Published in final edited form as:

PM R. 2010 July ; 2(7): 642–646. doi:10.1016/j.pmrj.2010.05.002.

Comparison of surface and ultrasound localization to identify forearm flexor muscles for botulinum toxin injections

M. Kristi Henzel, MD, PhD¹, Michael C. Munin, MD¹, Christian Niyonkuru, MS¹, Elizabeth R. Skidmore, PhD^{1,2}, Douglas J. Weber, PhD^{1,3}, and Ross D. Zafonte, DO⁴

¹Department of Physical Medicine and Rehabilitation, University of Pittsburgh School of Medicine

²Department of Occupational Therapy, University of Pittsburgh

³Department of Bioengineering, University of Pittsburgh

⁴Department of Physical Medicine and Rehabilitation, Harvard Medical School

Abstract

Objective—To determine if ultrasound (US) localization is equivalent to surface landmark localization to identify botulinum toxin (Btx) injection targets for forearm muscle spasticity.

Design—Observational

Setting—Outpatient spasticity clinic in a tertiary care center.

Subjects—18 patients with upper extremity flexor spasticity interfering with function were included. Individuals with severe fixed contractures or traumatic injury of the involved forearm were excluded.

Methods—Flexor pollicis longus (FPL), flexor carpi radialis (FCR), pronator teres (PT) and flexor digitorum superficialis (FDS) were identified by 2 separate localization techniques: the method of Delagi and Perotto for FCR, PT and FPL, and a surface landmark technique by Bickerton to identify the 4 muscle bellies of FDS. Proximodistal and lateral (radial) coordinates were recorded relative to a landmark line (LL) from the medial epicondyle to pisiform bone and percentage of LL distance was calculated. After surface measurements were collected, the best point for injection was determined using real time US with a 12 MHz linear transducer. US measurements were recorded using the same LL system.

Results—Localization techniques were compared using the Wilcoxon Signed Ranks Test. One-sample t-tests compared surface mapped lateral coordinates to ultrasound derived lateral coordinates with controls for multiple testing. Significant differences were observed between surface and ultrasound proximodistal and lateral coordinates for several flexor muscles.

Corresponding Author: Michael C. Munin, MD, Kaufmann Building, Suite 201, 3471 Fifth Avenue, Pittsburgh, PA 15213, Phone: (412) 648-6848, Fax: (412) 692-4410, muninmc@upmc.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Presented in part: AANEM Annual Scientific Meeting, September 2008, Providence, RI

Device Status: There are no novel medical devices used in this study.

Conclusions—Ultrasound should be considered as an adjunct for localization in patients with upper limb spasticity. US can improve accuracy of toxin placement and help to avoid injection into vascular and nerve structures.

Keywords

Ultrasonography; forearm; botulinum toxin; muscle spasticity

Introduction

Upper limb flexor hypertonicity often involves several key muscles that place the wrist in flexion and the fingers in a fist position.^{1,2} Specifically, forearm spastic postures are often driven by hypertonicity within the flexor digitorum superficialis (FDS), flexor digitorum profundus (FDP), flexor pollicis longus (FPL), flexor carpi radialis (FCR) and pronator teres (PT). Chemodenervation of these muscles with botulinum toxin (Btx) can lead to a dose-dependent decrease in muscle spasticity and strength. Although several previous studies have shown that treatment with Btx alone is effective in reducing spasticity after stroke, improvements in upper limb motor function in moderately to severely impaired chronic stroke survivors were not reported or not significant.^{3,4,5,6}

The reasons are unclear why function did not improve as anticipated in Btx studies treating upper limb flexor spasticity. Possible mechanical causes of failure include inaccurate localization of target muscles and unanticipated spread of toxin to non-targeted muscles, although other disease specific mechanisms interfering with functional recovery may exist. The accuracy of EMG needle placement in cadavers using surface landmark localization and blind needle placement can be unreliable,⁷ particularly in smaller or deeper muscles.⁸ If toxin is not delivered accurately within the fascial sheath of targeted muscles, there may be spread which could cause unanticipated weakness in adjacent muscles and suboptimal dosing in targeted muscles. We speculate that inaccurate targeting of involved spastic muscles, particularly in the forearm where many muscles overlap, may contribute to lack of functional gains with treatment.

Physicians have traditionally used several methods to locate targeted muscles for Btx injection including surface anatomy, electromyography (EMG) with surface anatomic landmarks guiding electrode placement and motor nerve branch stimulation.^{3,9,10} EMG alone is able to identify only whether a muscle is contracting or if the needle is localized in muscle tissue. When multiple muscles are adjacent, some superficial and some deep as in the forearm, it is easy for the EMG needle to pass through the target muscle into an adjacent muscle if both are active. Needle stimulation of motor branches requires deep probing of forearm muscles that is painful and does not avoid spread of toxin during blind injections through muscle fascial borders.

Musculoskeletal ultrasound guidance (US) has been used to deliver precisely localized Btx injections in pediatric lower limb and upper limb muscles,^{11, 12, 13} as well as the head and neck of adults with thoracic outlet syndrome.¹⁴ Recently, ultrasound guided Btx-injections to the gastrocnemius in children with cerebral palsy were found to improve gait patterns and hind foot positioning during stance, suggesting that this localization method may improve

function.¹⁵ However, application of ultrasound guidance to Btx injections in the upper limb in adults with spasticity has not been studied. US has the potential to provide real time imaging during injections and to identify fascial borders to minimize direct spread of toxin; these advantages may optimize the reduction in spasticity and increase functional gains. It may also prevent accidental injection into subcutaneous fat, tendon or fibrotic tissue, and help avoid complications such as injury to nerves or intravascular injections. This technique could also prove useful in patients who have mild restriction in forearm supination due to spasticity that limits ideal positioning.

As a first step to better understand the accuracy of Btx injections, our objective was to compare surface landmark localization using published techniques to US localization for identification of key spastic muscles in the forearm. Our initial hypothesis was that use of ultrasound guidance for muscle localization would yield different injection points when compared to surface landmark localization.

Methods

Participants with upper extremity flexor spasticity that interfered with function were part of a larger IRB-approved spasticity treatment study using Btx. Individuals with severe fixed contractures or traumatic injuries to the involved forearm were excluded. Prior to Btx injection, Modified Ashworth Scale (MAS) were recorded to document the degree of spasticity, with values greater or equal than 2 for all subjects at both the wrist and fingers.¹⁶

Muscles targeted for injection in this study included FPL, FCR, PT, and FDS which were identified by 2 separate surface landmark techniques and ultrasound. In each method, the arm was positioned with the shoulder abducted approximately forty-five degrees and the elbow extended to neutral. The forearm was then placed in full (or the maximum available degrees) supination. This positioning was feasible for all subjects since those with significant contractures were excluded.

Surface identification of the FCR, PT and FPL was performed using fingerbreadth measurements per the method of Delagi and Perotto,¹⁷ and a single skin mark was placed for each muscle. Per this method, the FCR injection site is located three to four fingerbreadths distal to the midpoint of a line connecting the medial epicondyle and the biceps tendon. The PT site is located two fingerbreadths distal to the midpoint of a line connecting the medial epicondyle and biceps tendon. Finally, the FPL site is marked volar to the radius at the halfway point of the forearm longitudinally from antecubital fossa to radial styloid.

The 4 muscle bellies of FDS were marked using a surface landmark technique by Bickerton,¹⁸ that was validated previously,¹⁹ to determine the optimal injection site for each belly. First, a landmark line (LL) was drawn from the medial epicondyle (starting point) to pisiform bone (distal point). Next, measuring perpendicularly to the LL, the FDS2 muscle belly is localized 14mm lateral to the proximodistal point measured at 72% of the distance along the LL (%LL) from the medial epicondyle. Similarly, FDS3 is localized 17mm lateral to the 54%LL point, FDS4 is localized 7mm lateral to the 49%LL point, and FDS5 6mm lateral to the 76%LL point. To record these measurements in a standardized protocol, we

used the same landmark line (LL) and recorded proximodistal measurements in centimeters along the LL for each identified muscle. Then, we measured lateral (radial) coordinates in millimeters perpendicularly from the proximodistal mark for each muscle.¹⁸ In this way, each injection site had a proximodistal and radial coordinate that could be accurately recorded. We also calculated the percentage of LL distance for proximodistal measurements to normalize the data for forearm length, although we did not normalize the radial coordinate per the methodology of Bickerton.¹⁸

After surface measurements were collected, the skin marks were removed and real time US (using a 12 MHz linear transducer) was performed by an experienced clinician board certified in physical medicine and rehabilitation and electrodiagnostic medicine, with training and over four years of clinical experience in neuromuscular ultrasound. We determined our “optimal injection site” to be the transverse (axial) view where the largest cross sectional area of the target muscle was visualized with minimal intervening muscles to permit the most direct injection path that also avoided neurovascular structures. Gentle passive movements were incorporated to help identify the target muscle. Skin was then marked and US measurements were recorded using the same LL system, as shown in Figure 1.

Localization techniques were compared using the Wilcoxon Signed Ranks Test. For muscles (FDS2, FDS3, FDS4, and FDS5) where the surface mapped lateral coordinates were the same per protocol for all subjects, we used one-sample t-tests to compare to ultrasound derived lateral coordinates. We examined the correlation between the amount of spasticity as measured by MAS and the difference between the mapped and ultrasound coordinates using the Spearman Rho correlation. We controlled for multiple testing²⁰ and analyses were done using SPSS 16 statistical software. A p-value of 0.05 was used for statistical significance.

Results

Eighteen subjects (7 male and 11 female) were $46 \text{ years} \pm 14$ and the average time since injury was 7 years. Causes of spasticity included hemorrhagic stroke ($n=1$), traumatic brain injury ($n=4$), thrombotic stroke ($n=10$) and other ($n=3$). Seventeen subjects had lesions that affected cortical regions and one was subcortical, with the right brain affected in 55.6% of subjects ($n=10$). MAS mean scores ($\pm$ standard deviation) were 2.6 ± 1.2 for elbow flexion, 2.8 ± 1.0 for the wrist flexors, 2.7 ± 0.90 for the finger flexors, and 1.6 ± 0.70 for thumb flexion.

Coordinates (mean $\pm$ standard deviation) of the injection site for each muscle as determined by ultrasound and surface localization are shown in Table 1 as proximodistal coordinates (in cm), with lateral coordinates (in mm) shown in Table 2. For the sample, US measurements revealed the following coordinates for the “optimal injection site,” expressed as %LL and lateral coordinates (mm): FCR (34.5%, 22), PT (36.4%, 39), FPL (64.4%, 39), FDS2 (69.0%, 15), FDS3 (54.7%, 20), FDS4 (50.4%, 9), and FDS5 (74.6%, 6).

The US coordinates were then compared to surface localization points for each muscle to see if there were significant differences between localization techniques. Significant

differences were observed between surface and US proximodistal coordinates for FPL ($p = 0.042$), PT ($p = 0.003$), and FCR trended towards significance ($p = 0.066$). For lateral coordinates, there were significant differences for FDS3 ($p = 0.011$) and FCR ($p = 0.022$). FDS2 and FDS4 trended towards significance ($p = 0.053$ and 0.088 , respectively). There were no significant correlations between spasticity and ultrasound deviations from the mapped coordinates.

During injection of Btx (performed as part of a larger study), we were able to verify that the US-selected muscle insertion points provided direct needle access to the target muscles. US-guided Btx injections were performed using the axial view where the real-time injection of toxin appears as an echogenic “blush,” or cloud in the muscle belly. A representative example of this injection technique is presented in Figure 2.

Discussion

Our data showed that US located certain forearm muscles at distinctly different points compared to those derived by surface measurements in patients with upper limb spasticity. Several factors may contribute to these differences. First, surface measurements using landmarks or fingerbreadths, which were originally based on cadaveric studies of normal individuals, may be inaccurate due to difficulty placing patients with spasticity in full supination and extension. Second, use of cadaveric specimens to determine surface localization points may have produced inaccurate measurements due to inherent problems with specimen dehydration and altered tissue resilience. Finally, in patients with spasticity, the typical three-dimensional structure of the forearm may be distorted or obscured due to severe muscle atrophy and fibrotic tissue replacing muscle.²⁴ These difficulties may be abated by the use of US localization for injections.

US localized the most direct injection to the PT laterally near its insertion at approximately 1/3 of forearm length. At the surface landmarked PT location¹⁷ distal to the midpoint between the biceps tendon and medial epicondyle, too many other muscles such as FDS, FDP, FCR, palmaris longus and flexor carpi ulnaris cross into view on ultrasound imaging. Optimal FPL location visualized using US was more distal than the middle of forearm used in surface measurements and avoided puncturing the radial artery.¹⁷ US showed that FCR was more accessible slightly more distal and lateral than surface landmarks suggest. Surface mapping of the FDS was accurate for all proximodistal measurements but we noted that FDS3 was located more laterally than previously described¹⁹ with FDS2 also trending similarly in a lateral direction.

Therapeutic benefit with Btx injections is based not only on accurate injection that stays within the muscle fascia, but also where the terminal nerve enters the muscle to maximize the number of endplates blocked.^{21, 22, 23} Muscles such as FDS are complex with 4 separate bellies with a large distribution of nerve branching points when measured as a percentage of forearm length. Interestingly, the FDS US locations are very close to anatomical dissections of nerve end twigs for the middle branch (45% to 63% forearm length) and distal branch (63% to 72%) of this muscle.^{21,22} FCR and FPL US locations also correlate with anatomic dissections showing highest density of nerve endings between 26% and 45% forearm length

and 46% to 80% length respectively.²³ PT is the only muscle where US visualization differs slightly from anatomical locations of terminal nerve endings (9% to 35% forearm length).²³

Ultrasound guidance may be especially useful if patient anatomy is challenging. For example, when using the surface landmark techniques of Perotto and Delagi, injection of FPL requires penetration of both FCR and FDS. Likewise, when targeting FCR, inserting too deeply will reach FPL and FDS and too laterally will reach PT. Additionally, EMG guidance will not identify which muscle is active if all are spastic, therefore US can provide useful feedback if targeting a particular forearm muscle to achieve clinical goals. During an injection, US can ensure that the injectate stays within the fascial borders and that the needle tip does not inadvertently go deeper or penetrate neurovascular structures. An additional benefit to US localization is less pain due to decreased blind probing of the EMG needle while searching for a targeted muscle or nerve.

Limitations of this technique include increased muscle echo intensity from fat and connective tissue replacement in patients with longstanding spasticity that could hinder muscle identification.²⁴ While severe muscle atrophy or increased echogenicity may cause difficulty with US localization, we suspect that when combined with EMG-guidance, this technique gives much better likelihood of targeting the desired muscle than surface landmarking with EMG-guidance due to the ability to determine muscle thickness and depth of needle penetration using US. However, determining whether or not US-guided toxin injection results in improved function will require a randomized controlled trial.

Supplemental training in neuromuscular US is needed in addition to the cost of purchasing a machine. There is a learning curve to ensure that the needle is placed under the US beam during the injection to maintain visibility, especially for deeper structures. Typically the assistance of another person to help position the limb and equipment is required. Finally, in our experience, the inclusion of US guidance may add 5 to 10 minutes to the average Btx injection visit; this may be a limiting factor for some busy clinics.

Conclusions

Our data suggests that US should be considered as an adjunct for localization in patients with upper limb spasticity. In addition, use of US may help avoid injection into vascular and nerve structures and minimize spread of toxin outside the targeted muscle belly. It remains unclear whether use of US guidance to deliver this medication makes a difference in decreasing spasticity or improving functional recovery. Therefore, future studies comparing functional improvement after toxin administration by US and surface landmark localization are required to determine best practice guidelines. Given that Btx injections for upper limb spasticity will likely become more common now that FDA indications are approved, it is imperative that techniques to ensure optimal drug delivery are established by evidence-based studies.

Acknowledgments

Funding Support: Supported in part by an unrestricted research grant from Allergan, Inc.. (MCM, CN, ERS, DJW) and the National Institutes of Health (ERS; K12 HD055931).

References

1. Watkins CL, Leathley MJ, Gregson JM, Moore AP, Smith TL, Sharma AK. Prevalence of spasticity post stroke. *Clin Rehabil.* 2002; 16:515–522. [PubMed: 12194622]
2. Lundström E, Terént A, Borg J. Prevalence of disabling spasticity 1 year after first-ever stroke. *Eur J Neurol.* 2008; 15:533–539. [PubMed: 18355307]
3. Chin TYP, Nattrass GR, Selber P, Graham K. Accuracy of intramuscular injection of Botulinum toxin A in juvenile cerebral palsy. *J Pediatr Orthop.* 2005; 25:286–291. [PubMed: 15832139]
4. Sheean GL. Botulinum treatment of spasticity: why is it so difficult to show a functional benefit? *Curr Opin Neurol.* 2001; 14(6):771–776. [PubMed: 11723387]
5. Smith SJ, Ellis E, White S, Moore AP. A double-blind placebo-controlled study of botulinum toxin in upper limb spasticity after stroke or head injury. *Clin Rehabil.* 2000; 14(1):5–13. [PubMed: 10688339]
6. Simpson DM, Alexander DN, O'Brien CF, Tagliati M, Aswad AS, Leon JM, et al. Botulinum toxin type A in the treatment of upper extremity spasticity: a randomized, double-blind, placebo-controlled trial. *Neurology.* 1996; 46(5):1306–1310. [PubMed: 8628472]
7. Haig AJ, Goodmurphy CW, Harris AR, Ruiz AP, Etemad J. The accuracy of needle placement in lower limb muscles: a blinded study. *Arch Phys Med Rehabil.* 2003; 84(6):877–882. [PubMed: 12808542]
8. Goodmurphy C, Chiodo A, Haig A. The accuracy of needle placement in extremity muscles: a blinded study. *J Clin Neurophysiol.* 2007; 24(4):366–378. [PubMed: 17938608]
9. Gracies JM, Lugassy M, Weisz D, Vecchio M, Flannagan S, Simpson DM. Botulinum toxin dilution and endplate targeting in spasticity: a double-blind controlled study. *Arch Phys Med Rehabil.* 2009; 90:9–16. [PubMed: 19154823]
10. Francisco GE, Boake C, Vaughn A. Botulinum toxin in upper limb spasticity after acquired brain injury: a randomized trial comparing dilution techniques. *Am J Phys Med Rehabil.* 2002; 81:355–363. [PubMed: 11964576]
11. Berweck S, Feldkamp A, Francke A, Nehles J, Schwerin A, Heinen F. Sonography-guided injection of botulinum toxin A in children with cerebral palsy. *Neuropediatrics.* 2002; 33:221–223. [PubMed: 12368994]
12. Oddy MJ, Brown C, Mistry R, Eastwood DM. Botulinum toxin injection site localization for the tibialis posterior muscle. *J Pediatr Orthop B.* 2006; 15:414–417. [PubMed: 17001247]
13. Depedibi R, Unlü E, Cevikol A, Akkaya T, Cakci A, Cerekçi R, Köse G, Unlüsoy D. Ultrasound-guided botulinum toxin type A injection to the iliopsoas muscle in the management of children with cerebral palsy. *NeuroRehabilitation.* 2008; 23(3):199–205. [PubMed: 18560136]
14. Jordan SE, Ahn SS, Gelabert HA. Combining ultrasonography and electromyography for botulinum chemodenervation treatment of thoracic outlet syndrome: comparison with fluoroscopy and electromyography guidance. *Pain Physician.* 2007; 10(4):541–546. [PubMed: 17660852]
15. Kwon, Jeong-Yi, MD, PhD, Hwang, Ji Hye, MD, PhD, Kim, Joon-Sung, MD, PhD. Botulinum Toxin A Injection into Calf Muscles for Treatment of Spastic Equinus in Cerebral Palsy: A Controlled Trial Comparing Sonography and Electric Stimulation-Guided Injection Techniques: A Preliminary Report. *Am J Phys Med Rehabil.* 2010; 89:279–286. [PubMed: 20068435]
16. Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. *Phys Ther.* 1987; 67:206–207. [PubMed: 3809245]
17. Delagi, EF., Perotto, A., Iazetti, J., Morrison, D. *Anatomic Guide for the Electromyographer: The Limbs and Trunk.* Fourth. Springfield, IL: CC Thomas; 2005.
18. Bickerton LE, Agur A, Ashby P. Flexor digitorum superficialis: locations of individual muscle bellies for botulinum toxin injections. *Muscle Nerve.* 1997; 20:1041–1043. [PubMed: 9236799]
19. Munin MC, Navalgund BK, Levitt DA, Breisinger TP, Zafonte RD. A novel approach to apply botulinum toxin to the flexor digitorum superficialis muscle in acquired brain injury. *Brain Inj.* 2004; 18:403–407. [PubMed: 14742153]
20. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society 1995, Series B.* 57:289–300.

21. Roberts C, Crystal R, Eastwood DM. Optimal injection points for neuromuscular blockade of forearm flexor muscle: a cadaveric study. *J Pediatr Orthop B*. 2006; 15:351–355. [PubMed: 16891963]
22. Liu J, Pho RWH, Pereira BP, Lau HK, Kumar VP. Distribution of primary motor nerve branches and terminal nerve entry points to the forearm muscles. *Anat Rec*. 1997; 248:456–463. [PubMed: 9214564]
23. Lepage D, Parratte B, Tatu L, Vuiller F, Monnier G. Extra and intramuscular nerve supply of the muscles of the anterior antebrachial compartment: applications for selective neurotomy and for botulinum toxin injection. *Surg Radiol Anat*. 2005; 27:420–430. [PubMed: 16308665]
24. Pillen S, Arts IM, Zwarts MJ. Muscle ultrasound in neuromuscular disorders. *Muscle Nerve*. 2008; 37:679–693. [PubMed: 18506712]

Figure 1. Ultrasound localization of forearm flexor muscles for optimal injection site
 Each muscle location is determined first by proximodistal percentage of landmark line (LL) drawn from medial epicondyle to pisiform. Then, a lateral (radial) coordinate measured in millimeters is created perpendicular to the LL.

Figure 2. Serial images of US-guided Btx injection into FDS4

Example of subject receiving US-guided Btx injection into FDS4 using the axial view. Scan A demonstrates the needle point as it appears into view in the muscle belly. Scans B and C demonstrate the enlarging “blush” of echogenic Btx in addition to the appearance of the needle’s shadow in the tissue.

Table 1

Proximodistal coordinates with 95% confidence intervals for the average difference between the mapping and ultrasound coordinates.

Muscle	Mapping Proximodistal Coordinates in cm	Ultrasound Proximodistal Coordinates in cm	95% CI
FDS2	19.3 ± 1.7	19.1 ± 1.9	[-0.15 0.69]
FDS3	15.1 ± 1.3	15.0 ± 1.5	[-0.31 0.51]
FDS4	13.8 ± 1.5	13.7 ± 1.5	[-0.30 0.45]
FDS5	20.5 ± 1.7	20.4 ± 1.5	[-0.26 0.36]
FCR	8.4 ± 3.0	9.3 ± 3.1	[-2.03 0.33]
PT	18.7 ± 2.6	17.9 ± 2.5	[0.01 1.61] *
FPL	4.7 ± 0.8	9.4 ± 3.0	[-6.70 -2.81] *

Significant differences (p<0.05) are denoted with an asterisk.

(FDS - flexor digitorum superficialis, FCR - flexor carpi radialis, PT - pronator teres and FPL - flexor pollicis longus.)

Table 2

Mapping and ultrasound lateral coordinates with 95% confidence intervals for their average differences. There are no standard deviations for the muscles FDS2, FDS3, FDS4, and FDS5 because all the subjects had the same mapping coordinates per protocol.

Muscle	Mapping Lateral Coordinates in mm	Ultrasound Lateral Coordinates in mm	95% CI
FDS2	14	15.4 ± 2.6	[-2.84 0.023]
FDS3	17	19.9 ± 4.1	[-5.00 -0.77] *
FDS4	7	8.8 ± 4.0	[-3.8 0.30]
FDS5	6	6.2 ± 2.9	[-1.69 1.34]
FCR	32.8 ± 13.7	21.9 ± 5.7	[2.28 19.38] *
PT	37.8 ± 8.6	39.0 ± 7.4	[-7.82 5.45]
FPL	39.2 ± 7.2	39.4 ± 8.7	[-5.71 5.31]

Significant differences ($p < 0.05$) are denoted with an asterisk.