US009764143B2

(12) **United States Patent**
Ghosh et al.

(10) **Patent No.: US 9,764,143 B2**
(45) **Date of Patent: *Sep. 19, 2017**

(54) **SYSTEMS AND METHODS FOR CONFIGURATION OF INTERVENTRICULAR INTERVAL**

(71) Applicant: **Medtronic, Inc.**, Minneapolis, MN (US)

(72) Inventors: **Subham Ghosh**, Blaine, MN (US); **Jeffrey Gillberg**, Coon Rapids, MN (US)

(73) Assignee: **Medtronic, Inc.**, Minneapolis, MN (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 19 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **14/703,348**

(22) Filed: **May 4, 2015**

(65) **Prior Publication Data**

US 2016/0045737 A1 Feb. 18, 2016

Related U.S. Application Data

(60) Provisional application No. 62/037,694, filed on Aug. 15, 2014.

(51) **Int. Cl.**
A61N 1/36 (2006.01)
A61N 1/368 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC ***A61N 1/3684*** (2013.01); ***A61B 5/0452*** (2013.01); ***A61B 5/04085*** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC A61N 1/3684; A61N 1/37247; A61N 1/3682; A61N 1/36514; A61B 5/7282;
(Continued)

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,233,987 A 11/1980 Feingold
4,402,323 A 9/1983 White
(Continued)

FOREIGN PATENT DOCUMENTS

CN 1043621 A 7/1990
CN 1253761 A 5/2000
(Continued)

OTHER PUBLICATIONS

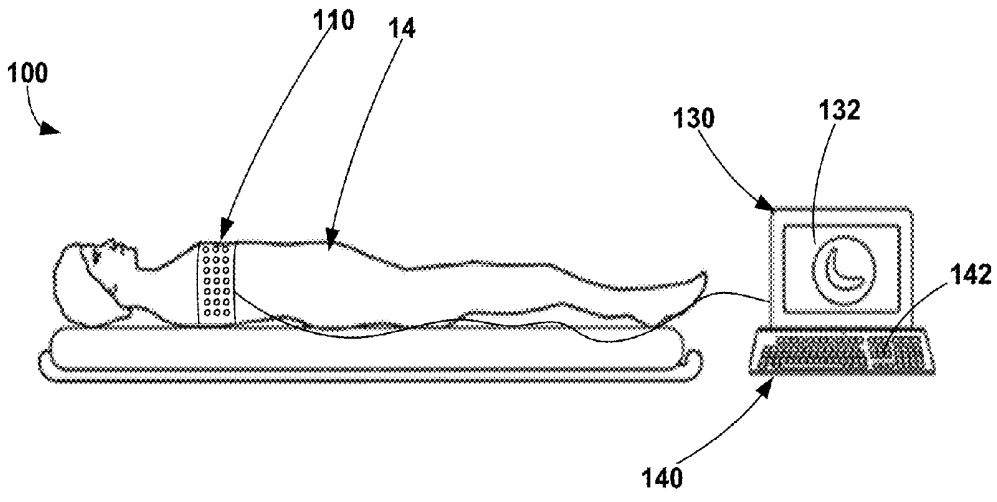
Botker MD, PhD., et al., "Electromechanical Mapping for Detection of Myocardial Viability in Patients with ischemia Cardiomyopathy," Circulation, Mar. 2001; vol. 103, No. 12, pp. 1631-1637.
(Continued)

Primary Examiner — Rex R Holmes

(57) **ABSTRACT**

Systems and methods are described herein for assisting a user in identification of interventricular (V-V) delay for cardiac therapy. The systems and methods may monitor electrical activity of a patient using external electrode apparatus to provide electrical heterogeneity information for a plurality of different V-V intervals and may identify a V-V interval based on the electrical heterogeneity information.

25 Claims, 12 Drawing Sheets



(51) **Int. Cl.**

A61N 1/372	(2006.01)
A61B 5/00	(2006.01)
A61B 5/0408	(2006.01)
A61B 5/0452	(2006.01)
A61N 1/365	(2006.01)

(52) **U.S. Cl.**
CPC ***A61B 5/7282*** (2013.01); ***A61N 1/37247*** (2013.01); *A61B 5/6805* (2013.01); *A61N 1/3682* (2013.01); *A61N 1/36514* (2013.01)

(58) **Field of Classification Search**
CPC .. A61B 5/04085; A61B 5/0452; A61B 5/6805
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,428,378	A	1/1984	Anderson et al.
4,497,326	A	2/1985	Curry
4,566,456	A	1/1986	Koning et al.
4,593,702	A	6/1986	Kepski
4,674,511	A	6/1987	Cartmell
4,763,660	A	8/1988	Kroll et al.
4,777,955	A	10/1988	Brayten et al.
4,787,389	A	11/1988	Tarjan
4,979,507	A	12/1990	Heinz et al.
5,052,388	A	10/1991	Sivula et al.
5,054,496	A	10/1991	Wen et al.
5,311,873	A	5/1994	Savard et al.
5,331,960	A	7/1994	Krenzke
5,334,220	A	8/1994	Sholder
5,443,492	A	8/1995	Stokes et al.
5,485,849	A	1/1996	Panescu et al.
5,514,163	A	5/1996	Markowitz et al.
5,552,645	A	9/1996	Weng
5,628,778	A	5/1997	Kruse et al.
5,671,752	A	9/1997	Sinderby et al.
5,683,429	A	11/1997	Mehra
5,683,432	A	11/1997	Goedeke et al.
5,687,737	A	11/1997	Branham et al.
5,810,740	A	9/1998	Paisner
5,876,336	A	3/1999	Swanson et al.
5,891,045	A	4/1999	Albrecht et al.
5,922,014	A	7/1999	Warman et al.
6,055,448	A	4/2000	Anderson et al.
6,128,535	A	10/2000	Maarse et al.
6,141,588	A	10/2000	Cox et al.
6,187,032	B1	2/2001	Ohyu et al.
6,205,357	B1	3/2001	Ideker et al.
6,226,542	B1	5/2001	Reisfeld
6,236,883	B1	5/2001	Ciaccio et al.
6,243,603	B1	6/2001	Ideker et al.
6,246,898	B1	6/2001	Vesely et al.
6,301,496	B1	10/2001	Reisfeld
6,311,089	B1	10/2001	Mann et al.
6,330,476	B1	12/2001	Ben-Haim et al.
6,358,214	B1	3/2002	Tereschouk
6,377,856	B1	4/2002	Carson
6,381,493	B1	4/2002	Stadler et al.
6,393,316	B1	5/2002	Gillberg et al.
6,418,346	B1	7/2002	Nelson et al.
6,442,433	B1	8/2002	Linberg
6,456,867	B2	9/2002	Reisfeld
6,473,638	B2	10/2002	Ferek-Petric
6,480,745	B2	11/2002	Nelson et al.
6,484,118	B1	11/2002	Govari
6,507,756	B1	1/2003	Heynen et al.
6,532,379	B2	3/2003	Stratbucker
6,584,343	B1	6/2003	Ransbury et al.
6,599,250	B2	7/2003	Webb et al.
6,625,482	B1	9/2003	Panescu et al.
6,640,136	B1	10/2003	Helland et al.
6,650,927	B1	11/2003	Keidar
6,766,189	B2	7/2004	Yu et al.
6,772,004	B2	8/2004	Rudy
6,804,555	B2	10/2004	Warkentin
6,847,836	B1	1/2005	Sujdak
6,856,830	B2	2/2005	He
6,882,882	B2	4/2005	Struble et al.
6,885,889	B2	4/2005	Chinchoy
6,915,149	B2	7/2005	Ben-Haim
6,968,237	B2	11/2005	Doan et al.
6,975,900	B2	12/2005	Rudy et al.
6,978,184	B1	12/2005	Marcus et al.
6,980,675	B2	12/2005	Evron et al.
7,016,719	B2	3/2006	Rudy et al.
7,031,777	B2	4/2006	Hine et al.
7,058,443	B2	6/2006	Struble
7,062,315	B2	6/2006	Koyrakh et al.
7,092,759	B2	8/2006	Nehls et al.
7,142,922	B2	11/2006	Spinelli et al.
7,184,835	B2	2/2007	Kramer et al.
7,215,998	B2	5/2007	Wesselink et al.
7,286,866	B2	10/2007	Okerlund et al.
7,308,297	B2	12/2007	Reddy et al.
7,308,299	B2	12/2007	Burrell et al.
7,313,444	B2	12/2007	Pianca et al.
7,321,677	B2	1/2008	Evron et al.
7,346,381	B2	3/2008	Okerlund et al.
7,398,116	B2	7/2008	Edwards
7,426,412	B1	9/2008	Schecter
7,454,248	B2	11/2008	Burrell et al.
7,499,743	B2	3/2009	Vass et al.
7,509,170	B2	3/2009	Zhang et al.
7,565,190	B2	7/2009	Okerlund et al.
7,587,074	B2	9/2009	Zarkh et al.
7,599,730	B2	10/2009	Hunter et al.
7,610,088	B2	10/2009	Chinchoy
7,613,500	B2	11/2009	Vass et al.
7,616,993	B2	11/2009	Müssig et al.
7,664,550	B2	2/2010	Eick et al.
7,684,863	B2	3/2010	Parikh et al.
7,742,629	B2	6/2010	Zarkh et al.
7,747,047	B2	6/2010	Okerlund et al.
7,751,882	B1	7/2010	Helland
7,769,451	B2	8/2010	Yang et al.
7,778,685	B2	8/2010	Evron et al.
7,778,686	B2	8/2010	Vass et al.
7,787,951	B1	8/2010	Min
7,813,785	B2	10/2010	Okerlund et al.
7,818,040	B2	10/2010	Spear et al.
7,848,807	B2	12/2010	Wang
7,860,580	B2	12/2010	Falk et al.
7,894,889	B2	2/2011	Zhang
7,912,544	B1	3/2011	Min et al.
7,917,214	B1	3/2011	Gill et al.
7,941,213	B2	5/2011	Markowitz et al.
7,953,475	B2	5/2011	Harlev et al.
7,953,482	B2	5/2011	Hess
7,983,743	B2	7/2011	Rudy et al.
7,996,063	B2	8/2011	Vass et al.
7,996,070	B2	8/2011	van Dam et al.
8,010,194	B2	8/2011	Muller
8,019,402	B1	9/2011	Kryzpow et al.
8,019,409	B2	9/2011	Rosenberg et al.
8,032,229	B2	10/2011	Gerber et al.
8,036,743	B2	10/2011	Savage et al.
8,060,185	B2	11/2011	Hunter et al.
8,150,513	B2	4/2012	Chinchoy
8,160,700	B1	4/2012	Ryu et al.
8,175,703	B2	5/2012	Dong et al.
8,180,428	B2	5/2012	Kaiser et al.
8,195,292	B2	6/2012	Rosenberg et al.
8,213,693	B1	7/2012	Li
8,214,041	B2	7/2012	Van Gelder et al.
8,265,738	B1	9/2012	Min et al.
8,285,377	B2	10/2012	Rosenberg et al.
8,295,943	B2	10/2012	Eggen et al.
8,326,419	B2	12/2012	Rosenberg et al.
8,332,030	B2	12/2012	Hess et al.
8,380,308	B2	2/2013	Rosenberg et al.
8,401,616	B2	3/2013	Verard et al.
8,478,388	B2	7/2013	Nguyen et al.
8,527,051	B1	9/2013	Hedberg et al.

(56) **References Cited**

U.S. PATENT DOCUMENTS

8,583,230 B2 11/2013 Ryu et al.
8,615,298 B2 12/2013 Ghosh et al.
8,617,082 B2 12/2013 Zhang et al.
8,620,433 B2 12/2013 Ghosh et al.
8,639,333 B2 1/2014 Stadler et al.
8,694,099 B2 4/2014 Ghosh et al.
8,738,132 B1 5/2014 Ghosh et al.
8,744,576 B2 6/2014 Munsterman et al.
8,768,465 B2 7/2014 Ghosh et al.
8,805,504 B2 8/2014 Sweeney
8,972,228 B2 3/2015 Ghosh et al.
9,037,238 B2 5/2015 Stadler et al.
9,155,897 B2 10/2015 Ghosh et al.
9,199,087 B2 12/2015 Stadler et al.
9,265,951 B2 2/2016 Sweeney
9,265,954 B2 2/2016 Ghosh
9,265,955 B2 2/2016 Ghosh
9,278,219 B2 3/2016 Ghosh
9,278,220 B2 3/2016 Ghosh
9,282,907 B2 3/2016 Ghosh
9,320,446 B2 4/2016 Gillberg et al.
2002/0087089 A1 7/2002 Ben-Haim
2002/0143264 A1 10/2002 Ding et al.
2002/0161307 A1 10/2002 Yu et al.
2002/0169484 A1 11/2002 Mathis et al.
2003/0018277 A1 1/2003 He
2003/0050670 A1 3/2003 Spinelli et al.
2003/0105495 A1 6/2003 Yu et al.
2003/0236466 A1 12/2003 Tarjan et al.
2004/0015081 A1 1/2004 Kramer et al.
2004/0059237 A1 3/2004 Narayan et al.
2004/0097806 A1 5/2004 Hunter et al.
2004/0102812 A1 5/2004 Yonce et al.
2004/0122479 A1 6/2004 Spinelli et al.
2004/0162496 A1 8/2004 Yu et al.
2004/0172078 A1 9/2004 Chinchoy
2004/0172079 A1 9/2004 Chinchoy
2004/0193223 A1 9/2004 Kramer et al.
2004/0215245 A1 10/2004 Stahmann et al.
2004/0215252 A1 10/2004 Verbeek et al.
2004/0220635 A1 11/2004 Burnes
2004/0267321 A1 12/2004 Boileau et al.
2005/0008210 A1 1/2005 Evron et al.
2005/0027320 A1 2/2005 Nehls et al.
2005/0090870 A1 4/2005 Hine et al.
2005/0096522 A1 5/2005 Reddy et al.
2005/0149138 A1 7/2005 Min et al.
2006/0074285 A1 4/2006 Zarkh et al.
2006/0224198 A1 10/2006 Dong et al.
2006/0235478 A1 10/2006 Van Gelder et al.
2006/0253162 A1 11/2006 Zhang et al.
2007/0142871 A1 6/2007 Libbus et al.
2007/0232943 A1 10/2007 Harel et al.
2007/0250129 A1 10/2007 Van Oort
2007/0265508 A1 11/2007 Sheikhzadeh-Nadjar et al.
2008/0021336 A1 1/2008 Dobak et al.
2008/0058656 A1 3/2008 Costello et al.
2008/0119903 A1 5/2008 Arcot-Krishnamurthy et al.
2008/0140143 A1 6/2008 Ettori et al.
2008/0146954 A1 6/2008 Bojovic et al.
2008/0242976 A1 10/2008 Robertson et al.
2008/0269818 A1 10/2008 Sullivan et al.
2008/0269823 A1 10/2008 Burnes et al.
2008/0281195 A1 11/2008 Heimdal
2008/0306567 A1 12/2008 Park et al.
2008/0306568 A1 12/2008 Ding et al.
2009/0005832 A1 1/2009 Zhu et al.
2009/0036947 A1 2/2009 Westlund et al.
2009/0043352 A1 2/2009 Brooke et al.
2009/0048528 A1 2/2009 Hopenfeld et al.
2009/0053102 A2 2/2009 Rudy et al.
2009/0054941 A1 2/2009 Eggen et al.
2009/0054946 A1 2/2009 Sommer et al.
2009/0084382 A1 4/2009 Jalde et al.
2009/0093857 A1 4/2009 Markowitz et al.
2009/0099468 A1 4/2009 Thiagalingam et al.
2009/0099469 A1 4/2009 Flores
2009/0099619 A1 4/2009 Lessmeier et al.
2009/0112109 A1 4/2009 Kuklik et al.
2009/0143838 A1 6/2009 Libbus et al.
2009/0157134 A1 6/2009 Ziglio et al.
2009/0157136 A1 6/2009 Yang et al.
2009/0198298 A1 8/2009 Kaiser et al.
2009/0216112 A1 8/2009 Assis et al.
2009/0232448 A1 9/2009 Barmash et al.
2009/0234414 A1 9/2009 Sambelashvili et al.
2009/0254140 A1 10/2009 Rosenberg et al.
2009/0270729 A1 10/2009 Corbucci et al.
2009/0270937 A1 10/2009 Yonce et al.
2009/0299201 A1 12/2009 Gunderson
2009/0299423 A1 12/2009 Min
2009/0306732 A1 12/2009 Rosenberg et al.
2009/0318995 A1 12/2009 Keel et al.
2010/0022873 A1 1/2010 Hunter et al.
2010/0049063 A1 2/2010 Dobak, III
2010/0069987 A1 3/2010 Min et al.
2010/0087888 A1 4/2010 Maskara
2010/0094149 A1 4/2010 Kohut et al.
2010/0113954 A1 5/2010 Zhou
2010/0114229 A1 5/2010 Chinchoy
2010/0121403 A1 5/2010 Schecter et al.
2010/0145405 A1 6/2010 Min et al.
2010/0174137 A1 7/2010 Shim
2010/0198292 A1 8/2010 Honeck et al.
2010/0228138 A1 9/2010 Chen
2010/0234916 A1 9/2010 Turcott et al.
2010/0254583 A1 10/2010 Chan et al.
2010/0268059 A1 10/2010 Ryu et al.
2011/0004111 A1 1/2011 Gill et al.
2011/0004264 A1 1/2011 Siejko et al.
2011/0022112 A1 1/2011 Min
2011/0054286 A1 3/2011 Crosby
2011/0054559 A1 3/2011 Rosenberg et al.
2011/0054560 A1 3/2011 Rosenberg et al.
2011/0075896 A1 3/2011 Matsumoto
2011/0092809 A1 4/2011 Nguyen et al.
2011/0112398 A1 5/2011 Zarkh et al.
2011/0118803 A1 5/2011 Hou et al.
2011/0137369 A1 6/2011 Ryu et al.
2011/0144510 A1 6/2011 Ryu et al.
2011/0172728 A1 7/2011 Wang
2011/0190615 A1 8/2011 Phillips et al.
2011/0201915 A1 8/2011 Gogin et al.
2011/0213260 A1 9/2011 Keel et al.
2011/0319954 A1 12/2011 Niazi et al.
2012/0004567 A1 1/2012 Eberle et al.
2012/0101543 A1 4/2012 Demmer et al.
2012/0101546 A1 4/2012 Stadler et al.
2012/0203090 A1 8/2012 Min
2012/0253419 A1 10/2012 Rosenberg et al.
2012/0283587 A1 11/2012 Gosh et al.
2012/0284003 A1 11/2012 Gosh et al.
2012/0296387 A1 11/2012 Zhang et al.
2012/0296388 A1 11/2012 Zhang et al.
2012/0302904 A1 11/2012 Lian et al.
2012/0303084 A1 11/2012 Kleckner et al.
2012/0310297 A1 12/2012 Sweeney
2012/0330179 A1 12/2012 Yuk et al.
2013/0006332 A1 1/2013 Sommer et al.
2013/0018250 A1 1/2013 Caprio et al.
2013/0018251 A1 1/2013 Caprio et al.
2013/0030491 A1 1/2013 Stadler et al.
2013/0060298 A1 3/2013 Splett et al.
2013/0072790 A1 3/2013 Ludwig et al.
2013/0096446 A1 4/2013 Michael et al.
2013/0116739 A1 5/2013 Brada et al.
2013/0131529 A1 5/2013 Jia et al.
2013/0131749 A1 5/2013 Sheldon et al.
2013/0131751 A1 5/2013 Stadler et al.
2013/0136035 A1 5/2013 Bange et al.
2013/0150913 A1 6/2013 Bornzin et al.
2013/0165983 A1 6/2013 Ghosh et al.
2013/0165988 A1 6/2013 Ghosh
2013/0261471 A1 10/2013 Saha et al.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2013/0261688	A1	10/2013	Dong et al.	
2013/0289640	A1	10/2013	Zhang et al.	
2013/0296726	A1	11/2013	Niebauer et al.	
2013/0304407	A1	11/2013	George et al.	
2013/0324828	A1	12/2013	Nishiwaki et al.	
2014/0005563	A1	1/2014	Ramanathan et al.	
2014/0018872	A1	1/2014	Siejko et al.	
2014/0135866	A1	5/2014	Ramanathan et al.	
2014/0135867	A1	5/2014	Demmer et al.	
2014/0163633	A1	6/2014	Ghosh et al.	
2014/0222099	A1	8/2014	Sweeney	
2014/0236252	A1	8/2014	Ghosh et al.	
2014/0276125	A1	9/2014	Hou et al.	
2014/0277233	A1	9/2014	Ghosh	
2014/0323882	A1	10/2014	Ghosh et al.	
2014/0323892	A1	10/2014	Ghosh et al.	
2014/0323893	A1	10/2014	Ghosh et al.	
2014/0371807	A1	12/2014	Ghosh et al.	
2014/0371808	A1	12/2014	Ghosh et al.	
2014/0371832	A1	12/2014	Ghosh et al.	
2014/0371833	A1	12/2014	Ghosh et al.	
2015/0032016	A1	1/2015	Ghosh	
2015/0032171	A1	1/2015	Ghosh	
2015/0032172	A1	1/2015	Ghosh	
2015/0032173	A1	1/2015	Ghosh	
2015/0045849	A1	2/2015	Ghosh et al.	
2015/0142069	A1	5/2015	Sambelashvili	
2015/0157225	A1	6/2015	Gillberg et al.	
2015/0157231	A1	6/2015	Gillberg et al.	
2015/0157232	A1	6/2015	Gillberg et al.	
2015/0157865	A1	6/2015	Gillberg et al.	
2015/0216434	A1	8/2015	Ghosh et al.	
2015/0265840	A1	9/2015	Ghosh et al.	
2016/0030747	A1	2/2016	Thakur et al.	
2016/0030751	A1*	2/2016	Ghosh	A61B 5/04085 607/18
2016/0045738	A1	2/2016	Ghosh et al.	
2016/0045744	A1	2/2016	Ghosh et al.	
2016/0184590	A1	6/2016	Gosh	

FOREIGN PATENT DOCUMENTS

CN	1878595	A	12/2006
CN	101073502	A	11/2007
EP	1 072 284	A2	1/2001
EP	1 504 713	A1	2/2005
EP	2016976	A1	1/2009
EP	2391270	A1	7/2011
EP	1 925 337	B1	3/2012
EP	2436309	A2	4/2012
EP	2 435 132	B1	8/2013
WO	WO 98/26712	A1	6/1998
WO	WO 99/06112	A1	2/1999
WO	WO 00/45700	A1	8/2000
WO	WO 01/67950	A1	9/2001
WO	WO 03/070323	A1	8/2003
WO	WO 2005/056108	A2	6/2005
WO	WO 2006/069215	A2	6/2006
WO	WO 2006/105474	A2	10/2006
WO	WO 2006/115777	A1	11/2006
WO	WO 2006/117773	A1	11/2006
WO	WO 2007/013994	A2	2/2007
WO	WO 2007/027940	A2	3/2007
WO	WO 2007/013994	A3	4/2007
WO	WO 2007/027940	A3	6/2007
WO	WO 2007/139456	A1	12/2007
WO	WO 2008/151077	A2	12/2008
WO	WO 2006/069215	A3	6/2009
WO	WO 2009/079344	A1	6/2009
WO	WO 2009/139911	A2	11/2009
WO	WO 2009/148429	A1	12/2009
WO	WO 2010/019494	A1	2/2010
WO	WO 2010/071520	A1	6/2010
WO	WO 2010/088040	A1	8/2010
WO	WO 2010/088485	A1	8/2010
WO	WO 2011/070166	A1	6/2011
WO	WO 2011/090622	A1	7/2011
WO	WO 2011/099992	A1	8/2011
WO	WO 2012/037471	A2	3/2012
WO	WO 2012/037471	A3	6/2012
WO	WO 2012/106297	A2	8/2012
WO	WO 2012/106297	A3	8/2012
WO	WO 2012/109618	A2	8/2012
WO	WO 2012/110940	A1	8/2012
WO	WO 2012/109618	A3	11/2012
WO	WO 2012/151364	A1	11/2012
WO	WO 2012/151389	A1	11/2012
WO	WO 2013/006724	A2	1/2013
WO	WO 2013/010165	A1	1/2013
WO	WO 2013/010184	A1	1/2013
WO	WO 2013/006724	A3	4/2013
WO	WO 2014/179454	A1	11/2014
WO	WO 2014/179459	A2	11/2014
WO	WO 2015/013271	A1	1/2015
WO	WO 2015/013493	A1	1/2015
WO	WO 2015/013574	A1	1/2015

OTHER PUBLICATIONS

Cuculich, P.S., et al., "The Electrophysiological Cardiac Ventricular Substrate in Patients After Myocardial Infection" *J. Am. Coll. Cardiol.* 2011; 58:1893-1902.

Dawoud, F. et al., "Inverse Electrocardiographic Imaging to Assess Electrical Dyssynchrony in Cardiac Resynchronization Therapy Patients," *Computing in Cardiology*, 2012; 39:993-996.

Fung et al., Chapter 20, Optimization of Cardiac Resynchronization Therapy, Cardiac Resynchronization Therapy, Second Edition, Copyright 2008, Blackwell Publishing Ltd., pp. 356-373.

Ghosh et al., "Electrophysiological Substrate and Intraventricular LV Dyssynchrony in Non-ischemic Heart Failure Patients Undergoing Cardiac Resynchronization Therapy," *Heart rhythm : the official journal of the Heart Rhythm Society*, 2011; 8(5):692-699.

Hopenfeld et al., "The Effect of Conductivity on ST -Segment Epicardial Potentials Arising from Subendocardial Ischemia," Annals of Biomedical Eng., Jun. 2005; vol. 33, No. 6, pp. 751-763.

Medtronic Vitatron CARELINK ENCORE® Programmer Model 29901 Reference Manual, 2013, Medtronic, Inc., Minneapolis, MN.

Miri et al., "Applicability of body surface potential map in computerized optimization of biventricular pacing," *Annals of Biomedical Engineering*, vol. 38, No. 3, Mar. 2010, pp. 865-875.

Miri et al., "Comparison of the electrophysiologically based optimization methods with different pacing parameters in patient undergoing resynchronization treatment," *30th Annual International IEEE EMS Conference*, Aug. 2008, pp. 1741-1744.

Miri et al., "Computerized Optimization of Biventricular Pacing Using Body Surface Potential Map," *31st Annual International Conference of the IEEE EMBS*, Sep. 2009, pp. 2815-2818.

Miri et al., "Efficiency of Timing Delays and Electrode Positions in Optimization of Biventricular Pacing: A Simulation Study," *IEEE Transactions on Biomedical Engineering*, Nov. 2009, pp. 2573-2582.

Nash et al., "An Experimental-Computational Framework for Validating in-vivo ECG Inverse Algorithms," International Journal of Bioelectromagnetism, vol. 2, No. 2, Dec. 31, 2000, 9 pp.

Potse et al., "Mathematical Modeling and Simulation of Ventricular Activation Sequences: Implications for Cardiac Resynchronization Therapy," *J. of Cardiovasc. Trans. Res.*, 2012; 5:146-158.

Prinzen et al., "Cardiac Resynchronization Therapy State-of-the-Art of Current Applications, Guidelines, Ongoing Trials, and Areas of Controversy" Circulation, 2013; 128: 2407-2418.

Strik et al., "Electrical and Mechanical Ventricular Activation During Left Bundle Branch Block and Resynchronization," *J. of Cardiovasc. Trans. Res.*, 2012; 5:117-126.

Svendsen et al., "Computational Models of Cardiac Electrical Activation," Chapter 5, Computational Nov. 2010, pp. 73-88.

Sweeney et al., QRS Fusion Complex Analysis Using Wave Interference to Predict Reverse Remodeling During Cardiac Resynchronization Therapy, heart Rhythm, 2014, 11:806-813.

(56) **References Cited**

OTHER PUBLICATIONS

Wang et al., "Application of the Method of Fundamental Solutions to Potential-based Inverse Electrocardiography," *Annals of Biomedical Engineering*, Aug. 2006, pp. 1272-1288.

Wellens, MD et al., "The Electrocardiogram 102 Years After Einthoven," Circulation, Feb. 2004; vol. 109, No. 5, pp. 562-564.

U.S. Appl. No. 14/173,288, filed Feb. 5, 2014, Sambelashvili.

U.S. Appl. No. 14/220,733, filed Mar. 20, 2014, Ghosh et al.

U.S. Appl. No. 14/227,719, filed Mar. 27, 2014, Gillberg et al.

U.S. Appl. No. 14/228,009, filed Mar. 27, 2014, Gillberg et al.

U.S. Appl. No. 14/228,024, filed Mar. 27, 2014, Ghosh et al.

U.S. Appl. No. 14/228,038, filed Mar. 27, 2014, Ghosh et al.

International Search Report and Written Opinion issued Nov. 7, 2014 for International Application No. PCT/US2014/036163; 12 pages.

International Search Report and Written Opinion issued Oct. 28, 2014 for International Application No. PCT/US2014/041928; 15 pages.

International Search Report and Written Opinion issued Oct. 24, 2014 for International Application No. PCT/US2014/041929; 14 pages.

International Search Report and Written Opinion issued on Mar. 9, 2015 for International Application No. PCT/US2014/069214; 11 pages.

International Search Report and Written Opinion issued on Mar. 17, 2015, for International Application No. PCT/US2014/069192; 11 pages.

International Search Report and Written Opinion issued on Mar. 16, 2015 for International Application No. PCT/US2014/069182; 11 pages.

International Search Report and Written Opinion issued on Apr. 8, 2015 for International Application No. PCT/US2014/069070; 11 pages.

Biffi et al., "Occurrence of Phrenic Nerve Stimulation in Cardiac Resynchronization Therapy Patients: the Role of Left Ventricular Lead Type and Placement Site," *Europace*, 2013; 15:77-82.

"CardioGuide System Enables Real-Time Navigation of Left Ventricular Leads During Medtronic CRT Implants," Press Release, Apr. 9, 2013, Medtronic, Inc., 2 pgs.

Czerwinska et al., "Method of Segmentation of Thorax Organs Images Applied to Modeling the Cardiac Electrical Field," *Engineering in Medicine and Biology Society*, Proceedings of the 22nd Annual International Conference of the IEEE, vol. 1, 23, Jul. 23, 2000.; pp. 402-405.

Freund et al., "A Decision-Theoretic Generalization of Online Learning and an Application to Boosting," *Journal of Computer and System Sciences*, 1997; 55(1):119-139.

Friedman, "Greedy Function Approximation: A Gradient Boosting Machine," *Annals of Statistics*, 2001; 29(5):1189-1232.

Friedman, "Stochastic Gradient Boosting," *Computational Statistics and Data Analysis*, 2002; 38(4):367-378.

Friedman et al., "Additive Logistic Regression: a Statistical View of Boosting," *Annals of Statistics*, 2000; 28(2):337-374.

Ghosh et al. "Accuracy of Quadratic Versus Linear Interpolation in Noninvasive Electrocardiographic Imaging (ECGI)," *Annals of Biomedical Engineering*, vol. 33, No. 9. Sep. 2005; pp. 1187-1201.

Ghosh et al., "Cardiac Memory in Patents with Wolff-Parkinson-White Syndrome: Noninvasive Imaging of Activation and Repolarization Before and After Catheter Ablation" *Circulation*, 2008; 118:907-915. Published online Aug. 12, 2008.

Ghosh et al. "Application of L1-Norm Regularization to Epicardial Potential Solution of the Inverse Electrocardiography Problem," *Annuals of Biomedical Engineering*, vol. 37, No. 5, May 2009; pp. 902-912.

Gold et al., "Comparison of Stimulation Sites within Left Ventricular Veins on the Acute Hemodynamic Effects of Cardiac Resynchronization Therapy" *Heart Rhythm*, Apr. 2005; 2(4):376-381.

Gulrajani, "The Forward and Inverse Problems of Electrocardiography," *IEEE Engineering in Medicine and Biology*, IEEE Service Center, vol. 17, No. 5, Sep. 1, 1988; pp. 84-101, 122.

Hansen, "Regularization Tools: A Matlab Package for Analysis and Solution of Discrete Ill-Posed Problems," Version 4.1 for Matlab 7.3; Mar. 2008; 128 pages. Retrieved from the Internet: Jun. 19, 2014 http://www.mathworks.com/matlabcentral/fileexchange/52-regtools.

Hayes et al., "Cardiac Resynchronization Therapy and the Relationship of Percent Biventricular Pacing to Symptoms and Survival," *Heart Rhythm*, Sep. 2011; 8(9):1469-1475.

"Heart Failure Management" datasheet [online]. Medtronic, Minneapolis, Minnesota, [Last updated on Jun. 3, 2013].Retrieved from the Internet: www.medtronic.com; 9 pages.

Jia et al., "Electrocardiographic Imaging of Cardiac Resynchronization Therapy in Heart Failure: Observation of Variable Electrophysiologic Responses," *Heart Rhythm*, vol. 3, No. 3; Mar. 1, 2006, pp. 296-310.

Kornreich, "Body Surface Potential Mapping of ST Segment Changes in Acute Myocardial Infarction," *Circulation*, 1993; 87: 773-782.

Modre et al., "Noninvasive Myocardial Activation Time Imaging: A Novel Inverse Algorithm Applied to Clinical ECG Mapping Data" *IEEE Transactions on Biomedical Engineering*, vol. 49; No. 10, Oct. 2002; pp. 1153-1161.

Ridgeway, "The State of Boosting," *Computing Science and Statistics*, 1999; 31:172-181.

Ryu et al., "Simultaneous Electrical and Mechanical Mapping Using 3D Cardiac Mapping System: Novel Approach for Optimal Cardiac Resynchronization Therapy," *Journal of Cardiovascular Electrophysiology*, Feb. 2010; 21(2):219-222.

Singh et al., "Left Ventricular Lead Position and Clinical Outcome in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT) Trial," *Circulation*, 2011; 123:1159-1166.

Sperzel et al., "Intraoperative Characterization of Interventricular Mechanical Dyssynchrony Using Electroanatomic Mapping System—A feasibility Study," *Journal of Interventional Cardiac Electrophysiology*, Nov. 2012; 35(2):189-96.

Steinhaus BM., "Estimating cardiac transmembrane activation and recovery times from unipolar and bipolar extracellular electrograms : a simulation study," Circulation Research, 1989, 64:449-462.

Sweeney et al., "Analysis of Ventricular Activation Using Surface Electrocardiography to Predict Left Ventricular Reverse Volumetric Remodeling During Cardiac Resynchronization Therapy," *Circulation*, Feb. 9, 2010; 121(5):626-634.

Turner et al, "Electrical and Mechanical Components of Dyssynchrony in Heart Failure Patients with Normal QRS Duration and Left Bundle-Branch Block," *Circulation* 2004; 109: 2544-2549.

van Deursen et al., "Vectorcardiography as a Tool for Easy Optimization of Cardiac Resynchronization Therapy in Canine Left Bundle Branch Block Hearts," *Circulation Arrhythmia and Electrophysiology*, Jun. 1, 2012; 5(3):544-552.

Vardas et al., The Task Force for Cardiac Pacing and Cardiac Resynchronization Therapy of the European Society of Cardiology. Developed in Collaboration with the European Heart Rhythm Association, *European Heart Journal*, 2007; 28:2256-2295.

Varma et al., "Placebo CRT," *Journal of Cardiovascular Electrophysiology*, vol. 19, Aug. 2008; p. 878.

Williams et al., "Short-Term Hemodynamic Effects of Cardiac Resynchronization Therapy in Patients With Heart Failure, a Narrow QRS Duration, and No Dyssynchrony," *Circulation*, Oct. 27, 2009; 120: 1687-1694.

Avari et al., "Cardiac Resynchronization Therapy in Pediatric Congenital Heart Disease: Insights from Noninvasive Electrocardiographic Imaging" *Heart Rhythm*, vol. 6, No. 8. Aug. 1, 2009; pp. 1178-1185 (as reproduced—NIH Public Access).

Silva et al., "Cardiac Resynchronization Therapy in Pediatric Congenital Heart Disease: Insights from Noninvasive Electrocardiographic Imaging" *Heart Rhythm*, vol. 6, No. 8. Aug. 1, 2009; pp. 1178-1185.

Cheng, Chien-Ming et al., "Comparison of quick optimization of interventricular delay between simple methods: Intracardiac

(56) **References Cited**

OTHER PUBLICATIONS

electrogram and surface electrocardiogram after cardiac resynchronization therapy", Europace, Sep. 2012; 4(9); 1317-23.

* cited by examiner

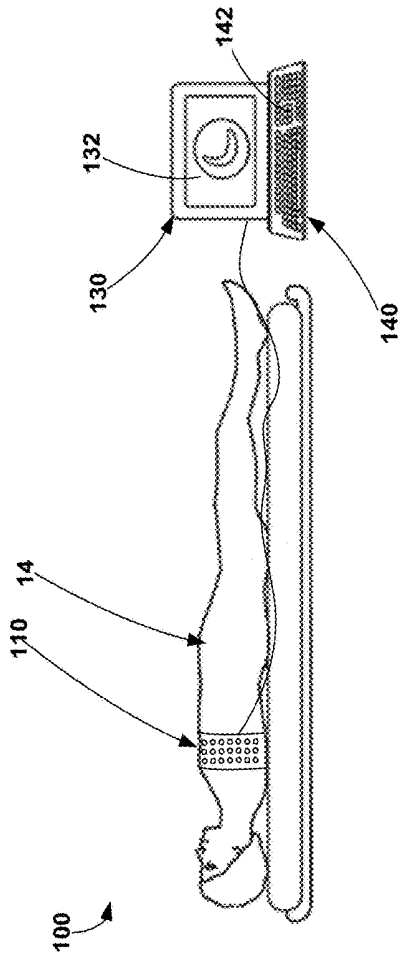


FIG. 1

FIG. 2

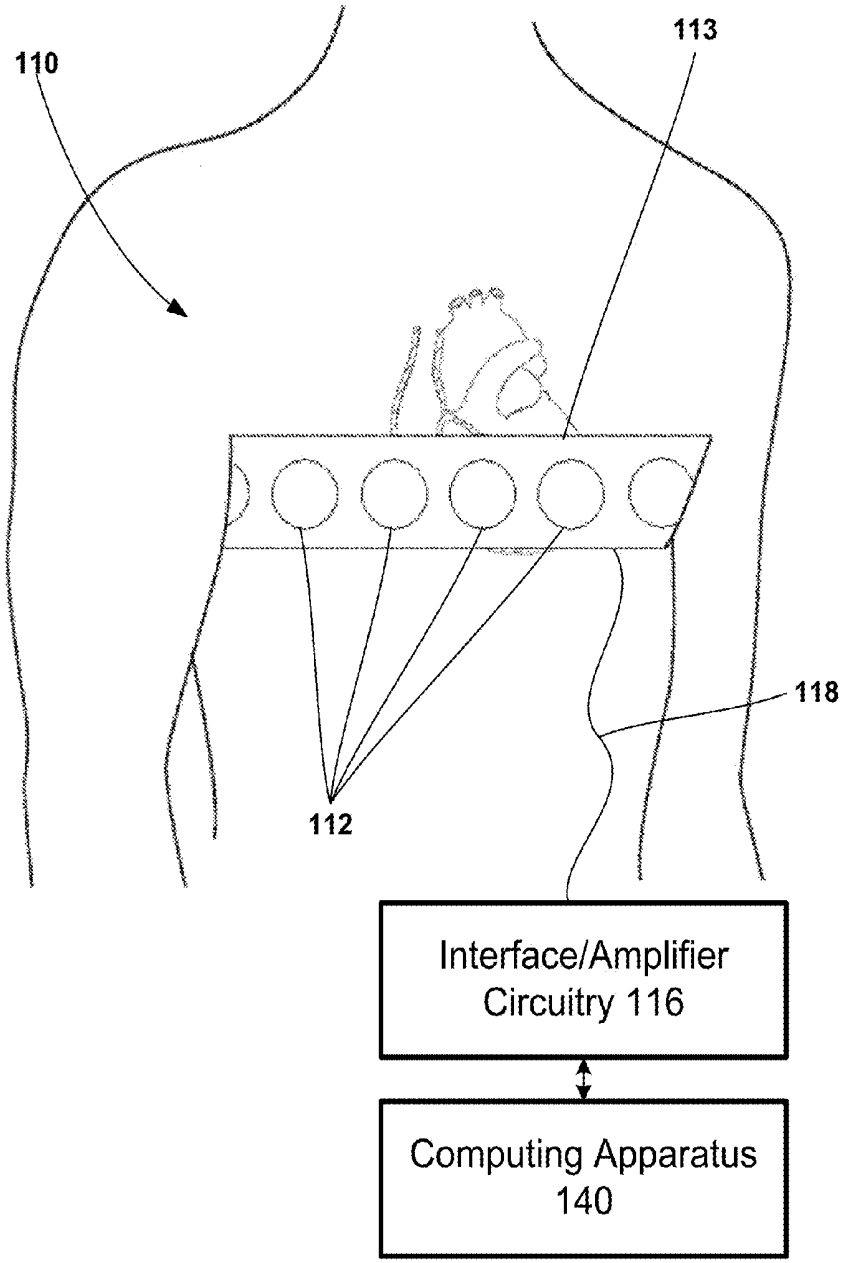

110
113
118
112
Interface/Amplifier Circuitry 116
Computing Apparatus 140

FIG. 3

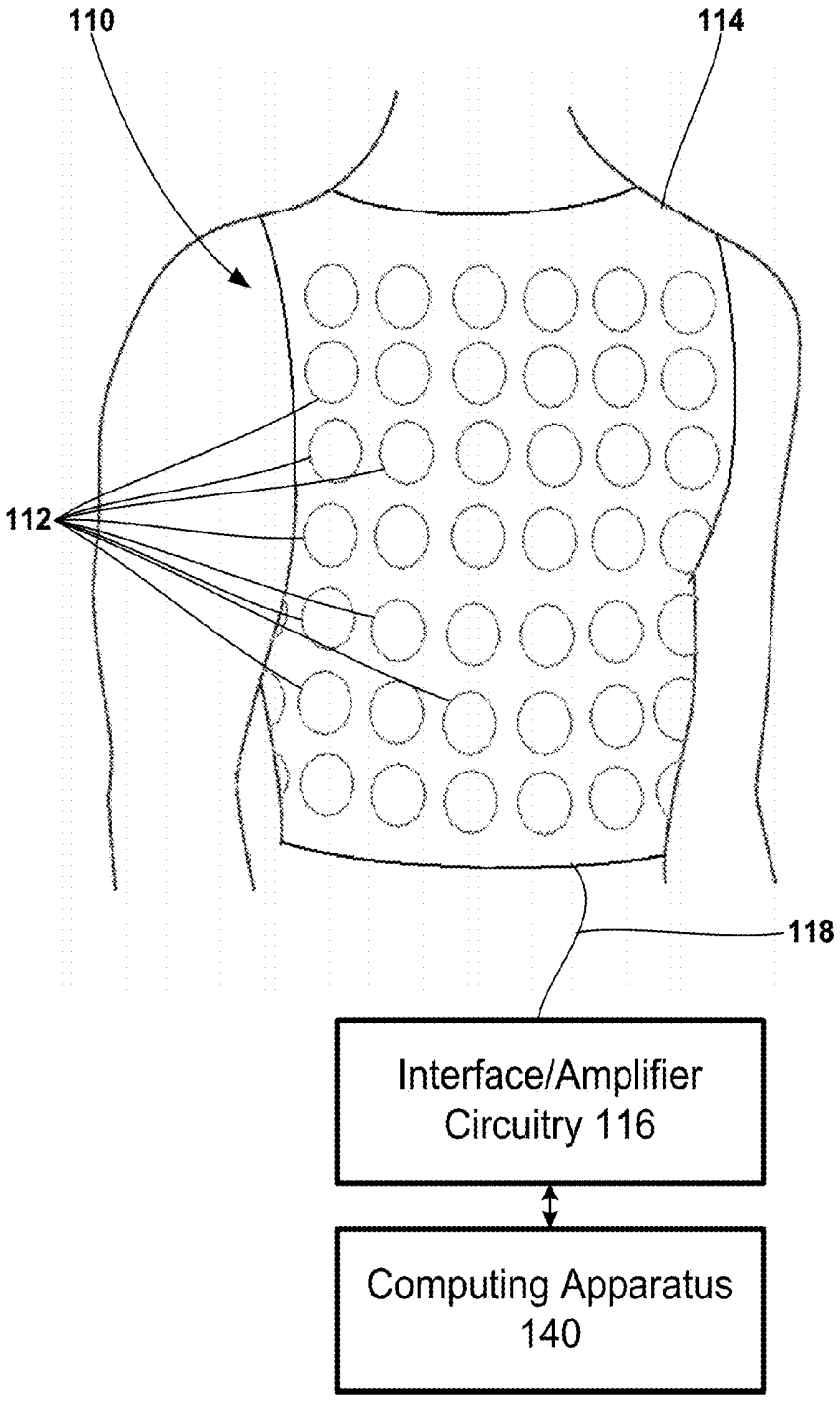

110
114
112
118
Interface/Amplifier Circuitry 116
Computing Apparatus 140

FIG. 4

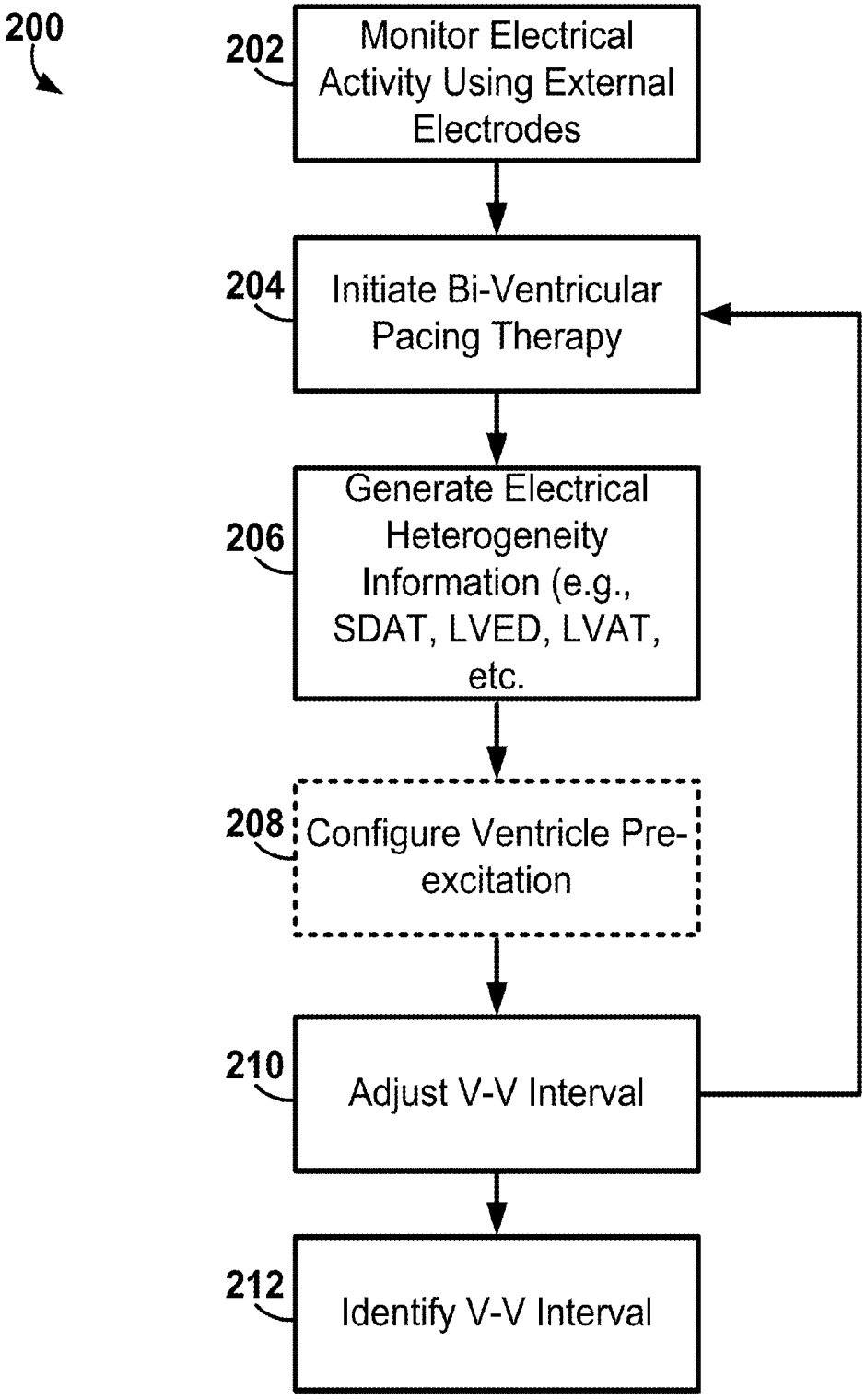

200
202
Monitor Electrical Activity Using External Electrodes
204
Initiate Bi-Ventricular Pacing Therapy
206
Generate Electrical Heterogeneity Information (e.g., SDAT, LVED, LVAT, etc.
208
Configure Ventricle Pre-excitation
210
Adjust V-V Interval
212
Identify V-V Interval

FIG. 5

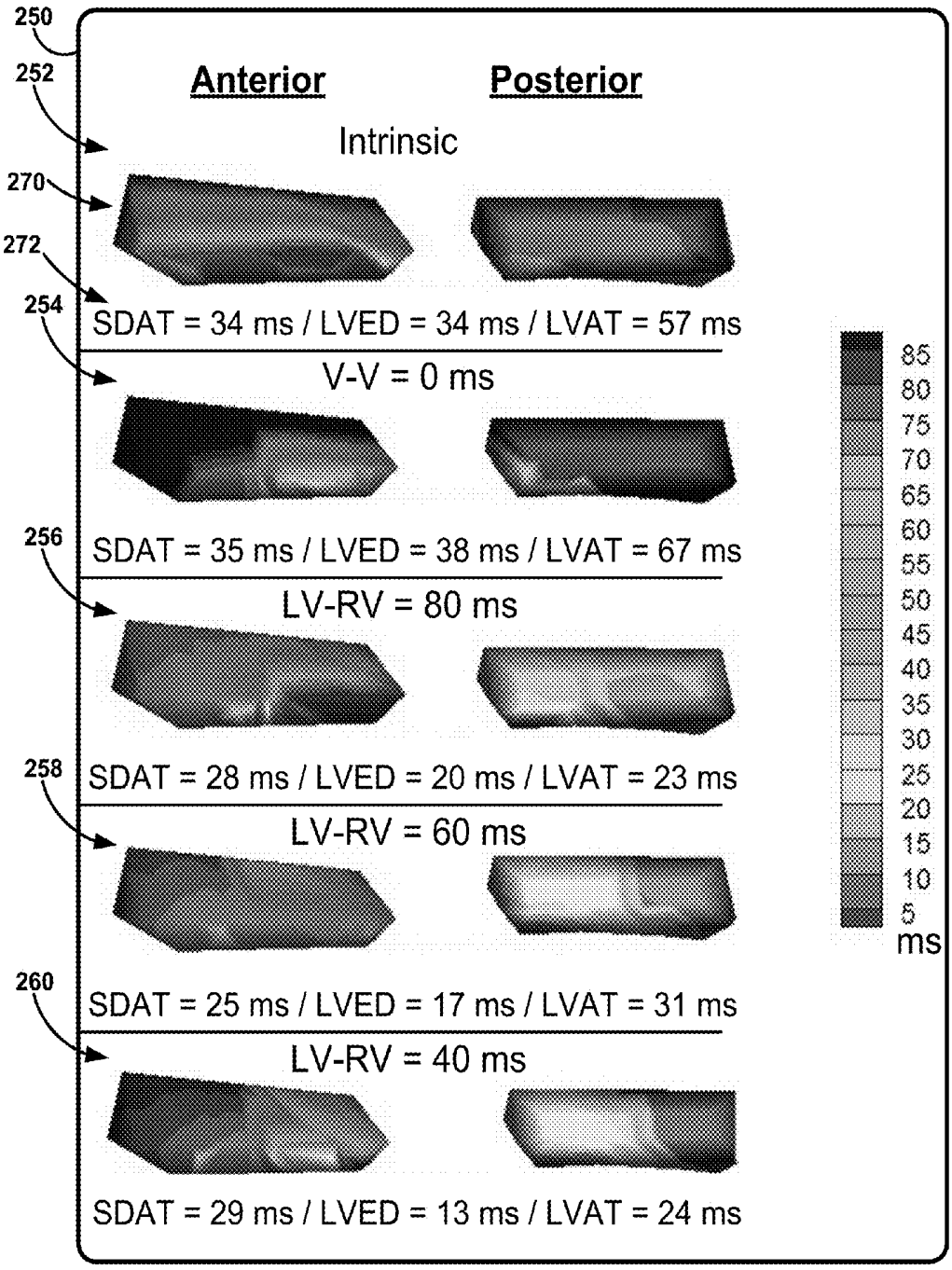

250
252
Anterior
Posterior
Intrinsic
270
272
254
SDAT = 34 ms / LVED = 34 ms / LVAT = 57 ms
V-V = 0 ms
256
SDAT = 35 ms / LVED = 38 ms / LVAT = 67 ms
LV-RV = 80 ms
258
SDAT = 28 ms / LVED = 20 ms / LVAT = 23 ms
LV-RV = 60 ms
260
SDAT = 25 ms / LVED = 17 ms / LVAT = 31 ms
LV-RV = 40 ms
SDAT = 29 ms / LVED = 13 ms / LVAT = 24 ms
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
ms

FIG. 6

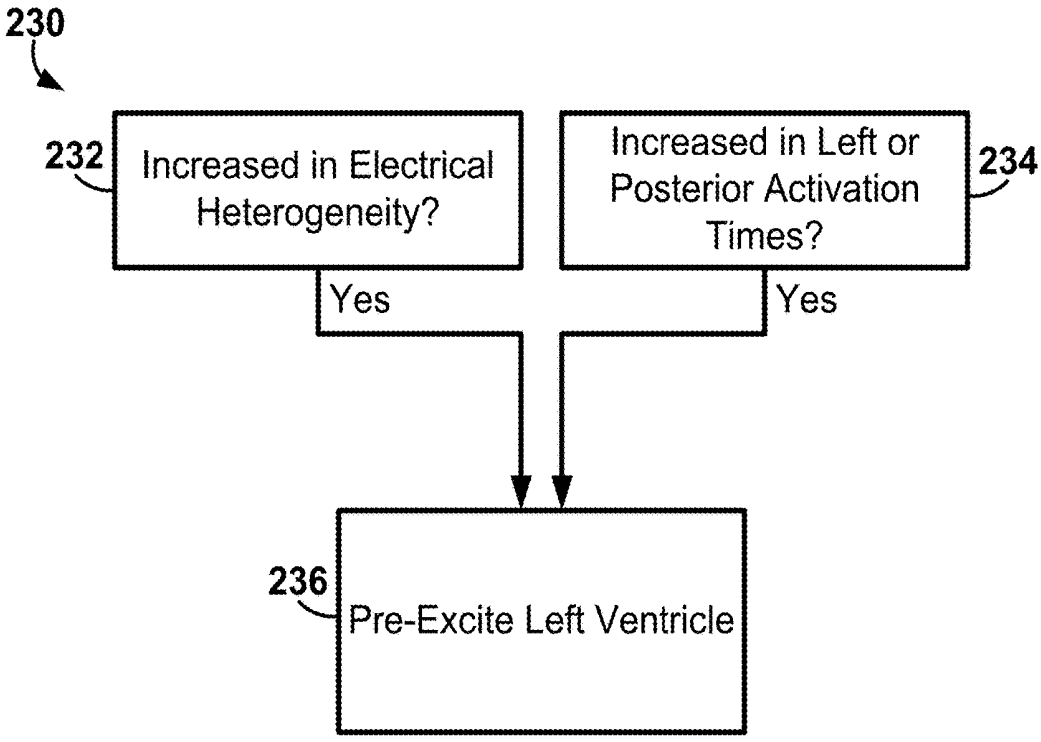

230
232
Increased in Electrical Heterogeneity?
Increased in Left or Posterior Activation Times?
234
Yes
Yes
236
Pre-Excite Left Ventricle

FIG. 7

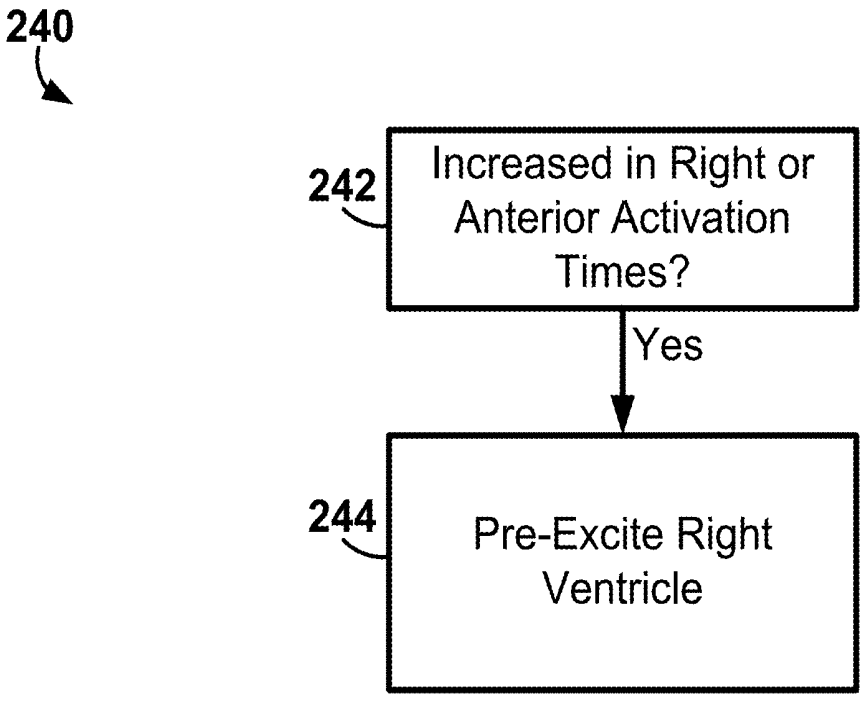
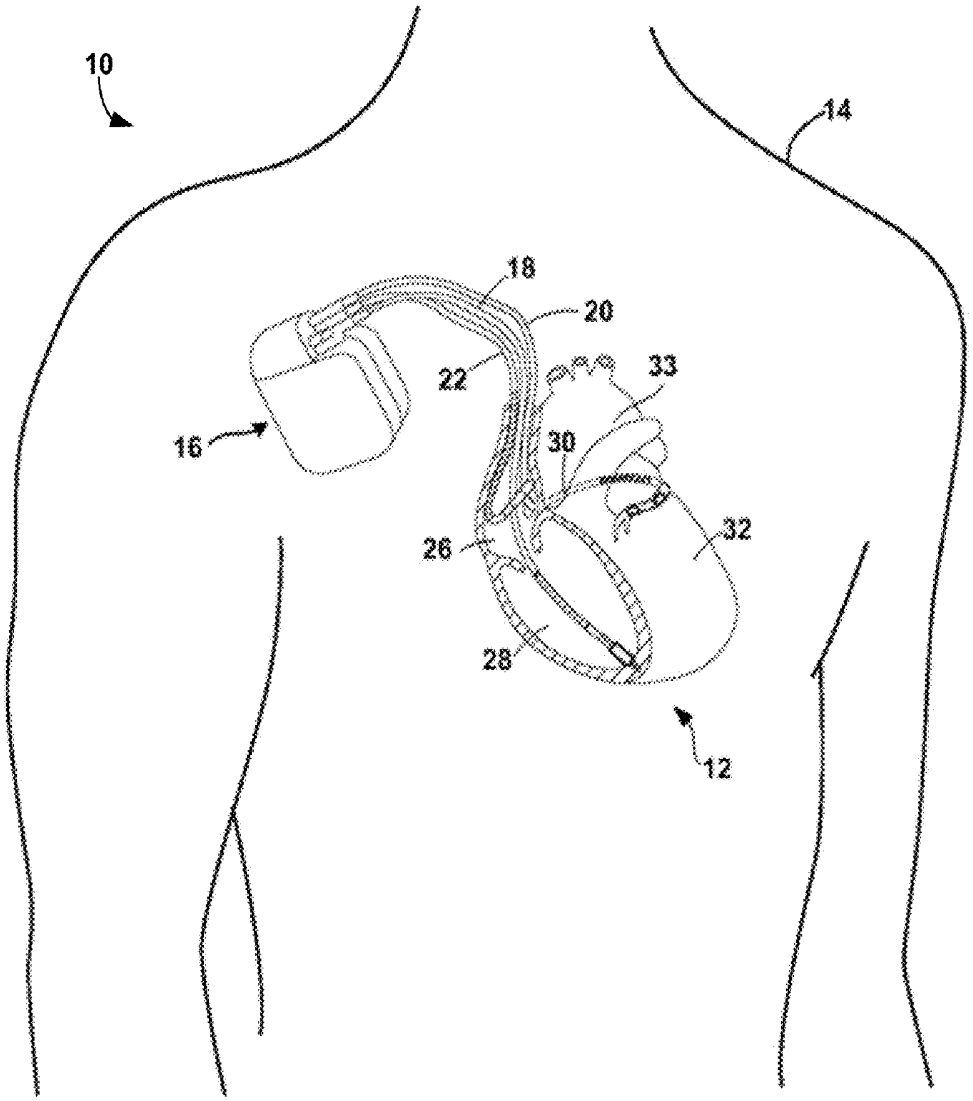

240
242
Increased in Right or Anterior Activation Times?
Yes
244
Pre-Excite Right Ventricle

FIG. 8



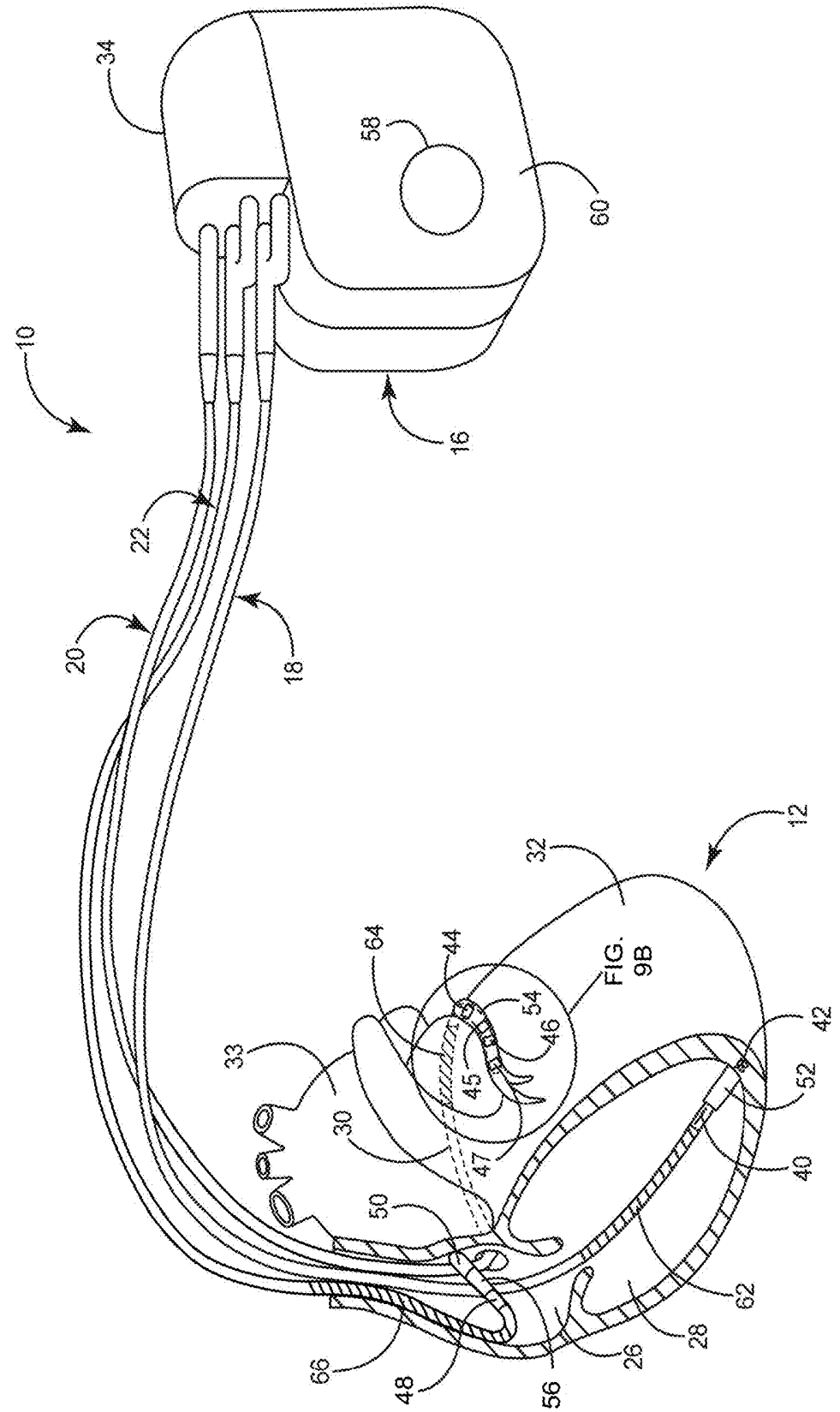

34
58
60
10
16
22
20
18
12
32
64
44
FIG. 9B
54
46
33
45
42
52
30
47
40
50
62
28
66
26
48
56

FIG. 9A

FIG. 9B

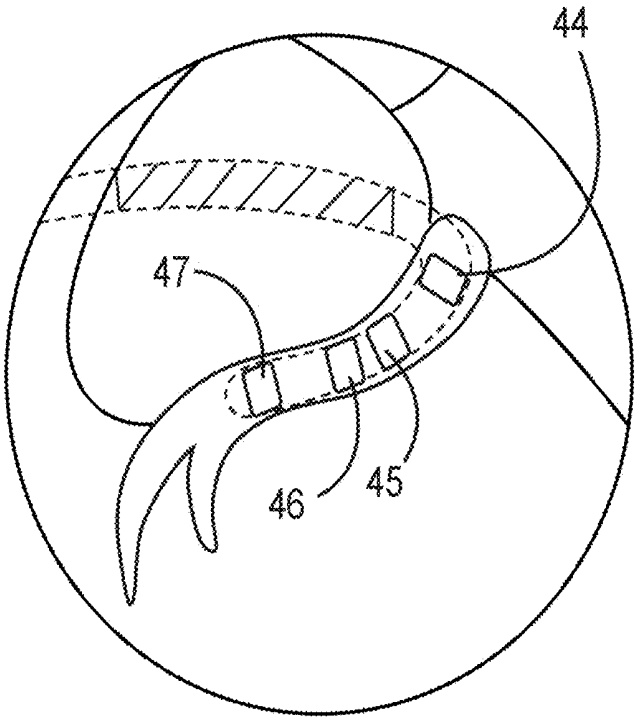
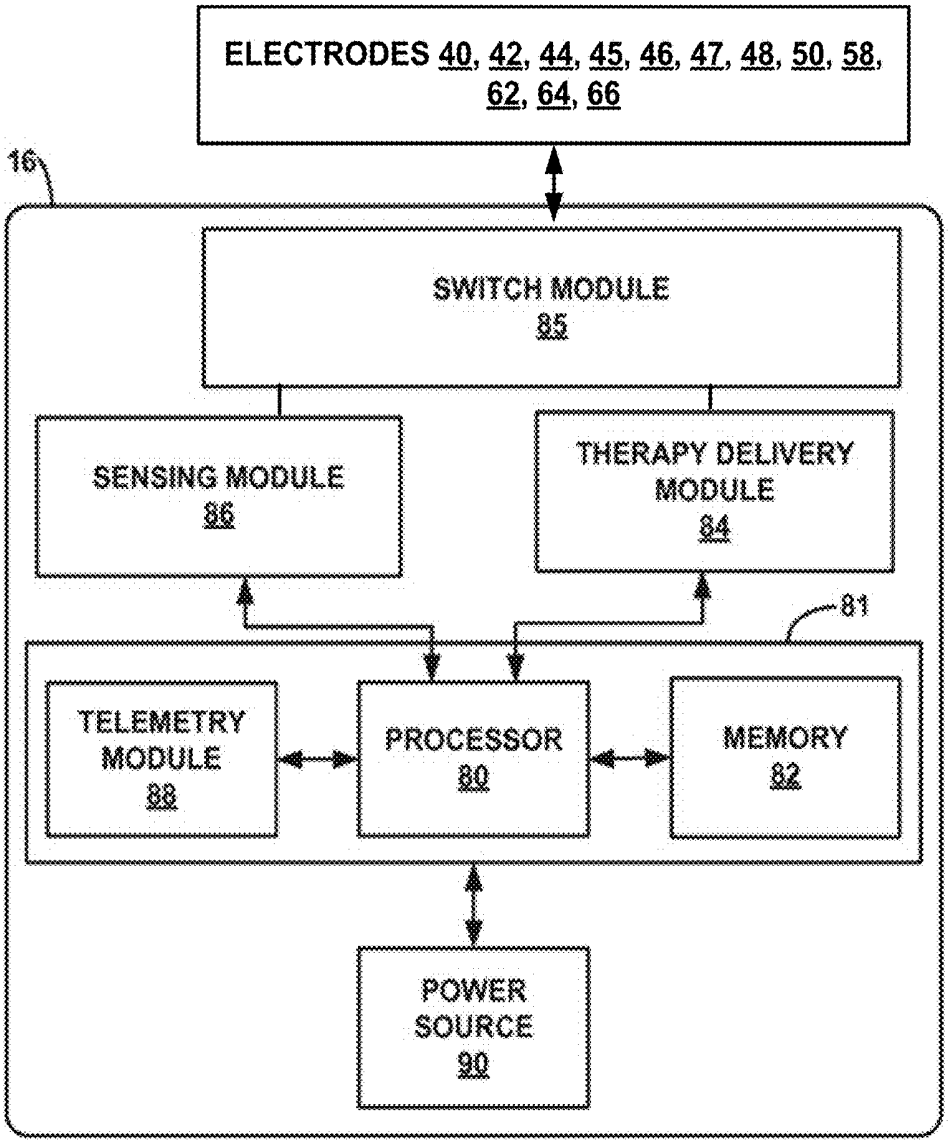


FIG. 10A


ELECTRODES 40, 42, 44, 45, 46, 47, 48, 50, 58, 62, 64, 66
16
SWITCH MODULE 85
SENSING MODULE 86
THERAPY DELIVERY MODULE 84
81
TELEMETRY MODULE 88
PROCESSOR 80
MEMORY 82
POWER SOURCE 90

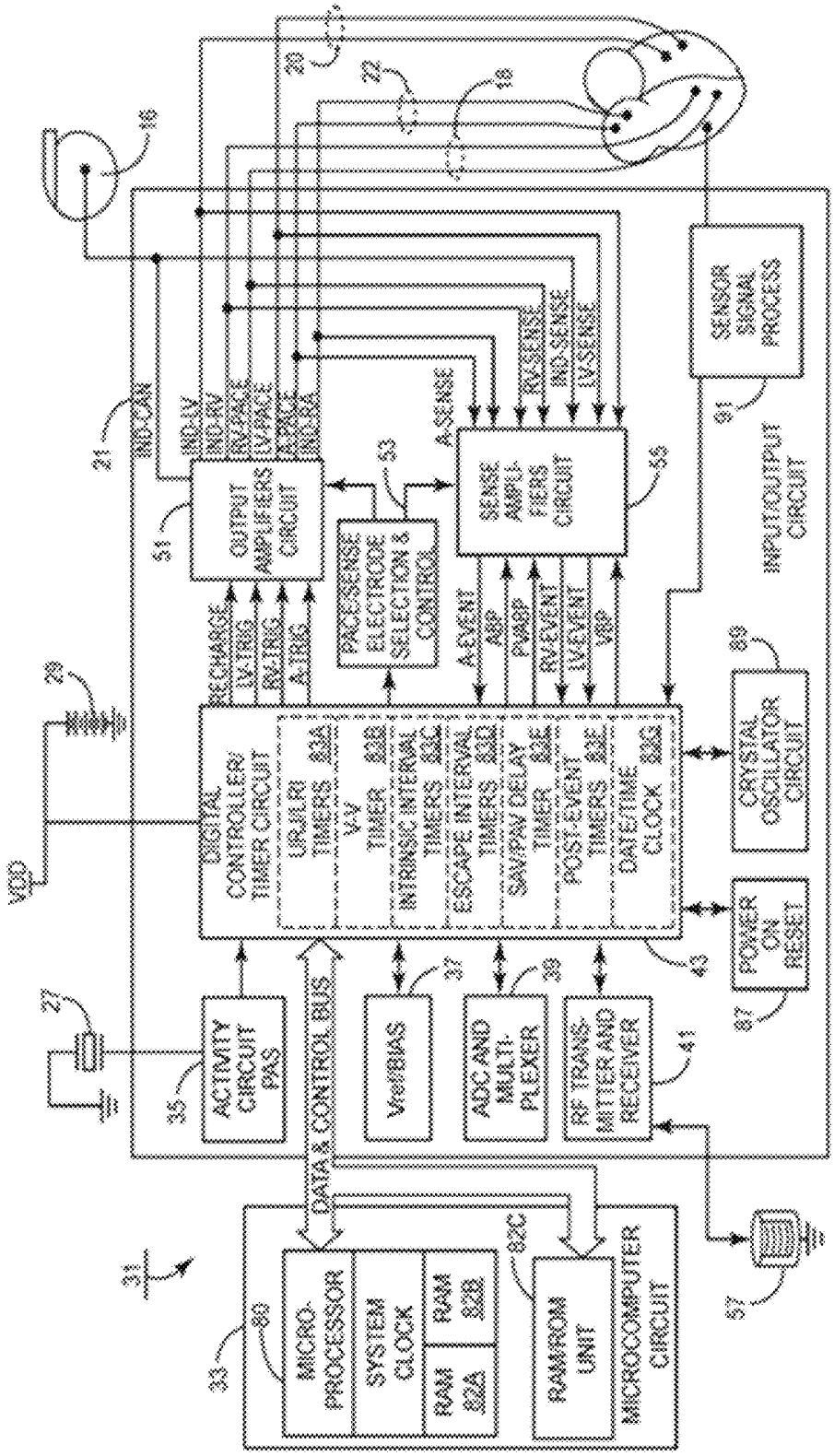

MICRO-PROCESSOR
SYSTEM CLOCK
RAM 82B
RAM 82A
RAM/ROM UNIT
MICROCOMPUTER CIRCUIT
DATA & CONTROL BUS
ACTIVITY CIRCUIT PAS
VrefBIAS
ADC AND MULTI-PLEXER
RF TRANS-MITTER AND RECEIVER
DIGITAL CONTROLLER/ TIMER CIRCUIT
URI/URI TIMERS
V-V TIMER
INTRINSIC INTERVAL TIMERS
ESCAPE INTERVAL TIMERS
SAV/PAV DELAY TIMER
POST-EVENT TIMERS
DATE/TIME CLOCK
CRYSTAL OSCILLATOR CIRCUIT
POWER ON RESET
OUTPUT AMPLIFIERS CIRCUIT
PACE/SENSE ELECTRODE SELECTION & CONTROL
SENSE AMPLI-FIERS CIRCUIT
SENSOR SIGNAL PROCESS
INPUT/OUTPUT CIRCUIT
VDD
IND.CAN
RECHARGE
LV.TRIG
RV.TRIG
A.TRIG
A.SENSE
RV.SENSE
IND.SENSE
LV.SENSE
A.EVENT
A.BP
PVBP
RV.EVENT
LV.EVENT
VBP

FIG. 10B

SYSTEMS AND METHODS FOR CONFIGURATION OF INTERVENTRICULAR INTERVAL

This application claims the benefit of U.S. Provisional Patent Application 62/037,694 entitled "Systems and Methods for Configuration of Interventricular Interval" and filed on Aug. 15, 2014, which is incorporated herein by reference in its entirety.

The disclosure herein relates to systems and methods for use in the configuration (e.g., optimization) of interventricular interval, or delay, for cardiac therapy being performed on a patient.

Cardiac therapy, such as cardiac resynchronization therapy (CRT), may correct symptoms of electrical dyssynchrony of a patient's heart by providing pacing therapy to one or both ventricles or atria, e.g., by providing pacing to encourage earlier activation of the left or right ventricles. By pacing, the ventricles may be controlled such that they contract in synchrony.

Providing cardiac therapy to a patient may involve determining effective programming of device parameters. For example, the selection of the timing of the pacing pulses delivered to the electrodes, such as atrioventricular (A-V) and interventricular (V-V) intervals, or delays, may be adjusted to deliver effective and/or optimal pacing therapy. Biventricular pacing includes the pacing (e.g., delivery of electrical stimulation) to both ventricles in a coordinated manner. V-V interval optimization may be challenging (e.g., especially in non-responder patients). Echocardiographic methods may be used for V-V interval optimization but may not be preferable.

SUMMARY

The exemplary systems, methods, and interfaces described herein may be configured to assist a user (e.g., a physician) in configuring cardiac therapy (e.g., cardiac therapy being performed on a patient during and/or after implantation of cardiac therapy apparatus). The systems, methods, and interfaces may be described as being noninvasive. For example, the systems, methods, and interfaces may not need implantable devices such as leads, probes, sensors, catheters, etc. to evaluate and configure the cardiac therapy. Instead, the systems, methods, and interfaces may use electrical measurements taken noninvasively using, e.g., a plurality of external electrodes attached to the skin of a patient about the patient's torso.

The exemplary systems and methods may monitor electrical activity using a plurality of external electrodes during the delivery of cardiac therapy using a plurality of different V-V intervals. The electrical activity may be used to generate electrical heterogeneity information (e.g., data) representative of mechanical cardiac functionality and/or electrical cardiac functionality of the patient for each of the plurality of different V-V intervals. One or more of the V-V intervals may be identified based on the electrical heterogeneity information (e.g., data) for each of the plurality of different V-V intervals.

The exemplary systems and methods may further determine which of the left ventricle or right ventricle should be pre-excited using a V-V interval based on baseline electrical heterogeneity information (e.g., data) from electrical activity monitored during delivery of cardiac therapy with an initial V-V interval (e.g., a V-V interval of 0 milliseconds).

One exemplary system for use in cardiac therapy may include electrode apparatus and computing apparatus coupled to the electrode apparatus. The electrode apparatus may include a plurality of external electrodes configured to be located proximate tissue of a patient (e.g., surface electrodes positioned in an array configured to be located proximate the skin of the torso of the patient). The computing apparatus may be configured to initiate delivery of bi-ventricular pacing therapy at a plurality of different V-V intervals (e.g., delivered by at least one implantable electrode coupled to at least one lead, bi-ventricular pacing therapy delivered at an optimized A-V interval, etc.), monitor electrical activity using the plurality of external electrodes for each of the plurality of V-V intervals during the delivery of bi-ventricular pacing therapy, and generate electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for each of the plurality of V-V intervals based on the monitored electrical activity. The computing apparatus may be further configured to identify a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information.

One exemplary method for use in cardiac therapy may include initiating delivery of bi-ventricular pacing therapy at a plurality of different V-V intervals, monitoring electrical activity using a plurality of external electrodes (e.g., surface electrodes positioned in an array configured to be located proximate the skin of the torso of the patient) for each of the plurality of V-V intervals during the delivery of bi-ventricular pacing therapy (e.g., delivered by at least one implantable electrode coupled to at least one lead, bi-ventricular pacing therapy delivered at an optimized A-V interval, etc.), and generating electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for each of the plurality of V-V intervals based on the monitored electrical activity. The exemplary method may further include identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information.

One exemplary system for use in cardiac therapy may include electrode means and computing means. The electrode means may include a plurality of external electrodes configured to be located proximate tissue of a patient (e.g., surface electrodes positioned in an array configured to be located proximate the skin of the torso of the patient). The computing means may be for initiating delivery of bi-ventricular pacing therapy at a plurality of different V-V intervals, monitoring electrical activity using the electrode means for each of the plurality of V-V intervals during the delivery of bi-ventricular pacing therapy (e.g., delivered by at least one implantable electrode coupled to at least one lead, bi-ventricular pacing therapy is delivered at an optimized A-V interval, etc.), and generating electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for each of the plurality of V-V intervals based on the monitored electrical activity. The computing means may further be for identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information.

One exemplary system for use in cardiac therapy may include electrode apparatus and computing apparatus coupled to the electrode apparatus. The electrode apparatus may include a plurality of external electrodes configured to be located proximate tissue of a patient (e.g., surface electrodes positioned in an array configured to be located proximate the skin of the torso of the patient). The computing apparatus may be configured to monitor electrical activity using the plurality of external electrodes, initiate delivery

of bi-ventricular pacing therapy at an initial V-V interval (e.g., delivered by at least one implantable electrode coupled to at least one lead, bi-ventricular pacing therapy is delivered at an optimized A-V interval, etc.), and generate initial electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for the initial V-V interval based on the electrical activity monitored during the delivery of bi-ventricular pacing therapy at the initial V-V interval. The computing apparatus may be further be configured to configure a plurality of different V-V intervals to pre-excite the left ventricle or the right ventricle based on the initial electrical heterogeneity information, initiate delivery of bi-ventricular pacing therapy at the plurality of different V-V intervals, generate electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for each of the plurality of different V-V intervals based on the monitored electrical activity, and identify a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information.

One exemplary method for use in cardiac therapy may include monitoring electrical activity using a plurality of external electrodes (e.g., surface electrodes positioned in an array configured to be located proximate the skin of the torso of the patient), initiating delivery of bi-ventricular pacing therapy at an initial V-V interval (e.g., delivered by at least one implantable electrode coupled to at least one lead, bi-ventricular pacing therapy is delivered at an optimized A-V interval, etc.), generating initial electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for the initial V-V interval based on the electrical activity monitored during the delivery of bi-ventricular pacing therapy at the initial V-V interval. The exemplary method may further include configuring a plurality of different V-V intervals to pre-excite the left ventricle or the right ventricle based on the initial electrical heterogeneity information, initiating delivery of bi-ventricular pacing therapy at the plurality of different V-V intervals, generating electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for each of the plurality of V-V intervals based on the electrical activity monitored during the delivery of bi-ventricular pacing therapy at the plurality of different V-V intervals; and identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information.

One exemplary system for use in cardiac therapy may include electrode means and computing means. The electrode means may include a plurality of external electrodes configured to be located proximate tissue of a patient (e.g., surface electrodes positioned in an array configured to be located proximate the skin of the torso of the patient). The computing means may be for monitoring electrical activity using the electrode means, initiating delivery of bi-ventricular pacing therapy at an initial V-V interval (e.g., delivered by at least one implantable electrode coupled to at least one lead, bi-ventricular pacing therapy is delivered at an optimized A-V interval, etc.), and generating initial electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for the initial V-V interval based on the electrical activity monitored during the delivery of bi-ventricular pacing therapy at the initial V-V interval. The computing means may be further for configuring a plurality of different V-V intervals to pre-excite the left ventricle or the right ventricle based on the initial electrical heterogeneity information, initiating delivery of bi-ventricular pacing therapy at the plurality of different V-V intervals, generating electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for each of the plurality of V-V intervals based on the electrical activity monitored during the delivery of bi-ventricular pacing therapy at the plurality of different V-V intervals, and identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information.

In one or more embodiments, the electrical heterogeneity information (e.g., data) may include a global standard deviation of surrogate electrical activation times monitored by the plurality of external electrodes, and identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information may include identifying the V-V interval from the plurality of different V-V intervals that generated the lowest global standard deviation of surrogate electrical activation times.

In one or more embodiments, the plurality of electrodes may include two or more left external electrodes configured to be located proximate the left side of the patient. In at least one embodiment, the electrical heterogeneity information may include a left standard deviation of surrogate electrical activation times monitored by the two or more left external electrodes and identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information may include identifying the V-V interval from the plurality of different V-V intervals that generated the lowest left standard deviation. In at least one embodiment, the electrical heterogeneity information may include a left average of surrogate electrical activation times monitored by the two or more left external electrodes, and identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information may include identifying the V-V interval from the plurality of different V-V intervals that generated the lowest left average.

In one or more embodiments, the plurality of different V-V intervals may be configured to pre-excite the left ventricle if the electrical heterogeneity information indicates an increase in heterogeneity in the electrical activity monitored by the plurality of external electrodes. For example, the plurality of electrodes may include two or more left external electrodes configured to be located proximate the left side of the patient and two or more posterior external electrodes configured to be located proximate the posterior side of the patient. The plurality of different V-V intervals may be configured to pre-excite the left ventricle if the monitored electrical activity indicates an increase in surrogate electrical activation times monitored by at least one of the two or more left external electrodes and the two or more posterior external electrodes. Further, for example, the plurality of electrodes may include two or more right external electrodes configured to be located proximate the right side of the patient and two or more anterior external electrodes configured to be located proximate the anterior side of the patient. The plurality of different V-V intervals may be configured to pre-excite the right ventricle if the monitored electrical activity indicates an increase in surrogate electrical activation times monitored by at least one of the two or more right external electrodes and the two or more anterior external electrodes.

In one or more embodiments, display apparatus may include, or be configured to display, a graphical user interface configured to present information for use in assisting a

user in evaluating and adjusting cardiac therapy delivered to a patient. The information may include the identified V-V interval and/or a graphical representation of surrogate electrical activation times monitored by the plurality of external electrodes about a portion of human anatomy monitored for each V-V interval of the plurality of different V-V intervals (e.g., color scaling the portion of human anatomy on the graphical user interface according to the surrogate electrical activation times).

It may be described that the exemplary systems and methods may focus on optimizing ventriculo-ventricular, or interventricular, (V-V) intervals, or delays, based on electrical activation and heterogeneity patterns monitored using a ECG electrode belt or a collection of surface ECG electrodes during cardiac resynchronization therapy (CRT) pacing. Further, the exemplary methods and systems may determine which ventricle to pre-excite and provide feedback identifying an optimal V-V delay.

The exemplary systems and methods may use one or more metrics, or indices, of electrical heterogeneity derived from ECG electrodes applied on the anterior as well as on posterior surfaces of the torso. The metrics of electrical heterogeneity may include a global metric, which includes a standard deviation of activation times (SDAT) from all electrodes, and two regional left-sided metrics. The two regional left-sided metrics may include one based on a standard deviation of activation times (LVED) from the left-sided electrodes and another based on a mean activation time (LVAT) of the left-sided electrodes. The exemplary systems and methods may provide V-V optimization that helps patients respond better to CRT therapy, especially when simultaneous biventricular pacing with an optimized atrioventricular delay fails to generate an effective response to CRT therapy.

The optimization of the V-V interval, or delay, which can be done either at implant or post-implant, may be based on the heterogeneity patterns during baseline biventricular pacing with zero V-V delay and an optimized A-V delay. In one or more embodiments, electrical activation times can be displayed in terms of color-coded maps (e.g., red for early activation times, blue for late activation times, etc.). If there is increased global heterogeneity (e.g., the SDAT is greater than or equal to about 25 milliseconds (ms)) and/or increased local heterogeneity (e.g., the LVED is greater than or equal to about 25 ms, the LVAT is greater than or equal to about 60 ms, etc.), it may indicate that conduction delay is present on the left side or posterior side of the patient and LV pre-excitation would be performed.

Different pre-excitation intervals, or delays, may be used, for example, starting from 10 ms to 100 ms in steps of 10 ms. In at least one embodiment, the interval that gives the least value of one or a combination of heterogeneity metrics may be identified as the optimal V-V interval. The optimal V-V interval may be programmed into the pacing apparatus used to deliver the biventricular pacing therapy.

If conduction delay is present on the right side or anterior side of the patient during simultaneous biventricular pacing at an optimized A-V interval, then the right ventricle may be pre-excited. Again, activation times for different V-V intervals starting from 10 ms to 100 ms may be evaluated and the settings that provide the least, or smallest, heterogeneity values may be chosen for pacing therapy.

It may be described that the present disclosure provides a roadmap to V-V interval optimization that can improve response in some CRT patients. Maximizing CRT response during simultaneous biventricular pacing can help identify areas of conduction delay and may localize, or identify, which ventricle is activating later than the other and can benefit from a possible pre-excitation interval. Further, the exemplary systems and methods can also provide feedback on what V-V interval gives the optimal setting.

The above summary is not intended to describe each embodiment or every implementation of the present disclosure. A more complete understanding will become apparent and appreciated by referring to the following detailed description and claims taken in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a diagram of an exemplary system including electrode apparatus, display apparatus, and computing apparatus.

FIGS. **2-3** are diagrams of exemplary external electrode apparatus for measuring torso-surface potentials.

FIG. **4** is a block diagram of an exemplary method for V-V interval identification (e.g., optimization).

FIG. **5** depicts five sets of graphical electrical activation information and electrical heterogeneity information for five different V-V intervals.

FIGS. **6-7** are block diagrams of exemplary methods for determining pre-excitation for V-V intervals.

FIG. **8** is a diagram of an exemplary system including an exemplary implantable medical device (IMD).

FIG. **9**A is a diagram of the exemplary IMD of FIG. **9**.

FIG. **9**B is a diagram of an enlarged view of a distal end of the electrical lead disposed in the left ventricle of FIG. **9**A.

FIG. **10**A is a block diagram of an exemplary IMD, e.g., the IMD of FIGS. **8-9**.

FIG. **10**B is another block diagram of an exemplary IMD (e.g., an implantable pulse generator) circuitry and associated leads employed in the system of FIG. **8**.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

In the following detailed description of illustrative embodiments, reference is made to the accompanying figures of the drawing which form a part hereof, and in which are shown, by way of illustration, specific embodiments which may be practiced. It is to be understood that other embodiments may be utilized and structural changes may be made without departing from (e.g., still falling within) the scope of the disclosure presented hereby.

Exemplary systems and methods shall be described with reference to FIGS. **1-10**. It will be apparent to one skilled in the art that elements or processes from one embodiment may be used in combination with elements or processes of the other embodiments, and that the possible embodiments of such methods and systems using combinations of features set forth herein is not limited to the specific embodiments shown in the Figures and/or described herein. Further, it will be recognized that the embodiments described herein may include many elements that are not necessarily shown to scale. Still further, it will be recognized that timing of the processes and the size and shape of various elements herein may be modified but still fall within the scope of the present disclosure, although certain timings, one or more shapes and/or sizes, or types of elements, may be advantageous over others.

Cardiac electrical activation times can be detected or estimated in proximity of a reference location (e.g., which can be a chosen location for a left ventricle lead during

implant) using unipolar electrocardiogram (ECG) recordings. The cardiac electrical activation times may be used to generate electrical heterogeneity information that may be used by a user (e.g., physician) to optimize one or more settings, or parameters, of pacing therapy. Further, the electrical activation times may be measured and displayed, or conveyed, to a user by a system. As described herein, electrical activation times and/or electrical heterogeneity information may be used in noninvasive configuration (e.g., optimization, adjustment, etc.) of cardiac therapy.

Various exemplary systems, methods, and interfaces may be configured to use electrode apparatus including external electrodes, display apparatus, and computing apparatus to noninvasively assist a user (e.g., a physician) in the configuration (e.g., optimization) of cardiac therapy. An exemplary system **100** including electrode apparatus **110**, display apparatus **130**, and computing apparatus **140** is depicted in FIG. **1**.

The electrode apparatus **110** as shown includes a plurality of electrodes incorporated, or included, within a band wrapped around the chest, or torso, of a patient **14**. The electrode apparatus **110** is operatively coupled to the computing apparatus **140** (e.g., through one or wired electrical connections, wirelessly, etc.) to provide electrical signals from each of the electrodes to the computing apparatus **140** for analysis, evaluation, etc. Exemplary electrode apparatus may be described in U.S. patent application Ser. No. 14/227,719 entitled "Bioelectric Sensor Device and Methods" and filed Mar. 27, 2014, which is incorporated herein by reference in its entirety. Further, exemplary electrode apparatus **110** will be described in more detail in reference to FIGS. **2-3**.

Although not described herein, the exemplary system **100** may further include imaging apparatus. The imaging apparatus may be any type of imaging apparatus configured to image, or provide images of, at least a portion of the patient in a noninvasive manner. For example, the imaging apparatus may not use any components or parts that may be located within the patient to provide images of the patient except noninvasive tools such as contrast solution. It is to be understood that the exemplary systems, methods, and interfaces described herein may further use imaging apparatus to provide noninvasive assistance to a user (e.g., a physician) to locate, or select, a pacing electrode or vector proximate the patient's heart in conjunction with the configuration of cardiac therapy.

For example, the exemplary systems, methods, and interfaces may provide image guided navigation that may be used to navigate leads including electrodes, leadless electrodes, wireless electrodes, catheters, etc., within the patient's body while also providing noninvasive cardiac therapy configuration including determining an effective, or optimal, V-V interval. Exemplary systems and methods that use imaging apparatus and/or electrode apparatus may be described in U.S. patent application Ser. No. 13/916,353 filed on Jun. 12, 2013 and entitled "Implantable Electrode Location Selection," U.S. patent application Ser. No. 13/916,377 filed on Jun. 12, 2013 and entitled "Implantable Electrode Location Selection," U.S. patent application Ser. No. 14/227,955 filed on Mar. 27, 2014 and entitled "Systems, Methods, and Interfaces for Identifying Effective Electrodes," U.S. patent application Ser. No. 14/227,919 filed on Mar. 27, 2014 and entitled "Systems, Methods, and Interfaces for Identifying Optimal Electrical Vectors," each of which is incorporated herein by reference in its entirety.

Exemplary imaging apparatus may be configured to capture x-ray images and/or any other alternative imaging modality. For example, the imaging apparatus may be configured to capture images, or image data, using isocentric fluoroscopy, bi-plane fluoroscopy, ultrasound, computed tomography (CT), multi-slice computed tomography (MSCT), magnetic resonance imaging (MRI), high frequency ultrasound (HIFU), optical coherence tomography (OCT), intra-vascular ultrasound (IVUS), two dimensional (2D) ultrasound, three dimensional (3D) ultrasound, four dimensional (4D) ultrasound, intraoperative CT, intraoperative MRI, etc. Further, it is to be understood that the imaging apparatus may be configured to capture a plurality of consecutive images (e.g., continuously) to provide video frame data. In other words, a plurality of images taken over time using the imaging apparatus may provide video frame, or motion picture, data. Additionally, the images may also be obtained and displayed in two, three, or four dimensions. In more advanced forms, four-dimensional surface rendering of the heart or other regions of the body may also be achieved by incorporating heart data or other soft tissue data from a map or from pre-operative image data captured by MRI, CT, or echocardiography modalities. Image datasets from hybrid modalities, such as positron emission tomography (PET) combined with CT, or single photon emission computer tomography (SPECT) combined with CT, could also provide functional image data superimposed onto anatomical data, e.g., to be used to navigate implantable apparatus to target locations within the heart or other areas of interest.

Systems and/or imaging apparatus that may be used in conjunction with the exemplary systems and methods described herein are described in U.S. Pat. App. Pub. No. 2005/0008210 to Evron et al. published on Jan. 13, 2005, U.S. Pat. App. Pub. No. 2006/0074285 to Zarkh et al. published on Apr. 6, 2006, U.S. Pat. App. Pub. No. 2011/0112398 to Zarkh et al. published on May 12, 2011, U.S. Pat. App. Pub. No. 2013/0116739 to Brada et al. published on May 9, 2013, U.S. Pat. No. 6,980,675 to Evron et al. issued on Dec. 27, 2005, U.S. Pat. No. 7,286,866 to Okerlund et al. issued on Oct. 23, 2007, U.S. Pat. No. 7,308,297 to Reddy et al. issued on Dec. 11, 2011, U.S. Pat. No. 7,308,299 to Burrell et al. issued on Dec. 11, 2011, U.S. Pat. No. 7,321,677 to Evron et al. issued on Jan. 22, 2008, U.S. Pat. No. 7,346,381 to Okerlund et al. issued on Mar. 18, 2008, U.S. Pat. No. 7,454,248 to Burrell et al. issued on Nov. 18, 2008, U.S. Pat. No. 7,499,743 to Vass et al. issued on Mar. 3, 2009, U.S. Pat. No. 7,565,190 to Okerlund et al. issued on Jul. 21, 2009, U.S. Pat. No. 7,587,074 to Zarkh et al. issued on Sep. 8, 2009, U.S. Pat. No. 7,599,730 to Hunter et al. issued on Oct. 6, 2009, U.S. Pat. No. 7,613,500 to Vass et al. issued on Nov. 3, 2009, U.S. Pat. No. 7,742,629 to Zarkh et al. issued on Jun. 22, 2010, U.S. Pat. No. 7,747,047 to Okerlund et al. issued on Jun. 29, 2010, U.S. Pat. No. 7,778,685 to Evron et al. issued on Aug. 17, 2010, U.S. Pat. No. 7,778,686 to Vass et al. issued on Aug. 17, 2010, U.S. Pat. No. 7,813,785 to Okerlund et al. issued on Oct. 12, 2010, U.S. Pat. No. 7,996,063 to Vass et al. issued on Aug. 9, 2011, U.S. Pat. No. 8,060,185 to Hunter et al. issued on Nov. 15, 2011, and U.S. Pat. No. 8,401,616 to Verard et al. issued on Mar. 19, 2013, each of which is incorporated herein by reference in its entirety.

The display apparatus **130** and the computing apparatus **140** may be configured to display and analyze data such as, e.g., electrical signals (e.g., electrocardiogram data), electrical heterogeneity information, etc. Electrical heterogeneity information, or electrical dyssynchrony information, may be representative of at least one of mechanical cardiac functionality and electrical cardiac functionality, surrogate

electrical activation information or data, etc. that is generated using electrical signals gathered, monitored, or collected, using the electrode apparatus **110**. In at least one embodiment, the computing apparatus **140** may be a server, a personal computer, or a tablet computer. The computing apparatus **140** may be configured to receive input from input apparatus **142** and transmit output to the display apparatus **130**. Further, the computing apparatus **140** may include data storage that may allow for access to processing programs or routines and/or one or more other types of data, e.g., for driving a graphical user interface configured to noninvasively assist a user in configuring one or more pacing parameters, or settings, such as, e.g., V-V interval, A-V interval, etc.

The computing apparatus **140** may be operatively coupled to the input apparatus **142** and the display apparatus **130** to, e.g., transmit data to and from each of the input apparatus **142** and the display apparatus **130**. For example, the computing apparatus **140** may be electrically coupled to each of the input apparatus **142** and the display apparatus **130** using, e.g., analog electrical connections, digital electrical connections, wireless connections, bus-based connections, network-based connections, internet-based connections, etc. As described further herein, a user may provide input to the input apparatus **142** to view and/or select one or more pieces of configuration information related to the cardiac therapy.

Although as depicted the input apparatus **142** is a keyboard, it is to be understood that the input apparatus **142** may include any apparatus capable of providing input to the computing apparatus **140** to perform the functionality, methods, and/or logic described herein. For example, the input apparatus **142** may include a mouse, a trackball, a touchscreen (e.g., capacitive touchscreen, a resistive touchscreen, a multi-touch touchscreen, etc.), etc. Likewise, the display apparatus **130** may include any apparatus capable of displaying information to a user, such as a graphical user interface **132** including one or more pacing parameters, electrical heterogeneity information, textual instructions, graphical depictions of electrical activation information, graphical depictions of anatomy of a human heart, images or graphical depictions of the patient's heart, graphical depictions of locations of one or more electrodes, graphical depictions of a human torso, images or graphical depictions of the patient's torso, graphical depictions or actual images of implanted electrodes and/or leads, etc. Further, the display apparatus **130** may include a liquid crystal display, an organic light-emitting diode screen, a touchscreen, a cathode ray tube display, etc.

The processing programs or routines stored and/or executed by the computing apparatus **140** may include programs or routines for computational mathematics, matrix mathematics, decomposition algorithms, compression algorithms (e.g., data compression algorithms), calibration algorithms, image construction algorithms, signal processing algorithms (e.g., various filtering algorithms, Fourier transforms, fast Fourier transforms, etc.), standardization algorithms, comparison algorithms, vector mathematics, or any other processing required to implement one or more exemplary methods and/or processes described herein. Data stored and/or used by the computing apparatus **140** may include, for example, electrical signal/waveform data from the electrode apparatus **110**, electrical activation times from the electrode apparatus **110**, graphics (e.g., graphical elements, icons, buttons, windows, dialogs, pull-down menus, graphic areas, graphic regions, 3D graphics, etc.), graphical user interfaces, results from one or more processing programs or routines employed according to the disclosure herein (e.g., electrical signals, electrical heterogeneity information, etc.), or any other data that may be necessary for carrying out the one and/or more processes or methods described herein.

In one or more embodiments, the exemplary systems, methods, and interfaces may be implemented using one or more computer programs executed on programmable computers, such as computers that include, for example, processing capabilities, data storage (e.g., volatile or non-volatile memory and/or storage elements), input devices, and output devices. Program code and/or logic described herein may be applied to input data to perform functionality described herein and generate desired output information. The output information may be applied as input to one or more other devices and/or methods as described herein or as would be applied in a known fashion.

The one or more programs used to implement the systems, methods, and/or interfaces described herein may be provided using any programmable language, e.g., a high level procedural and/or object orientated programming language that is suitable for communicating with a computer system. Any such programs may, for example, be stored on any suitable device, e.g., a storage media, that is readable by a general or special purpose program running on a computer system (e.g., including processing apparatus) for configuring and operating the computer system when the suitable device is read for performing the procedures described herein. In other words, at least in one embodiment, the exemplary systems, methods, and/or interfaces may be implemented using a computer readable storage medium, configured with a computer program, where the storage medium so configured causes the computer to operate in a specific and predefined manner to perform functions described herein. Further, in at least one embodiment, the exemplary systems, methods, and/or interfaces may be described as being implemented by logic (e.g., object code) encoded in one or more non-transitory media that includes code for execution and, when executed by a processor, is operable to perform operations such as the methods, processes, and/or functionality described herein.

The computing apparatus **140** may be, for example, any fixed or mobile computer system (e.g., a controller, a microcontroller, a personal computer, mini computer, tablet computer, etc.). The exact configuration of the computing apparatus **140** is not limiting, and essentially any device capable of providing suitable computing capabilities and control capabilities (e.g., graphics processing, etc.) may be used. As described herein, a digital file may be any medium (e.g., volatile or non-volatile memory, a CD-ROM, a punch card, magnetic recordable tape, etc.) containing digital bits (e.g., encoded in binary, trinary, etc.) that may be readable and/or writeable by computing apparatus **140** described herein. Also, as described herein, a file in user-readable format may be any representation of data (e.g., ASCII text, binary numbers, hexadecimal numbers, decimal numbers, graphically, etc.) presentable on any medium (e.g., paper, a display, etc.) readable and/or understandable by a user.

In view of the above, it will be readily apparent that the functionality as described in one or more embodiments according to the present disclosure may be implemented in any manner as would be known to one skilled in the art. As such, the computer language, the computer system, or any other software/hardware which is to be used to implement the processes described herein shall not be limiting on the scope of the systems, processes or programs (e.g., the functionality provided by such systems, processes or programs) described herein.

Electrical activation times of the patient's heart may be useful to evaluate cardiac therapy being delivered to a patient. Surrogate electrical activation information or data of one or more regions of a patient's heart may be monitored using electrode apparatus **110** as shown in FIG. **1** and in FIGS. **2-3**. The exemplary electrode apparatus **110** may be configured to measure body-surface potentials of a patient **14** and, more particularly, torso-surface potentials of a patient **14**. As shown in FIG. **2**, the exemplary electrode apparatus **110** may include a set, or array, of electrodes **112**, a strap **113**, and interface/amplifier circuitry **116**. The electrodes **112** may be attached, or coupled, to the strap **113** and the strap **113** may be configured to be wrapped around the torso of a patient **14** such that the electrodes **112** surround the patient's heart. As further illustrated, the electrodes **112** may be positioned around the circumference of a patient **14**, including the posterior, lateral, posterolateral, anterolateral, and anterior locations of the torso of a patient **14**.

Further, the electrodes **112** may be electrically connected to interface/amplifier circuitry **116** via wired connection **118**. The interface/amplifier circuitry **116** may be configured to amplify the signals from the electrodes **112** and provide the signals to the computing apparatus **140**. Other exemplary systems may use a wireless connection to transmit the signals sensed by electrodes **112** to the interface/amplifier circuitry **116** and, in turn, the computing apparatus **140**, e.g., as channels of data. For example, the interface/amplifier circuitry **116** may be electrically coupled to each of the computing apparatus **140** and the display apparatus **130** using, e.g., analog electrical connections, digital electrical connections, wireless connections, bus-based connections, network-based connections, internet-based connections, etc.

Although in the example of FIG. **2** the electrode apparatus **110** includes a strap **113**, in other examples any of a variety of mechanisms, e.g., tape or adhesives, may be employed to aid in the spacing and placement of electrodes **112**. In some examples, the strap **113** may include an elastic band, strip of tape, or cloth. In other examples, the electrodes **112** may be placed individually on the torso of a patient **14**. Further, in other examples, electrodes **112** (e.g., arranged in an array) may be part of, or located within, patches, vests, and/or other manners of securing the electrodes **112** to the torso of the patient **14**. Still further, in other examples, the electrodes **112** may be part of, or located within, two sections of material or two "patches." One of the two sections or patches may be located on the anterior side of the torso of the patient **14** (to, e.g., monitor electrical signals representative of the anterior side of the patient's heart, measure surrogate cardiac electrical activation times representative of the anterior side of the patient's heart, etc.) and the other section or patch may be located on the posterior side of the torso of the patient **14** (to, e.g., monitor electrical signals representative of the posterior side of the patient's heart, measure surrogate cardiac electrical activation times representative of the posterior side of the patient's heart, etc.).

The electrodes **112** may be configured to surround the heart of the patient **14** and record, or monitor, the electrical signals associated with the depolarization and repolarization of the heart after the signals have propagated through the torso of a patient **14**. Each of the electrodes **112** may be used in a unipolar configuration to sense the torso-surface potentials that reflect the cardiac signals. The interface/amplifier circuitry **116** may also be coupled to a return or indifferent electrode (not shown) that may be used in combination with each electrode **112** for unipolar sensing. In some examples, there may be about 12 to about 50 electrodes **112** spatially distributed around the torso of patient. Other configurations may have more or fewer electrodes **112**.

The computing apparatus **140** may record and analyze the torso-surface potential signals sensed by electrodes **112** and amplified/conditioned by the interface/amplifier circuitry **116**. The computing apparatus **140** may be configured to analyze the signals from the electrodes **112** to provide surrogate electrical activation information or data such as surrogate cardiac electrical activation times, e.g., representative of actual, or local, electrical activation times of one or more regions of the patient's heart as will be further described herein. For example, electrical signals measured at the left anterior surface location of a patient's torso may be representative, or surrogates, of electrical signals of the left anterior left ventricle region of the patient's heart, electrical signals measured at the left lateral surface location of a patient's torso may be representative, or surrogates, of electrical signals of the left lateral left ventricle region of the patient's heart, electrical signals measured at the left posterolateral surface location of a patient's torso may be representative, or surrogates, of electrical signals of the posterolateral left ventricle region of the patient's heart, and electrical signals measured at the posterior surface location of a patient's torso may be representative, or surrogates, of electrical signals of the posterior left ventricle region of the patient's heart. In one or more embodiments, measurement of activation times can be performed by measuring the period of time between an onset of cardiac depolarization (e.g., onset of QRS complex) and the next onset of cardiac depolarization. In one or more embodiments, measurement of activation times can be performed by picking an appropriate fiducial point (e.g., peak values, minimum values, minimum slopes, maximum slopes, zero crossings, threshold crossings, etc. of a near or far-field EGM) and measuring time between fiducial points (e.g., within the electrical activity).

Additionally, the computing apparatus **140** may be configured to provide graphical user interfaces depicting the surrogate electrical activation times obtained using the electrode apparatus **110**. Exemplary systems, methods, and/or interfaces may noninvasively use the electrical information collected using the electrode apparatus **110** to evaluate and configure cardiac therapy being delivered to the patient.

FIG. **3** illustrates another exemplary electrode apparatus **110** that includes a plurality of electrodes **112** configured to surround the heart of the patient **14** and record, or monitor, the electrical signals associated with the depolarization and repolarization of the heart after the signals have propagated through the torso of the patient **14**. The electrode apparatus **110** may include a vest **114** upon which the plurality of electrodes **112** may be attached, or to which the electrodes **112** may be coupled. In at least one embodiment, the plurality, or array, of electrodes **112** may be used to collect electrical information such as, e.g., surrogate electrical activation times. Similar to the electrode apparatus **110** of FIG. **2**, the electrode apparatus **110** of FIG. **3** may include interface/amplifier circuitry **116** electrically coupled to each of the electrodes **112** through a wired connection **118** and be configured to transmit signals from the electrodes **112** to computing apparatus **140**. As illustrated, the electrodes **112** may be distributed over the torso of a patient **14**, including, for example, the posterior, lateral, posterolateral, anterolateral, and anterior locations of the torso of a patient **14**.

The vest **114** may be formed of fabric with the electrodes **112** attached to the fabric. The vest **114** may be configured to maintain the position and spacing of electrodes **112** on the torso of the patient **14**. Further, the vest **114** may be marked

to assist in determining the location of the electrodes **112** on the surface of the torso of the patient **14**. In some examples, there may be about 25 to about 256 electrodes **112** distributed around the torso of the patient **14**, though other configurations may have more or fewer electrodes **112**.

As described herein, the electrode apparatus **110** may be configured to measure electrical information (e.g., electrical signals) representing different regions of a patient's heart. For example, activation times of different regions of a patient's heart can be approximated from surface electrocardiogram (ECG) activation times measured using surface electrodes in proximity to surface areas corresponding to the different regions of the patient's heart.

The exemplary systems and methods may be used to provide noninvasive assistance to a user in the evaluation and configuration of cardiac therapy (e.g., cardiac therapy being presently-delivered to a patient during implantation or after implantation). For example, the exemplary systems and methods may be used to assist a user in the configuration and/or adjustment of one or more cardiac therapy settings for the cardiac therapy being delivered to a patient. Specifically, the exemplary systems and methods may provide optimization of the V-V interval, or delay, of biventricular pacing therapy.

Exemplary method **200** depicted in FIG. **4** may be used to provide this functionality. The exemplary method **200** may be generally described to be used in the noninvasive evaluation and configuration (e.g., optimization) of cardiac therapy. The exemplary method **200** may be described as being noninvasive because the method does not use invasive apparatus to perform the evaluation and configuration of the cardiac therapy. The cardiac therapy being delivered, however, may be described as being invasive such as, e.g., one or more pacing electrodes implanted proximate a patient's heart. The exemplary method **200** may be used to evaluate and configure the invasive cardiac therapy. Further, the exemplary method **200** may be generally performed, or executed, after optimizing the A-V interval for the pacing therapy being performed. In other words, the exemplary method **200** may be used to adjust and/or optimize the V-V interval after the A-V interval has already been adjusted and/or optimized. Exemplary systems, methods, and apparatus for optimizing A-V interval may be described in U.S. Pat. No. 7,215,998 issued on May 8, 2007 to Wesselink et al., U.S. Pat. No. 7,848,807 issued on Dec. 7, 2010 to Li Wang, U.S. Pat. No. 6,507,756 issued on Jan. 14, 2003 to Heynen et al., and U.S. Pat. No. 8,214,041 issued to Gelder, et al. on Jul. 3, 2012, each of which is incorporated by reference in its entirety.

The exemplary method **200** may include monitoring, or measuring, electrical activity using a plurality of external electrodes **202**. The plurality of external electrodes may be similar to the external electrodes provided by the electrode apparatus **110** as described herein with respect to FIGS. **1-3**. For example, the plurality of external electrodes may be part, or incorporated into, a vest or band that is located about a patient's torso. More specifically, the plurality of electrodes may be described as being surface electrodes positioned in an array configured to be located proximate the skin of the torso of a patient. The electrical activity monitored during process **202** prior to the delivery of cardiac therapy may be referred to as "baseline" electrical activity because no therapy is delivered to the patient such that the patient's heart is in its natural, or intrinsic, rhythm.

During, or simultaneous with, the monitoring, or collecting, of electrical activity **202**, the exemplary method **200** may initiate the delivery of cardiac therapy **204** such as, e.g., biventricular pacing therapy. The cardiac therapy **204** may be delivered by at least one electrode configured to electrically stimulate (e.g., depolarize, pace, etc.) the patient's left ventricle and at least one electrode configured to electrically stimulate (e.g., depolarize, pace, etc.) the patient's right ventricle in a coordinated manner. The cardiac therapy may be delivered to both ventricles using an initial V-V interval or delay. In at least one embodiment, the initial V-V interval may be 0 milliseconds (ms) or zero delay.

In at least one embodiment, each of the electrodes may be coupled to one or more leads implanted in, or proximate to, the patient's heart. Further, in at least one embodiment, the cardiac therapy **204** may be delivered by one or more leadless electrodes. Exemplary cardiac therapy using an implantable electrode and lead may be further described herein with reference to FIGS. **8-10**. As described herein, although the cardiac therapy delivery may be described as being invasive, the exemplary methods and systems may be described as being noninvasive because the exemplary methods and systems may only initiate the delivery of and configure the cardiac therapy, and the exemplary methods and systems may further use electrical signals that are monitored, or taken, from the patient noninvasively.

The monitored electrical activity may be used to generate electrical heterogeneity information **206**. The electrical heterogeneity information may be described as information, or data, representative of at least one of mechanical cardiac functionality and electrical cardiac functionality. Electrical heterogeneity information and other cardiac therapy information may be described in U.S. Provisional Patent Application No. 61/834,133 entitled "METRICS OF ELECTRICAL DYSSYNCHRONY AND ELECTRICAL ACTIVATION PATTERNS FROM SURFACE ECG ELECTRODES" and filed on Jun. 12, 2013, which is hereby incorporated by reference it its entirety.

Electrical heterogeneity information may be defined as information indicative of at least one of mechanical synchrony or dyssynchrony of the heart and/or electrical synchrony or dyssynchrony of the heart. In other words, electrical heterogeneity information may represent a surrogate of actual mechanical and/or electrical functionality of a patient's heart. In at least one embodiment, relative changes in electrical heterogeneity information (e.g., changes relative to baseline electrical heterogeneity) may be used to determine a surrogate value representative of acute hemodynamic response as measured by changes in the left ventricle pressure gradients. The left ventricular pressure may be typically monitored invasively with a pressure sensor located in the left ventricular of a patient's heart. As such, the use of electrical heterogeneity information to determine a surrogate value representative of the left ventricular pressure may avoid invasive monitoring using a left ventricular pressure sensor.

In at least one embodiment, the electrical heterogeneity information may include a standard deviation of ventricular activation times measured using some or all of the external electrodes, e.g., of the electrode apparatus **110**. Further, local, or regional, electrical heterogeneity information may include standard deviations and/or averages of activation times measured using electrodes located in certain anatomic areas of the torso. For example, external electrodes on the left side of the torso of a patient may be used to compute local, or regional, left electrical heterogeneity information.

The electrical heterogeneity information may be generated using one or more various systems and/or methods. For example, electrical heterogeneity information may be generated using an array, or a plurality, of surface electrodes

and/or imaging systems as described in U.S. Pat. App. Pub. No. 2012/0283587 A1 published Nov. 8, 2012 and entitled "ASSESSING INRA-CARDIAC ACTIVATION PATTERNS AND ELECTRICAL DYSSYNCHRONY," U.S. Pat. App. Pub. No. 2012/0284003 A1 published Nov. 8, 2012 and entitled "ASSESSING INTRA-CARDIAC ACTIVATION PATTERNS", and U.S. Pat. No. 8,180,428 B2 issued May 15, 2012 and entitled "METHODS AND SYSTEMS FOR USE IN SELECTING CARDIAC PACING SITES," each of which is incorporated herein by reference in its entirety.

Electrical heterogeneity information may include one or more metrics or indices. For example, one of the metrics, or indices, of electrical heterogeneity may be a standard deviation of activation times (SDAT) measured using some or all of the electrodes on the surface of the torso of a patient. In some examples, the SDAT may be calculated using the estimated cardiac activation times over the surface of a model heart.

Another metric, or index, of electrical heterogeneity may be a left standard deviation of surrogate electrical activation times (LVED) monitored by external electrodes located proximate the left side of a patient. Further, another metric, or index, of electrical heterogeneity may include an average of surrogate electrical activation times (LVAT) monitored by external electrodes located proximate the left side of a patient. The LVED and LVAT may be determined (e.g., calculated, computed, etc.) from electrical activity measured only by electrodes proximate the left side of the patient, which may be referred to as "left" electrodes. The left electrodes may be defined as any surface electrodes located proximate the left ventricle, which includes region to left of the patient's sternum and spine. In one embodiment, the left electrodes may include all anterior electrodes on the left of the sternum and all posterior electrodes to the left of the spine. In another embodiment, the left electrodes may include all anterior electrodes on the left of the sternum and all posterior electrodes. In yet another embodiment, the left electrodes may be designated based on the contour of the left and right sides of the heart as determined using imaging apparatus (e.g., x-ray, fluoroscopy, etc.).

Another exemplary metric, or index, of dyssynchrony may be a range of activation times (RAT) that may be computed as the difference between the maximum and the minimum torso-surface or cardiac activation times, e.g., overall, or for a region. The RAT reflects the span of activation times while the SDAT gives an estimate of the dispersion of the activation times from a mean. The SDAT also provides an estimate of the heterogeneity of the activation times, because if activation times are spatially heterogeneous, the individual activation times will be further away from the mean activation time, indicating that one or more regions of heart have been delayed in activation. In some examples, the RAT may be calculated using the estimated cardiac activation times over the surface of a model heart.

Another exemplary metric, or index, of electrical heterogeneity information may include estimates of a percentage of surface electrodes located within a particular region of interest for the torso or heart whose associated activation times are greater than a certain percentile, such as, for example the 70th percentile, of measured QRS complex duration or the determined activation times for surface electrodes. The region of interest may, e.g., be a posterior, left anterior, and/or left-ventricular region. The exemplary metric, or index, may be referred to as a percentage of late activation (PLAT). The PLAT may be described as providing an estimate of percentage of the region of interest, e.g., posterior and left-anterior area associated with the left ventricular area of heart, which activates late. A large value for PLAT may imply delayed activation of a substantial portion of the region, e.g., the left ventricle, and the potential benefit of electrical resynchronization through CRT by pre-exciting the late region, e.g., of left ventricle. In other examples, the PLAT may be determined for other subsets of electrodes in other regions, such as a right anterior region to evaluate delayed activation in the right ventricle. Furthermore, in some examples, the PLAT may be calculated using the estimated cardiac activation times over the surface of a model heart for either the whole heart or for a particular region, e.g., left or right ventricle, of the heart.

In one or more embodiments, the electrical heterogeneity information may include indicators of favorable changes in global cardiac electrical activation such as, e.g., described in Sweeney et al., "Analysis of Ventricular Activation Using Surface Electrocardiography to Predict Left Ventricular Reverse Volumetric Remodeling During Cardiac Resynchronization Therapy," Circulation, 2010 Feb. 9, 121(5): 626-34 and/or Van Deursen, et al., "Vectorcardiography as a Tool for Easy Optimization of Cardiac Resynchronization Therapy in Canine LBBB Hearts," Circulation Arrhythmia and Electrophysiology, 2012 Jun. 1, 5(3): 544-52, each of which is incorporated herein by reference in its entirety. Electrical heterogeneity information may also include measurements of improved cardiac mechanical function measured by imaging or other systems to track motion of implanted leads within the heart as, e.g., described in Ryu et al., "Simultaneous Electrical and Mechanical Mapping Using 3D Cardiac Mapping System: Novel Approach for Optimal Cardiac Resynchronization Therapy," Journal of Cardiovascular Electrophysiology, 2010 February, 21(2): 219-22, Sperzel et al., "Intraoperative Characterization of Interventricular Mechanical Dyssynchrony Using Electroanatomic Mapping System—A Feasibility Study," Journal of Interventional Cardiac Electrophysiology, 2012 November, 35(2): 189-96, and/or U.S. Pat. App. Pub. No. 2009/0099619 A1 entitled "METHOD FOR OPTIMIZAING CRT THERAPY" and published on Apr. 16, 2009, each of which is incorporated herein by reference in its entirety.

The electrical heterogeneity information may be generated **206** for electrical activity monitored without, or before the delivery of, cardiac therapy, which may be referred to as baseline electrical heterogeneity information. The electrical heterogeneity information may be further generated **206** for electrical activity monitored during pacing therapy delivered at an initial, or first, V-V interval, which may be referred to as initial electrical heterogeneity information, and for electrical activity monitored during pacing therapy delivered at one or more V-V intervals that are adjusted following the initial, or first, V-V interval, which may be described as being subsequent, or following, electrical heterogeneity information.

After the initial, or first, V-V interval, the exemplary method **200** may further configure the following, or subsequent, V-V intervals of the biventricular pacing therapy **204** to pre-excite one of the left ventricle or right ventricle based on the monitored electrical activity and/or generated electrical heterogeneity information **208**. Pre-excitation may refer to the ventricle that is paced, or stimulated, using the biventricular pacing therapy first, or before the other ventricle. For example, if the left ventricle is to be pre-excited with a V-V delay of 50 ms, the left ventricle would be paced 50 ms before the right ventricle (in other words, the right ventricle would be paced 50 ms after the left ventricle).

Likewise, if the right ventricle is to be pre-excited with a V-V delay of 50 ms, the right ventricle would be paced 50 ms before the left ventricle (in other words, the left ventricle would be paced 50 ms after the right ventricle). Exemplary methods of determining ventricular pre-excitation are shown in FIGS. **6-7**. As shown, process step **208** is drawn using broken, or dotted, lines because determining ventricular pre-excitation may only occur after the initial V-V interval. In other words, after the ventricle to be pre-excited has been determined, it may not be determined again.

An exemplary method **230** of determining whether to pre-excite the patient's left ventricle is depicted in FIG. **6**. As shown, if the electrical heterogeneity information indicates an increase in heterogeneity **232**, the exemplary method **230** may determine and/or indicate that the left ventricle should be pre-excited **236**. An increase in heterogeneity **232** may be determined by comparing one or more indices or metrics of electrical heterogeneity information to one or more threshold values. For example, a SDAT that is greater than or equal to 25 ms may indicate an increase in heterogeneity **232**, and thus, the exemplary method **230** may determine that the left ventricle should be pre-excited **236**.

Further, if the electrical heterogeneity information indicates an increase in surrogate electrical activation times monitored by one or more left external electrodes (e.g., external electrodes located proximate the left side of the patient's torso) or one or more posterior external electrodes (e.g., external electrodes located proximate the posterior side of the patient's torso) **234**, the exemplary method **230** may determine and/or indicate that the left ventricle should be pre-excited **236**. An increase in left or posterior surrogate activation times may be determined by comparing one or more indices or metrics of electrical heterogeneity information to one or more threshold values. For example, a LVED that is greater than or equal to 25 ms may indicate an increase in left-sided activation times **234**, and thus, the exemplary method **230** may determine that the left ventricle should be pre-excited **236**. Further, for example, a LVAT that is greater than or equal to 70 ms may indicate an increase in left-sided activation times **234**, and thus, the exemplary method **230** may determine that the left ventricle should be pre-excited **236**. Still further, for example, if the LVAT of the left external electrodes exceeds the LVAT of the right external electrodes, the exemplary method **230** may determine that the left ventricle should be pre-excited **236**.

An exemplary method **240** of determining whether to pre-excite the patient's right ventricle is depicted in FIG. **7**. As shown, if the electrical heterogeneity information indicates an increase in surrogate electrical activation times monitored by one or more right external electrodes (e.g., external electrodes located proximate the right side of the patient's torso) **242**, the exemplary method **240** may determine and/or indicate that the right ventricle should be pre-excited **244**. For example, if the LVAT of the right external electrodes exceeds the LVAT of the left external electrodes, the exemplary method **240** may determine that the right ventricle should be pre-excited **242**.

The determination of whether to pre-excite one ventricle versus the other during biventricular pacing therapy may be based upon determination that cardiac resynchronization therapy delivered with simultaneous biventricular pacing at an optimal atrio-ventricular delay results in no change or increase in electrical heterogeneity metrics compared to the baseline. Then, the extent of electrical delay during biventricular pacing with zero V-V delay may be determined for both the anterior and posterior side. If the average activation time of the posterior electrodes exceeds the average activation time of the anterior electrodes, the left ventricle should be pre-excited. If the average activation time of the anterior electrodes exceed the average activation time of the posterior electrodes, the right ventricle should be pre-excited.

In another embodiment, the proportions of anterior and posterior electrodes activating late (e.g., later than 50% of the latest activation time or later than 50% of QRS duration) during biventricular pacing with zero V-V delay may be determined. If the proportion of posterior electrodes activating late exceeds the proportion of anterior electrodes activating late, the left ventricle may be pre-excited. Further, if the proportion of anterior electrodes activating late exceeds the proportion of posterior electrodes activating late, the right ventricle may be pre-excited.

Baseline, initial, and subsequent electrical heterogeneity information **250** for an exemplary patient is depicted in FIG. **5**. As shown, the baseline electrical heterogeneity information **252** was generated from electrical activity monitored without the delivery of cardiac therapy (e.g., the patient was in intrinsic rhythm) and indicated a SDAT of 35 ms, a LVED of 38 ms, and a LVAT of 67 ms. The initial electrical heterogeneity information **254** was generated from electrical activity monitored during the delivery of biventricular pacing therapy at a V-V interval of 0 ms and indicated a SDAT of 34 ms, a LVED of 34 ms, and a LVAT of 57 ms. As shown by comparing the baseline electrical heterogeneity information **252** and the initial electrical heterogeneity information **254**, the patient's overall heterogeneity did not improve with biventricular pacing therapy at a V-V interval of 0 ms (e.g., with an optimized A-V interval). Further, the extent of delay on posterior side was more than in the anterior side, which indicates that the V-V interval should be configured for left ventricular pre-excitation.

After selecting the left ventricle for pre-excitation **208**, the exemplary method **200** may adjust the V-V interval **210** from the previous V-V interval value, which if the V-V interval is the initial V-V interval, may be 0 ms. For example, the V-V interval may be selected to be a pre-determined value, or value within a range of values, that is different than the previous V-V interval. In at least one embodiment, the predetermined V-V interval may be about 80 milliseconds (ms). The predetermined V-V interval may be greater than or equal to about 50 ms, greater than or equal to about 60 ms, greater than or equal to about 70 ms, greater than or equal to about 80 ms, greater than or equal to about 90 ms, greater than or equal to about 100 ms, etc. Further, the predetermined V-V interval may be less than or equal to about 125 ms, less than or equal to about 115 ms, less than or equal to about 105 ms, less than or equal to about 95 ms, less than or equal to about 85 ms, less than or equal to about 75 ms, etc.

The exemplary method **200** may then deliver bi-ventricular pacing therapy **204**, monitor electrical activity **202**, and generate electrical heterogeneity information **206** for the predetermined V-V interval **210**. It may be described that the V-V interval is "swept" from the predetermined, long V-V interval until the V-V interval is back to 0. Thus, the method **200** may continue repeating the same cycle for a different V-V interval until, e.g., a plurality of V-V different intervals have been utilized and/or the V-V interval is adjusted to zero.

For example, the V-V interval may be decreased by a step size, or decrement, until the V-V interval is zero. In at least one embodiment, the step size, or increment, may be about 20 ms. The step size, or increment, may be greater than or about 5 ms, greater than or equal to about 10 ms, greater than or equal to about 15 ms, greater than or equal to about 20 ms, greater than or equal to about 25 ms, greater than or equal to about 30 ms, etc. Further, the step size, or decrement, may

be less than or equal to about 50 ms, less than or equal to about 40 ms, less than or equal to about 35 ms, less than or equal to about 30 ms, less than or equal to about 25 ms, etc.

In other words, the exemplary methods and systems initiate delivery of bi-ventricular pacing therapy at a plurality of different V-V intervals **204** (e.g., a different V-V interval for each cycle) and monitor the electrical activity **202** for each of the plurality of V-V intervals. Further, electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality may be generated **206** for each of the plurality of V-V intervals.

In FIG. **5**, the left ventricle was determined to be pre-excited and the V-V interval (i.e., left ventricle-to-right ventricle delay) was adjusted, or set, to 80 ms after the initial V-V interval (e.g., 0 ms). The V-V interval was then decremented by 20 ms for each cycle. As shown, the subsequent heterogeneity information **256** was generated from electrical activity monitored during the delivery of biventricular pacing therapy at a V-V interval of 80 ms and indicated a SDAT of 28 ms, a LVED of 20 ms, and a LVAT of 23 ms. The subsequent electrical heterogeneity information **256** indicates an improvement from the initial electrical heterogeneity information **254** that resulted from a V-V interval of 0 ms.

The V-V interval was then decremented by 20 ms to 60 ms and subsequent heterogeneity information **258** was generated from electrical activity monitored during the delivery of biventricular pacing therapy at a V-V interval of 60 ms. The subsequent heterogeneity information **258** indicated a SDAT of 25 ms, a LVED of 17 ms, and a LVAT of 31 ms.

The V-V interval was then further decremented by 20 ms to 40 ms and subsequent heterogeneity information **260** was generated from electrical activity monitored during the delivery of biventricular pacing therapy at a V-V interval of 40 ms. The subsequent heterogeneity information **260** indicated a SDAT of 29 ms, a LVED of 13 ms, and a LVAT of 24 ms.

After monitoring the electrical activity **202** for a plurality of different V-V intervals and generating electrical heterogeneity information **206** based on the monitored electrical activity for each of the plurality of different V-V intervals, the exemplary method **200** may identify one or more (e.g., one, two, etc.) V-V intervals of the plurality of different V-V intervals **212** based on the electrical heterogeneity information that may benefit the patient's cardiac therapy.

To identify one or more V-V intervals from the plurality of different V-V intervals **212**, the exemplary method **200** may use one or more metrics or indices of electrical heterogeneity, alone or together. For example, the V-V interval that generated the lowest global standard deviation of surrogate electrical activation times (SDAT), the lowest left standard deviation (LVED) and/or the lowest left average (LVAT) may be identified (e.g., identified as the optimal V-V interval).

When it is described that V-V intervals are identified, it is to be understood that the exemplary methods and systems may identify the V-V intervals in various different ways. For example, the identified V-V intervals may be displayed on a graphical user interface along with heterogeneity information. The heterogeneity information may be graphical and/or textual, and may include graphical maps of electrical activation times about one or more regions of the patient's torso and/or heart. In at least one embodiment, the heterogeneity information **250** of FIG. **5** may be depicted on a graphical user interface such that, e.g., a user may view the results from each of the different V-V intervals.

Additionally, the exemplary methods and systems may be further configured to select the identified V-V interval and program, or set, the cardiac therapy apparatus to use the identified V-V interval. In other embodiments, a user may use the exemplary systems and methods to program, or configure the cardiac therapy apparatus using the identified V-V interval as well as other parameters and settings.

In at least one embodiment, an exemplary graphical user interface may include, among other things, a graphical representation **270** of measured surrogate electrical activation times and electrical heterogeneity information **272**. The graphical representation **270** of measured surrogate cardiac electrical activation times may be depicted in a variety of fashions. As shown, the surrogate electrical activation times may be depicted as a color-coded, or color-scaled, segment (as shown, the color-coding is depicted in gray-scale). More specifically, anterior and posterior side color-coded segments graphically depicting surrogate electrical activation times measured, e.g., using the electrical apparatus described herein with reference to FIGS. **1-3**, are depicted in FIG. **5**. Further, the graphical representation **270** of measured surrogate cardiac electrical activation times for the anterior side may be measured using electrodes located on, or proximate to, the anterior side of the patient's torso, and likewise, the graphical representation **270** of measured surrogate cardiac electrical activation times for the posterior side may be measured using electrodes located on, or proximate to, the posterior side of the patient's torso. In other words, the graphical representation **270** of measured surrogate cardiac electrical activation times for the anterior side correlates to actual electrical signals measured using electrodes configured to measure electrical signals on the anterior side of the patient's torso, and the graphical representation **270** of measured surrogate cardiac electrical activation times for the posterior side of the human torso correlates to actual electrical signals measured using electrodes configured to measure electrical signals on the posterior side of the patient's torso.

Additional exemplary graphical representations of surrogate electrical activation times may be described in U.S. Patent Application Publication No. 2012/0284003 A1 published on Nov. 8, 2012 and entitled "Assessing Intra-Cardiac Activation Patterns" and U.S. Patent Application Publication No. 2012/0283587 A1 published on Nov. 8, 2012 and entitled "Assessing Intra-Cardiac Activation Patterns and Electrical Dyssynchrony," each of which is hereby incorporated by reference in its entirety.

The exemplary systems, methods, and graphical user interfaces described herein may be used with respect to the implantation and configuration of an implantable medical device (IMD) and/or one or more leads configured to be located proximate one or more portions of a patient's heart. For example, the exemplary systems, methods, and interfaces may be used in conjunction with an exemplary therapy system **10** described herein with reference to FIGS. **8-10**.

FIG. **8** is a conceptual diagram illustrating an exemplary therapy system **10** that may be used to deliver pacing therapy to a patient **14**. Patient **14** may, but not necessarily, be a human. The therapy system **10** may include an implantable medical device **16** (IMD), which may be coupled to leads **18**, **20**, **22**. The IMD **16** may be, e.g., an implantable pacemaker, cardioverter, and/or defibrillator, that delivers, or provides, electrical signals to and/or measures, or monitors electrical signals from the heart **12** of the patient **14** via electrodes coupled to one or more of the leads **18**, **20**, **22**.

The leads **18**, **20**, **22** extend into the heart **12** of the patient **14** to sense electrical activity of the heart **12** and/or to deliver

electrical stimulation to the heart **12**. In the example shown in FIG. **8**, the right ventricular (RV) lead **18** extends through one or more veins (not shown), the superior vena cava (not shown), and the right atrium **26**, and into the right ventricle **28**. The left ventricular (LV) coronary sinus lead **20** extends through one or more veins, the vena cava, the right atrium **26**, and into the coronary sinus **30** to a region adjacent to the free wall of the left ventricle **32** of the heart **12**. The right atrial (RA) lead **22** extends through one or more veins and the vena cava, and into the right atrium **26** of the heart **12**.

The IMD **16** may sense, among other things, electrical signals attendant to the depolarization and repolarization of the heart **12** via electrodes coupled to at least one of the leads **18**, **20**, **22**. In some examples, the IMD **16** provides pacing therapy (e.g., pacing pulses) to the heart **12** based on the electrical signals sensed within the heart **12**. The IMD **16** may be operable to adjust one or more parameters associated with the pacing therapy such as, e.g., V-V delay, A-V delay and other various timings, pulse wide, amplitude, voltage, burst length, etc. Further, the IMD **16** may be operable to use various electrode configurations to deliver pacing therapy, which may be unipolar, bipolar, quadripoloar, or further multipolar. For example, a multipolar lead may include several electrodes that can be used for delivering pacing therapy. Hence, a multipolar lead system may provide, or offer, multiple electrical vectors to pace from. A pacing vector may include at least one cathode, which may be at least one electrode located on at least one lead, and at least one anode, which may be at least one electrode located on at least one lead (e.g., the same lead, or a different lead) and/or on the casing, or can, of the IMD. While improvement in cardiac function as a result of the pacing therapy may primarily depend on the cathode, the electrical parameters like impedance, pacing threshold voltage, current drain, longevity, etc. may be more dependent on the pacing vector, which includes both the cathode and the anode. The IMD **16** may also provide defibrillation therapy and/or cardioversion therapy via electrodes located on at least one of the leads **18**, **20**, **22**. Further, the IMD **16** may detect arrhythmia of the heart **12**, such as fibrillation of the ventricles **28**, **32**, and deliver defibrillation therapy to the heart **12** in the form of electrical pulses. In some examples, IMD **16** may be programmed to deliver a progression of therapies, e.g., pulses with increasing energy levels, until a fibrillation of heart **12** is stopped.

FIGS. **9**A-**9**B are conceptual diagrams illustrating the IMD **16** and the leads **18**, **20**, **22** of therapy system **10** of FIG. **8** in more detail. The leads **18**, **20**, **22** may be electrically coupled to a therapy delivery module (e.g., for delivery of pacing therapy), a sensing module (e.g., for sensing one or more signals from one or more electrodes), and/or any other modules of the IMD **16** via a connector block **34**. In some examples, the proximal ends of the leads **18**, **20**, **22** may include electrical contacts that electrically couple to respective electrical contacts within the connector block **34** of the IMD **16**. In addition, in some examples, the leads **18**, **20**, **22** may be mechanically coupled to the connector block **34** with the aid of set screws, connection pins, or another suitable mechanical coupling mechanism.

Each of the leads **18**, **20**, **22** includes an elongated insulative lead body, which may carry a number of conductors (e.g., concentric coiled conductors, straight conductors, etc.) separated from one another by insulation (e.g., tubular insulative sheaths). In the illustrated example, bipolar electrodes **40**, **42** are located proximate to a distal end of the lead **18**. In addition, bipolar electrodes **44**, **45**, **46**, **47** are located proximate to a distal end of the lead **20** and bipolar electrodes **48**, **50** are located proximate to a distal end of the lead **22**.

The electrodes **40**, **44**, **45**, **46**, **47**, **48** may take the form of ring electrodes, and the electrodes **42**, **50** may take the form of extendable helix tip electrodes mounted retractably within the insulative electrode heads **52**, **54**, **56**, respectively. Each of the electrodes **40**, **42**, **44**, **45**, **46**, **47**, **48**, **50** may be electrically coupled to a respective one of the conductors (e.g., coiled and/or straight) within the lead body of its associated lead **18**, **20**, **22**, and thereby coupled to a respective one of the electrical contacts on the proximal end of the leads **18**, **20**, **22**.

Additionally, electrodes **44**, **45**, **46** and **47** may have an electrode surface area of about 5.3 mm^2 to about 5.8 mm^2. Electrodes **44**, **45**, **46**, and **47** may also be referred to as LV**1**, LV**2**, LV**3**, and LV**4**, respectively. The LV electrodes (i.e., left ventricle electrode **1** (LV**1**) **44**, left ventricle electrode **2** (LV**2**) **45**, left ventricle electrode **3** (LV**3**) **46**, and left ventricle **4** (LV**4**) **47** etc.) on the lead **20** can be spaced apart at variable distances. For example, electrode **44** may be a distance of, e.g., about 21 millimeters (mm), away from electrode **45**, electrodes **45** and **46** may be spaced a distance of, e.g., about 1.3 mm to about 1.5 mm, away from each other, and electrodes **46** and **47** may be spaced a distance of, e.g. 20 mm to about 21 mm, away from each other.

The electrodes **40**, **42**, **44**, **45**, **46**, **47**, **48**, **50** may further be used to sense electrical signals (e.g., morphological waveforms within electrograms (EGM)) attendant to the depolarization and repolarization of the heart **12**. The sensed electrical signals may be used to adjust one or more pacing parameters such as, e.g., A-V interval, V-V interval, etc. to provide optimal and/or effective cardiac functionality. The electrical signals are conducted to the IMD **16** via the respective leads **18**, **20**, **22**. In some examples, the IMD **16** may also deliver pacing pulses via the electrodes **40**, **42**, **44**, **45**, **46**, **47**, **48**, **50** to cause depolarization of cardiac tissue of the patient's heart **12**. In some examples, as illustrated in FIG. **9**A, the IMD **16** includes one or more housing electrodes, such as housing electrode **58**, which may be formed integrally with an outer surface of a housing **60** (e.g., hermetically-sealed housing) of the IMD **16** or otherwise coupled to the housing **60**. Any of the electrodes **40**, **42**, **44**, **45**, **46**, **47**, **48**, **50** may be used for unipolar sensing or pacing in combination with the housing electrode **58**. In other words, any of electrodes **40**, **42**, **44**, **45**, **46**, **47**, **48**, **50**, **58** may be used in combination to form a sensing vector, e.g., a sensing vector that may be used to evaluate and/or analyze the effectiveness of pacing therapy. It is to be understood by those skilled in the art that other electrodes can also be selected to define, or be used for, pacing and sensing vectors. Further, any of electrodes **40**, **42**, **44**, **45**, **46**, **47**, **48**, **50**, **58**, when not being used to deliver pacing therapy, may be used to sense electrical activity during pacing therapy.

As described in further detail with reference to FIG. **9**A, the housing **60** may enclose a therapy delivery module that may include a stimulation generator for generating cardiac pacing pulses and defibrillation or cardioversion shocks, as well as a sensing module for monitoring electrical signals of the patient's heart (e.g., the patient's heart rhythm). The leads **18**, **20**, **22** may also include elongated electrodes **62**, **64**, **66**, respectively, which may take the form of a coil. The IMD **16** may deliver defibrillation shocks to the heart **12** via any combination of the elongated electrodes **62**, **64**, **66** and the housing electrode **58**. The electrodes **58**, **62**, **64**, **66** may also be used to deliver cardioversion pulses to the heart **12**. Further, the electrodes **62**, **64**, **66** may be fabricated from any

suitable electrically conductive material, such as, but not limited to, platinum, platinum alloy, and/or other materials known to be usable in implantable defibrillation electrodes. Since electrodes **62**, **64**, **66** are not generally configured to deliver pacing therapy, any of electrodes **62**, **64**, **66** may be used to sense electrical activity (e.g., for use in determining electrode effectiveness, for use in analyzing pacing therapy effectiveness, etc.) and may be used in combination with any of electrodes **40**, **42**, **44**, **45**, **46**, **47**, **48**, **50**, **58**. In at least one embodiment, the RV elongated electrode **62** may be used to sense electrical activity of a patient's heart during the delivery of pacing therapy (e.g., in combination with the housing electrode **58**, or defibrillation electrode-to-housing electrode vector).

The configuration of the exemplary therapy system **10** illustrated in FIGS. **9-11** is merely one example. In other examples, the therapy system may include epicardial leads and/or patch electrodes instead of or in addition to the transvenous leads **18**, **20**, **22** illustrated in FIG. **8**. Additionally, in other examples, the therapy system **10** may be implanted in/around the cardiac space without transvenous leads (e.g., leadless/wireless pacing systems) or with leads implanted (e.g., implanted transvenously or using approaches) into the left chambers of the heart (in addition to or replacing the transvenous leads placed into the right chambers of the heart as illustrated in FIG. **8**). Further, in one or more embodiments, the IMD **16** need not be implanted within the patient **14**. For example, the IMD **16** may deliver various cardiac therapies to the heart **12** via percutaneous leads that extend through the skin of the patient **14** to a variety of positions within or outside of the heart **12**. In one or more embodiments, the system **10** may utilize wireless pacing (e.g., using energy transmission to the intracardiac pacing component(s) via ultrasound, inductive coupling, RF, etc.) and sensing cardiac activation using electrodes on the can/housing and/or on subcutaneous leads.

In other examples of therapy systems that provide electrical stimulation therapy to the heart **12**, such therapy systems may include any suitable number of leads coupled to the IMD **16**, and each of the leads may extend to any location within or proximate to the heart **12**. For example, other examples of therapy systems may include three transvenous leads located as illustrated in FIGS. **9-11**. Still further, other therapy systems may include a single lead that extends from the IMD **16** into the right atrium **26** or the right ventricle **28**, or two leads that extend into a respective one of the right atrium **26** and the right ventricle **28**.

FIG. **10**A is a functional block diagram of one exemplary configuration of the IMD **16**. As shown, the IMD **16** may include a control module **81**, a therapy delivery module **84** (e.g., which may include a stimulation generator), a sensing module **86**, and a power source **90**.

The control module **81** may include a processor **80**, memory **82**, and a telemetry module **88**. The memory **82** may include computer-readable instructions that, when executed, e.g., by the processor **80**, cause the IMD **16** and/or the control module **81** to perform various functions attributed to the IMD **16** and/or the control module **81** described herein. Further, the memory **82** may include any volatile, non-volatile, magnetic, optical, and/or electrical media, such as a random access memory (RAM), read-only memory (ROM), non-volatile RAM (NVRAM), electrically-erasable programmable ROM (EEPROM), flash memory, and/or any other digital media. An exemplary capture management module may be the left ventricular capture management (LVCM) module described in U.S. Pat. No. 7,684,863 entitled "LV THRESHOLD MEASUREMENT AND CAPTURE MANAGEMENT" and issued Mar. 23, 2010, which is incorporated herein by reference in its entirety.

The processor **80** of the control module **81** may include any one or more of a microprocessor, a controller, a digital signal processor (DSP), an application specific integrated circuit (ASIC), a field-programmable gate array (FPGA), and/or equivalent discrete or integrated logic circuitry. In some examples, the processor **80** may include multiple components, such as any combination of one or more microprocessors, one or more controllers, one or more DSPs, one or more ASICs, and/or one or more FPGAs, as well as other discrete or integrated logic circuitry. The functions attributed to the processor **80** herein may be embodied as software, firmware, hardware, or any combination thereof.

The control module **81** may control the therapy delivery module **84** to deliver therapy (e.g., electrical stimulation therapy such as pacing) to the heart **12** according to a selected one or more therapy programs, which may be stored in the memory **82**. More, specifically, the control module **81** (e.g., the processor **80**) may control various parameters of the electrical stimulus delivered by the therapy delivery module **84** such as, e.g., A-V delays, V-V delays, pacing pulses with the amplitudes, pulse widths, frequency, or electrode polarities, etc., which may be specified by one or more selected therapy programs (e.g., A-V and/or V-V delay adjustment programs, pacing therapy programs, pacing recovery programs, capture management programs, etc.). As shown, the therapy delivery module **84** is electrically coupled to electrodes **40**, **42**, **44**, **45**, **46**, **47**, **48**, **50**, **58**, **62**, **64**, **66**, e.g., via conductors of the respective lead **18**, **20**, **22**, or, in the case of housing electrode **58**, via an electrical conductor disposed within housing **60** of IMD **16**. Therapy delivery module **84** may be configured to generate and deliver electrical stimulation therapy such as pacing therapy to the heart **12** using one or more of the electrodes **40**, **42**, **44**, **45**, **46**, **47**, **48**, **50**, **58**, **62**, **64**, **66**.

For example, therapy delivery module **84** may deliver pacing stimulus (e.g., pacing pulses) via ring electrodes **40**, **44**, **45**, **46**, **47**, **48** coupled to leads **18**, **20**, **22** and/or helical tip electrodes **42**, **50** of leads **18**, **22**. Further, for example, therapy delivery module **84** may deliver defibrillation shocks to heart **12** via at least two of electrodes **58**, **62**, **64**, **66**. In some examples, therapy delivery module **84** may be configured to deliver pacing, cardioversion, or defibrillation stimulation in the form of electrical pulses. In other examples, therapy delivery module **84** may be configured deliver one or more of these types of stimulation in the form of other signals, such as sine waves, square waves, and/or other substantially continuous time signals.

The IMD **16** may further include a switch module **85** and the control module **81** (e.g., the processor **80**) may use the switch module **85** to select, e.g., via a data/address bus, which of the available electrodes are used to deliver therapy such as pacing pulses for pacing therapy, or which of the available electrodes are used for sensing. The switch module **85** may include a switch array, switch matrix, multiplexer, or any other type of switching device suitable to selectively couple the sensing module **86** and/or the therapy delivery module **84** to one or more selected electrodes. More specifically, the therapy delivery module **84** may include a plurality of pacing output circuits. Each pacing output circuit of the plurality of pacing output circuits may be selectively coupled, e.g., using the switch module **85**, to one or more of the electrodes **40**, **42**, **44**, **45**, **46**, **47**, **48**, **50**, **58**, **62**, **64**, **66** (e.g., a pair of electrodes for delivery of therapy using a bipolar or multipolar pacing vector). In other words,

each electrode can be selectively coupled to one of the pacing output circuits of the therapy delivery module using the switching module **85**.

The sensing module **86** is coupled (e.g., electrically coupled) to sensing apparatus, which may include, among additional sensing apparatus, the electrodes **40**, **42**, **44**, **45**, **46**, **47**, **48**, **50**, **58**, **62**, **64**, **66** to monitor electrical activity of the heart **12**, e.g., electrocardiogram (ECG)/electrogram (EGM) signals, etc. The ECG/EGM signals may be used to measure or monitor activation times (e.g., ventricular activations times, etc.), heart rate (HR), heart rate variability (HRV), heart rate turbulence (HRT), deceleration/acceleration capacity, deceleration sequence incidence, T-wave alternans (TWA), P-wave to P-wave intervals (also referred to as the P-P intervals or A-A intervals), R-wave to R-wave intervals (also referred to as the R-R intervals or V-V intervals), P-wave to QRS complex intervals (also referred to as the P-R intervals, A-V intervals, or P-Q intervals), QRS-complex morphology, ST segment (i.e., the segment that connects the QRS complex and the T-wave), T-wave changes, QT intervals, electrical vectors, etc.

The switch module **85** may also be used with the sensing module **86** to select which of the available electrodes are used, or enabled, to, e.g., sense electrical activity of the patient's heart (e.g., one or more electrical vectors of the patient's heart using any combination of the electrodes **40**, **42**, **44**, **45**, **46**, **47**, **48**, **50**, **58**, **62**, **64**, **66**). Likewise, the switch module **85** may also be used with the sensing module **86** to select which of the available electrodes are not to be used (e.g., disabled) to, e.g., sense electrical activity of the patient's heart (e.g., one or more electrical vectors of the patient's heart using any combination of the electrodes **40**, **42**, **44**, **45**, **46**, **47**, **48**, **50**, **58**, **62**, **64**, **66**), etc. In some examples, the control module **81** may select the electrodes that function as sensing electrodes via the switch module within the sensing module **86**, e.g., by providing signals via a data/address bus.

In some examples, sensing module **86** includes a channel that includes an amplifier with a relatively wider pass band than the R-wave or P-wave amplifiers. Signals from the selected sensing electrodes may be provided to a multiplexer, and thereafter converted to multi-bit digital signals by an analog-to-digital converter for storage in memory **82**, e.g., as an electrogram (EGM). In some examples, the storage of such EGMs in memory **82** may be under the control of a direct memory access circuit.

In some examples, the control module **81** may operate as an interrupt driven device, and may be responsive to interrupts from pacer timing and control module, where the interrupts may correspond to the occurrences of sensed P-waves and R-waves and the generation of cardiac pacing pulses. Any necessary mathematical calculations may be performed by the processor **80** and any updating of the values or intervals controlled by the pacer timing and control module may take place following such interrupts. A portion of memory **82** may be configured as a plurality of recirculating buffers, capable of holding one or more series of measured intervals (e.g., intrinsic A-V conduction times, intrinsic V-V conduction times, etc.), which may be analyzed by, e.g., the processor **80** in response to the occurrence of a pace or sense interrupt to determine whether the patient's heart **12** is presently exhibiting atrial or ventricular tachyarrhythmia.

The telemetry module **88** of the control module **81** may include any suitable hardware, firmware, software, or any combination thereof for communicating with another device, such as a programmer. For example, under the control of the processor **80**, the telemetry module **88** may receive downlink telemetry from and send uplink telemetry to a programmer with the aid of an antenna, which may be internal and/or external. The processor **80** may provide the data to be uplinked to a programmer and the control signals for the telemetry circuit within the telemetry module **88**, e.g., via an address/data bus. In some examples, the telemetry module **88** may provide received data to the processor **80** via a multiplexer.

The various components of the IMD **16** are further coupled to a power source **90**, which may include a rechargeable or non-rechargeable battery. A non-rechargeable battery may be selected to last for several years, while a rechargeable battery may be inductively charged from an external device, e.g., on a daily or weekly basis.

FIG. **10**B is another embodiment of a functional block diagram for IMD **16**. FIG. **10**B depicts bipolar RA lead **22**, bipolar RV lead **18**, and bipolar LV CS lead **20** without the LA CS pace/sense electrodes and coupled with an implantable pulse generator (IPG) circuit **31** having programmable modes and parameters of a bi-ventricular DDD/R type known in the pacing art. In turn, the sensor signal processing circuit **91** indirectly couples to the timing circuit **43** and via data and control bus to microcomputer circuitry **33**. The IPG circuit **31** is illustrated in a functional block diagram divided generally into a microcomputer circuit **33** and a pacing circuit **21**. The pacing circuit **21** includes the digital controller/timer circuit **43**, the output amplifiers circuit **51**, the sense amplifiers circuit **55**, the RF telemetry transceiver **41**, the activity sensor circuit **35** as well as a number of other circuits and components described below.

Crystal oscillator circuit **89** provides the basic timing clock for the pacing circuit **21** while battery **29** provides power. Power-on-reset circuit **87** responds to initial connection of the circuit to the battery for defining an initial operating condition and similarly, resets the operative state of the device in response to detection of a low battery condition. Reference mode circuit **37** generates stable voltage reference and currents for the analog circuits within the pacing circuit **21**. Analog-to-digital converter (ADC) and multiplexer circuit **39** digitize analog signals and voltage to provide, e.g., real time telemetry of cardiac signals from sense amplifiers **55** for uplink transmission via RF transmitter and receiver circuit **41**. Voltage reference and bias circuit **37**, ADC and multiplexer **39**, power-on-reset circuit **87**, and crystal oscillator circuit **89** may correspond to any of those used in exemplary implantable cardiac pacemakers.

If the IPG is programmed to a rate responsive mode, the signals output by one or more physiologic sensors are employed as a rate control parameter (RCP) to derive a physiologic escape interval. For example, the escape interval is adjusted proportionally to the patient's activity level developed in the patient activity sensor (PAS) circuit **35** in the depicted, exemplary IPG circuit **31**. The patient activity sensor **27** is coupled to the IPG housing and may take the form of a piezoelectric crystal transducer. The output signal of the patient activity sensor **27** may be processed and used as a RCP. Sensor **27** generates electrical signals in response to sensed physical activity that are processed by activity circuit **35** and provided to digital controller/timer circuit **43**. Activity circuit **35** and associated sensor **27** may correspond to the circuitry disclosed in U.S. Pat. No. 5,052,388 entitled "METHOD AND APPARATUS FOR IMPLEMENTING ACTIVITY SENSING IN A PULSE GENERATOR" and issued on Oct. 1, 1991 and U.S. Pat. No. 4,428,378 entitled "RATE ADAPTIVE PACER" and issued on Jan. 31, 1984, each of which is incorporated herein by reference in its

entirety. Similarly, the exemplary systems, apparatus, and methods described herein may be practiced in conjunction with alternate types of sensors such as oxygenation sensors, pressure sensors, pH sensors, and respiration sensors for use in providing rate responsive pacing capabilities. Alternately, QT time may be used as the rate indicating parameter, in which case no extra sensor is required. Similarly, the exemplary embodiments described herein may also be practiced in non-rate responsive pacemakers.

Data transmission to and from the external programmer is accomplished by way of the telemetry antenna **57** and an associated RF transceiver **41**, which serves both to demodulate received downlink telemetry and to transmit uplink telemetry. Uplink telemetry capabilities may include the ability to transmit stored digital information, e.g., operating modes and parameters, EGM histograms, and other events, as well as real time EGMs of atrial and/or ventricular electrical activity and marker channel pulses indicating the occurrence of sensed and paced depolarizations in the atrium and ventricle.

Microcomputer **33** contains a microprocessor **80** and associated system clock and on-processor RAM and ROM chips **82**A and **82**B, respectively. In addition, microcomputer circuit **33** includes a separate RAM/ROM chip **82**C to provide additional memory capacity. Microprocessor **80** normally operates in a reduced power consumption mode and is interrupt driven. Microprocessor **80** is awakened in response to defined interrupt events, which may include A-TRIG, RV-TRIG, LV-TRIG signals generated by timers in digital timer/controller circuit **43** and A-EVENT, RV-EVENT, and LV-EVENT signals generated by sense amplifiers circuit **55**, among others. The specific values of the intervals and delays timed out by digital controller/timer circuit **43** are controlled by the microcomputer circuit **33** by way of data and control bus from programmed-in parameter values and operating modes. In addition, if programmed to operate as a rate responsive pacemaker, a timed interrupt, e.g., every cycle or every two seconds, may be provided in order to allow the microprocessor to analyze the activity sensor data and update the basic A-A, V-A, or V-V escape interval, as applicable. In addition, the microprocessor **80** may also serve to define variable, operative V-V delay intervals, A-V delay intervals, etc. and the energy delivered to each ventricle and/or atrium.

In one embodiment, microprocessor **80** is a custom microprocessor adapted to fetch and execute instructions stored in RAM/ROM unit **82** in a conventional manner. It is contemplated, however, that other implementations may be suitable to practice the present invention. For example, an off-the-shelf, commercially available microprocessor or microcontroller, or custom application-specific, hardwired logic, or state-machine type circuit may perform the functions of microprocessor **80**.

Digital controller/timer circuit **43** operates under the general control of the microcomputer **33** to control timing and other functions within the pacing circuit **321** and includes a set of timing and associated logic circuits of which certain ones pertinent to the present invention are depicted. The depicted timing circuits include URI/LRI timers **83**A, V-V delay timer **83**B, intrinsic interval timers **83**C for timing elapsed V-EVENT to V-EVENT intervals or V-EVENT to A-EVENT intervals or the V-V conduction interval, escape interval timers **83**D for timing A-A, V-A, and/or V-V pacing escape intervals, an A-V delay interval timer **83**E for timing the A-LVp delay (or A-RVp delay) from a preceding A-EVENT or A-TRIG, a post-ventricular timer **83**F for timing post-ventricular time periods, and a date/time clock **83**G.

The A-V delay interval timer **83**E is loaded with an appropriate delay interval for one ventricular chamber (e.g., either an A-RVp delay or an A-LVp delay) to time-out starting from a preceding A-PACE or A-EVENT. The interval timer **83**E triggers pacing stimulus delivery, and can be based on one or more prior cardiac cycles (or from a data set empirically derived for a given patient).

The post-event timer **83**F times out the post-ventricular time period following an RV-EVENT or LV-EVENT or a RV-TRIG or LV-TRIG and post-atrial time periods following an A-EVENT or A-TRIG. The durations of the post-event time periods may also be selected as programmable parameters stored in the microcomputer **33**. The post-ventricular time periods include the PVARP, a post-atrial ventricular blanking period (PAVBP), a ventricular blanking period (VBP), a post-ventricular atrial blanking period (PVARP) and a ventricular refractory period (VRP) although other periods can be suitably defined depending, at least in part, on the operative circuitry employed in the pacing engine. The post-atrial time periods include an atrial refractory period (ARP) during which an A-EVENT is ignored for the purpose of resetting any A-V delay, and an atrial blanking period (ABP) during which atrial sensing is disabled. It should be noted that the starting of the post-atrial time periods and the A-V delays can be commenced substantially simultaneously with the start or end of each A-EVENT or A-TRIG or, in the latter case, upon the end of the A-PACE which may follow the A-TRIG. Similarly, the starting of the post-ventricular time periods and the V-A escape interval can be commenced substantially simultaneously with the start or end of the V-EVENT or V-TRIG or, in the latter case, upon the end of the V-PACE which may follow the V-TRIG. The microprocessor **80** also optionally calculates A-V delays, V-V delays, post-ventricular time periods, and post-atrial time periods that vary with the sensor based escape interval established in response to the RCP(s) and/or with the intrinsic atrial rate and/or intrinsic ventricular rate.

The output amplifiers circuit **51** contains a RA pace pulse generator (and a LA pace pulse generator if LA pacing is provided), a RV pace pulse generator, a LV pace pulse generator, and/or any other pulse generator configured to provide atrial and ventricular pacing. In order to trigger generation of an RV-PACE or LV-PACE pulse, digital controller/timer circuit **43** generates the RV-TRIG signal at the time-out of the A-RVp delay (in the case of RV pre-excitation) or the LV-TRIG at the time-out of the A-LVp delay (in the case of LV pre-excitation) provided by AV delay interval timer **83**E (or the V-V delay timer **83**B). Similarly, digital controller/timer circuit **43** generates an RA-TRIG signal that triggers output of an RA-PACE pulse (or an LA-TRIG signal that triggers output of an LA-PACE pulse, if provided) at the end of the V-A escape interval timed by escape interval timers **83**D.

The output amplifiers circuit **51** includes switching circuits for coupling selected pace electrode pairs from among the lead conductors and the IND-CAN electrode **20** to the RA pace pulse generator (and LA pace pulse generator if provided), RV pace pulse generator and LV pace pulse generator. Pace/sense electrode pair selection and control circuit **53** selects lead conductors and associated pace electrode pairs to be coupled with the atrial and ventricular output amplifiers within output amplifiers circuit **51** for accomplishing RA, LA, RV and LV pacing.

The sense amplifiers circuit **55** contains sense amplifiers for atrial and ventricular pacing and sensing. High impedance P-wave and R-wave sense amplifiers may be used to amplify a voltage difference signal that is generated across the sense electrode pairs by the passage of cardiac depolarization wavefronts. The high impedance sense amplifiers use high gain to amplify the low amplitude signals and rely on pass band filters, time domain filtering and amplitude threshold comparison to discriminate a P-wave or R-wave from background electrical noise. Digital controller/timer circuit **43** controls sensitivity settings of the atrial and ventricular sense amplifiers **55**.

The sense amplifiers may be uncoupled from the sense electrodes during the blanking periods before, during, and after delivery of a pace pulse to any of the pace electrodes of the pacing system to avoid saturation of the sense amplifiers. The sense amplifiers circuit **55** includes blanking circuits for uncoupling the selected pairs of the lead conductors and the IND-CAN electrode **20** from the inputs of the RA sense amplifier (and LA sense amplifier if provided), RV sense amplifier and LV sense amplifier during the ABP, PVABP and VBP. The sense amplifiers circuit **55** also includes switching circuits for coupling selected sense electrode lead conductors and the IND-CAN electrode **20** to the RA sense amplifier (and LA sense amplifier if provided), RV sense amplifier and LV sense amplifier. Again, sense electrode selection and control circuit **53** selects conductors and associated sense electrode pairs to be coupled with the atrial and ventricular sense amplifiers within the output amplifiers circuit **51** and sense amplifiers circuit **55** for accomplishing RA, LA, RV, and LV sensing along desired unipolar and bipolar sensing vectors.

Right atrial depolarizations or P-waves in the RA-SENSE signal that are sensed by the RA sense amplifier result in a RA-EVENT signal that is communicated to the digital controller/timer circuit **43**. Similarly, left atrial depolarizations or P-waves in the LA-SENSE signal that are sensed by the LA sense amplifier, if provided, result in a LA-EVENT signal that is communicated to the digital controller/timer circuit **43**. Ventricular depolarizations or R-waves in the RV-SENSE signal are sensed by a ventricular sense amplifier result in an RV-EVENT signal that is communicated to the digital controller/timer circuit **43**. Similarly, ventricular depolarizations or R-waves in the LV-SENSE signal are sensed by a ventricular sense amplifier result in an LV-EVENT signal that is communicated to the digital controller/timer circuit **43**. The RV-EVENT, LV-EVENT, and RA-EVENT, LA-SENSE signals may be refractory or non-refractory, and can inadvertently be triggered by electrical noise signals or aberrantly conducted depolarization waves rather than true R-waves or P-waves.

The techniques described in this disclosure, including those attributed to the IMD **16**, the computing apparatus **140**, and/or various constituent components, may be implemented, at least in part, in hardware, software, firmware, or any combination thereof. For example, various aspects of the techniques may be implemented within one or more processors, including one or more microprocessors, DSPs, ASICs, FPGAs, or any other equivalent integrated or discrete logic circuitry, as well as any combinations of such components, embodied in programmers, such as physician or patient programmers, stimulators, image processing devices, or other devices. The term "module," "processor," or "processing circuitry" may generally refer to any of the foregoing logic circuitry, alone or in combination with other logic circuitry, or any other equivalent circuitry.

Such hardware, software, and/or firmware may be implemented within the same device or within separate devices to support the various operations and functions described in this disclosure. In addition, any of the described units, modules, or components may be implemented together or separately as discrete but interoperable logic devices. Depiction of different features as modules or units is intended to highlight different functional aspects and does not necessarily imply that such modules or units must be realized by separate hardware or software components. Rather, functionality associated with one or more modules or units may be performed by separate hardware or software components, or integrated within common or separate hardware or software components.

When implemented in software, the functionality ascribed to the systems, devices and techniques described in this disclosure may be embodied as instructions on a computer-readable medium such as RAM, ROM, NVRAM, EEPROM, FLASH memory, magnetic data storage media, optical data storage media, or the like. The instructions may be executed by one or more processors to support one or more aspects of the functionality described in this disclosure.

This disclosure has been provided with reference to illustrative embodiments and is not meant to be construed in a limiting sense. As described previously, one skilled in the art will recognize that other various illustrative applications may use the techniques as described herein to take advantage of the beneficial characteristics of the apparatus and methods described herein. Various modifications of the illustrative embodiments, as well as additional embodiments of the disclosure, will be apparent upon reference to this description.

What is claimed:

1. A system for use in cardiac therapy comprising:

electrode apparatus comprising a plurality of external electrodes configured to be located proximate tissue of a patient; and

computing apparatus coupled to the electrode apparatus and configured to:

initiate delivery of bi-ventricular pacing therapy at a plurality of different V-V intervals,

monitor electrical activity using the plurality of external electrodes for each of the plurality of V-V intervals during the delivery of bi-ventricular pacing therapy,

generate electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for each of the plurality of V-V intervals based on the monitored electrical activity, and

identify a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information.

2. The system of claim **1**, wherein the electrical heterogeneity information comprises a global standard deviation of surrogate electrical activation times monitored by the plurality of external electrodes, wherein identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information comprises identifying the V-V interval from the plurality of different V-V intervals that generated the lowest global standard deviation of surrogate electrical activation times.

3. The system of claim **1**, wherein the plurality of electrodes comprises two or more left external electrodes configured to be located proximate the left side of the patient, wherein the electrical heterogeneity information comprises a

left standard deviation of surrogate electrical activation times monitored by the two or more left external electrodes, wherein identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information comprises identifying the V-V interval from the plurality of different V-V intervals that generated the lowest left standard deviation.

4. The system of claim **1**, wherein the plurality of electrodes comprises two or more left external electrodes configured to be located proximate the left side of the patient, wherein the electrical heterogeneity information comprises a left average of surrogate electrical activation times monitored by the two or more left external electrodes, wherein identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information comprises identifying the V-V interval from the plurality of different V-V intervals that generated the lowest left average.

5. The system of claim **1**, wherein the computing apparatus configures the plurality of different V-V intervals of the bi-ventricular pacing therapy to pre-excite the left ventricle if the electrical heterogeneity information indicates an increase in heterogeneity in the electrical activity monitored by the plurality of external electrodes.

6. The system of claim **1**, wherein the plurality of electrodes comprises two or more left external electrodes configured to be located proximate the left side of the patient, wherein the plurality of electrodes comprises two or more posterior external electrodes configured to be located proximate the posterior side of the patient,

wherein the computing apparatus configures the plurality of different V-V intervals of the bi-ventricular pacing therapy to pre-excite the left ventricle if the monitored electrical activity indicates an increase in surrogate electrical activation times monitored by at least one of the two or more left external electrodes and the two or more posterior external electrodes.

7. The system of claim **1**, wherein the plurality of electrodes comprises two or more right external electrodes configured to be located proximate the right side of the patient, wherein the plurality of electrodes comprises two or more anterior external electrodes configured to be located proximate the anterior side of the patient,

wherein the computing apparatus configures the plurality of different V-V intervals of the bi-ventricular pacing therapy to pre-excite the right ventricle if the monitored electrical activity indicates an increase in surrogate electrical activation times monitored by at least one of the two or more right external electrodes and the two or more anterior external electrodes.

8. The system of claim **1**, wherein the plurality of external electrodes comprises surface electrodes positioned in an array configured to be located proximate the skin of the torso of the patient.

9. The system of claim **1**, wherein the system further comprises:

display apparatus, wherein the display apparatus comprises a graphical user interface configured to present information for use in assisting a user in evaluating and adjusting cardiac therapy delivered to a patient,

wherein the computing apparatus is further configured to display at least the identified V-V interval on the graphical user interface.

10. The system of claim **9**, wherein the computing apparatus is further configured to display a graphical representation of surrogate electrical activation times monitored by the plurality of external electrodes about a portion of human anatomy monitored for each V-V interval of the plurality of different V-V intervals.

11. The system of claim **10**, wherein displaying the graphical representation of the surrogate cardiac electrical activation times about a portion of human anatomy comprises color scaling the portion of human anatomy on the graphical user interface according to the surrogate electrical activation times.

12. The system of claim **1**, wherein the pacing therapy is delivered by at least one implantable electrode coupled to at least one lead.

13. The system of claim **1**, wherein the bi-ventricular pacing therapy is delivered at an optimized A-V interval.

14. A system for use in cardiac therapy comprising:

electrode apparatus comprising a plurality of external electrodes configured to be located proximate tissue of a patient; and

computing apparatus coupled to the electrode apparatus and configured to:

monitor electrical activity using the plurality of external electrodes,

initiate delivery of bi-ventricular pacing therapy at an initial V-V interval,

generate initial electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for the initial V-V interval based on the electrical activity monitored during the delivery of bi-ventricular pacing therapy at the initial V-V interval,

configure a plurality of different V-V intervals to pre-excite the left ventricle or the right ventricle based on the initial electrical heterogeneity information,

initiate delivery of bi-ventricular pacing therapy at the plurality of different V-V intervals,

generate electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for each of the plurality of different V-V intervals based on the monitored electrical activity, and

identify a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information.

15. A method for use in cardiac therapy comprising:

initiating delivery of bi-ventricular pacing therapy at a plurality of different V-V intervals;

monitoring electrical activity using a plurality of external electrodes for each of the plurality of V-V intervals during the delivery of bi-ventricular pacing therapy;

generating electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for each of the plurality of V-V intervals based on the monitored electrical activity; and

identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information.

16. The method of claim **15**, wherein the electrical heterogeneity information comprises a global standard deviation of surrogate electrical activation times monitored by the plurality of external electrodes, wherein identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information comprises identifying the V-V interval from the plurality of different V-V intervals that generated the lowest global standard deviation of surrogate electrical activation times.

17. The method of claim 15, wherein the plurality of electrodes comprises two or more left external electrodes configured to be located proximate the left side of the patient, wherein the electrical heterogeneity information comprises a left standard deviation of surrogate electrical activation times monitored by the two or more left external electrodes, wherein identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information comprises identifying the V-V interval from the plurality of different V-V intervals that generated the lowest left standard deviation.

18. The method of claim 15, wherein the plurality of electrodes comprises two or more left external electrodes configured to be located proximate the left side of the patient, wherein the electrical heterogeneity information comprises a left average of surrogate electrical activation times monitored by the two or more left external electrodes, wherein identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information comprises identifying the V-V interval from the plurality of different V-V intervals that generated the lowest left average.

19. The method of claim 15, wherein the method further comprises configuring the plurality of different V-V intervals of the bi-ventricular pacing therapy to pre-excite the left ventricle if the electrical heterogeneity information indicates an increase in heterogeneity in the electrical activity monitored by the plurality of external electrodes.

20. The method of claim 15, wherein the plurality of electrodes comprises two or more left external electrodes configured to be located proximate the left side of the patient, wherein the plurality of electrodes comprises two or more posterior external electrodes configured to be located proximate the posterior side of the patient,

wherein the method further comprises configuring the plurality of different V-V intervals of the bi-ventricular pacing therapy to pre-excite the left ventricle if the monitored electrical activity indicates an increase in surrogate electrical activation times monitored by at least one of the two or more left external electrodes and the two or more posterior external electrodes.

21. The method of claim 15, wherein the plurality of electrodes comprises two or more right external electrodes configured to be located proximate the right side of the patient, wherein the plurality of electrodes comprises two or more anterior external electrodes configured to be located proximate the anterior side of the patient,

wherein the method further comprises configuring the plurality of different V-V intervals of the bi-ventricular pacing therapy to pre-excite the right ventricle if the monitored electrical activity indicates an increase in surrogate electrical activation times monitored by at least one of the two or more right external electrodes and the two or more anterior external electrodes.

22. The method of claim 15, wherein the plurality of external electrodes comprises surface electrodes positioned in an array configured to be located proximate the skin of the torso of the patient.

23. The method of claim 15, wherein the method further comprises displaying at least the identified V-V interval on a graphical user interface configured to present information for use in assisting a user in evaluating and adjusting cardiac therapy delivered to a patient.

24. The method of claim 23, wherein the method further comprises displaying, on the graphical user interface, a graphical representation of surrogate electrical activation times monitored by the plurality of external electrodes about a portion of human anatomy monitored for each V-V interval of the plurality of different V-V intervals.

25. A method for use in cardiac therapy comprising:

monitoring electrical activity using a plurality of external electrodes;

initiating delivery of bi-ventricular pacing therapy at an initial V-V interval;

generating initial electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for the initial V-V interval based on the electrical activity monitored during the delivery of bi-ventricular pacing therapy at the initial V-V interval;

configuring a plurality of different V-V intervals to pre-excite the left ventricle or the right ventricle based on the initial electrical heterogeneity information;

initiating delivery of bi-ventricular pacing therapy at the plurality of different V-V intervals;

generating electrical heterogeneity information representative of at least one of mechanical cardiac functionality and electrical cardiac functionality for each of the plurality of V-V intervals based on the electrical activity monitored during the delivery of bi-ventricular pacing therapy at the plurality of different V-V intervals; and

identifying a V-V interval from the plurality of different V-V intervals based on the electrical heterogeneity information.

* * * * *

专利名称(译)	用于配置室间隔的系统和方法		
公开(公告)号	US9764143	公开(公告)日	2017-09-19
申请号	US14/703348	申请日	2015-05-04
[标]申请(专利权)人(译)	美敦力公司		
申请(专利权)人(译)	美敦力公司，INC.		
当前申请(专利权)人(译)	美敦力公司，INC.		
[标]发明人	GHOSH SUBHAM GILLBERG JEFFREY		
发明人	GHOSH, SUBHAM GILLBERG, JEFFREY		
IPC分类号	A61N1/36 A61N1/372 A61N1/368 A61B5/00 A61B5/0408 A61B5/0452 A61N1/365		
CPC分类号	A61N1/3684 A61B5/0452 A61B5/04085 A61B5/7282 A61N1/37247 A61B5/6805 A61N1/3682 A61N1/36514 A61N1/36843		
优先权	62/037694 2014-08-15 US		
其他公开文献	US20160045737A1		
外部链接	Espacenet USPTO		

摘要(译)

本文描述了用于帮助用户识别心脏治疗的室间（V-V）延迟的系统和方法。该系统和方法可以使用外部电极设备监测患者的电活动，以提供多个不同V-V间隔的电异质性信息，并且可以基于电异质性信息识别V-V间期。