US010195429B1

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

(10) **Patent No.: US 10,195,429 B1**
(45) **Date of Patent: Feb. 5, 2019**

(54) **SYSTEMS AND METHODS FOR INTRAVASCULAR CATHETER POSITIONING AND/OR NERVE STIMULATION**

(71) Applicant: **Lungpacer Medical Inc.**, Burnaby (CA)

(72) Inventors: **Viral S. Thakkar**, Burnaby (CA); **Douglas G. Evans**, Downingtown, PA (US); **Matthew J. Gani**, Seattle, WA (US)

(73) Assignee: **Lungpacer Medical Inc.**, Burnaby (CA)

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

(21) Appl. No.: **15/666,989**

(22) Filed: **Aug. 2, 2017**

(51) **Int. Cl.**

A61N 1/36	(2006.01)
A61B 5/042	(2006.01)
A61N 1/05	(2006.01)
A61B 5/00	(2006.01)
A61B 5/0452	(2006.01)

(52) **U.S. Cl.**
CPC ***A61N 1/3601*** (2013.01); ***A61B 5/0422*** (2013.01); ***A61B 5/0452*** (2013.01); ***A61B 5/4893*** (2013.01); ***A61N 1/0551*** (2013.01)

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

(56) **References Cited**

U.S. PATENT DOCUMENTS

1,693,734	A	12/1928	Waggoner
2,532,788	A	12/1950	Sarnoff
2,664,880	A	1/1954	Wales, Jr.
3,348,548	A	10/1967	Chardack
3,470,876	A	10/1969	John

(Continued)

FOREIGN PATENT DOCUMENTS

CN	1652839	A	8/2005
CN	102143781	A	8/2011

(Continued)

OTHER PUBLICATIONS

Amit K. Gupta, "Respiration Rate Measurement Based on Impedance Pneumography", Texas Instruments, SBAA181—Feb. 2011, 11 pages.

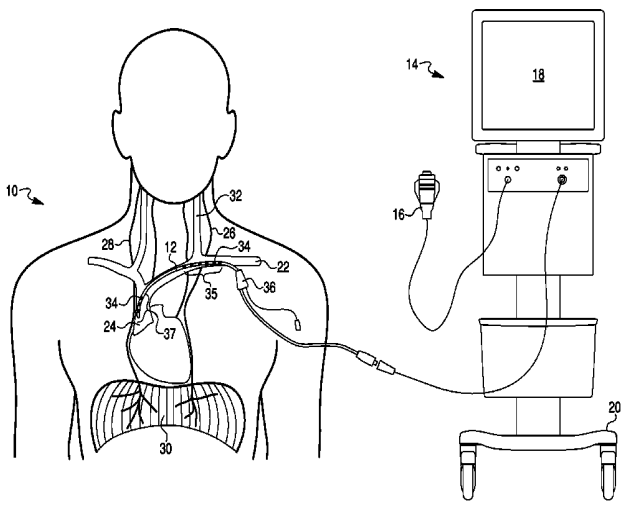
(Continued)

Primary Examiner — Brian T Gedeon
(74) *Attorney, Agent, or Firm* — Bookoff McAndrews, PLLC

(57) **ABSTRACT**

A method for positioning an intravascular catheter may include inserting the intravascular catheter into a venous system of a patient, wherein the catheter includes a plurality of electrodes, and multiple electrodes of the plurality of electrodes are configured to emit electrical signals; positioning a distal portion of the catheter in a first position; using one or more electrodes of the plurality of electrodes to acquire an ECG signal; based on the acquired ECG signal, adjusting the distal portion of the catheter to a second position different from the first position; identifying at least one first electrode of the plurality of electrodes to stimulate a first nerve; identifying at least one second electrode of the plurality of electrodes to stimulate a second nerve; and stimulating at least one of the first and second nerves to cause a contraction of a respiratory muscle.

27 Claims, 7 Drawing Sheets



(56) **References Cited**

U.S. PATENT DOCUMENTS

3,769,984 A 11/1973 Muench
3,804,098 A 4/1974 Friedman
3,817,241 A 6/1974 Grausz et al.
3,835,864 A 9/1974 Rasor et al.
3,847,157 A 11/1974 Caillouette et al.
3,851,641 A 12/1974 Toole et al.
3,896,373 A 7/1975 Stein
3,938,502 A 2/1976 Bom
3,983,881 A 10/1976 Wickham
4,054,881 A 10/1977 Raab
4,072,146 A 2/1978 Howes
4,114,601 A 9/1978 Abels
4,173,228 A 11/1979 Van Steenwyk et al.
4,249,539 A 2/1981 Vilkomerson et al.
4,317,078 A 2/1982 Weed et al.
4,380,237 A 4/1983 Newbower
4,407,294 A 10/1983 Vilkomerson
4,416,289 A 11/1983 Bresler
4,431,005 A 2/1984 McCormick
4,431,006 A 2/1984 Trimmer et al.
4,445,501 A 5/1984 Bresler
RE31,873 E 4/1985 Howes
4,573,481 A 3/1986 Bullara
4,586,923 A 5/1986 Gould et al.
4,587,975 A 5/1986 Salo et al.
4,643,201 A 2/1987 Stokes
4,674,518 A 6/1987 Salo
4,681,117 A 7/1987 Brodman et al.
4,683,890 A 8/1987 Hewson
4,697,595 A 10/1987 Breyer et al.
4,706,681 A 11/1987 Breyer et al.
4,771,788 A 9/1988 Millar
4,819,662 A 4/1989 Heil, Jr. et al.
4,827,935 A 5/1989 Geddes et al.
4,830,008 A 5/1989 Meer
4,840,182 A 6/1989 Carlson
4,852,580 A 8/1989 Wood
4,860,769 A 8/1989 Fogarty et al.
4,905,698 A 3/1990 Strohl, Jr. et al.
4,911,174 A 3/1990 Pederson et al.
4,934,049 A 6/1990 Kiekhafer et al.
4,944,088 A 7/1990 Doan et al.
4,951,682 A 8/1990 Petre
4,957,110 A 9/1990 Vogel et al.
4,989,617 A 2/1991 Memberg et al.
5,005,587 A 4/1991 Scott
5,036,848 A 8/1991 Hewson
5,042,143 A 8/1991 Holleman et al.
5,056,519 A 10/1991 Vince
5,115,818 A 5/1992 Holleman et al.
5,146,918 A 9/1992 Kallok et al.
5,170,802 A 12/1992 Mehra
5,184,621 A 2/1993 Vogel et al.
5,224,491 A 7/1993 Mehra
5,243,995 A 9/1993 Maier
5,265,604 A 11/1993 Vince
5,267,569 A 12/1993 Baer et al.
5,314,463 A 5/1994 Camps et al.
5,316,009 A 5/1994 Yamada
5,324,322 A 6/1994 Grill, Jr. et al.
5,330,522 A 7/1994 Kreyenhagen
5,345,936 A 9/1994 Pomeranz et al.
5,383,923 A 1/1995 Webster, Jr.
5,411,025 A 5/1995 Webster, Jr.
5,417,208 A 5/1995 Winkler
5,451,206 A 9/1995 Young
5,456,254 A 10/1995 Pietroski et al.
5,465,717 A 11/1995 Imran et al.
5,476,498 A 12/1995 Ayers
5,486,159 A 1/1996 Mahurkar
5,507,725 A 4/1996 Savage et al.
5,524,632 A 6/1996 Stein et al.
5,527,358 A 6/1996 Mehmanesh et al.
5,531,686 A 7/1996 Lundquist et al.
5,549,655 A 8/1996 Erickson
5,555,618 A 9/1996 Winkler
5,567,724 A 10/1996 Kelleher et al.
5,584,873 A 12/1996 Shoberg et al.
5,604,231 A 2/1997 Smith et al.
5,665,103 A 9/1997 Lafontaine et al.
5,678,535 A 10/1997 Dimarco
5,683,370 A 11/1997 Luther et al.
5,709,853 A 1/1998 Iino et al.
5,716,392 A 2/1998 Bourgeois et al.
5,733,255 A 3/1998 Dinh et al.
5,755,765 A 5/1998 Hyde et al.
5,776,111 A 7/1998 Tesio
5,779,732 A 7/1998 Amundson
5,782,828 A 7/1998 Chen et al.
5,785,706 A 7/1998 Bednarek
5,788,681 A 8/1998 Weaver et al.
5,813,399 A 9/1998 Isaza et al.
5,814,086 A 9/1998 Hirschberg et al.
RE35,924 E 10/1998 Winkler
5,824,027 A 10/1998 Hoffer et al.
5,827,192 A 10/1998 Gopakumaran et al.
5,916,163 A 6/1999 Panescu et al.
5,944,022 A 8/1999 Nardella et al.
5,954,761 A 9/1999 Machek et al.
5,967,978 A 10/1999 Littmann et al.
5,971,933 A 10/1999 Gopakumaran et al.
5,983,126 A 11/1999 Wittkampf
6,006,134 A 12/1999 Hill et al.
6,024,702 A 2/2000 Iversen
6,096,728 A 8/2000 Collins et al.
6,120,476 A 9/2000 Fung et al.
6,123,699 A 9/2000 Webster, Jr.
6,126,649 A 10/2000 Vantassel et al.
6,136,021 A 10/2000 Tockman et al.
6,157,862 A 12/2000 Brownlee et al.
6,161,029 A 12/2000 Spreigl et al.
6,166,048 A 12/2000 Bencherif
6,171,277 B1 1/2001 Ponzi
6,183,463 B1 2/2001 Webster, Jr.
6,198,970 B1 3/2001 Freed et al.
6,198,974 B1 3/2001 Webster, Jr.
6,201,994 B1 3/2001 Warman et al.
6,208,881 B1 3/2001 Champeau
6,210,339 B1 4/2001 Kiepen et al.
6,212,435 B1 4/2001 Lattner et al.
6,216,045 B1 4/2001 Black et al.
6,236,892 B1 5/2001 Feler
6,240,320 B1 5/2001 Spehr et al.
6,251,126 B1 6/2001 Ottenhoff et al.
6,269,269 B1 7/2001 Ottenhoff et al.
6,292,695 B1 9/2001 Webster, Jr. et al.
6,295,475 B1 9/2001 Morgan
6,360,740 B1 3/2002 Ward et al.
6,397,108 B1 5/2002 Camps et al.
6,400,976 B1 6/2002 Champeau
6,415,183 B1 7/2002 Scheiner et al.
6,415,187 B1 7/2002 Kuzma et al.
6,438,427 B1 8/2002 Rexhausen et al.
6,445,953 B1 9/2002 Bulkes et al.
6,449,507 B1 9/2002 Hill et al.
6,463,327 B1 10/2002 Lurie et al.
6,493,590 B1 12/2002 Wessman et al.
6,508,802 B1 1/2003 Rosengart et al.
6,526,321 B1 2/2003 Spehr
6,569,114 B2 5/2003 Ponzi et al.
6,584,362 B1 6/2003 Scheiner et al.
6,585,718 B2 7/2003 Hayzelden et al.
6,587,726 B2 7/2003 Lurie et al.
6,602,242 B1 8/2003 Fung et al.
6,610,713 B2 8/2003 Tracey
6,630,611 B1 10/2003 Malowaniec
6,643,552 B2 11/2003 Edell et al.
6,651,652 B1 11/2003 Waard
6,682,526 B1 1/2004 Jones et al.
6,702,780 B1 3/2004 Gilboa et al.
6,718,208 B2 4/2004 Hill et al.
6,721,603 B2 4/2004 Zabara et al.
6,757,970 B1 7/2004 Kuzma et al.
6,778,854 B2 8/2004 Puskas

(56) **References Cited**

U.S. PATENT DOCUMENTS

6,779,257 B2 8/2004 Kiepen et al.
6,844,713 B2 1/2005 Steber et al.
RE38,705 E 2/2005 Hill et al.
6,881,211 B2 4/2005 Schweikert et al.
6,885,888 B2 4/2005 Rezai
6,907,285 B2 6/2005 Denker et al.
6,934,583 B2 8/2005 Weinberg et al.
6,981,314 B2 1/2006 Black et al.
6,999,820 B2 2/2006 Jordan
7,018,374 B2 3/2006 Schon et al.
7,047,627 B2 5/2006 Black et al.
7,071,194 B2 7/2006 Teng
7,072,720 B2 7/2006 Puskas
7,077,823 B2 7/2006 McDaniel
7,082,331 B1 7/2006 Park et al.
7,130,700 B2 10/2006 Gardeski et al.
7,142,903 B2 11/2006 Rodriguez et al.
7,149,585 B2 12/2006 Wessman et al.
7,155,278 B2 12/2006 King et al.
7,168,429 B2 1/2007 Matthews et al.
7,184,829 B2 2/2007 Hill et al.
7,206,636 B1 4/2007 Turcott
7,212,867 B2 5/2007 Van Venrooij et al.
7,225,016 B1 5/2007 Koh
7,225,019 B2 5/2007 Jahns et al.
7,229,429 B2 6/2007 Martin et al.
7,231,260 B2 6/2007 Wallace et al.
7,235,070 B2 6/2007 Vanney
7,269,459 B1 9/2007 Koh
7,277,757 B2 10/2007 Casavant et al.
7,283,875 B2 10/2007 Larsson et al.
7,340,302 B1 3/2008 Falkenberg et al.
7,363,085 B1 4/2008 Benser et al.
7,363,086 B1 4/2008 Koh et al.
7,371,220 B1 5/2008 Koh et al.
7,416,552 B2 8/2008 Paul et al.
7,421,296 B1 9/2008 Benser et al.
7,454,244 B2 11/2008 Kassab et al.
7,519,425 B2 4/2009 Benser et al.
7,519,426 B1 4/2009 Koh et al.
7,522,953 B2 4/2009 Gharib et al.
7,553,305 B2 6/2009 Honebrink et al.
7,555,349 B2 6/2009 Wessman et al.
7,569,029 B2 8/2009 Clark et al.
7,591,265 B2 9/2009 Lee et al.
7,593,760 B2 9/2009 Rodriguez et al.
7,613,524 B2 11/2009 Jordan
7,636,600 B1 12/2009 Koh
7,670,284 B2 3/2010 Padget et al.
7,672,728 B2 3/2010 Libbus et al.
7,672,729 B2 3/2010 Koh et al.
7,676,275 B1 3/2010 Farazi et al.
7,676,910 B2 3/2010 Kiepen et al.
7,697,984 B2 4/2010 Hill et al.
7,747,323 B2 6/2010 Libbus et al.
7,771,388 B2 8/2010 Olsen et al.
7,783,362 B2 8/2010 Whitehurst et al.
7,794,407 B2 9/2010 Rothenberg
7,797,050 B2 9/2010 Libbus et al.
7,813,805 B1 10/2010 Farazi
7,819,883 B2 10/2010 Westlund et al.
7,840,270 B2 11/2010 Ignagni et al.
7,853,302 B2 12/2010 Rodriguez et al.
7,869,865 B2 1/2011 Govari et al.
7,891,085 B1 2/2011 Kuzma et al.
7,925,352 B2 4/2011 Stack et al.
7,949,409 B2 5/2011 Bly et al.
7,949,412 B1 5/2011 Harrison et al.
7,962,215 B2 6/2011 Ignagni et al.
7,970,475 B2 6/2011 Tehrani et al.
7,972,323 B1 7/2011 Bencini et al.
7,974,693 B2 7/2011 David et al.
7,974,705 B2 7/2011 Zdeblick et al.
7,979,128 B2 7/2011 Tehrani et al.
7,994,655 B2 8/2011 Bauer et al.
8,000,765 B2 8/2011 Rodriguez et al.
8,019,439 B2 9/2011 Kuzma et al.
8,021,327 B2 9/2011 Selkee
8,036,750 B2 10/2011 Caparso et al.
8,050,765 B2 11/2011 Lee et al.
8,052,607 B2 11/2011 Byrd
8,104,470 B2 1/2012 Lee et al.
8,116,872 B2 2/2012 Tehrani et al.
8,121,692 B2 2/2012 Haefner et al.
8,135,471 B2 3/2012 Zhang et al.
8,140,164 B2 3/2012 Tehrani et al.
8,147,486 B2 4/2012 Honour et al.
8,160,701 B2 4/2012 Zhao et al.
8,160,711 B2 4/2012 Tehrani et al.
8,195,297 B2 6/2012 Penner
8,200,336 B2 6/2012 Tehrani et al.
8,206,343 B2 6/2012 Racz
8,224,456 B2 7/2012 Daglow et al.
8,233,987 B2 7/2012 Gelfand et al.
8,233,993 B2 7/2012 Jordan
8,239,037 B2 8/2012 Glenn et al.
8,244,358 B2 8/2012 Tehrani et al.
8,244,359 B2 8/2012 Gelfand et al.
8,244,378 B2 8/2012 Bly et al.
8,255,056 B2 8/2012 Tehrani
8,256,419 B2 9/2012 Sinderby et al.
8,265,736 B2 9/2012 Sathaye et al.
8,265,759 B2 9/2012 Tehrani et al.
8,275,440 B2 9/2012 Rodriguez et al.
8,280,513 B2 10/2012 Tehrani et al.
8,315,713 B2 11/2012 Burnes et al.
8,321,808 B2 11/2012 Goetz et al.
8,335,567 B2 12/2012 Tehrani et al.
8,340,783 B2 12/2012 Sommer et al.
8,348,941 B2 1/2013 Tehrani
8,369,954 B2 2/2013 Stack et al.
8,374,704 B2 2/2013 Desai et al.
8,388,541 B2 3/2013 Messerly et al.
8,388,546 B2 3/2013 Rothenberg
8,391,956 B2 3/2013 Zellers et al.
8,401,640 B2 3/2013 Zhao et al.
8,401,651 B2 3/2013 Caparso et al.
8,406,883 B1 3/2013 Barker
8,406,885 B2 3/2013 Ignagni et al.
8,412,331 B2 4/2013 Tehrani et al.
8,412,350 B2 4/2013 Bly
8,428,711 B2 4/2013 Lin et al.
8,428,726 B2 4/2013 Ignagni et al.
8,428,730 B2 4/2013 Stack et al.
8,433,412 B1 4/2013 Westlund et al.
8,442,638 B2 5/2013 Libbus et al.
8,457,764 B2 6/2013 Ramachandran et al.
8,467,876 B2 6/2013 Tehrani
8,473,068 B2 6/2013 Farazi
8,478,412 B2 7/2013 Ignagni et al.
8,478,413 B2 7/2013 Karamanoglu et al.
8,478,426 B2 7/2013 Barker
8,483,834 B2 7/2013 Lee et al.
8,504,158 B2 8/2013 Karamanoglu et al.
8,504,161 B1 8/2013 Kornet et al.
8,509,901 B2 8/2013 Tehrani
8,509,902 B2 8/2013 Cho et al.
8,509,919 B2 8/2013 Yoo et al.
8,512,256 B2 8/2013 Rothenberg
8,522,779 B2 9/2013 Lee et al.
8,527,036 B2 9/2013 Jalde et al.
8,532,793 B2 9/2013 Morris et al.
8,554,323 B2 10/2013 Haefner et al.
8,560,072 B2 10/2013 Caparso et al.
8,560,086 B2 10/2013 Just et al.
8,571,662 B2 10/2013 Hoffer
8,571,685 B2 10/2013 Daglow et al.
8,615,297 B2 12/2013 Sathaye et al.
8,617,228 B2 12/2013 Wittenberger et al.
8,620,412 B2 12/2013 Griffiths et al.
8,620,450 B2 12/2013 Tockman et al.
8,626,292 B2 1/2014 McCabe et al.
8,630,707 B2 1/2014 Zhao et al.
8,644,939 B2 2/2014 Wilson et al.

(56) **References Cited**

U.S. PATENT DOCUMENTS

8,644,952 B2 2/2014 Desai et al.
8,646,172 B2 2/2014 Kuzma et al.
8,650,747 B2 2/2014 Kuzma et al.
8,676,323 B2 3/2014 Ignagni et al.
8,676,344 B2 3/2014 Desai et al.
8,694,123 B2 4/2014 Wahlstrand et al.
8,696,656 B2 4/2014 Abboud et al.
8,706,223 B2 4/2014 Zhou et al.
8,706,235 B2 * 4/2014 Karamanoglu A61B 5/042 607/42
8,706,236 B2 4/2014 Ignagni et al.
8,718,763 B2 5/2014 Zhou et al.
8,725,259 B2 5/2014 Kornet et al.
8,738,154 B2 5/2014 Zdeblick et al.
8,755,889 B2 6/2014 Scheiner
8,774,907 B2 7/2014 Rothenberg
8,781,578 B2 7/2014 McCabe et al.
8,781,582 B2 7/2014 Ziegler et al.
8,781,583 B2 7/2014 Cornelussen et al.
8,801,693 B2 8/2014 He et al.
8,805,511 B2 8/2014 Karamanoglu
8,838,245 B2 9/2014 Lin et al.
8,858,455 B2 10/2014 Rothenberg
8,863,742 B2 10/2014 Blomquist et al.
8,886,277 B2 11/2014 Kim et al.
8,897,879 B2 11/2014 Karamanoglu et al.
8,903,507 B2 12/2014 Desai et al.
8,903,509 B2 12/2014 Tockman et al.
8,909,341 B2 12/2014 Gelfand et al.
8,914,113 B2 12/2014 Zhang et al.
8,918,169 B2 12/2014 Kassab et al.
8,918,987 B2 12/2014 Kuzma et al.
8,923,971 B2 12/2014 Haefner et al.
8,942,823 B2 1/2015 Desai et al.
8,942,824 B2 1/2015 Yoo et al.
8,948,884 B2 2/2015 Ramachandran et al.
8,968,299 B2 3/2015 Kauphusman et al.
8,972,015 B2 3/2015 Stack et al.
8,983,602 B2 3/2015 Sathaye et al.
9,008,775 B2 4/2015 Sathaye et al.
9,026,231 B2 5/2015 Hoffer
9,037,264 B2 5/2015 Just et al.
9,042,981 B2 5/2015 Yoo et al.
9,072,864 B2 7/2015 Putz
9,072,899 B1 7/2015 Nickloes
9,108,058 B2 8/2015 Hoffer
9,108,059 B2 8/2015 Hoffer
9,125,578 B2 9/2015 Grunwald
9,138,580 B2 9/2015 Ignagni et al.
9,138,585 B2 9/2015 Saha et al.
9,149,642 B2 10/2015 McCabe et al.
9,168,377 B2 10/2015 Hoffer
9,205,258 B2 12/2015 Simon et al.
9,216,291 B2 12/2015 Lee et al.
9,220,898 B2 12/2015 Hoffer
9,226,688 B2 1/2016 Jacobsen et al.
9,226,689 B2 1/2016 Jacobsen et al.
9,242,088 B2 1/2016 Thakkar et al.
9,259,573 B2 2/2016 Tehrani et al.
9,295,846 B2 3/2016 Westlund et al.
9,314,618 B2 4/2016 Imran et al.
9,333,363 B2 5/2016 Hoffer et al.
9,345,422 B2 5/2016 Rothenberg
9,370,657 B2 6/2016 Tehrani et al.
9,398,931 B2 7/2016 Wittenberger et al.
9,415,188 B2 8/2016 He et al.
9,427,566 B2 8/2016 Reed et al.
9,427,588 B2 8/2016 Sathaye et al.
9,474,894 B2 10/2016 Mercanzini et al.
9,485,873 B2 11/2016 Shah et al.
9,498,625 B2 11/2016 Bauer et al.
9,498,631 B2 11/2016 Demmer et al.
9,504,837 B2 11/2016 Demmer et al.
9,532,724 B2 1/2017 Grunwald
9,533,160 B2 1/2017 Brooke et al.
9,539,429 B2 1/2017 Brooke et al.
9,545,511 B2 1/2017 Thakkar et al.
9,561,369 B2 2/2017 Burnes et al.
9,566,436 B2 2/2017 Hoffer et al.
9,572,982 B2 2/2017 Burnes et al.
9,597,509 B2 3/2017 Hoffer et al.
9,615,759 B2 4/2017 Hurezan
9,623,252 B2 4/2017 Sathaye et al.
9,662,494 B2 5/2017 Young et al.
9,682,235 B1 6/2017 O'Mahony et al.
9,694,185 B2 7/2017 Bauer
9,717,899 B2 8/2017 Kuzma et al.
9,724,018 B2 8/2017 Cho et al.
9,744,351 B1 8/2017 Gelfand et al.
9,776,005 B2 10/2017 Meyyappan
9,861,817 B2 1/2018 Cho et al.
9,872,989 B2 1/2018 Jung et al.
9,884,178 B2 2/2018 Bouton et al.
9,884,179 B2 2/2018 Bouton et al.
9,919,149 B2 3/2018 Imran et al.
9,931,504 B2 4/2018 Thakkar et al.
9,950,167 B2 4/2018 Hoffer et al.
9,956,396 B2 5/2018 Young et al.
9,968,785 B2 5/2018 Hoffer et al.
9,968,786 B2 5/2018 Bauer et al.
2001/0052345 A1 12/2001 Niazi
2002/0026228 A1 2/2002 Schauerte
2002/0056454 A1 5/2002 Samzelius
2002/0065544 A1 5/2002 Smits et al.
2002/0087156 A1 7/2002 Maguire et al.
2002/0128546 A1 9/2002 Silver
2002/0188325 A1 12/2002 Hill et al.
2003/0078623 A1 4/2003 Weinberg et al.
2003/0195571 A1 10/2003 Burnes et al.
2004/0003813 A1 1/2004 Banner et al.
2004/0010303 A1 1/2004 Bolea et al.
2004/0030362 A1 2/2004 Hill et al.
2004/0044377 A1 3/2004 Larsson et al.
2004/0064069 A1 4/2004 Reynolds et al.
2004/0077936 A1 4/2004 Larsson et al.
2004/0088015 A1 5/2004 Casavant et al.
2004/0111139 A1 6/2004 McCreery
2004/0186543 A1 9/2004 King et al.
2004/0210261 A1 10/2004 King et al.
2005/0004565 A1 1/2005 Vanney
2005/0013879 A1 1/2005 Lin et al.
2005/0021102 A1 1/2005 Ignagni et al.
2005/0027338 A1 2/2005 Hill
2005/0033136 A1 2/2005 Govari et al.
2005/0033137 A1 2/2005 Oral et al.
2005/0043765 A1 2/2005 Williams et al.
2005/0065567 A1 3/2005 Lee et al.
2005/0070981 A1 3/2005 Verma
2005/0075578 A1 4/2005 Gharib et al.
2005/0085865 A1 4/2005 Tehrani
2005/0085866 A1 4/2005 Tehrani
2005/0085867 A1 4/2005 Tehrani et al.
2005/0085868 A1 4/2005 Tehrani et al.
2005/0085869 A1 4/2005 Tehrani et al.
2005/0096710 A1 5/2005 Kieval
2005/0109340 A1 5/2005 Tehrani
2005/0113710 A1 5/2005 Stahmann et al.
2005/0115561 A1 6/2005 Stahmann et al.
2005/0131485 A1 6/2005 Knudson et al.
2005/0138791 A1 6/2005 Black et al.
2005/0138792 A1 6/2005 Black et al.
2005/0143787 A1 6/2005 Boveja et al.
2005/0165457 A1 7/2005 Benser et al.
2005/0182454 A1 8/2005 Gharib et al.
2005/0187584 A1 8/2005 Denker et al.
2005/0192655 A1 9/2005 Black et al.
2005/0251238 A1 11/2005 Wallace et al.
2005/0251239 A1 11/2005 Wallace et al.
2005/0288728 A1 12/2005 Libbus et al.
2005/0288730 A1 12/2005 Deem et al.
2006/0030894 A1 2/2006 Tehrani
2006/0035849 A1 2/2006 Spiegelman et al.
2006/0058852 A1 3/2006 Koh et al.
2006/0074449 A1 4/2006 Denker et al.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2006/0122661 A1 6/2006 Mandell
2006/0122662 A1 6/2006 Tehrani et al.
2006/0130833 A1 6/2006 Younes
2006/0142815 A1 6/2006 Tehrani et al.
2006/0149334 A1 7/2006 Tehrani et al.
2006/0155222 A1 7/2006 Sherman et al.
2006/0167523 A1 7/2006 Tehrani et al.
2006/0188325 A1 8/2006 Dolan
2006/0195159 A1 8/2006 Bradley et al.
2006/0217791 A1 9/2006 Spinka et al.
2006/0224209 A1 10/2006 Meyer
2006/0229677 A1 10/2006 Moffitt et al.
2006/0247729 A1 11/2006 Tehrani et al.
2006/0253161 A1 11/2006 Libbus et al.
2006/0253182 A1 11/2006 King
2006/0258667 A1 11/2006 Teng
2006/0259107 A1 11/2006 Caparso et al.
2006/0282131 A1 12/2006 Caparso et al.
2006/0287679 A1 12/2006 Stone
2007/0005053 A1 1/2007 Dando
2007/0021795 A1 1/2007 Tehrani
2007/0027448 A1 2/2007 Paul et al.
2007/0087314 A1 4/2007 Gomo
2007/0093875 A1 4/2007 Chavan et al.
2007/0106357 A1 5/2007 Denker et al.
2007/0112402 A1 5/2007 Grill et al.
2007/0112403 A1 5/2007 Moffitt et al.
2007/0118183 A1 5/2007 Gelfand et al.
2007/0150006 A1 6/2007 Libbus et al.
2007/0168007 A1 7/2007 Kuzma et al.
2007/0173900 A1 7/2007 Siegel et al.
2007/0191908 A1 8/2007 Jacob et al.
2007/0196780 A1 8/2007 Ware et al.
2007/0203549 A1 8/2007 Demarais et al.
2007/0208388 A1 9/2007 Jahns et al.
2007/0221224 A1 9/2007 Pittman et al.
2007/0240718 A1 10/2007 Daly
2007/0250056 A1 10/2007 Vanney
2007/0250162 A1 10/2007 Royalty
2007/0255379 A1 11/2007 Williams et al.
2007/0265611 A1 11/2007 Ignagni et al.
2007/0288076 A1 12/2007 Bulkes et al.
2008/0039916 A1 2/2008 Colliou et al.
2008/0065002 A1 3/2008 Lobl et al.
2008/0125828 A1 5/2008 Ignagni et al.
2008/0161878 A1 7/2008 Tehrani et al.
2008/0167695 A1 7/2008 Tehrani et al.
2008/0177347 A1 7/2008 Tehrani et al.
2008/0183186 A1 7/2008 Bly et al.
2008/0183187 A1 7/2008 Bly
2008/0183239 A1 7/2008 Tehrani et al.
2008/0183240 A1 7/2008 Tehrani et al.
2008/0183253 A1 7/2008 Bly
2008/0183254 A1 7/2008 Bly et al.
2008/0183255 A1 7/2008 Bly et al.
2008/0183259 A1 7/2008 Bly et al.
2008/0183264 A1 7/2008 Bly et al.
2008/0183265 A1 7/2008 Bly et al.
2008/0188903 A1 8/2008 Tehrani et al.
2008/0215106 A1 9/2008 Lee et al.
2008/0288010 A1 11/2008 Tehrani et al.
2008/0288015 A1 11/2008 Tehrani et al.
2008/0312712 A1 12/2008 Penner
2008/0312725 A1 12/2008 Penner
2009/0024047 A1 1/2009 Shipley et al.
2009/0036947 A1 2/2009 Westlund et al.
2009/0118785 A1 5/2009 Ignagni et al.
2009/0275956 A1 11/2009 Burnes et al.
2009/0275996 A1 11/2009 Burnes et al.
2009/0276022 A1 11/2009 Burnes et al.
2010/0022950 A1 1/2010 Anderson et al.
2010/0036451 A1 2/2010 Hoffer
2010/0077606 A1 4/2010 Black et al.
2010/0094376 A1 4/2010 Penner
2010/0114227 A1 5/2010 Cholette
2010/0114254 A1 5/2010 Kornet
2010/0198296 A1 8/2010 Ignagni et al.
2010/0204766 A1 8/2010 Zdeblick et al.
2010/0268311 A1 10/2010 Cardinal et al.
2010/0319691 A1 12/2010 Lurie et al.
2011/0060381 A1 3/2011 Ignagni et al.
2011/0077726 A1 3/2011 Westlund et al.
2011/0118815 A1 5/2011 Kuzma et al.
2011/0230932 A1 9/2011 Tehrani et al.
2011/0230935 A1 9/2011 Zdeblick
2011/0230945 A1 9/2011 Ohtaka et al.
2011/0270358 A1 11/2011 Davis et al.
2011/0288609 A1 11/2011 Tehrani et al.
2012/0035684 A1 2/2012 Thompson et al.
2012/0053654 A1 3/2012 Tehrani et al.
2012/0078320 A1 3/2012 Schotzko et al.
2012/0130217 A1 5/2012 Kauphusman et al.
2012/0158091 A1 6/2012 Tehrani et al.
2012/0209284 A1 8/2012 Westlund et al.
2012/0215278 A1 8/2012 Penner
2012/0323293 A1 12/2012 Tehrani et al.
2013/0018247 A1 1/2013 Glenn et al.
2013/0018427 A1 1/2013 Pham et al.
2013/0023972 A1 1/2013 Kuzma et al.
2013/0030496 A1 1/2013 Karamanoglu et al.
2013/0030497 A1 1/2013 Karamanoglu et al.
2013/0030498 A1 1/2013 Karamanoglu et al.
2013/0060245 A1 3/2013 Grunewald et al.
2013/0116743 A1 5/2013 Karamanoglu et al.
2013/0123891 A1 5/2013 Swanson
2013/0131743 A1 5/2013 Yamasaki et al.
2013/0158625 A1 6/2013 Gelfand et al.
2013/0165989 A1 6/2013 Gelfand et al.
2013/0167372 A1 7/2013 Black et al.
2013/0197601 A1 8/2013 Tehrani et al.
2013/0237906 A1 9/2013 Park et al.
2013/0268018 A1 10/2013 Brooke et al.
2013/0289686 A1 10/2013 Masson et al.
2013/0296964 A1 11/2013 Tehrani
2013/0296973 A1 11/2013 Tehrani et al.
2013/0317587 A1 11/2013 Barker
2013/0333696 A1 12/2013 Lee et al.
2014/0067032 A1 3/2014 Morris et al.
2014/0088580 A1 3/2014 Wittenberger et al.
2014/0114371 A1 4/2014 Westlund et al.
2014/0121716 A1 5/2014 Casavant et al.
2014/0128953 A1 5/2014 Zhao et al.
2014/0148780 A1 5/2014 Putz
2014/0316486 A1 10/2014 Zhou et al.
2014/0324115 A1 10/2014 Ziegler et al.
2014/0378803 A1 12/2014 Geistert et al.
2015/0018839 A1 1/2015 Morris et al.
2015/0034081 A1 2/2015 Tehrani et al.
2015/0045810 A1 2/2015 Hoffer et al.
2015/0045848 A1 2/2015 Cho et al.
2015/0119950 A1 4/2015 Demmer et al.
2015/0165207 A1 6/2015 Karamanoglu
2015/0196354 A1 7/2015 Haverkost et al.
2015/0196356 A1 7/2015 Kauphusman et al.
2015/0202448 A1 7/2015 Hoffer et al.
2015/0231348 A1 8/2015 Lee et al.
2015/0250982 A1 9/2015 Osypka
2015/0265833 A1 9/2015 Meyyappan et al.
2015/0283340 A1 10/2015 Zhang et al.
2015/0290476 A1 10/2015 Krocak et al.
2015/0359487 A1 12/2015 Coulombe
2015/0374252 A1 12/2015 De et al.
2015/0374991 A1 12/2015 Morris et al.
2016/0001072 A1 1/2016 Gelfand et al.
2016/0144078 A1 5/2016 Young et al.
2016/0193460 A1 7/2016 Xu et al.
2016/0228696 A1 8/2016 Imran et al.
2016/0239627 A1 8/2016 Cerny et al.
2016/0256692 A1 9/2016 Baru
2016/0310730 A1 10/2016 Martins
2016/0331326 A1 11/2016 Xiang et al.
2016/0367815 A1 12/2016 Hoffer
2017/0007825 A1 1/2017 Thakkar et al.
2017/0013713 A1 1/2017 Shah et al.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2017/0021166	A1	1/2017	Bauer et al.
2017/0028191	A1	2/2017	Mercanzini et al.
2017/0036017	A1	2/2017	Tehrani et al.
2017/0050033	A1	2/2017	Wechter
2017/0143973	A1	5/2017	Tehrani
2017/0143975	A1	5/2017	Hoffer et al.
2017/0196503	A1	7/2017	Narayan et al.
2017/0224993	A1	8/2017	Sathaye et al.
2017/0232250	A1	8/2017	Kim et al.
2017/0252558	A1	9/2017	O'Mahony et al.
2017/0291023	A1	10/2017	Kuzma et al.
2017/0296812	A1	10/2017	O'Mahony et al.
2017/0312006	A1	11/2017	McFarlin et al.
2017/0312507	A1	11/2017	Bauer et al.
2017/0312508	A1	11/2017	Bauer et al.
2017/0312509	A1	11/2017	Bauer et al.
2017/0326359	A1	11/2017	Gelfand et al.
2017/0347921	A1	12/2017	Haber et al.
2018/0001086	A1	1/2018	Bartholomew et al.
2018/0008821	A1	1/2018	Gonzalez et al.
2018/0110562	A1	4/2018	Govari et al.
2018/0117334	A1	5/2018	Jung

FOREIGN PATENT DOCUMENTS

EP	0993840	A1	4/2000
EP	1304135	A2	4/2003
EP	0605796	B1	8/2003
EP	2489395	A1	8/2012
FR	2801509	A1	6/2001
JP	H08510677	A	11/1996
JP	2003503119	A	1/2003
JP	2010516353	A	5/2010
JP	2011200571	A	10/2011
JP	2012000195	A	1/2012
WO	9407564	A2	4/1994
WO	9508357	A1	3/1995
WO	9964105	A1	12/1999
WO	9965561	A1	12/1999
WO	0100273	A1	1/2001
WO	02058785	A1	8/2002
WO	WO-03094855	A1	11/2003
WO	2006110338	A1	10/2006
WO	2006115877	A1	11/2006
WO	2007053508	A1	5/2007
WO	2008092246	A1	8/2008
WO	WO-2008094344	A1	8/2008
WO	2009006337	A1	1/2009
WO	WO-2009134459	A2	11/2009
WO	WO-2010029842	A1	3/2010
WO	WO-2010148412	A1	12/2010
WO	WO-2011158410	A1	12/2011
WO	2012106533	A2	8/2012
WO	2013131187	A1	9/2013
WO	WO-2013188965	A1	12/2013
WO	WO2014/008171	A1	1/2014

OTHER PUBLICATIONS

L. Salmela et al., "Verification of the position of a central venous catheter by intra-atrial ECG. When does this method fail?", Acta Anasthesiol Scand, 1993, vol. 37, Issue 1, pp. 26-28.

Antonica A., et al., "Vagal Control of Lymphocyte Release from Rat Thymus," Journal of the Autonomic Nervous System, Elsevier, vol. 48(3), Aug. 1994, pp. 187-197.

Whaley K., et al., "C2 Synthesis by Human Monocytes is Modulated by a Nicotinic Cholinergic Receptor," Nature, vol. 293, Oct. 15, 1981, pp. 580-582 (and reference page).

Borovikovaa L.V., et al., "Role of Vagus Nerve Signaling in CNI-1493-Mediated Suppression of Acute Inflammation," Autonomic Neuroscience: Basic and Clinical, vol. 85 (1-3), Dec. 20, 2000, pp. 141-147.

Borovikovaa L.V., et al., "Vagus Nerve Stimulation Attenuates the Systemic Inflammatory Response to Endotoxin," Nature, Macmillan Magazines Ltd, vol. 405, May 25, 2000, pp. 458-462.

Co-pending U.S. Appl. No. 15/606,867, filed on.

Extended European Search Report for Application No. 14864542.7, dated Jun. 2, 2017, 8 pages.

Fleshner M., et al., "Thermogenic and Corticosterone Responses to Intravenous Cytokines (IL-1β and TNF-α) are Attenuated by Subdiaphragmatic Vagotomy," Journal of Neuroimmunology, vol. 86, Jun. 1998, pp. 134-141.

Gaykema R.P.A. et al., "Subdiaphragmatic Vagotomy Suppresses Endotoxin-Induced Activation of Hypothalamic Corticotropin-Releasing Hormone Neurons and ACTH Secretion," Endocrinology, The Endocrine Society, vol. 136 (10), 1995, pp. 4717-4720.

Guslandi M., "Nicotine Treatment for Ulcerative Colitis," The British Journal of Clinical Pharmacology, Blackwell Science Ltd, vol. 48, 1999, pp. 481-484.

Japanese Office Action in corresponding Japanese Application No. 2014-560202, dated Dec. 6, 2016, 4 pages.

Kawashima K., et al., "Extraneuronal Cholinergic System in Lymphocytes," Pharmacology & Therapeutics, Elsevier, vol. 86, 2000, pp. 29-48.

Madretsma, G.S., et al., "Nicotine Inhibits the In-vitro Production of Interleukin 2 and Tumour Necrosis Factor-α by Human Mononuclear Cells," Immunopharmacology, Elsevier, vol. 35 (1), Oct. 1996, pp. 47-51.

Nabutovsky, Y., et al., "Lead Design and Initial Applications of a New Lead for Long-Term Endovascular Vagal Stimulation," PACE, Blackwell Publishing, Inc, vol. 30(1), Jan. 2007, pp. S215-S218.

Pavlovic D., et al., "Diaphragm Pacing During Prolonged Mechanical Ventilation of the Lungs could Prevent from Respiratory Muscle Fatigue," Medical Hypotheses, vol. 60 (3), 2003, pp. 398-403.

Planas R.F., et al., "Diaphragmatic Pressures: Transvenous vs. Direct Phrenic Nerve Stimulation," Journal of Applied Physiology, vol. 59(1), 1985, pp. 269-273.

Romanovsky, A.A., et al., "The Vagus Nerve in the Thermoregulatory Response to Systemic Inflammation," American Journal of Physiology, vol. 273 (1 Pt 2), 1997, pp. R407-R413.

Sandborn W.J., "Transdermal Nicotine for Mildly to Moderately Active Ulcerative Colitis," Annals of Internal Medicine, vol. 126 (5), Mar. 1, 1997, pp. 364-371.

Sato E., et al., "Acetylcholine Stimulates Alveolar Macrophages to Release Inflammatory Cell Chemotactic Activity," American Journal of Physiology, vol. 274 (Lung Cellular and Molecular Physiology 18), 1998, pp. L970-L979.

Sato, K.Z., et al., "Diversity of mRNA Expression for Muscarinic Acetylcholine Receptor Subtypes and Neuronal Nicotinic Acetylcholine Receptor Subunits in Human Mononuclear Leukocytes and Leukemic Cell Lines," Neuroscience Letters, vol. 266 (1), 1999, pp. 17-20.

Schauerte P., et al., "Transvenous Parasympathetic Nerve Stimulation in the Inferior Vena Cava and Atrioventricular Conduction," Journal of Cardiovascular Electrophysiology, vol. 11 (1), Jan. 2000, pp. 64-69.

Schauerte P.N., et al., "Transvenous Parasympathetic Cardiac Nerve Stimulation: An Approach for Stable Sinus Rate Control," Journal of Cardiovascular Electrophysiology, vol. 10 (11), Nov. 1999, pp. 1517-1524.

Scheinman R.I., et al., "Role of Transcriptional Activation of IκBα in Mediation of Immunosuppression by Glucocorticoids," Science, vol. 270, Oct. 13, 1995, pp. 283-286.

Sher, M.E., et al., "The Influence of Cigarette Smoking on Cytokine Levels in Patients with Inflammatory Bowel Disease," Inflammatory Bowel Diseases, vol. 5 (2), May 1999, pp. 73-78.

Steinlein, O., "New Functions for Nicotinic Acetylcholine Receptors?," Behavioural Brain Research, vol. 95, 1998, pp. 31-35.

Sternberg E.M., (Series Editor) "Neural-Immune Interactions in Health and Disease," The Journal of Clinical Investigation, vol. 100 (11), Dec. 1997, pp. 2641-2647.

Sykes., A.P., et al., "An Investigation into the Effect and Mechanisms of Action of Nicotine in Inflammatory Bowel Disease," Inflammation Research, vol. 49, 2000, pp. 311-319.

(56) **References Cited**

OTHER PUBLICATIONS

Toyabe S., et al., "Identification of Nicotinic Acetylcholine Receptors on Lymphocytes in the Periphery as well as Thymus in Mice," Immunology, vol. 92, 1997, pp. 201-205.

Van Dijk A.P.M., et al., "Transdermal Nicotine Inhibits Interleukin 2 Synthesis by Mononuclear Cells Derived from Healthy Volunteers," European Journal of Clinical Investigation, vol. 28, 1998, pp. 664-671.

Watkins L.R., et al., "Blockade of Interleukin-1 Induced Hyperthermia by Subdiaphragmatic Vagotomy: Evidence for Vagal Mediation of Immune-Brain Communication," Neuroscience Letters, vol. 183, 1995, pp. 27-31.

Watkins L.R., et al., "Implications of Immune-to-Brain Communication for Sickness and Pain," PNAS (Proceedings of the National Academy of Sciences of the USA), vol. 96 (14), Jul. 6, 1999, pp. 7710-7713.

PCT Search Report and Written Opinion dated Oct. 17, 2018 for PCT Application No. PCT/US2018/043661, 13 pages.

Ayas N.T., et al., "Prevention of Human Diaphragm Atrophy with Short periods of Electrical Stimulation," American Journal of Respiratory and Critical Care Medicine, Jun. 1999, vol. 159(6), pp. 2018-2020.

Borovikova, et al., "Role of the Vagus Nerve in the Anti-Inflammatory Effects of CNI-1493," Proceedings of the Annual Meeting of Professional Research Scientists: Experimental Biology 2000, Abstract 97.9, Apr. 15-18, 2000.

Chinese Search Report for Application No. CN2013/80023357.5, dated Jul. 24, 2015.

Daggeti, W.M. et al., "Intracaval Electrophrenic Stimulation. I. Experimental Application during Barbiturate Intoxication Hemorrhage and Gang," Journal of Thoracic and Cardiovascular Surgery, 1966, vol. 51 (5), pp. 676-884.

Daggeti, W.M. et al., "Intracaval electrophrenic stimulation. II. Studies on Pulmonary Mechanics Surface Tension Urine Flow and Bilateral Ph," Journal of Thoracic and Cardiovascular Surgery, 1970, vol. 60(1), pp. 98-107.

De Gregorio, M.A. et al., "The Gunther Tulip Retrievable Filter: Prolonged Temporary Filtration by Repositioning within the Inferior Vena Cava," Journal of Vascular and Interventional Radiology, 2003, vol. 14, pp. 1259-1265.

Deng Y-J et al., "The Effect of Positive Pressure Ventilation Combined with Diaphragm Pacing on Respiratory Mechanics in Patients with Respiratory Failure; Respiratory Mechanics," Chinese critical care medicine, Apr. 2011, vol. 23(4), pp. 213-215.

European Search Report for Application No. 13758363, dated Nov. 12, 2015.

European Search Report for Application No. EP17169051.4, dated Sep. 8, 2017, 7 pages.

Extended European Search Report for Application No. 15740415.3, dated Jul. 7, 2017.

Frisch S., "A Feasibility Study of a Novel Minimally Invasive Approach for Diaphragm Pacing," Master of Science Thesis, Simon Fraser University, 2009, p. 148.

Furman, S., "Transvenous Stimulation of the Phrenic Nerves," Journal of Thoracic and Cardiovascular Surgery, 1971, vol. 62 (5), pp. 743-751.

Hoffer J.A. et al., "Diaphragm Pacing with Endovascular Electrodes", IFESS 2010—International Functional Electrical Stimulation Society, 15th Anniversary Conference, Vienna, Austria, Sep. 2010.

Japanese Office Action in corresponding Japanese Application No. 2014-560202, dated Oct. 17, 2017, 5 pages.

Levine S., et al., "Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans," New England Journal of Medicine, 2008, vol. 358, pp. 1327-1335.

Lungpacer: Therapy, News.< http://lungpacer.com>. Accessed Dec. 27, 2016.

Marcy, T.W. et al., "Diaphragm Pacing for Ventilatory Insufficiency," Journal of Intensive Care Medicine, 1987, vol. 2 (6), pp. 345-353.

Meyyappan R., "Diaphragm Pacing during Controlled Mechanical Ventilation: Pre-Clinical Observations Reveal a Substantial Improvement in Respiratory Mechanics", 17th Biennial Canadian Biomechanics Society Meeting, Burnaby, BC, Jun. 6-9, 2012.

Notification of Reasons for Rejection and English language translation issued in corresponding Japanese Patent Application No. 2015-517565, dated Mar. 28, 2017, 6 pages.

Onders R.,, "A Diaphragm Pacing as a Short-Term Assist to Positive Pressure Mechanical Ventilation in Critical Care Patients," Chest, Oct. 24, 2007, vol. 132(4), pp. 5715-5728.

Onders R.,, "Diaphragm Pacing for Acute Respiratory Failure," Difficult Decisions in Thoracic Surgery, Chapter 37, Springer-Verlag, 2011, M.K. Ferguson (ed.), pp. 329-335.

Onders R, et al., "Diaphragm Pacing with Natural Orifice Transluminal Endoscopic Surgery: Potential for Difficult-To-Wean Intensive Care Unit Patients," Surgical Endoscopy, 2007, vol. 21, pp. 475-479.

Sandoval R., "A Catch/Ike Property-Based Stimulation Protocol for Diaphragm Pacing", Master of Science Coursework project, Simon Fraser University, Mar. 2013.

Sarnoff, S.J. et al., "Electrophrenic Respiration," Science, 1948, vol. 108, p. 482.

Wanner, A. et al., "Trasvenous Phrenic Nerve Stimulation in Anesthetized Dogs," Journal of Applied Physiology, 1973, vol. 34 (4), pp. 489-494.

Escher, Doris J.W. et al., "Clinical Control of Respiration by Transvenous Phrenic Pacing," American Society for Artificial Internal Organs: Apr. 1968—vol. 14—Issue 1—pp. 192-197.

Ishii, K. et al., "Effects of Bilateral Transvenous Diaphragm Pacing on Hemodynamic Function in Patients after Cardiac Operations," J. Thorac. Cardiovasc. Surg., 1990.

* cited by examiner

FIG. 1

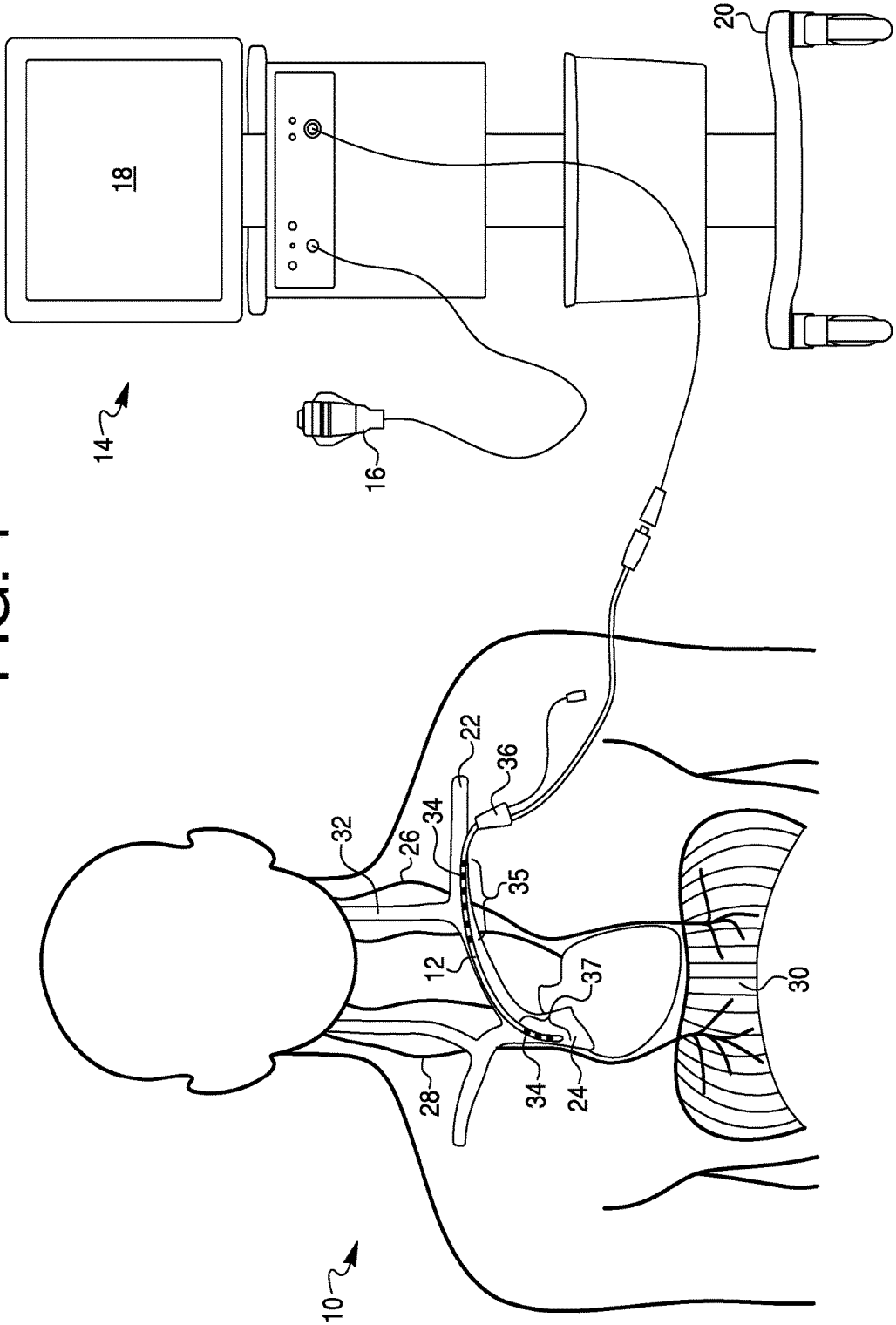


FIG. 2

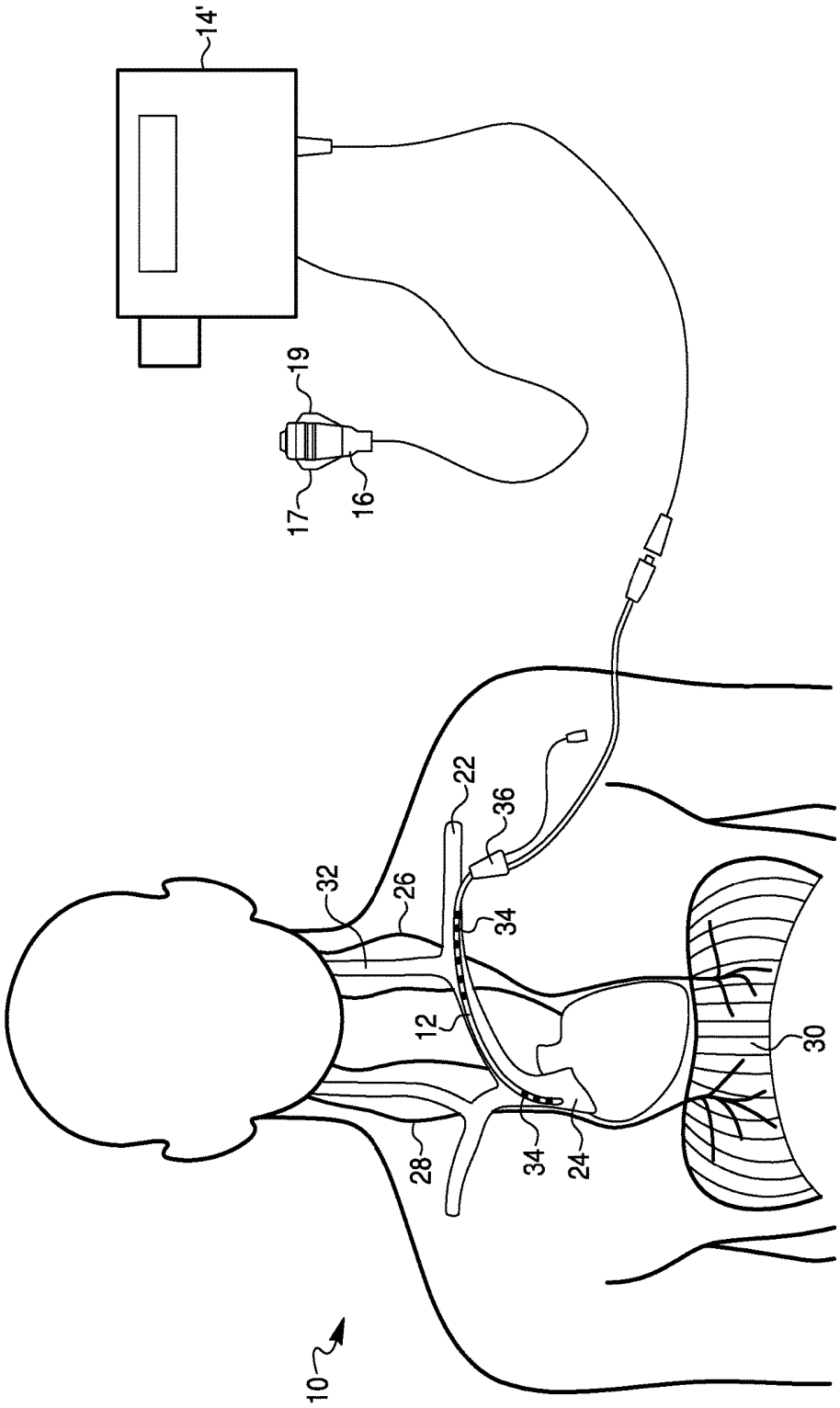


FIG. 3

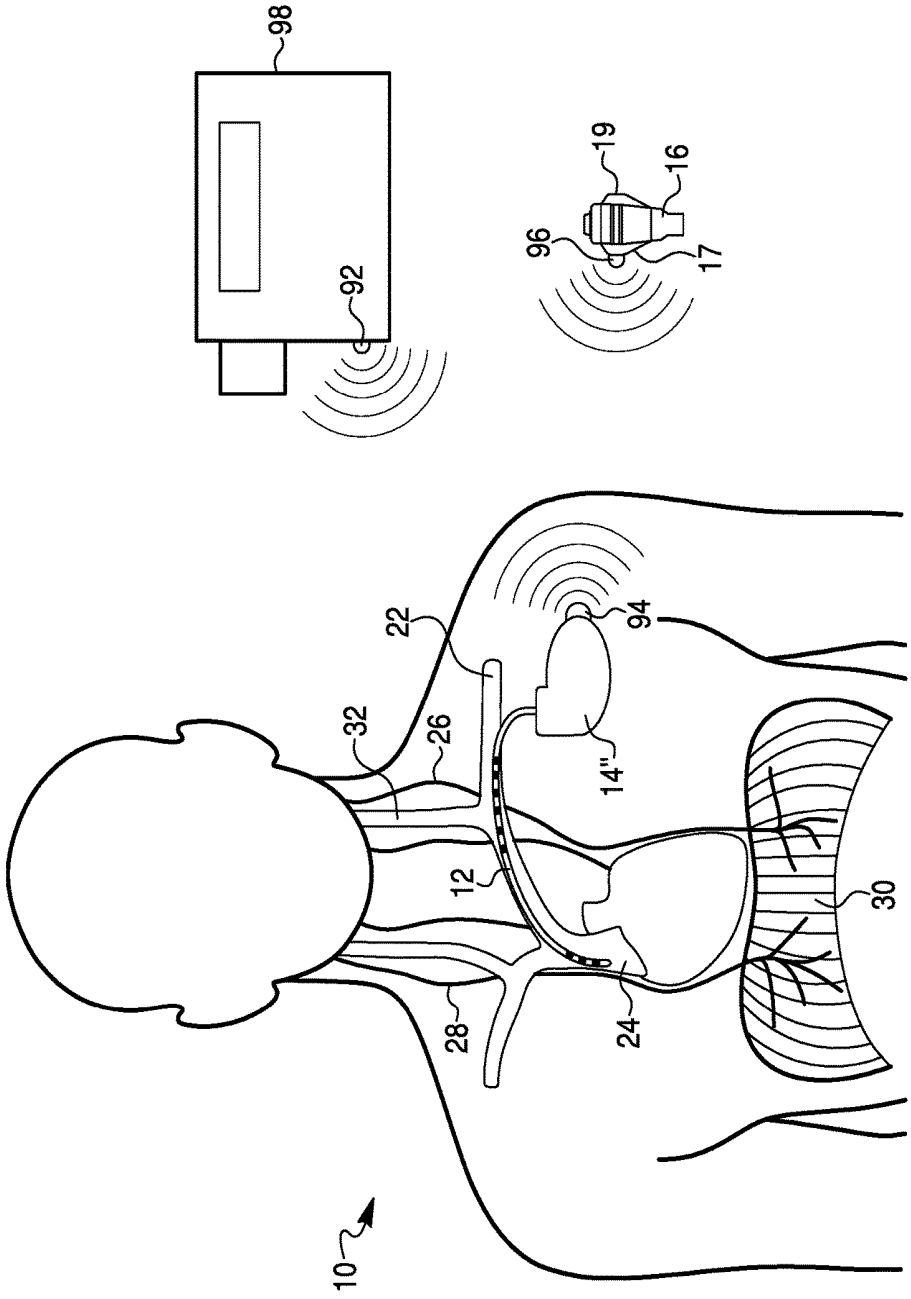


FIG. 4

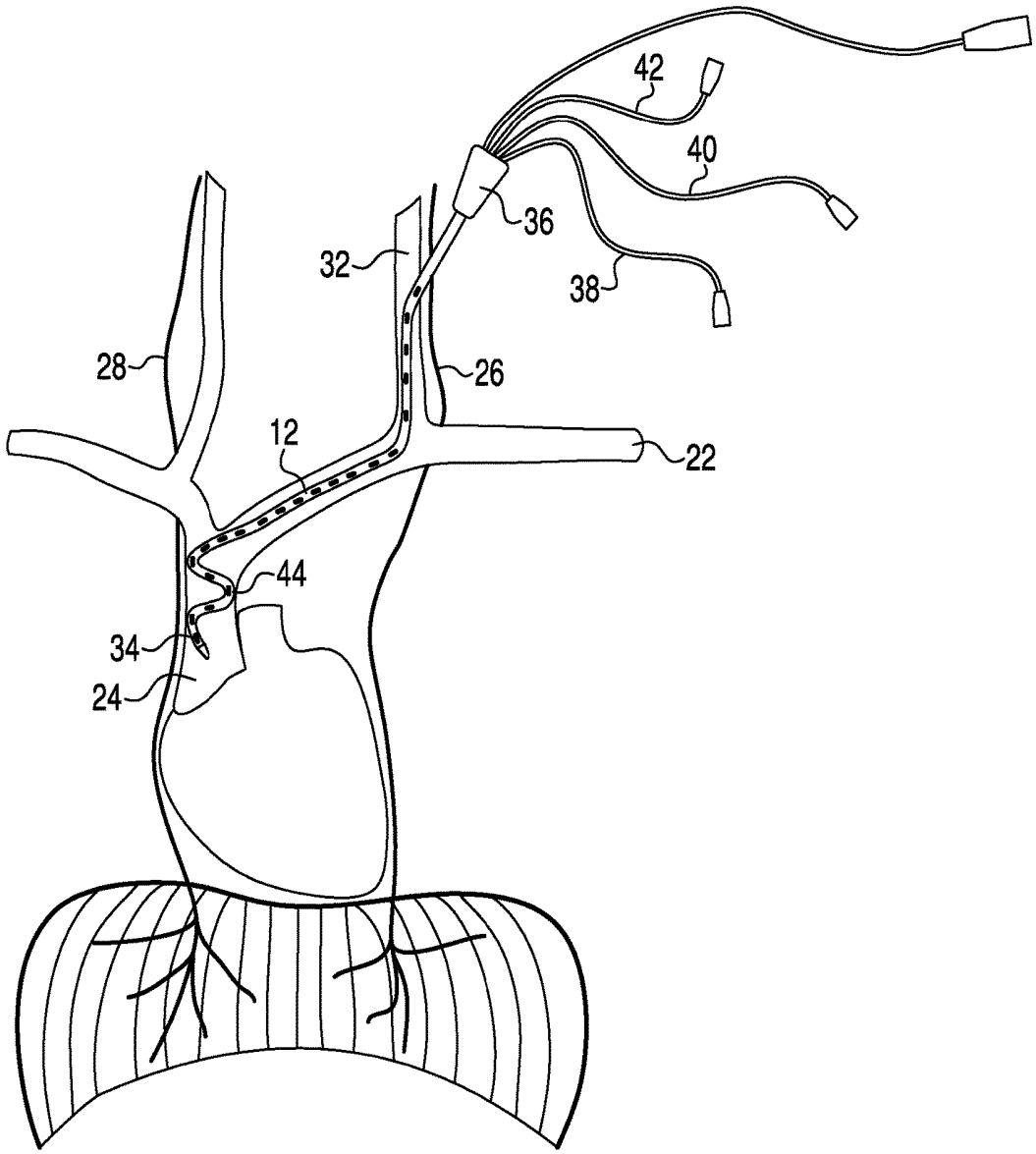


FIG. 5

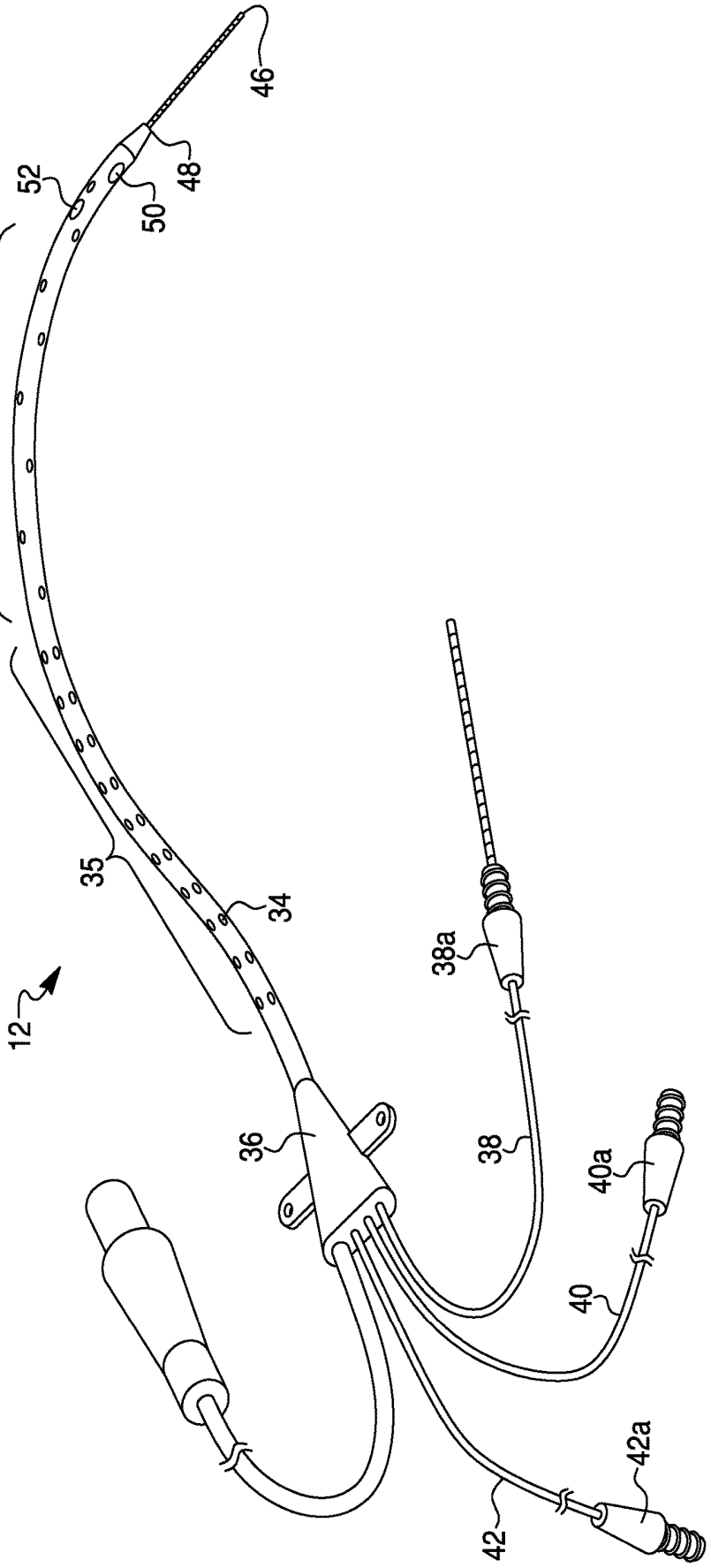


FIG. 6

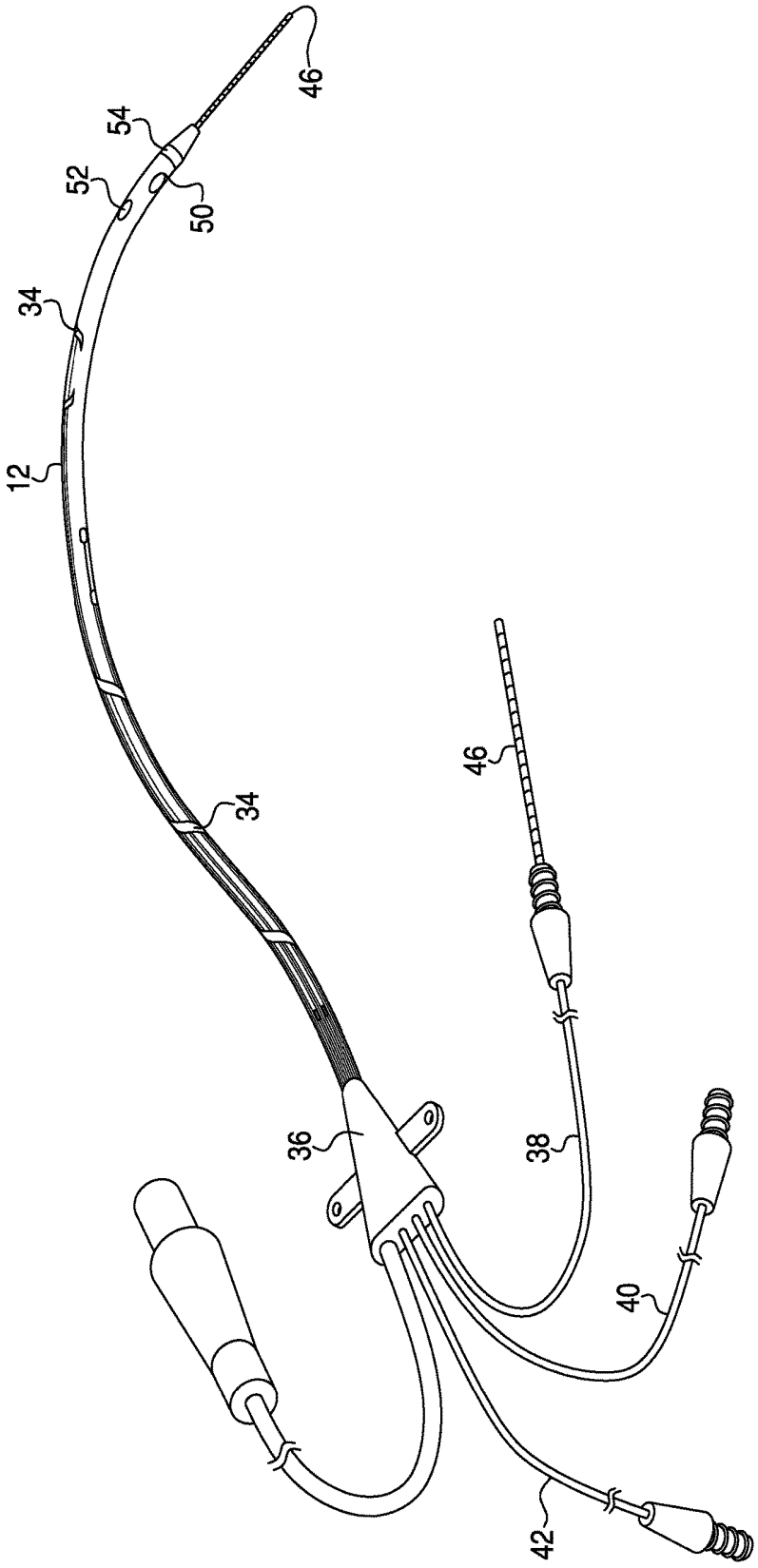
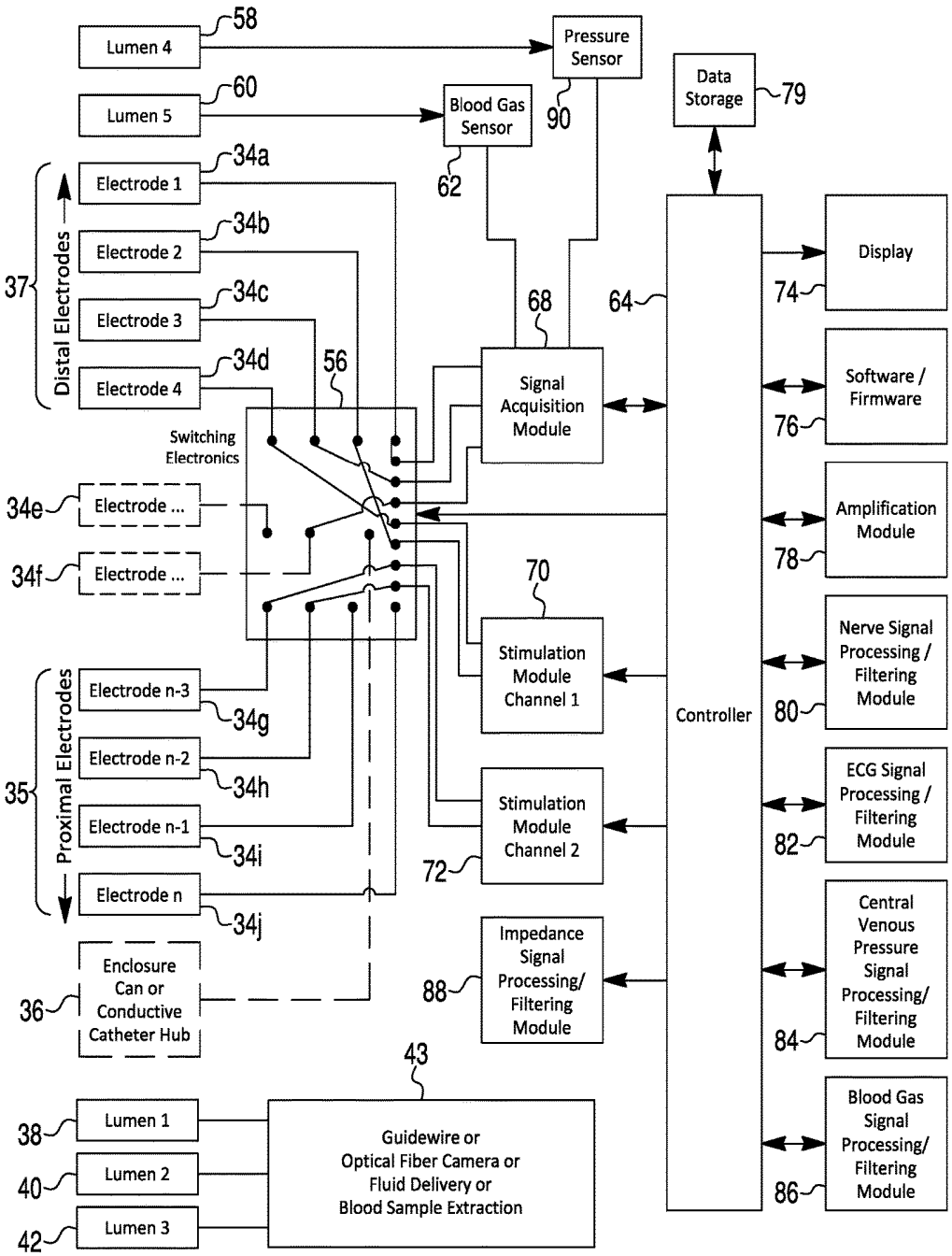


FIG. 7


Lumen 4
58
Pressure Sensor
Data Storage
79
Lumen 5
60
Blood Gas Sensor
90
62
Electrode 1
34a
Electrode 2
34b
Electrode 3
34c
Electrode 4
34d
Distal Electrodes
37
56
68
64
Signal Acquisition Module
Display
74
Software / Firmware
76
Switching Electronics
34e
Electrode ...
34f
Electrode ...
Amplification Module
78
70
Stimulation Module Channel 1
Nerve Signal Processing / Filtering Module
80
Controller
Electrode n-3
34g
Electrode n-2
34h
Electrode n-1
34i
Electrode n
34j
Proximal Electrodes
35
Stimulation Module Channel 2
72
ECG Signal Processing / Filtering Module
82
Central Venous Pressure Signal Processing/ Filtering Module
84
Impedance Signal Processing/ Filtering Module
88
Enclosure Can or Conductive Catheter Hub
36
43
Blood Gas Signal Processing/ Filtering Module
86
Lumen 1
38
Lumen 2
40
Lumen 3
42
Guidewire or Optical Fiber Camera or Fluid Delivery or Blood Sample Extraction

SYSTEMS AND METHODS FOR INTRAVASCULAR CATHETER POSITIONING AND/OR NERVE STIMULATION

TECHNICAL FIELD

This disclosure relates to systems, devices, and methods for one or more of positioning an intravascular nerve stimulation catheter, selecting electrodes for nerve stimulation, or stimulating nerves.

BACKGROUND

Electrical stimulation of nerves may be used to control muscle activity or to generate or attenuate sensations. Nerves and muscles may be stimulated by placing electrodes in, around, or near the nerves and muscles and by activating the electrodes by means of an implanted or external source of energy (e.g., electricity).

The diaphragm muscle provides an important function for the respiration of human beings. The phrenic nerves normally transmit signals from the brain to cause the contractions of the diaphragm muscle necessary for breathing. However, various conditions can prevent appropriate signals from being delivered to the phrenic nerves. These include: permanent or temporary injury or disease affecting the spinal cord or brain stem; Amyotrophic Lateral Sclerosis (ALS); decreased day or night ventilatory drive (e.g., central sleep apnea, Ondine's curse); and decreased ventilatory drive while under the influence of anesthetic agents and/or mechanical ventilation. These conditions affect a significant number of people.

Intubation and positive pressure mechanical ventilation (MV) may be used for periods of several hours or several days, sometimes weeks, to help critically ill patients breathe while in intensive care units (ICU). Some patients may be unable to regain voluntary breathing and thus require prolonged or permanent mechanical ventilation. Although mechanical ventilation can be initially lifesaving, it has a range of significant problems and/or side effects. Mechanical ventilation:

- often causes ventilator-induced lung injury (VILI) and alveolar damage, which can lead to accumulation of fluid in the lungs and increased susceptibility to infection (ventilator-associated pneumonia, VAP);
- commonly requires sedation to reduce discomfort and anxiety in acutely intubated patients;
- leads to rapid atrophy of the disused diaphragm muscle (ventilator-induced diaphragm dysfunction, VIDD);
- can adversely affect venous return because the lungs are pressurized and the diaphragm is inactive;
- interferes with eating and speaking;
- requires apparatus that is not readily portable; and
- increases the risk of dying if the patient fails to regain normal breathing and becomes ventilator-dependent.

A patient who is sedated and connected to a mechanical ventilator cannot breathe normally because the central neural drive to the diaphragm and accessory respiratory muscles are suppressed. Inactivity leads to muscle disuse atrophy and an overall decline in well-being. Diaphragm muscle atrophy occurs rapidly and can be a serious problem to the patient. According to a published study of organ donor patients (Levine et al., New England Journal of Medicine, 358: 1327-1335, 2008), after only 18 to 69 hours of mechanical ventilation, all diaphragm muscle fibers had shrunk on average by 52-57%. Muscle fiber atrophy results in muscle weakness and increased fatigability. Therefore, ventilator-induced diaphragm atrophy could cause a patient to become ventilator-dependent. It has been estimated that over 600,000 U.S. patients will be ventilator-dependent and require prolonged mechanical ventilation by the year 2020. Zilberberg et al., "Growth in adult prolonged acute mechanical ventilation: implications for healthcare delivery," Crit Care Med., 2008 May, 36(5): 1451-55.

SUMMARY

Embodiments of the present disclosure relate to, among other things, systems, devices, and methods for one or more of positioning an intravascular nerve stimulation catheter, selecting electrodes for nerve stimulation, or stimulating nerves. Each of the embodiments disclosed herein may include one or more of the features described in connection with any of the other disclosed embodiments.

In one example, a method for positioning an intravascular catheter may include inserting the intravascular catheter into a venous system of a patient, wherein the catheter includes a plurality of electrodes, and multiple electrodes of the plurality of electrodes are configured to emit electrical signals; positioning a distal portion of the catheter in a first position; using one or more electrodes of the plurality of electrodes to acquire an ECG signal; based on the acquired ECG signal, adjusting the distal portion of the catheter to a second position different from the first position; identifying at least one first electrode of the plurality of electrodes to stimulate a first nerve; identifying at least one second electrode of the plurality of electrodes to stimulate a second nerve; and stimulating at least one of the first and second nerves to cause a contraction of a respiratory muscle.

Any method described herein may additionally or alternatively include one or more of the following features or steps: inserting the intravascular catheter into the venous system may include inserting the intravascular catheter into: 1) at least one of a left subclavian, axillary, cephalic, cardiophrenic, brachial, radial, or left jugular vein, and 2) a superior vena cava; the first position may be proximate an atrium of a heart of the patient, and the second position may be in a superior vena cava; the ECG signal may be a first ECG signal, and the method may further comprise using one or more electrodes of the plurality of electrodes to acquire a second ECG signal; the one or more electrodes used to acquire the first ECG signal may be positioned on a proximal portion of the catheter and may be configured to stimulate the first nerve, and the one or more electrodes used to acquire the second ECG signal may be positioned on a distal portion of the catheter and may be configured to stimulate the second nerve; the method may further include comparing the first ECG signal to the second ECG signal, and based on the comparison, adjusting the distal portion of the catheter to the second position; the second position may be farther from a heart of the patient than the first position; the method may further include using one or more electrodes of the plurality of electrodes to sense at least one of an impedance or nerve activity; or each of the at least one first electrode and the at least one second electrode may be a combination of electrodes.

In another example, a method for positioning an intravascular catheter may include inserting the intravascular catheter into: 1) at least one of a left subclavian vein or a left jugular vein, and 2) a superior vena cava, wherein the catheter includes a plurality of electrodes, and the plurality of electrodes includes a proximal set of electrodes positioned proximate a left phrenic nerve and a distal set of

electrodes positioned proximate a right phrenic nerve; using one or more electrodes of the plurality of electrodes to acquire an ECG signal; based on a change in the ECG signal, withdrawing the catheter away from a heart of a patient; stimulating the left phrenic nerve using one or more electrodes of the proximal set of electrodes; and stimulating the right phrenic nerve using one or more electrodes of the distal set of electrodes.

Any method described herein may additionally or alternatively include one or more of the following features or steps: the change in the ECG signal may be a change in an amplitude of a P-wave, and the change may occur as a distal end of the catheter enters a region proximate an atrium of the heart; the step of withdrawing the catheter away from the heart may cause a change in the amplitude of the P-wave; the ECG signal may be a first ECG signal acquired by one or more electrodes of the proximal set of electrodes, and the method may further include using one or more electrodes of the distal set of electrodes to acquire a second ECG signal; the method may further include determining a difference between a P-wave of the first ECG signal and a P-wave of the second ECG signal, and withdrawing the catheter away from the heart of the patient when the difference exceeds a predetermined value; the difference may exceed the predetermined value when the catheter is advanced into an atrium of the heart; a hub coupled to the catheter and positioned exterior to the patient may be used with the one or more electrodes of the plurality of electrodes to acquire the ECG signal; or the method may further include monitoring the ECG signal as a distal end of the catheter is inserted into the at least one of the left subclavian vein or the left jugular vein and advanced into the superior vena cava.

In yet another example, a method for positioning an intravascular catheter may include inserting the intravascular catheter into a venous system of a patient, wherein the catheter includes a plurality of proximal electrodes and a plurality of distal electrodes; using one or more electrodes of the plurality of proximal electrodes to acquire a first ECG signal, and using one or more electrodes of the plurality of distal electrodes to acquire a second ECG signal; comparing the first ECG signal to the second ECG signal; based on the comparison between the first ECG signal and the second ECG signal, adjusting a position of the catheter; stimulating the first nerve using one or more of the plurality of proximal electrodes; and stimulating the second nerve using one or more of the plurality of distal electrodes.

Any method described herein may additionally or alternatively include one or more of the following features or steps: the first nerve may be a left phrenic nerve, and the second nerve may be a right phrenic nerve; comparing the first ECG signal to the second ECG signal may include comparing an amplitude of a portion of the first ECG signal to an amplitude of a portion of the second ECG signal; the step of comparing may occur a plurality of times during the inserting step; adjusting the position of the catheter may include moving the catheter away from a heart; at least one of stimulating the first nerve or stimulating the second nerve may cause a contraction of a diaphragm; or the method may further include sensing activity of the first nerve using one or more of the proximal electrodes and sensing activity of the second nerve using one or more of the distal electrodes

In another example, a method for positioning an intravascular catheter may include inserting the intravascular catheter into: 1) at least one of a left subclavian vein or a left jugular vein, and 2) a superior vena cava, wherein the catheter includes a plurality of proximal electrodes configured to be positioned proximate a left phrenic nerve and a plurality of distal electrodes configured to be positioned proximate a right phrenic nerve; at multiple positions of the catheter during the inserting step, using one or more electrodes of the plurality of proximal electrodes to acquire a first ECG signal, and using one or more electrodes of the plurality of distal electrodes to acquire a second ECG signal; comparing the first ECG signal to the second ECG signal at several of the multiple positions; based on the comparisons of the first ECG signal to the second ECG signal, determining a desired position of the catheter for nerve stimulation; stimulating the left phrenic nerve using one or more of the plurality of proximal electrodes; and stimulating the right phrenic nerve using one of more of the plurality of distal electrodes.

Any method described herein may additionally or alternatively include one or more of the following features or steps: the method may further include advancing a distal end of the catheter into a region proximate an atrium of a heart; one of the multiple positions may be a position in which the distal end of the catheter is proximate the atrium of the heart, and in the position, the comparison may indicate a difference between an amplitude of the first ECG signal and an amplitude of the second ECG signal that exceeds a predetermined value; the method may further include moving the catheter away from the heart; stimulating the left phrenic nerve may cause a diaphragm contraction, and stimulating the right phrenic nerve may cause a diaphragm contraction; the proximal electrodes used to acquire the first ECG signal may be configured to stimulate the left phrenic nerve, and the distal electrodes used to acquire the second ECG signal may be configured to stimulate the right phrenic nerve.

It may be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed. As used herein, the terms "comprises," "comprising," or any other variation thereof, are intended to cover a non-exclusive inclusion, such that a process, method, article, or apparatus that comprises a list of elements does not include only those elements, but may include other elements not expressly listed or inherent to such process, method, article, or apparatus. The term "exemplary" is used in the sense of "example," rather than "ideal."

BRIEF DESCRIPTION OF THE DRAWINGS

The accompanying drawings, which are incorporated in and constitute a part of this specification, illustrate exemplary embodiments of the present disclosure and together with the description, serve to explain the principles of the disclosure.

FIG. **1** illustrates a nerve stimulation system with an intravascular catheter positioned within a patient, according to an exemplary embodiment.

FIG. **2** illustrates a nerve stimulation system having a portable control unit, according to an exemplary embodiment.

FIG. **3** illustrates a wireless configuration of a nerve stimulation system, according to an exemplary embodiment.

FIG. **4** illustrates an intravascular catheter having a helical portion, according to an exemplary embodiment.

FIG. **5** illustrates an intravascular catheter having an optical fiber camera, according to an exemplary embodiment.

FIG. **6** illustrates an intravascular catheter having an ultrasound transducer, according to an exemplary embodiment.

FIG. **7** illustrates a block diagram of a nerve stimulation system having an intravascular catheter and a control unit, according to an exemplary embodiment.

DETAILED DESCRIPTION

When electrically stimulating nerves or muscles, a variety of goals may be considered. First, it may be desirable to place the electrodes in proximity to the phrenic nerves. Second, it may be desirable to avoid placing electrodes in close proximity to the sinoatrial (SA) node, atrioventricular (AV) node, or the His-Purkinje system located in heart tissue, as electrical stimulation of these anatomical features may cause arrhythmia. Third, when using a device that includes multiple electrodes, it may be desirable to identify particular electrodes that are in close proximity to the nerve. Identifying the proper electrodes may minimize the electrical charge required to effectively stimulate the nerves. Finally, as with any medical procedure, the risk of injury to the patient increases with the length and complexity of the medical procedure. Accordingly, it may be desirable to minimize the length of any procedure to electrically stimulate nerves or muscles.

There remains a need for cost-effective, practical, surgically simple, and minimally invasive devices and methods that address one or more of the above goals and can include one or more of a variety of functions, including: determining whether a nerve is the target nerve, stimulating breathing, delivering treatment (e.g., medications), sensing electrical signals from the body (e.g., ECG), sensing internal vascular blood pressure, heart rate, and electrical impedance, and performing tests, such as detecting respiration rate and blood gas levels (e.g, CO_2, O_2). There is also a need for devices and methods to help patients wean from mechanical ventilation and regain the ability to breathe naturally.

Accordingly, the present disclosure is drawn to systems, devices, and methods for one or more of positioning an intravascular catheter for nerve stimulation, selecting electrodes for nerve stimulation, and stimulating nerves. In particular, embodiments of the present disclosure may use various positioning features to obtain information useful for positioning a transvascular nerve stimulation catheter, or may use information gathered by sensors to select electrodes and parameters for nerve stimulation.

General System Overview

FIG. **1** illustrates a system **10** that includes a transvascular nerve stimulation catheter **12** and a control unit **14**. Catheter **12** may include a plurality of electrodes **34**. Catheter **12** may be operably connected (e.g., hardwired, wireless, etc.) to a control unit **14**. The control unit **14** may be programmed to perform any of the functions described herein in connection with system **10**. In some embodiments, the control unit **14** may include a remote controller **16** to allow a patient or health professional to control operation of the control unit **14** at a distance from the control unit **14**. The controller **16** may include a handheld device, as illustrated in FIG. **1**. In some examples, controller **16** may include a footswitch/pedal, a voice-activated, touch-activated, or pressure-activated switch, or any other form of a remote actuator. The control unit **14** may include a touch screen **18** and may be supported by a cart **20**.

During use, a proximal portion of catheter **12** may be positioned in a left subclavian vein **22**, and a distal portion of catheter **12** may be positioned in a superior vena cava **24**. Positioned in this manner, electrodes **34** on the proximal portion of catheter **12** may be positioned proximate a left phrenic nerve **26**, and electrodes **34** on the distal portion of catheter **12** may be positioned proximate a right phrenic nerve **28**. Left and right phrenic nerves **26**, **28** may innervate a diaphragm **30**. Accordingly, catheter **12** may be positioned to electrically stimulate one or both of the left and right phrenic nerves **26**, **28** to cause contraction of the diaphragm muscle **30** to initiate or support a patient breath. In other embodiments, the proximal portion of catheter **12** may be positioned in a left jugular vein **32**, and the distal portion of catheter **12** may be positioned in superior vena cava **24**.

In further examples, catheter **12** can be placed into and advanced through other vessels providing access to the locations adjacent the target nerve(s) (e.g., phrenic nerves), such as: the jugular, axillary, cephalic, cardiophrenic, brachial, or radial veins. In addition, catheter **12** may use other forms of stimulation energy, such as ultrasound, to activate the target nerves. In some examples, the system **10** can target other respiratory muscles (e.g., intercostal) either in addition to, or alternatively to, the diaphragm **30**. The energy can be delivered via one or more methods including transvascular, subcutaneous, nerve cuffs, transdermal stimulation, or other techniques known in the field.

FIG. **2** illustrates an alternative example of system **10**, in which control unit **14'** is portable. Portable control unit **14'** may include all of the functionality of control unit **14** of FIG. **1**, but it may be carried by a patient or other user to provide the patient with more mobility. In addition to carrying the control unit **14'**, the patient can wear control unit **14'** on a belt, on other articles of clothing, or around his/her neck, for example. In other examples, control unit **14'** may be mounted to a patient's bed to minimize the footprint of system **10** in the area around the patient, or to provide portable muscle stimulation in the event a bed-ridden patient needs to be transported or moved to another location.

Similar to FIG. **1**, the system of FIG. **2** may include a controller **16**, shown as a handheld controller **16**. Handheld controller **16** may include buttons **17**, **19** that can be pressed by a patient or other user to control breathing patterns. In one example, pressing one of buttons **17**, **19** can initiate a "sigh" breath, which may cause a greater volume of air to enter the patient's lungs than in a previous breath. A sigh breath may result when electrodes **34** of catheter **12** are directed to stimulate one or more of the phrenic nerves **26**, **28** at a higher level than a normal breath (i.e., a stimulation train having a longer duration of stimulation or having pulses with a higher amplitude, pulse width, or frequency). Higher amplitude stimulation pulses can recruit additional nerve fibers, which in turn can engage additional muscle fibers to cause stronger and/or deeper muscle contractions. Extended pulse widths or extended durations of the stimulation train can deliver stimulation over longer periods of time to extend the duration of the muscle contractions. In the case of diaphragm muscle stimulation, longer pulse widths have the potential to help expand the lower lung lobes by providing greater or extended negative pressure around the outside of the lungs. Such negative pressure has the potential to help prevent or mitigate a form of low pressure lung injury known as atelectasis. The increased stimulation of the one or more phrenic nerves **26**, **28** may result in a more forceful contraction of the diaphragm **30**, causing the patient to inhale a greater volume of air, thereby providing a greater amount of oxygen to the patient. Sigh breaths may increase patient comfort.

In other examples, buttons **17**, **19** may allow the patient or other user to start and stop stimulation therapy, or to increase or decrease stimulation parameters, including stimulation charge (amplitude×pulse width), frequency of pulses in a stimulation train, or breath rate. LED indicators or a small

LCD screen (not shown) on the controller may provide other information to guide or inform the operator regarding the stimulation parameters, the feedback from the system sensors, or the condition of the patient.

FIG. **3** illustrates another example of system **10** in which a control unit **14"** is implanted in the patient, along with catheter **12**. System **10** may further include remote controller **16** and a programmer **98** that communicates with control unit **14"** wirelessly. In this embodiment, each of programmer **98**, control unit **14"**, and remote controller **16** may include a wireless transceiver **92**, **94**, **96**, respectively, so that each of the three components can communicate wirelessly with each other. Control unit **14"** may include all of the electronics, software, and functioning logic necessary to perform the functions described herein. Implanting control unit **14"** as shown in FIG. **3** may allow catheter **12** to function as a permanent breathing pacemaker. Programmer **98** may allow the patient or health professional to modify or otherwise program the nerve stimulation or sensing parameters. Remote controller **16** may be used as described in connection with FIGS. **1** and **2**. In other examples, remote controller **16** may be in the form of a smartphone, tablet, watch or other wearable device.

Catheter Features

Referring to FIGS. **1-3**, catheter **12** may include a stimulation array comprising a plurality of electrodes **34** or other energy delivery elements. In one example, electrodes **34** may be surface electrodes located on an outer wall of catheter **12**. In another example, electrodes **34** may be positioned radially inward relative to the outer wall of catheter **12** (e.g., exposed through openings in the outer wall). In yet another example, the electrodes **34** may include printed electrodes as described in U.S. Pat. No. 9,242,088, which is incorporated by reference herein (see below).

Electrodes **34** may extend partially around the circumference of catheter **12**. This "partial" electrode configuration may allow electrodes **34** to target a desired nerve for stimulation, while minimizing application of electrical charge to undesired areas of the patient's anatomy (e.g., other nerves or the heart). As shown in FIG. **1**, catheter **12** may include a proximal set **35** of electrodes **34** configured to be positioned proximate to and stimulate left phrenic nerve **26** and a distal set **37** of electrodes **34** configured to be positioned proximate to and stimulate right phrenic nerve **28**. As shown in FIG. **5**, electrodes **34** may be arranged in rows extending along the length of catheter **12**. In one example, proximal set **35** may include two rows, and distal set **37** may include two rows.

Furthermore, the catheters described herein may include any features of the nerve stimulation devices described in the following documents, which are all incorporated by reference herein in their entireties: U.S. Pat. No. 8,571,662 (titled "Transvascular Nerve Stimulation Apparatus and Methods," issued Oct. 29, 2013); U.S. Pat. No. 9,242,088 (titled "Apparatus and Methods for Assisted Breathing by Transvascular Nerve Stimulation," issued Jan. 26, 2016); U.S. Pat. No. 9,333,363 (titled "Systems and Related Methods for Optimization of Multi-Electrode Nerve Pacing," issued May 10, 2016); U.S. application Ser. No. 14/383,285 (titled "Transvascular Nerve Stimulation Apparatus and Methods," filed Sep. 5, 2014); or U.S. application Ser. No. 14/410,022 (titled "Transvascular Diaphragm Pacing Systems and Methods of Use," filed Dec. 19, 2014). In addition, the control units described herein can have any of the functionality of the control units described in the above-referenced patent documents (e.g., the control units described herein can implement the methods of nerve stimulation described in the incorporated documents).

During nerve stimulation, one or more electrodes **34** may be selected from the proximal set **35** for stimulation of left phrenic nerve **26**, and one or more electrodes **34** may be selected from the distal set **37** for stimulation of right phrenic nerve **28**. Catheter **12** may stimulate nerves using monopolar, bipolar, or tripolar electrode combinations, or using any other suitable combination of electrodes **34**. In some examples, a second or third stimulation array can be used to stimulate other respiratory muscles. When multiple nerves or muscles are being stimulated, the controller and sensors described herein may be used to coordinate stimulation to achieve the desired muscle activation, breath, or level of respiratory support.

Catheter **12** may further include one or more lumens. Each lumen may extend from a proximal end of catheter **12** to a distal end of catheter **12**, or to a location proximate the distal end of catheter **12**. The lumens may contain medical devices, such as a guidewire or an optical fiber camera. Furthermore, the one or more lumens may be used for any suitable purpose, such as drawing blood samples or providing a pathway for delivering medications into the patient. In some examples, lumens may contain or be fluidly connected to sensors, such as blood gas sensors or pressure sensors.

In this disclosure, the figures illustrating catheter **12** may each illustrate different features and different combinations of features. However, catheter **12** may include any combination of the features that are described herein. Accordingly, the features of catheter **12** are not limited to the specific combinations shown in the various figures.

Referring to FIG. **2**, a hub **36** may be connected to the proximal end of catheter **12**. Hub **36** may include a conductive surface and can act as a reference electrode during monopolar stimulation or sensing. In some embodiments, hub **36** may be sutured on a patient's skin. In addition, hub **36** may be used as an ECG electrode.

FIG. **4** illustrates catheter **12** inserted into left jugular vein **32** and superior vena cava **24**. As described above, catheter **12** includes a plurality of electrodes **34**, with proximal electrodes **34** positioned near left phrenic nerve **26** and distal electrodes **34** positioned near right phrenic nerve **28**. Catheter **12** may further include three lumens (not shown) that connect with extension lumens **38**, **40**, **42** that extend proximally from hub **36**. The distal portion of catheter **12** may be configured to assume a helical shape **44** when positioned within the patient. Helical shape **44** may help anchor catheter **12** to the vessel wall to stabilize catheter **12** during nerve stimulation. Furthermore, helical shape **44** may allow electrodes **34** to be positioned at different radial positions within the vessel, which may be useful when selecting electrodes for nerve stimulation. For example, in certain instances it may be desirable to stimulate the nerve with electrodes **34** that are closer to the nerve (e.g., to obtain a stronger diaphragm response), and in other instances it may be desirable to stimulate the nerve with electrodes **34** that are farther away from the nerve (e.g., to obtain a weaker diaphragm response, or prevent stimulation of the vagus nerve).

In one example, helical shape **44** may be obtained by using a stiffening wire inserted into a lumen of catheter **12** via an extension lumen **38**, **40**, or **42**. The stiffening wire may include a shape-memory material (e.g., Nitinol) biased to a helical shape, stainless steel, or any other suitable material. The portion of catheter **12** configured to assume the helical shape **44** may include materials having a lower stiffness than other portions of catheter **12**. For example, the

materials along helical shape **44** may be thinner or more flexible than the materials along the remaining length of catheter **12**. In another example, catheter **12** may include a temperature-activated shape memory material (e.g., Nitinol) along a portion of its length, such that the shape-memory material of catheter **12** may have a substantially straight shape at room temperature and may assume a helical shape when heated within the patient's body.

In some examples, the proximal portion of catheter **12** additionally or alternatively may have a feature, similar to the distal portion of catheter **12**, to allow it to assume a helical shape when positioned within left jugular vein **32** (or left subclavian vein **22**). Any proximal helical shape may be obtained or result from any of the features described in connection with helical shape **44**. If both the proximal and distal portions of catheter **12** assume a helical shape when positioned within the patient, both the proximal and distal electrodes **34** may be fixed relative to the left and right phrenic nerves **26**, **28**, respectively. To account for body movements when the patient breathes or moves, catheter **12** may further include a helical shape along a central portion of catheter **12**. In one example, the diameter of an expanded helical shape in the central portion may be less than the diameter of the vessel wall, so that the central helical shape is not fixed relative to the vessel wall. Accordingly, the central helical portion may allow catheter **12** to freely expand and contract in length within the vessel as body movements cause the distance between the proximal helix and the distal helix (which may be fixed relative to the vessel walls) to vary. The central helical shape may be obtained or result from any of the features described in connection with helical shape **44**.

Referring to FIG. **5**, each of the extension lumens **38**, **40**, and **42** may end in a proximal-most port **38***a*, **40***a*, and **42***a*, respectively. Further, the lumens internal to catheter **12** may terminate in one or more distal ports. In one example, internal lumens that communicate with lumens **38**, **40**, and **42** terminate at a distal port **48**, medial port **50**, and proximal port **52**, respectively. Lumens **38**, **40**, **42** and their corresponding internal lumens may be used to transport fluid to and from the patient, such as to deliver medications or withdraw blood or other bodily fluids. In other examples, these lumens may be used to hold a guidewire, stiffening wire, optical fiber camera, sensors, or other medical devices. FIG. **5** illustrates an optical fiber camera **46** inserted into lumen **38**, extending through a corresponding internal lumen, and exiting from distal port **48**.

FIG. **6** illustrates another example of catheter **12**. Catheter **12** is similar to the catheter of FIG. **5**, except electrodes **34** may be formed by conductive inks (such as silver, gold, graphine, or carbon flakes suspended in polymer or other media) printed on the surface of catheter **12**, as described in U.S. Pat. No. 9,242,088, incorporated by reference herein (see above). These conductive inks may be deposited and adhered directly onto catheter **12** and sealed, except for the exposed electrodes **34**, with an outer polyurethane or other flexible insulative film. The exposed electrodes **34** may be coated (e.g., with titanium nitride) for purposes such as one or more of: enhancing electrical properties, such as conductivity and surface area; providing corrosion resistance; and reducing the potential for formation of silver oxide, which could be toxic. As can be seen in FIG. **6**, the conductive ink trace of distal electrodes may travel proximally along catheter **12** past the more proximal electrodes **34**. FIG. **6** further illustrates catheter **12** having an ultrasound transducer **54** at a distal end of catheter **12**, which will be described further below.

Detailed System Components

FIG. **7** illustrates a block diagram of the various components of system **10**. The electrodes **34***a*-**34***j*, hub **36**, and lumens **38**, **40**, **42**, **58**, and **60** may be part of catheter **12** described herein. Catheter **12** may have any number of electrodes and any number of lumens. Five lumens are illustrated in FIG. **7**, but in different examples, the catheter may include one, two, three, four, or more than five lumens. In one example, catheter **12** may have three lumens (e.g., extension lumens **38**, **40**, **42** and corresponding internal lumens), which each may hold one or more of a guidewire or optical fiber camera, or may be used for fluid delivery or blood sample extraction (box **43**). In another example, catheter **12** may include four lumens, with one lumen **58** holding or fluidly connected to a pressure sensor **90**, one lumen **60** holding or fluidly connected to a blood gas sensor **62**, and the other two lumens holding a guidewire or optical fiber camera and/or being used for fluid delivery or blood sample extraction. It should be understood that any lumen of system **10** may contain or be fluidly connected to any of the devices (e.g., sensors, guidewire, optical fiber camera) described herein and/or may be used for any of the functions described herein (e.g., fluid delivery, blood sample extraction).

System **10** may include a controller **64**, which may be part of any of the control units described herein. Each of the components of system **10** may be operably coupled to the controller **64**, and controller **64** may manage operation of electrodes **34** during nerve stimulation, control the gathering of information by various sensors and electrodes **34**, and control fluid delivery or extraction. It should be understood that the various modules described herein may be part of a computing system and are separated in FIG. **7** for explanatory purposes only; it is not necessary for the modules to be physically separate.

Electrodes **34***a*-**34***j* may be electronically coupled to switching electronics **56**, which may be communicably coupled to controller **64**. As shown in FIG. **7**, a portion of electrodes **34** may be distal electrodes **34***a*-**34***d*, and a portion of electrodes **34** may be proximal electrodes **34***g*-**34***j*. Other electrodes **34**, such as electrodes **34***e* and **34***f*, may be positioned between the proximal and distal electrodes and, depending on the placement of catheter **12**, may be used for stimulating either left or right phrenic nerves **26**, **28**. Hub **36** also may be connected to switching electronics **56** and may be used as an electrode.

Electrodes **34***a*-**34***j* may be used for both electrically stimulating nerves and for gathering physiological information. When being used for nerve stimulation, a first combination of electrodes (e.g., one, two, three, or more electrodes) may be electrically coupled to a first stimulation module channel **70** for stimulation of a first nerve (e.g., the right phrenic nerve) and a second combination of electrodes (e.g., one, two, three, or more electrodes) may be electrically coupled to a second stimulation module channel **72** for stimulation of a second nerve (e.g., the left phrenic nerve). Electrical signals may be sent from the first and second stimulation module channels **70**, **72** to the electrode combinations to cause the electrodes to stimulate the nerves. In other examples, more than two electrode combinations (e.g., 3, 4, or more) may be used to stimulate one or more target nerves, and system **10** may include more than two stimulation module channels.

Electrodes **34***a*-**34***f* may be further configured to sense physiological information from a patient, such as nerve activity, ECG, or electrical impedance, as will be described further below. When being used for sensing, one or more of

electrodes **34***a*-**34***f* may be electronically coupled to a signal acquisition module **68**. Signal acquisition module **68** may receive signals from electrodes **34**.

Switching electronics **56** may selectively couple electrodes **34** to first stimulation module channel **70**, second stimulation module channel **72**, or signal acquisition module **68**. For example, if an electrode **34** (e.g., electrode **34***a*) is being used to acquire a signal, such as an ECG signal, that electrode **34** may be coupled via switching electronics **56** to signal acquisition module **68**. Similarly, if a pair of electrodes (e.g., electrodes **34***b* and **34***d*) is being used to stimulate right phrenic nerve **28**, those electrodes may be coupled via switching electronics **56** to first stimulation module channel **70**. Finally, if a pair of electrodes (e.g., electrodes **34***g* and **34***h*) is being used to stimulate left phrenic nerve **26**, those electrodes may be coupled via switching electronics **56** to second stimulation module channel **72**. Switching electronics **56** may change which electrodes **34** are used for stimulation and which are used for sensing at any given time. In one example, any electrode **34** can be used for nerve stimulation and any electrode **34** can be used for sensing functions described herein. In other words, each electrode **34** may be configured to stimulate nerves, and each electrode **34** may be configured to sense physiological information.

Signal acquisition module **68** may further be coupled to one or more sensors configured to gather physiological information from a patient. For example, system **10** may include one or more of blood gas sensor **62** or pressure sensor **90**. These sensors may be located in lumens of catheter **12**, outside of the patient in fluid communication with a lumen, on an outer surface of catheter **12**, or in any other suitable location. In one example, blood gas sensor **62** may be housed in or fluidly connected to lumen **60**, while pressure sensor **90** may be housed in or fluidly connected to lumen **58**. Blood gas sensor **62** may measure the amount of O_2 or CO_2 in the patient's blood. Pressure sensor **90** may measure the central venous pressure (CVP) of the patient.

Signal acquisition module **68** may transmit the signals received from one or more of electrodes **34**, blood gas sensor **62**, and/or pressure sensor **90** to the appropriate processing/filtering module of system **10**. For example, signals from pressure sensor **90** may be transmitted to a central venous pressure signal processing/filtering module **84**, where the signals are processed and filtered to aid in interpretation of CVP information. Similarly, signals from blood gas sensor **62** may be transmitted to a blood gas signal processing/filtering module **86** for processing and filtering to determine blood gas levels. Signals from electrodes **34**, when they are used for sensing, may be sent to nerve signal processing/filtering module **80**, ECG signal processing/filtering module **82**, or impedance signal processing/filtering module **88**, as appropriate. Signals from electrodes **34** or other sensors may be sent to amplification module **78**, if necessary, to amplify the signals prior to being sent to the appropriate processing/filtering module.

Controller **64** may further communicate with display **74**, which may serve as a user interface and may have a touch screen **18** (see FIG. **1**). System **10** may further include software/firmware **76**, which may contain the instructions necessary for carrying out the various functions described herein. Finally, system **10** may include data storage **79**, for storing information gathered during sensing operations of catheter **12**, and/or for storing instructions related to the operation of any of the modules or instructions for carrying out any of the functions described herein. Catheter **12** may contain unique identification features (e.g., RFID), and in the event the system **10** described herein (e.g., having one or more of controllers/programmers **14**, **14'**, **14"**, **98**, **64**) is used to treat multiple patients concurrently, the catheter identification feature may allow the system **10** to uniquely identify each patient and access that patient's stored patient data.

Catheter Positioning

Catheter **12** may include a variety of positioning features that may help a user to position catheter **12** within a patient. Some positioning features may be visualization aids, such as optical fiber camera **46** shown in FIG. **5** or ultrasound transducer **54** shown in FIG. **6**. Other positioning features may be sensors to sense physiological parameters, such as pressure sensor **90**. Electrodes **34**, which can be used to stimulate a nerve, also may be used as sensors to gather information that can then be used to position catheter **12**. For example, electrodes **34** may gather information related to nerve activity (e.g., the left or right phrenic nerve), ECG signals, and/or impedance. Accordingly, a sensing electrode **34** may be considered a positioning feature. Each of the positioning features and how they are used to help position catheter **12** will be described in further detail below.

Catheter **12** may include any combination of positioning features, including one or more visualization aids, sensors (e.g., pressure), or electrodes capable of sensing various types of information. Similarly, the control units described herein, whether on a cart, wearable on a patient, or wireless, may be configured to process information gathered by the various positioning features described herein (e.g., visualization aids, sensors, and electrodes), as well as perform the various computerized functions described herein.

Referring back to FIG. **5**, optical fiber camera **46** may be positioned within extension lumen **38** and its corresponding internal lumen within catheter **12**, either temporarily or as an integral, permanent component of catheter **12**. It should be understood that optical fiber camera **46** could be inserted into any of the extension lumens **38**, **40**, **42** and internal lumens, and could exit any of the ports **48**, **50**, **52**. Optical fiber camera **46** may be used to aid in positioning of catheter **12** within the patient. For example, images from optical fiber camera **46** may be transmitted in real time to a health professional or other user during a procedure, who may rely on the images to guide catheter **12** through the patient's vessels and/or to adjust the position of the catheter within the vessels.

Referring back to FIG. **6**, ultrasound transducer **54** may be used in addition to or instead of optical fiber camera **46** to obtain information useful for positioning catheter **12** within the patient. Ultrasound transducer **54** may be secured temporarily or permanently to the exterior of catheter **12**, as shown in FIG. **6**, or may be positioned temporarily or permanently within a lumen of catheter **12** (e.g., positioned to extend from the distal end of a lumen of catheter **12**). Positioning ultrasound transducer **54** near the distal tip of catheter **12** may allow the user to view the inside of vessels and also ensure that the tip of catheter **12** is not positioned in an undesired location (e.g., in the atrium of the heart). For example, ultrasound transducer **54** may allow visualization of a heart valve, which could indicate that the catheter **12** has entered the atrium and may need to be retracted.

In addition to allowing a user to see the inside of the patient's vessels, the ultrasound images may provide information (e.g., calculated or visual) about the diameter of blood vessels and/or blood flow within the vessels. The user may then use vessel diameter information, blood flow, and real time images of the inside of the patient's vessels to position catheter **12** in a desired position.

CVP measurements from pressure sensor **90** may further aid in positioning catheter **12** within the patient. Normal values may vary between 4-12 cm H_2O. The CVP waveform may change based on the location, relative to the patient's heart, of the port (e.g., **46**, **48**, or **50**) in communication with pressure sensor **90**. In one example, CVP measurements may decline as the relevant port approaches the patient's heart. A user may read the changing CVP waveforms to help position the catheter **12** in a desired location relative to the patient's heart.

The CVP waveform has several components. The (a) wave corresponds to the right atrial contraction and correlates with the P wave on the ECG. The (c) wave corresponds to the cusp of the tricuspid valve protruding backwards through the atrium, as the right ventricle begins to contract. The (c) wave correlates with the end of the QRS complex on the ECG. The (x) descent corresponds to the movement of the right ventricle, which descends as it contracts. The downward movement decreases the pressure in the right atrium. At this stage, there is also atrial diastolic relaxation, which further decreases the right atrial pressure. The (x) descent happens before the T wave on the ECG. The (v) wave occurs as blood fills the right atrium and hits the tricuspid valve, causing a back-pressure wave. The (v) wave occurs after the T wave of the ECG. The (y) descent is a pressure decrease caused by the tricuspid valve opening in early ventricular diastole and occurs before the P wave of the ECG. The amplitudes of a, c, x, v, y may change depending on the position of the catheter with respect to the heart. The signature change of the CVP waveform can guide in the placement of catheter **12**.

In one example, a method for positioning intravascular catheter **12** may include positioning catheter **12** in a first position in a venous system of a patient, wherein catheter **12** includes a plurality of electrodes **34** and at least one lumen extending from a proximal end of catheter **12** to a distal end of catheter **12**, and each electrode **34** of the plurality of electrodes **34** is configured to emit electrical signals to stimulate a nerve; measuring a central venous pressure of the patient using a pressure sensor **90** fluidly connected to the at least one lumen; and based on the central venous pressure, adjusting catheter **12** to a second position different from the first position.

Nerve signals acquired by electrodes **34** also may be used to aid in positioning catheter **12** within a patient. The electrical signal from a nerve may be amplified by amplification module **78** and processed by nerve signal processing/filtering module **80**. The amplified and filtered signals from one or more electrodes **34** then may be compared to an expected signal from the targeted nerve (e.g., left or right phrenic nerve) to identify electrodes **34** in close proximity to the target nerve and to identify the optimal one or more electrodes for nerve stimulation. For example, electrodes **34** returning a higher strength and/or higher quality signal may be located closer to the target nerve.

More specifically, phrenic nerve activity can be recorded using bipolar or monopolar electrodes. Phrenic nerve discharge can be amplified and filtered (e.g., 100 Hz to 5 kHz), and a moving average can be obtained using a third-order Paynter filter with a 20 or 50 ms time constant. Phrenic nerve discharge also can be filtered at 10 Hz to 5 kHz for analysis of spectral composition. A sampling rate of 1-10 kHz can be used to capture the nerve activity.

The parameters acquired during nerve activity sensing can be used to detect if the signal is from the phrenic nerve or another nerve. Sensed parameters can include a number of physiological parameters, such as amplitude, inspiration duration, and/or breathing rate. For example, if the sensed amplitude shows proximity of the electrodes **34** to the nerve and the nerve is a phrenic nerve, the duration of pulses in a train should match the sensed inspiration duration, and the frequency of the trains should match the sensed breathing rate. Furthermore, the sensed signals from a nerve can be compared to known nerve signatures (e.g., of phrenic nerves) to confirm that the nerve signal is from the desired nerve.

Electrodes **34** (e.g., two or three) may be used to acquire ECG signals, with hub **36** optionally being used as a reference electrode. The ECG signal (e.g., morphology, amplitudes, and spectral content) may vary depending on the location, relative to the patient's heart, of the electrodes being used to measure the signal. Monitoring changes in the ECG signal as catheter **12** is being positioned may aid in identifying desired or undesired placement. For example, it may be undesired for catheter **12** to be placed in the atrium of the patient's heart.

In one example, one of the distal electrodes **34** on catheter **12** may be designated as a probe. Other electrodes along the length of catheter **12**, and in some cases in contact with the skin of the patient, may be used to detect an ECG signal, which can optionally be displayed by control unit **14** via screen **18**. Catheter **12** may be advanced through superior vena cava **24** towards the heart. As catheter **12** enters a region proximate the right atrium, or enters the right atrium, the P-wave portion of the ECG may become elevated and create an augmented peaked P-wave, indicating that the tip of the catheter **12** lies in or very close to the right atrium. The operator can observe the change in P-wave, or the control unit **14** can utilize an algorithm to detect the change and provide a visual, audible or other signal to the operator. For example, an LED on catheter hub **36**, control unit **14**, or remote controller **16** can change from green to yellow and then to red as the P-wave changes indicate that the catheter **12** is approaching and then is positioned within the right atrium. The catheter **12** can then be withdrawn slowly until the P-wave starts to diminish. The catheter **12** can then be withdrawn a further 1-2 cm, thereby positioning the catheter tip in the distal portion of superior vena cava **24**.

In this example, the positive deflection in the P-wave occurs when current flows to the probing electrode, and a negative deflection when it flows away. The P-wave depolarizes down the right atrium from the SA node, away from an electrode **34** in superior vena cava **24**, and is therefore negative. The amplitude of the P-wave is related to the inverse square rule, whereby the amplitude is inversely proportional to the square of the distance from the current source. Thus, the P-wave increases greatly in negative amplitude as catheter **12** approaches the atrium. When the tip enters the atrium, it is just beyond the SA node, and the first portion of the P-wave depolarizes towards it. This results in a brief, small positive deflection followed instantly by a deep negative deflection.

Alternatively, a distal combination of electrodes **34** (e.g., a distal pair) and a proximal combinations of electrodes **34** (e.g., a proximal pair) can be used to obtain, respectively, a distal and proximal ECG signal having a P-wave. The P-waves can be compared using standard signal processing techniques and a delta value can be determined as the catheter **12** is advanced through the vessel (e.g. superior vena cava **24**) towards the heart. As catheter **12** is advanced in close proximity to or into the atrium, the delta value will change significantly, exceeding a predetermined value. The system **10** can provide an indicator to the operator, as described previously, and catheter **12** can be withdrawn 1 to

2 cm. This method can also utilize one or more reference electrodes **34** located along the length of the catheter or positioned externally on the patient's body.

Electrodes **34** also may be used to measure impedance, which can provide information relevant to positioning catheter **12**. Impedance may be measured between any two electrodes **34** of catheter **12**. In one example, however, impedance may be measured between: a) either a proximal-most electrode **34** or hub **36**, and b) a distal-most electrode.

The impedance presented to injected current may be dependent on the conductivity of the fluid, or adjacent tissue, in the local area between a pair of sensing electrodes **34**. The conductivity further may depend on the cross-sectional area of the blood vessel at the site of the sending electrodes **34**. The impedance of an electrode **34** may vary depending on the medium in which it is resting. For example, an electrode **34** placed in a relatively large body of conductive fluid may have a lower impedance than one resting against a vessel wall. The impedance of an electrode **34** can therefore be used to determine whether it is adjacent to a vessel wall or resting in a larger body of conductive fluid.

In one example, when catheter **12** is inserted into a patient, electrodes **34** that are on a proximal portion of catheter **12** may have a higher impedance than other electrodes **34**, because the proximal portion of catheter **12** may be positioned in tissue (e.g., fatty) near an insertion site, rather than resting in the fluid of a blood vessel. Electrodes **34** farther down the shaft of catheter **12**, towards a central portion of catheter **12**, might have progressively lower impedances as the diameter of the vessel increases (e.g., as the vessel approaches superior vena cava **24**). Electrodes **34** on the portion of catheter **12** that is floating in fluid in superior vena cava **24** might have a low impedance. Electrodes **34** on the distal portion of catheter **12**, at or near the tip of catheter **12**, might be in direct contact with the vessel wall and therefore may have a higher impedance. A graph of the impedances of all of the electrodes **34** in this example may have a U-shaped curvature, as impedances may be higher at each end of catheter **12** and lower towards the central portion of catheter **12**. The change in impedance of an electrode **34** as it progresses through the patient's vessels can provide information about the location of that electrode **34**. In addition, the differences in impedances of electrodes **34** along the length of catheter **12** may provide information about the placement of catheter **12**.

In one example, catheter **12** may be placed in a vessel that varies in diameter, with distal electrodes **34** resting in a desired vessel (e.g., in superior vena cava **24**). The impedances of different, more proximal electrodes would be expected to vary depending on their position in the venous system. In one example, catheter **12**, when placed in a desired position, would be expected to include: 1) electrodes **34** whose impedances are reduced as the electrodes **34** approach the wall of a vessel (e.g., superior vena cava **24**); and 2) electrodes **34** having impedance profiles with a desired shape. In one example, measured impedances may be compared to impedance thresholds or profiles stored in data storage **79**, to determine if one or more electrodes **34** are properly placed.

In another example, the impedances of distal electrodes can be compared to the impedances of proximal electrodes as the catheter **12** is advanced through superior vena cava **24** towards the atrium. As the distal electrodes enter the atrium, the difference between the distal and proximal impedance measurements may exceed a predetermined threshold allowing the system **10** to provide an indication to the operator. Catheter **12** can then be withdrawn (or advanced depending on the application) to the desired location. Signal filtering, processing, and analytical techniques known in the art can be used to assess the impedance measurements in real time.

A catheter **12** that is under-inserted may have few or no electrodes **34** resting in the desired vessel (e.g., superior vena cava **24**), which would result in electrode impedance profiles having different shapes than the desired shape. In addition, a catheter **12** that is over-inserted may have one or more electrodes **34** that are close to, or in contact with, the atrium, which may also result in impedance profiles having different shapes than the desired shape. In one example, the impedance of one or more electrodes **34** is monitored as catheter **12** is inserted into the patient and electrodes **34** move through the patient's venous system. Changes in the impedance profiles can be displayed to the health professional performing the insertion, and the impedance profiles can be used to confirm proper placement of catheter **12**.

In one example, a method for positioning intravascular catheter **12** may include positioning catheter **12** in a first position in a venous system of a patient, wherein catheter **12** includes a plurality of electrodes **34**, and each electrode **34** of the plurality of electrodes **34** is configured to emit electrical signals to stimulate a phrenic nerve; measuring an impedance between a first electrode **34** of the plurality of electrodes **34** and a second electrode; and based on the measured impedance, adjusting catheter **12** to a second position different from the first position.

In other examples, catheter **12** may include a strain gauge and/or an accelerometer (not shown). Either the strain gauge or the accelerometer may be placed at or near the distal end of catheter **12**, in one of the lumens. The strain gauge could detect flex in a distal portion of catheter **12**, and the accelerometer could detect movement/acceleration of the distal portion of catheter **12**. Information from the strain gauge and/or accelerometer could be used to determine whether the distal end of catheter **12** is in the atrium (e.g., heartbeats may cause movement of the distal end of catheter **12**). The strain gauge or the accelerometer could be an integral, permanent part of catheter **12** or could be positioned in a lumen of catheter **12** temporarily during positioning of catheter **12**.

Electrode Selection and Determining Stimulation Parameters

Nerve signals acquired by sensing electrodes **34** may be used to select electrodes **34** for nerve stimulation. Electrodes **34** that are closer to a target nerve may sense nerve activity having a higher amplitude, while electrodes **34** that are farther from a target nerve may sense nerve activity having a lower amplitude. If a greater diaphragm response is desired, electrodes **34** that are closer to the nerve, as determined based on received nerve activity signals, may be selected for nerve stimulation. In other cases, if less diaphragm response is desired, electrodes **34** that are farther from the nerve, as determined based on received nerve activity signals, may be selected for nerve stimulation.

Typical nerve signals for, e.g., phrenic nerves, follow a pattern that has distinct characteristics (e.g., spectral characteristics and modulation over time). To select electrodes **34** for nerve stimulation, the sensed nerve signals from different electrodes **34** can be analyzed for their spectral and temporal characteristics. Of electrodes **34** having sensed signal patterns matching typical phrenic nerve activity, the optimal electrodes **34** can be selected based on the amplitude of the signal and how strongly the signal correlates to the typical pattern. In one example, a fast Fourier transform can be used to provide a correlation factor to a reference signal in near real-time. In another example, the sensed signals can

be frequency filtered in the frequency range of interest, based on the typical characteristics of the phrenic nerve signal, and then analyzed over time to observe periods or bursts of activity in the frequency range of interest.

In one example, a method for selecting one or more electrodes for nerve stimulation may include inserting intravascular catheter **12** into: a) at least one of left subclavian vein **22** or left jugular vein **32**, and b) superior vena cava **24**, wherein catheter **12** includes a plurality of electrodes **34**, and each electrode **34** of the plurality of electrodes **34** is configured to emit electrical signals to stimulate a nerve; using one or more electrodes **34** of the plurality of electrodes **34** to acquire an electrical signal emitted from the nerve; based on the acquired electrical signal, selecting an electrode **34** or an electrode combination for a nerve stimulation; and using the selected electrode **34** or electrode combination, stimulating the nerve.

The processed nerve activity waveforms additionally may be used to determine parameters for nerve stimulation. The processed waveforms may provide information regarding intrinsic breath rate (e.g., if the patient is attempting to breathe on his/her own) and nerve signal amplitude. The stimulation parameters may be adjusted based on the breath rate of previous stimulated breaths (e.g., to increase or decrease the breath rate, as sensed by the sensing electrodes) and nerve activity resulting from stimulation during previous breaths (e.g., to increase or decrease the strength of stimulation). Various parameters that may be adjusted include stimulation pulse amplitude, stimulation pulse width, stimulation pulse frequency, stimulation duration, and the interval between stimulations/pulse trains (e.g., stimulated breath rate). Accordingly, sensed nerve activity signals may be used to determine and adjust the nerve stimulation parameters in a closed-loop system.

Impedance information may be used to determine a breath rate of the patient in order to adjust nerve stimulation parameters (e.g., stimulation pulse amplitude, stimulation pulse width, stimulation pulse frequency, stimulation duration, and the interval between stimulations/pulse trains (e.g., stimulated breath rate)). Electrical impedance of lung tissue changes as a function of air content. Accordingly, the electrical impedance of the thorax changes during inhalation and exhalation. The thorax presents an electrical impedance that includes two components: a relatively constant value and a varying value. Changes in impedance may result from the following two effects during inspiration: 1) there is an increase in the gas volume of the chest in relation to the fluid volume, which may cause conductivity to decrease, and 2) the length of the conductance path (e.g., between two electrodes) increases when the lungs expand. These effects may cause impedance to increase during inspiration. There is an approximately linear correlation between the impedance changes and the volume of respirated air. The varying component of impedance (i.e., respirative impedance) generates a varying voltage component when current is injected (e.g., by electrodes **34**). This varying voltage component can then be used to determine the person's breathing rate.

Information from blood gas sensor **62** may be used by a health professional, or by controller **64**, to adjust stimulation parameters. For example, if blood O_2 levels are low (or blood CO_2 levels are high) controller **64** may send a signal to electrodes **34** to emit stimulation signals having a higher charge (amplitude×pulse width) or frequency, and may stimulate a sigh breath. Conversely, if blood O_2 levels are high (or blood CO_2 levels are low), controller **64** may cause electrodes **34** to emit stimulation signals having a lower charge or frequency. Based on information from blood gas sensor **62**, the following parameters can be adjusted: stimulation pulse amplitude, stimulation pulse width, stimulation pulse frequency, stimulation duration, and the interval between stimulations/pulse trains (e.g., stimulated breath rate).

For any of the parameter adjustments described herein, increasing stimulation pulse amplitude, width and/or frequency may increase lung volume during a stimulated breath. Increasing stimulation duration may increase lung volume and/or increase the amount of time air remains in the lungs during a stimulated breath, allowing for an extended gas exchange period. Increasing the stimulated breath rate may allow for additional gas exchange periods over a given period of time, which may increase the amount and/or speed of gas exchange.

The system **10** and catheter **12** described herein may include any combination of sensing features. For example, catheter **12** may be configured to sense ECG, impedance, nerve activity, blood gas levels, and CVP, and the system **10** may be configured to position catheter **12**, select electrodes **34** for stimulation, and select stimulation parameters based on one or more types of information received by sensors or electrodes **34**.

Accordingly, the various visualization and sensing functions of system **10** may assist a user in one or more of positioning a transvascular catheter, selecting optimal electrodes for nerve stimulation, or selecting or adjusting parameters for nerve stimulation.

While principles of the present disclosure are described herein with reference to illustrative embodiments for particular applications, it should be understood that the disclosure is not limited thereto. Those having ordinary skill in the art and access to the teachings provided herein will recognize additional modifications, applications, embodiments, and substitution of equivalents all fall within the scope of the embodiments described herein. Accordingly, the invention is not to be considered as limited by the foregoing description.

We claim:

1. A method for positioning an intravascular catheter, comprising:

inserting the intravascular catheter into a venous system of a patient, wherein the catheter includes a plurality of electrodes, and multiple electrodes of the plurality of electrodes are configured to emit electrical signals;

positioning a distal portion of the catheter in a first position;

using one or more electrodes of the plurality of electrodes to acquire a first ECG signal and a second ECG signal;

determining a difference between the first ECG signal and the second ECG signal;

comparing the difference to a value;

based on the comparison of the difference to the value, adjusting the distal portion of the catheter to a second position different from the first position;

identifying at least one first electrode of the plurality of electrodes to stimulate a first nerve;

identifying at least one second electrode of the plurality of electrodes to stimulate a second nerve; and

stimulating at least one of the first and second nerves to cause a contraction of a respiratory muscle.

2. The method of claim **1**, wherein inserting the intravascular catheter into the venous system includes inserting the intravascular catheter into: 1) at least one of a left subclavian, axillary, cephalic, cardiophrenic, brachial, radial, or left jugular vein, and 2) a superior vena cava.

3. The method of claim 1, wherein the first position is proximate an atrium of a heart of the patient, and the second position is in a superior vena cava.

4. The method of claim 1, wherein the first ECG signal is acquired by one or more electrodes that are positioned on a proximal portion of the catheter and are configured to stimulate the first nerve, and the second ECG signal is acquired by one or more electrodes that are positioned on a distal portion of the catheter and are configured to stimulate the second nerve.

5. The method of claim 1, wherein the second position is farther from a heart of the patient than the first position.

6. The method of claim 1, further comprising using one or more electrodes of the plurality of electrodes to sense at least one of an impedance or nerve activity.

7. The method of claim 1, wherein each of the at least one first electrode and the at least one second electrode is a combination of electrodes.

8. A method for positioning an intravascular catheter, comprising:

inserting the intravascular catheter into: 1) at least one of a left subclavian vein or a left jugular vein, and 2) a superior vena cava, wherein the catheter includes a plurality of electrodes, and the plurality of electrodes includes a proximal set of electrodes positioned proximate a left phrenic nerve and a distal set of electrodes positioned proximate a right phrenic nerve;

using one or more electrodes of the plurality of electrodes to acquire a first ECG signal and a second ECG signal;

determining a difference between the first ECG signal and the second ECG signal;

comparing the difference to a value;

based on the comparison of the difference to the value, withdrawing the catheter away from a heart of a patient;

stimulating the left phrenic nerve using one or more electrodes of the proximal set of electrodes; and

stimulating the right phrenic nerve using one or more electrodes of the distal set of electrodes.

9. The method of claim 8, wherein the step of withdrawing the catheter away from the heart causes a change in an amplitude of a P-wave of the first ECG signal or the second ECG signal.

10. The method of claim 8, wherein the first ECG signal is acquired by one or more electrodes of the proximal set of electrodes, and the second ECG signal is acquired by one or more electrodes of the distal set of electrodes.

11. The method of claim 8, wherein the difference between the first ECG signal and the second ECG signal is a difference between a P-wave of the first ECG signal and a P-wave of the second ECG signal.

12. The method of claim 8, wherein the difference exceeds the value when the catheter is advanced into an atrium of the heart.

13. The method of claim 8, wherein a hub coupled to the catheter and positioned exterior to the patient is used with the one or more electrodes of the plurality of electrodes to acquire the ECG signal.

14. The method of claim 8, further comprising monitoring the first ECG signal and the second ECG signal as a distal end of the catheter is inserted into the at least one of the left subclavian vein or the left jugular vein and advanced into the superior vena cava.

15. A method for positioning an intravascular catheter, comprising:

inserting the intravascular catheter into a venous system of a patient, wherein the catheter includes a plurality of proximal electrodes and a plurality of distal electrodes;

using one or more electrodes of the plurality of proximal electrodes to acquire a first ECG signal, and using one or more electrodes of the plurality of distal electrodes to acquire a second ECG signal;

determining a difference between the first ECG signal and the second ECG signal;

comparing the difference to a value;

based on the comparison of the difference to the value, adjusting a position of the catheter;

stimulating the first nerve using one or more of the plurality of proximal electrodes; and

stimulating the second nerve using one or more of the plurality of distal electrodes.

16. The method of claim 15, wherein the first nerve is a left phrenic nerve, and the second nerve is a right phrenic nerve.

17. The method of claim 15, wherein the difference between the first ECG signal and the second ECG signal is a difference between an amplitude of a portion of the first ECG signal and an amplitude of a portion of the second ECG signal.

18. The method of claim 15, wherein the steps of determining the difference and comparing occur a plurality of times during the inserting step.

19. The method of claim 15, wherein adjusting the position of the catheter includes moving the catheter away from a heart.

20. The method of claim 15, wherein at least one of stimulating the first nerve or stimulating the second nerve causes a contraction of a diaphragm.

21. The method of claim 15, further comprising sensing activity of the first nerve using one or more of the proximal electrodes and sensing activity of the second nerve using one or more of the distal electrodes.

22. A method for positioning an intravascular catheter, comprising:

inserting the intravascular catheter into: 1) at least one of a left subclavian vein or a left jugular vein, and 2) a superior vena cava, wherein the catheter includes a plurality of proximal electrodes configured to be positioned proximate a left phrenic nerve and a plurality of distal electrodes configured to be positioned proximate a right phrenic nerve;

at multiple positions of the catheter during the inserting step, using one or more electrodes of the plurality of proximal electrodes to acquire a first ECG signal, and using one or more electrodes of the plurality of distal electrodes to acquire a second ECG signal;

determining a difference between the first ECG signal and the second ECG signal at several of the multiple positions;

comparing each difference to a value;

based on the comparisons of each difference to the value, determining a desired position of the catheter for nerve stimulation;

stimulating the left phrenic nerve using one or more of the plurality of proximal electrodes; and

stimulating the right phrenic nerve using one of more of the plurality of distal electrodes.

23. The method of claim 22, further comprising advancing a distal end of the catheter into a region proximate an atrium of a heart.

24. The method of claim 23, wherein one of the multiple positions is a position in which the distal end of the catheter

is proximate the atrium of the heart, and in the position, the comparison indicates a difference between an amplitude of the first ECG signal and an amplitude of the second ECG signal that exceeds the value.

25. The method of claim **24**, further comprising moving the catheter away from the heart.

26. The method of claim **22**, wherein stimulating the left phrenic nerve causes a diaphragm contraction, and stimulating the right phrenic nerve causes a diaphragm contraction.

27. The method of claim **22**, wherein the proximal electrodes used to acquire the first ECG signal are configured to stimulate the left phrenic nerve, and the distal electrodes used to acquire the second ECG signal are configured to stimulate the right phrenic nerve.

* * * * *

专利名称(译)	用于血管内导管定位和/或神经刺激的系统和方法		
公开(公告)号	US10195429	公开(公告)日	2019-02-05
申请号	US15/666989	申请日	2017-08-02
[标]发明人	THAKKAR VIRAL S EVANS DOUGLAS G GANI MATTHEW J		
发明人	THAKKAR, VIRAL S. EVANS, DOUGLAS G. GANI, MATTHEW J.		
IPC分类号	A61N1/36 A61B5/042 A61N1/05 A61B5/00 A61B5/0452		
CPC分类号	A61N1/3601 A61N1/0551 A61B5/4893 A61B5/0422 A61B5/0452 A61B5/04001		
其他公开文献	US20190038897A1		
外部链接	Espacenet		

摘要(译)

用于定位血管内导管的方法可以包括将血管内导管插入患者的静脉系统，其中导管包括多个电极，并且多个电极中的多个电极配置为发射电信号;将导管的远端部分定位在第一位置;使用多个电极中的一个或多个电极来获取ECG信号;基于所获取的ECG信号，将导管的远端部分调节到不同于第一位置的第二位置;识别所述多个电极中的至少一个第一电极以刺激第一神经;识别多个电极中的至少一个第二电极以刺激第二神经;并且刺激第一和第二神经中的至少一个以引起呼吸肌的收缩。