

The effects of neurodynamic mobilization on fluid dispersion within the tibial nerve at the ankle: an unembalmed cadaveric study

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Objective: To evaluate the effects of neurodynamic mobilization on the fluid dynamics of the tibial nerve in cadavers.

Background: Evidence showing patients benefit from neural mobilization is limited. Mechanisms responsible for changes in patient symptoms are unclear.

Methods: Bilateral lower limbs of six unembalmed cadavers ($n=12$) were randomized into matched pairs and dissected to expose the tibial nerve proximal to the ankle. Dye composed of Toulidine blue and plasma was injected into the nerve. The longitudinal dye spread was measured pre- and post-mobilization. The experimental group received the intervention consisting of 30 repetitions of passive ankle range of motion over the course of 1 minute. The matched control limb received no mobilization. Data were analysed using a 2×2 repeated measures ANOVA with subsequent *t*-tests for pairwise comparisons.

Results: Mean dye spread was 23.8 ± 10.2 mm, a change of $5.4 \pm 4.7\%$ in the experimental limb as compared to 20.7 ± 6.0 mm, a change of $-1.5 \pm 3.9\%$ in the control limb. The ANOVA was significant ($P \leq 0.02$) for interaction between group (experimental/control) and time (pre-mobilization/post-mobilization). *t*-test results were significant between pre- and post-mobilization of the experimental leg ($P=0.01$), and between control and experimental limbs post-mobilization ($P \leq 0.02$).

Conclusion: Passive neural mobilization induces dispersion of intraneural fluid. This may be clinically significant in the presence of intraneural edema found in pathological nerves such as those found in compression syndromes.

Keywords: Cadaver, Compression, Entrapment, Nerve, Neurodynamic, Neuropathy, Tibial

Introduction

Clinicians incorporate neurodynamic techniques for assessment and treatment of neuromuscular disorders. These disorders include compression syndromes or other neuromuscular conditions that may be accompanied by neuropathic pain.¹⁻⁵ Damaged nerves exhibit predictable pathophysiological responses including impaired nerve mobility,⁶⁻⁹ increased mechanosensitivity,^{8,10} impaired nerve conduction,¹¹⁻¹³ nerve tissue ischemia,^{14,15} axonal transport inhibition,¹⁶⁻²² and intraneural edema.^{15,23-28} Impaired nerve mobility and increased mechanosensitivity provide the basis for existing studies of neurodynamic techniques. These studies examined neurodynamic techniques with respect to quantification of strain²⁹ and excursion,³⁰⁻³⁷ as well as symptom reproduction.^{8,34}

Impaired nerve mobility and mechanosensitivity can be clinically assessed by measuring changes in joint range of motion,^{38,39} pain reproduction,^{4,8,10,40-42} or change of symptoms following neurodynamic mobilization.⁴³ Some authors reported an improvement of symptoms⁴³ and increased mobility³⁹ when using neural mobilization as part of the treatment regime, while others found no significant improvement in pain or mobility following neural mobilization.⁴⁴ In a review of neural mobilization studies, Ellis and Hing found limited evidence to support the use of this modality.⁴⁵ To our knowledge, there is no published study to date that investigates neurodynamic techniques with respect to nerve function or other pathophysiological responses, such as ischemia, impaired axonal transport, or intraneural edema.

Intraneural edema is a common response to nerve injury,^{23,25-27} and is intimately involved in the proliferation of damage to nerve structure and function.^{25,46} Edema is found in peripheral nerves that have been

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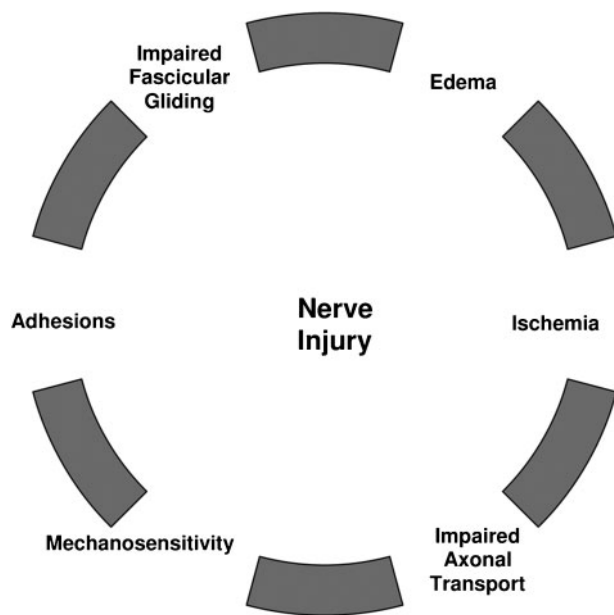


Figure 1 Pathophysiological responses due to nerve injury. Edema propagates the cycle.

subject to trauma such as compression,^{13,23,24,47} excessive tension events,^{14,20,48} or vibration.^{21,26} Even mild injury may result in epineurial edema,²³ but compression that is prolonged or of great magnitude leads to a breach of the diffusion barriers created by both the perineurium and microvasculature, resulting in endoneurial edema.²³ The absence of lymphatic vessels in the endoneurium limits drainage of this edema,⁴⁷ thereby creating a ‘mini-compartment syndrome’ within the nerve.²⁵ This ‘mini-compartment syndrome’, due to the increase in endoneurial pressure, subsequently leads to fibrosis and adhesions, impairing intrafascicular gliding. This loss of intrafascicular gliding creates an internal stretch lesion (Fig. 1).^{14,46,47,49} Fibrosis may be accompanied by nerve enlargement, resulting in additional compression due to intraneural thickening,⁵⁰ as well as increased extraneural compression from adjacent structures.^{51,52} The effects of this enlargement will be more pronounced when the nerve traverses a small space such as an osteofibrous tunnel that is often the site of a compression syndrome.^{51,52}

Neurodynamic mobilization techniques are often used clinically for restoring nerve mobility³⁹ and

decreasing pain.^{43,53,54} In the lower extremity, neurodynamic techniques incorporate ankle range of motion for neurodynamic testing^{2,4,29,40,41,55,56} and treatment.⁵⁷ Moreover, repetitive ankle motion (e.g. ankle dorsiflexion and plantar flexion) is often used clinically to assist in fluid dispersion in the presence of generalized ankle swelling, as well as increase ankle joint mobility regardless of effects on nerve mobility. Despite anecdotal reports of positive treatment outcomes when using neurodynamic techniques,^{5,43,53,54,57} the mechanisms responsible for these outcomes remain unclear. The reduction of neural edema has been cited as a possible benefit to neurodynamic mobilization techniques⁴³ but has not been demonstrated.

The purpose of this study was to examine the effects of neurodynamic mobilization on simulated intraneural edema in the tibial nerve at the ankle in cadavers. The current investigators hypothesized that neurodynamic mobilization performed by passive ankle dorsiflexion and plantar flexion would induce dispersion in the tibial nerve at the ankle. Demonstrating that intraneural fluid can be dispersed by means of ankle range of motion may help identify one mechanism responsible for the benefits of neurodynamic mobilization.

Materials and Methods

Specimens

Seven unembalmed cadavers (three females and four males) with a mean age of 72 ± 10.4 years, mean height of 166 ± 12.8 cm, and mean weight of 66 ± 15.5 kg (Table 1), were used for this pre-test–post-test matched control study. By random selection within each cadaver, one limb was designated as the experimental limb and the other limb was designated as a control limb. Data were not collected on one control limb due to loss of power in the digital caliper. Therefore, a total of six matched limb pairs ($n=12$) were used for analysis.

Position

Before stabilizing limb position, all ankles underwent repetitive ankle dorsiflexion and plantar flexion in order to break the mild but present rigor mortis. Cadaver position was standardized in supine with

Table 1 Cadaver demographics

Cadaver no.	Age	Sex	Height (cm)	Weight (kg)	Cause of death
1	80	F	149.8	43.2	Pneumonia
2	52	F	162.5	72.7	Metastatic carcinoma of anus, systemic HTN
3	74	M	175.2	68.2	Protein calorie malnutrition, prostate CA, RA, CAD, old CVA
4	71	F	154.9	50	CAD, HTN, COPD
5	74	M	182.8	81.8	CVA
6	80	M	172.7	77.3	COPD
Mean	72.0		166.0	66.0	
SD	10.36		12.72	15.50	

Note: CA=cancer; RA=rheumatoid arthritis; CAD=coronary artery syndrome; CVA=cerebral vascular disorder; HTN=hypertension; COPD=chronic obstructive pulmonary disorder.



Figure 2 Before dye injection, location of window for dissection was identified and marked starting just proximal to the distal tip of the medial malleolus. The skin flap was incised and the neurovascular bundle was separated in order to free the tibial nerve from all adjacent tissue. This was necessary in order to visualize and measure the nerve. The injection site was marked with a coloured marker as well as a T-pin.

limbs externally rotated at the hip to 25° and abducted to 10°. The amount of hip rotation was determined by the natural leg position, available range of motion, and ability to access the tibial nerve at the ankle during measurement trials. Wooden blocks and stabilization straps were used to stabilize the position of the limbs. The straps were placed in such a manner as to avoid compression on any part of the nerve and to stabilize without interfering with movement of the ankle.

Dissection

With the exception of the dissection window, the cadavers remained intact so as not to disturb the nerve bed proximal or distal to the ankle. A dissection window (10 × 4 cm) was incised just proximal to the distal tip of the medial malleolus and the resulting skin flap was retracted posteriorly. The subcutaneous tissue was excised proximal to the flexor retinaculum and retracted posteriorly along with the skin flap. The deep fascia was excised to expose the neurovascular bundle comprised of the tibial nerve, posterior tibial artery, and posterior tibial vein. The neurovascular bundle was separated by blunt dissection in order to free the tibial nerve and allow visualization of the length of the nerve within the dissection window. The vascular components were retracted and with 'T-pins' fixated posteriorly unless the anatomical arrangement required an anterior fixation to allow a better view of the tibial nerve. In order to maintain visualization of the initial injection site, the site was marked with a coloured marker and a 'T-pin' was inserted in the intact tissue anterior to the injection site as an additional reference point (Fig. 2).

Dye injection procedure

The dye mixture was composed of plasma and Toluidine blue used in a previous investigation.⁵⁸



Figure 3 Dye injection (pilot study). The injection amount and method were piloted on embalmed cadavers. The amount of dye needed was determined by the ability to create a bolus without leaking from the nerve. The needle was injected just beneath the external epineurium.

The dye injection procedure was piloted using embalmed cadavers and the amount of dye injected was determined by the amount needed to reach the threshold of leakage through the injection site. Using a syringe and a 0.45 × 23 mm needle, the predetermined amount of dye (0.2 cc), was injected with steady, mild pressure just beneath the epineurium⁵⁹ of the tibial nerve, 5 cm proximal to the distal edge of the medial malleolus (Fig. 3). This bolus of fluid created an initial dye spread, which was measured proximally and distally by means of a digital caliper (Wiha Digimax 6' precision digital caliper; Wihatools.com LLC, Monticello, MN, USA). The point of measurement was determined by the most distinct border. Indistinct, barely visible borders were not considered to be reliable sites for measurements (Fig. 4).



Figure 4 Caliper measurements. The measurements were made by one investigator who was blinded to the digital reading. The average of three successive measurements at each 2-minute interval was recorded.



Figure 5 Neural mobilization was performed through 30 repetitions of ankle dorsiflexion/plantar flexion to end range.

Measurements

Once the initial dye spread was established, longitudinal dye spread was measured at 2-minute intervals until stabilized. In order to reduce measurement errors, dye spread measurements were taken three times and averaged. Stabilization was determined by successive 2-minute interval dye spread measurements that were within 0.5 mm of each other. Once the dye spread stabilized, the neurodynamic mobilization intervention was performed.

Intervention

Repeated passive ankle dorsiflexion and plantar flexion to end range were used as the neurodynamic mobilization intervention. This motion is a component of treatment for lower extremity nerve pathology.^{40,53} According to Butler,⁴⁰ the full range of motion corresponds to a grade three mobilization as described by Maitland. The intervention for this study consisted of 1 minute of passive ankle dorsiflexion/plantar flexion repetitions performed rhythmically at a rate of 30 repetitions per minute. The rhythm was maintained at a constant rate by means of a software metronome (TempoPerfect v1.02). This rate of movement was established to create a clinically applicable intervention parameter and maximize performance uniformity (Fig. 5).

Statistical analysis

Reliability

Intrarater reliability of caliper measurements was assessed with data collected from four repeated measurements of both limbs from two embalmed cadavers taken during two separate trials. These measurements were taken at 2-minute intervals, similar to the same time interval used for the final data collection. As in the final data collection, the investigator taking the measurements was blinded to the results of the caliper measurements. Data were analysed by means of intraclass correlation coefficient (ICC).

Descriptive data

The range, mean, standard deviation, and confidence intervals were determined for the length of the dye spread from the time of injection, at each 2-minute interval and post-mobilization. The same descriptive information was determined for the percent change in dye following intervention, total change in dye length, and total range of motion at the ankle.

Inferential statistics

Statistical analysis was performed using SPSS (v17.0). The independent variables were group (control versus experimental limbs) and time (pre-mobilization versus post-mobilization). The dependent variable was the amount of longitudinal dye dispersion. Because ankle range of motion has clinical application, the total amount of range (from dorsiflexion to plantar flexion) was considered to be a possible influencing factor (covariate). Therefore, inferential analysis was performed with an ANCOVA using range of motion as a covariate in pre- and post-intervention in each group (i.e. control and experimental conditions). In the event that the results were not significant, that is, range of motion was not determined to be a covariate, inferential analysis was pre-planned to proceed using 2×2 repeated measures ANOVA. Any interaction was further analysed using *t*-tests for *post hoc* pairwise comparison. Since the pre-test data had been normalized to have a common baseline, there was no need to analyse the pre-control versus pre-experimental grouping. The pairwise comparisons were made between the following groups of limbs: (1) pre-control versus post-control; (2) post-control versus post-experimental; and (3) pre-experimental versus post-experimental.

Results

The results showed significant mobilization effects in that there was increased fluid dispersion within the tibial nerve after the intervention. This significance was found with respect to time/intervention (experimental limb, pre- versus post-mobilization) as well as across groups (experimental versus control limb) post-mobilization (Fig. 6).

Reliability

Intrarater reliability for caliper measurements of dye dispersion using ICC was found to be 0.987 with a 95% confidence interval of 0.949–0.997.

Descriptive statistics

Following the intervention in the experimental leg, the dye spread ranged from 13.8 to 37.0 mm with a mean \pm SD of 23.8 ± 10.2 mm. In the absence of the intervention, but within the same time period, the measurements of the control leg ranged from 12.6 to 30.3 mm with a mean \pm SD of 20.7 ± 6.0 mm. The mean total movement of dye was -0.2 ± 0.7 mm in

Fluid Dispersion with Neurodynamic Mobilization

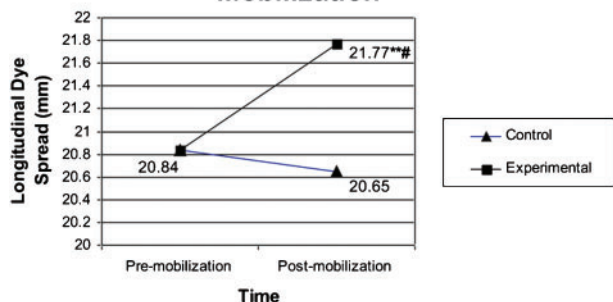


Figure 6 Mean fluid dispersion after mobilization. Statistical significance based on *t*-test results. At pre-test, the experimental group data were normalized to the control group data. ** $P \leq 0.05$, significantly different from pre-mobilization condition ($P=0.009$); # $P \leq 0.05$, significantly different from control group ($P=0.022$).****

the control leg and 0.9 ± 0.6 mm in the experimental leg (Table 2).

Inferential statistics

Owing to the variability of initial dye spread, the data were normalized in order to establish a standardized baseline (Table 3). According to the ANCOVA results, range of motion was not found to be a covariate. Therefore, as pre-planned, the effects of the intervention (repeated passive ankle dorsiflexion–plantar flexion to end range) were analysed by means of a repeated measures 2×2 ANOVA. The 2×2 ANOVA was found to be significant at $P \leq 0.022$ for interaction between groups (control and experimental) and time (pre- and post-mobilization). In order to clarify this interaction, subsequent *post hoc* pairwise analyses via *t*-tests were performed. No significance ($P \leq 0.539$) was found with analysis of the pre- and post-control group. The *t*-test analysis for the experimental group, pre- and post-test mobilization was significant ($P \leq 0.009$). Additionally, post-mobilization *t*-test comparing fluid dispersion between the

experimental group and control group was found to be significant ($P \leq 0.022$) (Table 4).

Discussion

Previous investigative studies of neurodynamic mobilization have focused on quantitative findings with respect to nerve mechanics during limb movement.^{29,30,34,60–62} While these studies provide valuable information regarding peripheral nerve movement and strain, they provide no insight into the mechanisms responsible for the benefits of using neurodynamic mobilization. Furthermore, no studies were found that address the effects of neurodynamic mobilization on nerves exhibiting pathophysiological responses such as impaired nerve conduction, ischemia, inhibited axonal transport, or intraneural edema.

The current study examined the effects of neurodynamic mobilization on intraneural edema in the cadaveric tibial nerve. The authors’ hypothesis that neurodynamic mobilization would induce fluid dispersion in the cadaveric tibial nerve at the ankle was supported by statistically significant dye dispersion after the mobilization. The dye in the control limb receded in three limbs and spread minimally in the other three, resulting in a ‘negative’ mean dye dispersion. It was surmised that without mechanical influence, the dye pooled due to the influence of gravity, and/or rebounded due to the change in pressure gradient after the injection. On the other hand, there was significant dye dispersion after the mobilization in the experimental limb indicating that there was a treatment effect due to the intervention. Comparison between the experimental limb and the control limb also produced significant results supporting the use of neurodynamic mobilization to induce fluid dispersion in the tibial nerve at the ankle.

The use of cadavers eliminated confounding physiological effects, such as changes due to blood

Table 2 Descriptive data

	Control leg			Experimental leg		
	Range	Mean \pm SD	95% confidence intervals	Range	Mean \pm SD	95% confidence intervals
Initial dye spread (mm)	6.6–29.5	17.1 \pm 8.5	10.3–23.9	10.1–33.6	20.9 \pm 9.6	13.2–28.6
Dye stabilized (mm)	13.8–29.7	20.8 \pm 5.6	15.0–26.7	12.1–36.2	22.9 \pm 10.5	11.9–33.8
Dye post-mobilization (mm)	12.6–30.3	20.7 \pm 6.0	14.4–26.9	13.8–37.0	23.8 \pm 10.2	13.1–34.5
Time to stabilize (min.)	10–22	14.0 \pm 4.4	10.5–17.5	10–16	13.0 \pm 2.1	11.3–14.7
Total length change (mm)	(–)1.2–0.6	(–)0.2 \pm 0.7	(–)0.7–0.4	0.3–1.6	0.9 \pm 0.6	0.5–1.4
Change post-mobilization (%)	(–)8.5–2.0	(–)1.5 \pm 3.9	(–)4.7–1.6	0.9–13.5	5.4 \pm 4.7	1.7 \pm 9.1
Total arc of motion	30–54°	38.7 \pm 6.3	32.1–45.2	23°–54°	41.3 \pm 10.7	30.1–52.6

Table 3 Normalized data

Cadaver	Control pre-mobilization (mm)	Control post-mobilization (mm)	Transformed experimental pre-mobilization (mm)	Transformed experimental post-mobilization (mm)
1	17.21	17.37	17.21	18.79
2	18.67	19.04	18.67	19.44
3	21.84	21.50	21.84	23.47
4	13.78	12.61	13.78	14.54
5	29.66	30.27	29.66	30.17
6	23.85	23.11	23.85	24.18
Mean	20.84	20.65	20.84	21.77
SD	5.58	5.96	5.58	5.40

Note: The pre-mobilization data were normalized by means of a constant determined by the difference between the stabilized (pre-mobilization) dye spread of the control and the experimental limbs. This established a standardized baseline. The constant was applied to the experimental limb in both pre- and post-mobilization measurements of dye spread. SD=standard deviation.

flow, axonal transport, or temperature, thus pointing to the purely mechanical effects of passive neural mobilization. Because the tibial nerve was dissected free of all adjacent tissue and eliminated any external interfaces, the response to the mobilization appeared to be due to intraneural mechanics.

The mechanisms responsible for the dye spread with mobilization may include fluid movement with intrafascicular gliding, and/or transverse contraction of the nerve as it lengthens.⁶³ Transverse contraction of the nerve results in an increase in intrafascicular pressure due to changes in volume.⁶³ During the mobilization technique, the tibial nerve alternately elongated and shortened which may have provided a temporary increase in intraneural pressure followed by a period of relaxation. Although speculative, it appears that this repetitive or 'pumping' action may have created a flushing of the dye and an alteration of the intraneural pressure as the intraneural fluid was dispersed.

The clinical importance of limiting intraneural pressure is supported by the results of studies that demonstrated the detrimental effects of increased levels of intraneural pressure on neural tissue.^{15,23} Maintaining healthy nerve function using neurodynamic techniques may occur by promoting uninterrupted axonal transport, thereby preventing deposition

of mechanosensitivity elements, the presence of which results in pain and limited neural movement.^{8,22} In the early stages of stretch injury or compression, the ability to prevent or at least reduce edema may prevent or slow the inhibition of blood flow,^{15,23} thus preventing the sequelae leading to impaired axonal transport,^{18,20} demyelination,^{11,24} loss of elasticity due to fibrosis or adhesions,^{46,63} and ultimately to alteration in nerve structure and function.^{19,24,27} The ability to promote fluid dispersion using range of motion may provide a means to break the cycle of edema formation leading to fibrosis,⁵⁰ which may in turn lead again to edema formation. These findings may be even more important when considering interventions for previously damaged nerves^{64,65,66,67} or nerves compromised by pathology such as diabetes.⁶⁸

In the current study, the limbs were positioned in hip and knee extension and the ankles were moved from plantar flexion to dorsiflexion in a manner that is consistent with the generally accepted position for performance of passive ankle range of motion in the clinic. It was assumed that the amount of strain reached at dorsiflexion was well within the limits of strain normally tolerated by the nerve.⁶⁹ Furthermore, the pressure created by normal elongation, which occurs during range of motion, was assumed to be well tolerated by the nerve.

Table 4 Inferential statistics

Test	Independent variables	F-Statistic	df	Effect size (partial eta squared)	Power	Statistical results ($P \leq 0.05$)
ANCOVA	Pre-control versus post-control	3.590	1	0.435	0.308	≤ 0.131
ANCOVA	Pre-experimental versus post-experimental	0.987	1	0.198	0.121	≤ 0.377
2 x 2 ANOVA (repeated measures)	Group [†] by time [‡] interaction	10.724	1	0.682	0.745	$\leq 0.022^{***}$
t-test	Pre-control versus post-control	0.435	1	0.08	0.084	≤ 0.539
t-test	Post-control versus post-experimental	10.724	1	0.682	0.745	$\leq 0.022^{***}$
t-test	Pre-experimental versus post-experimental	17.259	1	0.775	0.908	$\leq 0.009^{***}$

Note: *Group=control limb/experimental limb

[†]Time=pre-mobilization/post-mobilization

[‡]Significant at $P \leq 0.05$.

The ability to mechanically induce fluid dispersion by means of passive neurodynamic mobilization is a substantial finding as it sheds light on the physiological benefits of this technique that could ultimately influence neurophysiological function. Clinical conditions resulting in loss of active motion may prohibit more active participation in mobilization. This is especially important when endoneurial edema is present because of the limited physiological flushing or fluid dispersion due to the absence of an endoneurial lymphatic system.

The effects that gliding or compression from extraneural interfaces along the intact neurovascular bundle have on fluid dispersion are still unknown. A combination of the intraneural mechanical effects described in this study, along with extraneural mechanical and physiological effects may provide further collective beneficial effects on fluid dispersion in the nerve. Future studies should give consideration to examining the combination of the intraneural mechanical effects combined with extraneural effects. The effect of passive versus active neurodynamic mobilization also warrants investigation.

In vivo studies would be helpful in assessing the benefits of neurodynamic mobilization in both normal subjects and in those presenting with pathology. *In vivo* studies using diagnostic ultrasound (DUS) demonstrate that this type of imaging is a valid tool for use in measuring longitudinal and transverse movement of nerve tissue during neural mobilization.^{7,9,32,62,70} In addition, DUS has the ability to detect pathological changes in nerve morphology^{52,71,72} and can be useful in visualizing the structures within an osteofibrous tunnel.^{51,73} The ability of DUS to detect morphological changes as well as nerve movement makes this an excellent tool for further exploring the direct effects of neurodynamic mobilization on nerve tissue mechanics. Finally, limb position is an important consideration in the clinical use of neurodynamic mobilization as there is a mutual relationship between joint position and the amount of strain and excursion.^{29,34,60,61} Therefore, additional studies investigating various limb positions on fluid dispersion are warranted.

Limitations of this current study include the inability to generalize the findings to live subjects due to active physiological processes, the inability to completely generalize the results to other peripheral nerves or nerve roots, and the inability to generalize the findings to nerves exhibiting a loss of elasticity due to fibrosis or adhesions,^{46,63} which may alter the manner in which fluid is dispersed.

Conclusion

Passive mobilization in the form of ankle dorsiflexion and plantar flexion to end range induces a significant

increase in fluid dispersion in the tibial nerve of human cadaveric specimen. Neurodynamic mobilization may be beneficial in preserving nerve function by limiting intraneural fluid accumulation, thus preventing the adverse effects of intraneural edema.

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