



(51) International Patent Classification:

A61B 5/0452 (2006.01) A61B 5/00 (2006.01)
A61B 5/0464 (2006.01)

(21) International Application Number:

PCT/GB2015/052192

(22) International Filing Date:

29 July 2015 (29.07.2015)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

1414335.8 13 August 2014 (13.08.2014) GB

(72) Inventor; and

(71) Applicant : SAUMAREZ, Richard C. [GB/GB]; 21
Greenside, Waterbeach, Cambridge Cambridgeshire CB25
9HW (GB).

(74) Agents: TOLFREE, Adam et al.; TPT CAMBRIDGE,
Toll Drove, Manea Cambridgeshire PE15 0JX (GB).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,

BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,
SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ,
TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU,
TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,
LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK,
SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

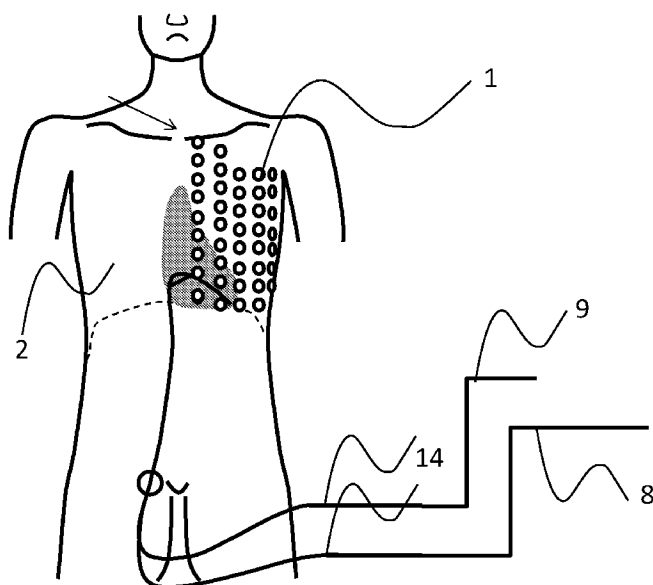
Published:

— with international search report (Art. 21(3))

— with amended claims (Art. 19(1))

(54) Title: APPARATUS FOR RECORDING AND ANALYSING A SURFACE ELECTROCARDIOGRAM (ECG) FOR DISTINGUISHING A PHYSIOLOGICAL SIGNAL FROM NOISE

Figure 2



(57) Abstract: There is described a technique using apparatus for recording and analysing a surface electrocardiogram (ECG) for distinguishing a physiological signal from noise. The technique involves aligning and averaging multiple surface electrogram records taken for repeated pacing sequence with the same interval between pacing stimuli.

**Apparatus for Recording and Analysing a Surface Electrocardiogram (ECG) for
Distinguishing a Physiological Signal From Noise**

Previous research has shown that the risk of sudden death due to cardiac arrhythmias can be predicted by observing the shape of recorded endocardial electrograms in response to pacing.

The diagnostic change in electrograms consists of small deflections in the recorded electrogram following early stimulation of the heart. The heart is stimulated with apparatus that generates a stimulation sequence at one site in the heart and records electrograms from other sites within the heart.

10 The above technique has been used to form intra-ventricular conduction curves in which the delay of each potential within an electrogram following an early stimulation of the heart is plotted against the interval between the stimulus and the last stimulus of a constant rate sequence of stimuli. Typically this involves between 230 and 250 early stimuli with the interval at which each early stimulus is applied is
15 reduced by one millisecond on each occasion. These curves have characteristic shapes that can be analysed to estimate the risk of sudden death. This technique is described in GB2439562.

In previous research using this technique, the diseases that affect the heart have been assumed to uniformly affect all of the tissue within the heart. In the case of patients
20 that have recovered myocardial infarction, the abnormalities are confined to the tissue that surrounds the infarct. While it is possible to make detailed endocardial recordings in that region, such a technique is too complex for routine use, because for example, the need for multiple left ventricular electrodes.

A surface electrocardiogram (ECG) consists of potentials measured on the torso
25 surface, these represent the weighted sum of all of the currents active within the heart. Surface ECGs are commonly used for diagnostic purposes.

The small deflections following an early stimulus can be detected using a surface ECG recording although the detected deflections are extremely small. Therefore a process needs to be carried out to distinguish these small deflections from noise.

5 A common technique is to average the signals to accentuate small potentials from the noise.

It is well known that some patients have small delayed potentials discernible in their average ECG during sinus rhythm and this has some association with the risk of sudden death.

10 According to a first aspect of the invention there is provided apparatus for recording and analysing a surface electrocardiogram (ECG) for distinguishing a physiological signal from noise; the apparatus comprising:

a) means to pace the heart in a pacing sequence comprising a number of stimuli with a constant interval followed by an early stimulus, in which the interval between the early stimulus and the preceding constant rate stimulus is smaller than the interval
15 between the constant rate stimuli;

b) means to repeat the pacing sequence multiple times with the same interval between the early stimulus and the preceding constant rate stimulus;

c) means to repeat the pacing sequence multiple times with a different interval between the early stimulus and the preceding constant rate stimulus;

20 d) means to create surface electrocardiogram records during the repeated pacing sequences in b) and c) ;

e) means to average the surface electrocardiogram records corresponding to each of the early stimuli paced in b); and

f) means to average the surface electrocardiogram records corresponding to each of the early stimuli paced in c).

The apparatus thereby provides the ability to determine changes in intraventricular conduction thereby building a conduction curve that is analogous to that obtained using endocardial measurements.

In a preferred embodiment, the apparatus comprises means to compare the averaged recorded surface electrocardiograms taken from e) and f) and to display the differences thereby displaying a conduction curve.

A surface electrocardiogram shows physiological variability in its shape as a consequence of respiration, blood pressure control cycles etc. In order to compensate for this, it is preferred that there is at least one sensing endocardial cardiac electrode and means for using a signal sensed by the at least one sensing endocardial cardiac electrode to compensate for delays and/or distortion of the surface electrocardiogram.

Preferably the at least one sensing endocardial cardiac electrode is used to derive an interval between the pacing stimulus provided by a pacing electrode and the onset of activation of myocardium in a region proximate to the pacing electrode. The variation in this interval represents stimulus to tissue latency and its measure allows alignment of the surface electrocardiogram signals to a common timing reference. Thus it is also preferred that the interval derived for each stimulus is used to align the surface ECG record corresponding to that stimulus to a common time reference.

By aligning of the surface ECG signals improved resolution of its features will be obtained following averaging as misaligned signals will tend to degrade detection of small potentials.

So that the conduction time between electrodes will be short as compared to the stimulus to tissue latency, it is preferred that the distance between the pacing

electrode and the at least one sensing endocardial cardiac electrode is substantially 1cm or less.

It is further preferable that the apparatus comprises a first sensing cardiac electrode that is proximate to a pacing electrode and a second sensing cardiac electrode that is
5 remote to the pacing electrode.

It is preferred that the pacing electrode, first sensing cardiac electrode, and where applicable second sensing cardiac electrode are located within the right ventricle of the heart. Thereby avoiding additional complexity of left ventricular catheterisation.

The apparatus may also comprise means to determine an interval between a signal
10 from the first sensing electrode resulting from the activation of myocardial tissue proximate the first electrode and a second signal from the second sensing electrode resulting from activation of myocardial tissue proximate the second electrode. This interval represents conduction velocity throughout the heart and may be used to time stretch or time compress the surface electrocardiogram records so that each record is
15 the same length. This has the effect also of increasing resolution of the averaged surface ECG signal as a result of better alignment of the potentials when averaging takes place.

The interval between potentials as sensed by the proximate electrode and remote electrode is measured, preferably by cross correlation. (Variations in the interval may
20 be caused by physiological effects such as respirations, fluctuations in blood pressure etc.) This allows stretching of the individual surface ECG records for each response to the early stimuli so as to become of equal length.

The timings of pacing stimuli are derived from a clock with a frequency of 1KHz resulting in 1ms time resolution. This frequency may result in stimuli that are
25 coherent with mains frequency interference and its harmonics. Therefore the noise in the surface ECG may not be truly random and so not eliminated by averaging. To

overcome this, it is preferred that a pseudo-random time jitter is introduced into the constant rate stimuli. More preferably the pseudo-random time jitter is introduced into the first constant rate stimulus of each pacing sequence. This will decouple the pacing sequence from AC noise.

- 5 A first assumption behind averaging is that each physiological signal being averaged is identical. A second assumption is that the measurements reflect a pure electrophysiological process, however, where there is progressive cardiac ischaemia conduction within the heart will be affected as the pacing proceeds that will alter the morphology of the surface ECG and in particular the responses associated with the
10 constant rate stimuli.

In order to identify progressive changes in shape of the response to constant rate stimuli, it is preferred that each ECG record is divided into sub records and the change in signal power (the square of the signal amplitude) is determined each a new record added to the average record. If the signal power fails to decline as new records
15 are added it will indicate progressive change in the ECG morphology and non stationarity of the averaging process which is indicative of ischemia.

The invention will now be described by example with reference to the following figures in which:

Figure 1 is a schematic of apparatus to stimulate a heart, make a surface ECG, and
20 subsequently analyse the resulting data;

Figure 2 is a schematic illustrating the electrodes used to pace the heart and take recording from within the heart and from the torso surface;

Figure 3 is an antero-posterior projection of the hearts showing the relative positions of the pacing electrode and sensing electrodes;

25 **Figure 4** is a schematic of the stimulation sequence used to pace the heart;

Figure 5 is a schematic indicating alignment of surface ECG responses for different coupling intervals being averaged;

Figure 6 is a simulated high-pass filtered surface electrocardiogram signal;

Figure 7 is the surface ECG signal of Fig 6 with added noise;

- 5 **Figure 8** is an averaged ECG signal (similar to Fig 7) illustrating the cancelling out of noise;

Figure 9 is a schematic showing pseudo-random jitter in a first constant rate stimulus in a sequence;

- 10 **Figure 10** is a schematic illustrating misalignment between successive potentials following an extra stimulus;

Figure 11 illustrate recorded endocardial electrograms following a constant rate stimulus;

Figure 12 is a plot showing delays of endocardial potentials following successive constant rate stimuli;

- 15 **Figure 13** illustrates the process of cross correlating signals from proximate and remote recording electrodes to derive the delay between them;

Figure 14 shows alignment of two signals using stimulus to tissue latency;

Figure 15 illustrates time compression and time dilation of electrograms to give a consistent length signal;

- 20 **Figure 16** show the results of averaging a non-stationary signal;

Figure 17 shows the segmentation of a signal into successive sub-records;

Figure 18 shows the power in selected sub records varying as the number of averages increases for a stationary signal; and

Figure 19 a similar plot to Fig 18 for the non-stationary signal illustrated in Fig 17.

With reference to Fig 1 there is shown apparatus comprising a recording, pacing and an analysis system. The system comprises an array of thoracic surface electrodes 1 that sense potentials from torso surface 2, illustrated in Fig 2. The sensed potentials are amplified by a multichannel amplifier system 3 and digitised with an analogue to digital converter 4 and the digital signals stored in a memory 5. The heart 6 is stimulated with a pacing system 7 having an electrode 8 placed within the heart. Further electrodes 9 placed at alternative positions within the heart, as shown in Fig 3 sense potentials from within the heart 6. The endocardial electrodes 8, 9 are inserted via catheters 14 into the right ventricle. The potentials sensed by electrodes 9 are amplified by amplifier 10, digitised by an ADC 11 and stored in memory 5. The stimulation of the heart and recording of the sensed potentials are controlled by a computer program 12. Following a recording process, the recorded data in memory 5 is analysed by a further program 13.

Figure 3 shows the pacing electrode 8 positioned at a tip of a catheter 15A used to stimulate the heart 6 and a second electrode 9A mounted on the same catheter 15A within 1cm of the pacing electrode 8 for recording a response. A second recording electrode 9B on a second catheter 15B is positioned in the right ventricle of the heart 6 as far as possible from the pacing electrode 8. In addition to pacing electrode 8 a further pacing electrode (not shown) can be used to stimulate the high right atrium to avoid fusion beats.

The heart 6 is paced with a pacing sequence comprising a number of constant rate stimuli (S1) followed by an extra stimulus S2. The S1-S2 interval is smaller than the S1-S1 interval. Figure 4 illustrates four of these sequences showing in this instance two S1-S2 intervals in the sequences S1-S2A, S1-S2B, S1-S2A, S1-S2B,... Alternatively the sequence may be delivered as S1-S2A, S1-S2A,... S1-S2B, S1-S2B,... Fig 4 shows these sequences repeated twice but in practice it is preferred that they are repeated several hundred times. The number of repeats may be determined by the convergence of the signal.

Although only two intervals are shown, in practice eight intervals used to achieve a study in a practical length of time. However, more intervals may be used where time allows.

Figure 5 illustrates the process of averaging each recorded signal in response to S2 stimuli following the same S1-S2 interval; in this case the intervals A and B as shown in Fig 4.

Each recorded signal of interval A 20 are aligned in time using the pacing stimulus 21 within the recording. The aligned recorded signals are then summed to form an average signal 22 of interval A. The same process is also performed on each recorded signal 23 of interval B to create an average recorded signal of interval B 24. The averaging process reduces the noise by the square root of the number of averages for a Gaussian noise. It is also known that the averaging process acts as a low-pass filter that acts selectively on the noise.

Figures 6, 7 and 8 illustrate an ideal process showing a simulated high-pass filtered surface ECG signal 30. Two hundred records the signal shown in Fig 6 are created to represent records taken following S2 stimuli, pseudo-random noise is added to each record 31, one of which is shown in figure 7. These are then averaged to give the signal 32 shown in Fig 8, where the small potentials 33 in the terminal portion are discernible.

In practice, this process will be degraded in a number of ways rendering small potentials indiscernible. These ways and their remedies described.

A fundamental assumption is that that noise is unrelated to the signal being detected. Conventionally stimuli are calculated in 1ms intervals and are timed using a 1KHz clock. This may create synchronisation of the pacing process with mains AC noise or its harmonics. This is overcome, as illustrated in Fig 9 by imposing a pseudo-random jitter 40 in the interval between the S2 stimulus and S1 stimulus following it. The subsequent stimuli in the sequence following the S1 stimulus maintain the same interval from each other such that in effect all the stimuli within a sequence are jittered by the same amount. This will decouple the pacing sequence from periodic signals in the noise.

Another problem is that signals following a S2 stimulus may be misaligned as a consequence of physiological processes such as respiration. Figure 10 shows the

misalignment of potentials between two recorded signals 50, 51 by an interval 52 caused by said physiological processes.

This misalignment results in small potentials being not added together and so will not be detected in the averaged signal 32.

- 5 Figure 11 shows two intracardiac electrograms 60 62 recorded by remote electrode 9B following an S1 stimulus. The electrograms 60 62 have been aligned using the S1 stimulus as the reference point. Notwithstanding this alignment, it can be seen that there remains miss-alignment between the significant potentials 61 63 of the signals 60 62.

10 The first potential 61A in signal 60 following a S1 stimulus precedes the first potential 63A in signal 62. This distance 64 between the first potentials 61A 63A and S1 stimulus represents the signal to tissue latency. The difference in time between the first potentials 61A 63A from the S1 stimulus represents variation in signal to tissue latency 64A.

15 Similarly the potential 61B in signal 60 precedes the equivalent potential 63B in signal 62 by a greater interval 65 than the stimulus to tissue latency indicating time dilation of signal 62 with respect to signal 60.

Figure 12 shows the delays 61 and 63 measured for successive S1 stimuli and each potential 61 63 is plotted as the ordinate against the time at which the stimulus occurred. The mean interval between the S1 stimulus and the first potentials 61A 63A are shown by line 70. Similarly the mean interval between the S1 stimulus and the potentials 61B is shown by line 71. This variation will degrade detection of potentials of short duration.

25 Line 72 is an interpolated version of data points 61A 61B. It has a periodicity of approximately 11.5 per minute that likely to be due to respiration. The degree of variation in stimulus to tissue latency and time dilation of the electrogram are comparable to the width the small potentials that one would wish to detect in the electrocardiogram and therefore this degree of signal variation is likely to degrade the results of signal averaging. It should be noted this effect is highly variable between patients.

This problem can be minimised by using intracardiac reference electrograms.

Figure 13 illustrates electrograms 80 81 taken from the proximate and remote sensing electrodes 9A 9B respectively. The stimulus to tissue latency 64 marked $\Delta T1$ is determined from the proximate electrode signal 80. The two electrograms 80 81 are cross-correlated to give the cross-correlation function 82 showing a peak when the two are most correlated. The delay 83 of this peak $\Delta T2$ gives the delay between the electrograms 80 81. The mean delay of $\Delta T2$ for all records at a particular S1-S2 interval is determined.

Provided that $\Delta T2$ for an individual record is close to the mean $\Delta T2$ of all records, it indicates that there has been no significant stretch in the individual record, and any misalignment is therefore due to stimulus to tissue latency.

Figure 14 shows two misaligned signals 90 91 from a surface ECG. The misalignments shown as 92 are due to stimulus to tissue latency. The signal 91 is shifted by the difference in stimulus to tissue latency from the mean, $\Delta T1^* 64$ derived using the endocardial electrograms so that it aligns with the signal 90.

Figure 15 shows two surface ECG records 100 101 in response to the same interstimulus interval, showing different stimulus to tissue latency and time dilation. A further signal 102 shows mean stimulus to tissue latency and time dilation. After correction of signals 100 101 for the stimulus to tissue latency, thereby aligning their first potential with that of record 102, record 100 is compressed according to the interval $\Delta T2 103$ derived for that record 100 and record 101 stretched using $\Delta T2 104$ derived for that record, so that both records 100 101 have a $\Delta T2$ that corresponds to the mean $\Delta T2$ for record 102. The stretching and compression is achieved by frequency domain interpolation and resampling on a constant time interval.

A portion 105 of each signal is believed to contain small physiologically derived signals and a later portion 106 is assumed to contain only noise.

We measure the sum of the power in the signals in the physiological region 105 and the noise region 106.

In practice stretching and compression may be by assuming that the degree of requirement of length change of an individual signal is a function of ΔT^2 that may be described by a few parameters, thereby allowing some degree of non-linearity in the stretching.

An objective function is defined which is the power in the assumed portion of the averaged signals following time stretching/compression divided by the power considered to be noise that is similarly stretched/compressed. Therefore the parameters of the stretching/compressing process may be determined by maximising this function using conventional numerical methods.

During a protracted pacing run myocardial ischemia may be provoked. It is known that that ischemia causes increased conduction delays and local block leading to lengthening and additional potentials in local endocardial electrograms which may be reflected in the surface ECG. This may be detected by identifying non-stationarity in the responses to S1 stimuli that should remain constant.

Figure 16 show a stimulated averaged signal derived from signals in response to an S1 stimulus having non-stationary potentials assumed to be caused from ischemia.

The effects of non-stationarity can be detected by segmenting each individual record 112 into sub-records 113 as shown in Figure 17. The average signal power (squared amplitude) in each sub record is calculated.

Figure 18 shows the logarithm of the power in each sub record 114 for a stationary signal as each record added to the average record. After roughly two hundred records have been averaged, the power in each sub record approaches a stable value 114A.

Figure 19 shows the results for a non stationary signal assumed to be caused by ischemia. The sub records 115 close to the end of the assumed physiological portion of the signal deviate with increasing number of averages as potentials in that sub

record increase or diminish. The final sub records 115A that are assumed to be noise only do not change.

Claims

1. Apparatus for recording and analysing a surface electrocardiogram (ECG) for distinguishing a physiological signal from noise; the apparatus comprising:
 - a) means to pace the heart in a pacing sequence comprising a number of stimuli with a constant interval followed by an early stimulus, in which the interval between the early stimulus and the preceding constant rate stimulus is smaller than the interval between the constant rate stimuli;
 - b) means to repeat the pacing sequence multiple times with the same interval between the early stimulus and the preceding constant rate stimulus;
 - 10 c) means to repeat the pacing sequence multiple times with a different interval between the early stimulus and the preceding constant rate stimulus;
 - d) means to create surface electrocardiogram records during the repeated pacing sequences in b) and c)
 - e) means to average the surface electrocardiogram records corresponding to each
15 of the early stimuli paced in b); and
 - f) means to average the surface electrocardiogram records corresponding to each of the early stimuli paced in c).
2. Apparatus according to claim 1 comprising means to compare the averaged recorded surface electrocardiogram taken from e) and f) and to display the
20 differences.

3. Apparatus according to claim 1 or 2 comprising at least one sensing cardiac electrode and means for using a signal sensed by the at least one sensing cardiac electrode to compensate for delays and/or distortion of the surface electrocardiogram.
- 5 4. Apparatus according to claim 3 wherein the at least one sensing cardiac electrode is used to derive an interval between the pacing stimulus provided by a pacing electrode and the onset of activation of myocardium in a region proximate to the pacing electrode (which represents stimulus to tissue latency).
- 10 5. Apparatus according to claim 4 wherein the interval derived in claim 4 for each stimulus is used to align the ECG record corresponding to that stimulus to a common time reference.
6. Apparatus according to claim 4 or 5 wherein the distance between the pacing electrode and the at least one sensing cardiac electrode is substantially 1cm or less.
15
- 7 Apparatus according to any claim 3 - 6 comprising a first sensing cardiac electrode that is proximate to a pacing electrode and a second sensing cardiac electrode that is remote to the pacing electrode.
8. Apparatus according to claim 7 comprising means to determine an interval
20 between a signal from the first sensing electrode resulting from the activation of myocardial tissue proximate the first electrode and a second signal from the second sensing electrode resulting from activation of myocardial tissue proximate the second electrode
9. Apparatus according to claim 8 wherein the interval between the signal from
25 the first sensing electrode and the second signal from the second sensing

electrode, is used to time stretch or time compress the individual surface electrocardiogram records so that each individual surface electrocardiogram record is the same length.

10. Apparatus according to any previous claim wherein a pseudo-random time jitter is introduced into the constant rate stimuli.
11. Apparatus according to claim 10 wherein the pseudo-random jitter is introduced into the first constant rate stimulus of each pacing sequence.
12. Apparatus according to any previous claim comprising means for determining the changes in duration of a response to stimuli over the course of the pacing sequences recorded in d) and e).
13. Apparatus according to claim 12 comprising means to create surface electrocardiogram records following constant rate stimuli, to divide each electrocardiogram record into sub-records, determine the power of the potential in each sub-record and to determine how the power changes in each sub-record as successive electrocardiogram records are added to form an averaged surface electrocardiogram record.

AMENDED CLAIMS

received by the International Bureau on 01 December 2015 (01.12.2015)

1. Apparatus to determine changes in intraventricular conduction and thereby build a conduction curve; the apparatus comprising means for recording and analysing a surface electrocardiogram (ECG) for distinguishing a physiological signal
5 from noise including:
- a) means to pace the heart in a pacing sequence comprising a number of stimuli with a constant interval followed by an early stimulus, in which the interval between the early stimulus and the preceding constant rate stimulus is smaller than the interval between the constant rate stimuli;
- 10 b) means to repeat the pacing sequence multiple times with the same interval between the early stimulus and the preceding constant rate stimulus;
- c) means to repeat the pacing sequence multiple times with a different interval between the early stimulus and the preceding constant rate stimulus;
- d) means to create surface electrocardiogram records during the repeated pacing
15 sequences in b) and c)
- e) means to average the surface electrocardiogram records corresponding to each of the early stimuli paced in b); and
- f) means to average the surface electrocardiogram records corresponding to each of the early stimuli paced in c).
- 20 2. Apparatus according to claim 1 comprising means to compare the averaged recorded surface electrocardiogram taken from e) and f) and to display the differences.

3. Apparatus according to claim 1 or 2 comprising at least one sensing cardiac electrode and means for using a signal sensed by the at least one sensing cardiac electrode to compensate for delays and/or distortion of the surface electrocardiogram.
- 5 4. Apparatus according to claim 3 wherein the at least one sensing cardiac electrode is used to derive an interval between the pacing stimulus provided by a pacing electrode and the onset of activation of myocardium in a region proximate to the pacing electrode (which represents stimulus to tissue latency).
- 10 5. Apparatus according to claim 4 wherein the interval derived in claim 4 for each stimulus is used to align the ECG record corresponding to that stimulus to a common time reference.
6. Apparatus according to claim 4 or 5 wherein the distance between the pacing electrode and the at least one sensing cardiac electrode is substantially 1cm or less.
15
- 7 Apparatus according to any claim 3 - 6 comprising a first sensing cardiac electrode that is proximate to a pacing electrode and a second sensing cardiac electrode that is remote to the pacing electrode.
8. Apparatus according to claim 7 comprising means to determine an interval
20 between a signal from the first sensing electrode resulting from the activation of myocardial tissue proximate the first electrode and a second signal from the second sensing electrode resulting from activation of myocardial tissue proximate the second electrode
9. Apparatus according to claim 8 wherein the interval between the signal from
25 the first sensing electrode and the second signal from the second sensing

electrode, is used to time stretch or time compress the individual surface electrocardiogram records so that each individual surface electrocardiogram record is the same length.

10. Apparatus according to any previous claim wherein a pseudo-random time jitter is introduced into the constant rate stimuli.
11. Apparatus according to claim 10 wherein the pseudo-random jitter is introduced into the first constant rate stimulus of each pacing sequence.
12. Apparatus according to any previous claim comprising means for determining the changes in duration of a response to stimuli over the course of the pacing sequences recorded in d) and e).
13. Apparatus according to claim 12 comprising means to create surface electrocardiogram records following constant rate stimuli, to divide each electrocardiogram record into sub-records, determine the power of the potential in each sub-record and to determine how the power changes in each sub-record as successive electrocardiogram records are added to form an averaged surface electrocardiogram record.

Figure 1

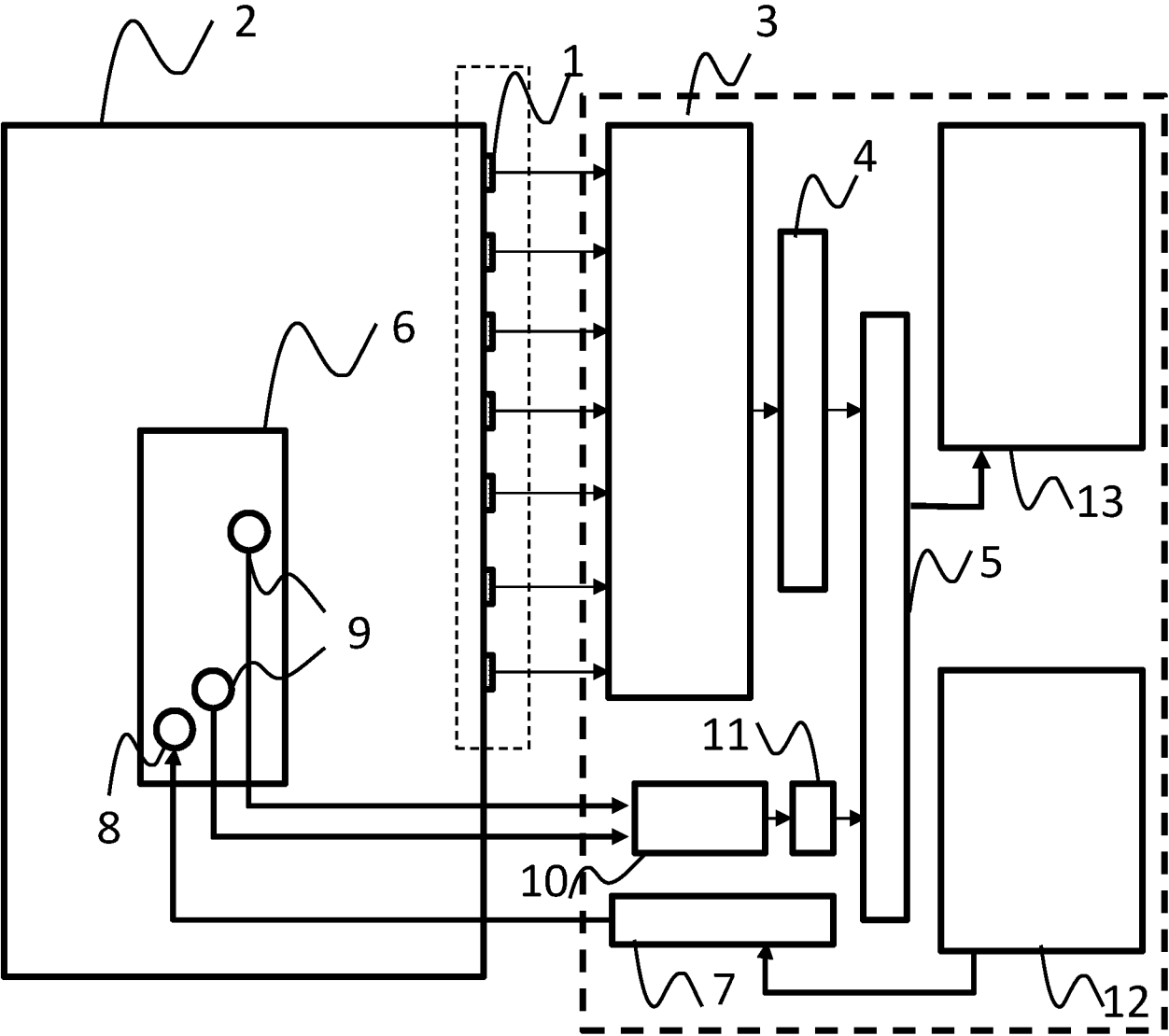


Figure 2

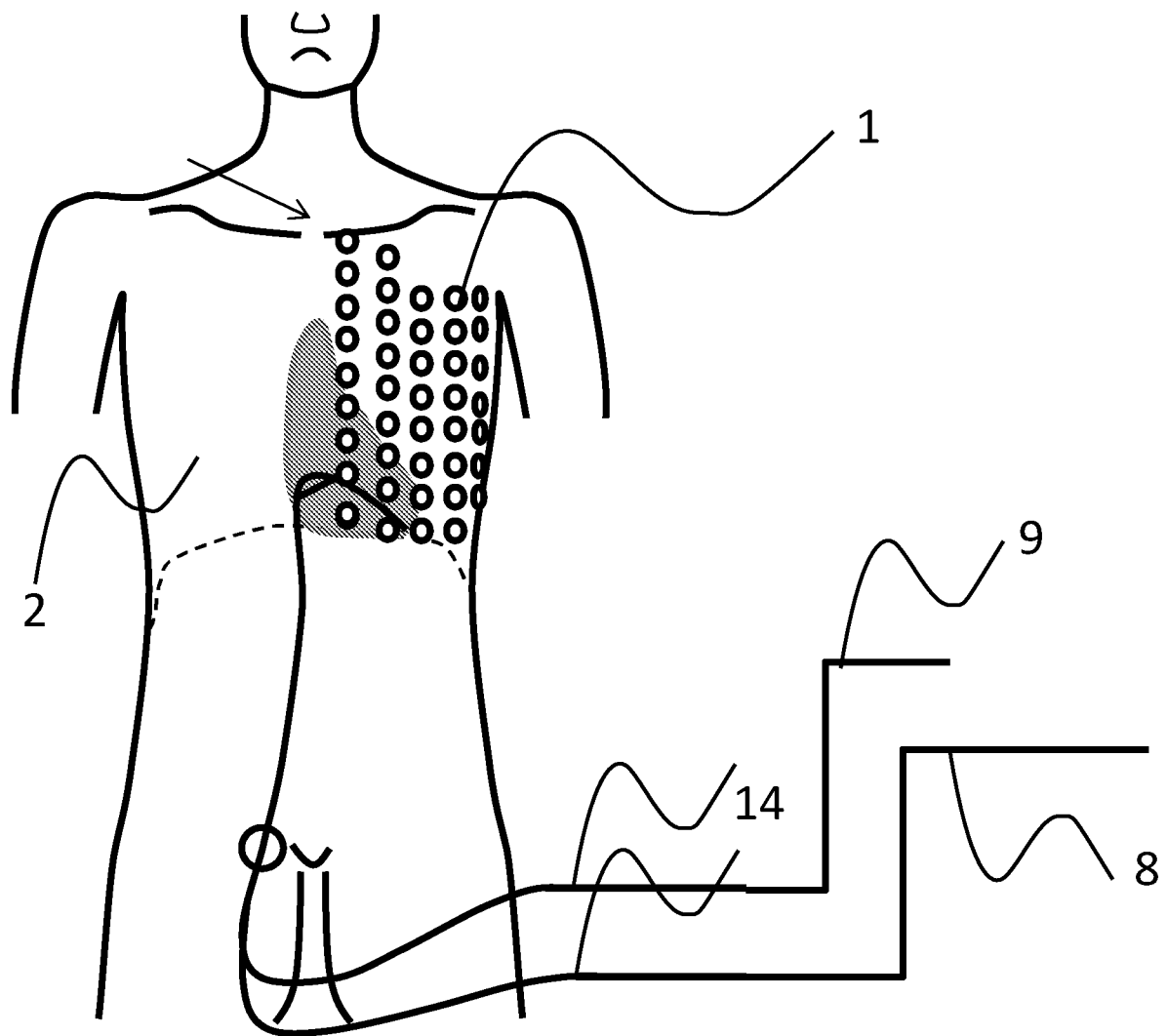


Figure 3

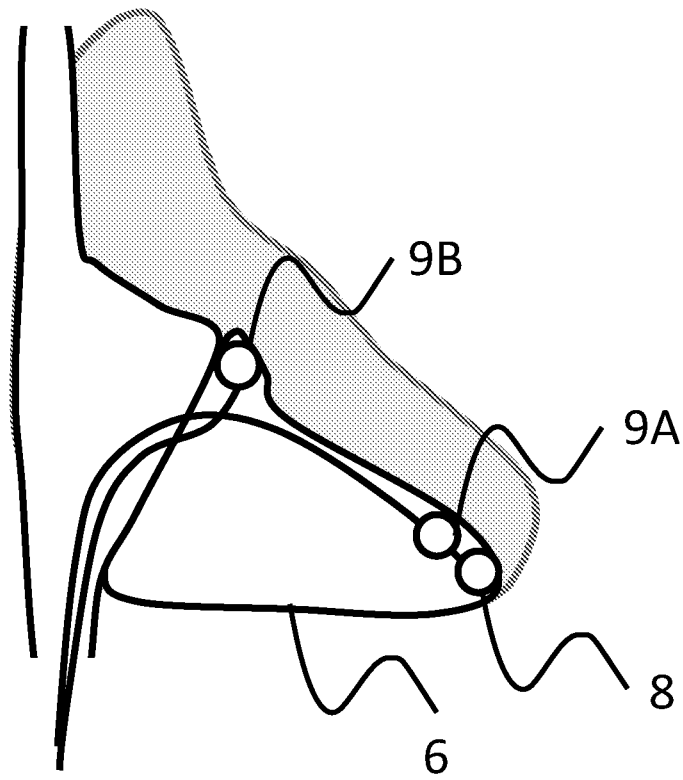


Figure 4

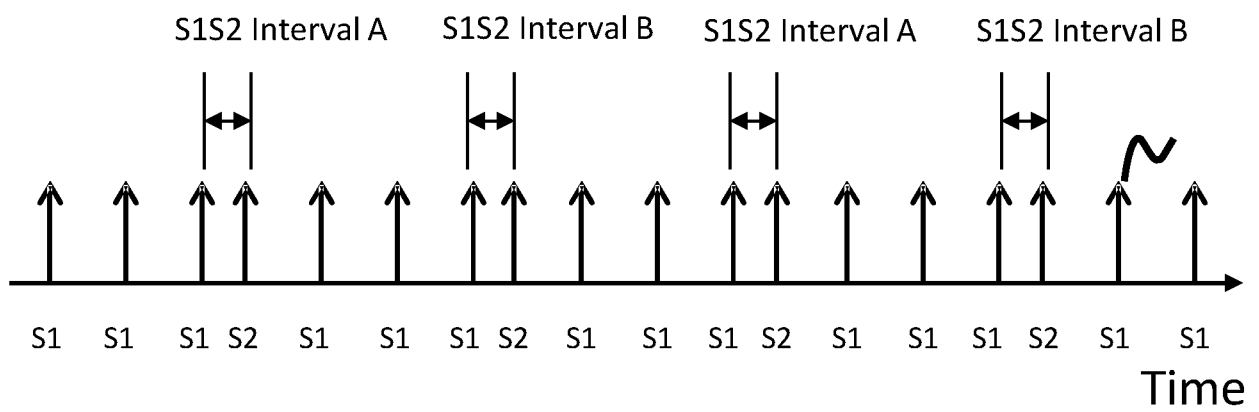


Figure 5

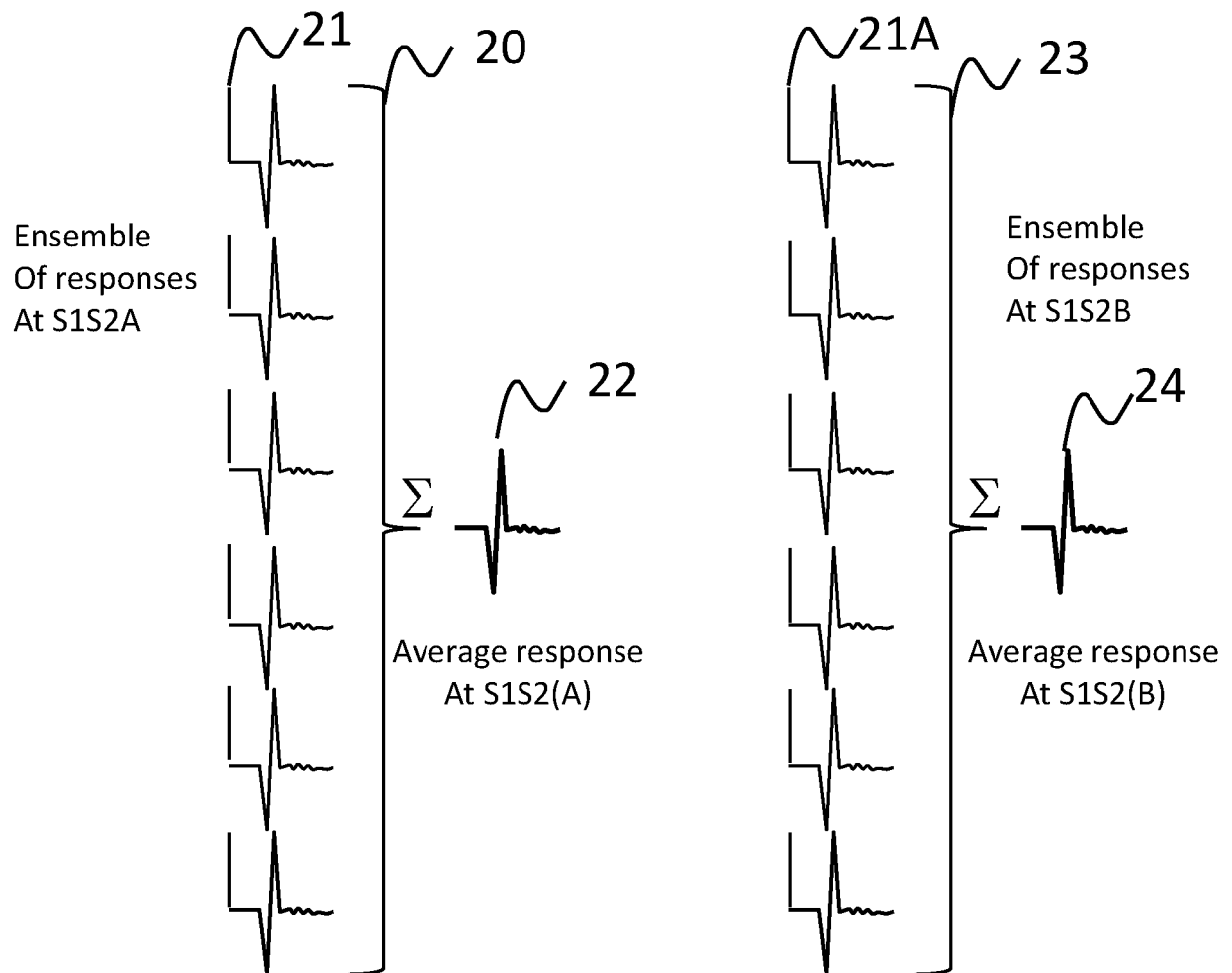
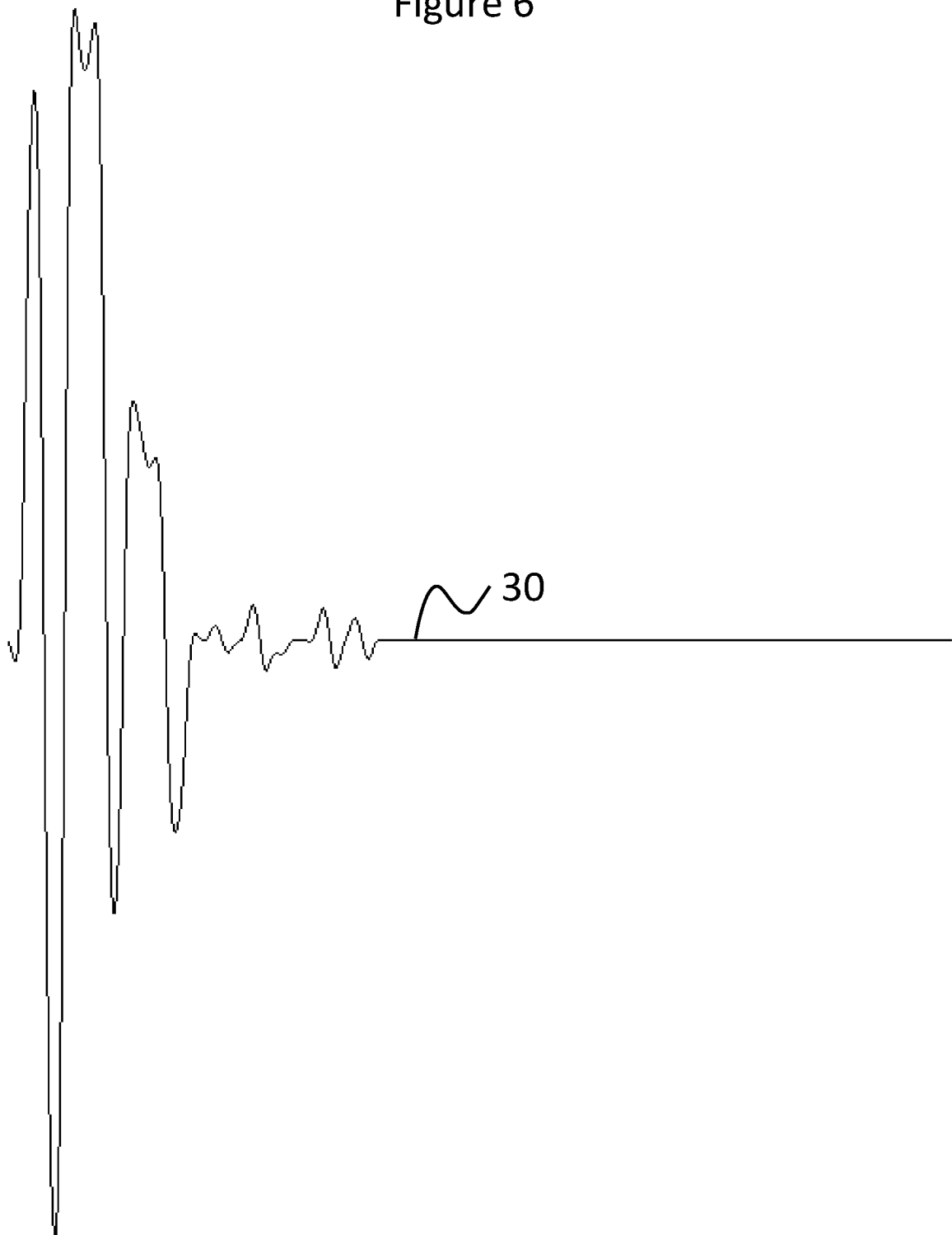


Figure 6



7/19

Figure 7

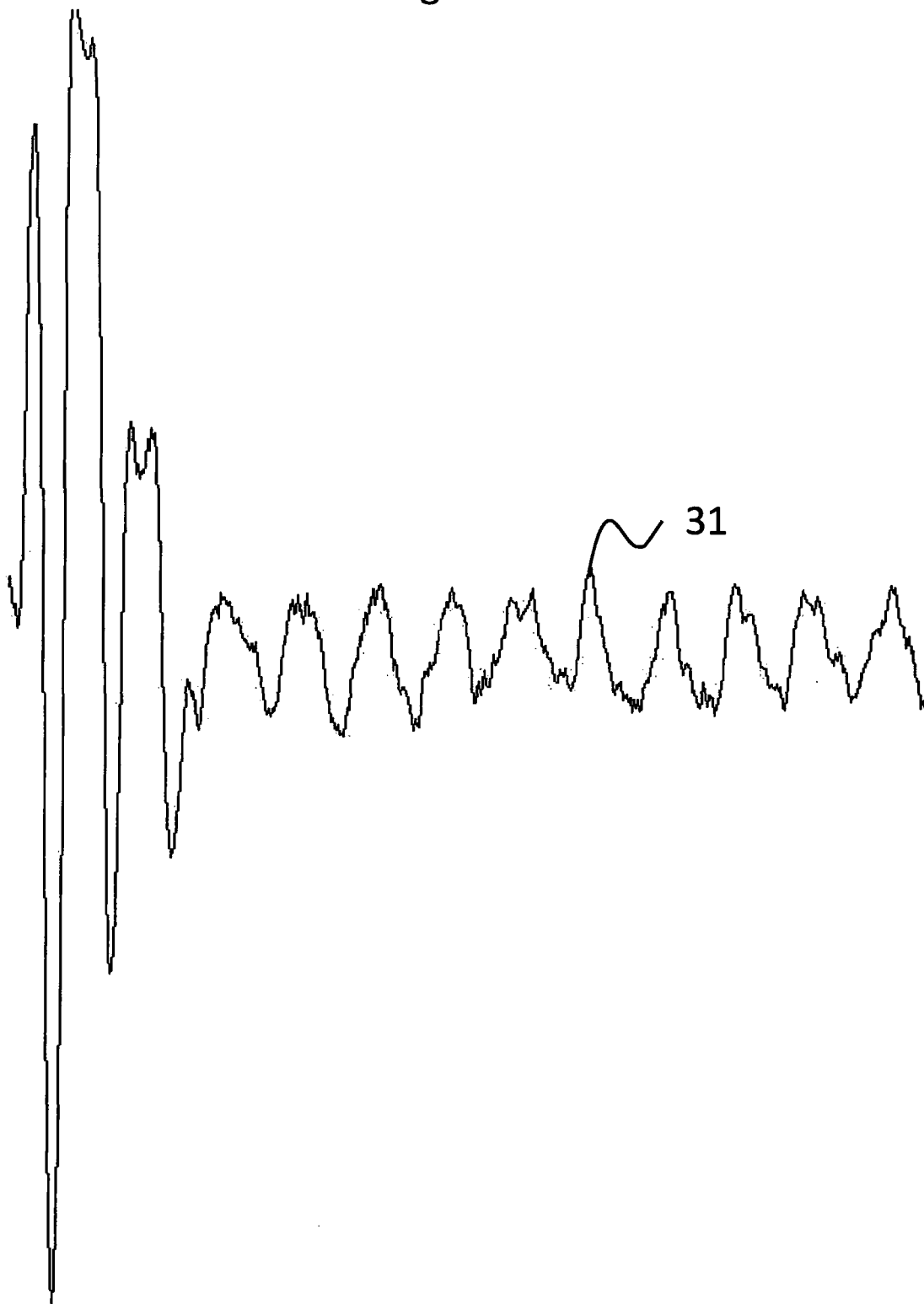


Figure 8

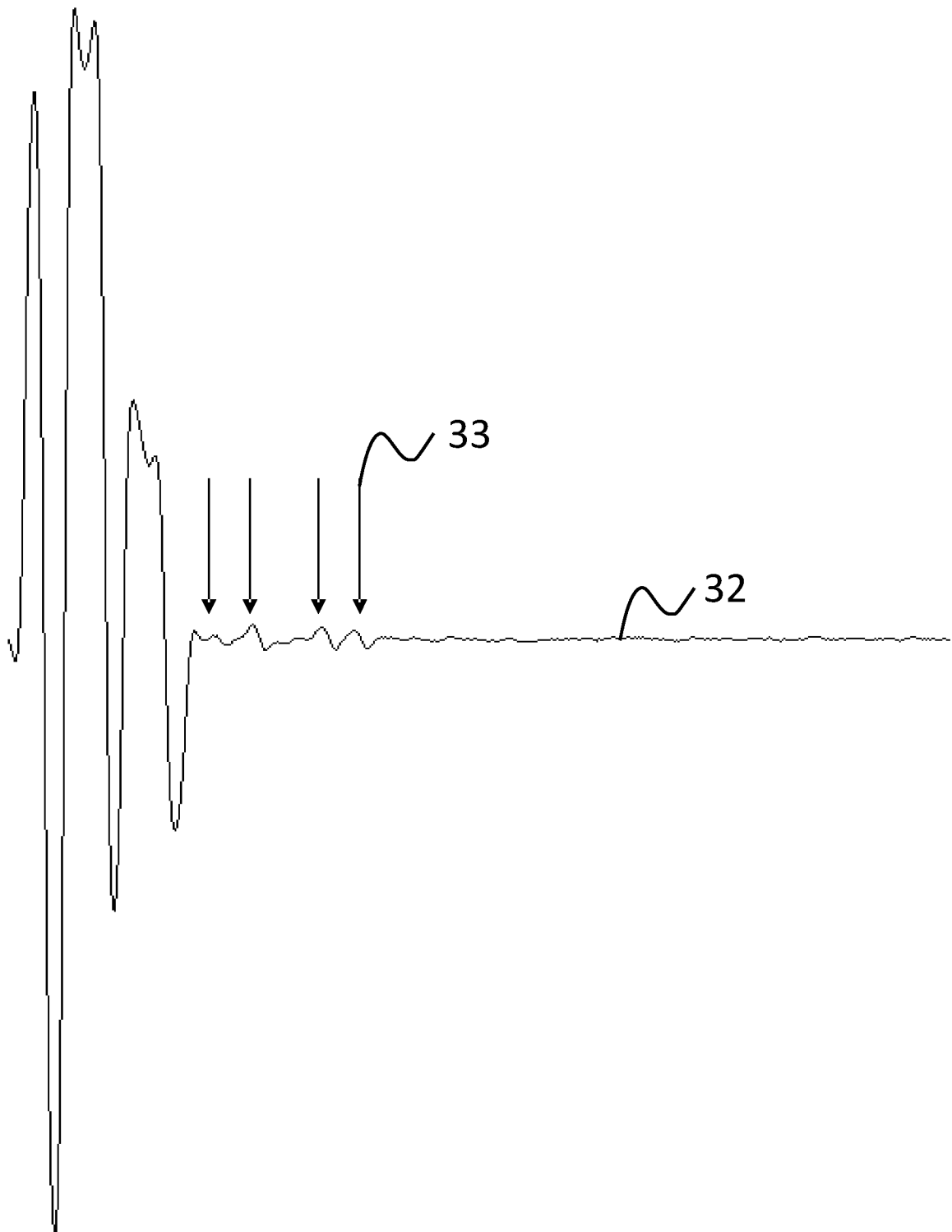


Figure 9

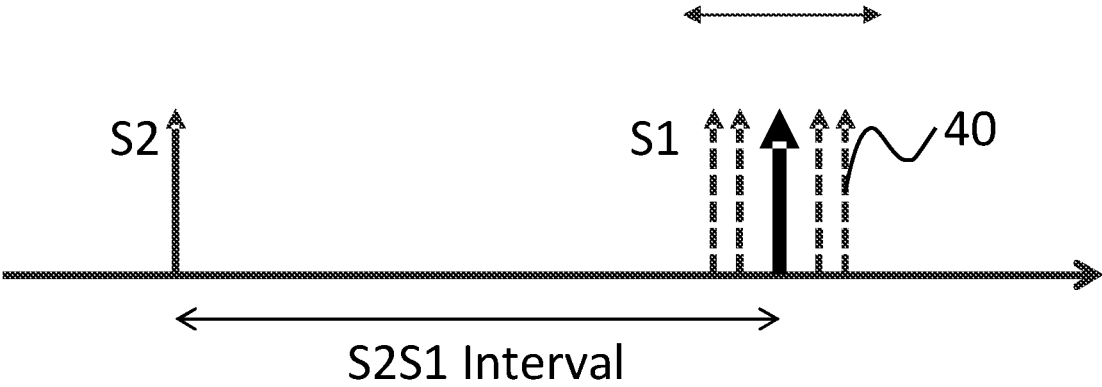


Figure 10

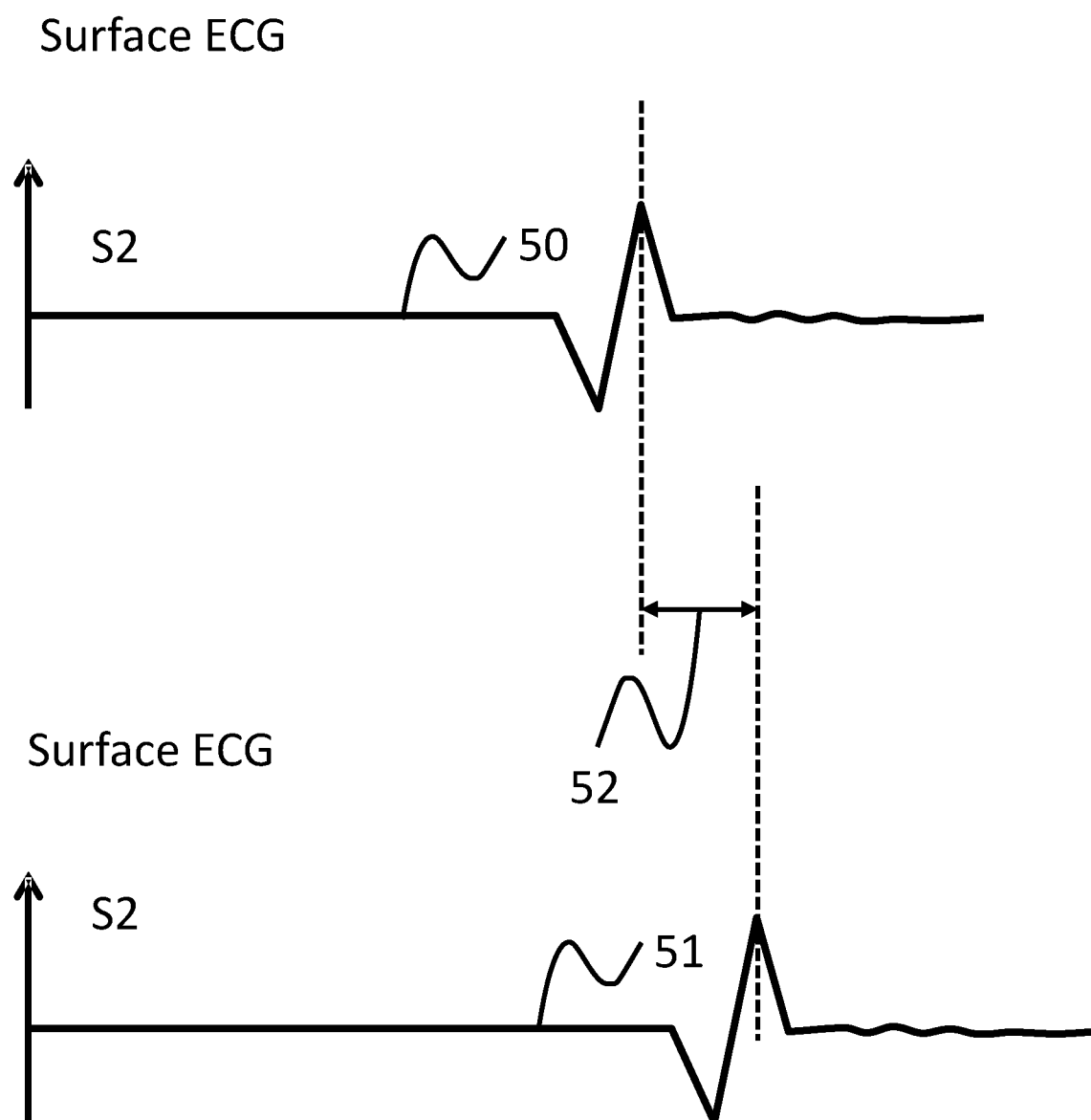
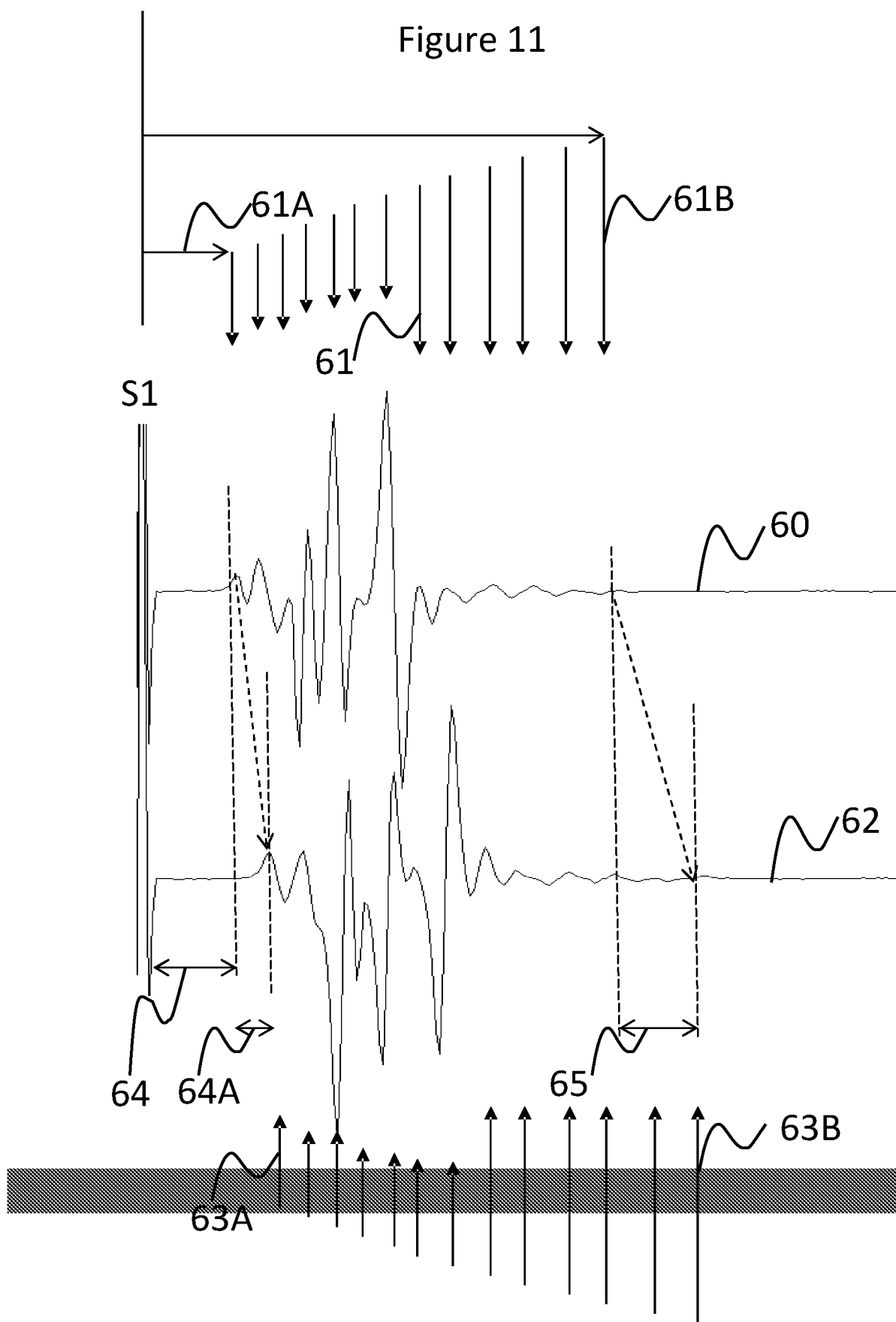


Figure 11



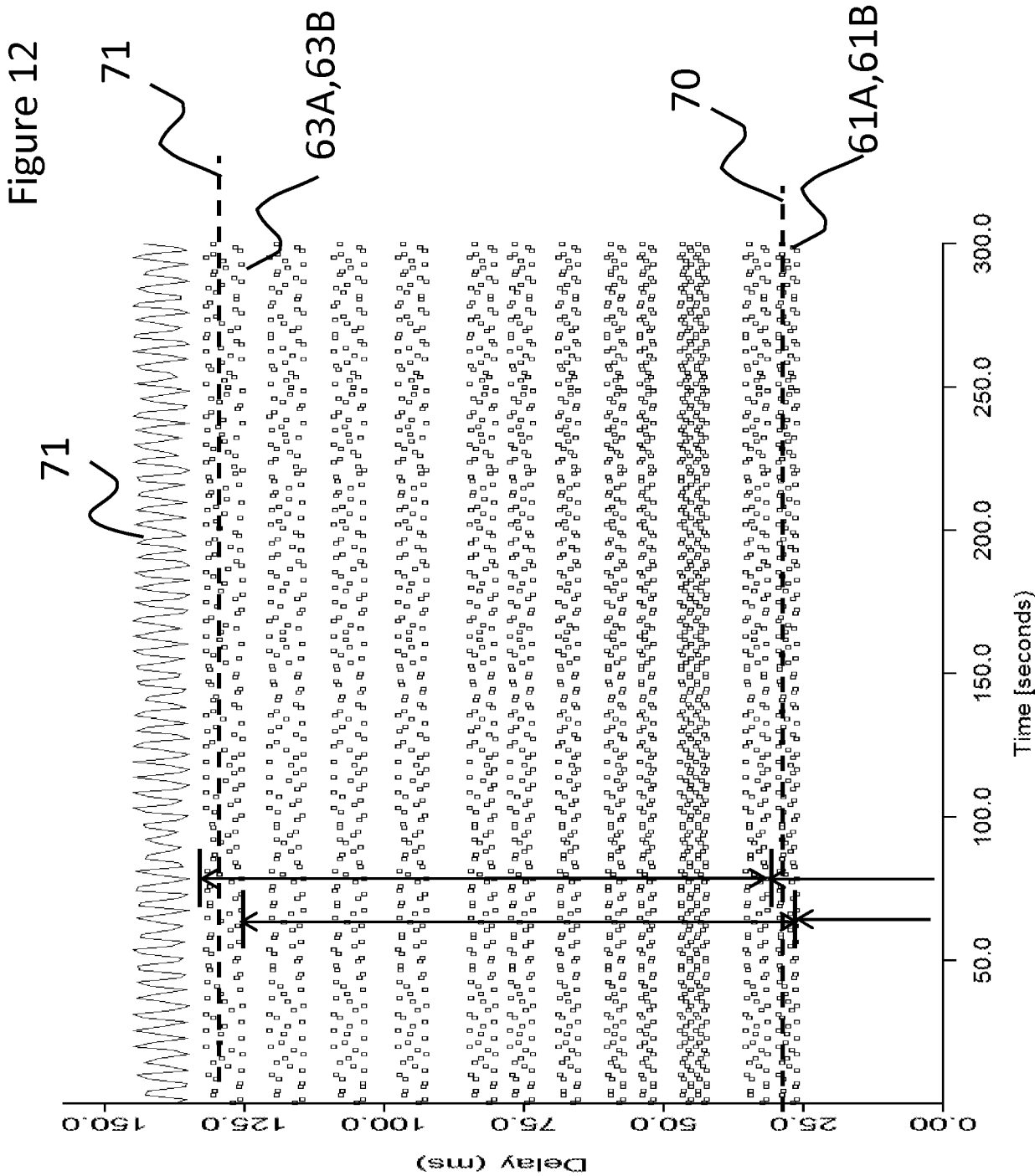
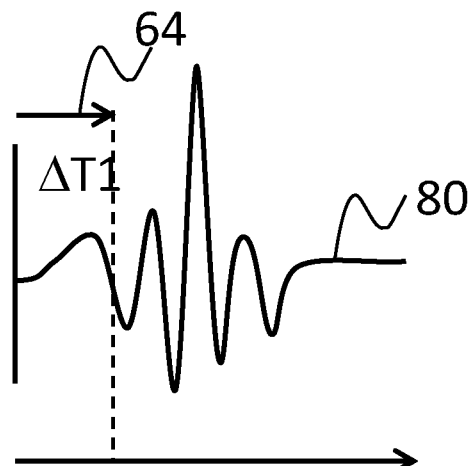


Figure 13

Electrogram adjacent to Pacing site



Electrogram remote from
pacing site

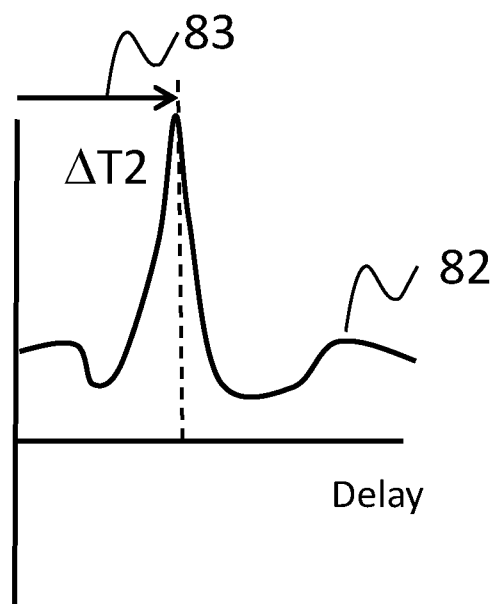
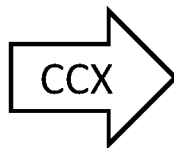
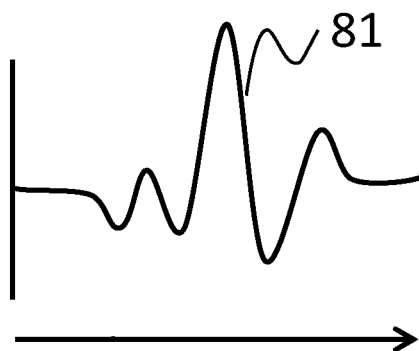


Figure 14

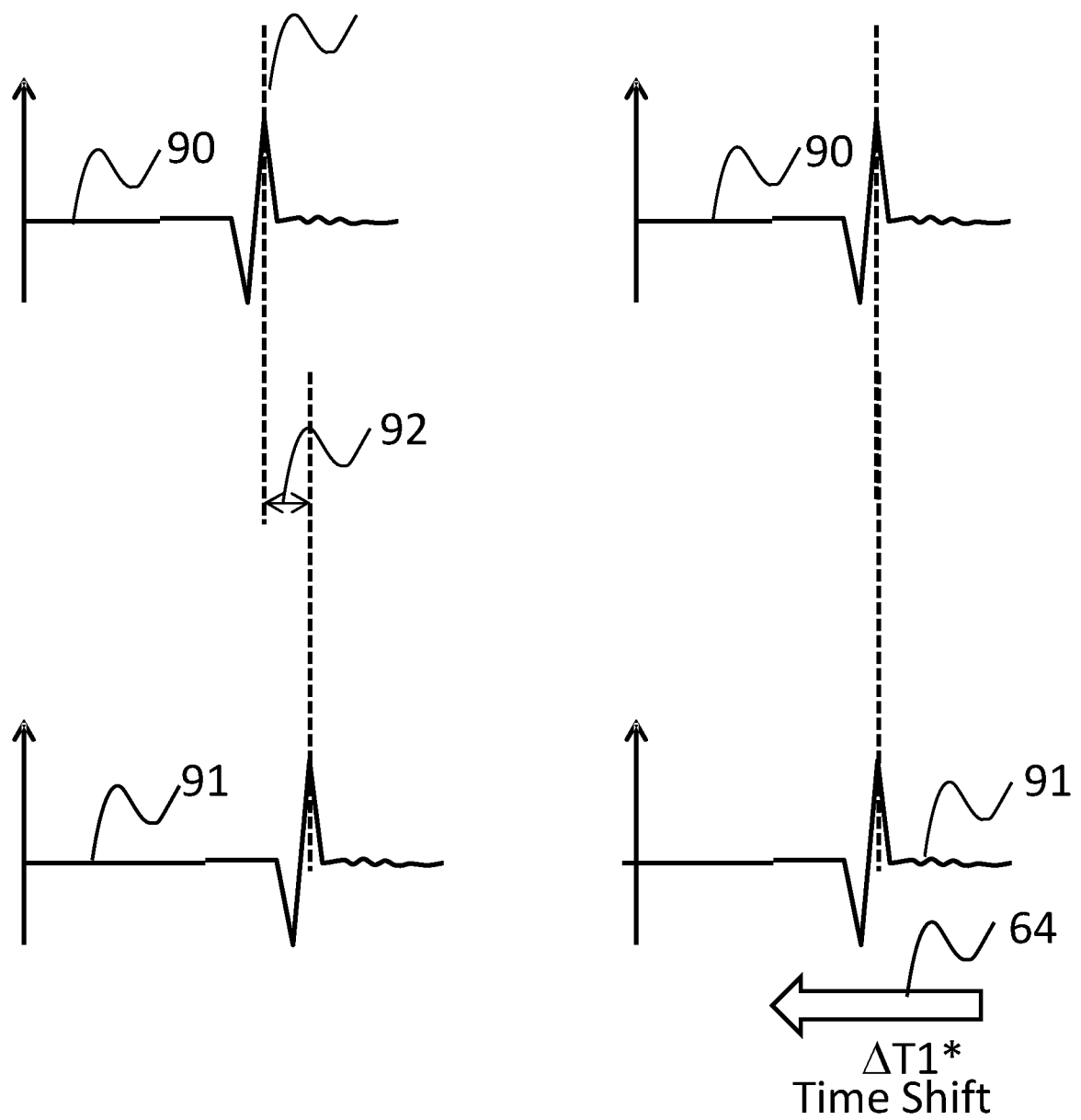


Figure 15

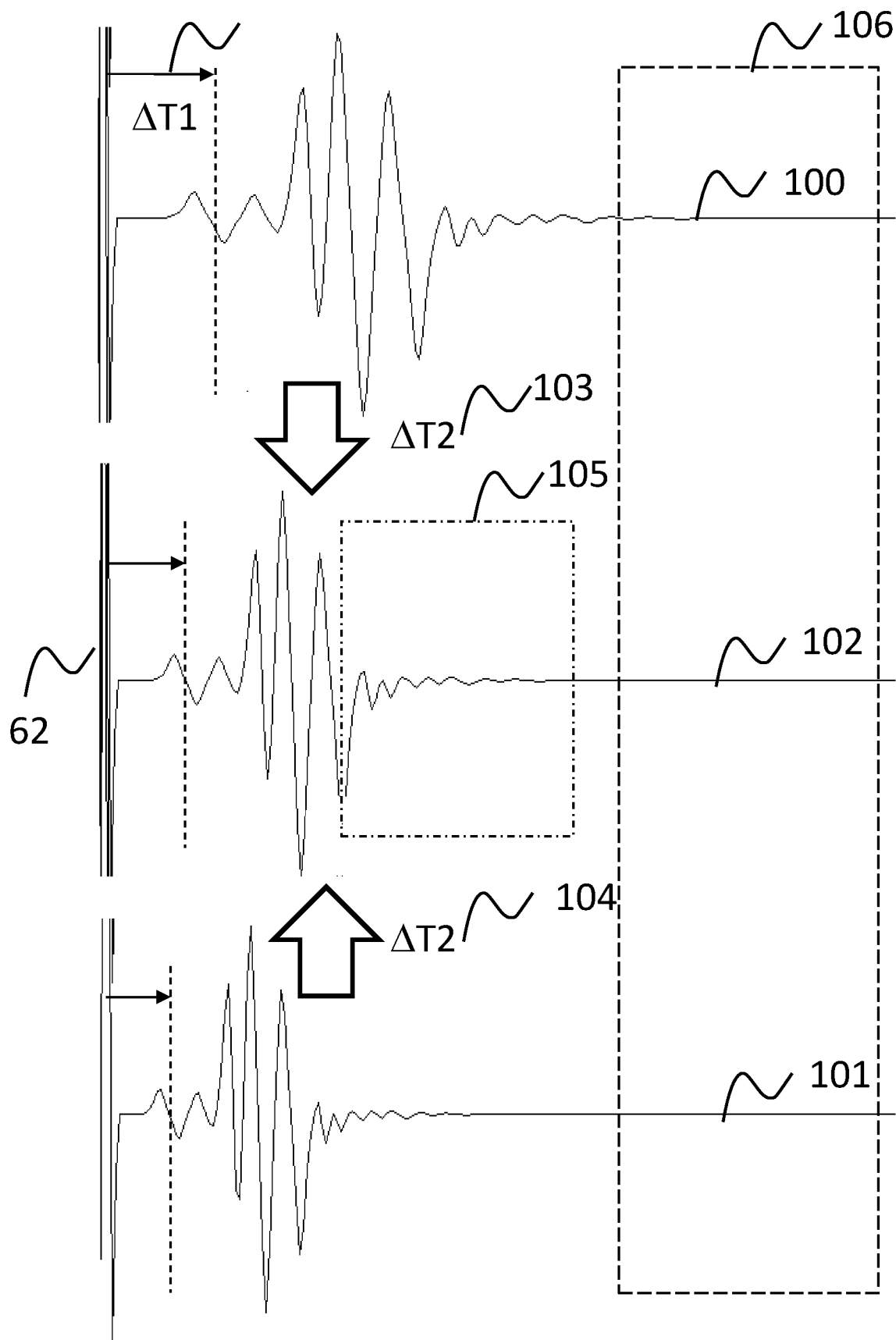


Figure 16

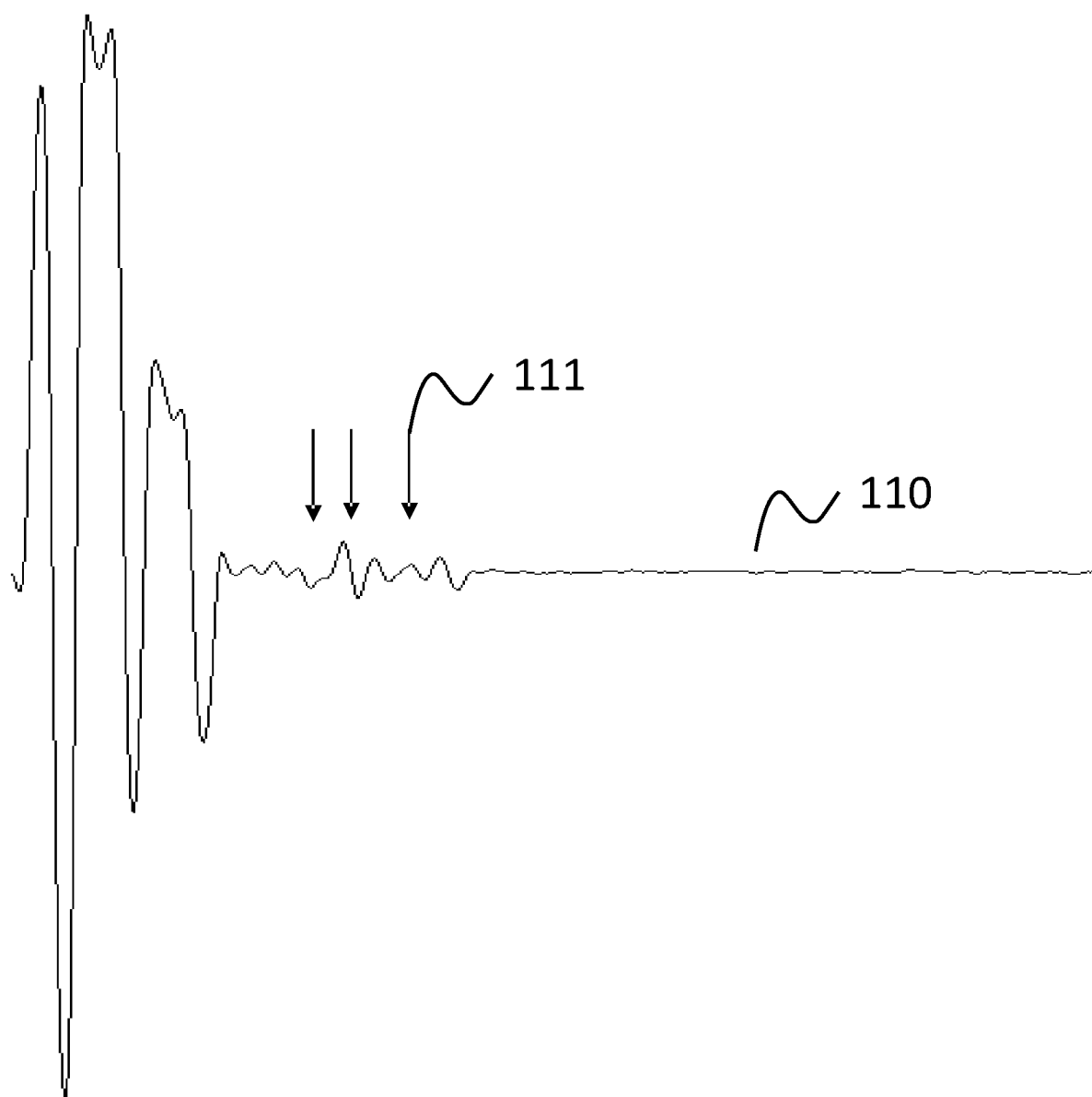


Figure 17

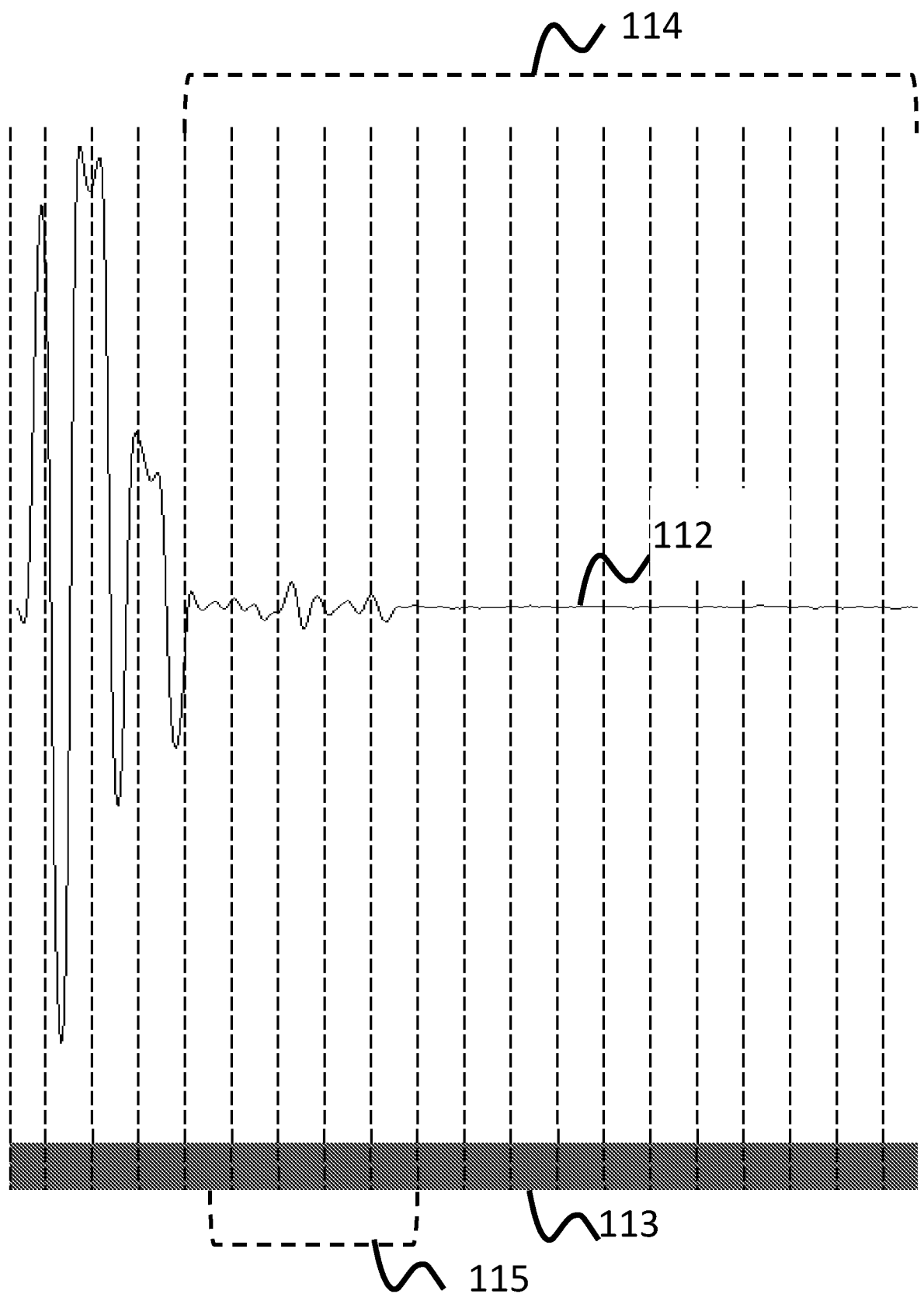


Figure 18

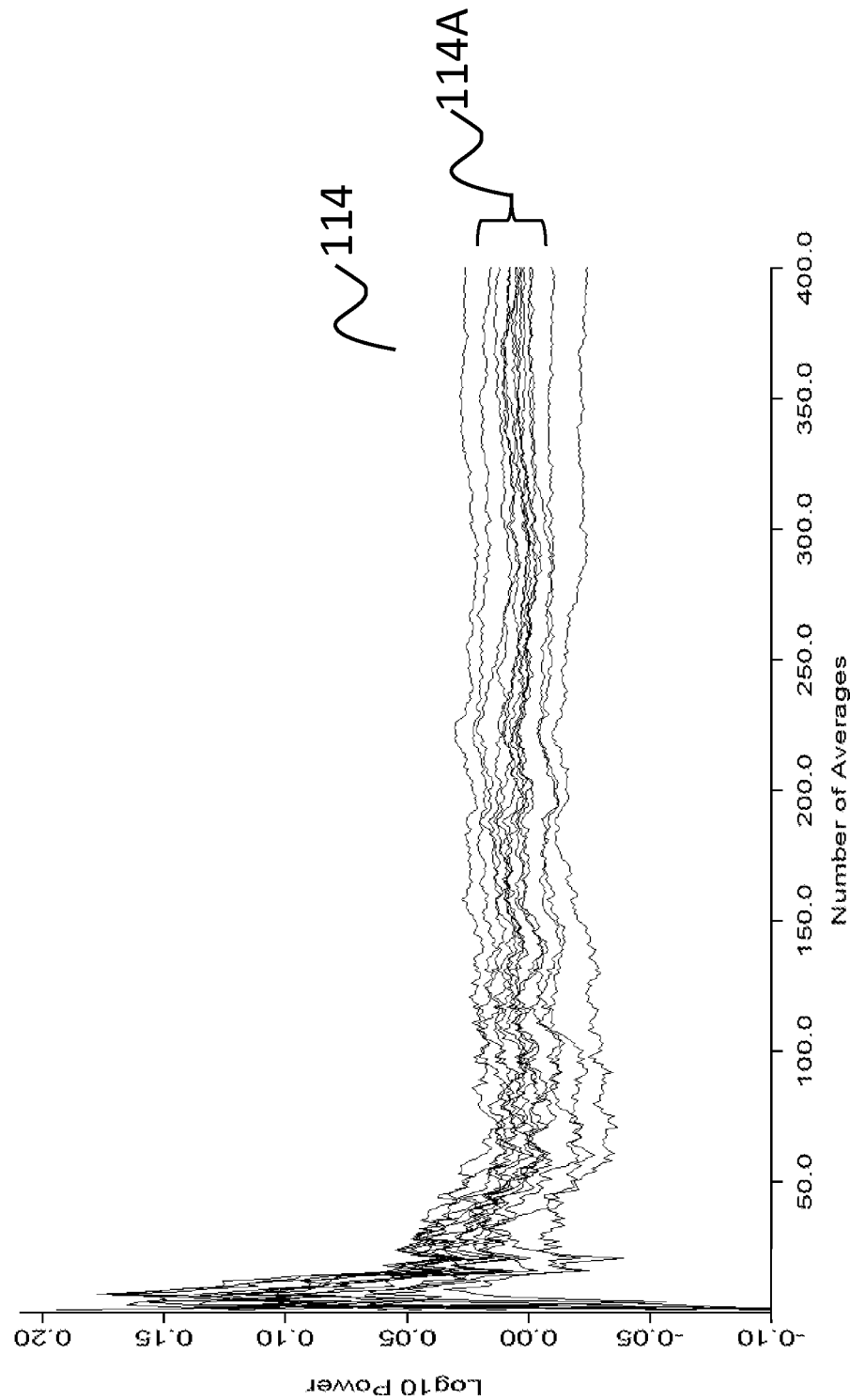
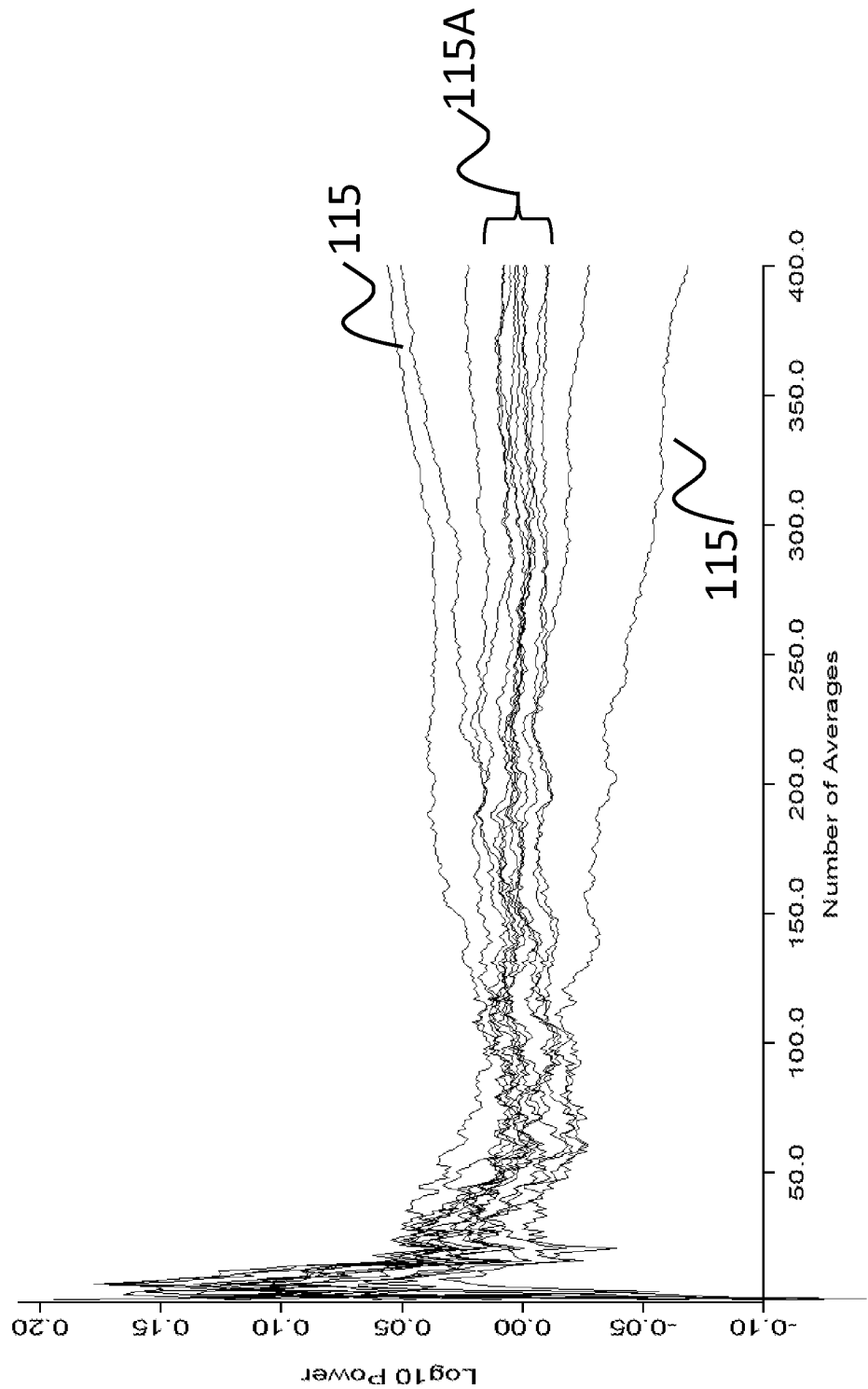


Figure 19



INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2015/052192

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/0452 A61B5/0464 A61B5/00
ADD.

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)
A61B

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, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/026123 A2 (NARAYAN SANJIV MATHUR [US]; BHARGAVA VALMIK [US]) 1 April 2004 (2004-04-01) page 4, line 25 - page 5, line 7 page 14, lines 1-17 page 15, line 21 - page 16, line 12 page 45, line 1 - page 51, line 8 page 58, line 4 - page 59, line 12 -----	1-13
A	WO 2012/097067 A1 (RHYTHMIA MEDICAL INC [US]; HARLEV DORON [US]; ELDAR ROTEM [IL]) 19 July 2012 (2012-07-19) page 19, line 16 - page 23, line 18 ----- -/--	1-13



Further documents are listed in the continuation of Box C.



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

"E" earlier application or patent 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

24 September 2015

Date of mailing of the international search report

01/10/2015

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Pohjamo, Terhi

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2015/052192

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 96/25096 A1 (EP TECHNOLOGIES [US]) 22 August 1996 (1996-08-22) page 5, line 4 - page 7, line 15 page 20, lines 3-31 page 31, line 23 - page 32, line 16 page 43, line 14 - page 44, line 7 page 51, line 13 - page 52, line 24 -----	1-13

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2015/052192

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004026123	A2	01-04-2004	AU 2003299035 A1 08-04-2004
			US 2004059237 A1 25-03-2004
			US 2007021679 A1 25-01-2007
			WO 2004026123 A2 01-04-2004

WO 2012097067	A1	19-07-2012	CA 2824234 A1 19-07-2012
			EP 2663227 A1 20-11-2013
			JP 2014503319 A 13-02-2014
			US 2012184858 A1 19-07-2012
			WO 2012097067 A1 19-07-2012

WO 9625096	A1	22-08-1996	NONE

专利名称(译)	用于记录和分析表面心电图 (ECG) 的装置，用于区分生理信号和噪声		
公开(公告)号	EP3179909A1	公开(公告)日	2017-06-21
申请号	EP2015747190	申请日	2015-07-29
[标]申请(专利权)人(译)	FEN EP LTD		
[标]发明人	SAUMAREZ RICHARD C		
发明人	SAUMAREZ, RICHARD C.		
IPC分类号	A61B5/0452 A61B5/0464 A61B5/00		
CPC分类号	A61B5/04085 A61B5/0452 A61B5/0464 A61B5/7203 A61B5/7217 A61N1/3625 A61N1/3702 A61B5/0402 A61B5/04012 A61B5/0432 A61B5/044 A61N1/025		
优先权	2014014335 2014-08-13 GB		
外部链接	Espacenet		

摘要(译)

描述了一种使用用于记录和分析表面心电图 (ECG) 的装置的技术，用于区分生理信号和噪声。该技术涉及对重复起搏序列采用的多个表面电描记录对齐和平均，并且在起搏刺激之间具有相同的间隔。