Changes in Sonoelastography After Using Botulinum Toxin Type A for the Treatment of the Patients with Post-stroke Spasticity: Report of 2 Cases

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We examined the biceps brachii and the medial head of the gastrocnemius muscles on the affected side of two patients with post-stroke spasticity. Sonoelastography was used to evaluate the changes in spastic muscles before treatment; and 2, 4, 8 and 12 weeks after treatment with botulinum toxin Type A. Modified Ashworth scale (MAS), and the passive range of motion of the elbow and the ankle joints, before and after the treatment, were also evaluated. Both patients engaged in outpatient rehabilitation and a home exercise program focused on stretching throughout the assessment period.
Sonoelastography enabled the visualization of the hardness of the spastic muscles using imaging and color scaling, and an objective evaluation of the hardness of the spastic muscles was performed by measuring the strain ratio(SR) using an acoustic coupler.
Both patients showed reductions in MAS score and SR for both the biceps brachii and medial gastrocnemius head at two and four weeks after injection with botulinum toxin Type A: subsequently, however, these two measures followed different patterns through week 12 of evaluation.
SR is an objective measure of spastic muscle hardness based on physical changes in their viscoelasticity, making it qualitatively different from the subjective ratings of the MAS. Sonoelastography offers clinicians a useful tool for visually and objectively monitoring complex pathologies characterized by muscle spasticity at all points in their course: before botulinum therapy and associated rehabilitation, during follow-up, and at the time of repeated injection(s). The information provided could help to select which muscle(s) to target for treatments, and to determine effective dosages.
Further accumulation of cases is needed to ascertain and establish useful roles for this tool in clinical practice.

Key words: post-stroke spasticity, botulinum toxin Type A, sonoelastography, Modified Ashworth Scale, Strain Ratio

INTRODUCTION

Spasticity is one of the symptoms of the upper motor neuron syndrome caused by diseases such as stroke, head injury, and spinal cord injury [1]. It is a motor disorder characterized by a velocity-dependent increase in the tonic stretch reflexes (muscle tone) with exaggerated tendon jerks (hyperreflexia) [2].

The characteristic findings of the upper motor neuron syndrome include negative and positive signs. Positive signs include spasticity, spastic dystonia, and pathological co-contraction, while hemiplegia and muscle weakness are the negative signs. In contrast, once the muscles become immobile due to motor paralysis, nonneuronal changes occur, including muscle rigidity, muscle fibrosis and muscle atrophy, and muscle viscoelasticity also changes at an increased rate. The changes in muscle viscoelasticity increase spasticity even further. Therefore, the motor disorders develop a far more complex pathology, involving not only spasticity and motor paralysis but also changes in viscoelasticity, which causes impairment and disability, making this an important issue in rehabilitation medicine.

Botulinum therapy for spasticity provides relief from troublesome symptoms such as pain and eases the burden of assistance as well. It may also act to improve function.

Generally, the modified Ashworth scale (MAS) [3] is used to evaluate the level of muscle spasticity at which the therapeutic preparations of botulinum toxin are indicated. MAS is also used to determine the posttreatment course and the timing of re-administration in clinical practice, but it provides a subjective evaluation only.

In contrast, it is also important to evaluate the changes occurring in muscle viscoelasticity because they worsen spasticity. This evaluation affects the decision-making, regarding the timing of treatment, as well.

In sonoelastography [4, 5], a probe is placed on the body, the minute displacement caused by the slight pressure of the probe is converted into strain, and this strain is imaged in real time. Soft tissue generates a large strain, while hard tissue generates only a small strain, which makes it possible to image the relative hardness of the tissues. Areas with smaller strains

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(relatively harder areas) are displayed in blue, while the areas with larger strains (relatively softer areas) are displayed in red. The hardness within these tissues can also be objectively evaluated by measuring the strain ratio (SR) using an acoustic coupler.

Here, we used sonoelastography to evaluate the changes in the viscoelasticity of the spastic muscles, visually and objectively, in two patients with post-stroke spasticity.

METHODS AND PATIENTS

We examined two patients with post-stroke spasticity. The biceps brachii and the medial gastrocnemius, as the main muscles involved in the spasticity treatment, were evaluated using sonoelastography; so that the changes in spastic muscle, before and after the treatment with botulinum toxin Type A, could be determined.

The modified Ashworth scale (MAS), and the passive range of motion of the elbow and the ankle joints, before and after the injection, were also evaluated.

Two patients engaged in outpatient rehabilitation and a home exercise program focused on stretching throughout the assessment period.

Procedures

The biceps brachii and the medial gastrocnemius muscles on the affected side were identified, and the needle puncture site on the epidermis was used as an identification mark.

Ultrasound equipment (M-turbo; SonoSite, USA) and a linear probe (HFL50x, 6–15MHz; SonoSite, USA) were used to identify and inject the botulinum toxin Type A into the muscles.

At the site marked on the epidermis, these muscles were also evaluated using sonoelastography.

Sonoelastography was performed via a linear probe (Hitachi Aloka Medical, Ltd., EUP-L65, 6–14MHz, Japan) with a dedicated acoustic coupler (Hitachi Aloka Medical, Ltd., EZU-TECPL1, Japan) fitted on the ultrasound equipment (Hitachi Aloka Medical, Ltd., Hi-vision Ascendus, Japan).

This equipment imaged the tissue hardness with color scaling, displaying hardness as colors in an easy-to-understand format, shown in the order of blue, green, yellow, and red (hard to soft).

The acoustic coupler was made of elastomer resin, and its elastic modulus was set at a constant pressure of 22.6 kPa.

SR was calculated as muscle strain/coupler strain, and the hardness of the muscle tissue was determined with the acoustic coupler. SR was smaller for the soft muscle tissues and larger for the hard muscle tissues.

Mean of the three SR values was reported as the result. Mean was used as it was considered more reliable than the individual values. The evaluation was performed by two clinical technologists with more than 20 years of experience.

Next, the probe was placed on the center of the site marking the muscles and an ultrasound-guided injection of botulinum toxin Type A was administered using the crossover method (out of line).

Sonoelastography was performed by aligning the center of the linear probe, fitted with an acoustic coupler, with the identification site, after the injection of the botulinum toxin.

Sonoelastographic evaluation and MAS scores for each muscle, and the passive range of motion (PROM) of dorsiflexion at the ankle joint and of extension at the elbow joint, were evaluated at 2, 4, 8, and 12 weeks after the injection.

The MAS measures resistance during passive soft-tissue stretching and is used as a simple measure of spasticity. The MAS grades spasticity as follows: 0 = Normal muscle tone; 1 = Slight increase in muscle tone; 1+ = Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM; 2 = marked increase in muscle tone through most of the ROM, but affected part(s) easily moved; 3 = Considerable increase in muscle tone, passive movement difficult; 4 = part(s) rigid in flexion or extension.

Case 1:

A 74-year-old man had a right caudate nucleus hemorrhage 20 years ago. He had residual left hemiplegia and spasticity in the left upper and lower limbs.

The left hemiplegia was classified as Brunnstrome stage Arm III, Hand III and Leg II. He wore a left ankle foot orthosis and walked with a T-cane and was independent in his activities of daily living. His total functional independence measure (FIM) score was 115 points (motor: 80 points; cognition: 35 points).

The results of the evaluation of spasticity in this patient were as follows: biceps brachii muscle: MAS 3; medial head of the gastrocnemius muscle: MAS 3; PROM of the left elbow for extension: -5°, PROM for flexion 135°; PROM at the left ankle for dorsiflexion: 0° and PROM for plantar flexion: 60°.

The Brunnstrom stages is a short and easily administered measure for assessing motor function. The Brunnstrom stages contains items:the upper limb (arm, hand), and the lower limb, all of which are rated on a 6-level Likert-type scale (levelI to VI). Higher levels represent better motor function.

The FIM is an 18-item of physical, psychological and social function. Contains 18 items composed of: 13 motor tasks, 5 cognitive tasks (considered basic activities of daily living). Scores range from 18 (lowest) to 126 (highest) indicating level of function. The tool is used to assess a patient's level of disability as well as change in patient status in response to rehabilitation or medical intervention.

The biceps brachii and the medial gastrocnemius muscles were identified, with the ultrasound equipment, in the center of the left upper arm, and five finger-breaths distal to the popliteal line on the medial side of the left lower leg, respectively. The location was marked on the epidermis.

The marking sites were evaluated using sonoelastography.

Next, a needle was inserted at the marking site, and an ultrasound-guided injection of botulinum toxin Type A was administered using the crossover method. We administered 50 units of botulinum toxin Type A to the biceps brachii muscle and 30 units to the medial head of the gastrocnemius muscle.

The marking site was again evaluated by sonoelastography to ensure that the site, after the injection, remained constant.

Sonoelastographic imaging of each muscle and SR, MAS, and PROM of dorsiflexion at the ankle joint and of extension at the elbow joint were evaluated before the injection and at 2, 4, 8, and 12 weeks after the injection.

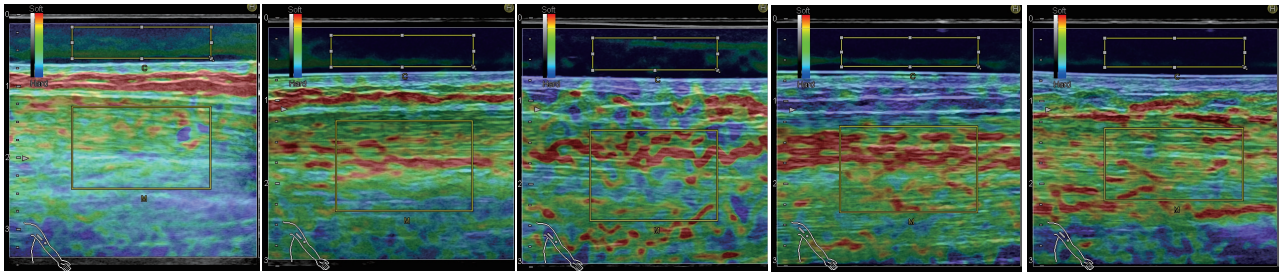
Results:

The red areas in the biceps brachii and the medial head of the gastrocnemius muscles had increased on the sonoelastographic imaging at 2 weeks after the injection. The red areas were present in the biceps brachii muscle until 12 weeks after the injection. Red areas were present in the medial head of the gastrocnemius muscle until 8 weeks after the injection but had lessened by 12 weeks after injection (Fig. 1, 2).

The evaluation of the biceps brachii muscle, before the injection, showed the following values: SR: 0.5, MAS: 3, and the elbow joint extension: -5°. At 2 weeks after the injection, the values were: SR: 0.24, MAS: 2 and the elbow joint extension: 0°. At 4 weeks after the injection, the values were: SR: 0.20, MAS: 2, and the elbow joint extension: 0°. At 8 weeks after the injection, the values were: SR: 0.09, MAS: 3, and the elbow joint extension: 0°. Finally, at 12 weeks after the injection, the values were: SR: 0.09, MAS: 3, and the elbow joint extension: 0°.

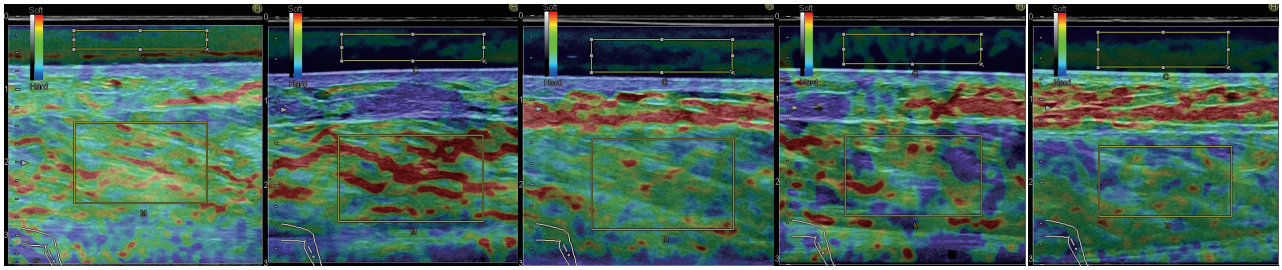
The evaluation of the medial head of the gastrocnemius muscle, before the injection, showed the following values: SR: 0.57, MAS: 3, and the ankle joint dorsiflexion: 0°.

At 2 weeks after the injection, the values were: SR: 0.18, MAS: 2, and the ankle joint dorsiflexion: 5°. At 4 weeks after the injection, the values were: SR: 0.47, MAS: 2, and the ankle joint dorsiflexion: 5°. At 8 weeks after the injection, the values were: SR 0.44, MAS 3, and the ankle joint dorsiflexion: 0°. Finally, at 12 weeks after the injection, the values were: SR: 0.80, MAS: 3, and the ankle joint dorsiflexion: 0° (Table 1).



before 2weeks 4weeks 8weeks 12weeks

Fig. 1 Sonoelastographic images of muscle spasticity (color scaling) in the left biceps brachii muscle of Case 1 (a 74-year-old man) before injection, and at 2, 4, 8 and 12 weeks after the injection of botulinum toxin Type A



before 2weeks 4weeks 8weeks 12weeks

Fig. 2 Sonoelastographic images of muscle spasticity (color scaling) in the medial head of the gastrocnemius muscle of Case 1 (a 74-year-old man) before injection, and at 2, 4, 8 and 12 weeks after the injection of botulinum toxin Type A

Table 1 Changes in SR, MAS, and PROM of the left biceps brachii and the medial head of the gastrocnemius muscles in Case 1 (a 74-year-old man) before injection, and at 2, 4, 8 and 12 weeks after the injection of botulinum toxin Type A

		Before	2weeks	4weeks	8weeks	12weeks
Biceps brachii						
	SR	0.50	0.24	0.20	0.09	0.09
	MAS	3	2	2	3	3
	PROM					
	(elbow for extension)	-5°	0°	0°	0°	0°
Gastrocnemius						
	SR	0.57	0.18	0.47	0.44	0.80
	MAS	3	2	2	3	3
	ROM					
	(ankle for dorsiflexion)	0°	5°	5°	0°	0°

Case 2:

A 54-year-old woman had right putaminal hemorrhage 10 years ago. She had residual left hemiplegia and spasticity in the left upper and lower limbs. The left hemiplegia was classified as Brunnstrome stage Arm II, Hand IV and Leg IV. She wore a left ankle foot orthosis and walked independently with a T-cane. Her total FIM score was 114 points (motor: 79 points; cognition: 35 points).

The results of the evaluation of spasticity in this patient were as follows: left biceps brachii muscle: MAS 3; medial head of the gastrocnemius muscle: MAS 3; PROM for extension of the left elbow: -35°; PROM for flexion: 130°; PROM for left ankle joint dorsiflexion: -15°; PROM for plantar flexion: 40°.

For the sonoelastographic evaluation and injection of the botulinum toxin Type A, same procedures as Case 1 were followed. We administered 50 units of botulinum toxin Type A to the biceps brachii muscle, and 50 units to the medial head of the gastrocnemius muscle.

Sonoelastographic imaging of each muscle and SR, MAS and PROM of the ankle joint dorsiflexion and the elbow joint extension were evaluated before the injection and at 2, 4, 8, and 12 weeks after the injection.

Results:

The red areas in the biceps brachii and the medial head of the gastrocnemius muscles had increased on sonoelastographic imaging at 2 weeks after the injection. The red areas were still present in the biceps brachii muscle until 8 weeks after the injection but had disappeared at 12 weeks after the injection. Red areas were still present in the medial head of the gastrocnemius muscle until 12 weeks after the injection (Fig. 3, 4).

The evaluation of the biceps brachii muscle, before the injection, showed the following values: SR: 1.63; MAS: 3; and the elbow joint extension: -35°. At 2 weeks after the injection, the values were: SR: 0.20; MAS: 2; and the elbow joint extension: -20°. At 4 weeks after the injection, the values were: SR: 0.15; MAS: 2; and

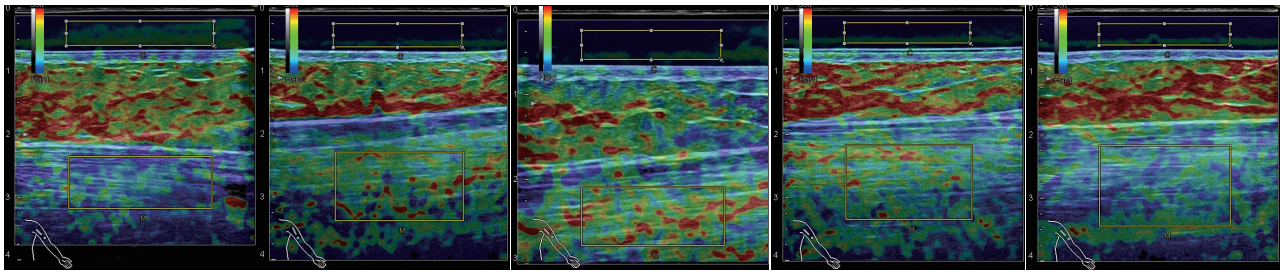


Fig. 3 Sonoelastographic images of muscle spasticity (color scaling) in the left biceps brachii muscle of Case 2 (a 54-year-old woman) before injection, and at 2, 4, 8 and 12 weeks after the injection of botulinum toxin Type A

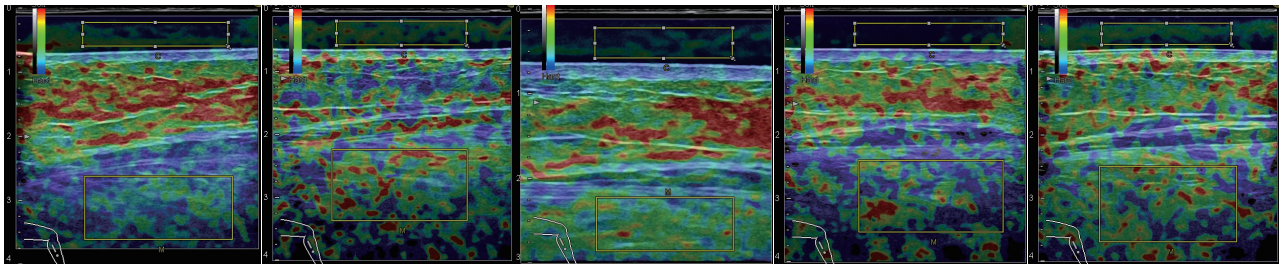


Fig. 4 Sonoelastographic images of muscle spasticity (color scaling) in the medial head of the gastrocnemius muscle of Case 2 (a 54-year-old woman) before injection, and at 2, 4, 8 and 12 weeks after the injection of botulinum toxin Type A

Table 2 Changes in SR, MAS, and PROM of the left biceps brachii and the medial head of the gastrocnemius muscles in Case 2 (a 54-year-old woman) before injection, and at 2, 4, 8 and 12 weeks after the injection of botulinum toxin Type A

		Before	2weeks	4weeks	8weeks	12weeks
Biceps brachii						
	SR	1.63	0.20	0.15	0.31	0.35
	MAS	3	2	2	2	2
	PROM					
	(elbow for extension)	-35°	-20°	-10°	0°	0°
Gastrocnemius						
	SR	1.42	0.7	0.44	0.29	0.72
	MAS	3	2	2	3	3
	ROM					
	(ankle for dorsiflexion)	-15°	0°	0°	0°	-5°

the elbow joint extension: -10°. At 8 weeks after the injection, the values were: SR: 0.31; MAS: 2; and the elbow joint extension: 0°. Finally, at 12 weeks after the injection, the values were: SR: 0.35; MAS: 2; and the elbow joint extension 0°.

The evaluation of the medial head of the gastrocnemius muscle, before the injection, showed the following values: SR: 1.42; MAS: 3; and the ankle joint dorsiflexion: -15°. At 2 weeks after the injection, the values were: SR: 0.70; MAS: 2; and the ankle joint dorsiflexion: 0°. At 4 weeks after the injection, the values were: SR: 0.44; MAS: 2, and the ankle joint dorsiflexion: 0°. At 8 weeks after the injection, the values were: SR: 0.29; MAS: 2; and the ankle joint dorsiflexion: 0°. Finally, at 12 weeks after the injection, the values were: SR: 0.72; MAS: 3; and the ankle joint dorsiflexion: -5° (Table 2).

DISCUSSION

This paper details our experiences using sonoelastography to evaluate post-stroke muscle spasticity in two individuals. Each patient was injected with botulinum toxin Type A in the biceps brachii and the medial head of the gastrocnemius muscle of the affected side, and then engaged in outpatient rehabilitation and a home exercise program focused on stretching. Sonoelastography data — i.e., SR values and color-scaled images — as well as MAS score for both muscles were successfully recorded over a lengthy follow-up period (12 weeks).

Kesikburun *et al.* [6] evaluated the gastrocnemius muscle in 26 stroke patients using sonoelastography and reported that the elasticity ratio on the affected side was significantly increased compared to that of the healthy side, suggesting that sonoelastography could be used to evaluate the hardness of the spastic gastrocnemius muscle in the stroke patients. Yasar *et al.* [7] also evaluated spastic muscle of the forearms of 23 post-stroke patients using sonoelastography and reported that the elasticity ratio on the affected side was significantly increased compared to that of the healthy side.

The results of this study on two patients also suggest that sonoelastography is useful as a diagnostic tool for evaluating the hardness of the spastic muscles, as reported by Kesikburun *et al.* and Yasar *et al.*

Case 1 showed reductions in the biceps brachii MAS score and SR compared with baseline through four weeks after treatment. While his MAS score returned to baseline by eight weeks, his SR had fallen even lower by eight and 12 weeks. This patient also showed reductions in the medial gastrocnemius MAS score and SR compared with baseline through four weeks after treatment. Here again, the MAS score returned to baseline by eight weeks; the SR reduction persisted through eight weeks, but rose above baseline by 12 weeks. The patient's ankle dorsiflexion initially improved, an effect that lasted through four weeks, but returned to the pre-injection ROM by eight weeks.

Case 2 also showed reductions in the biceps brachii MAS score and SR compared with baseline, but these persisted longer, through 12 weeks after treatment. This patient also showed reductions in medial gastrocnemius MAS score and SR compared with baseline through four weeks after treatment; her MAS score returned to baseline by eight weeks, but the SR reduction persisted through 12 weeks. The patient's ankle dorsiflexion initially improved, an effect that persisted through eight weeks, but started to subside by 12 weeks.

Gao *et al.* reported significant correlations between SR and MAS score in a feasibility study of ultrasound elastography, in which the technology was used to evaluate biceps brachii spasticity before botulinum toxin Type A treatment and thereafter (mean: 22 days) in seven stroke victims [8]. Picelli *et al.* similarly conducted a trial with sonoelastography in 21 patients before and one month after botulinum toxin Type A injection for post-stroke gastrocnemius spasticity. While the treatment had direct effects on ankle dorsiflexion PROM and calf muscle spasticity (as measured by Ashworth scale), it was not associated with any significant changes in ultrasonographic characteristics [9].

Both of our patients detailed here showed reductions in MAS score and SR in both the biceps brachii and medial gastrocnemius head at two and four weeks after injection with botulinum toxin Type A: subsequently, however, these two measures followed different patterns through week 12 of evaluation.

Botulinum therapy reduces muscle spasticity, which could have made it easier for our patients to engage in outpatient rehabilitation as well as stretching and other exercises, in turn leading to marked improvements in viscoelasticity.

The changes in muscle spasticity that occur after stroke are neurological in nature, making them qualitatively different from associated (non-neurological) changes in viscoelasticity. Sonoelastographic data — i.e., SR values and color-scaled images — reflect muscle viscoelasticity, and therefore may not necessarily agree with the MAS, which evaluates spasticity.

Greater viscoelasticity increases spasticity, while greater spasticity promotes viscoelasticity by immobilizing the muscle. Botulinum therapy is expected to reduce spasticity and alter viscoelasticity in spastic muscle; however, the effects of botulinum toxin Type A may vary depending on the muscle injected, the dosage, and rehabilitation program contents.

Sonoelastography can be used to evaluate the hardness of the spastic muscles relatively easily in routine practice.

Furthermore, sonoelastography offers clinicians a useful tool for visually and objectively monitoring complex pathologies characterized by muscle spasticity at all points in their course: before botulinum therapy and associated rehabilitation, during follow-up, and at the time of repeated injection(s). The information provided could help to select which muscle(s) to target for treatments, and to determine effective dosages.

Further examination of a large number of patients is needed to confirm the role of sonoelastography in clinical practice.

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