



US008663107B2

(12) **United States Patent**
Kiani

(10) **Patent No.:** **US 8,663,107 B2**
(45) **Date of Patent:** ***Mar. 4, 2014**

(54) **SEPSIS MONITOR**

(75) Inventor: **Massi E. Kiani**, Laguna Niguel, CA
(US)

(73) Assignee: **Cercacor Laboratories, Inc.**, Irvine, CA
(US)

(*) Notice: Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 0 days.

This patent is subject to a terminal dis-
claimer.

5,041,187 A	8/1991	Hink et al.
5,069,213 A	12/1991	Polczynski
5,163,438 A	11/1992	Gordon et al.
5,319,355 A	6/1994	Russek
5,337,744 A	8/1994	Branigan
5,341,805 A	8/1994	Stavridi et al.
D353,195 S	12/1994	Savage et al.
D353,196 S	12/1994	Savage et al.
5,377,676 A	1/1995	Vari et al.
D359,546 S	6/1995	Savage et al.
5,431,170 A	7/1995	Mathews
D361,840 S	8/1995	Savage et al.
D362,063 S	9/1995	Savage et al.
5,452,717 A	9/1995	Branigan et al.
D363,120 S	10/1995	Savage et al.

(Continued)

(21) Appl. No.: **13/100,172**

(22) Filed: **May 3, 2011**

(65) **Prior Publication Data**

US 2011/0208018 A1 Aug. 25, 2011

Related U.S. Application Data

(63) Continuation of application No. 11/803,936, filed on
May 15, 2007, now Pat. No. 7,941,199.

(60) Provisional application No. 60/800,629, filed on May
15, 2006.

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

(52) **U.S. Cl.**
USPC **600/301; 600/323; 600/324**

(58) **Field of Classification Search**
USPC **600/300, 301, 324, 500, 508, 529, 323;**
128/900

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,869,253 A	9/1989	Craig, Jr. et al.
4,960,128 A	10/1990	Gordon et al.
4,964,408 A	10/1990	Hink et al.

OTHER PUBLICATIONS

Angus, D.C., MD, MPH, FCCM, et al., "Epidemiology of Severe
Sepsis in the United States: Analysis of Incidence, Outcome, and
Associated Cost of Care," *Critical Care Medicine*, vol. 29, No. 7, pp.
1303-1310.

(Continued)

Primary Examiner — Bill Thomson

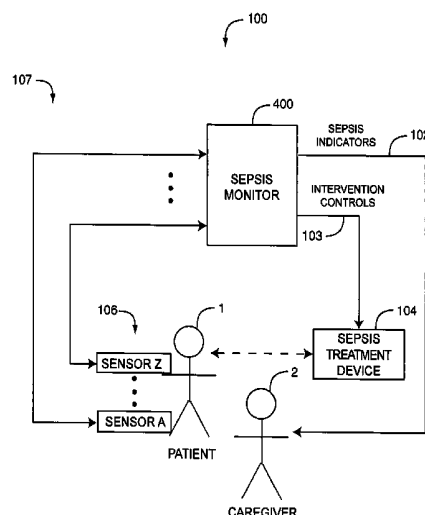
Assistant Examiner — Bobby Soriano

(74) *Attorney, Agent, or Firm* — Knobbe Martens Olson &
Bear LLP

(57) **ABSTRACT**

Sensors are attached to a living being so as to generate cor-
responding sensor signals. A monitor is in communications
with the sensors so as to derive physiological parameters
responsive to the sensor signals. Predetermined limits are
applied to the physiological parameters. At least one indicator
responsive to the physiological parameters and the predeter-
mined limits signal the onset of a sepsis condition in the living
being.

11 Claims, 6 Drawing Sheets



(56)

References Cited

U.S. PATENT DOCUMENTS

5,456,252 A	10/1995	Vari et al.	6,377,829 B1	4/2002	Al-Ali
5,479,934 A	1/1996	Imran	6,388,240 B2	5/2002	Schulz et al.
5,482,036 A	1/1996	Diab et al.	6,397,091 B2	5/2002	Diab et al.
5,490,505 A	2/1996	Diab et al.	6,430,437 B1	8/2002	Marro
5,494,043 A	2/1996	O'Sullivan et al.	6,430,525 B1	8/2002	Weber et al.
5,533,511 A	7/1996	Kaspari et al.	6,463,311 B1	10/2002	Diab
5,534,851 A	7/1996	Russek	6,470,199 B1	10/2002	Kopotic et al.
5,561,275 A	10/1996	Savage et al.	6,501,975 B2	12/2002	Diab et al.
5,562,002 A	10/1996	Lalin	6,505,059 B1	1/2003	Kollias et al.
5,590,649 A	1/1997	Caro et al.	6,515,273 B2	2/2003	Al-Ali
5,602,924 A	2/1997	Durand et al.	6,519,487 B1	2/2003	Parker
5,632,272 A	5/1997	Diab et al.	6,525,386 B1	2/2003	Mills et al.
5,638,816 A	6/1997	Kiani-Azarbayjany et al.	6,526,300 B1	2/2003	Kiani et al.
5,638,818 A	6/1997	Diab et al.	6,541,756 B2	4/2003	Schulz et al.
5,645,440 A	7/1997	Tobler et al.	6,542,764 B1	4/2003	Al-Ali et al.
5,685,299 A	11/1997	Diab et al.	6,580,086 B1	6/2003	Schulz et al.
D393,830 S	4/1998	Tobler et al.	6,584,336 B1	6/2003	Ali et al.
5,743,262 A	4/1998	Lepper, Jr. et al.	6,595,316 B2	7/2003	Cybulski et al.
5,758,644 A	6/1998	Diab et al.	6,597,932 B2	7/2003	Tian et al.
5,760,910 A	6/1998	Lepper, Jr. et al.	6,597,933 B2	7/2003	Kiani et al.
5,769,785 A	6/1998	Diab et al.	6,606,511 B1	8/2003	Ali et al.
5,782,757 A	7/1998	Diab et al.	6,632,181 B2	10/2003	Flaherty et al.
5,785,659 A	7/1998	Caro et al.	6,639,668 B1	10/2003	Trepagnier
5,791,347 A	8/1998	Flaherty et al.	6,640,116 B2	10/2003	Diab
5,810,734 A	9/1998	Caro et al.	6,643,530 B2	11/2003	Diab et al.
5,823,950 A	10/1998	Diab et al.	6,650,917 B2	11/2003	Diab et al.
5,830,131 A	11/1998	Caro et al.	6,654,624 B2	11/2003	Diab et al.
5,833,618 A	11/1998	Caro et al.	6,658,276 B2	12/2003	Kiani et al.
5,860,919 A	1/1999	Kiani-Azarbayjany et al.	6,661,161 B1	12/2003	Lanzo et al.
5,890,929 A	4/1999	Mills et al.	6,671,531 B2	12/2003	Al-Ali et al.
5,904,654 A	5/1999	Wohltmann et al.	6,678,543 B2	1/2004	Diab et al.
5,919,134 A	7/1999	Diab	6,684,090 B2	1/2004	Ali et al.
5,934,925 A	8/1999	Tobler et al.	6,684,091 B2	1/2004	Parker
5,940,182 A	8/1999	Lepper, Jr. et al.	6,697,656 B1	2/2004	Al-Ali
5,995,855 A	11/1999	Kiani et al.	6,697,657 B1	2/2004	Shehada et al.
5,997,343 A	12/1999	Mills et al.	6,697,658 B2	2/2004	Al-Ali
6,002,952 A	12/1999	Diab et al.	RE38,476 E	3/2004	Diab et al.
6,011,986 A	1/2000	Diab et al.	6,699,194 B1	3/2004	Diab et al.
6,027,452 A	2/2000	Flaherty et al.	6,714,804 B2	3/2004	Al-Ali et al.
6,036,642 A	3/2000	Diab et al.	RE38,492 E	4/2004	Diab et al.
6,045,509 A	4/2000	Caro et al.	6,721,582 B2	4/2004	Trepagnier et al.
6,067,462 A	5/2000	Diab et al.	6,721,585 B1	4/2004	Parker
6,081,735 A	6/2000	Diab et al.	6,725,075 B2	4/2004	Al-Ali
6,088,607 A	7/2000	Diab et al.	6,728,560 B2	4/2004	Kollias et al.
6,110,522 A	8/2000	Lepper, Jr. et al.	6,733,464 B2 *	5/2004	Olbrich et al. 600/538
6,124,597 A	9/2000	Shehada	6,735,459 B2	5/2004	Parker
6,128,521 A	10/2000	Marro et al.	6,745,060 B2	6/2004	Diab et al.
6,129,675 A	10/2000	Jay	6,760,607 B2	7/2004	Al-Ali
6,144,868 A	11/2000	Parker	6,770,028 B1	8/2004	Ali et al.
6,151,516 A	11/2000	Kiani-Azarbayjany et al.	6,771,994 B2	8/2004	Kiani et al.
6,152,754 A	11/2000	Gerhardt et al.	6,792,300 B1	9/2004	Diab et al.
6,157,850 A	12/2000	Diab et al.	6,813,511 B2	11/2004	Diab et al.
6,165,005 A	12/2000	Mills et al.	6,816,741 B2	11/2004	Diab
6,184,521 B1	2/2001	Coffin, IV et al.	6,822,564 B2	11/2004	Al-Ali
6,206,830 B1	3/2001	Diab et al.	6,826,419 B2	11/2004	Diab et al.
6,229,856 B1	5/2001	Diab et al.	6,830,711 B2	12/2004	Mills et al.
6,232,609 B1	5/2001	Snyder et al.	6,850,787 B2	2/2005	Weber et al.
6,236,872 B1	5/2001	Diab et al.	6,850,788 B2	2/2005	Al-Ali
6,241,683 B1	6/2001	Macklem et al.	6,852,083 B2	2/2005	Caro et al.
6,253,097 B1	6/2001	Aronow et al.	6,861,639 B2	3/2005	Al-Ali
6,256,523 B1	7/2001	Diab et al.	6,898,452 B2	5/2005	Al-Ali et al.
6,263,222 B1	7/2001	Diab et al.	6,920,345 B2	7/2005	Al-Ali et al.
6,278,522 B1	8/2001	Lepper, Jr. et al.	6,931,268 B1	8/2005	Kiani-Azarbayjany et al.
6,280,213 B1	8/2001	Tobler et al.	6,934,570 B2	8/2005	Kiani et al.
6,285,896 B1	9/2001	Tobler et al.	6,939,305 B2	9/2005	Flaherty et al.
6,301,493 B1	10/2001	Marro et al.	6,943,348 B1	9/2005	Coffin, IV
6,317,627 B1	11/2001	Ennen et al.	6,950,687 B2	9/2005	Al-Ali
6,321,100 B1	11/2001	Parker	6,961,598 B2	11/2005	Diab
6,325,761 B1	12/2001	Jay	6,970,792 B1	11/2005	Diab
6,334,065 B1	12/2001	Al-Ali et al.	6,979,812 B2	12/2005	Al-Ali
6,343,224 B1	1/2002	Parker	6,985,764 B2	1/2006	Mason et al.
6,349,228 B1	2/2002	Kiani et al.	6,993,371 B2	1/2006	Kiani et al.
6,360,114 B1	3/2002	Diab et al.	6,996,427 B2	2/2006	Ali et al.
6,368,283 B1	4/2002	Xu et al.	6,999,904 B2	2/2006	Weber et al.
6,371,921 B1	4/2002	Caro et al.	7,003,338 B2	2/2006	Weber et al.
			7,003,339 B2	2/2006	Diab et al.
			7,015,451 B2	3/2006	Dalke et al.
			7,024,233 B2	4/2006	Ali et al.
			7,027,849 B2	4/2006	Al-Ali

(56)

References Cited

U.S. PATENT DOCUMENTS

- 7,030,749 B2 4/2006 Al-Ali
7,039,449 B2 5/2006 Al-Ali
7,041,060 B2 5/2006 Flaherty et al.
7,044,918 B2 5/2006 Diab
7,067,893 B2 6/2006 Mills et al.
7,081,095 B2 * 7/2006 Lynn et al. 600/538
7,090,648 B2 * 8/2006 Sackner et al. 601/1
7,096,052 B2 8/2006 Mason et al.
7,096,054 B2 8/2006 Abdul-Hafiz et al.
7,132,641 B2 11/2006 Schulz et al.
7,142,901 B2 11/2006 Kiani et al.
7,149,561 B2 12/2006 Diab
7,186,966 B2 3/2007 Al-Ali
7,190,261 B2 3/2007 Al-Ali
7,215,984 B2 5/2007 Diab
7,215,986 B2 5/2007 Diab
7,221,971 B2 5/2007 Diab
7,225,006 B2 5/2007 Al-Ali et al.
7,225,007 B2 5/2007 Al-Ali
RE39,672 E 6/2007 Shehada et al.
7,239,905 B2 7/2007 Kiani-Azarbayjany et al.
7,245,953 B1 7/2007 Parker
7,252,637 B2 8/2007 Ebner et al.
7,254,429 B2 8/2007 Schurman et al.
7,254,431 B2 8/2007 Al-Ali
7,254,433 B2 8/2007 Diab et al.
7,254,434 B2 8/2007 Schulz et al.
7,272,425 B2 9/2007 Al-Ali
7,274,955 B2 9/2007 Kiani et al.
D554,263 S 10/2007 Al-Ali
7,280,858 B2 10/2007 Al-Ali et al.
7,289,835 B2 10/2007 Mansfield et al.
7,292,883 B2 11/2007 De Felice et al.
7,295,866 B2 11/2007 Al-Ali
7,328,053 B1 2/2008 Diab et al.
7,332,784 B2 2/2008 Mills et al.
7,340,287 B2 3/2008 Mason et al.
7,341,559 B2 3/2008 Schulz et al.
7,343,186 B2 3/2008 Lamago et al.
D566,282 S 4/2008 Al-Ali et al.
7,355,512 B1 4/2008 Al-Ali
7,356,365 B2 4/2008 Schurman
7,371,981 B2 5/2008 Abdul-Hafiz
7,373,193 B2 5/2008 Al-Ali et al.
7,373,194 B2 5/2008 Weber et al.
7,376,453 B1 5/2008 Diab et al.
7,377,794 B2 5/2008 Al-Ali et al.
7,377,899 B2 5/2008 Weber et al.
7,383,070 B2 6/2008 Diab et al.
7,415,297 B2 8/2008 Al-Ali et al.
7,428,432 B2 9/2008 Ali et al.
7,438,683 B2 10/2008 Al-Ali et al.
7,440,787 B2 10/2008 Diab
7,454,240 B2 11/2008 Diab et al.
7,467,002 B2 12/2008 Weber et al.
7,469,157 B2 12/2008 Diab et al.
7,471,969 B2 12/2008 Diab et al.
7,471,971 B2 12/2008 Diab et al.
7,483,729 B2 1/2009 Al-Ali et al.
7,483,730 B2 1/2009 Diab et al.
7,489,958 B2 2/2009 Diab et al.
7,496,391 B2 2/2009 Diab et al.
7,496,393 B2 2/2009 Diab et al.
D587,657 S 3/2009 Al-Ali et al.
7,499,741 B2 3/2009 Diab et al.
7,499,835 B2 3/2009 Weber et al.
7,500,950 B2 3/2009 Al-Ali et al.
7,509,154 B2 3/2009 Diab et al.
7,509,494 B2 3/2009 Al-Ali
7,510,849 B2 3/2009 Schurman et al.
7,526,328 B2 4/2009 Diab et al.
7,530,942 B1 5/2009 Diab
7,530,949 B2 5/2009 Al Ali et al.
7,530,955 B2 5/2009 Diab et al.
7,563,110 B2 7/2009 Al-Ali et al.
7,596,398 B2 9/2009 Al-Ali et al.
7,618,375 B2 11/2009 Flaherty
D606,659 S 12/2009 Kiani et al.
7,647,083 B2 1/2010 Al-Ali et al.
D609,193 S 2/2010 Al-Ali et al.
7,668,579 B2 * 2/2010 Lynn 600/323
D614,305 S 4/2010 Al-Ali et al.
RE41,317 E 5/2010 Parker
7,729,733 B2 6/2010 Al-Ali et al.
7,734,320 B2 6/2010 Al-Ali
7,761,127 B2 7/2010 Al-Ali et al.
7,761,128 B2 7/2010 Al-Ali et al.
7,764,982 B2 7/2010 Dalke et al.
D621,516 S 8/2010 Kiani et al.
7,791,155 B2 9/2010 Diab
7,801,581 B2 9/2010 Diab
7,822,452 B2 10/2010 Schurman et al.
RE41,912 E 11/2010 Parker
7,844,313 B2 11/2010 Kiani et al.
7,844,314 B2 11/2010 Al-Ali
7,844,315 B2 11/2010 Al-Ali
7,865,222 B2 1/2011 Weber et al.
7,873,497 B2 1/2011 Weber et al.
7,880,606 B2 2/2011 Al-Ali
7,880,626 B2 2/2011 Al-Ali et al.
7,891,355 B2 2/2011 Al-Ali et al.
7,894,868 B2 2/2011 Al-Ali et al.
7,899,507 B2 3/2011 Al-Ali et al.
7,899,518 B2 3/2011 Trepagnier et al.
7,904,132 B2 3/2011 Weber et al.
7,909,772 B2 3/2011 Popov et al.
7,910,875 B2 3/2011 Al-Ali
7,919,713 B2 4/2011 Al-Ali et al.
7,937,128 B2 5/2011 Al-Ali
7,937,129 B2 5/2011 Mason et al.
7,937,130 B2 5/2011 Diab et al.
2002/0103454 A1 * 8/2002 Sackner et al. 604/19
2003/0191373 A1 * 10/2003 Blike 600/300
2003/0208113 A1 * 11/2003 Mault et al. 600/316
2003/0214409 A1 * 11/2003 Hickie 340/573.1
2004/0039295 A1 2/2004 Olbrich et al.
2004/0078219 A1 4/2004 Kaylor et al.
2004/0186410 A1 * 9/2004 Davidner et al. 604/5.01
2004/0236229 A1 * 11/2004 Freeman et al. 600/474
2005/0001728 A1 1/2005 Appelt et al.
2005/0038332 A1 * 2/2005 Saidara et al. 600/347
2005/0054942 A1 * 3/2005 Melker et al. 600/532
2005/0065556 A1 * 3/2005 Reghabi et al. 607/5
2005/0101841 A9 * 5/2005 Kaylor et al. 600/300
2005/0143632 A1 * 6/2005 Elaz et al. 600/301
2005/0148832 A1 7/2005 Reghabi et al.
2005/0277912 A1 * 12/2005 John 604/890.1
2005/0288571 A1 * 12/2005 Perkins et al. 600/407
2006/0020179 A1 * 1/2006 Anderson et al. 600/309
2006/0155176 A1 * 7/2006 Ebner et al. 600/301
2006/0241358 A1 * 10/2006 Al-Ali et al. 600/301
2006/0276695 A9 * 12/2006 Lynn et al. 600/300
2007/0024946 A1 * 2/2007 Panasyuk et al. 359/253
2007/0032733 A1 * 2/2007 Burton 600/509
2007/0093701 A1 * 4/2007 Myers et al. 600/323
2007/0100213 A1 * 5/2007 Dossas et al. 600/300
2007/0129647 A1 * 6/2007 Lynn 600/538
2007/0191697 A1 * 8/2007 Lynn et al. 600/323
2007/0219434 A1 * 9/2007 Abreu 600/301
2007/0282212 A1 * 12/2007 Sierra et al. 600/529
2008/0051764 A1 * 2/2008 Dent et al. 604/890.1
2008/0221408 A1 * 9/2008 Hoarau et al. 600/310
2008/0286763 A1 * 11/2008 Russwurm et al. 435/6
2008/0306353 A1 * 12/2008 Douglas et al. 600/301
2009/0069642 A1 * 3/2009 Gao et al. 600/300
2009/0299154 A1 * 12/2009 Segman 600/301

OTHER PUBLICATIONS

- Dellinger, R.P., MD, et al., "Surviving Sepsis Campaign Guidelines for Management of Severe Sepsis and Septic Shock," *Critical Care Medicine*, vol. 32, No. 3, pp. 858-873.
Masimo, "SpCO™ Pulse CO-Oximetry™", pp. 1-4 (2005).
Ohashi, K., et al., "Elevated Methemoglobin in Patients with Sepsis," *ACTA Anaesthesiologica Scandinavica*, 42, pp. 713-716 (1998).

(56)

References Cited

OTHER PUBLICATIONS

www.ccmjournal.com/pt/re/ccm/fulltext.00003246-199806000-00019.htm;jsessionid=, "Septic Shock: An Analysis of Outcomes for Patients with Onset on Hospital Wards Versus Intensive Care Units," *Critical Care Medicine*, vol. 26(6), 9 pages (Jun. 1998), downloaded and printed from the World Wide Web on Feb. 1, 2006.

<http://www.ispub.com/ostia/index.php?xmlFilePath=journals/ijpn/vol2n2/sepsis.xml>, "Plasma Carbon Monoxide Levels in Pediatrics Sepsis Syndrome," *The Internet Journal of Pediatrics and Neonatology*, vol. 2, No. 2, 11 pages (2002), downloaded and printed from the World Wide Web on Oct. 14, 2005.

* cited by examiner

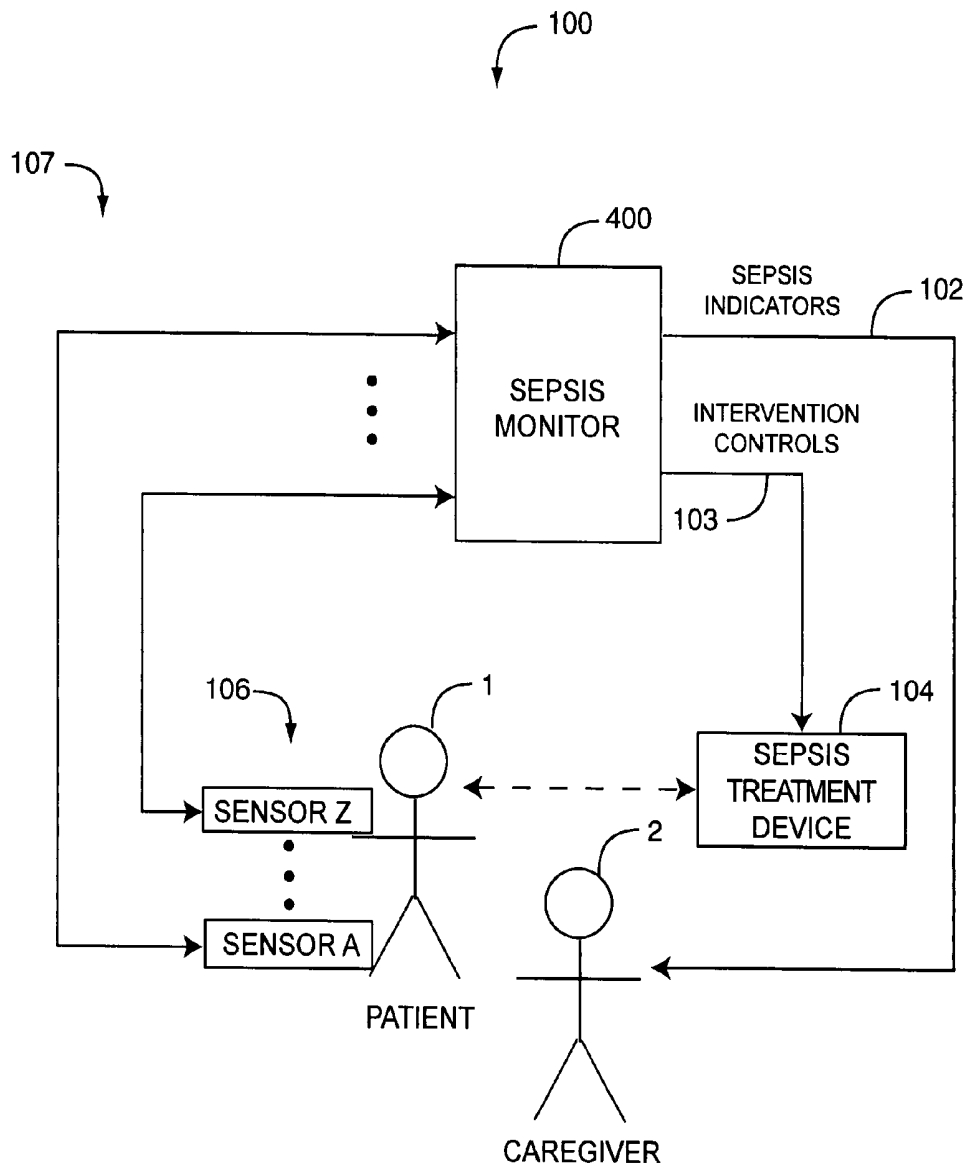


FIG. 1

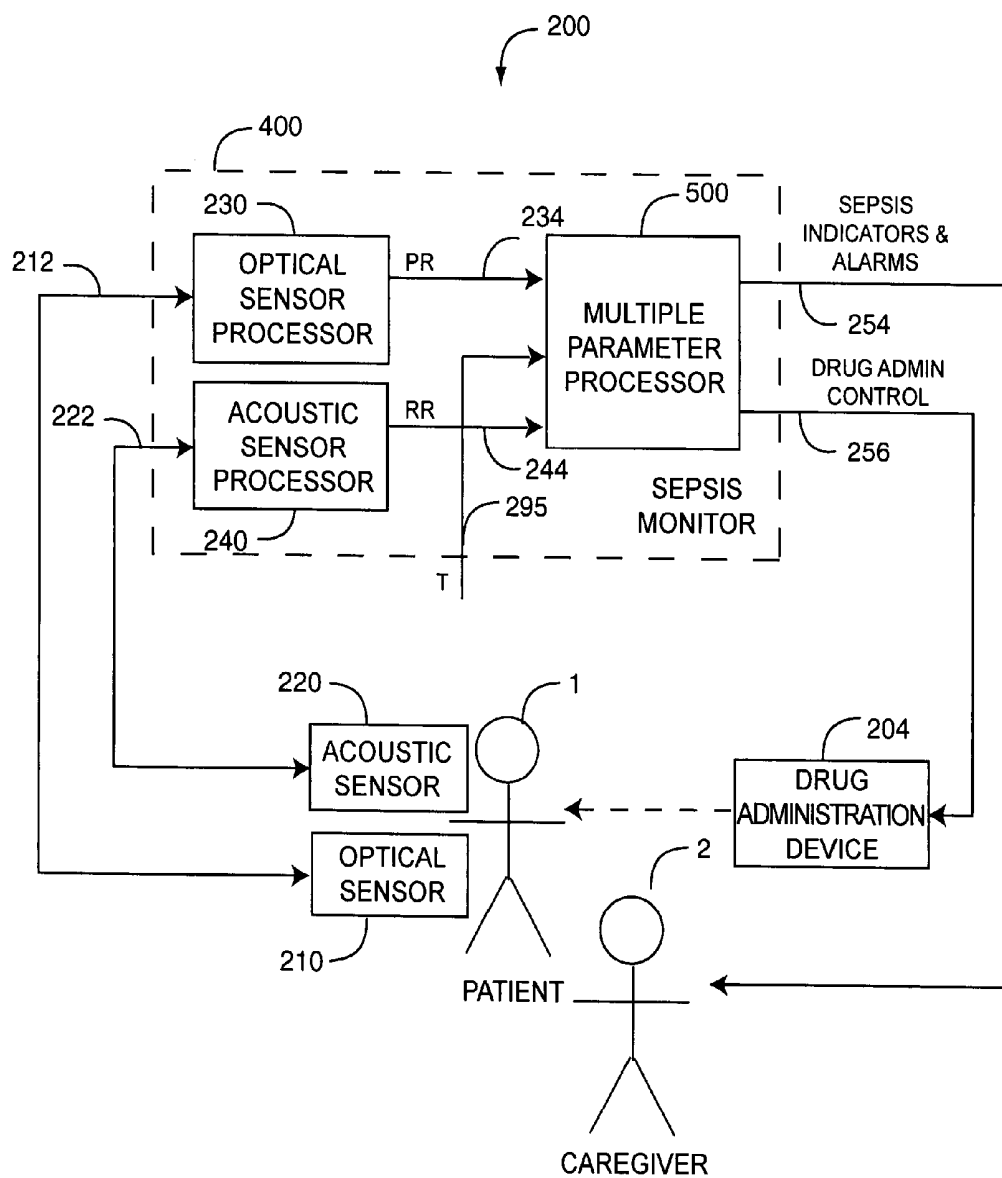


FIG. 2A

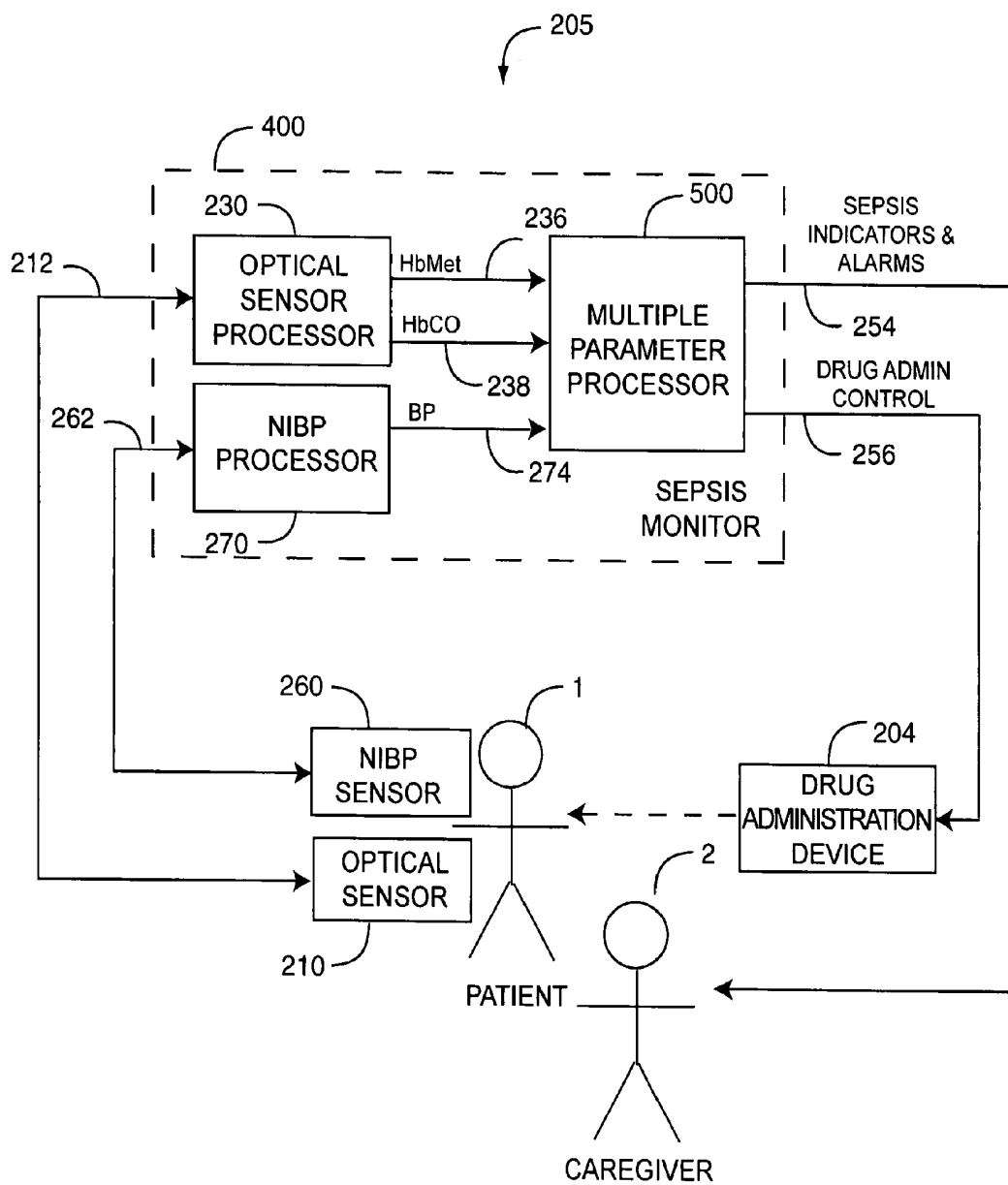


FIG. 2B

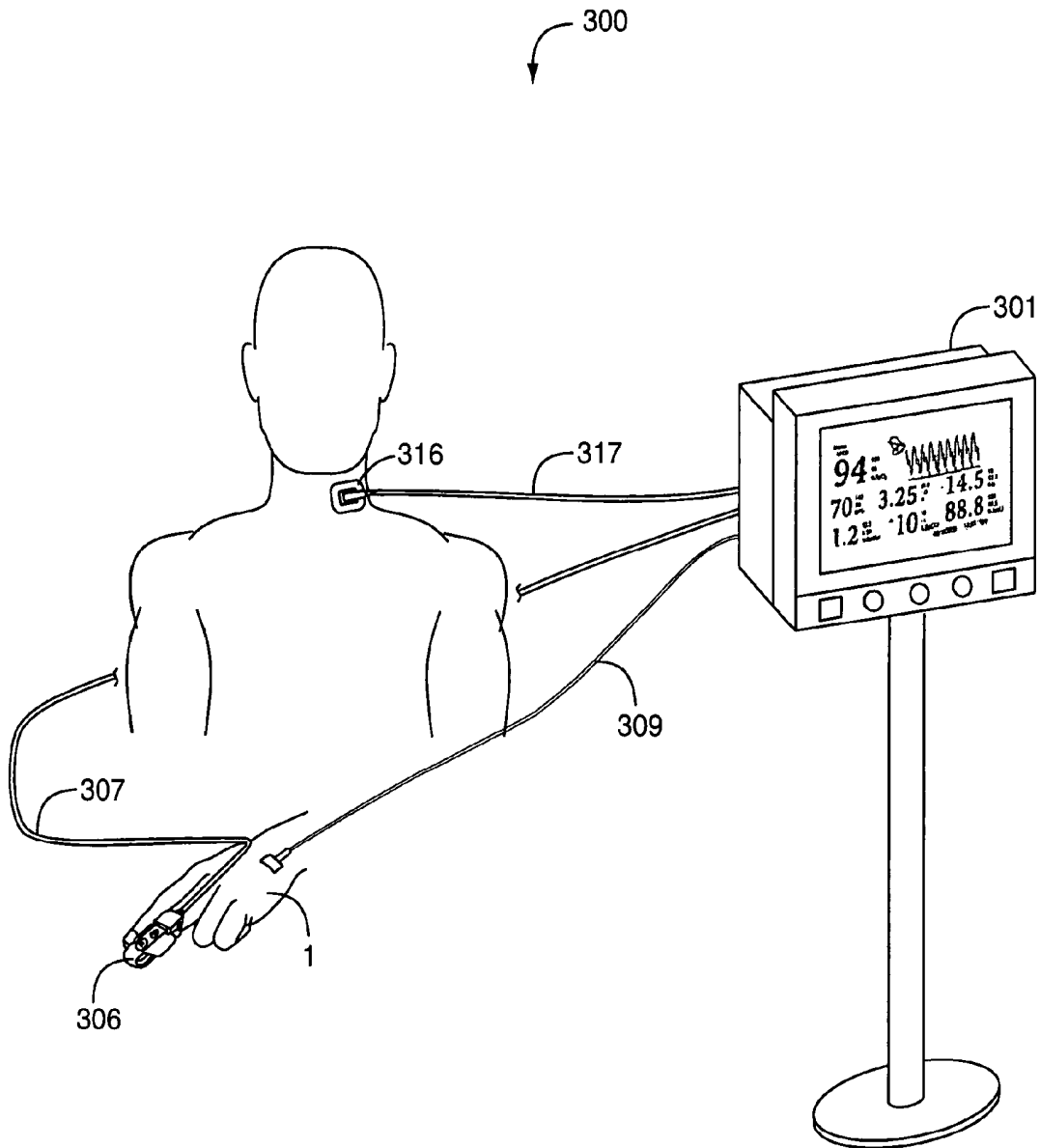


FIG. 3

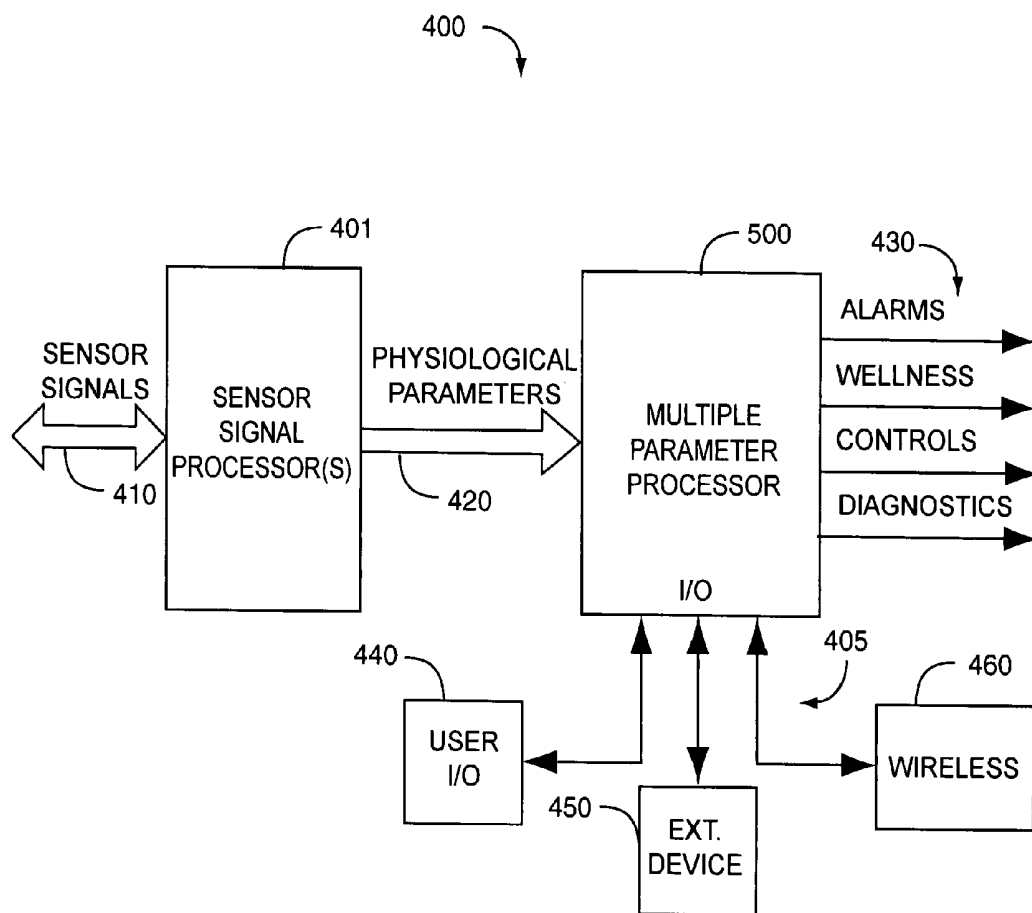


FIG. 4

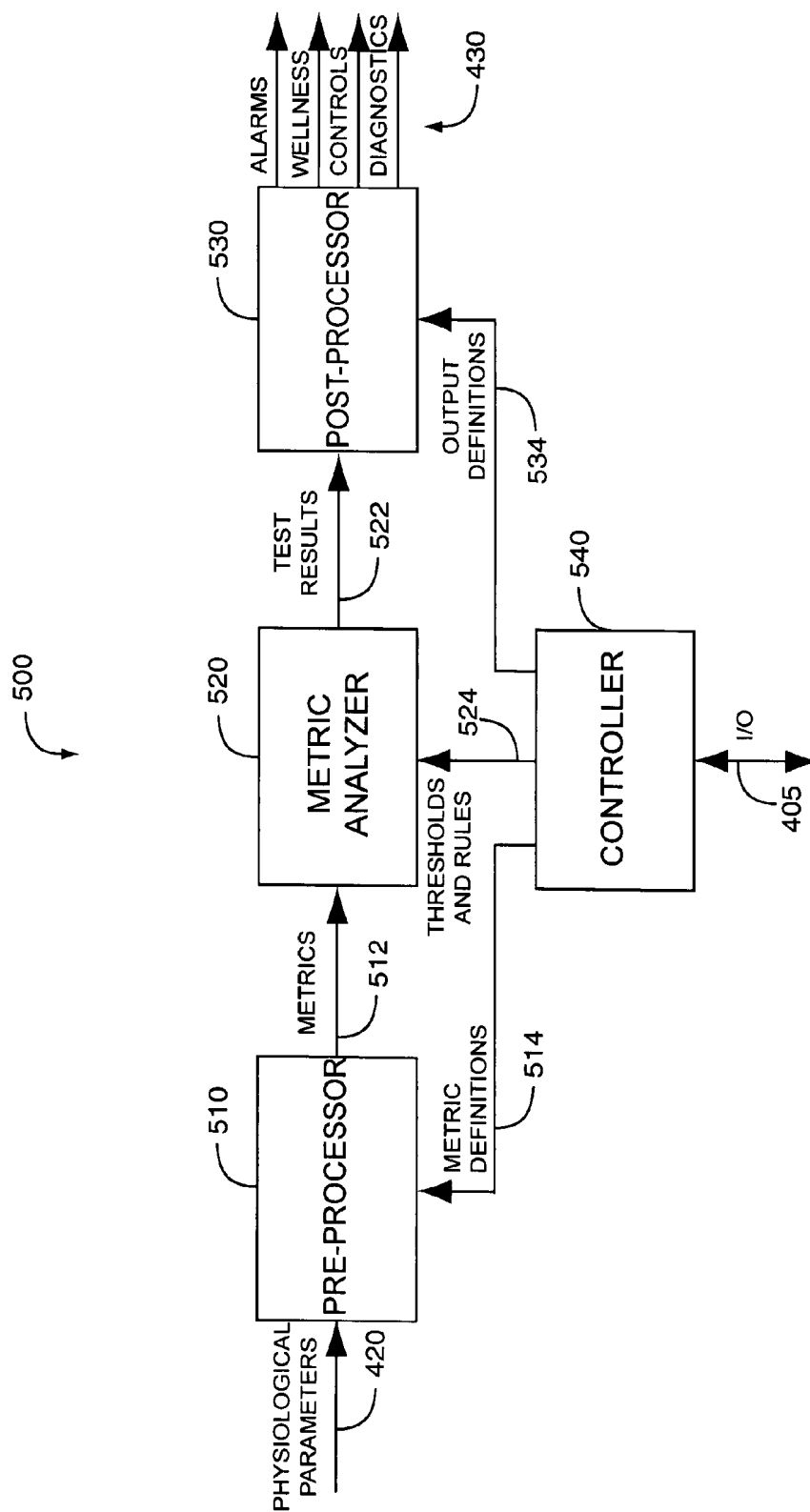


FIG. 5

1

SEPSIS MONITOR

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application claims priority benefit under 35 U.S.C. §120 to, and is a continuation of U.S. patent application Ser. No. 11/803,936, filed May 15, 2007 entitled "Sepsis Monitor," which claims priority benefit under 35 U.S.C. §119 (e) from U.S. Provisional Application No. 60/800,629, filed May 15, 2006, entitled "Septic Shock Monitor." The present application also incorporates the foregoing disclosures herein by reference.

BACKGROUND OF THE INVENTION

Sepsis is a serious medical condition caused by the body's response to an infection. The source of the infection can be any of a number of places throughout the body. Bacterial infections are the most common cause of sepsis, but sepsis can also be caused by fungal, parasitic, or viral infections. Toxins produced by an untreated or inadequately treated infection circulate in the bloodstream causing damage, for example, to the brain, heart, lungs, kidneys and liver. Severe sepsis can result in septic shock, a medical emergency in which the organs and tissues of the body are not receiving an adequate flow of blood.

SUMMARY OF THE INVENTION

The signs and symptoms of sepsis may be subtle. The unacceptably low survival rate of severe sepsis indicates that current patient identification strategies may be lacking. For example, conventional patient monitors give insufficient advance warning of deteriorating patient health or the onset of potentially serious physiological conditions resulting from sepsis. Advantageously, a sepsis monitor noninvasively measures patient condition so as to provide caregivers with an advanced warning or prediction of the onset sepsis. A sepsis monitor may also be configured to provide automatic intervention or treatment of sepsis.

SIRS (systemic inflammatory response syndrome) refers to the systemic activation of the body's immune response, such as from sepsis. SIRS is manifested by, for example, the presence of more than one of a temperature greater than 38° C. or less than 36° C.; a heart rate greater than 90 beats/min.; and a respiration rate greater than 20 breaths/min. Thus, in an embodiment, a sepsis monitor is responsive to more than one of pulse rate, respiration rate and temperature.

Sepsis also results in large amounts of nitrous oxide (NO) released into the blood. It has been shown that NO functions, in part, as a killer molecule that is activated by immune cells. The overproduction of NO during sepsis induces excessive vascular relaxation and a profound hypotension that is also a characteristic feature of sepsis. NO interacts rapidly with hemoglobin to form methemoglobin (HbMet). Thus, HbMet can function as a marker for NO generation in patients with sepsis. Further, endogenously produced CO functions as a messenger molecule as part of a complex cascade of mediators resulting from sepsis. A portion of the endogenous CO is exhaled and a portion is present as carboxyhemoglobin (HbCO). Thus, in an embodiment, a sepsis monitor is responsive to one or more of HbCO, HbMet and blood pressure.

In an embodiment, sepsis monitoring is based upon one or more physiological parameters and associated parameter limits, trends, patterns and variability, alone or in combination. The physiological parameters may include: blood parameters

2

derived from an optical sensor including one or more of oxygen saturation (SpO₂), pulse rate, HbCO and HbMet; respiration rate (RR) derived from an acoustic sensor or a capnography sensor, as examples; noninvasive blood pressure (NIBP) derived from a blood pressure sensor, such as an inflatable cuff and corresponding acoustic sensor, a continuous NIBP(CNIBP) measurement device or an intelligent cuff inflation (ICI) device, to name a few; and temperature manually measured or derived from a thermistor or other temperature transducer.

One aspect of a sepsis monitor is sensors attached to a living being so as to generate corresponding sensor signals. A monitor is in communications with the sensors so as to derive physiological parameters responsive to the sensor signals. Predetermined limits are applied to the physiological parameters. At least one indicator responsive to the physiological parameters and the predetermined limits signal the onset of a sepsis condition in the living being.

Another aspect of a sepsis monitor is identifying physiological parameters indicative of an onset of a sepsis condition in a living being. Sensor signals are generated that are responsive to the physiological parameters. The physiological parameters are computed from the sensor signals. Predetermined rules are applied to the physiological parameters so as to determine the onset of the sepsis condition. An indicator signals the potential existence and likely nonexistence of the sepsis condition.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a general block diagram of a sepsis monitoring system;

FIGS. 2A-B are detailed diagrams of sepsis monitoring system embodiments;

FIG. 3 is an illustration of a sepsis monitoring system embodiment;

FIG. 4 is a general block diagram of a sepsis monitor incorporating a multiple parameter processor; and

FIG. 5 is a detailed block diagram of a multiple parameter processor embodiment.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

FIG. 1 illustrates a sepsis monitoring system **100** having one or more sensors **106** generating sensor signals **107** in response to physiological states of a living being, such as a patient **1**. A sepsis monitor **400** processes the sensor signals **107** and generates sepsis indicators **102** or intervention controls **103** or both, in response. In an open-loop configuration, one or more sepsis indicators **102** are observed by a caregiver **2**, who administers treatment in response. Alternatively, or in addition, the caregiver **2** initiates, pauses, halts or adjusts the settings of a sepsis treatment device **104** in response to the sepsis indicators **102**. In an embodiment, the sepsis indicators **102** signal one or more of a prediction of the onset of sepsis, a sepsis condition, a prediction of the onset of septic shock and a septic shock condition. In a closed-loop configuration, the sepsis treatment device **104** is responsive to one or more intervention controls **103** so as to affect the treatment of the patient **1**, including, for example, initiating, pausing, halting or adjusting the dosage of administered drugs. In an embodiment, the intervention controls **103** are responsive to one or more of a prediction of the onset of sepsis, a sepsis condition, a prediction of the onset of septic shock and a septic shock condition.

As shown in FIG. 1, the sepsis treatment device **104** may be a drug infusion device, a medical gas inhalation device or a ventilation device to name a few. Drug infusion device and gas inhalation device control is described in U.S. patent application Ser. No. 11/654,904, filed Jan. 17, 2007, entitled Drug Administration Controller and incorporated by reference herein. Closed loop respirator control is described in U.S. patent application Ser. No. 11/585,678, filed Oct. 23, 2006, entitled Robust Ventilator Control and incorporated by reference herein.

As shown in FIG. 1, sensors **106** provide noninvasive measurements and include, for example, an optical sensor attached to a tissue site, such as a fingertip, for measuring one or more blood parameters. Noninvasive sensors **106** may also include acoustic sensors, blood pressure cuffs, ECG or EEG electrodes, CO₂ measuring capnography sensors and temperature sensors to name but a few. The sepsis monitor **400** is responsive to sensors signals **107** so as to generate parameter measurements, which may include SpO₂, pulse rate, perfusion index, perfusion variability index, HbCO, HbMet, total hemoglobin, fractional saturation, glucose, cyanide, respiration rate, blood pressure, CO₂, bilirubin, lung volume, cardiac output, temperature, consciousness and hydration measures, among other parameters. Such parameters may be measured intermittently or continuously. Although sensors **106** are described above with respect to noninvasive technologies, sensors **106** may be invasive or noninvasive. Invasive measurements may require a person to prepare a blood or tissue sample, which is then processed by an instrument or testing device, with the result read from the instrument or device and manually entered into the sepsis monitor **400**.

The sepsis monitor **400** may be a single instrument incorporating various hardware, software, circuits and code for processing sensor signals, deriving physiological parameters and processing those parameters to generate the indicators and controls described above. Alternatively, the sepsis monitor **400** may integrate one or more standalone instruments or plug-ins, each of which process specific sensor signals and derive particular physiological parameters. These may include blood parameter monitors, respiration rate monitors, blood pressure monitors, ECG and EEG monitors and capnometers, as a few examples.

In an embodiment, sensors **106** include a multiple wavelength optical sensor, such as described in U.S. patent application Ser. No. 11/376,013, filed Mar. 1, 2006 and entitled Multiple Wavelength Sensor Emitters; and the sepsis monitor **400** incorporates a patient monitor, such as described in U.S. patent application Ser. No. 11/367,033, filed Mar. 1, 2006 and entitled Noninvasive Multi-Parameter Patient Monitor, both patent applications assigned to Masimo Laboratories, Irvine, Calif. and both incorporated by reference herein.

In an embodiment, sensors **106** and measurement devices **108** include multiple wavelength sensors and corresponding noninvasive blood parameter monitors, such as Rainbow™ adhesive and reusable sensors and RAD-57™ and Radical-7™ monitors for measuring SpO₂, pulse rate, perfusion index, signal quality, HbCO and HbMet among other parameters. The Rainbow™ sensors and RAD-57™ and Radical-7™ monitors are available from Masimo Corporation, Irvine, Calif. In an embodiment, sensors **106** include a pulse oximetry sensor, such as described in U.S. Pat. No. 5,782,757 entitled Low Noise Optical Probes and the sepsis monitor **400** incorporates a pulse oximeter, such as described in U.S. Pat. No. 5,632,272 entitled Signal Processing Apparatus, both assigned to Masimo Corporation, Irvine, Calif. and both incorporated by reference herein. In other embodiments, sensors **106** also include any of LNOP® adhesive or reusable

sensors, SofTouch™ sensors, Hi-Fi Trauma™ or Blue™ sensor all available from Masimo Corporation, Irvine, Calif. Further, the sepsis monitor **400** may also include any of Radical®, SatShare™, Rad-9™, Rad-5™, Rad-5v™ or PPO+™ Masimo SET® pulse oximeters all available from Masimo Corporation, Irvine, Calif.

In another embodiment, the sepsis monitor **400** and the sepsis treatment device **104** are incorporated within a single unit. For example, the sepsis monitor **400** and treatment device **104** may be incorporated within a single housing, or the devices may be separately housed but physically and proximately connected.

FIGS. 2A-B illustrate sepsis monitoring system embodiments **200**, **205**. As shown in FIG. 2A with respect to a system embodiment **200**, a sepsis monitor **400** is in communications with an optical sensor **210** and an acoustic sensor **220** attached to a patient **1**. An optical sensor processor **230** generates pulsatile-blood related parameters, such as pulse rate (PR) **234**, in response to optical sensor signals **212**. An acoustic sensor processor **240** generates body-sound related parameters **244**, such as respiration rate (RR), in response to acoustic sensor signals **222**. A temperature parameter **295** is generated via a temperature sensor or manually entered. A multiple parameter processor **500** processes the parameter measurements **234**, **244**, **295** alone or in combination and generates sepsis indicators and alarms **254** or drug administration controls **256**, or both, in response. An acoustic sensor is described in U.S. Pat. No. 6,661,161 entitled Piezoelectric Biological Sound Monitor with Printed Circuit Board and a corresponding respirator rate monitor is described in International App. No. PCT/CA2005/000536 and Pub. No. WO 2005/096931, filed Apr. 8, 2005, both applications incorporated by reference herein.

As shown in FIG. 2B with respect to a system embodiment **205**, a sepsis monitor **400** is in communications with an optical sensor **210** and a NIBP sensor **260** attached to a patient **1**. An optical sensor processor **230** generates pulsatile-blood related parameters, such as such as HbCO **236** and HbMet **238** in response to optical sensor signals **212**. An NIBP processor **270** generates blood pressure (BP) parameters, in response to NIBP sensor signals **262**. A multiple parameter processor **500** processes the parameter measurements **236**, **238**, **274** alone or in combination and generates sepsis indicators and alarms **254** or drug administration controls **256**, or both, in response. A continuous NIBP (CNIBP) sensor and processor are described in U.S. Pat. No. 5,590,649 entitled Apparatus and Method for Measuring an Induced Perturbation to Determine Blood Pressure and an intelligent cuff inflation (ICI) sensor and processor are described in U.S. Pat. No. 5,785,659 entitled Automatically Activated Blood Pressure Measurement Device, both patents incorporated by reference herein.

Advantageously, the multiple parameter processor **500** is responsive to a combination of multiple physiological parameters to indicate sepsis so that an alert can be provided based upon these parameters. Further, the multiple parameter processor **500** responds not only to parameter limits but also to parameter trend information, parameter patterns and parameter variability, so as to reflect a patient condition over time. In an embodiment, sepsis indicators **254** include alarms and wellness indicators that indicate stages of sepsis from none, to the onset of sepsis, to severe sepsis and septic shock. These outputs, for example, provide a warning of a potential onset of sepsis at an early stage and can trigger alarms as sepsis symptoms progress. Further, drug administration control **256** controls the administration of drugs or alters drug doses in response to patient condition. In an embodiment, the multiple

parameter processor **500** compares parameter limits and rising or falling trends of the measurements **234**, **244**, **236**, **238**, **274**, **295** alone or in combination, with corresponding predetermined thresholds and generates indicators and alarms **254** or drug administration controls **256** in response. The comparisons utilize a rule-based metric analysis, as described in detail in respect to FIGS. 4-5, below.

In one embodiment, the sepsis indicators **254** include a green indicator signaling a stable condition, a yellow indicator signaling a less stable condition or a potential sepsis onset and a red indicator signaling an unstable or severe sepsis condition. The indicators **254** may be, for example, various display LEDs emitting wavelengths of the appropriate colors. In an embodiment, a sepsis monitor **400** provides indicators **254** according to TABLES 1 and 2 below.

In an embodiment according to TABLE 1, below, if a patient's pulse rate (PR) and respiration rate (RR) are less than predetermined maximum limits and their body temperature is within a predetermined normal range, then the sepsis monitor **400** displays a green indicator. However, if more than one of pulse rate, respiration rate and body temperature are changing, where applicable changes in pulse rate and respiration rate are rate increases, then the sepsis monitor **400** displays a yellow indicator, signaling a potential onset of sepsis. If more than one of pulse rate, respiration rate and temperature become abnormal, including pulse rate and respiration rate above a predetermined limit and temperature outside of a predetermined range, then the sepsis monitor **400** displays a red indicator, signaling a potential sepsis condition.

TABLE 1

Rule-Based Monitor Outputs	
RULE	OUTPUT
If PR < heart rate limit; RR < breathing rate limit; & T in normal range.	Then illuminate green indicator.
If PR rising > heart rate trend limit; RR rising > breathing rate trend limit; & T rising or fallina.	Then illuminate yellow indicator
If PR > heart rate limit; RR > breathing rate limit; & T outside normal range.	Then illuminate red indicator; Trigger audible alarm.

In an embodiment according to TABLE 2, below, if a patient's carboxyhemoglobin (HbCO), methemoglobin (HbMet) and blood pressure (BP) are normal, i.e. HbCO and HbMet less than predetermined maximum limits and BP greater than a predetermined minimum limit, then the sepsis monitor **400** displays a green indicator. However, if any of HbCO, HbMet and BP are changing, where applicable changes in HbCO and HbMet are increases and the applicable change in BP is a decrease, then the sepsis monitor **400** displays a yellow indicator, signaling a potential onset of sepsis. If any of HbCO, HbMet and BP change beyond predetermined limits, then the sepsis monitor **400** displays a red indicator, signaling a potential sepsis condition.

TABLE 2

Additional Rule-Based Monitor Outputs	
RULE	OUTPUT
If HbCO < CO limit; HbMet < Met limit; & BP > blood pressure limit.	Then illuminate green indicator.

TABLE 2-continued

Additional Rule-Based Monitor Outputs	
RULE	OUTPUT
If HbCO rising > CO trend limit; HbMet rising > Met trend limit or BP falling.	Then illuminate yellow indicator
If HbCO > HbCO limit threshold; HbMet > HbMet limit threshold; or BP < blood pressure limit.	Then trigger an alarm, such as An audible or a visual alert or both.

In other embodiments, a sepsis monitor **400** utilizes predetermined limits and ranges on any or all of PR, RR, T, HbCO, HbMet and BP to indicate no sepsis, a potential onset of sepsis or a sepsis condition, with green, yellow and red indicators or with other visual and audible indicators, displays and alarms. Other indicators, alarms, controls and diagnostics in response to various combinations of parameters and thresholds can be substituted for, or added to, the rule-based outputs illustrated in TABLES 1 and 2.

Other parameter measurements that may be input to the multiple parameter processor **500** include oxygen saturation (SpO₂) and perfusion index (PI) as derived from a pulse oximeter, EGG, EEG and ETCO₂, to name a few. All of these parameters may indicate real-time measurements and historical data such as measurement trends, patterns and variability. Signal quality measurements may also be input to the multiple parameter processor **500**. Pulse oximetry signal quality and data confidence indicators are described in U.S. Pat. No. 6,684,090 entitled Pulse Oximetry Data Confidence Indicator, a pattern recognition alarm indicator is described in U.S. Pat. No. 6,822,564 entitled Parallel Measurement Alarm Processor, both patents assigned to Masimo Corporation, Irvine, Ga. and incorporated by reference herein.

FIG. 3 illustrates a sepsis monitoring system **300** combining a sepsis monitor **400** (FIG. 1) and a drug administration device **204** (FIGS. 2A-B) into a drug infusion monitor **301**. The sepsis monitoring system **300** has an optical sensor **306** and a piezoelectric sensor **316** attached to a patient's body **1**. The optical sensor **306** detects pulsatile blood components and the piezoelectric sensor **316** detects tracheal sounds. The corresponding optical and acoustic sensor signals are transmitted to the drug infusion monitor **301** via an optical-sensor cable **307** and an acoustic-sensor cable **317**. The drug infusion monitor **301** generates blood parameter measurements such as PR, HbCO and HbMet and biological sound measurements such as respiration rate (RR) and processes the measurements to display sepsis indicators and administer corresponding treatments. In a particular embodiment, the drug infusion monitor **301** intravenously administers one or more drugs, such as recombinant activated protein C, to the patient **1** in doses and dose intervals so as to respond to varying stages of sepsis or the potential onset of sepsis and to transitions between less severe and more severe stages of sepsis.

FIG. 4 illustrates a sepsis monitor embodiment **400** having sensor signal processor(s) **401**, a multiple parameter processor **500**, sensor signal inputs **410** to the signal processor(s) **401** and monitor outputs **430** from the parameter processor **500**. Monitor outputs **430** may be sepsis alarms, wellness indicators, controls and sepsis diagnostics. Alarms may be used to alert medical personnel to a potential urgent or emergency medical condition in a patient under their care. Wellness indicators may be used to inform medical personnel as to patient condition stability or instability, such as a less urgent but potentially deteriorating medical state or condition. Diagnostics may be messages or other indicators used to assist medical personnel in diagnosing or treating a patient condi-

tion. Controls may be used to affect the operation of a medical treatment device, as described above, or other medical-related equipment.

In an embodiment, the multiple parameter processor **500** also has an input and output port (I/O) **405** that provides communications to the outside world. The I/O includes user I/O and external device communications to name a few. User I/O allows manual data entry and control. For example, a menu-driven operator display may be provided to allow entry of predetermined alarm thresholds. External device communications may include interfaces, networks or wireless communications to PCs, printers, chart recorders or displays to name a few.

FIG. 5 illustrates a sepsis monitor embodiment **500** having a pre-processor **510**, a metric analyzer **520**, a post-processor **530** and a controller **540**. The pre-processor **510** has inputs **420** that may be real-time physiological parameter measurements, historical physiological parameter measurements, signal quality measures or any combination of the above. The pre-processor **510** generates metrics **512** that may include historical or real-time parameter trends, detected parameter patterns, parameter variability measures and signal quality indicators to name a few. As examples, trend metrics may indicate if a physiological parameter is increasing or decreasing at a certain rate over a certain time, pattern metrics may indicate if a parameter is cyclical within a particular frequency range or over a particular time period, variability metrics may indicate the extent of parameter stability.

As shown in FIG. 5, the metric analyzer **520** is configured to provide test results **522** to the post-processor based upon various rules applied to the metrics **512** in view of various thresholds **524**. As an example, the metric analyzer **520** may output an alarm trigger **522** to the post-processor **530** when a parameter measurement **503** increases faster than a predetermined rate. This may be expressed, as an example, by a rule that states "if trend metric exceeds trend threshold then trigger alarm." TABLE 1 and TABLE 2, above, illustrate sepsis monitor rules applied to metrics including PR, RR, T, HbCO, HbMet and BP parameters and trends.

Also shown in FIG. 5, the post processor **530** inputs test results **522** and generates outputs **502** including alarms, wellness indicators, controls and diagnostics. Alarms may be, for example, audible or visual alerts warning of critical conditions that need immediate attention. Wellness indicators may be audible or visual cues, such as an intermittent, low-volume tone or a red/yellow/green light indicating a patient with a stable or unstable physiological condition, as examples. Controls may be electrical or electronic, wired or wireless or mechanical outputs, to name a few, capable of interfacing with and affecting another device. Diagnostics may indicate a particular patient condition, such as the potential onset of sepsis.

Further shown in FIG. 5, the controller **540** interfaces with I/O **509**. In one embodiment, the I/O **509** provides predetermined thresholds, which the controller **540** transmits to the metric analyzer **520**. The controller **540** may also define metrics **514** for the pre-processor **510** and define outputs **534** for the post-processor **530**.

A sepsis monitor has been disclosed in detail in connection with various embodiments. These embodiments are disclosed by way of examples only and are not to limit the scope of the claims that follow. One of ordinary skill in art will appreciate many variations and modifications.

What is claimed is:

1. A patient monitoring method seeking to identify a sepsis condition in said patient, said method comprising:

noninvasively generating a plurality of sensor signals responsive to physiological parameters indicative of an onset of a sepsis condition in a said patient, at least one of said sensor signals responsive to the output of a non-invasive optical sensor;

electronically computing measurements for said physiological parameters from the sensor signals, said parameters including at least, pulse rate, temperature, and respiration;

said respiration parameter responsive to measurements taken by an acoustic sensor applied to the neck, and said pulse rate parameter responsive to measurements taken by a pulse oximeter applied to a digit;

applying a plurality of predetermined rules to the physiological parameters so as to determine the onset of the sepsis condition; and

indicating to an observer the potential existence of the sepsis condition.

2. The sepsis monitoring method according to claim 1 wherein the acoustic sensor detects tracheal sounds of the living being.

3. The sepsis monitoring method according to claim 2 wherein the applying comprises determining if the temperature is outside a predetermined range.

4. The sepsis monitoring method according to claim 3 wherein the applying comprises determining if the pulse rate and the respiration rate are greater than a plurality of predetermined limits.

5. The sepsis monitoring method according to claim 4 wherein the indicating comprises activating a first colored light to indicate nonexistence of a sepsis condition and a second colored light to indicate a potential existence of a sepsis condition.

6. The sepsis monitoring method according to claim 1 further comprising sending a control signal to a drug administration device intravenously in communications with the living being in response to the applying step so as to provide treatment for the sepsis condition.

7. A method of electronically monitoring signals indicative of a patient condition to determine when to warn a caregiver that said patient condition is indicative of sepsis, the method comprising:

outputting a first signal from a noninvasive optical sensor applied to a digit indicative of an absorption of light by body tissue of said patient, said first signal also indicative of one or more physiological parameters of said patient including a pulse rate;

outputting a second signal from a noninvasive acoustic sensor applied to an area of skin around a patient's throat where said second signal is indicative of acoustically sensed tracheal sounds;

outputting a third signal from a thermal sensor wherein the signal is indicative of a temperature of the patient;

electronically processing with a processor said first signal to output measurement values for said one or more physiological parameters including at least the pulse rate, processing with said processor said second signal to output measurement values for respiration, and processing with said processor said third signal to output measurement values for said temperature;

electronically applying with said processor a plurality of predetermined rules to said measurement values; and when said application of said rules indicates said patient condition is indicative that sepsis potentially exists, or that sepsis likely exists, outputting at least one of an audio or visual indication to said caregiver that sepsis

potentially exists, or that sepsis likely exists respectively according to the indication from the application of the rules.

8. The method according to claim 7, wherein the audio or visual indication is a colored light. 5

9. The method according to claim 7, further comprising sending a control signal to a drug administration device intravenously in communications with said patient, said control signal responsive to said indication of said sepsis, said device providing treatment for said sepsis. 10

10. The method of claim 7, wherein the applying comprises determining if the pulse rate and the respiration rate are greater than a plurality of predetermined limits.

11. The method of claim 7, wherein the applying comprising determining if the temperature is outside a normal range. 15

* * * * *

专利名称(译)	败血症监测		
公开(公告)号	US8663107	公开(公告)日	2014-03-04
申请号	US13/100172	申请日	2011-05-03
[标]申请(专利权)人(译)	Kiani曾MASSIê		
申请(专利权)人(译)	Kiani曾 , MASSI E.		
当前申请(专利权)人(译)	CERCACOR LABORATORIES , INC.		
[标]发明人	KIANI MASSI E		
发明人	KIANI, MASSI, E.		
IPC分类号	A61B5/00		
CPC分类号	A61B2560/0276 A61B5/6826 A61B5/412 A61B5/6838 A61B5/08 A61B5/0205 A61B5/02455 A61B5/022 A61M5/1723 A61B5/14551 A61B5/082 A61B7/04		
优先权	60/800629 2006-05-15 US		
其他公开文献	US20110208018A1		
外部链接	Espacenet USPTO		

摘要(译)

传感器连接到生物上以产生相应的传感器信号。监视器与传感器通信，以便响应传感器信号导出生理参数。将预定限制应用于生理参数。响应于生理参数和预定限制的至少一个指示器指示生物体中败血症状况的发作。

