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(71) Applicant: MAX-PLANCK-GESELLSCHAFT ZUR FÖRDERUNG DER WISSENSCHAFTEN E.V. [DE/DE]; Hofgartenstraße 8, 80539 München (DE).

(72) Inventors: TOM WÖRDEN, Henrik; Insterburger Weg 10, 37083 Göttingen (DE). HORNUNG, Daniel; Wiesenstraße 28, 37073 Göttingen (DE). BAIG, Tariq; Goßlerstraße 44, 37075 Göttingen (DE).

(74) Agent: REHBERG HÜPPE + PARTNER PATENTANWÄLTE PARTG MBB; Robert-Gernhardt-Platz 1, 37073 Göttingen (DE).

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(54) Title: APPARATUS FOR TERMINATING OR UNPINNING ROTATING ELECTRIC ACTIVITY IN A CARDIAC TISSUE

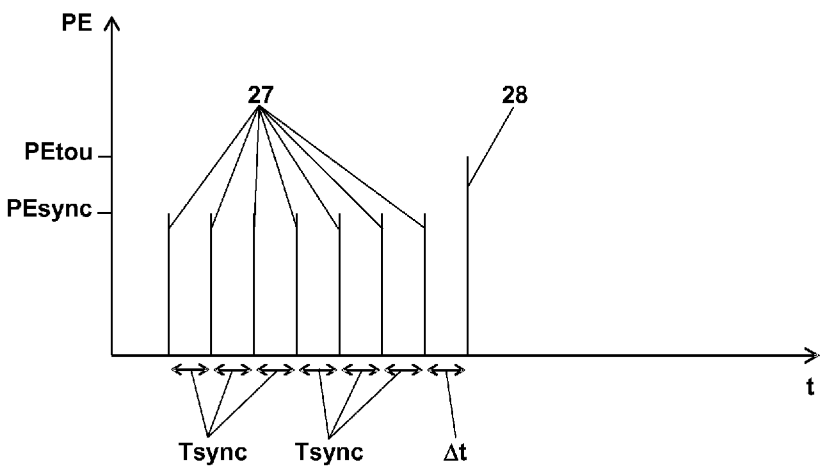

Fig. 3

(57) Abstract: An apparatus (1) for terminating or unpinning rotating electric activity (2) in a cardiac tissue (3), the apparatus (1) comprises an electric state sensor sensing at least one electric parameter of the cardiac tissue; an electric state analyzer (9) connected to the electric state sensor (8) and analyzing the at least one electric parameter for rotating electric activity (2) in the cardiac tissue (3); a pulse generator (19) connected to the electric state analyzer (9) and generating electric pulses in response to rotating electric activity (2) in the cardiac tissue (3); and a pulse applicator (20) connected to the pulse generator (19) and applying the electric pulses as electric field pulses extending across the cardiac tissue (3). The electric pulses include a rotating electric activity termination or unpinning pulse (28) and a plurality of rotating electric activity synchronization pulses (27) preceding the rotating electric activity termination or unpinning pulse (28). The rotating electric activity synchronization pulses (27) are arranged at first intervals (Tsync), and the rotating electric activity termination or unpinning pulse (28) is arranged at a second interval (At) in a range from 0.7 to 1.2 times one of the first intervals (Tsync) after the last one of the plurality of rotating electric activity synchronization pulses (27). At least one of a first maximum electric field strength (FSsync) as caused by each of the rotating electric activity synchronization pulses (27) and a first electric pulse energy (PEsync) delivered to the cardiac tissue (3) by each of the rotating electric activity synchronization pulses (27) is not more than 82 % of a second maximum electric field strength (FStou) as caused by the rotating electric activity termination or

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unpinning pulse (28) or not more than 67 % of a second electric pulse energy (PEtou) delivered to the cardiac tissue (3) by the rotating electric activity termination or unpinning pulse (28), respectively.

APPARATUS FOR TERMINATING OR UNPINNING ROTATING ELECTRIC ACTIVITY IN A CARDIAC TISSUE

TECHNICAL FIELD OF THE INVENTION

The present invention relates to an apparatus for terminating or unpinning rotating electric activity in a cardiac tissue. The rotating electric activity may, for example, be associated with an electric state of the cardiac tissue called fibrillation. The electric activity may include so-called scroll waves. The rotating electric activity may rotate about inhomogeneities of the cardiac tissue. The cardiac tissue may particularly be a living heart.

More particularly, the present invention relates to an apparatus for terminating or unpinning rotating electric activity in a cardiac tissue, the apparatus comprising an electric state sensor configured to sense at least one electric parameter of the cardiac tissue; an electric state analyzer connected to the electric state sensor and configured to analyze the at least one electric parameter sensed by the electric state sensor for rotating electric activity in the cardiac tissue; a pulse generator connected to the electric state analyzer and configured to generate electric pulses in response to the electric state analyzer analyzing that there is rotating electric activity in the cardiac tissue, the electric pulses including a rotating electric activity termination or unpinning pulse; and a pulse applicator connected to the pulse generator and configured to apply the electric pulses as electric field pulses extending across the cardiac tissue.

BACKGROUND

WO 2012/172027 A2 discloses an apparatus for terminating a high frequency arrhythmic electric state of a biological tissue. The known apparatus comprises a termination unit which determines from an electric signal representative of the present electric state of the biological tissue at least one dominant frequency. From the at least one dominant frequency the termination unit determines whether the present electric state of the biological tissue is a high frequency arrhythmic electric state. Further the determination unit determines from the electric signal a dominance level indicative of how dominant the at least one dominant frequency is in the high frequency arrhythmic electric state. At a point in time at which the dominance level exceeds a predefined threshold value, the determination unit triggers an electric pulse generator to generate at least one series of electric pulses at intervals depending on the at least one dominant frequency. These electric pulses are applied to the biological tissue via at least one electrode connected to the pulse generator. For determining the dominance level, the determination unit compares the intensity of the electric signal of the dominant frequency with the intensity of the electric signal at at least one neighboring frequency. The electric pulse generator generates electric pulses at a comparatively low electric energy as compared to a standard defibrillation energy used for defibrillation by means of a single pulse providing an electric shock. The electric pulse generator generates the individual electric pulses of the at least one series of electric pulses at such time intervals that the electric pulses raster scan the phase defined by the at least one dominant frequency at phase intervals. For this purpose, the electric pulse generator generates the electric pulses of the at least one series of electric pulses at time intervals deviating from the reciprocal value of the at least one dominant frequency by 1/32 to 1/5 of the reciprocal value of the at least one dominant frequency. Preferably, the intervals of the electric pulses exceed the reciprocal value of the dominant frequency. If the determination unit determines from the electrical signal that the biological tissue still is in the arrhythmic electric state after a first series of electric pulses has been applied, the electric pulse generator generates a further series of electric pulses at a higher voltage than the first series of electric pulses. Only if the termination unit, after a predefined number of series of electric pulses, determines that the biological tissues still is in the arrhythmic electric state, the electric pulse generator generates a single electric pulse of a standard heart defibrillation energy.

WO 2011/139596 A2 discloses a three-stage atrial cardioversion therapy. A first stage of the three-stage atrial cardioversion therapy has at least two and less than ten biphasic atrial cardioversion pulses of more than 10 V and less than 100 V with a pulse duration of less than 10 milliseconds and a pulse coupling interval of between 20 to 50 ms, wherein the first stage has a total duration of less than two of the cycle lengths of a detected atrial arrhythmia and is delivered within a ventricular refractory period with an energy of each biphasic atrial cardioversion pulse being less than 0.1 J to unpin one or more singularities associated with the atrial arrhythmia. A second stage of the three-stage atrial cardioversion therapy has at least five and less than ten far field pulses of less than a ventricular far-field excitation threshold with a pulse duration of more than 5 and less than 20 ms and a pulse coupling interval of between 70 to 90 % of the cycle length of the atrial arrhythmia, wherein the second stage prevents repining of the one or more singularities associated with the atrial arrhythmia that are unpinned by the first stage. The third stage of the three-stage cardioversion therapy has at least five and less than ten near field pulses of less than 10 V with a pulse duration of more than 0.2 and less than 5 ms and a pulse coupling interval of between 70 to 90 % of the cycle length of the atrial arrhythmia, wherein the third stage extinguishes the one or more singularities associated with the atrial arrhythmia that are unpinned by the first stage and prevented from repining by the second stage.

US 8,014,858 B1 discloses a method of terminating a fibrillation occurring in a heart of a person without applying shock pulses by applying electrical pulses to the heart at a rate greater than about 10 Hz, with a peak power that is less than about 100 W, wherein applying the pulses comprises applying a pulse having an amplitude less than about 50 mA, and terminating the electric pulses, whereby the steps of applying and terminating the electric pulses effectuate defibrillation of the heart. In the known method motion of the heart is sensed, and applying the pulses comprises modifying a characteristic of at least some of the pulses applied to the heart responsive to the sensed motion, and pacing the heart at approximately 1 Hz while applying the electrical pulses at the rate greater than about 10 Hz.

US 8,473,051 B1 discloses a method of treating atrial arrhythmias by delivering a multi-stage atrial cardioversion therapy. Each stage of the multi-stage atrial cardioversion therapy includes at least two and less than ten atrial cardioversion pulses of more than 10 volts and less than 500 V for the pulse duration of less than 10 ms, each pulse comprising multiple sub-pulses having a sub-pulse duration of less than 10 ms of increasing, decreasing or constant amplitudes.

There is still a need of an apparatus for terminating or unpinning rotating electric activity in a cardiac tissue which applies electric pulses to the cardiac tissue at a lower overall electric energy than known apparatuses but nevertheless effectively terminates or unpins the rotating electric activity.

SUMMARY

The present invention provides an apparatus for terminating or unpinning rotating electric activity in a cardiac tissue, the apparatus comprising the features of independent claim 1. The dependent claims define preferred embodiments of the apparatus.

DESCRIPTION OF THE INVENTION

The apparatus according to the invention comprises an electric state sensor configured to sense at least one electric parameter of the cardiac tissue; an electric state analyzer connected to the electric state sensor and configured to analyze the at least one electric parameter sensed by the electric state sensor for rotating electric activity in the cardiac tissue; a pulse generator connected to the electric state analyzer and configured to generate electric pulses in response to the electric state analyzer analyzing that there is rotating electric activity in the cardiac tissue; and a pulse applicator connected to the pulse generator and configured to apply the electric pulses as electric field pulses extending across the cardiac tissue. The electric pulses include a rotating electric activity termination or unpinning pulse and a plurality of rotating electric activity synchronization pulses preceding the rotating electric activity termination or unpinning pulse. The rotating electric activity synchronization pulses are arranged at first intervals, and the electric activity termination or unpinning pulse is arranged at a second interval in a range from 0.7 to 1.2 of each of the first intervals after the last of the plurality of rotating electric activity synchronization pulses. At least one of a first maximum electric field strength as caused by each of the rotating electric activity synchronization pulses and a first electric pulse energy delivered to the cardiac tissue by each of the rotating electric activity synchronization pulses is not more than 82 % of a second maximum electric field strength as caused by the rotating electric activity termination or unpinning pulse or not more than 67 % of a second electric pulse energy delivered to the cardiac tissue by the rotating electric activity termination or unpinning pulse, respectively.

The apparatus according to the present invention does not split up a single rotating electric activities unpinning or synchronization pulse into a plurality of rotating electric activity termination or unpinning pulses delivered at intervals to unpin or terminate rotating electric activity of different phases according to WO 2012/172027 A2. Instead, the rotating electric activity in the cardiac tissue is first synchronized with a plurality of rotating electric activity synchronization pulses and then terminated or unpinned by a single rotating electric activity termination or unpinning pulse or by two rotating electric activity termination or unpinning pulses. A second rotating electric activity termination or unpinning pulse already considerably increases the total energy applied to the cardiac tissue for terminating or unpinning the rotating electric activity. For this reason, groups of three or more separate rotating electric activity termination or unpinning pulses are not according to the present invention. The rotating electric activity synchronization pulses do not qualify as fully suitable rotating electric activity termination or unpinning pulses due to their lower maximum electric field strength and/or lower electric pulse energy. This does, however, not exclude that the rotating electric activity synchronization pulses do already terminate or unpin any weak rotating electric activity. With stronger rotating electric activity, however, the rotating electric activity synchronization pulses may, however, not be strong enough to terminate or unpin them. With regard to these stronger rotating electric activity, the rotating electric activity synchronization pulses will, however, be able to cause some kind of a synchronization such that they are prone to easy termination or unpinning by means of the following rotating electric activity termination or unpinning pulse. In other words, due to the application of the rotating electric activity synchronization pulses, it is not necessary to scan the phase with a plurality of rotating electric activity termination or unpinning pulses. Instead, a succeeding single rotating electric activity termination or unpinning pulse will be sufficient.

The total energy applied to the cardiac tissue for terminating or unpinning the rotating electric activity can thus be strongly reduced as compared to a plurality of rotating electric activity termination or unpinning pulses of equal electric field strength and electric pulse energy according to WO 2012/172027 A2, as the rotating electric activity synchronization pulses are of a considerably reduced maximum electric field strength and/or electric pulse energy.

Particularly, the first electric pulse energy delivered to the cardiac tissue by each of the rotating electric activity synchronization pulses being not more than 67 % of the second electric pulse energy delivered to the cardiac tissue by the rotating electric activity termination or unpinning pulse means that a ratio between the first and the second electric pulse energy is not more than about 2:3. Due to the fact that the electric energy depends on the square of the electric field strength, the first maximum electric field strength as caused by each of the rotating electric activity synchronization pulses being not more than 82 % of the second maximum electric field strength as caused by the rotating electric activity termination or unpinning pulse means about the same as the criterion on the first and second electric pulse energies with same shapes of the rotating electric activity synchronization and termination or unpinning pulses (82 % x 82 % = 67 %).

The final rotating electric activity termination or unpinning pulse delivered by the apparatus according to the present invention may be of a same second maximum electric field strength and/or second electric pulse energy as known as each pulse of a plurality of same rotating electric activity termination or unpinning pulses according to WO 2012/172027 A2.

In the apparatus according to the present invention a same pair of electrodes may both be part of the electric state analyzer and the pulse applicator.

Typically, a number of the rotating electric activity synchronization pulses preceding the rotating electric activity termination or unpinning pulse is at least 5. Often, this number is in a range from 10 to 30. Sometimes this number is about 15 to 25.

Often, it will be sufficient that the first maximum electric field strength as caused by each of the rotating electric activity synchronization pulses is not more than 71 % or not more than 50 % of the second maximum electric field strength as caused by the rotating electric activity termination or unpinning pulse. In absolute terms, the first maximum electric field strength as caused by all of the rotating electric activity synchronization pulses may be in a range from 20 to 300 V/m. Typically it is not more than 200 V/m. The first electric field strength caused by each of the rotating electric activity synchronization pulses may further be constant, i.e. the same with all of the rotating electric activity synchronization pulses.

The first electric pulse energy delivered to the cardiac tissue by each of the rotating electric activity synchronization pulses is preferably not more than 50 % or even not more than 25 % of the second electric pulse energy delivered to the cardiac tissue by the rotating electric activity termination or unpinning pulse. In absolute terms, the first electric pulse energy delivered to the cardiac tissue by each of the rotating electric activity synchronization pulses may be in a range from 0.005 to 20 J. This rather large range is due to the fact that the geometries under which electrodes for applying the pulses are arranged may vary strongly. Further, the first electric pulse energy delivered to the cardiac tissue by each of the rotating electric activity synchronization pulses may be constant, i.e. the same with all of the rotating electric activity synchronization pulses.

In the apparatus according to the invention, the electric state analyzer may be configured to analyze the at least one electric parameter sensed by the electric state sensor for a characteristic frequency of the rotating electric activity in the cardiac tissue. The pulse generator of the apparatus may then be configured to generate the rotating electric activity synchronization pulses of intervals which are smaller than the reciprocal value of this characteristic frequency. Further, the electric state analyzer may be configured to analyze the at least one electric parameter sensed by the electric state sensor for a dominant frequency as the characteristic frequency of the rotating electric activity in the cardiac tissue.

Preferably, the pulse generator is configured to generate the rotating electric activity synchronization pulses at intervals in a range from 0.6 times the reciprocal value of the characteristic frequency to 0.9 times the reciprocal value of the characteristic frequency.

The pulse applicator of the apparatus according to the present invention may be configured to generate the rotating electric activity synchronization pulses as unipolar electric pulses of a same polarity, and to generate the rotating electric activity termination or unpinning pulse as a bipolar electric pulse. The rotating electric activity termination or unpinning pulse being a bipolar electric pulse advantageously avoids electrically charging the cardiac tissue to a relevant extent. Nevertheless, the electric energy applied during a first part of the rotating electric activity termination or unpinning pulse may include more than 60 or 70 % of the electric energy applied by the entire rotating electric activity termination or unpinning pulse. The rotating electric activity synchronization pulses may also be bipolar. But this will normally not provide any additional benefit. The first part of the rotating electric activity termination or unpinning pulse may have the same or the opposite polarity as compared to the rotating electric activity synchronization pulses. However, the relative polarity of the rotating electric activity termination or unpinning pulse will have an influence on the optimum second interval at which the rotating electric activity termination or unpinning pulse is applied after the last rotating electric activity synchronization pulse.

The electric pulses generated by the pulse generator of the apparatus according to the invention may additionally include a plurality of anti-tachycardia pacing (ATP) pulses at intervals smaller than the reciprocal value of the characteristic frequency and succeeding the rotating electric activity termination or unpinning pulse. Such anti-tachycardia pacing pulses may be locally applied by a known bipolar electrode of standard ATP configuration, and they will be of a typical ATP electric pulse energy, i.e. of a much smaller electric pulse energy than both the second electric pulse energy of the rotating electric activity termination or unpinning pulse and the first electric pulse energy of the rotating electric activity synchronization pulses.

The pulse generator of the apparatus according the present invention may further be configured to generate further electric pulses in response to the electric state analyzer analyzing that there is still rotating electric activity in the cardiac tissue after the application of the electric pulses. I.e. the apparatus may try more than once to terminate or unpin the rotating electric activity by means of a plurality of electric activity synchronization pulses and a succeeding electric rotating activity termination or unpinning pulse.

The pulse applicator of the apparatus according to the present invention may be configured to apply all rotating electric activity synchronization and rotating electric activity termination or unpinning pulses as electric field pulses extending between a same electrode and a same counter electrode. This means that all electric pulses may have a same direction of the electrical field caused.

Advantageous developments of the invention result from the claims, the description and the drawings. The advantages of features and of combinations of a plurality of features mentioned at the beginning of the description only serve as examples and may be used alternatively or cumulatively without the necessity of embodiments according to the invention having to obtain these advantages. Without changing the scope of protection as defined by the enclosed claims, the following applies with respect to the disclosure of the original application and the patent: further features may be taken from the drawings, in particular from the illustrated designs and the dimensions of a plurality of components with respect to one another as well as from their relative arrangement and their operative connection. The combination of features of different embodiments of the invention or of features of different claims independent of the chosen references of the claims is also possible, and it is motivated herewith. This also relates to features which are illustrated in separate drawings, or which are mentioned when describing them. These features may also be combined with features of different claims. Furthermore, it is possible that further embodiments of the invention do not have the features mentioned in the claims.

The number of the features mentioned in the claims and in the description is to be understood to cover this exact number and a greater number than the mentioned number without having to explicitly use the adverb "at least". For example, if a pulse is mentioned, this is to be understood such that there is exactly one pulse or there are two pulses or more pulses. Additional features may be added to the features listed in the claims, or these features may be the only features of the respective apparatus.

The reference signs contained in the claims are not limiting the extent of the matter protected by the claims. Their sole function is to make the claims easier to understand.

BRIEF DESCRIPTION OF THE DRAWINGS

In the following, the invention is further explained and described with respect to preferred exemplary embodiments illustrated in the drawings.

Fig. 1 is a schematic drawing of an apparatus according to the present invention.

Fig. 2 is a flow chart illustrating the operation of the apparatus of the present invention.

Fig. 3 schematically shows the electric energy applied by electric pulses provided by the apparatus according to the invention and their temporal sequence according to a first embodiment, and

Fig. 4 schematically shows the electric energy applied by electric pulses provided by the apparatus according to the invention and their temporal sequence according to a second embodiment.

Fig. 5 depicts a time series of an electrocardiogram (ECG) showing successful termination of a ventricular fibrillation in a pig heart.

Fig. 6 depicts data of experiments with pig hearts and compares the voltage of rotating electric activity termination or unpinning pulses applied after rotating electric activity synchronization pulses with the voltage of each of a plurality of rotating electric activity termination or unpinning pulses applied according to WO 2012/172027 A2.

Fig. 7 depicts data of experiments with rabbit hearts which otherwise correspond to the experiments according to Fig. 6.

DESCRIPTION OF THE DRAWINGS

The apparatus 1 according to the present invention depicted in **Fig. 1** is configured to terminate or unpin rotating electric activity 2 in a cardiac tissue 3. The rotating electric activity 2 is schematically indicated here by a circular arrow 4 rotating about an inhomogeneity 5 of the cardiac tissue 3. A pair of electrodes 6, 7 provides an electric state sensor 8 which senses at least one electric parameter of the cardiac tissue, like for example a voltage between the electrodes 6 and 7. If the cardiac tissue 3 is a living heart, one of the electrodes, like for example the electrode 6, will typically be placed within the heart, whereas the other electrode, like for example the electrode 7, may be placed outside the heart and even outside a thorax surrounding the heart. The electric parameter sensed by the electric state sensor 8 including the electrodes 6 and 7 is analyzed by an electric state analyzer 9. The electric state analyzer 9 is located within a housing 10. The electrodes 6 and 7 are connected to the analyzer via external lines 11 and 12, connectors 13 and 14 provided at the housing 10 and internal lines 15 and 16. The electric state analyzer 9 analyzes the at least one electric parameter sensed by the electric state sensor 8 for rotating electric activity 2 in the cardiac tissue 3. If the electric state analyzer 9 analyzes that there is rotating electric activity 2 in the cardiac tissue 3, the analyzer determines a characteristic frequency of the rotating electric activity 2 and forwards control signals 17 and 18 which are indicative on the fact that there is rotating electric activity 2 in the cardiac tissue 3 and its characteristic frequency, respectively, to a pulse generator 19. The generator 19 then generates electric pulses which are applied to the cardiac tissue 3 via the electrodes 6 and 7 now acting as a pulse applicator 20 applying the electric pulses as electric field pulses extending across the cardiac tissue 3. These electric pulses include a plurality of rotating electric activity synchronization pulses followed by a rotating electric activity termination or unpinning pulse of a higher maximum electric field strength and electric pulse energy. The electrodes 6 and 7 are unipolar electrodes, they may be arranged in various geometries, and they may be supplemented by additional unipolar electrodes for applying the rotating electric activity synchronization pulses and the rotating electric activity termination or unpinning pulse as electric field pulses. Further, the pulse applicator 20 may include a bipolar electrode 30 for ATP also connected to the generator 20 and to the cardiac tissue 3.

The flow chart according to **Fig. 2** illustrates the operation of the apparatus 1 according to Fig. 1. The flow chart starts with a step 21 of sensing the at least one electric parameter of the cardiac tissue 3. In a next step 22, the electric parameter is analyzed for the presence of rotating electric activity 2. If there is no rotating electric activity, the operation of the apparatus 1 returns to step 21. If there is rotating electric activity 2, a characteristic frequency fcharea of the rotating electric activity is determined in a step 23. This characteristic frequency fcharea may be the dominant frequency of the rotating electric activity 2.

Next, in a step 24, various parameters of the electric pulses to be generated by the pulse generator 19 are set. These parameters include intervals Tsync, which are set smaller than a reciprocal value of the dominant frequency fcharea, a maximum field strength FSsync to be caused by the rotating electric activity synchronization pulses, and their pulse energy PEsync. Further, an interval Δt between the final rotating electric activity synchronization pulse and the rotating electric activity termination or unpinning pulse, a maximum field strength FStou and an electric pulse energy PEtou of the rotating electric activity termination or unpinning pulse are set. In a step 25, the rotating activity synchronization pulses and the rotating activity termination or unpinning pulse are generated according to the parameters set in step 24. In step 26 these electric pulses are applied to the cardiac tissue 3. Afterwards, the at least one electric parameter of the cardiac tissue 3 is sensed again and analyzed for the presence of rotating electric activity 2, i.e. the operation of the apparatus 1 once again starts with steps 21 and 22.

Fig. 3 indicates the electric pulse energies PEsync and PEtou depending on the maximum electric field strengths FSsync and FStou of seven electric activity synchronization pulses 27 followed by a single rotating electric activity termination or unpinning pulse 28. Fig. 3 shows that the electric pulse energy PEsync is the same for all electric activity synchronization pulses 27, and that the rotating electric activity synchronization pulses 27 are all arranged at same intervals Tsync in time t. The following rotating electric activity termination or unpinning pulse is arranged at the interval Δt which is typically smaller than the interval Tsync. Generally it is in a range of 0.7 to 1.2 times Tsync. Additionally, the electric pulse energy PEtou of the rotating electric activity termination or unpinning pulse 28 is clearly higher than the electric pulse energy PEsync. The same applies to the respective maximum electric field strengths FSsync and FStou. Both the maximum field strength FStou and the pulse energy of the rotating electric activity termination or unpinning pulse 28 are in ranges typical for rotating electric activity termination or unpinning pulses according to WO 2012/172027 A2. According to the invention, however, a single rotating activity termination or unpinning pulse 28 is sufficient due to the synchronization of the rotating electric activity by means of the rotating electric activity synchronization pulses 27 preceding the rotating electric activity termination or unpinning pulse 28.

Fig. 4, in addition to Fig. 3 also shows a plurality of anti-tachycardia pacing (ATP) pulses 29 succeeding the rotating activity termination or unpinning pulse 28. The anti-tachycardia pacing pulses 29 are applied by the bipolar electrode 30 of Fig. 1. The anti-tachycardia pacing pulses 29 are depicted as being arranged at same intervals in time as the rotating electric activity synchronization pulses 27 but as being of a much smaller electric pulse energy PEATP than the electric pulse energy PEsync of the rotating electric activity synchronization pulses 27. Further, the anti-tachycardia pacing pulses 29 may alternatively be arranged at different intervals in time as compared to the rotating electric activity synchronization pulses 27. Particularly, the parameters of the anti-tachycardia pacing pulses 29 may be set and the anti-tachycardia pacing pulses 29 may be applied according to the general knowledge of those skilled in the art of anti-tachycardia pacing.

Fig. 5 depicts a time series of an electrocardiogram (ECG) showing successful termination of ventricular fibrillation in a pig heart in a Langendorff perfusion setup at t = 6.1 s. This termination was achieved by applying 25 rotating electric activity synchronization pulses 27 starting at t = 2 s, and one rotating electric activity termination or unpinning pulse 28. The rotating electric activity termination or unpinning pulse 28 had a field strength of a comparable magnitude to that required in the same setup to terminate ventricular fibrillation according to WO 2012/172027 A2. The electric field strength of the rotating electric activity synchronization pulses was less than 11 % of the electric field strength of the rotating electric activity termination or unpinning pulse 28.

Fig. 6 depicts data of whole-heart Langendorff perfusion experiments with pig hearts and compares the voltage of the rotating electric activity termination or unpinning pulse 28 applied by the apparatus of the present invention with the voltage of rotating electric activity termination or unpinning pulses according to WO 2012/172027 A2, that are required for a probability of 0.5 to terminate ventricular fibrillation. Two dots connected by a line correspond to one experiment. The required voltages differ among the experiments, but within one experiment they are similar. As the rotating electric activity synchronization pulses are of much lower voltage, the total energy applied by the apparatus according to the present invention for terminating the ventricular fibrillation is significantly lower than the total energy applied by the apparatus according to WO 2012/172027 A2.

Fig. 7 depicts data of whole heart Langendorff perfusion experiments with rabbit hearts and compares the voltage of the rotating electric activity termination or unpinning pulse applied by the apparatus according to the present invention with the voltage of rotating electric activity termination or unpinning pulses applied according to WO 2012/172027 A2, that are required for a probability of 0.5 to terminate ventricular fibrillation. Two dots connected by a line correspond to one experiment. The required voltages differ among the experiments, but within one experiment they are similar. As the rotating electric activity synchronization pulses are of a much lower voltage, the total energy applied by the apparatus according to the present invention is significantly lower than the total energy applied by the apparatus according to WO 2012/172027 A2.

LIST OF REFERENCE NUMERALS

1	Apparatus
2	Rotating electric activity
3	Cardiac tissue
4	Circular arrow
5	Inhomogeneity
6	Electrode
7	Electrode
8	Electric state sensor
9	Electric state analyzer
10	Housing
11	External line
12	External line
13	Connector
14	Connector
15	Internal line
16	Internal line
17	Electric signal
18	Electric signal
19	Generator
20	Pulse applicator
21	Step of sensing
22	Step of analyzing
23	Step of determining
24	Step of setting
25	Step of generating
26	Step of applying
27	Rotating electric activity synchronization pulse
28	Rotating electric activity termination or unpinning pulse
29	Anti-tachycardia pacing pulse
30	Bipolar electrode
Tsync	Intervals of the rotating electric activity **sync**hronization pulses 27

FSsync	Maximum electric **f**ield **s**trength caused by the rotating electric activity **sync**hronization pulses 27
PEsync	**P**ulse **e**nergy of the rotating electric activity **sync**hronization pulses 27
Δt	Interval in **t**ime at which the rotating electric activity termination or unpinning pulse 28 is arranged after the last rotating electric activity synchronization pulse 27
FStou	Maximum **f**ield **s**trength of the rotating electric activity **t**ermination **o**r **u**npinning pulse 28
PEtou	**P**ulse **e**nergy of the rotating electric activity **t**ermination **o**r **u**npinning pulse 28
t	**T**ime
FS	**F**ield **s**trength
PE	**P**ulse **e**nergy
PEATP	**P**ulse **e**nergy of the **a**nti-**t**achycardia **p**acing pulses 29
fcharea	**Cha**racteristic **f**requency of the **r**otating **e**lectric **a**ctivity 2

CLAIMS

1. An apparatus (1) for terminating or unpinning rotating electric activity (2) in a cardiac tissue (3), the apparatus (1) comprising:

- an electric state sensor configured to sense at least one electric parameter of the cardiac tissue;
- an electric state analyzer (9) connected to the electric state sensor (8) and configured to analyze the at least one electric parameter sensed by the electric state sensor (8) for rotating electric activity (2) in the cardiac tissue (3);
- a pulse generator (19) connected to the electric state analyzer (9) and configured to generate electric pulses in response to the electric state analyzer analyzing that there is rotating electric activity (2) in the cardiac tissue (3), the electric pulses including a rotating electric activity termination or unpinning pulse (28); and
- a pulse applicator (20) connected to the pulse generator (19) and configured to apply the electric pulses as electric field pulses extending across the cardiac tissue (3);

characterized in

- that the electric pulses include a plurality of rotating electric activity synchronization pulses (27) preceding the rotating electric activity termination or unpinning pulse (28),
- wherein the rotating electric activity synchronization pulses (27) are arranged at first intervals (Tsync), and the rotating electric activity termination or unpinning pulse (28) is arranged at a second interval (Δt) in a range from 0.7 to 1.2 times one of the first intervals (Tsync) after the last one of the plurality of rotating electric activity synchronization pulses (27), and
- wherein at least one of
  - a first maximum electric field strength (FSsync) as caused by each of the rotating electric activity synchronization pulses (27) and
  - a first electric pulse energy (PEsync) delivered to the cardiac tissue (3) by each of the rotating electric activity synchronization pulses (27)

is not more than 82 % of a second maximum electric field strength (FStou) as caused by the rotating electric activity termination or unpinning pulse (28) or not more than 67 % of a second electric pulse energy (PEtou) delivered to the cardiac tissue (3) by the rotating electric activity termination or unpinning pulse (28), respectively.

2. The apparatus (1) of claim 1, **characterized in** that a number of the rotating electric activity synchronization pulses (27) preceding the rotating electric activity termination or unpinning pulse (28) is at least five.

3. The apparatus (1) of claim 2, **characterized in** that the number of the rotating electric activity synchronization pulses (27) preceding the rotating electric activity termination or unpinning pulse (28) is in a range from 10 to 30.

4. The apparatus (1) of any of the preceding claims, **characterized in** that the first maximum electric field strength (FSsync) as caused by each of the rotating electric activity synchronization pulses (27) is not more than 71 % or not more than 50 % of the second maximum electric field strength (FStou) as caused by the rotating electric activity termination or unpinning pulse (28).

5. The apparatus (1) of any of the preceding claims, **characterized in** that the first maximum electric field strength (FSsync) as caused by each of the rotating electric activity synchronization pulses (27) is in a range from 20 to 200 V/m.

6. The apparatus (1) of any of the preceding claims, **characterized in** that the first maximum electric field strength (FSsync) as caused by each of the rotating electric activity synchronization pulses (27) is constant.

7. The apparatus (1) of any of the preceding claims, **characterized in** that the first electric pulse energy (PEsync) delivered to the cardiac tissue (3) by each of the rotating electric activity synchronization pulses (27) is not more than 50 % or not more than 25 % of the second electric pulse energy (PEtou) delivered to the cardiac tissue (3) by the rotating electric activity termination or unpinning pulse (28).

8. The apparatus (1) of any of the preceding claims, **characterized in** that first the electric pulse energy (PEsync) delivered to the cardiac tissue (3) by each of the rotating electric activity synchronization pulses (27) is constant.

9. The apparatus (1) of any of the preceding claims, **characterized in** that the electric state analyzer (9) is configured to analyze the at least one electric parameter sensed by the electric state sensor (8) for a characteristic frequency (fcharea) of the rotating electric activity (2) in the

cardiac tissue (3), and that the pulse generator (19) is configured to generate the rotating electric activity synchronization pulses (27) at intervals of T < 1/ (fcharea).

10. The apparatus (1) of claim 9, **characterized in** that the electric state analyzer (9) is configured to analyze the at least one electric parameter sensed by the electric state sensor (8) for a dominant frequency as the characteristic frequency (fcharea) of the rotating electric activity (2) in the cardiac tissue (3).

11. The apparatus (1) of claim 9 or 10, **characterized in** that the pulse generator (19) is configured to generate the rotating electric activity synchronization pulses (27) at intervals of 0.6 x 1/ (fcharea) < T < 0.9 x 1/ (fcharea).

12. The apparatus (1) of any of the claims 9 to 11, **characterized in** that the electric pulses include a plurality of anti-tachycardia pacing pulses (29) at intervals of T < 1/ (fcharea) succeeding the rotating electric activity termination or unpinning pulse (28) .

13. The apparatus (1) of claim 9, **characterized in** that the pulse applicator (20) comprises a separate bipolar electrode (30) connected to the pulse generator (19) and configured to apply the anti-tachycardia pacing pulses (29) to the cardiac tissue.

14. The apparatus (1) of any of the preceding claims, **characterized in** that the pulse generator (19) is configured to generate further electric pulses in response to the electric state analyzer (9) analyzing that there is still rotating electric activity (2) in the cardiac tissue (3) after the application of the electric pulses.

15. The apparatus (1) of any of the preceding claims, **characterized in** that the pulse applicator (20) is configured to apply all rotating electric activity synchronization (27) and rotating electric activity termination or unpinning (28) pulses as electric field pulses extending between a same electrode and a same counter electrode.

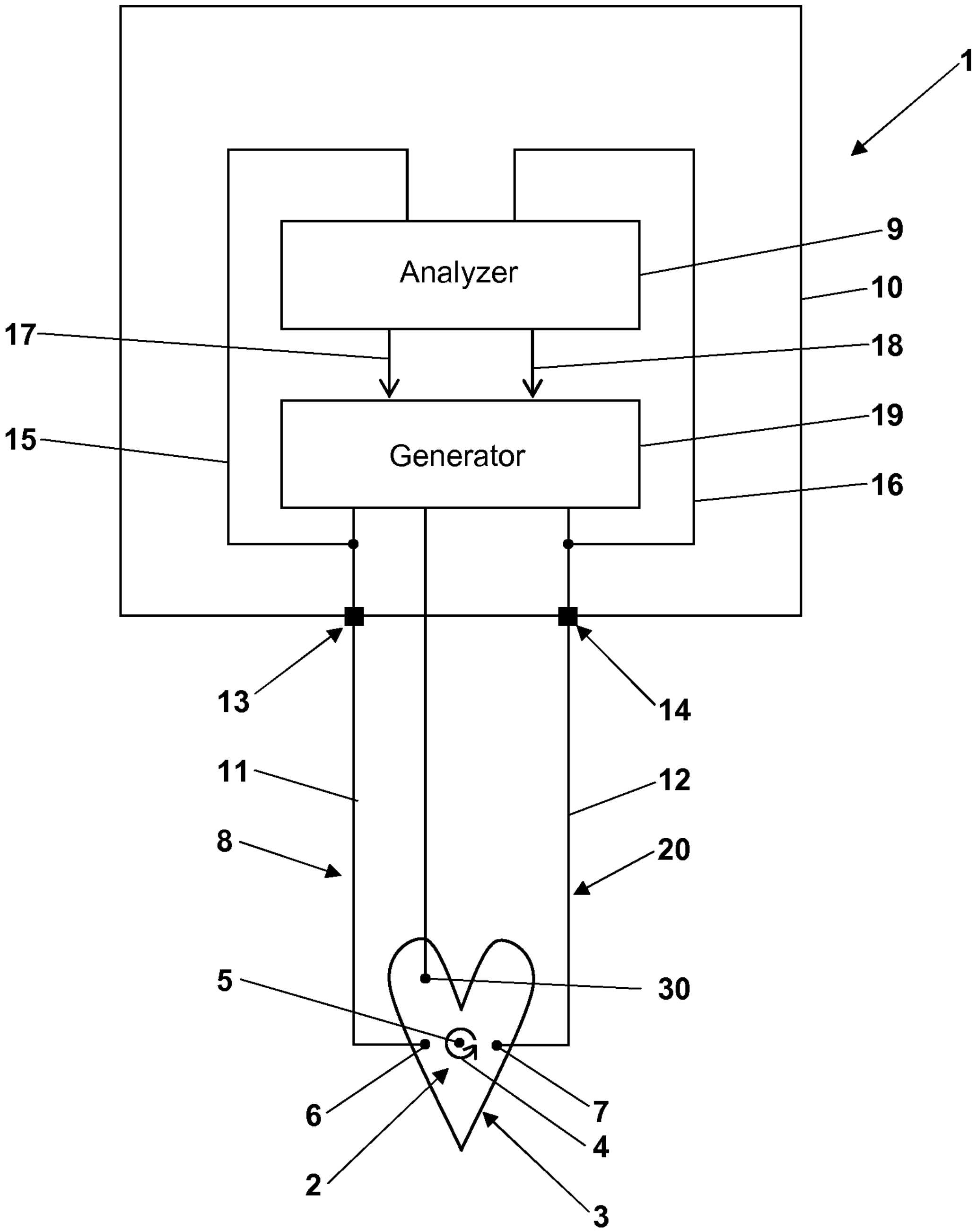
1
9
Analyzer
10
17
18
Generator
19
15
16
13
14
11
12
8
20
5
30
6
7
4
2
3

Fig. 1

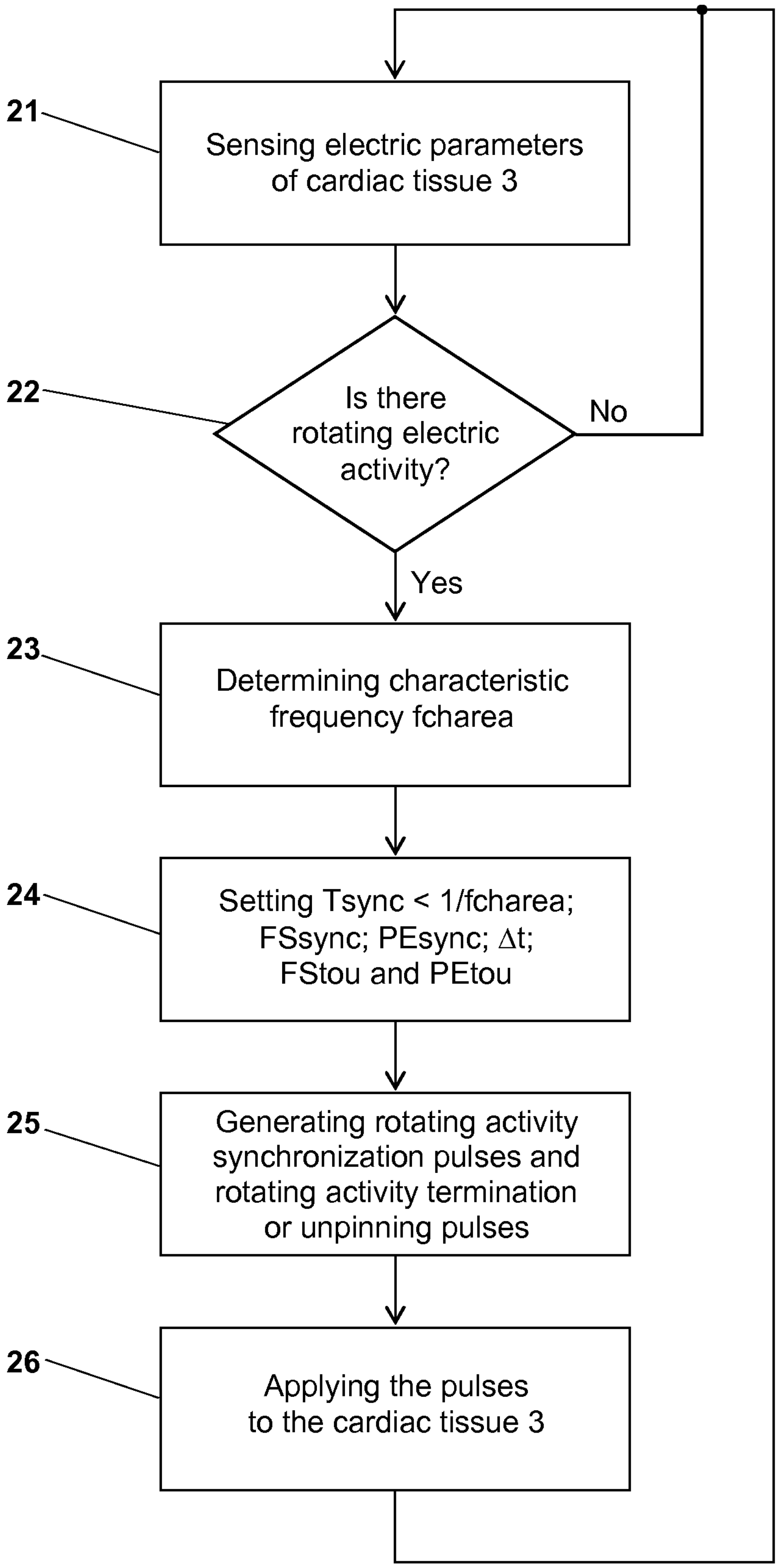
21
Sensing electric parameters of cardiac tissue 3
22
Is there rotating electric activity?
No
Yes
23
Determining characteristic frequency fcharea
24
Setting Tsync < 1/fcharea; FSsync; PEsync; Δt; FStou and PEtou
25
Generating rotating activity synchronization pulses and rotating activity termination or unpinning pulses
26
Applying the pulses to the cardiac tissue 3

Fig. 2

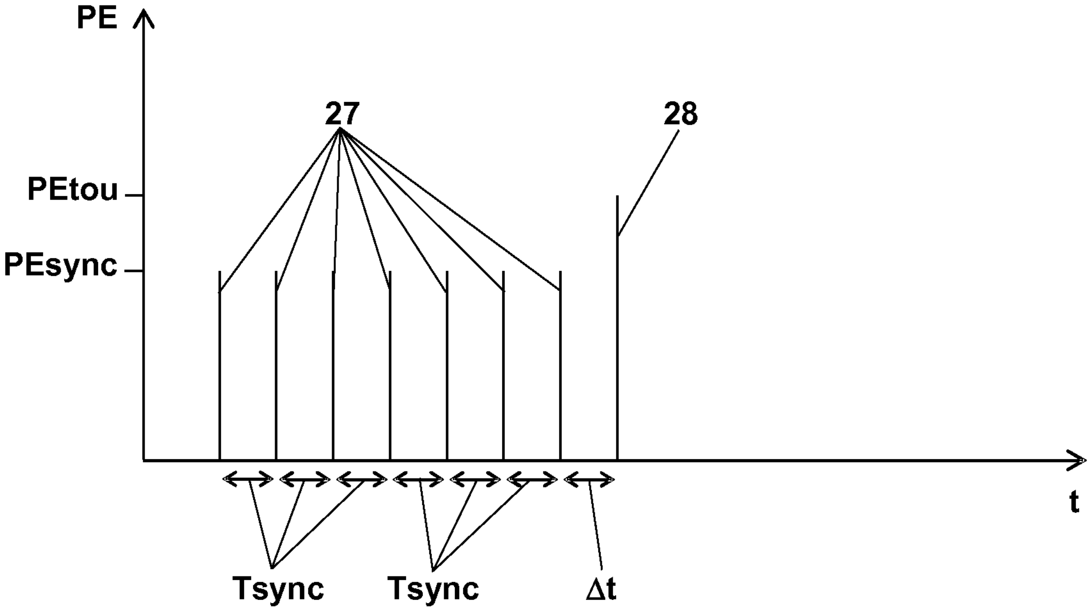
PE
27
28
PEtou
PEsync
t
Tsync
Tsync
Δt

Fig. 3

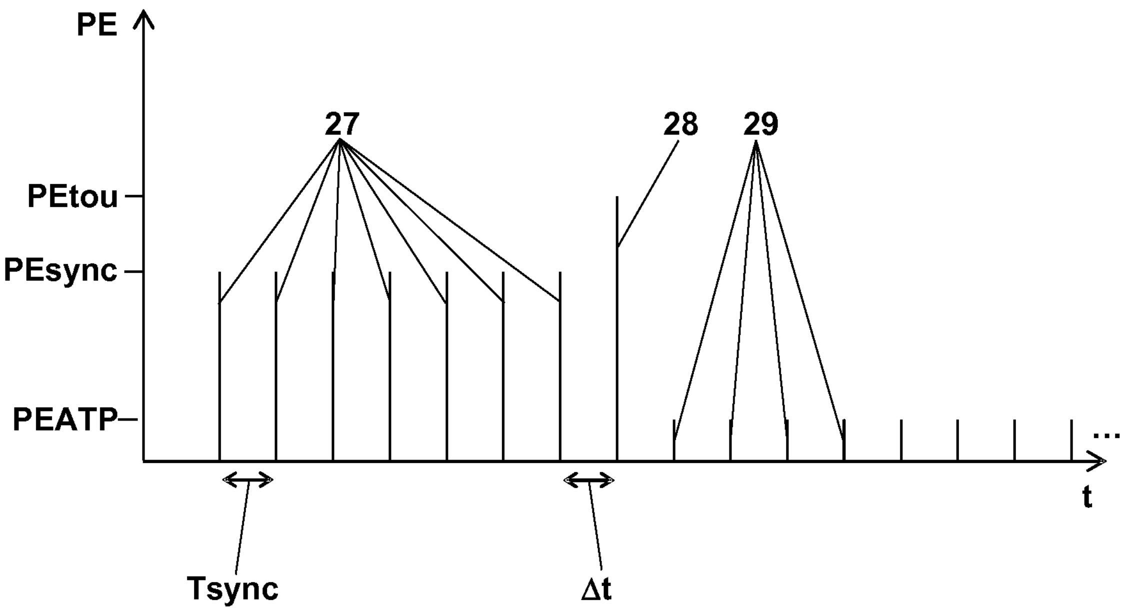
PE
27
28
29
PEtou
PEsync
PEATP
...
t
Tsync
Δt

Fig. 4

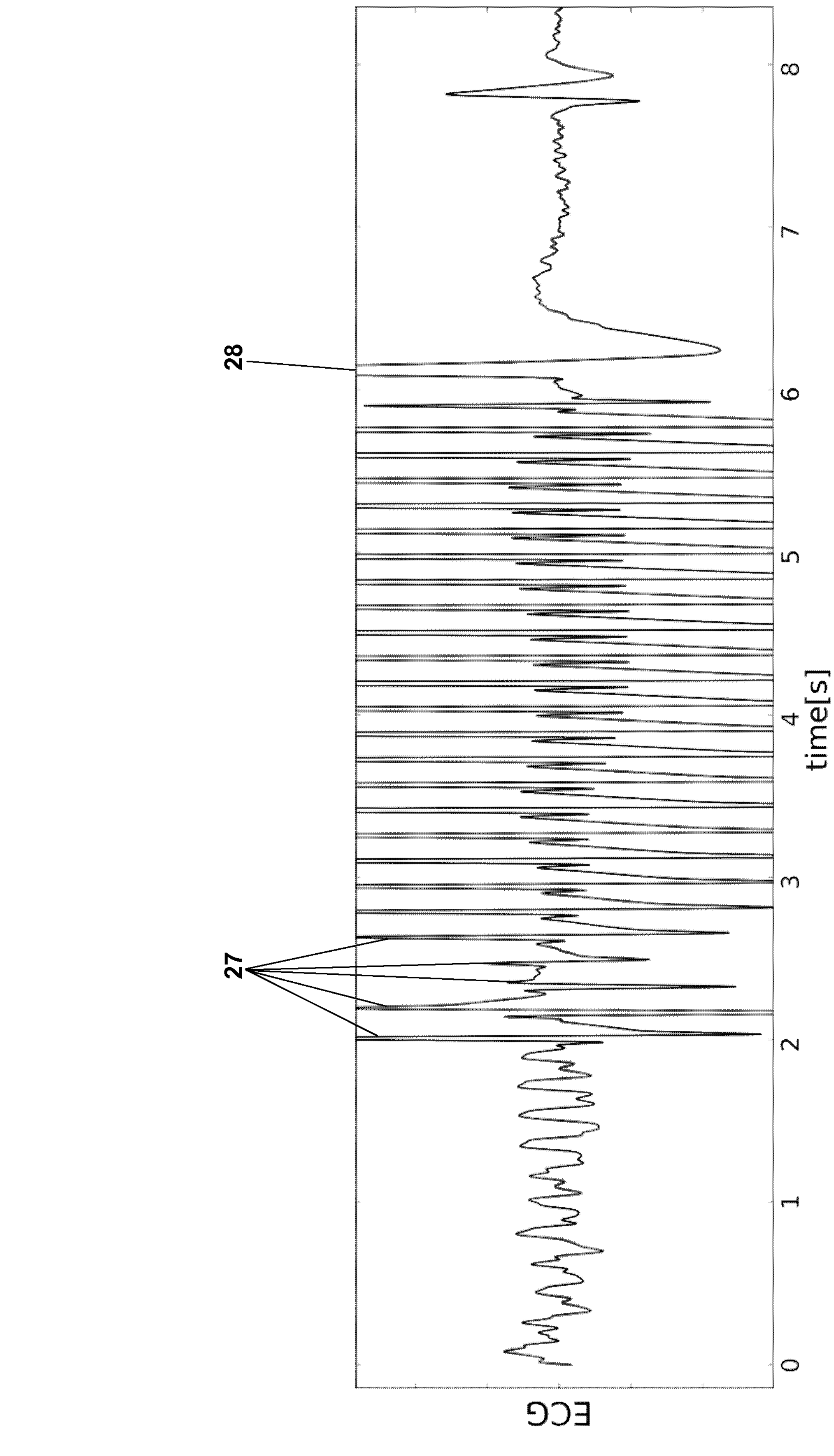

Fig. 5

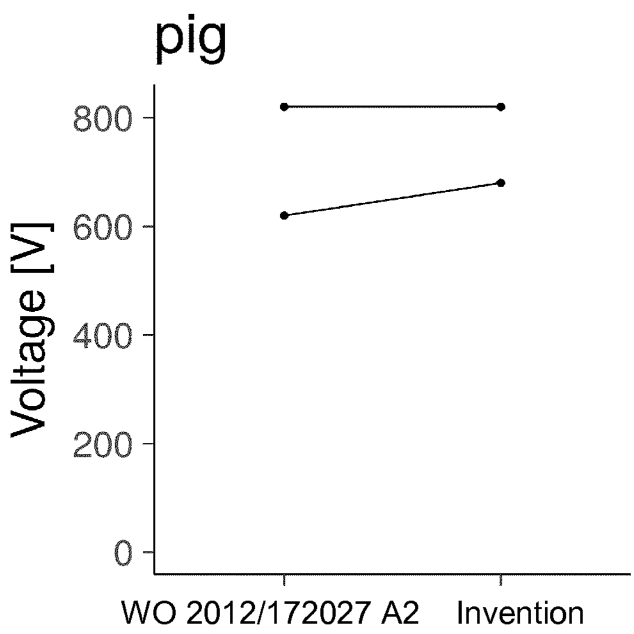
pig
Voltage [V]
800
600
400
200
0
WO 2012/172027 A2
Invention

Fig. 6

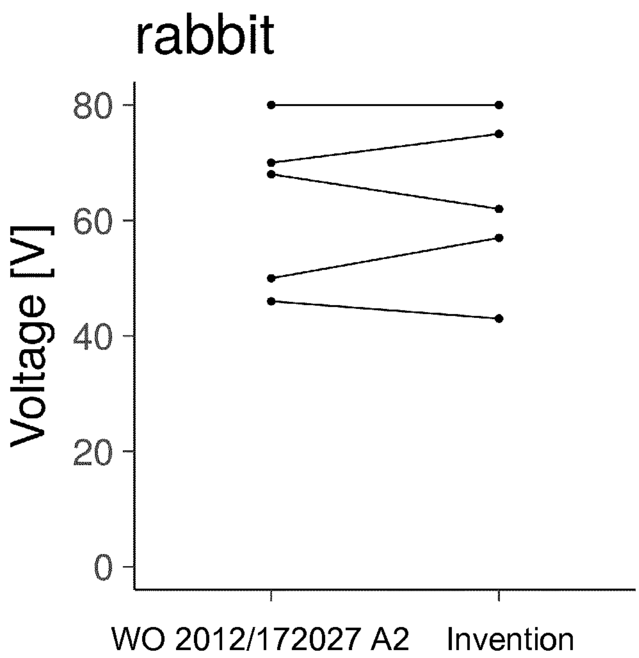
rabbit
Voltage [V]
80
60
40
20
0
WO 2012/172027 A2
Invention

Fig. 7

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2017/082048

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N1/39
ADD. A61N1/362

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)
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 practicable, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2004/172065 A1 (SIH HARIS J [US] ET AL) 2 September 2004 (2004-09-02) abstract; figures 1, 2, 5 paragraph [0001] paragraph [0015] - paragraph [0016] paragraph [0019] paragraph [0028] - paragraph [0044] paragraph [0056] - paragraph [0059] -----	1-15
A	US 2006/100670 A1 (SWEENEY ROBERT J [US]) 11 May 2006 (2006-05-11) the whole document -----	1-15
A	WO 2012/172027 A2 (MAX PLANCK GESELLSCHAFT [DE]; UNIV CORNELL [US]; LUTHER STEFAN [DE]; B) 20 December 2012 (2012-12-20) cited in the application the whole document -----	1-15

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

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

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"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
15 February 2018	04/04/2018

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, Fax: (+31-70) 340-3016	Molina Silvestre, A

1

International application No
PCT/EP2017/082048

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00/72918 A1 (IMPULSE DYNAMIC NV [NL]; BEN HAIM SHLOMO [IL]; DARVISH NISSIM [IL]; MI) 7 December 2000 (2000-12-07) the whole document -----	1-15

1

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Information on patent family members

International application No
PCT/EP2017/082048

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