

Combination Therapy for Treatment of Spasticity in Stroke Patients: A Case Study

DIMITRIOS ATHANASIADIS¹, ELEFThERIOS STEFAS²,
ATHINA KAPSOKOULOU³, JANNIS PAPATHANASIOU⁴, YANNIS DIONYSSIOTIS⁵

¹Physiotherapy Practice "Dimitrios Athanasiadis", Kavala, Greece

²Department of Physical Medicine and Rehabilitation, Rehabilitation Center EVEXIA, Chalkidiki, Greece

³School of Medicine, University of Patras, Patras, Greece

⁴Department of Kinesitherapy, Faculty of Public Health, Medical University of Sofia, Sofia, Bulgaria

⁵1st Physical Medicine and Rehabilitation Department, National Rehabilitation Center EKA, Athens, Greece

ABSTRACT: Background and purpose: Spasticity is a disorder of sensory-motor control that appears as an effect of a lesion in the upper motor neuron and demonstrates sustained or intermittent unintentional muscle activation. Many treatment interventions exist to treat spasticity, and in this study, three of them were combined: vibration, static positioning and transcutaneous nerve stimulation (TENS). Evidence exists regarding the application of each intervention per se, but not in combination. Hence, the aim of the study is to present an innovative treatment approach for spasticity and show the effects it produced on one patient. Methods: The study was a case report. The subject was a 31-year-old male patient who had ischemic stroke a year ago. He demonstrated severe plantar flexion of the left foot due to spasticity. There was a baseline assessment and measurement, one on the end of the intervention (10th week) and a follow-up 8 months after it. Assessment and measurement tools: a dynamic gait analysis on the treadmill by Zebris FDM-T system, electromyography testing (F-wave parameter and stretch reflex activity), the Modified Ashworth Scale (MAS), a standard goniometer, the Motricity index (MI) leg score and a pain dichotomous when stretching and while at rest. Intervention: The intervention lasted 10 weeks, 5 days per week for 30 minutes. The patient was standing on a 30-degree-inclination wedge. The wedge was positioned on a whole-body vibrator set to vibrate with 91Hz of frequency and 1.0mm amplitude. TENS was offered through surface electrodes which were placed on the tibialis anterior and triceps surae muscles, along the sural nerve (impulse frequency: 100Hz, pulse width: 250µs, intensity: 30mA). Results: The range of motion and the MI was increased and the swing-phase of the right foot as well as the standing-phase of the left foot were increased an hour after the intervention. The results were slightly diminished a day and a week after the intervention but a statistically significant improvement still remained. Conclusion: Combination therapy intervention could offer an alternative for treating spasticity. Further studies are needed to establish a treatment protocol and maybe combine other spasticity-centered treatment modalities in order to produce new interventions.

KEYWORDS: Combination therapy, TENS, positioning, vibration, spasticity.

Introduction

Stroke is one of the most lethal diseases worldwide [1].

Stroke is a disease in cerebral vasculature where oxygen fails to be supplied to the brain cells, leading them to death and can be classified as either ischemic or hemorrhagic [2].

Many physical disabilities could result from a stroke accident among which spasticity is one with long term effects on the patient's life [3].

Spasticity is most holistically defined as "disordered sensory-motor control, resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles" by Pandyan et al.'s [4].

However, another term is that of McCrea et al.'s [5] where spasticity is suggested to be used as an umbrella term for every positive, active symptom of the upper motor neurone syndrome that a therapist might confront in daily clinical

practice. Patients suffering from spasticity could be disabled by a mixture of soft tissue contracture, muscle overactivity and paresis [6].

According to a Cochrane review performed by Monaghan et al.'s [7], there are 25 different interventions employed to treat spasticity in the literature, among which: vibration, static positioning and transcutaneous nerve stimulation (TENS).

In this case report, there was a combination of the last three interventions.

According to Yetley et al.'s [8] case studies are in the lower middle part of the hierarchy of evidence pyramid, with the higher risk of bias and the lower quality of evidence.

However, it was considered best to use this research method, as it allows a detail exploratory examination of data, within a particular context [9].

Hence, the primary objective of this study is to present an innovative treatment intervention

and establish the proof-of-safety of the intervention.

The secondary objective was to present the effect that combination therapy had on a stroke patient, discuss the results and make some future recommendations.

Scientific Background

Given that spasticity is deeply affected by a muscle's length, the position of the patient's limb affects the result when assessing spasticity, especially when focusing on bi-articular muscles [10].

It has been demonstrated on the Root mean square (RMS) values that several positions affect the stretch reflex activity of muscles with spasticity [11].

That is presumably due to alterations of the inner muscle characteristics [7].

Notably, the stretch reflex activity is higher in an elongated muscle than in a shortened muscle [10].

In this case report, the static positioning was offered to the patient in the form of standing which has beneficial effects due to activity promotion from the anti-gravity muscles of the lower limbs and the trunk, neural alteration of spasticity triggered by changed sensory input and prolonged stretch, amelioration or preservation of the flexibility of joints or soft tissue, spasms decline on the lower limbs and, lastly, psychological effects [12-14].

Regarding vibration, it is considered to reduce the gamma-afferent fibers' activity through a decrease of impulses from the muscle spindles in a "nervous-system response" [15].

Additionally, vibratory stimulation elicit relaxation and strengthening of soft tissues and muscular tissues [15].

The aforementioned findings could interpret the alterations observed on the F-wave parameters of the excitability of the motor neuron which are being modified when applying external vibratory stimulation [7].

With regards to TENS, there is evidence in support of the application of TENS for inducing inhibitory effects, for a short period of time after the stimulation, on stretch reflex activity which is unnaturally increased due to spasticity that originates in the cerebrum; for reducing the spastic antagonists' co-contraction, and; for disinhibiting the voluntary motor commands of paretic muscles [16-17].

Noteworthy, the use of TENS in treating spasticity is supported by a plethora of studies [18-20].

Generally, it is supported that TENS application may have positive effect on treating spasticity [21].

Case Presentation

Although eight out of ten stroke patients belong to the ischemic stroke category [22], the subject of the current case report belongs to the hemorrhagic category as the patient suffered a saccular aneurysm [2] at the basilar artery on the September of 2016.

The subject is a male, 31-year-old ex-smoker, and his dominant side was the right one. Apart from the stroke accident, other inclusion criteria involved that the patient was treated early after stroke, was aged between 21 and 85 years old and that the patient presented lower-limb spasticity of at least 3 according to the Modified Ashworth Scale (MAS). Exclusion criteria were a Mini Mental Exam Status ≤ 24 , 2, significant neglect, and spatiotemporal or visual or vestibular deficits. As this patient was the first one to receive Combination Therapy in a monitored and regular manner, the sample had to be of convenience.

Moreover, the patient showed history of hyperlipidemia and hypertension.

Pharmaceutical treatment included: Lopresor, Salospir, Malortil, Ivor, Ovepin, Efiend in Blister (blis 2X10), Escitalo, Xanax and Proteins. Furthermore, the patient received two botulinum toxin injections in the 6th and 9th month after starting his treatment at the rehabilitation center. Given that the effects of botulinum toxin are known to fade away about 8 to 12 weeks after applying it to the patient [23], it was considered that the medicine had no effect over the effect of the treatment which started precisely 12 months after the first day of the patient's treatment at the rehabilitation clinic.

Additionally, the subject's spastic movement pattern involved a genu recurvatum type of gait which he tried to alter by activating muscles from the hip and back. The subject, also, presented foot drop with the ankle being impossible to dorsiflex from neutral and the toes being able to dorsiflex over 5° from neutral and only for the big toe. The subject had no sensory loss, no spatial or language impairment, was not overweight and had recovered most of his muscle strength and cardiovascular ability within his first year of rehabilitation. The patient gave a written informed consent to participate in the study. The baseline characteristics are shown on Table 1.

Table 1. Patient's baseline features.

Gender	Male
Age	31
Days Since Stroke	3
Hemiplegic Side	Right
Dominant Side	Right
Pain/No Pain when stretching and while at rest	No pain
Modified Asworth Scale	3
Motricity Index Leg Score	81
Maximum voluntary dorsiflexion range of ankle and big toe	0° and 5° from the neutral position

As it is already mentioned, the intervention was offered one year after the first day of the subject's rehabilitation program. Interventions employed separately before applying Combination Therapy included: manual stretching, electrotherapy, mat activities, splinting and vibration. The aforementioned program was offered for 1 hour daily, 5 times per week. Additionally, the patient was instructed to perform a stretching program at home.

The intervention lasted 30 minutes, 5 days per week for 10 weeks. Measurements and assessments were conducted thrice: once before the intervention, a second time on the end of the intervention (end of 10th week) and a third in a follow-up of 8 months after the end of the intervention (week 42). A physiotherapist was recruited to be the independent assessor. The assessor was blinded towards the intervention. On the contrary, no blinding was possible for the patient.

Measurement tools included: a dynamic gait analysis on the treadmill by Zebris FDM-T system in order to analyze gait and stance, the Modified Asworth Scale (MAS) to assess spasticity, a standard goniometer to measure range of motion (ROM) and the Motricity index (MI) leg score to assess muscle strength. To assess pain, VAS was overly criticized when used on stroke patients [24].

As a result, a pain dichotomous was preferred (pain versus no pain), a choice driven by older studies conducted on stroke patients [25].

This pain dichotomous was used when stretching the ankle and toes in dorsiflexion and while at rest. Regarding the measurement of range of motion, three measurements were conducted by a standard goniometer and the clinicians based their record according to the lowest of the three. The study's design abides by the CARE guidelines [26] for case reports.

To perform the intervention, the patient was asked to step on a solid plastic wedge of 30° angle which was placed over a whole-body

vibration plate. As seen in the attached video of the intervention, the whole-body vibration platform had support handles by each side.

While vibrating the body, the therapist was behind the patient in case of emergency.

Before every intervention, the patient's blood pressure and heart rate was checked. Recess was given whenever the patient wanted. A picture that most accurately depicts the intervention is given at Figure 1.

**Figure 1. Vibration+TENS+positioning.**

Focusing on the parameters of the intervention, the vibration was offered in a frequency of 91Hz and 1.0mm amplitude. The TENS was offered cutaneously through surface electrodes, which were placed along the sural nerve of the affected limb. The TENS was offered on an impulse frequency of 100Hz, pulse width of 0,25ms and intensity of 30mA. Apart from Combination Therapy, the patient also received classical physiotherapy which included stretching and mat activities for 30 minutes daily. Along with the Combination Therapy intervention, the patient was educated to perform a home-based stretching program. During the intervention period, no other intervention was offered. Lastly, it is important

to notice that the patient was making use of ankle-foot orthosis since day 1 of his rehabilitation in the clinic and henceforward.

The patient was informed about the purpose and content of the project and gave written informed consent to participate in the study, which conformed to the Declaration of Helsinki and was approved by the Local Ethical Committee.

Statistical methods applied in the experiment were determined before planning the experiment. Due to the inadequacy of the number of samples, the data's characteristics to be obtained by the experiment were determined and the statistical method to be used was decided. The Kruskal Wallis Analysis of Variance ($p > 0.05$) was implemented. Normality was tested by using the K-S test from the SPSS and the Mann-Whitney U Test was applied to

compare mean scores. Power analysis was performed which produced results above 80%.

Results

The results showed no pain increase due to the intervention either at calm or when stretching at neither week 10 nor follow-up measurement. Spasticity was reduced by 40%, while the Motricity Index Leg score showed an increase by 11%, both compared to baseline. The aforementioned scores were maintained at the follow-up. The range of motion was increased by 13° for the ankle and 19° for the big toe compared to baseline and these scores were marginally lessened by 2° for the ankle and 3° for the big toe on week 42. A summary of the results of the assessment is presented on Table 2.

Table 2. Scores at Baseline, Week 10 and Week 42.

Outcome Measures/Timing of the Intervention	Baseline	Week 10	Week 42
Pain/No Pain when stretching and while at rest	No pain	No pain	No pain
Modified Ashworth Scale	3	1	1
Motricity Index Leg Score	81	92	92
Maximum voluntary dorsiflexion range of ankle and big toe	0° and 5° from neutral position	13° and 24° from neutral position	11° and 21° from neutral position

Regarding the Zebris FDM-T measurements, Figure 2 depicts the foot prints produced while walking on the treadmill at baseline, week 10 and week 42. This illustrates how pressure

was allocated progressively throughout the experiment, as the patient was being able to make use of the whole area of the plantar surface of the foot.

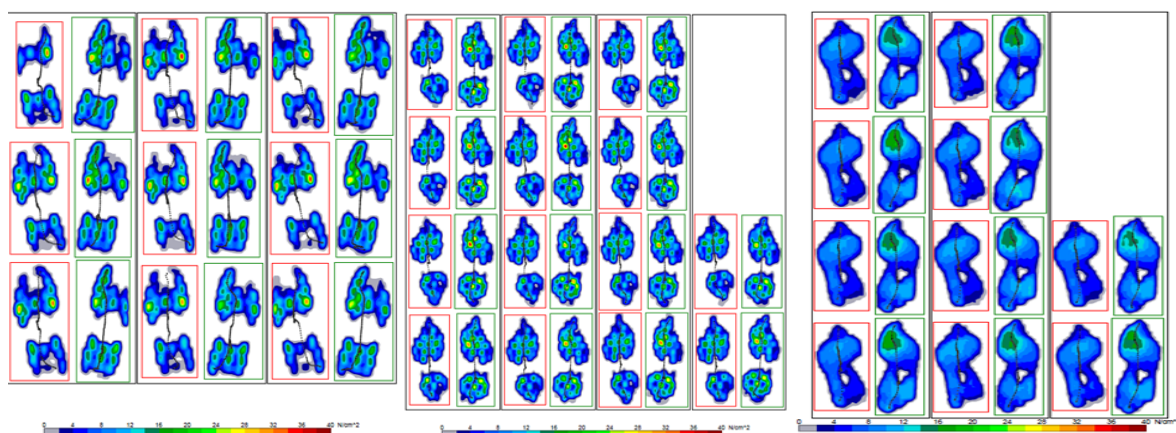


Figure 2. Foot prints pressure while walking in baseline, week 10 and week 42.

The following Figures 3, 4 and 5 illustrate the progression of force distribution changes in the static posture of the patient. Interestingly, the patient started the experiment with 40.9% of his pressure being laid on the left foot and 59.1% on the right foot, progressed to 45.1%-54.9%

respectively on week 10 and the follow-up on week 42 showed 41.1%-58.9% respectively.

Most of the pressure was laid on the foreword of the plantar surface of the foot than backwards in all three measurements.

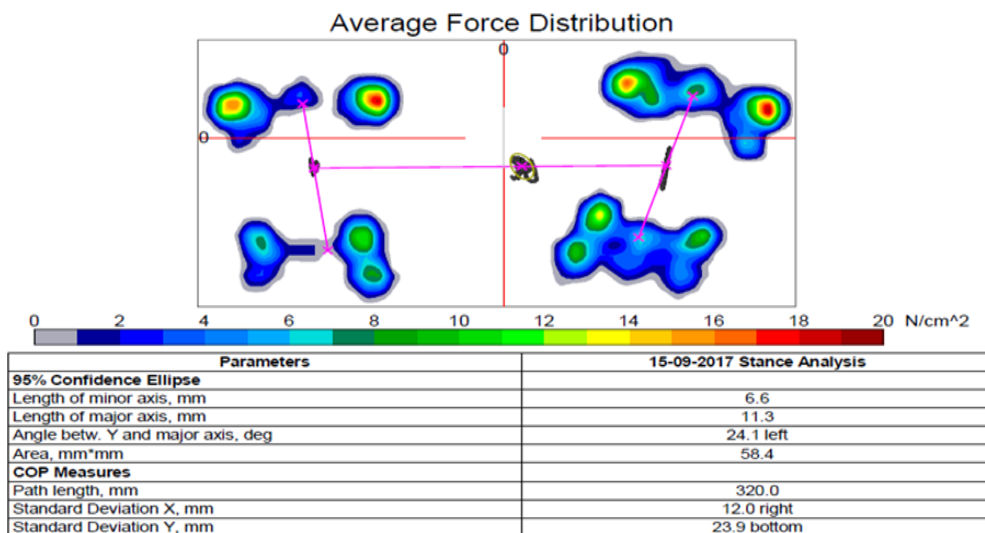


Figure 3. Stance analysis on baseline.

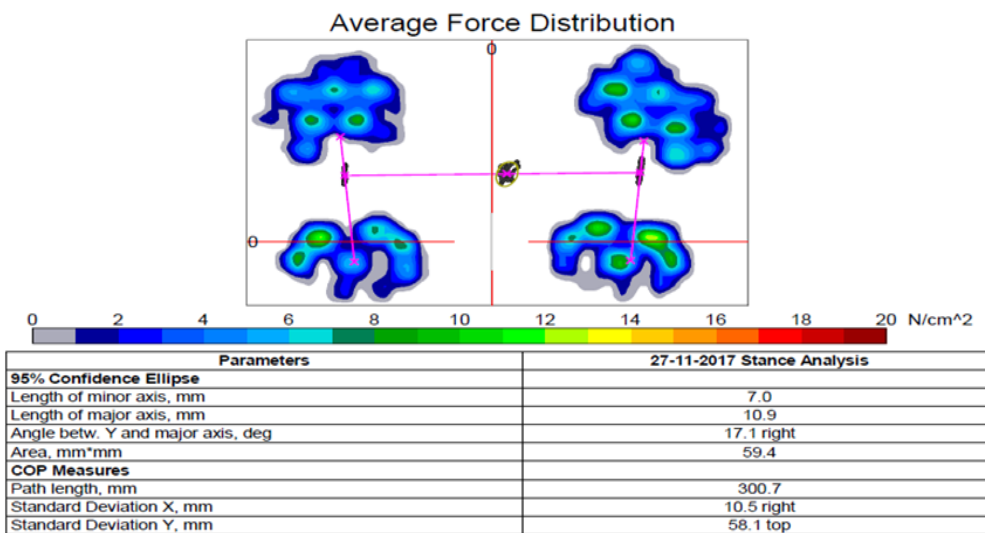


Figure 4. Stance analysis on week 10.

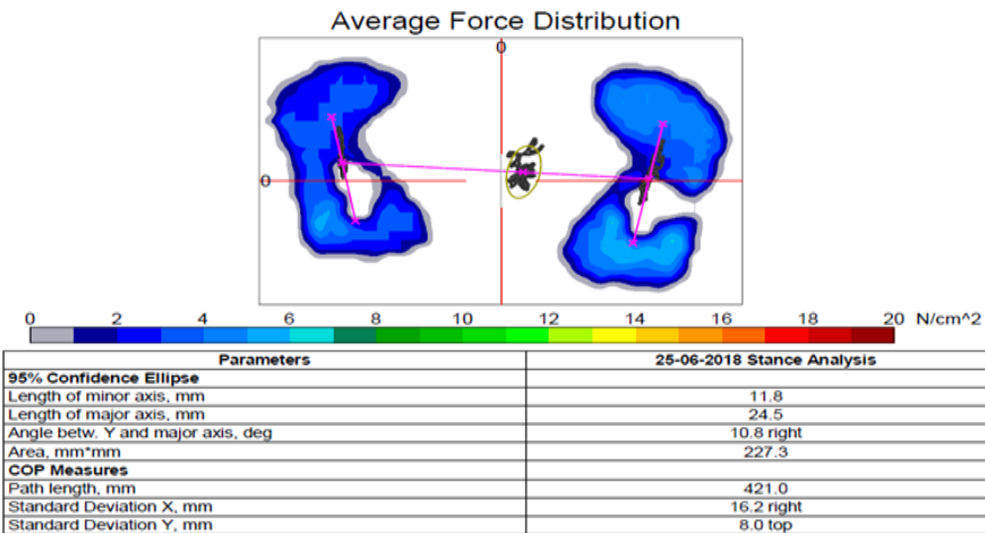


Figure 5. Stance analysis on week 42.

Moving deeper on the gait analysis, the results on baseline, week 10 and week 42 are thoroughly displayed on Figures 6, 7 and 8.

Almost 40% reduction on step width was revealed between the first two measurements which was maintained until week 42.

Moreover, the stride length was increased by 47% on week 10 compared to baseline and almost doubled on week 42.

Total double support was lessened by 16% and 33% on week 10 and week 42 respectively, compared to baseline.

About 31% was the decrease in stride time by the end of the experiment and it was further lowered in the follow-up when it reached 43% compared to baseline. Regarding the affected

limb, step length, single support during stance phase and the swing phase were significantly increased (44%, 16% and 41% respectively) and did not deteriorate on follow-up compared to baseline (66%, 43% and 64% respectively).

Noteworthy, the affected limb's step time, stance phase, pre-swing phase during stance phase and swing phase was decreased (37%, 9% and 31% respectively) and did not deteriorate on follow-up compared to baseline (49%, 13% and 46% respectively).

These results present an improvement on the stability the patient produced while walking, but also an amelioration in the movement patterns generated by the affected side and the whole body in general.

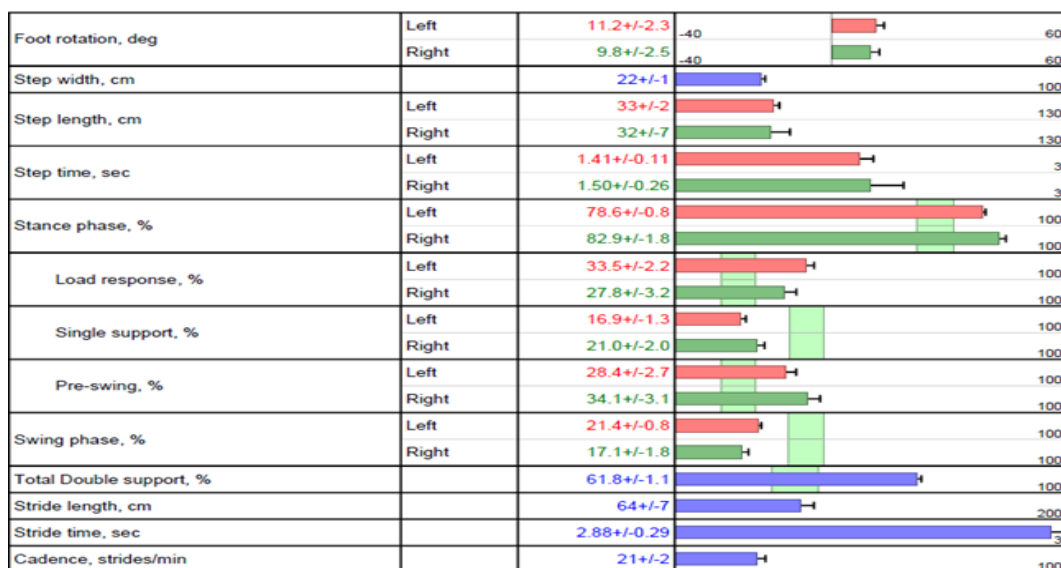


Figure 6. Gait analysis parameters on baseline.

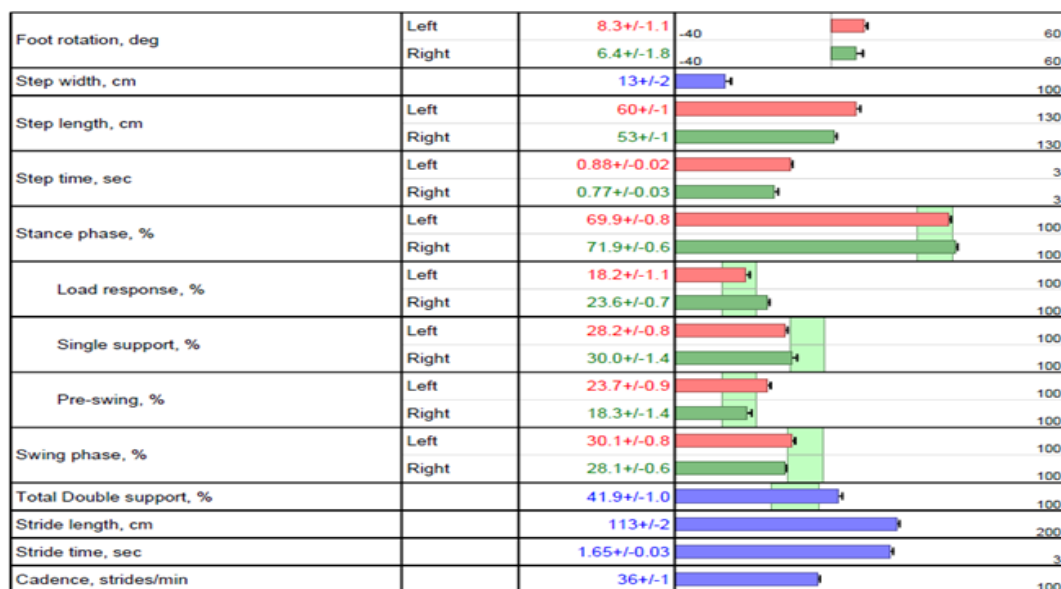


Figure 7. Gait analysis parameters on week 10.

Foot rotation, deg	Left	9.9+/-1.1		60
	Right	6.8+/-1.5		
Step width, cm		14+/-1		100
Step length, cm	Left	47+/-2		130
	Right	46+/-2		
Step time, sec	Left	1.03+/-0.06		3
	Right	0.94+/-0.05		
Stance phase, %	Left	74.1+/-1.5		100
	Right	75.9+/-1.3		
Load response, %	Left	23.7+/-1.7		100
	Right	26.2+/-1.8		
Single support, %	Left	24.2+/-1.4		100
	Right	25.9+/-1.2		
Pre-swing, %	Left	26.2+/-1.6		100
	Right	23.6+/-1.8		
Swing phase, %	Left	25.9+/-1.5		100
	Right	24.1+/-1.3		
Total Double support, %		50.0+/-1.9		100
Stride length, cm		94+/-3		200
Stride time, sec		1.98+/-0.07		3
Cadence, strides/min		30+/-1		100

Figure 8. Gait analysis parameters on week 42.

Lastly, some postural changes and movement variability throughout the experiment, can be seen on the butterfly parameters depicted on Figures 9, 10 and 11.

The butterfly parameters showed that the gait line length, the anterior/posterior variability, the

lateral symmetry and variability have all improved between the baseline and week 10.

Thereafter, for most of the aforementioned, the effects remained or further ameliorated, except from the lateral symmetry and the gait line length for the left foot, both of which were reduced back to the baseline.

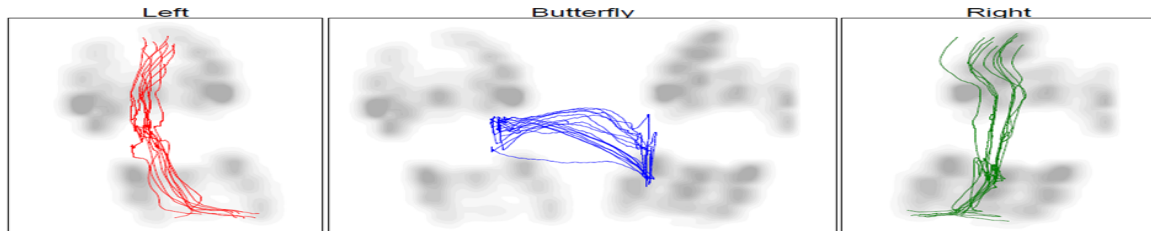


Figure 9. Butterfly parameters on baseline.

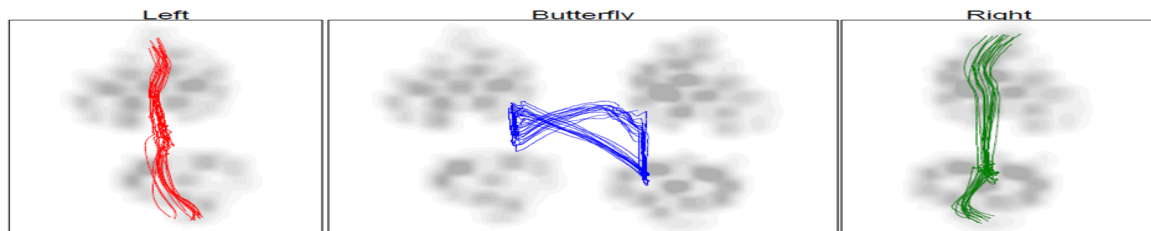


Figure 10. Butterfly parameters on week 10.

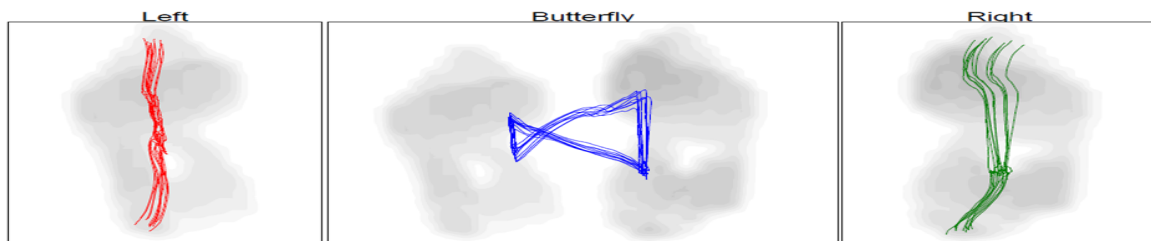


Figure 11. Butterfly parameters on week 42.

Discussion

The current piece of evidence is the first study on Combination Therapy for the treatment of spasticity in stroke patients. It verifies proof that the intervention might be safe to use.

Additionally, it suggests that Combination Therapy might have a positive effect on alleviating spasticity of the lower extremity in chronic stroke patients.

Reducing levels of spasticity implies an improvement in functional recovery with regards to gait pattern and dynamic stability.

This piece of evidence comes to be connected with previous studies that support the separate use of each of the combined treatment modalities for the purpose of decreasing spasticity [7].

Since this is the first study to combine different interventions, the study also ignites interest about what other combinations of treatment modalities could be recruited in order to decrease the levels of spasticity in either stroke or other patients.

It should be reminded to the reader that there are at least 25 different evidence-based interventions that have been applied to treat spasticity [7].

Regarding the measurement tools, the Modified Asworth Scale [27] was used which a highly-reliable assessment tool, supported by evidence in several aspects of its psychometrics regarding stroke patients [28-34].

However, it should be noted that it is a very ambiguous assessment tool because resistance to passive motion could be intercepted by several other factors [35] and this intermingles with other issues that interfere with the quantification of spasticity [36-37].

With regards to the assessment of motor function, the Motricity Index [38] was utilized which is a reliable [39-42], valid [39-40,43], sensitive [39] and highly-responsive [44] assessment tool for stroke patients.

However, it is supported to have poor ceiling effects when used for the lower extremity [45] and small sensitivity for over 3 months after stroke [46].

Especially on the lower extremity, the Motricity Index produced small sensitivity in the acute phase [47].

A standard goniometer was used to measure range of motion which had some disadvantages. Firstly, a joint's range of motion differentiates depending on gender, with males producing less

ROM, and age, with older populations presenting less ROM [48].

Secondly, the study of Gajdosik & Bohannon's [49] showed that the use of goniometer raises validity and reliability concerns.

Goniometer reliability depends on the time intervals between each measurement, with the longer being the least accurate, the different joints, with lower extremity to have lower inter-rater reliability than the upper, the procedure's standardization and the condition of each patient's problem [49].

All the above, combined with the size and weight of the patient's extremity and the position of the hip and knee, affect the measurements' validity [49].

In conclusion, a standard goniometer generates results regarding the ROM, but a potential error underlies every measurement, undermining the final outcome.

Besides the positive effects, this clinical trial gathers proof-of-safety for the intervention.

Pain when stretching and when at rest was absent before the intervention and remained absent even 42 weeks after.

This may further imply that the pain will not feel any pain in the future as this phenomenon is mostly prevalent at six months after stroke [50].

Moreover, no negative side-effect was apparent with regards to the increase of spasticity or decrease in muscle strength or range of motion.

Likewise, this patient may not have further worsening regarding spasticity given that spasticity could appear at the second week post-stroke the earliest [51] and its prevalence increases at the 3rd week [52] and the 6th week [53] post-stroke.

To further support, stroke patients with low sensory or motor deficits probably will not be further affected by spasticity [53-54].

Hence, this case study could support that Combination Therapy is a safe treatment approach towards chronic stroke patients.

Conclusions

In conclusion, the presented data create evidence that could possibly support the use of Combination

Therapy for the treatment of spasticity and, thus, functional improvement in chronic stroke patients.

Additionally, evidence for the proof-of-safety of the intervention was partially granted,

especially for younger populations of chronic stroke.

As this was the first study to research the specific area of interested, it is mandated to conduct more studies, with more subjects and more rigid and standardized procedures, in order to generalize the conclusions and validate the responsiveness of the effects to the greater stroke population.

Combination Therapy is a safe treatment option to be used in order to cope with spasticity in stroke patients.

However, caution should be taken as further studies are necessary to generalize the conclusions of the study to the entire stroke population.

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Conflict of interests

None to declare.

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Corresponding Author: Yannis Dionyssiotis, 1st Physical Medicine and Rehabilitation Department National Rehabilitation Center EKA-KAT, 13122 Ilion, Athens, Greece, e-mail: yannis_dionyssiotis@hotmail.com