenerative fascicular area, thus improving opportunities for nerve regeneration.

The current study presents valuable information for the determination of regenerative potential in nerve grafts. The study data showed that a larger regenerative fascicular area was present in the PNA compared with the CSNA. The PNA group showed a similar or larger regenerative fascicular area compared with the native nerve stump; however, the CSNA group had a significantly smaller regenerative fascicular area compared with the native nerve stump. Theoretically, a smaller fascicular area may limit the ability of regenerating axons to extend through the nerve graft to the distal target, which may inhibit axonal outgrowth. Future in vivo and clinical studies may improve our understanding as to the influence of fascicular area on functional outcomes.

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DISCLOSURES

Drs. Leversedge, Safa, and Iorio, are consultants of Axogen Corporation. Drs. Merced-O'Neill and Tajdaran are employees of Axogen Corporation. Dr. Lin has no financial interest to declare in relation to the content of this article.

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REFERENCES

1. Slutsky D. A practical approach to nerve grafting in the upper extremity. *Atlas of the Hand Clinics*. 2005;10:73–92.
2. Poppler LH, Davidge K, Lu JCY, et al. Alternatives to sural nerve grafts in the upper extremity. *HAND*. 2015;10:68–75.
3. Higgins JP, Fisher S, Serletti JM, et al. Assessment of nerve graft donor sites used for reconstruction of traumatic digital nerve defects. *J Hand Surg Am*. 2002;27:286–292.
4. Trumble TE, Vanderhooft E, Khan U. Sural nerve grafting for lower extremity nerve injuries. *J Orthop Trauma*. 1995;9:158–163.
5. Lee YH, Chung MS, Gong HS, et al. Sural nerve autografts for high radial nerve injury with nine centimeter or greater defects. *J Hand Surg*. 2008;33:83–86.
6. Ducic I, Yoon J, Buncke G. Chronic postoperative complications and donor site morbidity after sural nerve autograft harvest or biopsy. *Microsurgery*. 2020;40:710–716.
7. Park HD, Kwak HH, Hu KS, et al. Topographic and histologic characteristics of the sural nerve for use in nerve grafting. *J Craniofac Surg*. 2007;18:1434–1438.
8. Steele R, Coker C, Freed B, et al. Anatomy of the sural nerve complex: Unaccounted anatomic variations and morphometric data. *Ann Anat - Anatomischer Anzeiger*. 2021;238:151742.
9. Lans J, Eberlin K, Evans PJ, et al. A systematic review and meta-analysis of nerve gap repair: comparative effectiveness of allografts, autografts, and conduits. *Plast Reconstr Surg*. 2023:151:814e–827e.
10. Buncke G. Peripheral nerve allograft: how innovation has changed surgical practice. *Plast Aesthet Res*. 2022;9:38.
11. Hudson TW, Liu SY, Schmidt CE. Engineering an improved acellular nerve graft via optimized chemical processing. *Tissue Eng*. 2004;10:1346–1358.
12. Krekoski CA, Neubauer D, Zuo J, et al. Axonal regeneration into acellular nerve grafts is enhanced by degradation of chondroitin sulfate proteoglycan. *J Neurosci*. 2001;21:6206–6213.
13. Neubauer D, Graham J, Muir D. Chondroitinase treatment increases the effective length of acellular nerve grafts. *Exp Neurol*. 2007;207:163–170.
14. Axogen Corporation. Avance nerve graft. Available at https://www.axogeninc.com/products/avance-nerve-graft/. Published 2023. Accessed November 2, 2021.
15. Moore AM, Macewan M, Santosa KB, et al. Acellular nerve allografts in peripheral nerve regeneration: a comparative study. *Muscle & Nerve*. 2011;44:221–234.
16. Best TJ, Mackinnon SE, Evans PJ, et al. Peripheral nerve revascularization: histomorphometric study of small- and large-caliber grafts. *J Reconstr Microsurg*. 1999;15:183–190.
17. Whitlock EL, Tuffaha SH, Luciano JP, et al. Processed allografts and type I collagen conduits for repair of peripheral nerve gaps. *Muscle & Nerve*. 2009;39:787–799.
18. Tang P, Kilic A, Konopka G, et al. Histologic and functional outcomes of nerve defects treated with acellular allograft versus cabled autograft in a rat model. *Microsurgery*. 2013;33:460–467.
19. Tang P, Whiteman DR, Voigt C, et al. No difference in outcomes detected between decellular nerve allograft and cable autograft in rat sciatic nerve defects. *J Bone Joint Surg Am*. 2019;101:e42.
20. Chentanez V, Cha-Oumphol P, Kaewsema A, et al. Accuracy of the three-window sampling method in morphometric analysis of human sural nerve. *J Neurosci Methods*. 2006;157:154–157.
21. Chentanez V, Cha-oumphol P, Kaewsema A, et al. Morphometric data of normal sural nerve in Thai adults. *J Med Assoc Thai*. 2006;89:670–674.
22. Oliveira ALCRD, Fazan VPS, Marques W, et al. Dorsal cutaneous branch of the ulnar nerve: a light and electron microscopy histometric study. *J Peripher Nerv Syst*. 2011;16:98–101.

23. Chang W, Shah MB, Zhou G, et al. Polymeric nanofibrous nerve conduits coupled with laminin for peripheral nerve regeneration. *Biomed Mater.* 2020;15:035003.
24. Armstrong SJ, Wiberg M, Terenghi G, et al. ECM molecules mediate both Schwann cell proliferation and activation to enhance neurite outgrowth. *Tissue Eng.* 2007;13:2863–2870.
25. Wolford LM, Stevao ELL. Considerations in nerve repair. *Bayl Univ Med Cent Proc.* 2003;16:152–156.
26. Waters PM, Theodore Schwartz J. Posterior interosseous nerve: an anatomic study of potential nerve grafts. *J Hand Surg.* 1993;18:743–745.
27. Saheb-Al-Zamani M, Yan Y, Farber SJ, et al. Limited regeneration in long acellular nerve allografts is associated with increased Schwann cell senescence. *Exp Neurol.* 2013;247:165–177.
28. Hoben G, Yan Y, Iyer N, et al. Comparison of acellular nerve allograft modification with Schwann cells or VEGF. *Hand (N Y).* 2015;10:396–402.