US007396333B2

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

(10) **Patent No.: US 7,396,333 B2**
(45) **Date of Patent: Jul. 8, 2008**

(54) **PREDICTION OF DISORDERED BREATHING**

(75) Inventors: **Jeffrey E. Stahmann**, Ramsey, MN (US); **John D. Hatlestad**, Maplewood, MN (US); **Quan Ni**, Shoreview, MN (US); **Jesse Hartley**, Lino Lakes, MN (US); **Douglas R. Daum**, Oakdale, MN (US); **Kent Lee**, Fridley, MN (US)

(73) Assignee: **Cardiac Pacemakers, Inc.**, St. Paul, MN (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 728 days.

(21) Appl. No.: **10/643,016**

(22) Filed: **Aug. 18, 2003**

(65) **Prior Publication Data**

US 2005/0043644 A1 Feb. 24, 2005

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

(52) **U.S. Cl.** **600/529**

(58) **Field of Classification Search** 600/529–543
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,312,734	A		1/1982	Nichols
4,365,636	A	*	12/1982	Barker 600/529
4,390,405	A		6/1983	Hahn et al.
4,562,841	A		1/1986	Brockway et al.
4,702,253	A	*	10/1987	Nappholz et al. 607/20
4,777,962	A		10/1988	Watson et al.
4,784,162	A		11/1988	Ricks et al.
4,802,485	A		2/1989	Bowers et al.
4,813,427	A		3/1989	Schlaefke et al.
4,827,943	A		5/1989	Bornn et al.
4,875,477	A		10/1989	Waschke et al.
4,953,551	A		9/1990	Mehra et al.
4,958,632	A		9/1990	Duggan
4,961,423	A		10/1990	Canducci
4,972,842	A		11/1990	Korten et al.
4,982,738	A		1/1991	Griebel
5,010,888	A		4/1991	Jadvar et al.
5,047,930	A		9/1991	Martens et al.
5,063,927	A		11/1991	Webb et al.

(Continued)

FOREIGN PATENT DOCUMENTS

EP	1162125	12/2001

(Continued)

OTHER PUBLICATIONS

Waldemark, Katrina et al., Detection of Apnea Using Short Window FFT Technique and Artificial Neural Network, SPIE, International Society for Optical Engineering, vol. 3390, pp. 122-133 (1998).

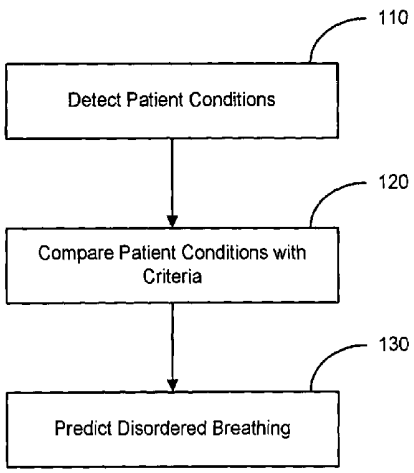
(Continued)

Primary Examiner—Charles A. Marmor, II
Assistant Examiner—Karen E Toth
(74) *Attorney, Agent, or Firm*—Hollingsworth & Funk, LLC

(57) **ABSTRACT**

An approach for predicting disordered breathing involves detecting one or more conditions associated with disordered breathing. The detected conditions are compared to disordered breathing prediction criteria. A prediction of disordered breathing is performed based on the comparison of the detected conditions to the prediction criteria. At least one of comparing the detected conditions to the prediction criteria and predicting disordered breathing is performed at least in part implantably.

75 Claims, 9 Drawing Sheets



U.S. PATENT DOCUMENTS

5,105,354 A 4/1992 Nishimura
5,123,425 A 6/1992 Shannon, Jr. et al.
5,133,353 A 7/1992 Hauser
5,156,157 A 10/1992 Valenta
5,170,784 A 12/1992 Ramon et al.
5,174,287 A 12/1992 Kallok et al.
5,179,945 A 1/1993 Van Hofwegen et al.
5,183,038 A 2/1993 Hoffman et al.
5,188,106 A 2/1993 Nappholz
5,199,424 A 4/1993 Sullivan et al.
5,209,229 A 5/1993 Gilli
5,259,373 A 11/1993 Gruenke et al.
5,261,400 A 11/1993 Bardy
5,275,159 A 1/1994 Griebel
5,292,338 A 3/1994 Bardy
5,300,106 A 4/1994 Dahl et al.
5,314,430 A 5/1994 Bardy
5,314,459 A 5/1994 Swanson et al.
5,318,597 A 6/1994 Hauck et al.
5,330,505 A 7/1994 Cohen
5,331,966 A 7/1994 Bennett et al.
5,353,788 A 10/1994 Miles
5,372,606 A 12/1994 Lang et al.
5,376,106 A 12/1994 Stahmann et al.
5,398,682 A 3/1995 Lynn
5,411,525 A 5/1995 Swanson et al.
5,411,539 A 5/1995 Neisz
5,439,482 A 8/1995 Adams et al.
5,441,518 A 8/1995 Adams et al.
5,466,245 A 11/1995 Heemels et al.
5,468,254 A 11/1995 Hahn et al.
5,483,969 A 1/1996 Testerman et al.
5,517,983 A 5/1996 Deighan et al.
5,522,382 A 6/1996 Sullivan et al.
5,531,779 A 7/1996 Dahl et al.
5,540,727 A 7/1996 Tockman et al.
5,540,732 A 7/1996 Testerman
5,540,734 A 7/1996 Zabara
5,545,186 A 8/1996 Olson et al.
5,545,202 A 8/1996 Dahl et al.
5,549,655 A 8/1996 Erickson
5,590,648 A 1/1997 Mitchell et al.
5,591,216 A 1/1997 Testerman et al.
5,603,732 A 2/1997 Dahl et al.
5,605,151 A 2/1997 Lynn
5,606,969 A 3/1997 Butler et al.
5,620,466 A 4/1997 Haefner et al.
5,622,178 A 4/1997 Gilham
5,634,938 A 6/1997 Swanson et al.
5,641,326 A 6/1997 Adams
5,645,570 A 7/1997 Corbucci
5,662,688 A 9/1997 Haefner et al.
5,693,000 A 12/1997 Crosby et al.
5,697,951 A 12/1997 Harpstead et al.
5,697,953 A 12/1997 Kroll et al.
5,701,894 A 12/1997 Cherry et al.
5,704,365 A 1/1998 Albrecht et al.
5,715,812 A 2/1998 Deighan et al.
5,724,984 A 3/1998 Arnold et al.
5,738,102 A 4/1998 Lemelson
5,800,470 A 9/1998 Stein et al.
5,826,579 A 10/1998 Remmers et al.
5,827,326 A 10/1998 Kroll et al.
5,861,011 A 1/1999 Stoop
5,876,353 A 3/1999 Riff
5,895,414 A 4/1999 Sanchez-Zambrano
5,919,141 A 7/1999 Money et al.
5,957,956 A 9/1999 Kroll et al.
5,961,446 A 10/1999 Beller et al.
5,961,450 A 10/1999 Merchant et al.
5,970,975 A 10/1999 Estes et al.
6,015,388 A 1/2000 Sackner et al.
6,021,351 A 2/2000 Kadhiresan et al.
6,045,513 A 4/2000 Stone et al.
6,047,203 A 4/2000 Sackner et al.
6,050,940 A 4/2000 Braun et al.
6,064,910 A 5/2000 Andersson et al.
6,105,575 A 8/2000 Estes et al.
6,144,866 A 11/2000 Miesel et al.
6,148,230 A 11/2000 KenKnight
6,155,976 A 12/2000 Sackner et al.
6,161,042 A 12/2000 Hartley et al.
6,168,568 B1 1/2001 Gavriely
6,181,961 B1 1/2001 Prass
6,212,435 B1 4/2001 Lattner et al.
6,236,873 B1 5/2001 Holmström
6,261,238 B1 7/2001 Gavriely
6,270,457 B1 8/2001 Bardy
6,272,377 B1 8/2001 Sweeney et al.
6,280,462 B1 8/2001 Hauser et al.
6,287,264 B1 9/2001 Hoffman
6,303,270 B1 10/2001 Naim
6,306,088 B1 10/2001 Krausman
6,312,378 B1 11/2001 Bardy
6,331,536 B1 12/2001 Radulovacki et al.
6,336,903 B1 1/2002 Bardy
6,357,444 B1 3/2002 Parker
6,360,127 B1 3/2002 Ding et al.
6,361,522 B1 3/2002 Scheiner et al.
6,368,284 B1 4/2002 Bardy
6,375,614 B1 4/2002 Braun et al.
6,375,623 B1 4/2002 Gavriely
6,397,845 B1 6/2002 Burton
6,398,728 B1 6/2002 Bardy
6,398,739 B1 6/2002 Sullivan et al.
6,409,675 B1 6/2002 Turcott
6,415,174 B1 7/2002 Bebehani et al.
6,415,183 B1 * 7/2002 Scheiner et al. 607/42
6,431,171 B1 8/2002 Burton
6,440,066 B1 8/2002 Bardy
6,442,413 B1 8/2002 Silver
6,450,957 B1 9/2002 Yoshimi
6,454,708 B1 9/2002 Ferguson et al.
6,463,326 B1 10/2002 Hartley et al.
6,468,219 B1 10/2002 Njemanze
6,491,639 B1 12/2002 Trucott
6,512,940 B1 1/2003 Brabec et al.
6,522,915 B1 2/2003 Ceballos et al.
6,564,106 B2 5/2003 Guck et al.
6,572,543 B1 6/2003 Christopherson et al.
6,574,507 B1 6/2003 Bonnet
6,580,944 B1 * 6/2003 Katz et al. 600/513
6,600,949 B1 7/2003 Turcott
6,606,993 B1 8/2003 Wiesmann et al.
6,607,509 B2 8/2003 Bobroff et al.
6,615,083 B2 9/2003 Kupper
6,622,046 B2 9/2003 Fraley et al.
6,628,986 B1 9/2003 Mouchawar et al.
6,641,542 B2 11/2003 Cho et al.
6,694,186 B2 2/2004 Bardy
6,704,590 B2 3/2004 Haldeman
6,708,058 B2 3/2004 Kim et al.
6,723,055 B2 4/2004 Hoffman
6,741,885 B1 * 5/2004 Park et al. 600/509
6,830,548 B2 12/2004 Bonnet et al.
6,890,306 B2 5/2005 Poezevera
6,892,095 B2 5/2005 Salo
6,964,641 B2 * 11/2005 Cho et al. 600/529
7,025,729 B2 4/2006 de Chazal et al.
7,025,730 B2 4/2006 Cho et al.
7,081,095 B2 7/2006 Lynn et al.
7,130,687 B2 10/2006 Cho et al.
7,155,278 B2 12/2006 King et al.
7,194,313 B2 3/2007 Libbus

7,207,945	B2	4/2007	Bardy	
7,225,013	B2 *	5/2007	Geva et al.	600/513
2001/0000346	A1	4/2001	Ruton et al.	
2001/0018547	A1	8/2001	Mechlenburg et al.	
2002/0035376	A1	3/2002	Bardy et al.	
2002/0035377	A1	3/2002	Bardy et al.	
2002/0035378	A1	3/2002	Bardy et al.	
2002/0035379	A1	3/2002	Bardy et al.	
2002/0035380	A1	3/2002	Rissmann et al.	
2002/0035381	A1	3/2002	Bardy et al.	
2002/0042629	A1	4/2002	Bardy et al.	
2002/0042630	A1	4/2002	Bardy et al.	
2002/0042634	A1	4/2002	Bardy et al.	
2002/0049475	A1	4/2002	Bardy et al.	
2002/0049476	A1	4/2002	Bardy et al.	
2002/0052636	A1	5/2002	Bardy et al.	
2002/0068958	A1	6/2002	Bardy et al.	
2002/0072773	A1	6/2002	Bardy et al.	
2002/0082652	A1	6/2002	Wentkowski et al.	
2002/0082658	A1	6/2002	Heinrich et al.	
2002/0091414	A1	7/2002	Bardy et al.	
2002/0095184	A1	7/2002	Bardy et al.	
2002/0103510	A1	8/2002	Bardy et al.	
2002/0107544	A1	8/2002	Ostroff et al.	
2002/0107545	A1	8/2002	Rissmann et al.	
2002/0107546	A1	8/2002	Ostroff et al.	
2002/0107547	A1	8/2002	Erlinger et al.	
2002/0107548	A1	8/2002	Bardy et al.	
2002/0107549	A1	8/2002	Bardy et al.	
2002/0107559	A1	8/2002	Sanders et al.	
2002/0120299	A1	8/2002	Ostroff et al.	
2002/0143264	A1	10/2002	Ding et al.	
2002/0169384	A1	11/2002	Kowallik et al.	
2003/0004546	A1	1/2003	Casey	
2003/0004552	A1	1/2003	Plombon et al.	
2003/0023175	A1	1/2003	Arzbaecher et al.	
2003/0036778	A1	2/2003	Ostroff et al.	
2003/0045904	A1	3/2003	Bardy et al.	
2003/0055348	A1	3/2003	Chazal et al.	
2003/0060848	A1	3/2003	Kieval et al.	
2003/0069609	A1	4/2003	Thompson	
2003/0088278	A1	5/2003	Bardy et al.	
2003/0088279	A1	5/2003	Rissmann et al.	
2003/0088280	A1	5/2003	Ostroff	
2003/0088281	A1	5/2003	Ostroff et al.	
2003/0088282	A1	5/2003	Ostroff	
2003/0088283	A1	5/2003	Ostroff	
2003/0088286	A1	5/2003	Ostroff et al.	
2003/0097153	A1	5/2003	Bardy et al.	
2003/0153953	A1	8/2003	Park et al.	
2003/0153954	A1	8/2003	Park et al.	
2003/0153955	A1	8/2003	Park et al.	
2003/0153956	A1	8/2003	Park et al.	
2003/0178031	A1	9/2003	Du Pen et al.	
2003/0195571	A1	10/2003	Burnes et al.	
2003/0199945	A1	10/2003	Ciulla	
2003/0204213	A1	10/2003	Jensen et al.	
2003/0212436	A1	11/2003	Brown	
2003/0216789	A1	11/2003	Deem et al.	
2004/0002742	A1	1/2004	Florio	
2004/0030362	A1	2/2004	Hill et al.	
2004/0059240	A1	3/2004	Cho et al.	
2004/0088027	A1	5/2004	Burnes et al.	
2004/0116981	A1 *	6/2004	Mazar	607/60
2004/0122488	A1 *	6/2004	Mazar et al.	607/60
2004/0128161	A1 *	7/2004	Mazar et al.	705/2
2004/0133079	A1 *	7/2004	Mazar et al.	600/300
2004/0176809	A1	9/2004	Cho et al.	
2004/0210261	A1	10/2004	King et al.	
2004/0249416	A1	12/2004	Yun et al.	
2005/0043652	A1	2/2005	Lovett et al.	
2005/0043772	A1 *	2/2005	Stahmann et al.	607/42
2005/0061315	A1	3/2005	Lee et al.	
2005/0065567	A1	3/2005	Lee et al.	
2005/0085865	A1	4/2005	Tehrani	
2005/0119711	A1	6/2005	Cho et al.	
2005/0145246	A1	7/2005	Hartley et al.	
2005/0288728	A1	12/2005	Libbus et al.	

FOREIGN PATENT DOCUMENTS

EP	1 172 125 A1	1/2002
EP	1172125	1/2002
WO	WO92/020402	11/1992
WO	WO00/017615	3/2000

OTHER PUBLICATIONS

U.S. Appl. No. 10/462,001, filed Jun. 13, 2003, Lovett et al.
U.S. Appl. No. 10/465,520, filed Nov. 18, 2004, Lindstrom.
U.S. Appl. No. 10/785,431, filed Feb. 24, 2004, Sanders.
U.S. Appl. No. 10/821,248, filed Apr. 8, 2004, Lovett et al.
U.S. Appl. No. 10/930,088, filed Aug. 31, 2004, Tockmann et al.
Balaban, Krzysztof W.; Cho, Yong; Mongeon, Luc; Liu, Lynn; Foldvary, Nancy; Burgess, Richard; Scharf, Reto Candinas, Christoph; and Wilkoff, Bruce L.; "Feasibility of Screening for Sleep Apnea using Pacemaker Impedance Sensor", Cleveland Clin. Fdn, Cleveland, OH, Medtronic, Inc., Minneapolis, MN, Strong Memorial Hosp., Rochester, NY and Univ. Hosp., Zurich, Switzerland, p. 313, 2001.
Bilgutay et al. A new concept in the treatment of hypertension utilizing an implantable electronical device: Baropacer. *Trans. Am. Society Artificial Internal Organs*. 1964. vol. 10, pp. 387-395.
Bradley et al, Cardiac Output Response To Continuous Positive Airway Pressure In Congestive Heart Failure, 145 Am. Rev. Respir. Dis. 377-382 (1992).
T. Douglas Bradley, MD and John S. Floras, MD,DPhIL, "Pathophysiologic and Therapeutic Implications of Sleep Apnea in Congestive Heart Failure", Toronto, Ontario, Canada, Journal of Cardiac Failure, vol. 2, No. 3, pp. 223-240, 1996.
Buda et al., Effect Of Intrathoracic Pressure On Left Ventricular Performance, 301 Engl. J. Med. 453-459 (1979). (Abstract only).
Calvin et al., Positive End-Expiratory Pressure (PEEP) Does Not Depress Left Ventricular Function In Patients With Pulmonary Edema, 124 Am. Rev. Respir. Dis. 121-128 (1981). (Abstract only).
Coleridge et al. "The distribution, connexions and histology of baroreceptors in the pulmonary artery, with some observations on the sensory innervation of the ductus arteriosus." *Physiology*. May 1961. vol. 156, pp. 591-602.
De Hoyos et al., Haemodynamic Effects Of Continuous Positive Airway Pressure In Humans With Normal And Impaired Left Ventricular Function, 88 Clin. Sci. (Lond). 173-8 (1995). (Abstract only).
Garrigue, S., MD et al., Benefit of Atrial Pacing in Sleep Apnea Syndrome, N. Engl. J. Med., vol. 346, No. 6, pp. 404-412 (Feb. 7, 2002).
Stephane Garrigue, MD, Philippe Bordier, MD, Meleze Hocini, MD, Pierre Jaïs, MD, Michel Haïssaguerre, MD and Jacques Clementy, MD, "Night Atrial Overdrive with DDD Pacing: A New Therapy for Sleep Apnea Syndrome", Hopital Cardiologique du Haut-Leveque, University of Bordeaux, Pessac-Bordeaux, France, p. 591.
Stephane Garrigue, Philippe Bordier, Meleze Hocini, Pierre Jais, Michel Haissaguerre and Jacques Clementy, Night Atrial Overdrive with DDD Pacing Results in a Significant Reduction of Sleep Apnea Episodes and QOL Improvement in Heart Failure Patients, Hosp. Cardiologique du Haut-Leveque, Bordeaux-Pessac, France, Abstract Session 25, p. 145, 2001.
Giardino et al., Respiratory Sinus Arrhythmia is Associated with the Efficiency of Pulmonary Gas Exchange in Healthy Humans, 284 Am. J. Physiol. H1585-1591 (2003). (Abstract only).
Rainer Gradaus M.D. et al., Nonthoracotomy Implantable Cardioverter Defibrillator Placement in Children: Use of a Subcutaneous Array Leads and Abdominally Placed Implantable Cardioverter Defibrillators in Children, J. of Cardiovascular Electrophysiology, vol. 12, No. 3, pp. 356-360 (Mar. 2001).
Hanson et al., Cardiac Gated Ventilation, 2433 SPIE 303-308 (1995).

Renee Hartz et al., New Approach to Defibrillator Insertion, J. Thoracic Cardiovascular Surgery, vol. 97, pp. 920-922 (1989).

Hilton, M.F., Bates, R.A., Godfery, K.R., Chappell, M.J. and Cayton, R.M., "Evaluation of Frequency and Time-frequency Spectral Analysis of Heart Rate Variability as a Diagnostic Marker of the Sleep Apnea Syndrome." Med Biol Eng Comput Nov. 1999, 37(6), 760-9. Abstract only.

Holger Steltner et al., Diagnosis of Sleep Apnea by Automatic Analysis of Nasal Pressure and Forced Oscillation Impedance. Am. Journal Respiratory Critical Care Medicine, vol. 165, pp. 940-944 (2002).

Javaheri, S., "A Mechanism of Central Sleep Apnea In Patients With Heart Failure." New England Journal of Medicine, Sep. 1999; 341(13):949-54.

S. Javaheri, MD, T.J.Parker, MD, J.D. Liming, MD, W.S. Corbett, BS, H. Nishiyama, MD, L. Wexler, MD and G.A. Roselle, MD, "Sleep Apnea in 81 Ambulatory Male Patients with Stable Heart Failure", from the Sleep Disorders Laboratory, Department of Veterans Affairs Medical Center, and the Department of Medicine, University of Cincinnati College of Medicine, Cincinnati, OH, pp. 2154-2159.

Kaye et al., Acute Effects Of Continuous Positive Airway Pressure On Cardiac Sympathetic Tone In Congestive Heart Failure, 103 Circulation 2336-24338 (2001).

Theofilos M. Kolettis, MD, PhD et al., Submammary Implantation of a Cardioverter-Defibrillator with a Nonthoractomy Lead System, Am. Heart J., vol. 126, pp. 1222-1223 (Nov. 1993).

Laude et al., Effects of Breathing Pattern on Blood Pressure and Heart Rate Oscillations in Humans, 20 Clin. Exp. Pharmol. Phisiol 619, 625 (1993). Abstract only.

Charles T. Leng et al., Lead Configuration for Defibrillator Implantation in a Patient with Congenital Heart Disease and a Mechanical Prosthetic Tricuspid Valve, PACE, vol. 24, No. 8, pp. 1291-1292 (Aug. 2001).

Lenique et al., Ventilatory And Hemodynamic Effects Of Continuous Positive Airway Pressure In Left Heart Failure, 155 Am. J. Respir. Crit. Care Med. 500-505 (1997). (Abstract only).

Lugaresi et al., Snoring, 39 Electroencephalogr. Clin. Neurophysiol. 59-64 (1975).

Mansfield, D. et al., Effects of Continuous Positive Airway Pressure on Lung Function in Patients with Chronic Obstructive Pulmonary Disease and Sleep Disordered Breathing, Respirology 365-70 (1999). Abstract only.

Mehta et al., Effects Of Continuous Positive Airway Pressure On Cardiac Volumes In Patients With Ischemic And Dilated Cardiomyopathy, 161 Am. J. Respir. Crit. Care Med. 128-134 (2000).

Naughton et al., Effects Of Continuous Positive Airway Pressure On Intrathoracic And Left Ventricular Transmural Pressure In Congestive Heart Failure, 91 Circulation 1725-1731 (1995), pp. 1-25.

Neil et al. "Effects of electrical stimulation of the aortic nerve on blood pressure and respiration in cats and rabbits under chloralose and nembutal anaesthesia." *Journal of Physiology*. Sep. 1949. vol. 109 (3-4), pp. 392-401.

Park & Pollock, Use of an Implantable Cardioverter Defibrillator in an Eight-Month-Old Infant with Ventricular Fibrillation Arising from a Myocardial Fibroma, PACE, vol. 22, No. 1, pp. 138-139 (Jan. 1999).

Peters et al. "Tempral and spatial summation caused by aortic nerve stimulation in rabbits. Effects of stimulation frequencies and amplitudes." *Journal of the Autonomic Nervous System*. 1989. vol. 27, pp. 193-205 (Abstract only).

Pinsky et al., Hemodynamic Effect Of Cardiac Cycle-Specific Increases In Intrathoracic Pressure, 6 J. Appl. Physiol. 604-612 (1986). (Abstract only).

Potkin et al., Effect of positive end-expiratory pressure on right and left ventricular function in patients with the adult respiratory distress syndrome, 135 Am. Rev. Respir. Dis. 307-311 (1987). (Abstract only).

Reddel et al., Analysis of Adherence to Peak Flow Monitoring When Recording of Data is Electronic, BMJ 146-147 (2002).

Roche, F., Gaspoz, J.M., Court-Fortune, I., Minini, P., Pichot, V., Duvermney, D., Costes, F., Lacour, J.R., Barthelemy and J.C., "Screening of Obstructive Sleep Apnea Syndrome by Heart Rate Variability Analysis." Circulation Sep. 28, 1999; 100(13):1411-5.

Sato et al. "Novel Therapeutic Strategy against Central Baroreflex Failure: A Bionic Baroreflex System." *Circulation*. Jul. 1999 vol. 100, pp. 299-304.

Satoh et al., "Role of Hypoxic Drive in Regulation of Postapneic Ventilation During Sleep in Patients with Obstructive Sleep Apnea", Am Rev Respir Dis, Mar. 1991 143 (3): 481-485.

Scharf, Effects Of Continuous Positive Airway Pressure On Cardiac Output In Experimental Heart Failure, 19 Sleep S240-2 (1996). (Abstract only).

John C. Schuder et al., Experimental Ventricular Defibrillation with an Automatic and Completely Implanted System, Trans. Am. Soc. Artif. Int. Organs, vol. 16, pp. 207-212 (1970).

John C. Schuder et al., Transthoracic Ventricular Defibrillation in the Dog with Truncated and Untruncated Exponential Stimuli, IEEE Trans. On Bio-Medical Engin., vol. BME-18, No. 6, pp. 410-415 (Nov. 1971).

John C. Schuder et al., Ventricular Defibrillation in the Dog Using Implanted and Partially Implanted Electrode Systems, Am. J. of Cardiology, vol. 33, pp. 243-247 (Feb. 1974).

Karel Smits & Marek Malik, Defibrillation Threshold (DFT) Model of a Fully Subcutaneous ICD System, Europace Supplements, vol. 2, Jun. 2001 at col. 778, p. B83.

N. Spector al. "Assessing and Managing Dyspnea." The University of Chicago Hospitals. Nursing Spectrum-Career Fitness Online. Self-Study Modules. pp. 1-13. http://nsweb.nursingspectrum.com/.

Stirbis et al., Optmizing the Shape of Implanted Artificial Pacemakers, Kaunas Medical Institute. Translated from Meditsinskaya Tekhnika, No. 6, pp. 25-27 (1986).

Thrasher et al. "Unloading arterial baroreceptors causes neurogenic hypertension." *American Journal Physiol. Regulatory Integrative Comp. Physiol.* 2002. vol. 282, R1044-R1053.

Vanninen, E., Tuunainen, A., Kansanen, M., Uusitupa, M. and Lansimies, E., "Cardiac Sympathovagal Balance During Sleep Apnea Episodes." Clin Physiol May 1996; 16(3):209-16.

Weber et al., Effects of CPAP and BIPAP on stroke volume in patients with obstructive sleep apnea syndrome. Pneumolgie Mar. 1995;49(3):233-5. Translated Abstract only.

Terry Young, Ph.D., Mari Palta, Ph.D., Jerome Dempsey, Ph.D., James Skatrud, MD, Steven Weber, Ph.D., and Safwan Badr, MD. "The Occurrence of Sleep-disordered Breathing Among Middle-aged Adults", The New England Journal of Medicine, vol. 328, No. 17, pp. 1230-1235.

* cited by examiner

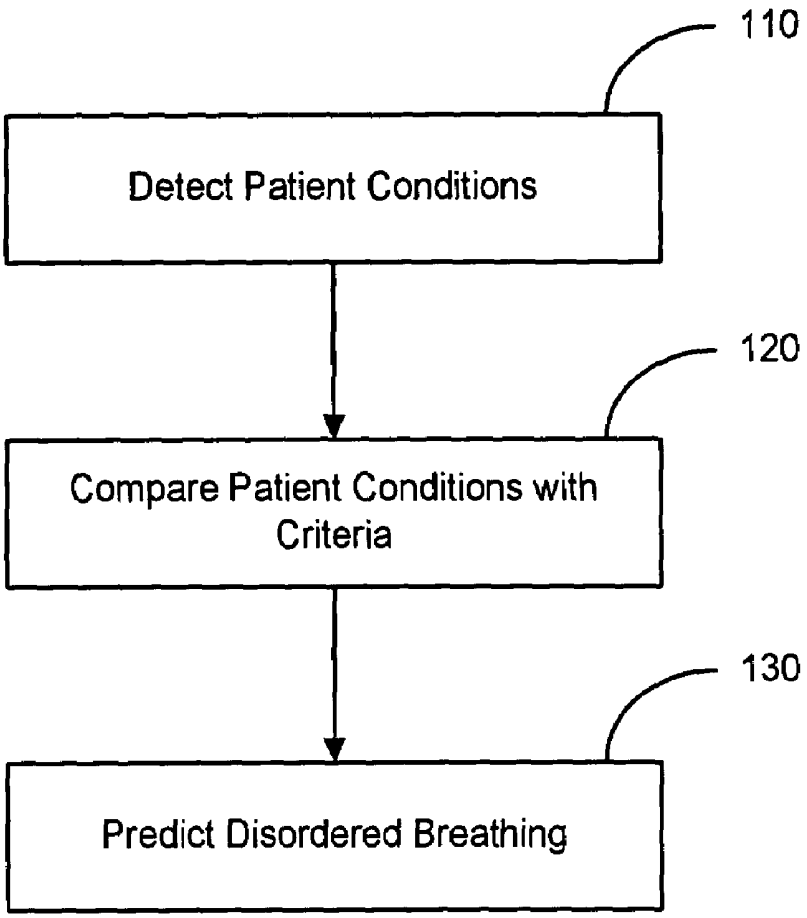

110
Detect Patient Conditions
120
Compare Patient Conditions with Criteria
130
Predict Disordered Breathing

Figure 1

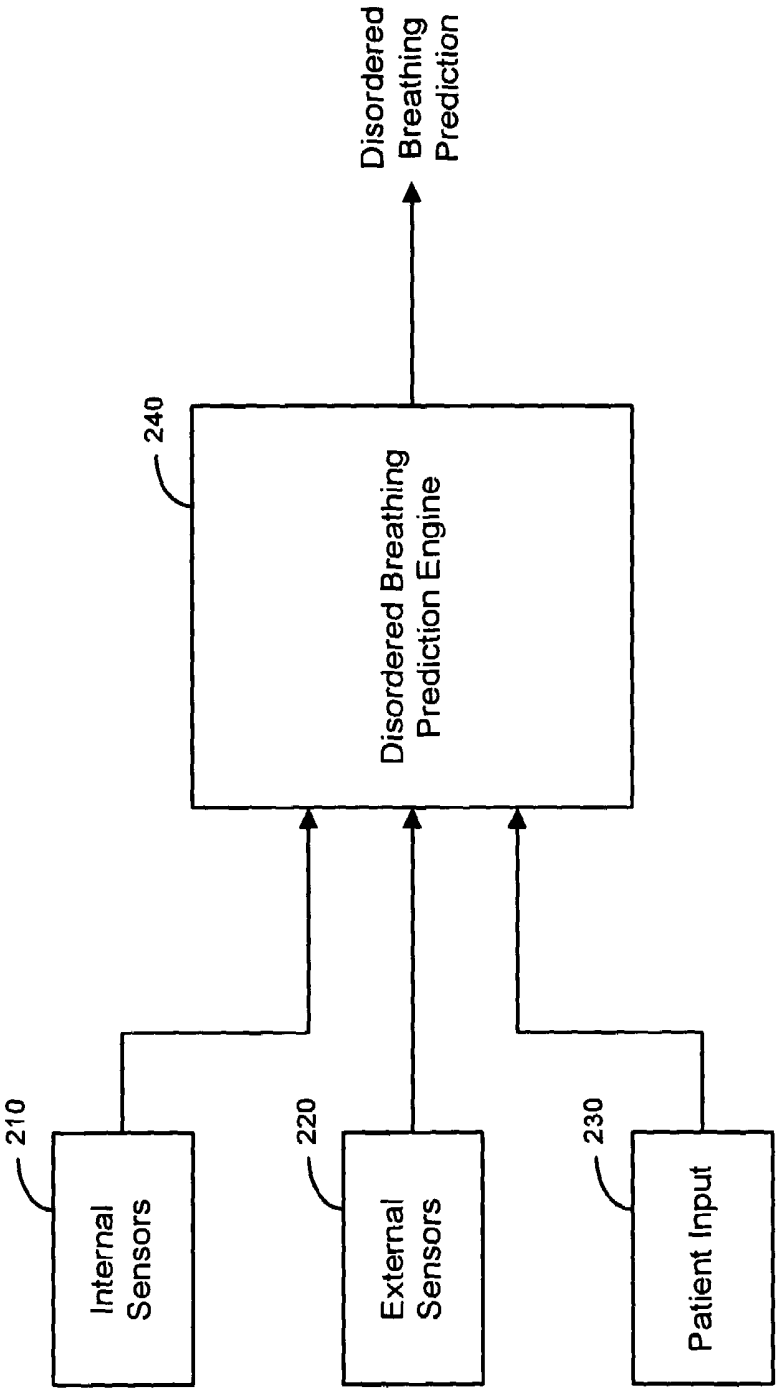

Disordered Breathing Prediction
240
Disordered Breathing Prediction Engine
210
Internal Sensors
220
External Sensors
230
Patient Input

Figure 2

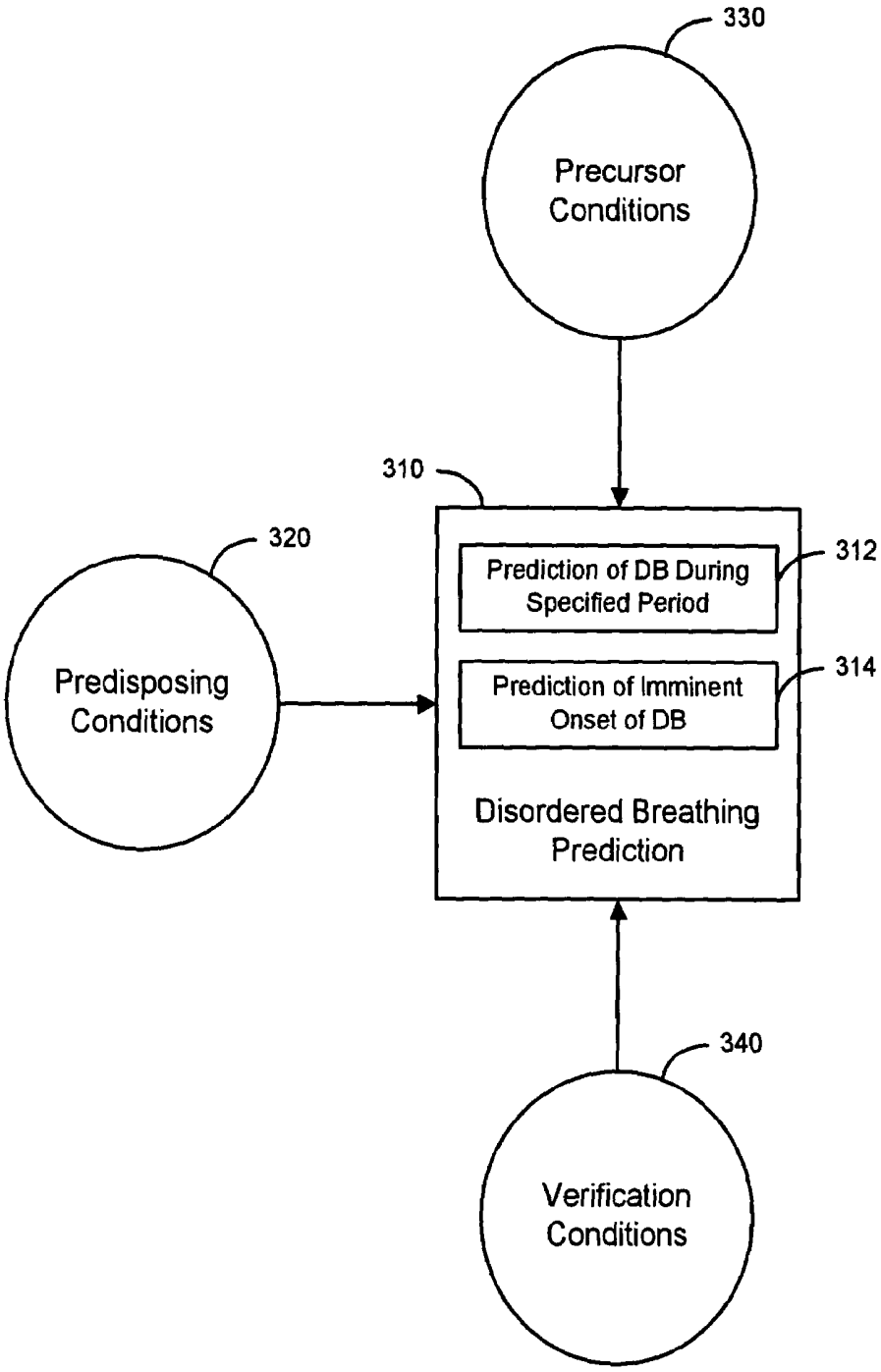

330
Precursor Conditions
310
320
Predisposing Conditions
Prediction of DB During Specified Period
312
Prediction of Imminent Onset of DB
314
Disordered Breathing Prediction
340
Verification Conditions

Figure 3

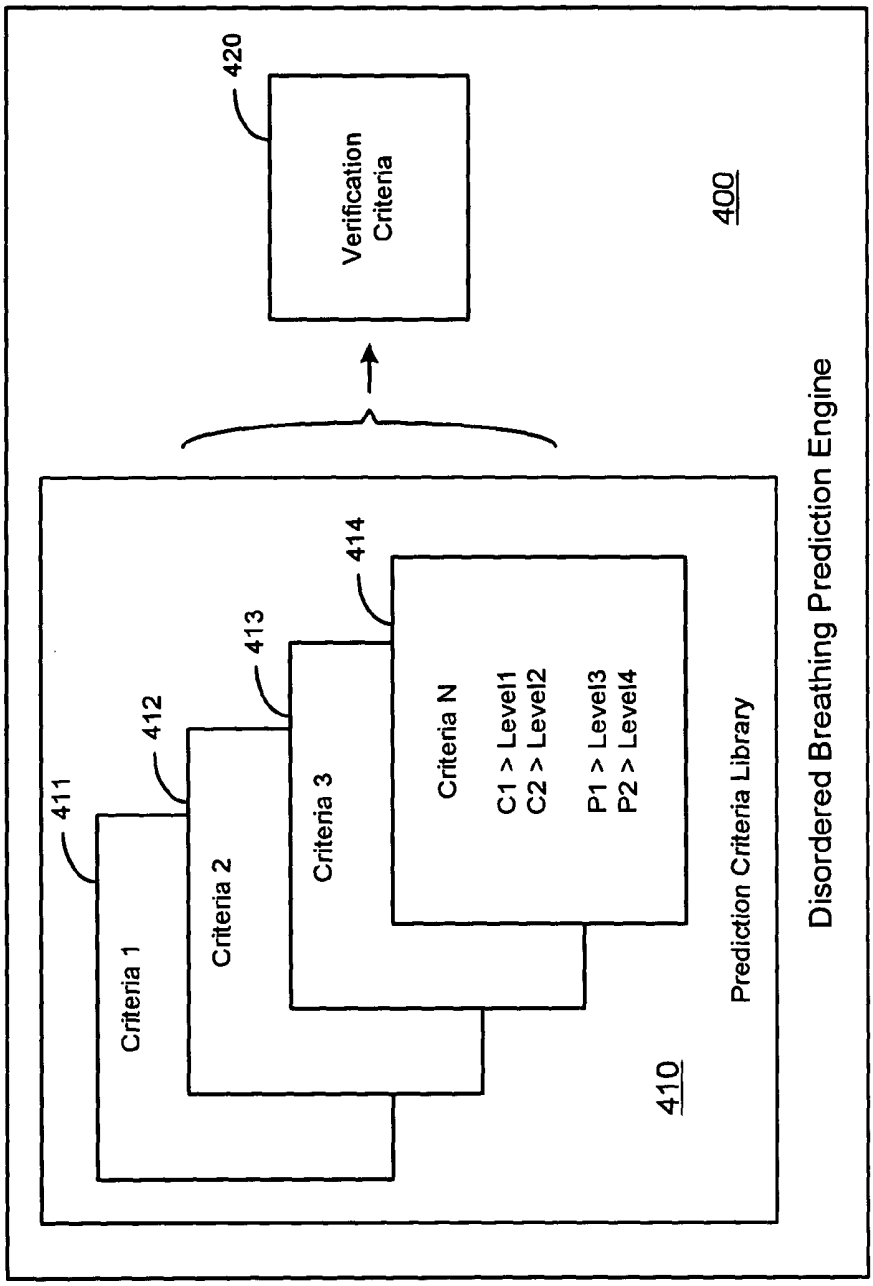

Disordered Breathing Prediction Engine
400
Verification Criteria
420
Prediction Criteria Library
410
Criteria 1
411
Criteria 2
412
Criteria 3
413
Criteria N
414
C1 > Level1
C2 > Level2
P1 > Level3
P2 > Level4

Figure 4

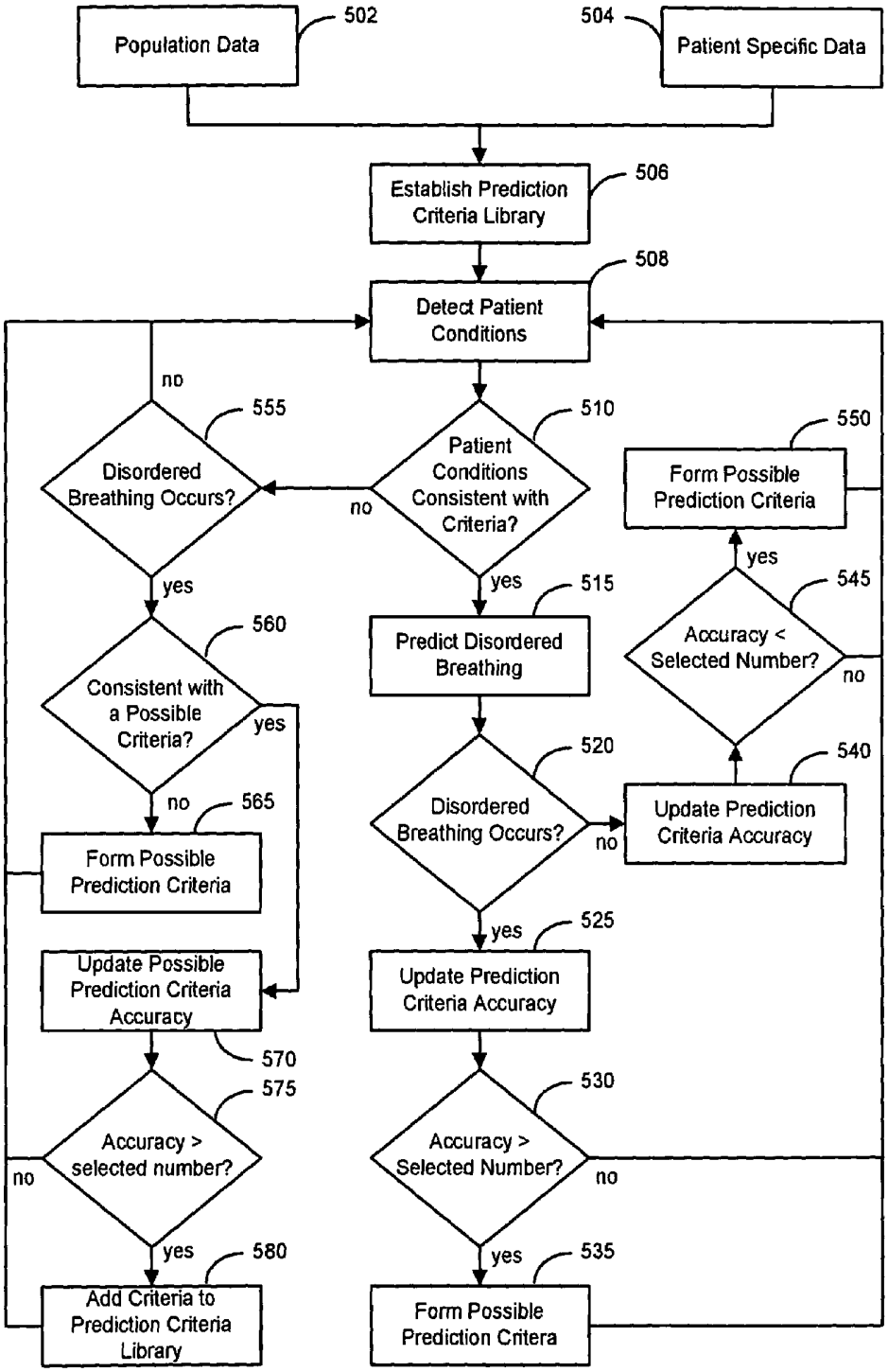

Population Data
502
Patient Specific Data
504
Establish Prediction Criteria Library
506
Detect Patient Conditions
508
Patient Conditions Consistent with Criteria?
510
Disordered Breathing Occurs?
555
Predict Disordered Breathing
515
Disordered Breathing Occurs?
520
Update Prediction Criteria Accuracy
525
Accuracy > Selected Number?
530
Form Possible Prediction Critera
535
Form Possible Prediction Criteria
550
Accuracy < Selected Number?
545
Update Prediction Criteria Accuracy
540
Consistent with a Possible Criteria?
560
Form Possible Prediction Criteria
565
Update Possible Prediction Criteria Accuracy
570
Accuracy > selected number?
575
Add Criteria to Prediction Criteria Library
580
yes
no

Figure 5

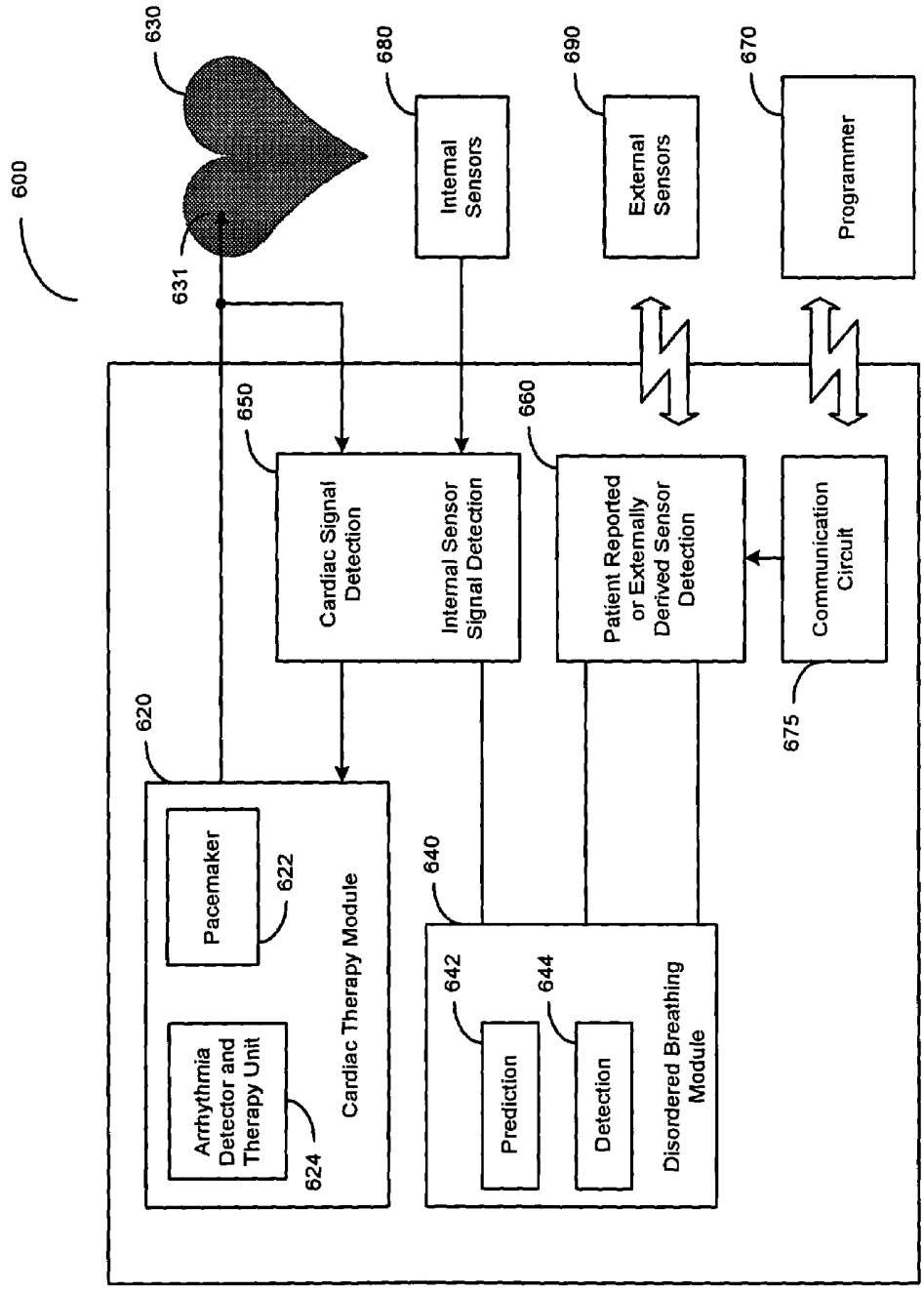

600
630
631
680
Internal Sensors
690
External Sensors
670
Programmer
650
Cardiac Signal Detection
Internal Sensor Signal Detection
660
Patient Reported or Externally Derived Sensor Detection
Communication Circuit
675
620
Pacemaker
622
Arrhythmia Detector and Therapy Unit
624
Cardiac Therapy Module
640
642
Prediction
644
Detection
Disordered Breathing Module

Figure 6

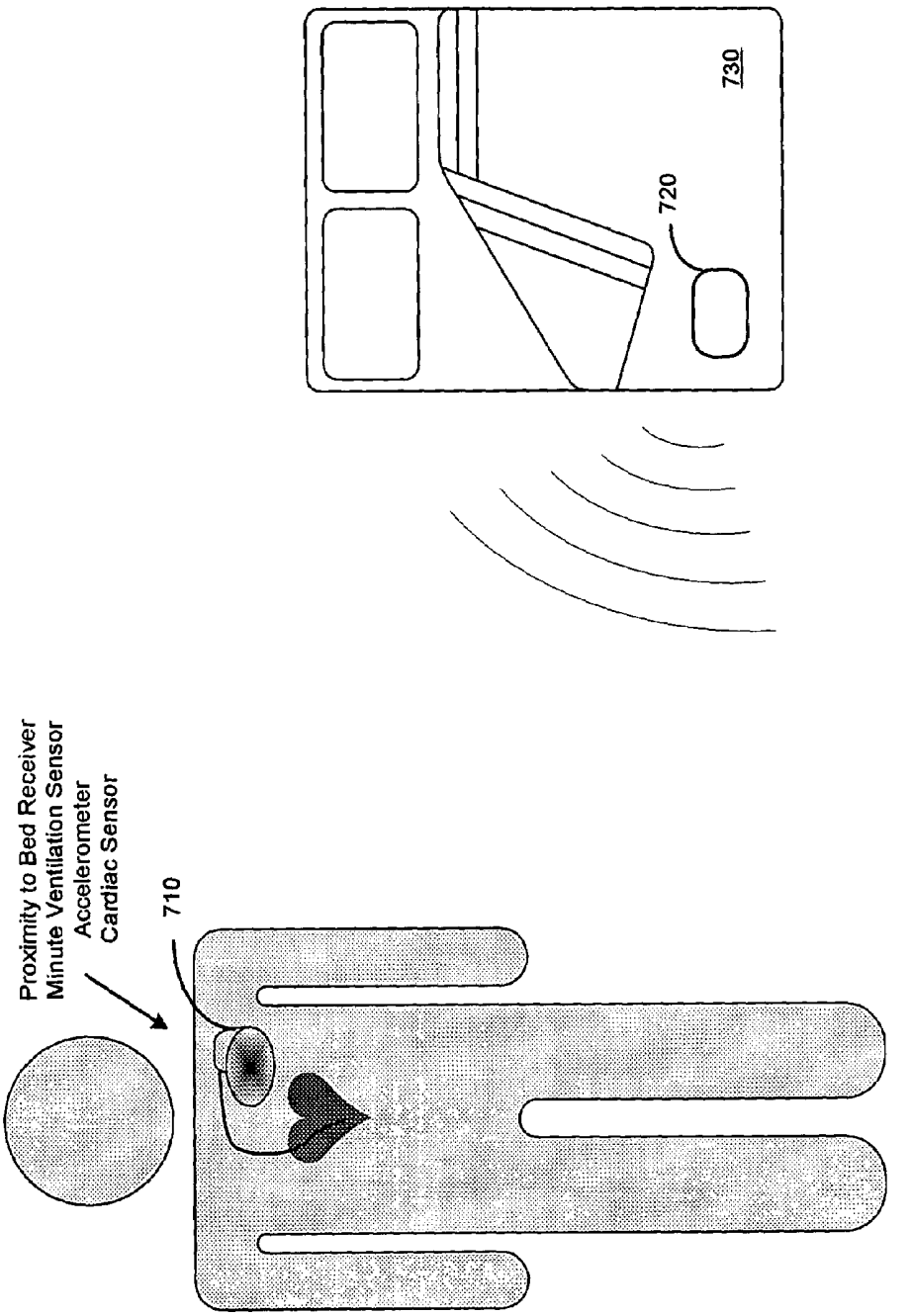

730
720
Proximity to Bed Receiver
Minute Ventilation Sensor
Accelerometer
Cardiac Sensor
710

Figure 7

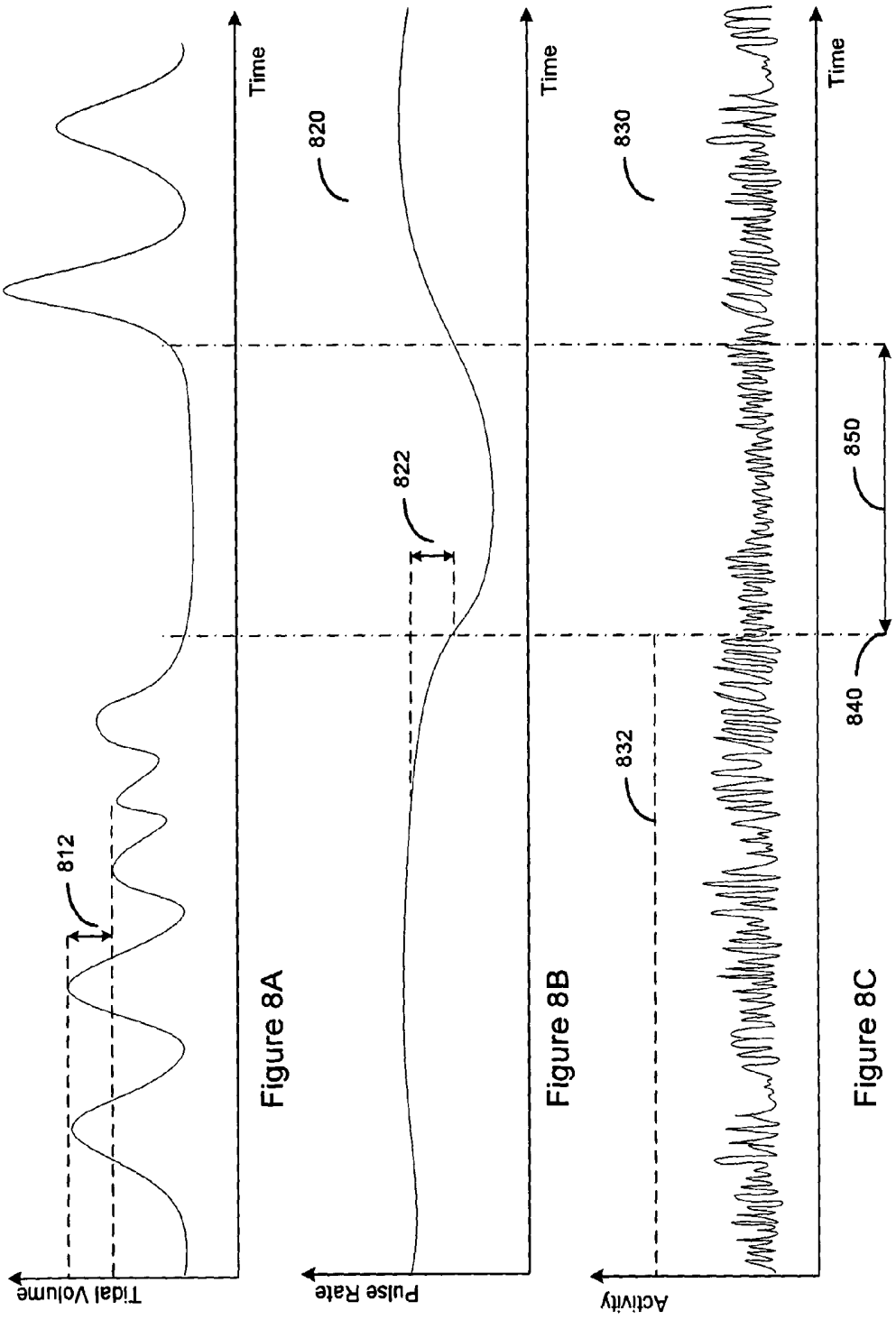


Figure 8A

Figure 8B

Figure 8C

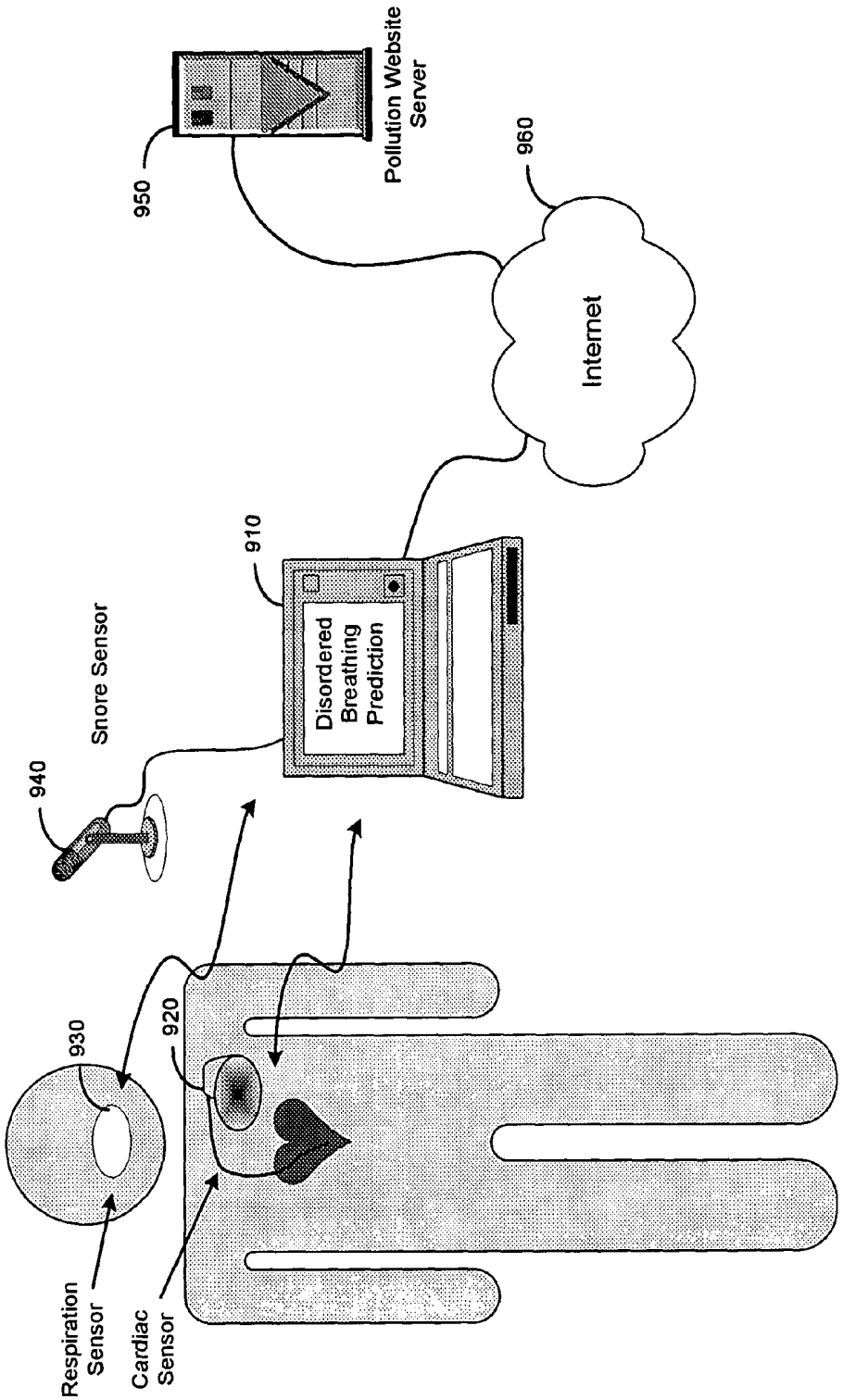

Pollution Website Server
950
960
Internet
910
Disordered Breathing Prediction
Snore Sensor
940
930
920
Respiration Sensor
Cardiac Sensor

Figure 9

PREDICTION OF DISORDERED BREATHING

FIELD OF THE INVENTION

The present invention relates generally to prediction of disordered breathing using an implantable device.

BACKGROUND OF THE INVENTION

Disordered breathing is associated with a wide spectrum of respiratory conditions that involve disruption of the normal respiratory cycle. Although disordered breathing typically occurs during sleep, the condition may also occur while the patient is awake. Respiratory disruption can be particularly serious for patients concurrently suffering from cardiovascular deficiencies, such as congestive heart failure. Unfortunately, disordered breathing is often undiagnosed. If left untreated, the effects of disordered breathing may result in serious health consequences for the patient.

Various types of disordered respiration have been identified, including apnea, hypopnea, tachypnea, and periodic breathing. Apnea is a fairly common disorder characterized by periods of interrupted breathing. Apnea is typically classified based on its etiology. One type of apnea, denoted obstructive apnea, occurs when the patient's airway is obstructed by the collapse of soft tissue in the rear of the throat. Central apnea is caused by a derangement of the central nervous system control of respiration. The patient ceases to breathe when control signals from the brain to the respiratory muscles are absent or interrupted. Mixed apnea is a combination of the central and obstructive apnea types. Regardless of the type of apnea, people experiencing an apnea event stop breathing for a period of time. The cessation of breathing may occur repeatedly during sleep, sometimes hundreds of times a night and sometimes for a minute or longer.

In addition to apnea, other types of disordered respiration have been identified, including hypopnea (shallow breathing), tachypnea (rapid breathing), hyperpnea (heavy breathing), and dyspnea (labored breathing). Combinations of the respiratory cycles described above may be observed, including, for example, periodic breathing and Cheyne-Stokes respiration (CSR). Periodic breathing is characterized by cyclic respiratory patterns that may exhibit rhythmic rises and falls in tidal volume. Cheyne-Stokes respiration is a specific form of periodic breathing wherein the tidal volume decreases to zero resulting in apneic intervals. The breathing interruptions of periodic breathing and CSR are predominantly central in nature but may occasionally be obstructive in nature. Cheyne-Stokes respiration is frequently observed in patients with congestive heart failure (CHF) and is associated with an increased risk of accelerated CHF progression.

Although disordered breathing is more common during sleep, disordered breathing may also occur while the patient is awake. When disordered breathing occurs during sleep, the patient may briefly arouse in order to resume breathing. The frequent interruptions during sleep result in extremely fragmented sleep of poor quality. An adequate duration and quality of sleep is required to maintain physiological homeostasis. Untreated, disordered breathing may have a number of adverse health and quality of life consequences ranging from high blood pressure and other cardiovascular diseases to cognitive impairment, headaches, impaired driving skills resulting in increased vehicular accidents, and degradation of social and work related activities.

SUMMARY OF THE INVENTION

Various embodiments of present invention involve methods, devices, and systems for predicting disordered breathing.

An embodiment of the invention involves an automated method of predicting disordered breathing in a patient. One or more conditions associated with disordered breathing are detected and compared to one or more sets of disordered breathing prediction criteria. Disordered breathing is predicted based on the comparison. At least one of comparing the conditions to the disordered breathing prediction criteria and predicting the disordered breathing is performed at least in part implantably.

In another embodiment of the invention, a method for predicting disordered breathing involves detecting one or more conditions predisposing a patient to disordered breathing. The predisposing conditions are compared to one or more sets of disordered breathing prediction criteria. Disordered breathing is predicted based on the comparison. At least one of comparing the predisposing conditions to the one or more sets of disordered breathing prediction criteria and predicting the disordered breathing is performed at least in part implantably.

Yet another embodiment of the invention involves detecting one or more precursor conditions associated with disordered breathing. The precursor conditions are compared to one or more sets of disordered breathing prediction criteria. Disordered breathing is predicted based on the comparison. At least one of comparing the precursor conditions to the one or more sets of disordered breathing prediction criteria and predicting the disordered breathing is performed at least in part implantably.

In a further embodiment of the invention, a medical device includes a detector system and a prediction engine. The detector system is configured to detect one or more conditions associated with disordered breathing. The prediction engine is coupled to the detector system and is configured to compare the one or more detected conditions to one or more sets of disordered breathing prediction criteria and to predict disordered breathing based on the comparison. The prediction engine includes at least one implantable component.

Another embodiment of the invention involves an automated disordered breathing prediction system. The system includes means for detecting one or more conditions associated with disordered breathing, means for comparing the detected one or more conditions to one or more sets of disordered breathing prediction criteria and means for predicting disordered breathing based on the comparison. At least one of the means for comparing and the means for predicting includes an implantable component.

In yet another embodiment of the invention, an automated system for predicting disordered breathing includes means for detecting conditions predisposing the patient to disordered breathing. The system further includes means for comparing the predisposing conditions to one or more sets of disordered breathing prediction criteria and means for predicting disordered breathing based on the comparison. At least one of the means for comparing the predisposing conditions to the one or more sets of prediction criteria, and the means for predicting disordered breathing includes an implantable component.

In yet a further embodiment of the invention, an automated system for predicting disordered breathing includes means for detecting precursor conditions associated with disordered breathing. The system further includes means for comparing the precursor conditions to one or more sets of disordered breathing prediction criteria and means for predicting disor-

dered breathing based on the comparison. At least one of the means for comparing the precursor conditions to the one or more sets of disordered breathing prediction criteria and means for predicting disordered breathing includes an implantable component.

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

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a flow graph of a method for predicting disordered breathing in accordance with embodiments of the invention;

FIG. **2** is a block diagram of a system for predicting disordered breathing in accordance with embodiments of the invention;

FIG. **3** illustrates conditions that are used to predict disordered breathing according to embodiments of the invention;

FIG. **4** is a block diagram of a disordered breathing prediction engine in accordance with embodiments of the invention;

FIG. **5** is a flow graph illustrating a method of updating a prediction criteria library according to embodiments of the invention;

FIG. **6** is a block diagram of a cardiac rhythm management system incorporating a disordered breathing prediction engine in accordance with embodiments of the invention;

FIG. **7** is a diagram illustrating a system for predicting disordered breathing in accordance with embodiments of the invention;

FIG. **8**A illustrates a representative graph of tidal volume signal used in connection with disordered breathing prediction in accordance with embodiments of the invention;

FIG. **8**B illustrates a representative graph of heart rate signal used in connection with disordered breathing prediction in accordance with embodiments of the invention;

FIG. **8**C illustrates a representative graph of an activity signal used in connection disordered breathing prediction in accordance with embodiments of the invention; and

FIG. **9** is a diagram illustrating a system for predicting disordered breathing in accordance with embodiments of the invention.

While the invention is amenable to various modifications and alternative forms, specifics thereof have been shown by way of example in the drawings and will be described in detail below. It is to be understood, however, that the intention is not to limit the invention to the particular embodiments described. On the contrary, the invention is intended to cover all modifications, equivalents, and alternatives falling within the scope of the invention as defined by the appended claims.

DETAILED DESCRIPTION OF VARIOUS EMBODIMENTS

In the following description of the illustrated embodiments, references are made to the accompanying drawings which form a part hereof, and in which are shown, by way of illustration, various embodiments by which the invention may be practiced. It is to be understood that other embodiments may be utilized. Structural and functional changes may be made without departing from the scope of the present invention.

A significant percentage of patients between the ages of 30 and 60 years experience some symptoms of disordered breathing. Sleep disordered breathing is associated with excessive daytime sleepiness, systemic hypertension, increased risk of stroke, angina, and myocardial infarction. Disordered breathing is particularly prevalent among congestive heart failure patients, and may contribute to the progression of heart failure.

Disordered breathing occurs most often when the patient is asleep and may result in highly fragmented sleep. Methods for collecting data and evaluating sleep quality are described in commonly owned U.S. Patent Application entitled "Sleep Quality Data Collection and Evaluation," identified under attorney docket number GUID.058PA, concurrently filed with this patent application and incorporated by reference in its entirety.

Various therapies have been developed to treat central or obstructive disordered breathing episodes. Obstructive apnea has been associated with prolapse of the tongue and its surrounding structure into the pharynx, thus occluding the respiratory pathway. A commonly prescribed treatment for obstructive apnea is continuous positive airway pressure (CPAP). A CPAP device delivers air pressure through a nasal mask worn by the patient. The application of continuous positive airway pressure keeps the patient's throat open, reducing or eliminating the obstruction causing apnea.

Another therapy directed to treating obstructive apnea involves nerve stimulation. Prolapse of the tongue muscles has been attributed to diminishing neuromuscular activity of the upper airway. A treatment for obstructive sleep apnea involves compensating for the decreased muscle activity by electrical activation of the tongue muscles. The hypoglossal nerve innervates the protrusor and retractor tongue muscles. An appropriately applied electrical stimulation to the hypoglossal nerve may prevent backward movement of the tongue, thus preventing the tongue from obstructing the airway.

Cardiac stimulation may be used as a therapy for disordered breathing. A therapy method using cardiac pacing is described in commonly owned U.S. Publication No. 2005/0039745, which was filed concurrently with this patent application, and incorporated herein by reference in its entirety. The cardiac stimulation methods described use adaptive therapy to reduce an impact of the therapy on the patient.

The present invention involves a method and system for predicting disordered breathing. Such a prediction may be used for example, for diagnostic purposes, to alert the patient that disordered breathing is likely to occur. Alternatively or additionally, the prediction may facilitate therapy by allowing the patient to take preventative steps, for example, by beginning a predetermined therapy regimen. Further, the prediction of disordered breathing may also be used to automatically initiate disordered breathing therapy to prevent or mitigate the predicted disordered breathing.

The flowchart of FIG. **1** illustrates a method for predicting disordered breathing according to various embodiments of the invention. The method involves detecting **110** conditions associated with disordered breathing and comparing **120** the detected conditions to one or more sets of disordered breathing prediction criteria. The detected conditions may include, for example, one or more of the representative set of conditions listed in Table 1 below. If the detected conditions are consistent with a set of prediction criteria, disordered breathing is predicted **130**. Optionally, a set of verification criteria may be checked prior to the final prediction determination to enhance prediction accuracy.

Conditions associated with disordered breathing used in connection with disordered breathing detection may include both physiological and contextual (e.g. non-physiological) conditions. The physiological conditions may include a broad category of conditions associated with the internal physiological conditions of the patient. Physiological conditions may be further subdivided, for example, into conditions of the cardiovascular, respiratory, and nervous systems, blood chemistry, body-related, e.g., posture and activity, in addition to respiration and/or sleep quality, and comfort during therapy as reported by the patient.

Contextual conditions generally encompass patient-external or background conditions. Contextual conditions may be broadly defined to include, for example, present environmental conditions such as patient location, ambient temperature, humidity, air pollution index, as well as historical/background conditions relating to the patient, including the patient's normal sleep time and the patient's medical history, for example. Methods and systems for detecting some contextual conditions, including, for example, proximity to bed detection, are described in commonly owned U.S. Publication No. 2004/0073093, which is incorporated by reference herein in its entirety.

Table 1 provides a representative set of conditions that may be used in connection with predicting disordered breathing. Table 1 also provides examples of sensing methods that may be employed to sense the conditions.

TABLE 1

Condition Type		Condition	Sensor type or Detection method
Physiological	Cardiovascular System	Heart rate	EGM, ECG
		Heart rate variability	
		QT interval	
		Ventricular filling pressure	Intracardiac pressure sensor
		Blood pressure	Blood pressure sensor
	Respiratory System	Snoring	Accelerometer
			Microphone
		Respiration pattern	Transthoracic impedance
		(Tidal volume Minute ventilation	sensor (AC)
		Respiratory rate)	
		Patency of upper airway	Intrathoracic impedance sensor
		Pulmonary congestion	Transthoracic impedance sensor (DC)
	Nervous System	Sympathetic nerve activity	Muscle sympathetic nerve Activity sensor
		Brain activity	EEG
	Blood Chemistry	CO2 saturation	Blood analysis
		O2 saturation	
		Blood alcohol content	
		Adrenalin	
		B-type Natriutetic Peptide (BNP)	
		C-Reactive Protein	
		Drug/Medication/Tobacco use	
	Muscle System	Muscle atonia	EMG
		Eye movement	EOG
		Patient activity	Accelerometer, MV, etc.
		Limb movements	Accelerometer, EMG
		Jaw movements	
Contextual (non-physiological)	Environmental	Ambient temperature	Thermometer
		Humidity	Hygrometer
		Pollution	Air quality website
		Time	Clock
		Barometric pressure	Barometer
		Ambient noise	Microphone
		Ambient light	Photodetector
	Body-related	Posture	Posture sensor
		Altitude	Altimeter
		Location	GPS, proximity sensor
		Proximity to bed	Proximity to bed sensor
	Historical/Background	Historical sleep time	Patient input, previously detected sleep onset times
		Medical history	Patient input device
		Age	
		Recent exercise	
		Weight	
		Gender	
		Body mass index	
		Neck size	
		Emotional state	
		Psychological history	
		Daytime sleepiness	
		Patient perception of sleep quality	
		Drug, alcohol, nicotine use	

FIG. **2** illustrates a block diagram of a system for detecting conditions associated with disordered breathing and predicting disordered breathing in accordance with embodiments of the invention. The system may use internal sensors **210**, implanted within the body of the patient, to detect physiological conditions affecting the patient. For example, the system may detect heart rate, tidal volume, and/or other physiological signals using an intracardiac electrocardiogram (EGM) signal detector and transthoracic impedance sensor that are part of an implanted cardiac rhythm management system such as a cardiac pacemaker or defibrillator.

The system may further use external sensors **220** and detect physiological or contextual conditions using signals from the external sensors **220**. In one scenario whether the patient is snoring may be useful in predicting disordered breathing. Snoring noises may be sensed using an external microphone or an implanted accelerometer. Signals representing the snoring noises may be transmitted from the sensors to the system and used to detect that the patient is snoring. In another situation, temperature and humidity may be factors in the patient's disordered breathing. Signals from temperature and humidity sensors may be used to aid in the prediction of disordered breathing.

Additionally, the system may use information input **230** by the patient to inform the disordered breathing prediction system of patient conditions. In various embodiments, the patient's medical history, self-described medication use, alcohol or tobacco use, day-time sleepiness, or perceptions of sleep quality over the past few nights may be useful in connection with the disordered breathing prediction.

Signals from one or more of the internal sensors **210**, external sensors **220**, and patient input **230** may be coupled to a disordered breathing prediction engine **240** for prediction analysis. In one example, the conditions associated with disordered breathing may be sensed and processed using implantable sensors **210** and the prediction analysis performed by an external disordered breathing prediction engine **240**. Some or all of the implantable sensors **210** may have remote communication capabilities, such as a wireless proprietary or a wireless Bluetooth communications link. The wireless communications link couples the implantable sensor or sensors **210** to the external disordered breathing prediction engine **240**. Electrical signals representing conditions associated with disordered breathing are produced by the implantable sensors **210** and transmitted to the external disordered breathing prediction engine **240**.

In another example, a disordered breathing prediction system is configured to include an implantable therapy device incorporating a disordered breathing prediction engine **240** and one or more external sensors **220**. Signals representing the detected conditions may be transmitted from the external sensors to the prediction engine **240** over a wireless communication link. The above examples provide only a few of the many possible configurations that may be used to predict disordered breathing.

In yet another example, internal sensors **210** may be coupled to an internal prediction engine **240** using a lead system. Various combinations of internal sensors **210**, external sensors **220**, and patient input devices **230** coupled through wireless or wired connections to the prediction engine **240** are possible.

Each of the conditions listed in Table 1 may serve a variety of purposes in predicting disordered breathing. Various subsets of the conditions listed in Table 1 may be detected as predisposing conditions, precursor conditions, and/or verification conditions useful in the prediction of disordered breathing. In one example, information regarding sleep onset may be employed in prediction of sleep disordered breathing. A subset of the conditions listed in Table 1 may be used to detect whether the patient is asleep and to track the various stages of sleep. Another subset of the conditions may be employed to detect and classify disordered breathing episodes. Table 2 below provides further examples of how the physiological and contextual conditions of the patient may be used in disordered breathing prediction.

TABLE 2

Condition	Examples of how condition is used in disordered breathing prediction
Heart rate	Decrease in heart rate may indicate disordered breathing episode. Decrease in heart rate may indicate the patient is asleep.
Heart rate variability	May be used to determine sleep state
Ventricular filling pressure	May be used to identify/predict pulmonary congestion associated with respiratory disturbance.
Blood pressure	Swings in on-line blood pressure measures are associated with apnea.
Snoring	Snoring is associated with a higher incidence of obstructive sleep apnea and may be used to detect disordered breathing.
Respiration signals/respiration patterns	Respiration patterns may be used to detect disordered breathing episodes. Respiration patterns may be used to determine the type of disordered breathing. Respiration patterns may be used to detect that the patient is asleep. Hyperventilation may be used to predict disordered breathing. Previous episodes of disordered breathing may be used to predict further episodes. One form of disordered breathing may be used to predict another form of disordered breathing
Patency of upper airway	Patency of upper airway is related to obstructive sleep apnea and may be used to detect episodes of obstructive sleep apnea.
Pulmonary congestion	Pulmonary congestion is associated with respiratory disturbances.
Sympathetic nerve activity	End of apnea associated with a spike in SNA
CO2 saturation	Low CO2 levels initiate central apnea.
O2 saturation	O2 desaturation occurs during severe apnea/hypopnea episodes.
Blood alcohol content	Alcohol tends to increase incidence of snoring & obstructive apnea.
Adrenalin	End of apnea associated with a spike in blood adrenaline.
BNP	A marker of heart failure status, which is associated with Cheyne-Stokes Respiration

TABLE 2-continued

Condition	Examples of how condition is used in disordered breathing prediction
C-Reactive Protein	A measure of inflammation that may be related to apnea.
Drug/Medication/Tobacco use	These substances may affect incidence of both central & obstructive apnea.
Muscle atonia	Muscle atonia may be used to detect REM and non-REM sleep.
Eye movement	Eye movement may be used to detect REM and non-REM sleep.
Temperature	Ambient temperature may be a condition predisposing the patient to episodes of disordered breathing.
Humidity	Humidity may be a condition predisposing the patient to episodes of disordered breathing.
Pollution	Pollution may be a condition predisposing the patient to episodes of disordered breathing.
Posture	Posture may be used to determine if the patient is asleep. Posture may be a condition predisposing the patient to episodes of disordered breathing.
Activity	Patient activity may be used in relation to sleep detection.
Sleep stage	NREM sleep is associated with a higher incidence of DB episodes
Location	Patient location may used to determine if the patient is in bed as a part of sleep detection.

FIG. **3** conceptually illustrates how conditions such as those listed in Table 1 and/or 2 may be used in predicting disordered breathing **310** according to embodiments of the invention. In one embodiment, the system tracks one or more of the conditions listed in Table 1 and/or 2 to predict disordered breathing. For example, over the course of a period of time, e.g., at least about a 16 hour window preceding and including the patient's historical sleep time, the system may track one or more conditions to determine the presence and/or level of each particular condition.

In one implementation, the system tracks conditions that have been determined to predispose **320** the patient to an attack of disordered breathing. Predisposing conditions represent conditions statistically associated with an onset of disordered breathing. Prediction of disordered breathing based on predisposing conditions may be performed in real-time. The presence of one or more predisposing conditions consistent with prediction criteria may indicate that disordered breathing is likely to occur within the next time period, such as during the current sleep period, or during the next time period of about eight hours. For example, the conditions predisposing the patient to disordered breathing may include the air pollution index of the patient's environment downloaded from an air quality website, recent tobacco use reported by the patient, the degree of the patient's pulmonary congestion detected by an implanted transthoracic impedance sensor, as well as other internally or externally detected predisposing conditions.

Additionally, or alternatively, the system may use previous episodes of disordered breathing to determine that the patient is predisposed to further episodes of disordered breathing within particular time period, such as during the night. For example, previous episodes of disordered breathing during a first interval within a sleep period may be an indication that additional episodes are likely to occur in a second and subsequent interval within the same sleep period. Therefore, the system may use the type, duration, frequency, and severity of the previous disordered breathing episodes to inform the disordered breathing prediction analysis.

The occurrence of one type of disordered breathing may predict another type. For example, the occurrence of obstructive sleep apnea episodes may be used to predict that central sleep apnea will occur later during the night. In another example, the occurrence of a hypopnea episode may be used to predict an apnea episode. Quantification of the severity, frequency, and duration of disordered breathing may be accomplished using any of a number of disturbed breathing measures, including, for example, percent time in disordered breathing and the apnea/hypopnea index.

A further example of a condition predisposing a patient to hypopnea or apnea is body posture. A supine posture is more likely to result in obstruction of the upper airway and can be used to predict episodes of obstructive hypopnea and apnea. Posture sensing may be implemented using a position sensitive switch coupled to the patient. Posture and/or torso orientation sensing may be accomplished, for example, using an implantable or external multiaxis accelerometer.

The patient's location may also be useful in prediction of disordered breathing. Because disordered breathing often occurs during sleep, the patient may be more likely to experience disordered breathing if the patient is in bed. A bed proximity sensor may be implemented by placing a beacon transmitter on the patient's bed. Receiver circuitry on or in the patient, for example, incorporated in the patient's pacemaker, receives the beacon signal and determines that the patient is in bed. A proximity to bed sensor methodology is further described in commonly owned U.S. Publication No. 2004/0073093.

Conditions that predispose the patient to disordered breathing **320** are conditions that, if detected, indicate the likelihood that one or more episodes of disordered breathing will occur during the next time period, such as over the course of the night. Based on predisposing conditions **320**, an onset of disordered breathing may be predicted **312** to occur within a time window that may include several hours, for example. A second set of factors, denoted herein as precursor conditions **330**, may be used to predict **314** an impending onset of disordered breathing. Precursor conditions **330** indicate that an episode of disordered breathing is imminent. Prediction of disordered breathing may be performed in real-time. The presence of precursor conditions consistent with prediction criteria may be used to predict that disordered breathing will occur within a time window that may be measured in terms of minutes or seconds, for example, within about the next five minutes.

Precursor conditions **330** indicative of an impending onset of disordered breathing may include, for example, pre-apnea or pre-hypopnea conditions. In one embodiment, decreased levels of CO_2 in a particular patient may be causal to central apnea. Therefore, a condition of pre-apnea may be detected

when a patient's CO_2 level, as measured by an external CO_2 sensor, falls below a selected level, indicating the impending onset of an apnea episode.

In another embodiment, a patient's heart rate variability may be significantly altered before, during, and after episodes of apnea. Heart rate variability may be used, for example, as a precursor condition to predict an impending episode of disordered breathing.

In yet another embodiment of the invention, a pre-disordered breathing condition, e.g., pre-apnea or pre-hypopnea, may be detected by analyzing the patient's respiration patterns or the morphology of a respiration signal. Respiration cycles just prior to an apnea event may exhibit a characteristic pattern. For example, an apnea event for many patients is preceded by a period of hyperventilation with a number of rapid, deep breaths. The pattern of hyperventilation may be detected by analyzing patient's transthoracic impedance signal to determine respiration rate and tidal volume.

Cheyne-Stokes respiration and some apnea/hypopnea episodes may exhibit a crescendo—decrescendo respiration pattern. The crescendo—decrescendo respiration pattern produces hyperventilation during the crescendo stage and hypoventilation during the decrescendo phase. Hyperventilation, secondary to pulmonary congestion, drives arterial partial pressure of carbon dioxide down. A decrease in arterial partial pressure of carbon dioxide below an apnea level may be a causal mechanism for central apnea. According to one embodiment of the invention, detection of an impending onset of disordered breathing may be implemented by detecting a series of increasing tidal volumes followed by a series of decreasing tidal volumes.

For some patients, disordered breathing occurs at regular intervals, allowing the periodicity of the disordered breathing episodes to be used as a precursor condition. If disordered breathing episodes of the patient occur at regular intervals, the next episode of disordered breathing may be predicted based on the time elapsed since the last episode was detected. Precursor conditions **330** may be analyzed individually, or in combination with one or more predisposing conditions **320**, to predict the impending onset of a disordered breathing episode.

Snoring is an example of a pre-apnea or pre-hypopnea condition. In many, patient snoring, or more generally any abnormal airflow in the upper airway detectable via acoustic means, precedes more significant sleep disordered breathing conditions such as hypopnea or apnea.

Yet another group of conditions may be used to verify a prediction of disordered breathing. For example, after a prediction of disordered breathing is made, one or more verification conditions **340** may be checked to confirm the prediction. The verification conditions, as well as the physiological and contextual conditions used in the first stage of the prediction analysis, may be highly patient specific.

In one example, a characteristic pattern of respiration is a reliable predictor of disordered breathing in a particular patient only when the patient is supine. If the prediction is made while the patient not supine, normal variations in respiration cycles in this particular patient may lead to an erroneous prediction of disordered breathing. Thus, before disordered breathing is predicted, the posture sensor signal is checked to verify that the patient is supine. If the patient is supine and the. patient's respiration cycles are consistent with criteria indicating that disordered breathing is likely, the prediction may be made.

In another example, the patient is known to suffer from episodes of apnea during sleep. The patient's sleep apnea may be predicted using a number of physiological and contexual conditions. The prediction of sleep apnea may be made after assessing that the patient's posture and location are consistent with sleep. Before a prediction of sleep apnea is made, the system confirms that the patient is lying down in bed by checking the signal from an implantable posture sensor and a bed proximity sensor.

Alternatively, or additionally, the system may detect that the patient is sleeping by examining the patient's respiration and/or activity prior to making a prediction regarding sleep disordered breathing. A method for determining that the patient is asleep is described in commonly owned U.S. Pat. No. 7,189,204, which is incorporated herein by reference in its entirety.

Episodes of disordered breathing are associated with acute physiological effects, including, for example, negative intrathoracic pressure, hypoxia, and arousal from sleep. During obstructive apnea, for example, the effort to generate airflow increases. Attempted inspiration in the presence of an occluded airway result in an abrupt reduction in intrathoracic pressure. The repeated futile inspiratory efforts associated with obstructive sleep apnea may trigger a series of secondary responses, including mechanical, hemodynamic, chemical, neural, and inflammatory responses.

Obstructive sleep apneas are terminated by arousal from sleep several seconds after the apneic peak, allowing the resumption of airflow. Coincident with arousal from sleep, surges in sympathetic nerve activity, blood pressure, and heart rate occur. The adverse effects of obstructive apnea are not confined to sleep. Daytime sympathetic nerve activity and systemic blood pressure may be increased. There may also be a sustained reduction in vagal tone, causing reduction in total heart rate variability during periods of wakefulness.

Central sleep apnea is generally caused by a failure of respiratory control signals from the brain and is a component of Cheyne-Stokes respiration (CSR), a respiration pattern primarily observed in patients suffering from chronic heart failure (CHF). Cheyne-Stokes respiration is a form of periodic breathing in which central apneas and hypopneas alternate with periods of hyperventilation causing a waxing-waning pattern of tidal volume. In some patients, obstructive sleep apnea and central sleep apnea may coexist. In these patients, there is generally a gradual shift from predominantly obstructive apneas at the beginning of the night to predominantly central apneas at the end of the night.

When CHF patients lie down, the prone posture may create central fluid accumulation and pulmonary congestion causing the patient to reflexively hyperventilate. Central apnea is usually initiated during sleep by an increase in ventilation and a reduction of arterial partial pressure of carbon dioxide ($PaCO_2$) that is triggered by spontaneous arousal. When $PaCO_2$ falls below the threshold level required to stimulate breathing, the central drive to the respiratory muscles and airflow cease, and central apnea ensues. Apnea persists until $PaCO_2$ rises above the threshold required to stimulate ventilation.

Arousals are not required in central sleep apneas for the resumption of breathing at the termination of the apneic event. In central apnea, the arousals follow the initiation of breathing and facilitate the development of oscillations in ventilation by recurrently stimulating hyperventilation and reducing $PaCO_2$ below the apneic threshold. Once triggered, the pattern of alternating hyperventilation and apnea is sustained by the combination of increased respiratory drive, pulmonary congestion, arousals, and apnea-induced hypoxia causing $PaCO_2$ oscillations above and below the apneic

threshold. Shifts in the patient's state of consciousness, particularly with repeated arousals, may further destabilize breathing.

With the transition from wakefulness to NREM sleep the waking neural drive to breathe is lost, and the threshold for a ventilatory response to CO_2 is increased. Therefore, if the patient's $PaCO_2$ level during wakefulness is below this higher sleeping threshold, the transition to NREM sleep may be accompanied by a transient loss of respiratory drive resulting in a central apnea. During the apnea, the $PaCO_2$ rises until it reaches the new higher threshold level and initiates breathing. If sleep becomes firmly established, regular breathing resumes. However, if an arousal should occur, the increased $PaCO_2$ level associated with sleep is now relatively too high for a state of wakefulness and will stimulate hyperventilation. Thus, although arousals terminate obstructive sleep apneas, arousals may trigger the respiratory oscillations associated with central apneas, particularly Cheyne-Stokes respiration.

In addition to the acute responses to central sleep apnea discussed above, central sleep apnea is also associated with a number of secondary responses, including, for example, decreased heart rate variability (HRV), and blood pressure changes. Patients with central sleep apnea may have higher urinary and circulating norepinephrine concentrations and lower $PaCO_2$ during both sleep and wakefulness.

The operation of a disordered breathing prediction engine **400**, according various to embodiments, is conceptually illustrated in the block diagram of FIG. **4**. Periodically, one or more conditions are detected and compared to a library **410** of prediction criteria. The prediction criteria library **410** may incorporate one or more sets of prediction criteria **411**, **412**, **413**, **414**. Each of these sets of criteria may be compared to the detected conditions. If the criteria of a prediction criteria set **411**, **412**, **413**, **414** are substantially consistent with the detected conditions, a preliminary disordered breathing prediction may be made.

In various embodiments, the prediction criteria sets **411**, **412**, **413**, **414** represent one or more condition thresholds associated with an onset of disordered breathing. In one embodiment, the level of one or more conditions may be compared to the prediction criteria sets **411**, **412** **413**, **414**. If the levels of the one or more conditions are substantially equal to or greater than the thresholds specified in a prediction criteria set **411**, **412**, **413**, **414**, a preliminary prediction of disordered breathing is made.

The example above and the examples that follow are described in terms of a condition being consistent with a prediction criteria when the condition exceeds a prediction criteria threshold. However, it will be understood by those skilled in the art that different threshold requirements may be defined for different conditions. For example, one condition may be defined to be consistent with a prediction criterion when the condition exceeds a prediction criterion threshold. Another condition may be defined to be consistent with a prediction criterion threshold when the condition falls below the threshold. In yet another example, a condition may be defined to be consistent with the prediction criterion when the condition falls within a specified range of values. A detected condition may be consistent with a particular prediction criteria in terms of a timing, a rate of change or a maximum or minimum value of the condition, for example.

In the example provided in FIG. **4**, the prediction criteria N **414** involves two contextual conditions, C**1** and C**2**, and two physiological conditions, P**1** and P**2**. In this particular example, if conditions C**1**, C**2**, P**1**, and P**2** exceed levels Level1, Level2, Level3, and Level4, respectively, the patient is likely to experience disordered breathing during the night. Therefore, when conditions C**1**, C**2**, and P**1**, P**2** reach the levels specified in criteria N **414**, preliminary prediction of disordered breathing is made.

In another embodiment of the invention, the relationships between the detected conditions are analyzed to predict disordered breathing. In this embodiment, the disordered breathing prediction may be based on the existence and relative values associated with two or more conditions. For example, if condition A is present at a level of x, then condition B must also be present at a level of f(x) before a disordered breathing prediction is made.

In yet another embodiment of the invention, the estimated probability, $P(C_n)$, that disordered breathing will occur if a particular condition level is detected may be expressed as a function of the ratio of the number of times disordered breathing occurred within a selected time interval following the detection of the particular condition level to the total number of observed occurrences of the condition level. The probability that disordered breathing will occur, $P(C_n)$, is compared to a threshold probability level to make the disordered breathing prediction. Other methods of calculating the estimated probability are also possible.

The prediction of disordered breathing may be based on the convergence or divergence of a number of conditions occurring within the same time period. In this situation, a composite probability score may be computed as a combination of the individual probabilities. In one embodiment, the probabilities are combined by adding the condition probabilities after multiplying each of the condition probabilities by a weighting factor. For example, if the disordered breathing prediction is based on four substantially simultaneous conditions, C_1, C_2, C_3, and C_4, the total probability score PS_S may be calculated as:

$$PS_T = A \times P(C_1) + B \times P(C_2) + C \times P(C_3) + D \times P(C_4), \quad [1]$$

where A, B, C, and D are scalar weighting factors that may be used to estimate the relative importance of each of the conditions C_1, C_2, C_3, and C_4. If the probability score exceeds a selected prediction criteria threshold, then disordered breathing is predicted.

Although the above process describes combining the estimated probabilities for each condition by adding each of the estimated probabilities, other methods are also possible. For example, a detected condition may operate against a prediction of disordered breathing. In this situation, the estimated probability, $P_n(C_n)$, that disordered breathing will not occur if a particular condition level is detected may be expressed as a function of the ratio of the number of times disordered breathing did not occur within a selected time interval following the detection of the particular condition level to the total number of observed occurrences of the condition level. This value may be subtracted from the total to determine the probability score. Non-linear methods of combining the estimated probabilities to arrive at a composite probability are also possible.

If the conditions affecting the patient are consistent with a prediction of disordered breathing, the prediction may be verified by comparing one or more verification conditions to verification criteria. If the verification conditions are consistent with the verification criteria, a prediction of disordered breathing is made.

In the embodiments described above, predictions of disordered breathing are based upon comparisons of one or more detected conditions to sets of prediction criteria. The initial data from which the initial prediction criteria sets are formed may be derived from past observations taken from population data, or from data collected from a particular patient. The

initial prediction criteria sets may then be modified as additional data are collected from the patient.

In one embodiment, an estimated accuracy for the prediction criteria is updated for every prediction event. The estimated positive predictive value (PPV) for a prediction criteria set N may be expressed as:

$$PPV_N = \frac{TP}{TP + FP} \quad [2]$$

where TP (true positive) is the number of times the prediction criteria set successfully predicted disordered breathing, and FP (false positive) is the number of times the prediction criteria erroneously predicted disordered breathing.

If the estimated accuracy of prediction criteria set N, PPV_N, falls below a predetermined level, for example, 0.7, the prediction criteria set N may be modified. In one embodiment, a possible prediction criteria set is formed, for example, by modifying the threshold level of one or more of the conditions represented by the. original prediction criteria set N. In one embodiment, each threshold in the original prediction criteria set N is modified by an incremental value, to make the prediction criteria set more accurate.

In another embodiment, conditions represented in the original prediction criteria set N are compared to the conditions that are present just prior to a disordered breathing occurrence to determine how the modification for the possible prediction criteria set should be implemented. For example, if the level of a particular condition just prior to the occurrence shows a relatively large variation just prior to the disordered breathing episode, but the levels of other conditions remain constant, then only the changing level may be modified in the possible prediction criteria set.

Each time the possible prediction criteria set is satisfied, no prediction of disordered breathing is made, however, the accuracy of the possible prediction criteria set is updated, for example, using an equation similar in form to Equation 2. If the accuracy of the possible prediction criteria set reaches a selected level, for example, 0.7, and the accuracy original prediction criteria set N remains below 0.7, the possible prediction criteria set may replace the original prediction criteria set N in the prediction criteria library.

According to various embodiments, new prediction criteria sets may be added to the prediction criteria library. In accordance with these embodiments, if a disordered breathing episode occurs without prediction, the levels of the detected conditions prior to the disordered breathing episode are saved as a possible prediction criteria set. Each time the possible prediction criteria set is satisfied, no prediction of disordered breathing is made, however, the accuracy of the possible prediction criteria set is updated, for example, using an equation similar in form to Equation 2. If the accuracy of the possible prediction criteria set reaches a selected level, for example, 0.7, the possible prediction criteria set may be added to the prediction criteria library.

The system may also be adjusted to provide increasingly sensitive disordered breathing prediction criteria sets, according to various embodiments. The estimated sensitivity for a prediction criteria set N may be expressed as:

$$Sensitivity_N = \frac{TP}{TP + FN} \quad [3]$$

where TP (true positive) is the number of times the prediction criteria successfully predicted disordered breathing, and FN (false negative) is the number of times the prediction criteria erroneously predicted that disordered breathing would not occur.

In one embodiment, if the prediction criteria accuracy for the prediction criteria set N becomes larger than a selected number, for example, 0.9, then the threshold levels of one or more of the conditions represented in the prediction criteria set N may be adjusted to provide enhanced sensitivity.

In one example, the threshold level of each condition represented in the prediction criteria set N is modified by an incremental value, thus making the prediction criteria set N more sensitive. In another embodiment, conditions represented in the prediction criteria set N are compared to the conditions that are present just prior to a disordered breathing occurrence to determine how the modification of the prediction criteria set N should be implemented. In yet another embodiment, a condition threshold level that is modified is based upon the relative importance of the condition in the overall prediction criteria. In another example, if the level of a particular condition is changing just prior to the occurrence of the disordered breathing episode, but the levels of other conditions remain constant, only the changing condition may be modified.

Following adjustment by any of the processes described above, the adjusted prediction criteria set may be designated as possible prediction criteria set. Each time the possible prediction criteria set is satisfied, no prediction of disordered breathing is made, however, the accuracy of the possible prediction criteria set is updated, for example, using Equation 2 or 3. If the accuracy of a possible prediction criteria set reaches a selected level, for example, 0.7, the possible prediction criteria set may be added to the prediction criteria library.

The system may also be adjusted to provide improved specificity or negative predictive value (NPV) of disordered breathing prediction criteria in a manner similar to the adaptive method described previously. Calculation of specificity and NPV for a prediction criteria N may be accomplished using equations 4 and 5 below.

$$Specificity_N = \frac{TN}{TN + FP} \quad [4]$$

$$NPV_N = \frac{TN}{TN + FN} \quad [5]$$

where TN (true negative) is the number of times the prediction criteria successfully predicted the absence of disordered breathing, FP (false positive) is the number of times the prediction criteria erroneously predicted disordered breathing and FN (false negative) is the number of times the prediction criteria erroneously predicted the absence of disordered breathing.

The flowchart of FIG. **5** illustrates a method for establishing and updating the prediction criteria library according to embodiments of the invention. Previous observations of disordered breathing may be assimilated from population data **502** or from past observation of the specific patient **504**. One or more prediction criteria sets are determined and organized in a prediction criteria library **506**.

Conditions associated with disordered breathing are periodically detected **508** and compared to the prediction criteria sets in the prediction criteria library. If the levels of the detected conditions are consistent **510** with any of the predic-

tion criteria sets in the library, then disordered breathing is predicted **515**. Within a time window following the disordered breathing prediction, the system determines if disordered breathing occurs **520**.

One method for detecting disordered breathing involves monitoring a respiratory waveform output, for example, using a transthoracic impedance sensor. When the tidal volume (TV) of the patient's respiration, as indicated by the transthoracic impedance signal, falls below a hypopnea threshold, then a hypopnea event is declared. For example, a hypopnea event may be declared if the patient's tidal volume fall below about 50% of the recent average tidal volume or other baseline tidal volume. When the patient's tidal volume falls further to an apnea threshold, e.g., about 10% of the recent average tidal volume, an apnea event is declared.

Another method for detecting disordered breathing involves defining and analyzing a number of respiratory cycle intervals. Such a method is described in commonly owned U.S. patent No. 7,252,640, which is incorporated herein by reference in its entirety.

If disordered breathing occurs **520**, the prediction criteria accuracy of the prediction criteria set used for the disordered breathing prediction is updated **525**. If the updated prediction criteria accuracy is greater **530** than a selected number, then a possible prediction criteria set is formed **535**. The possible prediction criteria set may be formed, for example, by substituting more sensitive condition levels when compared to the original prediction criteria set.

If disordered breathing is not detected **520** following the prediction, then the prediction criteria set accuracy is updated **540**. If the prediction criteria set accuracy decreases **545** below a selected number, then a possible prediction criteria set **550** is formed. The possible prediction criteria set may be formed, for example, by substituting more stringent condition levels to produce a more accurate prediction.

If the detected conditions are not consistent **510** with any of the prediction criteria sets in the prediction criteria library, disordered breathing is not predicted. Within a time window following the disordered breathing prediction, the system determines if disordered breathing occurs **555**. If disordered breathing occurs **555**, then the system checks to see if the conditions are consistent **560** with any of the possible prediction criteria sets. If the conditions are not consistent **560** with any of the possible prediction criteria sets, a possible prediction criteria set is formed **565**.

If the conditions are consistent **560** with a possible criteria set, the possible prediction criteria set accuracy is updated **570**. If the possible prediction criteria accuracy increases beyond a selected number **575**, the possible prediction criteria set is added **580** to the prediction criteria library.

The block diagram of FIG. **6** illustrates a system for predicting disordered breathing configured in accordance with embodiments of the invention. According to one embodiment, a disordered breathing prediction engine **642** is incorporated within a cardiac rhythm management system **600**. The cardiac rhythm management system may include, for example, a cardiac therapy module **620** including a pacemaker **622** and an arrhythmia detector/therapy unit **624**. The cardiac therapy module **620** is coupled to a lead system having electrodes **631** implanted to electrically couple the heart **630** to the cardiac rhythm management system **600**.

The cardiac rhythm management system **600** includes circuitry **650** for detecting signals from internal sensors such as the implanted cardiac electrodes **631**, and other internal sensors **680** such as the internal sensors listed in Table 1. The internal sensors **680**, may be coupled to the implanted signal detection circuitry **650** through conducting leads as shown, or through a wireless connection, for example.

The cardiac rhythm management system **600** may also include circuitry **660** for detecting signals from external sensors **690** located outside the patient's body and from patient reported input. The external sensors **690** may be coupled to the detection circuitry **660** through a wireless link. Signals representing patient reported data may be input through a programmer unit **670** that is wirelessly coupled to a telemetry circuit **675** within the cardiac rhythm management system **600**.

The cardiac therapy module **620** receives cardiac signals from the implanted cardiac electrodes **631** and analyzes the cardiac signals to determine an appropriate therapy. The cardiac therapy may include pacing therapy controlled by the pacemaker **622** to treat cardiac rhythms that are too slow. The pacemaker **622** controls the delivery of periodic low energy pacing pulses to one or more of the heart chambers through cardiac electrodes **631** to ensure that the periodic contractions of the heart are maintained at a hemodynamically sufficient rate.

The cardiac therapy may also include therapy to terminate tachyarrhythmia, wherein the heart rate is too fast. The arrhythmia detector/therapy unit **624** detects and treats episodes of tachyarrhythmia, including tachycardia and/or fibrillation. The arrhythmia detector/therapy unit **624** recognizes cardiac signals indicative of tachyarrhythmia and delivers high energy stimulations to the heart **630** through the implanted electrodes **631** to terminate the arrhythmia.

A disordered breathing module **640** incorporated within the cardiac rhythm management system **600** includes circuitry for disordered breathing detection **644**, as well as the disordered breathing prediction engine **642**. The implanted signal detection circuitry **650** and patient reported/external sensor detection circuitry **660** are coupled to the disordered breathing module **640**. The implanted signal detection circuitry **650** and patient reported/external sensor detection circuitry **660** provide signals associated with various conditions used for disordered breathing detection and prediction. A prediction of disordered breathing by the disordered breathing prediction engine **642** may be used to trigger cardiac pacing therapy delivered by the cardiac therapy module to mitigate disordered breathing as more fully described in commonly owned U.S. Publication No. 2005/0043772, which was filed concurrently with this patent application, and incorporated herein by reference in its entirety.

Although the disordered breathing prediction engine **642** is described in connection with FIG. **6** as a component of an implantable cardiac rhythm management system, the disordered breathing prediction engine **642** may be incorporated in various implantable or external therapeutic or diagnostic devices including cardiac monitors, pacemakers, defibrillators, and cardiac resynchronizers, for example.

FIGS. **7** through **9** illustrate systems that may be used to implement methods of disordered breathing prediction according to embodiments of the invention. FIG. **7** illustrates a system for predicting disordered breathing utilizing the cardiac rhythm management system **710** incorporating a disordered breathing prediction engine **710** as discussed in connection with FIG. **6**. In addition to the previously described implanted cardiac electrodes, the cardiac rhythm management system **710** also includes an accelerometer mounted within the housing of the cardiac rhythm management system for sensing patient activity.

In the embodiment of FIG. **7**, the cardiac rhythm management system **710** further includes a receiver for a proximity to bed signal that is generated by a proximity to bed beacon **720**

located on or near the patient's bed **730**. If the proximity to bed receiver detects a signal of sufficient strength from the proximity to bed beacon **720**, then the receiver signals that the patient is in bed.

The cardiac rhythm management system **710** includes a transthoracic impedance sensor used to determine conditions associated with disordered breathing including respiration rate, respiration rate variability, tidal volume, and minute ventilation, for example. In this example, the disordered breathing prediction engine located within the cardiac rhythm management system **710** predicts disordered breathing based primarily on the patient's heart rate and tidal volume. Two additional signals, the patient's activity level and proximity to bed, are used to verify the prediction of disordered breathing.

Data associated with disordered breathing prediction may be collected by the disordered breathing prediction engine, or other components, and stored in the memory of the cardiac rhythm management system or the disordered breathing prediction engine. The data may include, for example, the number and/or types of disordered breathing episodes predicted, the number and/or types of disordered breathing episodes detected, the accuracy of the predictions made by the prediction engine, or other data useful for diagnostic or therapeutic purposes. For example, the data stored may involve counting the number of successful disordered breathing predictions made and/or counting the number of unsuccessful disordered breathing predictions made. A system for predicting disordered breathing may include a display or other output device capable of displaying information associated with the disordered breathing predictions in the form of graphics, text, or other media. Alternatively or additionally, the collected data may be transmitted to a separate device for storage, display, report generation, further analysis, or other purposes.

The methods and systems for predicting disordered breathing as illustrated by the embodiments described herein may be used in cooperation with advanced patient management systems. Advanced patient management systems allow physicians to remotely and automatically monitor patient conditions and test physiological functions, including cardiac and respiratory functions, for example. In one example of advanced patient management, an implantable cardiac rhythm management system, such as cardiac pacemaker, defibrillator, or cardiac resynchronization device, may be equipped with various telecommunications and information technologies enabling real-time data collection, diagnosis, and treatment of the patient. Advanced patient management systems may be enhanced by real-time prediction of disordered breathing and/or long term collection of disordered breathing prediction data. Systems and methods involving advanced patient management techniques are described in U.S. Pat. Nos. 6,336,903, 6,312,378, 6,270,457, and 6,398,728 which are incorporated herein by reference in their respective entireties.

Representative graphs of the patient's tidal volume **810**, heart rate **820**, and activity level **830** during disordered breathing prediction are illustrated in FIGS. **8**A-**8**C. In this example, the patient's tidal volume **810** exhibits a characteristic decrease **812** just before the onset **840** of an episode of disordered breathing **850**. Accordingly, a first condition threshold for disordered breathing prediction is established as a percentage drop in tidal volume. Additionally, the patient's heart rate **820** exhibits a decrease **822** that occurs substantially simultaneously with the decrease in tidal volume **812**. A second condition threshold for disordered breathing detection is established as a percentage drop in heart rate.

If the system detects that the percent decrease in tidal volume and the percent decrease in heart rate exceed the established thresholds, a disordered breathing prediction is made subject to verification. The disordered breathing prediction is then verified by determining that the patient's activity signal **830**, as detected by the accelerometer, is below a resting threshold **832** and that the proximity to bed receiver indicates that the patient is in bed.

Another embodiment of a disordered breathing prediction system is illustrated in the diagram of FIG. **9**. In this embodiment, the prediction criteria for predicting disordered breathing are based on the patient's heart rate, respiration rate, the condition of patient snoring, and air quality.

In this embodiment, a heart rate signal is wirelessly transmitted from the cardiac rhythm management system **920** to an external disordered breathing prediction unit **910**. An external respiration monitor **930** produces respiration signals and wirelessly transmits the respiration signals to the disordered breathing prediction unit **910**. A snore sensor **940**, which may be implemented as a microphone or accelerometer, for example, is coupled through a lead to the disordered breathing prediction unit **910** for detection of patient snoring. The disordered breathing prediction unit **910** accesses an air quality website server **950** through a network, such as the internet **960**, and downloads information regarding air quality.

The examples presented herein represent a subset of many ways in which the described sensors and systems may be combined to implement disordered breathing prediction in accordance with principles of the invention. It will be appreciated that many combinations of physiological and/or environmental conditions may be detected and used to predict disordered breathing according to the methods and systems described herein.

The following commonly owned U.S. Patents Applications, some of which have been identified above, are hereby incorporated by reference in their respective entireties: U.S. patent application Ser. No. 10/309,770 now U.S. Pat. No. 7,252,640, U.S. patent application Ser. No. 10/309,771 now U.S. Pat. No. 7,189,204, U.S. Publication No. 2005/0042589, which was concurrently filed with this patent application, U.S. Publication No. 2005/0039745, which was filed concurrently with this patent application, U.S. Publication No. 2005/0043652, which was filed concurrently with this patent application, and U.S. Publication No. 2005/0043772, which was filed concurrently with this patent application.

Various modifications and additions can be made to the preferred embodiments discussed above without departing from the scope of the present invention. Accordingly, the scope of the present invention should not be limited by the particular embodiments described above, but should be defined only by the claims set forth below and equivalents thereof.

What is claimed is:

1. A method for predicting disordered breathing in a patient, comprising:

detecting one or more conditions associated with disordered breathing;

comparing the one or more conditions to one or more sets of disordered breathing prediction criteria;

predicting the disordered breathing based on the comparison, wherein at least one of comparing and predicting is performed at least in part implantably; and

counting the disordered breathing predictions.

2. The method of claim **1**, wherein predicting is performed at least in part implantably.

3. The method of claim **1**, wherein each of comparing and predicting is performed at least in part implantably.

4. The method of claim 1, wherein detecting the one or more conditions comprises detecting a physiological condition.

5. The method of claim 1, wherein detecting the one or more conditions comprises detecting a respiration quality condition.

6. The method of claim 1, wherein detecting the one or more conditions comprises detecting a body-related condition.

7. The method of claim 1, wherein each of the one or more sets of prediction criteria associated with disordered breathing comprises at least one threshold corresponding to at least one condition associated with disordered breathing.

8. The method of claim 1, wherein comparing the one or more conditions to the one or more sets of disordered breathing prediction criteria comprises comparing at least one of the one or more conditions associated with disordered breathing to a threshold corresponding to an onset of disordered breathing.

9. The method of claim 1, wherein comparing the one or more conditions to the one or more sets of prediction criteria comprises comparing a relationship between at least two of the one or more conditions to a relationship criterion corresponding to an onset of disordered breathing.

10. The method of claim 1, wherein comparing the one or more conditions to the one or more sets of prediction criteria comprises:

computing an estimated probability that disordered breathing will occur based on the one or more conditions; and

comparing the estimated probability to a threshold probability associated with an onset of disordered breathing.

11. The method of claim 10, wherein computing an estimated probability comprises computing a composite estimated probability score.

12. The method of claim 1, wherein predicting the disordered breathing comprises predicting the disordered breathing will occur if the one or more conditions are consistent with at least one set of prediction criteria.

13. The method of claim 1, further comprising establishing a particular set of prediction criteria based on the one or more conditions.

14. The method of claim 13, wherein establishing the particular set of prediction criteria is performed at least in part implantably.

15. The method of claim 1, further comprising adjusting a particular set of prediction criteria based on the one or more conditions.

16. The method of claim 15, wherein adjusting the particular set of prediction criteria is performed at least in part implantably.

17. The method of claim 15, wherein adjusting the particular set of prediction criteria comprises deleting the particular set of prediction criteria.

18. The method of claim 15, wherein adjusting the particular set of prediction criteria comprises:

calculating an estimated accuracy for the particular set of prediction criteria; and

adjusting the particular set of prediction criteria based on the estimated accuracy.

19. The method of claim 15, wherein adjusting the particular set of prediction criteria comprises:

calculating an estimated sensitivity for the particular set of prediction criteria; and

adjusting the particular set of prediction criteria based on the estimated sensitivity.

20. The method of claim 1, wherein predicting the disordered breathing comprises predicting the disordered breathing will occur within a particular time interval.

21. The method of claim 20, wherein predicting the disordered breathing will occur within the particular time interval comprises performing a real-time prediction of the disordered breathing.

22. The method of claim 1, further comprising collecting data associated with disordered breathing predictions.

23. The method of claim 22, wherein collecting the data associated with the disordered breathing predictions comprises collecting data associated with an accuracy of the disordered breathing predictions.

24. The method of claim 22, wherein collecting the data associated with the disordered breathing predictions comprises collecting data associated with the one or more conditions associated with disordered breathing.

25. The method of claim 1, further comprising:

collecting data associated with disordered breathing predictions; and

displaying the collected data.

26. The method of claim 1, further comprising:

collecting data associated with disordered breathing predictions; and

transmitting the data to a separate device.

27. The method of claim 1, wherein detecting the one or more conditions comprises detection a respiratory condition and one or more of an additional physiological condition, a sleep condition, a cardiovascular system condition, a nervous system condition, a blood chemistry system condition, a muscle system condition, a patient-history condition, a patient-reported condition, a condition used to verify the prediction of disordered breathing, patient posture, a non-physiological condition, an environmental condition, a contextual condition and air pollution.

28. A method for predicting disordered breathing in a patient, comprising:

detecting one or more conditions predisposing the patient to disordered breathing;

comparing the one or more predisposing conditions to one or more sets of prediction criteria associated with disordered breathing;

predicting the disordered breathing based on the comparison, wherein at least one of comparing and predicting is performed at least in part implantably; and

collecting data associated with an accuracy of the disordered breathing predictions.

29. The method of claim 28, wherein predicting the disordered breathing is performed at least in part implantably.

30. The method of claim 28, wherein each of comparing and predicting is performed at least in part implantably.

31. The method of claim 28, wherein detecting the one or more predisposing conditions comprises detecting a condition associated with an increased likelihood of disordered breathing.

32. The method of claim 28, wherein detecting the one or more predisposing conditions comprises detecting a physiological condition.

33. The method of claim 28, wherein detecting the one or more predisposing conditions comprises detecting snoring.

34. The method of claim 28, wherein:

detecting the one or more predisposing conditions comprises detecting a first type of disordered breathing; and

predicting the disordered breathing comprises predicting a second type or disordered breathing.

35. The method of claim 28, wherein predicting the disordered breathing comprises performing a real-time prediction of the disordered breathing.

36. The method of claim 35, wherein performing the real-time prediction of disordered breathing comprises predicting the disordered breathing will occur within about an 8 hour period following the disordered breathing prediction.

37. The method of claim 35, wherein performing the real-time prediction of disordered breathing comprises predicting the disordered breathing will occur during a next sleep time following the disordered breathing prediction.

38. An automated method for predicting disordered breathing in a patient, comprising:

detecting one or more precursor conditions associated with disordered breathing, the precursor conditions including at least a periodicity of occurrences of disordered breathing;

comparing the one or more precursor conditions to one or more sets of prediction criteria associated with disordered breathing; and

predicting the disordered breathing based on the comparison, wherein at least one of comparing and predicting is performed at least in part implantably.

39. The method of claim 38, wherein predicting the disordered breathing is performed at least in part implantably.

40. The method of claim 38, wherein each of comparing and predicting is performed at least in part implantably.

41. The method of claim 38, wherein detecting the one or more precursor conditions comprises detecting a condition associated with an impending onset of disordered breathing.

42. The method of claim 38, wherein detecting the one or more precursor conditions comprises detecting a respiratory system condition.

43. The method of claim 42, wherein detecting the respiratory system condition comprises detecting a respiration tidal volume pattern.

44. The method of claim 42, wherein detecting the one or more precursor conditions comprises detecting hyperventilation.

45. The method of claim 38, wherein predicting the disordered breathing comprises performing the disordered breathing prediction in real-time.

46. The method of claim 45, wherein performing the disordered breathing prediction in real-time comprises predicting the disordered breathing will occur within about a five minute period following the disordered breathing prediction.

47. An automated medical device, comprising:

a detector system configured to detect conditions associated with disordered breathing; and

a prediction engine coupled to the detector system and configured to compare the detected conditions to one or more sets of prediction criteria, predict the disordered breathing based on the comparison, and to count the disordered breathing predictions, wherein the prediction engine includes an implantable component.

48. The medical device of claim 47, wherein the detector system comprises an implantable sensor.

49. The medical device of claim 47, wherein the detector system comprises a patient-external sensor.

50. The medical device of claim 47, wherein the detector system comprises a patient input device.

51. The medical device of claim 47, wherein the detector system comprises a sensor configured to sense a physiological condition.

52. The medical device of claim 47, wherein the detector system comprises a sensor configured to sense a respiratory system condition.

53. The medical device of claim 47, wherein the detector system comprises at least one network-accessible component.

54. The medical device of claim 47, wherein the detector system comprises at least one wirelessly connected component.

55. The medical device of claim 47, wherein the prediction engine is configured to establish the one or more sets of prediction criteria based on the detected conditions.

56. The medical device of claim 47, wherein the prediction engine is configured to adjust a particular set of prediction criteria based on the detected conditions.

57. The medical device of claim 47, wherein the prediction engine is configured to calculate an estimated accuracy of a particular set of prediction criteria and adjust the particular set of prediction criteria based on the estimated accuracy.

58. The medical device of claim 47, wherein the prediction engine is configured to calculate an estimated sensitivity of a particular set of prediction criteria and adjust the particular set of prediction criteria based on the estimated sensitivity.

59. The medical device of claim 47, wherein the prediction engine is configured to predict the disordered breathing will occur within a particular time interval on a real-time basis.

60. The medical device of claim 47, wherein:

the detector system is configured to detect conditions predisposing the patient to the disordered breathing; and

the prediction engine is configured predict that the disordered breathing will occur within a period of about 8 hours based on the predisposing conditions.

61. The medical device of claim 47, wherein:

the detector system is configured to detect disordered breathing precursor conditions; and

the prediction engine is configured to predict that the disordered breathing will occur within a period of about five minutes following a disordered breathing prediction.

62. The medical device of claim 47, further comprising a data storage unit configured to store data associated with disordered breathing predictions.

63. The medical device of claim 62, wherein the data storage unit is configured to counting a number of disordered breathing predictions.

64. The medical device of claim 63, wherein the number of the disordered breathing predictions comprises a number of successful disordered breathing predictions.

65. The medical device of claim 63, wherein the number of the disordered breathing predictions comprises a number of unsuccessful disordered breathing predictions.

66. The medical device of claim 62, wherein the data storage unit is configured to collect data associated with an accuracy of the disordered breathing predictions.

67. The medical device of claim 62, wherein data storage unit is configured to collect data associated with the conditions associated with disordered breathing.

68. The medical device of claim 47, further comprising:

a data storage unit configured to collect and store data associated with disordered breathing predictions; and

a display unit configured to display the collected data.

69. The medical device of claim 47, further comprising:

a data storage unit configured to collect and store data associated with disordered breathing predictions; and

a transmitter configured to transmit the collected data to a separate device.

70. The device of claim 47, wherein the detector system is configured to detect a respiratory condition and one or more of an additional physiological condition, a sleep condition, a cardiovascular system condition, a nervous system condition,

a blood chemistry system condition, a muscle system condition, a patient-history condition, a patient-reported condition, a condition used to verify the prediction of disordered breathing, patient posture, a non-physiological condition, an environmental condition, a contextual condition and air pollution.

71. A disordered breathing prediction system, comprising:

means for detecting one or more conditions associated with disordered breathing of a patient;

means for comparing the one or more conditions to one or more sets of disordered breathing prediction criteria;

means for predicting the disordered breathing, wherein at least one of the means for comparing and the means for predicting include an implantable component; and

means for counting the disordered breathing predictions.

72. The system of claim **71**, further comprising means for establishing a particular set of prediction criteria.

73. The system of claim **71**, further comprising means for adjusting a particular set of prediction criteria.

74. An automated system for predicting disordered breathing in a patient, comprising:

means for detecting one or more conditions predisposing the patient to disordered breathing;

means for comparing the one or more predisposing conditions to one or more sets of disordered breathing prediction criteria;

means for predicting the disordered breathing based on the comparison, wherein at least one of the means for comparing and the means for predicting includes an implantable component; and

means for collecting data associated with an accuracy of the disordered breathing predictions.

75. A system for predicting disordered breathing in a patient, comprising:

means for detecting one or more precursor conditions associated with disordered breathing, the precursor conditions including at least a periodicity of occurrences of disordered breathing;

means for comparing the one or more precursor conditions to one or more sets of disordered breathing prediction criteria; and

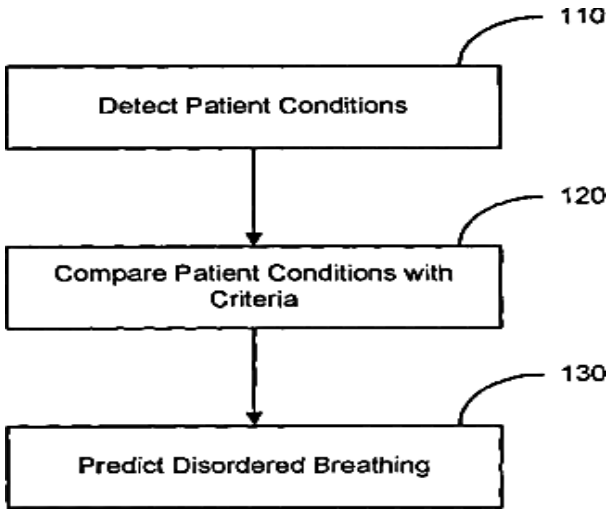
means for predicting the disordered breathing based on the comparison, wherein at least one of the means for comparing and the means for predicting includes an implantable component.

* * * * *

专利名称(译)	预测呼吸紊乱		
公开(公告)号	US7396333	公开(公告)日	2008-07-08
申请号	US10/643016	申请日	2003-08-18
[标]申请(专利权)人(译)	STAHMANN JEFFREYê HATLESTAD约翰·D· 倪泉 哈特利JESSE DAUM DOUGLAS - [R LEE KENT		
申请(专利权)人(译)	STAHMANN JEFFREY E. HATLESTAD约翰D. NI QUAN 哈特利JESSE DAUM DOUGLAS R. LEE KENT		
当前申请(专利权)人(译)	心脏起搏器，INC.		
[标]发明人	STAHMANN JEFFREY E HATLESTAD JOHN D NI QUAN HARTLEY JESSE DAUM DOUGLAS R LEE KENT		
发明人	STAHMANN, JEFFREY E. HATLESTAD, JOHN D. NI, QUAN HARTLEY, JESSE DAUM, DOUGLAS R. LEE, KENT		
IPC分类号	A61B5/00 A61B5/08 A61B5/11 A61N1/362 A61N1/365		
CPC分类号	A61B5/0031 A61B5/02405 A61B5/0816 A61B5/1116 A61B5/1118 A61B5/4815 A61B5/4818 A61N1/36514 A61B5/4812 A61B5/08 A61B2560/0242 A61B2562/0219 A61N1/362		
其他公开文献	US20050043644A1		
外部链接	Espacenet USPTO		

摘要(译)

预测呼吸紊乱的方法涉及检测与呼吸紊乱相关的一种或多种病症。将检测到的条件与无序呼吸预测标准进行比较。基于检测到的条件与预测标准的比较来执行无序呼吸的预测。将检测到的条件与预测标准进行比较并预测无序呼吸中的至少一个至少部分地被植入地执行。


110
Detect Patient Conditions
120
Compare Patient Conditions with Criteria
130
Predict Disordered Breathing