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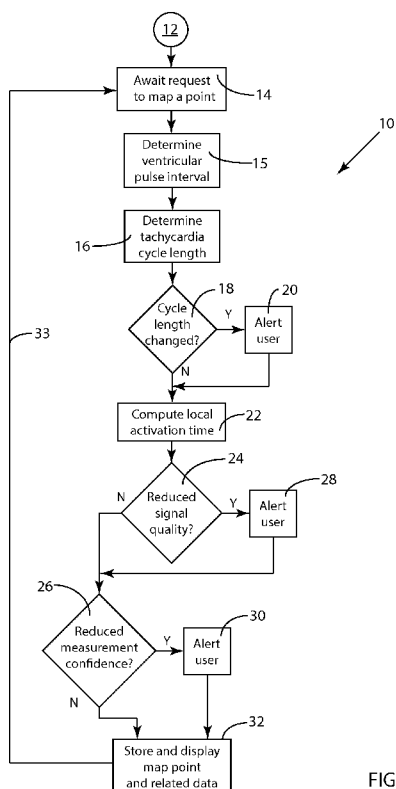


FIG. 1

(57) Abstract: An automatic method of determining local activation time (LAT) in multi-channel cardiac electrogram signals including at least two cardiac channels, one of the cardiac channels being a mapping channel and another cardiac channel being a reference channel, the method comprising: (a) estimating a cycle length CL in the reference channel; (b) determining a mapping-channel fiducial time t_M in the mapping channel signal; (c) determining a plurality of reference-channel fiducial times t_R ; (d) computing adjusted reference-channel fiducial times t_{RA} by adding or subtracting multiples of cycle length CL to each time t_R such that each time t_{RA} is within a time window of length CL surrounding mapping-channel fiducial time t_M ; (e) computing a single final reference-channel fiducial time t_{RF} from the plurality of adjusted reference-channel fiducial times t_{RA} ; and (f) computing the LAT as t_M minus t_{RF} .



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MULTI-CHANNEL CARDIAC MEASUREMENTS

FIELD OF THE INVENTION

This invention is related generally to the field of electrophysiology, and more particularly to technology for accurate measurement of parameters within body-surface ECG, intracardiac, and epicardial electrical signals such as heart rates and local activation times and the assessment of the quality of such measurements.

BACKGROUND OF THE INVENTION

The invention disclosed herein involves the processing of multiple channels of electrical signals which are produced by the heart. These channel signals include the ECG signals from body-surface electrodes and signals from electrodes within the body, *i.e.*, intracardiac signals from within vessels and chambers of the heart and epicardial signals from the outer surface of the heart. Throughout this document, the term "multi-channel cardiac electrogram" (or "MCCE") is used to refer to all of these types of channels, and when specific types are appropriate, specific nomenclature is used. This new terminology (MCCE) is used herein since the term "ECG" sometimes only refers to body-surface measurements of cardiac performance.

A major component in cardiac interventional procedures such as cardiac ablation is the display of cardiac data which is extracted from the MCCE signals captured by an array of electrodes placed on the body surface and within and on the structures of the heart itself. Among the important data which are displayed are ventricular pulse interval (time between heart beats), intracardiac cycle length (time between the activations in arrhythmias (such as atrial fibrillation), relative time differences between related activations in two intracardiac channels to generate activation maps, and assessments of signal strength, variability, and other measures of signal quality within MCCE signals.

Cardiac interventional electrophysiology procedures (*e.g.*, ablation) can be extremely time-consuming, and the reliable determination and presentation of such cardiac parameters is an important element in both the quality of the procedures and the speed with which they can be carried out. Often the data which are presented to the electrophysiology doctor during such procedures exhibit high variability

contributed not only by the performance of the heart itself but by unreliable detection of certain features of the MCCE signals. Therefore there is a need for more reliable and more rapid algorithms to process body surface and intracardiac signals obtained during an electrophysiology (EP) procedure.

5 MCCE electrodes capture the electrical signals in the cardiac muscle cells. As mentioned above, some MCCE electrodes may be attached to the body surface (ECG) and some may be positioned inside cardiac veins, arteries and chambers (intracardiac) and on the outer surface of the heart (epicardial) as conductive elements at the tips or along the lengths of catheters introduced into the body and maneuvered into position
10 by the EP doctor. The electrical signals within the heart muscles and which flow therefrom to other regions of the body have very low voltage amplitudes and therefore are susceptible to both external signal noise and internally-generated electrical variations (non-cardiac activity). In addition, cardiac arrhythmias themselves may be highly variable, which can make reliable extraction of cardiac parameters from MCCE
15 signals difficult.

One important cardiac parameter used during such procedures is the time difference between the activations occurring within two channels, both of which contain the electrical signals of an arrhythmia. This measurement is called local activation time (LAT), and measurement of a plurality of LATs is the basis for the
20 generation of an activation map. The map displays information about the sequence of activations of cardiac muscle cells relative to each other, and this sequence of information is combined with physical anatomical position information to form the map. An activation map then provides guidance to the EP doctor for the process of applying therapies to heart muscle cells which can terminate cardiac arrhythmias and
25 permanently affect the heart to prevent recurrence of such arrhythmias.

This entire process is referred to as mapping because all of the information generated by analysis of the MCCE signals is combined in a single computer display of a three-dimensional figure that has the shape of the heart chamber of interest and display of additional image qualities such as color that convey the sequence of
30 electrical activity (activation map) or possibly other qualities of the electrical activity (*e.g.*, voltage map). These images are similar in style to weather maps common today

in weather-forecasting. Such a cardiac map becomes a focus of attention for the EP doctor as he directs the motion of catheters in the heart to new positions, and an algorithm which processes the MCCE signals produces measurements from the electrodes in new positions. As this process continues, the map is updated with new colored points to represent additional information about the electrical activity of the heart.

The generation of position information and its combination with the cardiac timing information is outside the scope of the present invention. The focus of the present invention is the processing of MCCE signals to measure time relationships within the signals, the two most important of which are cycle length (CL) and local activation time (LAT).

Currently-available MCCE-processing algorithms are simplistic and often provide inaccurate measurements which cause the activation map and many other cardiac parameter values to be misleading. A misleading map may either (1) compel the doctor to continue mapping new points until apparent inconsistencies of the map are corrected by a preponderance of new, more-accurately measured map points or (2) convince the doctor to apply a therapy to a muscle region which actually makes little or no progress in the termination of an arrhythmia, again prolonging the procedure while the EP doctor maps more points in an attempt to locate new regions where therapy may be effective.

Currently, computer systems which assist doctors in the mapping process have manual overrides to allow a technician, or sometimes the EP doctor himself, to correct the measurements made by the system automatically. This requires a person to observe a computer display called the "Annotation Window" which shows a short length of the patient's heart rhythm, perhaps 3-5 heart beats as recorded in 3-8 channels (signals from MCCE electrodes).

The channels of the annotation window are of several types. Usually there will be a body surface ECG lead such as lead II that identifies when ventricular activity is occurring. (It is also possible that the ventricular activity may be sensed by an intracardiac channel electrode.) There is one channel, identified as a reference channel, the electrode of which remains in a fixed position during the entire mapping-

generating procedure. There is at least one other intracardiac channel (the mapping channel) which senses the electrical signal at a catheter tip, the precise three-dimensional position of which is determined by other means. The electrical activity in the mapping channel is compared to the activity in the reference channel to determine the local activation time (LAT) which is used to color the map at that precise three-dimensional position.

Intracardiac channels may be of either the bipolar or unipolar recording types, and the inventive measurement method disclosed herein can be applied to both types of signals. Also, since it is possible during arrhythmias for some chambers of the heart to be beating in a rhythm different from other chambers of the heart, the annotation window often contains additional channels to aid the doctor's interpretation of the data presented.

OBJECTS OF THE INVENTION

It is an object of this invention, in the field of electrophysiology, to provide an automatic method for accurate measurement of several parameters which characterize MCCE signals.

Another object of this invention is to provide an automatic method for such measurements which operates rapidly enough to not hinder an electrophysiologist performing procedures which utilize such a method.

Another object of this invention is to provide an automatic method for rapid and reliable measurement of cardiac cycle length (or heart rate).

Another object of this invention is to provide an automatic method for rapid and reliable measurement of cardiac parameters to reduce the length of time certain cardiac procedures require and also reduce the X-ray exposure times for the patients.

Another object of this invention is to provide an automatic method for rapid and reliable measurement of local activation times which are provided for the rapid generation of local activation time maps, determining the precise phase relationship between a reference channel and a mapping channel.

Still another object of this invention is to provide an automatic method for cardiac parameter measurement which can be used in real time during certain interventional cardiac procedures.

Another object of this invention is to provide an automatic method for rapid and reliable activation mapping which can continue providing LAT measurement when a reference signal degrades such that it is no longer useable as a reference signal.

Yet another object of the invention is to provide an automatic method for measuring cardiac parameters which is largely insensitive to the amplitude of the MCCE signals and almost entirely dependent on the timing information contained in such signals.

These and other objects of the invention will be apparent from the following descriptions and from the drawings.

SUMMARY OF THE INVENTION

The term "digitized signal" as used herein refers to a stream of digital numeric values at discrete points in time. For example, an analog voltage signal of an MCCE channel is digitized every millisecond (msec) using an analog-to-digital (A/D) converter to generate a series of sequential digital numeric values one millisecond apart. The examples presented herein use this sampling rate of 1kHz, producing streams of digital values one millisecond apart. This sampling rate is not intended to be limiting; other sampling rates may be used.

The term "velocity" as used herein refers to a signal the values of which are generally proportional to the time-rate-of-change of another signal.

The term "two differenced sequential boxcar filters" as used herein refers to two boxcar filters which operate in tandem and then the difference between the two boxcar filter values is computed. Such a filtering operation is one embodiment by which a low-pass filter followed by a first-difference filter is applied. Two differenced sequential boxcar filters are illustrated in FIGURE 3A and described in detail later in this document.

The term "dot-product autocorrelation" as used herein refers to a mathematical operation applied to a time series of digital values, and this operation is generally a signal-processing application of conventional autocorrelation. Applying conventional autocorrelation to a fixed-length time series of numeric values x_i generates another series of numeric values a_j which represents how well the signal x_i correlates with itself as a function of the time difference between the signal and the same signal displaced in time by a period of time called lag. In conventional autocorrelation of a fixed-length signal x_i having n values in a time interval,

$$a_j = \sum (x_i \cdot x_{i-j})$$

where the symbol $\sum$ indicates the sum over all $n-j$ values of x_i , i represents values of time, and j represents values of lag. As used herein, the dot-product autocorrelation may be adjusted by a scale factor K as a computational convenience, in which case,

$$a_j = K \cdot \sum (x_i \cdot x_{i-j})$$

again where the symbol $\sum$ indicates the sum over all $n-j$ values of x_i , i represents values of time, and j represents values of lag. Such an adjustment is not intended to be limiting to the meaning of the term. The maximum value of a_j is, of course, a_0 since at lag = 0, the signal perfectly correlates with itself. One such form of scale factor may include a_0 such that $K = k/a_0$ where k is a constant and its value is set for computational convenience.

The term "magnitude-coincidence autocorrelation" as used herein refers to a modification of dot-product autocorrelation. As used herein, magnitude-coincidence auto-correlation operates on signals which first have been rectified (an absolute-value filter has been applied). Each numeric value of a fixed-length time series x_i (all values of $x_i \geq 0$) is replaced by a 1 if the value x_i is equal to or greater than a threshold value T_{AC} and by a 0 if x_i is less than T_{AC} . Further, threshold T_{AC} is set at some multiple of the median of all n values of x_i in the fixed-length time series. Rectified cardiac signals such as those processed by the present invention contain noise which is typically substantially smaller than the peaks within such signals. Furthermore, over all n values of such a signal, a large number of values will be close to the noise level since there are substantial periods of time between signal (electrical events) representing a heart beat. Therefore, if threshold $T_{AC} = p \cdot \text{median}(x_i)$ and p is, e.g., 4,

threshold T_{AC} will be just above the baseline noise in the signal x_i , and the thresholded signal X_i will be equal to 1 only if a non-zero signal value is present which is generally not noise. Then, the magnitude-coincidence autocorrelation will have peaks for values of lag at which the time-distribution of the noise-free signal aligns
5 (correlates well) with itself. Magnitude-coincidence autocorrelation is particularly useful when the "time" information in a signal is of more interest than the "shape" or amplitude information in a signal.

The term "normal median" as used herein refers to the numeric value determined from a set of numeric values, such numeric value (median) being
10 computed according to the commonly-understood mathematical meaning of the term median. The normal median of a finite set of numeric values can be determined by arranging all the numeric values from lowest value to highest value and picking the middle value from the ordered set. If there is an even number of numeric values in the set, the normal median is defined to be the mean of the two middle values of the
15 ordered set.

The term "set-member median" as used herein refers to the numeric value determined from a set of numeric values in a manner modified from the above-described method of median determination. In this modified determination, if there is an even number of numeric values in the set, the set-member median is either one of
20 the two middle values in the ordered set such that the set-member median is always a member of the set of numeric values.

The term "intracardiac channel" as used herein refers to a channel of a set of MCCE signals which is connected to an internal lead, *i.e.*, connected to an internal-surface electrode such as is at the end or along the tip of a cardiac catheter. For
25 example, such an electrode may be in a blood vessel or in a chamber of a heart.

The term "ventricular channel" as used herein refers to a channel of a set of MCCE signals which exhibits the dominant response of the ventricles. This may most often be a channel which is connected to an external lead, *i.e.*, connected to a body-surface electrode. An epicardial or intracardiac channel may also sometimes be a
30 ventricular channel.

The term "activation" as used herein refers to a time segment within an MCCE signal which represents the passage of a depolarization wavefront within muscle cells adjacent to an MCCE electrode. An activation may sometimes be referred as an activity trigger.

5 The term "cycle length" as used herein refers to the time between neighboring activations in an MCCE signal, particularly in a reference-channel or mapping-channel signal. As used herein, the term "pulse interval" is used to connote the cycle length for a ventricular channel. The terms "ventricular pulse interval" and "intracardiac cycle length" are used to distinguish between these two measures of
10 repetitive signals. For example, if a cardiac patient is in a period of atrial fibrillation, there may be a significant difference between the rate of occurrence of electrical events in a ventricular channel and in some intracardiac channels. The ventricular cycle length, herein called ventricular pulse interval to further distinguish it from intracardiac cycle length, may be two or three times as long as the intracardiac cycle
15 length.

 As used herein, the terms "method" and "process" are sometimes used interchangeably, particularly in the description of the preferred embodiment as illustrated in the figures. The algorithms described as embodiments of the inventive automatic method of measuring parameters of multi-channel cardiac electrogram
20 signals are presented as a series of method steps which together comprise processes.

 As used herein, the terms "signal" and "channel" may be used interchangeably since the inventive automatic method described herein uses signal values in the channels of MCCE signals.

 The invention is an automatic method of determining local activation time
25 (LAT) in multi-channel cardiac electrogram signals including at least two cardiac channels, one of the cardiac channels being a mapping channel and another cardiac channel being a reference channel. The method comprises: (a) estimating a cycle length CL in the reference channel; (b) determining a mapping-channel fiducial time t_M in the mapping channel signal; (c) determining a plurality of reference-channel
30 fiducial times t_R ; (d) computing adjusted reference-channel fiducial times t_{RA} by adding or subtracting multiples of cycle length CL to each time t_R such that each time

t_{RA} is within a time window of length CL surrounding mapping-channel fiducial time t_M ; (e) computing a single final reference-channel fiducial time t_{RF} from the plurality of adjusted reference-channel fiducial times t_{RA} ; and (f) computing the LAT as t_M minus t_{RF} . In preferred embodiments, the time window of length CL surrounding t_M spans $\pm CL/2$ of t_M .

In some preferred embodiments of the automatic LAT-determination method, the adjusted reference-channel fiducial times t_{RA} used to compute final reference-channel fiducial time t_{RF} are a subset of the plurality of adjusted reference-channel fiducial times t^A . In some such embodiments, computing a single final reference-channel fiducial time t_{RF} comprises the steps of computing an average av_{RA} of the subset, including av_{RA} in the subset, and setting the final reference-channel fiducial time t_{RF} to the median of the subset, and in some of these embodiments, the median of the subset is the set-member median.

In other preferred embodiments of the automatic LAT-determination method, the adjusted fiducial times t_{RA} are a set of adjusted fiducial times and computing a single final reference-channel fiducial time t_{RF} comprises the steps of computing an average av_{RA} of the set, including av_{RA} in the set, and setting the final reference-channel fiducial time t_{RF} to the median of the set. In some of these embodiments, the median of the set is the set-member median.

In some highly-preferred embodiments, the mapping-channel fiducial time t_M is at a time of maximum negative velocity of the mapping-channel signal., and in some embodiments, the reference-channel fiducial times t_R are at times of maximum negative velocity of the reference-channel signal.

Further, in some highly-preferred embodiments of the automatic LAT-determination method, the steps (a) through (f) are repeated to generate a plurality of LAT values, the these values are displayed as an LAT map.

In other preferred embodiments of the automatic LAT-determination method, computing a single final reference-channel fiducial time t_{RF} from the plurality of adjusted reference-channel fiducial times t_{RA} includes ordering the plurality of adjusted reference-channel fiducial times t_{RA} and using a subset of times t_{RA} to

compute final reference-channel fiducial time t_{RF} . In some such embodiments, the subset of times t_{RA} is the interquartile set of times $t^{\wedge}$, and in some of these embodiments, the final reference-channel fiducial time t_{RF} is the median of the set. Further, in some of these embodiments, the median of the interquartile set is the set-member median.

Certain embodiments of the automatic LAT-determination method include computing a confidence interval for the determined LAT. In some such embodiments, computing an LAT confidence interval comprises computing an intermediate LAT value as $LAT = t_M - t_{RA}$ for each of the plurality of adjusted reference-channel fiducial times t_{RA} where the intermediate LAT values comprises a set of values, selecting the highest and lowest intermediate LAT values in the set, and computing the confidence interval as $\pm$ a fraction of the difference between the highest and lowest intermediate LAT values. In some of these embodiments, the fraction of the difference is one-half. Further, in some of the these embodiments, the set is a subset of the intermediate LAT values.

In certain other embodiments of the automatic LAT-determination method, estimating a cycle length CL in the reference channel comprises digitizing the reference-channel signal over a first preset time window, filtering the reference-channel signal to generate a reference-channel absolute-value velocity signal, autocorrelating the reference-channel absolute-value velocity signal, and selecting a peak value of the autocorrelation and setting the cycle length CL as the lag at the peak. Some of these embodiments include determining a CL confidence interval by setting a lag value L2 as the lag at a second autocorrelation peak near twice CL and setting the CL confidence interval at $\pm(L2 - 2CL)$.

In another aspect of this invention, the invention is an automatic method of measuring parameters of multi-channel cardiac electrogram signals which include at least one ventricular channel and at least two other cardiac channels. The inventive method comprises: (a) digitizing a first other cardiac signal and a ventricular-channel signal over a first preset time window; (b) filtering the ventricular-channel signal to generate a ventricular absolute-value velocity signal and filtering the digitized first other cardiac signal to generate a first other cardiac absolute-value velocity signal; (c)

estimating a pulse interval in the ventricular absolute-value velocity signal; (d) autocorrelating the first other cardiac absolute-value velocity signal; (e) selecting a peak value of the autocorrelation based on ventricular pulse-interval estimates; and (f) setting the cycle length of the first other cardiac signal to the lag value of the selected peak in the autocorrelation.

In some embodiments of the inventive method, the absolute-value velocity signals are each generated by applying a low-pass filter followed by a first-difference filter and an absolute-value filter. In some of these embodiments, each combination of low-pass filter and first-difference filter is two differenced sequential boxcar filters.

In highly-preferred embodiments of the inventive method, the first signal autocorrelation is calculated by magnitude-coincidence autocorrelation. In some other embodiments, the first signal autocorrelation is calculated by dot-product autocorrelation.

In certain preferred embodiments, the step of estimating the pulse interval includes determining ventricular-channel activations by measuring signal threshold-crossings. In some of these preferred embodiments, determining the ventricular-channel activations includes the steps of subdividing the first preset time window into three equal-length periods of time, determining the signal maximum in each of the three periods of time, setting the threshold to a fixed threshold-percentage of the minimum of the three signal maxima, and identifying ventricular-channel activation times at threshold-crossing times at which a threshold-crossing is preceded by at least a fixed below-threshold period. In some of these embodiments, the fixed threshold-percentage is about 50%, and in some, the below-threshold period is about 120 msec.

In other preferred embodiments, estimating the pulse interval includes the steps of computing all activation double-intervals, determining the median of all of the activation double-intervals, and setting the pulse interval to one-half of the median.

Some preferred embodiments of the inventive method include a step of determining a confidence interval for the pulse interval estimate. This determination comprises computing a set of activation intervals, identifying maximum and minimum

activation intervals in the set, and setting the confidence interval equal to the difference between the maximum and minimum activation intervals.

In highly-preferred embodiments, selecting a peak value of the autocorrelation includes the steps of: (1) determining the lag W of the minimum of the autocorrelation for lag less than a preset lag threshold; (2) determining the maximum peak P_j of the autocorrelation for lag CL_1 greater than W and setting an interim cycle length CL to CL_1 and an interim peak P_{CL} to P_1 ; (3) determining whether CL_1 is within a first lag interval of twice the pulse interval; (4) finding maximum P_2 in the autocorrelation at lag CL_2 within a second lag interval of the pulse interval, determining (a) whether the maximum P_2 is greater than $P_{CL}/2$ and (b) whether CL_2 is within a third lag interval of $CL/2$, and if (a) and (b) are true, setting CL to CL_2 and P_{CL} to P_2 ; (5) determining whether CL is within a fourth lag interval of the pulse interval; (6) finding maximum P_3 in the autocorrelation at lag CL_3 between a lag of $CL/6$ and a lag of $2CL/3$, determining (a) whether the maximum P_3 is greater than $P_{CL}/2$ and (b) whether either $2CL_3$ or $3CL_3$ is within a fifth lag interval of CL , and if both (a) and (b) are true, setting CL to CL_3 ; and (7) setting the cycle length of the first other cardiac signal to interim cycle length CL .

In certain highly-preferred embodiments of the inventive method, the first other cardiac signal is a reference signal and a second other cardiac signal is a mapping signal. In these embodiments, the method further includes the steps of: (a) computing a reference velocity signal; (b) selecting the mapping signal over a second preset time window, the second preset time window being a percentage of and overlapping the end of the first preset time window; (c) digitizing the mapping signal; (d) filtering the digitized mapping signal to generate a mapping velocity signal and an absolute-value mapping velocity signal; (e) determining mapping-signal activations by measuring signal threshold-crossings; (f) selecting a mapping-signal activation based on its time relative to the ventricular channel activation times; (g) finding time t_M of the maximum negative velocity in the selected mapping-signal activation; (h) finding the time t_R of the maximum negative velocity in the reference velocity signal within one half of the cycle length of the reference signal; and (i) computing local activation time as t_M minus t_R . Some of these embodiments include storing and displaying the

local activation time in a map and repeating steps (a) through (i) to store and display plural local activation times in a map.

Some embodiments of the inventive method include finding a plurality of times t_R , computing a plurality of interim local activation times t_{LAT} based on the times t_R , and determining the local activation time based on a subset of the plurality of times t_{LAT} . In some of these embodiments, the single local activation time is the median of the plurality of interim times t_{LAT} and in some, the plurality of times t_R includes all of the times of local negative velocity maxima in the reference signal, and the subset includes times t_{LAT} based on each time t_R . Further, in some, the plurality of times t_R includes all of the times of local negative velocity maxima in the reference signal, and the subset includes times t_{LAT} based on an interquartile set of times t_{LAT} .

In another aspect of the inventive method, wherein the at least one ventricular channel includes two or more ventricular channels, the method further includes automatically selecting the ventricular-channel signal from among the two or more ventricular channels. In some embodiments, the step of selecting the ventricular-channel signal comprises: (1) digitizing a plurality of candidate ventricular-channel signals over a first preset selection time window; (2) filtering each of the plurality of candidate signals to generate corresponding candidate absolute-value velocity signals; (3) dividing each candidate absolute-value velocity signal into a set of sequential, equal-length sub-signals; (4) estimating signal quality and pulse interval for each sub-signal of each candidate signal; (5) combining the sub-signal quality estimates of each candidate signal to generate a signal quality estimate SQ_{VC} for each candidate signal; (6) determining the maximum and minimum pulse intervals for each sub-signal and generating a pulse interval variability estimate VAR_{VC} for each candidate signal by selecting the maximum difference between sub-signal pulse-interval maxima and minima; (7) excluding candidate ventricular-channel signals with values VAR_{VC} above a variability threshold; and (8) selecting the ventricular channel as the non-excluded candidate channel with the highest signal quality estimate SQ_{VC} . In some of these embodiments, estimating signal quality for each sub-signal comprises the steps of dividing each sub-signal into three equal-length chunks, determining the maximum of each chunk, determining the maximum MAX and minimum MIN of the

three chunk maxima, computing the median of the sub-signal to generate a noise estimate N_s equal to twice the median, and calculating the signal-quality estimate as $2 \times \text{MFN} - \text{MAX} - 2 \times N_s$.

Certain preferred embodiments of the inventive method include automatically
 5 selecting the first other cardiac channel from among the at least two other cardiac channels. In certain of these embodiments, selecting the first other cardiac channel comprises: (1) digitizing a plurality of candidate other cardiac signals over a first preset selection time window; (2) filtering each of the plurality of candidate signals to generate corresponding candidate absolute-value velocity signals; (3) dividing each
 10 candidate velocity signal into a set of sequential, equal-length sub-signals; (4) estimating signal quality, cycle length and variability for each sub-signal of each candidate signal; (5) combining the sub-signal quality estimates of each candidate signal to generate a signal quality estimate SQ_{RC} for each candidate signal; (6) determining the maximum MAX_{CL} and minimum MIN_{CL} of the sub-signal cycle
 15 lengths and a cycle length variability VAR_{RC} for each candidate signal; (7) calculating a figure of merit value for each candidate signal based on signal quality SQ_{RC} , MAX_{CL} , MIN_{CL} , and VAR_{RC} ; and (8) selecting the other cardiac channel as the candidate channel with the highest figure of merit value.

In another aspect of the inventive method, wherein the at least two other
 20 cardiac channels includes three or more other cardiac channels, the method further includes selecting a reference channel and a mapping channel from among the other cardiac channels, monitoring the signal quality of each of the reference channel and at least one of the other cardiac channel, and if the signal quality of the reference channel falls below a signal quality threshold, replacing the reference channel with the other
 25 cardiac channel with a higher signal quality and calculating local activation time values based on the higher-signal-quality other cardiac channel.

In a further aspect of the inventive method, wherein multi-channel cardiac electrogram signals include a plurality of cardiac channels and at least one ventricular channel, a reference channel is automatically selected from the plurality of cardiac
 30 channels based on signal quality, cycle length, and cycle-length variability measurements of a subset of the plurality of cardiac channels. In some such

embodiments, the at least one ventricular channel is two or more ventricular channels and the method further includes automatically selecting a ventricular channel based on signal quality and variability of the ventricular channels.

5 In yet another aspect of the inventive method of automatic measurement of parameters of multi-channel cardiac electrogram signals, wherein there is a plurality of cardiac channels, some preferred embodiments include measuring and storing cardiac parameters in a first subset of channels, detecting activations in a second subset of channels, and computing local activation times for a plurality of pairs of channels, each pair including one channel from the first subset of channels and one
10 channel from the second subset of channels.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGURE 1 is a schematic block diagram of the inventive method for measuring parameters of MCCE signals, including intracardiac cycle lengths and local
15 activation times and estimates of signal and measurement quality. The steps of the method as illustrated in the block diagram of FIGURE 1 are further detailed in several other schematic block diagrams.

FIGURE 2 is a schematic block diagram illustrating steps of the inventive method to generate absolute-value velocity data of a selected digitized MCCE signal.

20 FIGURE 3A is an illustration of the operation of the filtering which occurs by applying two differenced sequential boxcar filters to a digitized signal.

FIGURE 3B depicts the absolute value of the output signal of the filtering operation illustrated in FIGURE 3A.

FIGURE 4A is a schematic block diagram of the process of determining
25 activations (activity triggers) in the absolute-value velocity signal from an MCCE channel. The steps of this process are applied to more than one channel signal in the inventive method.

FIGURE 4B illustrates the process of identifying activations in an example absolute-value velocity channel signal as processed by the process of FIGURE 4A.

FIGURE 5 is a schematic block diagram of the process of determining the ventricular-channel cycle length, herein called "pulse interval" when associated with a ventricular channel.

FIGURES 6A and 6B together are a schematic block diagram of the process of
5 determining the reference-channel cycle length in the embodiment of FIGURE 1.

FIGURES 7A and 7B together are a schematic block diagram of the process of determining local activation time (LAT) for a single mapping point in the embodiment of FIGURE 1.

FIGURE 7C is schematic block diagram of an alternative embodiment of the
10 inventive method to determine LAT for a single mapping point, using additional fiducial times within a reference-channel signal.

FIGURE 8A is a set of MCCE signal plots illustrating an example of the process of determining LAT for a single mapping point as shown in FIGURES 7A and 7B.

FIGURE 8B is a table which illustrates the process by which a specific
15 mapping-channel activation is selected for the determination of LAT for the example of FIGURE 8A.

FIGURE 8C-1 through FIGURE 8C-4 is a set of plots illustrating in detail a selected mapping-channel activation and its corresponding portion of the reference-
20 channel signal which, as illustrated in FIGURES 8A and 8B, are used to determine LAT for a single mapping point.

FIGURE 8D is a table illustrating an embodiment of a method to assess measurement confidence in the inventive method of FIGURE 1, using the examples of FIGURES 8A through FIGURE 8C-4. FIGURE 8D also illustrates a second
25 alternative embodiment of the inventive method to determine an LAT value for a single mapping point.

FIGURE 9 is a schematic diagram illustrating the inclusion of automatic selection of the ventricular and reference channels in the inventive automatic method of measuring parameters of MCCE signals.

FIGURE 10A is a schematic block diagram of the process of automatically selecting a ventricular channel from a set of candidate MCCE channels, specifically illustrating the determination of parameters for a single candidate ventricular channel.

FIGURE 10B is a schematic block diagram of the process of automatically selecting a ventricular channel from a set of candidate MCCE channels, specifically illustrating the automatic selection from among candidate ventricular channels which have had parameters determined in the automatic process of FIGURE 10A.

FIGURE 11A is a schematic block diagram of the process of automatically selecting a reference channel from a set of candidate MCCE channels, specifically illustrating the determination of parameters for a single candidate reference channel.

FIGURE 11B is a schematic block diagram of the process of automatically determining the variability parameter for a single candidate reference channel as used within the process illustrated in FIGURE 11A.

FIGURE 11C is a schematic block diagram of the process of automatically selecting a reference channel from a set of candidate MCCE channels, specifically illustrating the automatic selection from among candidate reference channels which have had parameters determined in the automatic process of FIGURES 11A and 11B.

FIGURE 12 is a matrix which schematically illustrates a series of reference channels and mapping channels among a set of MCCE signals which in an aspect of the inventive method may be processed in parallel to generate multiple LAT maps by various combinations of reference and mapping channels.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

FIGURE 1 illustrates one embodiment of the inventive method for measuring parameters of multi-channel ECG signals. FIGURE 1 is a high-level schematic block diagram of a method which measures intracardiac cycle lengths and local activation times on a near-real-time basis as part of a system to generate maps (*e.g.*, computer displayed 3D presentations of the distribution of voltages and activation times across cardiac structures) and provides feedback regarding signal quality and measurement confidence.

Several other figures in this document relate to the inventive method of FIGURE 1, and the steps presented in the schematic block diagrams of these other figures are nested within the high-level schematic block diagram of FIGURE 1, as will be described below. In addition, the inventive method also includes initial
5 channel selection steps which occur prior to the steps of FIGURE 1. These are illustrated and described later in this document, in FIGURES 9 through 11C.

Referring to FIGURE 1, an embodiment 10 of the inventive method includes a flow loop of method steps which is initiated by a request 12 to map a point, and each time a mapping-point request 12 is generated, the method proceeds through the steps
10 shown in FIGURE 1. The flow chart element labeled with reference number 14 indicates that the flow loop waits to receive request 12. During a procedure in which the inventive method is used, an electrophysiologist (EP doctor) is maneuvering an electrode-tipped catheter (mapping catheter) through and around the chambers, arteries and veins of a patient's heart. The electrode on this maneuvered catheter
15 provides the mapping-channel signal. When the EP doctor determines that the maneuvered catheter electrode is in a desired position, the EP doctor activates a signal as request 12 to map a point. A plurality of map points constitute the map.

Generating the map during this procedure involves time measurements made between the MCCE signals of the mapping electrode and a reference electrode. (As
20 used herein, electrodes are positioned to provide signals to channels. Thus, for example, the mapping electrode provides the signal for the mapping channel.) The reference electrode is positioned before mapping begins in a location that is expected to remain constant during the mapping process and that will generate stable and repetitive electrical signals.

25 Each electrode develops an electrical signal when muscle cells in contact with the electrode change their cell membrane potentials. These electric potentials change as the cells mechanically contract. Nerve cells, which do not contract, also can be in contact with electrodes and produce electrical signals.

The map being generated represents a particular heart rhythm being studied,
30 such as tachycardia. The reference-channel and mapping-channel signals are both cyclical and have substantially the same cycle length (CL). The reference-channel

signal represents a zero-phase or index moment of the particular cardiac cycle, and the local activation time (LAT) measurements (time difference between mapping and reference-channel signals) indicate the sequence of muscle and nerve cell activation of various points (map points) in the cardiac structure. This time sequence and its physical course around the anatomy of the heart are the information the EP doctor needs to determine how to apply therapy. The term "local" refers to the fact that the measurement applies to the heart cells in contact with the electrode and to signals with respect to a reference-channel signal, and this information is translated to a position on a three-dimensional (3D) image of the heart chamber.

Activation time is measured relative to one or more activations at the reference electrode and may be positive or negative. A local activation time which is negative by more than a half of one cycle length may also be recognized as being positive at a corresponding time less than a half of one cycle length. Local activation times may be defined as being relative to the nearest activation in the reference channel.

Positioning of the mapping catheter is guided at times by fluoroscopic imaging. At a position of interest, the EP doctor generates request 12 to trigger the system to make measurements from the MCCE signals available from the maneuvered catheter and other more stationary catheters and body surface electrodes. These measurements at mapping points are represented graphically, usually by color, on a 3D image of the heart chamber of interest. These points may be requested at irregular intervals of several seconds to perhaps minutes, depending on when the EP doctor maneuvers the mapping catheter to a point at which measurements should be taken.

When request 12 is received, measurements are made using an "epoch" of the most recent 6 seconds of MCCE signals. In embodiment 10, the 6-second length of this epoch should not be taken as limiting. The epoch is a preset time window of MCCE signals, and its 6-second length is chosen here in embodiment 10 such that selected signals during the preset time window contain a suitable number of electrical events to permit the analysis to be performed. During such mapping procedure, at least one mapping channel and at least one reference channel are used. At some points within embodiment 10, as will be described later in this document, the epoch is divided into three equal periods of time, and six seconds is chosen here since a 2-

second period will almost always contain at least one heart beat (or cell activation) for all heart rates above 30 beats per minute.

As the mapping catheter is moved, it is important that its electrode be in place at the selected location for a period of time (dwell time) long enough to obtain a suitable signal. In embodiment 10, such dwell time is about 2 seconds. Thus, when request 12 is received, the epoch consists of 6 seconds of data on other channels being used and 2 seconds of data on the mapping channel. (The 6 seconds of data may consist of the immediate past 4 seconds of the data plus 2 seconds of data generated after request 12 occurs. The 6 seconds of data in an epoch may also be the 6 seconds of data immediately preceding the request 12, since it may be that the mapping catheter has already been in a stable position for the 2 seconds prior to the triggering of request 12. Other possible strategies for acquiring the epochs of data are also possible.)

In the high-level schematic block diagram of FIGURE 1, after request 12 is received, ending the wait in method step 14, a determination of the pulse interval in the ventricular channel is performed in method step 15. Details of ventricular pulse interval determination 15 are detailed in the schematic block diagrams and example signals of FIGURE 2 through FIGURE 5, all of which will be described later in this document.

Following ventricular pulse interval determination 15, a determination 16 of the intracardiac cycle length in the reference channel is performed. (Method step 16 is shown in FIGURE 1 as determining tachycardia cycle length since the inventive method is intended primarily for monitoring cardiac parameters in the treatment of patients in tachycardia. The use of the term "tachycardia" is not intended to be limiting. The inventive method is applicable to measurement of all types of cardiac arrhythmias as well as normal heart rhythms.) Details of intracardiac cycle length determination 16 are detailed in the schematic block diagrams and example signals of FIGURES 2 through 4B and FIGURE 6, all of which will be described later in this document. Intracardiac cycle length determination 16 depends on the value of ventricular pulse interval established in determination 15.

Decision step 18 follows determination 16 such that the cycle length determined in step 16 is compared to a cycle-length-change criterion in decision step 18, and if the cycle length has not exceeded the cycle-length-change criterion, the inventive method proceeds. If, however, the cycle-length-change criterion is exceeded, the EP doctor is alerted in method step 20 in order that steps may be taken by the EP doctor during the mapping procedure to evaluate the impact of such a change.

A cycle-length-change criterion applied in method step 18 may be based on an absolute time difference in cycle length from a previous cycle length or on the average of a plurality of previous cycle lengths. Or it may be based on a percentage change from such quantities. One useful previous cycle length is the initial or starting cycle length of the reference channel, established at the beginning of the mapping procedure. A local activation time map is related to a particular rhythm so that if there is too great a change in cycle length, the EP doctor may choose to start a new map, or in fact may determine that mapping is no longer appropriate at such time. A value for the percentage change which triggers an alert in method step 20 may be that the current reference-channel cycle length (determined in method step 16) is found to differ from the starting cycle length by more than 10%. Such value is not intended to be limiting; other values may be found to provide adequate warning to the EP doctor.

Embodiment 10 of the inventive method then proceeds to a computation 22 of the local activation time (LAT) associated with the map point being analyzed. Details of local activation time computation 22 are detailed in the schematic block diagram of FIGURES 7A-7C which will be described later in this document, and examples of such determination are illustrated in FIGURES 8A through 8D.

Embodiment 10 of the inventive method for measuring parameters of MCCE signals includes steps for evaluation 24 of signal quality and evaluation 26 of measurement confidence, both of which are applied within embodiment 10 to monitor the measurement process. In each case, that is, reduced signal quality as determined in step 24 and reduced measurement confidence in step 26, the EP doctor is alerted (user alerts 28 and 30, respectively) that such conditions have been detected. One embodiment of a method to measure signal quality in method step 24 is included in

the steps illustrated in FIGURE 4A and will be discussed later in this document. One embodiment of a method to assess measurement confidence in method step 26 is illustrated in the example of FIGURE 8D described later in this document.

As shown in FIGURE 1, the method of embodiment 10 provides (in step 32) the map point and its related measurement data to a computer at least for display to the EP doctor during the procedure and for storage in memory for later analysis. The system then returns via loop path 33 to wait for the next mapping point request 12 at step 14.

FIGURES 2, 3A and 3B illustrate an embodiment of a portion of the steps of the inventive method further detailed in FIGURES 4A-11C. FIGURE 2 is a schematic block diagram illustrating detailed steps within embodiment 10 by which a selected digitized MCCE channel signal 36i is filtered to generate a corresponding absolute-value velocity signal 36o. The steps of FIGURE 2 are applied to various signals within embodiment 10 of the inventive method, as indicated later in the description below.

In FIGURE 2, the combined steps, low-pass filter 38, first-difference filter 40, and absolute-value filter 42, are together shown as an absolute-value velocity filter 34. The first two steps of absolute-value velocity filter 34, low-pass filter 38 and first-difference filter 40, are together shown as a bandpass filter 44 which generates a filtered velocity signal 41 of an input signal.

As shown in FIGURE 2, an input signal 36i is a 6-second preset time window (epoch) of digitized data from a selected MCCE signal. Low-pass filter 38 operates on input signal 36i followed by first-difference filter 40, and together these two filters generate a digital stream of data 41 which corresponds to the filtered velocity (first derivative) of input signal 36i with certain low and high frequencies filtered out. That is, filter 44 is a bandpass filter. Absolute-value filter 42 simply applies an absolute-value operation (rectification) to filtered velocity signal 41 from first-difference filter 40 to generate output signal 36o which is an absolute-value velocity signal of input signal 36i.

One embodiment of applying a combination 44 of low-pass filter 38 and first-difference filter 40 to a digitized signal is what is called herein "two differenced

sequential boxcar filters," and such filtering embodiment is illustrated in FIGURE 3A, in which an example digitized signal 46 is shown both graphically (46g) and numerically (46n). Seven pairs of "boxcars" 48b illustrate the sequential operation of boxcar filter 48.

5 Referring to FIGURE 3A, each pair of boxcars 48b in boxcar filter 48 is four time samples in length, and two boxcars 48b are such that one follows the other immediately in time. (Only two of the 14 boxcars 48b are labeled.) The sum of the four time samples of digitized signal 46 in each boxcar 48b is calculated. Thus, for example, the left boxcar 48b of the uppermost (first in time) pair as shown holds the
 10 sum of the four time samples it subtends, and the right boxcar 48b of this pair holds the sum of the four time samples it subtends. These two sums are 7 and 12, respectively, and the difference between the right boxcar value and the left boxcar value is $12 - 7 = 5$. This differenced value 5 is shown to the right of the uppermost boxcar 48b pair, and seven such values, indicated by reference number 50, are shown
 15 to the right of the seven example sequential boxcar 48b pairs. This output signal 50 is shown both numerically as 50n and graphically as 50g. Filter output signal 50 is shown for the seven time samples between the dotted lines labeled 52a and 52b.

In the example of FIGURE 3A, each boxcar 48b has a boxcar-width w_B of four samples. The value of w_B determines the frequency response of boxcar filter 48, or
 20 the amount of smoothing provided by boxcar filter 48. Larger values of w_B produce a lower central frequency of boxcar filter 48 and therefore more smoothing of the signal on which it operates. Such relationships are well-known to people skilled in the art of digital filtering. Any specific value for w_B used herein is not intended to be limiting. However, for the embodiments exemplified herein, it has been found that values of w_B
 25 of around 4 are appropriate for use on intracardiac signals, and values of w_B around 20 are appropriate for ventricular channels. For MCCE signals digitized every 1 millisecond and for sequential four-sample-long boxcar filters 48 ($w_B = 4$) illustrated in FIGURES 3A, 3B and 5, the resulting bandpass filter has a center frequency of 125Hz.

30 The operation of the two differenced sequential boxcar filters 48 performs low-pass filtering and differentiation to input signal 46 such that filter output 50 is

proportional to the velocity of bandpass-filtered digitized signal 46. No scaling has been applied in this example, but such lack of scaling is not intended to limit the meaning of the term two differenced sequential boxcar filters.

FIGURE 3B, shown below and to the left of FIGURE 3A, simply graphically illustrates the absolute value of output signal 50 as exemplified in FIGURE 3A. The absolute value of output signal 50 is processed by absolute-value filter 42 as shown in FIGURES 3A and 3B. This absolute-value velocity signal is output signal 36o of FIGURE 2.

Some steps of the inventive method as illustrated in embodiment 10 include the identification of activations or activity triggers within one or more channel signals of MCCE signals. Activations (activity triggers) are the electrical activity associated with the initiation of the depolarization of the heart muscle cells which occurs during a heart beat, progressing like a wave through the various portions of the cardiac structure and causing the heart to pump.

FIGURE 4A is a schematic block diagram of a process 58 of determining activations (activity triggers) in an absolute-value velocity signal. The steps of process 58 may be applied to more than one channel signal in the inventive method.

In the embodiment of FIGURE 4A, a signal 60 which is 6 seconds in duration (6-sec epoch) and is the absolute-value velocity of an MCCE channel signal, is divided into three 2-second "chunks" in method step 62. In method steps 64-1, 64-2 and 64-3, these three chunks are processed to find three signal maxima (max1, max2, and max3), one for each of the three signal chunks. These three values (max1, max2, and max3) are inputs to method step 66 which selects the maximum MAX among the three inputs and method step 68 which selects the minimum MIN among the three inputs. The values MAX and MIN are in turn inputs to method step 70 which determines an estimate SI for signal irregularity. In method step 70, signal irregularity SI is estimated as $SI = MAX - MIN$. A larger difference between the maximum (MAX) and minimum (MIN) values of the chunk maxima (max1, max2, and max3) indicates that there is more irregularity among the heart beats within epoch 60 being processed. Signal irregularity SI is related to the variations in the "shape" of the

activations in MCCE signals while other measurements described later in this document relate to variations in the time of activations.

The value MTN represents an estimate SS of signal strength. SS is multiplied by 0.5 (threshold factor) in method step 72 to determine a value for an activation threshold AT to be used in step 74 to determine the occurrence of activations within the MCCE signal being processed. The value (0.5) of the threshold factor applied in method step 72 of this embodiment is not intended to be limiting. Other values for the threshold factor may be applied in embodiments of the inventive method.

Signal irregularity SI and signal strength SS are used in conjunction with an estimate of signal noise N_s to provide an estimate of signal quality SQ in method step 79. In method step 78, signal 60 (provided by flow path 60a) is processed to compute its median over the entire 6-second epoch, and such median is multiplied by 2 to produce estimate N_s of signal noise. In method step 78, the calculation of the median of signal 60 may be done using a normal median or a set-member median. For such large data sets (*e.g.*; 6 seconds at 1,000 samples per second), it has been found that using the set-member median is computationally convenient and highly suitable. In step 79, signal quality SQ is computed as $SQ = SS - SI - 2N_s$.

The factor of 2 applied in method step 78 and the factor of 2 applied in method step 79 are both not intended to be limiting. Other values for such factors may be used. The size of the factor in step 78 is related to ensuring that the estimate of noise N_s in signal 60 is a good representation of the noise level in signal 60. The size of the factor in step 79 is related to the relative weight given to noise estimate N_s compared to those given to signal strength SS and signal irregularity SI in generating the estimate for signal quality SQ. The values of 2 for both of these factors have been found to provide good performance for estimating noise N_s and signal quality SQ.

FIGURE 4B illustrates method step 74 of FIGURE 4A, the process of identifying activations in an example absolute-value velocity channel signal 60 as processed by the method steps of FIGURE 4A. The signal of epoch 60 being processed is an input to method step 74 as indicated by the signal flow path 60a. A portion of example epoch 60 is illustrated in FIGURE 4B. Activation threshold AT is shown as a dotted line AT parallel to the time axis and intersecting signal 60 at points

76. (Eleven signal crossings are shown; one such point is labeled 76a, one is labeled 76b, and one is labeled 76c).

As indicated in method step 74 of FIGURE 4A, activations in epoch 60 being processed are indicated by identifying threshold crossings 76 before which signal 60 does not cross activation threshold AT for at least T_{BT} milliseconds. The value of
 5 before-threshold time T_{BT} chosen may vary according to the type of MCCE signal 60 being processed. For example, it has been found that $T_{BT} = 120\text{msec}$ is an appropriate value when a ventricular channel is being analyzed, and that $T_{BT} = 90\text{msec}$ is an appropriate value when an intracardiac channel is being analyzed. These values for
 10 T_{BT} are not intended to be limiting; the selection of a value for T_{BT} is based on choosing a value by which a reliable differentiation between subsequent activations and among threshold crossings 76 within an individual activation can be achieved.

In the example of FIGURE 4B, the activation labeled 75 shown includes six threshold crossings 76 as indicated by dotted circles occurring in rapid succession, the first being threshold crossing 76b and the last being threshold crossing 76c. A portion
 15 of a previous activation 77 within signal 60 is also shown in FIGURE 4B. In activation 77, five threshold crossings 76 occur in rapid succession, the last of which is labeled 76a.

The time difference between threshold crossing 76a associated with activation 77 and threshold crossing 76b associated with activation 75 is about 185msec as
 20 shown in FIGURE 4B. In this example, 185msec is longer than either of the example values for T_{BT} ; thus threshold crossing 76b is determined to be the leading edge of activation 75, and the time at which threshold crossing 76b occurs is determined to be activation time t_{ACT} . In this example, threshold 76b is the only such threshold crossing
 25 illustrated in FIGURE 4B.

FIGURE 5 is a schematic block diagram of an embodiment 80 of a process of determining the ventricular-channel pulse interval (heart rate). In the inventive automatic method of measuring parameters of MCCE signals, ventricular-channel pulse interval information is used in the calculations to determine intracardiac-channel
 30 parameter calculations. The steps of embodiment 80 of FIGURE 5 analyze an absolute-value velocity ventricular-channel signal epoch 82, again 6 seconds in

duration. In method step 84, activations within epoch 82 are identified by applying steps 58 as illustrated in FIGURE 4A. As indicated in method steps 82 and 84, when processing a ventricular channel, values for boxcar-width w_B and before-threshold time T_{BT} may differ from those used for intracardiac channels. In the embodiment of

5 FIGURE 5, these values are $w_B = 20$ and $T_{BT} = 120\text{msec}$.

Activations identified in method step 84 each have an activation time t_i , and for purposes of description, there are n such activation times. In method step 86, all activation intervals I_i are computed. There are $n-1$ activation intervals I_i computed as follows:

$$\begin{aligned}
 10 \quad & I_1 = t_2 - t_1 \\
 & \bullet \\
 & I_i = t_{i+1} - t_i \\
 & \bullet \\
 & I_{n-1} = t_n - t_{n-1}
 \end{aligned}$$

15 In method step 88, a maximum interval MAX_{PI} of the $n-1$ activation intervals I_i is computed, and in step 90, the minimum interval MIN_{PI} of the $n-1$ activation intervals I_i is computed. In method step 92, a range R_{PI} for activation intervals I_i is computed as the difference between MAX_{PI} and MIN_{PI} .

The n activation times t_i are also used in method step 94 to compute all

20 double-intervals D_i of ventricular-channel signal epoch 82. There are $n-2$ double-intervals D_i , and such double-intervals D_i are computed as follows:

$$\begin{aligned}
 & D_1 = t_3 - t_1 \\
 & \bullet \\
 & D_i = t_{i+2} - t_i \\
 & \bullet \\
 25 \quad & D_{n-2} = t_n - t_{n-2}
 \end{aligned}$$

In method step 96, the normal median M_{DI} of all double-intervals D_i is computed, and in step 98, the estimate PI of ventricular-channel pulse interval is computed as

$$PI = M_{DI}^{12}$$

30 Thus, method steps of process 80 generate an estimate of ventricular pulse interval PI and provide an estimate of the range R_{PI} over which ventricular pulse interval PI

varies. The value of pulse interval PI is used in the determination of reference-channel and mapping-channel cycle lengths and is reported as a heart rate HR for the patient being monitored. Heart rate HR in beats per minute (bpm) is determined in method step 99 from pulse interval PI (in msec). (For computational convenience in
 5 step 96, a set-member median calculation may be used in place of the normal median calculation.)

FIGURES 6A and 6B together are a schematic block diagram of a process 220 of determining the reference-channel cycle length CL. (Method step 16 of FIGURE 1 includes process 220 along with other elements of the reference-channel cycle-length
 10 determination as illustrated in the embodiments of FIGURES 2 through 4B.) The steps of FIGURES 6A and 6B process an absolute-value velocity reference-channel signal epoch 222, again 6 seconds in duration. In step 224, reference-channel signal strength SS, signal irregularity SI, and noise N_s are computed using the steps of FIGURE 4A. Method steps 72 and 74 of FIGURE 4A are not used in the processing
 15 of reference-channel absolute-value velocity signal 222; individual activations within signal 222 are not detected. Signal strength SS, signal irregularity SI, and noise N_s are used to determine signal quality SQ, and noise N_s is used in the computation of the magnitude-coincidence autocorrelation function ACF in method step 226.

In method step 226, a magnitude-coincidence autocorrelation is performed on
 20 the data in absolute-value velocity reference-channel signal epoch 222. (The computed autocorrelation function is indicated by the term ACF.) The threshold value for the magnitude-coincidence autocorrelation is dependent on noise N_s in signal 222 as described in the summary section above which defines magnitude-coincidence autocorrelation. As applied in method step 226, the value of the
 25 threshold T_{AC} is set to ensure that the thresholding process selects events which are significant events within input signal 222. In one embodiment,

$$T_{AC} = 2 \cdot N_s \text{ where noise } N_s = 2 \cdot (\text{median(input)} + 1).$$

The "1" is added to the median for computational convenience and to avoid singular conditions within the system. Values other than 1 may be used and other ways to set
 30 threshold T_{AC} may be used; this specific expression for T_{AC} is not intended to limit the scope of this invention.

The remaining method steps of process embodiment 220 in FIGURES 6A and 6B, steps 228-252, encompass analysis of ACF to determine reference-channel cycle length CL. As described above, ACF is a function of lag, and in this analysis, values of lag in ACF are analyzed with respect to ventricular-channel pulse interval PI such that reference-channel cycle-length CL is determined in process 220 based on estimates of pulse interval PI.

In method step 228, a minimum of ACF at values of lag less than about 200 msec is identified. (200msec is a preset lag threshold.) The lag at this minimum in ACF is labeled W and is an estimate of activity width. The lag threshold value of 200 msec for searching for activity width is chosen such that the width of activations expected for most intracardiac-channel signals will be found at lag values less than 200 msec. The search window (preset lag threshold) should be shorter than the shortest expected value of reference-channel cycle length and longer than the width of activations in the reference-channel signal. Since activations typically are significantly shorter than CL, it is straightforward to set the range to an appropriate value. 200msec has been found to be a useful value. However, the specific value of 200 msec for the preset lag threshold is not intended to be limiting.

In method step 230, the maximum peak P_j is found in ACF for values of lag greater than W; CL is set at the value of lag CL_1 where ACF has its maximum peak P_1 for lag greater than W; and an interim peak amplitude P_{CL} is set to PI. (P_{CL} , P_1 , P_2 , P_3 , CL_1 , CL_2 and CL_3 are interim values in the steps of process 220.) Then in method step 232, if CL_1 is very near (within ± 20 msec) double the ventricular pulse interval PI, then process 220 proceeds to method step 234. If CL_1 is not very near $2PI$, then process 220 proceeds to method step 242 in FIGURE 6B. (Points A and B in process 220 represent common points joining FIGURES 6A and 6B.) The situation of CL_1 being very near double the ventricular pulse interval PI may occur in a condition in which a slight alternation of ventricular pulse interval PI in a pattern of bigeminy (long, short, long, short, etc.) causes the autocorrelation to be slightly stronger at the repeating double interval. Consecutive single intervals are only slightly different, but magnitude-coincidence autocorrelation is very sensitive to the slight timing differences.

Throughout process embodiment 220 of determining reference-channel cycle length CL, there are several time intervals which are used to identify certain values in ACF such as the ± 20 msec "nearness" criterion in method step 232. These occur in method steps 232, 234, 238, 242, 248, and 250. In each such occurrence, these specific values have been found to perform well in the embodiment of process 220. (The "nearness" criteria are also referred to as lag intervals. The lag intervals in the method steps of process 220 are: step 232, a first lag interval; step 234, a second lag interval; step 238, a third lag interval; step 242, a fourth lag interval; and steps 248 and 250, a fifth lag interval.)

In method step 234, the maximum amplitude P_2 of ACF is identified within a lag interval of ± 40 msec of ventricular pulse interval PI, CL_2 is set to the value of lag at maximum P_2 , and process 220 proceeds to method step 236. In method step 236, if the amplitude P_2 is greater than half of peak amplitude P_{CL} and if, in method step 238, CL_2 is within 20 msec of $CL_1/2$, then in method step 240, CL is set to CL_2 , P_{CL} is set to P_2 , and process 220 proceeds to step 242. If both of these two conditions (in steps 236 and 238) are not true, process 220 proceeds to step 242 without setting CL to CL_2 and P_{CL} to P_2 . Method step 238 distinguishes peak P_2 from a maximum on one of the boundaries of the ± 40 msec lag interval in method step 234. If the P_2 is not greater than half of P_1 , then the process proceeds to method step 242.

In method step 238, if $CL_1/2$ is within 20 msec of CL_2 , then CL is set to CL_2 in method step 240 and the process proceeds to method step 242. If $CL_1/2$ is not within 20 msec of CL_2 , then the process proceeds to method step 242 without setting CL to CL_2 .

In method step 242, if CL (set in method step 230 or method step 240) is within 60 msec of ventricular pulse interval PI, then process 220 proceeds to method step 244. If CL is not within 60 msec of PI, then the process ends and the reference-channel cycle length is either $CL = CL_1$ as set in method step 230 or CL_2 as set in method step 240.

In method step 244, the maximum amplitude P_3 of ACF is identified within the lag interval between lag = $CL/6$ and lag = $2CL/3$, interim value CL_3 is set to the lag at maximum P_3 , and process 220 proceeds to method step 246. In method step

246, if amplitude P_3 is greater than half of the amplitude P_{CL} at CL (CL is either the lag CL_1 at peak P_j or the lag CL_2 at peak P_2), then process 220 proceeds to method steps 248 and 250. If the amplitude P_3 does not satisfy the criterion in method step 246, then process 220 ends and the value of reference-channel cycle length CL is
 5 either $CL = CL_1$ as set in method step 230 or CL_2 as set in method step 240.

It is possible that there may be a significant peak in ACF between lag = $CL/6$ and lag = $2CL/3$. Method steps 248 and 250 are parallel steps which, if either of the criteria in these steps is satisfied, process 220 proceeds to method step 252 in which the reference-channel cycle length CL is set to $CL = CL_3$ and process 220 ends. If
 10 neither of these two criteria is satisfied, process 220 ends and reference-channel cycle length CL is either $CL = CL_1$ as set in method step 230 or CL_2 as set in method step 240. The criteria in method steps 248 and 250 check whether peak P_3 has a value of lag wherein CL is within 20 msec of either $2CL_3$ or $3CL_3$. If either condition is true, then, as stated above, reference-channel cycle length CL is set to CL_3 and process 220
 15 ends. The situation of a proper reference-channel cycle length CL being at 1/3 or 1/2 of ventricular pulse interval PI is related to 3:1 or 2:1 atrio-ventricular conduction with the artificial enhancement of the ACF peak at pulse interval PI because of the ventricular artifact that occurs for some of the atrial activations.

The methods just described can be summarized as three distinct and separable
 20 strategies. First is the use of the autocorrelation function to identify repeating cycles in the cardiac rhythm with maximum use of all the data available and little dependance on shape, no dependance on threshold-crossing jitter, and robust-to-occasional noise glitches. The second important strategy is avoiding the choice of a false cycle length at twice the ventricular pulse interval because the ventricular
 25 response slightly alternates in a pattern of bigeminal timing. The third important strategy is avoiding the choice of a cycle length equal to the ventricular pulse interval because ventricular far-field distortions may occur in atrial signals during 2:1 or 3:1 atrio-ventricular conduction. These three strategies are useful separately but more so in combination.

30 FIGURES 7A and 7B together are a schematic block diagram of an embodiment 100 of the process of determining local activation time (LAT) for a

single mapping point in the inventive method of measuring parameters of MCCE signals. FIGURE 7A illustrates three MCCE signals (6-sec epochs) on which computations are performed, as has been described above, in order to provide results which are used in the determination of LAT for a single mapping point. A

5 ventricular-channel epoch 102 and a reference-channel epoch 108 are coincident in time, and a mapping-channel 2-sec epoch 114 is coincident with the last 2 seconds of epochs 102 and 108. FIGURE 7A includes a legend which defines the terminology used in FIGURES 7A and 7B.

In method step 104, ventricular-channel epoch 102 is processed with the steps
10 of FIGURE 4A and produces a set of ventricular-channel activation times $t_{v\text{ACT}}$ and estimates of signal quality SQ and signal irregularity SI for epoch 102. The ventricular-channel activation times $t_{v\text{ACT}}$ are used in the determination of LAT as indicated by the circle labeled V which is common with the same such circle in FIGURE 7B. In method step 106, ventricular-channel pulse interval PI and range of
15 pulse intervals R_{PI} are computed for presentation to the EP doctor using the steps shown in FIGURE 5.

In a similar fashion, in method step 110, reference-channel epoch 108 is processed with the steps of FIGURE 4A and produces estimates of signal quality SQ and signal irregularity SI for epoch 108. Within the method steps of FIGURE 4A, a
20 velocity signal for the reference channel is computed, and it is used in the determination of LAT as indicated by the circle labeled R_{vel} which is common with the same such circle in FIGURE 7B. In method step 112, reference-channel cycle length CL is determined using the steps shown in FIGURES 6A and 6B, and reference-channel cycle length CL is used in the determination of LAT as indicated by the circle
25 labeled CL which is common with the same such circle in FIGURE 7B.

In method step 114, mapping-channel epoch 114 is processed with the steps of FIGURE 4A and produces a set of mapping-channel activation times $t_{M\text{ACT}}$ and estimates of signal quality SQ for epoch 114. (Epoch 114 is not sufficiently long to determine a useful estimate of signal irregularity SI. However, if a longer epoch
30 length is used, SI may be estimated in method step 116.) Mapping-channel activation times $t_{M\text{ACT}}$ are used in the determination of LAT as indicated by the circle labeled M

which is common with the same such circle in FIGURE 7B. Within the steps of FIGURE 4A, a velocity signal for the mapping channel is computed, and it is used in the determination of LAT as indicated by the circle labeled M_{vel} which is common with the same such circle in FIGURE 7B.

5 FIGURE 7B shows a continuation of the flow chart of embodiment 100. Inputs to the method steps of FIGURE 7B have been computed in the method steps of FIGURE 7A, and these inputs are illustrated by the circles labeled as described above. In method step 118, a mapping-channel activation for LAT determination is selected from among the activations and corresponding mapping-channel activation times t_{M-}
10 t_{ACT} determined in method step 116. The selection of such activation in step 118 includes the maximization of an activation selection score A_{sc} , a value for which is computed for each candidate activation among the set of mapping-channel activations. Details of method step 118 are described later in this document in the discussion of the example of FIGURES 8A and 8B.

15 After selecting the specific mapping-channel activation to be used to determine LAT in method step 118, a mapping-channel fiducial time t_M is found in method step 120. In determining LAT, a more precise representation of event times is required than the threshold-crossing determination of activation detection in method step 74. In this document, "fiducial time" is the term used to indicate such a more
20 precise determination of an event (activation) time. "Fiducial time" as used herein represents the instant within an MCCE signal at which a depolarization wavefront passes below the positive recording electrode in either a bipolar or unipolar MCCE signal.

 As is well-known to those skilled in the field of electrophysiology, one good
25 representation of fiducial time is the instant at which a signal exhibits its maximum negative velocity. Thus, one embodiment of method step 120 includes determining mapping-channel fiducial time t_M as the time at which the maximum negative velocity occurs within the selected activation of the mapping channel. In a similar fashion, a reference-channel fiducial time t_R is found in method step 122. Reference-channel
30 fiducial time t_R is the time at which the maximum negative velocity occurs within $\pm CL/2$ of mapping-channel fiducial time t_M .

The use of the time of maximum negative velocity as the fiducial time is not intended to be limiting. Other indications of precise depolarization event times may be used in determining the fiducial times.

In method step 124, the local activation time LAT for a position at which the mapping-channel electrode is located within the heart is computed as $LAT = t_M - t_R$. Local activation time LAT is determined relative to the selected reference channel, and values of LAT at a plurality of locations within the region of the heart being mapped are determined during the process of building an LAT map. If the quality of the channel signals being processed degrades before mapping is complete such that mapping cannot be continued, a new map must be generated. Local activation times may be positive or negative times (occurring after or before the corresponding activation event in the reference channel).

FIGURE 7C is a schematic block diagram of an alternative embodiment 122' of the process by which an LAT value is determined for a single mapping point. (Embodiment 122' of FIGURE 7C is an alternative embodiment to method steps 122 and 124 of FIGURE 7B.) FIGURE 7C will be described later in this document, after the example of FIGURES 8A-8D is described.

FIGURE 8A through FIGURE 8D together illustrate in more detail the process of determining LAT for a single mapping-channel electrode location. FIGURE 8A is a set of exemplary MCCE signal plots. At the top of FIGURE 8A is a 6-second epoch of an ECG reference-channel signal 108. At the bottom of FIGURE 8A is a 6-second epoch of an ECG ventricular-channel signal 102 time-coincident with reference-channel signal 108. In the middle and to the right of FIGURE 8A is a 2-second epoch of an MCCE mapping-channel signal 114 time-coincident with the final 2 seconds of reference-channel signal 108 and ventricular-channel signal 102. (Note that in FIGURE 8A, the signal traces illustrated are the MCCE voltage signals, not absolute-value velocity signals which are created during signal processing represented in the steps 100 of FIGURE 7A.)

Also illustrated in FIGURE 8A is magnitude-coincidence autocorrelation ACF 126 of the absolute-value velocity of reference-channel signal 108. ACF 126 is used to determine reference-channel cycle length CL in a process such as embodiment 220

in FIGURES 6A and 6B. ACF 126 in FIGURE 8A is annotated to show activity width W . Peak P_j occurs at a lag value of 342 msec, and the lag at peak P_j is the reference-channel cycle length CL in this example.

Ventricular-channel activations identified in method step 104 are shown in FIGURE 8A. Nine such activations, represented by ventricular-channel activation times 128, were identified in ventricular-channel signal 102. In a similar fashion, mapping-channel activation times 130 are shown in FIGURE 8A; four mapping-channel activations were identified in method step 116. Note that in this example, the first and last activations in the 2-second epoch of mapping-channel signal 114 were not identified by the threshold-crossing activation detection process of method step 74 of FIGURE 4A. (For description purposes, all six activations in mapping-channel signal 114 are labeled 132a through 132f in FIGURE 8A even though only four such activation were detected. The number 132 is not repeated with the letters a-f for simplicity in the figure. Activations 132a and 132f were not detected.)

FIGURE 8B presents a table detailing method steps 118 by which a specific mapping-channel activation is selected for the determination of LAT for the example of FIGURE 8A. FIGURE 8B includes a legend further defining the terms utilized in construction of and computations within the table for this example. In method step 112 of FIGURE 7A, reference-channel cycle length CL was determined to be 342 milliseconds, shown in FIGURE 8B at the top of the table.

As mentioned above, local activation time (LAT) is measured by the time difference between a fiducial time t_M in an activation in the mapping channel and its corresponding fiducial time t_R in the reference channel. As part of this determination, an activation within the mapping-channel signal 114 must be selected for such computation, in method step 118. This selection process includes: (a) for each mapping-channel activation i , determining the time $t_{NV}(i)$ to the nearest ventricular-channel activation for each mapping-channel activation; (b) for each mapping-channel activation i , determining the deviation $D_p(i)$ from CL of the time to the previous mapping-channel activation $i-1$; and (c) for each mapping-channel activation i , determining the deviation $D_f(i)$ from CL of the time to the next (future) mapping-

channel activation $i+1$. The mathematical representations of these determinations are shown in the legend of FIGURE 8B.

To generate a full map of local activation times, often a large number of individual points must be determined. This can be a time-consuming process. It is therefore desirable to determine each individual value of LAT as quickly as possible once a new position of the mapping-channel electrode being manipulated by the EP doctor is established. It has been found that about 2 seconds is often required to make a good determination. At typical intracardiac heart rates being measured, only a few activations occur in the mapping channel during a 2-second epoch period, so it is helpful to increase the number of candidate activations by adapting to situations where an activation is "missing" due to a failed activation detection or to a simple epoch-end timing situation. The inventive method includes a beginning-of-data rule and an end-of-data rule to increase the number of candidate mapping-channel activations. These special rules are as follows:

Beginning-of-data rule: In some cases, the first detected activity may be very near the beginning of available data. If the expected previous activity to a detected activity would be located before the beginning of the mapping-channel epoch, then there is no evidence that detections failed and the value for $D_p(i)$ for such a candidate activation is presumed to be 0. However, if the amount of time in the available data in the mapping-channel epoch is longer than the expected cycle length CL, then it is likely that an activation failed to be detected due to some kind of noise in the mapping-channel signal, an irregular signal, or an insufficiency in the detection algorithm. In this case, $D_p(i)$ is set to $t_{\text{MAC}}(i) - \text{CL}$, but not less than 0, where CL is the reference-channel cycle length.

End-of-data rule: This rule is symmetrical to the beginning-of-data rule and is created to handle the same available data constraint at the end of the data. $D_p(i)$ for only the last candidate mapping-channel activation is set to 0 if the last detected activity is within one reference-channel cycle length CL of the end of data. However, there may be more time in the available mapping-channel epoch data than one CL after the last detected activation. In this case, it is very likely that some kind of noise in the mapping-channel signal, an irregular signal, or an insufficiency in the detection

algorithm caused a failed activation detection. In this case, the value of $D_F(i)$ is set to the length of available following data minus CL or $D_F(i) = t_{ME} - t_{M.ACT}(i) - CL$, but not less than 0, where t_{ME} is the mapping-channel epoch length, in this example, 2000msec, and CL is the reference-channel cycle length. Two such situations are

5 illustrated in the example of FIGURES 8A and 8B.

The mapping-channel activation which is selected is the activation for which activation selection score $A_{sc}(i)$ is a maximum. As shown in FIGURE 8B,

$$A_{sc}(i) = t_{NV}(i) - D_P(i) - D_F(i).$$

It is desirable that the selected mapping-channel activation be far in time from a

10 ventricular-channel activation and that the neighboring cycle lengths in the mapping channel be close to reference-channel cycle length CL. This mathematical construction of the activation selection score $A_{sc}(i)$ accomplishes this desired relationship.

The computations outlined above and represented in FIGURE 8B were carried

15 out for the four candidate mapping-channel activations 132b through 132e (having activation times labeled 130). The activations labeled 132a and 132f were not detected; activation 132a occurred too close to the beginning of epoch 114, and activation 132f was not large enough to trigger the threshold in activation detection step 74. Thus, as shown FIGURE 8B, both the beginning-of-data rule and the end-of-

20 data rule were applied in this example to determine values for activations 132b and 132e. In the row of data in the table for mapping-channel activation 132b, the value of $D_P = 40$ was determined by application of the beginning-of-data rule, and in the row of data in the table for mapping-channel activation 132e, the value of $D_F = 247$ was determined by application of the end-of-data rule.

25 Mapping-channel activation 132c is selected based on its maximum activation selection score $A_{sc} = 290$ among the candidate mapping-channel activations.

FIGURES 8C-1 through 8C-4 are a set of plots illustrating in detail method steps 120, 122, and 124 in which LAT is computed based on selected mapping-channel activation 132c and a reference-channel activation 134. (Note that reference-

30 channel activation 134 is not detected in the inventive method but it is clear in FIGURE 8A that activation 134 is an activation near in time to t_M .) As indicated

above, in this example, fiducial times t_M and t_R are the instants in the mapping-channel and reference-channel activations at which the maximum negative velocity occurs.

FIGURE 8C-1 illustrates an expanded signal of mapping-channel activation 132c, and

FIGURE 8C-3 illustrates an expanded signal of mapping-channel activation velocity

5 132c:v. Mapping-channel fiducial time t_M is indicated by the dotted line labeled 136.

The value of t_M in this example is 4716 msec as indicated to the left of mapping-channel activation 132c in FIGURE 8A.

Reference-channel activation 134 is the activation in reference-channel signal 108 which is located within $\pm CL/2$ along the time axis of reference-channel signal

10 108. FIGURE 8C-2 illustrates an expanded signal of reference-channel activation

134, and FIGURE 8C-4 illustrates an expanded signal of reference-channel activation

velocity 134:v. Reference-channel fiducial time t_R , indicated by the dotted line

labeled 138, is clearly located within ± 17 msec ($\pm CL/2$) of t_M .

In this example, reference-channel activation 134 occurs after mapping-

15 channel activation 132c, and the local activation time $LAT = t_M - t_R = -15$ msec. This

value of LAT provides a single point in the generation of an LAT map. As mentioned above, an LAT map is based a single reference channel with its electrode placed at the same point in the cardiac structure throughout the entire generation of the map. A plurality of LAT measurements is used to generate an LAT map, each such point

20 being made available for display by the inventive system.

In FIGURE 7C, an alternative embodiment 122' for LAT determination is illustrated. Alternative embodiment 122' takes advantage of the fact that multiple

fiducial times t_R are available in reference-channel signal 108 to which mapping-

channel fiducial time t_M may be compared. In method step 200, the times t_R of

25 maximum negative velocity generated in method step 110 of FIGURE 7A are

identified in reference-channel signal 108. (As described above, activations in the reference channel are not detected using a threshold-crossing technique; rather a

simple numerical search method may be used to find the times t_R of local relative

negative-velocity maxima in signal 108.) In method step 202, the four nearest values

30 t_R to mapping-channel fiducial time t_M are selected from among the values of t_R , and in

method step 204, each of these four times t_R are adjusted by adding or subtracting

multiples of reference-channel cycle length CL until each adjusted value t_{RA} is within $\pm CL/2$ of t_M so that t_{RA} now represents its relative time position within one cycle length CL. In method step 206, these four values are averaged and this average av_{RA} is included with the set of four values of t_{RA} in method step 208, creating a set of five
 5 time values. In method step 210, the median med_{jRA} of this set is found and in method step 212, LAT is determined as $LAT = t_M - med_{jRA}$.

Referring again to FIGURE 8A, reference-channel signal 108 is shown with a set of numerical values 135 next to each activation in signal 108. (Only one such triplet 135 of values is labeled with reference number 135 to avoid clutter within
 10 FIGURE 8A.) There are 14 such triplets 135 of values, and each triplet consists of (1) a fiducial time t_R of the maximum negative velocity in signal 108 (the number in parentheses), (2) the adjusted time t_{RA} by adding or subtracting multiples of cycle length CL to place t_{RA} within $\pm CL/2$ of t_M , and (3) the time difference between t_M and t_{jRA} , also referred to as intermediate LAT values. This set of time values is also shown
 15 in the table of FIGURE 8D.

Referring to FIGURE 8D, rows A, B, and C correspond to the time value triplets described in the above paragraph. Row D is an ordered list of the intermediate LAT values in row C. Due to variations in measurement conditions or sources of variability, outlier values may be present at either end of this ordered list. To avoid
 20 such outliers (such as the two highest values in row D, 44 and 161), an interquartile set of values is selected in row E, dropping the lowest and highest 25% of values from the ordered list. This interquartile list may then be used to provide an estimate of a measurement confidence interval for method step 26 in FIGURE 1. The range of this interval is indicated by the end values of row E which range from -15 to -11, or a ± 2
 25 msec LAT measurement confidence interval. Further, a measurement-confidence criterion for method step 26 in FIGURE 1 may be as follows: if the width of the measurement confidence interval (in this example, 4) is greater than some percentage of cycle length CL, then alert the EP doctor in method step 30. This width percentage criterion may be about 5% but this value is not intended to be limiting. An absolute
 30 width, say 15 msec, may also be used as the criteria; again such absolute width criterion value is not intended to be limiting.

Referring to FIGURE 8D to illustrate the alternative method of LAT determination described in FIGURE 7C, the four times t_R indicated by reference number 214 are the four nearest times t_R which encompass mapping-channel fiducial time t_M , forming a set 214 of four values t_R (in row A) as described in method step 5 202. The four values are adjusted as described above and form the set of four values t_{jRA} (in row B) described in method step 204. The average of these four values t_{RA} is computed in method step 206 ($av_{RA} = 4730.25$ msec), This value av_{RA} is added to set 214 to form a set of five values as indicated in method step 208. The set of five values is now the set (4727, 4729, 4730.25, 4731, 4734). The median $med^{\wedge}$ of this 10 set is 4730.25 as found in method step 210, and LAT is determined by $LAT = t_M - med_{jRA}$, or $LAT = 4716 - 4730.25 = -14.25$ msec. One advantage of such an embodiment is that some additional computational precision occurs with the use of the averaging step.

The use of the four nearest times t_R which encompass t_M is not intended to be 15 limiting. Other choices for the number of values t_R used in the LAT determination may be employed.

Additionally, the steps described with respect to FIGURE 8D also form a second alternative embodiment for LAT determination, potentially taking into account even more reference-channel fiducial times t_R in the estimate of LAT. In this second 20 alternative embodiment, the median value of the interquartile set of intermediate LAT values may be used as the LAT value for the current mapping point. As shown in FIGURE 8D, the median value in row D is -13, the LAT value for this second alternative method of LAT determination. Again as above, other choices maybe made for the number of values of t_R used in the determination of LAT.

25 Signal quality SQ as determined in method step 79 of FIGURE 4A is also applicable for use within method step 24 of FIGURE 1 in which signal quality is monitored to provide alert 28 when signal quality SQ degrades. One criterion by which to assess signal quality in method step 79 of FIGURE 1 is simply to determine if all three signal quality values (ventricular channel, reference channel and mapping 30 channel) are positive. The signal quality SQ determination for the mapping channel differs from that of the other two channels in that it does not include a signal

irregularity SI term *{i.e.,* $SQ = SS - 2N_s$ for the mapping channel) since the 2-second epoch of the mapping channel is too short to generate a meaningful value for signal irregularity SI. The decision of method step 79 is in the affirmative if any of the three signal quality SQ values is negative, at which time an alert is given to the EP doctor.

5 Other criteria may be used in method step 24 to trigger user alert 20.

As described above, activation maps are used during certain cardiac procedures. But during such procedures, a variety of other cardiac parameters may advantageously displayed. Among these may be: (1) a value for starting reference-channel cycle length; (2) a value for current reference-channel cycle length CL with a
10 confidence interval; (3) a value for LAT with a confidence interval; and (4) a value for ventricular-channel pulse interval PI with a confidence interval. All of these quantities are generated by the inventive method disclosed herein. For example, a confidence interval for current reference-channel cycle length CL may be determined from the lag L2 of a peak in ACF near twice the cycle length CL, with the confidence
15 interval being $\pm(L2 - 2CL)$ interval. A confidence interval for the LAT measurement may be $\pm$ half the interquartile range as described above. A confidence interval for ventricular pulse interval PI may be represented by range $R_{PI} (\pm R_{PI}/2)$ as computed in method step 92 of FIGURE 5.

As described above, an activation map comprises a plurality of LAT
20 measurements all of which are made relative to a particular reference-channel signal. One aspect of the inventive automatic method of measuring parameters of multi-channel cardiac electrogram signals includes the ability to compensate for signal degradation in the reference channel during the creation of an activation map. Since LAT maps are made relative to a specific reference channel, if the reference-channel
25 signal being used degrades during mapping below a useful level of signal quality, the inventive method enables another reference channel to be selected and recreates the set of LAT measurements based on the new reference channel and generates a new map. This is possible since the inventive method computes reference-channel parameters as described above for several reference channels in real-time and stores
30 the necessary parameters for use if needed. Very fast computation available with present computing equipment enables these "extra" channels to be recorded and

analyzed in real-time without hindering the operation of the "current" channels being used to create a map.

As seen above, a ventricular channel and a reference channel from among the channels of the MCCE signals are used in the automatic method of the present invention. The processes of selecting these channels automatically are among the various aspects of the inventive automatic method. FIGURE 9 is a schematic diagram illustrating the inclusion of automatic selection of the ventricular and reference channels to the inventive automatic method of measuring parameters of MCCE signals. The steps of this overall combination are indicated by reference number 140.

Referring to FIGURE 9, these automatic initialization steps include automatic selection of a ventricular channel, indicated by reference number 144. The method steps of an embodiment of automatic process 144 are illustrated in FIGURES 10A and 10B and described in detail below. Following the selection of a ventricular channel, a reference channel is automatically selected as indicated by reference number 164, and the method steps of an embodiment of automatic process 164 are illustrated in FIGURES 11A-11C.

The entire automatic method of the invention disclosed herein is under the control of the electrophysiologist (EP doctor) as indicated above. At the time of a medical procedure, there may be overriding medical or technical reasons for the EP doctor to reject a channel or the channels which have been automatically selected, so automatic method 140 includes a confirmation step 142 in which the EP doctor performing the procedure may accept or reject the channels which have been automatically selected. If the EP doctor rejects one or both of these selections, indicated by the "N" option on confirmation step 142, channel selection may be done manually or channels may be selected automatically as indicated by pathway 142n.

Upon final selection of ventricular and reference channels, automatic process 140 continues with the method steps of mapping as indicated by reference number 10 and as described in detail above.

FIGURES 10A and 10B are schematic diagrams of embodiment 144 of the process of automatically selecting a ventricular channel from a set of candidate MCCE channels. The ventricular channel is selected from a set of candidate channels

for use within the inventive automatic method of measuring parameters of MCCE signals. It is desirable that the ventricular channel selected be a channel which exhibits high signal quality and provides a stable representation of the action of the ventricles of the heart. As mentioned above, the ventricular channel of choice is most often connected to a body surface electrode, but other channels such as an epicardial electrode or an intracardiac electrode may provide the most useful signal among the set of candidate ventricular channels.

Referring to FIGURE 10A, in one embodiment of automatic process 144 for selection of the ventricular channel, an initial time period for capturing and assessing signal characteristics from all candidate channels is employed. Data is captured during the time period represented by five epochs E1 through E5. (Epochs E1 through E5 are also called sub-signals E1 through E5.) In the embodiment of FIGURE 10A, this initial period is 30 seconds long. The signal from each candidate channel is an absolute-value velocity signal generated as described above. During the ventricular-channel selection process, there may be numerous possible channels being evaluated, the candidate set of channels including body-surface channels as well as some epicardial and intracardiac channels, depending on the strength of the ventricular signal in such channels. The process illustrated in FIGURES 10A is applied to the waveform signals of each channel individually, generating for each channel two measures by which the ventricular-channel selection is made.

Referring again to FIGURE 10A, a 30-second signal 148 from each candidate channel is divided into five 6-second epochs (sub-signals) E1 through E5. The 30-second period, 6-second epoch length and number of epochs in the initial period are not intended to be limiting. FIGURE 10A illustrates the process for just one such candidate channel; a plurality of candidate channels is processed concurrently within ventricular-channel selection process 144.

As illustrated in FIGURE 10A, the signals in each epoch E1-E5 are processed to determine the corresponding signal quality SQ_i in method step 150. (Five such separate signal quality calculations are performed; only one is labeled with reference number 150, but the marking SQ_i indicates this calculation being performed sequentially five times, each producing a value SQ_i for the signal quality of the

corresponding epoch E_i .) Signal quality calculation 150 is carried out as illustrated in FIGURE 4A.

In method step 154, the five signal quality values SQ_i are summed to produce an overall signal quality value SQ_{VC} for each candidate ventricular channel.

5 Also illustrated in FIGURE 10A, the signals in each epoch E1-E5 are processed in method steps 152 to determine a value for pulse interval variability VAR_i for each of the five epochs (as found in the steps of FIGURE 5). Five such variability calculations are performed; one is labeled with reference number 152, but the markings indicate that this calculation is performed sequentially five times, each
 10 producing a value VAR_i for the variability of the corresponding epoch. In this embodiment, variability VAR_i for each epoch is the difference between its maximum MAX_{E1} and minimum MIN_{E1} pulse-interval values during the 6-second epoch. This is illustrated for epoch E1 in the detailed method step 152a as follows:

$$VAR_i = MAX_{E1} - MIN_{E1}$$

15 Similar relationships for each epoch are calculated to generate the variability VAR_i for each epoch E1 through E5.

In method step 156, the maximum value of variability among the five values of variability is set as the variability VAR_{VC} of the candidate ventricular channel.

At this stage in the automatic ventricular-channel selection process, each
 20 ventricular channel in the set of candidate ventricular channels has a channel signal quality assessment value SQ_{VC} and a channel pulse-interval variability assessment value VAR_{VC} which will be used to complete the automatic ventricular-channel selection process.

FIGURE 10B illustrates the final portion of ventricular-channel selection
 25 process 144 for this embodiment. In general, it is desirable to select a ventricular channel with high signal quality and acceptable variability. Thus, FIGURE 10B illustrates an embodiment which selects the channel with the highest signal quality but excludes channels from this choice which have especially high variability. Variability in such signals is expected. However, the reason that some channels are excluded is
 30 that these channels have variability values which are remarkably higher than those of

other channels, indicating that the algorithm may be failing to detect activations properly in such channels.

In FIGURE 10B, the wide arrows labeled 156a (two such arrows) and 154e represent a plurality of values as indicated. Arrows 156a therefore represent that the channel variability values for each of the channels are all inputs to the method steps 158 and 160. In method step 158, a ventricular-channel variability threshold T_{vc} is calculated as follows:

$$T_{vc} = 2 \cdot [\text{median}(\text{VAR}_{vc}) + A_{vc}]$$

where A_{vc} is a small increment of time which may be added into this calculation simply as a computational convenience, such as to avoid singular calculations or to avoid excluding too many channels when the variability of some channels is extremely small. The inclusion of increment A_{vc} in the embodiment of FIGURE 10B is not intended to be a limitation; A_{vc} may have a value of 0 or other computationally-convenient value. In FIGURE 10B, A_{vc} has a value of 5 milliseconds.

Ventricular-channel variability threshold T_{vc} is a threshold value above which the variability of a channel is deemed to be unacceptably high. In method step 160, the variability VAR_{vc} for each channel is compared with ventricular-channel variability threshold T_{vc} , and channels for which VAR_{vc} is equal to or exceeds threshold T_{vc} are excluded from being the selected ventricular-channel VC_S .

Other computational assessments of signal quality and variability for each channel and for the exclusion of channels on the basis of high variability are of course possible. The specifics of these assessment embodiments are not intended to be limiting.

Wide arrow 154e represents one or more ventricular-channel signal quality values SQ_{vc} for channels which have not been excluded in method step 160. Each channel represented in the set of values 154e is a possible selected ventricular-channel VC_S . In method step 162, the channel with the highest value of channel signal quality SQ_{vc} is then selected as the ventricular-channel VC_S within the inventive automatic method of measuring parameters of MCCE signals. (The method therefore also knows which channels are, for example, "second best" and "third best" among the candidate channels.)

After ventricular-channel VC_S has been selected using ECG signals over an initial period of time (30 seconds in the embodiment of FIGURES 10A and 10B), MCCE signals from the initial period of time or from an additional period of time are used to select a reference channel to be used within the inventive automatic method of measuring parameters of MCCE signals. FIGURES 11A through 11C are schematic diagrams of embodiment 164, 166 of the process of automatically selecting a reference channel from a set of candidate channels.

Body surface electrode channels are generally known not to be good choices for reference channels for many arrhythmias; thus, the reference channel is typically selected from the remaining set of MCCE channels for use within the inventive automatic method of measuring parameters of MCCE signals. It is desirable that the reference channel selected be a channel which exhibits high signal quality and low cycle-length variability and also which exhibits a fast heart rate. For physiological reasons related to the cardiac measurements for which the present invention is intended to be used, it is also desirable that the selected reference channel indicate the shortest cycle length CL. All of these criteria are used to select a reference channel from among the set of candidate reference channels.

Referring to FIGURE 11A, in automatic process 164 for selection of the reference channel, an initial time period for capturing and assessing signal characteristics from all candidate channels is employed. Data is captured during the time period represented by five epochs, labeled E6 through E10. (Epochs E6 through E10 are also called sub-signals E6 through E10.) In the embodiment of FIGURE 11A, this additional initial period is 30 seconds long. The signal from each candidate reference channel is an absolute-value velocity signal generated as described above. During the reference-channel selection process, there may be numerous possible channels being evaluated. What specific channels are candidate reference channels for cardiac mapping are well-known to those skilled in electrophysiology. The process illustrated in FIGURE 11A is applied to the waveform signals of each candidate channel individually, generating for each channel two measures by which the reference-channel selection is made.

Referring again to FIGURE 11A, a 30-second signal 168 from each candidate channel is divided into five 6-second epochs (sub-signals) E6 through E10. The 30-second period, 6-second epoch length and number of epochs in the initial period are not intended to be limiting in anyway. FIGURE 11A illustrates the process for just one such candidate channel; a plurality of candidate channels is processed concurrently within reference-channel selection process 164.

As illustrated in FIGURE 11A, the signals in each epoch E6-E10 are processed to determine the corresponding signal quality SQ_i in method step 170. (Five such separate signal quality calculations are performed; only one is labeled with reference number 170, but the marking SQ_i indicates this calculation being performed sequentially five times, each producing a value SQ_i for the signal quality of the corresponding epoch E_i .) Signal quality calculation 170 is carried out as illustrated in the steps of FIGURE 4A.

In method step 174, the five signal quality values SQ_i are summed to produce an overall signal quality value SQ_{RC} for each candidate reference channel.

Also illustrated in FIGURE 11A, the signals in each epoch E6-E10 are processed in method steps 172 to determine a cycle length CL_i and a value VAR_i for cycle-length variability for each of the five epochs. The cycle length determination is performed using the method steps described in detail above and illustrated in FIGURES 6A and 6B (and as referred to in FIGURE 11B). The determination of cycle-length variability (and cycle length) for each epoch is described using the schematic diagram of FIGURE 11B, which illustrates this process 172a for epoch E6 as indicated by the dotted-line ellipse in FIGURE 11A. Five such cycle length and cycle-length variability calculations as illustrated in FIGURE 11B are performed; one is labeled with reference number 172a, but the markings of each such element in FIGURE 11A indicate that this calculation is performed sequentially five times, each producing a value VAR_i for the cycle-length variability of the corresponding epoch.

In the method steps illustrated in FIGURE 11B, F6 is the magnitude-coincidence autocorrelation function of epoch signal E6 as calculated in method step 178. The threshold value for the magnitude-coincidence autocorrelation is a function of the noise in signal being processed as described in the summary section which

defines magnitude-coincidence autocorrelation and with respect to method step 226 of FIGURE 6A. Cycle length CL is computed in method step 182 as indicated, using steps outlined in FIGURES 6A and 6B. Then, in method step 186, a peak in F6 near a value of lag near 2 times CL is identified, and an interim variable DCL is set to the lag at such peak. In method step 188, another interim variable CL_A is set to $DCL - CL$. The value for the variability VAR_6 of epoch E6 is then calculated as follows in method step 190:

$$VAR_6 = |CL - CL_A|$$

Similar relationships for each epoch are calculated to generate the variability VAR_i for each epoch E6 through E10.

Referring again to FIGURE 11A, in method step 176, three additional values (in addition to SQ_{RC}) are determined for each epoch E6 through E10 by which to select from among the candidate reference channels: VAR_{RC} ; MAX_{CL} , and MIN_{CL} . MAX_{CL} is the maximum cycle length CL_i among the five cycle-length values. MIN_{CL} is the minimum cycle length CL_i among the five cycle-length values. VAR_{RC} is the maximum variability value VAR_i among the five variability values.

At this stage in the automatic reference-channel selection process, each reference channel in the set of candidate reference channels has a channel signal quality assessment value SQ_{RC} , a channel variability assessment value VAR_{RC} , and maximum and minimum cycle length values MAX_{CL} and MIN_{CL} which will be used to complete the automatic reference-channel selection process.

FIGURE 11C illustrates the final portion of reference-channel selection process 164 for this embodiment. In general, it is desirable to select a reference channel with high signal quality, low variability, and short cycle length, as indicated above. FIGURE 11C illustrates an embodiment which selects the channel with these characteristics.

In FIGURE 11C, the wide arrows labeled 174a, 176v, 176x, and 176n each represent a plurality of values as indicated. Wide arrow 174a represents all values of SQ_{RC} from the candidate reference channels; wide arrow 176v represents all values of VAR_{RC} from the candidate reference channels; wide arrow 176x represents all values

of MAX_{CL} from the candidate reference channels; and wide arrow 176n represents all values of MIN_{CL} from the candidate reference channels.

In method step 192, a figure-of-merit FM_{RC} is evaluated for each candidate reference channel. FM_{RC} for each candidate reference channel is computed as follows:

$$5 \quad FM_{RC} = SQ_{RC}/S_{RC} - MAX_{RC} - MIN_{RC} - S_{VAR} \cdot VAR_{RC}$$

where S_{RC} is an arbitrary scale factor and S_{VAR} is an arbitrary scale factor. The two scale factors are chosen such that a useful tradeoff within the figure-of-merit FM_{RC} is created. When signal quality values SQ_{RC} are in microvolts and cycle lengths are in milliseconds, a value of S_{RC} of 32 and a value of S_{VAR} of 2 have been found to yield a
 10 useful tradeoff among cycle lengths, variability, and signal quality and also to be computationally convenient.

The FM_{RC} values for each candidate reference channel are output from method step 192 as indicated by wide arrow 194. In method step 196, the channel with the highest value of FM_{RC} is the selected reference-channel RC_S .

15 Other computational assessments of signal quality, variability, and cycle length for each channel are of course possible. The specifics of these assessment embodiments are not intended to be limiting.

As described above, one aspect of the inventive automatic method of measuring parameters of multi-channel cardiac electrogram signals includes the
 20 ability to compensate for signal degradation in the reference channel during the creation of an activation map by selecting a new reference channel and recreating the set of LAT measurements based on the new reference channel and generating a new map. During the initial selection process for the reference channel, the inventive method keeps track of the reference channels which have values for FM_{RC} just below
 25 the selected reference channel RC_S so that if necessary, these "second best" reference channels can be substituted for the selected reference channel and the mapping process can continue without losing the valuable time and effort that has already been spent on the mapping process.

In another aspect of the inventive method, multiple mapping channels may
 30 also be employed, and the processing steps outlined herein applied to multiple mapping channels as well as multiple reference channels. Some catheters which are

used in cardiac procedures may include multiple electrodes in a variety of configurations. In addition, multiple catheters may be employed. The speed of computer processing available enables numerous calculations to be done very rapidly such that multiple mapping channels may be supported to generate a plurality of maps as the EP doctor moves the mapping electrodes throughout chambers and vessels of the heart.

FIGURE 12 is a matrix which schematically illustrates a series of reference channels and mapping channels from among a set of MCCE signals which in an aspect of the inventive method may be processed in parallel to generate multiple LAT maps as well as track the other cardiac parameters measured with the inventive method in a variety of combinations of reference and mapping channels. Some channels may be displayed for the EP doctor in parallel while others may serve of possible backups in case of signal degradation as explained above.

Referring to FIGURE 12, the table 260 shown is an 8x8 matrix (eight reference channels R_1 through R_8 and eight mapping channels M_1 through M_8). The number of channels illustrated is not intended to be limiting, but rather to illustrate the concept of flexible configuration combinations of reference and mapping channels. In fact, a set of MMCE signals is typically much larger than the eight illustrated here. Eight channels in the MCCE set of signals is only for purposes of illustration.) The "✓" symbols indicate that the mapping channel and reference channel at such an intersection together can generate a map. In other words, as shown in table 260 of FIGURE 12, each channel M_1 through M_8 can be paired with any other channel R_1 through R_8 , and any combination of these pairings can be created. The "-" simply indicate redundancy in table 260. The "-" symbol is located along the diagonal of table 260 indicating that any channel is not usefully paired with itself. Further, some channels among the set of channels may in fact be ventricular channels (primarily exhibiting ventricular signal characteristics) and therefore also not good candidates for either a reference or mapping channel.

The advantages of such multiple-channel processing configurations are that procedure time may be shortened but also that a much richer array of measurements may be obtained to provide better information to the EP doctor to ameliorate the

cardiac deficiency being treated. Further, as described above, backup channels can be available to deal with lost or degraded signals during a procedure without the need to start the procedure over again.

5 It is possible in some multi-channel configurations that certain information may be shared among several parallel computations. For example, it is possible that ventricular pulse interval values may be used for the determination of several reference-channel cycle lengths, and ventricular-channel activation times may be shared for use with more than one mapping channel. And many other combinations other than those exemplified here are possible with the multi-channel processing of the
10 inventive method described herein.

In embodiment 10 of the inventive automatic method of measuring parameters of multichannel cardiac signals described in detail above, contiguous 6-second epochs of MCCE signal data are used. Alternatively, a moving-window format of selecting epoch starting and end points may be used, such as the next epoch in a series of
15 epochs consisting of the last 5 seconds of the previous epoch and a new sixth second. Other epoch-forming strategies may be used, depending on the computational advantages which may be possible and on the desired speed of analysis.

While the principles of this invention have been described in connection with specific embodiments, it should be understood clearly that these descriptions are made
20 only by way of example and are not intended to limit the scope of the invention.

CLAIMS

1. An automatic method of determining local activation time (LAT) in multi-channel cardiac electrogram signals including at least two cardiac channels, one of the cardiac channels being a mapping channel and another cardiac channel being a reference channel, the method comprising:
- (a) estimating a cycle length CL in the reference channel;
 - (b) determining a mapping-channel fiducial time t_M in the mapping channel signal;
 - 10 (c) determining a plurality of reference-channel fiducial times t_R ;
 - (d) computing adjusted reference-channel fiducial times t_{RA} by adding or subtracting multiples of cycle length CL to each time t_R such that each time t_{RA} is within a time window of length CL surrounding mapping-channel fiducial time t_M ;
 - 15 (e) computing a single final reference-channel fiducial time t_{RF} from the plurality of adjusted reference-channel fiducial times t_{RA} ; and
 - (f) computing the LAT as t_M minus t_{RF} .
2. The automatic LAT-determination method of claim 1 wherein the time window of length CL surrounding t_M spans $\pm CL/2$ of t_M .
- 20 3. The automatic LAT-determination method of claim 1 wherein the adjusted reference-channel fiducial times t_{RA} used to compute final reference-channel fiducial time t_{RF} are a subset of the plurality of adjusted reference-channel fiducial times $t^\wedge$.

25

4. The automatic LAT-determination method of claim 3 wherein computing a single final reference-channel fiducial time t_{RF} comprises the steps of:

- computing an average av_{RA} of the subset;
- including av_{RA} in the subset; and
- 5 • setting the final reference-channel fiducial time t_{RF} to the median of the subset.

5. The automatic LAT-determination method of claim 4 wherein the median of the subset is the set-member median.

10

6. The automatic LAT-determination method of claim 1 wherein the adjusted fiducial times t_{RA} are a set of adjusted fiducial times and computing a single final reference-channel fiducial time t_{RF} comprises the steps of:

- computing an average av_{RA} of the set;
- 15 • including av_{RA} in the set; and
- setting the final reference-channel fiducial time t_{RF} to the median of the set.

7. The automatic LAT-determination method of claim 6 wherein the median of the set is the set-member median.

20

8. The automatic LAT-determination method of claim 1 wherein the mapping-channel fiducial time t_M is at a time of maximum negative velocity of the mapping-channel signal.

25 9. The automatic LAT-determination method of claim 1 wherein the reference-channel fiducial times t_R are at times of maximum negative velocity of the reference-channel signal.

30 10. The automatic LAT-determination method of claim 1 further including repeating steps (a) through (f) to generate a plurality of LAT values and displaying the plurality of LAT values as an LAT map.

11. The automatic LAT-determination method of claim 1 wherein computing a single final reference-channel fiducial time t_{RF} from the plurality of adjusted reference-channel fiducial times t_{RA} includes ordering the plurality of adjusted reference-channel fiducial times t_{RA} and using a subset of times t_{RA} to compute final
5 reference-channel fiducial time t_{RF} .

12. The automatic LAT-determination method of claim 11 wherein the subset of times t_{RA} is the interquartile set of times $t^\wedge$.

10 13. The automatic LAT-determination method of claim 12 wherein the final reference-channel fiducial time t_{RF} is the median of the set.

14. The automatic LAT-determination method of claim 13 wherein the median of the interquartile set is the set-member median.

15

15. The automatic LAT-determination method of claim 1 further including computing a confidence interval for the determined LAT.

16. The automatic LAT-determination method of claim 15 wherein computing
20 an LAT confidence interval comprises:

- computing an intermediate LAT value as $LAT = t_M - t_{RA}$ for each of the plurality of adjusted reference-channel fiducial times $t^\wedge$, the intermediate LAT values comprising a set of values;
- selecting the highest and lowest intermediate LAT values in the set; and
- 25 • computing the confidence interval as $\pm$ a fraction of the difference between the highest and lowest intermediate LAT values.

17. The automatic LAT-determination method of claim 16 wherein the fraction of the difference is one-half.

30

18. The automatic LAT-determination method of claim 16 wherein the set is a subset of the intermediate LAT values.

19. The automatic LAT-determination method of claim 18 wherein the
5 fraction of the difference is one-half.

20. The automatic LAT-determination method of claim 1 wherein estimating a cycle length CL in the reference channel comprises:

- digitizing the reference-channel signal over a first preset time window;
- 10 • filtering the reference-channel signal to generate a reference-channel absolute-value velocity signal;
- autocorrelating the reference-channel absolute-value velocity signal; and
- selecting a peak value of the autocorrelation and setting the cycle length CL as the lag at the peak.

15

21. The automatic LAT-determination method of claim 20 further including determining a CL confidence interval by setting a lag value L2 as the lag at a second autocorrelation peak near twice CL and setting the CL confidence interval at $\pm(L2 - 2CL)$.

20

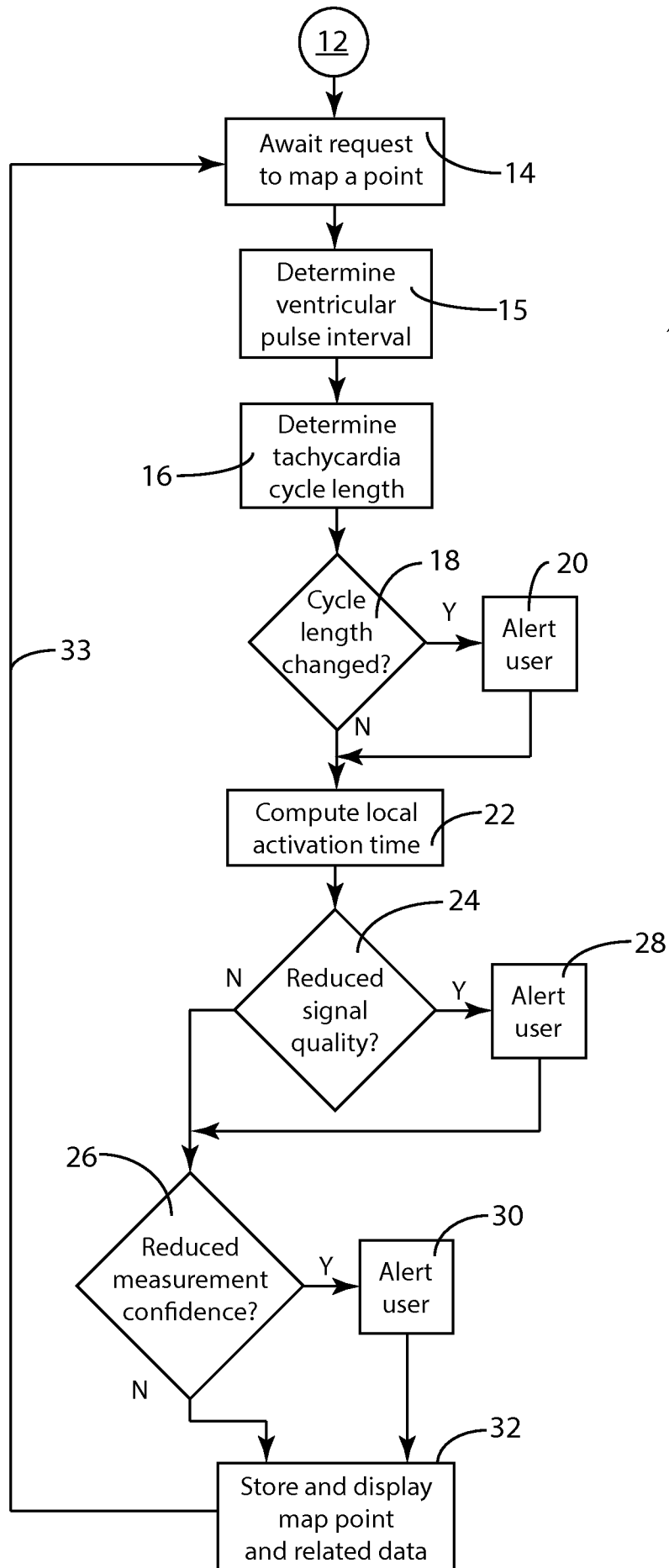


FIG. 1

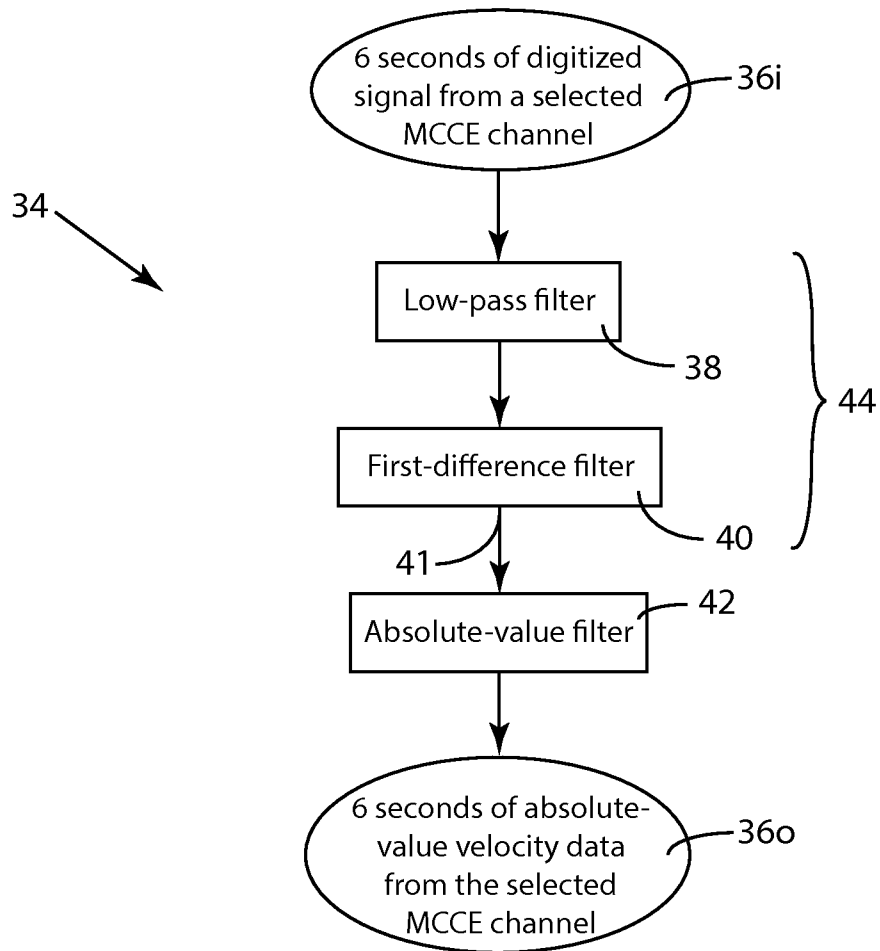
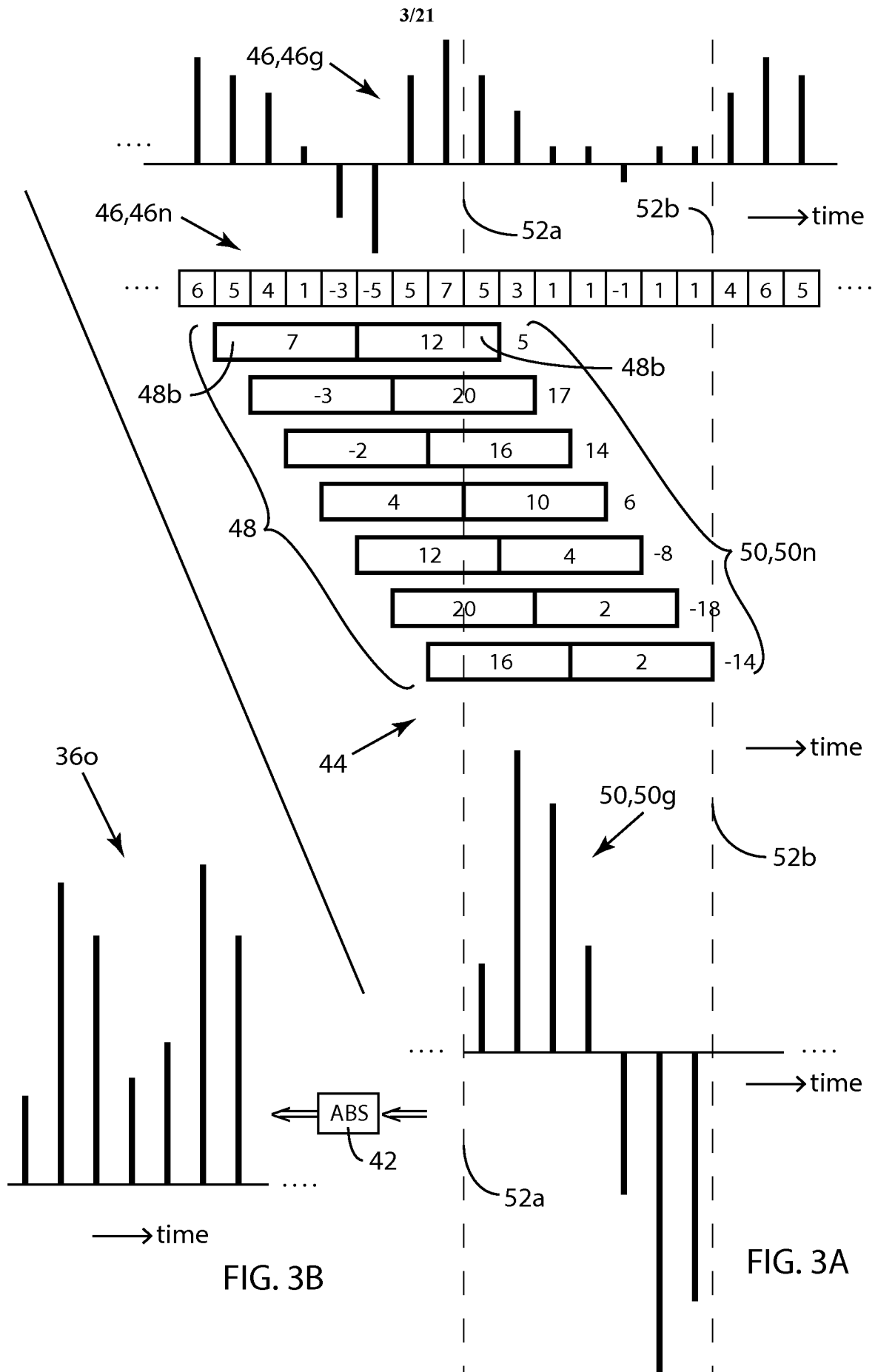


FIG. 2



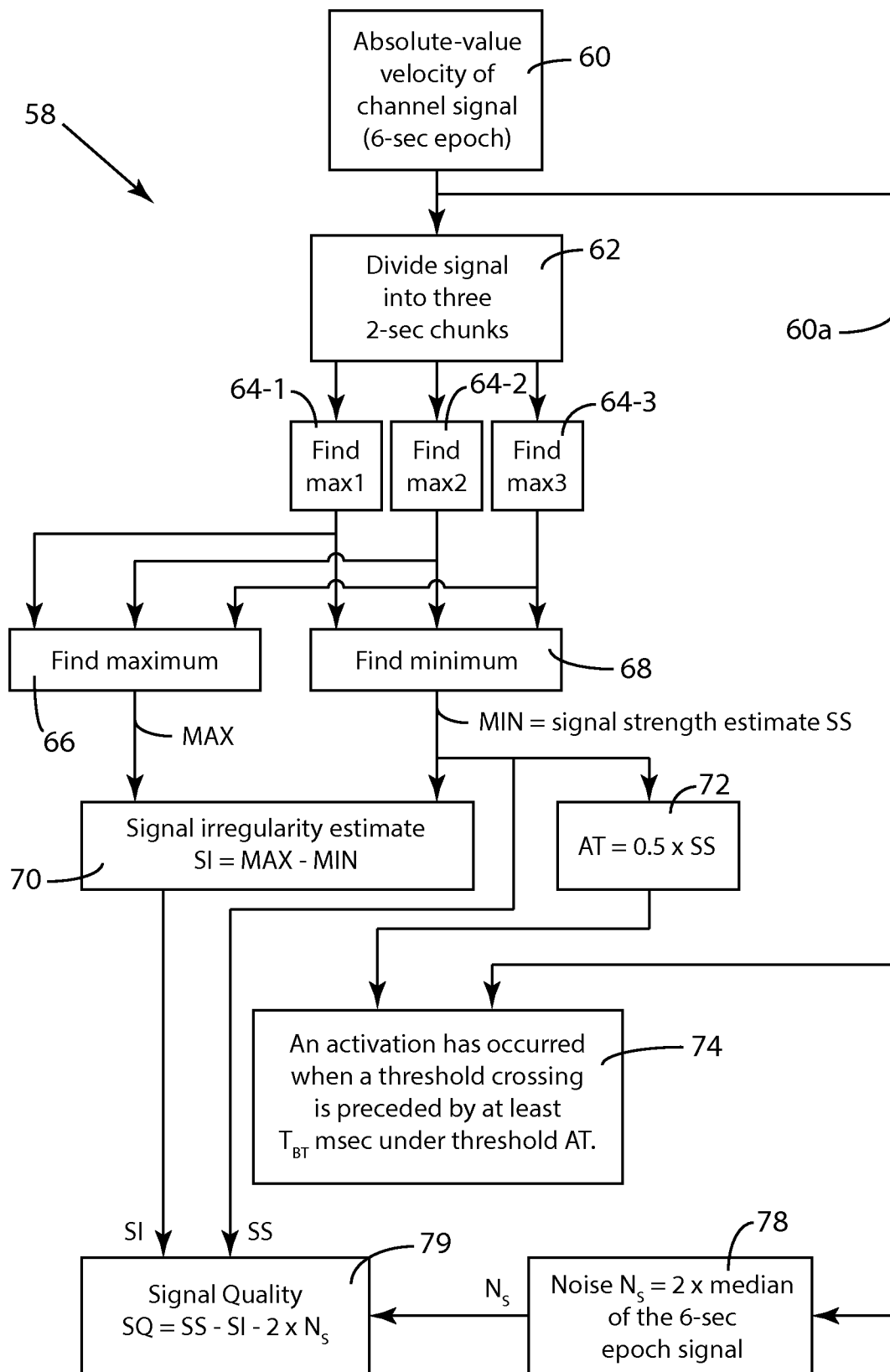


FIG. 4A

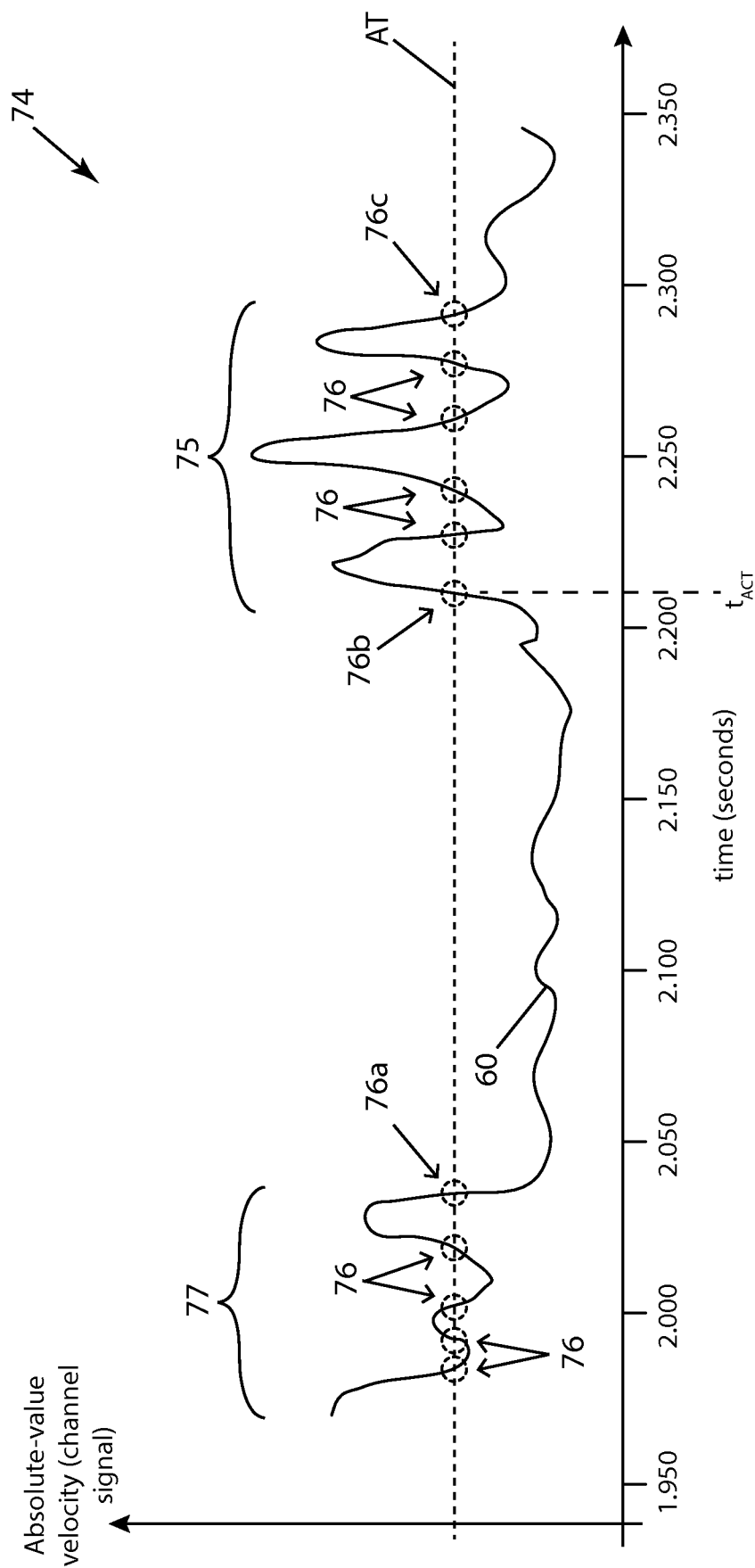


FIG. 4B

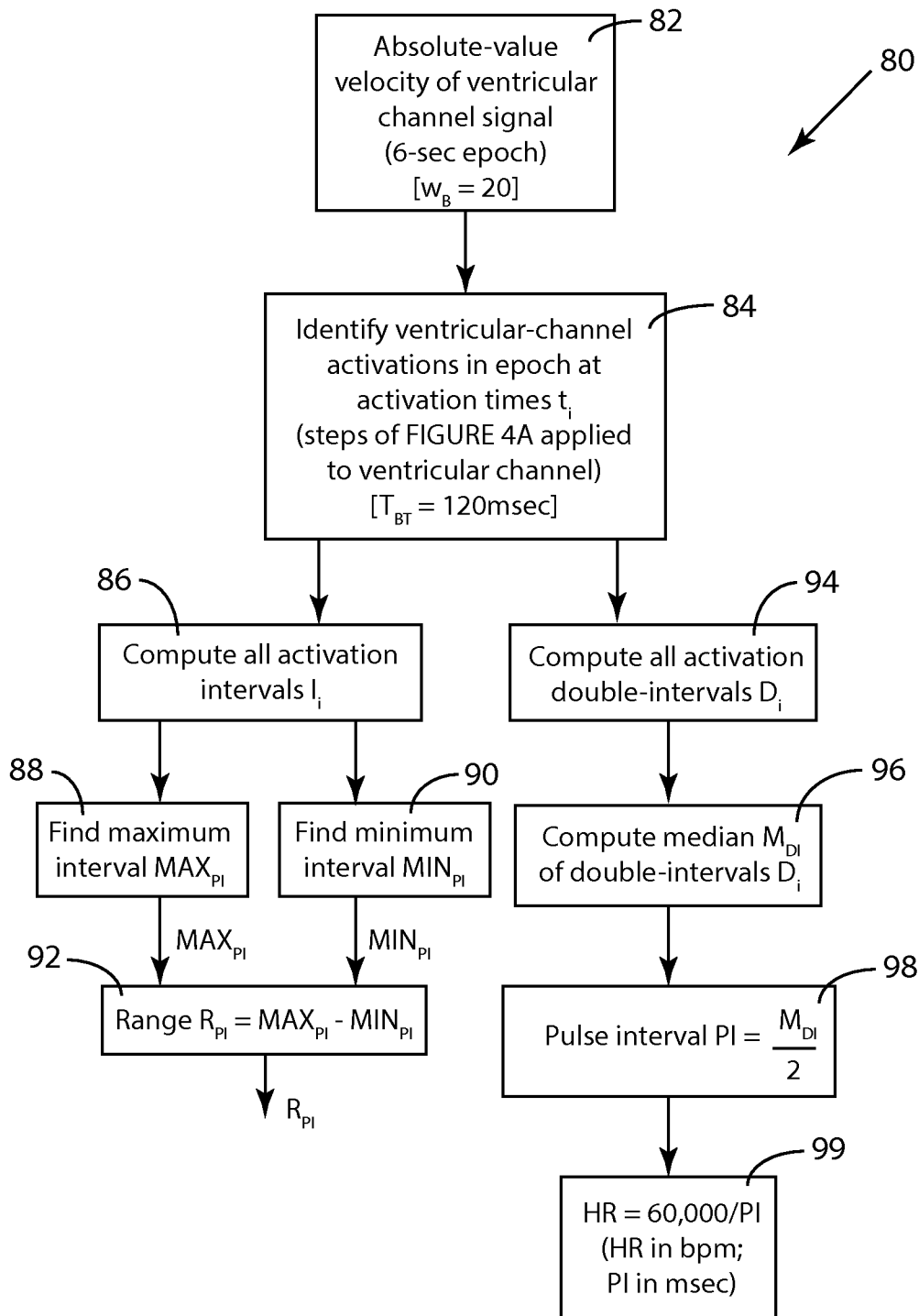


FIG. 5

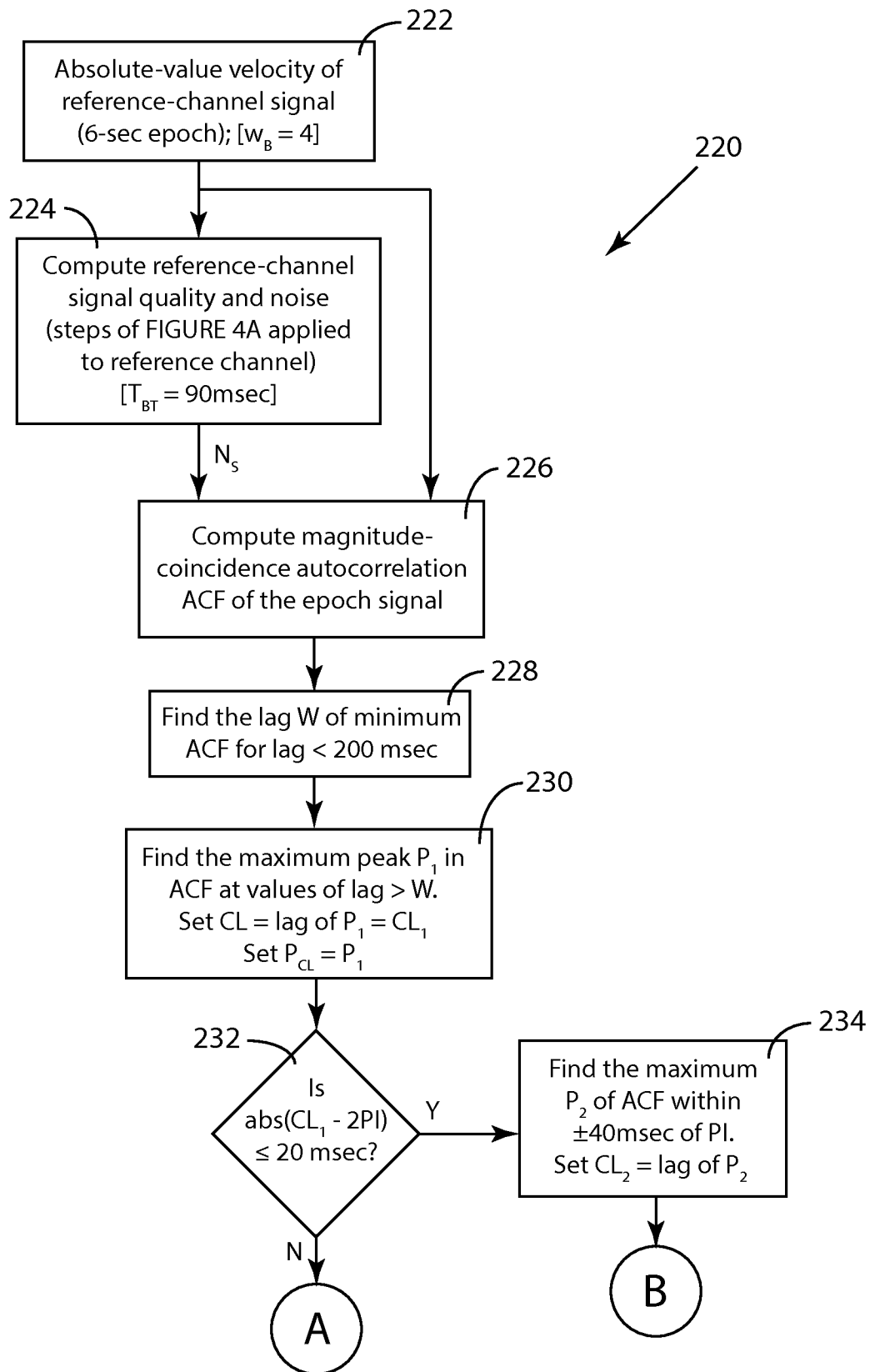


FIG. 6A

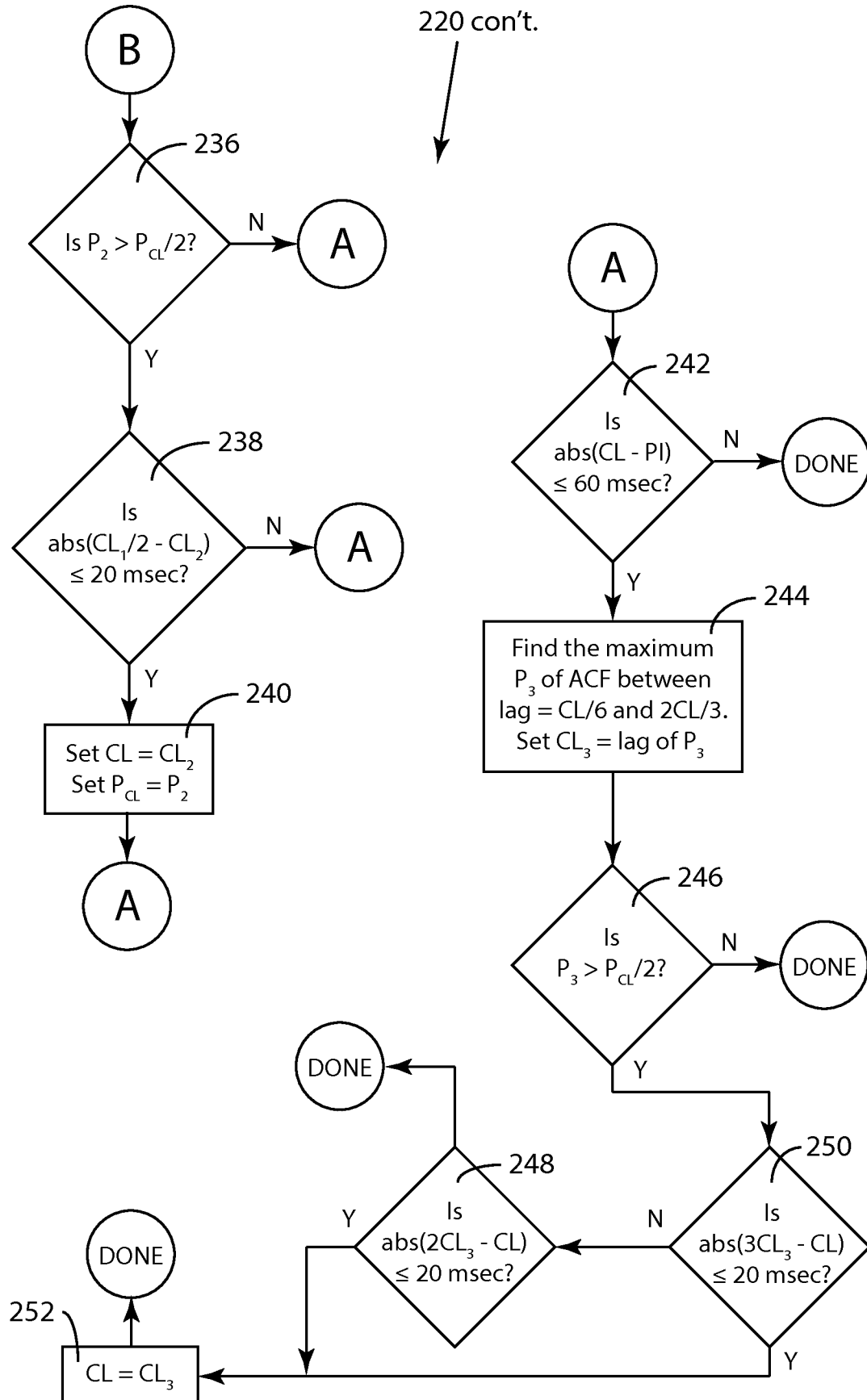


FIG. 6B

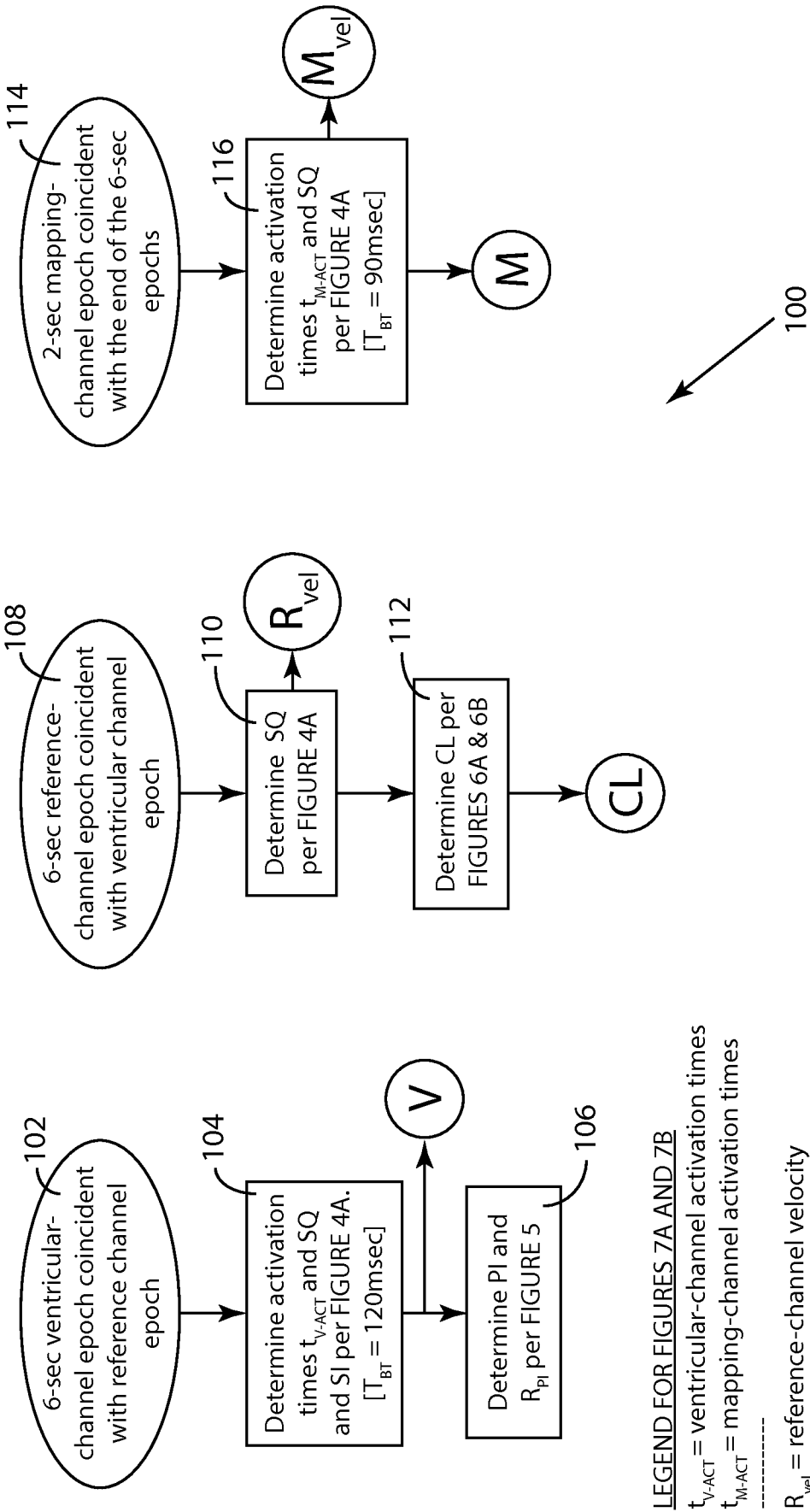


FIG. 7A

LEGEND FOR FIGURES 7A AND 7B
 t_{V-act} = ventricular-channel activation times
 t_{M-act} = mapping-channel activation times
 R_{vel} = reference-channel velocity
 M_{vel} = mapping-channel velocity
 t_r = reference-channel fiducial time (max. neg. velocity)
 t_m = mapping-channel fiducial time (max. neg. velocity)
 LAT = local activation time = $t_m - t_r$

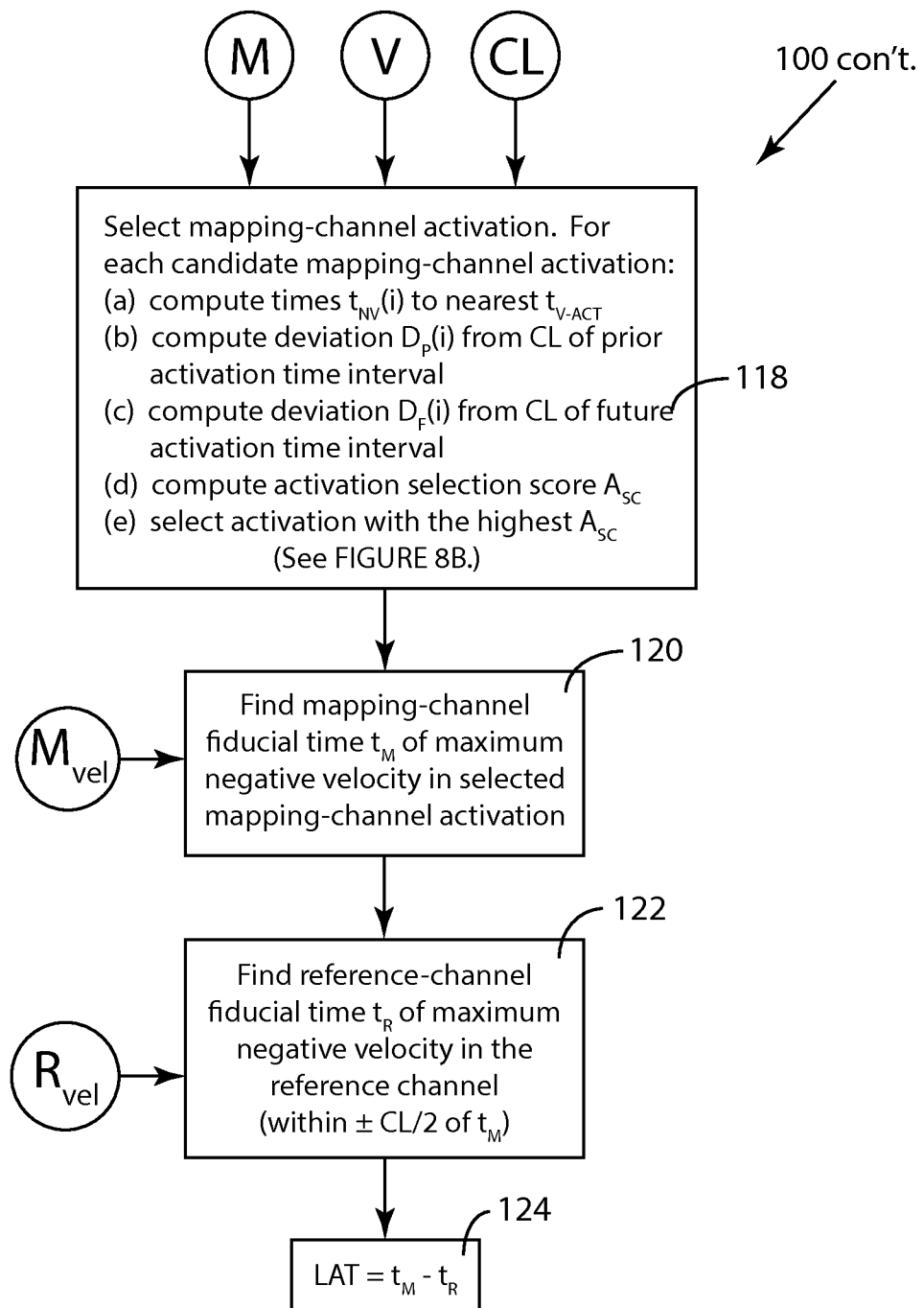


FIG. 7B

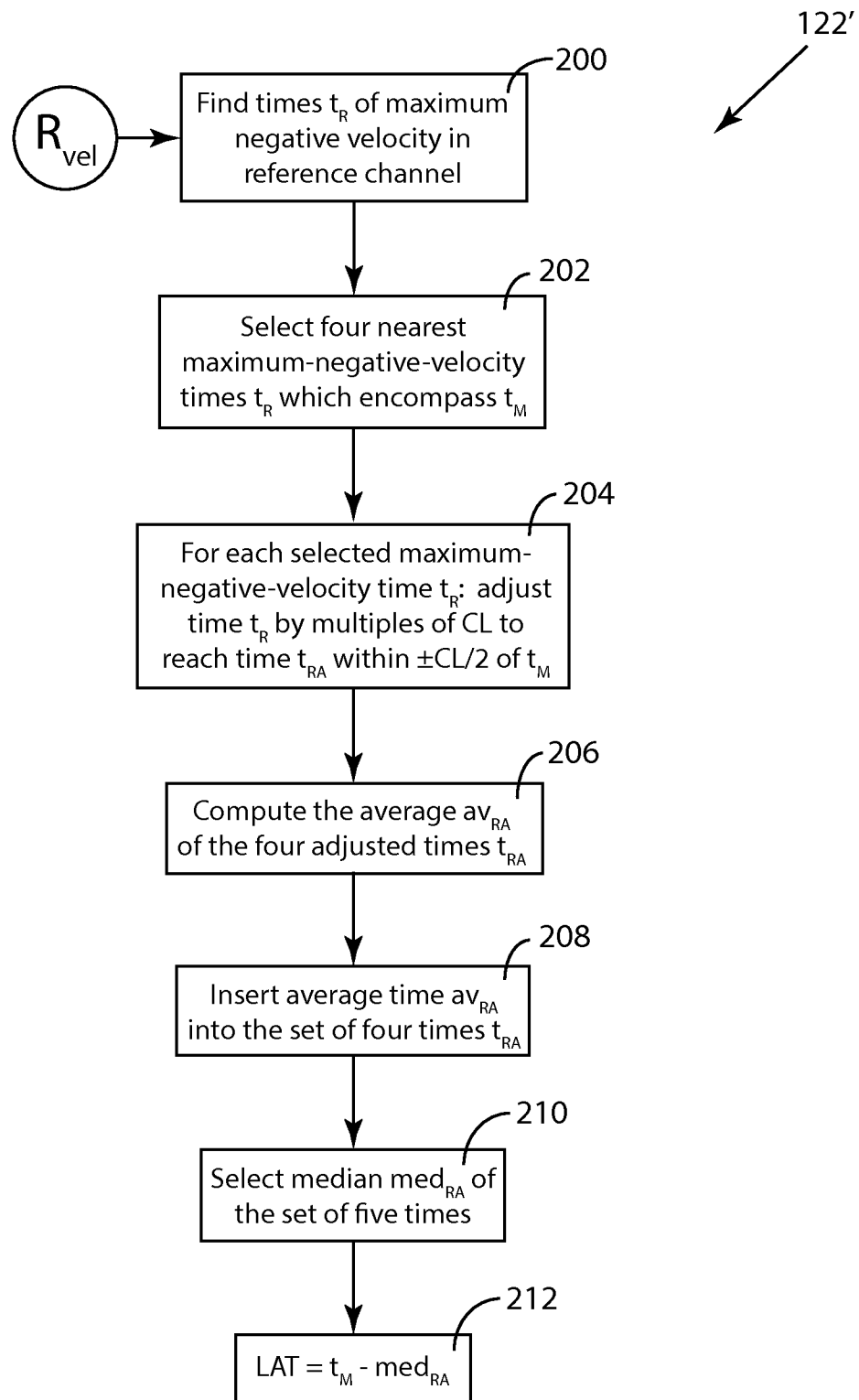
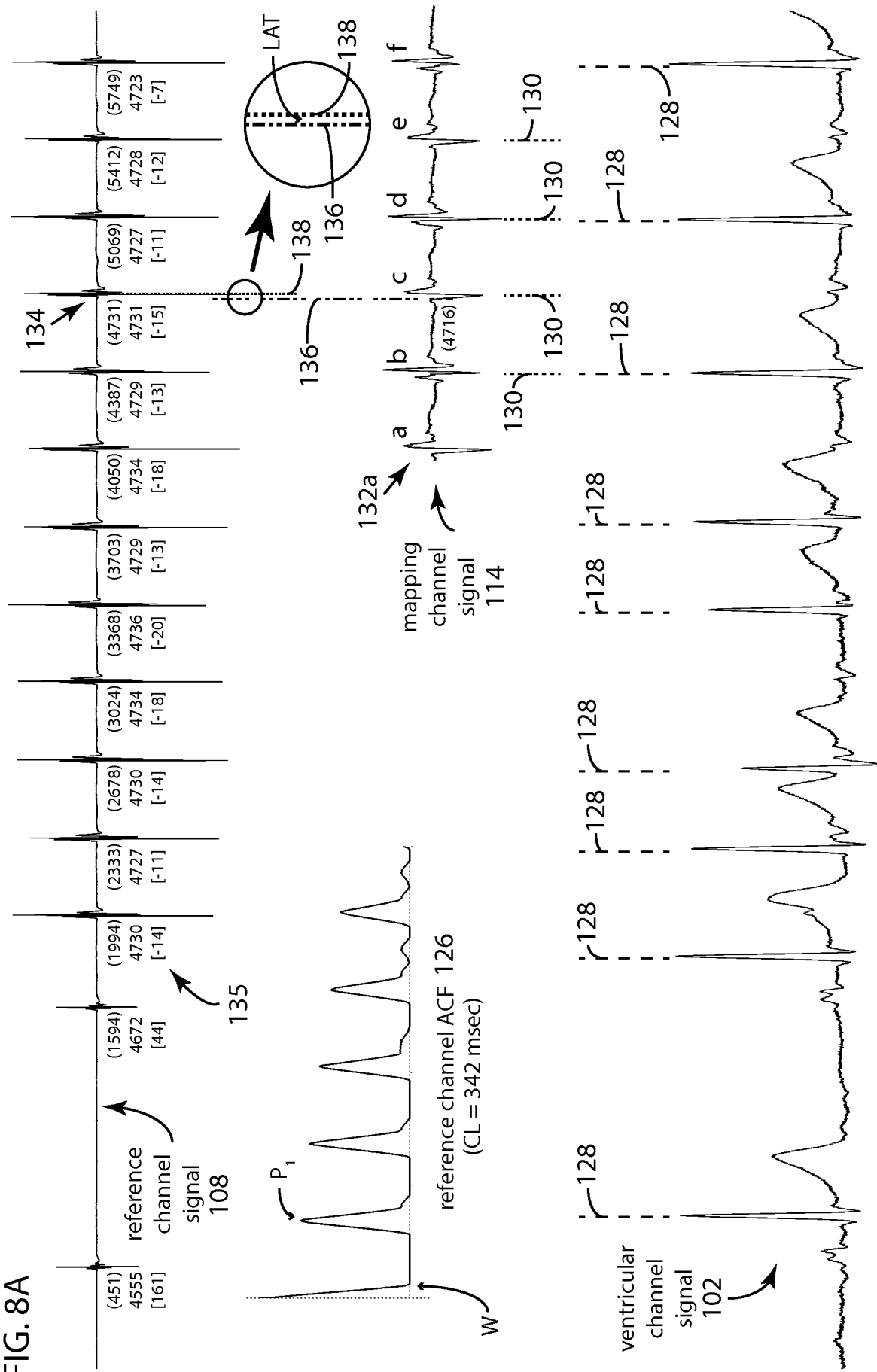


FIG. 7C

FIG. 8A



118



CL = 342 msec						Comment
ACT	t_{M-ACT}	t_{NV}	D_P	D_F	A_{SC}	
132a						not detected - too early
132b	4382	11	40	8	-37	beginning-of-data rule
132c	4732	314	8	16	290	selected activation
132d	5058	12	16	11	-15	
132e	5411	320	11	247	62	end-of-data rule
132f						not detected - too small

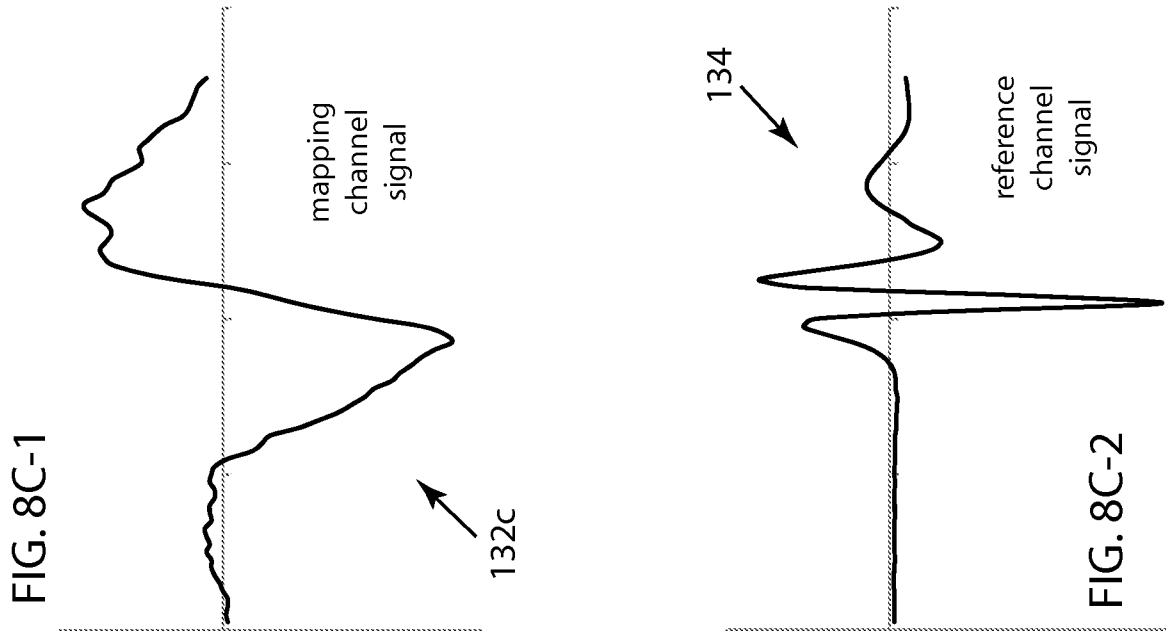
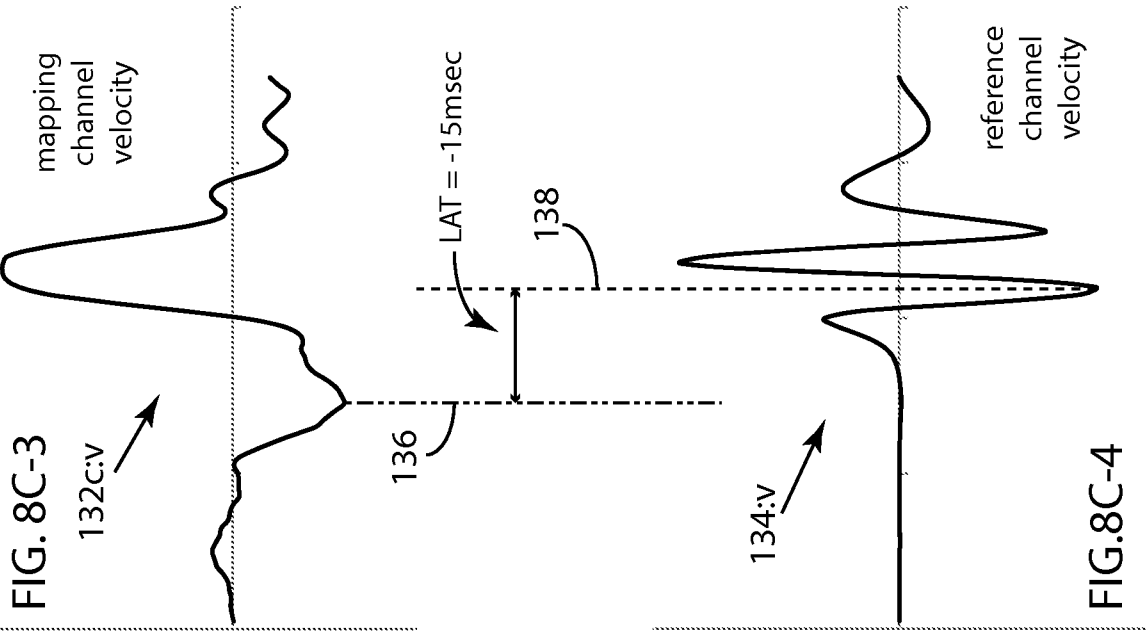
[all values in the table in msec]

TABLE LEGEND

CL = reference-channel cycle length

 $t_{M-ACT}(i)$ = mapping-channel activation times $t_{V-ACT}(i)$ = ventricular-channel activation times $t_{NV}(i) = \min_{\text{all } t_{V-ACT}} (|t_{M-ACT}(i) - t_{V-ACT}|)$ = time to nearest ventricular-channel activation $D_P(i) = t_{M-ACT}(i) - t_{M-ACT}(i-1) - CL$ = deviation of prior interval from CL $D_F(i) = t_{M-ACT}(i+1) - t_{M-ACT}(i) - CL$ = deviation of future interval from CL $A_{SC}(i) = t_{NV}(i) - D_P(i) - D_F(i)$ = mapping-channel activation selection score

FIG. 8B



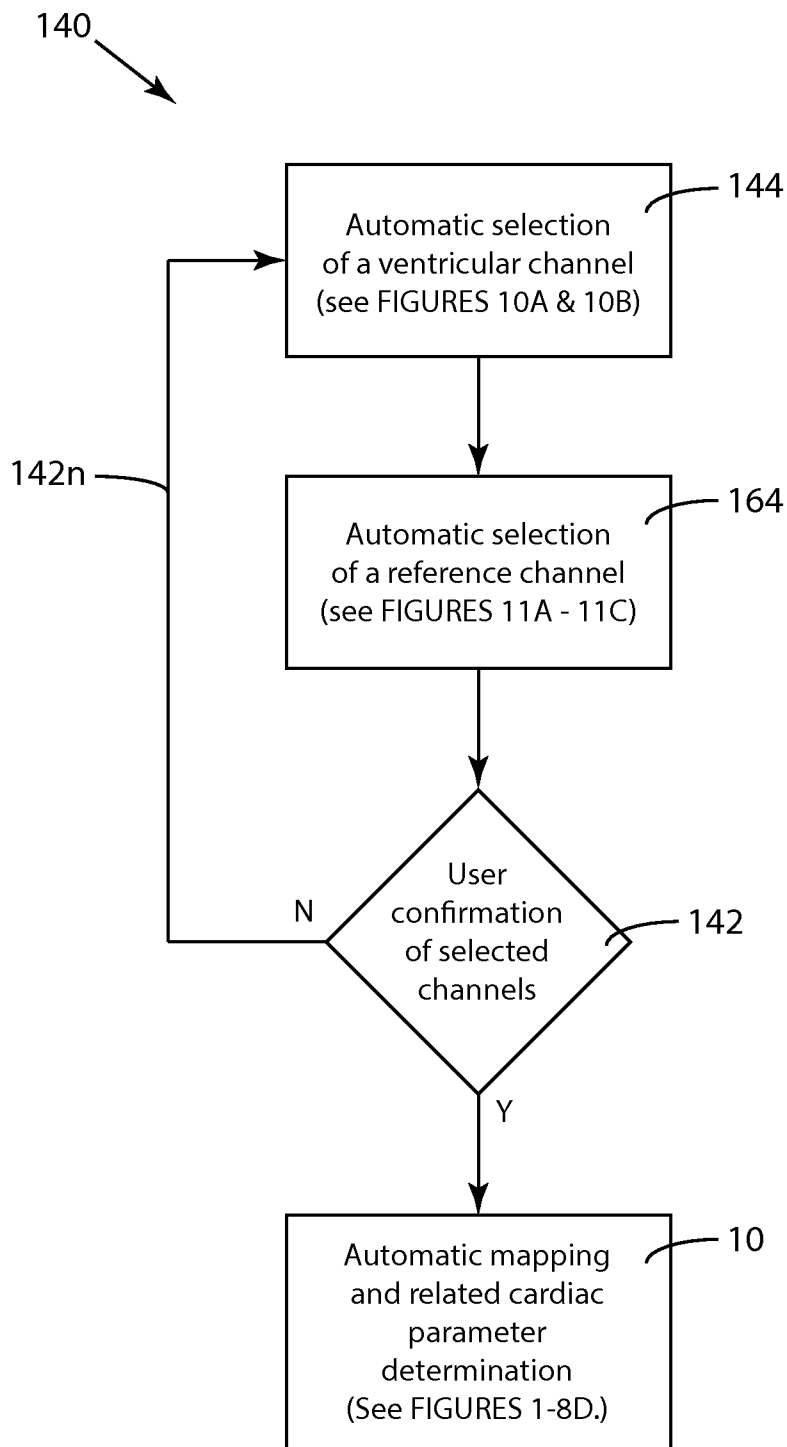


FIG. 9

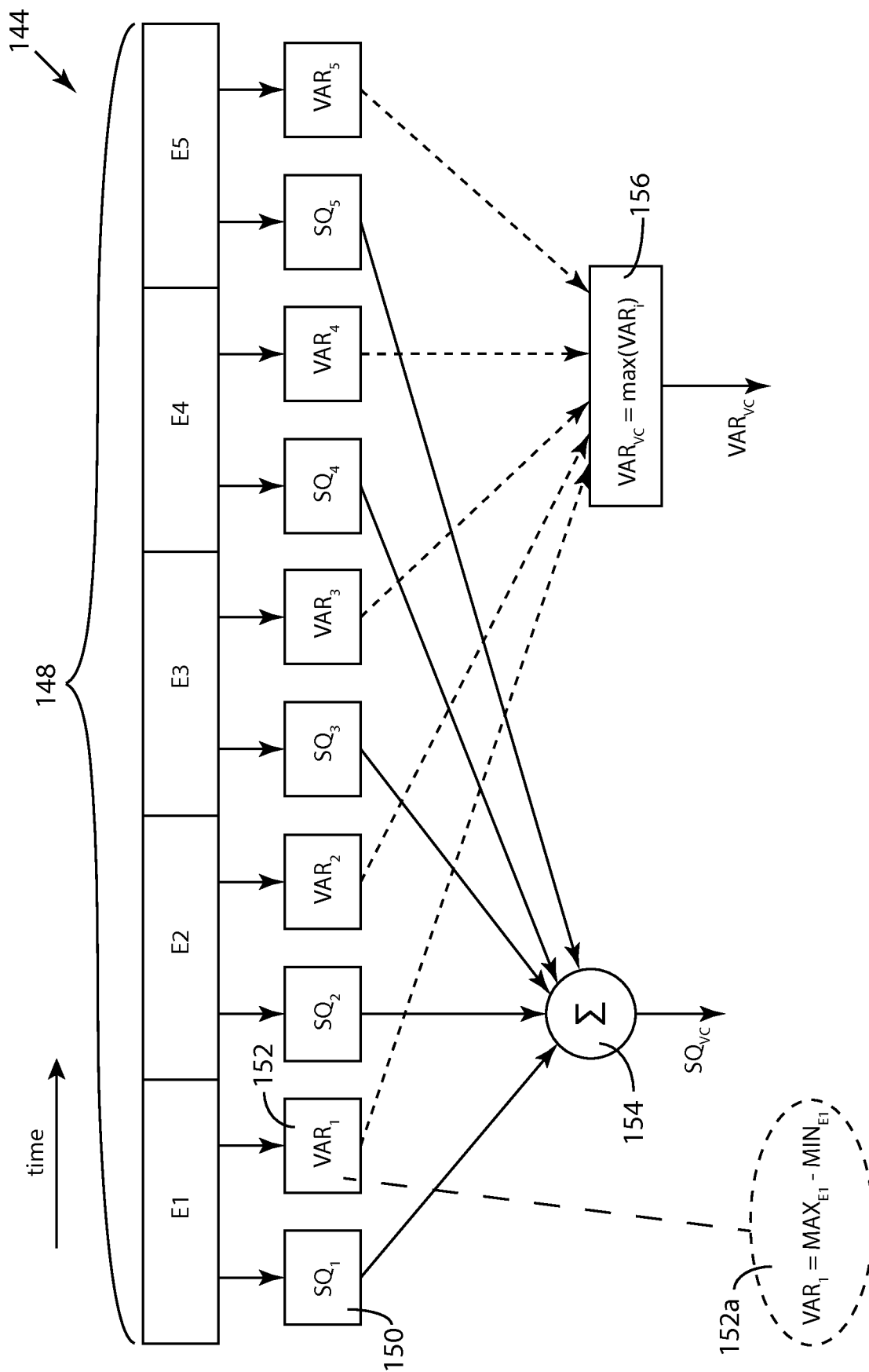
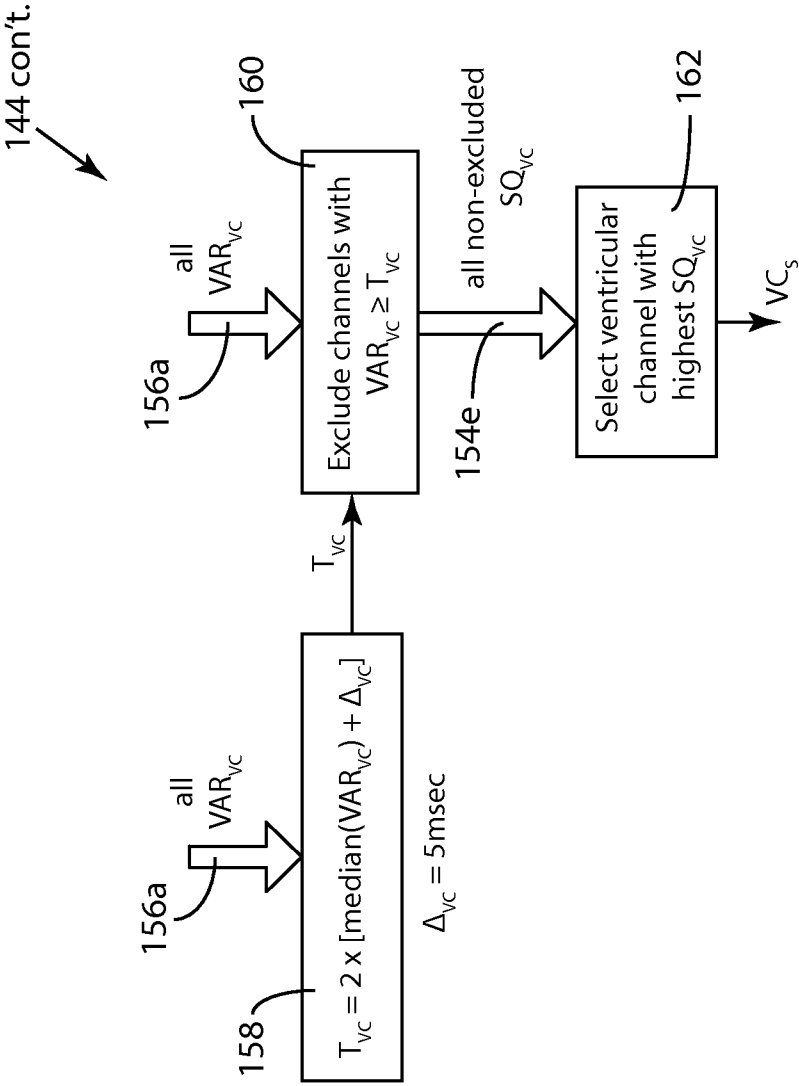


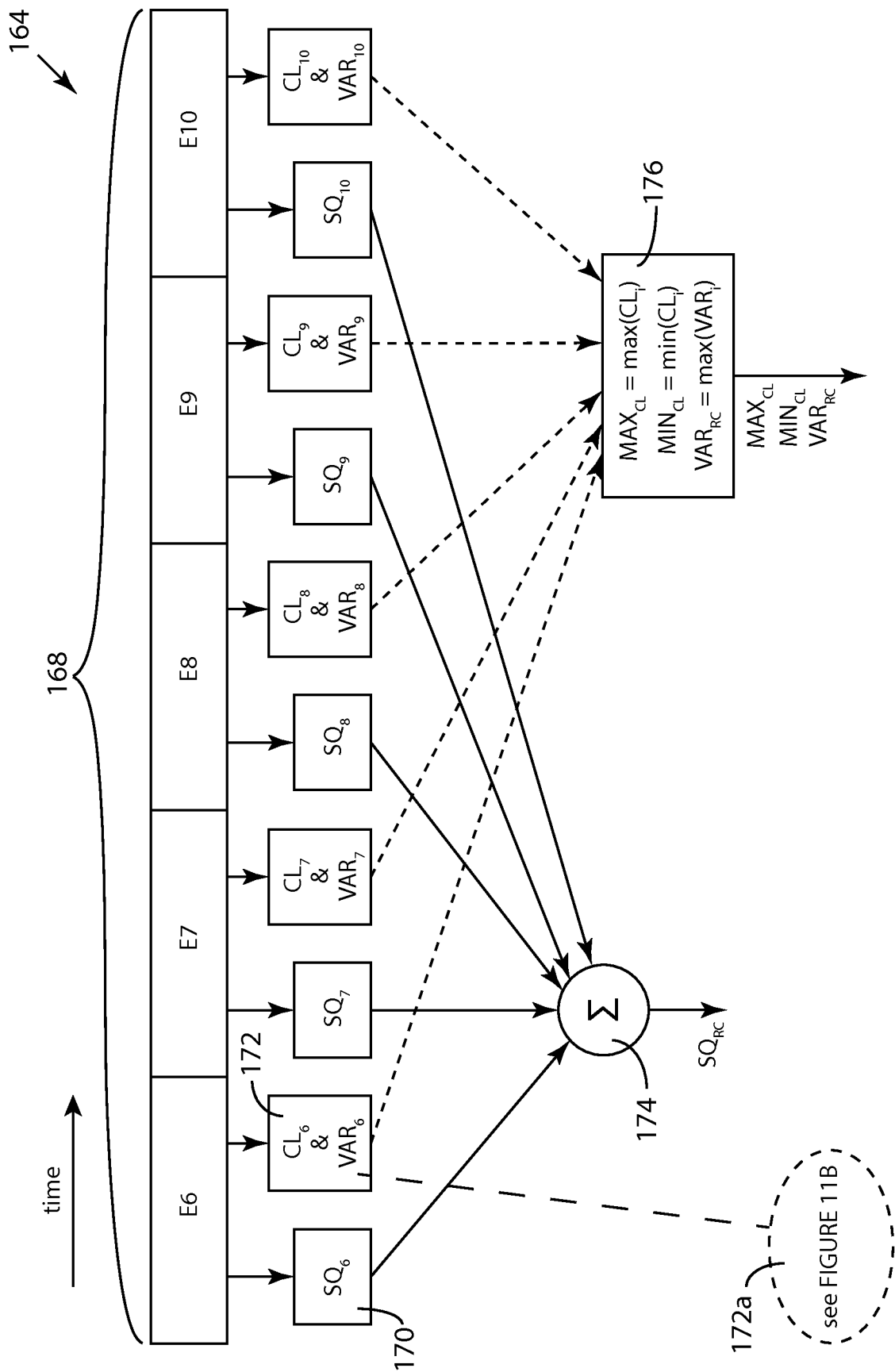
FIG. 10A

Automatic Ventricular-Channel Selection



Automatic Ventricular-Channel Selection

FIG. 10B



Automatic Reference-Channel Selection

FIG. 11A

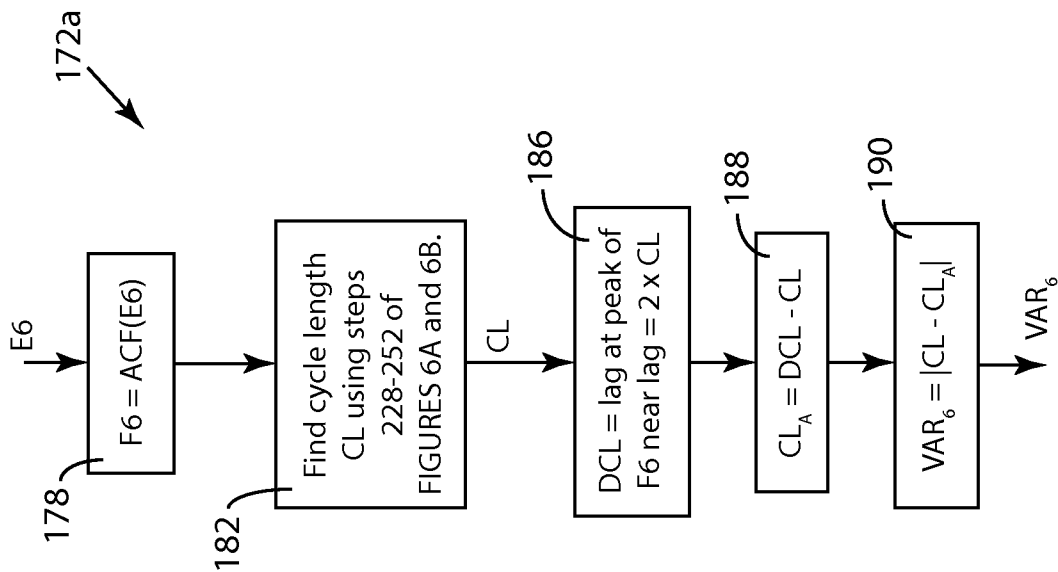


FIG. 11B

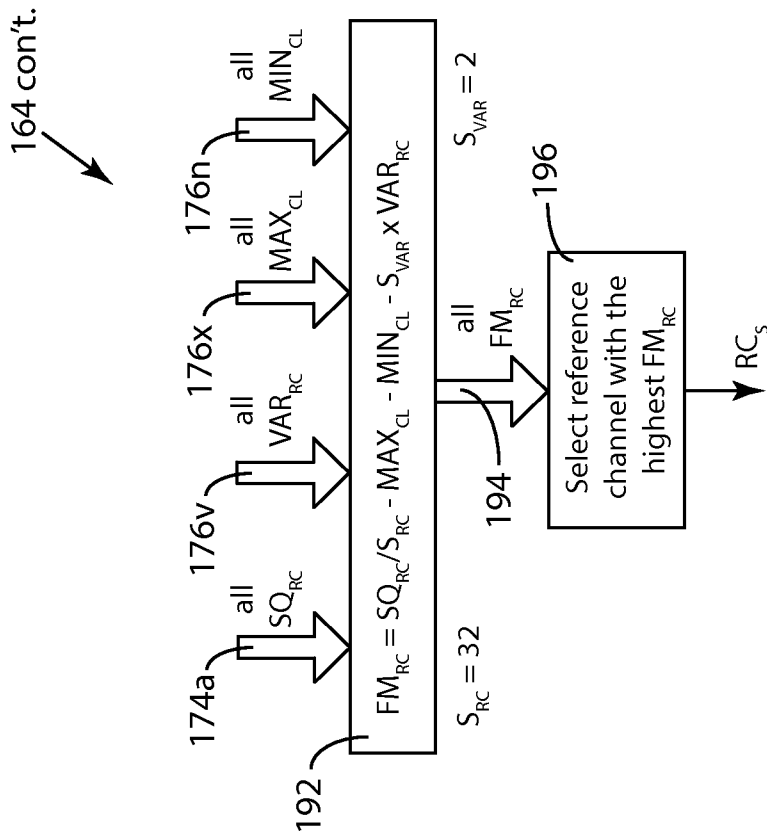
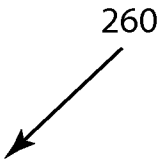


FIG. 11C

Automatic Reference-Channel Selection



	M ₁	M ₂	M ₃	M ₄	M ₅	M ₆	M ₇	M ₈
R ₁	-	✓	✓	✓	✓	✓	✓	✓
R ₂	-	-	✓	✓	✓	✓	✓	✓
R ₃	-	-	-	✓	✓	✓	✓	✓
R ₄	-	-	-	-	✓	✓	✓	✓
R ₅	-	-	-	-	-	✓	✓	✓
R ₆	-	-	-	-	-	-	✓	✓
R ₇	-	-	-	-	-	-	-	✓
R ₈	-	-	-	-	-	-	-	-

FIG. 12

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/23321

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 5/046 (2014.01)

USPC - 600/515, 509

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(8) - A61B 5/046 (2014.01)

USPC - 600/515, 509

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
600/515-518, 519; 600/481, 508, 509-525; A61B 5/0452 - 5/0472
(Search term limited; see below)

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

PubWest (PGPB, USPT, EPAB, JPAB); Google; PatBase (All);

Search Terms: Local activation time, LAT, activation time, reference, fiducial, mapping, determine, calculate, compute, equation, formula, subtract, minus, difference, average, weighted, time window, adjust, correcting, correction, active, measurement, channel, electrode, lead

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2012/0035488 A1 (MACADAM et al.) 09 February 2012 (09.02.2012) Entire document, especially Abstract, para[0036]- para[0038] and para[0050].	1-21
A	US 201 1/0282226 A1 (BENSER et al.) 17 November 2011 (17.11.2011) Entire document, especially para[0059]- para[0061].	1-21
A	US 6,236,883 B1 (CIACCIO et al.) 22 May 2001 (22.05.2001) Entire document, especially col 6, ln 1-18 and col 2, ln 35-62	1-21
A	US 2012/0184864 A1 (HARLEV et al.) 19 July 2012 (19.07.2012) Entire document, especially Abstract, para[0021], para[0314] and para[0367]- para[00369].	1-21



Further documents are listed in the continuation of Box C.



* 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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"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

05 June 2014 (05.06.2014)

Date of mailing of the international search report

09 JUL 2014

Name and mailing address of the ISA/US

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Authorized officer:

Lee W. Young

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PCT OSP: 571-272-7774

专利名称(译)	多通道心脏测量		
公开(公告)号	EP2967403A1	公开(公告)日	2016-01-20
申请号	EP2014770815	申请日	2014-03-11
[标]申请(专利权)人(译)	APN健康有限责任公司		
申请(专利权)人(译)	APN健康, LLC		
当前申请(专利权)人(译)	APN健康, LLC		
[标]发明人	BRODNICK DONALD SRA JASBIR		
发明人	BRODNICK, DONALD SRA, JASBIR		
IPC分类号	A61B5/046 A61B5/00 A61B5/04 A61B5/0408 A61B5/042 A61B5/0464 A61B5/0468		
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优先权	13/888070 2013-05-06 US 13/842994 2013-03-15 US		
其他公开文献	EP2967403A4		
外部链接	Espacenet		

摘要(译)

一种确定包括至少两个心脏通道的多通道心电图信号中的局部激活时间 (LAT) 的自动方法, 其中一个心脏通道是映射通道而另一个心脏通道是参考通道, 该方法包括: (a) 估计参考信道中的周期长度CL; (b) 确定映射信道信号中的映射信道基准时间tM; (c) 确定多个参考通道基准时间tR; (d) 通过向每个时间tR加上或减去周期长度CL的倍数来计算调整的参考信道基准时间tRA, 使得每个时间tRA在围绕映射信道基准时间tM的长度CL的时间窗内; (e) 从多个调整的参考信道基准时间tRA计算单个最终参考信道基准时间tRF; (f) 将LAT计算为tM减去tRF。