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Caregiver Delivered Sensory Electrical Stimulation for Post Stroke Upper Limb Spasticity: A Single Blind Crossover Randomized Feasibility Study

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Abstract

We developed a 64 channel sensory electrical stimulator which delivers a dynamic and variable ‘Sensory Barrage’ Stimulation (SBS). Our aim was to assess the feasibility of caregivers delivering the stimulation in the community for a clinical trial comparing single channel Transcutaneous Electrical Nerve Stimulation (TENS) with SBS for post stroke upper limb spasticity. We trained caregivers of 16 participants with post stroke upper limb spasticity to sequentially administer SBS and TENS for 60 min daily for four weeks each, with a washout period of two weeks in between. Outcome measures tested were recruitment and retention rates, compliance with interventions and daily recording of Participant -reported Numerical Rating Scale (NRS). We also collected results of Action Research Arm Test (ARAT), Leeds Arm Spasticity Impact Scale (LASIS) and Modified Ashworth Scale (MAS) for spasticity. Out of 21 potential participants, 16 consented and 15 completed the protocol. Ten participants received TENS for 80% (23/28) of the intended hours. Eleven participants completed NRS for at 80% (45/56) of the study days. All participants attended all visits. The MAS reduced by at least one in five participants after SBS and in three after TENS. Minimal Clinically Important Difference (MCID) of four points increase in ARAT was seen in five participants following TENS, and in four following SBS. A MCID of 18% decrease in NRS was reported by eight participants after TENS and three after SBS. This study demonstrated the feasibility of undertaking a trial of sensory electrical stimulation for post-stroke spasticity with caregivers delivering intervention in community. The study was not powered to detect efficacy of the interventions. **Trial registration number:** NCT02907775. Date 20-9-2016.

Keywords Stroke · Spasticity · Caregiver · Electrical stimulation · Transcutaneous electrical nerve stimulation · Sensory barrage stimulation

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1 Introduction

Spasticity is frequent sequelae of stroke and is associated with increased utilization of health care resources. [1, 2] Caregivers of stroke survivors with spasticity are more likely to experience anxiety and depression [3]. Spasticity is a significant impedance for recovery of arm function following stroke [4]. One in four stroke survivors develop spasticity within the first 2 weeks of the stroke and by 12 months 39% experience spasticity [5, 6]. Oral antispasticity drugs often result in side effects including sedation, weakness and floppiness [7, 8]. Compliance with oral antispasticity drugs among patients with spasticity following a stroke is only around 50% [9].

Only a few exploratory studies on sensory stimulation using Transcutaneous Electrical Nerve Stimulation (TENS) for spasticity exist [10–13]. A Cochrane review in 2013 did not find evidence at present to support its routine use [14]. A recent systematic review and meta-analysis published in 2018 was also inconclusive due to the limited number of studies [15]. TENS is a single-or dual channel, single strength and fixed duration stimulation to which the nervous system may get habituated, meaning that muscle responsiveness to the treatment may lessen [16].

As part of a previous National Institute for Health Research (NIHR)-funded project the Sheffield Teaching Hospitals team had developed ‘ShefStim’; a unique miniaturised (130x65x25mm) 64-channel programmable electrical stimulator for treating drop foot. For this upper limb study, the team re-engineered it to deliver novel sensory stimulation (ShefStim-SBS) and achieved a further 40% reduction in its size: to 150x58x15mm (Fig. 1). Unlike conventional stimula-



Fig. 1 Sensory barrage stimulator (ShefStim-SBS 64-independent channel stimulator)

tors, ShefStim-SBS enables the intensity and timing of the stimulation from each of the 64 electrodes to be controlled independently. The electrodes were arranged to form an 8 by 8 array and with this configuration ShefStim-SBS was able to programmatically control both the spatial and temporal characteristics of the stimulation. The original ShefStim stimulator was trialed for use as an orthotic aid to walking for people with stroke and multiple sclerosis [17, 18]. During the course of this upper limb project using the new ShefStim-SBS, we pioneered the SBS technique of rapid simultaneous stimulation at multiple sites, in a constantly changing pseudo-random pattern. Non-impaired volunteers described it as a novel, intense and tolerable sensation. This technique allowed us to stimulate a wider area of the body and to vary the timing and strength of each stimulus pulse in a random way employing its 64 independent channels compared to the single-site constant stimulation with standard TENS. As the stimulation provides a larger area of continuously changing sensory input, we have termed it Sensory Barrage Stimulation (SBS). We hypothesise that this approach will significantly reduce habituation compared to single site stimulation, thus providing a logical expansion of the paired associative stimulation approach described by Ridding and Uy [19]

As a precursor to this current study, we had conducted a hospital-based double blind randomized crossover exploratory trial comparing SBS with TENS for the treatment of spasticity affecting the elbow flexor muscles [20]. Immediately after a single 60 min session, both TENS and SBS groups showed a reduction in spasticity. 70% participants continued to respond (i.e. reduced spasticity) at 60 min after SBS, this reduced to 40% continuing to respond at 60 min after TENS. All participants tolerated both interventions well and none had any significant adverse effects. A potential barrier for use of electrical stimulation in treatment of spasticity is difficulty in providing the treatment at home. The aim of this study was to assess the feasibility of a clinical trial with caregivers delivering SBS and TENS in the domiciliary setting, for the treatment of post stroke spasticity affecting the elbow flexors.

2 Materials and Methods

The protocol for this study was approved by the Yorkshire and Humber Research Ethics Committee- Sheffield (IRAS project ID: 202450). This trial was registered with the [ClinicalTrials.gov](https://www.clinicaltrials.gov) (NCT02907775).

The trial was a single blind randomized crossover trial; the assessor was blind to the intervention. The investigator delivering the intervention was not involved in the assessment of outcomes. The data analysis was done by an investigator who was not involved in delivering interventions or assessing outcomes.

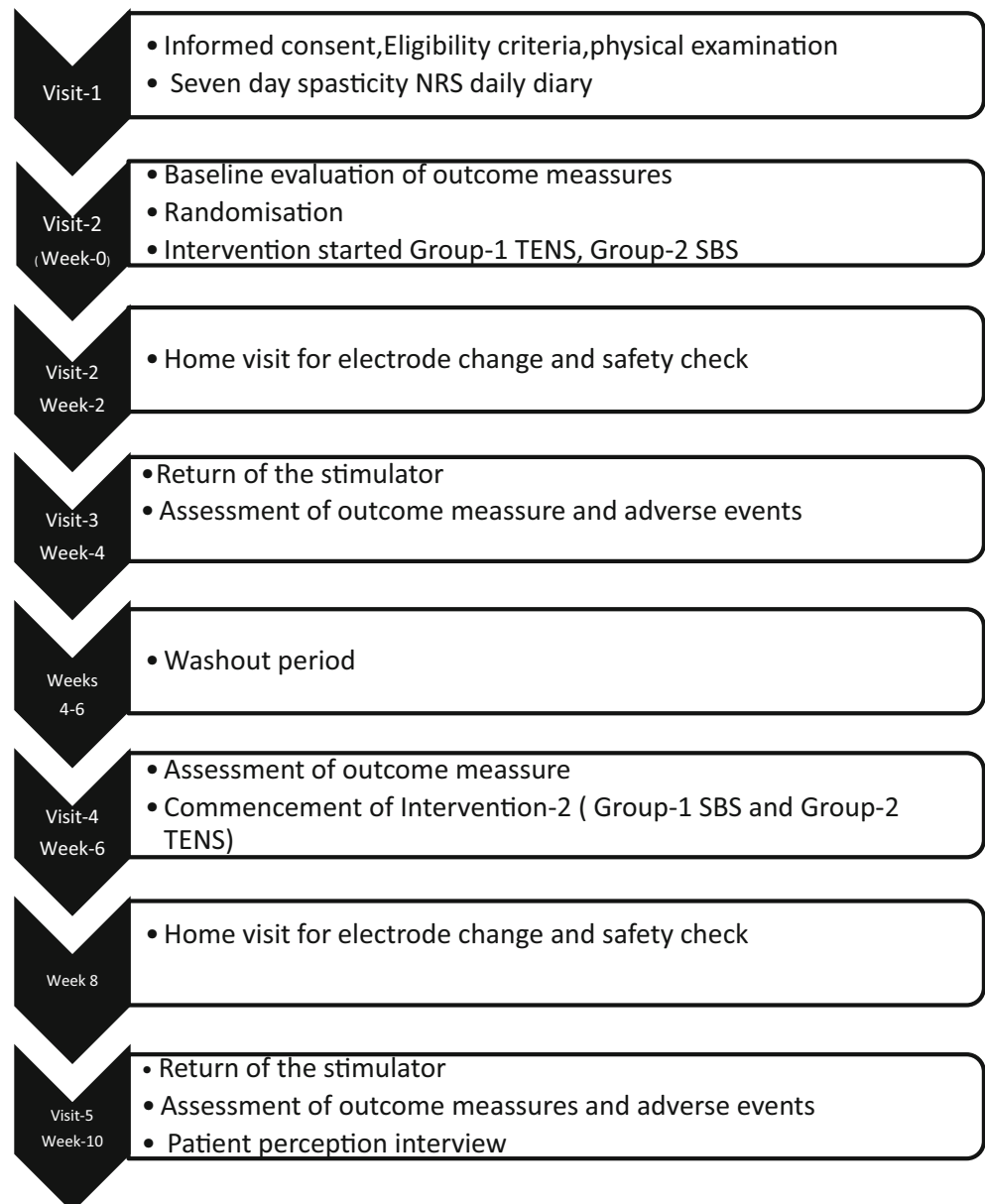
2.1 Participants

Participants were identified from the hospital clinics and community stroke services. When a potential participant with post stroke spasticity of upper limb was identified, a member of the treatment team invited them to take part in the trial and provided the participant and the caregiver with separate information leaflets on the study. After 7 to 14 days a member of the study team contacted the participant and the caregiver. Those who agreed to participate in the study were invited to attend a face to face appointment with a member of the study team at the hospital. The study protocol is shown on Fig. 2.

2.2 Study Protocol

Visit 1: During this visit participants and caregivers discussed the study with the principal investigator, who obtained separate informed consents from the participant and the caregiver. The participants were screened according to the following criteria. The inclusion criteria were 1) age 18 and above; 2) stroke at least six months previously and 3) spasticity at elbow flexor muscles of grade 2 or more on the Modified Ashworth Scale (MAS). The exclusion criteria were 1) cognitive impairment that would interfere with their ability to comply with the experimental protocol or provide an informed consent; 2) dermatological, rheumatologic or orthopedic conditions of the affected arm interfering with movement of the elbow; 3)

Fig. 2 Study protocol



pre-existing severe systemic disorders such as cardiovascular disease, active cancer or renal disease, end stage pulmonary or cardiovascular disease, psychiatric disorders including severe alcohol or drug abuse and depression; 4) inability to perform the baseline assessments; 5) severe tactile hypersensitivity; 6) participation in other, spasticity related studies; 7) within 12 weeks of receiving Botulinum toxin injections; 8) poorly controlled epilepsy; 9) pacemaker or any other implanted devices, 10) inability of the caregiver to deliver the intervention and 11) pregnancy.

The participants and caregivers were trained to record the severity of spasticity in a paper diary daily between 6 pm and 9 pm on a Numerical Rating Scale (NRS) ranging from 0 to 10; 0 -no spasticity, 10 -worst spasticity one can imagine [21]. The participants were asked to complete the NRS diary for 7 days immediately prior to their randomization visit at the clinical research facility.

Visit 2: The participants were randomly allocated to either group-1 or group-2 using an online randomization website; www.randomization.com. Initially the baseline outcome measures were carried out by the assessor (who was blinded to the allocation). Another researcher then setup the device for the participant and demonstrated the use of the device. For their first intervention participants in group-1 received TENS and those in group-2 received SBS. The TENS or SBS were setup over the extensor aspect of the affected upper arm and stimulation was done for 60 min. The initial intervention was done at the Clinical Research Facility within the Royal Hallamshire Hospital, Sheffield, United Kingdom. The strength of stimulation was set just below the motor threshold or the maximum tolerable stimulation whichever was lower. The researcher checked for any adverse effects after the intervention. The participants and caregivers were trained to apply the electrodes and deliver the intervention at home for 60 min a day for the next four weeks. After 2 weeks each participant was visited at home by the researcher to check for any adverse events, ensure they were correctly setting up the intervention, and to replace the electrodes.

Visit 3: The participants and caregivers returned after four weeks of intervention. The participant was assessed with outcome measures and adverse events. The outcome measures were carried out by an assessor who did not know about the type of intervention received by the participants. No interventions were performed for the next two weeks.

Visit 4: After the two week washout period, the participants attended the clinical research facility for the setup of the second intervention. This time participants in group-1 received SBS and group -2 received TENS. Before the second intervention was started the outcome measures were carried out by the assessor who was blinded to the intervention. The intervention was then setup by the other researcher and tested for 60 min, checking for any adverse effects. The participants and caregivers were trained to apply the electrodes and deliver the intervention at home for 60 min a day for the next four weeks. Two weeks into the

intervention period the researcher carried out another home visit to check for any adverse events, ensure they were correctly setting up the intervention, and to replace the electrodes.

Visit 5: The blinded researcher assessed the outcome measures and looked for any adverse event after the intervention.

2.3 Interventions

SBS: Participants and caregivers were issued our 64-independent channel stimulator (ShefStim-SBS) with a 64-channel electrode array contained in a custom made arm strap (Fig. 1). ShefStim-SBS enables stimulation to be applied in complex spatial and temporal patterns to be applied via an array of 64 electrodes. The stimulation patterns used in this study were the same as in our previous published hospital based study [20]. The participants with help from caregivers applied the electrode array over the extensor aspect of the affected upper arm. An adhesive hydrogel sheet (ST GEL-high impedance grade SCBZAB-05 M, Sekisui Plastics, Japan) with a resistivity of $1.3 \text{ k}\Omega\cdot\text{m}$ and a thickness of 0.5 mm was laid over the surface of the electrode array to act as the interface between the electrodes and the skin. In this study we used a custom-made arm strap for holding the stimulating electrode array in place for ease of home use. At the start of the first session, intensity of stimulation was increased until a muscle movement was first observed. The intensity level would then be set at 90% of this value, or the maximum tolerable level; whichever was lower. Stimulation continued at this level with the site moving around the array electrodes for 60 min [20]. On the 15th day, one of the researchers visited the participants at home to check whether there were any issues and to change the hydrogel sheet. Participants and caregivers returned to the Clinical Research Facility at the end of the fourth week to return equipment and had the outcome assessments done.

TENS: We used the stimulation techniques tested in the previous studies, including our trial [10–13, 20]. The participants, with help from caregivers, applied the single channel TENS surface electrodes over the extensor aspect of the affected upper arm – following prior training, placement was intended to be over the radial nerve in the radial groove. The intensity of stimulation was set to 90% of the motor threshold and TENS was applied for 60 min daily for four weeks.

2.4 Outcome Measures

The criteria for trial feasibility were: (1) 60% or more of eligible participants being consented for the trial and (2) 85% of the recruited participants completing the protocol. We also collected data on adherence with the intervention, adherence with completion of daily diary recording of NRS, attendance for the follow up appointments, rate of completion of the outcome measures and perception of the participants and caregivers about study. We assessed adherence of treatment by using the TENS user record program which showed time use for TENS. We defined good

compliance as use of at least 23 h and not more than the 28 h. The compliance of recording diary was noted by manually counting the NRS data entries recorded by participants in their daily diaries. We considered 80% or more days with legible diary entry as good adherence.

The outcome measures tested were participant reported NRS for spasticity, Action Research Arm Test (ARAT) [22], Leeds Adult Spasticity Impact Scale (LASIS) [23], Modified Ashworth Scale (MAS) for spasticity of elbow flexor muscles, muscle strength in affected elbow flexion and extension using Medical Research Council (MRC) grading and a questionnaire designed to capture participant's perception towards efficacy and acceptability of treatment. [24]. We used the Minimal Clinically Important Difference (MCID) established in the literature for defining response. The participants who had a reduction in NRS of at least 18% after four weeks of intervention were considered as responders [21]. Participants with an increase in ARAT of at least 4 in raw score were also considered as responders [25]. Currently there are no reported MCID for MRC grade, MAS or LASIS.

2.5 Analysis

Analyses of the data were performed by two authors who were not involved in the data collection or delivery of intervention. As it was a feasibility study we focused on feasibility issues and sample size calculations. We calculated recruitment rate, reason for non-participation, adherence with the protocol, acceptability, participants' perceptions about the devices and adverse events. All statistical analyses were performed using SPSS Statistics version 18.0 (SPSS, Inc., Chicago, IL, USA). A p value < 0.05 was considered to be statistically significant. The sample size was calculated using nQuery Advisor version 5.0. It was based on a two group t-test for equal means to conduct a three arm randomized control trial of SBS, TENS and 'usual care' control, to have 90% power to demonstrate a MCID reduction of 18% in NRS at the 1% significance level, to allow for multiple testing [26, 27].

3 Results

We approached 21 potential participants with post stroke upper limb spasticity, of whom 16 consented to take part in the study (76%). Of the five who chose not to participate; three did not give any reason and one had previous allergic reaction for the TENS stimulation electrode. We excluded one participant after screening as the participant had elbow flexor spasticity of less than grade 2 on MAS. The consort diagram of the study is shown on Fig. 3. One of the recruited participants dropped out after randomization before starting the first intervention. This participant was excluded from analysis. Overall 15 participants completed the study (94%), seven of whom

(47%) were men, and the age ranged from 28.8 to 70.5 years (54.5 ± 12.4 years). One of the participants was of Afro-Caribbean ethnic origin. All others were Caucasians. Five had right-sided stroke and ten had left-sided stroke. All 16 participants had spasticity of elbow flexor muscles of MAS of 2 or more.

Ten participants (67%) showed good adherence with the intervention and 11 (73%) showed good adherence in recording NRS daily during the intervention period. All tolerated the interventions well. There were four adverse events reported by three participants. The adverse events were: 1) vasovagal syncope during TENS period 2) headache and tingling feeling down left arm in washout period 3) seizure at 18 h after the application of SBS 4) nausea within TENS period. None of the adverse events occurred while using TENS or SBS.

The MAS of the elbow reduced by at least 1 grade in five participants after SBS and in three participants after TENS. For the ARAT, a Minimal Clinically Important Difference (MCID) of four points increase was seen in five participants following TENS, and in four following SBS. A MCID of 18% decrease in NRS was reported by eight participants after TENS and in three after SBS. The LASIS score improved in 12 participants after TENS and in seven after SBS.

Fourteen participants (93%) completed the Participants' Perception Questionnaire (Table 1), which sought feedback on their experiences in using the two stimulation technologies and in completing the outcome measures. Eight participants preferred TENS while six preferred SBS. The most common reasons behind participant's choice of preference were ease of administration (8), nature of the sensation (8) and perceived effectiveness of the treatment (8). Eight participants offered suggestions to improve the design of future studies, which included aiding electrode placement for TENS (1), improving SBS usability (4), such as facilitating single handed application and the addition of a timer function. Other comments included requests for a future study to include the shoulder, and, a longer duration for each intervention period. Despite the earlier SBS usability suggestions, one respondent commented that they found SBS more convenient to use than TENS and one noticed improvements in hand function following SBS.

Two participants did not agree that the ARAT was an appropriate outcome measure, commenting that it was too difficult to complete or it led to frustration for their level of arm function. Twelve of the 14 respondents would be prepared to participate in a follow-up study (Table 2).

The sample size calculation for a two group t-test for equal means showed that to conduct a three arm randomized control trial of SBS, TENS and 'usual care' control, we would need 68 subjects per group (total 204 participants) to have 90% power to demonstrate a MCID reduction of 18% in NRS at the 1% significance level to allow for multiple testing [26, 27].

4 Discussion

This study demonstrated that it is feasible to conduct a trial of electrical sensory stimulation in the community with caregivers assisting in the delivery of the intervention. The recruitment and retention rates in this study are similar to recruitment and retention rates of participants in other randomized controlled trials done in UK [28].

One of the difficulties in clinical trials with electrical stimulation is delivery of the interventions in the community. The interventions could take weeks and it is not practical for participants to visit research facilities regularly for the

intervention. It is also not cost effective or practical for research therapists to do home visits to deliver such interventions. Our results showed that it is possible to train participants and caregivers to deliver electrical stimulation for treating elbow spasticity at home. Around two thirds (67%) showed good adherence with the protocol. This is similar to the rate of adherence of stroke survivors with home exercises program (65%) and adherence across all types of medications (69%) [29, 30] and better than the 50% adherence reported for oral anti-spasticity medications. Future studies using electrical stimulation at home should include an objective measure of adherence such as an inbuilt user record within devices. We

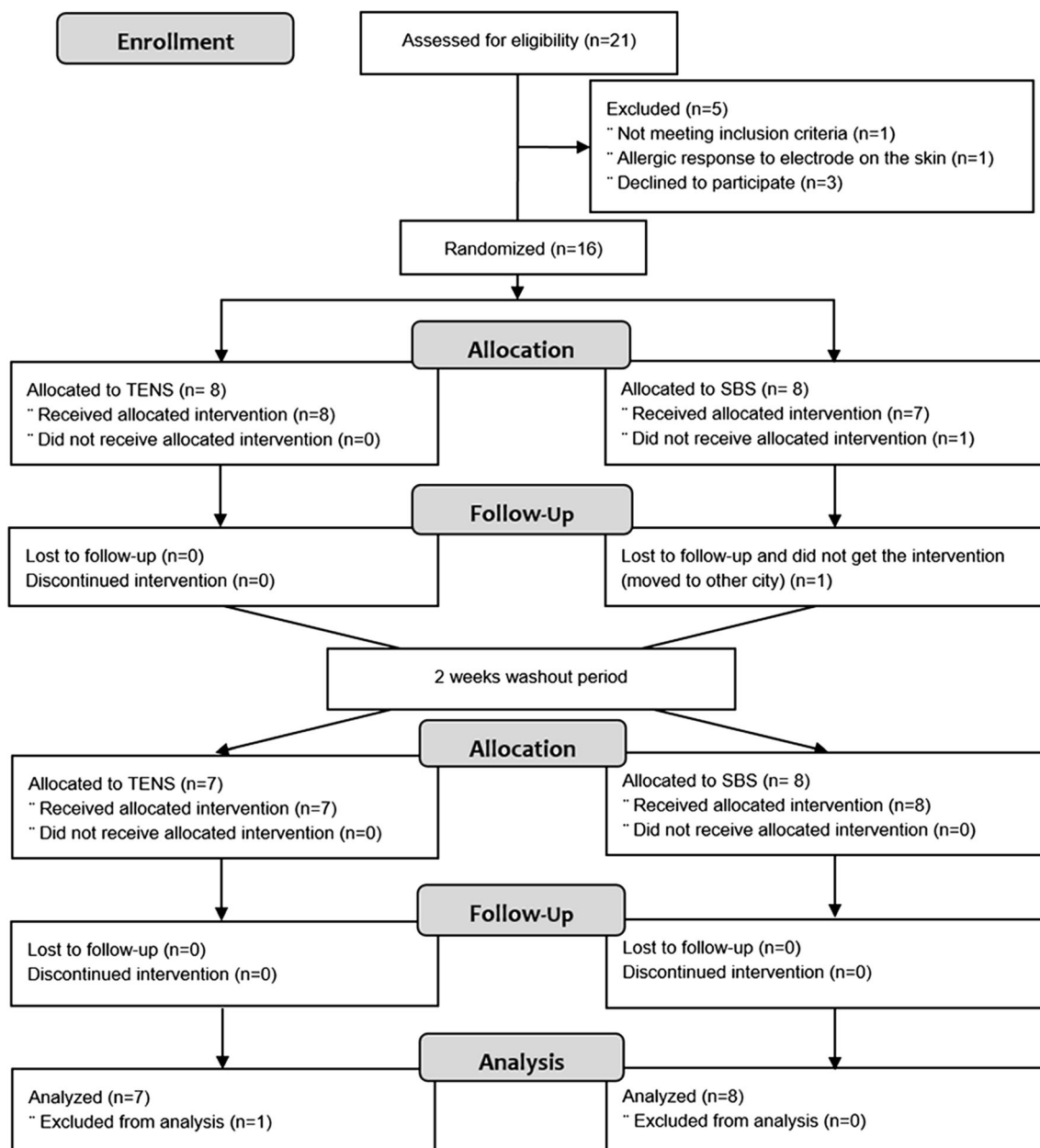


Fig. 3 CONSORT flow diagram showing number of participants through each stage of the randomized crossover trial

Table 1 Outcomes before and after interventions

	TENS			SBS		
	pre-intervention	post-intervention	<i>p</i> value	pre-intervention	post-intervention	<i>p</i> value
Spasticity NRS	5 (4,6)	4 (4,6)	0.072 *	5 (5,6.5)	6 (4,7)	0.748 *
ARAT	28 (3,39)	28 (1,46)	0.102 *	36 (4,45)	33 (3,50)	0.504 *
LASIS	1.2 + 0.2	0.9 + 0.2	0.010†	1.2 + 0.2	1.2 + 0.2	0.915†
MAS	1.5 (1.5,2.0)	1.5 (1.5,2.0)	1.000 *	2.0 (1.5,2.0)	1.5 (1.0,2.0)	0.131 *
MRC grade (Elbow extension)	3 (2,4)	3 (2,4)	0.655 *	3 (2,4)	3 (2,4)	1.000 *
MRC grade (Elbow Flexion)	3 (2,4)	3 (3,4)	0.257 *	4 (2,4)	3 (2,4)	0.414 *

*Wilcoxon signed ranks test (value is median, Q1, Q3)

† paired t-test (value is mean + SEM)

Abbreviations: NRS = Numeric Rating Scale, ARAT = Action Research Arm Test, LASIS = Leeds Adult Spasticity Impact Scale, MAS = Modified Ashworth Scale, MRC = Medical Research Council

Table 2 Participants' Perception Questionnaires

Questions	Answer			
	Yes	No	N/A	Comments
1. Is the ARAT an appropriate test to assess the functioning of your arm?	12	2	–	1. Because of no hand function on right side due to tone, cannot complete test. 2. It's far too hard. Frustrating for the stage I am at.
2. Is the Leeds Spasticity Impact Scale an appropriate questionnaire to assess the spasticity of your arm?	14	–	–	
4. Is TENS an appropriate treatment for you?	12	1	1	
5. Is SBS an appropriate treatment for you?	11	2	1	
6. Do you have any preferences between TENS and SBS?	14	–	–	
- 8 participants choose TENS				
- 6 participants choose SBS				
What are the reasons behind your choice?				
- Effectiveness of the treatment	8	3	3	1. Familiar
- Nature of the sensation	8	4	3	2. TENS-occasionally noticed ongoing tingling of forearm after use for an hour but not uncomfortable
- Ease of administration	8	5	1	
- Side effects	–	11	3	
- Others	2	3	9	
7. Do you have any concerns about this study?	2	11	1	1. Not specified 2. Number of visits and home visit acceptable
8. Will you consider participating in future research using TENS or SBS?	12	–	2	
9. Have you any suggestions to improve the design of future studies using TENS and SBS?	8	2	4	1. Design of application of SBS for ease of use 2. Ease of use for SBS, number of visits to be reduced for convenience 3. Having the times on SBS would help as it's easy to forget to set the separate times 4. To make easier to apply on own (need 2 hands to apply) 5. Small cuff 6. SBS hard to get on by self. Better if it was something you could pull on 7. We should look at shoulder. This study looked at elbow. 8. Better way of marking arm for correct position of pads
10. Any other comments?	4	–	10	1. Further study with longer duration of each intervention period. 2. Enjoyed taking part. Feel left arm is not as tight. Increased use of Lt. arm in activity of daily living. 3. SBS more convenient to use. 4. SBS helped with moving left fingers on their own.

Abbreviations: N/A = not answer

plan to refine the ShefStim-SBS device further to include concurrent usage monitoring.

Participant reported outcome measures are important in studies of post stroke spasticity. We used NRS and LASIS. LASIS is recommended by the Royal College of Physicians UK as an outcome measure for post stroke upper limb spasticity [24]. Further research is required to establish MCID on LASIS. Recording LASIS was successful in all our participants, who also felt that this is an appropriate measure to study. During treatment with TENS participants reported improvement on LASIS. Our study had only 16 participants and used multiple outcome measures. In view of these limitations further research is required to establish whether TENS improve LASIS in people with post stroke upper limb spasticity.

The participant reported NRS is a well-accepted outcome measure for spasticity with a moderate to high level of correlation with other clinician rated instruments used to assess spasticity [31]. This measure was used successfully to get FDA approval for Nabiximols for treatment of spasticity in multiple sclerosis [32]. One of the issues is that participants or caregivers need to record the NRS daily. This could be a problem for studies where intervention could last several weeks. In our study we noted that 11 out of 15 participants/caregivers recorded NRS for more than 80% of the days, using a paper diary. An electronic diary with automated daily reminders could improve the capture of the NRS and we plan to deliver and investigate this in a follow-up study.

This study demonstrated that sensory electrical stimulation delivered by caregivers in the community is a safe and well tolerated by participants with post stroke upper limb spasticity. Six participants preferred SBS and eight preferred TENS. The SBS was delivered using a prototype device which was more cumbersome to don and doff and difficult to operate. Improvements in design, especially ease of application of the wearable arm sleeve with integrated electrode array and incorporation of a timer are expected to further improve the acceptability of the SBS and this work is planned.

4.1 Limitations

Our data did not show any conclusive evidence that multi-channel stimulation was superior to single channel stimulation for post stroke upper limb spasticity. As a feasibility trial, this study was not designed to evaluate the efficacy of the interventions. Hence these data should not be used to justify or refute the use of electrical sensory stimulation as a treatment for post stroke upper limb spasticity. The study recruited only participants with spasticity six months or more after stroke and who had a caregiver able to administer the intervention. Hence the results are not generalizable to all participants with post stroke spasticity and in fact may have focused on participants with less resolvable spasticity. The World Health Organization's 'International Classification of Functioning,

Disability and Health' (ICF) provides a framework that allows the systematic categorization of clinical observations [33]. The areas include impairment, activity limitation, restriction in participation and quality of life. We measured impairment using MRC grading of muscle power and muscle tone using MAS. The ARAT and LASIS reflect limitation of activities involving upper limb function. We did not record measures of social participation or quality of life (QoL) in this study. A future study planned will include the EQ-5D, an internationally recognized and validated QoL tool, or potentially the spasticity-related QoL tool, the SQoL-6D [34], which is still in final validation.

Commercially available TENS devices are regulated for managing pain and not as a spasticity therapy, so such usage is restricted to a research setting. The use of separate single-channel TENS as a comparator to SBS was a further study limitation. While it enabled the stimulation modality to be investigated and contrasted scientifically, it resulted in some of the potential advantages of the ShefStim-SBS being artificially restricted, in that its 64 stimulating channels could have been distributed across several joints. Single channel TENS can only stimulate one joint, and thus to contrast like-with-like, only one joint, the elbow, could be treated in this study. Furthermore, the use of two different stimulators meant that the participants were aware of the differences in the interventions. A future study of a refined ShefStim-SBS will offer two potential benefits.

1. Its 64 independent channel programmability, together with new electrode designs, will permit the same ShefStim-SBS device to simulate and deliver single channel TENS thus providing device blinding for the TENS intervention arm.
2. In addition, it would be possible to utilize the ShefStim-SBS stimulating channels across several joints of the upper limb to maximize therapeutic effect.

Work is underway to develop and test new preparation techniques to improve and prolong hydrogel performance to reduce researcher visits and participant /carer burden.

5 Conclusions

Multichannel sensory electrical stimulation of the upper arm using the unique 64-independent channel ShefStim-SBS is safe and well tolerated by participants with post stroke spasticity. It is feasible to train caregivers to deliver sensory electrical stimulation at home, and conduct a randomized controlled trial to test single and multi-channel sensory electrical stimulation in a domiciliary setting. Our suggestions for this follow-up trial include:

- (1) a randomized control design
- (2) 204 participants divided into three arms ('usual care' control, TENS and SBS)
- (3) use of electronic reminders for delivery of intervention and recording NRS
- (4) inclusion of measures of quality of life and social participation
- (5) utilizing a refined ShefStim-SBS device to provide blinded TENS and SBS intervention arms and
- (6) investigating the utility of ShefStim-SBS concurrent multi-joint sensory stimulation for upper limb spasticity therapy using different electrode array configurations. Further studies on sensory electrical stimulation in acute and subacute phases of stroke are also warranted and may prove more receptive to spasticity improvement.

The research should also explore the option of combining sensory electrical stimulation with other interventions to improve upper limb function such as motor electrical stimulation (which could be achieved with ShefStim-SBS) or Constraint Induced Movement Therapy (CIMT) [35].

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Authors' contributions M Slovak, M Reeves, T. J Healey and A.N. Ali contributed to the design of the study. M Slovak and M Reeves trained the participants and care givers on use of TENS and SBS. KPS Nair was the principal investigator for the study and did participant recruitment, consenting and data analysis. L Patterson, K Lavender and L Strachan did collection of outcome measures and study management. C Chotiyarnwong performed the data analysis and prepared the manuscript. K Baster helped with data analysis. All authors contributed to preparation of the final manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing of interests.

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References

1. Kheder A, Nair KP. Spasticity: pathophysiology, evaluation and management. *Pract Neurol*. Oct 2012;12(5):289–98.
2. Tyry T, Salter A, Largent J, Marrie RA. The impact of spasticity severity on healthcare utilization among MS participants: a large-scale six-year follow-up study. *J Neurol Sci*. 2013;333:e376–7.
3. Denno MS, Gillard PJ, Graham GD, DiBonaventura MD, Goren A, Varon SF, et al. Anxiety and depression associated with caregiver burden in caregivers of stroke survivors with spasticity. *Arch Phys Med Rehabil*. Sep 2013;94(9):1731–6.
4. Intercollegiate Stroke Working Party. National clinical guideline for stroke. 3rd ed: London: Royal College of Physicians; 2008.
5. Hsieh YW, Wu CY, Lin KC, Chang YF, Chen CL, Liu JS. Responsiveness and validity of three outcome measures of motor function after stroke rehabilitation. *Stroke*. Apr 2009;40(4):1386–91.
6. Watkins CL, Leathley MJ, Gregson JM, Moore AP, Smith TL, Sharma AK. Prevalence of spasticity post stroke. *Clin Rehabil*. Aug 2002;16(5):515–22.
7. Goldstein EM. Spasticity management: an overview. *J Child Neurol*. Jan 2001;16(1):16–23.
8. Bethoux F. Spasticity management after stroke. *Phys Med Rehabil Clin N Am*. Nov 2015;26(4):625–39.
9. Halpern R, Gillard P, Graham GD, Varon SF, Zorowitz RD. Adherence associated with oral medications in the treatment of spasticity. *PM & R : the journal of injury, function, and rehabilitation*. Sep 2013;5(9):747–56.
10. Armutlu K, Meric A, Kirdi N, Yakut E, Karabudak R. The effect of transcutaneous electrical nerve stimulation on spasticity in multiple sclerosis participants: a pilot study. *Neurorehabil Neural Repair*. Jun 2003;17(2):79–82.
11. Ping Ho Chung B, Kam Kwan Cheng B. Immediate effect of transcutaneous electrical nerve stimulation on spasticity in Participants with spinal cord injury. *Clinical rehabilitation*. Mar 2010;24(3):202–210.
12. Lin Z, Yan T. Long-term effectiveness of neuromuscular electrical stimulation for promoting motor recovery of the upper extremity after stroke. *J Rehabil Med*. May 2011;43(6):506–10.
13. Miller L, Mattison P, Paul L, Wood L. The effects of transcutaneous electrical nerve stimulation (TENS) on spasticity in multiple sclerosis. *Mult Scler*. May 2007;13(4):527–33.
14. Amatya B, Khan F, La Mantia L, Demetrios M, Wade DT. Non pharmacological interventions for spasticity in multiple sclerosis. *The Cochrane database of systematic reviews*. Feb 28 2013(2):CD009974.
15. Mahmood A, Veluswamy SK, Hombali A, Mullick A, N M, Solomon JM. Effect of Transcutaneous Electrical Nerve Stimulation on Spasticity in Adults With Stroke: A Systematic

- Review and Meta-analysis. *Archives of physical medicine and rehabilitation*. Nov 16 2018.
16. Spielholz NNM. Conventional TENS and the phenomena of accommodation, adaption, habituation, and electrode polarization. *J Clin Electrophysiol*. 1995;7:16–9.
 17. Prenton S, Kenney LP, Stapleton C, Cooper G, Reeves ML, Heller BW, et al. Feasibility study of a take-home array-based functional electrical stimulation system with automated setup for current functional electrical stimulation users with foot-drop. *Arch Phys Med Rehabil*. Oct 2014;95(10):1870–7.
 18. Heller BW, Clarke AJ, Good TR, Healey TJ, Nair S, Pratt EJ, et al. Automated setup of functional electrical stimulation for drop foot using a novel 64 channel prototype stimulator and electrode array: results from a gait-lab based study. *Med Eng Phys*. Jan 2013;35(1):74–81.
 19. Ridding MC, Uy J. Changes in motor cortical excitability induced by paired associative stimulation. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*. Aug 2003;114(8):1437–44.
 20. Slovak M, Chindo J, Nair KP, Reeves ML, Heller B, Barker AT. Sensory barrage stimulation in the treatment of elbow spasticity: a crossover double blind randomized pilot trial. *Neuromodulation : journal of the International Neuromodulation Society*. Feb 2016;19(2):220–6.
 21. Farrar JT, Troxel AB, Stott C, Duncombe P, Jensen MP. Validity, reliability, and clinical importance of change in a 0-10 numeric rating scale measure of spasticity: a post hoc analysis of a randomized, double-blind, placebo-controlled trial. *Clin Ther*. May 2008;30(5):974–85.
 22. Sivan M, O'Connor RJ, Makower S, Levesley M, Bhakta B. Systematic review of outcome measures used in the evaluation of robot-assisted upper limb exercise in stroke. *J Rehabil Med*. Feb 2011;43(3):181–9.
 23. Ashford S, Slade M, Malaprade F, Turner-Stokes L. Evaluation of functional outcome measures for the hemiparetic upper limb: a systematic review. *J Rehabil Med*. Nov 2008;40(10):787–95.
 24. Royal College of Physicians, BSoRM, Chartered Society of Physiotherapy, Association of Chartered Physiotherapist Interested in Neurology. Spasticity in adults: management using botulinum toxin. *National guidelines*. 1st ed: London: Royal College of Physicians; 2009.
 25. Lin JH, Hsu MJ, Sheu CF, Wu TS, Lin RT, Chen CH, et al. Psychometric comparisons of 4 measures for assessing upper extremity function in people with stroke. *Phys Ther*. Aug 2009;89(8):840–50.
 26. Dixon WJ, Massey FJ. Introduction to statistical analysis. 4th ed. New York: McGraw-Hill; 1983.
 27. O'Brien RG, Muller KE. Applied analysis of variance in behavioral science. New York: Marcel Dekker; 1993.
 28. Walters SJ, Bonacho Dos Anjos Henriques-Cadby I, Bortolami O, et al. Recruitment and retention of participants in randomised controlled trials: a review of trials funded and published by the United Kingdom Health Technology Assessment Programme. *BMJ open*. Mar 20 2017;7(3):e015276.
 29. Miller KK, Porter RE, DeBaun-Sprague E, Van Puymbroeck M, Schmid AA. Exercise after stroke: patient adherence and beliefs after discharge from rehabilitation. *Top Stroke Rehabil*. Mar 2017;24(2):142–8.
 30. Cheiloudaki E, Alexopoulos EC. Adherence to Treatment in Stroke Participants. *International journal of environmental research and public health*. Jan 11 2019;16(2).
 31. Anwar K, Barnes MP. A pilot study of a comparison between a patient scored numeric rating scale and clinician scored measures of spasticity in multiple sclerosis. *NeuroRehabilitation*. 2009;24(4):333–40.
 32. Wade DT, Collin C, Stott C, Duncombe P. Meta-analysis of the efficacy and safety of Sativex (nabiximols), on spasticity in people with multiple sclerosis. *Mult Scler*. Jun 2010;16(6):707–14.
 33. Kostanjsek N. Use of The International Classification of Functioning, Disability and Health (ICF) as a conceptual framework and common language for disability statistics and health information systems. *BMC public health*. May 31 2011;11 Suppl 4: S3.
 34. Cicely Saunders Institute Of Palliative Care, Policy & Rehabilitation. The spasticity-related quality of life tool (SQoL-6D). Available: <https://www.kcl.ac.uk/cicelysaunders/resources/tools/the-sqol-6d-2.pdf> [Accessed 5 November, 2019].
 35. Kwakkel G, Veerbeek JM, van Wegen EE, Wolf SL. Constraint-induced movement therapy after stroke. *The Lancet Neurology*. Feb. 2015;14(2):224–34.

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