Morphological changes in *rectus femoris* muscle: advanced image processing technique and 3-dimensional visualization to monitor denervated and degenerated muscles treated with functional electrical stimulation

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Abstract

This study demonstrates qualitatively and quantitatively how functional electrical stimulation (FES) restores volume and morphology to denervated degenerate muscle. To this purpose a novel technique was developed to isolate and monitor muscle growth. During 3 years of electrical stimulation, complete 3-dimensional reconstructions of *rectus femoris* muscles from patients with long-term flaccid paraplegia were made. Spiral computer tomography and advanced image processing tools were developed and used to monitor and measure select muscle regions influenced by the stimulation. The complete morphology of *rectus femoris* muscle (RFM) was reconstructed at different therapy stages.

The results show remarkable changes of shapes and volume: 3-dimensional imaging of *rectus femoris* muscle demonstrates the restoration process during the therapy.

Key Words: 3-dimensional reconstruction, Modeling, Electrical stimulation, Denervated degenerated muscle, FES, Lower motor neuron lesion, Rehabilitation.

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Experimental and clinical research provides strong evidence of FES being a powerful tool for regeneration, functional restoration and maintenance of denervated musculature. The European project called RISE (QLG5-CT-2001-02191) proposes a novel clinical rehabilitation method for patients with permanent and non-recoverable muscle denervation in their legs [4, 8]. The main goal of the RISE project is to use electrical stimulation to restore standing in paraplegics with long-term DDM.

There being no possibility of re-innervation, patients with long term denervated degenerated muscles were refused FES-training for years. It was also widely believed that FES was unsuitable in DDM-training. Kern, however, not only showed that DDM patients can indeed be trained with FES using surface-electrodes, but also that FES training is able to restore the ability of muscles to perform tetanic contractions, that, in fact, are essential to prevent/recover atrophy by loading the muscles [1, 2, 5-7, 9].

The crucial indicator for the therapy is, of course, muscle growth. The effects of the treatment were monitored, e.g., by morphological and histochemical analysis of muscle biopsies as well as by clinical neurological, neurophysiological mechanical, and radiological methods [7, 8]. To track changes in the size and shape of the quadriceps muscle, computer tomography (CT) scans were taken at 10 cm intervals from the trochanter major to the knee [7]. A comparison of two scans taken at the same level at different times shows the muscle growth in that specific place during the period between the two scans. Comparing five scans, taken at 10 cm intervals, yields an estimate of the total muscle growth and changes in fat and bone tissue. It does not, however, show the growth of the whole muscle, as data from only 5 scans are not sufficient to make a three-dimensional model of muscle, bone, or other tissue. Additionally, denervated musculature loses its normal morphological shape over time, making both localization and identification of the different muscle tissue difficult.

This paper describes a method to isolate the RFM from the other muscles of the thigh and to measure volume and density during 3 years of electrical stimulation. Through an accurate 3-dimensional reconstruction, the morphological changes are visualized and monitored.

Material and Methods

Spiral CT

Every four months a spiral CT was taken of the RISE Study's Icelandic subgroup of three patients with a complete spinal cord injury of flaccid type.

The spiral CT scan starts above the head of the femur and continues down to the knee joint, both legs being covered by one scan. They are taken with a pitch of approximately 0.625 mm, resulting in a total of about 750-900 CT slices, depending on the patient's size. Each slice has 512 × 512 pixels, and each pixel has a grey value in the Hounsfield scale of 4096 grey scale values, meaning that it is represented with a 12-bit value.

A total data set from a single scan is therefore 512×512×750×12= 2.36 GBit, approximately 300 MB. This data set gives a complete three-dimensional description of the tissue, including the muscles and bones in both upper legs [2].

Area of Interest

The CT scan data were imported into a special image processing and editing computer program called MIMICS [2]. These files are rather big, considerably limiting the computer processing capacity; they were, therefore, preliminarily divided in two: one file for the right leg and another for the left.

The area on the thigh where the quadriceps muscle is stimulated is of particular interest. The goal was to select the muscle bellies most influenced by electrical stimulation and monitor their changes during therapy. Another reason is the importance of developing a methodology allowing duplication of the same area at different times. According to the RISE protocol large surface electrodes were applied on the quadriceps muscle.

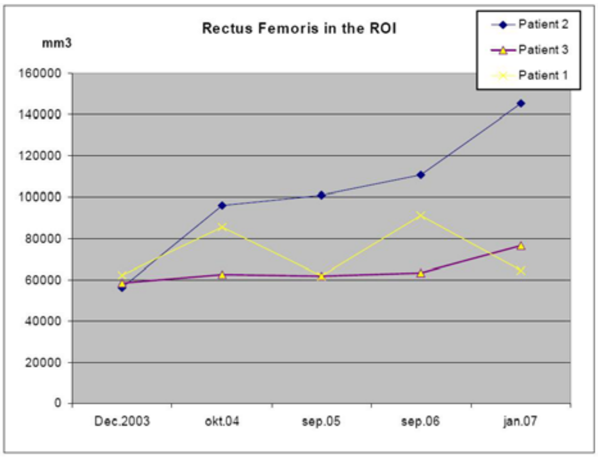

Figure 1. Changes of Rectus Femoris Volume during FES Therapy.

Because of muscle morphology, the *rectus femoris* is the most exposed part of the quadriceps to direct stimulation. The RFM was therefore chosen as the region of interest and monitored during the therapy.

Muscle segmentation

Objects scanned by CT are coded according to the Hounsfield scale, a quantitative scale for describing radio density where different values are ascribed to air, water, fat, bone and muscle. Image processing tools are used to segment the images and differentiate the diverse objects represented on the CT slide. The first step in image segmentation is thresholding: individual pixels with certain HU value are marked if their value is included in the customized HU interval representing muscles. The HU interval chosen in this application is -37 to 129 which guarantees clear differentiation and visualization of muscle tissue from other elements. The next step is to isolate the RFM from its surrounding muscles. The main difficulty in the segmentation process is the continuity, in term of HU values, between the RFM and the adjacent muscle tissue making conventional image processing tools useless for this purpose. The muscle was therefore segmented manually, directly on the CT slide, using advanced editing tools and the following method: the trans axial slide that visualizes RFM close to the patella is selected. A contour is drawn manually around the muscle; all pixels inside the curve are marked. The shape created on the first slide is projected on to the next. The muscle border on the new slide is slightly different, and the shape will therefore be adapted to fit the new muscle contour. Again all pixels inside the curve are marked and the shape projected forward. This process continues until the muscle ends on the pelvis. Finally the RFM is completely isolated from its surroundings. A mask containing the selected pixels is created This mask represents the RFM and includes information on muscle density and volume.

Using special software tools the *rectus femoris* mask can be converted into a 3D object allowing monitoring

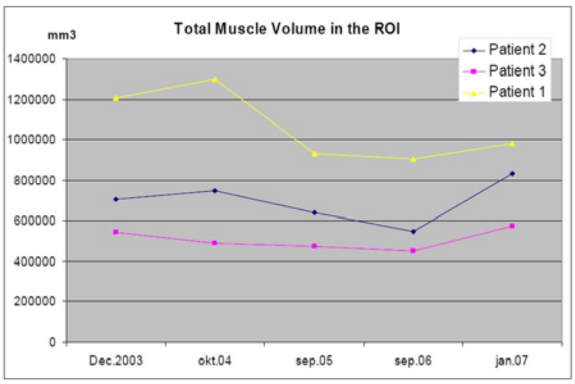

Figure 2. Changes of Total Volume of Thigh Muscles during FES Therapy.

of shapes and morphologies. Finally, using standard image processing tools, femur and patella bones are also reconstructed in 3-D. In this way RFM can be represented correctly and its changes during the FES therapy easily localized and understood.

Measurements

In this work the RFM from one Icelandic patient (named Patient 2) was isolated and monitored according to the RISE stimulation protocol from December 2003 to January 2007. The patient has been denervated since July 1999.

Some measurements were also performed on the two other Icelandic RISE patients (Patient 1 has been denervated since February 2003 and Patient 3 from January 1996). Both patients began the stimulation program at the end of 2003. For these measurements a Region of Interest (ROI) is defined: 140 mm below the head of the femur and 100 mm above the knee joint.

The *rectus femoris* is the quadriceps muscle most exposed to the stimulation; changes in this muscle are an index to validate the RISE therapy. The following data are presented:

- Monitor changes in shape and morphology: 3-Dimensional reconstruction of *rectus femoris* at different times during the therapy (Figure 3).

Results

The data in Figure 1 show volume growth of *Rectus Femoris* among the three Icelandic RISE patients. The growth rate is very different between patients:

- RFM in Patient 1 has an oscillating trend due long interruption of treatment during the FES therapy. December 2003 – January 2007, RFM growth: +4%
- RFM in Patient 2 show the best growth rate. Especially in the years 2004 and 2006, patient was more compliant, and then the volume growth was better. December 2003 – January 2007, RFM growth: +84%
- RFM in Patient 3 has a very slow, but continue growth rate due long denervation time. December 2003 – January 2007, RFM growth: +20%

The data in Figure 2 show the total volume growth in the thigh, among the three Icelandic RISE patients.

- Patient 1: December 2003 – January 2007, Volume in the thigh: -16%
- Patient 2: December 2003 – January 2007, Volume in the thigh: +20%
- Patient 3: December 2003 – January 2007, Volume in the thigh: +8%

Figure 3 shows the results from the 3-dimensional reconstruction of RFM at different times during the therapy. Remarkable improvements are naked-eye recognized, clearly demonstrating the restoration process toward a normal shape.

Conclusion

FES stops muscle degeneration and promotes muscle growth in the regions where it is applied. The new technique implements segmentation of muscle bellies and isolation of RFM improving the monitoring of the RISE therapy. Compared with the old method where muscle changes were only estimated on a few trans axial slides at fixed positions on the thigh, the new monitoring technique allows measures of volume and density on the whole muscle belly. Additionally, the combination of volume data with 3-dimensional imaging of the muscle provides qualitative and quantitative information on the otherwise hidden muscle behaviour.

In this paper data from the monitoring of the *rectus femoris* of one Icelandic RISE patient (patient 2) is published. Four data sets were developed with the new monitoring technique: at the beginning of the project and approximately once a year during the therapy period.

The results clearly demonstrate muscle growth and restoration of normal muscle shape and morphology. In three years of stimulation, *rectus femoris* has almost doubled its volume.

Though the stimulation was applied to the whole quadriceps muscle, it seems that the RFM is the only muscle truly gaining from the therapy. An explanation could be that the thicker fat layer surrounding the other quadriceps muscles prevents the stimulation from being

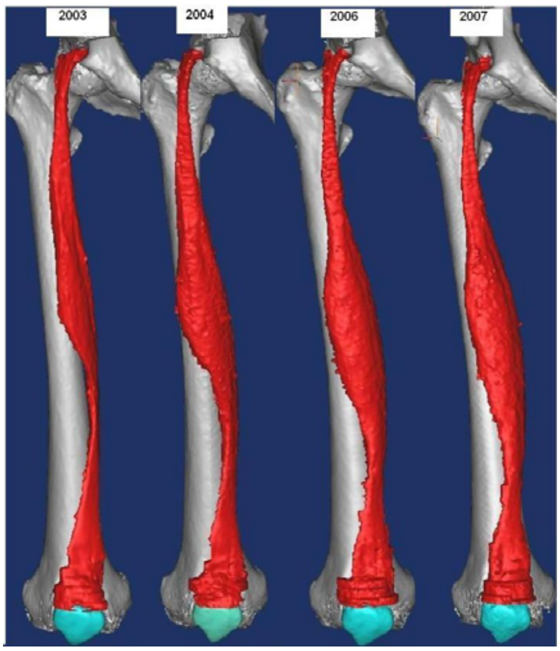

Figure 3. Total Muscle Volume Changes during FES. The 3-dimensional reconstruction of RFM at different times during the therapy show remarkable improvement, clearly demonstrating the restoration process of normal morphological shape.

as effective.

The next step, therefore, would be to implement this methodology: measure other patients and segment and measure all the muscles in the thigh.

The muscle growth rate is of course influenced by patient compliance and by possible clinical problems affecting the patients during therapy. For instance, having to stop the stimulation protocol for a few weeks can lead to the loss of a muscle mass previously gained over several months. It is crucial to correlate and measure muscle changes in order to understand how denervated musculature grows and to measure changes in volume and density at different regimes of stimulation. Segmentation of muscles can be a highly useful tool to perform such investigations.

Information from RFM segmentation contributes to the adjustment and improvement of the stimulation protocol, for instance in changing electrode position or stimulation patterns. Furthermore this information on muscle behaviour is an important basis for new development such as: stimulator, electrodes and implantable devices.

Finally the segmentation process and monitoring methodology developed in this work is an accurate tool to validate the RISE therapy and provide a better understanding of denervated muscle behaviour.

Abbreviations

FES: Functional Electrical Stimulation; DDM: Denervated Degenerate Muscle; RFM: *Rectus Femoris* Muscle; HU: Hounsfield units; ROI: Region of Interest.

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