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Functional Electrical Stimulation
Introduction

The reanimation of contractile function of muscle is an important advance in the field of reconstructive surgery. Contraction can be either done voluntarily after a few months when the muscle's nerve is coapted (e.g. dynamic reanimation in patients with facial paralysis\(^1\)) or with the help of an external stimulator. The latter is needed when there is an upper motor neuron injury.\(^2\) In this situation the paralyzed muscles have an intact lower motor neuron pathway from the spinal cord to the muscle endplate. To activate the paralyzed muscles an external electrical stimulus is needed. External stimulation is also required when a muscle is transposed and has to perform a function different from its native one even with intact nerve supply.\(^3\) The most optimal would be an electrical stimulation system that imitates the natural activation of skeletal muscle. The physiological route for activating skeletal muscle is via a complex mechanism in which the brain, spinal cord and peripheral nervous system are involved and interact.\(^4\) The activity imposed by chronic electrical stimulation is simple but on the other hand can have adverse effects because of improper use. Therefore, by understanding the basic knowledge of physiologic and electrical muscle stimulation one can better understand and approach the problems encountered with electrical muscle stimulation.

Functional Electrical Stimulation (FES)

Functional electrical stimulation (FES) covers the general field of using electrical stimulation to recover a lost function. This applies to the central nervous system directly (e.g., cerebellar stimulation\(^5\)), to cranial nerves (e.g., auditory prostheses\(^6\)) and to the peripheral nervous system.\(^7\) When applied in the last group to achieve functional movement, it is often referred to as functional neuromuscular stimulation (FNS). FNS is generally applied to stable neurological lesions where no further recovery is expected and it is accepted that the procedure should be effective for the lifetime of the user. Peripheral nerve stimulation also covers therapeutic stimulation, which is usually applied to enhance residual or temporarily diminished voluntary function and is of shorter duration. Finally peripheral nerve stimulation covers the field of dynamic myoplasty.

Peripheral Nerve Stimulation Physiology

Stimulation of excitable tissue is initiated by depolarizing the cell membrane. The resting transmembrane potential arises as a result of an ionic concentration difference in the intracellular and extracellular fluids of the cell
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body and axon. Normally, action potentials are generated by membrane potential changes following synaptic currents. Lowering this potential artificially results in the generation of a propagated action potential. Unmyelinated axons carry the action potential smoothly, while myelinated axons carry it in discrete steps but at faster speeds. The threshold of stimulation is the minimum stimulus amplitude or duration needed to initiate an axon potential, and this translates to a minimum amount of cathodic charge transfer necessary. Peripheral nerve stimulation to gain muscle contraction depends on delivering a controllable amount of charge to the nerve through an extracellular electrode. Action potentials can also be generated by anodic break currents. Since the thresholds for these are much higher, for practical FNS cathodic stimulation is universally used. The amplitude of the pulse needed to start an action potential is greater for pulses of shorter duration. Though one would use long duration pulses to minimize the current amplitude needed, total charge transfer should be minimized to decrease the chance of tissue injury. The threshold charge also increases with pulse width increase. This increase is due to the fact that with long duration pulses, the charge is distributed rather than being concentrated at the excitation site.

In myelinated axons there is a constant relationship between the internodal distance and the diameter of the axon (internodal distance = 100 x diameter). Thus large-diameter axons have nodes further apart than small-diameter axons. As a result, under a uniform electrical field the large fibers have a larger potential difference between adjacent nodes. The result of this is that larger fibers have lower thresholds and fire before smaller fibers, which is the reversal of the physiologic recruitment order. Although this does not affect applications where the stimulation is delivered to the muscle through epimysial or intramuscular routes, it does have importance in nerve cuff applications. Techniques have been developed using a special stimulation waveform to recruit small fibers before large. In applications in which direct nerve cuff stimulation is used, the diameter of the axons in the nerve and their distances from the stimulating electrodes have an effect on the recruitment domain and order. There are strategies by which axons can be selectively activated. Thus, only large fibers or small fibers or a group of localized fibers can be stimulated. During epimysial and intramuscular stimulation the muscle is activated by direct nerve stimulation of the intramuscular muscle branches and not through muscle fiber stimulation. The thresholds for muscle fiber activation are much higher for direct muscle stimulation as compared to direct nerve stimulation.
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Electrophysiology

The use of metal electrodes for electrical stimulation necessitates the flow of ionic charge into tissues. This can occur by capacitative or faradic mechanisms. In the former there is alternate attraction and repulsion of ions but no net transfer of electrons. Thus there is no chance of chemical changes occurring. This is an ideal mechanism of charge injection, but is limited by the maximal amount of charge that can be transferred before the dielectric breaks down. Because the charge required for physiological stimulation far exceeds that available from capacitative mechanisms, FNS depends on faradic charge injection. Faradic mechanisms involve transfer of electrons, which means that some chemicals are oxidized or reduced. This can be reversible, as when an opposing current reverses the chemical changes of the preceding stimulation pulse and no new chemicals are formed or destroyed. Thus there is no corrosion of the electrode. In irreversible processes, material is lost into the extracellular fluid.

The guiding principle for selection of electrode materials and stimulation protocols is chemical reversibility. For a particular electrode material, there is a limit to the amount of charge that can be injected before reaching the limits of the reversible processes. This charge limit depends on the electrode material, its shape and size, and the stimulation waveform. The temporal pattern of the stimulus waveform is probably the most important criteria. The least damaging waveforms are biphasic with no net direct current and charge densities within the reversible spectrum. The charges in each half of the waveform may be balanced with a symmetrical or asymmetric wave and there may be delays between the two parts of the biphasic pulse.

Biomaterials

Platinum and its alloys with iridium have been most widely used for electrical stimulation. Platinum is ideal for peripheral applications, while the addition of iridium oxide coatings allows smaller sized electrodes to be used. Of the non-noble metals, 316L stainless steel has been widely used for intramuscular electrodes.

Leads are one of the critical parts of any stimulation system, either percutaneous or implanted, since they have to be able to withstand fatigue failure from shear and joint movement. The implanted stimulators are packaged in titanium with hermetic feedthroughs for the leads. With this type of packaging, the receiving coil has to be outside the main package to avoid significant loss of radiofrequency signal. They also have been packaged in ceramic material, which allows all the components to be in one package, thus reducing the size of the stimulation device.
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Adverse Effects

Potential adverse effects of peripheral neuromuscular stimulation are the possibility of tissue damage, unwanted spillover patterns and pain. The mechanism of tissue damage falls into two categories: first, from toxicity from products of electrode dissolution, and second, from non-electrochemical mechanisms like vascular damage or neural membrane damage from passage of the electrical current. The electrochemical problem can be mitigated by following safe stimulation techniques as previously discussed. Long-term stimulation of muscles using intramuscular or epimysial electrodes can be done with no deleterious effects. Nerve cuff electrodes have the potential for causing greater damage, but careful regulation of the stimulation parameters, charge densities, total charge delivered, and electrode configurations can minimize this.

Nerve cuff electrodes have been used for many applications ranging from phrenic nerve stimulation for respiratory assist to dynamic cardiomyoplasty. As various the applications are as diverse the long-term effects are, even within the application. Glenn et al. reported a study in which quadriplegic patients with respiratory paralysis have been treated by electrical stimulation of the phrenic nerves to pace the diaphragm. The average time the 13 patients have had bilateral diaphragm pacemakers is 26 months. Injury to the phrenic nerves either by initial trauma to the cervical cord or during operation for implantation of the nerve cuff was the most significant complication. In spite of this, nerve damage from prolonged electrical stimulation has not been a problem in this study.

Application Basics

Stimulation parameters selected for electrical stimulation have the objective of depolarizing the specific fibers in the peripheral nerve generally to effect movement of a particular muscle group or groups without evoking an undesirable sensation. Because recruitment is affected by the number of active motor units and the rate of their firing, the stimulation parameters must allow these two variables (i.e., recruitment and temporal summation). There are different anatomic routes and sites for the placement of electrodes, and this diversity affects the efficacy, selectivity, adverse effects, and the stimulation parameters needed. Three types of electrodes are used, classified by invasiveness as surface, percutaneous, and implanted. With each of these electrodes, stimulation can be monopolar or bipolar. The stimulus waveform used to affect excitation is generally a biphasic current controlled waveform with equal charge contained under the negative and positive going components of the stimulus and waveform. The current controlled phase (in
contrast to using a voltage controlled phase) insures delivery of the desired amount of current to the nerve regardless of tissue impedance changes that might occur at the electrode with encapsulation.

Control of activation of the number of motor units is obtained by increasing either the current or the pulsewidth of the stimulation. Recruitment obtained in this way activates more and more motor units as either the stimulus amplitude or pulse width is increased. However, recruitment is a nonlinear property and the force versus stimulus characteristics generally show no force generated up to a specific stimulation level (known as threshold), followed by a nonlinear in the magnitude of force with increasing magnitude of stimulation. The specific relationship between the stimulus input and the force developed is unpredictable and depends significantly on the geometric relationship of the electrode to the desired nerve fibers. Thus this must be determined experimentally.

In a case of muscle-based electrodes, muscular contraction is elicited through activation of the peripheral nerve, but the electrode generally is not immediately adjacent to the nerve itself, but is rather based on or in the muscle. These electrode types generally are thus less efficient in affecting neural activation and may require a stimulus as high as 20 mA and a stimulus pulse width of as high as 200 µsec to affect strong activation of the muscle.

**Muscle Fatigue**

**General**

A universal complication of all functional electrical stimulated muscle in situ or transferred muscle (dynamic myoplasty) is muscle fatigue. Muscles require maintenance of adenosine triphosphate (ATP) within the myofibers to generate force through the contractile interaction of actin and myosin proteins. In the absence of adequate oxygen delivery, muscle dependence upon aerobic mechanisms of metabolism for ATP generation will become limited and dependence upon anaerobic metabolic mechanisms will prevail. A consequence of this shift to anaerobic metabolism is a reduction in ATP production and an increase in lactic acid production. While the etiology of muscle fatigue is complex and can result from many contributing factors, the combination of decreased ATP availability and decreased intracellular pH from lactic acidosis certainly contribute to the failure of muscle to produce contractile force. 

In activation of muscle, electrical stimulation provides an unnatural means of eliciting firing of the motor units. All other factors considered equal, the recruitment order achieved for electrical stimulation is through large motor units (innervating fast-contracting, fast-fatiguing motor units) being excited at lower thresholds than those for slow contracting, slow twitch motor units.
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This is the reverse order of recruitment of that achieved during normal voluntary contraction. In actual implementation the activation pattern is considerably more complex because smaller motor units may be closer to the electrode than larger motor units. Thus, the inverse size principle may not be as critical in differentiating the recruitment order. These alterations of the metabolic properties of the muscle are important in its ultimate clinical use. In particular one encounters reductions in either the maximum force that can be generated or the ability to sustain muscle contraction.

With regard to fatigue, two properties are known to be most important. They are the metabolic profile of the muscle which is being excited and the frequency of stimulation which is delivered to the nerve. For the metabolic profile it is well known that most muscles are composed of motor units that possess different contractile properties, which allow them to act over a wide range of speed of contraction and endurance. In upper motor neuron injury paralyzed muscle is distinguished by having lost many characteristics and is composed of a greater uniformity of fibers, which contractile speeds are similar to fast contracting and relaxing and fast fatiguing. Because of this, electrically stimulated muscle fatigues quite rapidly and generates little force. A second factor with a significant influence on muscle fatigue is the frequency of activation. It is well known that the muscle generates greater force at higher stimulus frequencies and that a minimum stimulus frequency of 10 to 15 Hz is required to produce a fused contraction of a muscle with slow contraction characteristics. Stimulation at low frequencies is desired, because the force-time properties of the muscle are extended. Thus, in obtaining functional use of muscle, one desires low frequencies for greater endurance but higher frequencies for increased force.

Fatigue in FES

Various methods have been used to reduce fatigue in functional electrical stimulation. These include 1. Chronic electrical stimulation in an attempt to convert fast type II fatigue prone fibers to slow type I fatigue resistant fibers; 2. Modulation of electrical parameters; 3. Alternate stimulation, whereby the different muscles that do the same function are stimulated alternately (e.g. stimulating different muscles in the lower limb alternately to maintain tedious tasks as standing); 4. Sequential stimulation and 5. Varying regimens of nerve stimulation. Each of these methods has its advantages and disadvantages. In dynamic myoplasty typically muscles are moved to new locations while maintaining only one neurovascular pedicle and then forced through extraneous pulse generators to functionally perform in this new location. The new functional demand is not normal for this muscle and thus fatigues fairly easily. In dynamic myoplasty muscle fatigues primarily for two reasons: they have inadequate perfusion and or they are stimulated to contract at a
frequency that is incompatible with their basic muscle fiber type (the latter being in all functional electrical stimulation applications). The use of extraneous stimulation devices produces skeletal muscle contractions capable of generating significant force but the muscle cannot maintain force generation due to fatigue of the muscle. As an anatomical muscle contracts, the individual myofibers within the muscle place significant pressure on the blood vessels within the muscle. Due to these high transmural pressures, a tetanic contraction has the effect of occluding blood flow through the muscle during contraction. This reduction of perfusion due to internal muscle pressure contributes to the failure to deliver adequate oxygen and nutrients to the contracting muscle and precipitates fatigue of the muscle and failure to generate force despite continued stimulation.

Another factor in dynamic myoplasty that indirectly contributes to fatigue might be the unfavorable resting length from which the muscle has to start contracting. It is known that the length of the muscle in terms of bridge kinetics has a determining influence on the force it can generate. In a sphincter model the muscle is wrapped in the shape of a cylinder. Since the muscle is no longer fixed via its tendons it shortens because of its elastic components. In the shortened position maximum contractile strength cannot be developed since there is not an optimum overlap of actin and myosin filaments.

**Training Regimen**

An approach used in dynamic myoplasty to avoid muscle failure due to fatigue is to train the muscle to enhance fatigue resistance. Training protocols currently in use require an 8 week period of stimulation at increasing frequency until the muscle is converted to a fatigue resistant fiber type. Skeletal or striated muscles are normally a mixture of fatigue-prone, fast-twitch, glycolytic (type II) and fatigue-resistant, slow-twitch, oxidative (type I) muscle fibers. The innervation and the function of the muscle determine the predominance of one fiber type over another and all fiber types in a given motor unit are the same. But striated muscle is plastic in nature and the training regimen transforms the muscle to predominantly type I. The trade-off for producing fatigue resistance is a slower contracting muscle capable of generating less power than its innate character.

**Sequential Stimulation**

While there are many factors that probably contribute to the found difficulties in using a training protocol to enhance fatigue resistance, one reason for the variable outcomes could relate to the way the muscle is being electrically stimulated. Under normal circumstances, a given anatomical muscle can respond and adapt to generation of fine control, prolonged sustained activity,
or brief intense activity. The response generated by muscle depends upon the types of motor units (and therefore myofiber types) contained within the muscle and the pattern of activity in which they are engaged. Current applications of dynamic myoplasty call for tetanic stimulation and contraction of all myofibers simultaneously. This tetanic type contraction occurs rarely in normal conditions and can lead to irreversible muscle damage. On the basis of the earlier described drawbacks of training regimens an entirely different -more physiologic- approach to minimize skeletal muscle fatigue was developed by Zonnevijlle et al. Rather than stimulating an entire gracilis muscle in one electrical burst and thus recruiting the same fibers simultaneously, they studied the feasibility of stimulating different gracilis muscle segments sequentially. This approach allows parts of the muscle to rest while other parts work. This sequential segmental neuromuscular stimulation (SSNS) of the gracilis significantly enhanced resistance to fatigue in comparison with whole muscle stimulation. These findings agreed with literature addressing endurance enhancement in neuromuscular prosthesis research for gait, in which alternation between agonistic muscles proved to be beneficial. They are also in agreement with observations described in the literature concerning the indirect or neural multichannel stimulation, which was also developed to sequentially recruit separate parts of a muscle.

Feedback Control
The control paradigms used in FNS have been described as open-loop and closed-loop systems. In the open-loop paradigm, a single command or group of commands is used to supply a stimulus to the muscle, which then for example generates a force acting across the joint. The resulting torque is balanced by the load, gravity, or an opposing muscle. In the open-loop system, a single command is used to simultaneously control the stimulus levels, which are provided to an entire group of muscles that generate a coordinated action. This system does not incorporate any changes in the performance of the muscle, such as fatigue or changes in the load, in the predicted performance. Rather, the subject has the entire responsibility of using the command to regulate the output performance. In contrast, closed-loop control uses sensors to alter the performance of the system. An example of a closed-loop system would be one in which detection of muscle force is required because of fatigue. In this case, by measuring muscle force, the control system can automatically compensate for changes in the muscle force due to an alteration in muscle performance. There are many other examples of such closed-loop control systems, including walking systems, in which the contact of the foot on the floor is used to regulate subsequent stimulus actions, and control systems, in which a sensor is provided to the joint to ensure that the joint moves through its desired trajectory at a known rate. Closed-loop systems
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clearly require sensors as a critical element in their implementation. Significant effort has gone into developing sensors for measuring parameters such as foot to floor contact, force grasp, individual muscle force through the bioelectric signal, intramuscular bioelectrical signal, intramuscular pressure and tendon force, joint angle and so forth. Complex arm movements, involving grasp and release control of the forearm, wrist, elbow, and shoulder, have been achieved by using feedback control.

SSNS was introduced by Zonnevijlle et al. to reduce muscle fatigue in applications like graciloplasty, so that a prolonged training period could be avoided and the neo-sphincter could be activated soon after surgery to improve patient quality of life more immediately than current approaches permit. To produce this most desired effect, the muscle was proposed to animate in a fashion that allowed it to contract according to need. A normally functioning native sphincter utilizes control mechanisms to regulate when and to what degree contraction occurs, thus maintaining continence without resorting to maximal sphincter contraction for prolonged periods of time. Therefore, closed-loop control of the force generated by the neo-sphincter was applied and combined with SSNS to mimic true physiologic sphincter function. This study showed that closed loop control and sequential segmental stimulation can be effectively combined to acutely control force generation.
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