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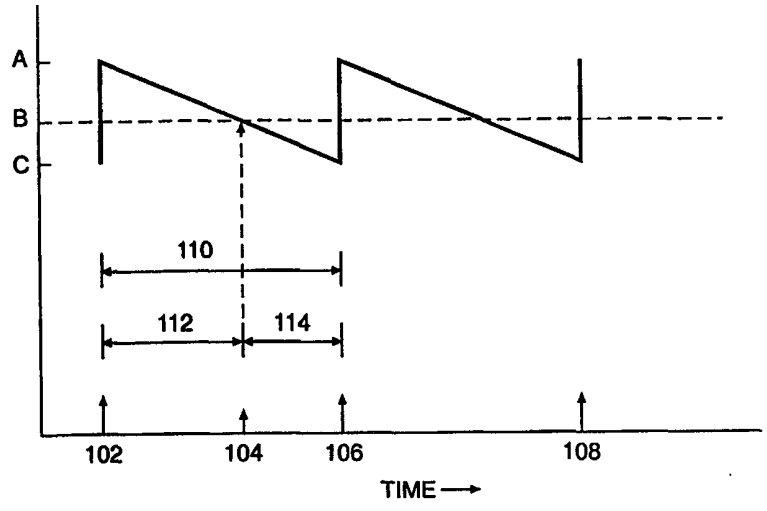

(57) Abstract

Method and apparatus for cyclic ventricular pacing starting at a rate just above the intrinsic atrial firing rate (overdrive pacing), followed by relaxation to a rate just below the intrinsic atrial firing rate (ventricular escape). The method and apparatus can be applied to one or both ventricles, and can utilize one or more electrodes per ventricle. The electrode(s) can be applied to inner or outer ventricular surfaces. Relaxation protocols as a function of time can be linear, curvilinear to include exponential, or mixtures thereof. Furthermore, relaxation protocols can include one or more periods of time during which the pacing rate is held constant. Typically, the average ventricular pacing rate using this invention will be slightly greater than the intrinsic atrial firing rate, though alternate embodiments that encompass average ventricular pacing rates that are equal to or slightly less than the intrinsic atrial firing rate are also envisioned. Application of this method and apparatus to a heart in need thereof will produce a heart with an optimally minimized energy output requirement.

METHOD ALLOWING CYCLIC PACING WITH AVERAGE RATE JUST ABOVE THE INTRINSIC RATE

Field of the Invention

The present invention relates generally to pacemakers to control the beating of hearts. In particular, the present invention relates to pacemakers used to promote, on a cyclic basis, ventricular tracking of atrial firing by overdriving ventricular pacing at a rate slightly over the intrinsic heart (atrial) rate, followed by gradual relaxation of the rate of ventricular stimulation to the point of decoupling of ventricular beating from atrial firing, especially in conjunction with ventricular synchronizing techniques such as biventricular pacing, biphasic pulsing, and/or multiple-site ventricular pacing.

Background of the Invention

A-V blocks, encountered frequently in cardiac patients, arise when electrical impulses flowing from the SA node along the conduction bundles are delayed when they reach the A-V junction/A-V node. In some pathologies, if an A-V delay is sufficiently great, the ventricles will beat at their own intrinsic and slower rate. With A-V blocks in other pathologies, the ventricles can beat at a variable and/or intermittent rate, or ectopic foci can appear, potentially leading to life threatening ventricular fibrillation.

A variety of strategies have been employed for pacemakers to overcome the adverse physiological effects of A-V blocks. One such strategy is overdriving or overpacing, in which the pacemaker stimulates the ventricles at a faster rate than the atrial beating rate. A problem encountered with such strategies is that the atrial and ventricular beating can not be coordinated for optimal pumping efficiency. Another problem is that such fast ventricular pacing rates fatigue the heart because physiological and biochemical functioning generally are not optimized. Furthermore, such additional fatigue only imposes greater restraints on the already limited life style of the typical cardiac patient. Thus, the patient with an already weakened heart can be subjected to unnecessary overstimulation, and be stressed and further weakened as a result of application of current pacemaking protocols.

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Patented technologies relating to overdriving pacing with subsequent relaxation of the pacing rate include U.S. Patent No. 5,626,620 to Kieval, et al., which discloses a pacemaker stimulation protocol in which fusion and/or near fusion beats are detected by monitoring changes in the characteristics of the evoked QRS. The protocol is adjustable to allow selection of an acceptable percentage of fusion beats. When an unacceptable fusion percentage is measured, the A-V delay is automatically decreased to lead to a higher ventricular beating rate from the pacemaker's synchronous pace pulses (ventricular "capture"). Once ventricular capture is maintained for a predetermined time interval or number of cycles without an unacceptable rate of fusion, the A-V interval is incrementally increased to produce a beating rate toward the rate at which fusion had previously occurred. Upon again meeting an unacceptable fusion percentage, the A-V delay is automatically decreased, and the cycle continues so as to approximate the longest A-V interval (i.e., the slowest ventricular beating rate) consistent with avoiding fusion.

U.S. Patent No. 5,527,347 to Shelton, et al. discloses a pacemaker ventricular stimulation protocol in which the A-V delay is slowly increased until fusion occurs, at which point the A-V delay is decreased slightly. The cycle is then repeated. Thus, the A-V delay is cyclically maintained in a small range of about that corresponding to fusion, to slightly lower values (i.e., higher ventricular beating rate).

U.S. Patent No. 5,522,858 to van der Veen discloses a pacemaker stimulation protocol in which A-V delays are gradually decreased until ventricular tracking of atrial firing occurs. In particular, the ventricles are stimulated after the atrial depolarization impulse reaches the ventricles, but are not stimulated during the ventricular refractory period. The net effect is to decrease the prolonged A-V delay period, and thus increase the ventricular beating rate. In small increments, the A-V delay period then is further decreased until ventricular tracking is observed.

U.S. Patent No. 5,480,413 to Greenhut, et al. discloses a means for using a pacemaker to correct ventricular beating rate instability in the presence of atrial fibrillation/tachyarrhythmia. First, ventricular beating is decoupled from atrial beating by gradually increasing the ventricular beating rate (dual or multichamber pacemakers are switched to a single chamber pacing mode) via appropriately spaced electrical stimulations. Once a stabilized beating rate is achieved at the higher ventricular beating rate, then the rate

of ventricular stimulation is slowly decreased to the lowest rate that provides ventricular rate stability, and held at this rate until the atrial tachyarrhythmia/fibrillation disappears. Dual or multi-chamber (atria and ventricles) pacemaking is then resumed.

U.S. Patent No. 5,441,522 to Schüller discloses a dual chamber pacemaker stimulation protocol in which the A-V interval is cycled between two values when retrograde conduction from ventricular stimulation renders the atria refractory to the normally timed stimulation by the pacemaker. When such a condition is sensed, the A-V interval is shortened to one value. Once a predetermined time or number of pulses has occurred, or once a spontaneous ventricular reaction is sensed within the shortened A-V interval, then the longer A-V interval is restored.

U.S. Patent No. 5,340,361 to Sholder discloses a ventricular stimulation protocol in which the A-V interval is automatically adjusted to just less than that for the intrinsic (and pathological) rhythm to produce a ventricular firing that is slightly in advance of the intrinsic ventricular firing time. This invention overcomes the problem of abnormal A-V delay, which decreases cardiac efficiency due to non-optimal atrial-ventricular synchronization. The rates of atrial firing and ventricular firing are equal in this invention.

U.S. Patent No. 5,334,220 to Sholder discloses a ventricular stimulation protocol in which the A-V interval is automatically adjusted to avoid ventricular stimulation at a time that would result in fusion (at the cross-over point) with the endogenous ventricular stimulation. A final A-V value is selected by incrementally adjusting the A-V interval until the crossover point is reached with respect to the R wave. The final A-V value that is set is based on the determined cross-over point, adjusted by a small margin. Thus, this procedure overdrives the intrinsic rhythm to ensure a suitably short A-V interval/delay that, otherwise, would impair cardiac pumping efficiency. When this procedure is invoked (automatically) too frequently, it is suspended for a predetermined period.

U.S. Patent No. 5,105,810 to Collins, et al. discloses a cyclic protocol for achieving the minimum voltage for ventricular pacing for the purpose of extending the life of batteries used in pacemakers. The protocol uses a series of bradycardia support pacing pulses at a predetermined voltage, and ventricular pressure measurements are analyzed during the pulse train to determine if capture has occurred. If capture has occurred during the pulse train, bradycardia support pacing pulses again are delivered once the stimulus voltage has been

decreased by a step. If capture is the result, then the decremental voltage stepping and capture assessing is continued until capture is lost, at which point the voltage is incrementally increased until capture occurs.

U.S. Patent No. 4,503,857 to Boute, et al. discloses a ventricular pacing protocol in which either spontaneous bradycardia or tachycardia is altered first by ventricular capture, followed by gradual increase or decrease, respectively, in the rate of pulse pacing until a normal programmed pacing rate is reached.

As can be seen from earlier inventions, pacemakers utilize overdrive ventricular pacing that adjusts the A-V interval/delay in a manner that avoids fusion, and that controls ventricular firing solely by the imposed pacing impulses. However, such protocols have not been optimally designed to minimize the energy expenditure of the already compromised patient's heart. Generally, the above references are designed to change the stimulation rate by adjustment of the A-V interval/delay in order to achieve a predetermined rate or a physiological standard.

What is needed is a pacemaker with a ventricular firing protocol that minimizes the energy of the heart used for contraction/pumping work. Furthermore, what is needed is a pacemaker with a ventricular firing protocol in which the maximum overdrive pacing rate is only slightly (i.e., only a few beats per minute -- ideally two or three beats per minute) greater than the atrial firing rate at the commencement of the first cycle of the protocol. In addition, what is needed is a pacemaker for ventricular firing that uses a pacing protocol that achieves re-synchronization/fusion, so as to produce the least amount of stress on a heart which may already be in a weakened condition.

Lastly, 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, is also desired.

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.

Summary of the Invention

It is therefore an object of the present invention to provide a pacemaker with a ventricular firing protocol that minimizes the energy required for contraction and pumping of the heart of a cardiac patient.

It is another object of the present invention to provide a pacemaker with a ventricular firing protocol that uses ventricular overdrive pacing only to a minimal degree; i.e., overdrive pacing is just a few beats per minute greater than the intrinsic atrial firing rate.

It is a further object of the present invention to provide a pacemaker with a ventricular firing protocol with a pacing relaxation period in which the ventricular pacing rate is slowly decreased to just slightly less (i.e., by only 1-2 beats per minute) than the intrinsic atrial firing rate before commencement of the next cycle.

It is a further object of the present invention to directly adjust the ventricular pacing cycle length, rather than the A-V delay.

It is a further object of the present invention to provide rate modulation in conjunction with multiple-site ventricular pacing.

The present invention accomplishes the above objectives by providing a ventricular firing protocol that is initiated by synchronization with the QRS complex of the electrocardiogram. The time from one QRS complex to the next constitutes a practical definition of the length of a heart beat, thereby providing the control circuit with a ready, strong reference point that serves as a timing mark for the timing of the firing trigger of the first electrical impulse to the ventricle(s). In theory, a P wave with an appropriate time interval could work. However, the weak P wave could disappear in the presence of conditions such as atrial fibrillation. This is particularly true in the case of pathological hearts. Therefore, the QRS complex, because of its large amplitude, serves as the best reference point available in the electrocardiogram. However, it is to be understood that the practice of the initial phase of this invention amounts to indirect timing/coordination with respect to atrial firing and contraction, as this is required for optimal total cardiac functioning.

The ventricular firing protocol is activated upon detection of a QRS complex, and is

set at an overdrive rate of only a few beats per minute (i.e., no more than 3-5 beats per minute) greater than the intrinsic atrial firing rate. Next, the ventricular firing rate is slowly decreased ("relaxed") to a rate just a few beats per minute (i.e., no more than 2-3 beats per minute; ideally, only 1-2 beats per minute) below the intrinsic atrial firing rate, which leads to ventricular escape (i.e., atrial firing and contraction no longer coordinate perfectly with ventricular firing and contraction).

Subsequently, a new cycle is commenced.

Thus, the present invention uses a stimulation rate that is continuously cycled from a highest rate that is just barely above the intrinsic atrial firing rate, to a rate just barely below the intrinsic atrial firing rate. Such a stimulation protocol is expected *a priori* to provide a good approximation of an optimal lowest energy requiring protocol. Therefore, the limited energy of the cardiac patient can be used wisely and optimally to the benefit of the already compromised patient. In summary, this technique allows pacing at an average rate that is just above the intrinsic heart rate so as to maximize inotropic pacing effects at minimal heart rates, and thereby conserve the precious energy of the patient's heart.

Additionally, the ventricular firing protocol of the present invention can be used in conjunction with biphasic pacing. The method and apparatus relating to biphasic pacing 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 fifth alternative embodiment the first phase is administered over 200 milliseconds after completion of a cardiac beating/pumping cycle. 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

Figure 1 shows a cyclic saw tooth (linear decay) stimulation-relaxation protocol for ventricular pacing.

Figure 2 shows a cyclic exponential decay stimulation-relaxation protocol for ventricular pacing.

Figure 3 is a schematic representation of leading anodal biphasic stimulation.

Figure 4 is a schematic representation of leading cathodal biphasic stimulation.

Figure 5 is a schematic representation of leading anodal stimulation of low level and long duration, followed by cathodal stimulation.

Figure 6 is a schematic representation of leading anodal stimulation of ramped low level and long duration, followed by cathodal stimulation.

Figure 7 is a schematic representation of leading anodal stimulation of low level and short duration administered in a series, followed by cathodal stimulation.

Description of the Preferred Embodiments

The fundamentals of the present invention can be understood with reference to Figures 1 and 2, which depict two cyclic stimulation-relaxation protocols for ventricular pacing, in which the maximum rate of ventricular overdrive pacing is followed by relaxation to a rate just less than the intrinsic atrial firing rate (which corresponds to ventricular escape). Figure 1 shows a cyclic saw tooth (linear decay) stimulation-relaxation protocol. Figure 2 shows a cyclic exponential decay stimulation-relaxation protocol.

Referring to Figure 1, a cyclic saw tooth stimulation-relaxation protocol for ventricular pacing is depicted with time points **102**, **106**, and **108** to illustrate initiation of ventricular overdrive pacing at maximum pacing rate **A**, followed by linear decay/relaxation of the rate of pacing to minimum pacing rate **C**. Each cycle has total time length **110**. Intrinsic atrial firing rate **B** is shown as a dashed reference line. Rate difference **A-B** is greater than rate difference **B-C** in this example. During the course of linear relaxation of the ventricular pacing rate, crossover point **104** is reached when the ventricular pacing rate equals intrinsic atrial firing rate **B**. Thus, the period between time point **102** and crossover point **104** represents linear ventricular overdrive pacing period **112**, and the period between crossover point **104** and time point **106** represents linear ventricular escape period **114.** It is

evident that linear ventricular overdrive pacing period **112** is a longer time period than linear ventricular escape period **114.** Therefore, the average ventricular firing rate for this protocol, with the above given relative parameters, will always be slightly greater than intrinsic atrial firing rate **B.**

Referring to Figure 2, a cyclic exponential decay stimulation-relaxation ventricular pacing protocol is shown with ventricular overdrive pacing to maximum pacing rate **A** being initiated at time points **202, 206** and **208,** followed by exponential relaxation of the rate of pacing to minimum pacing rate **C**. Each cycle has total time length **210**. The time course of the pacing rate during the relaxation phase will be proportional to the time course of the product obtained by multiplying maximum pacing rate **A** (or the quantity **A** minus a selected "factor") by the proportionality $e^{1/\tau}$, where τ is the time constant. The selected "factor" typically will have a value less than **C**. As in Figure 1, dashed line **B** represents the reference line of intrinsic atrial firing rate. Compared to Figure 1, two parameters have been adjusted in Figure 2. First, the relaxation of pacing rate is an exponential function of time instead of a linear function of time. Second, minimum ventricular pacing rate **C** is closer to intrinsic atrial firing rate **B.**

As in Figure 1, the period between time point **202** and crossover point **204** represents exponential ventricular overdrive pacing period **212,** and the period between crossover point **204** and time point **206** represents exponential ventricular escape period **214**. Rate difference **A-B** is the same in Figures 1 and 2, as are cycle lengths **110** and **210**. This combination of parameters produces a protocol in which exponential ventricular overdrive pacing period **212** of Figure 2 is shorter than linear ventricular overdrive pacing period **112** of Figure 1.

In the case of a curvilinear (including exponential) relaxation protocol with cycle length **210**, comparison of ventricular overdrive pacing period **212** and ventricular escape period **214** of Figure 2 reveals that their magnitudes effectively are controlled by variations in two parameters: **(A-B)/(B-C)**, and ventricular overdrive pacing period **212.**

Referring again to Figure 1, in the case of a linear relaxation protocol with cycle length **110**, comparison of linear ventricular overdrive pacing period **112** and linear ventricular escape period **114** reveals that their magnitudes are controlled by variation in single parameter **(A-B)/(B-C)**, or any mathematical equivalent, such as **(102-104)/(104-106)**.

It is anticipated that different relaxation protocols will be required for different pathologies and different medical situations. In addition, a virtually infinite array of relaxation protocols are possible in theory. Thus, the preferred embodiment of the present invention contemplates any monotonic relaxation protocol, where "monotonic" indicates a unidirectional change in the applied ventricular pacing rate. Further, "unidirectional change" is to be understood to refer to a change in ventricular pacing rate that is in the direction of decreasing ventricular pacing rate, and to include periods of time in which there is no change in ventricular pacing rate.

Therefore, the preferred embodiment of the present invention contemplates relaxation protocols beyond the two depicted in Figures 1 and 2, as long as the relaxation protocol embodies unidirectional change in ventricular pacing rate as defined above. Thus, the shapes of the relaxation curves can generally be decreasing linear, decreasing curvilinear, decreasing in an exponential fashion, include one or more periods at a constant pacing rate, or combinations of these. For example, with reference to Figure 1, one can imagine a protocol in which, between time points **102** and **104**, there is a small time segment over which the voltage is constant, followed by linear relaxation at the same or a different rate of relaxation (i.e., the same or a different slope) compared to the initial rate of relaxation. In one embodiment, the same or different rate of relaxation that follows the brief period of constant voltage is maintained up to time point **106**, which marks the end of one cycle and the beginning of the next cycle.

Alternate embodiments encompass relaxation protocols in which ventricular pacing rates are not monotonic; i.e., as the ventricular pacing rate is declining in a given cycle, time periods in which the ventricular pacing rates are increased slightly can be included. Further alternative embodiments can include the use of combinations of different rates of relaxation within a single cycle, for example, within time segment **102 - 106**, or **202 - 206**.

Typically, physiological data from one or more sensing electrodes (including electrodes that perform both pacing and sensing) are used to determine whether an "action criterion" has been met, in order to initiate a cyclic pacing protocol if the situation so demands. Such sensing may be directed to detecting such nonlimiting physiological parameters as abnormal or unacceptably long A-V delays, whether atrial firing entrains both

left and right ventricles, length of the QRS complex, magnitude of the QRS complex, heart rate, arterial and/or venous blood pressure, ventricular fibrillation, atrial fibrillation, and probability density function ("PDF"). At the end of such a cyclic pacing protocol, sensing again is performed to determine if additional pacing is required. Alternatively, sensing can be conducted concurrently with a cyclic pacing protocol.

The ventricular firing protocol is activated upon detection of a QRS complex, and is set at an overdrive rate of only a few beats per minute (i.e., no more than 3-5 beats per minute) greater than the intrinsic atrial firing rate. Next, the ventricular firing rate is slowly decreased ("relaxed") to a rate just a few beats per minute (i.e., no more than 2-3 beats per minute; ideally, only 1-2 beats per minute) below the intrinsic atrial firing rate, which leads to ventricular escape (i.e., atrial firing and contraction no longer coordinate perfectly with ventricular firing and contraction). Heart rates could vary from about 40 to 120 beats per minute, with these rates being largely determined by the intrinsic physiology of the heart. Rates that vary greatly from this 40 to 120 beats per minute range would not be beneficial physiologically.

What is central to the present invention is that the ventricular pacing rates hover not far from the intrinsic atrial firing rate so as to minimize the energy requirements of the myocardium. Generally, practice of the present invention will result in an average ventricular beating rate that is just slightly greater than the intrinsic atrial firing rate. However, it is anticipated that some pathological/medical conditions will minimize the cardiac energy requirements with a relaxation protocol that results in an average ventricular beating rate that is equal to, or just slightly less than, the intrinsic atrial firing rate; and such relaxation protocols are well within the scope of the present invention.

The application of cyclic ventricular pacing with any of the above range of relaxation protocols pertains not only to mono-ventricular pacing, but also to biventricular pacing, and/or pacing from multiple sites. In the case of biventricualr pacing, right and left ventricles can be cyclically paced either on the same or similar time protocol or independently of one another. Furthermore, one pacing electrode or multiple pacing electrodes can be employed per ventricle, and the pacing electrodes can be applied to the external surfaces of the ventricles and/or to the internal surfaces. Typically, internal pacing electrodes will be applied via the vena cava and the right atrium to the right ventricle only; however, multiple internal

pacing electrodes are also contemplated for the left ventricle.

Additional embodiments encompass the use of monophasic stimulation, as well as biphasic stimulation. Furthermore, the monophasic stimulation and the biphasic stimulation can be applied to either atria or ventricles. Monophasic stimulation can be either cathodal or anodal, and is known to those skilled in the art. Biphasic cardiac stimulation is disclosed in United States Patent Application No. 08/699,552 to Mower, which is hereby incorporated by reference in its entirety.

Typically, a cyclic pacing/relaxation period will fall within the three to 30 second range; however, longer periods also are contemplated, particularly for patients with more "difficult" pathologies.

Figure 3 depicts biphasic electrical stimulation wherein a first stimulation phase, comprising anodal stimulus **302**, is administered having amplitude **304** and duration **306**. This first stimulation phase is immediately followed by a second stimulation phase comprising cathodal stimulation **308** of equal intensity and duration.

Figure 4 depicts biphasic electrical stimulation wherein a first stimulation phase, comprising cathodal stimulation **402** having amplitude **404** and duration **406**, is administered. This first stimulation phase is immediately followed by a second stimulation phase comprising anodal stimulation **408** of equal intensity and duration.

Figure 5 depicts a preferred embodiment of biphasic stimulation wherein a first stimulation phase, comprising low level, long duration anodal stimulation **502** having amplitude **504** and duration **506**, is administered. This first stimulation phase is immediately followed by a second stimulation phase comprising cathodal stimulation **508** of conventional intensity and duration. In differing alternative embodiments, anodal stimulation **502** is: 1) at maximum subthreshold amplitude; 2) less than three volts; 3) of a duration of approximately two to eight milliseconds; and/or 4) administered over 200 milliseconds post heart beat. Maximum subthreshold amplitude is understood to mean the maximum stimulation amplitude that can be administered without eliciting a contraction. In differing alternative embodiments, cathodal stimulation **508** is: 1) of a short duration; 2) approximately 0.3 to 1.5 milliseconds; 3) of a high amplitude; 4) in the approximate range of three to twenty volts; and/or 5) of a duration less than 0.3 millisecond and at a voltage greater than twenty volts. In a preferred embodiment, cathodal stimulation is about 0.8

millisecond. In the manner disclosed by these embodiments, as well as those alterations and modifications which can become obvious upon the reading of this specification, a maximum membrane potential without activation is achieved in the first phase of stimulation.

Figure 6 depicts an alternative preferred embodiment of biphasic stimulation wherein a first stimulation phase, comprising anodal stimulation **602**, is administered over period **604** with rising intensity level **606**. The ramp of rising intensity level **606** can be linear or non-linear, and the slope can vary. This anodal stimulation is immediately followed by a second stimulation phase comprising cathodal stimulation **608** of conventional intensity and duration. In alternative embodiments, anodal stimulation **602**: (1) rises to a maximum subthreshold amplitude less than three volts; (2) is of a duration of approximately two to eight milliseconds; and/or (3) is administered over 200 milliseconds post heart beat. In yet other alternative embodiments, cathodal stimulation **608** is: (1) of a short duration; (2) approximately 0.3 to 1.5 milliseconds; (3) of a high amplitude; (4) in the approximate range of three to twenty volts; and/or (5) of a duration less than 0.3 milliseconds and at a voltage greater than twenty volts. In the manner disclosed by these embodiments, as well as those alterations and modifications which can become obvious upon the reading of this specification, a maximum membrane potential without activation is achieved in the first phase of stimulation.

Figure 7 depicts biphasic electrical stimulation wherein a first stimulation phase, comprising series **702** of anodal pulses, is administered at amplitude **704**. In one embodiment, rest period **706** is of equal duration to stimulation period **708**, and is administered at baseline amplitude. In an alternative embodiment, rest period **706** is of a differing duration than stimulation period **708**, and is administered at baseline amplitude. Rest period **706** occurs after each stimulation period **708**, with the exception that a second stimulation phase, comprising cathodal stimulation **710** of conventional intensity and duration, immediately follows the completion of series **702**. In alternative embodiments: (1) the total charge transferred through series **702** of anodal stimulation is at the maximum subthreshold level; and/or (2) the first stimulation pulse of series **702** is administered over 200 milliseconds post heart beat. In yet other alternative embodiments, cathodal stimulation **710** is: (1) of a short duration; (2) approximately 0.3 to 1.5 milliseconds; (3) of a high amplitude; (4) in the approximate range of three to twenty volts, and/or (5) of a duration less

than 0.3 milliseconds and at a voltage greater than twenty volts.

The preferred practice of the present invention is directed to ventricular pacing where the pacing rate skirts just above and below the intrinsic atrial pacing rate, and is timed (albeit indirectly) relative to intrinsic atrial firing in order to achieve optimal coordinated cardiac function. However, situations can be anticipated in which ventricular pacing is effected independently of intrinsic atrial firing.

Furthermore, when atrial rhythmicity is pathologic, the present invention can be practiced with respect to the rhythmicity of pacemaker paced atria. In embodiments in which atria are paced by extrinsic pacemakers, the clinical practitioner first sets the rate of atrial pacing, which can be fixed, or can be variable to permit appropriate response to changes in physical activity or other change which would require a change in heart rate, for example, an increased heart rate during a period of fever. Second, the ventricular firing protocol is selected according to the principles described and disclosed herein. It is to be emphasized that selection of the ventricular firing protocol generally will be a decision that is made independently of the atrial beating pattern, whether the atrial beating pattern is set intrinsically or extrinsically, for example, by a pacemaker. However, it is within the scope of the present invention to apply the teachings herein to cases in which decisions regarding extrinsically controlled atrial and ventricular beating protocols are considered in a linked, integrated manner.

In addition, testing procedures can be applied to achieve optimal parameters for a given patient with a particular constellation of pathologies. Thus, it is within the scope of the present invention to test, and vary, alternative stimulation pulse waveforms, for example, durations, amplitudes, and shapes of the various waveforms required to reach optimal physiological parameters for a particular patient at a given time. Further, various measurable parameters may be used to assess the effects of changes in stimulus waveforms, for example, the effects on pulse pressure, duration of the QRS complex, maximum fusion, and production of a minimal intrinsic heart rate, to name but a few.

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. Accordingly, the invention is limited only by the following claims and equivalents thereto.

Claims

1. A method for cardiac pacing for a heart having an intrinsic atrial firing rate, comprising:

applying a series of pacing stimuli to at least one ventricle having an initial pacing rate,

where the initial pacing rate is slightly greater than the intrinsic atrial firing rate;

and

decreasing the pacing rate over time from the initial pacing rate to a minimum pacing rate that is slightly less than the intrinsic atrial firing rate.

2. The method for cardiac pacing according to claim 1, further comprising sensing physiological parameters to determine if additional cardiac pacing is needed.

3. The method for cardiac pacing according to claim 2, where the physiological parameters are selected from the group consisting of A-V interval, atrial entrainment of left and right ventricles, length of QRS complex, magnitude of QRS complex, arterial blood pressure, venous blood pressure, heart rate, ventricular fibrillation, atrial fibrillation, and probability density function.

4. The method for cardiac pacing according to claim 1, where applying the pacing stimuli and decreasing the pacing rate is repeated in a cyclic pattern.

5. The method for cardiac pacing according to claim 1, where a protocol for decreasing the pacing rate over time is selected from the group consisting of linear, curvilinear, exponential, and combinations thereof.

6. The method for cardiac pacing according to claim 5, where the protocol for decreasing the pacing rate includes one or more periods of time in which the pacing rate is held constant.

7. The method for cardiac pacing according to claim 1, where a protocol for decreasing the pacing rate includes one or more periods of time in which the pacing rate is held constant.

8. The method for cardiac pacing according to claim 1, where the initial pacing

rate
minus the intrinsic atrial firing rate is greater than the intrinsic atrial firing rate minus the minimum pacing rate.

9. The method for cardiac pacing according to claim 1, where the initial pacing rate
minus the intrinsic atrial firing rate is equal to the intrinsic atrial firing rate minus the minimum pacing rate.

10. The method for cardiac pacing according to claim 1, where the initial pacing rate
minus the intrinsic atrial firing rate is less than the intrinsic atrial firing rate minus the minimum pacing rate.

11. The method for cardiac pacing according to claim 1, where the pacing stimuli are
selected from the group consisting of monophasic stimulation and biphasic stimulation.

12. The method for cardiac pacing according to claim 11, where the monophasic stimulation is selected from the group consisting of cathodal stimulation and anodal stimulation.

13. The method for cardiac pacing according to claim 11, where the biphasic stimulation comprises an anodal stimulation phase followed by a cathodal stimulation phase.

14. The method for cardiac pacing according to claim 13, where the anodal stimulation phase:
has a magnitude equal to or less than a maximum subthreshold amplitude; and
has an approximate shape selected from the group consisting of square wave, increasing ramp, and series of short duration square waves.

15. The method for cardiac pacing according to claim 1, where the pacing stimuli are
applied via multiple electrodes to at least one ventricle.

16. A method for cardiac pacing for a heart with a paced atrial firing rate, comprising:
applying a series of pacing stimuli to at least one ventricle, where the initial ventricular pacing rate is slightly greater than the paced atrial firing rate; and

decreasing the initial ventricular pacing rate over time to a minimum pacing rate that is slightly less than the paced atrial firing rate.

17. The method for cardiac pacing according to claim 16, wherein applying the pacing stimuli and decreasing the pacing rate is repeated in a cyclic pattern.

18. The method for cardiac pacing according to claim 16, where a protocol for decreasing the initial ventricular pacing rate over time is selected from the group consisting of linear, curvilinear, exponential, and combinations thereof.

19. The method for cardiac pacing according to claim 18, where the protocol for decreasing the initial pacing rate includes one or more periods of time in which the pacing rate is held constant.

20. The method for cardiac pacing according to claim 16, where a protocol for decreasing the pacing rate includes one or more periods of time in which the pacing rate is held constant.

21. The method for cardiac pacing according to claim 16, where the initial ventricular pacing rate minus the paced atrial firing rate is greater than the paced atrial firing rate minus the minimum ventricular pacing rate.

22. The method for cardiac pacing according to claim 16, where the initial ventricular pacing rate minus the paced atrial firing rate is equal to the paced atrial firing rate minus the minimum ventricular pacing rate.

23. The method for cardiac pacing according to claim 16, where the initial ventricular pacing rate minus the paced atrial firing rate is less than the paced atrial firing rate minus the minimum ventricular pacing rate.

24. The method for cardiac pacing according to claim 16, where the pacing stimuli are selected from the group consisting of monophasic stimulation and biphasic stimulation.

25. The method for cardiac pacing according to claim 24, where the monophasic stimulation is selected from the group consisting of cathodal stimulation and anodal

stimulation.

26. The method for cardiac pacing according to claim 24, where the biphasic stimulation comprises an anodal stimulation phase followed by a cathodal stimulation phase.

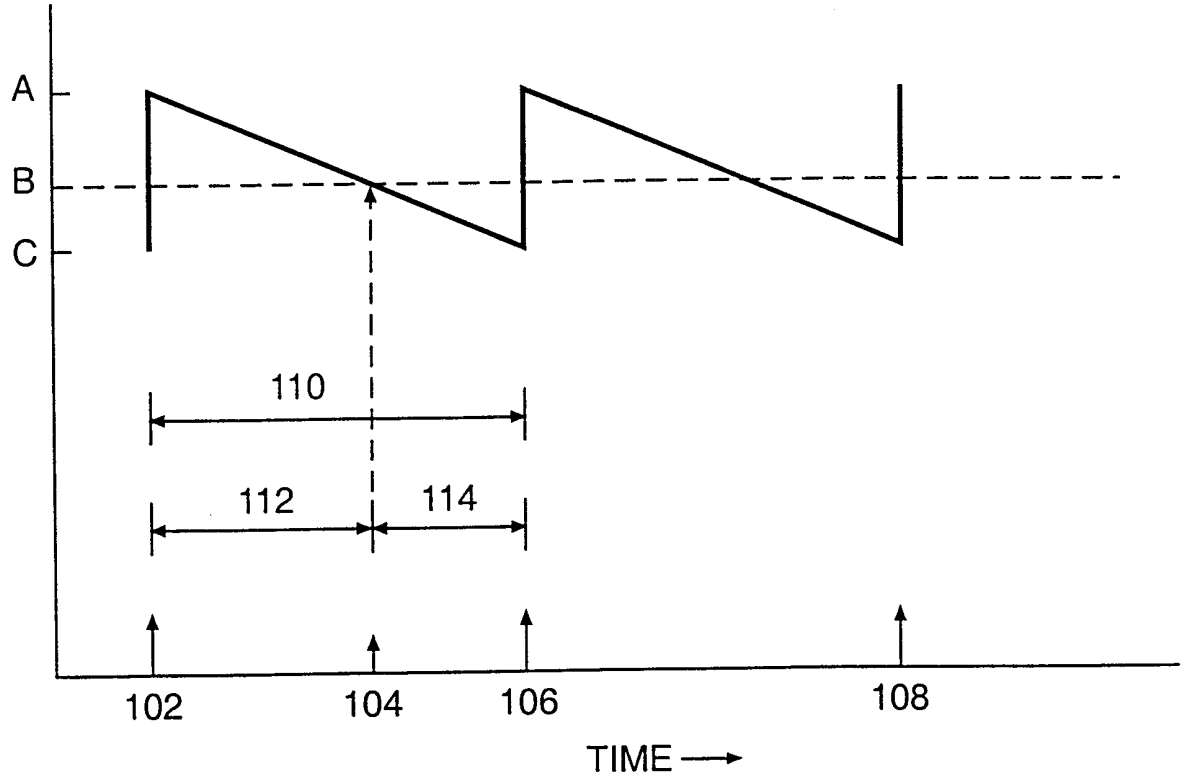
27. The method for cardiac pacing according to claim 26, where the anodal stimulation phase:

has a magnitude equal to or less than a maximum subthreshold amplitude; and

has an approximate shape selected from the group consisting of square wave, increasing ramp, and series of short duration square waves.

28. The method for cardiac pacing according to claim 16, where the pacing stimuli are

applied via multiple electrodes to at least one ventricle.


A
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C
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106
108
TIME

FIG. 1

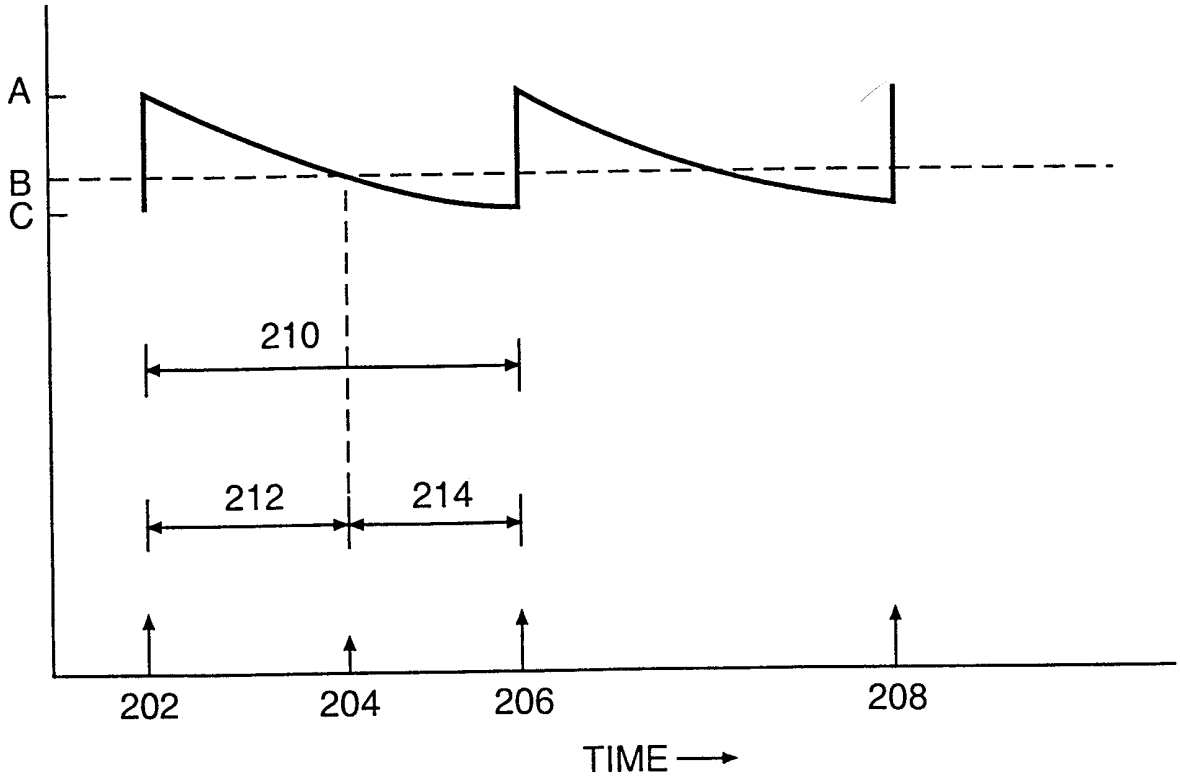
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FIG. 2

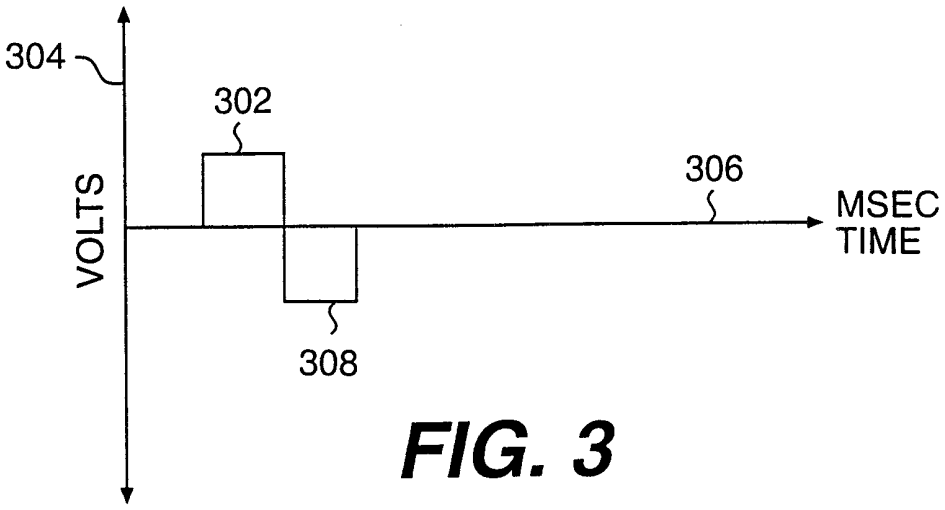
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FIG. 3

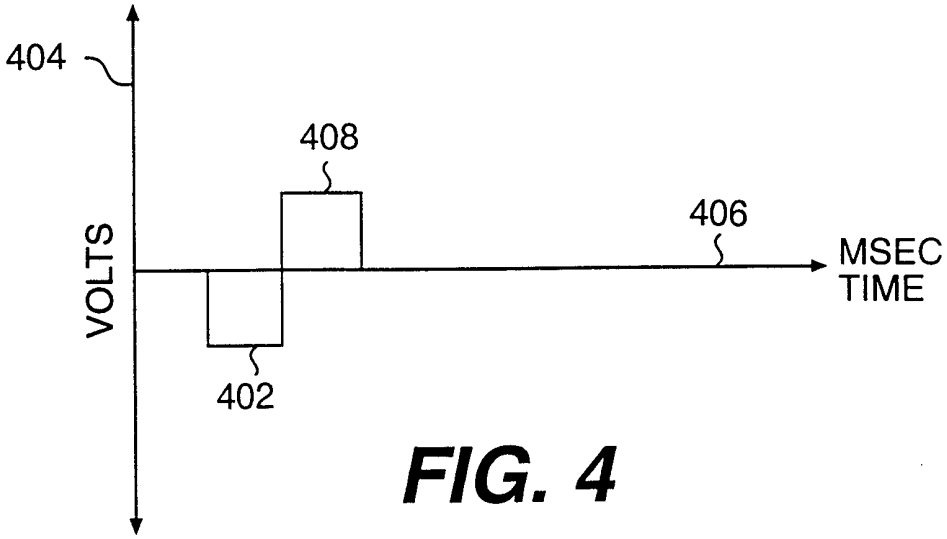
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FIG. 4

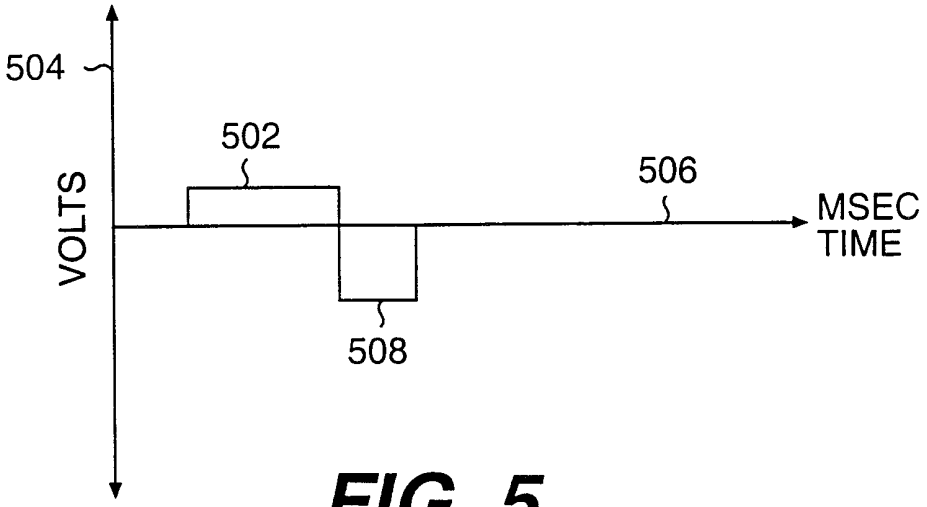
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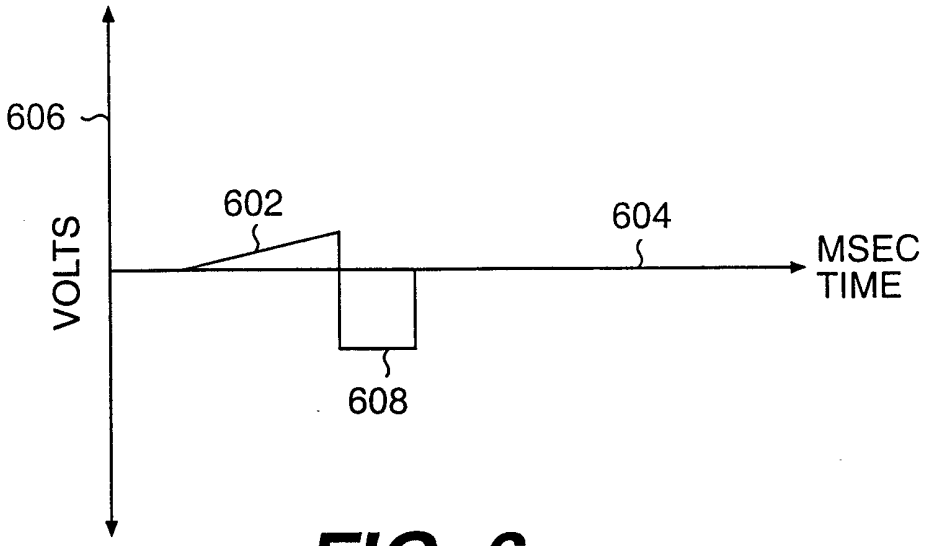
FIG. 5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608

FIG. 6

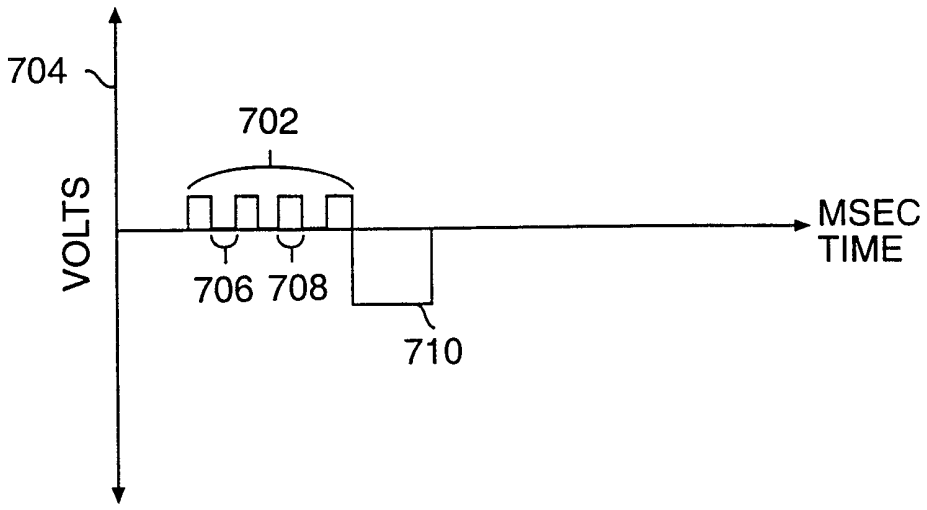

FIG. 7

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/11375

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61N1/368

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 480 413 A (GREENHUT SAUL ET AL) 2 January 1996 (1996-01-02) cited in the application	
A	EP 0 600 631 A (SIEMENS AG) 8 June 1994 (1994-06-08) cited in the application	
P,A	US 5 871 506 A (MOWER MORTON M) 16 February 1999 (1999-02-16) cited in the application	
A	US 5 713 929 A (MEADOR JOHN T ET AL) 3 February 1998 (1998-02-03)	
P,A	FR 2 763 247 A (ELA MEDICAL SA) 20 November 1998 (1998-11-20)	

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 August 1999	03/09/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Allen, E

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

.ternational application No.
PCT/US 99/ 11375

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 1-28
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US 99/11375

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although the claims are directed to a method of treatment of the human/ animal body, the search has been carried out and based on a device to carry out the method of claims 1 and 16.

Continuation of Box I.1

Claims Nos.: 1-28

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int tional Application No
PCT/US 99/11375

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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