Increasing Muscle Mass in Spinal Cord Injured Persons With a Functional Electrical Stimulation Exercise Program

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Objective: To determine the magnitude of changes in muscle mass and lower extremity body composition that could be induced with a regular regimen of functional electrical stimulation (FES)-induced lower-extremity cycling, as well as the distribution of changes in muscle mass among the thigh muscles in persons with spinal cord injury (SCI).

Study Design: Thirty men with neurologically complete motor sensory SCI underwent a 3-phase, FES-induced, ergometer exercise program: phase 1, quadriceps strengthening; phase 2, progressive sequential stimulation to achieve a rhythmic pedaling motion (surface electrodes placed over the quadriceps, hamstrings, and gluteal muscles); phase 3, FES-induced cycling for 30 minutes. Participants moved from one phase to the next when they met the objectives for the current phase.

Measures: Computed tomography of legs to assess muscle cross-sectional area and proportion of muscle and adipose tissue. Scans were done at baseline (before subjects started the program), at first follow-up, typically after 65.4 ± 5.6 (SD) weekly sessions, and at second follow-up, typically after 98.1 ± 9.1 sessions.

Results: Increases in cross-sectional areas were found in the following muscles: rectus femoris (31%, p < .001), sartorius (22%, p < .025), adductor magnus-hamstrings (26%, p < .001), vastus lateralis (39%, p = .001), vastus medialis-intermedius (31%, p = .025). Cross-sectional area of adductor longus and gracilis muscles did not change. The ratio of muscle to adipose tissue increased significantly in thighs and calves. There was no correlation among the total number of exercise sessions and the magnitude of muscle hypertrophy.

Conclusions: Muscle cross-sectional area and the muscle to adipose tissue ratio of the lower extremities increased during a regular regimen of 2.3 FES-induced lower extremity cycling sessions weekly. The distribution of changes was related to the proximity of muscles to the stimulating electrodes.

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FUNCTIONAL ELECTRICAL stimulation (FES) is potentially useful in the rehabilitation of patients with spinal cord injury (SCI). Claimed benefits include improvement of contractures, neurogenic osteoporosis, deep venous thrombosis, and edema, as well as amelioration of spasticity.1-9 Another potential use of FES is as an aid in standing and ambulation.10-13 Many of these applications require development of adequate muscle power, which must be preceded by at least a partial reversal of the profound muscle atrophy that occurs at levels below the SCI lesion.

Resistive exercise increases muscle mass in human subjects and experimental animals.14-21 FES has been reported to prevent disuse atrophy of the quadriceps in able-bodied patients after surgery.22,23 Baldi and colleagues24 reported prevention of muscle atrophy in SCI subjects by FES cycle ergometry when it was used within 3 months after injury. Information on effects of FES on muscle mass in long-term SCI subjects, however, is fragmentary.25,26 and the persistence of changes and the relations of these changes to the duration of FES training have not been established.

This work was designed to test if a prolonged exercise regime of FES-induced lower-extremity cycling (FESILEC) could improve muscle mass, and to determine the magnitude and distribution of the effect in the thigh and leg. We used computed tomography (CT) of the lower extremity to evaluate muscle cross-sectional area and the proportion of muscle to adipose tissue, a method validated against cadaver information27 and the standard against which other techniques are evaluated.28

MATERIAL AND METHODS

Subjects

Admission criteria for the study included a neurologically complete SCI lesion (American Spinal Injury Association [ASIA] Impairment Scale A29), presence of spasticity, and range of motion of hip, knee, and ankle within limits compatible with safe operation of the Regys ergometer.2 Characteristics of the 13 men admitted to the study are summarized in table 1. All subjects gave informed consent on a protocol approved by the Human Subjects Committee of the West Los Angeles VA Medical Center.

Exclusion criteria were: implanted pacemaker, unhealed lower extremity fracture, history of hip or knee dislocation or subluxation, presence of plates, screws, or pins in femurs, poorly controlled autonomic dysreflexia, active heterotopic ossification, extreme osteoporosis with positive history of fracture, severe uncontrollable spasticity in lower extremities, presence of pressure sores in areas of treatment, acute medical intercurrence, recent history of alcohol abuse for which treatment was recommended, cardiovascular disease, and moderate to severe pulmonary disease. Twelve potential subjects were excluded from the study on the basis of these criteria.

At admission to the study, subjects received a complete physical examination and, after informed consent, the following evaluations: x-rays of spine, hip, femur, tibia, fibula, and
FES-INDUCED CYCLING TO INCREASE MUSCLE MASS, Scremin

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<th>Body Mass (kg)</th>
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Mean (SD) 10.0 (5.0) 34.0 (6.9) 75.9 (14.3) 10.3 (6.8)

Analysis of CT Scans

CT scans were performed before phase 1 began and then as close as possible to the end of phase 3a (on average, after 65 sessions) and at midpoint within phase 3b (on average, after 98 sessions) of FESILEC (fig 1): the first CT was done to obtain a baseline (pre-FESILEC) measurement before the exercise protocol started; the second CT was done when workload reached a stable level (first follow-up CT); and the third CT was done during the maintenance regime of phase 3b (second follow-up CT). Three CT planes perpendicular to the limb major axis were defined in the thigh. One (midthigh) was at the midpoint between the anterior superior iliac spine and the knee joint line. Two other planes were 5cm above (proximal thigh) and 5cm below (distal thigh) the first plane (midthigh). Two planes were defined in the leg. One (proximal leg) was at the point of maximal circumferential distance, and another (distal leg) 2cm below. Three methods quantified these images. (1) Tracing of areas with density levels of muscle tissue in digitized CT scans with subtraction of intramuscular areas with density levels of adipose tissue (adipose tissue-free muscle area). In this analysis, the three levels in the thigh (defined above) were studied; (2) A tracing of areas with density levels of muscle tissue was done without subtraction of intramuscular fat (anatomical muscle area). Individual muscles were identified with anatomic data from Eyecleshymer and Schoemaker. This analysis was limited to the midthigh level. (3) Semiautomatic calculation of area occupied by muscle tissue, adipose tissue, and bone was done using standard software available on the GE Highlight Advantage CT scanner. The range of densities used to differentiate tissues were: adipose tissue, $-190$ to $-20$; muscle tissue, $+20$ to $+100$; bone, $+200$ to $+2,000$. In this analysis three levels in the thigh and two levels in the leg (defined above) were studied. The first two analyses were performed after CT scan films were digitized in a Hewlett-Packard Scanjet 4C/T scanner. Images were analyzed using SigmaScan Pro 4 software. Only one operator performed each

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Table 1: Patient Characteristics

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Feet; blood tests, including complete blood count, chemistry panel, and hematocrit and hemoglobin levels, routine urinalysis; and a resting 12-lead electrocardiogram and cardiopulmonary exercise stress test by arm crank ergometry.

FESILEC Protocol

Patients were treated with muscle stimulation in sessions of 30 minutes' duration, performed $2.32 \pm 0.26$ (SD) times per week in a Regys 1 System. Stimulation was applied with carbon-filled silastic surface electrodes taped to the skin. A conducting jelly was applied between the skin and the electrode. Stimulation parameters were as follows: pulse frequency, 30Hz; pulse duration, 300~sec; on/off ramp duration, 1sec; train duration, 10sec. These parameters were controlled by a microprocessor modulating six channels of stimulation. A set of electrodes to produce 45° of active extension followed, during flexion, by passive flexion. Treatment began without load. Initially, subjects pedalled against 0 kilopond (kp) resistive load for 5 minutes or as long as the subject could tolerate (up to a maximum of 30 minutes). This was followed until the schedule was completed and then each succeeding session increased progressively until the subject was able to pedal for 30min in two consecutive sessions. In phase 3a (training protocol), subjects performed three 30-minute sessions of FESILEC per week, initially unloaded (0 kp). Once the patient could complete two consecutive 30-minute sessions at a given workload, the load was increased by 6.1W (1/8kp). If during the training session the patient fatigued (ie, revolutions per minutes decreased to <35), then the workload was reduced to the previous level and exercise continued until the total of 30min was accomplished. Two subjects could only cycle without load and are listed with a maximum training workload of 0 in table 1. In phase 3b, the protocol was similar to 3a, except that simultaneous arm ergometry was performed. This phase was initiated after completion of phase 3a with at least 24 sessions of 30-minute cycling completed. Average durations (in weeks) of each phase were: phase 1, 7.5; phase 2, 8.9; phase 3a, 14.4; Phase 3b, 21.9. The average protocol duration (sum of all phases' average durations listed above) was 52.8 weeks.

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Phases of training protocol and timing of CT measurements.

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methodology, and this person was blind to the treatment and to subject identity. Not all the subjects were included in all three analysis methods because some of the software was not available in the initial stages of the study and some of the CT scans had characteristics that did not permit anatomic delineation of the individual muscles.

**Statistical Analysis**

Ratios of cross-sectional area of the first and second follow-up CT scans and that of baseline (pre-FESILEC) were calculated to cancel out the variance between subjects. Statistical significance of these ratios against 1 were calculated from the t distribution. A Bonferroni correction for two simultaneous contrasts (first and second intervals against baseline) was applied to the percentage increases in anterior and posterior muscle mass. Statistical significance of differences was assumed for probabilities <.05. Results were presented as percentage of baseline (ratio × 100).

**RESULTS**

Initial analysis indicated that there were no statistically significant side to side differences within individual subjects; therefore, cross-sectional areas from both sides were averaged for each subject.

Cross-sectional scans of the thigh (fig 2) showed that adipose tissue-free skeletal muscle increased significantly in anterior (fig 3) and posterior (fig 4) compartments when measured at the first follow-up interval. No further increase was observed at the second follow-up interval.

Analysis of individual muscles’ cross-sectional areas (anatomic skeletal muscle) is shown in figure 5. The percent increases over baseline (before FESILEC started) were: rectus femoris, 31% (p < .001); sartorius, 22% (p < .025); adductor magnus-hamstrings, 26% (p < .001); vastus lateralis, 39% (p = .001); vastus medialis-intermedius, 31% (p = .025). Cross-sectional area of adductor longus and gracilis muscles did not change. There were no correlations among the total number of FESILEC sessions and the magnitude of muscle hypertrophy.

Evaluation of the areas occupied by different tissues (fig 6) indicated statistically significant increases in muscle tissue in thigh and leg, no changes in adipose tissue, and a significant increase in the ratio of muscle to adipose tissue.

**DISCUSSION**

This study found a generalized increase in skeletal muscle cross-sectional area, with no change in adipose tissue, and a consequent increase in the ratio of muscle to adipose tissue. This phenomenon was present in both the thigh and the leg. Although no electrodes were applied over the leg, proximity of the posterior electrodes to the sciatic nerve activated leg muscles. The greater effect observed in the anterior compartment may relate to the fact that only the quadriceps muscles were stimulated in the strengthening period in phase 1. In addition, the posterior compartment included the gracilis and adductor longus muscles, which did not increase in mass, probably because motor points for these muscles were not close to the stimulating electrodes.

Increased muscle mass was observed at the first follow-up evaluation, after completion of the resistive part of the training. This type of exercise has been shown to induce greater muscle hypertrophy in animals and humans than aerobic exercise.33 The lack of further increase in muscle mass beyond the first follow-up CT is probably related to the fact that workload was not incremented after that time.

FES has been shown previously to prevent decreases in leg...
leak body mass in SCI subjects when it is applied within 3 months after injury; Baldi and associates\textsuperscript{24} observed a decrease of 21\% in lean lower limb mass after a 6-months postinjury period in untreated patients, whereas patients treated with FESILEC (three times a week) showed a small but statistically significant increase compared with pretreatment mass. The smaller increase (9\%) found by Baldi than found in the present study (about 30\% increase in the thigh) may be attributable to differences in time after injury or underestimations in the Baldi study because of the indirect estimates of muscle mass recorded by x-ray absorptiometry.

In our study, muscle cross-sectional area increases were comparable to those described with resistance exercise in able-bodied subjects. In healthy men of ages comparable to those of our subjects, after 6 months of weight training on alternate days with six series of eight unilateral leg extensions at 80\% of one repetition maximum, cross-sectional area increased by 13\% to 19.3\% at different sectors of the quadriceps muscle.\textsuperscript{14} In subjects over the age of 55 years, 6 months of isometric quadriceps strength training induced a 4\% to 4.9\% increase in thigh circumference.\textsuperscript{15} In the upper arm, cross-sectional areas of biceps and triceps increased by 12.6\% and 25.1\%, respectively, after 12 weeks of intensified resistance training in college men.\textsuperscript{16} The cross-sectional area of medial and lateral knee extensors of bodybuilders has been reported to be 29\% and 49\% greater, respectively, than that of nontrained controls of comparable ages.\textsuperscript{32}

The ability of the presently reported FES exercise program to increase muscle mass in men with SCI may be related to the strength training characteristics of phases 1 and 3a, in which

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Figure 3. Thigh anterior compartment: percentage change in cross-sectional area of adipose tissue-free skeletal muscle in 8 subjects. Left and right sides were averaged because no side differences were present. Results are expressed as percentage of baseline (\textsuperscript{C}, pre-FESILEC [100\%]). The first follow-up CT measurement (\textsuperscript{II}) was taken after 65 ± 5 sessions. The second follow-up CT measurement (\textsuperscript{II}) was taken after 98 ± 9 sessions. *p < .025; **p < .001.

Figure 4. Thigh posterior compartment: percentage change in cross-sectional area of adipose tissue-free skeletal muscle in 8 subjects. Left and right sides were averaged because no side differences were present. Results are expressed as percentage of baseline (\textsuperscript{C}, pre-FESILEC [100\%]). The first follow-up CT measurement (\textsuperscript{II}) was taken after 65 ± 5 sessions. The second follow-up CT measurement (\textsuperscript{II}) was taken after 98 ± 9 sessions. *p < .025; **p < .001.

Figure 5. Individual skeletal muscles (thigh): percent change in cross-sectional area between baseline and first follow-up CT in 9 subjects. Results are expressed as percent of baseline (pre-FESILEC, 100\%). *p < .025; **p < .001.

Figure 6. Cross-sectional area occupied by muscle (\textsuperscript{C}) and by adipose tissue (\textsuperscript{II}), and the ratio of muscle to adipose tissue (\textsuperscript{II}): percent changes between baseline and first follow-up CT in 6 subjects. Tissue components were calculated by segmenting image density levels into Hounsfield unit ranges: adipose tissue, -190 to -20; muscle tissue, -19 to +150. T1, proximal thigh; T2, midthigh; T3, distal thigh; L1, proximal leg; L2, distal leg. Results are expressed as percentage of baseline (pre-FESILEC, 100\%). *p < .025.
progressive loads are used. The fact that the gain in muscle cross-sectional area was recorded at the end of phase 3a, with no further gain at a later follow up seems to support this interpretation. The anaerobic nature of FESILEC training may also contribute to its effect on muscle mass. In young subjects, when the quadriceps performs long, fatiguing contractions, a significantly greater increase in cross-sectional area is observed than when short contractions are performed followed by longer intervals—a difference that has been attributed to a greater metabolite accumulation during the first type of exercise. 33 FESILEC induces a large increase in blood lactate. 34 Moreover, our previous studies of muscle blood flow in SCI subjects on FES-induced exercise showed a larger increase in blood flow and a slower return to preexercise blood flow levels than in able bodied subjects performing a mechanically equivalent voluntary exercise. 35 These findings suggest a greater accumulation and slower washout of metabolites in this type of FES exercise. The phenomenon may relate to the tetanic and synchronous nature of FESILEC muscle contraction that interferes with local circulation.

Our results in the present study showed no change in adipose tissue cross-sectional area in the legs after FESILEC. Only one study has examined this issue before and it claimed that adipose tissue area decreased in one of the studied FES regimens. 36 This conclusion was based on the analysis of a small group of patients (n = 4) and use of nonadjusted multiple contrast statistics. In the presence of an increase in muscle cross-sectional area, the muscle to adipose tissue ratio of the lower extremities in our experiments was enhanced by FESILEC.

CONCLUSION

FESILEC increased muscle mass of thighs and legs, and enhanced the muscle to adipose tissue ratio of SCI subjects. These effects were sustained by continuous training over 1 year.

References


 Suppliers
a. Therapeutic Alliances, 333 North Broad Street, Fairborn, OH 45324.
b. GE Medical Systems, 25925 Telegraph Road, Southfield, Milwau-kee, WI 48034.
c. Hewlett-Packard, 3000 Hanover Street, Palo Alto, CA 94304-1185.
d. Jandel Scientific, PO Box 7005, San Rafael, CA 94912-7005.