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1 **Title:**

2 IS MAXIMUM STIMULATION INTENSITY REQUIRED IN THE ASSESSMENT OF  
3 MUSCLE ACTIVATION CAPACITY?

4

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8

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14

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17

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23

24 **Abstract**

25 Voluntary activation assessment using the interpolation twitch technique (ITT) has almost  
26 invariably been applied using maximal stimulation intensity, i.e., an intensity beyond which  
27 no additional joint moment or external force is produced by increasing further the intensity  
28 of stimulation. The aim of the study was to identify the minimum stimulation intensity at  
29 which percutaneous ITT yields valid results. Maximal stimulation intensity and the force  
30 produced at that intensity were identified for the quadriceps muscle using percutaneous  
31 electrodes in eight active men. The stimulation intensities producing 10 to 90% (in 10%  
32 increments) of that force were determined and subsequently applied during isometric  
33 contractions at 90% of maximum voluntary contraction (MVC) via twitch doublets. Muscle  
34 activation was calculated with the ITT and pain scores were obtained for each stimulation  
35 intensity and compared to the respective values at maximum stimulation intensity. Muscle  
36 activation at maximal stimulation intensity was 91.6 (2.5)%. The lowest stimulation  
37 intensity yielding comparable muscle activation results to maximal stimulation was 50%  
38 (88.8 (3.9)%,  $p < 0.05$ ). Pain score at maximal stimulation intensity was 6.6 (1.5) cm and it  
39 was significantly reduced at 60% stimulation intensity (3.7 (1.5) cm,  $p < 0.05$ ) compared to  
40 maximal stimulation intensity. Submaximal stimulation can produce valid ITT results while  
41 reducing the discomfort obtained by the subjects, widening the assessment of ITT to  
42 situations where discomfort may otherwise impede maximal electrostimulation.

43

44

## 45 **Introduction**

46 Muscle strength, measured as joint moment or force applied externally during a maximum  
47 voluntary contraction (MVC), is determined by a number of biological factors, including  
48 the size of the agonist muscles and their moment arms, the joint angle tested which affects  
49 muscle length, the specific tension of the muscle, antagonist muscle co-contraction, and the  
50 level of voluntary agonist muscle activation during the test. The assessment of this last  
51 factor, voluntary activation, requires the application of artificial stimulation and this has  
52 been routinely applied in several populations, including children [O'Brien et al, 2010;  
53 O'Brien et al, 2008], older individuals [Morse et al., 2008; Reeves et al, 2003], patients with  
54 musculoskeletal disorders [Rutherford et al, 1986; Suter et al, 1998] and in intervention  
55 studies involving various types of exercise training [e.g., Knight and Kamen, 2001;  
56 Maffiuletti et al, 2000; Selkowitz, 1985] and disuse [e.g., de Boer et al, 2007; Lewek et al,  
57 2001; Sisk et al, 1987].

58 Voluntary activation is typically assessed by some variant of the interpolated twitch  
59 technique (ITT [Merton, 1954]), according to the equation:

$$60 \text{ Activation level (\%)} = (1 - SI / R) \times 100 \quad (\text{eq. 1})$$

61 where, SI is the additional joint moment (or external force) produced by superimposing the  
62 electrical stimulus on the MVC and R is the joint moment (or external force) produced by  
63 the same stimulus applied at rest. Investigators generally strive to use maximal stimulation  
64 for the ITT [Babault et al, 2003; Bampouras et al, 2006; Behm et al, 2001; De Serres and  
65 Enoka, 1998; Kent-Braun and Le-Blanc, 1996; Morse et al, 2008; O'Brien et al, 2008], but  
66 there is often some confusion as to what maximality means and whether it is essential for  
67 the reliable estimation of voluntary activation. To obtain the maximum force from a muscle

68 it is necessary that all motor units are activated and that they are stimulated at frequencies,  
69 generally in the order of 30-100 Hz [Gerritts et al, 1999], that generate maximum force.  
70 Percutaneous stimulation of a large muscle such as the quadriceps is unlikely ever to  
71 activate all motor units. Activation of all motor units can be achieved with direct  
72 stimulation of the femoral nerve. Possibly the only time that true maximality of stimulation  
73 was achieved during a voluntary contraction was with tetanic stimulation of the femoral  
74 nerve with increasing stimulus intensity [Bigland-Ritchie et al, 1978], but this is not a  
75 procedure that is well tolerated by most subjects. Irrespective of whether all motor units  
76 are activated, it is very unlikely that they will be producing their maximum force since most  
77 ITT tests involve using twitches or doublets rather than tetanic trains.

78 One issue associated with using twitches or doublets to stimulate the resting muscle is that  
79 the relatively small and transitory forces will be recorded as smaller tension transients due  
80 to stretching of the series elastic components of the apparatus and in the muscle-tendon  
81 unit. When superimposed on a voluntary contraction where the series elements are already  
82 stretched the tension transient will more faithfully reflect the force produced by the muscle.  
83 This will tend to increase the SI/R ratio and thus give a false low value for voluntary  
84 activation. One way of reducing the series compliance of the quadriceps is to flex the knee  
85 and it has been shown that the ITT value for the quadriceps muscle was higher by 9-18%  
86 (depending on the stimuli number) at more flexed (more stretched muscle-tendon unit) than  
87 extended (slacker muscle-tendon unit) knee positions [Bampouras et al, 2006].

88 Another possible way of avoiding the problems associated with comparing twitches of  
89 resting with active muscle is by using the Central Activation Ratio (CAR) which only  
90 depends on the superimposed force or joint moment during MVC and not the stimulation at

91 rest ( $CAR = MVC/(MVC+SI)$ ) [Bampouras et al, 2006]. However, it is very unlikely that  
92 the superimposed stimulation will maximally activate all the muscle.

93 The question is therefore how much of the muscle needs to be activated to achieve a  
94 reliable answer using the ITT. Behm et al [1996] and de Ruiter et al [2004] suggest that it is  
95 necessary to stimulate nearly all the muscle. However, Rutherford et al [1986] compared  
96 femoral nerve stimulation, which was assumed to activate all motor units, and percutaneous  
97 quadriceps muscle stimulation that activated only a portion of the muscle, and found no  
98 differences in the SI/R ratio between the two stimulation modes. When using percutaneous  
99 stimulation, Rutherford et al [1986] state that they adjusted the stimulus intensity used for  
100 the superimposed twitches in relation to the proportion of the MVC force generated when  
101 stimulating at 30 Hz. However, they did not specify what that force was nor present any  
102 evidence as to what the minimum required force might be. Consequently, the aim of the  
103 present study was to identify the minimum stimulation intensity at which muscle activation  
104 could be validly assessed, reducing the discomfort associated with high intensity  
105 stimulation and thus widening the applicability of ITT assessment to a greater range of  
106 subjects and patients.

107

## 108 **Methods**

### 109 **Subjects**

110 Eight healthy, physically active men (mean (SD): age 28.9 (5.0) years, height 1.80 (0.09)  
111 m, body mass 83.9 (15.3) kg) volunteered to participate in the study. To ensure consistency  
112 in performance, all subjects were familiar with the experimental procedures involved  
113 [Button and Behm, 2008] and were tested in the laboratory on a single occasion.

114 Ethical approval for the study was granted by the Ethics Committee of the Institute for  
115 Biomedical Research into Human Movement and Health of Manchester Metropolitan  
116 University, UK. All subjects provided written informed consent prior to any testing. The  
117 study complied with the Declaration of Helsinki.

### 118 **Isometric knee extension test**

119 The mechanical output of isometric knee extension was measured as force applied  
120 externally in the sagittal plane at the level of the ankle, at right angles to the longitudinal  
121 axis of the lower leg. The subjects sat in the chair of a custom-made dynamometer [de  
122 Ruiter et al, 2004; Kooistra et al, 2007], with the hip joint angle at 85° (supine position =  
123 0°) and the right leg at a knee joint angle of 90° (full knee extension = 0°). Straps were  
124 positioned over the hips and tested thigh to prevent extraneous movement and the lower leg  
125 was securely strapped to a force-transducer (KAP, E/200 Hz, Bienfait B.V. Haarlem, The  
126 Netherlands) at the ankle. Force signals were corrected for passive tension of the knee  
127 extensors and real-time force readings were displayed online and recorded for further  
128 analysis (Matlab, The Mathworks, Natick, MA).

### 129 **Electrical stimulation**

130 Two 7 x 12.5-cm self-adhesive carbon rubber electrodes (Versa-Stim, ConMed, New York,  
131 USA) were placed on the proximal and distal regions of the quadriceps muscle group with  
132 the cathode being the proximal electrode. Stimuli of 200- $\mu$ s pulse width and 10-ms inter-  
133 stimulus gap were generated by an electrical stimulator (model DS7, Digitimer stimulator,  
134 Welwyn, Garden City, UK) modified to deliver a maximum of 1,000 mA output. Electrical  
135 stimuli application was displayed online along with the force signal.

#### 136 Procedures

##### 137 Maximal stimulation intensity

138 Maximal stimulation intensity was determined by application of single twitches at rest, with  
139 the voltage set at 300 V and the current intensity increasing by 50 mA for each application.

140 Maximal stimulation intensity (hereafter called the maximal intensity) was determined as  
141 that beyond which a further increase in current by 50 mA failed to increase the twitch force  
142 further.

##### 143 Percentages of the maximal intensity twitch force

144 The stimulation intensities required to produce 10 to 100% (in 10% increments) of the force  
145 at maximal intensity were determined in a randomized order. Typically, this procedure  
146 required application of 2-3 twitches at each percentage of the maximal intensity to identify  
147 the appropriate current. Duration of rest between stimuli applications was 2-3 min. These  
148 stimulation intensities were then used for the rest of the experiment (hereafter called  
149 percentage intensities).

##### 150 Stimulation during voluntary contractions

151 Subjects performed an MVC and all subsequent test contractions were performed at 90% of  
152 MVC. This contraction level was selected as our laboratory and others have found it to be a



153 near-maximal contraction level that subjects can achieve consistently [Bampouras et al,  
154 2006; Behm et al, 1996; Bülow et al, 1993]. A target line indicating 90% of MVC was  
155 displayed on the same screen as the force from which the subjects received visual feedback  
156 to help them maintain a steady and consistent force.

157 The subjects were required to perform 9 trials at 90% of MVC with 3-4 min rest interval.  
158 Typically, these trials lasted ~2 s. During each trial, two stimuli (doublet) were applied as  
159 soon as a force plateau occurred (determined visually) while a second doublet was applied  
160 exactly three seconds later, during complete relaxation (resting doublet). The doublet was  
161 selected over a higher number of stimuli based on our previous finding of no differences  
162 between a doublet and a quadruplet or an octuplet on the ITT value for the quadriceps  
163 muscle (Bampouras et al, 2006). The ITT (eq.1) value for each percentage intensity was  
164 calculated.

165 To assess the level of discomfort associated with a given percentage intensity, an unmarked  
166 10 mm visual analog pain intensity scale (VAS [Collins et al, 1997]), with 'No pain' at one  
167 end and 'Worst pain' at the other end, was used to record the level of discomfort  
168 experienced by the subjects after each stimulus intensity. Scores above 5.4 cm indicate  
169 severe pain, while scores above 3 cm indicate moderate pain [Collins et al, 1997].

#### 170 Statistical analysis

171 Normality of data was examined using the Shapiro-Wilk test and was subsequently  
172 confirmed for all variables (90% MVC, activation level, VAS pain scores). A repeated  
173 measures analysis of variance was used to ascertain comparability of 90% MVC force  
174 across the trials with the different percentage intensities.

175 Differences between percentage intensities and maximal intensity for activation level and  
176 VAS scores were examined using Dunnett's test. This test is more appropriate in situations  
177 where several treatments are to be compared against a control or reference treatment only,  
178 rather than comparisons between all treatments [Dunnett, 1955]. The smallest percentage  
179 intensity for which muscle activation did not differ significantly from that of the maximal  
180 intensity was considered to be the minimum intensity able to yield valid results.  
181 Significance was set at  $p < 0.05$ . Values are presented as mean (SD), unless otherwise  
182 indicated.  
183

184 **Results**

185 The subjects' MVC force was 748 (130) N. The 90% MVC force was not significantly  
186 different ( $p = 0.477$ ) between the trials with the different percentage intensities (Table 1)  
187 and demonstrated low variability (coefficient of variation 2.5 (1.2) %). The resting stimulus  
188 force at maximal intensity was 302 (62) N (Figure 1).

189 Table 1

190 Figure 1

191 Muscle activation at maximal stimulation intensity was 91.6 (2.5)%. Percentage intensities  
192 of 90-50% yielded similar muscle activation values compared to the maximal intensity ( $p >$   
193  $0.05$ ). However, the percentage intensities of 40-10% produced significantly different  
194 muscle activation values ( $p < 0.05$ ) than maximal intensity (Figure 2). Therefore, 50% of  
195 maximal intensity was the mean lowest percentage intensity yielding a valid ITT outcome  
196 (muscle activation 88.8 (3.9) %). However, visual inspection of individual graphs indicated  
197 that in some subjects a valid ITT outcome could be obtained with intensities around 30%  
198 of maximal intensity.

199 Figure 2

200 Figure 3

201 VAS indicated that pain at percentage intensities of 90-70% was similar to the pain  
202 experienced at maximal intensity. However, pain at 60-10% stimulation intensities was  
203 significantly lower ( $p < 0.05$ ). The pain scores were reduced from 6.6 (1.5) cm at maximal  
204 intensity to 3.7 (1.5) cm at 60% percentage intensity (Table 1).

205

206

**207 Discussion**

208 The aim of the study was to identify the minimum stimulation intensity that will yield valid  
209 muscle activation values, similar to those obtained with maximal intensity. We found that  
210 stimulation at 50% of maximal intensity is sufficient to obtain a valid ITT outcome. The  
211 discomfort experienced by the subjects at this stimulation intensity was also reduced from  
212 severe to moderate compared to maximal stimulation.

213 Many previous authors have used what they term “maximal” stimulation intensities in an  
214 attempt to activate the largest portion of muscle possible and avoid erroneous ITT estimates  
215 [Behm et al, 2001; de Ruiter et al, 2004; Kent-Braun and Le-Blanc, 1996; Knight and  
216 Kamen, 2001; Kooistra et al, 2007; Morse et al, 2008; O’Brien et al, 2008; Reeves et al,  
217 2003]. However, a comparison between percutaneous muscle stimulation, which only  
218 activates a proportion of the muscle, and nerve stimulation, which activates all the motor  
219 units [Rutherford et al, 1986], showed no differences in the ITT outcome between the two  
220 techniques, suggesting that valid results can be achieved as long as the portion of the  
221 muscle activated at rest and during contraction remains the same. The findings of the  
222 current study support those of Rutherford et al [1986], indicating that reliable ITT results  
223 can be obtained even when activating relatively small portions of the quadriceps muscle.

224 The mechanisms underlying the pattern of the ITT and the results obtained in the present  
225 study can be better understood by considering the changes with percentage intensity and the  
226 magnitude of the corresponding mean values of the superimposed and resting doublets  
227 independently (Figure 1). At lower stimulation intensities (10% and 20% of maximal  
228 intensity), a very small proportion of inactive muscle would become activated by the  
229 superimposed doublet. Although this stimulation intensity suffices to produce a detectable

230 force increment when the doublet is applied at rest, it is difficult to detect the superimposed  
231 doublet since any force increment is small in relation to the oscillation of the voluntary  
232 force trace. This results in zero SI/R ratios and a misleading conclusion of complete  
233 activation. At 30% and 40% of maximal intensity a larger portion of muscle becomes  
234 activated and the magnitude of the superimposed doublet increases rapidly. Following that  
235 point the stimulation intensity reaches a level that is sufficiently high to induce both  
236 detectable increases in the superimposed stimulus as well as sufficiently stretch the series  
237 elastic components at rest, resulting in a constant SI/R ratio and, thus, in valid ITT results.

238 Maximal stimulation is an imprecise term since it can vary with the type of stimulator, the  
239 type, size and position of the electrodes as well as the conductivity of the skin and  
240 subcutaneous fat and the size of the muscle. It is therefore more useful to define the  
241 minimum requirements for testing activation in terms of the force generated by the  
242 electrical stimulation as a percentage of the likely MVC force. In our subjects the mean  
243 90% of MVC was 635 N and reliable estimates of ITT were obtained with a percentage  
244 intensity that generated a mean force of 181 N in the resting muscle. Consequently, we  
245 recommend that the stimulation intensity should be set to generate at least one third of the  
246 estimated MVC.

247 A concern with electrical stimulation is sometimes the discomfort experienced by subjects  
248 [Behm et al, 2001; Chae et al, 1998; Delitto et al, 1992; Han et al, 2006; Miller et al, 2003;  
249 Valli et al, 2002]. Two studies have indicated high levels of discomfort in older subjects  
250 [Valli et al, 2003] and patients [Chae et al, 1998], subject groups where it is particularly  
251 important to assess the ability to activate their muscles [Bampouras et al, 2006; Chae et al,  
252 1998]. Subject discomfort was investigated by Miller et al [2003] by inducing pulse trains

253 of different lengths and durations. Less discomfort was reported with shorter pulse  
254 durations without a change in the activation results. Suggestions were made for more  
255 research into protocols that can assess muscle activation reliably, with reduced discomfort  
256 of the subjects. The present findings suggest that discomfort was significantly reduced at  
257 percentage intensities below 60%. The average difference in VAS scores was reduced by  
258 2.9 cm. Previous studies suggested 2 cm as the minimum clinically significant change when  
259 using VAS [DeLoach et al, 1998]. Therefore, our results indicate a reduction from severe  
260 pain to moderate pain, which is important because it widens the applicability of ITT  
261 assessment to subjects who are less tolerant of high intensity stimulation.

262 Another potential problem with the application of transcutaneous electrical stimulation for  
263 assessing activation capacity using the ITT method is co-contraction of: a) nearby agonist  
264 muscles due to current spread [Taylor, 2009], b) antagonist muscles due to activation of  
265 cutaneous receptors [Belanger and McComas, 1981; Poumarat et al, 1991] and c)  
266 antagonist muscles due to discomfort [Paillard et al, 2005]. The latter effect will be less of a  
267 problem with submaximal stimulation. Nevertheless, electromyography can be used to  
268 detect any artifactual co-contractions from non-studied muscles and make appropriate  
269 relevant adjustments (e.g., alter size or position of stimulating electrodes).

270 In conclusion, this study shows that maximal stimulation is not necessary to obtain a valid  
271 ITT outcome. Our results for the knee extensor muscles of healthy young adults show that  
272 valid ITT results for contractions at 90% of MVC can be obtained with just 50% of  
273 maximal intensity. Practically, a more useful guide is that the force generated by  
274 stimulation of the resting muscle should be approximately one third of the anticipated MVC  
275 force.

276

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## Figure captions

Figure 1. Mean superimposed (left y axis) and resting (right y axis) doublet magnitudes across all percentage intensities. Vertical bars denote SD.

Figure 2. Mean muscle activation values across all percentage intensities. Vertical bars denote SD. \* indicates significant difference ( $P < 0.05$ ) compared to maximal intensity.

Figure 3. Muscle activation values across all percentage intensities for a single subject, showing a plateau in muscle activation occurring below 30% percentage intensity.

Figure 1.

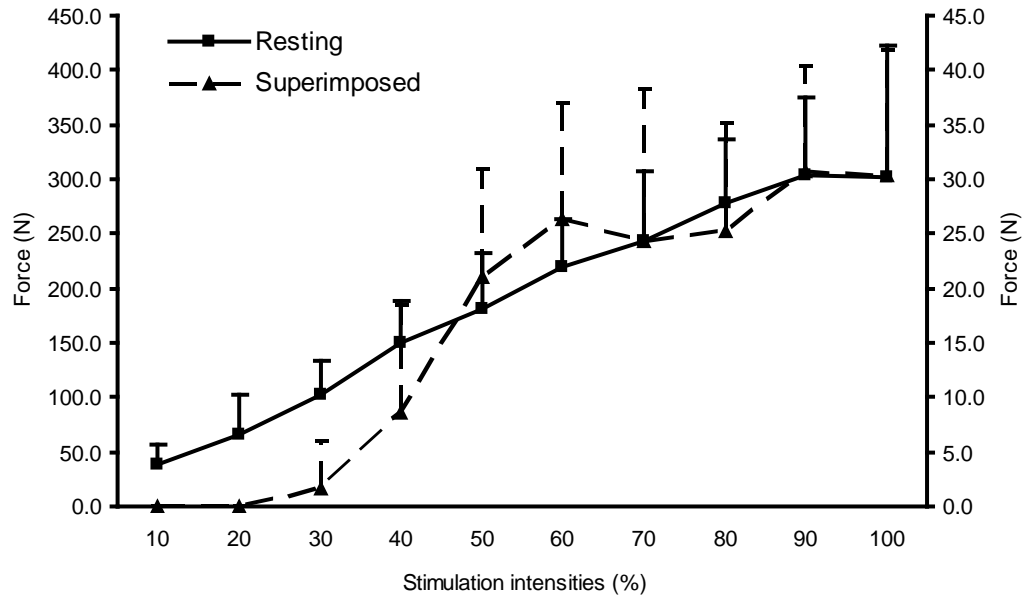


Figure 2.

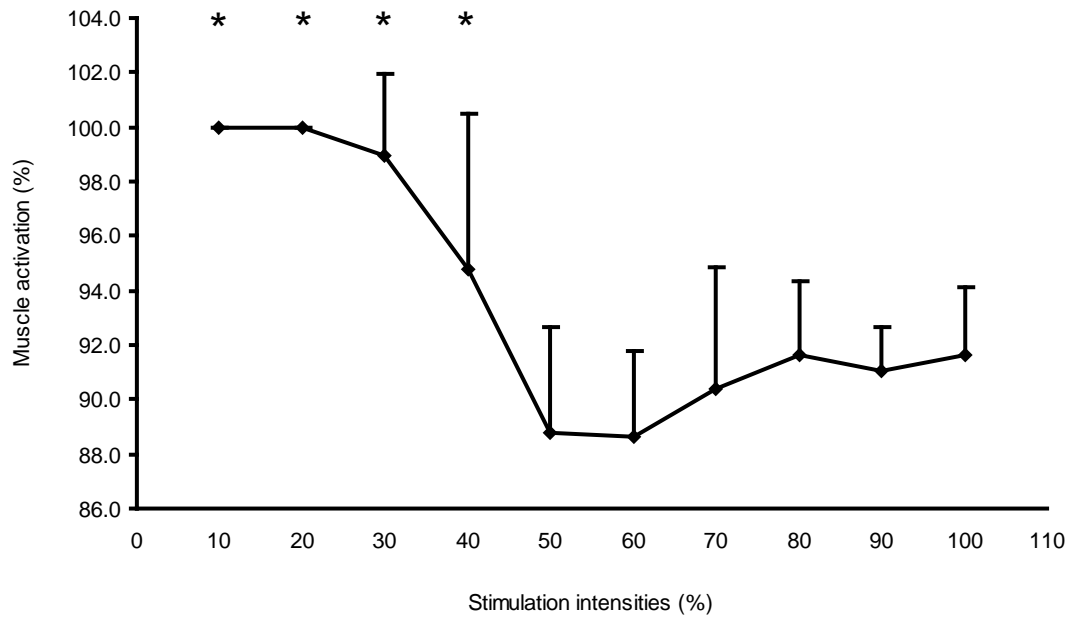
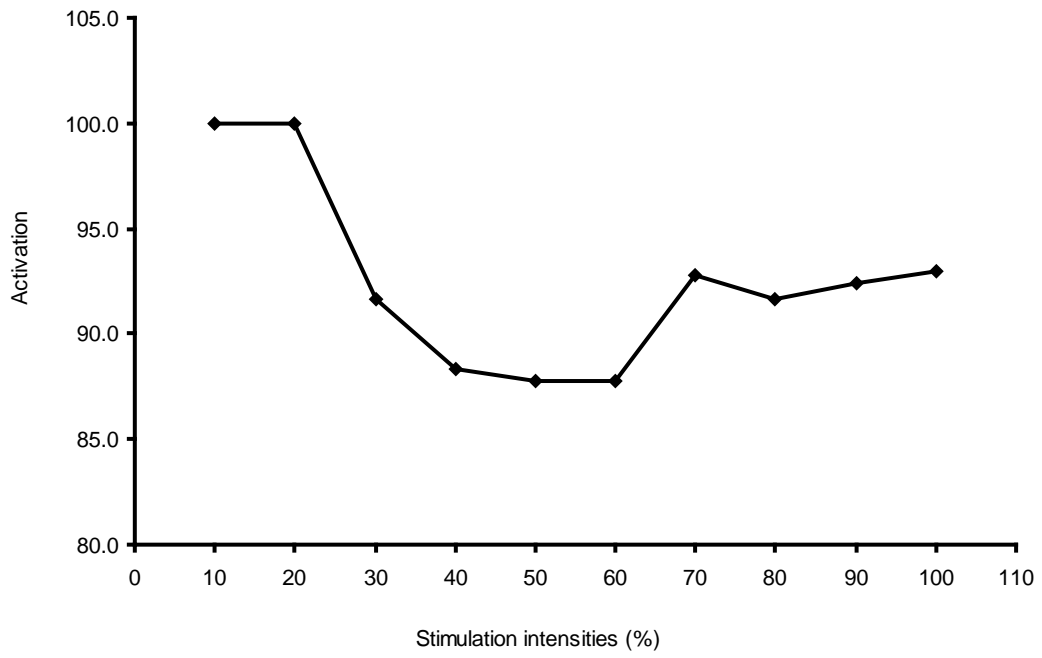


Figure 3.





## Tables

Table 1. 90% of MVC force values and VAS pain scores for each percentage intensity.

Data are presented as mean (SD). \* indicates significant difference between a given percentage intensity and the maximal intensity.

	<b>10</b>	<b>20</b>	<b>30</b>	<b>40</b>	<b>50</b>	<b>60</b>	<b>70</b>	<b>80</b>	<b>90</b>	<b>100</b>
<b>90% MVC (N)</b>	639	643	631	631	628	641	626	639	634	636
	(102)*	(110)*	(119)*	(116)*	(114)	(108)	(106)	(108)	(115)	(117)
<b>VAS (cm)</b>	1.5	1.4	1.6	3.0	4.0	3.7	4.4	4.9	6.4	6.6
	(1.9)*	(1.3)*	(1.2)*	(1.7)*	(2.2)*	(1.5)*	(1.7)	(2.3)	(2.5)	(1.5)