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(54) **ANALYZING AND MAPPING ECG SIGNALS AND DETERMINING ABLATION POINTS TO ELIMINATE BRUGADA SYNDROME**

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(73) Assignee: **Biosense Webster (Israel) Ltd.**, Yokneam (IL)

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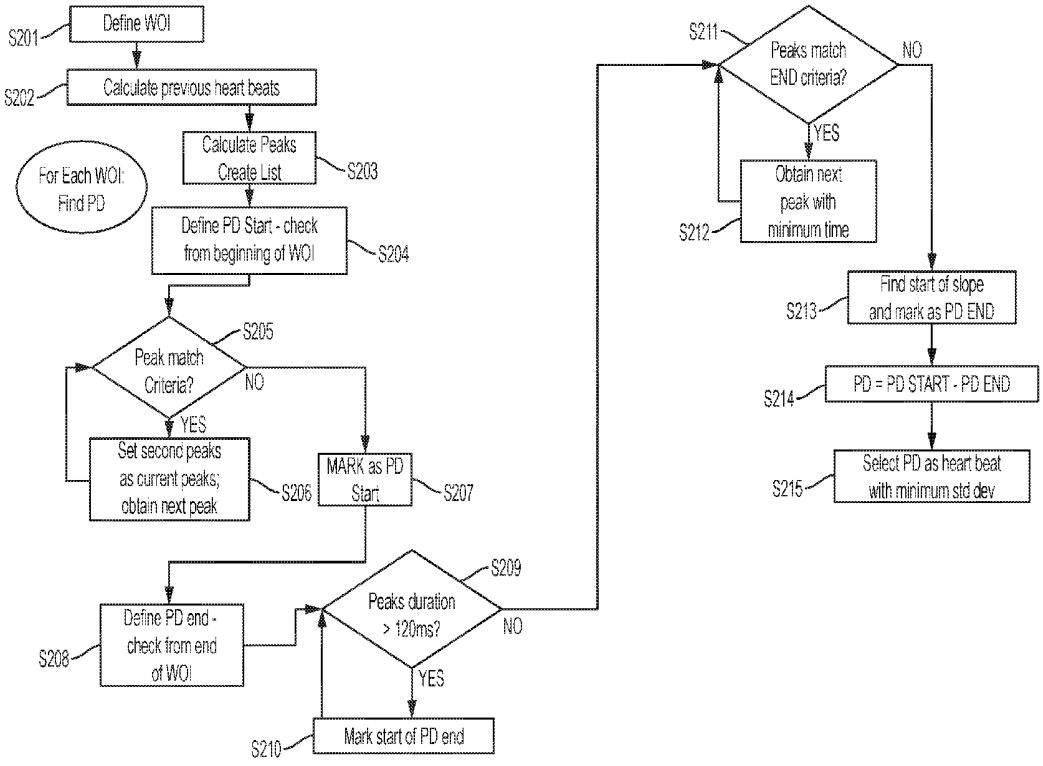
A61B 5/04	(2006.01)

(52) **U.S. Cl.**

CPC ***A61B 5/042*** (2013.01); ***A61B 5/6852*** (2013.01); *A61B 2034/2046* (2016.02); ***A61B 5/0472*** (2013.01); ***A61B 5/04012*** (2013.01); ***A61B 18/1492*** (2013.01)

(57) **ABSTRACT**

A system and method for Brugada syndrome epicardial ablation comprising preparing an endocardial duration map; preparing a baseline epicardial duration map comprising at least one or more areas of delimination; and when some of the areas of delimination are greater than 200 ms, performing epicardial ablation of the areas of delimination greater than 200 ms. The method may further comprise preparing an updated epicardial duration map after performing epicardial ablation, and determining whether or not a BrS pattern appears in the updated epicardial duration map; and when the BrS pattern appears, performing epicardial ablation. The method may further comprise preparing an updated epicardial duration map after performing epicardial ablation, and determining whether or not an abnormal EGM exists in the updated epicardial duration map; and when the abnormal EGM exists, performing epicardial ablation. The method may further comprise preparing an updated epicardial map comprising maintaining anatomical volume data and adding electroanatomical data.



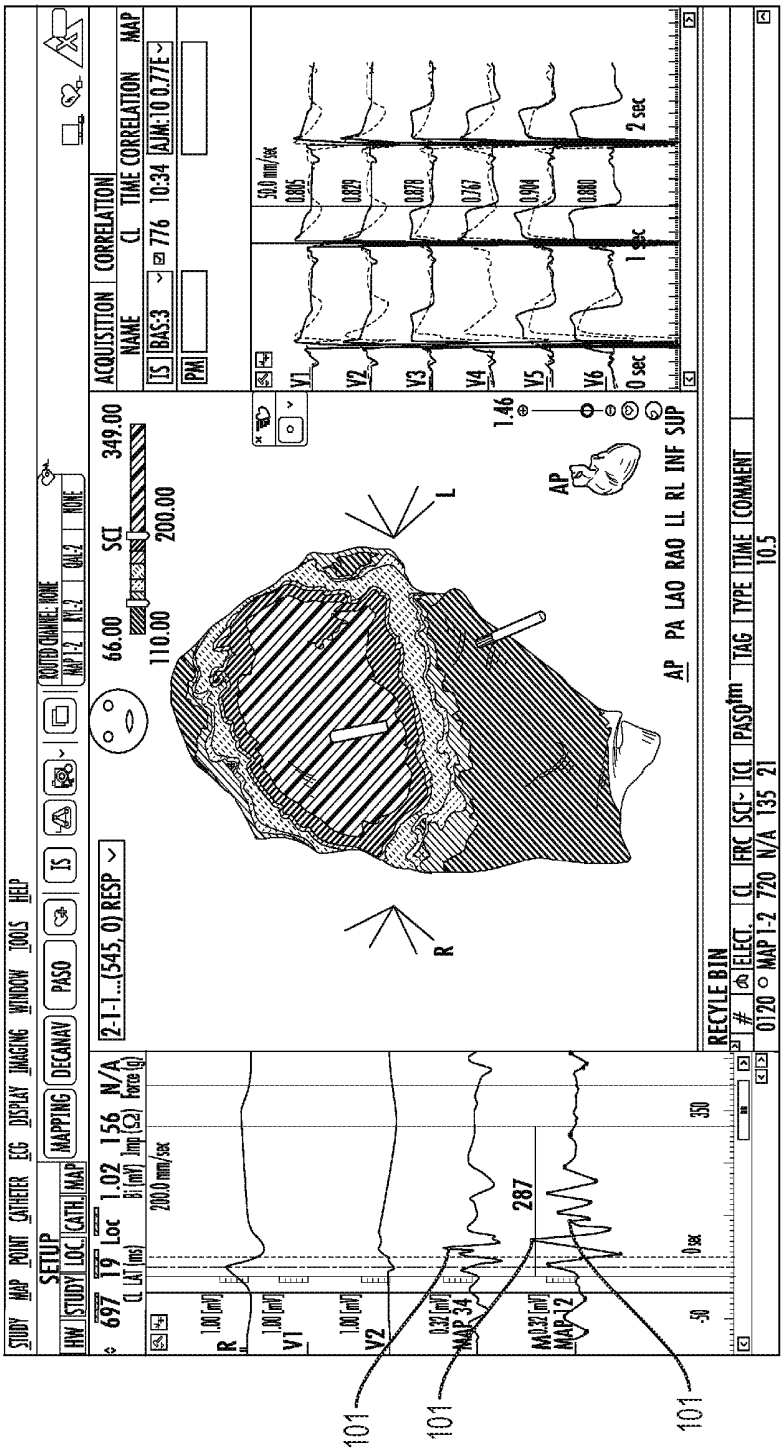


FIG. 1

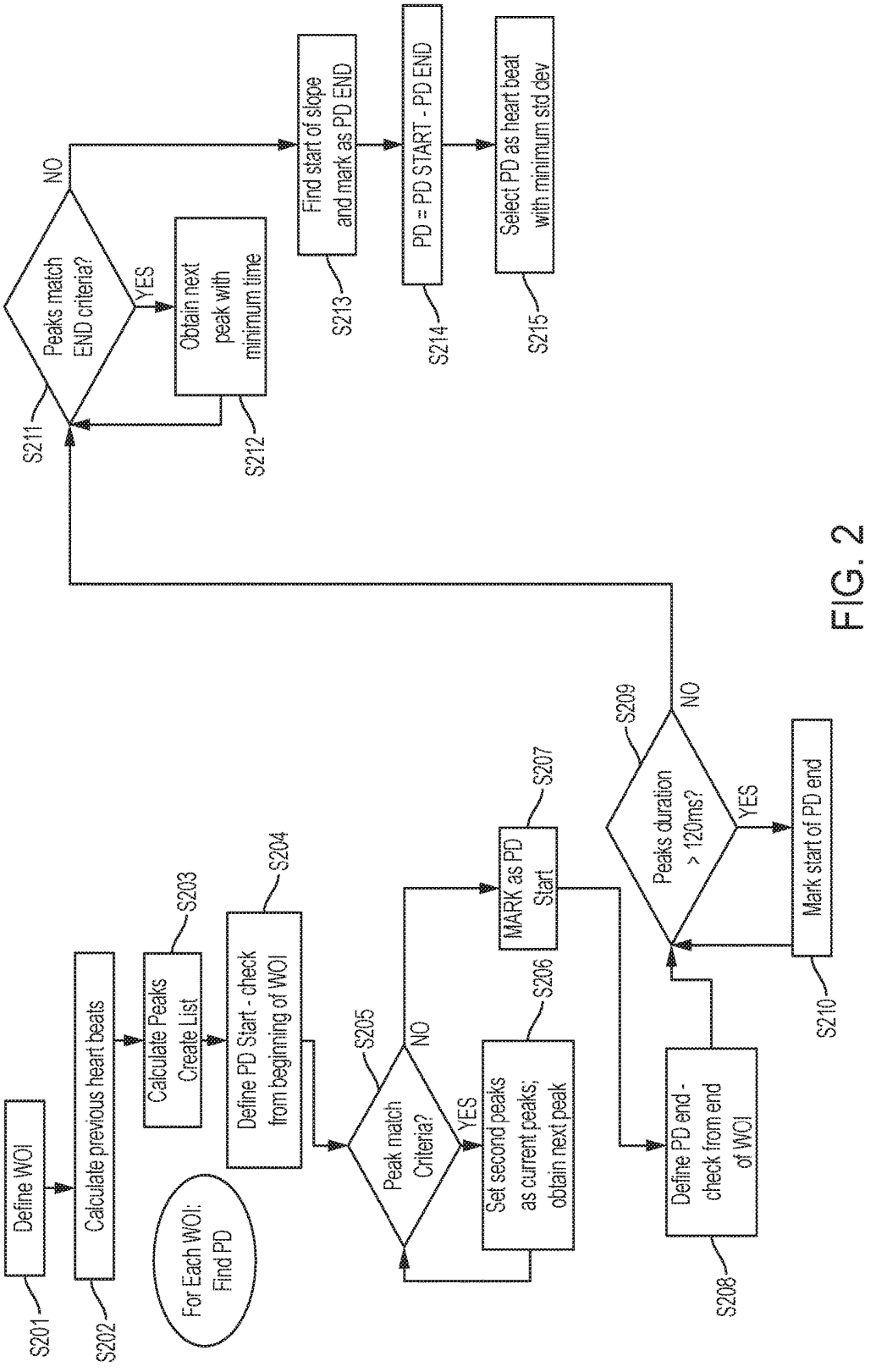

Define WOI
S201
Calculate previous heart beats
S202
For Each WOI: Find PD
Calculate Peaks Create List
S203
Define PD Start - check from beginning of WOI
S204
Peak match Criteria?
S205
NO
YES
Set second peaks as current peaks; obtain next peak
S206
MARK as PD Start
S207
Define PD end - check from end of WOI
S208
Peaks duration > 120ms?
S209
NO
YES
Mark start of PD end
S210
Peaks match END criteria?
S211
NO
YES
Obtain next peak with minimum time
S212
Find start of slope and mark as PD END
S213
PD = PD START - PD END
S214
Select PD as heart beat with minimum std dev
S215

FIG. 2

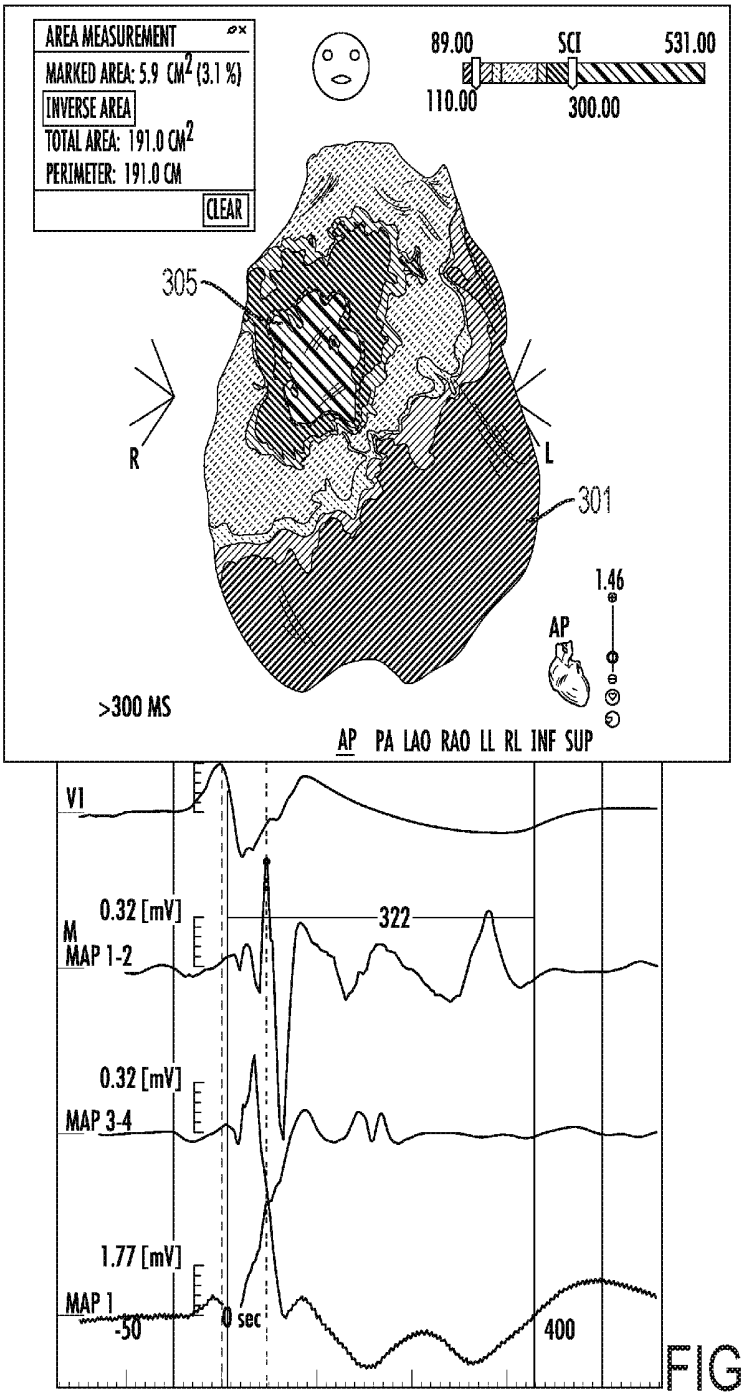

AREA MEASUREMENT
MARKED AREA: 5.9 CM2 (3.1 %)
INVERSE AREA
TOTAL AREA: 191.0 CM2
PERIMETER: 191.0 CM
CLEAR
89.00
SCI
531.00
110.00
300.00
305
R
L
301
1.46
AP
>300 MS
AP PA LAO RAO LL RL INF SUP
V1
0.32 [mV]
M
MAP 1-2
322
0.32 [mV]
MAP 3-4
1.77 [mV]
MAP 1
-50
0 sec
400

FIG. 3A

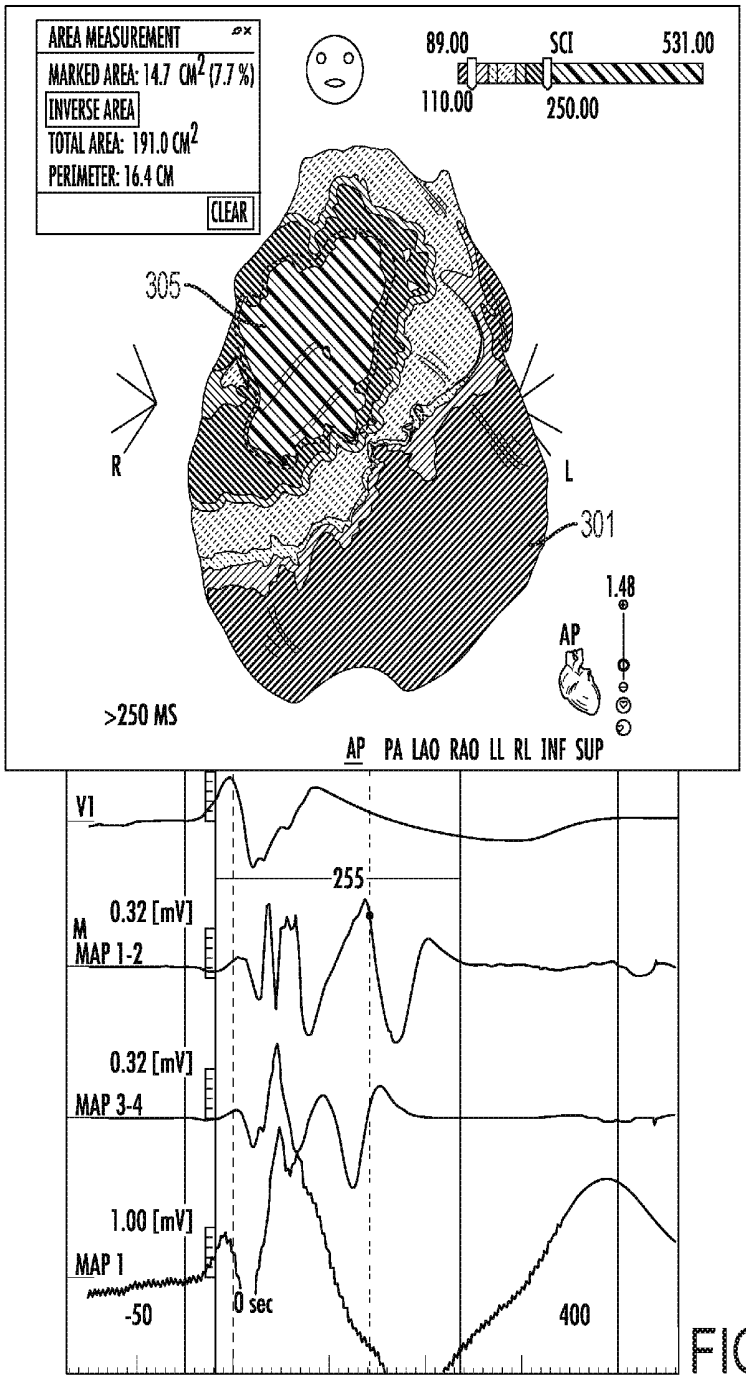

AREA MEASUREMENT
MARKED AREA: 14.7 CM2 (7.7 %)
INVERSE AREA
TOTAL AREA: 191.0 CM2
PERIMETER: 16.4 CM
CLEAR
89.00
SCI
531.00
110.00
250.00
305
R
L
301
1.48
AP
>250 MS
AP PA LAO RAO LL RL INF SUP
V1
255
0.32 [mV]
M
MAP 1-2
0.32 [mV]
MAP 3-4
1.00 [mV]
MAP 1
-50
0 sec
400

FIG. 3B

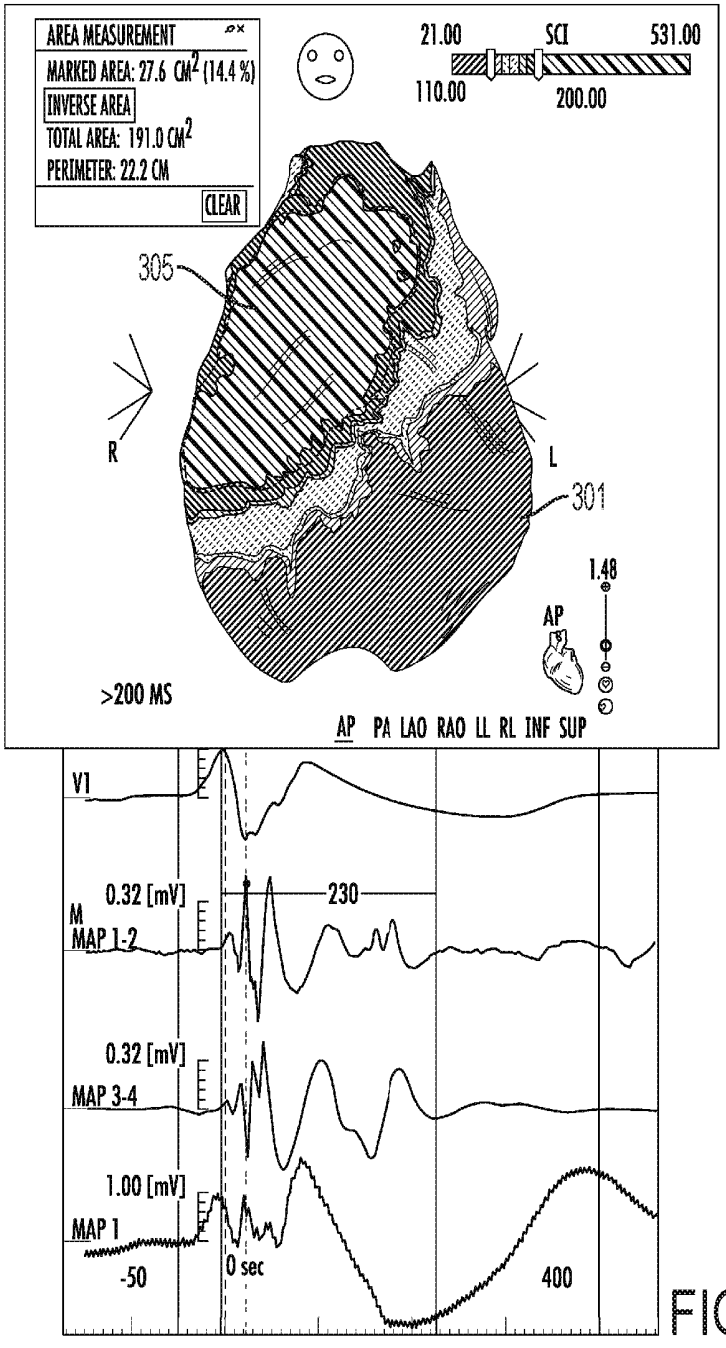

AREA MEASUREMENT
MARKED AREA: 27.6 CM2 (14.4 %)
INVERSE AREA
TOTAL AREA: 191.0 CM2
PERIMETER: 22.2 CM
CLEAR
21.00
SCI
531.00
110.00
200.00
305
R
L
301
1.48
AP
>200 MS
AP PA LAO RAO LL RL INF SUP
V1
0.32 [mV]
230
M
MAP 1-2
0.32 [mV]
MAP 3-4
1.00 [mV]
MAP 1
-50
0 sec
400

FIG. 3C

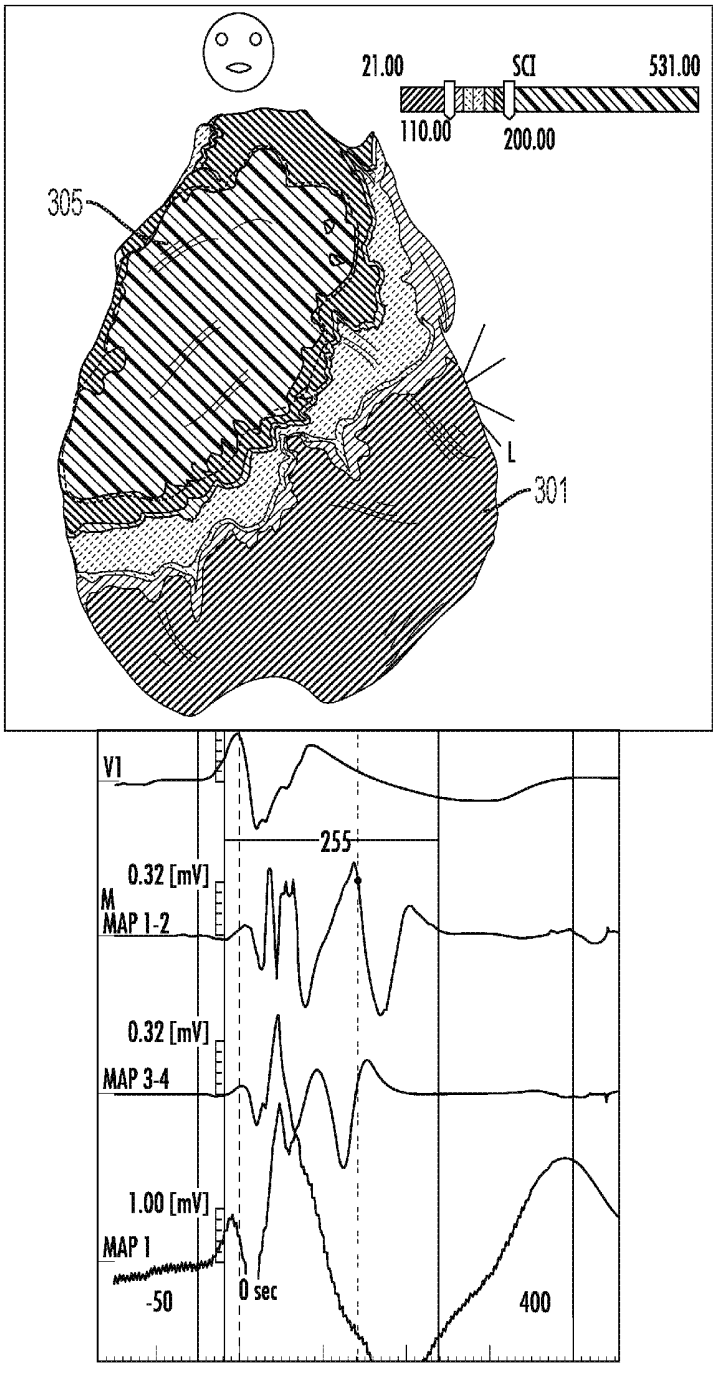

21.00
SCI
531.00
110.00
200.00
305
L
301
V1
255
0.32 [mV]
M
MAP 1-2
0.32 [mV]
MAP 3-4
1.00 [mV]
MAP 1
-50
0 sec
400

FIG. 4A

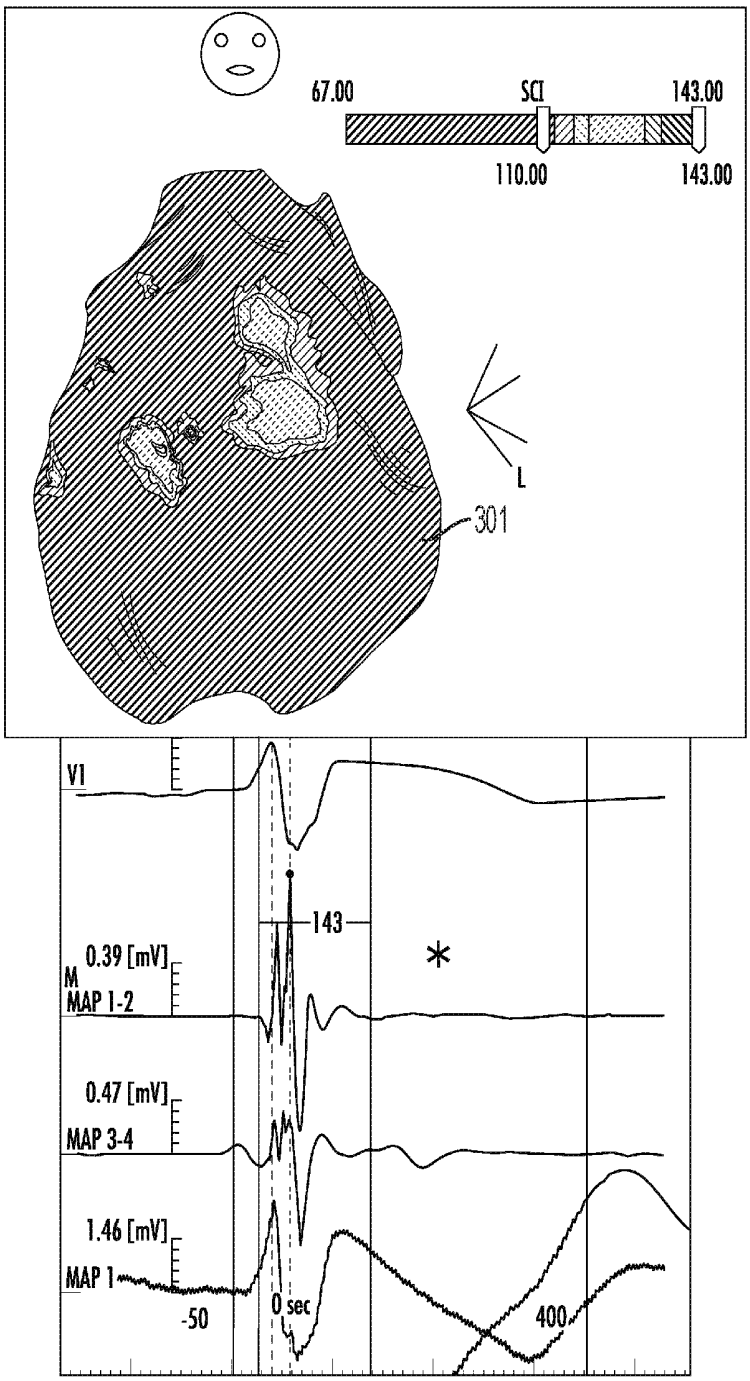

67.00
SCI
143.00
110.00
143.00
L
301
V1
143
0.39 [mV]
M
MAP 1-2
0.47 [mV]
MAP 3-4
1.46 [mV]
MAP 1
-50
0 sec
400

FIG. 4B

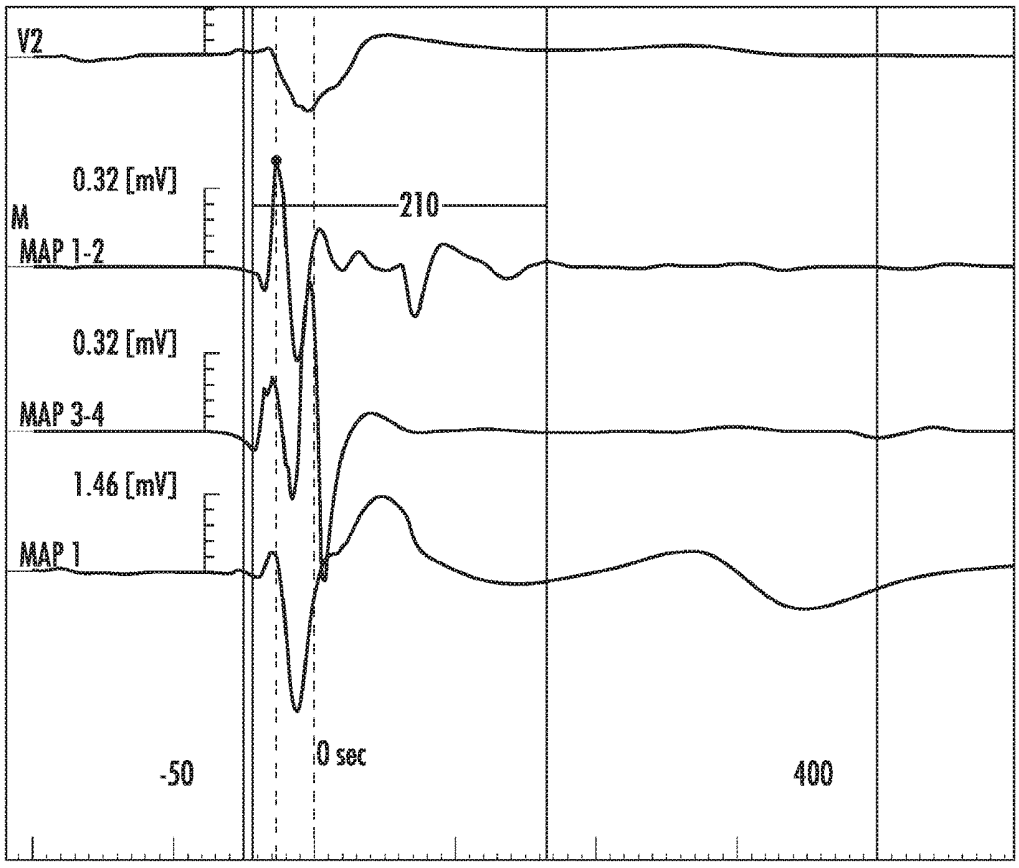


FIG. 5

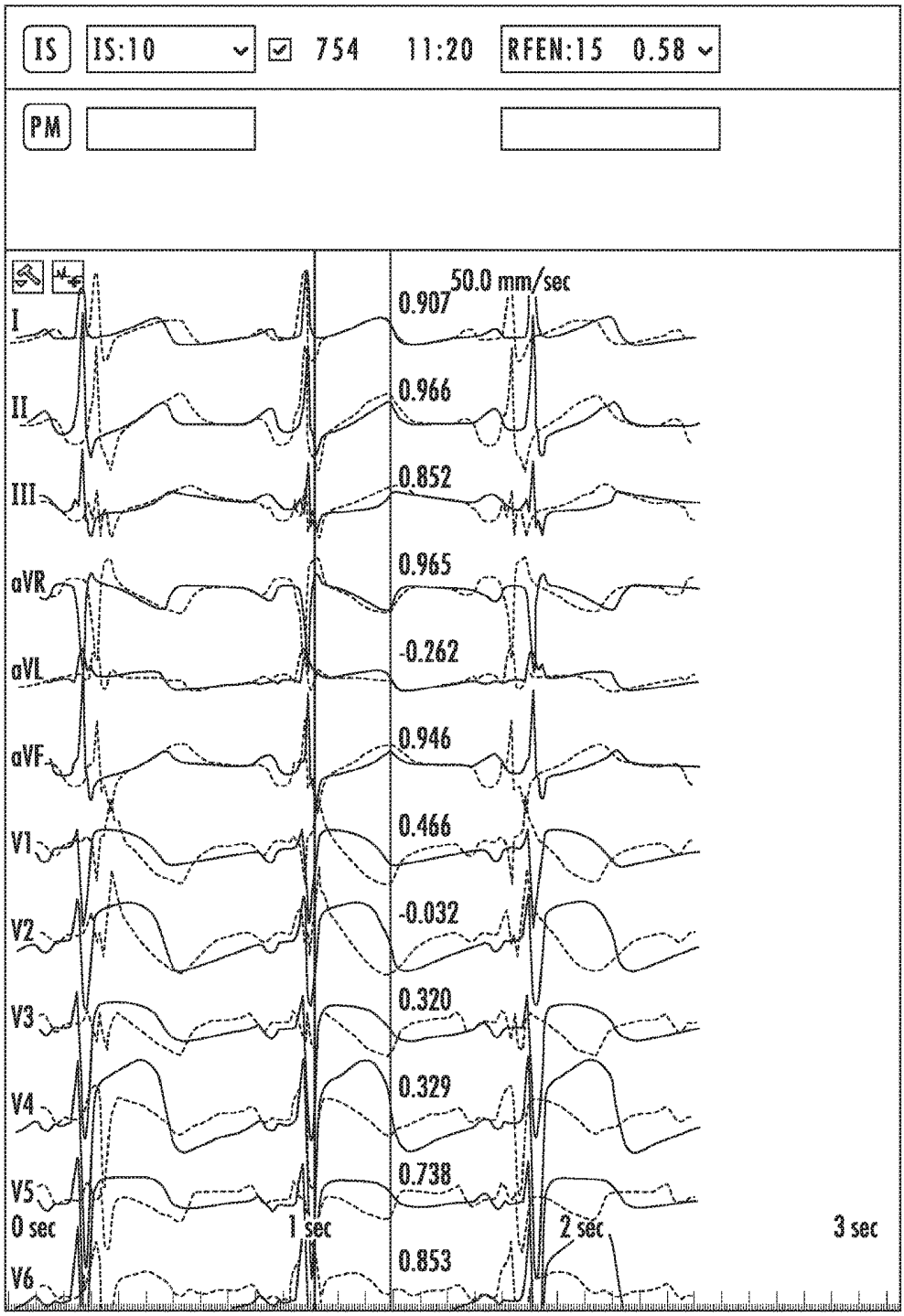

IS
IS:10
754
11:20
RFEN:15 0.58
PM
50.0 mm/sec
I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6
0.907
0.966
0.852
0.965
-0.262
0.946
0.466
-0.032
0.320
0.329
0.738
0.853
0 sec
1 sec
2 sec
3 sec

FIG. 6

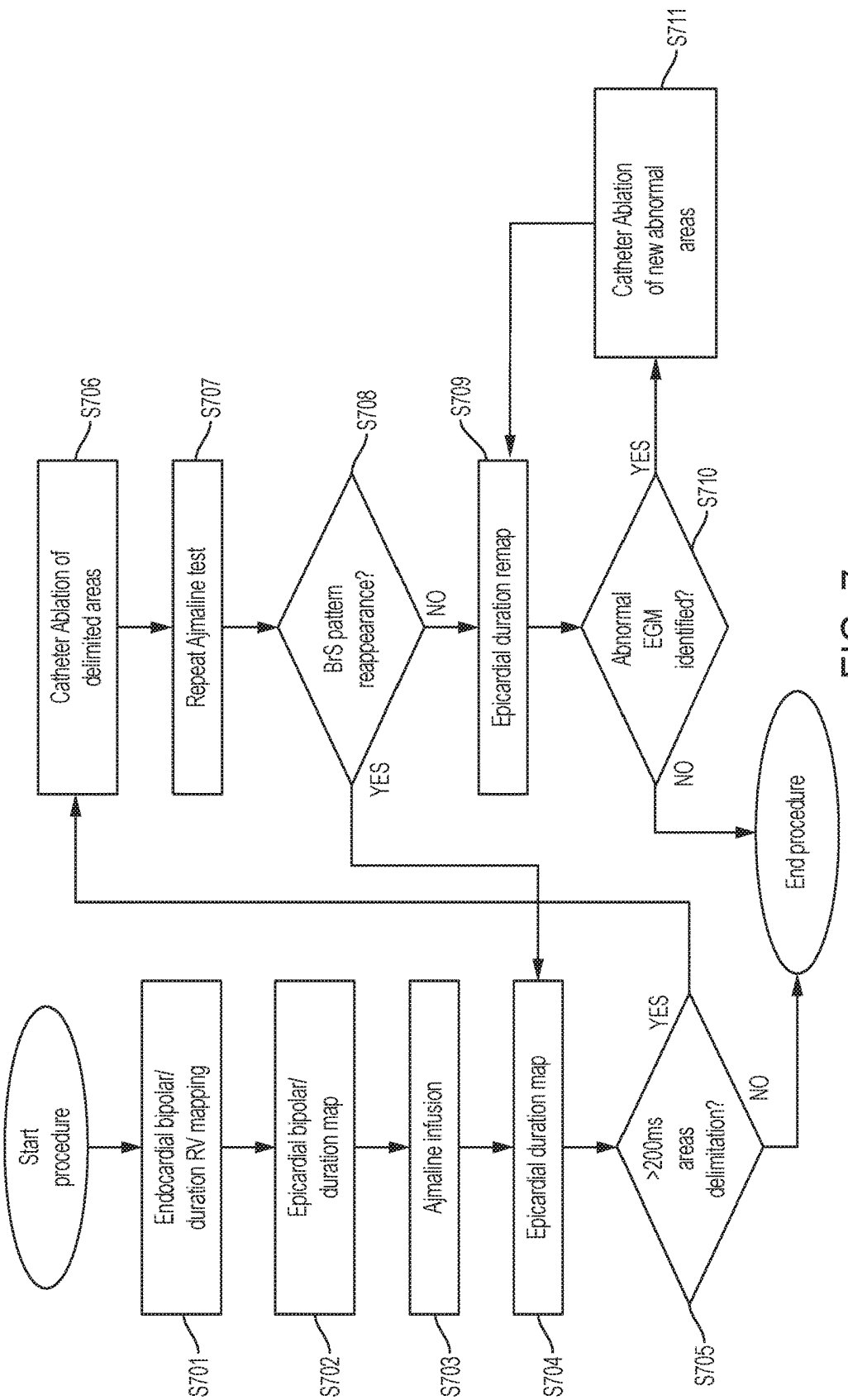

Start procedure
Endocardial bipolar/ duration RV mapping
S701
Epicardial bipolar/ duration map
S702
Ajmaline infusion
S703
Epicardial duration map
S704
>200ms areas delimitation?
S705
YES
NO
End procedure
Catheter Ablation of delimited areas
S706
Repeat Ajmaline test
S707
BrS pattern reappearance?
S708
YES
NO
Epicardial duration remap
S709
Abnormal EGM identified?
S710
YES
NO
Catheter Ablation of new abnormal areas
S711

FIG. 7

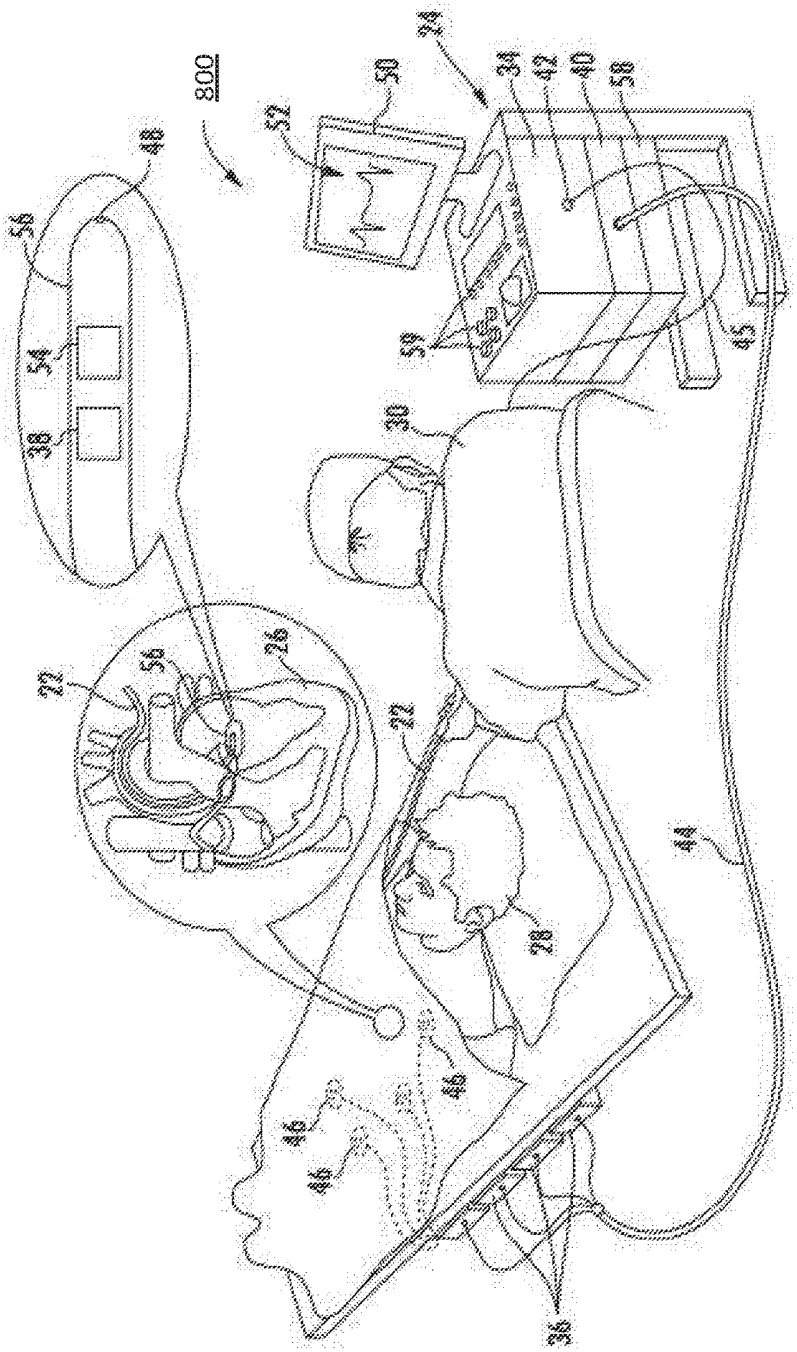

800
74
34
42
40
58
50
52
48
56
54
38
59
45
30
26
72
58
22
44
78
49
46
46
36

FIGURE 8

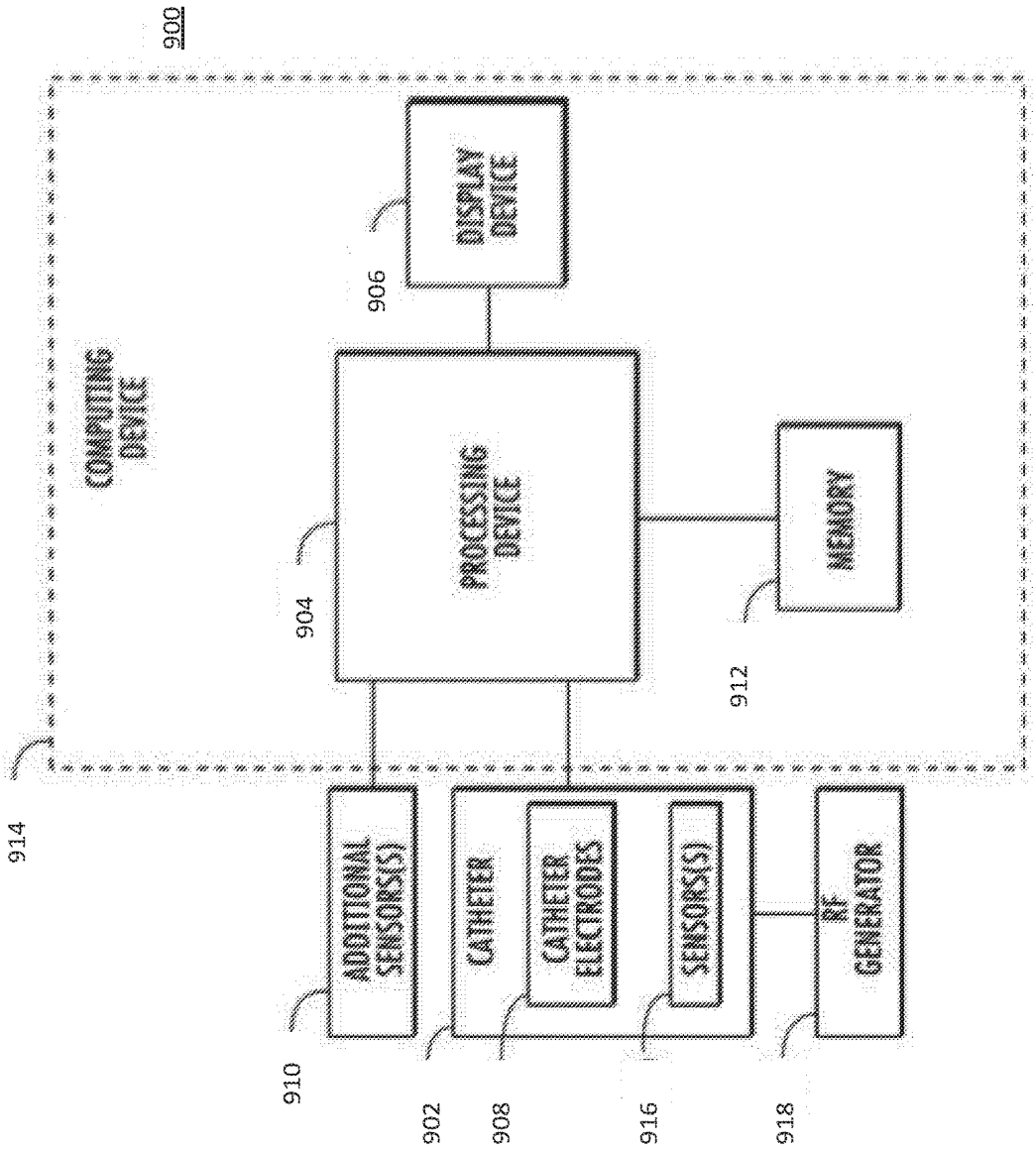

900
COMPUTING DEVICE
914
DISPLAY DEVICE
906
PROCESSING DEVICE
904
MEMORY
912
ADDITIONAL SENSOR(S)
910
CATHETER
902
CATHETER ELECTRODES
908
SENSOR(S)
916
RF GENERATOR
918

FIGURE 9

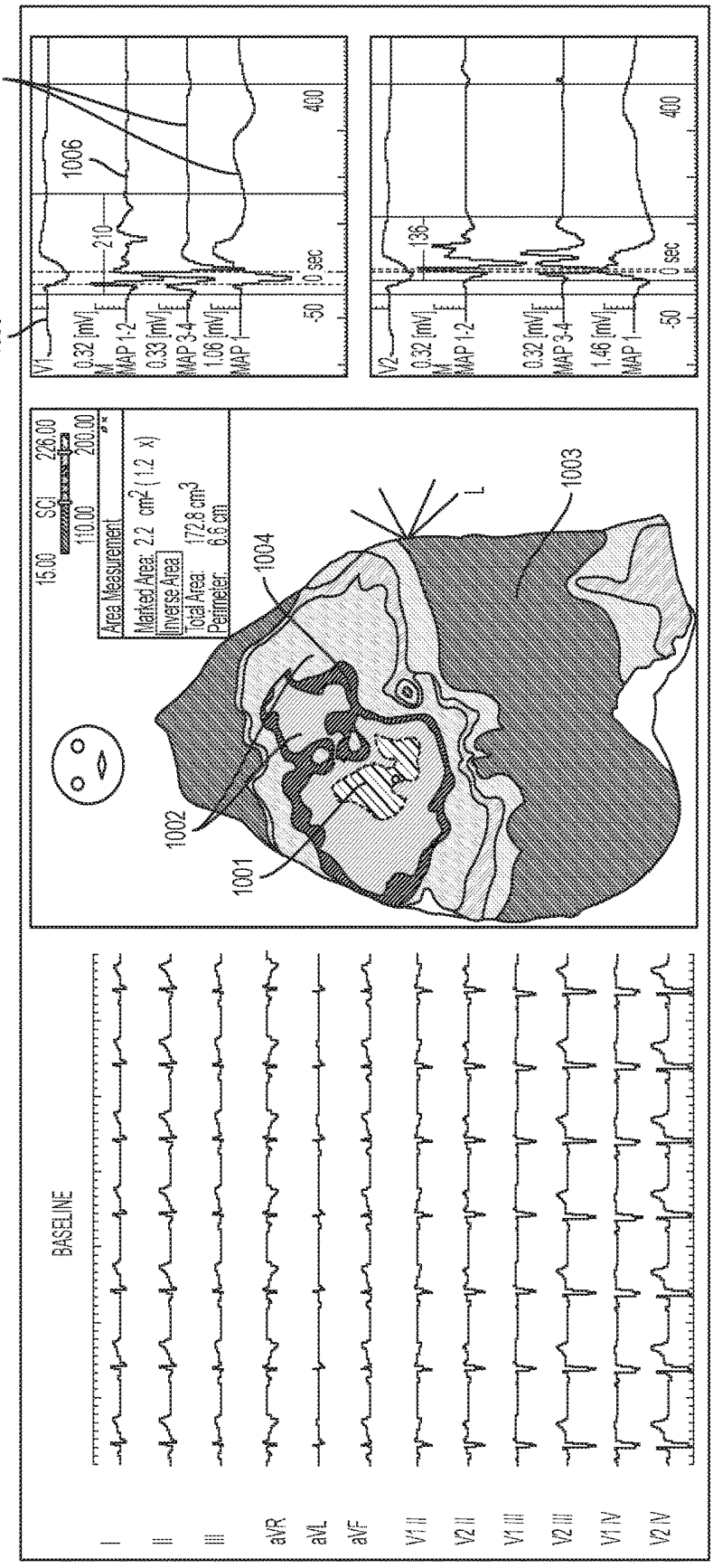

1007
1005
1006
1004
1003
1002
1001
BASELINE
I
II
III
aVR
aVL
aVF
V1 II
V2 II
V1 III
V2 III
V1 IV
V2 IV
Area Measurement
Marked Area: 2.2 cm² (1.2 x)
Inverse Area
Total Area: 172.8 cm³
Perimeter: 6.6 cm
15.00 SCI 226.00
110.00 200.00
V1
V2
MAP 1-2
MAP 3-4
MAP 1
0.32 [mV]
0.33 [mV]
1.06 [mV]
1.46 [mV]
210
136
400
-50
10 sec
0 sec
L

FIG. 10A

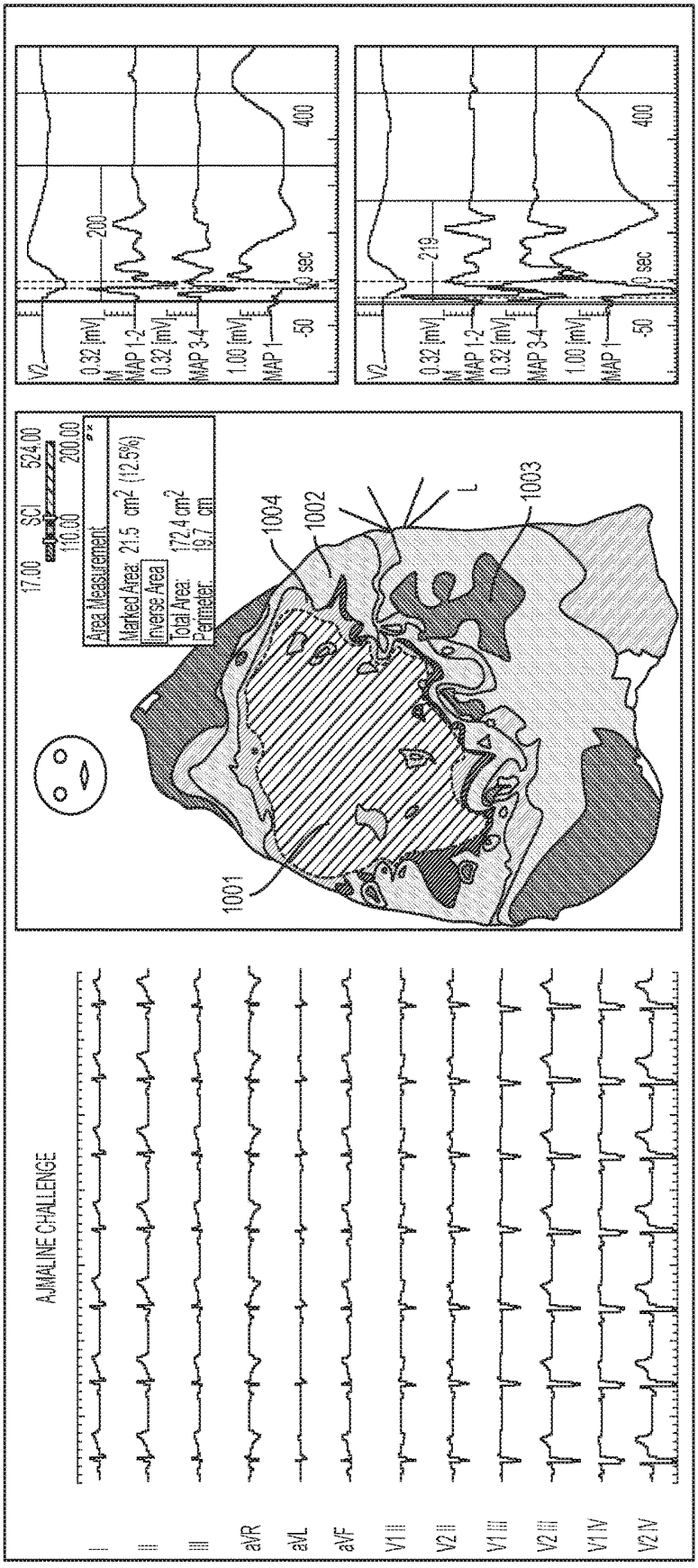

AJMALINE CHALLENGE
I
II
III
aVR
aVL
aVF
V1 III
V2 II
V1 III
V2 III
V1 IV
V2 IV
17.00
SCI
524.00
110.00
200.00
Area Measurement
Marked Area: 21.5 cm² (12.5%)
Inverse Area
Total Area: 172.4 cm²
Perimeter: 19.7 cm
1001
1002
1003
1004
L
V2
0.32 [mV]
MAP 1-2
MAP 3-4
MAP 1
200
219
400
-50
0 sec

FIG. 10B

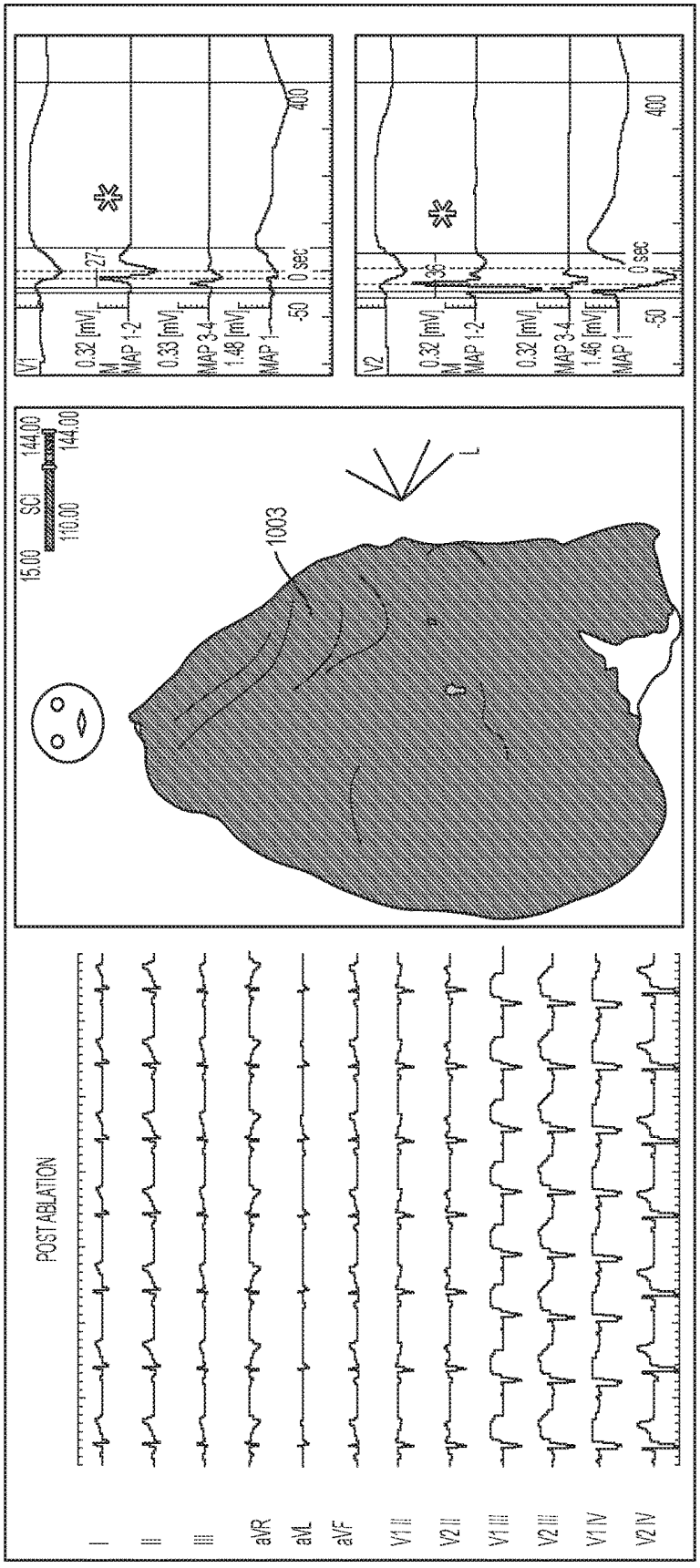

POST ABLATION
I
II
III
aVR
aVL
aVF
V1 II
V2 II
V1 III
V2 III
V1 IV
V2 IV
15.00 SCI 144.00
110.00 144.00
1003
L
V1
0.32 [mV]
MAP 1-2
0.33 [mV]
MAP 3-4
1.46 [mV]
MAP 1
-50
400
0 sec
V2
0.32 [mV]
MAP 1-2
0.32 [mV]
MAP 3-4
1.46 [mV]
MAP 1
-50
400
0 sec

FIG. 10C

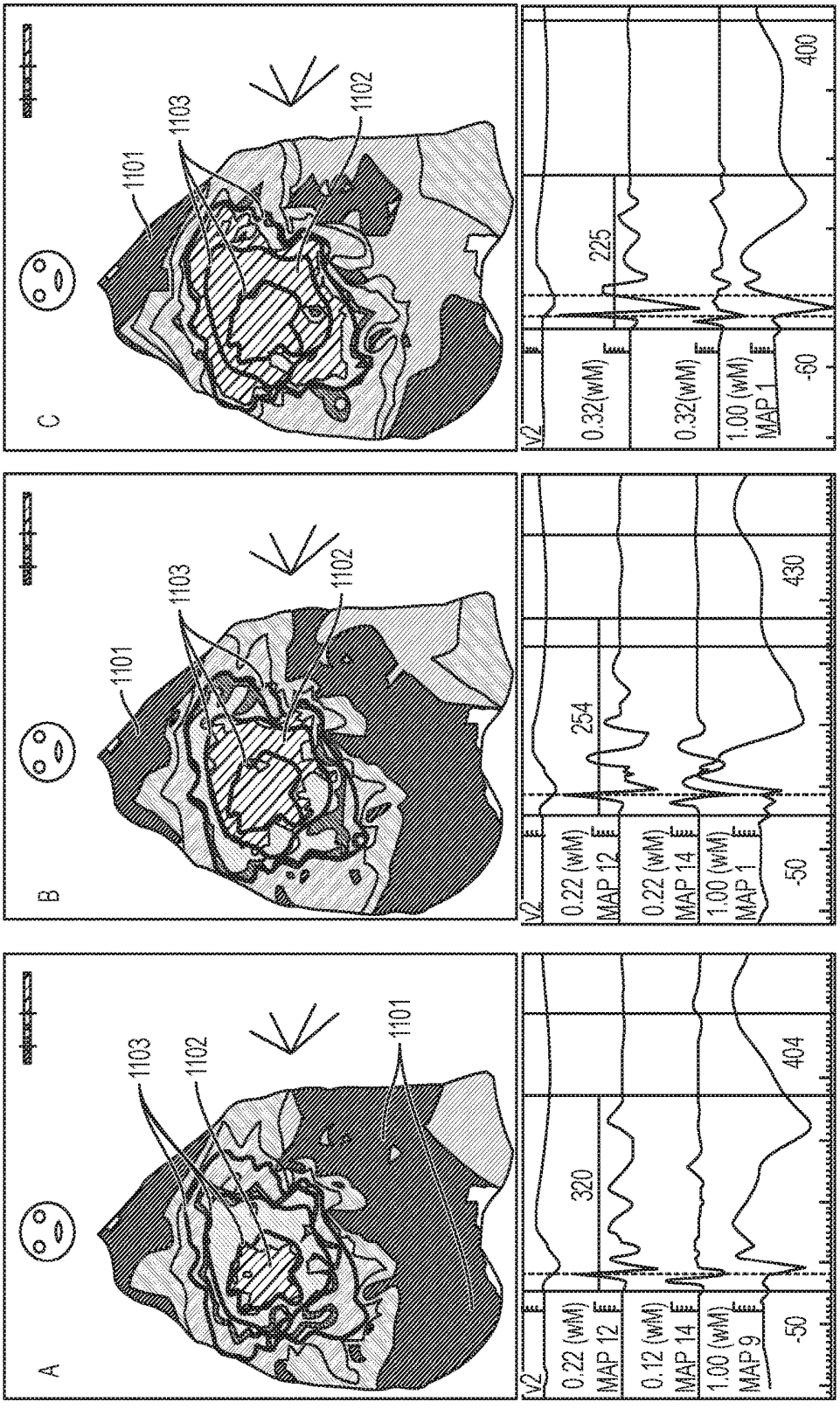

A
1103
1102
1101
V2
0.22 (wM)
MAP 12
320
0.12 (wM)
MAP 14
1.00 (wM)
MAP 9
404
-50
B
1101
1103
1102
V2
0.22 (wM)
MAP 12
254
0.22 (wM)
MAP 14
1.00 (wM)
MAP 1
430
-50
C
1101
1103
1102
V2
0.32(wM)
225
0.32(wM)
1.00 (wM)
MAP 1
400
-60

FIG. 11

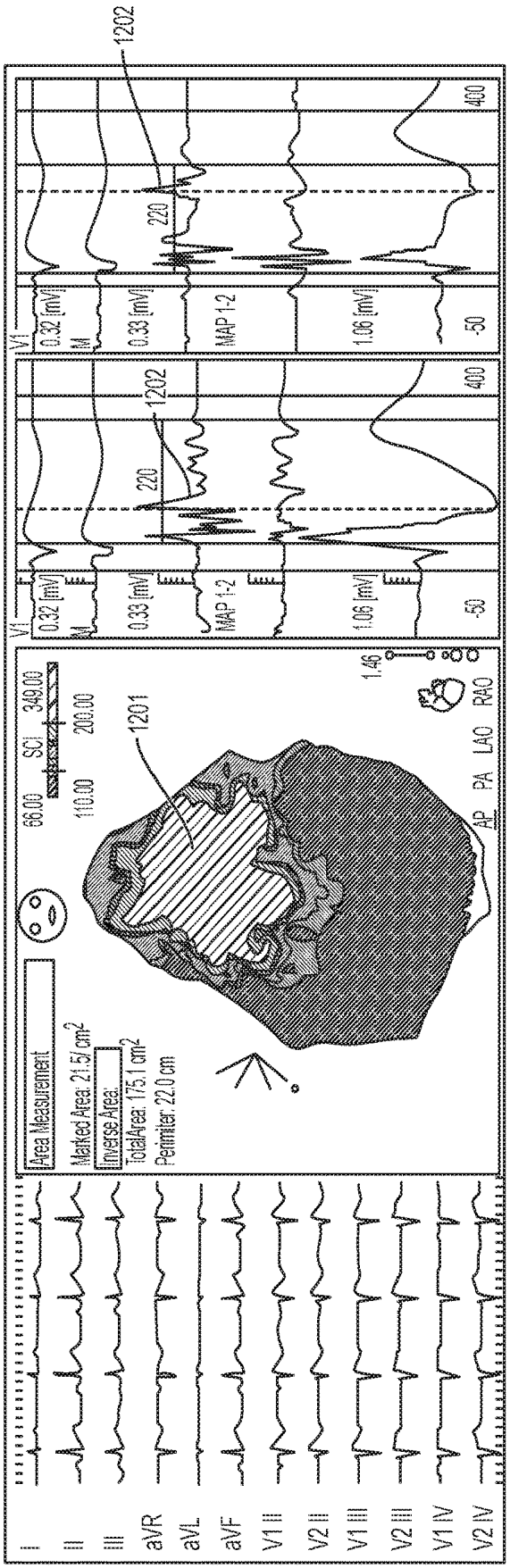

1202
1201
Area Measurement
Marked Area: 21.5 cm2
Inverse Area:
TotalArea: 175.1 cm2
Perimiter: 22.0 cm
66.00
SCI
349.00
110.00
200.00
0.32 [mV]
0.33 [mV]
MAP 1-2
1.06 [mV]
220
400
-50
1.46
AP
PA
LAO
RAO
I
II
III
aVR
aVL
aVF
V1 III
V2 II
V1 III
V2 III
V1 IV
V2 IV

FIG. 12

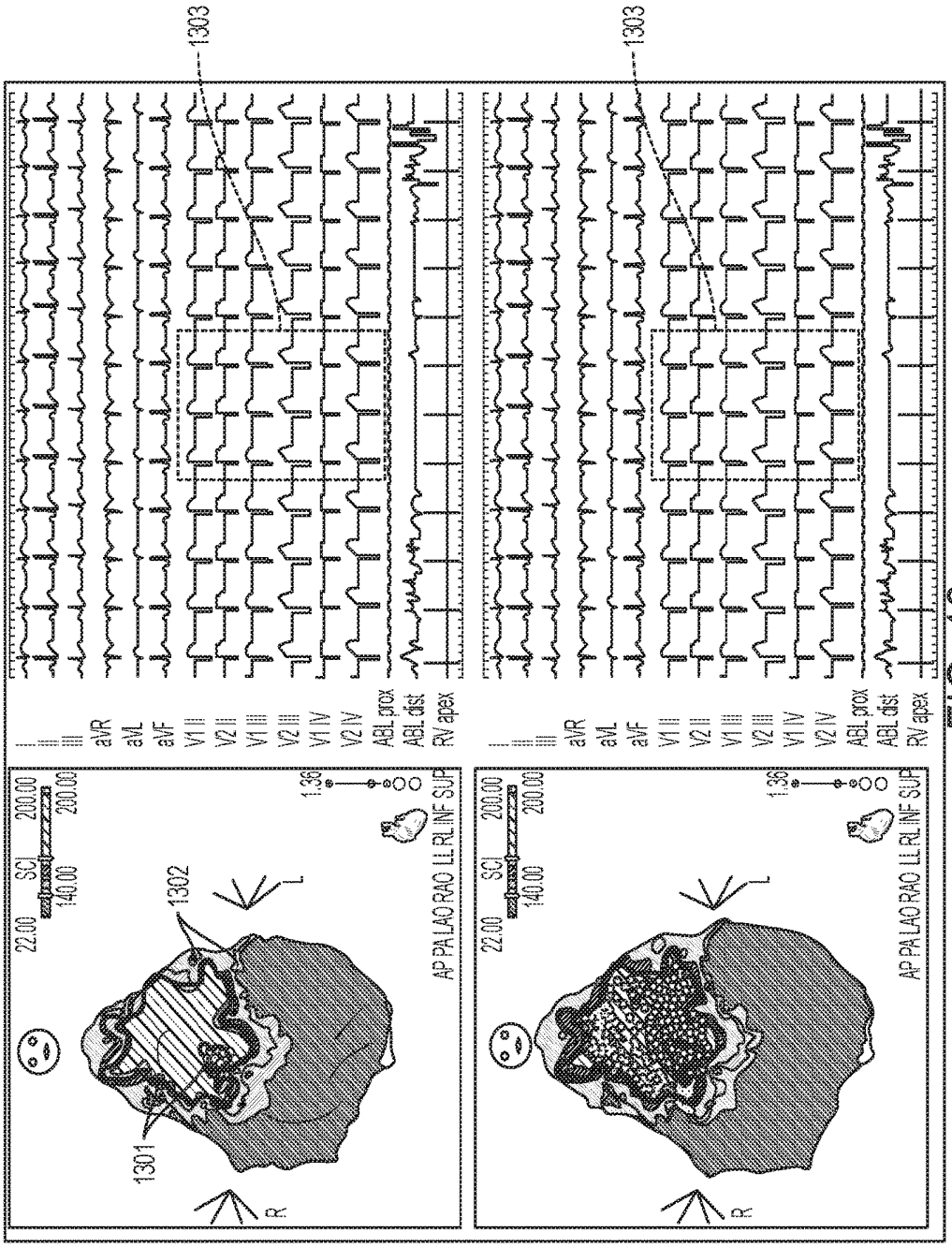

1303
1303
I
II
III
aVR
aVL
aVF
V1 II
V2 II
V1 III
V2 III
V1 IV
V2 IV
ABL prox
ABL dist
RV apex
22.00
SCI
200.00
140.00
200.00
1.36
1302
1301
L
R
AP PA LAO RAO LL RL INF SUP

FIG. 13

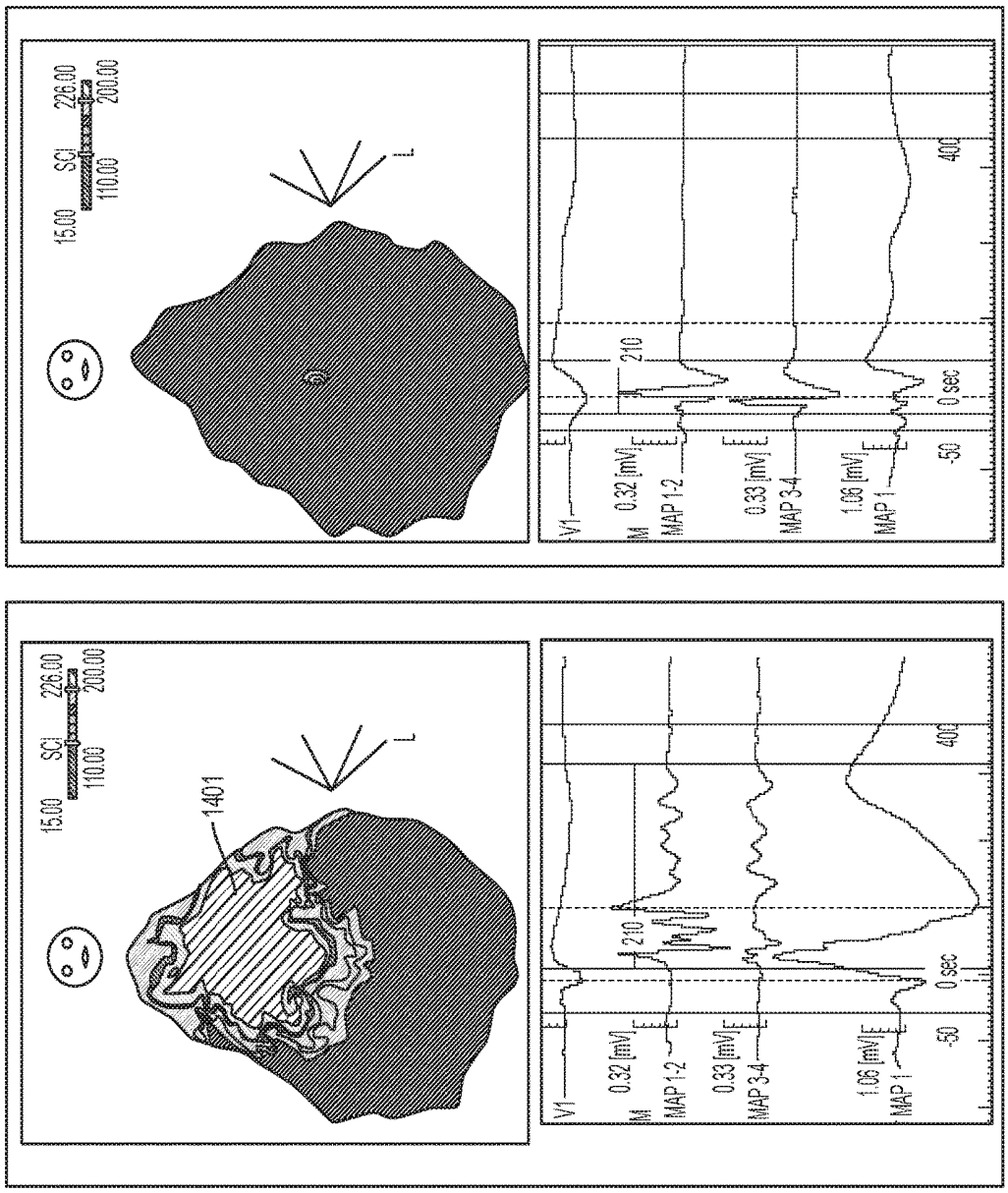

15.00
SCI
110.00
226.00
200.00
L
1401
V1
0.32 [mV]
MAP 1-2
0.33 [mV]
MAP 3-4
1.06 [mV]
MAP 1
210
400
0 sec
-50

FIG. 14

FIGURE 15

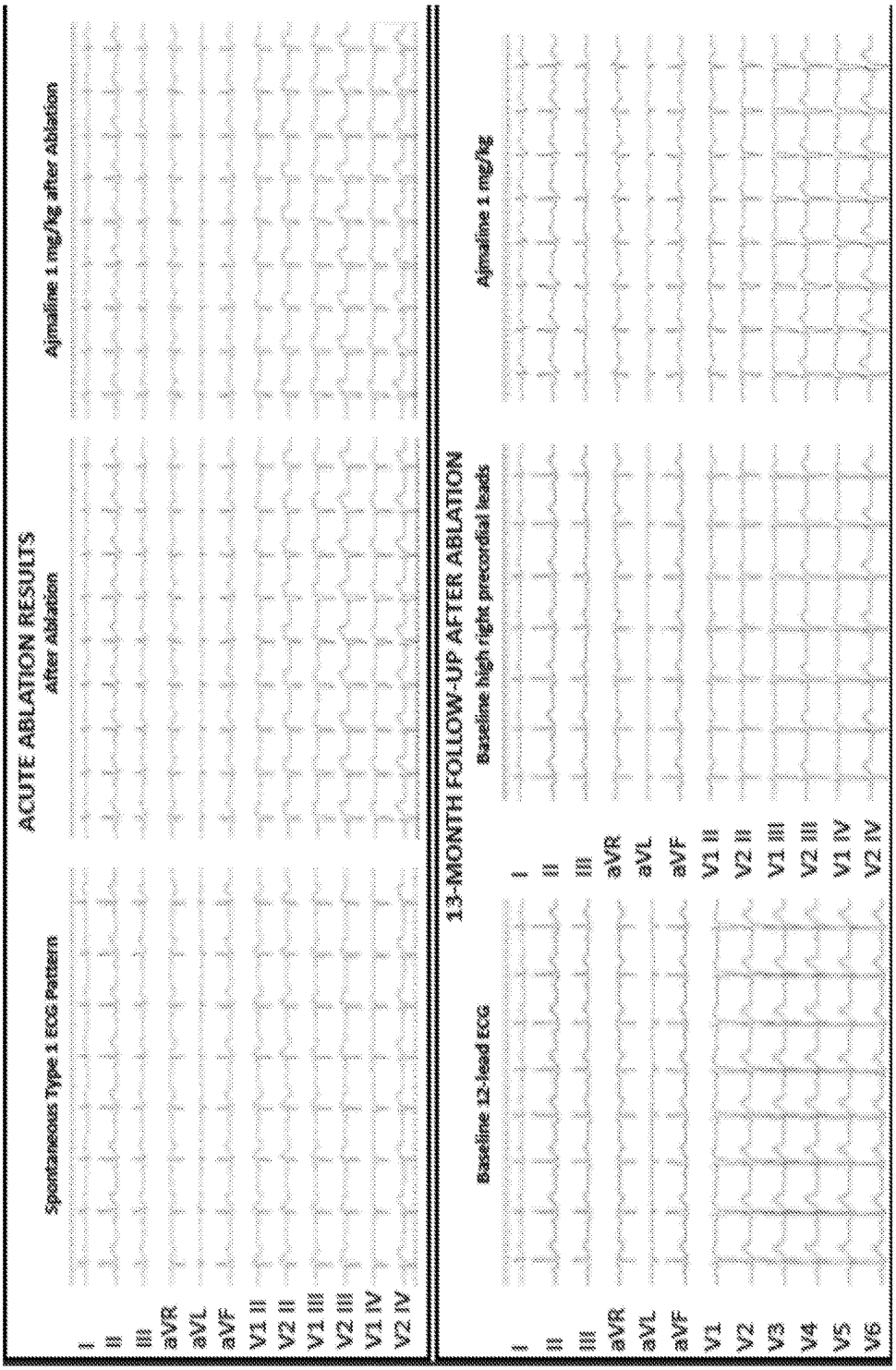

Spontaneous Type 1 ECG Pattern
ACUTE ABLATION RESULTS
After Ablation
Ajmaline 1 mg/kg after Ablation
I
II
III
aVR
aVL
aVF
V1 II
V2 II
V1 III
V2 III
V1 IV
V2 IV
13-MONTH FOLLOW-UP AFTER ABLATION
Baseline 12-lead ECG
Baseline high right precordial leads
Ajmaline 1 mg/kg
I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6
V1 II
V2 II
V1 III
V2 III
V1 IV
V2 IV

FIGURE 16

Electrophysiological characteristics of study population according to the clinical presentation

Characteristics	Group 1		Group 2 (N=72)	P-Value*	
	*Worst (N=38)	*Not worst (N=24)			
Baseline abnormal area, cm²				0.013	
Median	8.0	7.0	4.6		a vs b P=0.234
IQR	5.4-12.3	3.6-11.4	2.5-9.4		a vs c P=0.004
Min-Max	0.5-58.6	0-23.9	0-17.4		b vs c P=0.229
Abnormal area after ajmaline, cm²					
<200 ms				0.001	
Median	20.0	19.2	15.7		a vs b P=0.692
IQR	17.9-22.4	14.4-28.1	13.0-19.1		a vs c P<0.001
Min-Max	9.3-64.2	11.9-36.6	5-51		b vs c P=0.033
<250 ms				0.004	
Median	10.0	9.2	7.3		a vs b P=0.373
IQR	7.3-11.3	5.6-11.9	3.2-9.1		a vs c P=0.001
Min-Max	4.5-31.0	2.5-16.9	1-23.5		b vs c P=0.143
<280 ms				<0.001	
Median	6.5	5.2	4.8		a vs b P=0.337
IQR	4.7-7.3	4.3-7.2	2.9-5.6		a vs c P<0.001
Min-Max	1.9-22.1	0.6-12.3	0.4-12.3		b vs c P=0.028
Baseline potential duration, ms				0.003	
Median	230	185	177		a vs b P=0.031
IQR	192-284	157-227	150-226		a vs c P=0.001
Min-Max	129-310	124-310	123-323		b vs c P=0.408
Potential duration after ajmaline, ms				0.003	
Median	330	310	300		a vs b P=0.061
IQR	310-333	280-330	260-330		a vs c P<0.001
Min-Max	219-423	226-405	219-400		b vs c P=0.372
Baseline local activation time, ms				0.132	
Median	71	66	73		
IQR	64-76	62-76	64-81		
Min-Max	59-84	53-83	53-89		
Local activation time after ajmaline, ms				0.126	
Median	82	78	83		
IQR	75-89	74-89	77-94		
Min-Max	70-96	68-93	68-103		
Baseline low-voltage area, cm²				<0.001	
Median	1	0	0		a vs b P=<0.001
IQR	0-7	0-0	0-0		a vs c P=<0.001
Min-Max	0-13	0-1	0-2		b vs c P=0.614
Low-voltage area after ajmaline, cm²				<0.001	
Median	2	0	0		a vs b P=<0.001
IQR	0-12	1-0	0-0		a vs c P=<0.001
Min-Max	0-21	0-2	0-4		b vs c P=0.392

*By Kruskal-Wallis H Test with Dunn's test for multiple comparisons

FIGURE 17

Clinical Characteristics of the Study Patients according to clinical presentation

Characteristics	Group 1		Group 2	P-Value
	Worst (N=39)	Not worst (N=24)	(N=72)	
Male sex — no. (%)	29 (74.4)	18 (75.0)	59 (81.9)	0.584
Age — yr				0.974*
Mean±SD	39.9±11.4	39.3±9.7	39.6±11.7	
Min-Max	22-63	21-59	18-71	
BrS-ECG pattern — no. (%)				0.833
Type 1	8 (20.5)	7 (29.2)	16 (22.2)	
Type 2	15 (38.5)	7 (25.0)	26 (36.1)	
Type 3	16 (41.0)	11 (45.8)	30 (41.7)	
Family history of SD — no. (%)	6 (15.4)	6 (25.0)	15 (20.8)	0.630
Probands — no. (%)	9 (23.1)	5 (20.8)	8 (11.1)	0.213
Relatives — no. (%)	4 (10.3)	2 (8.3)	12 (16.7)	0.465
Positive SCN5A — no. (%)	12 (30.8)	7 (29.2)	13 (18.1)	0.254
Pre-RFA ICD therapy — no. (%)	27 (69.2)	4 (16.7)	1 (1.4)	<0.001
Post-RFA ICD therapy — no. (%)	2 (5.1)	0 (0)	0 (0)	0.112
Follow-up — months				0.188†
Median	10	12	9	
IQR	7-12	8-12	7-11.8	
Min-Max	3-13	5-13	3-13	

*By one-way ANOVA
†By Kruskal-Wallis H Test

ANALYZING AND MAPPING ECG SIGNALS AND DETERMINING ABLATION POINTS TO ELIMINATE BRUGADA SYNDROME

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application incorporates by reference as if fully set forth Attorney Docket No. JNJ-BI05744USNP titled "A Method And System For Eliminating A Broad Range Of Cardiac Conditions By Analyzing Intracardiac Signals, Providing A Detailed Map And Determining Potential Ablation Points" filed on the same date as the present application. This application claims benefit of U.S. Provisional Application No. 62/450,388, filed on Jan. 25, 2017, which is incorporated by reference as if fully set forth.

SUMMARY

[0002] There is provided according to embodiments of a system and method that enables improved analysis of electrocardiography (ECG) signals to eliminate Brugada syndrome. (BrS) The system and method can create a potential duration map (PDM) by automatically measuring duration of signals and annotating ventricular eletrogram (EGM) duration from onset to offset.

[0003] The method of Brugada syndrome epicardial ablation may comprise preparing an endocardial duration map, preparing a baseline epicardial duration map comprising at least one or more areas of delimination, and when some of the areas of delimination are greater than 200 ms, performing epicardial ablation of the areas of delimination greater than 200 ms. The method may further comprise preparing an updated epicardial duration map after performing epicardial ablation, and determining whether or not a BrS pattern appears in the updated epicardial duration map; and when the BrS pattern appears, performing epicardial ablation. The method may further comprise preparing an updated epicardial duration map after performing epicardial ablation, and determining whether or not an abnormal EGM exists in the updated epicardial duration map; and when the abnormal EGM exists, performing epicardial ablation. The method may further comprise preparing an updated epicardial map comprising maintaining anatomical volume data and adding electroanatomical data. The method may further comprise the baseline epicardial duration map, and the updated epicardial map displaying concentric areas having cut-off intervals. The method may further comprise, in the step of preparing a baseline epicardial duration map, defining a window of interest (WOI) comprising at least a cycle length, calculating previous heart beats based on the cycle length and reference annotation, assigning the heart beats within the cycle length of the WOI to the WOI, finding a start potential duration and an end potential duration, and selecting an ablation point based on a heart beat having a minimum standard deviation from the heart beats assigned to the WOI.

[0004] The system for Brugada syndrome epicardial ablation in a heart may comprise a catheter for measuring ECG signals, a computer adapted to: prepare an endocardial duration map; prepare a baseline epicardial duration map comprising at least one or more areas of delimination; and when one or more of the areas of delimination are greater than 200 ms, performing epicardial ablation of the areas of delimination greater than 200 ms; and a display device for displaying the endocardial duration map and the baseline epicardial map. The computer in the system may further be adapted to prepare an updated epicardial duration map after performing epicardial ablation, and determine whether or not a BrS pattern appears in the updated epicardial duration map, and when the BrS pattern appears, perform epicardial ablation. The computer in the system may further be adapted to prepare an updated epicardial duration map after performing epicardial ablation, and determine whether or not an abnormal EGM exists in the updated epicardial duration map, and when the abnormal EGM exists, perform epicardial ablation. The system may further comprise a tool for injecting ajamline into the heart. The computer in the system may further be adapted to prepare an updated epicardial map after performing epicardial ablation, comprising maintaining anatomical volume data and adding electroanatomical data. The computer in the system may further be adapted to display concentric areas having cut-off intervals on the baseline epicardial duration map and the updated epicardial map. The computer in the system may further be adapted to prepare the baseline epicardial duration map by performing steps of defining a WOI comprising at least a cycle length, calculating previous heart beats based on the cycle length and reference annotation, assigning the heart beats within the cycle length of the WOI to the WOI, finding a start potential duration and an end potential duration, and selecting an ablation point based on a heart beat having a minimum standard deviation from the heart beats assigned to the WOI.

[0005] A computer program product for Brugada syndrome epicardial ablation is also presented.

[0006] These and other objects, features and advantages of the present invention will be apparent from the following detailed description of illustrative embodiments thereof, which is to be read in connection with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0007] For a better understanding of the present invention, reference is made to the detailed description of the invention, by way of example, which is to be read in conjunction with the following drawings, wherein like elements are given like reference numerals.

[0008] FIG. **1** shows a Potential Duration Map (PDM).

[0009] FIG. **2** is a flow diagram of an example method in an embodiment.

[0010] FIGS. **3**A, **3**B, **3**C show Brugada syndrome concentric substrate distribution.

[0011] FIGS. **4**A, **4**B show a PDM before and after radiofrequency ablation.

[0012] FIG. **5** shows a calculation of potential duration.

[0013] FIG. **6** shows changes in BS ECG signal.

[0014] FIG. **7** is a work flow diagram of Brugada syndrome epicardial ablation in one embodiment.

[0015] FIG. **8** shows an example mapping system for real-time mapping of cardiac ablation in accordance with an embodiment, in which the inventive technique is used.

[0016] FIG. **9** is a block diagram illustrating example components of a medical system in one embodiment.

[0017] FIGS. **10**A, **10**B, **10**C illustrate test results for one example patient.

[0018] FIG. **11** illustrates additional test results for one patient.

[0019] FIG. **12** shows a spontaneous type 1 Brugada pattern for one patient.

[0020] FIG. **13** shows RF ablation in spontaneous type 1 Brugada pattern for one patient.

[0021] FIG. **14** shows a PDM before and after RF ablation for an example patient.

[0022] FIG. **15** shows ECG changes for the example patient.

[0023] FIG. **16** shows a table of ablation results for the example patient.

[0024] FIG. **17** shows a table of electrophysiological characteristics of study population.

DETAILED DESCRIPTION OF THE INVENTION

[0025] Brugada syndrome (BrS) is an ECG abnormality with a high incidence of sudden death in patients with structurally normal hearts. This syndrome or disorder is characterized by sudden death associated with one of several ECG patterns characterized by incomplete right bundle-branch block and ST-segment elevations in the anterior precordial leads.

[0026] BrS is a genetically determined disease predisposing to sudden cardiac death due to ventricular malignant arrhythmias. A first aspect of the present system and method is treating Brugada syndrome by analyzing the EGM signals, determining the ablation points, and manually editing the calipers on the mapping catheter to set the duration. A second aspect of the present system is an example method, presented below, which enables visualization of the abnormal substrate according to the EGMs' duration found on the epicardial layer of BrS patients.

[0027] FIG. **1** shows a Potential Duration Map (PDM) (e.g., RV epicarial Map), in the center, a selected point viewer in the left column, and Paso viewer in the right column. The PDM uses a scale of Shortex Complex Interval (SCI) which ranges from 15.0 ms to 171.0 ms. The PDM is created using the present system to measure the Potential Duration for each point that the EGM automatically creates in accordance with the mapping method. The EGM shown in FIG. **1**, left side, includes MAP**1-2** and MAP**3-4**, each having peaks **101** that indicate changes in direction of the tracings of the mapping catheter.

[0028] The example method is performed to visualize the abnormal substrate according to the EGMs duration found on the epicardial layer of BrS patients. Using, for example, the Complex Fractionated Atrial Electrograms (CFAE) module of the CARTO®3 system (Biosense Webster), for each electroanatomical acquired point, two calipers are manually moved by placing the first on the onset and the second on the offset of the EGM recorded. Note that CFAE performs calculations using the fragmentation in Bipolar EGM signal in the acquired point. The fragmentation is marked as interval duration with left and right borders. The present method results in the exact measurement of the ventricular EGM duration, enabling the creation of a PDM that may comprise a coded mapping, such as a color-coded map (color shown using different hatching patterns), showing different degrees of prolongation. The appropriate characterization of the abnormal substrate along with the localization of such EGMs helps to establish the appropriate target for catheter ablation in order to achieve a successful procedure, and the PDM enables such characterization.

[0029] As shown in FIG. **1**, the present system can be used to automatically annotate and measure EGM signals (as shown in the left panel) to create the PDM for Brugada syndrome elimination by ablation. This system uses an annotation technique to improve conventional software, such as CARTO®3, by automating the process of detecting where to ablate.

[0030] FIG. **2** is a flow diagram of an example method for automatically determining ablation points in Brugada syndrome is presented. As shown in FIG. **2**, the method is performed as follows.

[0031] In step **5201**, a Window Of Interest (WOI) is defined, the WOI being the interval in the EGM and/or ECG which is normally used to calculate the voltage amplitude (peak to peak mV) and the signal duration. An example EGM is shown in FIG. **1**.

[0032] In step S**202**, at least two previous heart beats are calculated based on cycle length and reference annotation, and a WOI is assigned for two of the heart beats. Note that each electroanatomical acquired point (e.g., point EGM) contains data to be used for coloring the Map according to Map Type, such as PDM, CFAE, LAT, Bipolar Voltage etc. Example maps are shown in FIGS. **10-14**, (described hereinafter). In one acquired point, for example, a window equal to 2500 ms of ECG and EGM is recorded. For example, if the reference annotation for a heart beat lays at 2000 ms, the first WOI [−50 ms, 350 ms] goes from 2000 ms−50 ms (e.g., 1950 ms) to 2000 ms+350 ms (e.g., 2350 ms). If the heart beat cycle length is 800 ms, there is more than one heart beat in the 2500 ms WOI. The previous heart beat reference lays at 1200 ms (2000 ms−800 ms [e.g., 1200 ms]) and the WOI will be from 1200 ms−0 ms (e.g., 1150 ms) to 1200 ms+350 ms (e.g., 1550 ms). It should be noted that the abovementioned time intervals have been used by way of example and should not be considered as limiting.

[0033] Next, for each WOI of each heart beat, the Potential Duration is calculated as shown in steps S**203-211**, as follows.

[0034] In step S**203**, the peaks are calculated based on a predetermined threshold in WOI and a list of peaks in WOI are created. The EGM signal values are measured in mV, and, in one example, a peak with mV value greater than 0.05 mV is marked. However, it should be noted that the peak threshold may be set by the physician.

[0035] In step S**204**, Potential Duration Start (PD-Start) is defined by checking from the beginning of the WOI, as shown in steps S**205**-S**207** as follows.

[0036] In step S**205**, it is determined whether or not two consecutive peaks have the same sign and the same peaks absolute values are less than 2*Min.

[0037] In step S**206**, if S**205**=YES (two consecutive peaks have the same sign and the absolute value of the consecutive peaks is less than 2*Min), the current peak is set as the second peak, the next peak is obtained and the method returns to step S**205**.

[0038] In step S**207**, if S**205**=NO (two consecutive peaks do not have the same sign and/or the absolute value of the consecutive peaks is greater than or equal to 2*Min), the start of the slope before the current peak is found and marked it as Start potential duration.

[0039] In step S**208**, Potential Duration End (PD-END) is defined, checking from the ending of the WOI, as shown in steps S**209**-S**210** as follows.

[0040] In step S**209**, it is determined whether or not two consecutive peaks' distance is greater than 120 ms.

[0041] In step S**210**, if S**209**=YES (two consecutive peaks are greater than 120 ms), the start of PD-End portion is marked as the peak with minimum time of the two consecutive peaks and the method returns to step S**209**.

[0042] In step S**211**, if S**209**=NO (two consecutive peaks do not have distance greater than 120 ms), then in step S**211**, it is determined whether two consecutive peaks have the same sign and the peaks' absolute values are less than 2*Min Threshold, whether the time between two consecutive peaks is greater than 120 ms or whether the time between two consecutive peaks is less than 25 ms.

[0043] Keeping in mind that the stability and reproducibility of the duration of the potential can be a crucial factor, in one embodiment, the present technique can consider another factor; the technique can verify, in the presence of a double or late potential, that the late activity is also present in all the beats included in the 2500 ms recording window.

[0044] In step S**212**, if S**211**=YES (two consecutive peaks have the same sign and the peaks' absolute values are less than 2*Min, the time between two consecutive peaks is greater than 120 ms or the time between two consecutive peaks is less than 25 ms), the next peak is obtained with minimum time, and the method returns to step S**211**.

[0045] In step S**213**, if S**211**=NO (two consecutive peaks do not have the same sign, the peaks absolute values are equal to or greater than 2*Min or the time between two consecutive peaks is less than or equal to than 120 ms or the time between two consecutive peaks is greater than or equal to 25 ms), the start of the slope after the current peak is found and marked as End Potential Duration.

[0046] In step S**214**, the Potential Duration value is calculated as the difference between potential duration Start and potential duration End in ms.

[0047] In step S**215**, the selected point potential duration value is set as the heart beat which has the minimum standard deviation of the positions on each heart beat WOI. Note that the area measurement between the BS ECG IS when inducing the BrS and the BS ECG IS after treating the BrS can provide the indication of when to stop the procedure.

[0048] In accordance with the PDM and the analysis described above, any EGM showing a duration ≥200 ms may be considered abnormal, and thus represents a target for catheter ablation. Three different concentric areas are identified according to the degree of prolongation by setting different cut-off intervals, for example, ≥300 ms, ≥250 ms and ≥200 ms, respectively. The different cut-offs are necessary to guide the ablation procedure, starting from the small "core" of the substrate (area showing EGM duration ≥300 ms) and subsequently moving to the larger regions having potential duration ≥250 ms and ≥200 ms, respectively, as shown in FIGS. **3**A, **3**B and **3**C, described in more detail below.

[0049] The inventive technique may enable the elimination of all delayed and prolonged EGM activities located in the abovementioned regions. Class IC drug challenge is performed at the end of ablation in order to ensure successful abolition of all abnormal potentials and stable BrS-ECG pattern elimination. In cases of BrS-ECG pattern reappearance after drug challenge, the epicardial PDM is a remap of the epicardial using PDM to identify target locations with PDM bigger than 200 ms for ablation. This is repeated to identify any residual or additional abnormal signals for further RF applications in order to completely normalize the ECG pattern. The final end-point, e.g., ablation point, is obtained by the elimination and the non-inducibility of the BrS ECG pattern proved by the Class IC drug test and the abolition, using RF catheter ablation, of any prolonged and fragmented potential identified during the mapping procedure.

[0050] FIGS. **3**A, **3**B and **3**C show Brugada Syndrome concentric substrate distribution, that is, each of these figures show an epicardial PDM after Class IC drug-challenge. The maps are reconstructed by collecting the duration of each bipolar EGM. The color-code (shown as different hatching patterns) ranges from red **301** to purple **305**, where red **301** is showing regions exhibiting less than 110 ms duration. Purple **305** is representing areas with longer EGM duration (≥300 ms in FIG. **3**A, ≥250 ms in FIG. **3**B and ≥200 ms in FIG. **3**C). Additional colors (not shown) represent areas >110 ms to 300 ms. According to the different cut-off applied, a concentric distribution is shown, where the longest potentials (≥300 ms duration) are located in the inner circle (FIG. **3**A), whilst the relatively shorter ones, but still ≥200 ms, are in the outer circle (FIG. **3**C). The regions showing longer potential duration have different dimensions (≥300 area is 5.9 cm^2, ≥250 area is 14.7 cm^2 and ≥200 ms area is 27.6 cm^2, respectively). Below each map in FIGS. **3**A, **3**B, **3**C, an example of the EGM recorded in the purple **305** area when the coved-type pattern occurs after ajmaline test is shown (EGMs of 322 ms, 255 ms and 230 ms duration in each panel of FIG. **3**A, **3**B, **3**C, respectively).

[0051] The QRS complex is a name for the combination of three of the graphical deflections seen on a typical electrocardiogram, e.g., EGM or ECG. QRS is usually the central and most visually obvious part of the tracing. It corresponds to the depolarization of the right and left ventricles of the human heart. In adults, deflections normally last 0.06-0.10 seconds; in children and during physical activity, it may be shorter. The Q, R, and S waves occur in rapid succession, do not all appear in all leads, and reflect a single event, and thus are usually considered together. A Q wave is any downward deflection after the P wave. An R wave follows as an upward deflection, and the S wave is any downward deflection after the R wave. The T wave follows the S wave, and in some cases an additional U wave follows the T wave. The late activity is extended after the QRS termination and it is characterized by a fragmented and discrete late component. QRS represents simultaneous activation of the right and left ventricle.

[0052] In each EGM panel shown in the lower portion of FIGS. **3**A, **3**B and **3**C, V1 ECG lead, distal, proximal bipolar and unipolar signals are shown at 200 mm/sec speed, from top to bottom, respectively.

[0053] The technique described herein will improve the existing process of manual measurements for duration map construction. The physician will no longer need to manually move and measure the two duration calipers for each point taken during duration map reconstruction. By using the present method to calculate each acquired point potential duration, the system can automatically annotate the ventricular EGMs duration from the onset to its offset, and automatically measure signals duration to create the PDM for Brugada syndrome substrate characterization.

[0054] Moreover, the process of prolonged EGMs detection and their quantification in terms of potential duration is

enhanced by the present technique. This approach creates PDM with objective annotation, correctly identifying the adequate ablation target areas. The system automatically acquires bipolar and potential duration information by an ablation and/or multielectrode mapping (MEM) catheter to speed up the procedure. The method can be performed on two heart beats on the 2.5 seconds of the mapping bipolar signal of the acquired point, and the potential duration on the heart beat with the best positions stability can be selected. This enables positions stability to be considered in calculating potential duration, which cannot be done manually.

[0055] FIGS. **4**A and **4**B show a PDM before and after RF ablation. FIG. **4**A top shows the PDM before ablation, while FIG. **4**A bottom shows an example of prolonged and fragmented potential found in the purple area **305** (distal bipolar EGM 255 ms duration "DP-EMG"). After ablation, FIG. **4**B top shows the PDM with the disappearance of abnormally prolonged EGMs, highlighting that the late component (activation after the QRS—peaks above 0.05 mV where Potential duration is bigger than 200 ms) has been abolished (EGMs duration of 143 ms; FIG. **4**B bottom). The asterisk in FIG. **4**B bottom indicates the disappearance of the late components that had been recorded prior to ablation. The EGM showed in FIG. **4**B has been registered in the same region that was previously exhibiting the prolonged and fragmented potential, illustrated in FIG. **4**A. In each EGM panel, V1 II ICS ECG lead, distal, proximal bipolar, and unipolar signals recorded are shown from top to bottom, respectively. Of note, in FIG. **4**A bottom, the V1 lead is showing a typical coved-type pattern, whereas in FIG. **4**B bottom, the same ECG lead is demonstrating that the BrS pattern has been modified, showing a horizontal and flat ST-segment elevation after ablation.

[0056] FIG. **5** shows a calculation of Potential Duration which is marked by the two vertical lines or borders, R**1** and R**2**. These borders indicate WOI[−50,400] from 2000 ms−50 ms (1950 ms) to 2000 ms+400 ms (2400 ms). As shown, the Potential Duration is greater than 200 ms. Around the dotted vertical line is the QRS; the late component appears in the right part of the Potential Duration marked with the two borders R**1** and R**2**.

[0057] FIG. **6** shows changes in BS ECG signal, that is, the changes of the BS ECG Signals **601** when the BrS is induced, and the BS ECG Signals **602** after treating the BrS with ablation. Accordingly, ECG **602** refers to end of class IC drug injection and ECG **601** refers to end of RF ablation.

[0058] FIG. **7** is a work flow diagram of Brugada syndrome epicardial ablation. In step S**701**, endocardial bipolar/duration RV mapping is performed. In step S**702**, epicardial bipolar/duration mapping is performed, creating a baseline PDM as shown, for example, in FIG. **1**. In step S**703**, an ajmaline infusion is administered and an ajmaline test is performed. In step S**704**, an updated epicardial duration map, which maintains the FAM (anatomical volume) data and adds electro-anatomical data is produced. In step S**705**, it is determined whether or not there are areas of delimination, that is, areas in which the duration of potentials exceed a threshold amount, for example, a threshold greater than 200 ms. If so (S**705**=YES), in step S**806** catheter ablation of the area(s) of delimination is performed. In step S**707**, the ajmaline test is repeated; this test had been initially performed in step S**703**.

[0059] In step S**708**, it is determined whether or not the BrS pattern reappears. If the BrS pattern does reappear (S**708**=YES), the procedure continues at step S**704**. If the BrS pattern does not reappear (S**708**=N**0**), at step S**709**, an updated epicardial duration re-map is created. In step S**710**, it is determined whether or not any abnormal EGMs are identified. If there are none (S**710**=NO), the procedure ends.

[0060] If one or more abnormal EGMs are identified (S**710**=YES), at step S**711**, catheter ablation of the new abnormal EGM areas is prepared and the process continues at step S**709**.

[0061] If the areas of delimination are less than or equal to 200 ms (S**805**=NO), then the procedure ends.

[0062] FIG. **8** is an illustration of an example medical system **800** that may be used to generate and display information **52** (e.g., PDM and other maps and anatomical models of a portion of a patient and signal information). Tools, such as tool **22**, can be any tool used for diagnostic or therapeutic treatment, such as for example, a catheter having a plurality of electrodes for mapping electrical potentials in a heart **26** of a patient **28**. Alternatively, tools may be used, mutatis mutandis, for other therapeutic and/or diagnostic purposes of different portions of anatomy, such as in the heart, lungs or other body organs, such as the ear, nose, and throat (ENT). Tools may include, for example, probes, catheters, cutting tools and suction devices.

[0063] An operator **30** may insert the tool **22** into a portion of patient anatomy, such as the vascular system of the patient **28** so that a tip **56** of the tool **22** enters a chamber of the heart **26**. The control console **24** may use magnetic position sensing to determine 3-D position coordinates of the tool (e.g., coordinates of the tip **56**) inside the heart **26**. To determine the position coordinates, a driver circuit **34** in the control console **24** may drive, via connector, **44**, field generators **36** to generate magnetic fields within the anatomy of the patient **28**.

[0064] The field generators **36** include one or more emitter coils (not shown in FIG. **8**), placed at known positions external to the patient **28**, which are configured to generate magnetic fields in a predefined working volume that contains a portion of interest of the patient anatomy. Each of the emitting coils may be driven by a different frequency to emit a constant magnetic field. For example, in the example medical system **800** shown in FIG. **8**, one or more emitter coils can be placed below the torso of the patient **28** and each configured to generate magnetic fields in a predefined working volume that contains the heart **26** of the patient.

[0065] As shown in FIG. **8**, a magnetic field location sensor **38** is disposed at the tip **56** of tool **22**. The magnetic field location sensor **38** generates electrical signals, based on the amplitude and phase of the magnetic fields, indicating the 3-D position coordinates of the tool (e.g., position coordinates of the tip **56**). The electrical signals may be communicated to the control console **24** to determine the position coordinates of the tool. The electrical signals may be communicated to the control console **24** via wire **45**.

[0066] Alternatively, or in addition to wired communication, the electrical signals may be wirelessly communicated to the control console **24**, for example, via a wireless communication interface (not shown) at the tool **22** that may communicate with input/output (I/O) interface **42** in the control console **24**. For example, U.S. Pat. No. 6,266,551, whose disclosure is incorporated herein by reference, describes, inter alia, a wireless catheter, which is not physically connected to signal processing and/or computing apparatus and is incorporated herein by reference. Rather, a

transmitter/receiver is attached to the proximal end of the catheter. The transmitter/receiver communicates with a signal processing and/or computer apparatus using wireless communication methods, such as IR, RF, Bluetooth, or acoustic transmissions. The wireless digital interface and the I/O interface **42** may operate in accordance with any suitable wireless communication standard that is known in the art, such as for example, IR, RF, Bluetooth, one of the IEEE 802.11 family of standards (e.g., Wi-Fi), or the HiperLAN standard.

[0067] Although FIG. **8** shows a single magnetic field location sensor **38** disposed at the tip **56** of tool **22**, tools may include one or more magnetic field location sensors each disposed at any tool portion. The magnetic field location sensor **38** may include one or more miniature coils (not shown). For example, a magnetic field location sensor may include multiple miniature coils oriented along different axes. Alternatively, the magnetic field location sensor may comprise either another type of magnetic sensor or position transducers of other types, such as impedance-based or ultrasonic location sensors.

[0068] The signal processor **40** is configured to process the signals to determine the position coordinates of the tool **22**, including both location and orientation coordinates. The method of position sensing described hereinabove is implemented in the CARTO™ mapping system produced by Biosense Webster Inc., of Diamond Bar, Calif., and is described in detail in the patents and the patent applications cited herein.

[0069] The tool **22** may also include a force sensor **54** contained within the tip **56**. The force sensor **54** may measure a force applied by the tool **22** (e.g., the tip **56** of the tool) to the endocardial tissue of the heart **26** and generate a signal that is sent to the control console **24**. The force sensor **54** may include a magnetic field transmitter and a receiver connected by a spring in the tip **56**, and may generate an indication of the force based on measuring a deflection of the spring. Further details of this sort of probe and force sensor are described in U.S. Patent Application Publications 2009/0093806 and 2009/0138007, whose disclosures are incorporated herein by reference. Alternatively, the tip **56** may include another type of force sensor that may use, for example, fiber optics or impedance measurements.

[0070] The tool **22** may also include an electrode **48** coupled to the tip **56** and configured to function as an impedance-based position transducer. Additionally or alternatively, the electrode **48** may be configured to measure a certain physiological property, for example the local surface electrical potential (e.g., of cardiac tissue) at one or more locations. The electrode **48** may be configured to apply RF energy to ablate endocardial tissue in the heart **26**.

[0071] Although the example medical system **800** may be configured to measure the position of the tool **22** using magnetic-based sensors, other position tracking techniques may be used (e.g., impedance-based sensors). Magnetic position tracking techniques are described, for example, in U.S. Pat. Nos. 5,391,199, 5,443,489, 6,788,967, 6,690,963, 5,558,091, 6,172,499 6,177,792, the disclosures of which are incorporated herein by reference. Impedance-based position tracking techniques are described, for example, in U.S. Pat. Nos. 5,983,126, 6,456,828 and 5,944,022, the disclosures of which are incorporated herein by reference.

[0072] The I/O interface **42** may enable the control console **24** to interact with the tool **22**, the body surface electrodes **46** and any other sensors (not shown). Based on the electrical impulses received from the body surface electrodes **46** and the electrical signals received from the tool **22** via the I/O interface **42** and other components of medical system **900**, the signal processor **40** may determine the location of the tool in a 3-D space and generate the display information **52**, which may be shown on a display **50**.

[0073] The signal processor **40** may be included in a general-purpose computer, with a suitable front end and interface circuits for receiving signals from the tool **22** and controlling the other components of the control console **24**. The signal processor **40** may be programmed, using software, to perform the functions that are described herein. The software may be downloaded to the control console **24** in electronic form, over a network, for example, or it may be provided on non-transitory tangible media, such as optical, magnetic or electronic memory media. Alternatively, some or all of the functions of the signal processor **40** may be performed by dedicated or programmable digital hardware components.

[0074] In the example shown at FIG. **8**, the control console **24** is connected, via cable **44**, to body surface electrodes **46**, each of which are attached to patient **28** using patches (e.g., indicated in FIG. **8** as circles around the electrodes **46**) that adhere to the skin of the patient. Body surface electrodes **46** may include one or more wireless sensor nodes integrated on a flexible substrate. The one or more wireless sensor nodes may include a wireless transmit/receive unit (WTRU) enabling local digital signal processing, a radio link, and a miniaturized rechargeable battery. In addition or alternative to the patches, body surface electrodes **46** may also be positioned on the patient using articles worn by patient **28** which include the body surface electrodes **46** and may also include one or more position sensors (not shown) indicating the location of the worn article. For example, body surface electrodes **46** can be embedded in a vest that is configured to be worn by the patient **28**. During operation, the body surface electrodes **46** assist in providing a location of the tool (e.g., catheter) in 3-D space by detecting electrical impulses generated by the polarization and depolarization of cardiac tissue and transmitting information to the control console **24**, via the cable **44**. The body surface electrodes **46** can be equipped with magnetic location tracking and can help identify and track the respiration cycle of the patient **28**. In addition to or alternative to wired communication, the body surface electrodes **46** may communicate with the control console **24** and one another via a wireless interface (not shown).

[0075] During the diagnostic treatment, the signal processor **40** may present the display information **52** and may store data representing the information **52** in a memory **58**. The memory **58** may include any suitable volatile and/or non-volatile memory, such as random access memory or a hard disk drive. The operator **30** may be able to manipulate the display information **52** using one or more input devices **59**. Alternatively, the medical system **800** may include a second operator that manipulates the control console **24** while the operator **30** manipulates the tool **22**. It should be noted that the configuration shown in FIG. **8** is exemplary. Any suitable configuration of the medical system **800** may be used and implemented.

[0076] FIG. **9** is a block diagram illustrating example components of a medical system **900** in which features

described herein can be implemented. As shown in FIG. **9**, the system **900** includes catheter **902**, processing device **904**, display device **906** and memory **912**. As shown in FIG. **9**, the processing device **904**, display device **906** and memory **912** are a part of computing device **914**. In some embodiments, the display device **906** may be separate from computing device **914**. Computing device **914** may also include an I/O interface, such as I/O interface **42** shown in FIG. **9**.

[0077] Catheter **902** includes a plurality of catheter electrodes **908** for detecting the electrical activity of the heart over time. Catheter **902** also includes sensor(s) **916**, which include, for example, sensors (e.g., a magnetic field location sensor) for providing location signals to indicate the location of the catheter **902** in a 3-D space as well as sensors (e.g., position sensors, pressure or force sensors, temperature sensors, impedance sensors) for providing ablation parameter signals during the ablation of the heart tissue. The example system **900** also includes one or more additional sensors **910**, separate from the catheter **902**, used to provide location signals indicating the location of the catheter **902** in a 3D space.

[0078] The system **902** shown in example system **900** also includes an RF generator **918**, which supplies high-frequency electrical energy, via catheter **902**, for ablating tissue at locations engaged by the catheter **902**. Accordingly, catheter **902** may be used to acquire electrical activity for generating mapping of the heart as well ablating cardiac tissue. As described above, however, embodiments may include catheters used to acquire the electrical activity for generating mapping of the heart while not used to ablate cardiac tissue.

[0079] Processing device **904** may include one or more processors each configured to process the ECG signals, record ECG signals over time, filter ECG signals, fractionate ECG signals into signal components (e.g., slopes, waves, complexes) and generate and combine ECG signal information for displaying the plurality of electrical signals on display device **906**. Processing device **904** may also generate and interpolate mapping information for displaying maps of the heart on display device **906**. Processing device **904** may include one or more processors (e.g., signal processor **40**) configured to process the location information acquired from sensors (e.g., additional sensor(s) **910** and catheter sensor(s) **916**) to determine location and orientation coordinates.

[0080] Processing device **904** is also configured to drive display device **906** to display dynamic maps (i.e., spatio-temporal maps) of the heart and the electrical activity of the heart using the mapping information and the ECG data. Display device **906** may include one or more displays each configured to display maps of the heart representing spatio-temporal manifestations of the electrical activity of the heart over time and display the ECG signals acquired from the heart over time.

[0081] The catheter electrodes **908**, catheter sensor(s) **916** and additional sensor(s) **910** may be in wired or wireless communication with processing device **904**. Display device **906** may also be in wired or wireless communication with processing device **904**.

[0082] The methods provided can be implemented in a general purpose computer, a processor, or a processor core. Suitable processors include, by way of example, a general purpose processor, a special purpose processor, a conventional processor, a digital signal processor (DSP), a plurality of microprocessors, one or more microprocessors in association with a DSP core, a controller, a microcontroller, Application Specific Integrated Circuits (ASICs), Field Programmable Gate Arrays (FPGAs) circuits, any other type of integrated circuit (IC), and/or a state machine. Such processors can be manufactured by configuring a manufacturing process using the results of processed hardware description language (HDL) instructions and other intermediary data including netlists (such instructions capable of being stored on a computer readable media). The results of such processing can be maskworks that are then used in a semiconductor manufacturing process to manufacture a processor which implements features of the disclosure.

[0083] The methods or flow charts provided herein can be implemented in a computer program, software, or firmware incorporated in a non-transitory computer-readable storage medium for execution by a general purpose computer or a processor. Examples of non-transitory computer-readable storage mediums include a read only memory (ROM), a random access memory (RAM), a register, cache memory, semiconductor memory devices, magnetic media such as internal hard disks and removable disks, magneto-optical media, and optical media such as CD-ROM disks, and digital versatile disks (DVDs).

[0084] An example study employing the present method is presented. In this example study, a patient population is obtained comprising consecutive selected symptomatic patients diagnosed with type 1 BrS-ECG pattern either spontaneously or after ajmaline administration; each patient also had an ICD implanted. Ajmaline administration (1 mg/Kg in 5 minutes) was considered positive if the typical coved-type ECG pattern appeared in more than one right precordial lead (V1-V3).

[0085] Patients underwent a combined epi-endocardial mapping procedure (examples of mapping shown in FIGS. **10-15**, described below). Under general anesthesia, an invasive arterial pressure line was obtained through radial artery access. The ECG was continuously recorded during the procedure. After femoral venous access, a multipolar diagnostic catheter was positioned at the RV apex. The epicardial access was gained by a percutaneous subxyphoid access to the pericardial space, as is known in the art. Three dimensional RV endocardial and epicardial mapping, using CARTO®3, was performed in all patients during stable sinus rhythm and presence of type 1 BrS-ECG pattern. Epicardial mapping was systematically performed after endocardial mapping, in order to have adequate delimination of the RV boundaries when mapping the epicardium. Epicardial RV mapping and ablation catheter manipulation were assisted by a steerable sheath, such as Agilis EPI, St. Jude Medical, St. Paul, Minn. BrS epicardial substrate identification consisted in mapping the entire RV epicardial surface under baseline conditions and after ajmaline infusion (imp/Kg in 5 minutes). Three groups of RV epicardial electrograms properties are obtained using a CARTO®3 mapping system: 1) bipolar/unipolar voltage map, 2) local activation time map (LAT), and 3) potential duration map (PDM) in which abnormal long-duration bipolar electrograms were defined as low-frequency (up to 100 Hz) prolonged duration (>200 ms) bipolar signals with delayed activity extending beyond the end of the QRS complex. FIGS. **10-12**, which are described below, illustrate this. The bipolar electrograms were filtered from 16 Hz to 500 Hz, displayed at a speed of 200 ms and were recorded between the distal electrode pair.

Electrograms were excluded if their technical quality was insufficient or if catheter-induced extrasystoles occurred.

[0086] Voltage mapping, in this example study is described as follows. Color-coded electroanatomical voltage (not shown), activation (not shown) and duration maps (shown in FIG. **10**A, **10**B, **10**C using various hash patterns to indicate various colors) were performed and superimposed to cardiac anatomy. Red color **1003** indicates low-voltage dense scar that arbitrarily was defined as bipolar signal amplitude <0.5 mV, while purple color **1001** indicates voltage areas >1.5 mV. Areas of low voltage were identified using standard voltage cut-off values for dense scar (<0.5 mV) and border zone (BZ) (<1.5 mV). Electrograms below the 0.0 5mV threshold were not considered.

[0087] LAT mapping in this example study is described as follows. To study activation, the local activation time was asssessed, defined as the interval (in milliseconds) from a peak of QRS in lead II to the steepest negative change in voltage over time (dV/dt) of the intrinsic deflection in the bipolar electrogram. Activation-duration was defined as the interval (in milliseconds) between the earliest activation time of any electrogram (activation-start) and the latest activation time of any electrogram (activation-end).

[0088] Potential Duration Mapping (PDM) in this example study is described as follows. The maximum electrogram duration was the longest electrogram with continuous deflections without an intervening isoelectric line as recorded with a 0.45 sec window of interest (WOI). Fractionation of electrograms was defined as the presence of more than two intrinsic deflections and expressed as number of intrinsic deflections per electrogram. Electrogram duration was measured before and after ajmaline in the bipolar signal as the interval between the onset of the first and the offset of the last component of the electrogram, measured at the time scale of 200 mm/sec, and expressed as mean bipolar electrogram duration (in milliseconds). A cut-off range from 100 ms to 200 ms, 250 ms and 280 ms was used for defining color-coded duration maps. As a result, a color-code map was obtained showing the regions displaying the shortest (<110 ms cut-off, red **1003**) and the longest duration (>200 ms cut-off, purple **1001**), respectively. The degree of duration of the potentials was displayed from the longest (purple **1001**) to the shortest potential (red **1003**) using different duration cut-off values (illustrated in FIGS. **10-14**). According to the selected cut-offs, three different concentric circles were drawn around purple areas as shown in FIG. **11**. The PDM was performed by collecting the duration of each bipolar electrogram using the CARTO®3 system.

[0089] Substrate-based ablation in this example study is described as follows. Epicardial ablation was performed during sinus rhythm using a stepwise strategy in a descending order of abnormal potential duration as displayed on the map and beginning from the longest potentials. The longest-duration potential area was displayed in purple by setting the color-bar upper limit (300 ms) in the three-dimensional duration map, as created simultaneously during voltage and LAT mapping. Afterwards, RF ablation was performed sequentially by gradually moving at substrate sites towards areas with less prolonged late (250 ms and 200 ms) potentials according to the stepwise strategy. RF was delivered with an externally irrigated 3.5 mm tip ablation catheter. A power control mode having from 35 W up to 45 W was used. The irrigation rate was 17 mL/min for RF ablation, which was delivered by a dragging strategy, up to complete elimination of all long-duration, delayed activity.

[0090] FIG. **15** shows BrS-ECG pattern changes during epicardial RF ablation that were analyzed by continuous ECG monitoring. The ST-segment modifications were evaluated using a correlation software, such as PASO in CARTO®3. Immediate ablation endpoint was the elimination of all abnormally prolonged late activity with normalization of BrS-ECG pattern, as shown in FIG. **15**.

[0091] Ajmaline was systematically re-infused after RF ablation to ensure abolition of all abnormal ventricular potentials while confirming the BrS-ECG pattern elimination. In patients in whom the BrS-ECG pattern reappeared during infusion, epicardial duration maps were repeated to identify any residual or additional abnormal signals for further RF applications in order to definitively normalize the ECG pattern. Once a stable BrS-ECG pattern elimination was obtained, VT/VF inducibility was assessed. Intrapericardial liquid was permanently withdrawn through the deflectable sheet during the procedure to avoid serum accumulation.

[0092] The end-point of the example study was elimination of all abnormal electrical ventricular potentials before and after ajmaline, leading to ECG normalization and non-inducibility of ventricular tachycardia (VT) with respect to ventricular fibrillation (VF), e.g., VT/VF.

[0093] BrS was diagnosed in the presence of a coved-type ST elevation of >2 mm as documented in more than one lead from V1 to V3 positioned in the second, third, or fourth intercostal space. Because of the variable nature of the BrS-ECG pattern, BrS patients were classified according to their ECG at the time of the presentation and defined as spontaneous ECG pattern. Three BrS patient groups (BrS-**1** to BrS-**3**) were defined as coved-type (BrS-**1**), saddleback ST configuration (BrS-**2**), and either type 1 or type 2 but with <2 mm of ST segment elevation (BrS-**3**). BrS patients with typical BrS-related symptoms included those with documented VF or polymorphic VT at the time of symptoms. BrS patients without typical BrS-related symptoms were considered as patients with different symptoms (from dizziness to palpitations) without ECG documentation at the time of events but all with inducible VT/VF. Patients with the worst clinical presentation were defined as those who experienced cardiac arrest or syncope due to documented ventricular fibrillation. A proband was defined as the first patient diagnosed with Brugada syndrome in a family on the basis of a type 1 Brugada ECG pattern. Major complications were defined as those that required prolonged hospitalization.

[0094] Procedural data in the example study include the following. The median procedure, fluoroscopy and RF application times were 169 minutes (Inter-quartil (IQR) 160-214, min-max 105-266), 8 minutes (IQR 7-9, min-max 6-14) and 18 minutes (IQR 17-21, min-max 12-31), respectively. During the procedure, the activation, voltage and duration maps were successfully acquired during sinus rhythm and after ajmaline-induced type 1 BrS-ECG pattern in all patients. At baseline, epicardial activation started in the lower septum/apex and subsequently diverged toward the tricuspid annulus and RVOT. As shown in FIGS. **10-14**, for example, the red areas indicate short activation times while blue areas indicate longer activation times. No apparent conduction block was observed in any patient. After ajmaline infusion, the epicardial activation time was slightly longer without

change in the sequence activation pattern, but this difference was not statistically significant, as shown in the table in FIG. **16**. Overall, electro-anatomical voltage maps showed very small low-voltage areas in RVOT, which were larger in Group **1**, particularly in patients with the worst clinical presentation than in Group **2** ($P<0.001$ as shown in FIG. **16**). Before and after ajmaline, 3D epicardial duration maps displayed large areas of variable size with abnormally prolonged potentials in the RVOT, which contrasted with normal signals in the surrounding areas.

[0095] Electrophysiciological substrate characteristics according to spontaneous ECG pattern in the example study are as follows. Baseline clinical and ECG characteristics did not differ between the two groups including patients with the worst clinical presentation; spontaneous type 1 BrS-ECG pattern was less frequently found regardless of clinical presentation, as shown in the table in FIG. **17**. CARTO®3 maps identified epicardial areas of abnormal prolonged electrical signals over the RVOT (>75%) extending after ajmaline to RV free wall (see FIGS. **10-14**). The area of electrical substrate significantly increased in size after ajmaline in both groups as shown in the table in FIG. **16**. Before and after ajmaline, Group **1** showed wider area and more prolonged and abnormal potentials than Group **2**, although the increase in Group **2** was three times higher as compared with baseline values shown in the table in FIG. **16**. Of note, regardless of clinical presentation, before and after ajmaline the epicardial electrical substrate was larger in men than women. Areas with the longest abnormal potentials (>280 ms) in different RV regions appeared on color-coded maps to be smaller, displaying a characteristic onion-like substrate of concentric circles showing in the center of the area with the widest electrograms (see FIG. **11**).

[0096] Electrophysiological substrate characteristics according to spontaneous ECG pattern in the example study are described as follows. There was no difference in clinical characteristics between patients with and without spontaneous type 1 ECG pattern including age, sex, or family history of sudden death of those less than 45 years old. Large abnormal areas and wider abnormal electrograms were found in patients with type 1 ECG pattern than in patients without. The localization of abnormal areas did not differ between patients with and without type 1 ECG pattern. Baseline ST segment elevation did not differ between Group **1** and Group **2**, but after ajmaline the increase was significantly higher in Group **1**. Overall, after ajmaline the degree of type 1 ST-segment elevation correlated with the magnitude of the wider area ($r=0.682$, $p<0.001$).

[0097] Substrate-based epicardial ablation in the example study can be described as follows. Once the areas targeted for ablation were established on the map of electrogram duration, RF started beginning on areas with the widest electrical potentials, which during ablation disappeared without significant change in voltage-amplitude after RF was turned off. Elimination of abnormal signals was confirmed by remap and ajmaline reinfusion. Seventy-eight patients after ajmaline reinfusion showed reappearance of suspicious coved ECG pattern requiring further RF ablation to eliminate any residual abnormal potentials. Ablation at these sites eliminated the type 1 ECG pattern with successful suppression of VT/VF. Characteristically, during initial delivery of RF energy on the longest potential duration areas, the type 1 ECG pattern increased for some seconds, to progressively invert the ST segment slope from descending to ascending (see FIG. **12**), and the increase was higher in Group **1**. Immediately after, there was a typical flat ST-segment elevation progressively becoming ascendant in V1 and V2, which was not further modified by ajmaline and isoproterenol infusion.

[0098] FIGS. **10-17** illustrate the example study. Note that different hatching patterns are used to show different colors, e.g., color-coding, in FIGS. **10-15**. FIGS. **10** and **11** illustrate a 39-year-old Brugada Syndrome (BrS) patient, presenting with a family history of BrS and syncope, who had an ICD implantation. The patient had positive ajmaline test and VT/VF inducibility during an electrophysiological study.

[0099] FIG. **10**A shows baseline BrS-ECG pattern and epicardial color-coded duration CARTO® maps. A saddleback pattern is evident in V2 (II intercostal space) with a corresponding small (2.2 cm^2) purple area **1001** of abnormally prolonged potentials (210 ms in the example). The border-zone area (green/blue area **1002** greater than 110 ms and less than 200 ms) shows potentials with relatively shorter duration (136 ms).

[0100] FIG. **10**B shows BrS-ECG pattern and color-coded duration maps after ajmaline. After type 1 ajmaline-induced ECG pattern, the abnormal purple area **1001** significantly increased to 21.5 cm^2. Examples of abnormal and prolonged electrograms (EGMs) found in the purple area **1001** after ajmaline test are shown beside the map (289 ms and 219 ms).

[0101] FIG. **10**C shows BrS-ECG pattern and color-coded duration maps after RF ablation of epicardial substrate. After ajmaline re-challenge at the end of the procedure, the ECG showed a horizontal and ascendant ST-segment elevation, with minimal intraventricular conduction delay characterized by slight QRS broadening with a more pronounced S wave in leads I and II and qR morphology in a VII. Abnormally prolonged fragmented and delayed EGMs disappeared (87 ms and 96 ms, light-blue color **1004**).

[0102] The two examples of ventricular EGMs shown on the right side of FIGS. **10**A, **10**B and **10**C (one above the other) were recorded from the previously abnormal area, and the red asterisks indicate disappearance of the late components. The two EGM panels in each of FIGS. **10**A, **10**B and **10**C are from the CARTO®3 system and each ECG panel shows V2 ECG lead (top), distal (second from top), proximal bipolar (third from top) and unipolar (bottom) signals at a speed of 200 ms. Of note, in FIG. **10**B, V2 lead shows a typical coved-type pattern, which after ablation was modified into a horizontal and flat ST-segment elevation.

[0103] FIG. **11** shows a Potential Duration Map and Concentric 'Onion-like' Substrate. This is the same patient as in FIG. **10**. The epicardial map shows a concentric 'onion-like' substrate distribution after ajmaline. White lines delimitate multiple areas exhibiting electrograms (EGMs) with different duration (≥300 panel A, ≥250 panel B, and ≥200 ms panel C). Areas with the longest potential duration (≥300 ms) are in the inner circle (panel A), while relatively shorter areas (≥250 and ≥200 ms) are in the outer circle (panels B and C). In FIG. **11**, red regions **1101** represent areas with EGM potential duration ≤110 ms. Below each map, there is an example of the EGM recorded in the purple area **1102** (320 ms duration in panel A, 264 in B and 225 in C, respectively). Each EGM panel from the CARTO® system shows V2 ECG lead (top), distal (second from top), proximal bipolar (third from top) and unipolar (bottom) signals at speed of 200 ms speed.

[0104] FIG. **12** shows spontaneous type 1 Brugada pattern. The figure refers to a 32-year old patient with spontaneous type 1 Brugada pattern implanted with an ICD due to history of frank syncope without prodromes and an electrophysiological study (EPS) positive for VT/VF induction. In the left panel, the 12-lead ECG with precordial leads placed in V1 and V2 at higher intercostal spaces (II, III and IV ICS) shows typical type 1 Brugada pattern particularly evident in V1 and V2 II ICS and in V1 III ICS. The middle panel of FIG. **12**, shows the epicardial PDM in which the purple area **1201** exhibits long duration potentials (≥200 ms; dimensions 21.5 cm^2). The two right panels show two examples of electrograms (EGMs) found in the most fragmented and prolonged region (purple area **1201**). Of note, typical EGM of wide duration with low voltage and fragmented delayed components are shown in the distal bipolar (second line from top) signal, 320 and 280 ms duration, respectively). In each EGM panel, V1 and V2 II ICS ECG lead (top), distal (second from top), proximal bipolar (third from top) and unipolar (bottom) signals are shown at speed of 200 ms.

[0105] FIG. **13** shows RF ablation in spontaneous type 1 Brugada pattern, using the same patient as in FIG. **12**. The top left panel shows the PDM with white circles **1301** delimitating the areas exhibiting potentials duration ≥300 ms (inner circle) and ≥200 ms (outer circle). RF ablation in the inner circle (red dots **1302**) determined initial ascending and horizontal ST-segment elevation in the high right precordial leads, shown in the top panel on the right, box **1303**. In the left bottom panel, the complete set of lesions has been delivered in the whole area ≥200 ms resulting in persistent horizontal and flat ST elevation in the right precordial leads, which are not showing the Brugada type 1 pattern at the end of ablation (right bottom panel, red box **1303**).

[0106] FIG. **14** shows a PDM before and after RF ablation, using the same patient as in FIG. **12**. The left-top panel shows the PDM before ablation. The left-bottom panel shows an example of a wide and fragmented potential discovered in the purple area **1401** (distal bipolar EGM 320 ms duration). After ablation, the PDM in the right-top panel shows the disappearance of abnormally prolonged EGMs, highlighting that the late component has been abolished by ablation (EGM duration 69 ms, right-bottom panel, red asterisk). The EGM showed in the right-bottom panel has been recorded in the same region that had previously exhibited the prolonged and fragmented potential illustrated in the left-bottom panel. The ablation catheter shadow in both CARTO® maps indicates the location where such potentials have been recorded. In each EGM panel, (bottom left and right) V2 II ICS ECG lead (top), distal (second from top), proximal bipolar (third from top) and unipolar (bottom) signals are shown at speed of 200 ms. Of note, in the left-bottom panel, the V2 lead is showing typical coved-type pattern, whereas in the right-bottom panel, the same ECG lead is demonstrating that the Brugada pattern has been modified, showing a horizontal and flat ST segment elevation after ablation.

[0107] FIG. **15** shows ECG changes immediately after ablation and thirteen months following the procedure, using the same patient as in FIG. **12**. The top panel shows the acute disappearance of the type 1 pattern after RF ablation of the area showing fragmented and prolonged potentials. On the left, the baseline Brugada ECG is followed by the disappearance of the type 1 pattern immediately after ablation (top-middle panel), proved by the final ajmaline challenge repeated at the end of the procedure (top-right panel). The high right precordial leads show horizontal and flat ST-segment elevation that disappears during the follow-up (bottom panel). The bottom panel shows the persistent disappearance of Brugada type 1 pattern, proved by ajmaline challenge thirteen months after ablation. Ajmaline infusion determines PR interval prolongation with QRS broadening and slight ST segment horizontal elevation without the morphological characteristics of the coved-type ECG. From left to right, baseline 12-leads ECG, ECG with high right precordial leads at baseline and after ajmaline administration are shown.

[0108] It will be appreciated by persons skilled in the art that the present teachings are not limited to what has been particularly shown and described herein. Instead, the scope of the present teachings include both combinations and sub-combinations of the various features described herein, as well as variations and modifications thereof that are not in the prior art, which would occur to persons skilled in the art upon reading the foregoing description.

What is claimed is:

1. A method for Brugada syndrome epicardial ablation in a heart, comprising:

preparing an endocardial duration map;

preparing a baseline epicardial duration map comprising at least one or more areas of delimination; and

when one or more of the areas of delimination are greater than 200 ms, performing epicardial ablation of the areas of delimination greater than 200 ms.

2. The method according to claim **1**, further comprising:

after performing epicardial ablation, preparing an updated epicardial duration map and determining whether or not a BrS pattern appears in the updated epicardial duration map; and

when the BrS pattern appears, performing epicardial ablation.

3. The method according to claim **1**, further comprising:

after performing epicardial ablation, preparing an updated epicardial duration map and determining whether or not an abnormal EGM exists in the updated epicardial duration map; and

when the abnormal EGM exists, performing epicardial ablation.

4. The method according to claim **1**, further comprising injecting ajamline into the heart.

5. The method according to claim **1**, further comprising after performing epicardial ablation, preparing an updated epicardial map comprising maintaining anatomical volume data and adding electroanatomical data.

6. The method according to claim **1**, the baseline epicardial duration map, the updated epicardial map displaying concentric areas having cut-off intervals.

7. The method according to claim **1**, the step of preparing a baseline epicardial duration map comprising:

defining a window of interest (WOI) comprising at least a cycle length;

calculating previous heart beats based on the cycle length and reference annotation;

assigning the heart beats within the cycle length of the WOI to the WOI;

finding a start potential duration and an end potential duration; and

selecting an ablation point based on a heart beat having a minimum standard deviation from the heart beats assigned to the WOI.

8. A system for Brugada syndrome epicardial ablation in a heart, comprising:

a catheter for measuring ECG signals;

a computer adapted to:

prepare an endocardial duration map;

prepare a baseline epicardial duration map comprising at least one or more areas of delimination; and

when one or more of the areas of delimination are greater than 200 ms, performing epicardial ablation of the areas of delimination greater than 200 ms; and

a display device for displaying the endocardial duration map and the baseline epicardial map.

9. The system according to claim **8**, the computer further adapted to:

after performing epicardial ablation, prepare an updated epicardial duration map and determine whether or not a BrS pattern appears in the updated epicardial duration map; and

when the BrS pattern appears, perform epicardial ablation.

10. The system according to claim **8**, the computer further adapted to:

after performing epicardial ablation, prepare an updated epicardial duration map and determine whether or not an abnormal EGM exists in the updated epicardial duration map; and

when the abnormal EGM exists, perform epicardial ablation.

11. The system according to claim **8**, the system further comprising a tool for injecting ajamline into the heart.

12. The system according to claim **8**, the computer further adapted to, after performing epicardial ablation, prepare an updated epicardial map comprising maintaining anatomical volume data and adding electroanatomical data.

13. The system according to claim **8**, the computer further adapted to display concentric areas having cut-off intervals on one or both of the baseline epicardial duration map, and the updated epicardial map.

14. The system according to claim **8**, the computer further adapted to prepare the baseline epicardial duration map by performing steps of:

defining a window of interest (WOI) comprising at least a cycle length;

calculating previous heart beats based on the cycle length and reference annotation;

assigning the heart beats within the cycle length of the WOI to the WOI;

finding a start potential duration and an end potential duration; and

selecting an ablation point based on a heart beat having a minimum standard deviation from the heart beats assigned to the WOI.

15. A computer software product for improving ablation procedures, including a non-transitory computer readable storage medium in which computer program instructions are stored, which instructions, when executed by a computer, cause the computer to perform the steps of:

preparing an endocardial duration map;

preparing a baseline epicardial duration map comprising at least one or more areas of delimination;

when one or more of the areas of delimination are greater than 200 ms, performing epicardial ablation of the areas of delimination greater than 200 ms.

16. The computer software product according to claim **15**, further comprising:

after performing epicardial ablation, preparing an updated epicardial duration map and determining whether or not a BrS pattern appears in the updated epicardial duration map; and

when the BrS pattern appears, performing epicardial ablation.

17. The computer software product according to claim **15**, further comprising:

after performing epicardial ablation, preparing an updated epicardial duration map and determining whether or not an abnormal EGM exists in the updated epicardial duration map; and

when the abnormal EGM exists, performing epicardial ablation.

18. The computer software product according to claim **15**, further comprising after performing epicardial ablation, preparing an updated epicardial map comprising maintaining anatomical volume data and adding electroanatomical data.

19. The computer software product according to claim **15**, wherein the baseline epicardial duration map, the updated epicardial map displaying concentric areas having cut-off intervals.

20. The computer software product according to claim **15**, the step of preparing the baseline epicardial duration map comprising:

defining a window of interest (WOI) comprising at least a cycle length;

calculating previous heart beats based on the cycle length and reference annotation;

assigning the heart beats within the cycle length of the WOI to the WOI;

finding a start potential duration and an end potential duration; and

selecting an ablation point based on a heart beat having a minimum standard deviation from the heart beats assigned to the WOI.

* * * * *

专利名称(译)	分析和映射ECG信号并确定消融点以消除brugada综合征		
公开(公告)号	US20180206750A1	公开(公告)日	2018-07-26
申请号	US15/854485	申请日	2017-12-26
[标]申请(专利权)人(译)	韦伯斯特生物官能(以色列)有限公司		
申请(专利权)人(译)	生物传感韦伯斯特（以色列）LTD.		
当前申请(专利权)人(译)	生物传感韦伯斯特（以色列）LTD.		
[标]发明人	PAPPONE CARLO TURGEMAN AHARON POZZI PAOLO ROBERTO NATALIZIA ANDREA		
发明人	PAPPONE, CARLO TURGEMAN, AHARON POZZI, PAOLO ROBERTO NATALIZIA, ANDREA		
IPC分类号	A61B5/042 A61B5/00 A61B18/14 A61B5/0472 A61B5/04		
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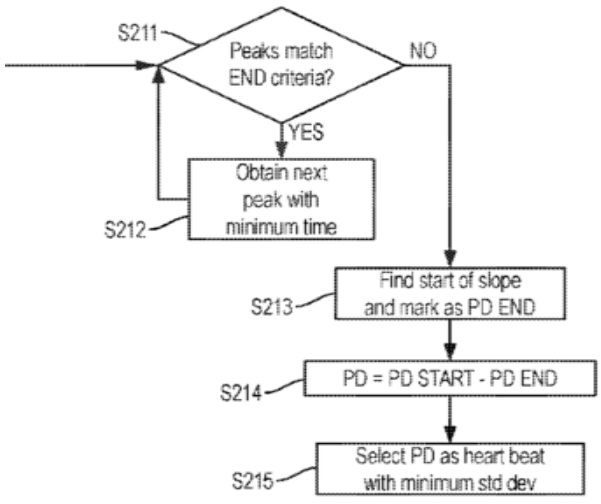
优先权	62/450388 2017-01-25 US		
外部链接	Espacenet USPTO		

摘要(译)

用于Brugada综合征心外膜消融的系统和方法包括制备心内膜持续时间图;准备包括至少一个或多个消除区域的基线心外膜持续时间图;当某些消除区域大于200毫秒时，对大于200毫秒的消除区域进行心外膜消融。该方法还可以包括在执行心外膜消融之后准备更新的心外膜持续时间图，以及确定BrS图案是否出现在更新的心外膜持续时间图中;当出现BrS模式时，进行心外膜消融。该方法还可以包括在执行心外膜消融之后准备更新的心外膜持续时间图，以及确定更新的心外膜持续时间图中是否存在异常EGM;当存在异常EGM时，进行心外膜消融。该方法可以进一步包括准备更新的心外膜图，包括维护解剖体积数据和添加电解剖数据。