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Multi-channel functional electrical stimulation with motor point tracking for sustainable muscle contraction

筋収縮維持可能な motor point 追従刺激を用いた機能的電気刺激についての研究

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Abstract

Functional electrical stimulation (FES) has become an important option to recover motor defects due to stroke and other illnesses. However the decline of muscle contraction during FES is still a problem in its clinical use. The purpose of this study is to improve the evoked contraction by periodically shifting the stimulating pair of electrodes on the same muscle. Motor point moves depending on arm movement, so we assumed that muscle contraction can be stable when the position of stimulation electrode shifts in response to the movement of motor point. In order to investigate the effect of the novel FES method, we placed two pairs of surface electrodes over the biceps brachii's motor point at elbow flexion and elbow extension. and stimulated the muscle with two shifting methods. One is a stimulation method which is called time based shifting stimulation (TSS). TSS changed the stimulating pair of electrode periodically from the distal pair to the proximal pair with 0.5 seconds offset. The other method is called joint angle based shifting stimulation (JASS). JASS shifts stimulation electrode based on elbow angle. It is know that elbow angle is correlated with the movement of motor point. The improvement of maintenance of muscle contraction was assessed by the angle of motion induced by FES. The effect of proposed methods was evaluated by the comparison of proposed methods and the other control method (simultaneous stimulation: SS, simultaneous stimulation with 1.5 seconds stimulation duration: SS-1.5s, opposite phase time based shifting stimulation: OFTSS). Eight healthy male subjects performed 180 contractions induced by each FES methods (TSS, JASS, SS, SS-1.5s, and OFTSS) in 15 minutes. 1 week rest was taken between two tests. As a result, TSS realized significantly larger angle of motion than the other control method. The effect of TSS on maintaining angle of motion showed that shifting stimulation position contributed to stable muscle contraction and shifting direction should be as same as the movement direction of motor point. JASS also significantly improved the maintenance of angle of motion. The result can be an evidence to support that motor point tracking stimulation improved the maintenance of muscle contraction.

Contents

Chapter1 Introduction

1.1 Motor Deficit due to Stroke

Strokes have been among the top 3 leading cause of death over the last 50 years[Ministry of Health, Labour and Welfare 2010]. A stroke is caused by the cutting off of the blood supply to a part of the brain. The brain cells cannot get oxygen from the blood and die off rapidly. Motor defects are a common symptom of strokes [Krakauer 2011]. For example people who suffer from a stroke experience muscle weakness or paralysis. The motor deficit affects mobility or balance.
In Japan, a decrease of the number of mortalities from strokes over the last few decades has been observed (**Figure 1.1**) but the number of people who are diagnosed is increasing[Ministry of Health, Labour and Welfare 2013] (**Figure 1.2**).

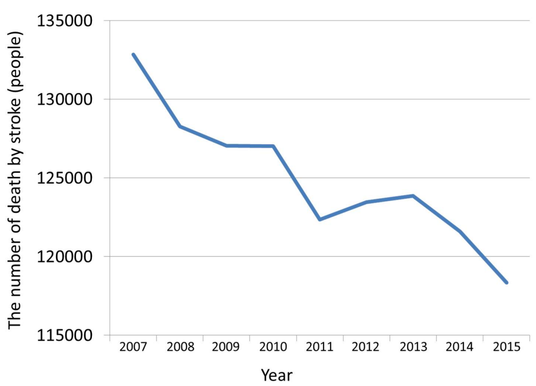


Fig.1.1　The number of death by stroke

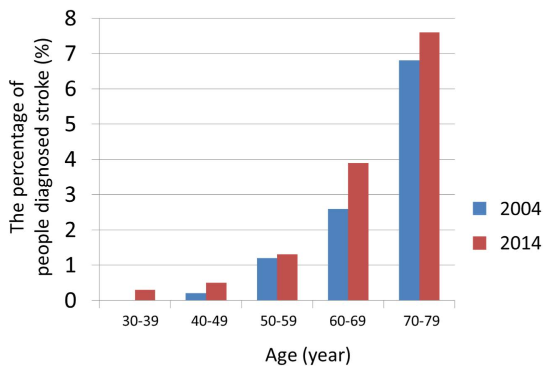


Fig.1.2　The number of people who was diagnosed stroke

1.2 Rehabilitation to Recover Motor Function

There are two important factors in the beginning of rehabilitation. One is to set proper rehabilitation tasks depending on the patient's remaining motor functions. The other is to start rehabilitation as soon as possible after injury.
Rehabilitation tasks differ depending on the location or severity of the lesion. The Brunnstrom Approach set 6 different stages (Brunnstrom stages) of motor recovery after

stroke. Brunnstrom stage has been proved to assess the motor recovery[Naghdi 2010]. It is important to carry out proper rehabilitation tasks depending on the Brunnstrom stage. Most patients who have suffered from a stroke recover their motor function considerably in the first few months [Wade 1985]. However most of their recovery reaches its limitation within 6 months[Kuptniratsaikul 2011]. The early initiation of rehabilitation and intensive rehabilitation support effective recovery from strokes.

Figure 1.3 shows the recovery score of several methods. FuglMeyer leg score (FM-leg),

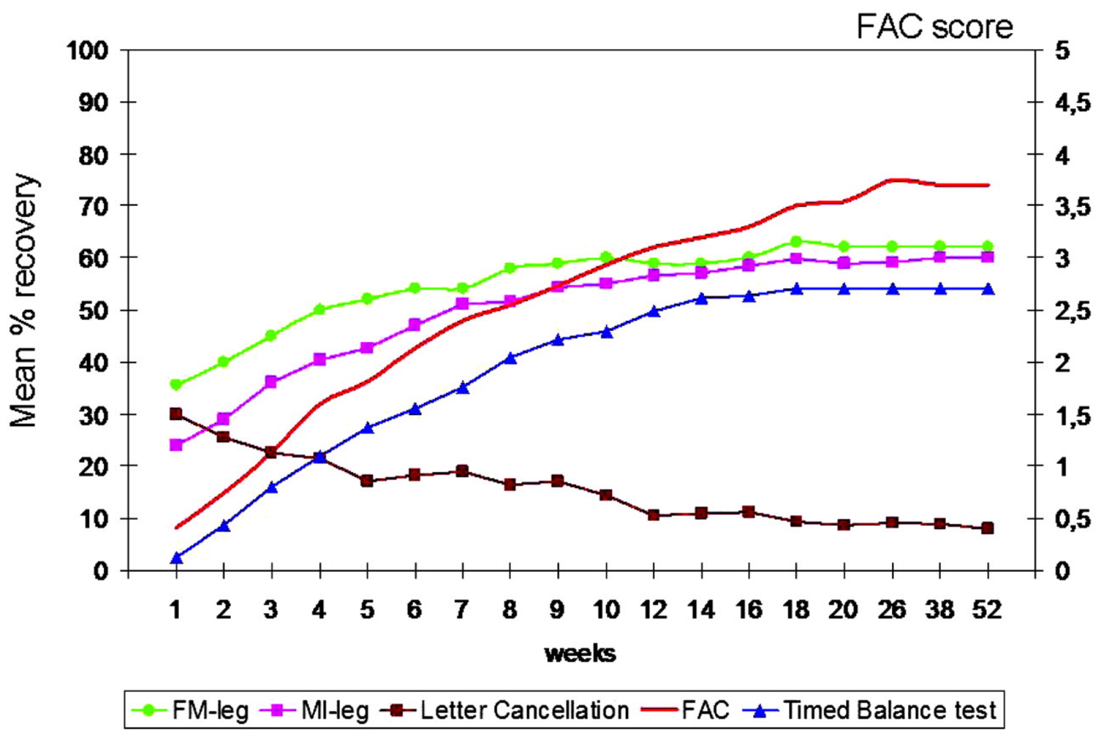


Fig.1.3 Improvement of Recovery score for 1 year [Kuptniratsaikul 2011]

Motricity index leg score (MI-leg), letter cancellation task (LCT), Fugl-Meyer balance (FM-balance), timed balance test (TBT), functional ambulation categories (FAC).

1.3 How to Restore Motor Deficit

Nudo et. al. suggested afferent input in response to associated motion is effective in the improvement of motor function[Nudo 1996]. Thier study showed rehabilitation for patients paralyzed after a stroke must involve not only supporting limb motion but afferent input, for example somatic or cutaneous sensory input. Kawahira et. al demonstrated repetitive facilitation exercises with their facilitation technique was influenced on motor recovery for hemiplegic patients [Kawahira 2010] (**Figure 1.4**). Their facilitation technique involved passive limb movement with afferent input. The afferent input involved tapping or rubbing on the muscle which is associated with the limb motion.

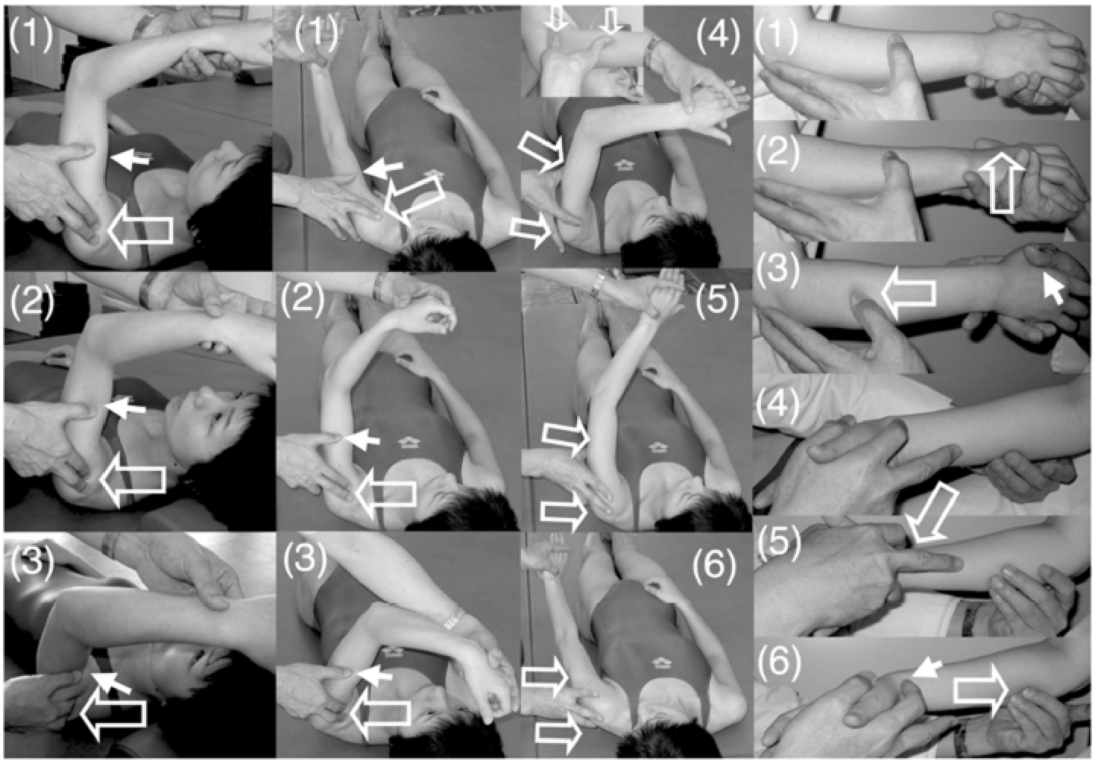


Fig.1.4 Repetitive facilitation exercises [Kawahira 2010]

1.4 Rehabilitation Methods for Patients

Various rehabilitation methods have studied for post stroke patients, for instance constraint-induced movement therapy with a physiotherapist [Page 2001], transcranial magnetic stimulation (TMS) [Takeuchi 2001], a robot suit with exoskeleton [Ogata 2001], and functional electrical stimulation (FES) [Popovic 2001].
Rehabilitation with a physiotherapist cannot continue for a long time because the reha-

bilitation time for each patient is limited in a hospital. It is important for patients to continue individual rehabilitation without a physiotherapist.

TMS is a non-invasive method for clinical rehabilitation for recovering motor functions by inducing cortical excitement (**Figure 1.5**). The excitement was effect on motor skill acquisition[Kim 2006], hand dexterity [Liepert 2007], rip force [Dafotakis 2008] in stroke patient.

For instance of an exoskeleton type robot suit for assisting voluntary contractions, The effect of the hybrid assistive limb (HAL) [Fujii 2016] on functional recovery (**Figure 2.3**). TMS and robot suit with exoskeleton have an effect on motor recovery. HAL supports in voluntary knee and hip joint motion by detecting bio-electrical signal but their equipment is too big or complicated to use for individual rehabilitation at home or in the patient's room.

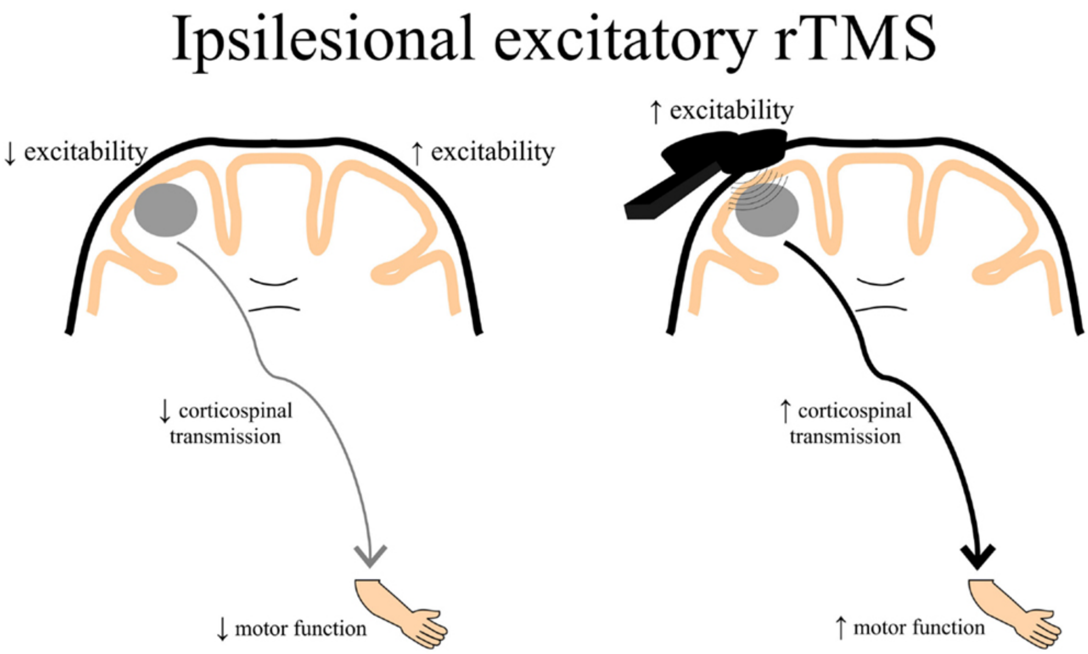


Fig.1.5 transcranial magnetic stimulation [Auriat 2015]

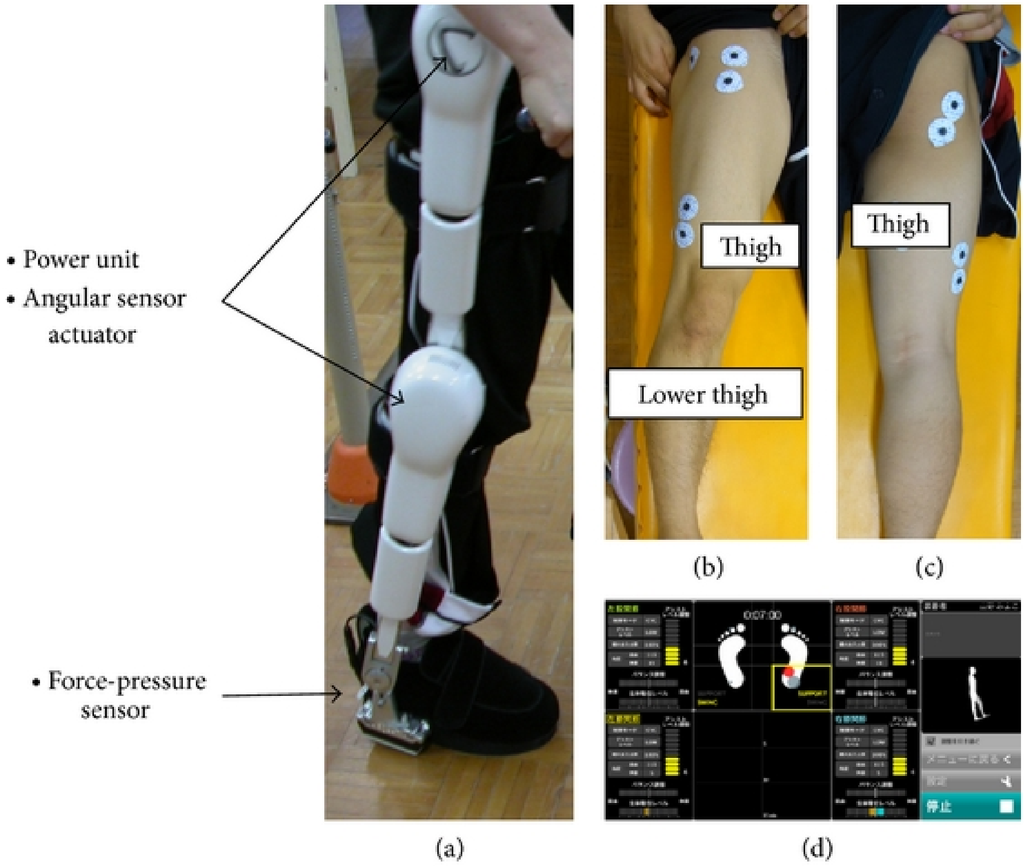


Fig.1.6 Hybrid Assistive Limb(HAL) [Fujii 2016]

1.5 Functional Electrical Stimulation: FES

FES is conducted by comparatively small devices. Popovic et. al. showed FES was effective at improving motor functions [Popovic 2001]. The electrical stimulation is applied from a pair of electrodes. A basic FES device consists of a pair of electrodes which serve as anode and cathode, a stimulator (ES devise), battery, stimulation switch, and voltage controller. Voltage controller can modify FES parametes without PC, so it will portable and it can be useful in home care. (**Figure 1.8**). FES is categorized by the placement of electrodes (**Figure 1.7**). Transcutaneous-FES is applied stimulation from surface electrodes on the skin. Precutaneous-FES is applied stimulation from implanted electrodes [Popovic 2004].

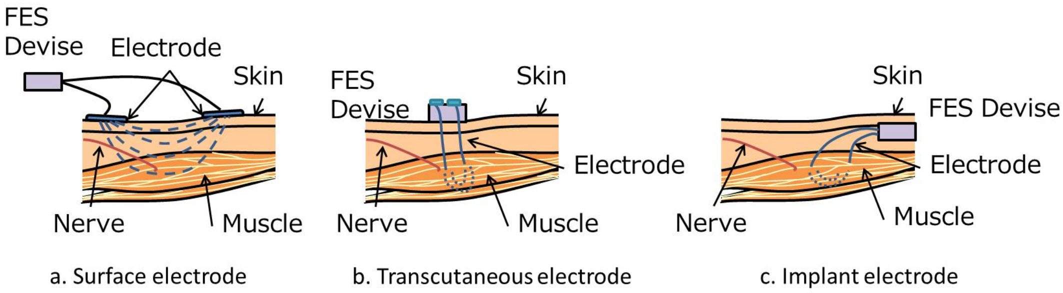


Fig.1.7 Categorization of FES

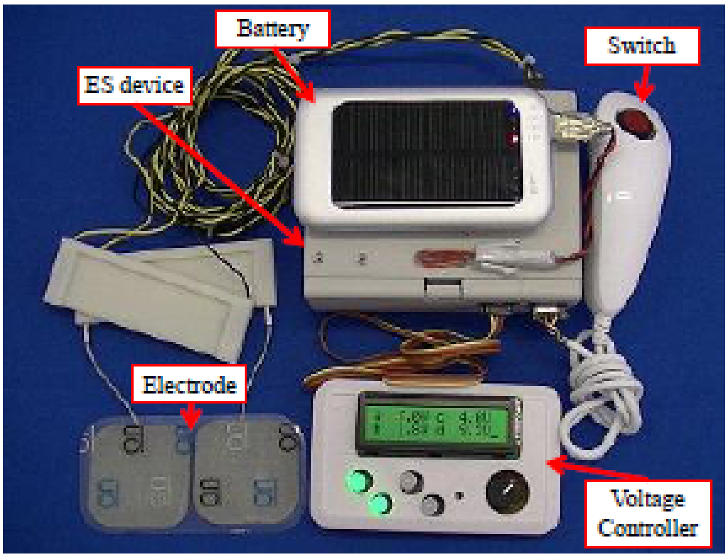


Fig.1.8 Components of FES system

1.6 Limitations of FES

FES is applied to muscle produces muscle contraction and supports therapeutic rehabilitation, for instance standing or walking. However, one of the biggest limitations of non-invasive FES is that it ccauses a rapid decrease in muscle contraction and weakening of muscle response [Binder-Macleod 1993]. This limitation can decrease the angular torque and/or angle of motion induced by the stimulation. The decrease of the maintenance of muscle contraction leads to difficulties in continuing rehabilitation for sufficient length of time and may delay the restoration of motor function.

1.7 Motivation

FES is a novel rehabilitation method in terms of inducing afferent input and muscle contraction at the same time. However, the support of limb motion by FES will be unstable or unsustainable because of the rapid reduction of muscle strength. This limitation will lead not only delayed recovery but being in danger during the rehabilitation involving dynamic exercise such as walking or standing up. Delaying the onset of the reduction of muscle strength can be lead to better clinical efficacy.
An desired FES system should support the patient's limb motion stably. Biologically there is a certain position called motor point which can activate muscle contraction efficiently [Gobbo 2014]. Continuous stimulation to motor point will induce stable muscle contraction. However current path in the body or skin surface is too complicated to quantify. Due to spreading stimulation around the stimulated position and activate another muscle group, limb motion may be interfered. It will be necessary to apply stimulation to the desired position accurately in order to maintain muscle contraction.

1.8 Aim and Objectives

The final aim of this study is to realizing the method for improving the maintenance of muscle contraction. By developing a multi-channel FES system, stimulation can be applied to motor point. Multi-channel stimulation selector was firstly developed by Sato et al. [Sato 2013]. In this study, desired FES system will be developed to optimize for the requirement of this study.
The objective required to complete the final aim are:

1. **Development of a novel FES system**: A novel FES system requires to change

stimulation electrode in response to limb motion. Stimulation position will be controlled based on limb angle.

2. **Efficacy evaluation**: The effect of the novel FES system on inducing stable muscle contraction will be investigated in experiments of able-bodied subjects.

1.9 Thesis Outline

These aims and objectives will be realized in this thesis. The thesis is structured as follow.

Chapter 2: The possibility of FES in clinical treatment and the limitation of FES will be mentioned in this chapter. A throughout background of FES will be introduced. Subsequently after mentioning the limitation of FES, current understanding of the cause of the reduction of muscle contraction will be introduced. In order to avoid the reduction of muscle contraction, several previous studies will be reviewed in this chapter. The idea of proposed method will be mentioned.

Chapter 3: Based on the previous study, research hypothesis will be introduced. In order to realize the proposed methods, multi-channel FES system involving stimulation controlling principle will be explained. Overall structure of the novel FES system and each module in the structure will be described. Then the experimental procedure and experimental protocol will be introduced.

Chapter 4: Experimental results of 8 able-bodied subjects will be shown in this chapter. Proposed methods were compared several control methods for investigating the effect of motor point tracking stimulation.

Chapter 5: This chapter discuss about main outcome of this research. The results are summarized and evaluate the hypothesis of this study. Considerable mechanisms of the reduction of muscle contraction will be discussed.

Chapter2 The Possibilities of FES and its Limitations

2.1 The possibilities of FES

FES is able to not only induce limb motion but also apply afferent stimulation at the same time (**Figure 2.1**) thefore FES is an effective treatment method in clinical rehabilitation. Previous studies have shown several effects of FES in preventing muscle atrophy [Gould 1982] and reducing spasticity [Lo 2009]. FES also has an influence on improving motor functions such as walking speed [Marsden 2013] and balance in the standing posture [Kim 2012].

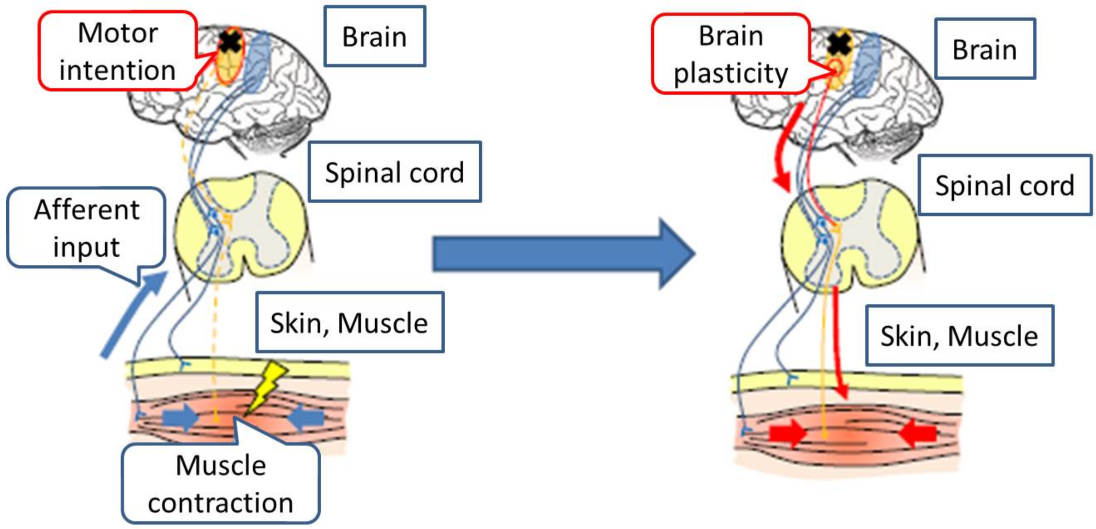


Fig.2.1 The effectiveness of FES

2.1.1 Electric Model of Muscle and Surface Skin

Takayama et. al. suggested an electrodermal activity model considering skin potential and skin impedance[Takayama 2000](**Figure 2.2**). According to their model, alternating electrical stimulation will be applicable for the penetration of electrical stimulation. There are some FES parameters in order to generate effective stimulation for activating strong muscle contraction.

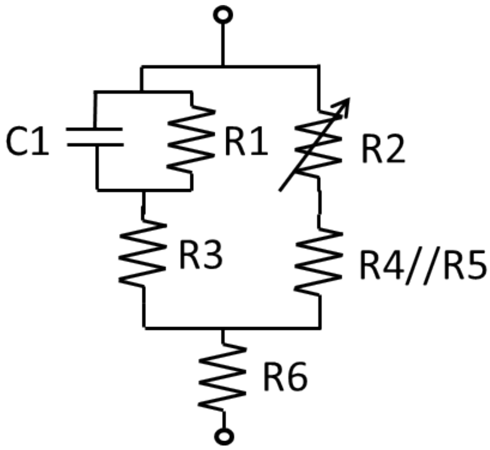
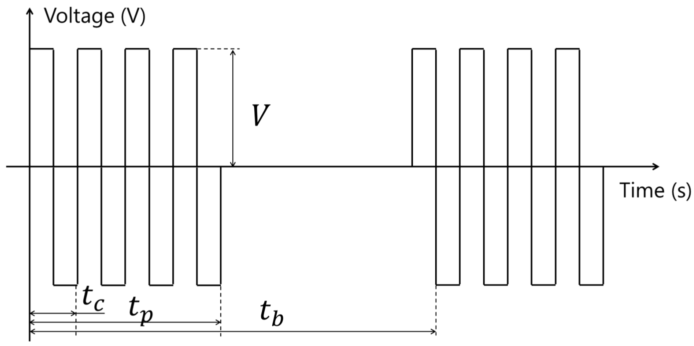


Fig.2.2 Electrical model of skin surface [Takayama 2000]

2.1.2 Parameters of EFS

There are several FES parameters which include stimulation shape or stimulation frequency. Petrofsky showed that sine waves passed ealiry through the skin and fat layer whereas square waves hardly transmit [Petrofsky 2004] because a RC low pass filter was created by the skin and fat layer.
There is mainly 4 parameters for stimulation frequency. One is carrier frequency, a second is burst frequency, the two others are duty ratio and amplitude. Muscle contraction can be change by modifying these 4 parameters. Ward et al. mentioned the typical range for burst frequency is 1-150 Hz [Ward 2002] and investigated pain and motor thresholds depending on 1-10 k Hz carrier frequency. Subjects felt less pain at higher frequencies but induced stronger muscle contraction at lower frequency [Ward 1998]. In order to show the effect of duty datio, Ward et al conducted a data analysis using Andrianova et al.'s published data[Andrianova 1971] because they didn not make any statistical comparison [Ward 2002(a)]. They showed that significantly stronger torque was produced by burst modulated stimulation (Duty: 50 %) than by continuous stimulation (**Figure 3.9**).



$f_c(=1/t_c)$	Carrier Frequency (Hz)
$f_b(=1/t_b)$	Burst Frequency (Hz)
t_c/t_b	Duty Ratio (%)
V	Voltage (V)

Fig.2.3 Stimulation shape of FES

2.1.3 How Muscle Contracts with FES

When electrical stimulation is applied to human muscle, muscle contraction is induced by the depolarizing motor axon beneath the stimulation electrode [Collins 2007].The depolarization in a muscle fiber is caused by the neurotransmitter. When an electrical signal from the motor neuron reaches axon terminal, it triggers a chain of chemical reactions in the axon terminal. Calcium ion going into the axon terminal initiates the release of the neurotransmitter.

It is well known that in order to activate stable muscle contraction stimulation applied to motor points induces muscle contraction with the least electric input [Gobbo 2011]. Motor point is a junction between motor nerve and branches of motor nerve.

2.2 The Limitations of FES

Muscle fatigue is defined by the deduction of required force. As previously mentioned, muscle contraction induced by FES is much easier to fatigue than voluntary muscle contraction.

2.2.1 Possible Causes of the Reduction of Muscle Contraction

Binder-Macleod el al. showed that muscle force induced by FES decreased to a greater extent than that of voluntary contraction [Binder-Macleod 1993]. However the mechanism behind the reduction of muscle strength by FES is not fully understood. Currently there are three hypothesised mechanisms which may result in the muscle strength reduction. One is that FES sctivates motor neurons in the opposite order to natural recruitment according to the size principle [Hamada 2004]. FES is activated from larger motor neurons to smaller motor neurons. The other is that muscle fibers are activated synchronously by FES but muscle fibers are activated asynchronously during voluntary contraction. The other is FES activate fast fatigable motor units first and then slow fatigue-resistant motor units.

2.3 Previous Methods to Improve the FES Limitation

Various research was studied in order to develop a technique to improve the maintenance of muscle contraction.

2.3.1 Random Modulation of Stimulation Frequency

Two studies suggested an FES method using random modulation of stimulation parameters in order to continuously change the firing rate [Thrasher 2005][Graupe 2006]. The random modulation of stimulation parameters aimed to decrease the number of activated motor units and to increase muscle fatigue resistance. The modulation was varied by 15% of the mean value of each stimulation parameter. Mean stimulation frequency was 40 Hz, mean stimulation duration was 250 μs, and the amplitude was between 34 and 110 mA. The duration of muscle contraction at 75 % of maximum isometric force induced by FES was compared in constant stimulation, randomized frequency stimulation, randomized amplitude stimulation, and randomized pulse width stimulation. Consequently there was no significant difference. Therefore the result showed that randomizing stimulation parameters had no effect at increasing muscle fatigue resistance.

2.3.2 Progressively Altering Stimulation Frequency

Another study tested a method which changed the stimulation parameters periodically [Kesar 2008]. 12 able bodied subjects were recruited. In this previous study, three different methods were evaluated in terms of isometric peak force and the maintenance of muscle force. These three protocols were progressively increasing pulse frequency, progressively increasing pulse duration and maintaning constant pulse frequency and duration. This previous study showed that the frequency-modulation method produced better isometric muscle performance in peak force and force maintenance than that of pulse-duration-modulation and no-modulation. Furthermore, the fatigue level was similar for all 3 methods. The fatigue level was quantified by the ratio between torque induced by stimulation at 20 Hz and torque at 60 Hz [Russ 1999].
The effect of progressively altering stimulation frequency was studied in another research by measuring the isometric thenar muscle force and the amplitude of M-wave induced by three different protocols [Griffin 2007]. M-wave is muscle action potential induced by electrical stimulation [Hicks 1985]. When stimulation is applied to a motor axon, the efferent signal (M-wave) will be produced. 23 able-bodied subject was recruited. In this previous study, gradually increasing frequency (20-40 Hz), gradually decreasing frequency and constant frequency. There was no significant difference in force-time integration between these three protocols.
Another study investigated the effect of progressively changing pulse amplitude [Doix 2014]. The effect was evaluated by comparing torque-time integration between constant stimulation and progressively changing pulse amplitude. There was no significant difference between the two FES protocols.
The comparison between progressively modulating frequency, amplitude, and both was showed by measuring the maintenance of muscle force. The experiment was carried out with patients suffering from spinal cord injury [Chou 2008(a)] and able-bodied people

[Chou 2008(b)]. Progressively increasing both frequency and amplitude showed better performance than progressively increasing either frequency or amplitude alone.

2.3.3 Variable Frequency Train

The effect on force production of variable frequency train was studied by comparing mixed stimulation of variable frequency train and constant frequency train with constant frequency train. Variable frequency train stimulation consisted of several frequency stimulations in a stimulation train [Deleym 2014]. 13 able-bodied subjects were recruited. The mean torque induced by the mixed stimulation showed an improvement on the other method.

2.3.4 Spatially Distributed Sequential Stimulation

Recently Nguyen et al., have shown that a method of using multichannel FES called Spatially Distributed Sequential Stimulation (SDSS) is effective in mainteining muscle torque [Nguyen 2011] (**Figure 2.4**). SDSS uses three or four active electrodes which are placed on different muscle groups and one reference electrode. The stimulation electrode is shifted periodically between these three or four active electrodes in order to prolong the muscle contraction of each muscle group. As a result, SDSS improved the maintenance of muscle contraction.

In this previous study, SDSS applied to triceps surea. There are two big muscle group (Lateral head and Medial head) which induce plantar flexion. No matter which muscle group is stimulated, plantar flexion is induced, so SDSS switch stimulation electrode one after another. However if there is one muscle group which is related to angle of motion, it is difficult for SDSS to be applied, for example biceps brachii, triceps brachii, or anterior tibialis.

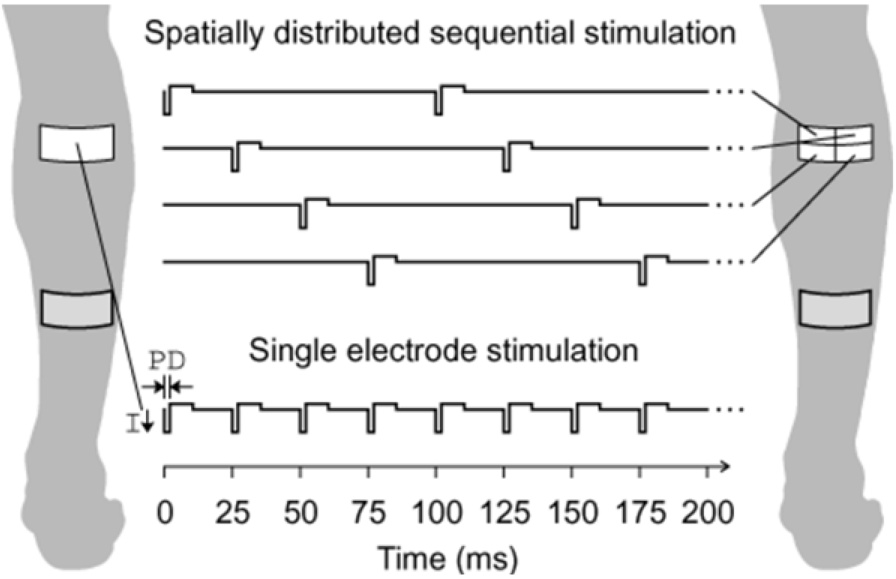


Fig.2.4 Spatially Distributed Sequential Stimulation [Nguyen 2011]

2.3.5 Type of Contraction

Subjects in previous studies frequently performed isometric contraction in order to quantify the muscle fatigue [Kesar 2008] [Thrasher 2005] [Deleym 2014] [Nguyen 2011]. However, it is more important that muscle strength does not decrease in dynamic motion for instance walking standing up, or moving an object to certain potion rather than in static contraction. In clinical rehabilitation, passive range of motion is one of the important indexes used to assess motor recovery [de Jong 2012]. However most of previous researches were studied under isometric condition. In the practical use, dynamic exercise is always involved, therefore The method need to be considered during dynamic exercise.

2.3.6 Proposed Method

During dynamic exercise it can be important to apply stimulation to motor points continuously for maintaining stable muscle contraction. Stimulation position need to change because motor points moves in response to angle of motion.

Chapter3 Methods and Limitation

3.1 Research Hypothesis

Muscle contraction can be induced strongly when electrical stimulation is applied to a motor point [Gobbo 2014]. However, during dynamic exercise the position of the motor point moves in response to limb motion [Nishihara 2013]. If the stimulation is applied to a certain position, muscle strength can weaken because the stimulation is out of position of the motor point after a limb moves. Nishihara et. al [Nishihara 2013] showed that the position of the motor point was correlated to angle of motion, so in present study the position of motor point was determined by measuring the angle of motion.

The main hypothesis of this study is that stimulation which can follow the position of motor point during dynamic exercise can improve the maintenance of muscle contraction. Previous studies were tested under static contraction conditions, so the previous methods may be difficult to apply to support muscle contraction involving dynamic exercise due to the movement of the motor point. In order to evaluate the effect of motor point tracking stimulation, the following two main hypotheses are offered.

1. **The effect of changing stimulation position periodically**: The motor point of the biceps moves from the distal position to the proximal position when the arm is flexed. Stimulation can be periodically applied to the motor point during dynamic exercise when the stimulating electrode periodically shifts from the distal electrode to the proximal. This method is called Time based Shifting Stimulation (TSS). It can be assumed that that TSS can induce stable muscle contractions.
2. **The effect of changing stimulation position based on joint angle** : The position of the motor point of the biceps is correlated to elbow angle, so the position of the motor point can be presumed based on joint angle. Stimulation can be applied to the motor point continuously.

3.2 Requirements of Multi-Channel FES for Motor Point Tracking Stimulation

FES systems do not typically include an angular measurement system which can control stimulation timing, so it is necessary to realize an external stimulation controller which communicates with the FES system and determine the stimulation electrode in response to the angle of motion.
The main role of a multi-channel stimulator is to switch stimulation electrodes one after another in response to the position of the motor point. The stimulation the position is determined based on the law of linear correlation between the position of the motor point and the angle of motion.

1. **Generating a stimulation trigger in response to the angle of motion**
2. **Switch stimulation electrodes one after an other**:

3.3 Multi-channel Stimulation System

3.3.1 Overview of Multi-channel Stimulation System

A multi-channel stimulation system consists of three modules, a stimulation generator, a trigger generator, and an electrode selector (see **Figure 3.4**).

1. **Stimulation Generator**: Stimulation is generated and stimulation duration and stimulation parameters are set in this module. Stimulation and On-Off signal of stimulation are input to the electrode selector module.
2. **Electrode Selector**: The stimulation electrode is selected in this module and is changed in response of the angle of motion.
3. **Trigger Generator**: The angle of motion is monitored in this module and a signal sent to choose which electrode need to be selected.

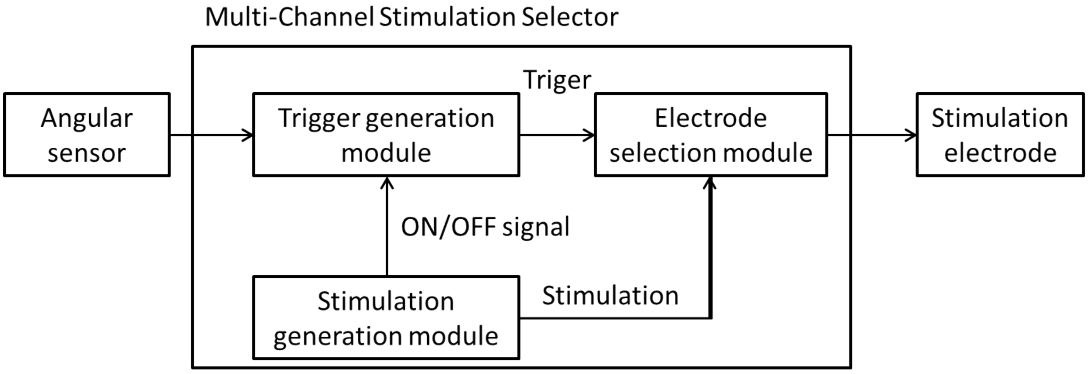


Fig.3.1 Block diagram of multi-channel stimulator

3.3.2 Trigger Generator

The position of the motor point is assumed at this module and a command is generated that decides which electrode should be active in response to the angle of motion. The position of stimulation: x is defined by the following equation (3.3-1).

$$x = x_{init} + \frac{x_{final} - x_{init}}{\theta_{final} - \theta_{init}} (\theta - \theta_{init}) \tag{3.3-1}$$

x_{final} means the stimulation position at θ_{final}(full extension) and x_{init} means the stimulation position at θ_{init}(full flexion).

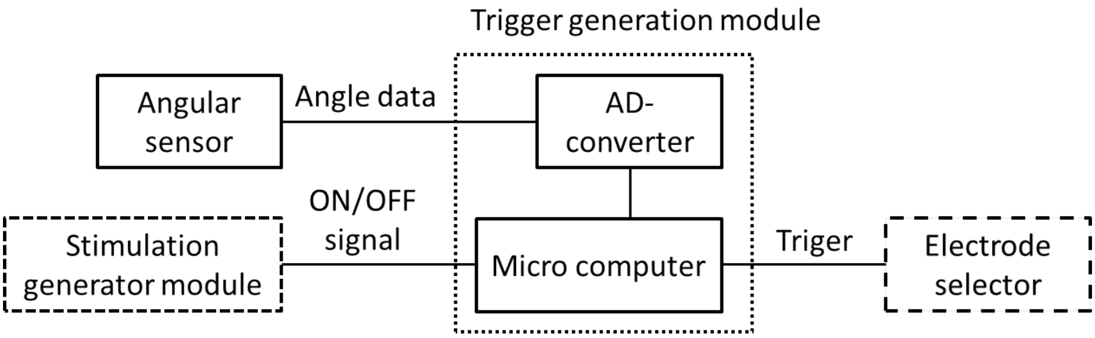


Fig.3.2 Block diagram of Trigger generation module

3.3.3 Electrode Selector

We used a novel FES selector developed by Sato et al. [Sato 2013]. This FES selector consists of two structures.One is the signal generator of electrode selection and the other is the interface between stimulator and electrodes. The overview of the selector is shown in **Figure 3.3**. 12 pairs of electrodes can be controlled individually by this selector.

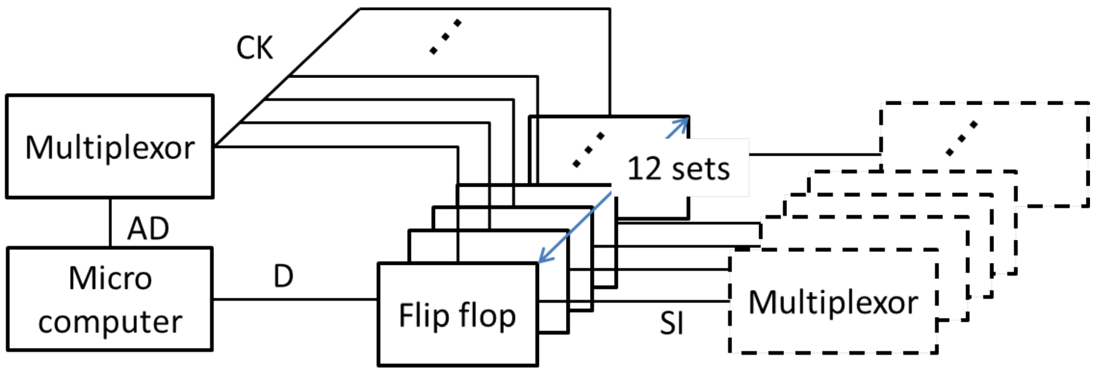


Fig.3.3 Block diagram of electrode selector

Signal Generator of Electrode Selection

The signal generator selects the desired electrode for stimulation. The signal generator can select at most 8 different stimulation electrodes (the anode and cathode of 4 channels). The signal generator consists of 36 sets of two multiplexors (74HC138) and a flip flop (74HC175). **Figure 3.5** gives an overview of the Signal Generator.

AD: Signal to multiplexor for Electrode selection

D: Signal to flip flop for Channel selection

CK: Signal to flip flop for Electrode selection

SI : finalized Signal to multiplexor for Electrode selection.

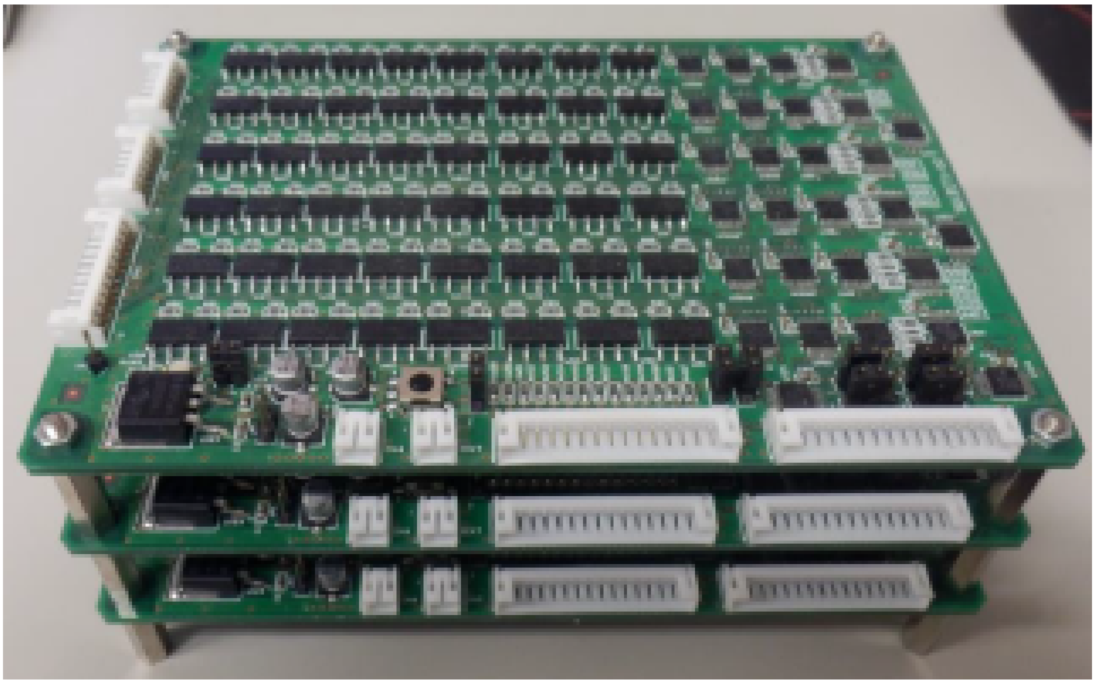


Fig.3.4 Electrode Selector

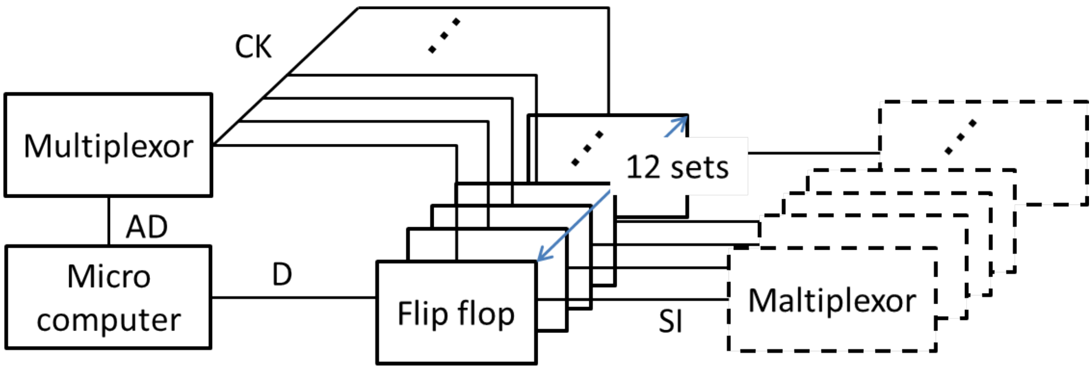


Fig.3.5 Block diagram of Signal Generator of Electrode Selection

The interface between stimulator and electrodes

For safety, the stimulation channel must not be allowed to be short-circuited, therefore the interface prevents the circuit from shortening by incorporating a change-over contact switch. The change-over contact switch was designed with a NOT element (74HC04) and break contact relay element (AQW210S) (see **Figure 3.6**).

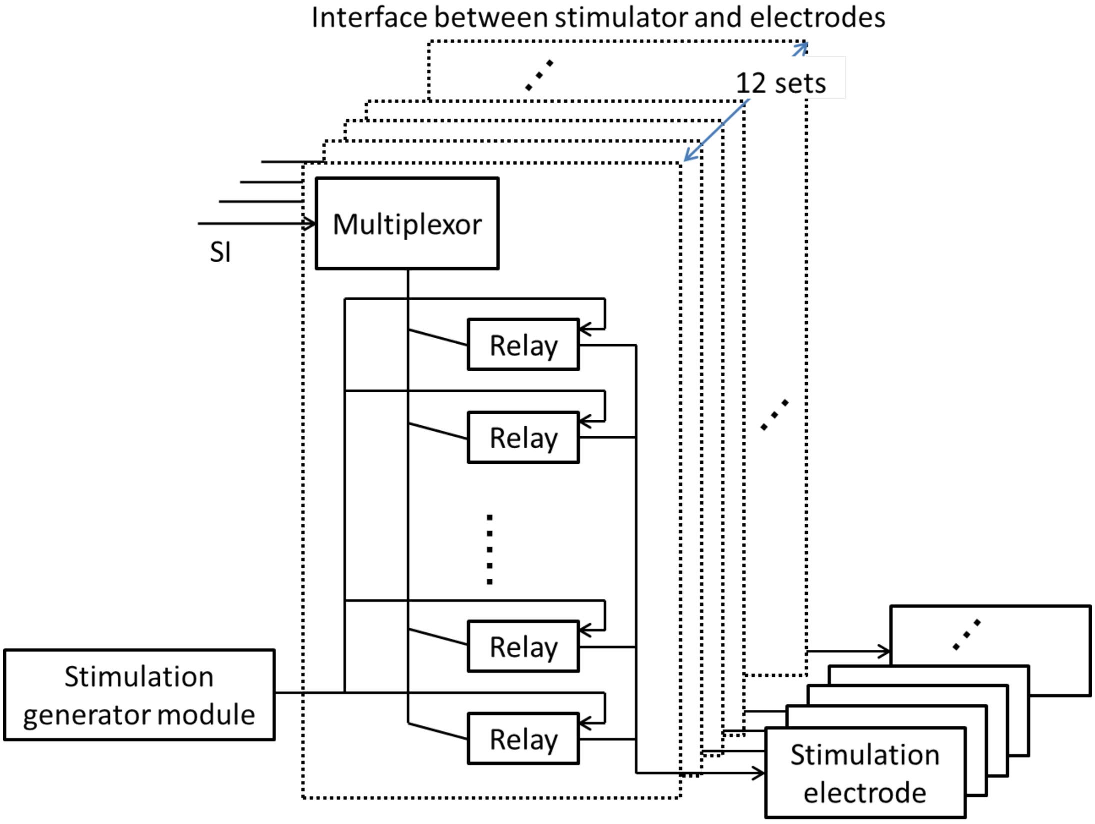


Fig.3.6 Overview of the interface between stimulator and electrodes

3.3.4 Stimulation Generator

A programmable 4-ch constant voltage FES stimulator (System Instruments Co., Ltd.) was used to generate electrical stimulation **3.7**. Stimulation parameters and duration of stimulation and rest time period were set at this module.

3.4 Subjects

10 healthy male subjects in their twenties were recruited. Two subjects could not finish all the protocols due to their schedule. The study was approved by the ethical committee

Fig.3.7 Stimulation Generator

at The University of Electro-Communications. Each subject signed a written informed consent form before the experiment.

3.5 Apparatus

3.5.1 Measurement Device

Elbow angle (θ in **Figure 3.12**) was measured using an electro-goniometer with a sampling frequency of 100 Hz (Model SG150 twin-axis goniometer; Biometric Ltd., Ladysmith, VA).

3.5.2 Stimulation

Self-adhesive circular electrodes (radius: 5 cm) were placed over the motor point of the biceps **Figure 3.8**. Orange circle expresses the position of motor point at elbow extension and blue circle expresses the position of motor point at elbow flexion. Pair of electrodes was placed vertical to mucle fiber. Stimulation was alternating current with 2000 Hz carrier frequency (pulse width: 500 μs) modulated at 100 Hz (duty cycle: 50%)**Figure 3.9**. The burst modulated alternating current stimulation was suggested to induce muscle strength with less discomfort [Selkowitz 2009]. Stimulation intensity was adjusted based on the angle of motion generated by FES. Stimulation intensity was set to the minimum voltage which was able to rotate the elbow angle more than 40 degrees from the initial position.

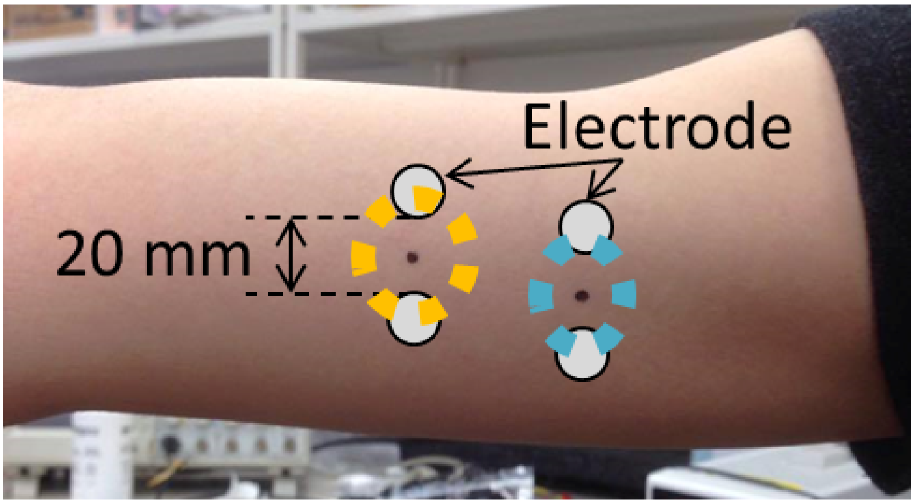
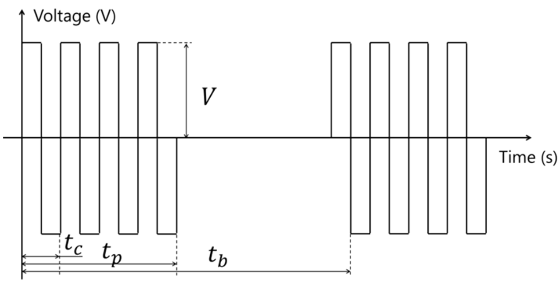


Fig.3.8 Electrode placement



$f_c(=1/t_c)$	Carrier Frequency (Hz)	2000Hz
$f_b(=1/t_b)$	Burst Frequency (Hz)	100Hz
t_c/t_b	Duty Ratio (%)	50%
V	Voltage (V)	5-28 V

Fig.3.9 Stimulation form

3.5.3 Target Muscle Group

The elbow flexor was chosen as the target muscle because the elbow flexor, biceps brachii is one of the muscles which the previous method, SDSS, is difficult to apply. The biceps brachii has two muscle groups including a long head bundle and a short head bundle. Stimulation was applied to short head bundle in paticular because it was shown that short head is relatively efficient at elbow flexion [Jarrett 2011]. Therefore target muscle of this study is short head of biceps brachii **Figure 3.10**

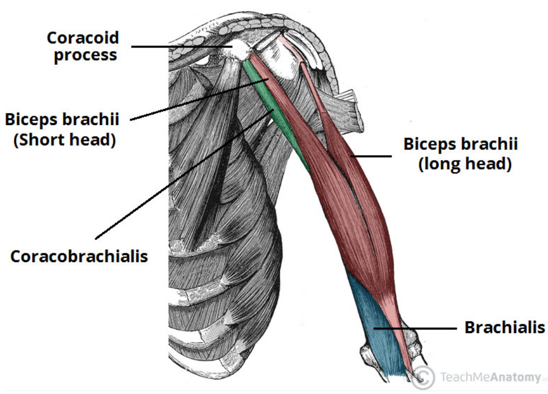


Fig.3.10 Target muscle

3.5.4 Electrode Preparation

Before every test, the position of the motor point was searched for with a pen type stimulator at elbow extension position and flexion position. Pairs of electrodes were placed vertically on the biceps. The motor point was in the middle of one set of electrode. The distance between electrode was 20 mm. In order to maintain a good contact state, skin stratum corneum was removed before the electrode placement.

3.6 Experimental Procedure

3.6.1 Study Design

All participants participated in 5 days for the experiment. One out of 5 intervention(SS, TSS, OPTSS, SS-1.5, JASS) was applied on each day. Between each test at least 1 week rest was provided **Figure 3.11**.

Day1 (90 min)	Warm up & familiarization Test(SS)
Rest	At least 1 week
Day2 (90 min)	Warm up & familiarization Test (TSS)
Rest	At least 1 week
Day13(90 min)	Warm up & familiarization Test(OFTSS)
Rest	At least 1 week
Day4(90 min)	Warm up & familiarization Test(SS-1.5)
Rest	At least 1 week
Day5 (90 min)	Warm up & familiarization Test(MPTS)

Fig.3.11 Time schedule of the experiment

3.6.2 Experimental Setting

Before the experiment, the positions of the motor point were searched for with a pen electrode when the arm was flexed and extended. Two pairs of stimulation electrodes were placed over the two positions.

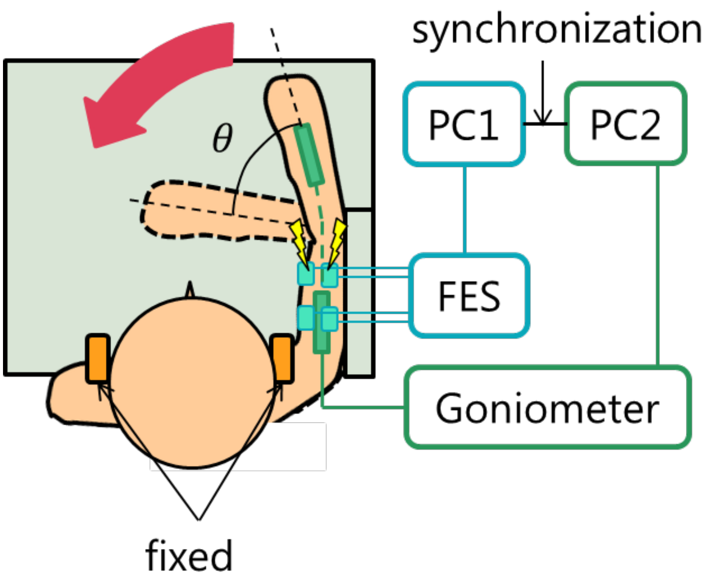


Fig.3.12 Experimental environment

3.6.3 Warm-up and Familiarization

Before the test, subjects were asked to perform a short warm-up session of 5 sets of isometric voluntary contraction for 10 seconds. As a familiarization session, subjects performed 1 set of flexion induced by FES and voluntary extension.

3.6.4 Task

Each subject made his/her arm perform elbow flexion by FES on the transverse plane (range of motion: 98.2-71.3 (degrees)) and returned his/her arm to full extension position voluntarily in one set. The rest time period between each contraction was 3.5 seconds. One trial consisted of continuous 180 sets of exercise (15 minutes). The days of each test were separated by 1 week to allow the subjects to have enough rest.

3.6.5 Proposed Method

Time Based Shifting Stimulation

In order to investigate the effect of periodically changing stimulation position on inducing stable muscle contractions, TSS shifted the stimulating position from the distal electrode to the proximal electrode. This electrode shifting direction is the same as the movement of the motor point in the biceps. Stimulation timing is shown in **Figure 3.13**. Stimulation from channel 2 was applied 0.5 seconds after the stimulation from channel 1. The stimulation duration of both channels was 1 second. Stimulation duration for one section was 5 seconds.

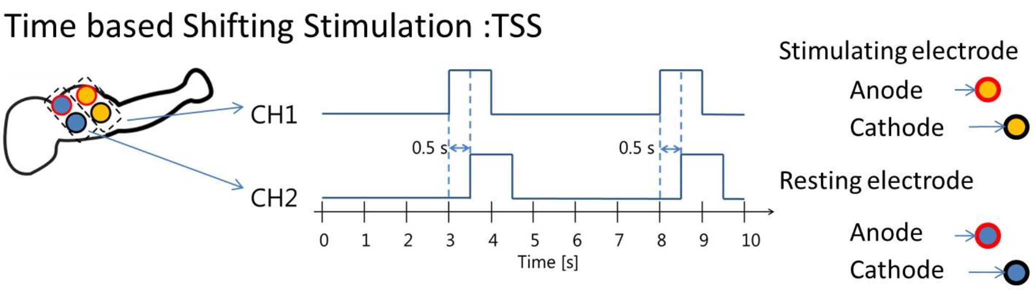


Fig.3.13 Stimulation timing of Time Shifting Stimulation

Joint Angle Based Shifting Stimulation

In order to investigate the effect of joint angle based changing stimulation position on inducing stable muscle contractions, JASS shifted stimulation electrode based on elbow angle. In the begining of the experiment, the maximum range of elbow angle was measured for each subject. Based on **Equation 3.3-1** stimulation position was determined. First stimulation from channel 1 was applied in one third of the range of motion, and stimulation from both channels was applied in the next third of the range of motion. Stimulation from channel 2 was then applied in the last third of the range of motion.

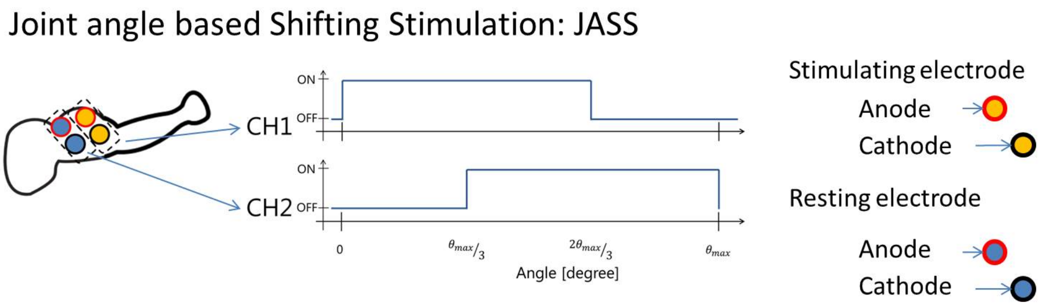


Fig.3.14 Motor Point Tracking Stimulation

3.6.6 Control Method

In order to evaluate the effect of TSS and JASS , we conducted the following control experiments.

Simultaneous Stimulation

The stimulation output from each channel was same as for TSS. This stimulation protocol was used for the investigation of the effect of changing the stimulating the position under the conditions of the same stimulation output from each channel. Stimulation timing is shown in **Figure 3.15**. Stimulation from both channels was applied at the same time and the duration of each was 1 second.

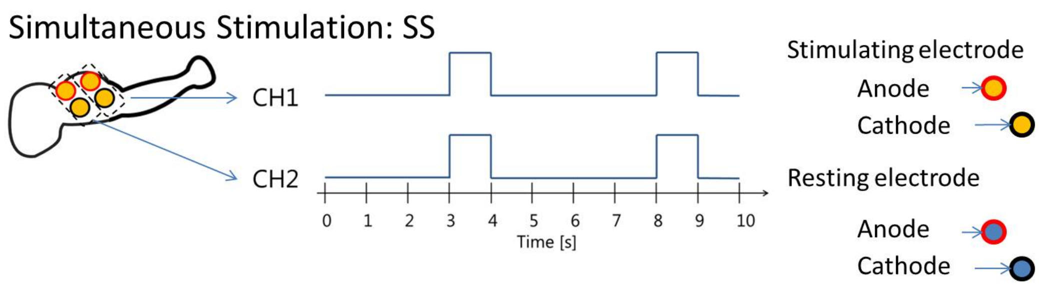


Fig.3.15 Stimulation timing of Simultaneous Stimulation

Simultaneous Stimulation with duration of 1.5 seconds

The total stimulation duration was the same as for TSS. This stimulation protocol was used for the investigation of the effect of changing the stimulating position under the conditions of the same total stimulation duration. Stimulation timing was shown in **Figure 3.16**. Stimulation from both channels was applied at the same time and lasts 1.5 seconds.

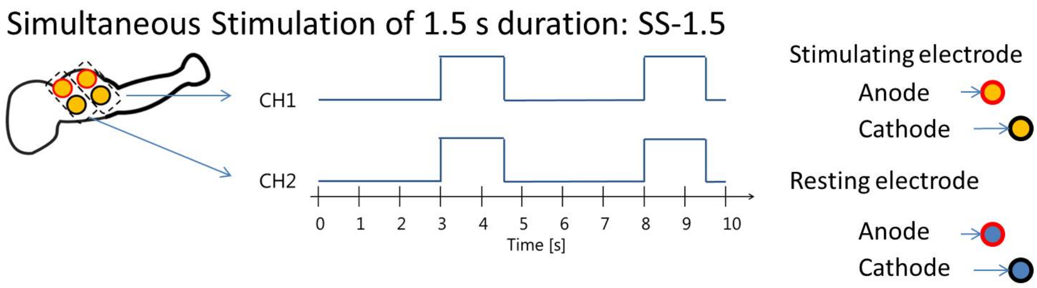


Fig.3.16 Simultaneous Stimulation with 1.5 seconds stimulation duration

Opposite Phase Time based Shifting Stimulation

The stimulation phase was the opposite of TSS. This stimulation protocol was used for the investigation of the effect of changing stimulating position order under the condition of same total stimulation duration. Stimulation timing is shown in **Figure 3.17**. Stimulation from channel 1 was applied 0.5 seconds after the stimulation from channel 2. Stimulation duration of both channels was 1 second.

3.7 Data Analysis

3.7.1 Participant Exclusion

The experimental data of certain participants were excluded based on the following criteria. One participant was excluded based on the results of SS and SS-1.5s. **Figure**

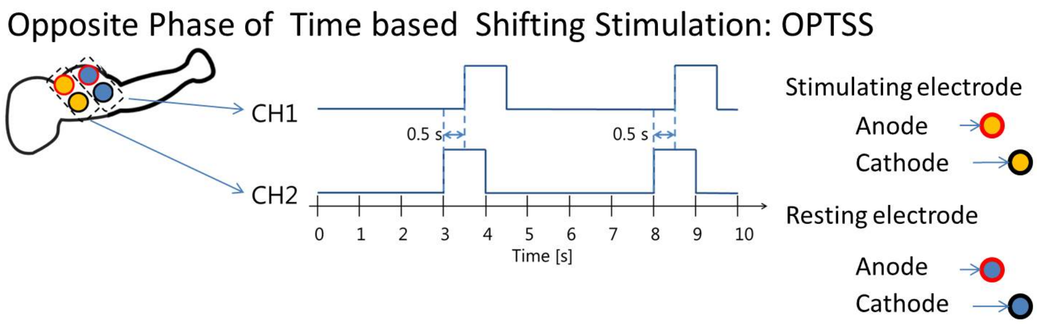


Fig.3.17 Opposite Phase Time Shifting Stimulation

3.18 shows the ratio of the mean angle of motion induced by SS and SS-1.5s. One participant (Sub.3) out of 8 participants induced a 2.3 times larger angle of motion by SS than the other participants. Stimulation duration was decreased in the same stimulation method but the angle of motion was greatly increased. The experiment on this subject can be considered to have not been properly conducted, so the data of this subject was excluded from the following analyses.

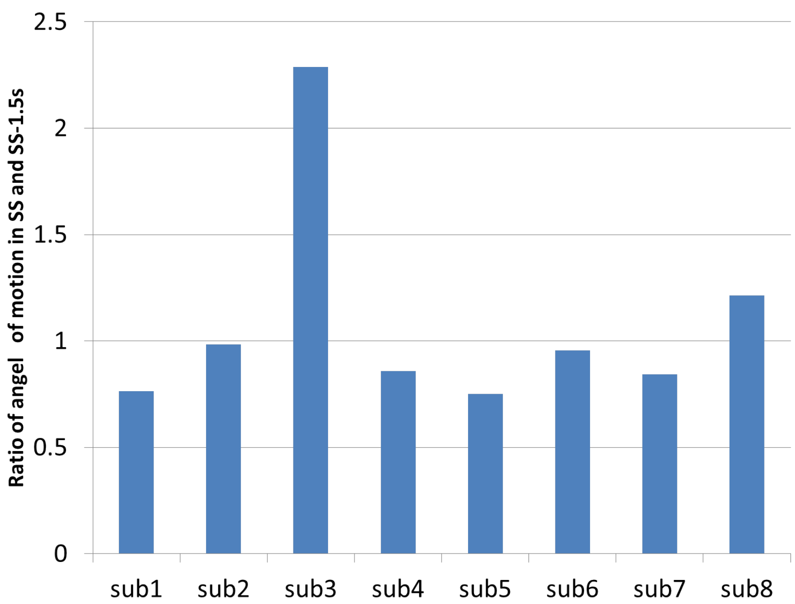


Fig.3.18 Ratio of the angle of motion in SS and SS-1.5s

The mean angle of motion over 180 contractions was averaged across the 8 subjects. One way factional ANOVA and Tukey's Honest Significant Difference method was performed to compare TSS, SS, SS-1.5s, and OPTSS, and JASS, SS, SS-1.5s, and OFTSS.

Chapter4 Results

4.1 The effect of stimulation with time shifting

4.1.1 Comparison between TSS and SS

Figure 4.1(a) shows the time series of the elbow angle of a typical subject. The elbow angle induced by SS continued to go up and down but the elbow angle induced by TSS constantly maintained at a high level for 15 minutes.
The angle positions in the first 90 contractions are shown in **Figure 4.1(b)**. Each point indicates the peak angle of motion in one contraction. In the first 90 seconds, the difference between the maximum angle of motion and minimum angle of motion was 39.2 degree at SS and 8.8 degrees at TSS. The reduction of angle of motion of TSS was much less than that of SS.

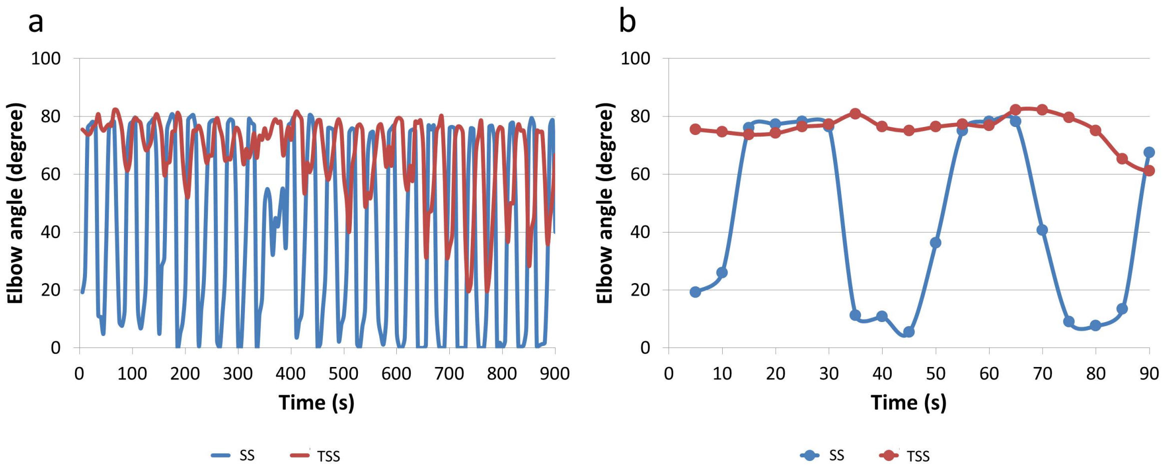


Fig.4.1 Elbow angle in one representative subject with TSS and SS (a) Time series data of peak angle of motion induced by FES with 180 contractions (15 minutes). Blue: SS, Red: TSS. (b) Peak elbow angle of the representative subject in first 18 contractions (90 seconds). Each point shows peak angle of motion in one contraction

This result showed that the maintenance of muscle contraction can be improved by periodically changing the position of the stimulation electrode. The muscle strength became stable with TSS even though stimulation duration from both channels were the same, so presumably the stimulation order is important in maintaining the wide angle of motion. However, the total stimulation duration of TSS was longer than that of SS. TSS applied stimulation 1.5s in one effort and SS applied stimulation 1s. Next, we compare the maintenance of angle of motion between SS-1.5s condition.

4.1.2 Comparison between TSS and SS-1.5

This test compared TSS and SS-1.5. The total stimulation duration of both interventions was the same 1.5 s. **Figure 4.2(a)** shows the time series of the elbow angle of a typical subject. The angle positions in the first 90 contractions are shown in Figure 4.2(b). Each point indicates the peak angle of motion in one contraction.

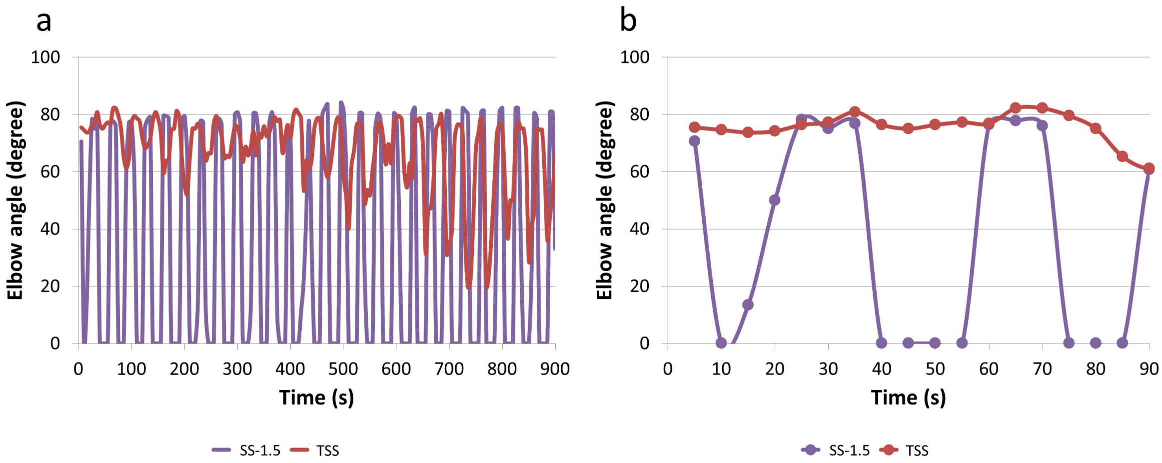


Fig.4.2 Elbow angle of a typical subject with TSS and SS-1.5 (a) Time series data of peak angle of motion induced by FES with 180 contractions (15 minutes). Purple: SS-1.5, Red: TSS. (b) Peak elbow angle of the representative subject in first 18 contractions (90 seconds). Each point is shown peak angle of motion in one contraction

This result showed that the angle of motion varied drastically in SS-1.5. As shown in **figure 4.2 (b)** , the angle of motion induced by SS-1.5 became zero frequently while the angle of motion elicited by TSS was stable.
Even though the total stimulation duration of SS-1.5 was same as that of TSS, muscle

contraction maintained stability in TSS. This result supplied an evidence for the importance of the shifting of the stimulation electrode for stable muscle contraction. Since the current flow applied by FES to human body is too complicated to monitor from outside, it is unclear whether the stimulation sequence had an effect on sustainable muscle contraction or whether stimulation shifting itself is important regardless of the shifting order.

4.1.3 Comparison between TSS and OPTSS

In order to investigate the effect of the sequence of the stimulation electrode on maintaining muscle contraction the following test compared TSS and OFTSS. **Figure 4.3(a)** shows the time series data for the elbow angle of a representative subject. The angle positions in the first 90 contractions are shown in **Figure 4.3(b)**. Each point indicates the peak angle of motion in one contraction.

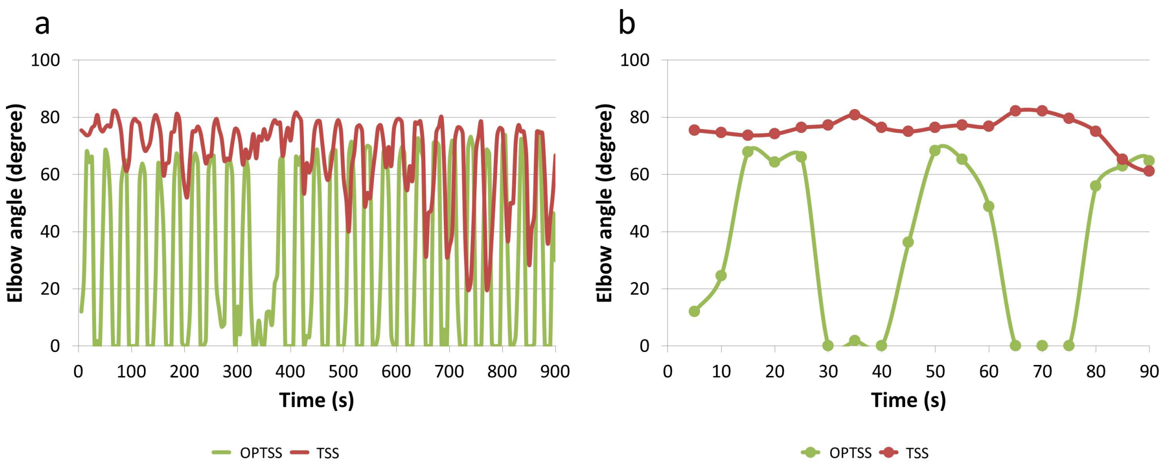


Fig.4.3 angle of a typical subject with TSS and OFTSS (a) Time series data of peak angle of motion induced by FES with 180 contractions (15 minutes). Green: OFTSS, Red: TSS. (b) Peak elbow angle of the representative subject in first 18 contractions (90 seconds). Each point showed peak angle of motion in one contraction

This result showed that when the stimulation order was opposite phase of TSS, the angle of motion induced by OFTSS was consistently less than that induced by TSS. The effect of stimulation shifting order on the maintenance of muscle contraction was demonstrated.

4.1.4 Comparison between TSS and SS, SS-1,5, and OFTSS

Figure 4.4 shows the mean angle of motion of 180 contractions (15 minutes) was averaged across 7 subjects (ANOVA: $p \leq 0.05$). TSS significantly improved the maintenance of muscle contraction compared to the other three interventions. P-value between TSS and SS-1.5 and between TSS and SS, and between TSS and OPTSS was $p \leq 0.01$.

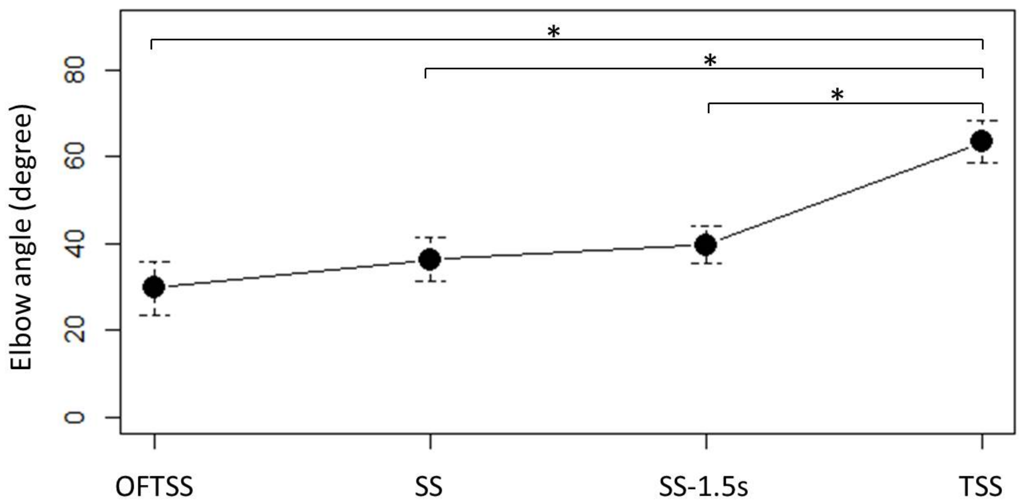


Fig.4.4 Average elbow angle of seven subjects

This result demonstrates that the muscle contracted stably when stimulation shifted periodically in response to the limb motion.

4.2 The effect of Joint Angle Based Shifting Stimulation

With TSS, changing the stimulation position in response to limb motion had the effect of maintaining of the angle of motion. TSS did not actually follow the motor point, however stimulation would be applied to the motor point by the time shifting stimulation electrode. The next study shows the effect of JASS. JASS determined the stimulating position by the elbow angle, so stimulation could be applied to motor point more accurately.

4.2.1 Comparison between JASS and SS

Figure 4.5(a) shows the time series data for the elbow angle of a typical subject. The angle positions in the first 90 contractions are shown in **figure 4.5(b)**. Each point indicates the peak angle of motion in one contraction.

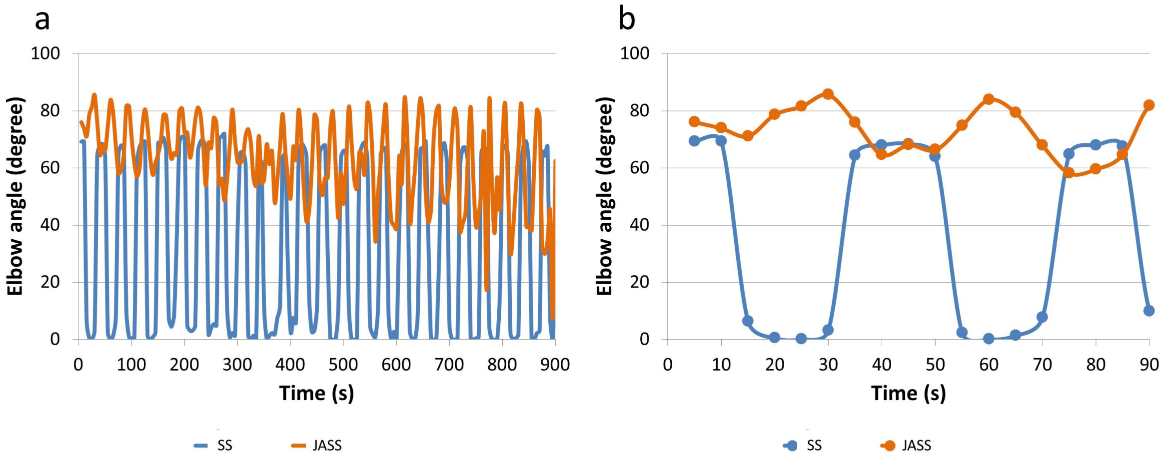


Fig.4.5 Elbow angle in one representative subject with JASS and SS (a) Time series data of peak angle of motion induced by FES with 180 contractions (15 minutes). Blue: SS, Orange: JASS. (b) Peak elbow angle of the representative subject in first 18 contractions (90 seconds). Each point is shown peak angle of motion in one contraction

4.2.2 Comparison between JASS and SS-1.5

Figure 4.6(a) shows the time series data for the elbow angle of a representative subject. The angle positions in the first 90 contractions are shown in **figure 4.6(b)**. Each point indicates the peak angle of motion in one contraction.

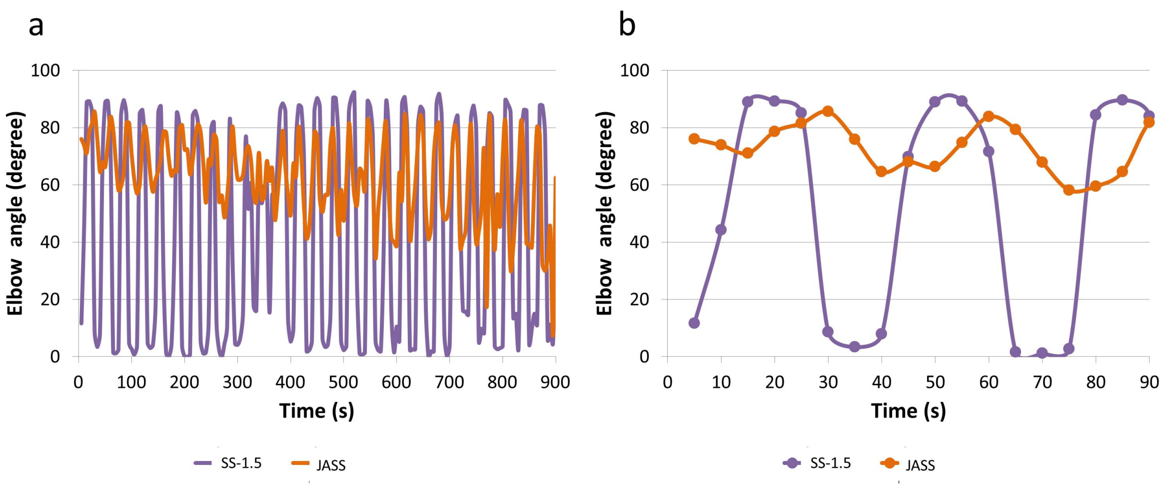


Fig.4.6 Elbow angle in one representative subject with JASS and SS-1.5s (a) Time series data of peak angle of motion induced by FES with 180 contractions (15 minutes). Blue: SS-1.5s, Orange: JASS. (b) Peak elbow angle of the representative subject in first 18 contractions (90 seconds). Each point shows peak angle of motion in one contraction

4.2.3 Comparison between JASS and OPTSS

Figure 4.7(a) shows the time series data for the elbow angle of a representative subject. The angle positions in the first 90 contractions are shown in **figure 4.7(b)**. Each point indicates the peak angle of motion in one contraction.

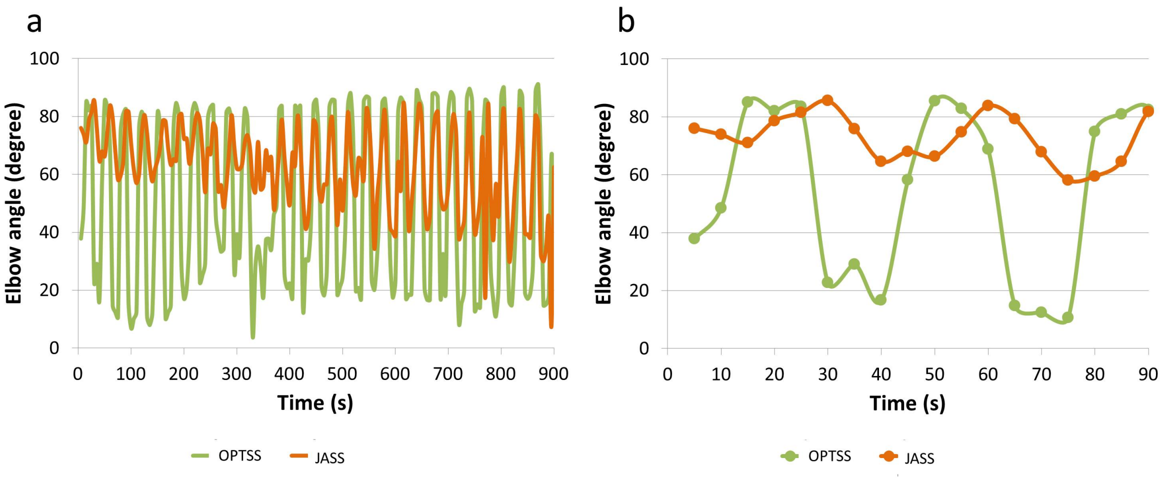


Fig.4.7 Elbow angle in one representative subject with JASS and OPTSS (a) Time series data of peak angle of motion induced by FES with 180 contractions (15 minutes). Green: OPTSS, Orange: JASS. (b) Peak elbow angle of the representative subject in first 18 contractions (90 seconds). Each point shows peak angle of motion in one contraction

4.2.4 Comparison between JASS and SS, SS-1,5, and OPTSS

Figure 5.1 showed the mean angle of motion of 180 contractions (15 minutes) was averaged across 7 subjects. JASS improved the maintenance of muscle contraction significantly compared to the other three interventions. P-value between TSS and SS-1.5 and between TSS and SS, and between TSS and OPTSS was $p \leq 0.01$.

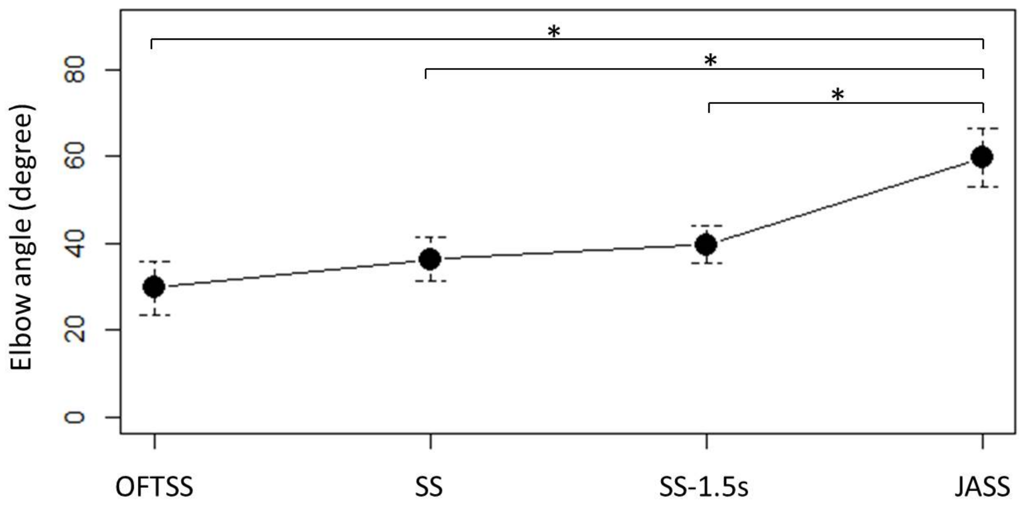


Fig.4.8 Average elbow angle of seven subjects: The mean angle of motion was averaged across the seven subjects

Chapter5 Discussion

5.1 The Effect of Periodically Changing Stimulating Position

In the comparison between TSS and SS, SS-1.5, and OPTSS, the effect of TSS on maintaining muscle contraction was demonstrated by a wide angle of motion in 7 healthy subjects (see Figure 4.4).

In the comparison between TSS and SS, even though the stimulation output from each channel was same, the stimulation method involving time based shifting stimulation significantly improved the maintenance of angle of motion. This result demonstrated the effect of periodically changing the stimulation electrode. However, the total stimulation duration was different between TSS and SS. It is unclear whether or not the difference of angle of motion between TSS and SS was produced as an effect of changing the stimulation position periodically.

The comparison between TSS and SS-1.5s showed the effect of periodically changing stimulation position. Even though the total stimulation duration was the same in TSS and SS-1.5s and stimulation output of SS-1.5s from each channel larger than that of TSS, TSS produced a significantly better effect on the maintenance of angle of motion. These results clearly demonstrated the effects of changing stimulation position periodically.

5.2 The Effect of The Shifting Direction

From the above result, it is uncertain whether the effect of TSS was produced by the effect of stimulation shifting itself, or by the effect the order of stimulation shifting. The comparison between TSS and OPTSS investigated the effect of shifting direction of the stimulating electrode. TSS induced a significantly larger angle of motion than OPTSS. This result showed the shifting direction had influenced on the stable muscle contraction. In order to produce stable muscle contractions that the shifting direction needs to be the same direction as the movement of motor point during elbow flexion.
From these comparisons it was demonstrated that there was the effect of the stimulation electrode shifting from the distal electrode to the proximal electrode. Two electrodes were placed over the motor point position when the arm extended and flexed. Stimulation was shifted from the distal pair of electrodes to the proximal pair based on the fact that elbow muscle contraction made the motor point moved from the distal position to the proximal position during elbow flexion. It can be presumed that TSS may effectively cause stimulation over the motor point. According to these results we hypothesised that shifting the stimulating position in response to the movement of the motor point may be effective in maintaining stable muscle contraction.

5.3 The Effect of Joint Angle based Shifting Stimulation

Although the stimulation direction is the same as the motor point movement, TSS shifts the stimulating position regardless of the position of the motor point. JASS shifts the stimulating position based on the angle of motion. The angle of motion of the elbow is correlated with the position of the motor point, so JASS can apply stimulation to the motor point continuously. Regarding the comparison between TSS and SS, SS-1.5s, and OPTSS, there were significant differences between JASS and SS, SS-1.5s, and OPTSS, thus demonstrating the effect of JASS. From these results, we concluded that stimulation shifting in response to the movement of the motor point can improve the maintenance of muscle contraction.

5.4 The maintenance of stable muscle contraction in Clinical Application

Consequently the effect of TSS and JASS on improving the maintenance of muscle contraction achieved a similar result. In terms of clinical rehabilitation, the level of muscle strength induced by FES differs depending on the patient, so angular velocity can be slower than the time shifting of stimulating electrode. It may be difficult to apply TSS to patients in various conditions. In contract, JASS shifts the stimulation electrode in response to the angle of motion. Stimulation can be applied to the motor point continuously. JASS can therefore be applicable to various kind of patients.

5.5 The Possibility Cause of the Reduction Muscle Contraction

From these result, both proposed methods was significantly better than the other control conditions in terms of the maintenance of muscle contraction. Yoshida et al. found muscle fatigue was related the amount of axonal population activated by stimulation overlap of two electrodes [Yoshida 1993].Initial stimulation from channel 2 of SS, SS-1.5s and OPTSS may induce muscle fatigue and lead the reduction of muscle contraction.

5.6 Limitations

5.6.1 Model of Motor point movement based shifting stimulation

Stimulation shift of JASS was proportional to elbow angle. However the relationship of the position of motor point and elbow angle may be non-linear. The proportional stimulation shifting may not be effective on such non-linear system. The model of the relationship between the position of motor point and elbow angle will be effective of decide the stimulation position in order to apply stimulation from nearest pair of electrode.

5.6.2 The Electrode Size of Multi-Channel FES for the fine stimulation shift

There was stimulation overlap in JASS. The maintenance of muscle contraction can be improved by avoiding the overlap. increasing the number of small electrode will be effective way to avoid overlap and to realize more accurate stimulation to motor point.

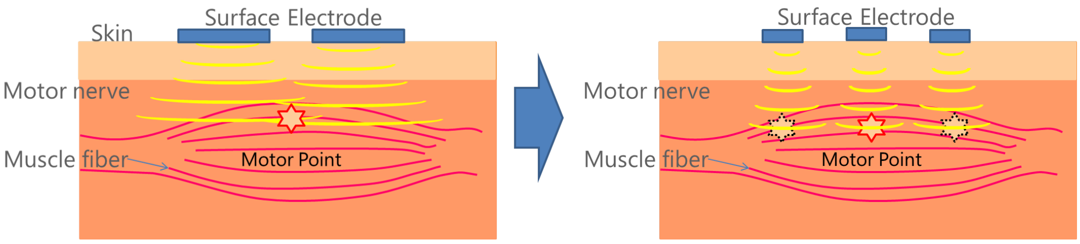


Fig.5.1 Increasing the number of small electrode for avoiding stimulation overlap

Chapter6 Conclusion

In this study, we proposed the method that shifted the stimulation electrode in response to the elbow angle for improving the maintenance of angle of motion during dynamic exercise. This method was based on the fact that the position of motor point was related to angle of motion.
proposed methods
In order to assess the effect of proposed methods, several experiment was conducted involving dynamic exercise. As a result, JASS and TSS significantly improved the maintenance of muscle contraction. From these result motor point tracking stimulation can be an effective method to maintain stable muscle contraction.

TSS shifted the stimulating position periodically The effect of motor point tracking stimulation on the maintenance of muscle contraction was demonstrated by the investigation of the effect of JASS and TSS. In the clinical use, JASS can be an effective method to produce stable muscle contraction.

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2017 年

References

[Ministry of Health, Labour and Welfare 2013] Ministry of Health, Labour and Welfare: Summary Report of Comprehensive Survey of Living Conditions 2013, Long-Term Care

[Ministry of Health, Labour and Welfare 2010] Ministry of Health, Labour and Welfare: Summary Report of Comprehensive Survey of Living Conditions 2010, Long-Term Care

[Takayama 2000] Takayama, K., Isosak, K., Yamamoto, Y., Nakamura, T. (2000). Modeling of Electrodermal Activity. The Institute of Electronics, Information and Communication Engineers. *IEICE technical report.* ME and bio cybernetics. 99(688), 85-90.

[Popovic 2001] Popovic, M.R., Curt, A., Keller, T., and Dietz, V. (2001). Functional electrical stimulation for grasping and walking: indications and limitations. *Spinal Cord.* 39(8), 403412.

[Qian 2015] Qian, J. G., Rong, K., Qian, Z., Wen, C., and Zhang, S. (2015). Effects of a multichannel dynamic functional electrical stimulation system on hemiplegic gait and muscle forces. *Journal of Physical Therapy Science.* 27(11), 35413544.

[Binder-Macleod 1993] Binder-Macleod, S. A., and Snyder-Mackler, L. (1993) .Muscle fatigue: clinical implications for fatigue assessment and neuromusclar electrical stimulation. *Physical Therapy Journal.* 73(12), 902-910.

[Selkowitz 2009] Selkowitz, D. M., Rossman, E. G., and Fitzpatrick, S. (2009). Effect of burst-modulated alternating current carrier frequency on current amplitude required to produce maximally tolerated electrically stimulated quadriceps femoris knee extension torque. *American Journal of Physical Medicine and Rehabilitation.* 88(12), 973-978.

[Nguyen 2011] Nguyen, R., Masani, K., Micera, S., Morari, M., and Popovic, MR.. (2011). Spatially distributed sequential stimulation reduces fatigue in paralyzed triceps surae muscles: a case study. *Artificial Organs.* 35(12) 1174-1180.

[Pournezam 1988] Pournezam, M., Andrews, B. J., Baxendale, R. H., Phillips, G. F., and Paul, J. P., (1988). Reduction of muscle fatigue in man by cyclical stimulation. *Journal of Biomedical Engineering.*10(2), 196-200.

[Thrasher 2005] Thrasher, A., Graham, G. M., and Popovic, M. R., (2005). Reducing muscle fatigue due to functional electrical stimulation using random modulation of stimulation parameters. Artificial Organs. 29(6), 453458.

[Gobbo 2014] Gobbo, M., Maffiuletti, N. A., Orizio, C., and Minetto, M. A., 2014. Muscle motor point identification is essential for optimizing neuromuscular electrical stimulation use. *Journal of NeuroEngineering and Rehabilitation.* 13(76), from https://jneuroengrehab.biomedcentral.com/articles/10.1186/1743-0003-11-17.

[John 1993] John, H. W. (1993) The Extremities and The Head, Neck, and Trunk: Muscle and Motor Points, Lea and Febiger.

[de Jong 2012] de Jong, L. D., Dijkstra, P. U., Stewart, R. E., and Postema, K. (2012). Repeated measurements of arm joint passive range of motion after stroke: interobserver reliability and sources of variation. *Physical Therapy Journal.* 92(8), 10271035.

[Pelletier 2011] Pelletier, C. A., and Hicks, A. L. (2011). Muscle fatigue characteristics in paralyzed muscle after spinal cord injury. *Spinal Cord.* 49(1), 125130.

[Ning 2012] Ning, L. and Xin, H. (2012). Fusimotor control of spindle sensitivity regulates central and peripheral coding of joint angles. *Frontiers in Computational Neuroscience.* 66(6), from http://journal.frontiersin.org/article/10.3389/fncom.2012.00066/full.

[Downey 2015] Downey, R. J., Bellman, M. .J, Kawai, H., Gregory, C. M., Dixon, W. E. (2015).Comparing the Induced Muscle Fatigue Between Asynchronous and Synchronous Electrical Stimulation in Able-Bodied and Spinal Cord Injured Populations.*IEEE Transactions on Neural Systems and Rehabilitation Engineering.* 23(6), 964-972.

[Krakauer 2011] Krakauer, J. W., Lang, C. E., Corbetta, M., Fitzpatrick, S. M.(2011). Neurological principles and rehabilitation of action disorders: common clinical deficits. *Neurorehabilitation and Neural Repair.* 25(5), 21S32S.

[Kuptniratsaikul 2011] Kuptniratsaikul, V., Kovindha, A., Suethanapornkul, S., Massakulpan, P., Permsirivanich, W., Kuptniratsaikul, PS. (2017). Motor recovery of stroke patients after rehabilitation: one-year follow-up study. *The International journal of neuroscience.* 127(1), 37-43.

[Wade 1985] Wade, D. T., Wood, V. A., Hewer, R. L., (1985). Recovery after stroke–the first 3 months. *Journal of Neurology, Neurosurgery and Psychiatry.* 48(1):7-13.

[Naghdi 2010] Naghdi, S., Ansari, N. N., Mansouri, K., Hasson, S., (2010). A neurophysiological and clinical study of Brunnstrom recovery stages in the upper limb following stroke. *Brain Injury.* 24(11),1372-1378

[Hara 2008] Hara, Y. (2008). Neurorehabilitation with new functional electrical stimulation for hemiparetic upper extremity in stroke patients. *Journal of Nippon Medical School.* 75(1), 4-14.

[Nudo 1996] Nudo, R. J., Wise, B. M., SiFuentes, F., Milliken, G. W. (1996). Neural substrates for the effects of rehabilitative training on motor recovery after ischemic infarct. *Science.* 272(5269), 1791-1794.

[Kawahira 2010] Kawahira, K., Shimodozono, M., Etoh, S., Kamada, K., Noma, T., and Tanaka, T. (2010). Effects of intensive repetition of a new facilitation technique on motor functional recovery of the hemiplegic upper limb and hand. *Brain Injury.* 24(10), 12021213.

[Page 2001] Page, S. J., Sisto, S. A., Levine, P., Johnston, M. V., Hughes, M. (2001). Modified constraint induced therapy: a randomized feasibility and efficacy study. *Journal of Rehabilitation Research and Development.* 38(5), 583-590.

[Takeuchi 2001] Takeuchi, N., Chuma, T., Matsuo, Y., Watanabe, I., Ikoma, K. (2005). Repetitive transcranial magnetic stimulation of contralesional primary motor cortex improves hand function after stroke. Stroke, 36(12), 2681-2686, study. *Journal of Rehabilitation Research and Development.* 38(5), 583-590.

[Ogata 2001] Ogata, T., Abe, H., Samura, K., Hamada, O., Nonaka, M., Iwaasa, M., Higashi, T., Fukuda, H., Shiota, E., Tsuboi, Y., and Inoue, T. (2015). Hybrid Assistive Limb (HAL) Rehabilitation in Patients with Acute Hemorrhagic Stroke. *Neurologia medico-chirurgica.* 55(12), 901-906.

[Popovic 2004] Popovic, M. R., and Thrasher, T. A. (2004). "Neuroprostheses," in Encyclopedia of biomaterials and biomedical engineering. 1056-1065.

[Petrofsky 2004] Petrofsky, J. (2008). The effect of the subcutaneous fat on the transfer of current through skin and into muscle. *Medical Engineering and Physics.* 30(9), 1168-1176

[Ward 2002] Ward AR, Robertson VJ, Makowski RJ. (2002). Optimal frequencies for electric stimulation using medium-frequency alternating current. *Archives of Physical Medicine and Rehabilitation.* 83(7), 1024-1027.

[Ward 1998] Ward, A. R. and Robertson, V. J. (1998). Variation in torque production with frequency using medium frequency alternating current. *Archives of Physical Medicine and Rehabilitation.* 79(11), 1399-1404.

[Ward 2002(a)] Ward, A. R. and Shkuratova, N. (2002) Russian electrical stimulation: the early experiments. *Physical Therapy.* 82(10). 1019-1030.

[Andrianova 1971] Andrianova, G. G., Kots, Y. M., Marmyanov, V. A., Xvilon, V. A. (1971). Primenenie elektrostimuliatsii dlia trenirovki mishechnoj sili. *Novosti Meditsinskogo Priborostroeniia.* 3, 4047.

[Collins 2007] Collins,D. F. (2007). Central contributions to contractions evoked by tetanic neuromuscular electrical stimulation. *Exercise and Sport Sciences Reviews.* 35(3),102-109.

[Gobbo 2011] Gobbo, M., Gaffurini, P., Bissolotti, L., Esposito, F., Orizio, C. (2011). Transcutaneous neuromuscular electrical stimulation: influence of electrode positioning and stimulus amplitude settings on muscle response. *European Journal of Applied Physiology.* 111(10), 2451-2459.

[Hamada 2004] Hamada, T., Kimura, T., Moritani, T. (2004). Selective fatigue of fast motor units after electrically elicited muscle contractions. *Journal of Electromyography and Kinesiology.* 14(5), 531-538.

[Thrasher 2005] Thrasher, A., Graham, G. M., Popovic, M. R. (2005). Reducing muscle fatigue due to functional electrical stimulation using random modulation of stimulation parameters. *Artificial Organs.* 29(6), 453-458.

[Graupe 2000] Graupe, D., Suliga, P., Prudian, C., Kohn, K. H. (2000). Stochastically-modulated stimulation to slow down muscle fatigue at stimulated sites in paraplegics using functional electrical stimulation for leg extension. *Neurological Research.* 22(7), 703-704.

[Graupe 2006] Graham, G. M., Thrasher, T. A., Popovic, M. R. (2006). The effect of random modulation of functional electrical stimulation parameters on muscle fatigue. *IEEE Transactions on Neural Systems and Rehabilitation Engineering.* 14(1),38-45.

[Russ 1999] Russ, D. W., Binder-Macleod, S. A. (1999). Variable-frequency trains offset low-frequency fatigue in human skeletal muscle. *Muscle and Nerve.* 22(7), 874-882.

[Kesar 2008] Kesar, T., Chou, L. W., Binder-Macleod, S. A. (2008) Effects of stimulation frequency versus pulse duration modulation on muscle fatigue. *Journal of Electromyography and Kinesiology.* 18(4), 662-671.

[Griffin 2007] Griffin, L., Jun, B. G., Covington, C., Doucet, B. M. (2007). Force output during fatigue with progressively increasing stimulation frequency. *Journal of Electromyography and Kinesiology.* 18(3), 426-33.

[Doix 2014] Doix, A. C., Matkowski, B., Martin, A., Roeleveld, K., Colson, S. S. (2014). Effect of neuromuscular electrical stimulation intensity over the tibial nerve trunk on triceps surae muscle fatigue. *European Journal of Applied Physiology.* 114(2), 317-29

[Chou 2008(a)] Chou, L. W., Lee, S. C., Johnston, T. E., Binder-Macleod, S. A. (2008). The effectiveness of progressively increasing stimulation frequency and intensity to maintain paralyzed muscle force during repetitive activation in persons with spinal cord injury. *Archives of Physical Medicine and Rehabilitation.* 89(5), 856-864.

[Chou 2008(b)] Chou, L. W., Kesar, T. M., Binder-Macleod, S. A. Using customized rate-coding and recruitment strategies to maintain forces during repetitive activation of human muscles. *Physical Therapy Journal.* 88(3), 363-375.

[Deleym 2014] Deleym, G., Laroche, D., Babault, N. (2014). Effects of electrical stimulation pattern on quadriceps force production and fatigue. *Muscle and Nerve.* 49(5), 760-763.

[Nishihara 2013] Nishihara, K., Kawai, H., Chiba, Y., Kanemura, N., Gomi, T. (2013). Investigation of innervation zone shift with continuous dynamic muscle contraction. *Computational and Mathematical Methods in Medicine* from https://www.hindawi.com/journals/cmmm/2013/174342/

[Sato 2013] Sato, Y., Suzuki, M., Kato, R., Yokoi, H., Decision technique of the most suitable placement of the stimulation electrode for limbs control using surface electrical stimulation : Design of a pulse select circuit selecting the most suitable electrodes from many electrodes, Mechanical Engineering Congress, Japan 2013.

[Jarrett 2011] Jarrett, C. D., Weir, D. M., Stuffmann, E. S., Jain, S., Miller, M. C., Schmidt, C. C. (2011). Anatomic and biomechanical analysis of the short and long head components of the distal biceps tendon. *Journal of Shoulder and Elbow Surgery.* 21(7), 942-948

[Lo 2009] Lo H. C., Tsai, K. H., Su, F. C., Chang, G. L., Yeh, C. Y. (2009). Effects of a functional electrical stimulation-assisted leg-cycling wheelchair on reducing spasticity of patients after stroke. *Journal of Rehabilitation Medicine.* 41(4), 242-246.

[Gould 1982] Gould, N., Donnermeyer, D., Pope, M., Ashikaga, (1982) T. Transcutaneous muscle stimulation as a method to retard disuse atrophy. *Clinical Orthopaedics and Related Research.* (164), 215-220.

[Marsden 2013] Marsden, J., Stevenson, V., McFadden, C., Swain, I., Taylor, P. (2013). The effects of functional electrical stimulation on walking in hereditary and spontaneous spastic paraparesis, *Journal of the International Neuromodulation Society.* 16(3), 256-260.

[Kim 2012] Mee-Young, Kim., Ju-Hyun, Kim., Jeong-Uk, Lee., Na-Mi, Yoon., Bokyung, Kim., Junghwan, Kim. (2012). The Effects of Functional Electrical Stimulation on Balance of Stroke Patients in the Standing Posture. *Journal of Physical Therapy Science.* 24(1), 77.

[Kim 2006] Kim, Y. H., You, S. H., Ko, M. H., Park, J. W., Lee, K. H., Jang, S. H., Yoo, W. K., Hallett, M. (2006). Repetitive transcranial magnetic stimulation-induced corticomotor excitability and associated motor skill acquisition in chronic stroke. *Stroke.* 37(6). 1471-1476.

[Liepert 2007] Liepert, J., Zittel, S., Weiller, C. (2007). Improvement of dexterity by single session low-frequency repetitive transcranial magnetic stimulation over the contralesional motor cortex in acute stroke: a double-blind placebo-controlled crossover trial. *Restorative Neurology Neuroscience.* 25(5-6), 461-465

[Dafotakis 2008] Dafotakis, M., Grefkes, C., Eickhoff, S. B., Karbe, H., Fink, G. R., Nowak, D. A. (2008). Effects of rTMS on grip force control following subcortical stroke. *Experimental Neurology*, 211(2), 407-412.

[Fujii 2016] Fujii, K., Abe, T., Kubota, S., Marushima, A., Kawamoto, H., Ueno, T., Matsushita, A., Nakai, K., Saotome, K., Kadone, H., Endo, A., Haginoya, A., Hada, Y., Matsumura, A., Sankai, Y., Yamazaki, M. (2016). The voluntary driven exoskeleton Hybrid Assistive Limb (HAL) for postoperative training of thoracic ossification of the posterior longitudinal ligament: a case report. *The Journal of Spinal Cord Medicine.* 9,1-7.

[Hicks 1985] Hicks, A., Fenton, J., Garner, S., McComas, A. J. (1985). M wave potentiation during and after muscle activity. *Journal of Applied Physiology.* 66(6), 2606-2610.

[Yoshida 1993] Yoshida, K., Horch, K. (1993). Reduced fatigue in electrically stimulated muscle using dual channel intrafascicular electrodes with interleaved stimulation. *Annals Biomedical Engineering.* 21(6), 709-714.

[Auriat 2015] Auriat, A. M., Neva, J. L., Peters, S., Ferris, J. K., Boyd, L. A. (2015). A Review of Transcranial Magnetic Stimulation and Multimodal Neuroimaging to Characterize Post-Stroke Neuroplasticity. *Frontiers in Neurology.*

Publication

International Journal

Rintaro KAMIHIRA, Misato KASUYA, Yinlai JIANG, Shunta TOGO, Masao SUGI, Hiroshi YOKOI :
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Awards received

The best presentation award of 2016 International Conference on Biomedical Signal and Bioinformatics.

Patent

Patent pending: The invention of motor point tracking stimulation.