

***In vitro* and *in vivo* mechanical properties of human ulnar and median nerves**

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Abstract: Peripheral nerves are often subjected to mechanical stretching, which in excess results in various degrees of impairment of their function. An understanding of the biomechanical behavior of peripheral nerves is important to the prevention of nerve injury during surgical manipulation. Here, *in vitro* mechanical properties and viscoelastic behavior of human ulnar/median nerves were measured with a tensile tester. *In vivo* stress and deformation of an ulnar nerve was also examined in continuity during a surgical procedure. Finite element models were developed to determine *in vitro* and *in vivo* viscoelastic parameters of the nerves.

The results show that *in vitro* mechanical properties of fresh ulnar nerve are different from those measured *in vivo*. Several factors that are possibly attributed to the difference were analyzed. The *in situ* strain of the nerves is one of the major factors that must be considered to obtain accurate strain–stress relationship in the *in vivo* measurement. © 2013 Wiley Periodicals, Inc. *J Biomed Mater Res Part A* 101A: 2718–2725, 2013.

Key Words: peripheral nerve, mechanical properties, finite element methods, hyperelastic, biomechanics

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INTRODUCTION

Carpal and cubital tunnel syndromes, affecting the median and ulnar nerves at the wrist and elbow respectively, are the most common nerve disorders in the peripheral nervous system. Other types of nerve entrapment affect the neck, shoulder, arm, hand, lower back, buttock, leg, and foot. Minor compression or tension to peripheral nerves can cause muscle weakness, sensory changes such as numbness and pain, while major injuries can result in a total loss of motor and sensory functions.^{1,2} Over 80 million people in the United States currently suffer from different degrees of nerve disorders and related diseases.³ Various treatments including physical therapy and orthopedic surgery have been used to treat such nerve injuries.⁴ One of the challenges faced by orthopedic surgeons during nerve surgery is the evaluation of the allowable magnitude of intraoperative nerve tension. The clinical effect of nerve elongation has been shown to depend upon both the magnitude and rate of lengthening.^{5–9} An abrupt traction on nerves can result in serious injury, while a nerve may function

normally if a slower stretching rate within certain limits is applied.^{10,11} However, the level of strain that a nerve can tolerate and the functional deficits that result from exceeding this threshold are not thoroughly understood yet. Characterizing the mechanical properties of peripheral nerves is the first step toward understanding the mechanisms of mechanical nerve injury and can be useful in improving patient diagnosis and treatment following nerve trauma. Relevant work has been done on describing the stress and strain of the peripheral nerves,^{12,13} and on finding the limits of elongation beyond which histological and functional changes in the nerve become irreversible.^{14–17} Little is known, however, about *in vivo* biomechanical properties of human peripheral nerves.

Finite element (FE) analysis provides an attractive, non-invasive mean to study the potential pathological contact stresses that may develop during nerve manipulation.¹⁸ Recently, FE methods have been widely used in the field of clinical medical research.^{19–22} For example, three-dimensional FE models of human foot were created to

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investigate the effects of insoles on foot plantar pressure redistributions.²¹ FE methods were also implemented to simulate the fluid pressure within the carpal tunnel and in median nerves,^{18,23} intraocular pressure and related stress within the optic nerve head,^{24,25} and injury in central nervous system.^{26,27} Based on computed tomography scan images, a three-dimensional FE model of the carpal tunnel modeled as a tunnel structure was constructed to study the effects of mechanical properties of the transverse carpal ligament on its morphological changes.²⁸ More recently, FE methods were applied to assess materials properties of tendons or nerves by matching experimentally measured data.^{29,30} Apparent hyperelastic coefficients (μ and α) for a first-order Ogden material property definition were extracted from experimental data in conjunction with an FE-based optimization routine to determine. The stress/pressure and the material properties determined with the help of FE models in these studies can be useful in better understanding the functional mechanics of soft tissues and possible mechanisms of peripheral nerve compressive insult, which may lead to the onset of nervous injury and diseases.

The aim of this study was to investigate and compare the mechanical properties of human ulnar nerves between *in vitro* and *in vivo* measurements. In the first step, ulnar and median nerves extracted from cadavers were tested on a tensile test machine. Next, the properties of an ulnar nerve were measured *in vivo* during surgical manipulation on a patient. Finally, FE models with parametric analysis were matched with experimental data to determine *in vitro* and *in vivo* material properties.

METHODS

Experimental measurements

All tissues used in this study were handled in strict accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals. The experimental protocol for human samples was approved by our Institutional Animal Care and Use Committee.

***In vitro* tensile test of ulnar/median nerves.** Median and ulnar nerves were harvested from cadavers (Fig. 1) and stored frozen at -20°C . Before testing, segments of the frozen nerve specimens were cut and thawed at room temperature (20°C). Two pieces of 40 mm long median and four pieces of 60 mm long ulnar nerve specimens were tested. Both ends of the samples were rigidly clamped and the clamp on one end was attached to a load cell (LSB200 Miniature S Beam, FUTEK Advanced Sensor Technology, Irvine, CA) and a motorized linear translation stage (MTS25X, THORLABS, Newton, NJ) with a motion resolution of 0.001mm (Fig. 2). The gauge length was approximately 44 mm for ulnar nerves and 22 mm for median nerves. A laser alignment tool was used to align the sample during clamping. Tensile tests were carried out on the ulnar nerves at a linear translational rate of 0.05 mm/s. Stress relaxation tests were carried out on the median nerves with an initial ramp up strain of 10% at a rate of 0.05 mm/s and the applied strain was held constant for about 250 s. Load and



FIGURE 1. An as-received sample of human ulnar nerve. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

displacement data were recorded in each measurement digitally by a computer at a rate of 10 Hz.³¹ To exclude the possible influence of external vibration, the tensile tester was installed on a vibration isolation platform (BM-8 Bench Top Vibration Isolation Platform, Minus K Technology, Inglewood, CA).

Intraoperative lengthening of ulnar nerve. Our clinical case involved repair and transposition of an injured ulnar nerve in an adult male. Several fascicles within the patient's ulnar nerve were damaged through a penetration of a sharp object. The aim of the surgery was to repair the epineurium with sutures so that the damaged fascicles could recover their function. The ulnar nerve of the patient was manipulated as required in such surgical procedure. The manipulation on the ulnar nerve under the *in vivo* condition was recorded using camera and video apparatus. The first step in the surgical procedure was to expose the ulnar nerve and separate it from connective tissues. A ruler was used to measure the major and minor diameters and the exposed length of the ulnar nerve. A silicon vessel loop (Blue Maxi Vessel Loop, Aspen Surgical, Caledonia, MI) was looped

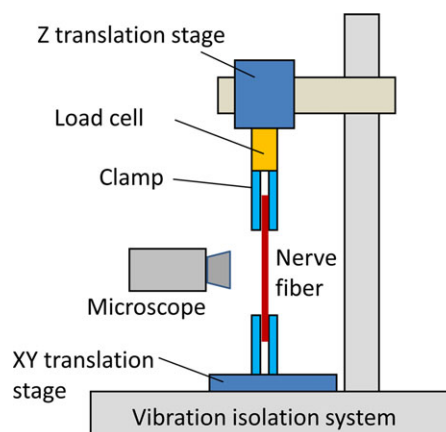


FIGURE 2. Schematic of experimental setup for tensile test of ulnar and median nerves. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

around the exposed nerve intraoperatively and secured with a pair of forceps. Lengthening a nerve through a vessel loop reduces the incidence of over stretching and the impact of possible high instantaneous applied force (e.g., stress concentration). Figure 3(a) schematically shows the lengthening of an ulnar nerve using a vessel loop during surgery. The displacement, δ [Fig. 3(b)], was measured during manipulation and used to calculate the stress in the never lengthening. The deformation of the vessel loop was also measured during the lengthening. The applied force, F [Fig. 3(b)], was obtained by subsequent calibration of the force-displacement curve of the vessel loop.

FE modeling

Three-dimensional FE models were created to simulate both *in vitro* and *in vivo* tensile characteristics of ulnar/median nerves. Because of the tissue incompressibility, the hybrid elements (with pressure as an additional variable) were chosen in ABAQUS (v6.9-1, Simulia, Providence, RI). An Ogden hyperelastic constitutive definition was adopted for describing the mechanical behaviors of the nerves.^{32–34} In this material model, strain energy W is a function of deviatoric principal stretches (λ_n):

$$W(\lambda_1, \lambda_2, \lambda_3) = \sum_{i=1}^N \frac{2\mu_i}{\alpha_i^2} (\lambda_1^{\alpha_i} + \lambda_2^{\alpha_i} + \lambda_3^{\alpha_i} - 3) \quad (1)$$

where the coefficients μ_i and α_i predominately reflect the low-strain slope and the higher strain curvature, respectively, of the resultant stress-strain curve.

To take viscoelasticity into account, the Ogden model was integrated with another suitable mathematical expression

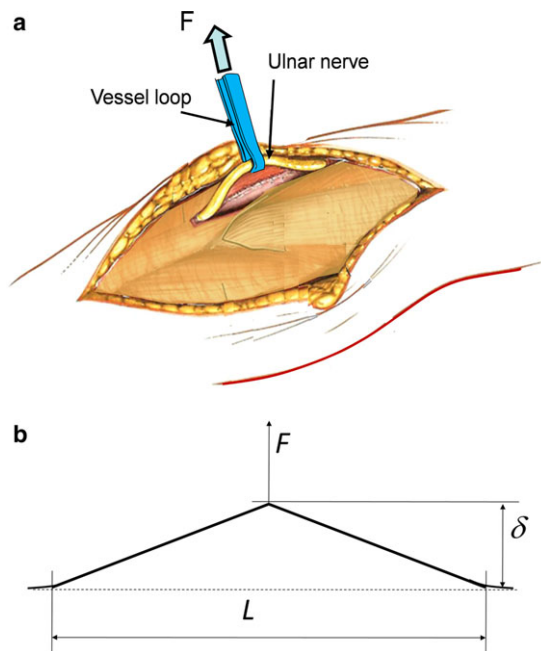


FIGURE 3. (a) Schematic of *in vivo* measurement of ulnar nerve by lengthening and (b) configuration of ulnar nerve during length. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com).]

such that the time effect is included, namely the stress relaxation (or creep) effects that all soft tissues exhibit over time when a certain load or deformation is exerted. In stress relaxation, the material stiffness is reduced over time when a deformation is kept constant. The most popular mathematical form of this behavior is given by the Prony series as^{25,35–37}:

$$\mu_i(t) = \mu_i^0 \left(1 - \sum_{i=1}^N g_i (1 - e^{-t/\tau_i}) \right) \quad (2)$$

where g_i is a material constant and τ_i is the relaxation time, $\mu_i(t)$ and μ_i^0 are the time dependent and the initial shear modulus, respectively. In this work, we have chosen the first-order Ogden and relaxation model of $N = 1$.

FE method was used to determine the coefficients in Eqs. (1) and (2) to best replicate the *in vitro* tensile behavior of each specimen (same lengths and diameters as measured *in vitro*). To this end, four provisional values for the Ogden hyperviscoelastic coefficients were loaded into an initial FE input file, run in ABAQUS, and the stress/strain data from the analysis were extracted from the FE output files. The FE results were interpolated so as to have stress values registered at identical strain values as recorded during the actual physical test. Then, using a least-squares nonlinear optimization function we made incremental adjustments to the coefficients to reduce the sum of the squared error between the experimental and interpolated FE stress values.

The *in vivo* lengthening of ulnar nerve was also simulated using ABAQUS. A FE model [Fig. 4(b)] was constructed based on the human anatomy of arms [Fig. 4(a)], the surgical images and the experimental measurement during lengthening procedure. Basically, in human anatomy, all of the nerves that travel down the arm pass through the *axilla* (the armpit) just under the shoulder joint. The ulnar nerve passes posterior to the medial humeral epicondyle and gives off branches to the elbow joint. It then passes under the arcuate ligament of osborne, and proceeds through the common origin of the exor and pronator muscles.²⁵ Figure 4(a) schematically shows the cross section of an upper arm in the middle of the arm. The ulnar nerve is surrounded by soft tissue and located at about 10 mm under the skin. In this study, the exposed part of ulnar nerve (about 56 mm in length) was located approximately in the middle of patient's upper arm. The total length of patient's upper arm from shoulder to elbow was about 300 mm, and the nerve in the upper arm was estimated to be 250 mm. We assume that the armpit and elbow (the nerve branching point) are two anchor points for the ulnar nerve, and the embedded length on each side of the exposed part is thus about 100 mm. In this study, utilizing symmetry, we modeled only one-half of the exposed nerve and connective tissue of the cubital tunnel. The FE model is composed of (i) an ulnar nerve with an elliptic cross-section (major diameter: $d_1 = 5$ mm and minor diameter $d_2 = 3.8$ mm), an exposed length of $l_1 = 28$ mm, and an embedded length of $l_2 = 100$ mm in the cubital tunnel and (ii) the soft surrounding tissue of whole upper arm with the bone area fixed. These data including the

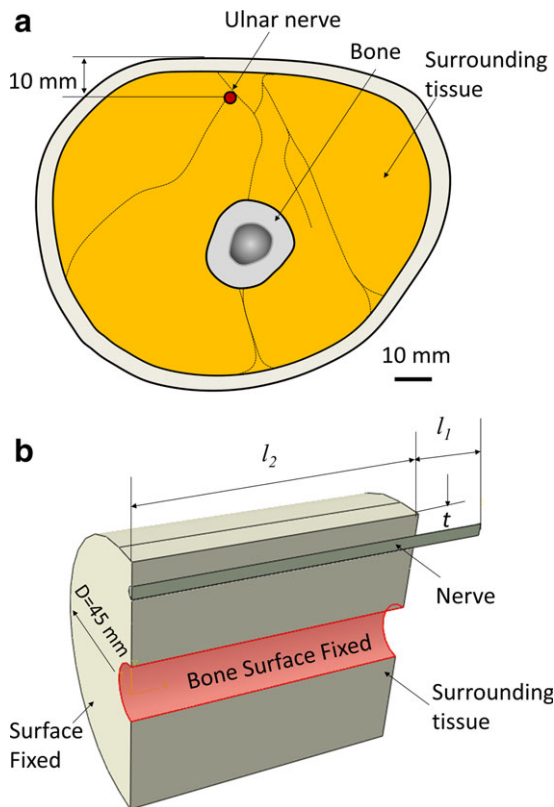


FIGURE 4. (a) Schematic of cross-section of human upper arm in the middle of the arm and (b) FE models of *in vivo* lengthening of ulnar nerve, constructed based on (a). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

elliptic cross-section and the exposed length were obtained from the surgical procedure. The bone was not explicitly modeled; instead, the surrounding tissue attached to it was fixed as a constraint boundary condition. The three-dimensional model had 18,200 elements: 1600 hexahedral solid elements for the nerve, and 16,600 hexahedral elements for the surrounding tissues. The ends of the tissue mesh were constrained against axial displacements along the original nerve axial direction during an analysis. This boundary condition is considered because the armpit and elbow act as two anchor points for the ulnar nerve. The contact between the nerve and the surrounding tissue was simulated using contact mode with a frictional coefficient of $m = 0.1$. The vessel loop was not explicitly modeled in this study. The ulnar nerve was directly tensioned by pulling up the nerve end under displacement-controlled boundary conditions. The total physical time simulated was 1.5 s, as did in lengthening procedure.

The Ogden hyperviscoelastic constitutive model was used to describe the intrinsic mechanical behaviors of the nerves. The mechanical properties of the surrounding tissue are important to accurately predict the behavior of the ulnar nerve. Since the surrounding tissues of carpal tunnel have been reported to follow the first-order Ogden hyperelastic constitutive definition,³⁰ for the purpose of this study, the same viscoelastic constitutive model was adopted for the surround-

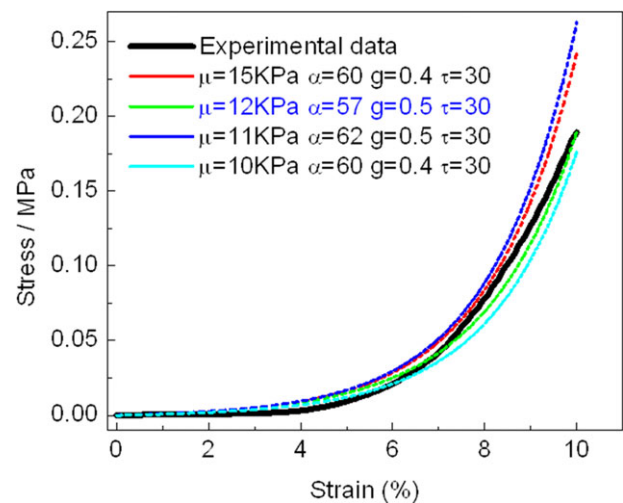


FIGURE 5. Stress-strain curves of human ulnar nerve and the fitting curves from FE analysis. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

ing tissues as that of carpal tunnel. The average values of Ogden coefficients for the carpal tunnel ($\mu = 36.0$ kPa, $\alpha = 9.14$)³⁰ were used for the surrounding tissue in this study.

RESULTS AND DISCUSSION

In vitro mechanical properties of ulnar/median nerves

A typical stress-strain curve of the *in vitro* tensile tests on ulnar nerve is shown in Figure 5 (i.e., experimental data). Both ulnar and median nerves exhibited strong hyperelastic and viscoelastic behaviors. During in-line tension, the stress was initially zero and increased rapidly as the strain increased beyond 6–8%. In the stress relaxation tests, the stress response in the initial ramp up stage was similar to those observed in tensile tests, while the stress in the nerve dropped rapidly at first and then gradually leveled off over time when displacement was held constant^{26,27} (Fig. 6).

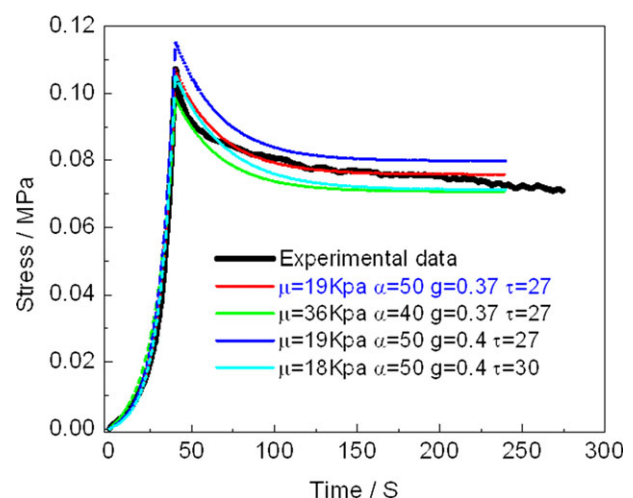


FIGURE 6. Tensile stress as a function of time during stretch-relaxation test of human median nerve and fitting curves by FE analysis. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

The material parameters of the ulnar and median nerves determined via the FE method gave visually acceptable fits to experimental data. Systematic changes were made for each individual coefficient while holding the others fixed, and then the error between the experimental and FE data associated with each individual coefficient was evaluated. Further adjustments were made to optimize all the coefficients until the error fell in an acceptable range. Some typical FE results during the fitting processes for in-line tension and stress relaxation tests were plotted in Figures 5 and 6, respectively. The material parameters that lead to a best fit of the experimental data are listed in Table I, and the mean parameters as determined by FE method for all the experimental results were shown in Figure 7. It is found that the *in vitro* modulus of the median nerve was higher than that of the ulnar nerve.

In vivo stress and strain on ulnar nerve

Figure 8(a) shows a digital image of human ulnar nerve during lengthening using a vessel loop in surgical procedure. In the clinical transposition, a pulling force of $F = 1.23$ N was applied through a vessel loop on the nerve with a gauge length of $L = 56$ mm, resulting in a lifting distance of $\delta = 8$ mm at the midpoint of the exposed ulnar nerve [Fig. 3(b)]. The pulling force F was calculated by measuring the deformation (strain) of the vessel loop during the lengthening. The lengthening was completed in about 1.5 s according to the video recording of the lengthening procedure. Under such loading condition, the stress and strain of the ulnar nerve can be determined based on the configuration shown in Figure 3(b) with an assumption that the two ends of the nerve are fixed at the exposed edges. The strain of the nerve was calculated by $\varepsilon = \sqrt{1 - (2\delta/L)^2} - 1$, whereas the stress in the nerve was determined by $\sigma = F/(A\sqrt{2})$, where A is the cross-sectional area of the nerve. A simple calculation shows that the applied stress and strain are 0.0583 MPa and 4.1%, respectively. The applied strain rate was thus approximately $2.73 \times 10^{-3} \text{ s}^{-1}$. This stress was over seven times higher than that measured in the *in vitro* experiment at the same strain (0.0082 MPa).

FE models, which accounted for deformation of surrounding tissue and possible slip of the nerve within the cubital tunnel in the upper arm, were used to simulate the *in vivo* lengthening process [Fig. 8(b)]. The *in vitro* material

TABLE I. Typical Mechanical Properties of Human Nerve, Calculated with FE Method by Fitting Experimental Results

	Modulus, μ (kPa)	Material Constant, α	Material Constant, g	Relaxation Time, τ (s)
Ulnar nerve (<i>in vitro</i>)	12	57	0.5	30
Median nerve (<i>in vitro</i>)	19	50	0.37	27
Ulnar nerve (<i>in vivo</i>)	54	57	0.5	30
Surrounding tissue ³⁰	36	9.14		

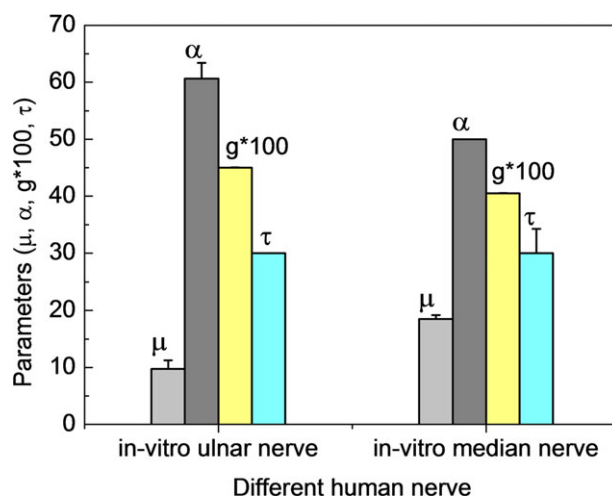


FIGURE 7. The mean and standard deviation of mechanical properties calculated with FE method by fitting experimental results (two pieces of 40 mm median and four pieces of 60 mm ulnar nerve specimens). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

properties of human ulnar nerve ($\mu = 12$ kPa, $\alpha = 57$, $g = 0.5$, and $\tau = 30$ s) and the surrounding tissue listed in Table I were used in the modeling. In this simulation, the nerve was pulled in the same way as in the experiment until the displacement at the midpoint reached the value of $\delta = 8$ mm as measured in the surgical procedure. The

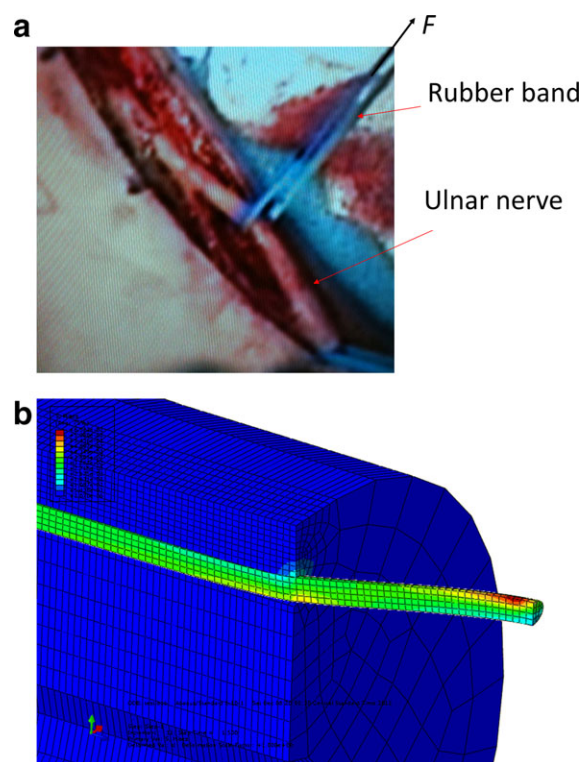


FIGURE 8. (a) Digital image showing lengthening of human ulnar nerve using silicon vessel loop during surgical operation and (b) the FE simulation result of the surgical operation process. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

pulling force derived from the simulation was $F = 0.16$ N, which was roughly eight times smaller than the real life data (i.e., $F = 1.23$ N).

The above discrepancy between the lengthening experiment and FE simulation is attributed to several factors including the *in situ* strain, the surrounding tissue, the applied boundary conditions, the frozen process, the injury, the moisture and temperature, and so forth. We first discuss the *in situ* strain of live nerves, which was not included in the current calculation. In fact, a normal peripheral nerve is always under tension in human body.^{10,11,28} With such *in situ* loading, the peripheral nerve can withstand a certain degree of stress and deformation without adverse effects during normal daily activities. The *in situ* strain corresponds approximately to the transition between the toe region and linear region of the stress-strain curve of the nerve.^{11,38} According to our *in vitro* tensile test data of human ulnar nerve, the *in situ* strain was determined to be about 6–8% in our case. We have recalculated the pulling force by introducing 7% *in situ* strain in the nerve in the lengthening simulation. Although the calculated force (0.36 N) was now closer to the experimental results, there was still a large difference between the prediction and experiment.

Other factors for the discrepancy could be related to the *in vivo* environment which is quite different from the *in vitro* testing. We have studied the effect of the frictional coefficient of the nerve against the tunnel wall, as well as the embedded length and shape of the nerve. There was no report on the frictional coefficient of human ulnar nerve against cubital tunnel wall. Measured frictional coefficient for human synovial joint bone was estimated to be 0.0032, while the frictional coefficient for human skin was measured in the order of 0.5.^{39,40} The embedded length of ulnar nerve could change from 75 to 125 mm, depending on the upper arm length. While the coefficient change from 0.1 to 0.5 results in an increase of 0.01% in the pulling force, respectively, the change of the embedded length from 75 to 125 mm leads to a variation of 0.02% in pulling force. In fact, the frictional coefficient of the ulnar nerve against cubital tunnel could be very low because of the existence of fluid that provides lubrication.¹¹ The nerve with a circular cross section but the same area as the elliptical one showed nearly the same pulling force as that for the elliptical nerve (difference <0.01%). Thus, the interfacial friction, embedded length and shape are not the dominant factors for the discrepancy. We also studied the influence of the materials properties of the surrounding tissue on the pulling force. It was reported that the modulus of the carpal tunnel varies from 24 to 42 kPa with an average value of 36 kPa, a nearly twofold change in material property.³⁰ Our simulation results show that the pulling force decreases by 14% when the modulus of the surrounding tissue reduces from 42 to 24 kPa. Thus, the FE simulation could introduce an error of $\pm 7\%$ for the estimate of nerve properties in the *in vivo* test. However, it is not the major factor responsible for the four time difference between the *in vivo* and *in vitro* measurement after the *in situ* strain is introduced.

The *in vivo* experiment was conducted on an injured nerve/tissue. Despite the patient's nerve injury was relatively subtle compared to diameter of the nerve, it may also be one of the factors that resulted in the above-mentioned difference. However, even if the injury weakened the nerve, the effect would make the apparent properties of the nerve closer to the *in vitro* measurement. Thus, it is concluded that the *in vivo* materials properties were different from those in the *in vitro* measurement. Similar *in vitro* and *in vivo* results were reported on peripheral nerves.^{11,41} Milesi et al. measured the mechanical properties of the nerve. They showed that measurements of the load necessary to achieve certain elongations on specimens outside the body did not correspond with *in situ* measurements. The necessary load was influenced by the presence or absence of branches and by the amount of fibrosis. Because of transverse contraction, elongation beyond a certain limit substantially decreases intrafascicular volume, leading to increased intrafascicular pressure.⁴¹ We have fitted the experimental *in vivo* pulling force, by changing one material coefficient while fixing the other three coefficients. The results are also listed in Table I. Although the material properties were different between *in vivo* and *in vitro* measurements, they were still in the same order of magnitude.

Because there are four parameters that define the mechanical behavior of the nerve, we studied the effect of each material parameter on the pulling force. In this parametric study, systematic changes were made to each individual coefficient while the others were fixed. The pulling force was then evaluated with the change of individual coefficients. Figure 9 shows the effect of different individual coefficient on the pulling force. Obviously among all these coefficients, modulus μ and material constant α were much more significant than material constant g and relaxation time τ . Because the time duration was short (1.5 s in this case), the viscoelastic material coefficients g and τ did not affect the pulling force very much. Therefore, it is

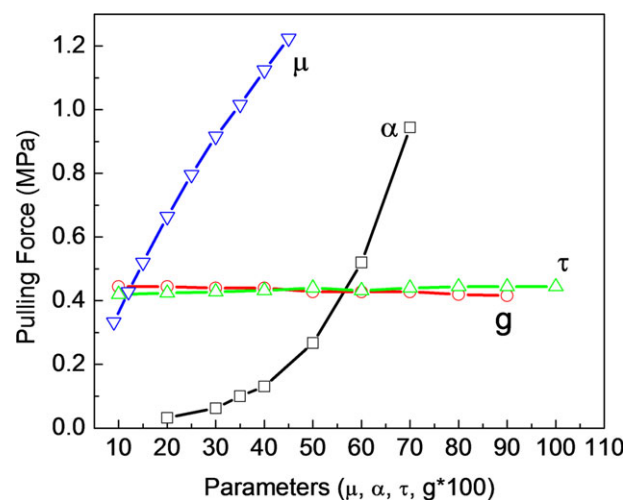


FIGURE 9. The effect of different individual coefficients (μ (kPa), α , τ (s), and g) on the pulling force. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

reasonable that nerve deformation during fast lengthening procedure can be described as hyperelastic materials without considering its viscoelastic properties.

CONCLUSIONS

Human ulnar and median nerves were tested to obtain *in vitro* and *in vivo* biomechanical properties, upon which a FE method was developed to extract the corresponding material parameters through a data fitting process. The experimental results showed that the ulnar and median nerves exhibited typical hyperelastic and viscoelastic properties as expected for biological tissues. Hyperviscoelastic material parameters derived from the *in vitro* measurements of ulnar and median nerves are comparable, while the corresponding parameters for the ulnar nerve during a surgical procedure has to be adjusted for matching with experiment, indicating nontrivial amount of variation had occurred after the nerve had been harvested from its local position. Although inconclusive, *in situ* strain, surrounding tissue and the defect of injured nerves do have a strong effect on the mechanical characteristics of *in vivo* nerves. A systematic parametric study was further carried out to fill up the gaps of the uncertainty and/or discrepancy in terms of material parameters. It shows that the ulnar nerve during fast lengthening procedure can be considered as hyperelastic materials without considering its viscoelastic properties.

REFERENCES

- Verdugo RJ, Salinas RA, Castillo JL, Cea JG. Surgical versus non-surgical treatment for carpal tunnel syndrome. *Cochrane Database Syst Rev* 2008;4:1–15.
- Robinson LR. Traumatic injury to peripheral nerves. *Muscle Nerve* 2000;23:863–873.
- MD Consult: Carpal Tunnel Syndrome: Comprehensive Version, May 12, 2009. <http://www.mdconsult.com/das/patient/body/173125082-2/0/10041/9479.html>.
- Campbell WW. Evaluation and management of peripheral nerve injury. *Clin Neurophysiol* 2008;119:1951–1965.
- Borschel GH, Kia KF, Kuzon WM, Dennis RG. Mechanical properties of acellular peripheral nerve. *J Surg Res* 2003;114:133–139.
- Fiford RJ, Bilston LE. The mechanical properties of rat spinal cord *in vitro*. *J Biomech* 2005;38:1509–1515.
- George GA, Walbeehm ET, Tillett R, Afoke A, Brown RA, Phillips JB. Investigating the mechanical shear-plane between core and sheath elements of peripheral nerves. *Cell Tissue Res* 2005;320:229–234.
- Li J, Shi R. Stretch-induced nerve conduction deficits in guinea pig *ex vivo* nerve. *J Biomech* 2007;40:569–578.
- Tillett RL, Afoke A, Hall SM, Brown RA, Phillips JB. Investigating mechanical behavior at a core-sheath interface in peripheral nerve. *J Peripher Nerv Syst* 2004;9:255–262.
- Bueno FR, Shah SB. Implications of tensile loading for the tissue engineering of nerves. *Tissue Eng B* 2008;14:219–233.
- Topp KS, Boyd BS. Structure and biomechanics of peripheral nerves: Nerve responses to physical stresses and implications for physical therapist practice. *Phys Ther* 2006;86:92–109.
- Chen RJ, Lin CCK, Ju MS. *In situ* biomechanical properties of normal and diabetic nerves: An efficient quasi-linear viscoelastic approach. *J Biomech* 2010;43:1118–1124.
- Haftek J. Stretch injury of peripheral nerve. *J Bone Joint Surg* 1970;52B:354–365.
- Babbage CS, Coppieters MW, McGowan CM. Strain and excursion of the sciatic nerve in the dog: Biomechanical considerations in the development of a clinical test for increased neural mechanosensitivity. *Vet J* 2007;174:330–336.
- Byl C, Puttlitz C, Byl N, Lotz J, Topp K. Strain in the median and ulnar nerves during upper-extremity positioning. *J Hand Surg Am* 2002;27:1032–1040.
- Li J, Shi R. A device for the electrophysiological recording of peripheral nerves in response to stretch. *J Neurosci Methods* 2006;154:101–108.
- Singh A, Lu Y, Chen C, Cavanaugh JM. Mechanical properties of spinal nerve roots subjected to tension at different strain rates. *J Biomech* 2006;39:1669–1676.
- Ko C, Brown TD. A fluid-immersed multi-body contact finite element formulation for median nerve stress in the carpal tunnel. *Comput Methods Biomech Biomed Eng* 2007;10:343–349.
- Bellezza AJ, Hart RT, Burgoyne CF. The optic nerve head as a biomechanical structure: Initial finite element modeling. *Invest Ophthalmol Vis Sci* 2000;41:2991–3000.
- Chen DT, Zeltzer D. Pump it up: Computer animation of a biomechanically based model of muscle using the finite element method. *Comput Graphics* 1992;26:89–98.
- Chen WP, Ju CW, Tang FT. Effects of total contact insoles on the plantar stress redistribution: A finite element analysis. *Clin Biomech* 2003;18:S17–S24.
- Sigal IA, Flanagan JG, Tertinegg I, Etbier CR. Finite element modeling of optic nerve head biomechanics. *Invest Ophthalmol Vis Sci* 2004;45:4378–4387.
- Myers RR, Murakami H, Powell HC. Reduced nerve blood flow in edematous neuropathies: A biomechanical mechanism. *Microvasc Res* 1986;32:145–151.
- Loocke MV, Lyons CG, Simms CK. Viscoelastic properties of passive skeletal muscle in compression: Stress-relaxation behavior and constitutive modeling. *J Biomech* 2008;41:1555–1566.
- Gonzalez MH, Lotfi P, Bendre A, Mandelbroyt Y, Lieska N. The ulnar nerve at the elbow and its local branching: An anatomic study. *J Hand Surg Br* 2001;26B:142–144.
- Wall EJ, Kwan MK, Rydevik BL, Woo SL, Garfin SR. Stress relaxation of a peripheral nerve. *J Hand Surg Am* 1991;16:859–863.
- Toby EB, Rotramel J, Jayaraman G, Struthers A. Changes in the stress relaxation properties of peripheral nerve after transection. *J Hand Surg Am* 1999;24:694–699.
- Kwan MK, Wall EJ, Massie J, Garfin SR. Strain, stress and stretch of peripheral nerve. *Acta Orthop Scand* 1992;63:267–272.
- Henderson J, Thoreson A, Yoshii Y, Zhao KD, Amadio PC, An KN. Finite element model of subsynovial connective tissue deformation due to tendon excursion in the human carpal tunnel. *J Biomech* 2011;44:150–155.
- Main EK, Goetz JE, Rudert MJ, Goreham-Voss CM, Brown TD. Apparent transverse compressive material properties of the digital flexor tendons and the median nerve in the carpal tunnel. *J Biomech* 2011;44:863–868.
- Abrahams M. Mechanical behavior of tendon *in vitro*. *Med Boil Eng* 1967;5:433–443.
- Nicholson DW, Nelson NW, Lin B, Farinella A. Finite element analysis of hyperelastic components. *Appl Mech Rev* 1998;51:303–320.
- Beda T. Modeling hyperelastic behavior of rubber: A novel invariant-based and a review of constitutive models. *J Polym Sci Part B: Polym Phys* 2007;45:1713–1732.
- Li-Rong W, Zhen-Hua L. Modeling method of constitutive law of rubber hyperelasticity based on finite element simulations. *Rubber Chem Technol* 2003;76:271–285.
- Ghoreishy MHR. Determination of the parameters of the Pony series in hyper-viscoelastic materials models using the finite element method. *Mater Design* 2012;35:791–797.
- Park SW, Schapery RA. Methods of interconversion between linear viscoelastic material functions. Part I—A numerical method based on Prony series. *Int J Solids Struct* 1999;36:1653–1675.
- Singh R, Davies P, Bajaj AK. Estimation of the dynamical properties of polyurethane foam through use of Prony series. *J Sound Vib* 2003;264:1005–1043.
- Layton BE, Sastry AM. A mechanical model for collagen fibril load sharing in peripheral nerve of diabetic and nondiabetic rats. *J Biomech Eng* 2004;126:803–814.
- Fung YC. *Biomechanics: Mechanical Properties of Living Tissue*. Berlin, Germany: Springer; 1981.

40. Zhang M, Mak AFT. In vivo friction properties of human skin. *Prosthet Orthot Int* 1999;23:135–141.
41. Millesi H, Zöch G, Reihnsner R. Mechanical properties of peripheral nerves. *Clin Orthop Relat Res* 1995;314:76–83.
42. Bellezza AJ, Hart RT, Burgoyne CF. The optic nerve head as a biomechanical structure: initial finite element modeling. *Invest Ophthalmol Vis Sci* 2000;41:2991–3000.
43. Sigal IA, Flanagan JG, Tertinegg I, Ethier CR. Finite element modeling of optic nerve head biomechanics. *Invest Ophthalmol Vis Sci* 2004;45:4378–4387.
44. Maikos JT, Qian Z, Metaxas D, Shreiber DI. Finite element analysis of spinal cord injury in the rat. *J Neurotrauma* 2008;25:795–816.
45. Miller K, Chinzei K, Orssengo G, Bednarz P. Mechanical properties of brain tissue in-vivo: Experiment and computer simulation. *J Biomechanics* 2000;33:1369–1376.
46. Guo X, Fan Y, Li Z-M. Three dimensional finite element analysis on the morphological change of the transverse carpal ligament. In: *IEEE/ICME International Conference on Complex Medical Engineering, CME 2007, Beijing; 2007*. p 1866–1869.