AUGMENTATION OF MUSCLE CONTRACTILITY BY BIPHASIC STIMULATION

166166

Inventor: Morton M. Mower, M.D.

RELATED APPLICATION DATA

The present disclosure is a continuation-in-part application related to the U.S. Patent Application entitled AElectrical Conduction and Contractility by Biphasic Cardiac Pacing Administered Via the Cardiac Blood Pool,@ Serial No. 09/008,636, filed January 16, 1998, which is a continuation-in-part application related to the U.S. Patent Application entitled AAugmentation of Electrical Conduction and Contractility by Biphasic Cardiac Pacing,@ Serial No. 08/699,552, filed August 8, 1996.

FIELD OF THE INVENTION

This invention relates generally to a method for the stimulation of muscle tissue. In particular, this invention relates to a method for stimulation of muscle tissue with biphasic waveforms that reduce the electrical energy required to elicit contraction.

BACKGROUND OF THE INVENTION

The function of the cardiovascular system is vital for survival. Through blood circulation, body tissues obtain necessary nutrients and oxygen, and discard waste substances. In the absence of circulation, cells begin to undergo irreversible changes that lead to death. The muscular contractions of the heart are the driving force behind circulation.

In cardiac muscle, the muscle fibers are interconnected in branching networks that spread in all directions through the heart. When any portion of this net is stimulated, a depolarization wave passes to all of its parts and the entire structure contracts as a unit. Before a muscle fiber can be stimulated to contract, its membrane must be polarized. A muscle fiber generally remains polarized until it is stimulated by some change in its environment. A membrane can be stimulated electrically, chemically, mechanically or by temperature change. The minimal stimulation strength needed to elicit a contraction is known as the threshold stimulus. The maximum stimulation amplitude that may be administered

G00002

without eliciting a contraction is the maximum subthreshold amplitude.

Where the membrane is stimulated electrically, the impulse amplitude required to elicit a response is dependent upon a number of factors. First, is the duration of current flow. Since the total charge transferred is equal to the current amplitude times the pulse duration, increased stimulus duration is associated with a decrease in threshold current amplitude. Second, the percentage of applied current that actually traverses the membrane varies inversely with electrode size. Third, the percentage of applied current that actually traverses the membrane varies directly with the proximity of the electrode to the tissue. Fourth, the impulse amplitude required to elicit a response is dependent upon the timing of stimulation within the excitability cycle.

Throughout much of the heart are clumps and strands of specialized cardiac muscle tissue. This tissue comprises the cardiac conduction system and serves to initiate and distribute depolarization waves throughout the myocardium. Any interference or block in cardiac impulse conduction may cause an arrhythmia or marked change in the rate or rhythm of the heart

Sometimes a patient suffering from a conduction disorder can be helped by an artificial pacemaker. Such a device contains a small battery powered electrical stimulator. When the artificial pacemaker is installed, electrodes are generally threaded through veins into the right ventricle, or into the right atrium and right ventricle, and the stimulator is planted beneath the skin in the shoulder or abdomen. The leads are planted in intimate contact with the cardiac tissue. The pacemaker then transmits rhythmic electrical impulses to the heart, and the myocardium responds by contracting rhythmically. Implantable medical devices for the pacing of the heart are well known in the art and have been used in humans since approximately the mid 1960s.

Either cathodal or anodal current may be used to stimulate the myocardium. However anodal current is thought not to be useful clinically. Cathodal current comprises electrical pulses of negative polarity. This type of current depolarizes the cell membrane by discharging the membrane capacitor, and directly reduces the membrane potential toward threshold level. Cathodal current, by directly reducing the resting membrane potential toward threshold, has a one-half to one-third lower threshold current in late diastole than does anodal current. Anodal current comprises electrical pulses of positive polarity. The effect of anodal current is to hyperpolarize the resting membrane. On sudden termination of the anodal pulse, the membrane potential returns towards resting level, overshoots to threshold, and a

propagated response occurs. The use of anodal current to stimulate the myocardium is generally discouraged due to the higher stimulation threshold, which leads to use of a higher current, resulting in a drain on the battery of an implanted device and impaired longevity. Additionally, the use of anodal current for cardiac stimulation is discouraged due to the suspicion that the anodal contribution to depolarization can, particularly at higher voltages, contribute to arrhythmogenesis.

Virtually all artificial pacemaking is done using stimulating pulses of negative polarity, or in the case of bipolar systems, the cathode is closer to the myocardium than is the anode. Where the use of anodal current is disclosed, it is generally as a charge of minute magnitude used to dissipate residual charge on the electrode. This does not affect or condition the myocardium itself. Such a use is disclosed in U.S. Patent No. 4,543,956 to Herscovici.

The use of a triphasic waveform has been disclosed in U.S. Patent Nos. 4,903,700 and 4,821,724 to Whigham et al., and U.S. Patent No. 4,343,312 to Cals et al. Here, the first and third phases have nothing to do with the myocardium per se, but are only envisioned to affect the electrode surface itself. Thus, the charge applied in these phases is of very low amplitude.

Lastly, biphasic stimulation is disclosed in U.S. Patent No. 4,402,322 to Duggan. The goal of this disclosure is to produce voltage doubling without the need for a large capacitor in the output circuit. The phases of the biphasic stimulation disclosed are of equal magnitude and duration.

What is needed is an improved means for stimulating muscle tissue, wherein the contraction elicited is enhanced and the damage to the tissue adjacent to the electrode is diminished.

Enhanced myocardial function is obtained through the biphasic pacing of the present invention. The combination of cathodal with anodal pulses of either a stimulating or conditioning nature, preserves the improved conduction and contractility of anodal pacing while eliminating the drawback of increased stimulation threshold. The result is a depolarization wave of increased propagation speed. This increased propagation speed results in superior cardiac contraction leading to an improvement in blood flow. Improved stimulation at a lower voltage level also results in reduction in power consumption and increased life for pacemaker batteries.

As with the cardiac muscle, striated muscle may also be stimulated electrically, chemically, mechanically or by temperature change. Where the muscle fiber is stimulated by

a motor neuron, the neuron transmits an impulse which activates all of the muscle fibers within its control, that is, those muscle fibers in its motor unit. Depolarization in one region of the membrane stimulates adjacent regions to depolarize as well, resulting in a wave of depolarization traveling over the membrane in all directions away from the site of stimulation. Thus, when a motor neuron transmits an impulse, all the muscle fibers in its motor unit are stimulated to contract simultaneously.

The minimum strength to elicit a contraction is called the threshold stimulus. Once this level of stimulation has been met, the generally held belief is that increasing the level will not increase the contraction. Additionally, since the muscle fibers within each muscle are organized into motor units, and each motor unit is controlled by a single motor neuron, all of the muscle fibers in a motor unit are stimulated at the same time. However, the whole muscle is controlled by many different motor units that respond to different stimulation thresholds. Thus, when a given stimulus is applied to a muscle, some motor units may respond while others may not.

The combination of cathodal and anodal pulses of the present invention also provides improved contraction of striated muscle where electrical muscular stimulation is indicated due to neural or muscular damage. Where nerve fibers have been damaged due to trauma or disease, muscle fibers in the regions supplied by the damaged nerve fiber tend to undergo atrophy and waste away. A muscle that cannot be exercised may decrease to half of its usual size in a few months. Where there is no stimulation, not only will the muscle fibers decrease in size, but they will become fragmented and degenerated, and replaced by connective tissue. Through electrical stimulation, one may maintain muscle tone such that, upon healing or regeneration of the nerve fiber, viable muscle tissue remains, and the overall regenerative process is thereby enhanced and assisted.

Striated muscle stimulation can also serve to preserve the neural pathway, such that, upon healing of the nerve fibers associated with the stimulated tissue, the patient Aremembers@ how to contract that particular muscle. Enhanced striated muscle contraction is obtained through the biphasic stimulation of the present invention. The combination of cathodal with anodal pulses of either a stimulating or conditioning nature results in contraction of a greater number of motor units at a lower voltage level, leading to superior muscle response.

Lastly, biphasic stimulation as provided by the present invention may be desirable to stimulate smooth muscle tissue, such as those muscles responsible for the movements that

force food through the digestive tube, constrict blood vessels and empty the urinary bladder. For example, appropriate stimulation could rectify the difficulties associated with incontinence.

SUMMARY OF THE INVENTION

It is therefore an object of the present invention to provide improved electrical stimulation of muscle tissue.

It is another object of the present invention to extend battery life of implantable electrical stimulation devices.

It is a further object of the present invention to obtain effective muscle stimulation at a lower voltage level.

It is a further object of the present invention to provide improved stimulation of muscle tissue, particularly striated muscle.

It is a further object of the present invention to provide contraction of a greater number of muscle motor units at a lower voltage level.

It is a further object of the present invention to provide contraction of a greater number of muscle motor units at a lower level of electrical current.

A method and apparatus for muscular stimulation in accordance with the present invention includes the administration of biphasic stimulation to the muscle tissue, wherein both cathodal and anodal pulses are administered.

According to a still further aspect of this invention, the stimulation is administered to muscle tissue to evoke muscular response. Stimulation may be administered directly or indirectly to muscle tissue, where indirect administration includes stimulation through the skin. Using the present invention, lower levels of electrical energy (voltage and/or current) are needed to reach the threshold stimulus, compared to conventional stimulation methods. Muscle tissue that may benefit from stimulation according to the present invention include skeletal (striated) muscle, cardiac muscle, and smooth muscle.

The electronics required for the implantable stimulation devices needed to practice the method of the present invention are well known to those skilled in the art. Current implantable stimulation devices are capable of being programmed to deliver a variety of pulses, including those disclosed herein. In addition, the electronics required for indirect muscle stimulation are also well known to those skilled in the art and are readily modified to

practice the method of the present invention.

The method and apparatus of the present invention comprises a first and second stimulation phase, with each stimulation phase having a polarity, amplitude, shape, and duration. In a preferred embodiment, the first and second phases have differing polarities. In one alternative embodiment, the two phases are of differing amplitude. In a second alternative embodiment, the two phases are of differing duration. In a third alternative embodiment, the first phase is in a chopped wave form. In a fourth alternative embodiment, the amplitude of the first phase is ramped. In a preferred alternative embodiment, the first phase of stimulation is an anodal pulse at maximum subthreshold amplitude for a long duration, and the second phase of stimulation is a cathodal pulse of short duration and high amplitude. It is noted that the aforementioned alternative embodiments can be combined in differing fashions. It is also noted that these alternative embodiments are intended to be presented by way of example only, and are not limiting.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a schematic representation of leading anodal biphasic stimulation.

Fig. 2 is a schematic representation of leading cathodal biphasic stimulation.

Fig. 3 is a schematic representation of leading anodal stimulation of low level and long duration, followed by conventional cathodal stimulation.

Fig. 4 is a schematic representation of leading anodal stimulation of ramped low level and long duration, followed by conventional cathodal stimulation.

Fig. 5 is a schematic representation of leading anodal stimulation of low level and short duration, administered in series, followed by conventional cathodal stimulation.

Fig. 6 graphs conduction velocity transverse to the fiber vs. pacing duration resulting from leading anodal biphasic pulse.

Fig. 7 graphs conduction velocity parallel to the fiber vs. pacing duration resulting from leading anodal biphasic pulse.

DETAILED DESCRIPTION

The present invention relates to the biphasic electrical stimulation of muscle tissue. Fig.

1 depicts biphasic electrical stimulation wherein a first stimulation phase, comprising anodal stimulus **102**, is administered having amplitude **104** and duration **106**. This first stimulation phase is immediately followed by a second stimulation phase comprising cathodal stimulation **108** of equal intensity and duration.

Fig. 2 depicts biphasic electrical stimulation wherein a first stimulation phase, comprising cathodal stimulation **202** having amplitude **204** and duration **206**, is administered. This first stimulation phase is immediately followed by a second stimulation phase comprising anodal stimulation **208** of equal intensity and duration.

Fig. 3 depicts a preferred embodiment of the present invention wherein a first stimulation phase, comprising low level, long duration anodal stimulation **302** having amplitude **304** and duration **306**, is administered. This first stimulation phase is immediately followed by a second stimulation phase comprising cathodal stimulation **308** of conventional intensity and duration. In an alternative embodiment of the invention, anodal stimulation **302** is at maximum subthreshold amplitude. In yet another alternative embodiment of the invention, anodal stimulation **302** is less than three volts. In another alternative embodiment of the invention, anodal stimulation **302** is a duration of approximately two to eight milliseconds. In yet another alternative embodiment of the invention, cathodal stimulation **308** is of a short duration. In another alternative embodiment of the invention, cathodal stimulation **308** is approximately 0.3 to 0.8 millisecond. In yet another alternative embodiment of the invention, cathodal stimulation **308** is of a high amplitude. In another alternative embodiment of the invention, cathodal stimulation **308** is in the approximate range of three to twenty volts. In yet another alternative embodiment of the present invention, cathodal stimulation **308** is of a duration less than 0.3 millisecond and at a voltage greater than twenty volts. In another alternative embodiment of the present invention, cathodal stimulation **308** lasts as long as 6.0 milliseconds and has a voltage as low as 200 millivolts. In the manner disclosed by these embodiments, as well as those alterations and modifications which may become obvious upon the reading of this specification, a maximum membrane potential without activation is achieved in the first phase of stimulation.

Fig. 4 depicts an alternative preferred embodiment of the present invention wherein a first stimulation phase, comprising anodal stimulation **402**, is administered over period **404** with rising intensity level **406**. The ramp of rising intensity level **406** may be linear or non-linear, and the slope may vary. This anodal stimulation is immediately followed by a second

stimulation phase comprising cathodal stimulation **408** of conventional intensity and duration. In an alternative embodiment of the invention, anodal stimulation **402** rises to a maximum subthreshold amplitude. In yet another alternative embodiment of the invention, anodal stimulation **402** rises to a maximum amplitude that is less than three volts. In another alternative embodiment of the invention, anodal stimulation **402** is a duration of approximately two to eight milliseconds. In yet another alternative embodiment of the invention, cathodal stimulation **408** is of a short duration. In another alternative embodiment of the invention, cathodal stimulation **408** is approximately 0.3 to 0.8 millisecond. In yet another alternative embodiment of the invention, cathodal stimulation **408** is of a high amplitude. In another alternative embodiment of the invention, cathodal stimulation **408** is in the approximate range of three to twenty volts. In yet another alternative embodiment of the present invention, cathodal stimulation **408** is of a duration less than 0.3 milliseconds and at a voltage greater than twenty volts. In another alternative embodiment of the present invention, cathodal stimulation **408** lasts as long as 6.0 milliseconds and has a voltage as low as 200 millivolts. In the manner disclosed by these embodiments, as well as those alterations and modifications which may become obvious upon the reading of this specification, a maximum membrane potential without activation is achieved in the first phase of stimulation.

Fig. 5 depicts biphasic electrical stimulation wherein a first stimulation phase, comprising series **502** of anodal pulses, is administered at amplitude **504**. In one embodiment, rest period **506** is of equal duration to stimulation period **508**, and is administered at baseline amplitude. In an alternative embodiment, rest period **506** is of a differing duration than stimulation period **508** and is administered at baseline amplitude. Rest period **506** occurs after each stimulation period **508**, with the exception that a second stimulation phase, comprising cathodal stimulation **510** of conventional intensity and duration, immediately follows the completion of series **502**. In an alternative embodiment of the invention, the total charge transferred through series **502** of anodal stimulation is at the maximum subthreshold level. In another alternative embodiment of the invention, cathodal stimulation **510** is of a short duration. In yet another alternative embodiment of the invention, cathodal stimulation **510** is approximately 0.3 to 0.8 millisecond. In another alternative embodiment of the invention, cathodal stimulation **510** is of a high amplitude. In yet another alternative embodiment of the invention, cathodal stimulation **510** is in the approximate range of three to twenty volts. In another alternative embodiment of the invention, cathodal

stimulation **510** is of a duration less than 0.3 millisecond and at a voltage greater than twenty volts. In another alternative embodiment of the present invention, cathodal stimulation **510** lasts as long as 6.0 milliseconds and has a voltage as low as 200 millivolts.

EXAMPLE 1

Stimulation and propagation characteristics of the myocardium were studied in isolated hearts using pulses of differing polarities and phases. The experiments were carried out in five isolated Langendorff perfused rabbit hearts. Conduction velocity on the epicardium was measured using an array of bipolar electrodes. Measurements were made between six millimeters and nine millimeters from the stimulation site. Transmembrane potential was recorded using a floating intracellular microelectrode. The following protocols were examined: monophasic cathodal pulse, monophasic anodal pulse, leading cathodal biphasic pulse, and leading anodal biphasic pulse.

Table 1 discloses the conduction speed transverse to fiber direction for each stimulation protocol administered, with stimulations of three, four and five volts and two millisecond pulse duration.

TABLE 1

Conduction Speed Transverse to Fiber Direction, 2 msec duration

	3 V	4 V	5 V
Cathodal Monophasic	18.9 ± 2.5 cm/sec	21.4 ± 2.6 cm/sec	23.3 ± 3.0 cm/sec
Anodal Monophasic	24.0 ± 2.3 cm/sec	27.5 ± 2.1 cm/sec	31.3 ± 1.7 cm/sec
Leading Cathodal Biphasic	27.1 ± 1.2 cm/sec	28.2 ± 2.3 cm/sec	27.5 ± 1.8 cm/sec
Leading Anodal Biphasic	26.8 ± 2.1 cm/sec	28.5 ± 0.7 cm/sec	29.7 ± 1.8 cm/sec

Table 2 discloses the conduction speed along fiber direction for each stimulation protocol administered, with stimulations of three, four and five volts and two millisecond pulse duration.

TABLE 2

Conduction Speed Along Fiber Direction, 2 msec stimulation

	3 V	4 V	5 V
Cathodal Monophasic	45.3 ± 0.9 cm/sec	47.4 ± 1.8 cm/sec	49.7 ± 1.5 cm/sec
Anodal Monophasic	48.1 ± 1.2 cm/sec	51.8 ± 0.5 cm/sec	54.9 ± 0.7 cm/sec

Leading Cathodal Biphasic	50.8 ± 0.9 cm/sec	52.6 ± 1.1 cm/sec	52.8 ± 1.7 cm/sec
Leading Anodal Biphasic	52.6 ± 2.5 cm/sec	55.3 ± 1.5 cm/sec	54.2 ± 2.3 cm/sec

The differences in conduction velocities between the cathodal monophasic, anodal monophasic, leading cathodal biphasic and leading anodal biphasic were found to be significant ($p < 0.001$). From the transmembrane potential measurements, the maximum upstroke ((dV/dt)max) of the action potentials was found to correlate well with the changes in conduction velocity in the longitudinal direction. For a four volt pulse of two millisecond duration, (dV/dt)max was 63.5 ± 2.4 V/sec for cathodal and 75.5 ± 5.6 V/sec for anodal pulses.

EXAMPLE 2

The effects of varying pacing protocols on cardiac electrophysiology were analyzed using Langendorff prepared isolated rabbit hearts. Stimulation was applied to the heart at a constant voltage rectangular pulse. The following protocols were examined: monophasic anodal pulse, monophasic cathodal pulse, leading anodal biphasic pulse, and leading cathodal biphasic pulse. Administered voltage was increased in one volt steps from one to five volts for both anodal and cathodal stimulation. Duration was increased in two millisecond steps from two to ten milliseconds. Epicardial conduction velocities were measured along and transverse to the left ventricular fiber direction at a distance between three to six millimeters from the left ventricular free wall. Figs. 6 and 7 depict the effects of stimulation pulse duration and the protocol of stimulation administered on the conduction velocities.

Fig. 6 depicts the velocities measured between three millimeters and six millimeters transverse to the fiber direction. In this region, cathodal monophasic stimulation **602** demonstrates the slowest conduction velocity for each stimulation pulse duration tested. This is followed by anodal monophasic stimulation **604** and leading cathodal biphasic stimulation **606**. The fastest conduction velocity is demonstrated by leading anodal biphasic stimulation **608**.

Fig. 7 depicts the velocities measured between three millimeters and six millimeters parallel to the fiber direction. In this region, cathodal monophasic stimulation **702** demonstrates the slowest conduction velocity for each stimulation pulse duration tested. Velocity results of anodal monophasic stimulation **704** and leading cathodal biphasic

stimulation **706** are similar to those with anodal monophasic stimulation, but demonstrating slightly quicker speeds. The fastest conduction velocity is demonstrated by leading anodal biphasic stimulation **708**.

In one aspect of the invention, electrical stimulation is administered to the cardiac muscle. The anodal stimulation component of biphasic electrical stimulation augments cardiac contractility by hyperpolarizing the tissue prior to excitation, leading to faster impulse conduction, more intracellular calcium release, and the resulting superior cardiac contraction. The cathodal stimulation component eliminates the drawbacks of anodal stimulation, resulting in effective cardiac stimulation at a lower voltage level than would be required with anodal stimulation alone. This, in turn, extends pacemaker battery life and reduces tissue damage.

In a second aspect of the invention, biphasic electrical stimulation is administered to the cardiac blood pool, that is, the blood entering and surrounding the heart. This enables cardiac stimulation without the necessity of placing electrical leads in intimate contact with cardiac tissue, thereby diminishing the likelihood of damage to this tissue. The stimulation threshold of biphasic stimulation administered via the blood pool is in the same range as standard stimuli delivered directly to the heart muscle. Through the use of biphasic electrical stimulation to the cardiac blood pool it is therefore possible to achieve enhanced cardiac contraction, without skeletal muscle contraction, cardiac muscle damage or adverse effects to the blood pool.

In a third aspect of the invention, biphasic electrical stimulation is applied to striated (skeletal) muscle tissue. The combination of anodal with cathodal stimulation results in the contraction of a greater number of muscle motor units at lower levels of voltage and/or electrical current, resulting in improved muscle response. The benefits of the present invention are realized both when there is direct stimulation, as well as when the stimulation is indirect (through the skin). Benefits may be realized in physical therapy and muscle rehabilitation contexts, for example, stimulation of muscles over time while waiting for damaged nerves to regenerate.

In a fourth aspect of the invention, biphasic electrical stimulation is applied to smooth muscle tissue. Visceral smooth muscle is found in the walls of hollow visceral organs such as the stomach, intestines, urinary bladder and uterus. The fibers of smooth muscles are capable of stimulating each other. Thus, once one fiber is stimulated, the depolarization wave moving over its surface may excite adjacent fibers, which in turn stimulate still others. Benefits of

such stimulation can be realized, for example, in situations where incontinence has been caused by trauma or disease.

Having thus described the basic concept of the invention, it will be readily apparent to those skilled in the art that the foregoing detailed disclosure is intended to be presented by way of example only, and is not limiting. Various alterations, improvements and modifications will occur and are intended to those skilled in the art, but are not expressly stated herein. These modifications, alterations and improvements are intended to be suggested hereby, and within the scope of the invention. Further, the stimulating pulses described in this specification are well within the capabilities of existing electronics with appropriate programming. Biphasic stimulation as provided by the present invention may be desirable in additional situations where electrical stimulation is indicated; such as, nerve tissue stimulation and bone tissue stimulation. Accordingly, the invention is limited only by the following claims and equivalents thereto.

CLAIMS

What is claimed is:

1. A method for stimulating muscle tissue, comprising:

defining a first stimulation phase with a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation;

defining a second stimulation phase with a polarity opposite to the first phase polarity, a second phase amplitude, a second phase shape, and a second phase duration; and

applying the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle.

2. The method for stimulating muscle tissue with biphasic waveforms according to claim 6, where the first phase amplitude is equal to or less than a maximum subthreshold amplitude.

3. The method for stimulating muscle tissue according to claim 1, where the first phase polarity is positive.

4. The method for stimulating muscle tissue according to claim 1, where the absolute value of the first phase amplitude is less than the absolute value of the second phase amplitude.

5. The method for stimulating muscle tissue according to claim 1, where the absolute value of the first phase amplitude is less than the absolute value of the second phase amplitude.

6. A method for stimulating muscle tissue with biphasic waveforms, comprising:

defining a first stimulation phase with a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation;

defining a second stimulation phase with a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

applying the first stimulation phase and the second stimulation phase in sequence to

the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the first phase amplitude is ramped from a baseline value to a second value.

7. A method for stimulating muscle tissue with biphasic waveforms, comprising:

defining a first stimulation phase with a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation;

defining a second stimulation phase with a polarity opposite to the first phase polarity, a second phase amplitude, a second phase shape, and a second phase duration; and

applying the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the first phase amplitude is ramped from a baseline value to a second value, and wherein the absolute value of the second value is equal to the absolute value of the second phase amplitude.

8. A method for stimulating muscle tissue with biphasic waveforms, comprising:

defining a first stimulation phase with a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation;

defining a second stimulation phase with a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

applying the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the first stimulation phase further comprises a series of stimulating pulses of a predetermined amplitude, polarity, and duration.

9. The method for stimulating muscle tissue with biphasic waveforms according to claim 8, where the first stimulation phase further comprises a series of rest periods.

10. The method for stimulating muscle tissue with biphasic waveforms according to

claim 9, where applying the first stimulation phase further comprises applying a rest period of a baseline amplitude after at least one stimulating pulse.

11. The method for stimulating muscle tissue with biphasic waveforms according to claim 10, where the rest period is of equal duration to the duration of the stimulating pulse.

12. A method for stimulating muscle tissue with biphasic waveforms, comprising:

defining a first stimulation phase with a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation;

defining a second stimulation phase with a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

applying the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the first phase polarity is positive and the maximum subthreshold amplitude is about 0.5 to 3.5 volts.

13. The method for stimulating muscle tissue according to claim 1, where the first phase duration is at least as long as the second phase duration.

14. A method for stimulating muscle tissue with biphasic waveforms, comprising:

defining a first stimulation phase with a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation;

defining a second stimulation phase with a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

applying the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the first phase duration is at least as long as the second phase duration and the first phase duration is about one to nine milliseconds.

15. A method for stimulating muscle tissue with biphasic waveforms, comprising:

defining a first stimulation phase with a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation;

defining a second stimulation phase with a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

applying the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the first phase duration is at least as long as the second phase duration and the second phase duration is about 0.2 to 0.9 millisecond.

16. A method for stimulating muscle tissue with biphasic waveforms, comprising:

defining a first stimulation phase with a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation;

defining a second stimulation phase with a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

applying the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the second phase amplitude is about two volts to twenty volts.

17. A method for stimulating muscle tissue with biphasic waveforms, comprising:

defining a first stimulation phase with a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation;

defining a second stimulation phase with a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

applying the first stimulation phase and the second stimulation phase in sequence to

the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the second phase duration is less than 0.3 milliseconds and the second phase amplitude is greater than twenty volts.

18. The method for stimulating muscle tissue with biphasic waveforms according to claim 6, where the second value is at a maximum subthreshold amplitude.

19. The method for stimulating muscle tissue with biphasic waveforms according to claim 18, where the maximum subthreshold amplitude is about 0.5 to 3.5 volts.

20. The method for stimulating muscle tissue with biphasic waveforms according to claim 6, where the first phase duration is at least as long as the second phase duration.

21. The method for stimulating muscle tissue with biphasic waveforms according to claim 6, where the first phase duration is about one to nine milliseconds.

22. The method for stimulating muscle tissue with biphasic waveforms according to claim 6, where the second phase duration is about 0.2 to 0.9 millisecond.

23. The method for stimulating muscle tissue with biphasic waveforms according to claim 6, where the second phase amplitude is about two volts to twenty volts.

24. The method for stimulating muscle tissue with biphasic waveforms according to claim 6, where the second phase duration is less than 0.3 millisecond, and the second phase amplitude is greater than 20 volts.

25. A method for stimulating muscle tissue according to claim 1, where the stimulation to the muscle is selected from the group consisting of direct stimulation to the muscle and indirect stimulation to the muscle.

26. A method for stimulating muscle tissue with biphasic waveforms, comprising:

defining a first stimulation phase with a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation;

defining a second stimulation phase with a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

applying the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the stimulation to the muscle is selected from the group consisting of direct stimulation to the muscle and indirect stimulation to the muscle; and

wherein the indirect stimulation is administered through skin.

27. The method for stimulating muscle tissue with biphasic waveforms according to claim 6, where the second phase duration is less than approximately 6 milliseconds and the second phase amplitude is at least 200 millivolts.

28. A method for stimulating muscle tissue with biphasic waveforms, comprising the steps of:

defining a first stimulation phase with a positive polarity, a first phase amplitude, a first phase shape and a first phase duration, where the first phase amplitude is about 0.5 to 3.5 volts, and the first phase duration is about one to nine milliseconds;

defining a second stimulation phase with a negative polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape and a second phase duration, where the second phase amplitude is about two volts to twenty volts, and the second phase duration is about 0.2 to 0.9 millisecond; and

applying the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle, and wherein the stimulation to the muscle is selected from the group consisting of direct stimulation to the muscle and indirect stimulation to the muscle.

29. An apparatus for stimulating muscle tissue with biphasic waveforms, comprising:

pulse generation electronics that generates a pulse, the pulse defining a first stimulation phase and defining a second stimulation phase, wherein the first stimulation phase has a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation, and wherein the second stimulation phase has a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

leads connected to the pulse generation electronics and being adapted to apply the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the first phase amplitude is ramped from a baseline value to a second value.

30. An apparatus for stimulating muscle tissue with biphasic waveforms, comprising:

pulse generation electronics that generates a pulse, the pulse defining a first stimulation phase and defining a second stimulation phase, wherein the first stimulation phase has a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation, and wherein the second stimulation phase has a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

leads connected to the pulse generation electronics and being adapted to apply the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the first phase amplitude is ramped from a baseline value to a second value, and wherein the absolute value of the second value is equal to the absolute value of the second phase amplitude.

31. An apparatus for stimulating muscle tissue with biphasic waveforms, comprising:

pulse generation electronics that generates a pulse, the pulse defining a first stimulation phase and defining a second stimulation phase, wherein the first stimulation phase has a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation, and wherein the second stimulation phase has a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

leads connected to the pulse generation electronics and being adapted to apply the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and

mixed muscle;

wherein the first stimulation phase further comprises a series of stimulating pulses of a predetermined amplitude, polarity, and duration.

32. An apparatus for stimulating muscle tissue with biphasic waveforms, comprising:

pulse generation electronics that generates a pulse, the pulse defining a first stimulation phase and defining a second stimulation phase, wherein the first stimulation phase has a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation, and wherein the second stimulation phase has a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

leads connected to the pulse generation electronics and being adapted to apply the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the first phase polarity is positive and the maximum subthreshold amplitude is about 0.5 to 3.5 volts.

33. An apparatus for stimulating muscle tissue with biphasic waveforms, comprising:

pulse generation electronics that generates a pulse, the pulse defining a first stimulation phase and defining a second stimulation phase, wherein the first stimulation phase has a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation, and wherein the second stimulation phase has a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

leads connected to the pulse generation electronics and being adapted to apply the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the first phase duration is at least as long as the second phase duration and the first phase duration is about one to nine milliseconds.

34. An apparatus for stimulating muscle tissue with biphasic waveforms, comprising:

pulse generation electronics that generates a pulse, the pulse defining a first stimulation phase and defining a second stimulation phase, wherein the first stimulation phase has a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation, and wherein the second stimulation phase has a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

leads connected to the pulse generation electronics and being adapted to apply the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the first phase duration is at least as long as the second phase duration and the second phase duration is about 0.2 to 0.9 millisecond.

35. An apparatus for stimulating muscle tissue with biphasic waveforms, comprising:

pulse generation electronics that generates a pulse, the pulse defining a first stimulation phase and defining a second stimulation phase, wherein the first stimulation phase has a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation, and wherein the second stimulation phase has a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

leads connected to the pulse generation electronics and being adapted to apply the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the second phase amplitude is about two volts to twenty volts.

36. An apparatus for stimulating muscle tissue with biphasic waveforms, comprising:

pulse generation electronics that generates a pulse, the pulse defining a first stimulation phase and defining a second stimulation phase, wherein the first stimulation phase has a first phase polarity, a first phase amplitude, a first phase shape, and a first phase

duration for preconditioning the muscle tissue to accept subsequent stimulation, and wherein the second stimulation phase has a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

leads connected to the pulse generation electronics and being adapted to apply the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the second phase duration is less than 0.3 milliseconds and the second phase amplitude is greater than twenty volts.

37. An apparatus for stimulating muscle tissue with biphasic waveforms, comprising:

pulse generation electronics that generates a pulse, the pulse defining a first stimulation phase and defining a second stimulation phase, wherein the first stimulation phase has a first phase polarity, a first phase amplitude, a first phase shape, and a first phase duration for preconditioning the muscle tissue to accept subsequent stimulation, and wherein the second stimulation phase has a polarity opposite to the first phase polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration; and

leads connected to the pulse generation electronics and being adapted to apply the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle;

wherein the stimulation to the muscle is selected from the group consisting of direct stimulation to the muscle and indirect stimulation to the muscle; and

wherein the indirect stimulation is administered through skin.

38. An apparatus for stimulating muscle tissue with biphasic waveforms, comprising:

pulse generation electronics that generates a pulse, the pulse defining a first stimulation phase and defining a second stimulation phase;

wherein the first stimulation phase has a positive polarity, a first phase amplitude, a first phase shape, and a first phase duration, where the first phase amplitude is about 0.5 to 3.5 volts, and the first phase duration is about one to nine milliseconds; and

wherein the second stimulation phase has a negative polarity, a second phase amplitude that is larger in absolute value than the first phase amplitude, a second phase shape, and a second phase duration, where the second phase amplitude is about two volts to twenty volts, and the second phase duration is about 0.2 to 0.9 millisecond; and

leads connected to the pulse generation electronics and being adapted to apply the first stimulation phase and the second stimulation phase in sequence to the muscle tissue, wherein the muscle tissue is selected from the group consisting of striated muscle, smooth muscle and mixed muscle, and wherein the stimulation to the muscle is selected from the group consisting of direct stimulation to the muscle and indirect stimulation to the muscle.