Blood Perfusion Changes during Sacral Nerve Root Stimulation versus Surface Gluteus Electrical Stimulation in Seated Spinal Cord Injury

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Abstract

Objective: To examine dynamic changes of ischial blood perfusion during sacral nerve root stimulation against surface functional electrical stimulation (FES). **Methods:** Fourteen adults with suprasacral complete spinal cord injury were recruited. The gluteal maximus was activated by surface FES or stimulating sacral nerve roots by functional magnetic stimulation (FMS) or a sacral anterior root stimulator implant (SARS). Ischial skin index of haemoglobin (IHB) and oxygenation (IOX) was measured. **Results:** Skin blood perfusion was significantly higher during FMS than the baseline (IHB 1.05±0.21 before vs. 1.08±0.02 during stimulation, P=0.03; IOX 0.18 ± 0.21 before vs. 0.46 ± 0.30, P=0.01 during stimulation, n=6). Similarly, when using the SARS implant, we also observed that blood perfusion significantly increased (IHB 1.01 ± 0.02 before vs. 1.07 ±0.02 during stimulation, P=0.003; IOX 0.79±0.81 before vs. 2.2±1.21 during stimulation, P=0.03, n=6). However, there was no significant change of blood perfusion during surface FES. Among 4 participants who completed both the FMS and FES studies, the magnitude of increase in both parameters was significantly higher during FMS. **Conclusion:** This study demonstrates that using SARS implant is more efficient to activate gluteal muscles and confer better benefit on blood perfusion than applying traditional FES in SCI population.

Key words: electrical stimulation**,** pressure ulcer, sacral nerve roots, spinal cord injury, gluteal muscles, ischial tuberosity, blood perfusion.

INTRODUCTION:

Pressure ulcer is one of the most devastating conditions for people with Spinal Cord Injury (SCI)[1]. It is reported that up to 85% of adults with SCI will develop a pressure ulcer at some point during their lifetimes[1-5], and 7-8% of those who develop pressure ulcers will die from related complications. [6]

According to National/ European Pressure Ulcer Advisory Panel guideline, pressure ulcer has been newly named as pressure injury, which is described as an area of localised injury to the

skin as a result of prolonged pressure alone, or pressure in combination with shearing forces.[7] It is typically categorised into four key stages depending on severity. The higher the grade is, the more severe the injury to the skin and underlying tissue will be. In stage one, the skin is not broken but is red or discoloured; the redness or change in colour does not fade within thirty minutes after pressure is removed. In stage two, the epidermis or topmost layer of the skin is broken, creating a shallow open sore and drainage may, or may not, be present. At stage three, the break in the skin extends through the dermis (second skin layer) into the subcutaneous and fat tissue and the wound is deeper than in stage two. In stage four, the breakdown extends into the muscle and can extend to the bone. At this stage, there is often a large amount of dead tissue and drainage.

Following SCI, the interruption of spinal vasomotor pathways results in loss of vasomotor control over skeletal muscle and skin, which lowers the tone of vascular bed below the level of lesion. Impaired vascular patency causes vessels to be less able to withstand normal loading conditions. Concurrent with loss of capillary networks due to lost muscle bulk, the volume of blood in the tissues is reduced [8-10]. Previous clinical studies have shown that tissue blood volume/perfusion was lower and tissue reperfusion was impaired in people with SCI in comparison with able-bodied subjects.[11-14] For instance, Jan and colleagues measured sacral skin perfusion in 14 people with SCI and 14 healthy subjects during sitting[11]. They found skin perfusion declined more in people with SCI during constant sitting than able-bodied subjects. Furthermore, impaired vascular function in people with SCI has been reported by other studies.[12,13] Makhsous and colleagues [12] measured transcutaneous partial pressures of oxygen and carbon dioxide of the buttock overlying the ischial tuberosity in 20 paraplegic individuals, 20 tetraplegic individuals, and 20 able-bodied subjects. They found that recovery time during offloading was significantly longer in both paraplegic and tetraplegic participants in comparison with able-bodied individuals. As a result, people living with SCI have a higher risk of developing pressure ulcers than able-bodied individuals

Once a pressure ulcer is formed, it is very difficult to achieve a full repair or it takes a particularly long period of time to heal for severe cases. In addition, those who suffer a pressure ulcer may be subjected to longer hospital stays, delayed rehabilitation and a significant loss of independence, which adds another burden to the psychological trauma of SCI, as well as the reduced quality of life.[15] If a pressure ulcer is severe, it can lead to further disabilities, the need for surgical interventions and even fatal infections.[2,15] In addition to the

detrimental personal effect, a pressure ulcer also represents a significant cost burden for health and social care systems. Although the exact cost of pressure ulcer management in people living with SCI is unknown in the United Kingdom, the average cost to treat one stage 4 pressure ulcer is £14,108 per episode in the general population[16]. Given the significant personal consequences and serious health care burden, effective prevention of pressure ulcer is undoubtedly important for people living with SCI.

Thus far, preventing pressure ulcer tends to focus on methods to reduce external pressure. These efforts range from using pressure-relieving devices, to patients performing 'pressure relief' manoeuvres themselves, such as frequent repositioning, 'push-ups' or 'leaning forward [17-20]. However, these efforts are only partially effective at best in people living with SCI. Poor compliance from patients to carry out the frequent pressure relief activities together with intrinsic changes in the paralyzed individuals such as reduced vascular response to loading, reduced muscular tone and progressive loss of muscle bulk may contribute to the high incidence of pressure ulcer in this population[21-22]. Despite simple pressure relief methods providing benefits in reducing local pressure at bony prominences, such approaches were not aimed to prevent muscle atrophy or to improve muscular tone and tissue blood volume. Therefore, in conjunction to pressure relief strategies, alternative means of improving tissue health should be explored in this population for pressure ulcer prevention.

In fact, activating paralyzed gluteal muscles to modify tissue blood circulation by using surface functional electrical stimulation (FES) has been explored in SCI for 30 years.[23-25] For instance, back in the 1990s, Levine and colleagues[19] examined ischial blood flow in six people with acute SCI during electrical stimulation of gluteus maximus. They found that skin blood flow increased during stimulation for all participants. Similarly, Gyawali and colleagues[24] measured loaded gluteal tissue oxygenation during 7s or 13s of continuous electrical stimulation and 3s burst electrical stimulation of gluteus maximus using surface electrode in 17 patients with SCI who had a mean age of 37 years. They reported that both continuous and burst electrical stimulation of gluteal muscles induced significant increases in tissue oxygenation assessed using T_2*-weighted magnetic resonance imaging techniques. However, the gluteus maximus has been difficult to stimulate by surface electrodes due to its greater mass covered by adipose tissue[26]. In addition, surface FES requires repeated application of large electrodes to the buttocks to stimulate the gluteal muscles, which can cause local dermatitis and excoriation. Importantly, muscles will eventually re-atrophy if stimulation is not continued[26]. Therefore, surface FES has significant limitations if used for sustained benefit. Interestingly, implanted muscular electrical stimulation of gluteal muscles

has been shown to benefit seat pressure and tissue oxygenation in people living with SCI[26,27]. For instance, Wu and colleagues measured transcutaneous oxygen tension bilaterally over the ischia in seven patients living with SCI who had intramuscular electrodes implanted for combined trunk and gluteal muscles. Trunk and gluteal stimulation was applied concurrently at 20-Hz frequency and 20-mA pulse amplitude for 5 minutes in their study. They reported that mean ischial transcutaneous oxygen tension increased during neuromuscular electrical stimulation and remained elevated after the intervention.

Alternatively, sacral nerve roots stimulation has been reported to activate gluteal maximus in the able bodied and people with SCI.[28,29] Sacral anterior root stimulator (SARS) implant is a well-established device for individuals with SCI to empty their bladder and bowel, where the electrodes are usually implanted intra- or extra-durally on bilateral S2, S3 or S4 sacral nerve roots. This implant has proven to be very cost effective and results in significant improvement in limiting urinary tract infections and increasing quality of life in people with SCI. Yet, such implant hasn't been clinically applied for pressure ulcer prevention. Indeed, our previous studies have demonstrated that sacral nerve roots stimulation can induce sufficient gluteal muscle contraction to reduce interface pressure and increase blood perfusion under the ischial tuberosity.[28,29] For instance, FMS was first explored in able-bodies participants for pressure changes under the ischial tuberosity[28]. The primary objective of that study was to demonstrate the utility of FMS as an assessment tool, and map the optimal FMS stimulation parameters and the positioning of stimulating coil to be able to activate the S2 nerve root. Secondly in order to test the feasibility and viability of stimulating the S2 nerve root using a well-established implant for activating gluteal muscles, we stimulated the S2 nerve root alone in those patients who have a SARS implant for their daily bladder/bowl management. The results showed that S2 nerve root stimulation, either by FMS or using SARS implant, induced gluteus maximus contraction sufficient for significant reductions in ischial pressures during sitting in five able-bodied and six individuals with SCI who had a SARS implant respectively.

Later, the FMS was further investigated in five patients with SCI for pressure changes under the ischial tuberosity[29]. In addition to ischial pressure measurement, skin blood perfusion changes were also simultaneously measured during the S2 nerve root stimulation in five patients during FMS and six patients with a SARS implant. Our results demonstrated that ischial pressures significantly decreased and cutaneous haemoglobin and oxygenation significantly increased during sacral nerve root stimulation via FMS or a SARS implant in all 11 participants.

To compare the effect of S2 nerve root stimulation with traditional FES using surface electrodes, we then reported another study[30], in which the magnitude of pressure changes during S2 nerve root stimulation was compared with the pressure changes during traditional FES delivered by surface electrodes. Six patients with complete SCI were studied in each group. Interestingly, the results indicated that the magnitude of ischial pressure decrease was significantly greater during S2 nerve root stimulation via FMS or SARS implant than that obtained in participants who applied traditional FES.

However, even S2 nerve root stimulation produce better benefits in reducing ischial pressure than traditional FES using surface electrodes. Skin blood perfusion has been suggested as a fundamental element for practical benefit in terms of pressure ulcer prevention. There was a consensus that the prolonged pressure loading sufficient to produce ischemia, cell deformation and reperfusion injury was identified as an important process of pressure ulcer formation[31,32]. Moreover, previous studies indicated that interface pressure alone does not provide complete information about the effectiveness of pressure relief[12]. So far, there are no published papers that directly compare the skin blood perfusion by sacral nerve root stimulation to traditional surface FES of gluteal muscles itself.

Therefore, the objective of this study was to compare the magnitude of skin blood perfusion during gluteal maximus contraction through the stimulation of sacral nerve roots with the skin blood perfusion changes achieved using traditional surface FES in patients with SCI.

METHODS

The project was approved by the National Health Service (NHS) research ethics committee, XXXX Hospital NHS Trust. All participants gave their informed consent.

Study design

Three individual studies (FMS, SARS implant and surface FES) were conducted separately during a 12-month period. Each participant was invited to attend the research lab for 1.5-2 hours. Before the experiment, all participants were asked to empty their bladder and bowel.

Participants

Subjects who had suprasacral complete SCI were aged between 18-65 years old and were recruited in FMS and surface ES studies. All six participants who completed the FMS study were invited for surface FES study, four of them accepted the invitation. Individuals with an

electrode implanted on S2 nerve root in their SARS implant for bladder and/or bowel management were recruited for SARS implant study.

Individuals who were pregnant or using a cardiac pacemaker were excluded for the FMS study; any subject with a current pressure ulcer over the gluteal region or a history of severe autonomic dysreflexia was excluded.

Sacral nerve roots stimulation

FMS study:

FMS was delivered using a magnetic stimulator (MagPro, Dantec Medical A/S, and Denmark) with a large circular coil (120mm diameter, producing maximum field strength of 2 Tesla) placed over the sacrum area. To obtain a smooth tetanic fused contraction of the gluteal muscles, stimulation frequencies in the available range of 15-25pps for two seconds were utilized. Stimulation intensities were adjusted individually by starting from the lowest level from 30% in steps of 5% (stimulation strength is indicated as percentage of the maximum output) to the highest level of patients' tolerance. The maximum level of intensity used was 80%. To activate bilateral gluteus muscles, the coil position was placed at the sacrum midline, 6cm below iliac crest for participants without sclerosis.

A Fintech-Brindley SARS implant:

Electrical stimulation was applied bilaterally through a Finetech-Brindley SARS implant (Finetech Medical Ltd, UK). A stimulation program was manually set up from an external control box. To avoid bladder/bowel activation, S3 & S4 stimulators were switched off. Only the S2 nerve root was stimulated. In order to obtain a smooth tetanic contraction, stimulation frequency of 20pps and duration of stimulation of 8-second were utilized. All patients were given lowest amplitude '1' (highest amplitude was '3') to avoid activating deeper muscles or organs such as bladder and bowel. The stimulation pulse width was adjusted individually by starting from the lowest pulse width of 8μs to the highest level of patients' tolerance; the maximum pulse width used was 700 μs.

Surface FES:

Electrical stimulation was provided through large surface electrodes (PALS/Platinum, Model 895240, Nidd Valley Medical Ltd, UK) using Stock Microstim2, a dual-channel neuromuscular stimulator. The specifications of the Microstim2 (v2) are: 1) stimulation frequencies are 20Hz and 40 Hz; 2) maximum pulse width is 330μs; 3) maximum output amplitude is 100mA; 4) the stimulation waveform is square with passive charge balancing. In order to be comparable with SARS, the stimulation frequency and duration of stimulation were set at 20 Hz and 8 seconds respectively. As per the stimulation amplitude, all

participants started from the lowest level of '1' to highest level of patients' tolerance, the maximum level of amplitude was level '9'.

Ischial skin Haemoglobin and Oxygenation

Tissue Reflectance Spectrometry (TRS) (MCS521 spectrometer, Carl Zeiss, Germany) in the visible spectrum was used to measure skin haemoglobin and oxygenation under ischial tuberosity. The TRS uses the characteristic absorption of light by the constituents of skin to measure the various constituents present. The theory of tissue reflectance spectrometry is based on a simple anatomical model[33]. A thin flexible optical probe was designed, which does not cause loading artefact during sitting. This probe incorporated two plastic optical fibres (1 mm diameter with 1 mm spacing) that were bonded in a Shore D60 flat flexible polyurethane sheath (Flexane 60L, Devcon Ltd, Ireland) for a transmission of incident and reflected light from the skin surface to the tissue reflectance spectrometry. The theoretical skin penetration depth was 500 um.

Before each experiment, the TRS was always allowed to equilibrate for 30 minutes. The flexible thin flat optical probe was placed in the dark, then being placed onto a standard white surface to determine the reference light intensity. The sample rate for data acquisition of a full-spectrum was 2Hz with an integration time of 500ms and a cycle time of 0.5s. The absorption values for each wavelength increment of 1nm between 450 and 650nm were stored on a PC for offline processing. After data acquisition, the data were converted to ASCII text and exported to Microsoft Excel 2007. The indices of skin haemoglobin (IHB) and oxygenation (IOX) were calculated using modified version of a method by Feather *et al*[29,33]. No melanin compensation was used. However, all participants were Caucasian with very little melanin over the skin covering the ischial tuberosity. Skin haemoglobin and oxygenation data were analysed by comparing IHB and IOX before and during stimulation when participants were sitting in the chair. During sitting, IHB would be close to 0. In order to prevent negative IOX, all IHB values were offset by a value of '1'. This was to make interpretation of IOX easier.

Experiment setting:

FMS and SARS studies:

Prior to the experiment, participants were asked to rest 5-10 minutes and were given an introduction regarding the experiment. Following this, each participant was carefully transferred to a standard wheelchair with a standard foam cushion (high resilience foam, density 45kg/m3) and fitted arm and footrest. All participants had stabilized in a standard sitting position defined as: 1) back rest-to-seat angle of at least 80 degrees; 2) footrest

adjusted to keep the thighs parallel to the seat. The probe was then placed on the skin under the left/right ischial tuberosity with double-sided adhesive tape. The left or right ischial tuberosity was randomly selected. Spectral response of haemoglobins was continually monitored before and during maximal tolerated stimulation.

Surface FES study:

After they had entered the research lab and received an introduction to the experiment, each participant was helped to lie down on a standard hospital bed in a prone position. Two large rectangle electrodes (5cm×9cm) were placed onto each side of the gluteus maximus. The stimulating anodes were then placed bilaterally just below the posterior superior iliac crest. The participants were then carefully transferred to the study wheelchair. The skin probe placement and blood perfusion measurement was same as FMS and SARS studies.

Statistical analysis

Descriptive statistics were calculated using Excel 2007 and SPSS (IBM SPSS Statistics 19). All data were examined for normality using a Kolmogorov-Smirnov test. For comparison between before and during stimulation within same subjects, or comparison between FMS and surface FES within same subjects, paired sample t-test was used. Due to the small sample size of each study, non-parametric tests were also used to confirm the results from parametric tests where appropriate. Wilcoxon Signed-rank test was applied for comparison between before and during stimulation within same subjects. P-values were two-tailed and differences were considered to be statistically significant for P-value less than 0.05. In addition to p value, Cohen's d value was further reported to provide an estimate of the magnitude of differences associated with t-tests. Cohen's effect size *d* value of 0.2 or less represents a small effect or low practical significance, around 0.5 an intermediate effect and 0.8 or greater represents a large effect or high practical significance.

RESULTS

All participants who completed the studies tolerated stimulation well and no adverse events were reported. The skin areas where the electrodes and skin probe were placed were then inspected after each experiment. Baseline characteristics of all fourteen subjects are summarized in Table 1.

FMS study

Table 2 illustrates the FMS parameters in all 6 participants who completed FMS study. During optimal FMS, IHB and IOX increased in all 6 participants. As a group, IHB and IOX during stimulation were significantly higher than the baseline.

SARS study

Optimal stimulation of S2 nerve root at frequency of 20 pps and amplitude of '1' was utilised in the 6 individual participants. The pulse width varies among individual subjects ranging from 64 to 600μs. As a whole group, the average pulse width was 256μs. Table 3 demonstrated optimal stimulation parameters in 6 participants with a SARS Implant.

For the whole group of six participants, IHB and IOX were significantly higher during stimulation than baseline. Figure 1 demonstrates the value of IHB and IOX before and during SARS in six participants with a SARS implant.

Surface FES study

Out of six participants, five of them tolerated the highest level of amplitude of '9' and one participant tolerated '7'. Table 4 demonstrates optimal FES parameters in six participants who had surface gluteal FES. During maximum tolerated stimulation, there was an increase of skin blood perfusion under the ischial tuberosity in all six participants. However, the increase was not statistically significant. Details of skin blood perfusion in the three studies are summarised in table 5.

Comparison of blood perfusion during sacral nerve root stimulation and surface ES

For those four participants who received both FMS and surface FES, the magnitude of increase in both IHB and IOX was significantly higher during FMS than surface FES (IHB mean difference=0.175±0.031, p=0.04, paired t-test; p=0.04, nonparametric Wilcoxon Signed-Rank test; IOX mean difference=0.133±0.265, p=0.03, paired t-test; p=0.04, nonparametric Wilcoxon Signed-Rank test).

DISCUSSION

The primary objective of this study was to compare dynamic effects of ischial blood perfusion changes during sacral nerve root stimulations and gluteal muscle stimulation using traditional electrodes. In addition, this study investigated the feasibility of the customized flexible probe for real-time measuring of blood perfusion during sitting in those individuals living with SCI. The results from the study demonstrate that S2 nerve root stimulation through a SARS implant can induce gluteus muscle contractions sufficient to achieve a significant increase in skin blood perfusion during sitting. By using traditional surface electrodes to activate gluteal muscles, there was no significant change in blood perfusion during surface FES.

Indeed, the inconsistency of findings in blood flow during stimulating gluteal muscles using surface electrodes has been previously reported in SCI.[24,25,20,]. While some of those studies reported a significant increase in regional tissue oxygenation or blood flow during the

stimulation, other studies reported an insignificant increase of tissue oxygenation. For instance, Smit and colleagues[25] applied electrical stimulation to gluteal and hamstring muscles through surface electrodes and measured tissue blood flow and oxygenation in 12 male patients with SCI aged 26–52 years old using a commercial instrument (Oxygen To See device) with a rigid probe. The device adopted a combination of reflection spectroscopy and laser Doppler technique. They reported that there were no significant changes of mean blood flow and oxygenation during electrical stimulation as compared with the rest, although there was a significant difference in peak blood flow during electrical stimulation as compared with the rest. Conversely, Levine and colleagues examined ischial blood flow in six acute patients with SCI during electrical stimulation of gluteus maximus[23]. They found that skin blood flow increased during stimulation for all participants.

While the exact mechanism of improving local tissue oxygenation and blood flow during the ES remains unclear, increased blood perfusion may result from muscle contraction allowing higher oxygen delivery rates and metabolite removal, or neuronal excitation may contribute to the increase of blood perfusion. Alternatively, a dynamic 'pressure relief' caused by gluteus muscle contractions and/or pelvic tilt, which dilates the micro-vessels underlying the ischial skin, may be partly attributable. While previous studies investigated the interface pressure and tissue oxygenation or blood flow simultaneously during gluteal electrical stimulation e[24-27], these studies, in general, had a small sample size without control groups. None of those studies proved the hypothesis that electrical stimulation induced muscle activation would directly increase blood flow and oxygenation. Increasing sample size and recording more subjects' characteristic factors in the future studies may help understand the findings of this study.

In theory, all muscles consist of a number of motor units and the fibres belonging to a motor unit are dispersed and interlink amongst fibres of other units. A motor unit normally consists of one motor neuron and all of the muscle fibres it stimulates. The muscle fibres belonging to one motor unit can be spread throughout a part, or most of the entire muscle, depending on the number of fibres and size of the muscle. When a motor neuron is activated, all of the muscle fibres innervated by the motor neuron are stimulated and contracted. The activation of single motor neuron results in a weak distributed muscle contraction (twitch contraction). In contrast, the activation of more motor neurons will result in more muscle fibres being activated, and therefore a stronger muscle contraction (tetanic contraction) was produced. The higher the recruitment of motor unit, the stronger the muscle contraction will be. The activation of more motor neurons will result in more muscle fibers being activated, and

therefore a stronger muscle contraction[34]. In comparison, between sacral nerve root stimulation versus traditional surface FES of gluteal muscles, the larger numbers of motor neurones recruitment in sacral nerve roots stimulation may produce stronger contraction than surface FES. Therefore it can activate gluteus muscles more efficiently. Sacral nerve root stimulation can efficiently activate all motor neurons that innervate gluteal maximus, whereas surface FES of gluteus maximus maybe limited by the size of electrodes and the depth of electrical signal to reach the muscle motor points.

It is worth noting that although the index of haemoglobin and oxygenation was increased during the S2 nerve root stimulations in this study, it is difficult to compare the magnitude of changes with other studies in the literature. A variety of stimulation parameters used alongside different modalities employed blood perfusion measurement among each study was identified. In terms of blood perfusion measurement techniques, previous studies that investigated acute effect of electrical stimulation on blood circulation utilized various modalities, which include laser Doppler flowmetry, transcutaneous oximeters and near-infrared spectroscopy [24-27, 35]. So far, regardless of the modalities adopted, the dermal probes were rigid, which can potentially increase local pressure during sitting, or have movement artefact. In the present study, tissue reflectance spectrometry was utilised, which is an optical technique and offers the distinct advantages of being non-invasive with no artefact of movement and real-time recording. More importantly, a customised thin flexible dermal probe was applied for the real-time blood perfusion measurement during sitting. The inter-fiber cross talk was tested and coupling was not found. A flexible dermal probe such as this has potential for future monitoring studies during sitting, and examining key factors in pressure ulcer development.

The long-term goal of such research is to reverse gluteus muscle atrophy, build up muscle bulk and improve tissue viability by stimulating gluteus maximus through a SARS implant in people with supra-sacral spinal lesions. Traditional surface FES is a well-established technique to activate paralysed muscles including gluteal maximus in SCI. Yet it is not particularly practical or efficient in the long term or for sustained effect in SCI. It would be better to deliver gluteal electrical stimulation through implanted electrodes, and better still if this could be achieved using a durable SARS stimulator such as Fintech SARS. The results from current study indicate that sacral nerve root stimulation via implanted electrodes can induce sufficient gluteus maximus contraction to significantly increase cutaneous haemoglobin and oxygenation during sitting. Compare to our previous study[30], which we reported sacral nerve root stimulation confer better modulation of sitting pressure than

traditional surface FES, the conclusions from this study are that stimulation via an implanted SARS may be useful for gluteus muscle bulking and improving vascularisation for preventing ischial pressure injuries. In addition to restoring bladder control with a SARS implant, implanted S2 nerve-root electrodes may also provide frequent, convenient, and sufficient stimulation of gluteus muscles and has the potential to improve tissue heath in SCI population.

Study limitations

One of the limitations of our study was the small sample size along with the pilot study design. Unmatched age, body mass index, gluteal mass and level and duration of injuries were not addressed. However, four participants who completed FMS were recruited and agreed to participate FES studies, which allowed us to perform a paired sample t test and Wilcoxon signed-rank nonparametric test in the four subjects.

Another limitation was the use of a single skin probe to measure blood perfusion in the study. While non-invasive tissue reflectance spectrometry incorporated with customised probe provides real-time data, using only one skin probe with a limited skin area restricted us to compare blood perfusion changes on both sides within each subject. Developing a dual probe to measure skin blood perfusion bilaterally with a high sampling frequency, deep penetration and multiple skin area measurements should be considered in future studies.

Finally, the stimulation was only applied in a single burst to investigate the dynamic effect of sacral nerve stimulations on gluteus maximus. Due to the limitations of FMS over-heating and being ill-defined, it is impossible to apply more cycles of stimulation in the protocol presented in this study. Nevertheless, our study provides the basis of designing future rigorous studies by investigating more cycles of stimulation over longer periods, and modifying electrical stimulation parameters such as frequency, pulse width and durations, alongside using the customised thin, flexible skin probe for real-time blood perfusion measurement.

CONCLUSION

Gluteal muscle activity via S2 nerve root can induce sufficient gluteus maximus contraction in SCI to promote blood flow. Skin blood perfusion was significantly increased during sacral nerve root stimulation, but the change was not significant during traditional FES using surface electrodes. SARS implant may be more convenient and more efficient in activating gluteal muscles compared to traditional surface FES. This study confirmed that the S2 stimulation through an implant is viable and has potential for gluteal pressure ulcer prevention in SCI. However, in order to justify adding S2 stimulating electrodes in those patients who have

opted for an implantable SARS for their bladder and bowel management, future well designed, large sample studies are warranted to confirm current findings.

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Table 1 Demographic characteristic of all participants in three studies

Variables	**FMS (n=6)***	**SARS (n=6)**	**Surface ES (n=6)***
Age (mean ± SD)	40.33±9.69	44.50±10.07	41.50±4.97
Gender (F/M)	1/5	1/5	1/5
BMI (mean ± SD)	23.78±2.64	24.77±6.06	25.65±5.09
Level of injury	C5/6-T10/11	T3 –T10/11	T4/5-T10/11
Years of injury (mean ± SD)	8.17±6.11	14.33±6.47	8.33±5.05

FMS=Functional magnetic stimulation; SARS=Sacral anterior root simulator; ES=Electrical stimulation

*Four participants completed both FMS and Surface ES study

Table 2 Optimal stimulation parameters in 6 participants who had functional magnetic stimulation

Participant	Duration	Optimal Frequency (Hz)	maximal tolerated Intensity (%)	Vertical Optimal coil location (distance to iliac crest)	Optimal coil location for bilateral response
1	2	25	60%	60mm	midline
2	2	20	50%	60mm	20mm to right
3	2	20	60%	60mm	midline
4	2	20	65%	60mm	midline
5	2	20	80%	60mm	20mm to left
6	2	20	60%	60mm	midline

Table 3 Optimal stimulation parameters in six participants who used a SARS Implant.

Patients	Duration	Frequency(Hz)	Amplitude	Optimal Pulse Width
1	8s	20	1	256 μsec
2	8s	20	1	128 μsec
3	8s	20	1	600 μsec
4	8s	20	1	256 μsec
5	8s	20	1	128 μsec
6	8s	20	1	512 μsec

Table 4 Optimal stimulation parameters in six participants who used surface electrodes

Patients	Duration	Frequency(Hz)	Amplitude	Optimal Pulse Width
1	8s	20	8	330μsec
2	8s	20	7	330 μsec
3	8s	20	8	330 μsec
4	8s	20	9	330 μsec
5	8s	20	9	330 μsec
6	8s	20	8	330 μsec

Table 5 Skin blood perfusion before and during stimulations in the three studies

Variables	FMS (n=6)	SARS (n=6)	Surface ES (n=6)
Skin blood content			
Baseline (mean ± SD)	1.05±0.21	1.01 ± 0.02	1.05 ± 0.01
Stimulation (mean ± SD)	1.08±0.02	1.07 ±0.02	1.06 ±0.01
Paired sample t-test			
t value (degree of freedom)	t(5)=2.9	t(5)=5.5	t(5)=2.3
P value	0.03	0.003	0.07
Cohen's effect size (d)	0.2*	6.0***	0.4*
Skin blood oxygenation			
Baseline (mean ± SD)	0.18 ± 0.21	0.79±0.81	0.56±0.39
Stimulation (mean ± SD	0.46 ± 0.30	2.2±1.27	0.86±0.41
Paired sample t-test			
t value (degree of freedom)	t(5)=3.6	t(5)=3.0	t(5)=1.8
P value	0.01	0.03	0.12 (NS)
Cohen's effect size (d)	1.0***	3.4***	0.4*

P value<0.05;

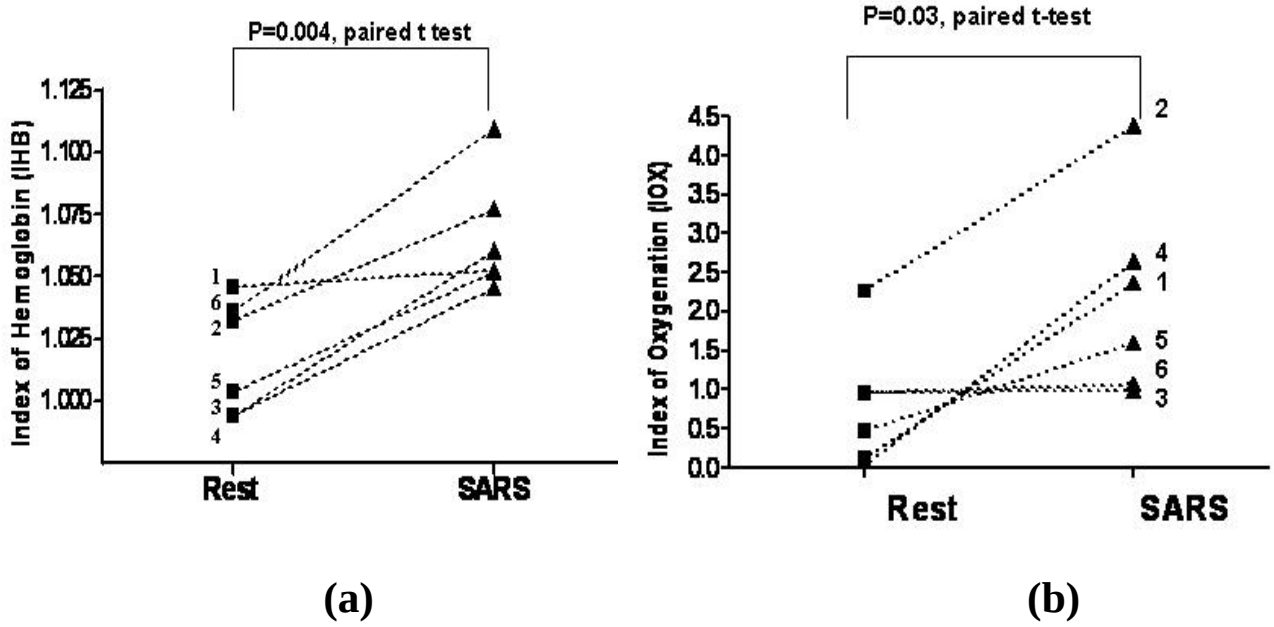
***Cohen's effect size value d>0.8 suggested a high practical significance;

** Cohen's effect size value 0.5 <d<0.8 suggested a medium practical significance;

* Cohen's effect size value d<0.5 suggested a low practical significance

SD=Standard deviation

Figure 1 The value of Index of haemoglobin and Oxygenation before and during electrical stimulation in six participants using a sacral anterior root implant



(a) **(b)**