

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

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8

9 **Abstract**

10 **Objective:** To examine dynamic changes of ischial blood perfusion during sacral nerve root
11 stimulation against surface functional electrical stimulation (FES). **Methods:** Fourteen adults
12 with suprasacral complete spinal cord injury were recruited. The gluteal maximus was
13 activated by surface FES or stimulating sacral nerve roots by functional magnetic stimulation
14 (FMS) or a sacral anterior root stimulator implant (SARS). Ischial skin index of haemoglobin
15 (IHB) and oxygenation (IOX) was measured. **Results:** Skin blood perfusion was significantly
16 higher during FMS than the baseline (IHB 1.05 ± 0.21 before vs. 1.08 ± 0.02 during stimulation,
17 $P=0.03$; IOX 0.18 ± 0.21 before vs. 0.46 ± 0.30 , $P=0.01$ during stimulation, $n=6$). Similarly,
18 when using the SARS implant, we also observed that blood perfusion significantly increased
19 (IHB 1.01 ± 0.02 before vs. 1.07 ± 0.02 during stimulation, $P=0.003$; IOX 0.79 ± 0.81 before vs.
20 2.2 ± 1.21 during stimulation, $P=0.03$, $n=6$). However, there was no significant change of
21 blood perfusion during surface FES. Among 4 participants who completed both the FMS and
22 FES studies, the magnitude of increase in both parameters was significantly higher during
23 FMS. **Conclusion:** This study demonstrates that using SARS implant is more efficient to
24 activate gluteal muscles and confer better benefit on blood perfusion than applying traditional
25 FES in SCI population.

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

28 **INTRODUCTION:**

29 Pressure ulcer is one of the most devastating conditions for people with Spinal Cord Injury
30 (SCI)¹. It is reported that up to 85% of adults with SCI will develop a pressure ulcer at some
31 point during their lifetimes¹⁻⁵, and 7-8% of those who develop pressure ulcers will die from
32 related complications.⁶

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

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

45
46 Following SCI, the interruption of spinal vasomotor pathways results in loss of vasomotor
47 control over skeletal muscle and skin, which lowers the tone of vascular bed below the level
48 of lesion. Impaired vascular patency causes vessels to be less able to withstand normal
49 loading conditions. Concurrent with loss of capillary networks due to lost muscle bulk, the
50 volume of blood in the tissues is reduced⁸⁻¹⁰. Previous clinical studies have shown that tissue
51 blood volume/perfusion was lower and tissue reperfusion was impaired in people with SCI in
52 comparison with able-bodied subjects.¹¹⁻¹⁴ For instance, Jan and colleagues measured sacral
53 skin perfusion in 14 people with SCI and 14 healthy subjects during sitting¹¹. They found skin
54 perfusion declined more in people with SCI during constant sitting than able-bodied subjects.
55 Furthermore, impaired vascular function in people with SCI has been reported by other
56 studies.^{12,13} Makhsous and colleagues¹² measured transcutaneous partial pressures of oxygen
57 and carbon dioxide of the buttock overlying the ischial tuberosity in 20 paraplegic individuals,
58 20 tetraplegic individuals, and 20 able-bodied subjects. They found that recovery time during
59 offloading was significantly longer in both paraplegic and tetraplegic participants in
60 comparison with able-bodied individuals. As a result, people living with SCI have a higher
61 risk of developing pressure ulcers than able-bodied individuals

62
63 Once a pressure ulcer is formed, it is very difficult to achieve a full repair or it takes a
64 particularly long period of time to heal for severe cases. In addition, those who suffer a
65 pressure ulcer may be subjected to longer hospital stays, delayed rehabilitation and a
66 significant loss of independence, which adds another burden to the psychological trauma of
67 SCI, as well as the reduced quality of life.¹⁵ If a pressure ulcer is severe, it can lead to further
68 disabilities, the need for surgical interventions and even fatal infections.^{2,15} In addition to the

69 detrimental personal effect, a pressure ulcer also represents a significant cost burden for
70 health and social care systems. Although the exact cost of pressure ulcer management in
71 people living with SCI is unknown in the United Kingdom, the average cost to treat one stage
72 4 pressure ulcer is £14,108 per episode in the general population¹⁶. Given the significant
73 personal consequences and serious health care burden, effective prevention of pressure ulcer
74 is undoubtedly important for people living with SCI.

75 Thus far, preventing pressure ulcer tends to focus on methods to reduce external pressure.
76 These efforts range from using pressure-relieving devices, to patients performing ‘pressure
77 relief’ manoeuvres themselves, such as frequent repositioning, ‘push-ups’ or ‘leaning forward
78 ¹⁷⁻²⁰. However, these efforts are only partially effective at best in people living with SCI.
79 Poor compliance from patients to carry out the frequent pressure relief activities together with
80 intrinsic changes in the paralyzed individuals such as reduced vascular response to loading,
81 reduced muscular tone and progressive loss of muscle bulk may contribute to the high
82 incidence of pressure ulcer in this population²¹⁻²². Despite simple pressure relief methods
83 providing benefits in reducing local pressure at bony prominences, such approaches were not
84 aimed to prevent muscle atrophy or to improve muscular tone and tissue blood volume.
85 Therefore, in conjunction to pressure relief strategies, alternative means of improving tissue
86 health should be explored in this population for pressure ulcer prevention.

87 In fact, activating paralyzed gluteal muscles to modify tissue blood circulation by using
88 surface functional electrical stimulation (FES) has been explored in SCI for 30 years.²³⁻²⁵ For
89 instance, back in the 1990s, Levine and colleagues¹⁹ examined ischial blood flow in six
90 people with acute SCI during electrical stimulation of gluteus maximus. They found that skin
91 blood flow increased during stimulation for all participants. Similarly, Gyawali and
92 colleagues²⁴ measured loaded gluteal tissue oxygenation during 7s or 13s of continuous
93 electrical stimulation and 3s burst electrical stimulation of gluteus maximus using surface
94 electrode in 17 patients with SCI who had a mean age of 37 years. They reported that both
95 continuous and burst electrical stimulation of gluteal muscles induced significant increases in
96 tissue oxygenation assessed using T₂*-weighted magnetic resonance imaging techniques.
97 However, the gluteus maximus has been difficult to stimulate by surface electrodes due to its
98 greater mass covered by adipose tissue²⁶. In addition, surface FES requires repeated
99 application of large electrodes to the buttocks to stimulate the gluteal muscles, which can
100 cause local dermatitis and excoriation. Importantly, muscles will eventually re-atrophy if
101 stimulation is not continued²⁶. Therefore, surface FES has significant limitations if used for
102 sustained benefit. Interestingly, implanted muscular electrical stimulation of gluteal muscles

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

110 Alternatively, sacral nerve roots stimulation has been reported to activate gluteal maximus in
111 the able bodied and people with SCI.^{28,29} Sacral anterior root stimulator (SARS) implant is a
112 well-established device for individuals with SCI to empty their bladder and bowel, where the
113 electrodes are usually implanted intra- or extra-durally on bilateral S2, S3 or S4 sacral nerve
114 roots. This implant has proven to be very cost effective and results in significant improvement
115 in limiting urinary tract infections and increasing quality of life in people with SCI. Yet, such
116 implant hasn't been clinically applied for pressure ulcer prevention. Indeed, our previous
117 studies have demonstrated that sacral nerve roots stimulation can induce sufficient gluteal
118 muscle contraction to reduce interface pressure and increase blood perfusion under the ischial
119 tuberosity.^{28,29} For instance, FMS was first explored in able-bodied participants for pressure
120 changes under the ischial tuberosity²⁸. The primary objective of that study was to demonstrate
121 the utility of FMS as an assessment tool, and map the optimal FMS stimulation parameters
122 and the positioning of stimulating coil to be able to activate the S2 nerve root. Secondly in
123 order to test the feasibility and viability of stimulating the S2 nerve root using a well-
124 established implant for activating gluteal muscles, we stimulated the S2 nerve root alone in
125 those patients who have a SARS implant for their daily bladder/bowel management. The
126 results showed that S2 nerve root stimulation, either by FMS or using SARS implant, induced
127 gluteus maximus contraction sufficient for significant reductions in ischial pressures during
128 sitting in five able-bodied and six individuals with SCI who had a SARS implant respectively.

129
130 Later, the FMS was further investigated in five patients with SCI for pressure changes under
131 the ischial tuberosity²⁹. In addition to ischial pressure measurement, skin blood perfusion
132 changes were also simultaneously measured during the S2 nerve root stimulation in five
133 patients during FMS and six patients with a SARS implant. Our results demonstrated that
134 ischial pressures significantly decreased and cutaneous haemoglobin and oxygenation
135 significantly increased during sacral nerve root stimulation via FMS or a SARS implant in all
136 11 participants.

137

138 To compare the effect of S2 nerve root stimulation with traditional FES using surface
139 electrodes, we then reported another study³⁰, in which the magnitude of pressure changes
140 during S2 nerve root stimulation was compared with the pressure changes during traditional
141 FES delivered by surface electrodes. Six patients with complete SCI were studied in each
142 group. Interestingly, the results indicated that the magnitude of ischial pressure decrease was
143 significantly greater during S2 nerve root stimulation via FMS or SARS implant than that
144 obtained in participants who applied traditional FES.

145

146 However, even S2 nerve root stimulation produce better benefits in reducing ischial pressure
147 than traditional FES using surface electrodes. Skin blood perfusion has been suggested as a
148 fundamental element for practical benefit in terms of pressure ulcer prevention. There was a
149 consensus that the prolonged pressure loading sufficient to produce ischemia, cell
150 deformation and reperfusion injury was identified as an important process of pressure ulcer
151 formation^{31,32}. Moreover, previous studies indicated that interface pressure alone does not
152 provide complete information about the effectiveness of pressure relief¹². So far, there are no
153 published papers that directly compare the skin blood perfusion by sacral nerve root
154 stimulation to traditional surface FES of gluteal muscles itself.

155

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

159

160 **METHODS**

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

163 **Study design**

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

167 **Participants**

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

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

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

176 **Sacral nerve roots stimulation**

177 *FMS study:*

178 FMS was delivered using a magnetic stimulator (MagPro, Dantec Medical A/S, and Denmark)
179 with a large circular coil (120mm diameter, producing maximum field strength of 2 Tesla)
180 placed over the sacrum area. To obtain a smooth tetanic fused contraction of the gluteal
181 muscles, stimulation frequencies in the available range of 15-25pps for two seconds were
182 utilized. Stimulation intensities were adjusted individually by starting from the lowest level
183 from 30% in steps of 5% (stimulation strength is indicated as percentage of the maximum
184 output) to the highest level of patients' tolerance. The maximum level of intensity used was
185 80%. To activate bilateral gluteus muscles, the coil position was placed at the sacrum midline,
186 6cm below iliac crest for participants without sclerosis.

187 *A Finetech-Brindley SARS implant:*

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

197 **Surface FES:**

198 Electrical stimulation was provided through large surface electrodes (PALS/Platinum, Model
199 895240, Nidd Valley Medical Ltd, UK) using Stock Microstim2, a dual-channel
200 neuromuscular stimulator. The specifications of the Microstim2 (v2) are: 1) stimulation
201 frequencies are 20Hz and 40 Hz; 2) maximum pulse width is $330\mu s$; 3) maximum output
202 amplitude is 100mA; 4) the stimulation waveform is square with passive charge balancing. In
203 order to be comparable with SARS, the stimulation frequency and duration of stimulation
204 were set at 20 Hz and 8 seconds respectively. As per the stimulation amplitude, all

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

207 **Ischial skin Haemoglobin and Oxygenation**

208 Tissue Reflectance Spectrometry (TRS) (MCS521 spectrometer, Carl Zeiss, Germany) in the
209 visible spectrum was used to measure skin haemoglobin and oxygenation under ischial
210 tuberosity. The TRS uses the characteristic absorption of light by the constituents of skin to
211 measure the various constituents present. The theory of tissue reflectance spectrometry is
212 based on a simple anatomical model³³. A thin flexible optical probe was designed, which does
213 not cause loading artefact during sitting. This probe incorporated two plastic optical fibres (1
214 mm diameter with 1 mm spacing) that were bonded in a Shore D60 flat flexible polyurethane
215 sheath (Flexane 60L, Devcon Ltd, Ireland) for a transmission of incident and reflected light
216 from the skin surface to the tissue reflectance spectrometry. The theoretical skin penetration
217 depth was 500 μm .

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

232 **Experiment setting:**

233 *FMS and SARS studies:*

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

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

243 *Surface FES study:*

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

250 **Statistical analysis**

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

263

264 **RESULTS**

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

269 **FMS study**

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

273 **SARS study**

274 Optimal stimulation of S2 nerve root at frequency of 20 pps and amplitude of '1' was utilised
275 in the 6 individual participants. The pulse width varies among individual subjects ranging
276 from 64 to 600 μ s. As a whole group, the average pulse width was 256 μ s. Table 3
277 demonstrated optimal stimulation parameters in 6 participants with a SARS Implant.
278 For the whole group of six participants, IHB and IOX were significantly higher during
279 stimulation than baseline. Figure 1 demonstrates the value of IHB and IOX before and during
280 SARS in six participants with a SARS implant.

281 **Surface FES study**

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

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

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

294

295 **DISCUSSION**

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

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

307 stimulation, other studies reported an insignificant increase of tissue oxygenation. For
308 instance, Smit and colleagues²⁵ applied electrical stimulation to gluteal and hamstring
309 muscles through surface electrodes and measured tissue blood flow and oxygenation in 12
310 male patients with SCI aged 26–52 years old using a commercial instrument (Oxygen To See
311 device) with a rigid probe. The device adopted a combination of reflection spectroscopy and
312 laser Doppler technique. They reported that there were no significant changes of mean blood
313 flow and oxygenation during electrical stimulation as compared with the rest, although there
314 was a significant difference in peak blood flow during electrical stimulation as compared with
315 the rest. Conversely, Levine and colleagues examined ischial blood flow in six acute patients
316 with SCI during electrical stimulation of gluteus maximus²³. They found that skin blood flow
317 increased during stimulation for all participants.

318 While the exact mechanism of improving local tissue oxygenation and blood flow during the
319 ES remains unclear, increased blood perfusion may result from muscle contraction allowing
320 higher oxygen delivery rates and metabolite removal, or neuronal excitation may contribute to
321 the increase of blood perfusion. Alternatively, a dynamic ‘pressure relief’ caused by gluteus
322 muscle contractions and/or pelvic tilt, which dilates the micro-vessels underlying the ischial
323 skin, may be partly attributable. While previous studies investigated the interface pressure and
324 tissue oxygenation or blood flow simultaneously during gluteal electrical stimulation e²⁴⁻²⁷,
325 these studies, in general, had a small sample size without control groups. None of those
326 studies proved the hypothesis that electrical stimulation induced muscle activation would
327 directly increase blood flow and oxygenation. Increasing sample size and recording more
328 subjects’ characteristic factors in the future studies may help understand the findings of this
329 study.

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

341 therefore a stronger muscle contraction³⁴. In comparison, between sacral nerve root
342 stimulation versus traditional surface FES of gluteal muscles, the larger numbers of motor
343 neurones recruitment in sacral nerve roots stimulation may produce stronger contraction than
344 surface FES. Therefore it can activate gluteus muscles more efficiently. Sacral nerve root
345 stimulation can efficiently activate all motor neurons that innervate gluteal maximus, whereas
346 surface FES of gluteus maximus maybe limited by the size of electrodes and the depth of
347 electrical signal to reach the muscle motor points.

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

364 The long-term goal of such research is to reverse gluteus muscle atrophy, build up muscle
365 bulk and improve tissue viability by stimulating gluteus maximus through a SARS implant in
366 people with supra-sacral spinal lesions. Traditional surface FES is a well-established
367 technique to activate paralysed muscles including gluteal maximus in SCI. Yet it is not
368 particularly practical or efficient in the long term or for sustained effect in SCI. It would be
369 better to deliver gluteal electrical stimulation through implanted electrodes, and better still if
370 this could be achieved using a durable SARS stimulator such as Fintech SARS. The results
371 from current study indicate that sacral nerve root stimulation via implanted electrodes can
372 induce sufficient gluteus maximus contraction to significantly increase cutaneous
373 haemoglobin and oxygenation during sitting. Compare to our previous study³⁰, which we
374 reported sacral nerve root stimulation confer better modulation of sitting pressure than

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

380 **Study limitations**

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

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

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

400 **CONCLUSION**

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

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

410

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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 μ sec
2	8s	20	1	128 μ sec
3	8s	20	1	600 μ sec
4	8s	20	1	256 μ sec
5	8s	20	1	128 μ sec
6	8s	20	1	512 μ sec

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

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

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			
<i>t value (degree of freedom)</i>	t(5)=2.9	t(5)=5.5	t(5)=2.3
<i>P value</i>	0.03	0.003	0.07
<i>Cohen's effect size (d)</i>	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			
<i>t value (degree of freedom)</i>	t(5)=3.6	t(5)=3.0	t(5)=1.8
<i>P value</i>	0.01	0.03	0.12 (NS)
<i>Cohen's effect size (d)</i>	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

