1 Title Page

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3	EFFECT OF EARLY IMPLEMENTATION OF ELECTRICAL MUSCLE
4	STIMULATION TO PREVENT MUSCLE ATROPHY AND WEAKNESS IN
5	PATIENTS AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION
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#### 31 ABSTRACT

#### 32 **Objective**

Following anterior cruciate ligament (ACL) reconstruction, restricted weight bearing
and immobilization results in thigh and calf muscle atrophy and weakness. The
purpose of this study was to assess the effect of electrical muscle stimulation (EMS)
on prevention of muscle atrophy in patients during the early rehabilitation stage after
ACL reconstruction.

#### 38 Methods

Twenty patients with acute ACL tears were divided into two groups randomly. The control group (CON group) participated in only the usual rehabilitation program. In addition to this protocol, the electrical muscle stimulation group (EMS group) received EMS training using the wave form of 20 Hz exponential pulse from the 2nd post-operative day to 4 weeks after the surgery.

#### 44 **Results**

45 Muscle thickness of vastus lateralis and calf increased significantly 4 weeks after 46 surgery in the EMS group, while it decreased significantly in the CON group. The 47 decline of knee extension strength was significantly less in the EMS group than in 48 the CON group at 4 weeks after the surgery, and the EMS group showed greater

49	recovery of knee extension strength at 3 months after surgery.
50	Conclusions
51	EMS implemented during the early rehabilitation stage is effective in maintaining
52	and increasing muscle thickness and strength in the operated limb.
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#### 67 INTRODUCTION

69 Following anterior cruciate ligament (ACL) reconstruction, immobilization and 70 restricted motion of the operated limb lead to unloading of the knee joint and 71 restricted weight bearing for 4 weeks after surgery, resulting in atrophy and 72 weakness of the quadriceps femoris and triceps surae muscles. Quadriceps atrophy 73 and strength loss often exceed 20% and 30%, respectively, during the first three 74 months following ACL reconstruction, and a 10% to 20% deficit in quadriceps size 75 and strength can persist for years after surgery, despite concentrated rehabilitation efforts<sup>12</sup>. In addition, Nicholas et al. reported that ACL reconstruction resulted in a 76 significant decrease in thigh and calf girth at 3 weeks postoperation<sup>24</sup>. Therefore, a 77 78 primary focus of ACL rehabilitation protocols is the preservation and prompts 79 recovery of quadriceps femoris and triceps surae force production and function. We 80 believe it is important that patients start to exercise the quadriceps femoris and 81 triceps surae muscles during the early post-operative period in order to prevent 82 muscle atrophy and maintain muscle strength. One conventional choice for solving 83 this serious problem is electrical muscle stimulation (EMS). EMS elicits skeletal 84 muscle contractions through percutaneous electrodes that depolarize underlying

85	motor nerves. EMS using percutaneous electrodes is noninvasive and easy-to-use.
86	Several EMS studies have shown the potential advantages, both physiological and
87	clinical <sup>9, 20, 29</sup> . These previous studies have shown that EMS can be used to mimic
88	voluntary exercise and improve neuromuscular functions. There are other studies
89	showing better results of voluntary training versus electrical stimulation training and
90	that this varies depending on the type of individuals tested (healthy versus patients) <sup>4</sup> ,
91	5, 18, 30

92 Previous studies had EMS protocols specific to each study's purpose, making it 93 difficult to define the relationship between the EMS protocol and its effects. So it is 94 quite difficult to prescribe a flexible EMS protocol appropriate for the desired 95 purpose and participant's condition. Our laboratory has focused on EMS protocols, especially stimulus frequency characteristics. For example, our previous studies 96 97 demonstrated in human participants that 1) training with 20 Hz frequency 98 stimulation is more effective than 50 or 80 Hz frequency stimulations for inducing muscle hypertrophy<sup>22</sup>, 2) EMS significantly increases glucose disposal rate (GDR) 99 during euglycemic clamp studies<sup>15</sup>, and a single bout of EMS to the lower 100 extremities can significantly enhance energy consumption, carbohydrate oxidation, 101 and whole body glucose uptake with low-intensity exercise<sup>13</sup>, and 3) EMS induces 102

103	selective fast-twitch MU activation of knee extensor muscles <sup>14</sup> . However, the
104	effects of long-term EMS training using our protocol are still unknown. Further
105	studies are necessary to test the therapeutic efficacy of our EMS device and
106	stimulation protocol. In most studies investigating the efficacy of EMS in patients
107	after knee surgery, the start time of the electric stimulation was often late (2-6 weeks
108	after surgery) and the muscles had already deteriorated and lost strength <sup>2, 6, 19, 25, 31, 32</sup> .
109	No one has reported the effects of EMS treatment implemented during the early
110	rehabilitation stage for prevention of muscle atrophy in patients with ACL
111	reconstruction. Moreover, there are no reports that evaluate changes in muscle
112	thickness of individual muscles during EMS training.
113	The purpose of this study was to determine the effects of electrical muscle
114	stimulation on the prevention of muscle atrophy in patients during the early

rehabilitation stage after ACL reconstruction using a modified EMS device andstimulation protocol.

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#### 118 MATERIALS AND METHODS

119 Participants and Informed Consent

120	Twenty patients (16 male, 4 female), ranging in age from 13 to 54 years (26.3 $\pm$
121	11.8 years) participated in this study. All patients had suffered an acute tear of the
122	ACL, and underwent an arthroscopically assisted semitendinosus autograft
123	reconstruction. The time from ACL tear until surgery were $3.1 \pm 1.4$ months. They
124	had no history of neuromuscular disorders except for ACL injury. Each participant
125	provided informed consent prior to experimentation. The study protocol was
126	approved by the Medical Ethics Committee of our hospital.

#### 128 Experimental Design

129 Twenty consecutive patients who underwent ACL reconstruction were 130 randomized and assigned to one of two groups: the control group (CON group) 131 included 10 patients (8 male, 2 female, age: 29.4±14.1 years, height: 165.9±5.9 cm, weight: 60.1 $\pm$ 10.1 kg, time from injury: 3.1 $\pm$ 1.4 months) and the electrical muscle 132 133 stimulation group (EMS group) included 10 patients (8 male, 2 female, age: 23.5 $\pm$ 9.3 years, height: 171.0 $\pm$ 3.9 cm, weight: 68.1 $\pm$ 6.3 kg, time from injury: 3.1 $\pm$ 134 1.4 months). There were no significant differences between the groups in age, 135 physical characteristic, and the time from injury. The CON group received only the 136 137 usual rehabilitation program determined by our institute. In addition to this

138	standard rehabilitation protocol, the EMS group received EMS training for 4 weeks
139	beginning on post-operative day 2. Table 1 represents the rehabilitation program
140	determined by our institute, in which all patients in the study participated. To
141	determine the effects of EMS, we measured muscle thickness of the rectus femoris
142	(RF), vastus intermedius (VI), vastus lateralis (VL), and calf muscle (CA) before
143	surgery and at 4 weeks and 3 months after surgery. We also measured changes in
144	knee extensor muscle strength in isometric and isokinetic contractions before
145	surgery and at 4 weeks and 3 months after surgery. Moreover, we measured lower
146	extremity function using the Lysholm score before and at 6 months after the surgery.

#### 148 EMS Training Protocol

The quadriceps femoris, hamstrings, tibialis anterior muscle, and triceps surae were selected for EMS training in this study. The EMS training was performed on the operated limb in patients of the EMS group, beginning the second day after surgery and performed 5 days per week for a period of 4 weeks. Contractions of the knee extensor, knee flexor, dorsi flexor, and plantar flexor muscles were elicited simultaneously without involving movement of the joint by percutaneous muscle stimulation for 20 minutes with the patient lying supine on a bed.

156	We used a specially designed handheld muscle stimulator (Homer Ion Co. LTD.,
157	Tokyo, Japan) powered by a 15-V battery for EMS training in this investigation (Fig.
158	1). The stimulator current waveform was designed to produce co-contractions in
159	the lower extremity muscle groups at a frequency of 20 Hz with a pulse width of 250
160	$\mu s.$ The duty cycle was a 5 s stimulation with a 2 s pause for a period of 20 min.
161	Moreover, we used an exponential climbing pulse to reduce discomfort during
162	muscle stimulation (Fig. 2). Impulses were delivered through eight silicon-rubber
163	electrodes on the operated limb with tightly fitted shorts and leg band (Wacoal Co.
164	LTD., Kyoto, Japan). The EMS device (Homer Ion Co. LTD., Tokyo, Japan) and
165	specially designed stimulation shorts (Wacoal Co. LTD., Kyoto, Japan) jointly
166	developed have been processed for its patents, and thus not yet commercially
167	available.

All patients were treated at the highest stimulation intensity they could tolerate (peak intensity: 74–107 mA). In every training session, the stimulus intensity was individually increased as high as possible, without causing discomfort. None of the patients complained of knee pain or skin discomfort during or after EMS training, and there were no abnormal findings in periodic examinations by their attending doctors.

175 Muscle Thickness Analysis

176 Muscle thickness on the operated limb was measured using ultrasound still 177 images (GE Yokokawa Medical Co. LTD., Tokyo, Japan) obtained using an 8.0 MHz 178 probe with the patient lying supine or prone. Ultrasound is particularly useful 179 because it is safe, noninvasive, and portable. Strong correlations have been reported 180 between muscle thickness measured by B-mode ultrasound and site-matched skeletal muscle mass measured by MRI<sup>7, 11, 21, 28, 34</sup>. Therefore, it is plausible to use 181 182 muscle thickness measurements to estimate muscle size and degree of muscle 183 atrophy. Previous studies have shown the reliability of the ultrasound technique for measuring muscle thickness<sup>1, 17, 26, 33</sup>. Also, we measured the reliability of the 184 185 ultrasonographic measurement in this study. The intraclass correlation coefficients 186 in RF, VI, VL, and CA were 0.97 (0.88 – 0.99), 0.96 (0.85 – 0.99), 0.99 (0.97 – 1.0), 187 and 0.99 (0.96 - 1.0), respectively. Muscle thicknesses of the RF and VI were 188 measured at the level of the half distance between the anterior superior iliac spine 189 (ASIS) and the upper pole of the patella and on the line which linked the two points. 190 Muscle thickness of VL was measured at the level of lower one-thirds of the 191 distance between the ASIS and the upper pole of the patella, and 3 cm lateral from

the line which linked the patella to the ASIS in the supine position. Muscle thickness of CA was measured at the level of the half distance between the head of fibula and the lateral malleolus in the prone position. We measured muscle thickness with the probe placed in the transverse plane. Measurements were performed before surgery and at 4 weeks and 3 months after surgery.

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198 Analysis of Knee Extensor Muscle Strength

199 We analyzed knee extensor muscle strength by measuring the maximal 200 voluntary isometric contraction of the quadriceps femoris using the CYBEX HUMAC NORM<sup>®</sup> (Computer Sports Medicine, Inc., MA, USA.) dvnamometer 201 before surgery and at 4 weeks and 3 months after surgery. The patients were 202 203 seated and stabilized in an electromechanical dynamometer with the knee flexed at 204 90 degrees where they attempted to maximally contract the quadriceps femoris 205 muscles for 5 seconds while verbal encouragement from the tester and visual 206 feedback from the dynamometer were provided. Similarly, we measured the maximal isokinetic knee extension force with an angular velocity of 60 207 208 degrees/second before surgery and at 3 months after surgery. The peak torque measured using the CYBEX HUMAC NORM<sup>®</sup> was normalized with respect to 209

210	patient's body weight, which was then expressed as the percent body weight (%BW).
211	This would allow a better understanding of the patient capacity (or muscle strength)
212	with respect to his/or her own body weight that needs to cope with in daily life. We
213	also calculated the ratio of changes at 4 weeks and 3 months after surgery in
214	comparison to the pre-operation.
215	
216	Analysis of Lower Extremity Function
217	We measured lower extremity function using the Lysholm score before and at 6
218	months after the surgery.
219	
220	Statistics
221	We calculated the mean and standard error of the mean (SE) for all variables.
222	A two-way analysis of variance (ANOVA) followed by Fisher's post-hoc test
223	procedure was used to test differences in the effects of EMS training on dependent
224	variables (muscle thickness and muscle strength in isometric and isokinetic
225	contraction) before surgery and after 4 weeks and 3 months. Also we calculated
226	the change ratio on operated side for muscle strength of knee extensor at 4 weeks

and 3 months after surgery in comparison to the pre-operation, and conducted a

228	two-way ANOVA followed by Fisher's post-hoc test procedure to test differences in
229	effects of EMS training on dependent variables. The factors included in the two
230	way analysis of variance were time course (pre operation, 4 weeks after surgery, and
231	3 months after surgery) and training group (CON group and EMS group).
232	
233	RESULTS
234	
235	Changes in Muscle Thickness
236	Fig. 3a shows RF muscle thickness of the operated side at pre-operation (PRE),
237	4 weeks post-operation (4WPO) and 3 months post-operation (3MPO) for both CON
238	and EMS groups. Two-way ANOVA with Fisher's post-hoc test indicated that in
239	the EMS group there was no significant decline in RF muscle thickness between
240	PRE and 4WPO while the muscle thickness was significantly increased (p=0.003) at
241	3MPO. In contrast, RF muscle thickness decreased significantly (p=0.0001) at
242	4WPO compared to PRE and increased significantly (p=0.0006) at 3MPO compared
243	to 4WPO in the CON group.
244	Fig. 3b shows the time-course changes of VI muscle thickness. There were no
245	significant changes between PRE and 4WPO and VI muscle thickness increased

significantly (p=0.007) at 3MPO compared to 4WPO in the EMS group. For the
CON group, VI muscle thickness decreased significantly (p=0.0000004) at 4WPO
compared to PRE and increased significantly (p=0.00001) at 3MPO compared to
4WPO, respectively.

Fig. 3c shows the time-course changes of VL muscle thickness, which increased significantly at 4WPO (p=0.0004) in the EMS group, while it decreased significantly at 4WPO (p=0.0000) but increased significantly at 3MPO (p=0.00007) compared to 4WPO in the CON group. VL muscle thickness was significantly (p=0.000003) higher at 3MPO than at PRE in the EMS group while it was significantly (p=0.017) lower at 3MPO than at PRE in the CON group.

Fig. 3d shows the time course changes of CA muscle thickness, which increased significantly at 4WPO (p=0.016) in the EMS group, while it decreased significantly at 4WPO (p=0.0002) but increased significantly at 3MPO (p=0.0002) compared to 4WPO in the CON group. CA thickness was significantly (p=0.004) higher at 3MPO than at PRE in the EMS group while we observed no significant difference between PRE and 3MPO in the CON group.

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263 Changes in Muscle Strength

264	Fig. 4a shows the time-course changes of isometric knee extension strength
265	expressed as percentage of body weight (%BW) at PRE, 4WPO and 3MPO in both
266	groups. Isometric strength decreased significantly at 4WPO (p=0.001) and
267	increased significantly at 3MPO (p=0.00008) in the CON group, while there were no
268	significant changes between PRE and 4WPO and a significant increase at 3MPO
269	(p=0.001) in the EMS group. The changes in these values are shown in Fig. 4b.
270	Change ratios in the EMS group were significantly higher than the CON group at 4
271	weeks after surgery (-1.2% vs. 39.2%, p=0.008) and tended to be higher at 3 months
272	after surgery (52.7% vs. 16.3%, p=0.072), respectively.
273	Change ratios in isokinetic muscle strength measured at angular velocity of 60
274	degrees/sec at 3 months after surgery tended to be higher in the EMS group than in
275	the CON group (62.2% vs. 13.8%), but the difference did not reach the statistical

276 significance.

277

#### 278 Changes in Lower Extremity Function

Lysholm scores for the CON and EMS groups were  $59.2\pm7.8$  vs.  $63.6\pm4.9$  at pre operation, and  $95.2\pm3.2$  vs.  $96.4\pm6.2$  at 6 months after surgery, respectively. There were no significant differences in Lysholm scores between the CON and the EMS 282 groups at 6months after the surgery.

#### 283 DISCUSSION

284

285 The significant finding of this study was that 4 weeks of 20 Hz EMS training 286 beginning in the early rehabilitation stage following ACL reconstruction prevented muscle atrophy and weakness. There have been some controversial findings 287 regarding the effects of EMS following ACL reconstruction. Sisk et al.<sup>31</sup> 288 289 demonstrated that there was no significant difference in strength between treatment 290 groups, but there was a significant difference in strength between competitive and recreational athletes. Moreover, Lieber et al.<sup>19</sup> demonstrated that 50 Hz 291 292 neuromuscular electrical stimulation and voluntary muscle contraction treatments, 293 when performed at the same intensity, are equally effective in strengthening skeletal 294 muscle that has been weakened by surgical repair of the ACL. On the other hand, Delito et al.<sup>6</sup> reported that patients in the EMS group finished a three-week training 295 296 regimen with higher percentages of both extension and flexion torque when compared to patients in the voluntary exercise group. Arvidsson et al.<sup>2</sup> studied 297 298 different parts of the quadriceps in female patients and found less atrophy of the vastus medialis after electrical stimulation. Snyder-Mackler et al.<sup>32</sup> reported that 299

300 quadriceps strength averaged at least 70% of the strength on the uninvolved side in 301 patients treated with high-intensity electrical stimulation (either alone or combined 302 with low-intensity electrical stimulation), 57% in patients treated with high-level 303 active exercise, and 51% in patients treated only with low-intensity electrical stimulation. Moreover, Fitzgerald et al.<sup>10</sup> reported that use of the modified EMS 304 305 protocol as an adjunct to rehabilitation resulted in modest increases in quadriceps torque output after 12 weeks of rehabilitation and in self-reported knee function at 306 307 12 and 16 weeks of rehabilitation, when compared to subjects who underwent 308 rehabilitation without EMS treatment.

Our present results confirmed significant efficacy of EMS training following ACL surgery, but differ from previous studies on some points. Our current data indicated that EMS training not only prevented muscle atrophy following ACL reconstruction, but also resulted in VL and CA hypertrophy, which have not been reported previously. We believe these different results are caused by differences in the start timing of EMS, the EMS protocol, and the electrodes.

However, there were no significant differences in Lysholm scores between the CON and the EMS groups. here were no significant differences in Lysholm scores between the CON and the EMS groups at 6months after the surgery. The

318 non-significant difference in the Lysholm scores might have been due to the fact that 319 the scores for the activity and knee static instability affected had already recovered 320 for all participants by this time. On the other hand, the recovery of knee pain and 321 swelling varied among different individuals, regardless of the way of training. For 322 these reasons, there were no significant differences in Lysholm scores between both 323 groups at 6 months after surgery.

324

#### 325 Timing of EMS Treatment Initiation

326 The EMS program in most of the previous studies started after the affected muscles had already begun to lose strength. Delito et al.<sup>7</sup> started EMS within the 327 328 first 6 weeks after the operation and demonstrated that the EMS group had a 329 significantly smaller loss of isometric knee extension strength than the control group, 330 but the treatment was not complete and was not enough to prevent muscle atrophy. Lieber et al.<sup>19</sup> compared EMS training with voluntary contraction training in 331 332 patients 2-6 weeks after ACL reconstruction and reported equal effects of the two 333 training protocols. In contrast, patients in our study began the EMS program on the 334 2nd post-operative day and were able to keep muscle strength. We succeeded in 335 starting the EMS training just after surgery because we could train the operated limb

336 safely without involving movement of the joint by using the EMS device to induce337 co-contraction of the quadriceps, hamstrings, tibialis anterior, and calf muscles.

338 It is unavoidable that muscle atrophy and weakness occur immediately after 339 In addition, we knew that muscle atrophy and weakness following ACL injury. 340 ACL reconstruction would begin immediately following surgery and that significant 341 disuse atrophy could occur as early as the first several days after surgery because patients are forced to be non-weight-bearing and immobilized during this time. 342 343 Patients are also restricted from knee extension muscle training to protect the 344 reconstructed ligament during the early rehabilitation stage. Therefore, we believe 345 that EMS training should start as early as possible following ACL reconstruction.

346

347 EMS Protocol

The quadriceps femoris, hamstrings, tibialis anterior muscle, and triceps surae were selected for EMS training. When EMS is used, the fatigue can be subdivided into low-frequency fatigue and high-frequency fatigue. Low-frequency fatigue is evident when the active force is depressed at frequencies that previously elicited submaximal force. Long-term low-frequency stimulation produces greater depressions of active force (called low frequency fatigue) than high-frequency

stimulation in post-stimulation periods<sup>30</sup>. Impaired excitation-contraction coupling 354 355 is responsible for low-frequency fatigue, which is prolonged and preferentially affects fast-twitch fibers<sup>8</sup>. High-frequency fatigue is evident when the active force is 356 357 depressed at frequencies that previously elicited maximal force. High-frequency 358 fatigue induces excessive loss of force, which can be due to electrical propagation failure with a rapid decline in the evoked action potential amplitude. Jones et al.<sup>16</sup> 359 demonstrated that a reduction in extracellular  $[Na^+]$  (or accumulation of  $[K^+]$ ) 360 361 accelerates the rate of force fatigue in an isolated preparation, as did an increase in stimulus frequency. Moritani et al.<sup>22</sup> have demonstrated that significantly less force 362 is generated after 30 seconds of high-frequency stimulation (50 Hz or 80 Hz) than 363 364 after a similar period of MVC. During this period of high-frequency force fatigue, considerably greater force is generated at 20 Hz stimulation $^{22}$ . 365 Thus, 366 high-frequency fatigue could be largely accounted for by a failure of electrical transmission that may be due to reduced muscle membrane excitability leading to a 367 reduction in the evoked potential amplitude and conduction time<sup>3, 16, 22</sup>. 368 Most of the previous studies reported the efficacy of EMS using very 369

370 high-frequency (2500 Hz) or high-frequency stimulations (50 Hz or 80 Hz)<sup>19, 31, 32</sup>.

371 Eriksson et al.<sup>9</sup> showed that muscle enzyme activities, fiber size, and mitochondrial

372 properties in the quadriceps femoris did not change with 50 Hz EMS training 373 sessions over 4-5 weeks. Thus, patients in previous studies employing 374 high-frequency (50Hz or 80Hz) EMS training might have suffered from 375 high-frequency fatigue, so that the intended muscles were not effectively contracted. 376 This evidence indicates that 20 Hz EMS has the potential to elicit more effective 377 muscular improvement (a combined adaptation of neural factors and morphological 378 changes) than high-frequency (50 Hz or 80 Hz) EMS. Our present results are in agreement with this previous evidence. Rebai et al.<sup>25</sup> demonstrated that twelve 379 380 weeks after surgery, the quadriceps peak torque deficit in the operated limb with 381 respect to the non-operated limb at 180 degrees/s and 240 degrees/s was 382 significantly less in the 20 Hz group than in the 80 Hz group. Our data also 383 suggest that low-frequency (20 Hz) EMS training is effective in muscle training. 384 We specifically avoided the use of high frequency (50 Hz, 80 Hz, and more higher) 385 stimulations due to "high frequency fatigue", i.e. a reduction of muscle membrane 386 excitability due to extracellular K+ accumulation which in turn results in force loss. In 387 other words, high frequency stimulations reduce the time necessary to fully perform 388 depolarization/repolarization to maintain the muscle membrane excitability. Use of 389 high frequency EMS would reduce the pain to a greater extent, but neurologically and

390 metabolically less effective when compared with low frequency stimulations. We have 391 shown this phenomenon with intramuscularly recorded M-wave and force measurements $^{22, 23}$ . We have also directly measured muscle energy metabolism during 392 393 low and high frequency stimulations and found that high frequency stimulations (50, 394 80Hz) resulted in significantly lower energy utilization due to "high frequency 395 fatigue"<sup>13</sup>. Also, in our earlier preliminary studies, we have tried various stimulation 396 protocols (20, 50, 80Hz and different duty cycle) and measured directly the rate of 397 muscle fatigue, oxygen extraction level by near infrared spectroscopy, and 398 mechanomyogram (MMG). We found the presently used protocol is the best in terms 399 of avoiding fatigue accumulation without compromising muscular hypertrophy effects.

400

#### 401 Wave Pattern and Electrodes

We used our original stimulus wave pattern and electrodes in the present study. It is generally difficult to increase stimulus intensity to the level necessary for effective muscle contraction using 20 Hz low-frequency stimulation because of skin pain or discomfort. We were able to increase the stimulus intensity higher than in previous studies without causing skin discomfort because we used an exponential climbing pulse instead of a rectangular pulse (Fig 2). Moreover, our original 408 electrodes were large, wet-gel type electrodes that reduced source impedance so that 409 there were no complaints of skin discomfort during or after EMS training, and no abnormal findings reported by the attending doctors. In our earlier studies<sup>13, 15</sup>, we 410 411 used square pulses without exponential climbing procedure. This stimulation 412 technique accompanied a quite pain on the skin surface, particularly when 413 stimulating at higher intensities. We therefore asked the EMS manufacture to invent 414 a new stimulation procedure to reduce such discomfort as much as possible by 415 avoiding initial sudden electrical discharge to the skin surface. A newly invented 416 this climbing pulse stimulation procedure has been successfully adopted in the 417 present study. This procedure includes initial phase of 10% of the final stimulus 418 voltage and gradually reaching the final intensity with in 100 msec.

419

#### 420 Conclusion

We were able to prevent muscle weakness in patients with ACL reconstruction by implementing our EMS protocol early in the rehabilitation stage following surgery. The decrease in the quadriceps peak torque of the operated limb was significantly less in the EMS group (1.2%) than in the CON group (39.2%) 4 weeks after surgery. The recovery ratio in the EMS group was higher than in the CON

426	group at 3 months. We believe that the difference in muscle strength between the
427	EMS and CON groups at 3MPO was brought about by the prevention of muscle
428	atrophy by EMS training for 4 weeks. Consequently, we suggest that EMS training
429	with 20 Hz exponential climbing pulse beginning immediately after surgery can
430	prevent muscle atrophy and weakness in patients recovering from ACL
431	reconstruction using semitendinosus autograft.
432	
433	
434	
435	REFERENCES
435 436	REFERENCES 1. Abe T, Kondo M, Kawakami Y, Fukunaga T. Prediction equations for body
436	1. Abe T, Kondo M, Kawakami Y, Fukunaga T. Prediction equations for body composition of Japanese adults by B-mode ultrasound. American Journal of
436 437	1. Abe T, Kondo M, Kawakami Y, Fukunaga T. Prediction equations for body composition of Japanese adults by B-mode ultrasound. American Journal of
436 437 438	1. Abe T, Kondo M, Kawakami Y, Fukunaga T. Prediction equations for body composition of Japanese adults by B-mode ultrasound. American Journal of
436 437 438 439	<ol> <li>Abe T, Kondo M, Kawakami Y, Fukunaga T. Prediction equations for body composition of Japanese adults by B-mode ultrasound. American Journal of Human Biology 1994; 6: 161–70.</li> </ol>
436 437 438 439 440	<ol> <li>Abe T, Kondo M, Kawakami Y, Fukunaga T. Prediction equations for body composition of Japanese adults by B-mode ultrasound. American Journal of Human Biology 1994; 6: 161–70.</li> <li>Arvidsson I, Arvidsson H, Eriksson E, et al. Prevention of quadriceps wasting</li> </ol>

444	3. Bigland-Ritchie B, Jones DA, and Woods JJ. Excitation frequency and muscle
445	fatigue. Electrical responses during human voluntary and stimulated contractions.
446	Experimental Neurology 1979; 64: 414-27.
447	
448	4. Currier DP, Lehman J, Lightfoot P, Electrical stimulation in exercise of the
449	quadriceps femoris muscle. Physical Therapy 1979; 59: 1508-12.
450	
451	5. Currier DP and Mann R. Muscular strength development by electrical stimulation
452	in healthy individuals. Physical Therapy 1983; 63: 915-21.
453	
454	6. Delitto A, Rose SJ, McKowen JM, et al. Electrical stimulation versus voluntary
455	exercise in strengthening thigh musculature after anterior cruciate ligament
456	surgery. Physical Therapy 1988; 68: 660-63.
457	
458	7. Dupont AC, Sauerbrei EE, Fenton, PV, Shragge, PC, Loeb GE, Richmond FJ.
459	Real-time sonography to estimate muscle thickness: comparison with MRI and
460	CT. Journal of Clinical Ultrasound 2001; 29: 230–36.
461	

462	8. Edwards RH, Hill DK, Jones DA, and Merton PA. Fatigue on long duration in
463	human skeletal muscle after exercise. Journal of Physiology 1977; 272: 769-78.
464	
465	9. Eriksson E, Haggmark T, Kiessling KH, and Karlsson J. Effects of electrical
466	stimulation on human skeletal muscle. International Journal of Sports Medicine
467	1981; 2: 18-22.
468	
469	10. Fitzgerald G K, Piva SR, and Irrgang JJ. A modified neuromuscular electrical
470	stimulation protocol for quadriceps strength training following anterior cruciate
471	ligament reconstruction. Journal of Orthopedic and Sports Physical Therapy 2003;
472	33: 492-501.
473	
474	11. Fukunaga T, Miyatani M, Tachi M, Kouzaki M, Kawakami Y, Kanehisa H.
475	Muscle volume is a major determinant of joint torque in humans. Acta
476	Physiological Scand 2001; 172: 249–55.
477	
478	12. Gerber JP, Marcus RL, Dibble LE, Greis PE, Burks RT, LaStayo PC. Effects of
479	early progressive eccentric exercise on muscle structure after anterior cruciate

ligament reconstruction. J Bone Joint Surg Am 2007; 89: 559-70.

481

482	13. Hamada T, Hayashi T, Kimura T, Nakano K, and Moritani T. Electrical
483	stimulation of human lower extremities enhances energy consumption,
484	carbohydrare oxidation, and whole body glucose uptake. Journal of Applied
485	physiology 2004; 96: 911-16.

486

487 14. Hamada T, Kimura T, and Moritani T. Selective fatigue of motor units after
488 electrically elicited muscle contractions. Journal of Electromyography and
489 Kinesiology 2004; 14: 531-38.

490

491 15. Hamada T, Sasaki H, Hayashi T, Moritani T, and Nakano K. Enhancement of
492 whole body glucose uptake during and after human skeletal muscle
493 low-frequency electrical stimulation. Journal of Applied Physiology 2003; 94:
494 2107-12.

495

496 16. Jones DA, Bigland-Ritchie B, and Edwards RHT. Excitation frequency and
497 muscle fatigue: mechanical responses to voluntary and stimulated contractions.

498	Experime	ntal Neurology	1979; 64:	401-13.
-----	----------	----------------	-----------	---------

500	17. Kellis E, Galanis N, Natsis K, Kapetanos G. Validity of architectural properties
501	of the hamstring muscles: correlation of ultrasound findings with cadaveric
502	dissection. Journal of Biomechanics 2009; 42: 2549-54.
503	
504	18. Laughman RK, Youdas JW, Garrett TR, et al. Strength changes in normal
505	quadriceps femoris muscle as a result of electrical stimulation. Physical Therapy
506	1983; 63: 494-99.
507	
508	19. Lieber RL, Silva PD, and Daniel DM. Equal effectiveness of electrical and
509	volitional strength training for quadriceps femoris muscles after anterior cruciate
510	ligament surgery. Journal of Orthopedic Research 1996; 14: 131-38.

512 20. Martin L, Cometti G, Pousson M, and Morlon B. Effect of electrical
513 stimulation training on the contractile characteristics of the triceps surae muscle.
514 European Journal of Applied Physiology and Occupational Physiology 1993; 67:
515 457-61.

517	21. Miyatani M, Kanehisa H, Ito M, Kawakami Y, Fukunaga T. The accuracy of
518	volume estimates using ultrasound muscle thickness measurements in different
519	muscle groups. European Journal of Physiology 2004; 91: 264-72.
520	
521	22. Moritani T, Muro M, and Kijima A. Electromechanical changes during
522	electrically induced and maximal voluntary contractions: electrophysiolosic
523	responses of different muscle fiber types during stimulated contractions.
524	Experimental Neurology 1985; 88: 471-83.
525	
526	23. Moritani, T., Muro, M., Kijima, A., Gaffney, F.A., and Persons, D.
527	Electromechanical changes during electrically induced and maximal voluntary
528	contractions: Surface and intramuscular EMG responses during sustained
529	maximal voluntary contraction. Experimental Neurology 1985; 88: 484-99.
530	
531	24. Nicholas SJ, Tyler TF, McHugh MP, Gleim GW. The effect on leg strength of
532	tourniquet use during anterior cruciate ligament reconstruction: A prospective
533	randomized study. Arthroscopy 2001; 17 (6): 603-07.

535	25. Rebai H, Barra V, Laborde A, et al. Effect of two electrical stimulation
536	frequencies in yhigh muscle after knee surgery. International Journal of Sports
537	Medicine 2002; 23: 604-09.
538	
539	26. Reeves ND, Maganaris CN, Narici MV. Ultrasonographic assessment of human
540	skeletal muscle size. European Journal of Physiology 2004; 91: 116–18.
541	
542	27. Sale DG. Influence of exercise and training on motor unit activation. Exercise
543	and Sports Science Reviews 1987; 15 :95-151.
544	
545	28. Sanada K, Kearns C, Midorikawa T, Abe T. Prediction and validation of total and
546	regional skeletal muscle mass by ultrasound in Japanese adults. European
547	Journal of Physiology 2006; 96: 24–31.
548	
549	29. Scremin AME, Kurta L, Gentile A, Wiseman B, Perell K, Kunkel C, and
550	Scremin OU. Increasing muscle mass in spinal cord injured persons with a
551	functional electrical stimulation exercise program. Archives of Physical

Medicine and Rehabilitation 1999; 80: 1531-36.

553

30. Selkowitz DM. Improvement in isometric strength of the quadriceps femoris
muscle after training with electrical stimulation. Physical Therapy 1985; 65:
186-96.

557

31. Sisk TD, Stralka SW, Deering MB, Griffin JW. Effect of electrical stimulation on
quadriceps strength after reconstructive surgery of the anterior cruciate ligament.
American Journal of Sports Medicine 1987; 15: 215-20.

561

32. Snyder-Mackler L, Delitto A, Bailey SL, Stralka SW. Strength of the quadriceps
femoris muscle and functional recovery after reconstruction of the anterior
cruciate ligament. A prospective, randomized clinical trial of electrical
stimulation. Journal of Bone Joint Surgery 1995; 77: 1166-73.

566

33. Thoirs K, English C. Ultrasound measures of muscle thickness: intra- examiner
reliability and influence of body position. Clinical Physiology and Functional
Imaging 2009; 29: 440–46.

5	7	0
$\mathcal{I}$	1	U

571	34. Walton JM, Roberts N, Whitehouse GH. Measurement of the quadriceps femoris
572	muscle using magnetic resonance and ultrasound imaging. British Journal of
573	Sports Medicine 1997; 31: 59–64.
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578	Table 1. Rehabilitation Protocol in the Rehabilitation Unit of Kyoto University
579	Hospital

Post-operation time	weight-bearing	ROM ex	training	cycle ergometer
2 days	NWB※1		non-oprerated leg training walking exercise on crutches muscle training around hip joint	
1 week	1/3PWB <b>※</b> 2	0° <b>~</b> 90°	isometric knee extention with knee flexed to 90° straight leg raise quadriceps setting exercise CKC training quarter squat (1/3PWB) CKC training calf raise (1/3PWB) bridge exercise with both legs	10 watts ×20 min
2 weeks	1/2PWB	0°~110°	knee flex exercise with weight band CKC training quarter squat (1/2PWB) CKC training calf raise (1/2PWB) bridge exercise with the operative leg	30 watts ×20 min
3 weeks	2/3PWB	0°~120°	CKC training quarter squat (2/3PWB) CKC training calf raise (2/3PWB) static squating	60 watts ×20 min
4 weeks	FWB <b>%</b> 3	0° <b>~</b> 130°	isokinetic muscle training of knee extension with knee flexed $60^{\circ} \sim 90^{\circ}$ knee bent walking knee flex exercise with tube forward and side lunge balance reach leg exercise	100 watts × 20 min
5 weeks		0° <b>~</b> 140°	long stride walking balance reach arm exercise	
6 weeks		full range	step exercise	
8 weeks			isokinetic muscles training of knee extension with knee flexed $45^{\circ} \sim 90^{\circ}$ squat with the operative leg stand up exercise with the operative leg quadriceps setting exercise on standing	150 watts × 30 sec × 4 set
12 weeks			jogging side jump with both legs	
16 weeks			sprint run side jump with the operative leg jumping long stride walking ladder plyometric exercise	
6-8 months			return to sports	

581 %1 Non-Weight-Bearing %2 Partial Weight-Bearing %3 Full Weight-Bearing

584	Figure Legends
585	
586	Figure 1. Patient with EMS device.
587	
588	Figure 2. The illustrations of pulses (the conventional rectangular pulse and
589	an exponential climbing pulse)
590	
591	Figure 3. Time course change of muscle thickness
592	
593	Figure 3a. RF muscle thickness (mm) at pre-operation (PRE), 4 weeks
594	post-operation (4WPO) and 3 months post-operation (3MPO) for the CON and the
595	EMS groups.
596	Significantly different among the evaluation times; **p<0.01. Significantly different
597	from the CON group; $^{\dagger\dagger}p$ <0.01. Values are expressed as means $\pm$ SE (CON; n=10,
598	EMS; n=10).
599	
600	Figure 3b. VI muscle thickness (mm) at pre-operation (PRE), 4 weeks
601	post-operation (4WPO) and 3 months post-operation (3MPO) for the CON and the

- 602 EMS groups.
- 603 Significantly different among the evaluation times; \*\* p<0.01. Values are expressed as
- 604 means  $\pm$  SE (CON n=10, EMS n=10).

- 606 Figure 3c. VL muscle thickness (mm) at PRE, 4WPO and 3MPO for the CON group
- 607 and the EMS group.
- 608 Significantly different among the evaluation times; \*\*p<0.01. Significantly different
- from the CON group;  $^{\dagger\dagger}p < 0.01$ ,  $^{\dagger}p < 0.05$ . Values are expressed as means  $\pm$  SE (CON;

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610 n=10, EMS; n=10).
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611

Figure 3d. CA muscle thickness (mm) at PRE, 4WPO and 3MPO for the CON andthe EMS groups.

- 614 Significantly different among the evaluation times; \*\*p<0.01. Significantly different
- 615 from the CON group; <sup>††</sup>p<0.01. Values are expressed as means  $\pm$  SE (CON; n=10,
- 616 EMS n=10).

617

618 Figure 4. Time course change of muscle strength

621	pre-operation (PRE), 4 weeks post-operation (4WPO) and 3 months post-operation
622	(3MPO) for the CON and the EMS groups.
623	Significantly different among the evaluation times; **p<0.01. Significantly different
624	from the CON group; <sup>†</sup> p<0.05. Values are expressed as means $\pm$ SE (CON; n=10,
625	EMS; n=10).
626	
627	Figure 4b. Changes ratios of isometric knee extension strength at 4WPO and 3MPO
628	compared to pre-operation in both the CON and EMS groups.
629	Significantly different; ** $p$ <0.01. Values are expressed as means ± SE (CON n=10,
630	EMS n=10).

Figure 4a. The isometric knee extension strength on an operated side at

# EMS Device and Tight-fitting flexible electrodes

# Patient with EMS device

# Stimulator

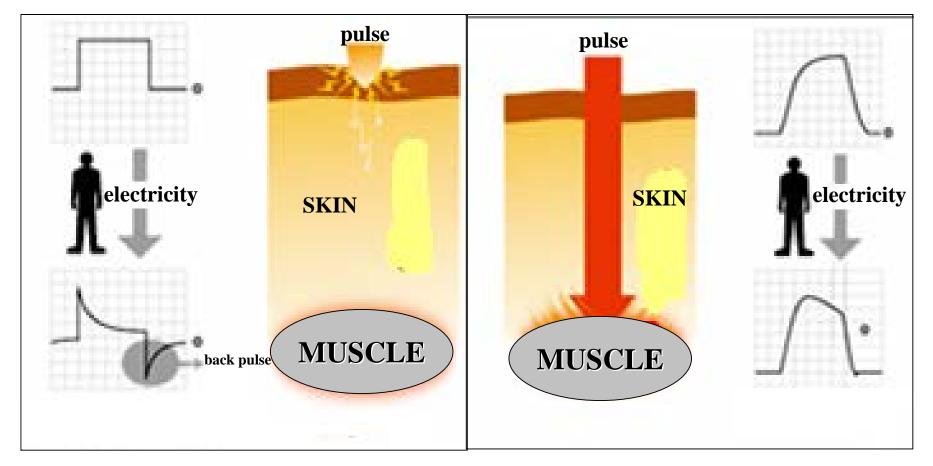


### Figure 1

# illustrations of pulses

## rectangular pulse

# exponential climbing pulse



#### Figure 2

