



US009538960B2

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

(10) **Patent No.:** **US 9,538,960 B2**
(45) **Date of Patent:** ***Jan. 10, 2017**

- (54) **INJECTABLE PHYSIOLOGICAL MONITORING SYSTEM**
- (71) Applicant: **Medtronic Monitoring, Inc.**, San Jose, CA (US)
- (72) Inventors: **Scott T. Mazar**, Woodbury, MN (US); **Mark J. Bly**, Falcon Heights, MN (US)
- (73) Assignee: **Medtronic Monitoring, Inc.**, San Jose, CA (US)
- (*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **14/921,827**

(22) Filed: **Oct. 23, 2015**

(65) **Prior Publication Data**
US 2016/0045169 A1 Feb. 18, 2016

Related U.S. Application Data
(63) Continuation of application No. 12/209,479, filed on Sep. 12, 2008, now Pat. No. 9,186,089.
(Continued)

(51) **Int. Cl.**
A61B 5/00 (2006.01)
A61B 5/042 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC **A61B 5/7282** (2013.01); **A61B 5/0031** (2013.01); **A61B 5/0205** (2013.01);
(Continued)

(58) **Field of Classification Search**
None
See application file for complete search history.

(56) **References Cited**
U.S. PATENT DOCUMENTS

834,261 A 10/1906 Chambers
2,087,124 A 7/1937 Smith et al.
(Continued)

FOREIGN PATENT DOCUMENTS

AU 2003-220574 A8 10/2003
EP 1487535 A2 12/2004
(Continued)

OTHER PUBLICATIONS

Young, David B. Control of Cardiac Output, Chapt. 6, Morgan and Claypool Lifesciences, San Rafael, CA, 2010 chapter 6, section 6.4, para 7.*

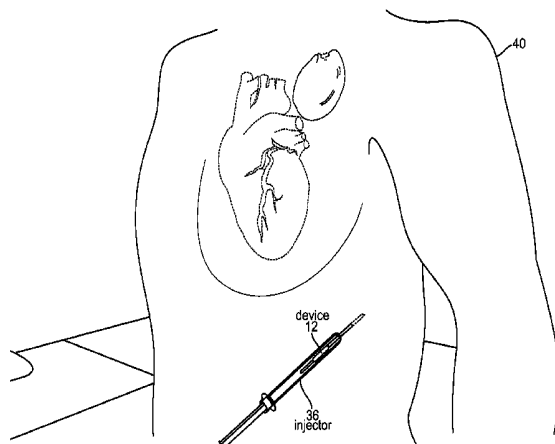
(Continued)

Primary Examiner — Brian T Gedeon
(74) *Attorney, Agent, or Firm* — Billion & Armitage;
Michael A. Collins

(57) **ABSTRACT**

An injectable device for use in a subcutaneous physiological monitoring of a patient includes a body, a plurality of sensors, and a monitoring unit. The plurality of sensors provide an indication of at least one physiological event of a patient, wherein the plurality of sensors includes two or more electrodes in contact with tissue of the patient. The monitoring unit is located within the body and is coupled to the plurality of sensors and configured to monitor a physiologic signal of the patient using the electrodes, wherein the physiologic signal includes an impedance signal related to hydration of tissue of the patient and wherein the monitoring unit is further configured to, based at least in part on the impedance signal measured from the patient, detect an impending cardiac decompensation of the patient.

18 Claims, 16 Drawing Sheets



Related U.S. Application Data				
		4,733,107 A	3/1988	O'Shaughnessy et al.
		4,781,200 A	11/1988	Baker
		4,793,362 A	12/1988	Tedner
(60)	Provisional application No. 61/055,666, filed on May 23, 2008, provisional application No. 60/972,336, filed on Sep. 14, 2007, provisional application No. 60/972,537, filed on Sep. 14, 2007, provisional application No. 60/972,329, filed on Sep. 14, 2007, provisional application No. 60/972,354, filed on Sep. 14, 2007.	4,838,273 A	6/1989	Cartmell
		4,838,279 A	6/1989	Fore
		4,850,370 A	7/1989	Dower
		4,880,004 A	11/1989	Baker, Jr. et al.
		4,895,163 A	1/1990	Libke et al.
		4,911,175 A	3/1990	Shizgal
		4,945,916 A	8/1990	Kretschmer et al.
		4,955,381 A	9/1990	Way et al.
		4,966,158 A	10/1990	Honma et al.
(51)	Int. Cl.	4,981,139 A	1/1991	Pfohl
	<i>A61B 5/0205</i> (2006.01)	4,988,335 A	1/1991	Prindle et al.
	<i>A61B 5/07</i> (2006.01)	4,989,612 A	2/1991	Fore
	<i>A61B 5/145</i> (2006.01)	5,001,632 A	3/1991	Hall-Tipping
	<i>A61B 5/053</i> (2006.01)	5,012,810 A	5/1991	Strand
	<i>A61N 1/372</i> (2006.01)	5,020,612 A	6/1991	Williams
	<i>A61B 5/11</i> (2006.01)	5,025,791 A	6/1991	Niwa
		5,027,824 A	7/1991	Dougherty et al.
(52)	U.S. Cl.	5,063,937 A	11/1991	Ezenwa et al.
	CPC <i>A61B 5/02055</i> (2013.01); <i>A61B 5/0422</i> (2013.01); <i>A61B 5/053</i> (2013.01); <i>A61B 5/07</i> (2013.01); <i>A61B 5/076</i> (2013.01); <i>A61B 5/14503</i> (2013.01); <i>A61B 5/4875</i> (2013.01); <i>A61B 5/686</i> (2013.01); <i>A61B 5/1118</i> (2013.01); <i>A61B 5/7232</i> (2013.01); <i>A61B 2560/0214</i> (2013.01); <i>A61B 2560/0468</i> (2013.01); <i>A61B 2562/0219</i> (2013.01); <i>A61B 2562/04</i> (2013.01); <i>A61B 2562/06</i> (2013.01); <i>A61B 2562/16</i> (2013.01); <i>A61N 1/37205</i> (2013.01)	5,080,099 A	1/1992	Way et al.
		5,083,563 A	1/1992	Collins
		5,086,781 A	2/1992	Bookspan
		5,113,869 A	5/1992	Nappholz et al.
		5,125,412 A	6/1992	Thornton
		5,133,355 A	7/1992	Strand et al.
		5,140,985 A	8/1992	Schroeder et al.
		5,150,708 A	9/1992	Brooks
		5,168,874 A	12/1992	Segalowitz
		5,226,417 A	7/1993	Swedlow et al.
		5,241,300 A	8/1993	Buschmann
		5,257,627 A	11/1993	Rapopot
		5,271,411 A	12/1993	Ripley et al.
		5,273,532 A	12/1993	Niezink et al.
		5,282,840 A	2/1994	Hudrlik
		5,291,013 A	3/1994	Nafarrate et al.
		5,297,556 A	3/1994	Shankar
		5,300,079 A	4/1994	Niezink et al.
		5,301,677 A	4/1994	Hsung
		5,319,363 A	6/1994	Welch et al.
		5,331,966 A	7/1994	Bennett et al.
		5,335,664 A	8/1994	Nagashima
		5,343,869 A	9/1994	Pross et al.
		5,353,793 A	10/1994	Bornn
		5,362,069 A	11/1994	Hall-Tipping
		5,375,604 A	12/1994	Kelly et al.
		5,411,530 A	5/1995	Akhtar
		5,437,285 A	8/1995	Verrier et al.
		5,443,073 A	8/1995	Wang et al.
		5,449,000 A	9/1995	Libke et al.
		5,450,845 A	9/1995	Axel
		5,454,377 A	10/1995	Dzwonczyk et al.
		5,464,012 A	11/1995	Falcone
		5,469,859 A	11/1995	Tsoglin et al.
		5,482,036 A	1/1996	Diab et al.
		5,503,157 A	4/1996	Sramek
		5,511,548 A	4/1996	Riazz
		5,511,553 A	4/1996	Segalowitz
		5,518,001 A	5/1996	Snell
		5,523,742 A	6/1996	Simkins et al.
		5,529,072 A	6/1996	Sramek
		5,544,661 A	8/1996	Davis et al.
		5,558,638 A	9/1996	Evers et al.
		5,560,368 A	10/1996	Berger
		5,564,429 A	10/1996	Bornn et al.
		5,564,434 A	10/1996	Halperin et al.
		5,566,671 A	10/1996	Lyons
		5,575,284 A	11/1996	Athan et al.
		5,607,454 A	3/1997	Cameron et al.
		5,632,272 A	5/1997	Diab et al.
		5,634,468 A	6/1997	Platt et al.
		5,642,734 A	7/1997	Ruben et al.
		5,673,704 A	10/1997	Marchlinski et al.
		5,678,562 A	10/1997	Sellers
		5,687,717 A	11/1997	Halpern et al.
		5,718,234 A	2/1998	Warden et al.
		5,724,025 A	3/1998	Tavori
		5,738,107 A	4/1998	Martinsen et al.
(56)	References Cited			
	U.S. PATENT DOCUMENTS			
	2,184,511 A	12/1939	Bagno et al.	
	3,170,459 A	2/1965	Phipps et al.	
	3,232,291 A	2/1966	Parker	
	3,370,459 A	2/1968	Cescati	
	3,517,999 A	6/1970	Weaver	
	3,620,216 A	11/1971	Szymanski	
	3,677,260 A	7/1972	Funfstuck et al.	
	3,805,769 A	4/1974	Sessions	
	3,845,757 A	11/1974	Weyer	
	3,874,368 A	4/1975	Asrican	
	3,882,853 A	5/1975	Gofman et al.	
	3,942,517 A	3/1976	Bowles et al.	
	3,972,329 A	8/1976	Kaufman	
	4,008,712 A	2/1977	Nyboer	
	4,024,312 A	5/1977	Korpman	
	4,077,406 A	3/1978	Sandhage et al.	
	4,121,573 A	10/1978	Crovella et al.	
	4,141,366 A	2/1979	Cross, Jr. et al.	
	RE30,101 E	9/1979	Kubicek et al.	
	4,185,621 A	1/1980	Morrow	
	4,216,462 A	8/1980	DiGiacomo et al.	
	4,300,575 A	11/1981	Wilson	
	4,308,872 A	1/1982	Watson et al.	
	4,358,678 A	11/1982	Lawrence	
	4,409,983 A	10/1983	Albert	
	4,450,527 A	5/1984	Sramek	
	4,451,254 A	5/1984	Dinius et al.	
	4,478,223 A	10/1984	Allor	
	4,498,479 A	2/1985	Martio et al.	
	4,522,211 A	6/1985	Bare et al.	
	4,661,103 A	4/1987	Harman	
	4,664,129 A	5/1987	Helzel et al.	
	4,669,480 A	6/1987	Hoffman	
	4,673,387 A	6/1987	Phillips et al.	
	4,681,118 A	7/1987	Asai et al.	
	4,692,685 A	9/1987	Blaze	
	4,699,146 A	10/1987	Sieverding	
	4,721,110 A	1/1988	Lampadius	
	4,730,611 A	3/1988	Lamb	

(56)

References Cited

U.S. PATENT DOCUMENTS

5,748,103	A	5/1998	Flach et al.	6,315,721	B2	11/2001	Schulman et al.
5,767,791	A	6/1998	Stoop et al.	6,327,487	B1	12/2001	Stratbucker
5,769,793	A	6/1998	Pincus et al.	6,330,464	B1	12/2001	Colvin, Jr. et al.
5,772,508	A	6/1998	Sugita et al.	6,336,903	B1	1/2002	Bardy
5,772,586	A	6/1998	Heinonen et al.	6,339,722	B1	1/2002	Heethaar et al.
5,778,882	A	7/1998	Raymond et al.	6,343,140	B1	1/2002	Brooks
5,788,643	A	8/1998	Feldman	6,347,245	B1	2/2002	Lee et al.
5,803,915	A	9/1998	Kremenchugsky et al.	6,358,208	B1	3/2002	Lang et al.
5,807,272	A	9/1998	Kun et al.	6,385,473	B1	5/2002	Haines et al.
5,814,079	A	9/1998	Kieval	6,398,727	B1	6/2002	Bui et al.
5,817,035	A	10/1998	Sullivan	6,400,982	B2	6/2002	Sweeney et al.
5,833,603	A	11/1998	Kovacs et al.	6,409,674	B1	6/2002	Brockway et al.
5,836,990	A	11/1998	Li	6,411,853	B1	6/2002	Millot et al.
5,855,614	A	1/1999	Stevens et al.	6,416,471	B1	7/2002	Kumar et al.
5,860,860	A	1/1999	Clayman	6,440,069	B1	8/2002	Raymond
5,862,802	A	1/1999	Bird	6,442,422	B1	8/2002	Duckert
5,862,803	A	1/1999	Besson et al.	6,450,820	B1	9/2002	Palsson et al.
5,865,733	A	2/1999	Malinouskas et al.	6,450,953	B1	9/2002	Place et al.
5,876,353	A	3/1999	Riff	6,454,707	B1	9/2002	Casscells, III et al.
5,904,708	A	5/1999	Goedeke	6,454,708	B1	9/2002	Ferguson et al.
5,935,079	A	8/1999	Swanson et al.	6,459,930	B1	10/2002	Takehara et al.
5,941,831	A	8/1999	Turcott	6,463,328	B1	10/2002	John
5,944,659	A	8/1999	Flach et al.	6,473,640	B1	10/2002	Erlebacher
5,949,636	A	9/1999	Johnson et al.	6,480,733	B1	11/2002	Turcott
5,957,854	A	9/1999	Besson et al.	6,480,734	B1	11/2002	Zhang et al.
5,957,861	A	9/1999	Combs et al.	6,480,734	B1	11/2002	Zhang et al.
5,964,703	A	10/1999	Goodman et al.	6,490,478	B1	12/2002	Zhang et al.
5,970,986	A	10/1999	Bolz et al.	6,491,647	B1	12/2002	Bridger et al.
5,984,102	A	11/1999	Tay	6,494,829	B1	12/2002	New, Jr. et al.
5,987,352	A	11/1999	Klein et al.	6,496,715	B1	12/2002	Lee et al.
6,007,532	A	12/1999	Netherly	6,512,949	B1	1/2003	Combs et al.
6,027,523	A	2/2000	Schmieding	6,520,967	B1	2/2003	Cauthen
6,045,513	A	4/2000	Stone et al.	6,527,711	B1	3/2003	Stivoric et al.
6,047,203	A	4/2000	Sackner et al.	6,527,729	B1	3/2003	Turcott
6,047,259	A	4/2000	Campbell et al.	6,544,173	B2	4/2003	West et al.
6,049,730	A	4/2000	Kristbjarnarson	6,544,174	B2	4/2003	West et al.
6,050,267	A	4/2000	Nardella et al.	6,551,251	B2	4/2003	Zuckerwar et al.
6,050,951	A	4/2000	Friedman et al.	6,551,252	B2	4/2003	Sackner et al.
6,051,017	A	4/2000	Loeb et al.	6,569,160	B1	5/2003	Goldin et al.
6,052,615	A	4/2000	Feild et al.	6,572,557	B2	6/2003	Tchou et al.
6,067,467	A	5/2000	John	6,572,636	B1	6/2003	Hagen et al.
6,080,106	A	6/2000	Lloyd et al.	6,577,139	B2	6/2003	Cooper
6,081,735	A	6/2000	Diab et al.	6,577,893	B1	6/2003	Besson et al.
6,095,991	A	8/2000	Krausman et al.	6,577,897	B1	6/2003	Shurubura et al.
6,102,856	A	8/2000	Groff et al.	6,579,231	B1	6/2003	Phipps
6,104,949	A	8/2000	Pitts et al.	6,580,942	B1	6/2003	Willshire
6,112,224	A	8/2000	Peifer et al.	6,582,441	B1	6/2003	He et al.
6,117,077	A	9/2000	Del Mar et al.	6,584,343	B1	6/2003	Ransbury et al.
6,125,297	A	9/2000	Siconolfi	6,587,715	B2	7/2003	Singer
6,129,744	A	10/2000	Boute et al.	6,589,170	B1	7/2003	Flach et al.
6,141,575	A	10/2000	Price	6,595,927	B2	7/2003	Pitts-Crick et al.
6,144,878	A	11/2000	Schroepel et al.	6,595,929	B2	7/2003	Stivoric et al.
6,164,284	A	12/2000	Schulman et al.	6,600,949	B1	7/2003	Turcott
6,181,963	B1	1/2001	Chin et al.	6,602,201	B1	8/2003	Hepp et al.
6,185,452	B1	2/2001	Schulman et al.	6,605,038	B1	8/2003	Teller et al.
6,190,313	B1	2/2001	Hinkle	6,611,705	B2	8/2003	Hopman et al.
6,190,324	B1	2/2001	Kieval et al.	6,616,606	B1	9/2003	Petersen et al.
6,198,394	B1	3/2001	Jacobsen et al.	6,622,042	B1	9/2003	Thacker
6,198,955	B1	3/2001	Axelgaard et al.	6,636,754	B1	10/2003	Baura et al.
6,208,894	B1	3/2001	Schulman et al.	6,641,542	B2	11/2003	Cho et al.
6,212,427	B1	4/2001	Hoover	6,645,153	B2	11/2003	Kroll et al.
6,213,942	B1	4/2001	Flach et al.	6,649,829	B2	11/2003	Garber et al.
6,225,901	B1	5/2001	Kail, IV	6,650,917	B2	11/2003	Diab et al.
6,245,021	B1	6/2001	Stampfer	6,650,943	B1*	11/2003	Whitehurst A61N 1/36007
6,259,939	B1	7/2001	Rogel	6,658,300	B2	12/2003	Govari et al.
6,272,377	B1	8/2001	Sweeney et al.	6,659,947	B1	12/2003	Carter et al.
6,277,078	B1	8/2001	Porat et al.	6,659,949	B1	12/2003	Lang et al.
6,287,252	B1	9/2001	Lugo	6,687,540	B2	2/2004	Marcovecchio
6,289,238	B1	9/2001	Besson et al.	6,697,658	B2	2/2004	Al-Ali
6,290,646	B1	9/2001	Cosentino et al.	RE38,476	E	3/2004	Diab et al.
6,295,466	B1	9/2001	Ishikawa et al.	6,699,200	B2	3/2004	Cao et al.
6,305,943	B1	10/2001	Pougatchev et al.	6,701,271	B2	3/2004	Willner et al.
6,306,088	B1	10/2001	Krausman et al.	6,711,423	B2	3/2004	Colvin, Jr.
6,308,094	B1	10/2001	Shusterman et al.	6,714,813	B2	3/2004	Ishigooka et al.
6,312,378	B1	11/2001	Bardy	RE38,492	E	4/2004	Diab et al.
				6,721,594	B2	4/2004	Conley et al.
				6,728,572	B2	4/2004	Hsu et al.
				6,748,269	B2	6/2004	Thompson et al.
				6,749,566	B2	6/2004	Russ

607/39

(56)

References Cited

U.S. PATENT DOCUMENTS

6,751,498	B1	6/2004	Greenberg et al.	7,212,849	B2	5/2007	Zhang et al.
6,760,617	B2	7/2004	Ward et al.	7,215,984	B2	5/2007	Doab et al.
6,773,396	B2	8/2004	Flach et al.	7,215,991	B2	5/2007	Besson et al.
6,775,566	B2	8/2004	Nissila	7,238,159	B2	7/2007	Banet et al.
6,790,178	B1	9/2004	Mault et al.	7,248,916	B2	7/2007	Bardy
6,795,722	B2	9/2004	Sheraton et al.	7,251,524	B1	7/2007	Hepp et al.
6,814,706	B2	11/2004	Barton et al.	7,257,438	B2	8/2007	Kinast
6,816,744	B2	11/2004	Garfield et al.	7,261,690	B2	8/2007	Teller et al.
6,821,249	B2	11/2004	Casscells et al.	7,277,741	B2	10/2007	Debreczeny et al.
6,824,515	B2	11/2004	Suorsa et al.	7,284,904	B2	10/2007	Tokita et al.
6,827,690	B2	12/2004	Bardy	7,285,090	B2	10/2007	Stivoric et al.
6,829,503	B2	12/2004	Alt	7,294,105	B1	11/2007	Islam
6,858,006	B2	2/2005	MacCarter et al.	7,295,879	B2	11/2007	Denker et al.
6,871,211	B2	3/2005	Labounty et al.	7,297,119	B2	11/2007	Westbrook et al.
6,878,121	B2	4/2005	Krausman et al.	7,318,808	B2	1/2008	Tarassenko et al.
6,879,850	B2	4/2005	Kimball	7,319,386	B2	1/2008	Collins et al.
6,881,191	B2	4/2005	Oakley et al.	7,336,187	B2	2/2008	Hubbard, Jr. et al.
6,885,895	B1	4/2005	Whitehurst et al.	7,346,380	B2	3/2008	Axelgaard et al.
6,887,201	B2	5/2005	Bardy	7,382,247	B2	6/2008	Welch et al.
6,890,096	B2	5/2005	Tokita et al.	7,384,398	B2	6/2008	Gagnadre et al.
6,893,396	B2	5/2005	Schulze et al.	7,390,299	B2	6/2008	Weiner et al.
6,894,204	B2	5/2005	Dunshree	7,395,106	B2	7/2008	Ryu et al.
6,906,530	B2	6/2005	Geisel	7,423,526	B2	9/2008	Despotis
6,912,414	B2	6/2005	Tong	7,423,537	B2	9/2008	Bonnet et al.
6,936,006	B2	8/2005	Sabra	7,443,302	B2	10/2008	Reeder et al.
6,940,403	B2	9/2005	Kail	7,450,024	B2	11/2008	Wildman et al.
6,942,622	B1	9/2005	Turcott	7,460,913	B2	12/2008	Kuzma et al.
6,952,695	B1	10/2005	Trinks et al.	7,468,032	B2	12/2008	Stahmann et al.
6,970,742	B2	11/2005	Mann et al.	7,510,699	B2	3/2009	Black et al.
6,972,683	B2	12/2005	Lestienne et al.	7,701,227	B2	4/2010	Saulnier et al.
6,978,177	B1	12/2005	Chen et al.	7,813,778	B2	10/2010	Benaron et al.
6,980,851	B2	12/2005	Zhu et al.	7,881,763	B2	2/2011	Brauker et al.
6,980,852	B2	12/2005	Jersey-Willuhn et al.	7,942,824	B1	5/2011	Kayyali et al.
6,985,078	B2	1/2006	Suzuki et al.	8,005,543	B2*	8/2011	Libbus A61N 1/36114
6,987,965	B2	1/2006	Ng et al.				607/18
6,988,989	B2	1/2006	Weiner et al.	8,057,486	B2	11/2011	Hansen
6,993,378	B2	1/2006	Wiederhold et al.	8,160,680	B2	4/2012	Boyden et al.
6,997,879	B1	2/2006	Turcott	8,364,280	B2	1/2013	Marnfeldt et al.
7,003,346	B2	2/2006	Singer	8,774,944	B2	7/2014	Thenuwara et al.
7,009,362	B2	3/2006	Tsakamoto et al.	2001/0047127	A1	11/2001	New, Jr. et al.
7,010,340	B2	3/2006	Scarantino et al.	2002/0019586	A1	2/2002	Teller et al.
7,018,338	B2	3/2006	Vetter et al.	2002/0019588	A1	2/2002	Marro et al.
7,020,508	B2	3/2006	Stivoric et al.	2002/0022786	A1	2/2002	Takehara et al.
7,027,862	B2	4/2006	Dahl et al.	2002/0028989	A1	3/2002	Pelletier et al.
7,041,062	B2	5/2006	Friedrichs et al.	2002/0032581	A1	3/2002	Reitberg
7,044,911	B2	5/2006	Drinan et al.	2002/0045836	A1	4/2002	Alkawwas et al.
7,047,067	B2	5/2006	Gray et al.	2002/0088465	A1	7/2002	Hill
7,050,846	B2	5/2006	Sweeney et al.	2002/0099277	A1	7/2002	Harry et al.
7,054,679	B2	5/2006	Hirsh	2002/0103510	A1	8/2002	Bardy et al.
7,059,767	B2	6/2006	Tokita et al.	2002/0116009	A1	8/2002	Fraser et al.
7,088,242	B2	8/2006	Aupperle et al.	2002/0123672	A1	9/2002	Christophersom et al.
7,113,826	B2	9/2006	Henry et al.	2002/0123674	A1	9/2002	Plicchi et al.
7,118,531	B2	10/2006	Krill	2002/0138017	A1	9/2002	Bui et al.
7,127,370	B2	10/2006	Kelly et al.	2002/0167389	A1	11/2002	Uchikoba et al.
7,129,836	B2	10/2006	Lawson et al.	2003/0009092	A1	1/2003	Parker
7,130,396	B2	10/2006	Rogers et al.	2003/0023184	A1	1/2003	Pitts-Crick et al.
7,130,679	B2	10/2006	Parsonnet et al.	2003/0028221	A1	2/2003	Zhu et al.
7,133,716	B2	11/2006	Kraemer et al.	2003/0028321	A1	2/2003	Upadhyaya et al.
7,136,697	B2	11/2006	Singer	2003/0051144	A1	3/2003	Williams
7,136,703	B1	11/2006	Cappa et al.	2003/0055460	A1	3/2003	Owens et al.
7,142,907	B2	11/2006	Xue et al.	2003/0083581	A1	5/2003	Taha et al.
7,149,574	B2	12/2006	Yun et al.	2003/0085717	A1	5/2003	Cooper
7,149,773	B2	12/2006	Haller et al.	2003/0087244	A1	5/2003	McCarthy
7,151,961	B1	12/2006	Whitehurst et al.	2003/0092975	A1	5/2003	Casscells, III et al.
7,153,262	B2	12/2006	Stivoric et al.	2003/0093125	A1	5/2003	Zhu et al.
7,156,807	B2	1/2007	Carter et al.	2003/0093298	A1	5/2003	Hernandez et al.
7,156,808	B2	1/2007	Quy et al.	2003/0100367	A1	5/2003	Cooke
7,160,252	B2	1/2007	Cho et al.	2003/0105411	A1	6/2003	Smallwood et al.
7,160,253	B2	1/2007	Missila et al.	2003/0135127	A1	7/2003	Sackner et al.
7,166,063	B2	1/2007	Rahman et al.	2003/0143544	A1	7/2003	McCarthy
7,167,743	B2	1/2007	Heruth et al.	2003/0149349	A1	8/2003	Jensen
7,184,821	B2	2/2007	Belalcazar et al.	2003/0187370	A1	10/2003	Kodama
7,191,000	B2	3/2007	Zhu et al.	2003/0191503	A1	10/2003	Zhu et al.
7,194,306	B1	3/2007	Turcott	2003/0212319	A1	11/2003	Magill
7,206,630	B1	4/2007	Tarler	2003/0221687	A1	12/2003	Kaigler
				2003/0233129	A1	12/2003	Matos
				2004/0006279	A1	1/2004	Arad (Abboud)
				2004/0010303	A1	1/2004	Bolea et al.
				2004/0015058	A1	1/2004	Besson et al.

(56)

References Cited

U.S. PATENT DOCUMENTS

2004/0019292	A1	1/2004	Drinan et al.	2005/0228234	A1	10/2005	Yang
2004/0044293	A1	3/2004	Burton	2005/0228238	A1	10/2005	Monitzer
2004/0049132	A1	3/2004	Barron et al.	2005/0228244	A1	10/2005	Banet
2004/0064133	A1	4/2004	Miller et al.	2005/0239493	A1	10/2005	Batkin et al.
2004/0068204	A1	4/2004	Imran et al.	2005/0240087	A1	10/2005	Keenan et al.
2004/0073094	A1	4/2004	Baker	2005/0251044	A1	11/2005	Hoctor et al.
2004/0073126	A1	4/2004	Rowlandson	2005/0256418	A1	11/2005	Mietus et al.
2004/0077954	A1	4/2004	Oakley et al.	2005/0261598	A1	11/2005	Banet et al.
2004/0100376	A1	5/2004	Lye et al.	2005/0261743	A1	11/2005	Kroll
2004/0102683	A1	5/2004	Khanuja et al.	2005/0267376	A1	12/2005	Marossero et al.
2004/0106951	A1	6/2004	Edman et al.	2005/0267377	A1	12/2005	Marossero et al.
2004/0106954	A1*	6/2004	Whitehurst A61M 5/14276 607/3	2005/0267381	A1	12/2005	Benditt et al.
2004/0122489	A1	6/2004	Mazar et al.	2005/0273023	A1	12/2005	Bystrom et al.
2004/0127790	A1	7/2004	Lang et al.	2005/0277841	A1	12/2005	Shennib
2004/0133079	A1	7/2004	Mazar et al.	2005/0277842	A1	12/2005	Silva
2004/0133081	A1	7/2004	Teller et al.	2005/0277992	A1	12/2005	Koh et al.
2004/0134496	A1	7/2004	Cho et al.	2005/0280531	A1	12/2005	Fadem et al.
2004/0143170	A1	7/2004	DuRousseau	2005/0283197	A1	12/2005	Daum et al.
2004/0147969	A1	7/2004	Mann et al.	2005/0288601	A1	12/2005	Wood et al.
2004/0152956	A1	8/2004	Korman	2006/0004300	A1	1/2006	Kennedy
2004/0158132	A1	8/2004	Zaleski	2006/0004377	A1	1/2006	Keller
2004/0167389	A1	8/2004	Brabrand	2006/0009697	A1	1/2006	Banet et al.
2004/0172080	A1	9/2004	Stadler et al.	2006/0009701	A1	1/2006	Nissila et al.
2004/0199056	A1	10/2004	Husemann et al.	2006/0010090	A1	1/2006	Brockway et al.
2004/0215240	A1	10/2004	Lovett et al.	2006/0020218	A1	1/2006	Freeman et al.
2004/0215247	A1	10/2004	Bolz	2006/0025661	A1	2/2006	Sweeney et al.
2004/0220639	A1	11/2004	Mulligan et al.	2006/0030781	A1	2/2006	Shennib
2004/0225199	A1	11/2004	Evanyk et al.	2006/0030782	A1	2/2006	Shennib
2004/0225203	A1	11/2004	Jemison et al.	2006/0031102	A1	2/2006	Teller et al.
2004/0243018	A1	12/2004	Organ et al.	2006/0041280	A1	2/2006	Stahmann et al.
2004/0267142	A1	12/2004	Paul	2006/0047215	A1	3/2006	Newman et al.
2005/0015094	A1	1/2005	Keller	2006/0052678	A1	3/2006	Drinan et al.
2005/0015095	A1	1/2005	Keller	2006/0058543	A1	3/2006	Walter et al.
2005/0020935	A1	1/2005	Helzel et al.	2006/0058593	A1	3/2006	Drinan et al.
2005/0027175	A1	2/2005	Yang	2006/0064030	A1	3/2006	Cosentino et al.
2005/0027204	A1	2/2005	Kligfield et al.	2006/0064040	A1	3/2006	Berger et al.
2005/0027207	A1	2/2005	Westbrook et al.	2006/0064142	A1	3/2006	Chavan et al.
2005/0027918	A1	2/2005	Govindarajulu et al.	2006/0066449	A1	3/2006	Johnson
2005/0043675	A1	2/2005	Pastore et al.	2006/0074283	A1	4/2006	Henderson et al.
2005/0054944	A1	3/2005	Nakada et al.	2006/0074462	A1	4/2006	Verhoef
2005/0059867	A1	3/2005	Chung	2006/0075257	A1	4/2006	Martis et al.
2005/0065445	A1	3/2005	Arzbaecher et al.	2006/0084881	A1	4/2006	Korzinov et al.
2005/0065571	A1	3/2005	Imran	2006/0085049	A1	4/2006	Cory et al.
2005/0070768	A1	3/2005	Zhu et al.	2006/0089679	A1	4/2006	Zhu et al.
2005/0070778	A1	3/2005	Lackey et al.	2006/0094948	A1	5/2006	Gough et al.
2005/0079132	A1	4/2005	Wang et al.	2006/0095078	A1	5/2006	Tronnes
2005/0080346	A1	4/2005	Gianchandani et al.	2006/0102476	A1	5/2006	Niwa et al.
2005/0080460	A1	4/2005	Wang et al.	2006/0116592	A1	6/2006	Zhou et al.
2005/0080463	A1	4/2005	Stahmann et al.	2006/0122474	A1	6/2006	Teller et al.
2005/0085734	A1	4/2005	Tehrani	2006/0135858	A1	6/2006	Nidd et al.
2005/0091338	A1	4/2005	de la Huerga	2006/0142654	A1	6/2006	Rytky
2005/0096513	A1	5/2005	Ozguz et al.	2006/0142820	A1	6/2006	Von Arx et al.
2005/0107870	A1	5/2005	Wang et al.	2006/0149168	A1	7/2006	Czarnek
2005/0113703	A1	5/2005	Farringdon et al.	2006/0155174	A1	7/2006	Glukhovskiy et al.
2005/0124878	A1	6/2005	Sharony	2006/0155183	A1	7/2006	Kroecker et al.
2005/0124901	A1	6/2005	Misczynski et al.	2006/0155200	A1	7/2006	Ng
2005/0124908	A1	6/2005	Belalcazar et al.	2006/0161073	A1	7/2006	Singer
2005/0131288	A1	6/2005	Turner et al.	2006/0161205	A1	7/2006	Mitrani et al.
2005/0137464	A1	6/2005	Bomba	2006/0161459	A9	7/2006	Rosenfeld et al.
2005/0137626	A1	6/2005	Pastore	2006/0167374	A1	7/2006	Takehara et al.
2005/0148895	A1	7/2005	Misczynski et al.	2006/0173257	A1	8/2006	Nagai et al.
2005/0158539	A1	7/2005	Murphy et al.	2006/0173269	A1	8/2006	Glossop
2005/0177038	A1	8/2005	Kolpin et al.	2006/0195020	A1	8/2006	Martin et al.
2005/0187482	A1	8/2005	O'Brien et al.	2006/0195039	A1	8/2006	Drew et al.
2005/0187796	A1	8/2005	Rosenfeld et al.	2006/0195097	A1	8/2006	Evans et al.
2005/0192488	A1	9/2005	Bryenton et al.	2006/0195144	A1	8/2006	Giftakis et al.
2005/0197654	A1	9/2005	Edman et al.	2006/0202816	A1	9/2006	Crump et al.
2005/0203433	A1	9/2005	Singer	2006/0212097	A1	9/2006	Varadan et al.
2005/0203435	A1	9/2005	Nakada	2006/0224051	A1	10/2006	Teller et al.
2005/0203436	A1	9/2005	Davies	2006/0224072	A1	10/2006	Shennib
2005/0203637	A1	9/2005	Edman et al.	2006/0224079	A1	10/2006	Washchuk
2005/0206518	A1	9/2005	Welch et al.	2006/0235281	A1	10/2006	Tuccillo
2005/0215914	A1	9/2005	Bornzin et al.	2006/0235316	A1	10/2006	Ungless et al.
2005/0215918	A1	9/2005	Frantz et al.	2006/0235489	A1	10/2006	Drew et al.
				2006/0241641	A1	10/2006	Albans et al.
				2006/0241701	A1	10/2006	Markowitz et al.
				2006/0241722	A1	10/2006	Thacker et al.
				2006/0247545	A1	11/2006	St. Martin
				2006/0252999	A1	11/2006	Devaul et al.

(56)

References Cited

U.S. PATENT DOCUMENTS

2006/0253005	A1	11/2006	Drinan et al.	2007/0208262	A1	9/2007	Kovacs
2006/0253044	A1	11/2006	Zhang et al.	2007/0232867	A1	10/2007	Hansmann
2006/0258952	A1	11/2006	Stahmann et al.	2007/0244403	A1	10/2007	Natarajan et al.
2006/0264730	A1	11/2006	Stivoric et al.	2007/0249946	A1	10/2007	Kumar et al.
2006/0264767	A1	11/2006	Shennib	2007/0250121	A1	10/2007	Miesel et al.
2006/0264776	A1	11/2006	Stahmann et al.	2007/0255120	A1	11/2007	Rosnov
2006/0271116	A1	11/2006	Stahmann et al.	2007/0255153	A1	11/2007	Kumar et al.
2006/0276714	A1	12/2006	Holt et al.	2007/0255184	A1	11/2007	Shennib
2006/0281981	A1	12/2006	Jang et al.	2007/0255531	A1	11/2007	Drew
2006/0281996	A1	12/2006	Kuo et al.	2007/0260133	A1	11/2007	Meyer
2006/0293571	A1	12/2006	Bao et al.	2007/0260155	A1	11/2007	Rapoport et al.
2006/0293609	A1	12/2006	Stahmann et al.	2007/0260289	A1	11/2007	Giftakis et al.
2007/0010702	A1	1/2007	Wang et al.	2007/0265582	A1	11/2007	Kaplan et al.
2007/0010721	A1	1/2007	Chen et al.	2007/0273504	A1	11/2007	Tran
2007/0010750	A1	1/2007	Ueno et al.	2007/0276273	A1	11/2007	Watson, Jr.
2007/0015973	A1	1/2007	Nanikashvili et al.	2007/0282173	A1	12/2007	Wang et al.
2007/0015976	A1	1/2007	Miesel et al.	2007/0299325	A1	12/2007	Farrell et al.
2007/0016089	A1	1/2007	Fischell et al.	2008/0004499	A1	1/2008	Davis
2007/0021678	A1	1/2007	Beck et al.	2008/0004904	A1	1/2008	Tran
2007/0021790	A1	1/2007	Kieval et al.	2008/0021336	A1	1/2008	Dobak
2007/0021792	A1	1/2007	Kieval et al.	2008/0024293	A1	1/2008	Stylos
2007/0021794	A1	1/2007	Kieval et al.	2008/0024294	A1	1/2008	Mazar
2007/0021796	A1	1/2007	Kieval et al.	2008/0033260	A1	2/2008	Sheppard et al.
2007/0021797	A1	1/2007	Kieval et al.	2008/0039700	A1	2/2008	Drinan et al.
2007/0021798	A1	1/2007	Kieval et al.	2008/0058614	A1	3/2008	Banet et al.
2007/0021799	A1	1/2007	Kieval et al.	2008/0058656	A1	3/2008	Costello et al.
2007/0027388	A1	2/2007	Chou	2008/0059239	A1	3/2008	Gerst et al.
2007/0027497	A1	2/2007	Parnis	2008/0091089	A1	4/2008	Guillory et al.
2007/0032749	A1	2/2007	Overall et al.	2008/0114220	A1	5/2008	Banet et al.
2007/0038038	A1	2/2007	Stivoric et al.	2008/0120784	A1	5/2008	Warner et al.
2007/0038078	A1	2/2007	Osadchy	2008/0139934	A1	6/2008	McMorrow et al.
2007/0038255	A1	2/2007	Kieval et al.	2008/0146892	A1	6/2008	LeBoeuf et al.
2007/0038262	A1	2/2007	Kieval et al.	2008/0167538	A1	7/2008	Teller et al.
2007/0043301	A1	2/2007	Martinsen et al.	2008/0171918	A1	7/2008	Teller et al.
2007/0043303	A1	2/2007	Osypka et al.	2008/0171922	A1	7/2008	Teller et al.
2007/0048224	A1	3/2007	Howell et al.	2008/0171929	A1	7/2008	Katims
2007/0060800	A1	3/2007	Drinan et al.	2008/0183052	A1	7/2008	Teller et al.
2007/0060802	A1	3/2007	Ghevondian et al.	2008/0200774	A1	8/2008	Luo
2007/0073132	A1	3/2007	Vosch	2008/0214903	A1	9/2008	Orbach
2007/0073168	A1	3/2007	Zhang et al.	2008/0220865	A1	9/2008	Hsu
2007/0073181	A1	3/2007	Pu et al.	2008/0221399	A1	9/2008	Zhou et al.
2007/0073361	A1	3/2007	Goren et al.	2008/0221402	A1	9/2008	Despotis
2007/0082189	A1	4/2007	Gillette	2008/0224852	A1	9/2008	Dicks et al.
2007/0083092	A1	4/2007	Rippo et al.	2008/0228084	A1	9/2008	Bedard et al.
2007/0092862	A1	4/2007	Gerber	2008/0275465	A1	11/2008	Paul et al.
2007/0104840	A1	5/2007	Singer	2008/0287751	A1	11/2008	Stivoric et al.
2007/0106132	A1	5/2007	Elhag et al.	2008/0287752	A1	11/2008	Stroetz et al.
2007/0106137	A1	5/2007	Baker, Jr. et al.	2008/0293491	A1	11/2008	Wu et al.
2007/0106167	A1	5/2007	Kinast	2008/0294019	A1	11/2008	Tran
2007/0118039	A1	5/2007	Bodecker et al.	2008/0294020	A1	11/2008	Sapounas
2007/0123756	A1	5/2007	Kitajima et al.	2008/0318681	A1	12/2008	Rofougaran et al.
2007/0123903	A1	5/2007	Raymond et al.	2008/0319279	A1	12/2008	Ramsay et al.
2007/0123904	A1	5/2007	Stad et al.	2008/0319282	A1	12/2008	Tran
2007/0129622	A1	6/2007	Bourget et al.	2008/0319290	A1	12/2008	Mao et al.
2007/0129643	A1	6/2007	Kwok et al.	2009/0005016	A1	1/2009	Eng et al.
2007/0129769	A1	6/2007	Bourget et al.	2009/0018410	A1	1/2009	Coene et al.
2007/0142715	A1	6/2007	Banet et al.	2009/0018456	A1	1/2009	Hung
2007/0142732	A1	6/2007	Brockway et al.	2009/0048526	A1	2/2009	Aarts
2007/0149282	A1	6/2007	Lu et al.	2009/0054737	A1	2/2009	Magar et al.
2007/0150008	A1	6/2007	Jones et al.	2009/0062670	A1	3/2009	Sterling et al.
2007/0150009	A1	6/2007	Kveen et al.	2009/0073991	A1	3/2009	Landrum et al.
2007/0150029	A1	6/2007	Bourget et al.	2009/0076336	A1	3/2009	Mazar et al.
2007/0162089	A1	7/2007	Mosesov	2009/0076340	A1	3/2009	Libbus et al.
2007/0167753	A1	7/2007	Van Wyk et al.	2009/0076341	A1	3/2009	James et al.
2007/0167848	A1	7/2007	Kuo et al.	2009/0076342	A1	3/2009	Amurthur et al.
2007/0167849	A1	7/2007	Zhang et al.	2009/0076343	A1	3/2009	James et al.
2007/0167850	A1	7/2007	Russell et al.	2009/0076344	A1	3/2009	Libbus et al.
2007/0172424	A1	7/2007	Roser	2009/0076345	A1	3/2009	Manicka et al.
2007/0173705	A1	7/2007	Teller et al.	2009/0076346	A1	3/2009	James et al.
2007/0180047	A1	8/2007	Dong et al.	2009/0076348	A1	3/2009	Manicka et al.
2007/0180140	A1	8/2007	Welch et al.	2009/0076349	A1	3/2009	Libbus et al.
2007/0191723	A1	8/2007	Prystowsky et al.	2009/0076350	A1	3/2009	Bly et al.
2007/0207858	A1	9/2007	Breving	2009/0076363	A1	3/2009	Bly et al.
2007/0208233	A1	9/2007	Kovacs	2009/0076364	A1	3/2009	Libbus et al.
2007/0208235	A1	9/2007	Besson et al.	2009/0076397	A1	3/2009	Libbus et al.
				2009/0076401	A1	3/2009	Mazar et al.
				2009/0076405	A1	3/2009	Amurthur et al.
				2009/0076410	A1	3/2009	Libbus et al.
				2009/0076559	A1	3/2009	Libbus et al.

(56)

References Cited

U.S. PATENT DOCUMENTS

2009/0177145	A1	7/2009	Ohlander et al.
2009/0182204	A1	7/2009	Semler et al.
2009/0204180	A1	8/2009	Gelbart
2009/0234410	A1	9/2009	Libbus et al.
2009/0292194	A1	11/2009	Libbus et al.
2009/0306633	A1	12/2009	Trovato et al.
2010/0056881	A1	3/2010	Libbus et al.
2010/0191310	A1	7/2010	Bly et al.
2011/0144470	A1	6/2011	Mazar et al.
2011/0245711	A1	10/2011	Katra et al.
2011/0270049	A1	11/2011	Katra et al.

FOREIGN PATENT DOCUMENTS

EP	1579801	A1	9/2005
JP	2005-521448	A	7/2005
WO	00/79255	A1	12/2000
WO	01/89362	A2	11/2001
WO	02/92101	A1	11/2002
WO	03/082080	A2	10/2003
WO	2005/051164	A2	6/2005
WO	2005/104930	A1	11/2005
WO	2006/008745	A2	1/2006
WO	2006/102476	A2	9/2006
WO	2006/111878	A1	10/2006
WO	2007/041783	A1	4/2007
WO	2007/106455	A2	9/2007
WO	2009/116906	A1	9/2009

OTHER PUBLICATIONS

- Cooley, "The Parameters of Transthoracic Electrical Conduction", *Annals of the New York Academy of Sciences*, vol. 170 (2), 1970, pp. 702-713.
- Cowie, et al., "Hospitalization of patients with heart failure. A population-based study", *European Heart Journal*, vol. 23 (11), 2002, pp. 877-885.
- Dimri, "Chapter 1: Fractals in geophysics and semiology: an introduction", *Fractal Behaviour of the Earth System*, Springer Berlin Heidelberg, 2005, pp. 1-22.
- El-Dawlatly, et al., "Impedance cardiography: noninvasive assessment of hemodynamics and thoracic fluid content during bariatric surgery", *Obesity Surgery*, vol. 15 (5), May 2005, pp. 655-658.
- EM Microelectronic, "Plastic Flexible LCD", Product Brochure, retrieved from <http://www.emmicroelectronic.com/Line.asp?IdLine=48>, 2009, 2 pages.
- Erdmann, "Editorials: The value of diuretics in chronic heart failure demonstrated by an implanted hemodynamic monitor", *European Heart Journal*, vol. 23 (1), 2002, pp. 7-9.
- FDA—Medtronic Inc., "Chronicle 9520B Implantable Hemodynamic Monitor Reference Manual", 2007, 112 pages.
- Flach, "U.S. Appl. No. 60/006,600, filed Nov. 13, 1995".
- Fonarow, "How well are chronic heart failure patients being managed", *Rev Cardiovasc Med.*, vol. 7 Suppl 1, 2006, pp. S3-11.
- Fonarow, "Maximizing Heart Failure Care", PowerPoint Presentation, downloaded from <http://www.medreviews.com/media/MaxHFCare.ppt>, date unknown, 130 pages.
- Fonarow, "Proactive monitoring and management of the chronic heart failure patient", *Rev Cardiovasc Med.*, vol. 7 Suppl 1, 2006, pp. S1-S2.
- Fonarow, et al., "Risk stratification for in-hospital mortality in acutely decompensated heart failure: classification and regression tree analysis", *JAMA*, vol. 293 (5), Feb. 2, 2005, pp. 572-580.
- Fonarow, "The Acute Decompensated Heart Failure National Registry (ADHERE): opportunities to improve care of patients hospitalized with acute decompensated heart failure", *Rev Cardiovasc Med.*, vol. 4 Suppl 7, 2003, pp. S21-S30.
- Ganion, et al., "Intrathoracic impedance to monitor heart failure status: a comparison of two methods in a chronic heart failure dog model", *Congest Heart Fail.*, vol. 11 (4), 2005, pp. 177-181, 211.
- Gass, et al., "Critical pathways in the management of acute decompensated heart failure: A CME-Accredited monograph", Mount Sinai School of Medicine, 2004, 32 pages.
- Gheorghiadu, et al., "Congestion is an important diagnostic and therapeutic target in heart failure", *Rev Cardiovasc Med.*, vol. 7 Suppl 1, 2006, pp. 12-24.
- Gilliam, III, et al., "Changes in heart rate variability, quality of life, and activity in cardiac resynchronization therapy patients: results of the HF-HRV registry", *Pacing and Clinical Electrophysiology*, vol. 30 (1), Jan. 18, 2007, pp. 56-64.
- Gilliam, III, et al., "Prognostic value of heart rate variability footprint and standard deviation of average 5-minute intrinsic R-R intervals for mortality in cardiac resynchronization therapy patients", *J Electrocardiol.*, vol. 40 (4), Oct. 2007, pp. 336-342.
- Gniadecka, et al., "Localization of dermal edema in lipodermatosclerosis, lymphedema, and cardiac insufficiency high-frequency ultrasound examination of intradermal echogenicity", *J Am Acad Dermatol*, vol. 35 (1), Jul. 1996, pp. 37-41.
- Goldberg, et al., "Randomized trial of a daily electronic home monitoring system in patients with advanced heart failure: The Weight Monitoring in Heart Failure (WHARF) Trial", *American Heart Journal*, vol. 416 (4), Oct. 2003, pp. 705-712.
- Grap, et al., "Actigraphy in the Critically Ill: Correlation with Activity, Agitation, and Sedation", *American Journal of Critical Care*, vol. 14, 2005, pp. 52-60.
- Gudivaka, et al., "Single and multifrequency models for bioelectrical impedance analysis of body water compartments", *J Appl Physiol*, vol. 87 (3), 1999, pp. 1087-1096.
- Guyton, et al., "Unit V: The Body Fluids and Kidneys, Chapter 25: The Body Fluid Compartments: Extracellular and Intracellular Fluids; Interstitial Fluid and Edema", Guyton and Hall Textbook of Medical Physiology 11th Edition, Saunders, 2005, pp. 291-306.
- Hadase, et al., "Very low frequency power of heart rate variability is a powerful predictor of clinical prognosis in patients with congestive heart failure", *Circ J.*, vol. 68 (4), 2004, pp. 343-347.
- Hallstrom, et al., "Structural relationships between measures based on heart beat intervals: potential for improved risk assessment", *IEEE Biomedical Engineering*, vol. 51 (8), 2004, pp. 1414-1420.
- HRV Enterprises LLC, "Heart Rate Variability Seminars", downloaded from <http://hrventerprise.com>, downloaded Apr. 24, 2008, 3 pages.
- HRV Enterprises LLC, "LoggerPro HRV Biosignal Analysis", downloaded from <http://hrventerprise.com/products.html>, downloaded Apr. 24, 2008, 3 pages.
- Hunt, et al., "ACC/AHA Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.", Developed in Collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: Endorsed by the Heart Rhythm Society, *Circulation*, vol. 112, 2005, E154-E235.
- Hunt, et al., "ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult: Executive Summary A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines", *Circulation*, vol. 104, 2001, pp. 2996-3007.
- Imhoff, et al., "Noninvasive whole-body electrical bioimpedance cardiac output and invasive thermodilution cardiac output in high-risk surgical patients", *Critical Care Medicine*, vol. 28 (8), 2000, pp. 2182-2188.
- Jaeger, et al., "Evidence for Increased Intrathoracic Fluid Volume in Man at High Altitude", *J Appl Physiol.*, vol. 47 (6), 1979, pp. 670-676.
- Jaio, et al., "Variance fractal dimension analysis of seismic refraction signals", WESCANEX 97: Communications, Power and Computing, *IEEE Conference Proceedings*, May 22-23, 1997, pp. 163-167.
- Jerant, et al., "Reducing the cost of frequent hospital admissions for congestive heart failure: a randomized trial of a home telecare intervention", *Medical Care*, vol. 39 (11), 2001, pp. 1234-1245.
- Kasper, et al., "A randomized trial of the efficacy of multidisciplinary care in heart failure outpatients at high risk of hospital readmission", *J Am Coll Cardiol*, vol. 39, 2002, pp. 471-480.

(56)

References Cited

OTHER PUBLICATIONS

- Kaukinen, "Cardiac output measurement after coronary artery bypass grafting using bolus thermodilution, continuous thermodilution, and whole-body impedance cardiography", *Journal of Cardiothoracic and Vascular Anesthesia*, vol. 17 (2), 2003, pp. 199-203.
- Kawaguchi, et al., "Combined ventricular systolic and arterial stiffening in patients with heart failure and preserved ejection fraction: implications for systolic and diastolic reserve limitations", *Circulation*, vol. 107, 2003, pp. 714-720.
- Kawasaki, et al., "Heart rate turbulence and clinical prognosis in hypertrophic cardiomyopathy and myocardial infarction", *Circ J*, vol. 67 (7), 2003, pp. 601-604.
- Kearney, et al., "Predicting death due to progressive heart failure in patients with mild-to-moderate chronic heart failure", *J Am Coll Cardiol*, vol. 40 (10), 2002, pp. 1801-1808.
- Kitzman, et al., "Pathophysiological characterization of isolated diastolic heart failure in comparison to systolic heart failure", *JAMA*, vol. 288 (17), Nov. 2002, pp. 2144-2150.
- Koobi, et al., "Non-invasive measurement of cardiac output: whole-body impedance cardiography in simultaneous comparison with thermodilution and direct oxygen Fick methods", *Intensive Care Medicine*, vol. 23 (11), 1997, pp. 1132-1137.
- Koyama, et al., "Evaluation of heart-rate turbulence as a new prognostic marker in patients with chronic heart failure", *Circ J*, vol. 66 (10), 2002, pp. 902-907.
- Kristofer, et al., "U.S. Appl. No. 60/972,336", filed Sep. 14, 2007.
- Kristofer, et al., "U.S. Appl. No. 60/972,340", filed Sep. 14, 2007.
- Kristofer, et al., "U.S. Appl. No. 60/972,343", filed Sep. 14, 2007.
- Krumholz, et al., "Predictors of readmission among elderly survivors of admission with heart failure", *American Heart Journal*, vol. 139 (1), 2000, pp. 72-77.
- Kyle, et al., "Bioelectrical Impedance Analysis—part I: review of principles and methods", *Clin Nutr.*, vol. 23 (5), Oct. 2004, pp. 1226-1243.
- Kyle, et al., "Bioelectrical Impedance Analysis—part II: utilization in clinical practice", *Clin Nutr.*, vol. 23 (5), Oct. 2004, pp. 1430-1453.
- Landrum, "U.S. Appl. No. 61/079,746", filed Jul. 10, 2008.
- Lee, et al., "Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model", *JAMA*, vol. 290 (19), 2003, pp. 2581-2587.
- Leier, "The Physical Examination in Heart Failure—Part I", *Congest Hear Fail.*, vol. 13 (1), Jan.-Feb. 2007, pp. 41-47.
- Libbus, et al., "U.S. Appl. No. 61/055,662", filed May 23, 2008.
- Libbus, et al., "U.S. Appl. No. 60/972,316", filed Sep. 12, 2008.
- Libbus, et al., "U.S. Appl. No. 60/972,512", filed Sep. 14, 2007.
- Libbus, et al., "U.S. Appl. No. 60/972,581", filed Sep. 14, 2007.
- Libbus, et al., "U.S. Appl. No. 60/972,616", filed Sep. 14, 2007.
- Libbus, et al., "U.S. Appl. No. 61/035,970", filed Mar. 12, 2008.
- Libbus, et al., "U.S. Appl. No. 61/047,875", filed Apr. 25, 2008.
- Libbus, et al., "U.S. Appl. No. 61/055,656", filed May 23, 2008.
- Liu, et al., "Fractal analysis with applications to seismological pattern recognition of underground nuclear explosions", *Signal Processing*, vol. 80 (9), Sep. 2000, pp. 1849-1861.
- Lozano-Nieto, "Impedance ratio in bioelectrical impedance measurements for body fluid shift determination", *Proceedings of the IEEE 24th Annual Northeast Bioengineering Conference*, Apr. 9-10, 1998, pp. 24-25.
- Lucreziotti, et al., "Five-minute recording of heart rate variability in severe chronic heart failure: Correlates with right ventricular function and prognostic implications", *American Heart Journal*, vol. 139 (6), 2000, pp. 1088-1095.
- Luthje, et al., "Detection of heart failure decompensation using intrathoracic impedance monitoring by a triple-chamber implantable defibrillator", *Heart Rhythm*, vol. 2 (9), Sep. 2005, pp. 997-999.
- Magalski, et al., "Continuous ambulatory right heart pressure measurements with an implantable hemodynamic monitor: a multi-center, 12-Month Follow-Up Study of Patients with Chronic Heart Failure", *J Card Fail*, vol. 8 (2), 2002, pp. 63-70.
- Mahlberg, et al., "Actigraphy in agitated patients with dementia: Monitoring treatment outcomes", *Zeitschrift fur Gerontologie and Geriatrie*, vol. 40 (3), Jun. 2007, pp. 178-184.
- Manicka, et al., "U.S. Appl. No. 60/972,329", filed Sep. 14, 2007.
- Manicka, et al., "U.S. Appl. No. 60/972,537", filed Sep. 14, 2007.
- Manicka, et al., "U.S. Appl. No. 61/055,666", filed May 23, 2008.
- Matthie, et al., "Analytic assessment of the various bioimpedance methods used to estimate body water", *Appl Physiol*, vol. 84 (5), 1998, pp. 1801-1816.
- Matthie, et al., "Second generation mixture theory equation for estimating intracellular water using bioimpedance spectroscopy", *J Appl Physiol*, vol. 99, 2005, pp. 780-781.
- Mazar, et al., "U.S. Appl. No. 60/972,354", filed Sep. 14, 2007.
- Mazar, et al., "U.S. Appl. No. 61/046,196", filed Apr. 18, 2008.
- McMurray, et al., "Heart Failure: Epidemiology, Aetiology, and Prognosis of Heart Failure", *Heart*, vol. 83, 2000, pp. 596-602.
- Miller, "Home monitoring for congestive heart failure patients", *Caring Magazine*, Aug. 1995, pp. 53-54.
- Moser, et al., "Improving outcomes in heart failure: it's not unusual beyond usual Care", *Circulation*, vol. 105, 2002, pp. 2810-2812.
- Nagels, et al., "Actigraphic measurement of agitated behaviour in dementia", *International Journal of Geriatric Psychiatry*, vol. 21 (4), 2009, pp. 388-393.
- Nakamura, et al., "Universal scaling law in human behavioral organization", *Physical Review Letters*, vol. 99 (13), Sep. 28, 2007, 4 pages.
- Nakaya, "Fractal properties of seismicity in regions affected by large, shallow earthquakes in western Japan: Implications for fault formation processes based on a binary fractal fracture network model", *Journal of Geophysical Research*, vol. 11 (B1), Jan. 2005, pp. B01310.1-B01310.15.
- Naylor, et al., "Comprehensive discharge planning for the hospitalized elderly: a randomized clinical trial", *Amer. College Physicians*, vol. 120 (12), 1994, pp. 999-1006.
- NESIRITIDE (NATRECOR), "Acutely Decompensated Congestive Heart Failure: Burden of Disease", Presentation, Downloaded from <http://www.huntsvillehospital.org/foundation/events/cardiologupdate/CHF.ppt>, date unknown, 39 pages.
- Nieminen, et al., "EuroHeart Failure Survey II (EHFSII): a survey on hospitalized acute heart failure patients: description of population", *European Heart Journal*, vol. 27 (22), 2006, pp. 2725-2736.
- Nijssen, et al., "The potential value of three-dimensional accelerometry for detection of motor seizures in severe epilepsy", *Epilepsy Behav.*, vol. 7 (1), Aug. 2005, pp. 74-84.
- Noble, et al., "Diuretic induced change in lung water assessed by electrical impedance tomography", *Physiol. Meas.*, vol. 21 (1), 2000, pp. 155-163.
- Noble, et al., "Monitoring patients with left ventricular failure by electrical impedance tomography", *Eur J Heart Fail.*, vol. 1 (4), Dec. 1999, pp. 379-384.
- O'Connell, et al., "Economic impact of heart failure in the United States: time for a different approach", *J Heart Lung Transplant.*, vol. 13 (4), Jul.-Aug. 1994, p. S107-S112.
- Ohlsson, et al., "Central hemodynamic responses during serial exercise tests in heart failure patients using implantable hemodynamic monitors", *Eur J Heart Fail.*, vol. 5 (3), Jun. 2003, pp. 253-259.
- Ohlsson, et al., "Continuous ambulatory monitoring of absolute right ventricular pressure and mixed venous oxygen saturation in patients with heart failure using an implantable hemodynamic monitor", *European Heart Journal*, vol. 22 (11), 2001, pp. 942-954.
- Packer, et al., "Utility of impedance cardiography for the identification of short-term risk of clinical decompensation in stable patients with chronic heart failure", *J. Am. Coll Cardiol*, vol. 47 (11), 2006, pp. 2245-2252.
- Palatini, et al., "Predictive value of clinic and ambulatory heart rate for mortality in elderly subjects with systolic hypertension", *Arch Intern Med.*, vol. 162, 2002, pp. 2313-2321.
- Piirra, et al., "Crackles in patients with fibrosing alveolitis bronchiectasis, COPD, and Heart Failure", *Chest*, vol. 99 (5), May 1991, pp. 1076-1083.

(56)

References Cited

OTHER PUBLICATIONS

- Pocock, et al., "Predictors of mortality in patients with chronic heart failure", *Eur Heart J*, vol. 27, 2006, pp. 65-75.
- Poole-Wilson, et al., "Importance of control of fluid volumes in heart failure", *European Heart Journal*, vol. 22 (11), 2000, pp. 893-894.
- Raj, et al., Letter Regarding Article by Adamson et al. "Continuous Autonomic Assessment in Patients with Symptomatic Heart Failure: Prognostic Value of Heart Rate Variability Measured by an Implanted Cardiac Resynchronization Device", *Circulation*, vol. 112, 2005, pp. E37-E38.
- Ramirez, et al., "Prognostic value of hemodynamic findings from impedance cardiography in hypertensive stroke", *AJH*, vol. 18 (20), 2005, pp. 65-72.
- Rich, et al. "A multidisciplinary intervention to prevent the readmission of elderly patients with congestive heart failure", *New Engl. J. Med.*, vol. 333, 1995, pp. 1190-1195.
- Roglieri, et al., "Disease management interventions to improve outcomes in congestive heart failure", *Am J. Manag. Care.*, vol. 3 (12), Dec. 1997, pp. 1831-1839.
- Sahalos, et al., "The electrical impedance of the human thorax as a guide in evaluation of intrathoracic fluid volume", *Phys. Med. Biol.*, vol. 31, 1986, pp. 425-439.
- Saxon, et al., "Remote active monitoring in patients with heart failure (rapid-rf): design and rationale", *Journal of Cardiac Failure*, vol. 13 (4), 2007, pp. 241-246.
- Scharf, et al., "Direct digital capture of pulse oximetry waveforms", *Proceedings of the Twelfth Southern Biomedical Engineering Conference*, 1993, pp. 230-232.
- Shabetai, "Monitoring heart failure hemodynamics with an implanted device: its potential to improve outcome", *J Am Coll Cardiol*, vol. 41, 2003, pp. 572-573.
- Small, "Integrating monitoring into the infrastructure and workflow of routine practice: OptiVol", *Rev Cardiovasc Med.*, vol. 7 Suppl 1, 2006, pp. S47-S55.
- "Acute Decompensated Heart Failure", *Wikipedia Entry*, downloaded from http://en.wikipedia.org/wiki/Acute_decompensated_heart_failure, downloaded Feb. 11, 2011, 6 pages.
- "AD5934: 250kSPS 12-Bit Impedance Converter Network Analyzer, Analog Devices", retrieved from http://www.analog.com/static/imported-files/data_sheets/AD5934.pdf, date unknown, 40 pages.
- "FDA—Draft questions for Chronicle Advisory Panel Meeting", retrieved from http://www.fda.gov/ohrms/dockets/ac/07/questions/2007-4284q1_draft.pdf, 2007, 3 pages.
- "FDA—Medtronic Chronicle Implantable Hemodynamic Monitoring System P050032", Panel Package Section 11: Chronicle IHM Summary of Safety and Effectiveness, 2007, 77 pages.
- "FDA—References for Circulatory System Devices Panel", retrieved from http://www.fda.gov/OHRMS/DOCKETS/AC/07/briefing/2007-4284bib1_01.pdf, Mar. 1, 2007, 1 page.
- "FDA Executive Summary Memorandum, meeting of the Circulatory Systems Devices Advisory Panel", P050032 Medtronic, Inc. Chronicle Implantable Hemodynamic Monitor (IHM) System, retrieved from http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4284b1_02.pdf, Mar. 1, 2007, 23 pages.
- "FDA Executive Summary, Medtronic Chronicle Implantable Hemodynamic Monitoring System P050032: Executive Summary", Panel Package Sponsor Executive Summary, vol. 1, Sec. 4, retrieved from http://www.fda.gov/OHRMS/DOCKETS/AC/07/briefing/2007-4284b1_03.pdf, 2007, 12 pages.
- "FDA Panel Recommendation", *Chronicle Analysis*, Mar. 1, 2007, 14 pages.
- "Heart Failure", *Wikipedia Entry*, downloaded from http://en.wikipedia.org/wiki/Heart_failure, downloaded Feb. 11, 2011, 17 pages.
- "HFSA Comprehensive Heart Failure Practice Guideline—Executive Summary: HFSA Comprehensive Heart Failure Practice Guideline", *Journal of Cardiac Failure*, vol. 12 (1), 2006, pp. 10-e38.
- "HFSA Comprehensive Heart Failure Practice Guideline—Section 12: Evaluation and Management of Patients with Acute Decompensated Heart Failure", *Journal of Cardiac Failure*, vol. 12 (1), 2006, pp. E86-E103.
- "HFSA Comprehensive Heart Failure Practice Guideline—Section 2: Conceptualization and Working Definition of Heart Failure", *Journal of Cardiac Failure*, vol. 12 (1), 2006, pp. E10-E11.
- "HFSA Comprehensive Heart Failure Practice Guideline—Section 4: Evaluation of Patients for Ventricular Dysfunction and Heart Failure", *Journal of Cardiac Failure*, vol. 12 (1), 2006, pp. E16-E25.
- "HFSA Comprehensive Heart Failure Practice Guideline—Section 8: Disease Management in Heart Failure Education and Counseling", *Journal of Cardiac Failure*, vol. 12 (1), 2006, pp. E58-E68.
- "HFSA Comprehensive Heart Failure Practice Guideline—Section 3: Prevention of Ventricular Remodeling Cardiac Dysfunction, and Heart Failure Overview", *Journal of Cardiac Failure*, vol. 12 (1), 2006, pp. E12-E15.
- "LifeShirt Model 200 Directions for Use, Introduction", *VivoMetrics, Inc.*, date unknown, 9 pages.
- 3M Corporation, "3M Surgical Tapes—Choose the Correct Tape", *quicksheet*, 2004.
- Abraham, "New approaches to monitoring heart failure before symptoms appear", *Rev. Cardiovasc. Med.*, vol. 7 Suppl 1, 2006, pp. 33-41.
- Adams, Jr., "Guiding heart failure care by invasive hemodynamic measurements: possible or useful?", *Journal of Cardiac Failure*, vol. 8 (2), 2002, pp. 71-73.
- Adamson, et al., "Continuous autonomic assessment in patients with symptomatic heart failure: prognostic value of heart rate variability measured by an implanted cardiac resynchronization device", *Circulation*, vol. 110, 2004, pp. 2389-2394.
- Adamson, "Integrating device monitoring into the infrastructure and workflow of routine practice", *Rev. Cardiovasc. Med.*, vol. 7 Suppl 1, 2006, pp. 42-60.
- Adamson, et al., "Ongoing right ventricular hemodynamics in heart failure", *J. Am. Coll. Cardiol*, vol. 41, 2003, pp. 565-570.
- Adhere, "Insights from the Adhere Registry: Data from over 1000,000 patient cases", *Presentation*, date unknown, 70 pages.
- ADVAMED, "Health Information Technology: Improving Patient Safety and Quality of Care", *Jun. 2005*, 23 pages.
- Aghababian, "Acutely decompensated heart failure: opportunities to improve care and outcomes in the emergency department", *Rev. Cardiovasc. Med.*, vol. 3 Suppl 4, 2002, pp. S3-9.
- Albert, "Bioimpedance to prevent heart failure hospitalization", *Curr Heart Fail Rep.*, vol. 3 (3), Sep. 2006, pp. 136-142.
- American Heart Association, "Heart Disease and Stroke Statistics—2006 Update", 2006, 43 pages.
- American Heart Association, "Heart Disease and Stroke Statistics—2007 Update", A Report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee; *Circulation*, 115, 2007, pp. e69-e171.
- Amurthur, et al., "U.S. Appl. No. 60/972,359", filed Sep. 14, 2007.
- Amurthur, et al., "U.S. Appl. No. 60/972,363", filed Sep. 14, 2007.
- Belalcazar, et al., "Monitoring lung edema using the pacemaker pulse and skin electrodes", *Physiol. Meas.*, vol. 26, 2005, pp. S153-S163.
- Bennett, "Development of implantable devices for continuous ambulatory monitoring of central hemodynamic values in heart failure patients", *PACE*, vol. 28, Jun. 2005, pp. 573-584.
- Bly, et al., "U.S. Appl. No. 60/972,333", filed Sep. 14, 2007.
- Bly, et al., "U.S. Appl. No. 60/972,629", filed Sep. 14, 2007.
- Bly, et al., "U.S. Appl. No. 61/055,645", filed May 23, 2008.
- Bly, "U.S. Appl. No. 61/084,567", filed Jul. 29, 2008.
- Bourge, "Case studies in advanced monitoring with the chronicle device", *Rev Cardiovasc Med.*, vol. 7 Suppl 1, 2006, pp. S56-S61.
- Braunschweig, "Continuous hemodynamic monitoring during withdrawal of diuretics in patients with congestive heart failure", *European Heart Journal*, vol. 23 (1), 2002, pp. 59-69.
- Braunschweig, "Dynamic changes in right ventricular pressures during hemodialysis recorded with an implantable hemodynamic monitor", *Nephrol Dial Transplant*, vol. 21, 2006, pp. 176-183.
- Brennan, "Measuring a Grounded Impedance Profile Using the AD5933", *Analog Devices*, retrieved from <http://www.analog.com/>

(56)

References Cited

OTHER PUBLICATIONS

- static/imported-files/application_notes/427095282381510189AN847_0.pdf, date unknown, 12 pages.
- Buono, et al., "The effect of ambient air temperature on whole-body bioelectrical impedance", *Physiol. Meas.*, vol. 25, 2004, pp. 119-123.
- Burkhoff, et al. "Heart failure with a normal ejection fraction: Is it really a disorder of diastolic function?", *Circulation*, vol. 107, 2003, pp. 656-658.
- Burr, et al., "Heart rate variability and 24-hour minimum heart rate", *Biological Research for Nursing*, vol. 7 (4), 2006, pp. 256-267.
- CardioNet, "CardioNet Mobile Cardiac Outpatient Telemetry: Addendum to Patient Education Guide", CardioNet, Inc., 2007, 2 pages.
- CardioNet, "Patient Education Guide", CardioNet, Inc., 2007, 7 pages.
- Charach, et al., "Transthoracic monitoring of the impedance of the right lung in patients with cardiogenic pulmonary edema", *Crit Care Med*, vol. 29 (6), 2001, pp. 1137-1144.
- Charlson, et al., "Can disease management target patients most likely to generate high costs? The Impact of Comorbidity", *Journal of General Internal Medicine*, vol. 22 (4), 2007, pp. 464-469.
- Chaudhry, et al., "Telemonitoring for patients with chronic heart failure: a systematic review", *J Card Fail.*, vol. 13 (1), Feb. 2007, pp. 56-62.
- Chung, et al., "White coat hypertension: Not so benign after all?", *Journal of Human Hypertension*, vol. 17, 2003, pp. 307-809.
- Cleland, et al., "The EuroHeart Failure survey programme—a survey on the quality of care among patients with heart failure in Europe—Part I: patient characteristics and diagnosis", *European Heart Journal*, vol. 24 (5), 2003, pp. 442-463.
- Smith, et al., "Outcomes in heart failure patients with preserved ejection fraction: mortality, readmission, and functional decline", *J Am Coll Cardiol*, vol. 41, 2003, pp. 1510-1518.
- Starling, "Improving care of chronic heart failure: advances from drugs to devices", *Cleveland Clinic Journal of Medicine*, vol. 70 (2), Feb. 2003, pp. 141-146.
- Steijaert, et al., "The use of multi-frequency impedance to determine total body water and extracellular water in obese and lean female individuals", *International Journal of Obesity*, vol. 21 (10), Oct. 1997, pp. 930-934.
- Stewart, et al., "Effects of a home-based intervention among patients with congestive heart failure discharged from acute hospital care", *Arch Intern Med.*, vol. 158, 1998, pp. 1067-1072.
- Stewart, et al., "Effects of a multidisciplinary, home-based intervention on planned readmissions and survival among patients with chronic congestive heart failure: a randomized controlled study", *The Lancet*, vol. 354 (9184), Sep. 1999, pp. 1077-1083.
- Stewart, et al., "Home-based intervention in congestive heart failure: long-term implications on readmission and survival", *Circulation*, vol. 105, 2002, pp. 2861-2866.
- Stewart, et al., "Prolonged beneficial effects of a home-based intervention on unplanned readmissions and mortality among patients with congestive heart failure", *Arch Intern Med.*, vol. 159, 1999, pp. 257-261.
- Stewart, et al., "Trends in Hospitalization for Heart Failure in Scotland. An Epidemic that has Reached Its Peak?", *European Heart Journal*, vol. 22 (3), 2001, pp. 209-217.
- Swedberg, et al., "Guidelines for the diagnosis and treatment of chronic heart failure: executive summary: The task force for the diagnosis and treatment of chronic heart failure of the European Society of Cardiology", *Eur Heart J.*, vol. 26 (11), Jun. 2005, pp. 1115-1140.
- Tang, "Case studies in advanced monitoring: OptiVol", *Rev Cardiovasc Med.*, vol. 7 Suppl 1, 2006, pp. S62-S66.
- The Economist, "Something in the way he moves", retrieved from <http://www.economist.com/science/printerFriendly.cfm?storyid=9861412>, 2007.
- The Escape Investigators, "Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness", *JAMA*, vol. 294, 2005, pp. 1625-1633.
- Tosi, et al., "Seismic signal detection by fractal dimension analysis", *Bulletin of the Seismological Society of America*, vol. 89 (4), Aug. 1999, pp. 970-977.
- Van De Water, et al., "Monitoring the chest with impedance", *Chest*, vol. 64, 1973, pp. 597-603.
- Van Someren, "Actigraphic monitoring of movement and rest-activity rhythms in aging, Alzheimer's disease, and Parkinson's disease", *IEEE Transactions on Rehabilitation Engineering*, vol. 5 (4), Dec. 1997, pp. 394-398.
- Vasan, et al., "Congestive heart failure in subjects with normal versus reduced left ventricular ejection fraction", *J Am Coll Cardiol*, vol. 33, 1999, pp. 1948-1955.
- Verdecchia, et al., "Adverse prognostic value of a blunted circadian rhythm of heart rate in essential hypertension", *Journal of Hypertension*, vol. 16 (9), 1998, pp. 1335-1343.
- Verdecchia, et al., "Ambulatory pulse pressure: a potent predictor of total cardiovascular risk in hypertension", *Hypertension*, vol. 32, 1998, pp. 983-988.
- Vollmann, et al., "Clinical utility of intrathoracic impedance monitoring to alert patients with an implanted device of deteriorating chronic heart failure", *European Heart Journal Advance Access*, downloaded from <http://eurheartj.oxfordjournals.org/cgi/content/full/ehl506v1>, Feb. 19, 2007, 6 pages.
- Vukanovic, et al., "Effect of posture on heart rate variability spectral measures in children and young adults with heart disease", *International Journal of Cardiology*, vol. 101 (2), 2005, pp. 273-278.
- Wang, et al., "Feasibility of using an implantable system to measure thoracic congestion in an ambulatory chronic heart failure canine model", *PACE*, vol. 28 (5), 2005, pp. 404-411.
- Wickemeyer, et al., "Association between atrial and ventricular tachyarrhythmias, intrathoracic impedance and heart failure decompensation in CRT-D Patients", *Journal of Cardiac Failure*, vol. 13 (6), 2007, pp. S131-S132.
- Williams, et al., "How do different indicators of cardiac pump function impact upon the long-term prognosis of patients with chronic heart failure", *American Heart Journal*, vol. 150 (5), date unknown, pp. E1-E983.
- Wonisch, et al., "Continuous hemodynamic monitoring during exercise in patients with pulmonary hypertension", *Int J Cardiol.*, vol. 101 (3), Jun. 8, 2005, pp. 415-420.
- Wynne, et al., "Impedance cardiography: a potential monitor for hemodialysis", *Journal of Surgical Research*, vol. 133 (1), 2006, pp. 55-60.
- Yancy, "Current approaches to monitoring and management of heart failure", *Rev Cardiovasc Med.*, vol. 7 Suppl 1, 2006, pp. S25-S32.
- Ypenburg, et al., "Intrathoracic Impedance Monitoring of Predict Decompensated Heart Failure", *Am J Cardiol*, vol. 99 (4), 2007, pp. 554-557.
- Yu, et al., "Intrathoracic Impedance Monitoring in Patients with Heart Failure: Correlation with Fluid Status and Feasibility of Early Warning Preceding Hospitalization", *Circulation*, vol. 112, 2005, pp. 841-848.
- Zannad, et al., "Incidence, clinical and etiologic features, and outcomes of advanced chronic heart failure: The EPICAL Study", *J Am Coll Cardiol*, vol. 33 (3), 1999, pp. 734-742.
- Zile, "Heart failure with preserved ejection fraction: is this diastolic heart failure?", *J Am Coll Cardiol.*, vol. 41 (9), 2003, pp. 1519-1522.

* cited by examiner

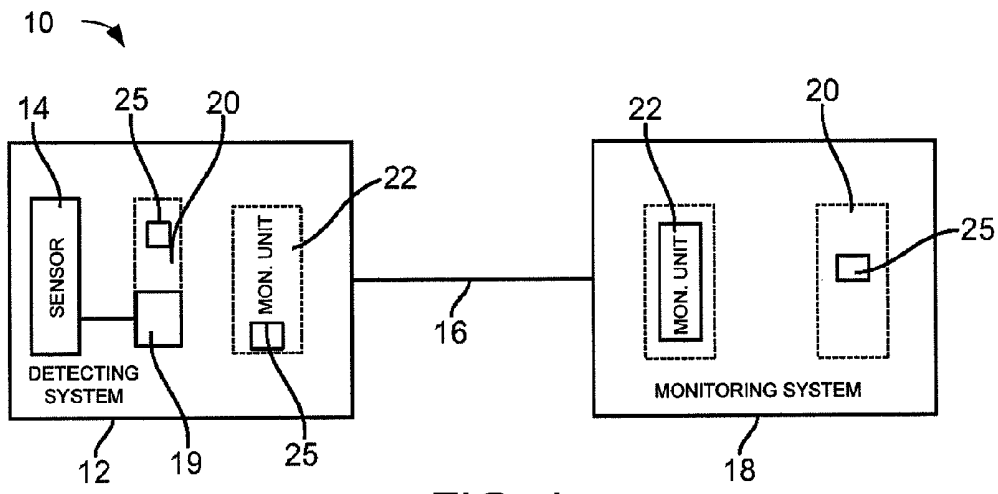


FIG. 1

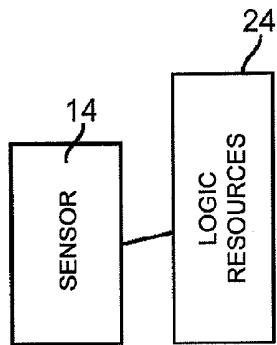


FIG. 4

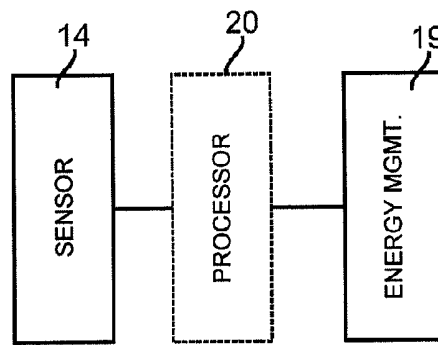


FIG. 3

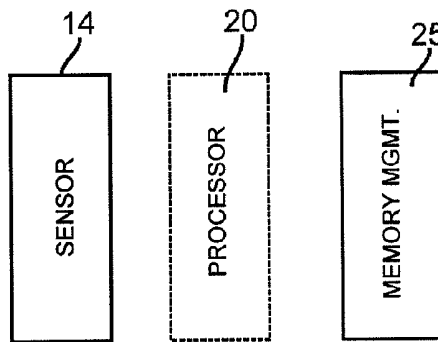


FIG. 5

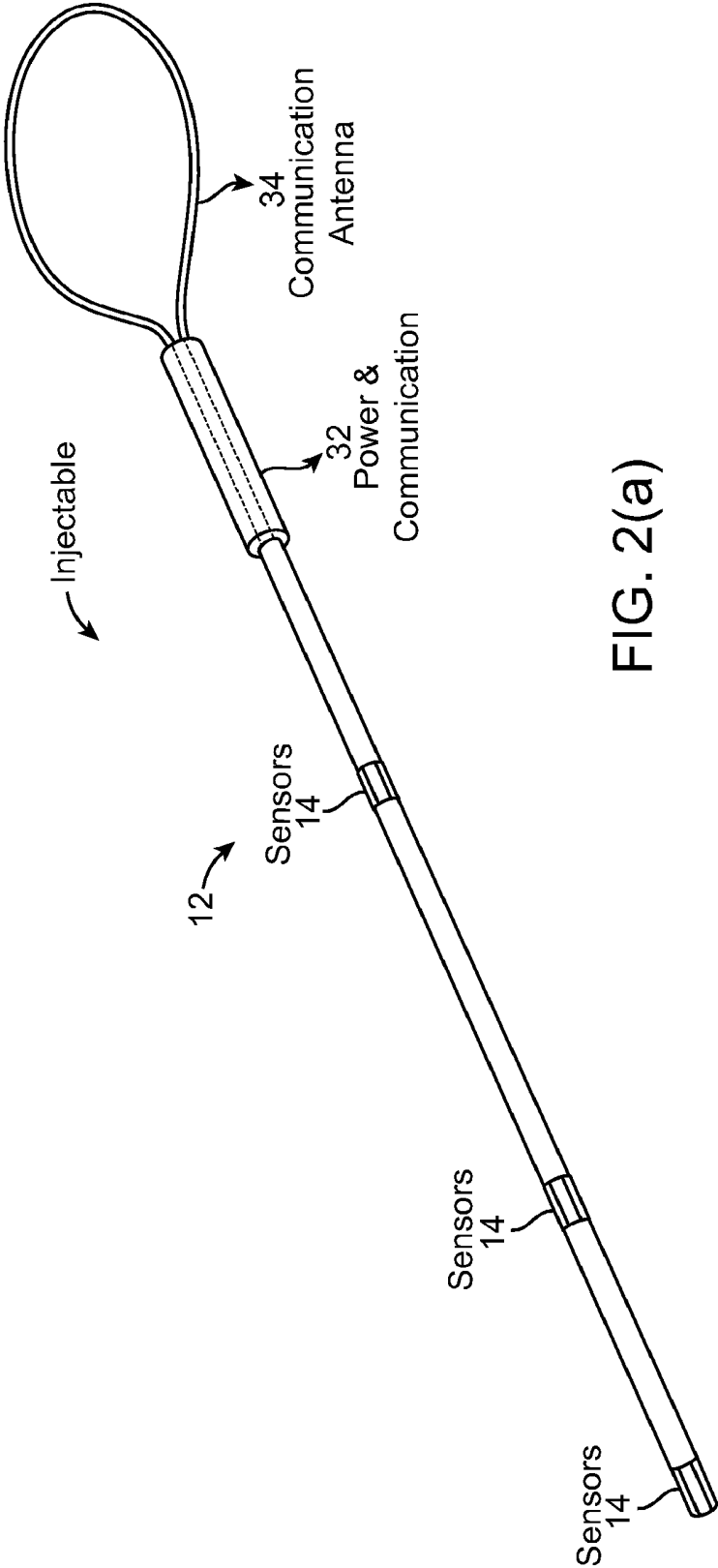


FIG. 2(a)

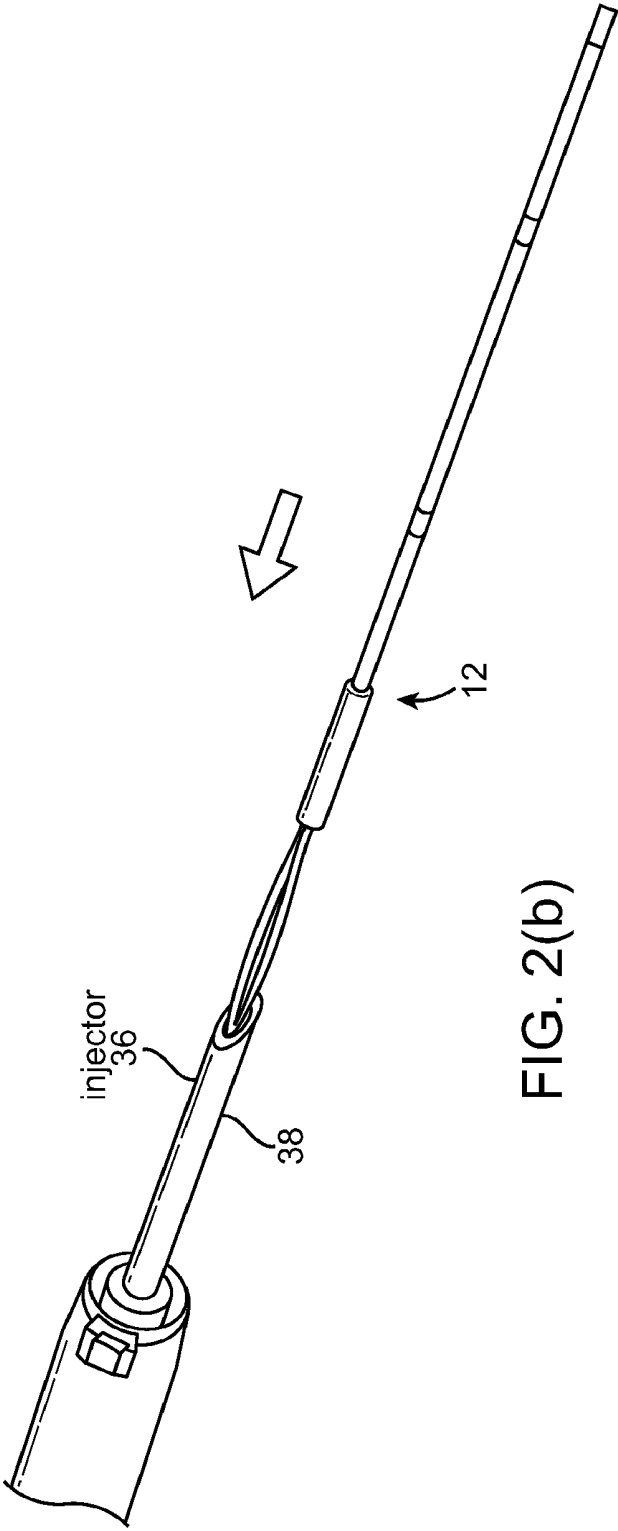


FIG. 2(b)

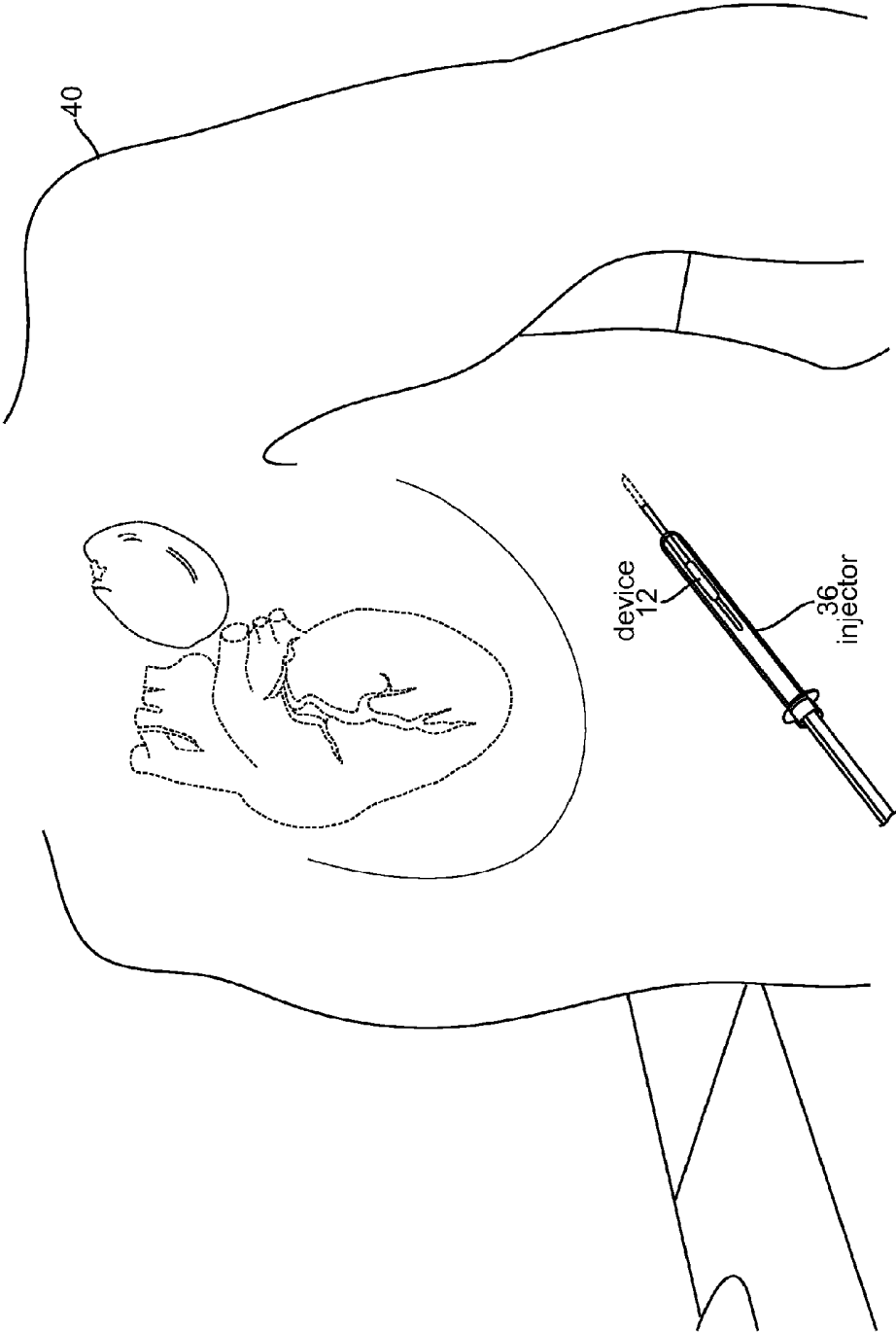


FIG. 2(c)

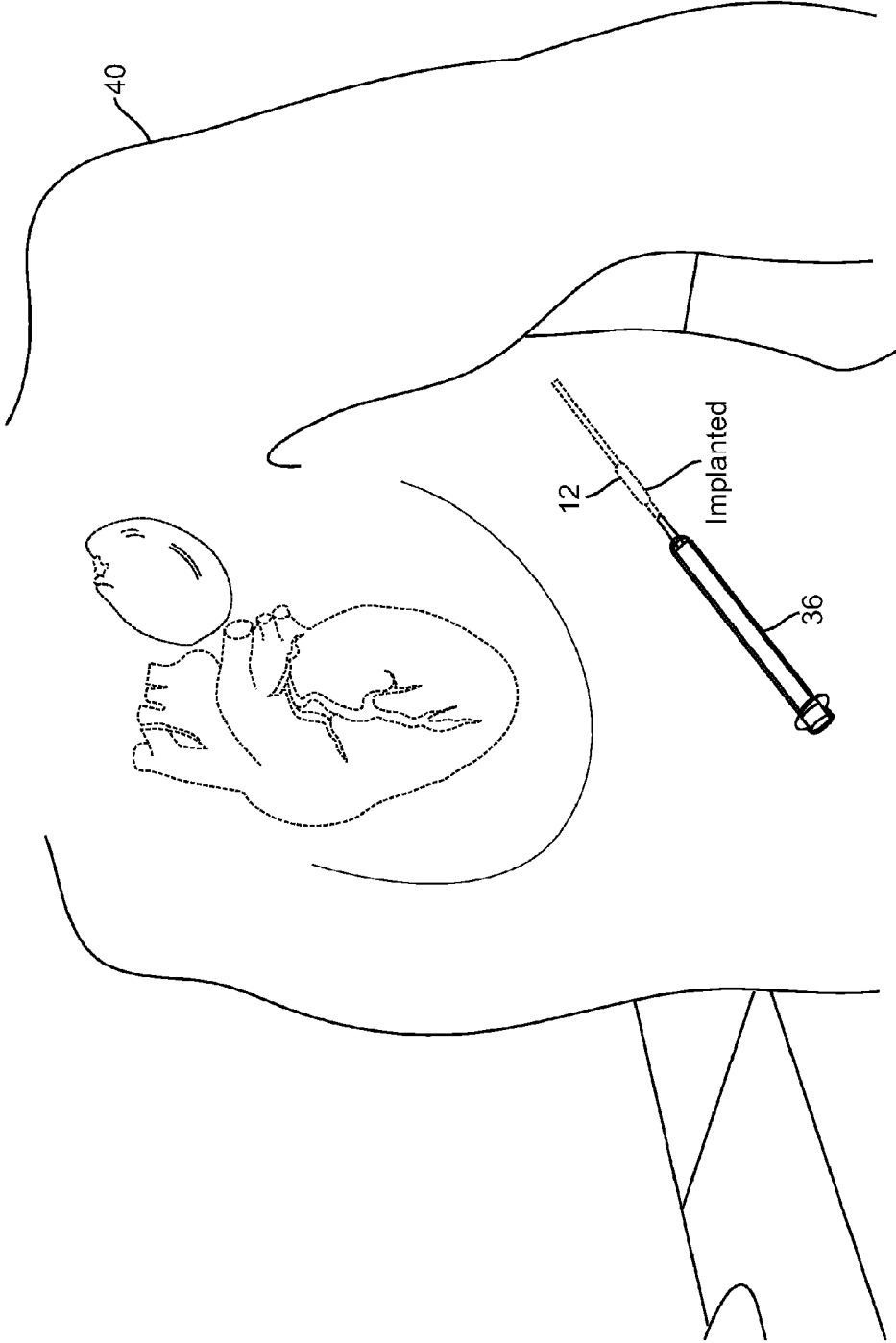


FIG. 2(d)

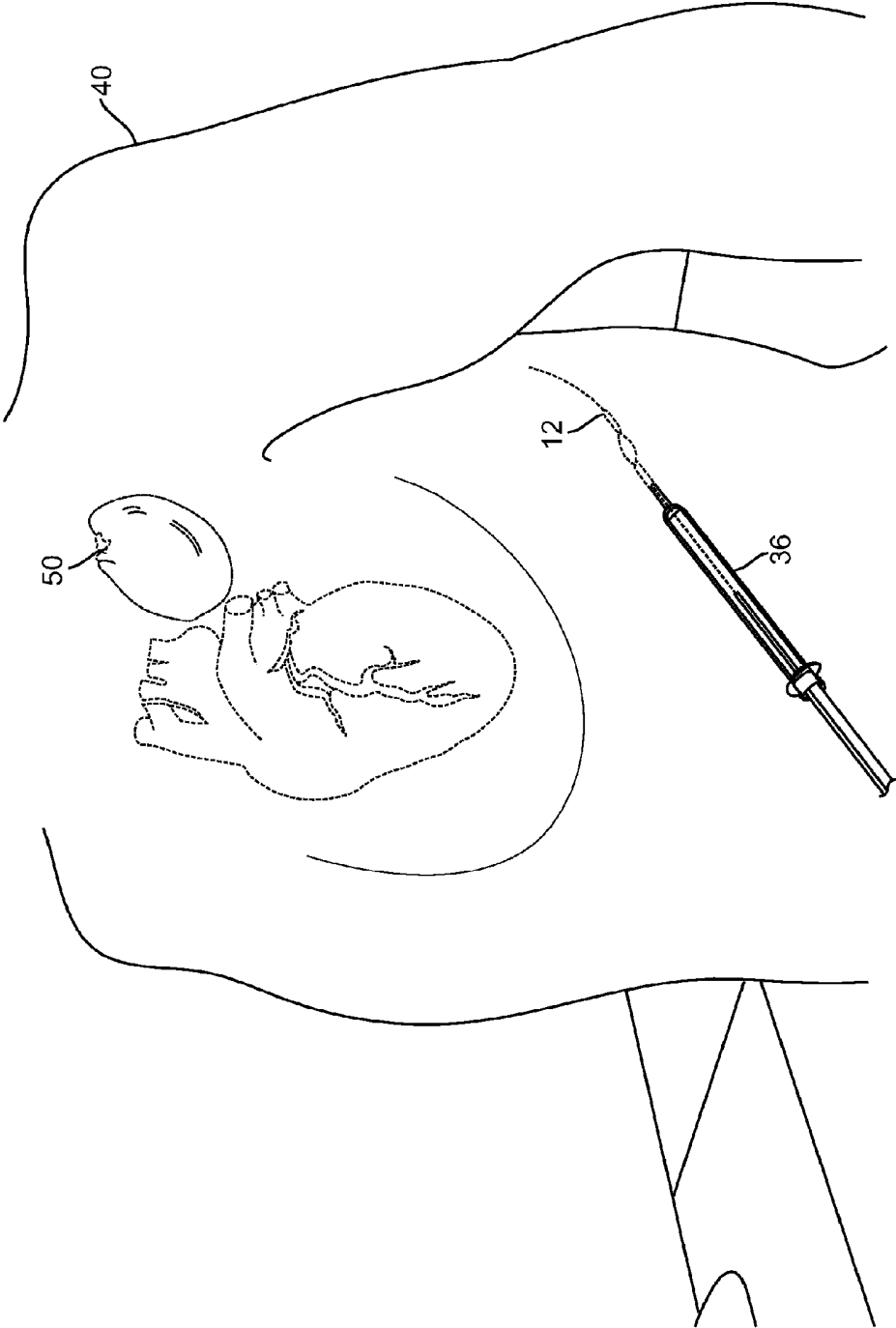


FIG. 2(e)

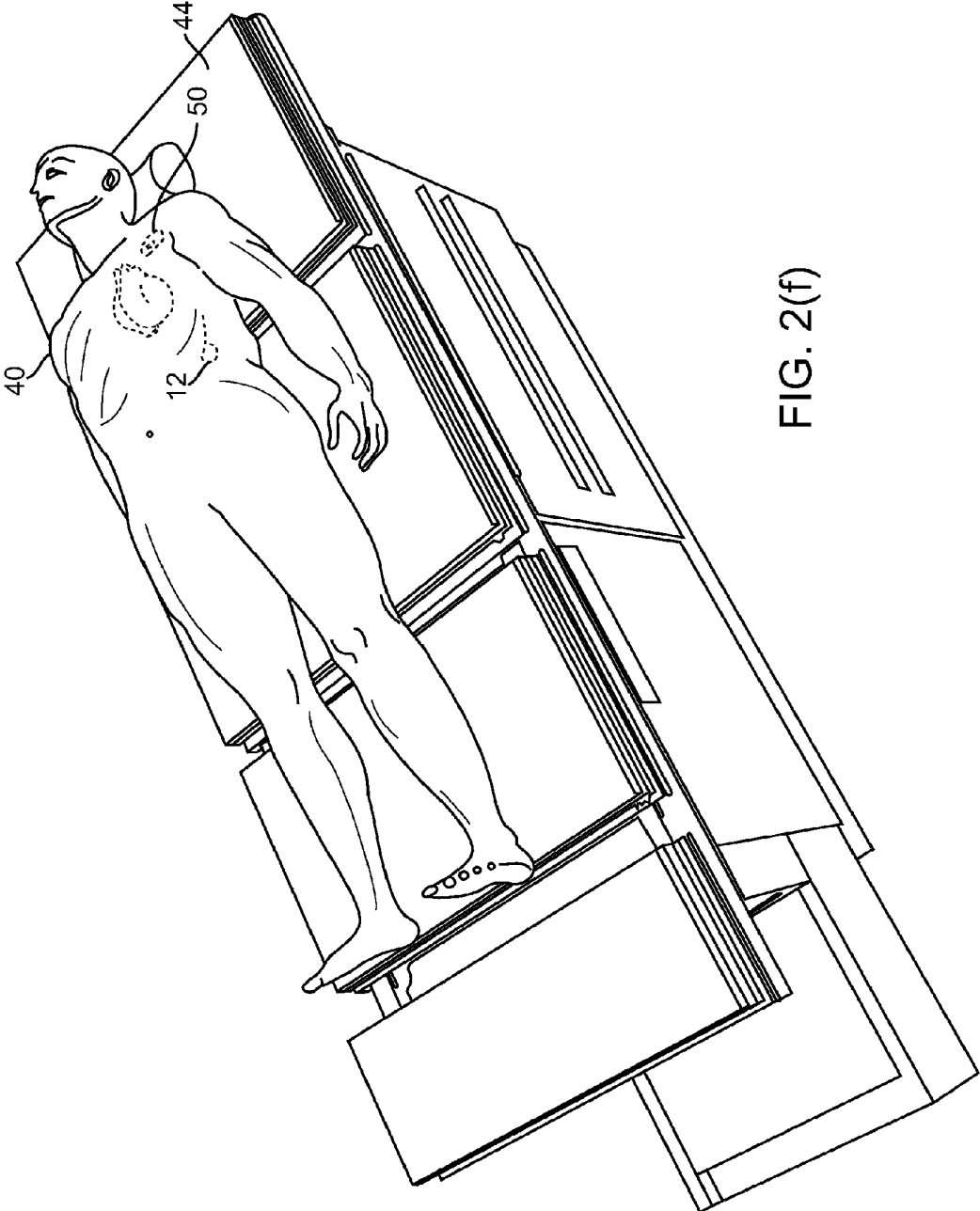


FIG. 2(f)

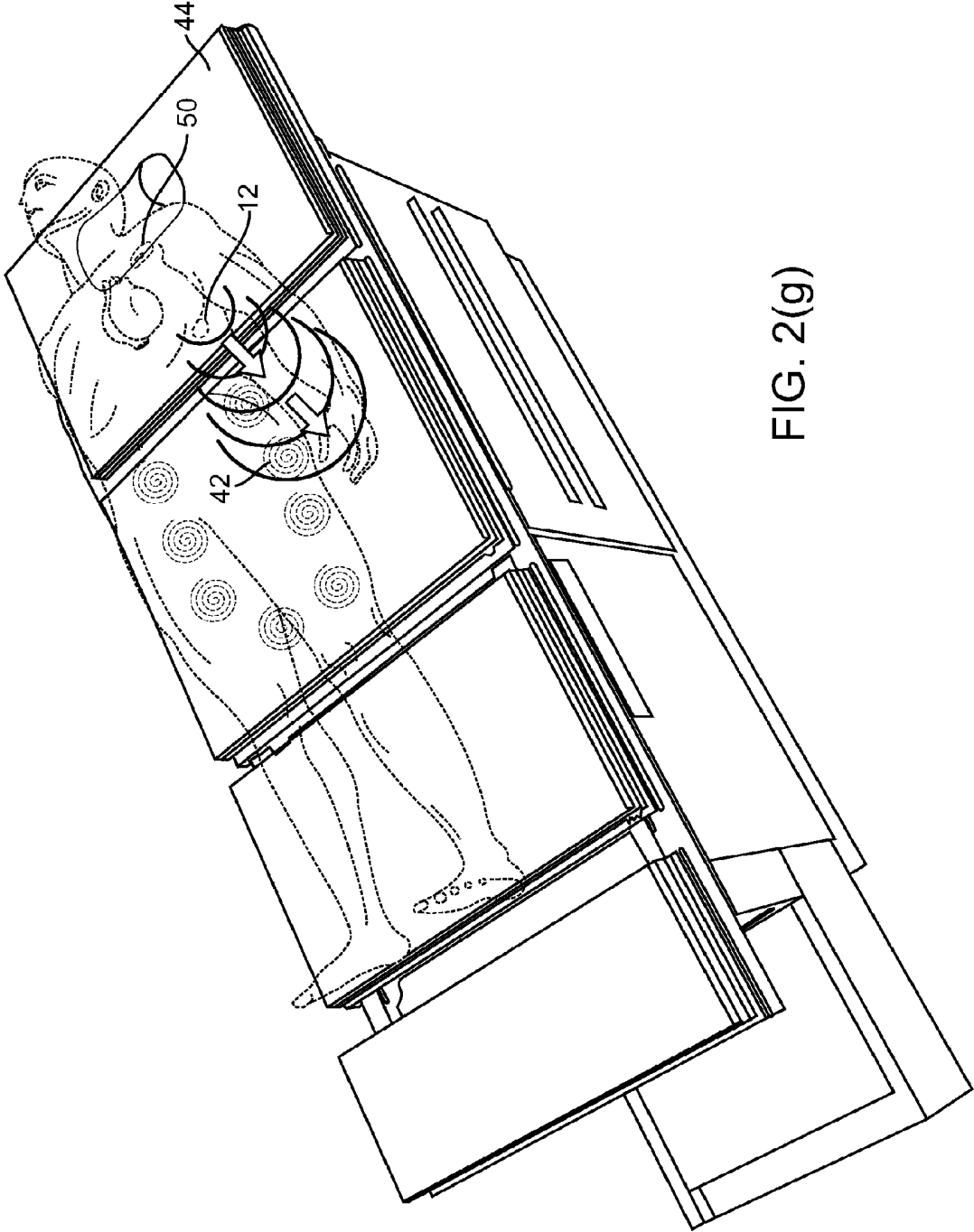


FIG. 2(g)

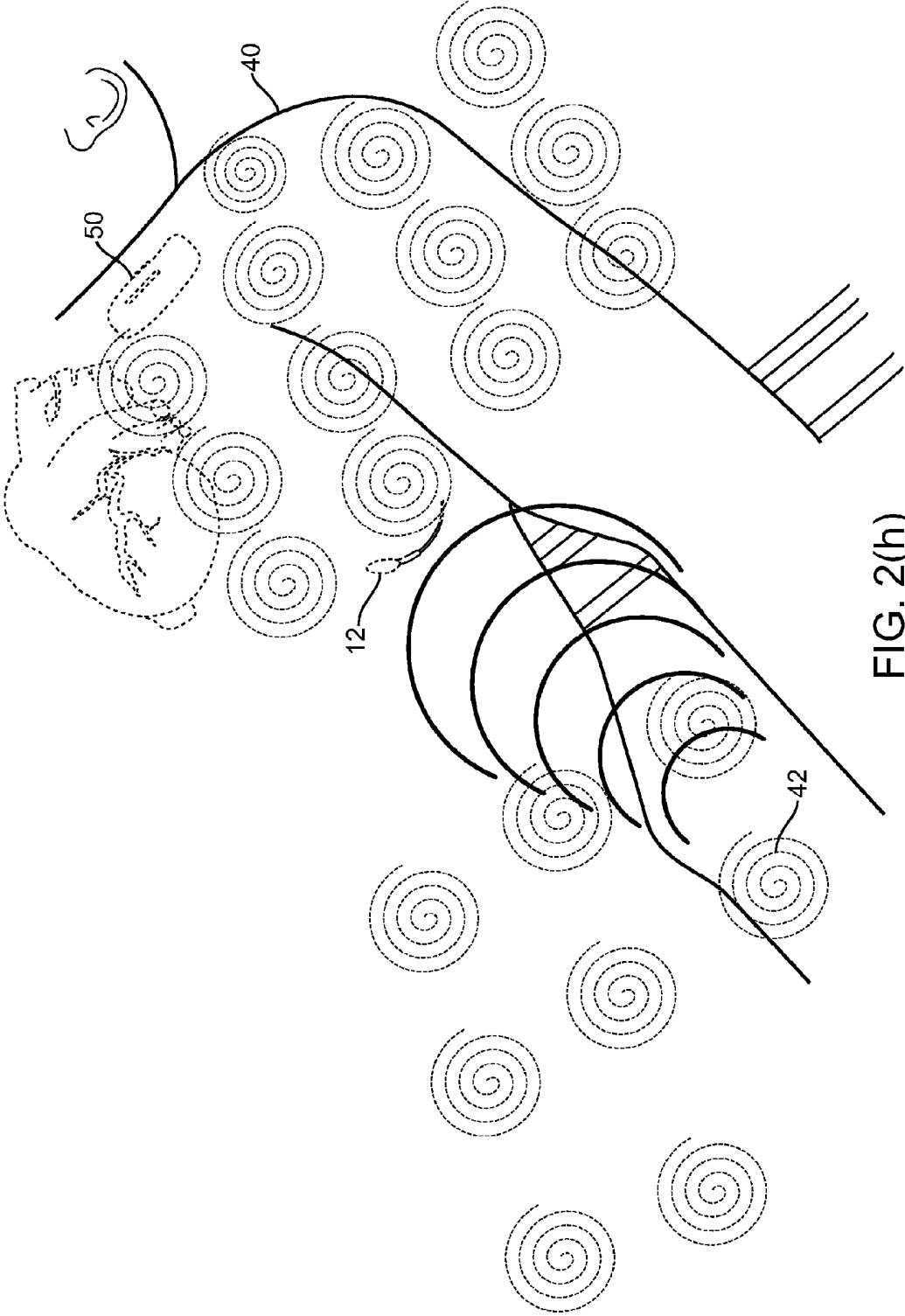


FIG. 2(h)

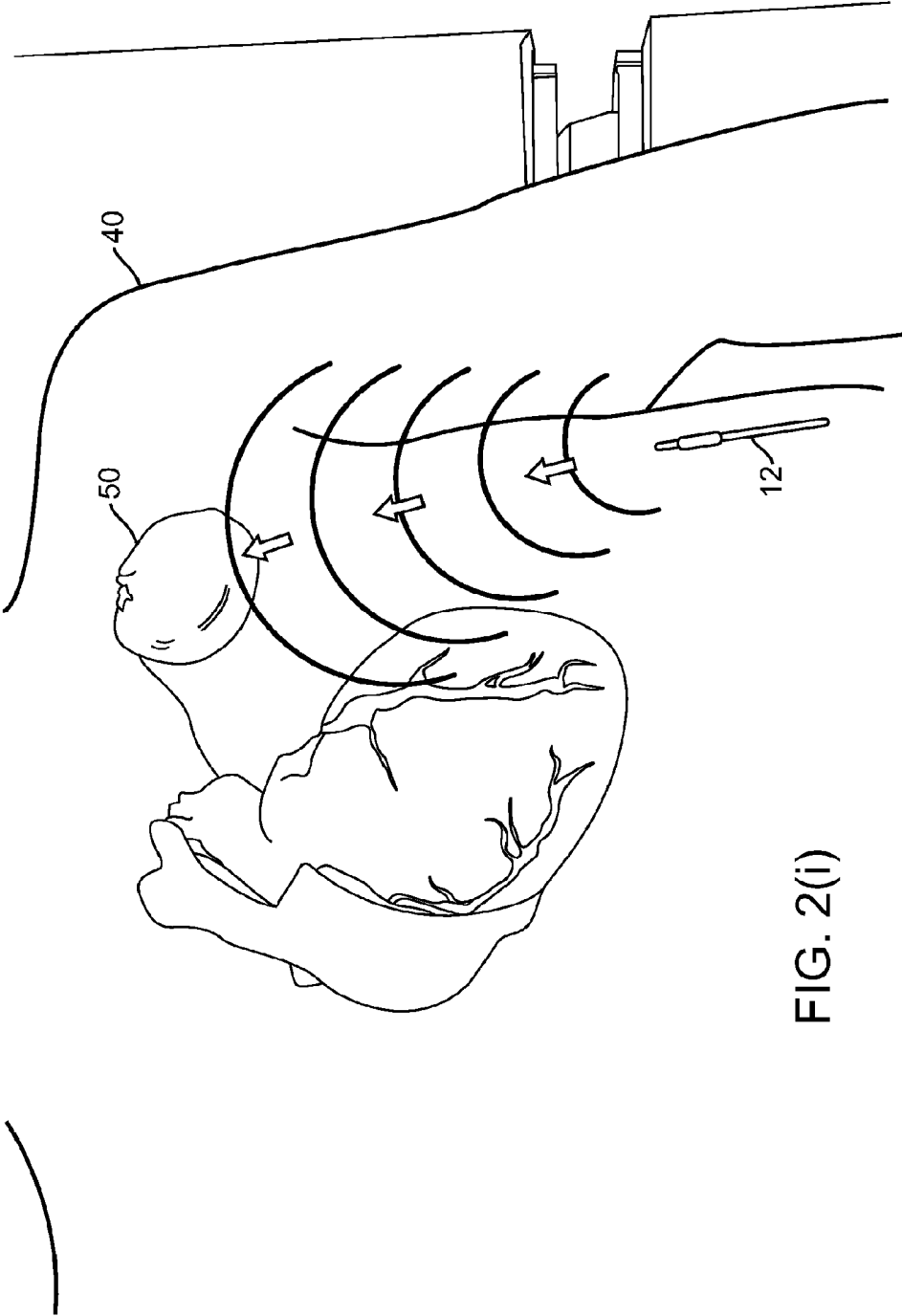


FIG. 2(i)

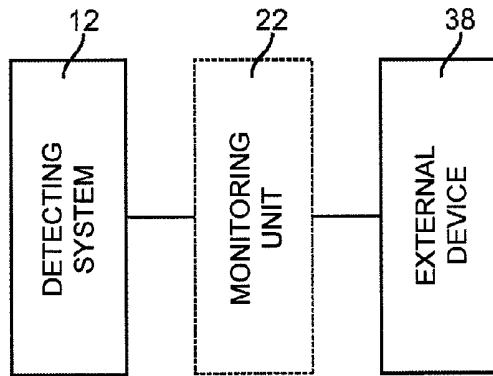


FIG. 6

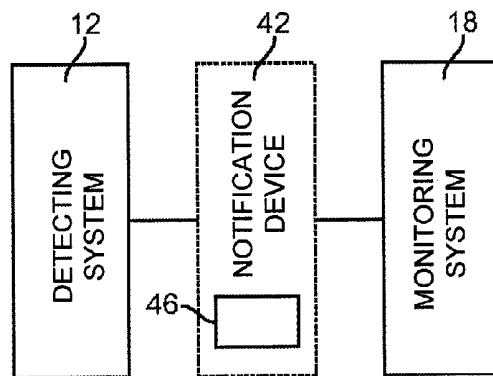


FIG. 7

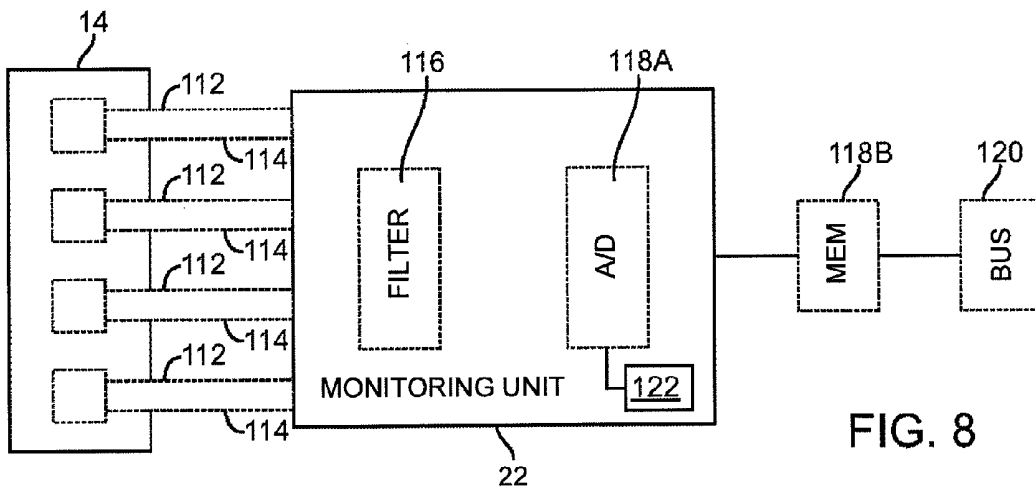


FIG. 8

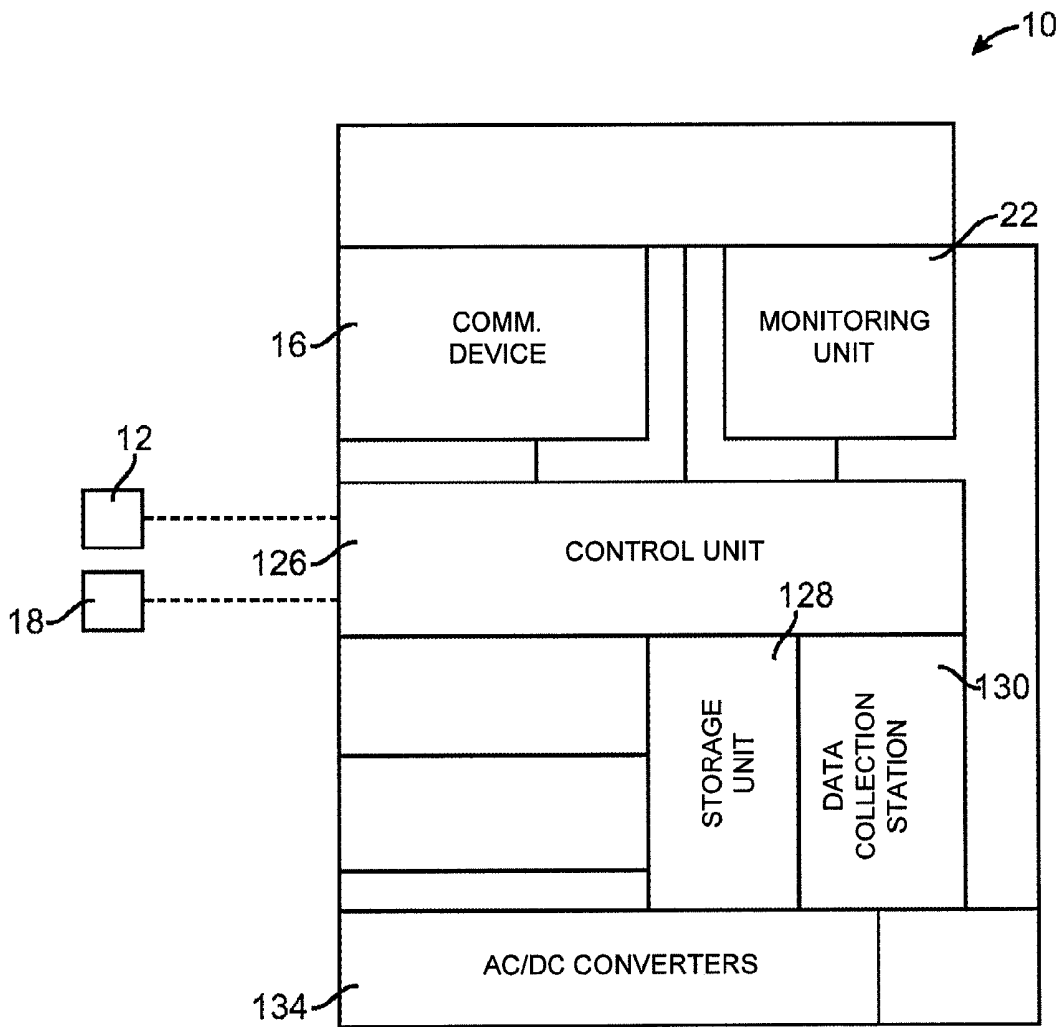


FIG. 9

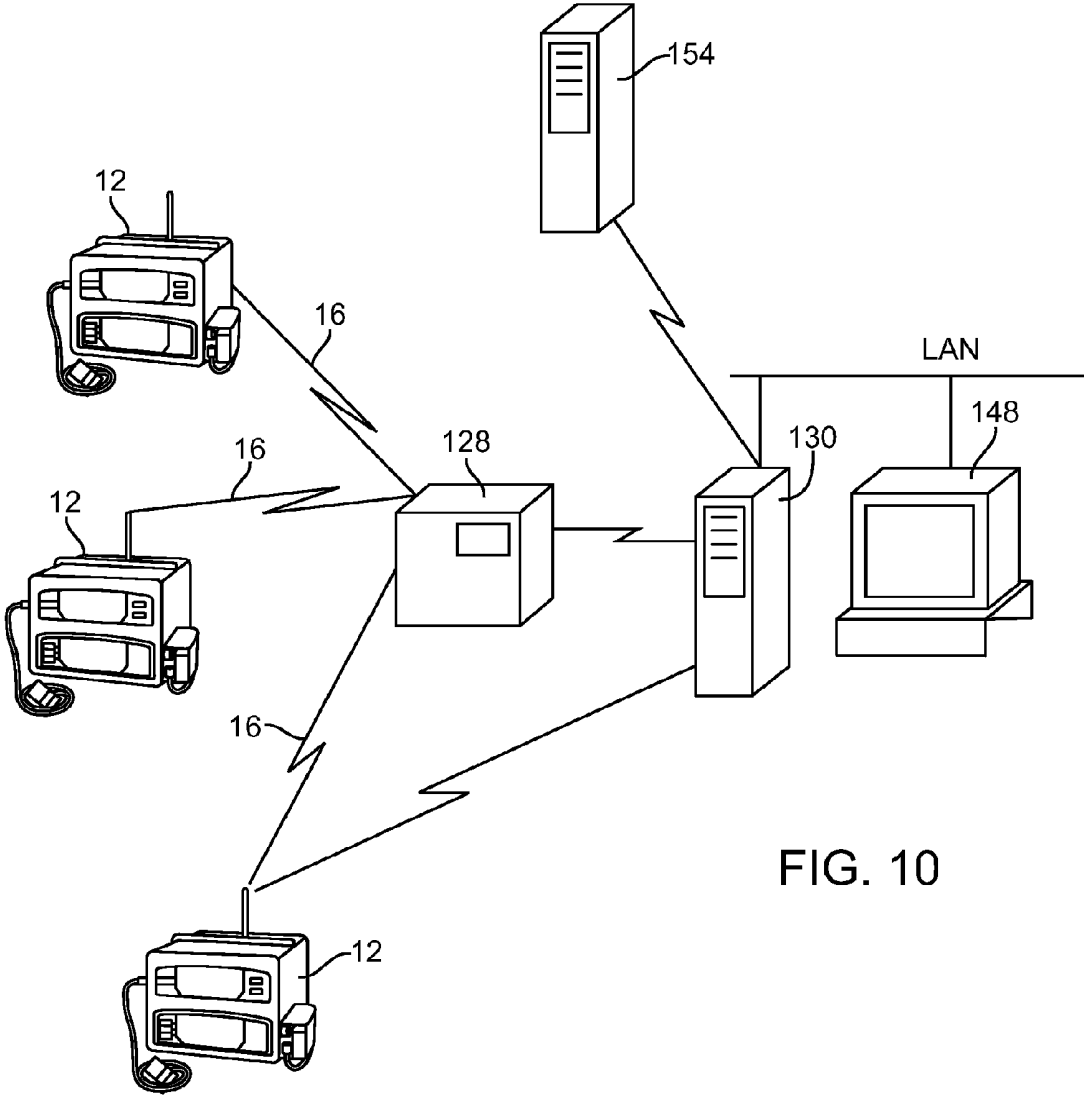


FIG. 10

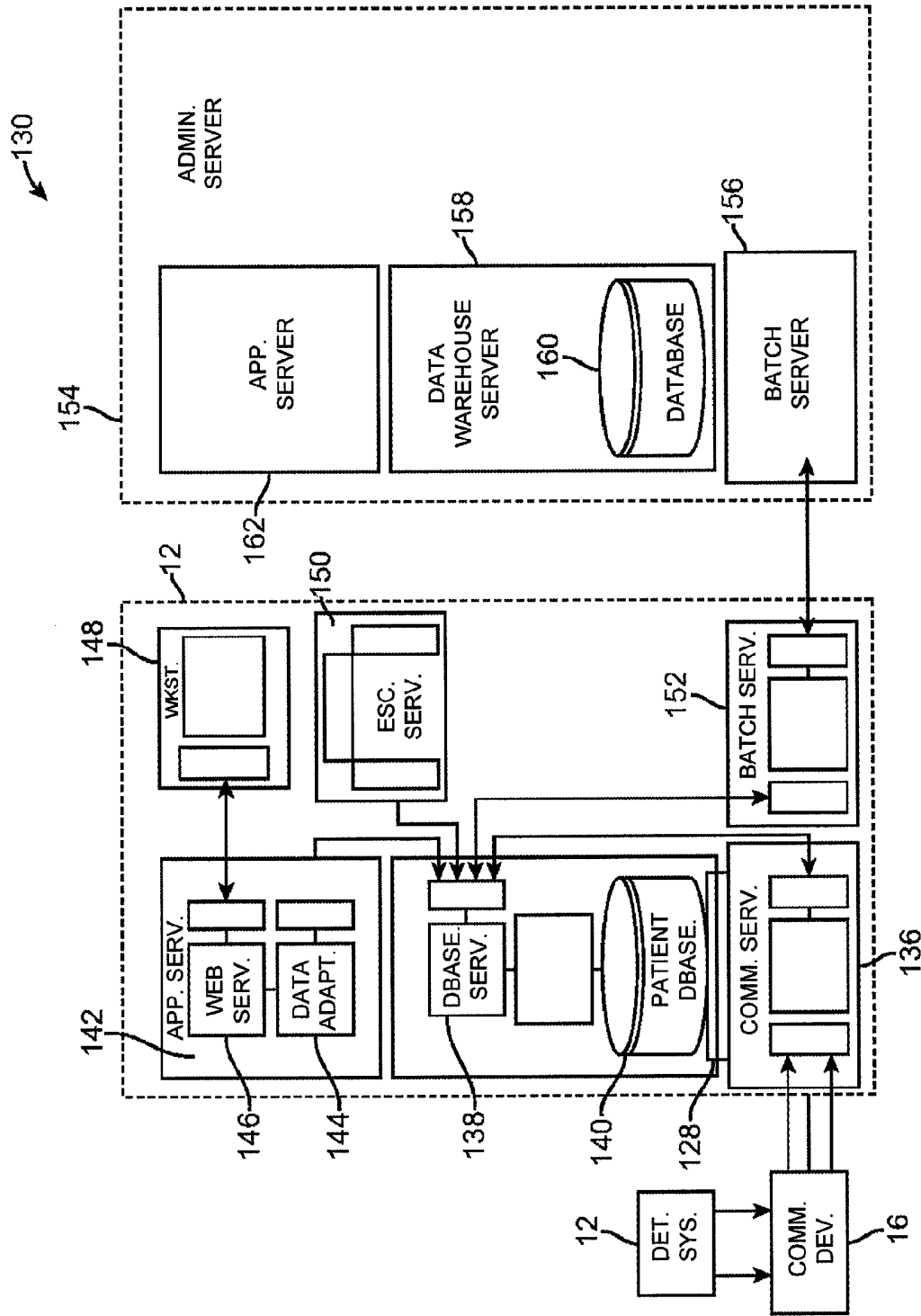


FIG. 11

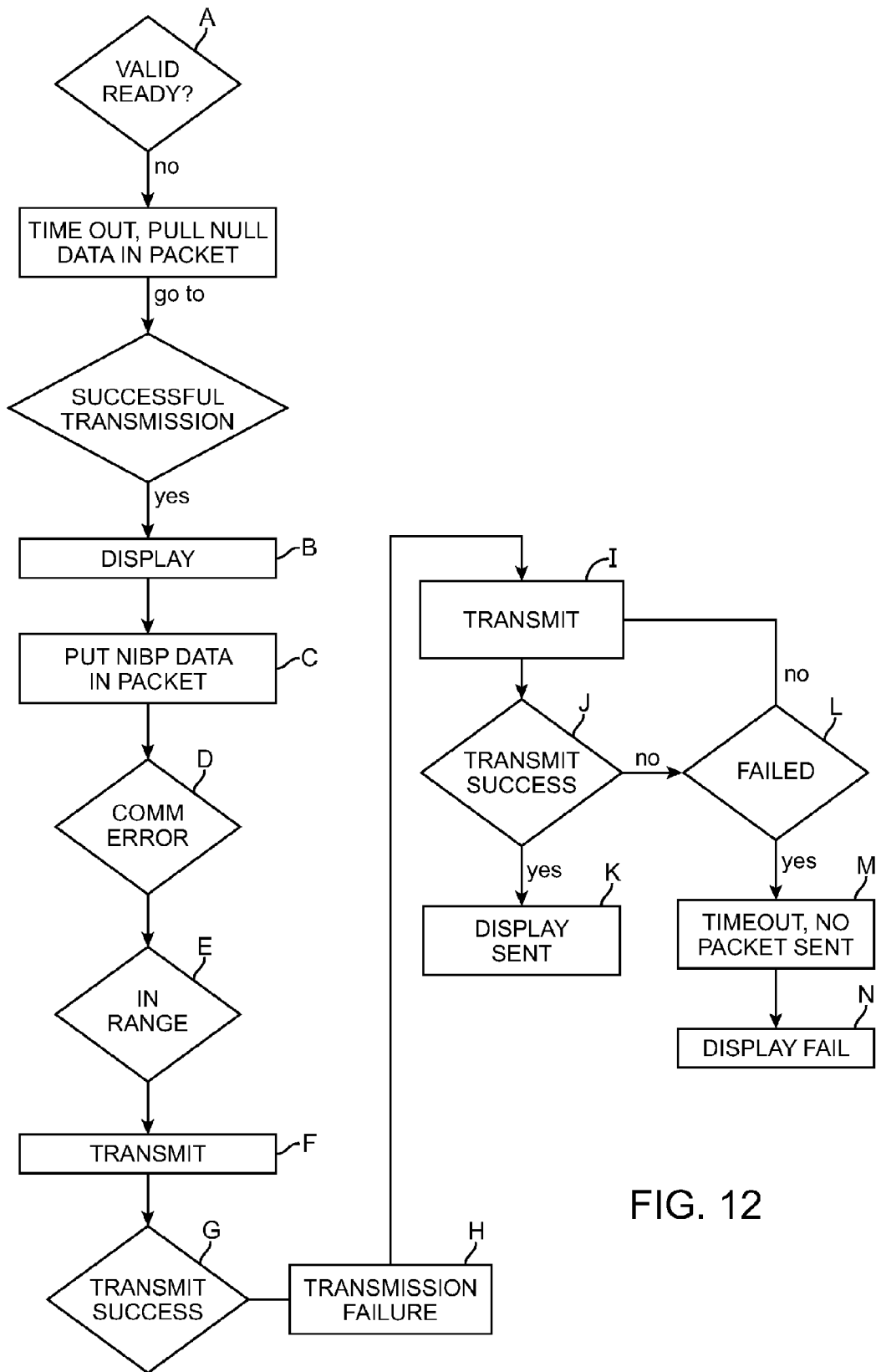


FIG. 12

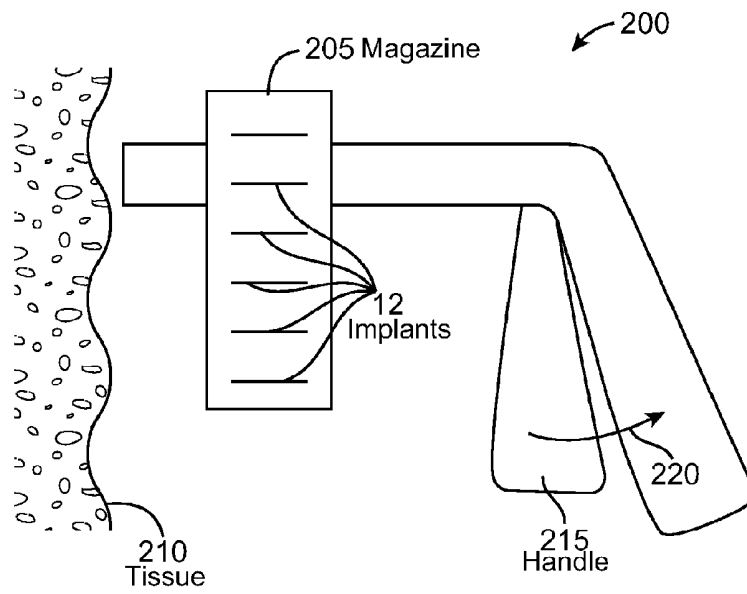


FIG. 13

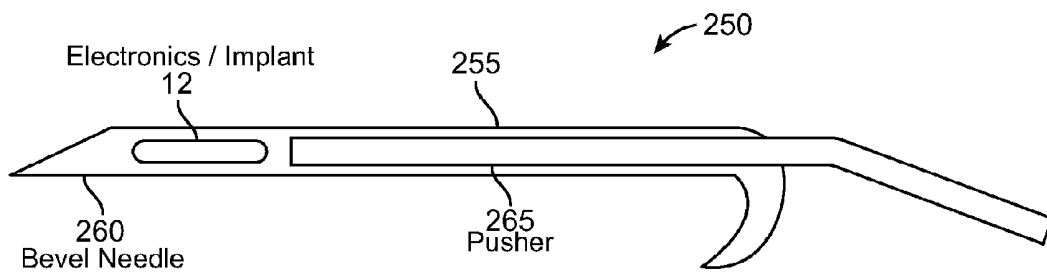


FIG. 14

INJECTABLE PHYSIOLOGICAL MONITORING SYSTEM

CROSS-REFERENCES TO RELATED APPLICATIONS

This application is a Continuing application of U.S. application Ser. No. 12/209,479, filed on 12 Sep. 2008, which claims the benefit under 35 USC 119(e) of U.S. Provisional Application Nos. 60/972,329, 60/972,336, 60/972,354 and 60/972,537, all filed Sep. 14, 2007, and 61/055,666 filed May 23, 2008; the full disclosures of which are incorporated herein by reference in their entirety. A claim of priority to all, to the extent appropriate, is made.

BACKGROUND OF THE INVENTION

Field of the Invention

This invention relates generally to systems and methods for remote patient monitoring, and more particularly to an injectable physiological monitoring system for decompensation prediction of a heart failure patient.

Frequent monitoring of patients permits the patients' physician to detect worsening symptoms as they begin to occur, rather than waiting until a critical condition has been reached. As such, home monitoring of patients with chronic conditions is becoming increasingly popular in the health care industry for the array of benefits it has the potential to provide. Potential benefits of home monitoring are numerous and include: better tracking and management of chronic disease conditions, earlier detection of changes in the patient condition, and reduction of overall health care expenses associated with long term disease management. The home monitoring of a number of diverse "chronic diseases" is of interest, where such diseases include diabetes, dietary disorders such as anorexia and obesity, anxiety, depression, epilepsy respiratory diseases, AIDS and other chronic viral conditions, conditions associated with the long term use of immunosuppressant's, e.g. in transplant patients, asthma, chronic hypertension, chronic use of anticoagulants, and the like.

Of particular interest in the home monitoring sector of the health care industry is the remote monitoring of patients with heart failure (HF), also known as congestive heart failure. HF is a syndrome in which the heart is unable to efficiently pump blood to the vital organs. Most instances of HF occur because of a decreased myocardial capacity to contract (systolic dysfunction). However, HF can also result when an increased pressure-stroke-volume load is imposed on the heart, such as when the heart is unable to expand sufficiently during diastole to accommodate the ventricular volume, causing an increased pressure load (diastolic dysfunction).

In either case, HF is characterized by diminished cardiac output and/or damming back of blood in the venous system. In HF, there is a shift in the cardiac function curve and an increase in blood volume caused in part by fluid retention by the kidneys. Indeed, many of the significant morphologic changes encountered in HF are distant from the heart and are produced by the hypoxic and congestive effects of the failing circulation upon other organs and tissues. One of the major symptoms of HF is edema, which has been defined as the excessive accumulation of interstitial fluid, either localized or generalized.

HF is the most common indication for hospitalization among adults over 65 years of age, and the rate of admission for this condition has increased progressively over the past

two decades. It has been estimated that HF affects more than 3 million patients in the U.S. (O'Connell, J. B. et al., *J. Heart Lung Transpl.*, 13(4):S107-112 (1993)).

In the conventional management of HF patients, where help is sought only in crisis, a cycle occurs where patients fail to recognize early symptoms and do not seek timely help from their care-givers, leading to emergency department admissions (Miller, P. Z., *Home monitoring for congestive heart failure patients*, *Caring Magazine*, 53-54 (August 1995)).

Recently, a prospective, randomized trial of 282 patients was conducted to assess the effect of the intervention on the rate of admission, quality of life, and cost of medical care. In this study, a nurse-directed, multi-disciplinary intervention (which consisted of comprehensive education of the patient and family, diet, social-service consultation and planning, review of medications, and intensive assessment of patient condition and follow-up) resulted in fewer readmissions than the conventional treatment group and a concomitant overall decrease in the cost of care (Rich, M. W. et al., *New Engl. J. Med.*, 333:1190-95 (1995)).

Similarly, comprehensive discharge planning and a home follow-up program was shown to decrease the number of readmissions and total hospital charges in an elderly population (Naylor, M. et al., *Amer. College Physicians*, 120: 999-1006 (1994)). Therefore, home monitoring is of particular interest in the HF management segment of the health care industry.

Another area in which home-monitoring is of particular interest is in the remote monitoring of a patient parameter that provides information on the titration of a drug, particularly with drugs that have a consequential effect following administration, such as insulin, anticoagulants, ACE inhibitors, beta-blockers, diuretics and the like.

Although a number of different home monitoring systems have been developed, there is continued interest in the development of new monitoring systems. Of particular interest would be the development of a system that provides for improved patient compliance, ease of use, etc. Of more particular interest would be the development of such a system that is particularly suited for use in the remote monitoring of patients suffering from HF.

Subcutaneous implantation of sensors has been achieved with an insertion and tunneling tool. The tunneling tool includes a stylet and a peel-away sheath. The tunneling tool is inserted into an incision and the stylet is withdrawn once the tunneling tool reaches a desired position. An electrode segment is inserted into the subcutaneous tunnel and the peel-away sheath is removed. In another delivery device, a pointed tip is inserted through the skin and a plunger is actuated to drive the sensor to its desired location.

In other delivery systems, an implant trocar includes a cannula for puncturing the skin and an obturator for delivering the implant. A spring element received within the cannula prevents the sensor from falling out during the implant process. Another sensor delivery device includes an injector that has a tubular body divided into two adjacent segments with a hollow interior bore. A pair of laterally adjacent tines extend longitudinally from the first segment to the distal end of the tubular body. A plunger rod has an exterior diameter just slightly larger than the interior diameter of the tubular body. With the second segment inserted beneath the skin, the push rod is advanced longitudinally through the tubular body, thereby pushing the sensor through the bore. As the implant and rod pass through the second segment, the tines are forced radially away from each other,

thereby dilating or expanding the incision, and facilitating implant. The instrument is removed from the incision following implantation.

For the above and other reasons, it would be desirable to provide a non-surgical instrument and method for subcutaneous implantation of sensors and solid materials that preferably does not require an incision preparatory to instrument insertion. It would also be desirable to provide an improved home monitoring of patients with chronic conditions and improved percutaneous sensor delivery devices.

BRIEF SUMMARY OF THE INVENTION

In a first aspect, embodiments of the present invention provide a system for decompensation prediction of a heart failure patient. The system comprises one or more injectable detecting systems having a plurality of sensors that provide an indication of at least one physiological event of a patient, a wireless communication device coupled to the one or more injectable detecting systems and configured to transfer patient data directly or indirectly from the one or more injectable detecting systems to a remote monitoring system, and a remote monitoring system coupled to the wireless communication device, the remote monitoring system using processed data to determine heart failure status and predict impending decompensation of the patient.

In another aspect, embodiments of the present invention provide a system for decompensation prediction of a heart failure patient. The system comprises one or more injectable detecting systems having a plurality of sensors that provide an indication of at least one physiological event of a patient, the one or more injectable detecting systems being inserted below the skin of the patient, the one or more injectable detecting systems being injected below the skin of the patient by gun or syringe injection, a wireless communication device coupled to the one or more injectable detecting systems and configured to transfer patient data directly or indirectly from the one or more injectable detecting systems to a remote monitoring system, and a remote monitoring system coupled to the wireless communication device, the remote monitoring system using processed data to determine heart failure status and predict impending decompensation of the patient.

In another aspect, embodiments of the present invention provide a method for decompensation prediction of a heart failure patient. The method comprising injecting subcutaneously one or more injectable detecting systems having a plurality of sensors that provide an indication of at least one physiological event of a patient, wirelessly transferring patient data directly or indirectly from the one or more injectable detecting systems to a remote monitoring system via a wireless communication device coupled to the one or more injectable detecting systems, and processing the data using the remote monitoring system to determine heart failure status and predict impending decompensation of the patient.

In many embodiments, the one or more injectable detecting systems are inserted below the skin of the patient by at least one of, catheter delivery, blunt tunneling and needle insertion.

In many embodiments, the systems and methods further comprise an imaging system to assist in guiding the injectable detecting system to a desired location.

In many embodiments, each of a sensor is selected from at least one of, bioimpedance, heart rate, heart rhythm, HRV, HRT, heart sounds, respiratory sounds, respiratory rate and

respiratory rate variability, blood pressure, activity, posture, wake/sleep, orthopnea, temperature, heat flux and an accelerometer.

In many embodiments, each of a sensor is an activity sensors selected from at least one of, ball switch, accelerometer, minute ventilation, HR, bioimpedance noise, skin temperature/heat flux, BP, muscle noise and posture.

In many embodiments, the injectable detecting systems include a power source, a memory, logic resources and an antenna. In many embodiments the power source is a rechargeable battery transcutaneously with an external unit.

In many embodiments, at least a portion of the injectable detecting systems have a drug eluting coating.

In many embodiments, the one or more injectable detecting systems are anchored in the patient by at least one of, barbs, anchors, tissue adhesion pads, suture loops, shape of device, self-expanding metal structure, wherein self-expanding metal structure is made of Nitinol.

In another aspect, embodiments of the present invention provide and injection system for injecting one or more injectable physiological monitoring systems for use in physiological monitoring of a patient. The system includes a body capable of holding one or more injectable physiological monitoring systems, the body having a proximal end and distal end, wherein the distal end is shaped to penetrate tissue, a a pusher configured to engage the one or more injectable physiological monitoring systems within the body and a movable handle coupled to a pusher configured to distally advance the one or more injectable physiological monitoring systems through the body.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a block diagram illustrating one embodiment of a patient monitoring system of the present invention.

FIG. 2(a) illustrates one embodiment of an injectable detecting system of the present invention that is injectable and includes multiple sensors, power and communication and a communication antenna.

FIG. 2(b) illustrates the insertion of the device of FIG. 2(a) into an injector.

FIG. 2(c) illustrates the device of FIG. 2(a) in the injector and ready to be introduced into the patient.

FIG. 2(d) illustrates the implanted sensor device of FIG. 2(a).

FIG. 2(e) illustrates the implanted sensor device of FIG. 2(a) as it flexes from a rigid state in the body.

FIG. 2(f) illustrates a patient laying on top of a matt that has coils, where downloading of patient data and recharging can occur via the matt or also through an adherent patch or wearable device by the patient.

FIG. 2(g) illustrates the patient laying on top of the matt from FIG. 2(f) and the downloading of data from the sensors to the matt.

FIG. 2(h) is a close up view of FIG. 2(g) showing the downloading of data from the sensors to the matt, and then transfer of the data from the matt to a modem.

FIG. 2(i) illustrates a patient with an implanted device, such as a pacing device, and the implanted device of FIG. 2(a) in communication with the implanted device.

FIG. 3 illustrates one embodiment of an energy management device that is coupled to the plurality of sensors of FIG. 1.

FIG. 4 illustrates one embodiment of present invention illustrating logic resources configured to receive data from the sensors and/or the processed patient for monitoring purposes, analysis and/or prediction purposes.

FIG. 5 illustrates an embodiment of the patient monitoring system of the present invention with a memory management device.

FIG. 6 illustrates an embodiment of the patient monitoring system of the present invention with an external device coupled to the sensors.

FIG. 7 illustrates an embodiment of the patient monitoring system of the present invention with a notification device.

FIG. 8 is a block diagram illustrating an embodiment of the present invention with sensor leads that convey signals from the sensors to a monitoring unit at the detecting system, or through a wireless communication device to a remote monitoring system.

FIG. 9 is a block diagram illustrating an embodiment of the present invention with a control unit at the detecting system and/or the remote monitoring system.

FIG. 10 is a block diagram illustrating an embodiment of the present invention where a control unit encodes patient data and transmits it to a wireless network storage unit at the remote monitoring system.

FIG. 11 is a block diagram illustrating one embodiment of an internal structure of a main data collection station at the remote monitoring system of the present invention.

FIG. 12 is a flow chart illustrating an embodiment of the present invention with operation steps performed by the system of the present invention in transmitting information to the main data collection station.

FIG. 13 shows one embodiment of an injection system for use with multiple injectable detecting systems.

FIG. 14 shows one embodiment of an injection system that includes a bevel needle shaped to receive the injectable detecting system.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed to a heart failure patient management system consisting of one or more subcutaneously injectable physiological monitoring systems inserted below the patient's skin. The system continuously monitors physiological parameters, communicates wirelessly with a remote center, and provides alerts when necessary. A variety of delivery devices and methods are also disclosed.

The system monitors physiological parameters and uses a proprietary algorithm to determine heart failure status and predict impending decompensation. The injectable system communicates with a remote center, preferably via an intermediate device in the patient's home. In some embodiments, the remote center receives the data and applies the prediction algorithm. When a flag is raised, the center may communicate with the patient, hospital, nurse, and/or physician to allow for therapeutic intervention to prevent decompensation.

The injectable system may be inserted with one of the following techniques: catheter delivery, blunt tunneling (with either a separate tunneling tool or a wire-stiffened lead), and insertion with a needle. The injectable system may be injected with a gun or syringe-like device. The injectable system may be flexible, and may be implanted with a stiffening wire or stylet.

The injectable system may be implanted in a non-sterile, non-surgical setting. Implantation may occur with or without local anesthesia, and with or without imaging assistance.

The system may consist of an implantable component and an external component. In such an embodiment, the injected component, with or without physiological sensing elec-

trodes, would be used to anchor an external electronics unit. The anchoring mechanism may be magnetic or mechanical.

The injectable system may contain one of the following features to facilitate subsequent extraction: an isodiametric profile, a breakaway anchor, a bioabsorbable material, coatings to limit tissue in-growth, and an electrically activated or fusible anchor. The injectable system may be modular, containing multiple connected components, a subset of which is easily extractable.

While the present invention is intended for heart failure patient monitoring, the system may be applicable to any human application in which wireless physiological monitoring and prediction is required.

In one embodiment, illustrated in FIG. 1, the present invention is a system that delivers a percutaneous sensing device for remote patient monitoring. The remote monitoring tracks the patient's physiological status, detects and predicts negative physiological events. In one embodiment, the implanted sensing device includes a plurality of sensors that are used in combination to enhance detection and prediction capabilities as more fully explained below.

Referring again to FIG. 1, in one embodiment, the system 10 includes an injectable detecting system 12 that includes a plurality of sensors 14 and/or electrodes, that provide an indication of at least one physiological event of a patient. The injectable detecting system 12 is inserted subcutaneously. In one embodiment the injectable detecting system 12 is inserted in the patient's thorax. The system 10 also includes a wireless communication device 16, coupled to the plurality of sensors 14. The wireless communication device transfers patient data directly or indirectly from the plurality of sensors 14 to a remote monitoring system 18. The remote monitoring system 18 uses data from the sensors to determine the patient's status. The system 10 can continuously, or non-continuously, monitor the patient, alerts are provided as necessary and medical intervention is provided when required. In one embodiment, the wireless communication device 16 is a wireless local area network for receiving data from the plurality of sensors.

The sensors 14 are subcutaneously inserted with the injectable detecting system 12 that is catheter based, blunt tunneling (with either a separate tunneling tool or a wire-stiffened lead), needle insertion gun or syringe-like injection. The injectable detecting system 12 can be flexible, and be used with a stiffening wire, stylet, catheter or guidewire. The injectable detecting system 12 can include any of the following to assist in subsequent extraction: (i) an isodiametric profile, (ii) a breakaway anchor, (iii) a bioabsorbable material, (iv) coatings to limit tissue in-growth, (v) an electrically activated or fusible anchor, and the like. The injectable detecting system 12 can be modular, containing multiple connected components, a subset of which is easily extractable.

The injectable detecting system 12 can be inserted in the patient in a non-sterile or sterile setting, non-surgical setting or surgical setting, implanted with or without anesthesia and implanted with or without imaging assistance from an imaging system. The injectable detecting system 12 can be anchored in the patient by a variety of means including but not limited to, barbs, anchors, tissue adhesion pads, suture loops, with sensor shapes that conform to adjacent tissue anatomy or provide pressure against the adjacent tissue, with the use of self-expanding materials such as a nitinol anchor and the like.

FIG. 2(a) shows one embodiment of the injectable detecting system 12 with sensors 14 that is introduced below the skin surface. The device includes power and communication

elements **32**, and a communication antenna **34**. The antenna may be a self expanding antenna expandable from a first compressed shape to a second expanded shape, such as disclosed in U.S. Provisional Application No. 61/084,567, filed Jul. 29, 2008 entitled "Communication-Anchor Loop For Injectable Device", the full disclosure of which is incorporated herein by reference. FIG. 2(b) illustrates the injectable detecting system **12** being loaded into an injector **36** having a needle end **38**. FIG. 2(c) shows the injectable detecting system **12** being introduced subcutaneously into a patient **40**. FIG. 2(d) shows the injectable detecting system **12** being implanted subcutaneously from the injector **36**. In FIG. 2(e), the injector **36** is removed and the injectable detecting system **12** flexes from a rigid configuration.

In one embodiment, illustrated in FIGS. 2(f) and 2(g), recharging coils **42** are placed in a mat **44** on the patient's bed, such as under a mattress pad. Recharging of the sensors/battery and data transfer can occur during sleep of the patient. The rechargeable batteries can be transcutaneously charged with an external unit other than the mat. FIG. 2(g) shows downloading from the sensors and data transfer during sleep of the patient. In FIG. 2(h), the injectable detecting system **12** downloads data to the mat and a modem is used from data transfer. In FIG. 2(i), an implantable device **50**, such as a pacing device communicates with the injectable detecting system **12** of FIG. 2(a).

In one embodiment, the wireless communication device **16** is configured to receive instructional data from the remote monitoring system and communicate instructions to the injectable detecting system.

As illustrated in FIG. 3, an energy management device **19** is coupled to the plurality of sensors. In one embodiment, the energy management device **19** is part of the detecting system. In various embodiments, the energy management device **19** performs one or more of, modulate drive levels per sensed signal of a sensor **14**, modulate a clock speed to optimize energy, watch cell voltage drop - unload cell, coulomb-meter or other battery monitor, sensor dropoff at an end of life of a battery coupled to a sensor, battery end of life dropoff to transfer data, elective replacement indicator, call center notification, sensing windows by the sensors **14** based on a monitored physiological parameter and sensing rate control.

In one embodiment, the energy management device **19** is configured to manage energy by at least one of, a thermoelectric unit, kinetics, fuel cell, nuclear power, a micro-battery and with a rechargeable device.

The system **10** is configured to automatically detect events. The system **10** automatically detects events by at least one of, high noise states, physiological quietness, sensor continuity and compliance. In response to a detected physiological event, patient states are identified when data collection is inappropriate. In response to a detected physiological event, patient states are identified when data collection is desirable. Patient states include, physiological quietness, rest, relaxation, agitation, movement, lack of movement and a patient's higher level of patient activity.

The system uses an intelligent combination of sensors to enhance detection and prediction capabilities, as more fully discloses in U.S. patent application Ser. Nos. 60/972,537 filed Sep. 14, 2008 and 61/055,666 filed May 23, 2008, both titled "Adherent Device with Multiple Physiological Sensors", incorporated herein by reference, and as more fully explained below.

In one embodiment, the injectable detecting system **12** communicates with the remote monitoring system **18** periodically or in response to a trigger event. The trigger event

can include but is not limited to at least one of, time of day, if a memory is full, if an action is patient initiated, if an action is initiated from the remote monitoring system, a diagnostic event of the monitoring system, an alarm trigger, a mechanical trigger, and the like.

The injectable detecting system **12** can continuously, or non-continuously, monitor the patient, alerts are provided as necessary and medical intervention is provided when required. In one embodiment, the wireless communication device **16** is a wireless local area network for receiving data from the plurality of sensors in the injectable detecting system.

A processor **20** is coupled to the plurality of sensors **14** in the injectable detecting system **12**. The processor **20** receives data from the plurality of sensors **14** and creates processed patient data. In one embodiment, the processor **20** is at the remote monitoring system **18**. In another embodiment, the processor **20** is at the detecting system **12**. The processor **20** can be integral with a monitoring unit **22** that is part of the injectable detecting system **12** or part of the remote monitoring system **18**.

The processor **20** has program instructions for evaluating values received from the sensors **14** with respect to acceptable physiological ranges for each value received by the processor **20** and determine variances. The processor **20** can receive and store a sensed measured parameter from the sensors **14**, compare the sensed measured value with a predetermined target value, determine a variance, accept and store a new predetermined target value and also store a series of questions from the remote monitoring system **18**.

As illustrated in FIG. 4, logic resources **24** are provided that take the data from the sensors **14**, and/or the processed patient data from the processor **20**, to predict an impending decompensation. The logic resources **24** can be at the remote monitoring system **18** or at the detecting system **12**, such as in the monitoring unit **22**.

In one embodiment, a memory management device **25** is provided as illustrated in FIG. 5. In various embodiments, the memory management device **25** performs one or more of data compression, prioritizing of sensing by a sensor **14**, monitoring all or some of sensor data by all or a portion of the sensors **14**, sensing by the sensors **14** in real time, noise blanking to provide that sensor data is not stored if a selected noise level is determined, low-power of battery caching and decimation of old sensor data.

The injectable detecting system **12** can provide a variety of different functions, including but not limited to, initiation, programming, measuring, storing, analyzing, communicating, predicting, and displaying of a physiological event of the patient. The injectable detecting system **12** can be sealed, such as housed in a hermetically sealed package. In one embodiment, at least a portion of the sealed packages include a power source, a memory, logic resources and a wireless communication device. In one embodiment, an antenna is included that is exterior to the sealed package of the injectable detecting system **12**. In one embodiment, the sensors **14** include, flex circuits, thin film resistors, organic transistors and the like. The sensors **14** can include ceramics, titanium PEEK, along with a silicon, PU or other insulative adherent sealant, to enclose the electronics. Additionally, the injectable detecting system **12** can include drug eluting coatings, including but not limited to, an antibiotic, anti-inflammatory agent and the like.

A wide variety of different sensors **14** can be utilized, including but not limited to, bioimpedance, heart rate, heart rhythm, HRV, HRT, heart sounds, respiration rate, respiration rate variability, respiratory sounds, SpO₂, blood pres-

sure, activity, posture, wake/sleep, orthopnea, temperature, heat flux, an accelerometer, glucose sensor, other chemical sensors associated with cardiac conditions, and the like. A variety activity sensors can be utilized, including but not limited to a, ball switch, accelerometer, minute ventilation, HR, bioimpedance noise, skin temperature/heat flux, BP, muscle noise, posture and the like.

The output of the sensors **14** can have multiple features to enhance physiological sensing performance. These multiple features have multiple sensing vectors that can include redundant vectors. The sensors **14** can include current delivery electrodes and sensing electrodes. Size and shape of current delivery electrodes, and the sensing electrodes, can be optimized to maximize sensing performance. The system **10** can be configured to determine an optimal sensing configuration and electronically reposition at least a portion of a sensing vector of a sensing electrode. The multiple features enhance the system's **10** ability to determine an optimal sensing configuration and electronically reposition sensing vectors. In one embodiment, the sensors **14** can be partially masked to minimize contamination of parameters sensed by the sensors **14**.

The size and shape of current delivery electrodes, for bioimpedance, and sensing electrodes can be optimized to maximize sensing performance. Additionally, the outputs of the sensors **14** can be used to calculate and monitor blended indices. Examples of the blended indices include but are not limited to, heart rate (HR) or respiratory rate (RR) response to activity, HR/RR response to posture change, HR+RR, HR/RR+bioimpedance, and/or minute ventilation/accelerometer and the like.

The sensors **14** can be cycled in order to manage energy, and different sensors **14** can sample at different times. By way of illustration, and without limitation, instead of each sensor **14** being sampled at a physiologically relevant interval, e.g. every 30 seconds, one sensor **14** can be sampled at each interval, and sampling cycles between available sensors.

By way of illustration, and without limitation, the sensors **14** can sample 5 seconds for every minute for ECG, once a second for an accelerometer sensor, and 10 seconds for every 5 minutes for impedance.

In one embodiment, a first sensor **14** is a core sensor **14** that continuously monitors and detects, and a second sensor **14** verifies a physiological status in response to the core sensor **14** raising a flag. Additionally, some sensors **14** can be used for short term tracking, and other sensors **14** used for long term tracking.

The injectable detecting system **12** is inserted into the patient by a variety of means, including but not limited to, catheter delivery, blunt tunneling, insertion with a needle, by injection, with a gun or syringe device with a stiffening wire and stylet and the like. The sensors **14** can be inserted in the patient in a non-sterile or sterile setting, non-surgical setting or surgical setting, injected with or without anesthesia and injected with or without imaging assistance. The injectable detecting system **12** can be anchored in the patient by a variety of means including but not limited to, barbs, anchors, tissue adhesion pads, suture loops.

The injectable detecting system **12** can come in a variety of different form factors including but not limited to, cylinder, dog-bone, half dog-bone, trapezoidal cross-section, semicircular cross-section, star-shaped cross-section, v-shaped cross-section, L-shaped, canted, W shaped, or in other shapes that assist in their percutaneous delivery, S-shaped, sine-wave shaped, J-shaped, any polygonal shape, helical/spiral, fin electrodes, and linear device with a radius

of curvature to match a radius of the injection site and the like. Further, the injectable detecting system **12** can have flexible body configurations. Additionally, the injectable detecting system **12** can be configured to deactivate selected sensors **14** to reduce redundancy.

The sensors **14** can be made of a variety of materials, including but not limited to, silicone, polyurethane, Nitinol, a biocompatible material, a bioabsorbable material and the like. Electrode sensors **14** can have a variety of different conductors, including but not limited to, platinum, MP35N which is a nickel-cobalt-chromium-molybdenum alloy, MP35N/Ag core, platinum/tantalum core, stainless steel, titanium and the like. The sensors **14** can have insulative materials, including but not limited to, polyetheretherketone (PEEK), ethylene-tetrafluoroethylene (ETFE), polytetrafluoroethylene (PTFE), polyimide, silicon, polyurethane, and the like. Further, the sensors **14** can have openings, or an absorbent material, configured to sample a hydration level or electrolyte level in a surrounding tissue site at the location of the sensor **14**. The sensor **14** electrodes can be made of a variety of materials, including but not limited to platinum, iridium, titanium, and the like. Electrode coatings can be included, such as iridium oxide, platinum black, TiN, and the like.

The injectable detecting system **12** can include one or more a rechargeable batteries **36** that can be transcutaneously chargeable with an external unit.

Referring to FIG. 6, in one embodiment, an external device **38**, including a medical treatment device, is coupled to the injectable detecting system **12**. The external device **38** can be coupled to a monitoring unit **22** that is part of the injectable detecting system **12**, or in direct communication with the sensors **14**. A variety of different external devices **38** can be used, including but not limited to, a weight scale, blood pressure cuff, cardiac rhythm management device, a medical treatment device, medication dispenser, glucose monitor, insulin pump, drug delivery pumps, drug delivery patches, and the like. Suitable cardiac rhythm management devices include but are not limited to, Boston Scientific's Latitude system, Medtronic's CareLink system, St. Jude Medical's HouseCall system and the like. Such communication may occur directly or via an external translator unit.

The external device **38** can be coupled to an auxiliary input of the monitoring unit **22** at the injectable detecting system **12** or to the monitoring system **22** at the remote monitoring system **18**. Additionally, an automated reader can be coupled to an auxiliary input in order to allow a single monitoring unit **22** to be used by multiple patients. As previously mentioned above, the monitoring unit **22** can be at the remote monitoring system **18** and each patient can have a patient identifier (ID) including a distinct patient identifier. In addition, the ID identifier can also contain patient specific configuration parameters. The automated reader can scan the patient identifier ID and transmit the patient ID number with a patient data packet such that the main data collection station can identify the patient.

It will be appreciated that other medical treatment devices can also be used. The injectable detecting system **12** can communicate wirelessly with the external devices **38** in a variety of ways including but not limited to, a public or proprietary communication standard and the like. The injectable detecting system **12** can be configured to serve as a communication hub for multiple medical devices, coordinating sensor data and therapy delivery while transmitting and receiving data from the remote monitoring system **18**.

In one embodiment, the injectable detecting system **12** coordinate data sharing between the external systems **38**

allowing for sensor integration across devices. The coordination of the injectable detecting system 12 provides for new pacing, sensing, defibrillation vectors, and the like.

In one embodiment, the processor 20 is included in the monitoring unit 22 and the external device 38 is in direct communication with the monitoring unit 22.

In another embodiment, illustrated in FIG. 7, a notification device 42 is coupled to the injectable detecting system 12 and the remote monitoring system 18. The notification device 42 is configured to provide notification when values received from the sensors 14 are not within acceptable physiological ranges. The notification device 42 can be at the remote monitoring system 18 or at the monitoring unit 22 that is part of the injectable detecting system 12. A variety of notification devices 42 can be utilized, including but not limited to, a visible patient indicator, an audible alarm, an emergency medical service notification, a call center alert, direct medical provider notification and the like. The notification device 42 provides notification to a variety of different entities, including but not limited to, the patient, a caregiver, the remote monitoring system, a spouse, a family member, a medical provider, from one device to another device such as the external device 38, and the like.

Notification can be according to a preset hierarchy. By way of illustration, and without limitation, the preset hierarchy can be, patient notification first and medical provider second, patient notification second and medical provider first, and the like. Upon receipt of a notification, a medical provider, the remote monitoring system 18, or a medical treatment device can trigger a high-rate sampling of physiological parameters for alert verification.

The system 10 can also include an alarm 46, that can be coupled to the notification device 42, for generating a human perceptible signal when values received from the sensors 14 are not within acceptable physiological ranges. The alarm 46 can trigger an event to render medical assistance to the patient, provide notification as set forth above, continue to monitor, wait and see, and the like.

When the values received from the sensors 14 are not within acceptable physiological ranges the notification is with the at least one of, the patient, a spouse, a family member, a caregiver, a medical provider and from one device to another device, to allow for therapeutic intervention to prevent decompensation.

In another embodiment, the injectable detecting system 12 can switch between different modes, wherein the modes are selected from at least one of, a stand alone mode with communication directly with the remote monitoring system 18, communication with an implanted device, communication with a single implanted device, coordination between different devices (external systems) coupled to the plurality of sensors and different device communication protocols.

By way of illustration, and without limitation, the patient can be a congestive heart failure patient. Heart failure status is determined by a weighted combination change in sensor outputs and be determined by a number of different means, including but not limited to, (i) when a rate of change of at least two sensor outputs is an abrupt change in the sensor outputs as compared to a change in the sensor outputs over a longer period of time, (ii) by a tiered combination of at least a first and a second sensor output, with the first sensor output indicating a problem that is then verified by at least a second sensor output, (iii) by a variance from a baseline value of sensor outputs, and the like. The baseline values can be defined in a look up table.

In another embodiment, heart failure status is determined using three or more sensors by at least one of, (i) when the

first sensor output is at a value that is sufficiently different from a baseline value, and at least one of the second and third sensor outputs is at a value also sufficiently different from a baseline value to indicate heart failure status, (ii) by time weighting the outputs of the first, second and third sensors, and the time weighting indicates a recent event that is indicative of the heart failure status and the like.

In one embodiment, the wireless communication device 16 can include a, modem, a controller to control data supplied by the injectable detecting system 12, serial interface, LAN or equivalent network connection and a wireless transmitter. Additionally, the wireless communication device 16 can include a receiver and a transmitter for receiving data indicating the values of the physiological event detected by the plurality of sensors, and for communicating the data to the remote monitoring system 18. Further, the wireless communication device 16 can have data storage for recording the data received from the injectable detecting system 12 and an access device for enabling access to information recording in the data storage from the remote monitoring system 18.

In various embodiments, the remote monitoring system 18 can include a, receiver, a transmitter and a display for displaying data representative of values of the one physiological event detected by the injectable detecting system 12. The remote monitoring system can also include a, data storage mechanism that has acceptable ranges for physiological values stored therein, a comparator for comparing the data received from the injectable detecting system 12 with the acceptable ranges stored in the data storage device and a portable computer. The remote monitoring system 18 can be a portable unit with a display screen and a data entry device for communicating with the wireless communication device 16.

Referring now to FIG. 8, for each sensor 14, a sensor lead 112 and 114 conveys signals from the sensor 14 to the monitoring unit 22 at the injectable detecting system 12, or through the wireless communication device 16 to the remote monitoring system 18.

In one embodiment, each signal from a sensor 14 is first passed through a low-pass filter 116, at the injectable detecting system 12 or at the remote monitoring system 18, to smooth the signal and reduce noise. The signal is then transmitted to an analog-to-digital converter 118A, which transforms the signals into a stream of digital data values that can be stored in a digital memory 118B. From the digital memory 118B, data values are transmitted to a data bus 120, along which they are transmitted to other components of the circuitry to be processed and archived. From the data bus 120, the digital data can be stored in a non-volatile data archive memory. The digital data can be transferred via the data bus 120 to the processor 20, which processes the data based in part on algorithms and other data stored in a non-volatile program memory.

The injectable detecting system 12 can also include a power management module 122 configured to power down certain components of the system, including but not limited to, the analog-to-digital converters 118A and 124, digital memories 118B and the non-volatile data archive memory and the like, between times when these components are in use. This helps to conserve battery power and thereby extend the useful life. Other circuitry and signaling modes may be devised by one skilled in the art.

As can be seen in FIG. 9, a control unit 126 is included at the detecting system 12, the remote monitoring system 18, or at both locations.

In one embodiment, the control unit 126 can be a micro-processor, for example, a Pentium or 486 processor. The control unit 126 can be coupled to the sensors 14 directly at the injectable detecting system 12, indirectly at the injectable detecting system 12 or indirectly at the remote monitoring system 18. Additionally the control unit 126 can be coupled to one or more devices, for example, a blood pressure monitor, cardiac rhythm management device, scale, a device that dispenses medication, a device that can indicate the medication has been dispensed, and the like.

The control unit 126 can be powered by AC inputs which are coupled to internal AC/DC converters 134 that generate multiple DC voltage levels. After the control unit 126 has collected the patient data from the sensors 14, the control unit 126 encodes the recorded patient data and transmits the patient data through the wireless communication device 16 to transmit the encoded patient data to a wireless network storage unit 128 at the remote monitoring system 18, as shown in FIG. 10. In another embodiment, wireless communication device 16 transmits the patient data from the injectable detecting system 12 to the control unit 126 when it is at the remote monitoring system 18.

Every time the control unit 126 plans to transmit patient data to a main data collection station 130, located at the remote monitoring system 18, the control unit 126 attempts to establish a communication link. The communication link can be wireless, wired, or a combination of wireless and wired for redundancy, e.g., the wired link checks to see if a wireless communication can be established. If the wireless communication link 16 is available, the control unit 126 transmits the encoded patient data through the wireless communication device 16. However, if the wireless communication device 16 is not available for any reason, the control unit 126 waits and tries again until a link is established.

Referring now to FIG. 11, one embodiment of an internal structure of a main data collection station 130, at the remote monitoring system 18, is illustrated. The patient data can be transmitted by the remote monitoring system 18 by either the wireless communication device 16 or conventional modem to the wireless network storage unit 128. After receiving the patient data, the wireless network storage unit 128 can be accessed by the main data collection station 130. The main data collection station 130 allows the remote monitoring system 18 to monitor the patient data of numerous patients from a centralized location without requiring the patient or a medical provider to physically interact with each other.

The main data collection station 130 can include a communications server 136 that communicates with the wireless network storage unit 128. The wireless network storage unit 128 can be a centralized computer server that includes a unique, password protected mailbox assigned to and accessible by the main data collection station 130. The main data collection station 130 contacts the wireless network storage unit 128 and downloads the patient data stored in a mailbox assigned to the main data collection station 130.

Once the communications server 136 has formed a link with the wireless network storage unit 128, and has downloaded the patient data, the patient data can be transferred to a database server 138. The database server 138 includes a patient database 140 that records and stores the patient data of the patients based upon identification included in the data packets sent by each of the monitoring units 22. For example, each data packet can include an identifier.

Each data packet transferred from the remote monitoring system 18 to the main data collection station 130 does not

have to include any patient identifiable information. Instead, the data packet can include the serial number assigned to the specific injectable detecting system 12. The serial number associated with the detecting system 12 can then be correlated to a specific patient by using information stored on the patient database 138. In this manner, the data packets transferred through the wireless network storage unit 128 do not include any patient-specific identification. Therefore, if the data packets are intercepted or improperly routed, patient confidentiality can not be breached.

The database server 138 can be accessible by an application server 142. The application server 142 can include a data adapter 144 that formats the patient data information into a form that can be viewed over a conventional web-based connection. The transformed data from the data adapter 144 can be accessible by propriety application software through a web server 146 such that the data can be viewed by a workstation 148. The workstation 148 can be a conventional personal computer that can access the patient data using proprietary software applications through, for example, HTTP protocol, and the like.

The main data collection station further can include an escalation server 150 that communicates with the database server 138. The escalation server 150 monitors the patient data packets that are received by the database server 138 from the monitoring unit 22. Specifically, the escalation server 150 can periodically poll the database server 138 for unacknowledged patient data packets. The patient data packets are sent to the remote monitoring system 18 where the processing of patient data occurs. The remote monitoring system 18 communicates with a medical provider in the event that an alert is required. If data packets are not acknowledged by the remote monitoring system 18. The escalation server 150 can be programmed to automatically deliver alerts to a specific medical provider if an alarm message has not been acknowledged within a selected time period after receipt of the data packet.

The escalation server 150 can be configured to generate the notification message to different people by different modes of communication after different delay periods and during different time periods.

The main data collection station 130 can include a batch server 152 connected to the database server 138. The batch server 152 allows an administration server 154 to have access to the patient data stored in the patient database 140. The administration server 154 allows for centralized management of patient information and patient classifications.

The administration server 154 can include a batch server 156 that communicates with the batch server 152 and provides the downloaded data to a data warehouse server 158. The data warehouse server 158 can include a large database 160 that records and stores the patient data.

The administration server 154 can further include an application server 162 and a maintenance workstation 164 that allow personnel from an administrator to access and monitor the data stored in the database 160.

The data packet utilized in the transmission of the patient data can be a variable length ASCII character packet, or any generic data formats, in which the various patient data measurements are placed in a specific sequence with the specific readings separated by commas. The control unit 126 can convert the readings from each sensor 14 into a standardized sequence that forms part of the patient data packet. In this manner, the control unit 126 can be programmed to convert the patient data readings from the sensors 14 into a

standardized data packet that can be interpreted and displayed by the main data collection station 130 at the remote monitoring system 18.

Referring now to the flow chart of FIG. 12, if an external device 38 fails to generate a valid reading, as illustrated in step A, the control unit 126 fills the portion of the patient data packet associated with the external device 38 with a null indicator. The null indicator can be the lack of any characters between commas in the patient data packet. The lack of characters in the patient data packet can indicate that the patient was not available for the patient data recording. The null indicator in the patient data packet can be interpreted by the main data collection station 130 at the remote monitoring system 18 as a failed attempt to record the patient data due to the unavailability of the patient, a malfunction in one or more of the sensors 14, or a malfunction in one of the external devices 38. The null indicator received by the main data collection station 130 can indicate that the transmission from the injectable detecting system 12 to the remote monitoring system 18 was successful. In one embodiment, the integrity of the data packet received by the main data collection station 130 can be determined using a cyclic redundancy code, CRC-16, check sum algorithm. The check sum algorithm can be applied to the data when the message can be sent and then again to the received message.

After the patient data measurements are complete, the control unit 126 displays the sensor data, including but not limited to blood pressure cuff data and the like, as illustrated by step B. In addition to displaying this data, the patient data can be placed in the patient data packet, as illustrated in step C.

As previously described, the system 10 can take additional measurements utilizing one or more auxiliary or external devices 38 such as those mentioned previously. Since the patient data packet has a variable length, the auxiliary device patient information can be added to the patient data packet being compiled by the remote monitoring unit 22 during patient data acquisition period being described. Data from the external devices 38 is transmitted by the wireless communication device 16 to the remote monitoring system 18 and can be included in the patient data packet.

If the remote monitoring system 18 can be set in either the auto mode or the wireless only mode, the remote monitoring unit 22 can first determine if there can be an internal communication error, as illustrated in step D.

A no communication error can be noted as illustrated in step E. If a communication error is noted the control unit 126 can proceed to wireless communication device 16 or to a conventional modem transmission sequence, as will be described below. However, if the communication device is working, the control unit 126 can transmit the patient data information over the wireless network 16, as illustrated in step F. After the communication device has transmitted the data packet, the control unit 126 determines whether the transmission was successful, as illustrated in step G. If the transmission has been unsuccessful only once, the control unit 126 retries the transmission. However, if the communication device has failed twice, as illustrated in step H, the control unit 126 proceeds to the conventional modem process if the remote monitoring unit 22 was configured in an auto mode.

When the control unit 126 is at the injectable detecting system 12, and the control unit 126 transmits the patient data over the wireless communication device 16, as illustrated in step I, if the transmission has been successful, the display of the remote monitoring unit 22 can display a successful

message, as illustrated in step J. However, if the control unit 126 determines in step K that the communication of patient data has failed, the control unit 126 repeats the transmission until the control unit 126 either successfully completes the transmission or determines that the transmission has failed a selected number of times, as illustrated in step L. The control unit 126 can time out the and a failure message can be displayed, as illustrated in steps M and N. Once the transmission sequence has either failed or successfully transmitted the data to the main data collection station, the control unit 126 returns to a start program step O.

As discussed previously, the patient data packets are first sent and stored in the wireless network storage unit 128. From there, the patient data packets are downloaded into the main data collection station 130. The main data collection station 130 decodes the encoded patient data packets and records the patient data in the patient database 140. The patient database 140 can be divided into individual storage locations for each patient such that the main data collection station 130 can store and compile patient data information from a plurality of individual patients.

A report on the patient's status can be accessed by a medical provider through a medical provider workstation that is coupled to the remote monitoring system 18. Unauthorized access to the patient database can be prevented by individual medical provider usernames and passwords to provide additional security for the patient's recorded patient data.

The main data collection station 130 and the series of work stations 148 allow the remote monitoring system 18 to monitor the daily patient data measurements taken by a plurality of patients reporting patient data to the single main data collection station 130. The main data collection station 130 can be configured to display multiple patients on the display of the workstations 148. The internal programming for the main data collection station 130 can operate such that the patients are placed in a sequential top-to-bottom order based upon whether or not the patient can be generating an alarm signal for one of the patient data being monitored. For example, if one of the patients monitored by monitoring system 130 has a blood pressure exceeding a predetermined maximum amount, this patient can be moved toward the top of the list of patients and the patient's name and/or patient data can be highlighted such that the medical personnel can quickly identify those patients who may be in need of medical assistance. By way of illustration, and without limitation, the following paragraphs is a representative order ranking method for determining the order which the monitored patients are displayed:

Alarm Display Order Patient Status Patients are then sorted 1 Medical Alarm Most alarms violated to least alarms violated, then oldest to newest 2 Missing Data Alarm Oldest to newest 3 Late Oldest to newest 4 Reviewed Medical Alarms Oldest to newest 5 Reviewed Missing Data Oldest to newest Alarms 6 Reviewed Null Oldest to newest 7 NDR Oldest to newest 8 Reviewed NDR Oldest to newest

As listed in the above, the order of patients listed on the display can be ranked based upon the seriousness and number of alarms that are registered based upon the latest patient data information. For example, if the blood pressure of a single patient exceeds the tolerance level and the patient's heart rate also exceeds the maximum level, this patient will be placed above a patient who only has one alarm condition. In this manner, the medical provider can quickly determine which patient most urgently needs medical attention by simply identifying the patient's name at the top of the patient list. The order which the patients are

displayed can be configurable by the remote monitoring system **18** depending on various preferences.

As discussed previously, the escalation server **150** automatically generates a notification message to a specified medical provider for unacknowledged data packets based on user specified parameters.

In addition to displaying the current patient data for the numerous patients being monitored, the software of the main data collection station **130** allows the medical provider to trend the patient data over a number of prior measurements in order to monitor the progress of a particular patient. In addition, the software allows the medical provider to determine whether or not a patient has been successful in recording their patient data as well as monitor the questions being asked by the remote monitoring unit **22**.

As previously mentioned, the system **10** uses an intelligent combination of sensors to enhance detection and prediction capabilities. Electrocardiogram circuitry can be coupled to the sensors **14**, or electrodes, to measure an electrocardiogram signal of the patient. An accelerometer can be mechanically coupled, for example adhered or affixed, to the sensors **14**, adherent patch and the like, to generate an accelerometer signal in response to at least one of an activity or a position of the patient. The accelerometer signals improve patient diagnosis, and can be especially useful when used with other signals, such as electrocardiogram signals and impedance signals, including but not limited to, hydration respiration, and the like. Mechanically coupling the accelerometer to the sensors **14**, electrodes, for measuring impedance, hydration and the like can improve the quality and/or usefulness of the impedance and/or electrocardiogram signals. By way of illustration, and without limitation, mechanical coupling of the accelerometer to the sensors **14**, electrodes, and to the skin of the patient can improve the reliability, quality and/or accuracy of the accelerometer measurements, as the sensor **14**, electrode, signals can indicate the quality of mechanical coupling of the patch to the patient so as to indicate that the device is connected to the patient and that the accelerometer signals are valid. Other examples of sensor interaction include but are not limited to, (i) orthopnea measurement where the breathing rate is correlated with posture during sleep, and detection of orthopnea, (ii) a blended activity sensor using the respiratory rate to exclude high activity levels caused by vibration (e.g. driving on a bumpy road) rather than exercise or extreme physical activity, (iii) sharing common power, logic and memory for sensors, electrodes, and the like.

FIG. **13** shows one embodiment of an injection system **200** for use with multiple injectable detecting systems **12** that includes a body having a magazine **205** with several injectable detecting systems **12** loaded therein. A needle portion of the injection system **200** can be placed against the tissue **210**, as shown. A handle **215** can be pulled proximally **220** and a pusher is advanced to inject one of the injectable detecting systems **12** out of the needle end into the patient **40**, and injectable detecting systems **12** in the magazine **205** are advanced such that the next injectable detecting system **12** is ready for injection at a subsequent location.

FIG. **14** shows one embodiment of an injection system **250** that includes a body with a needle **255** configured to hold one or more injectable detecting systems **12**. The needled **255** includes a bevel needle shaped tip **265**, that is inserted into the tissue with the injectable detecting system **12** loaded into the needle **255**. A pusher **265** is advanced distally in the body to advance the injectable detecting system **12** into the tissue after the needle tip has penetrated the tissue

While the invention is susceptible to various modifications and alternative constructions, certain illustrated embodiments thereof are shown in the drawings and have been described above in detail. It should be understood, however, that there is no intention to limit the invention to the specific form or forms disclosed, but on the contrary, the intention is to cover all modifications, alternative constructions, and equivalents falling within the spirit and scope of the invention.

The invention claimed is:

1. An injectable device for use in subcutaneous physiological monitoring of a patient, the injectable device comprising:

a body;

a plurality of sensors that provide an indication of at least one physiological event of a patient, wherein the plurality of sensors include current delivery electrodes and sensing electrodes in contact with tissue of the patient and spaced along the body of the injectable device; and a monitoring unit located within the body and coupled to the plurality of sensors and configured to monitor a bioimpedance of the patient using the current delivery electrodes and sensing electrodes, wherein the monitoring unit utilizes the monitored bioimpedance to determine a hydration of surrounding tissue and wherein the monitoring unit is further configured to, based at least in part on the determined hydration, detect an impending cardiac decompensation of the patient.

2. The injectable device of claim **1**, further including electrocardiogram circuitry coupled to the two or more electrodes to measure an electrocardiogram signal of the patient.

3. The injectable device of claim **2**, wherein the monitoring unit utilizes the measured impedance signal to monitor a respiration signal associated with the patient.

4. The injectable device of claim **3**, wherein the monitoring unit compares the monitored hydration, the respiration signal and the electrocardiogram signal to baseline values established for each, wherein the monitoring unit sets a flag indicating cardiac decompensation based on a combination of the compared values.

5. The injectable device of claim **1**, further including an accelerometer located within the body that generates an activity signal in response to at least one of an activity or a position of the patient.

6. The injectable device of claim **5**, wherein the accelerometer is a three-axis accelerometer configured to measure at least one inclination, a position, an orientation, and an acceleration of the patient in three dimensions.

7. The injectable device of claim **5**, wherein the accelerometer is comprised of at least one of a piezoelectric accelerometer, a capacitive accelerometer, or an electromechanical accelerometer.

8. The injectable device of claim **5**, wherein the monitoring unit utilizes activity data received from the accelerometer to detect physiological events and identify patient states when data collection is desirable.

9. The injectable device of claim **8**, wherein patient states in which data collection is desirable include rest states.

10. The injectable device of claim **1**, wherein the body has a proximal end and a distal end, wherein the distal end is shaped to penetrate tissue.

11. The injectable device of claim **1**, wherein the injectable device can be inserted in the patient in one or more of a non-sterile setting, sterile setting, non-surgical setting, and surgical setting.

19

12. An injectable device for use in subcutaneous physiological monitoring of a patient, the injectable device comprising:

a hermetically sealed body;

a plurality of sensors that provide an indication of at least one physiological event of a patient, wherein the plurality of sensors includes an accelerometer located within the body that generates an activity signal in response to at least one of a activity or a position of the patient and at least two electrodes spaced along the hermetically sealed body of the injectable device and in contact with tissue of the patient for monitoring a physiological signal associated with the patient; and

a monitoring unit located within the body and coupled to the accelerometer and the at least two electrodes, wherein the at least two electrodes are utilized to measure an impedance signal related, wherein the monitoring unit utilizes the measured impedance to determine a hydration of surrounding tissue of the patient and wherein the monitoring unit is further configured to, based at least in part on the determined hydration and the activity level of the patient, detect an impending cardiac decompensation of the patient.

20

13. The injectable device of claim 12, wherein the accelerometer is a three-axis accelerometer configured to measure at least one inclination, a position, an orientation, and an acceleration of the patient in three dimensions.

14. The injectable device of claim 12, wherein the monitoring unit utilizes the monitored activity level of the patient to identify patient states when data collection is appropriate.

15. The injectable device of claim 14, wherein patient states in which data collection is appropriate includes rest states.

16. The injectable device of claim 12, further including electrocardiogram circuitry coupled to the two or more electrodes to measure an electrocardiogram signal of the patient.

17. The injectable device of claim 16, wherein the monitoring unit utilizes the measured impedance signal to monitor a respiration signal associated with the patient.

18. The injectable device of claim 16, wherein the monitoring unit compares the monitored hydration, the respiration signal and the electrocardiogram signal to baseline values established for each, wherein the monitoring unit sets a flag indicating cardiac decompensation based on a combination of the compared values.

* * * * *

专利名称(译)	可注射的生理监测系统		
公开(公告)号	US9538960	公开(公告)日	2017-01-10
申请号	US14/921827	申请日	2015-10-23
[标]申请(专利权)人(译)	美敦力监控公司		
申请(专利权)人(译)	美敦力公司监测, INC.		
当前申请(专利权)人(译)	美敦力公司监测, INC.		
[标]发明人	MAZAR SCOTT T BLY MARK J		
发明人	MAZAR, SCOTT T. BLY, MARK J.		
IPC分类号	A61B5/00 A61B5/053 A61B5/042 A61B5/0205 A61B5/07 A61B5/145 A61B5/11 A61N1/372		
CPC分类号	A61B5/7282 A61B5/0031 A61B5/0205 A61B5/02055 A61B5/0422 A61B5/053 A61B5/07 A61B5/076 A61B5/14503 A61B5/4875 A61B5/686 A61B5/1118 A61B5/7232 A61B2560/0214 A61B2560/0468 A61B2562/0219 A61B2562/04 A61B2562/06 A61B2562/16 A61N1/37205		
代理人(译)	COLLINS, MICHAEL A.		
优先权	61/055666 2008-05-23 US 60/972336 2007-09-14 US 60/972537 2007-09-14 US 60/972329 2007-09-14 US 60/972354 2007-09-14 US		
其他公开文献	US20160045169A1		
外部链接	Espacenet USPTO		

摘要(译)

一种用于患者的皮下生理监测的可注射装置包括主体, 多个传感器和监测单元。所述多个传感器提供患者的至少一个生理事件的指示, 其中所述多个传感器包括与患者的组织接触的两个或更多个电极。监测单元位于体内并且耦合到多个传感器并且被配置为使用电极监测患者的生理信号, 其中生理信号包括与患者的组织的水合相关的阻抗信号, 并且其中监测单元还被配置为至少部分地基于从患者测量的阻抗信号来检测患者的即将发生的心脏代偿失调。

