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(54) **METHODS AND APPARATUS FOR FLOW RESTORATION**

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(56) **References Cited**

U.S. PATENT DOCUMENTS

2,709,999 A 6/1955 Nagel
3,174,851 A 3/1965 Buehler et al.
(Continued)

FOREIGN PATENT DOCUMENTS

BR 9604566 A 9/1998
CA 2389374 A1 5/2001
(Continued)

OTHER PUBLICATIONS

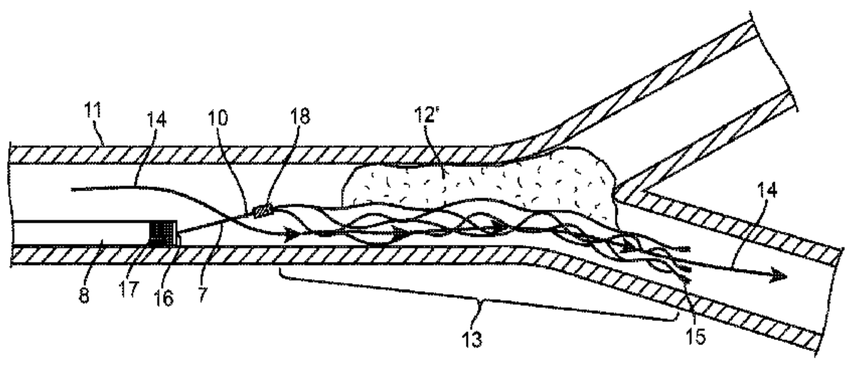
US 6,056,761 A, 05/2000, Gia (withdrawn)
(Continued)

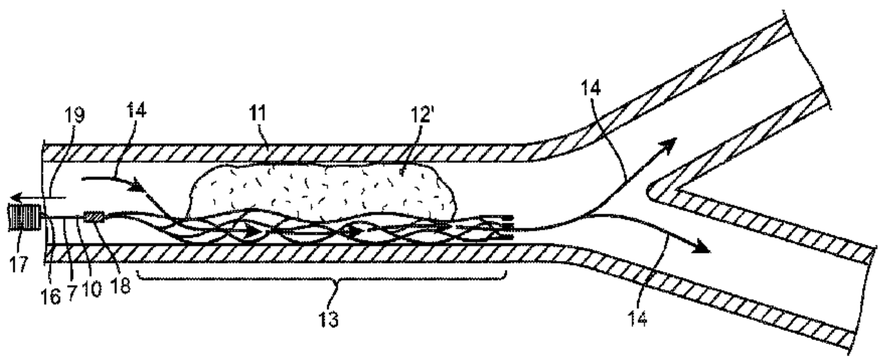
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(57) **ABSTRACT**

Methods for restoring blood flow in occluded blood vessels using an apparatus having a self-expandable distal segment that is pre-formed to assume a superimposed structure in an unconstrained condition but can be made to take on a volume-reduced form making it possible to introduce it with a microcatheter and a push wire arranged at the proximal end, with the distal segment in its superimposed structure assuming the form of a longitudinally open tube and having a mesh structure of interconnected strings or filaments or struts. In a preferred embodiment, the distal segment has a tapering structure at its proximal end where the strings or filaments or struts converge at a connection point.

34 Claims, 10 Drawing Sheets





Related U.S. Application Data

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(58) **Field of Classification Search**

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See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,351,463	A	11/1967	Rozner
3,506,171	A	4/1970	Rupert
3,753,700	A	8/1973	Harrison et al.
3,996,938	A	12/1976	Clark, III
4,046,150	A	9/1977	Schwartz et al.
4,299,255	A	11/1981	Miller
4,347,846	A	9/1982	Dormia
4,403,612	A	9/1983	Fogarty
4,611,594	A	9/1986	Grayhack et al.
4,612,931	A	9/1986	Dormia
4,650,466	A	3/1987	Luther
4,655,771	A	4/1987	Wallsten
4,733,665	A	3/1988	Palmaz
4,739,762	A	4/1988	Palmaz
4,793,348	A	12/1988	Palmaz
4,890,611	A	1/1990	Monfort et al.
4,993,481	A	2/1991	Kamimoto
4,998,539	A	3/1991	Delsanti
5,035,686	A	7/1991	Crittenden
5,057,114	A	10/1991	Wittich
5,071,407	A	12/1991	Termin et al.
5,100,423	A	3/1992	Fearnot
5,102,417	A	4/1992	Palmaz
5,190,058	A	3/1993	Jones et al.
5,192,286	A	3/1993	Phan et al.
5,195,984	A	3/1993	Schatz
5,197,978	A	3/1993	Hess
5,217,484	A	6/1993	Marks
5,222,964	A	6/1993	Cooper
5,222,971	A	6/1993	Willard et al.
5,275,622	A	1/1994	Lazarus
5,312,344	A	5/1994	Grinfeld et al.
5,327,885	A	7/1994	Griffith
5,330,482	A	7/1994	Gibbs et al.
5,344,395	A	9/1994	Whalen
5,354,295	A	10/1994	Guglielmi et al.
5,370,653	A	12/1994	Cragg
5,411,549	A	5/1995	Peters
5,423,829	A	6/1995	Pham et al.
5,425,739	A	6/1995	Jessen
5,449,372	A	9/1995	Schmaltz et al.
5,456,667	A	10/1995	Ham et al.
5,490,859	A	2/1996	Mische et al.
5,496,330	A	3/1996	Bates et al.
5,501,694	A	3/1996	Ressemann et al.
5,527,282	A	6/1996	Segal
5,527,326	A	6/1996	Hermann et al.
5,540,680	A	7/1996	Guglielmi et al.
5,540,707	A	7/1996	Ressemann et al.
5,569,245	A	10/1996	Guglielmi et al.
5,571,122	A	11/1996	Kelly et al.
5,573,520	A	11/1996	Schwartz et al.
5,624,449	A	4/1997	Pham et al.
5,643,309	A	7/1997	Myler et al.
5,649,906	A	7/1997	Gory et al.
5,653,743	A	8/1997	Martin
5,669,933	A	9/1997	Simon et al.
5,681,336	A	10/1997	Clement et al.
5,683,449	A	11/1997	Marcade
5,690,667	A	11/1997	Gia
5,695,469	A	12/1997	Segal
5,695,519	A	12/1997	Summers et al.
5,718,724	A	2/1998	Goicoechea et al.
5,720,764	A	2/1998	Naderlinger
5,743,905	A	4/1998	Eder et al.
5,749,883	A	5/1998	Halpern
5,759,192	A	6/1998	Saunders
5,769,882	A	6/1998	Fogarty et al.
5,792,145	A	8/1998	Bates et al.
5,792,157	A	8/1998	Mische et al.
5,795,322	A	8/1998	Boudewijn
5,800,454	A	9/1998	Jacobsen et al.
5,800,457	A	9/1998	Gelbfih
5,800,519	A	9/1998	Sandock
5,800,520	A	9/1998	Fogarty et al.
5,800,525	A	9/1998	Bachinski et al.
5,814,064	A	9/1998	Daniel et al.
5,824,037	A	10/1998	Fogarty et al.
5,827,304	A	10/1998	Hart
5,827,324	A	10/1998	Cassell et al.
5,836,868	A	11/1998	Ressemann et al.
5,848,964	A	12/1998	Samuels
5,851,206	A	12/1998	Guglielmi et al.
5,853,419	A	12/1998	Imran
5,855,578	A	1/1999	Guglielmi et al.
5,882,329	A	3/1999	Patterson et al.
5,891,128	A	4/1999	Gia et al.
5,895,385	A	4/1999	Guglielmi et al.
5,895,398	A	4/1999	Wensel et al.
5,897,567	A	4/1999	Ressemann et al.
5,904,698	A	5/1999	Thomas et al.
5,911,717	A	6/1999	Jacobsen et al.
5,911,734	A	6/1999	Tsugita et al.
5,913,895	A	6/1999	Burpee et al.
5,916,235	A	6/1999	Guglielmi
5,919,187	A	7/1999	Guglielmi et al.
5,922,019	A	7/1999	Hankh et al.
5,925,037	A	7/1999	Guglielmi et al.
5,925,061	A	7/1999	Ogi et al.
5,928,226	A	7/1999	Guglielmi et al.
5,928,260	A	7/1999	Chin et al.
5,935,139	A	8/1999	Bates
5,938,671	A	8/1999	Katoh et al.
5,938,697	A	8/1999	Killion et al.
5,941,869	A	8/1999	Patterson et al.
5,941,895	A	8/1999	Myler et al.
5,944,714	A	8/1999	Guglielmi et al.
5,947,962	A	9/1999	Guglielmi et al.
5,947,995	A	9/1999	Samuels
5,948,016	A	9/1999	Jang
5,951,599	A	9/1999	McCrory
5,954,743	A	9/1999	Jang
5,961,547	A	10/1999	Razavi
5,964,797	A	10/1999	Ho
5,968,013	A	10/1999	Smith et al.
5,972,016	A	10/1999	Morales
5,972,019	A	10/1999	Engelson et al.
5,972,219	A	10/1999	Habets et al.
5,976,120	A	11/1999	Chow
5,976,126	A	11/1999	Guglielmi
5,976,131	A	11/1999	Guglielmi et al.
5,980,514	A	11/1999	Kupiecki et al.
5,984,929	A	11/1999	Bashiri et al.
6,001,118	A	12/1999	Daniel et al.
6,010,449	A	1/2000	Selmon et al.

(56) **References Cited**

U.S. PATENT DOCUMENTS

6,010,498	A	1/2000	Guglielmi
6,010,521	A	1/2000	Lee et al.
6,013,093	A	1/2000	Nott et al.
6,015,424	A	1/2000	Rosenbluth et al.
6,039,721	A	3/2000	Johnson
6,051,020	A	4/2000	Goicoechea et al.
6,059,814	A	5/2000	Ladd
6,063,070	A	5/2000	Eder
6,063,100	A	5/2000	Diaz et al.
6,063,104	A	5/2000	Villar et al.
6,063,111	A	5/2000	Hieshima et al.
6,066,149	A	5/2000	Samson et al.
6,066,158	A	5/2000	Engelson et al.
6,077,260	A	6/2000	Wheelock et al.
6,083,220	A	7/2000	Guglielmi et al.
6,093,199	A	7/2000	Brown
6,096,034	A	8/2000	Kupiecki et al.
6,096,053	A	8/2000	Bates
6,099,549	A	8/2000	Bosma et al.
6,106,548	A	8/2000	Roubin et al.
6,110,198	A	8/2000	Fogarty et al.
6,117,167	A	9/2000	Goicoechea et al.
6,118,001	A	9/2000	Owen et al.
6,123,115	A	9/2000	Greenhalgh
6,123,714	A	9/2000	Gia et al.
6,129,755	A	10/2000	Mathis et al.
6,136,006	A	10/2000	Johnson et al.
6,146,396	A	11/2000	Konya et al.
6,156,061	A	12/2000	Wallace et al.
6,159,238	A	12/2000	Killion et al.
6,159,239	A	12/2000	Greenhalgh
6,164,339	A	12/2000	Greenhalgh
6,165,178	A	12/2000	Bashiri et al.
6,165,213	A	12/2000	Goicoechea et al.
6,168,592	B1	1/2001	Kupiecki et al.
6,168,603	B1	1/2001	Leslie et al.
6,168,604	B1	1/2001	Cano
6,179,857	B1	1/2001	Diaz et al.
6,187,017	B1	2/2001	Gregory, Jr.
6,190,358	B1	2/2001	Fitzmaurice et al.
6,190,394	B1	2/2001	Lind et al.
6,192,944	B1	2/2001	Greenhalgh
6,193,708	B1	2/2001	Ken et al.
6,193,745	B1	2/2001	Fogarty et al.
6,203,552	B1	3/2001	Bagley et al.
6,210,364	B1	4/2001	Anderson et al.
6,214,025	B1	4/2001	Thistle et al.
6,217,609	B1	4/2001	Haverkost
6,221,096	B1	4/2001	Aiba et al.
6,231,598	B1	5/2001	Berry et al.
6,238,412	B1	5/2001	Dubrul et al.
6,238,430	B1	5/2001	Klumb et al.
6,241,746	B1	6/2001	Bosma et al.
6,245,089	B1	6/2001	Daniel et al.
6,254,571	B1	7/2001	Hart
6,254,628	B1	7/2001	Wallace et al.
6,264,686	B1	7/2001	Rieu et al.
6,264,687	B1	7/2001	Tomonto
6,267,777	B1	7/2001	Bosma et al.
6,273,900	B1	8/2001	Nott et al.
6,277,125	B1	8/2001	Barry et al.
6,277,126	B1	8/2001	Barry et al.
6,280,413	B1	8/2001	Clark
6,283,940	B1	9/2001	Mulholland
6,283,992	B1	9/2001	Hankh et al.
6,290,720	B1	9/2001	Khosravi et al.
6,302,906	B1	10/2001	Goicoechea et al.
6,305,436	B1	10/2001	Andersen et al.
6,306,141	B1	10/2001	Jervis
6,312,463	B1	11/2001	Rourke et al.
6,322,585	B1	11/2001	Khosravi et al.
6,325,815	B1	12/2001	Kusleika et al.
6,325,820	B1	12/2001	Khosravi et al.
6,325,822	B1	12/2001	Chouinard et al.
6,336,934	B1	1/2002	Gilson et al.
6,344,041	B1	2/2002	Kupiecki et al.
6,361,558	B1	3/2002	Hieshima et al.
6,371,969	B1	4/2002	Tsugita et al.
6,379,329	B1	4/2002	Naglreiter et al.
6,383,205	B1	5/2002	Samson et al.
6,390,993	B1	5/2002	Cornish et al.
6,402,771	B1	6/2002	Palmer et al.
6,409,721	B1	6/2002	Wheelock et al.
6,425,893	B1	7/2002	Guglielmi
6,425,914	B1	7/2002	Wallace et al.
6,428,558	B1	8/2002	Jones et al.
6,432,122	B1	8/2002	Gilson et al.
6,443,971	B1	9/2002	Boylan et al.
6,443,972	B1	9/2002	Bosma et al.
6,454,775	B1	9/2002	Demarais et al.
6,454,780	B1	9/2002	Wallace
6,458,139	B1	10/2002	Palmer et al.
6,468,266	B1	10/2002	Bashiri et al.
6,468,301	B1	10/2002	Amplatz et al.
6,475,236	B1	11/2002	Roubin et al.
6,475,237	B2	11/2002	Drasler et al.
6,485,500	B1	11/2002	Kokish et al.
6,485,509	B2	11/2002	Killion et al.
6,485,524	B2	11/2002	Strecker
6,491,719	B1	12/2002	Fogarty et al.
6,500,182	B2	12/2002	Foster
6,514,273	B1	2/2003	Voss et al.
6,520,968	B2	2/2003	Bates et al.
6,530,935	B2	3/2003	Wensel et al.
6,533,811	B1	3/2003	Ryan et al.
6,537,294	B1	3/2003	Boyle et al.
6,551,341	B2	4/2003	Boylan et al.
6,551,342	B1	4/2003	Shen et al.
6,553,810	B2	4/2003	Webb et al.
6,554,842	B2	4/2003	Heuser et al.
6,554,849	B1	4/2003	Jones et al.
6,554,856	B1	4/2003	Doorly et al.
6,558,405	B1	5/2003	McInnes
6,562,066	B1	5/2003	Martin
6,569,179	B2	5/2003	Teoh et al.
6,569,193	B1	5/2003	Cox et al.
6,572,648	B1	6/2003	Klumb et al.
6,575,995	B1	6/2003	Huter et al.
6,575,997	B1	6/2003	Palmer et al.
6,589,230	B2	7/2003	Gia et al.
6,589,236	B2	7/2003	Wheelock et al.
6,589,265	B1	7/2003	Palmer et al.
6,592,607	B1	7/2003	Palmer et al.
6,592,615	B1	7/2003	Marcade et al.
6,605,057	B2	8/2003	Fitzmaurice et al.
6,610,077	B1	8/2003	Hancock et al.
6,616,617	B1	9/2003	Ferrera et al.
6,620,152	B2	9/2003	Guglielmi
6,629,953	B1	10/2003	Boyd
6,632,241	B1	10/2003	Hancock et al.
6,635,081	B2	10/2003	Khosravi et al.
6,638,294	B1	10/2003	Palmer
6,641,590	B1	11/2003	Palmer et al.
6,645,224	B2	11/2003	Gilson et al.
6,652,505	B1	11/2003	Tsugita
6,652,548	B2	11/2003	Evans et al.
6,652,576	B1	11/2003	Stalker
6,656,214	B1	12/2003	Fogarty et al.
6,660,014	B2	12/2003	Demarais et al.
6,660,021	B1	12/2003	Palmer et al.
6,663,607	B2	12/2003	Slaikeu et al.
6,663,650	B2	12/2003	Sepetka et al.
6,666,829	B2	12/2003	Cornish et al.
6,669,723	B2	12/2003	Killion et al.
6,673,025	B1	1/2004	Richardson et al.
6,673,106	B2	1/2004	Mitelberg et al.
6,679,893	B1	1/2004	Tran
6,685,722	B1	2/2004	Rosenbluth et al.
6,685,738	B2	2/2004	Chouinard et al.
6,692,508	B2	2/2004	Wensel et al.
6,695,813	B1	2/2004	Boyle et al.
6,702,782	B2	3/2004	Miller et al.
6,702,843	B1	3/2004	Brown et al.
6,709,440	B2	3/2004	Callol et al.

(56) **References Cited**

U.S. PATENT DOCUMENTS

6,716,178	B1	4/2004	Kilpatrick et al.	
6,716,238	B2	4/2004	Elliott	
6,723,108	B1	4/2004	Jones et al.	
6,723,112	B2	4/2004	Ho et al.	
6,730,104	B1	5/2004	Sepetka et al.	
6,733,519	B2	5/2004	Lashinski et al.	
6,743,236	B2	6/2004	Barry et al.	
6,746,468	B1	6/2004	Sepetka et al.	
6,764,506	B2	7/2004	Roubin et al.	
6,773,454	B2	8/2004	Wholey et al.	
6,790,237	B2	9/2004	Stinson	
6,795,979	B2	9/2004	Fournier	
6,802,851	B2	10/2004	Jones et al.	
6,811,560	B2	11/2004	Jones et al.	
6,818,013	B2	11/2004	Mitelberg et al.	
6,818,015	B2	11/2004	Hankh et al.	
6,821,291	B2	11/2004	Bolea et al.	
6,824,558	B2	11/2004	Parodi	
6,833,002	B2	12/2004	Stack et al.	
6,833,003	B2	12/2004	Jones et al.	
6,840,958	B2	1/2005	Nunez et al.	
6,878,151	B2	4/2005	Carrison et al.	
6,881,220	B2	4/2005	Edwin et al.	
6,887,268	B2	5/2005	Butaric et al.	
6,893,413	B2	5/2005	Martin	
6,913,612	B2	7/2005	Palmer et al.	
6,921,414	B2	7/2005	Klumb et al.	
6,945,977	B2	9/2005	Demarais et al.	
6,949,620	B2	9/2005	Aida et al.	
6,953,468	B2	10/2005	Jones et al.	
6,953,472	B2	10/2005	Palmer et al.	
6,955,685	B2	10/2005	Escamilla et al.	
6,960,227	B2	11/2005	Jones et al.	
6,960,228	B2	11/2005	Mitelberg et al.	
6,974,473	B2	12/2005	Barclay et al.	
6,989,020	B2	1/2006	Jones et al.	
6,991,641	B2	1/2006	Diaz et al.	
6,994,723	B1	2/2006	McMahon	
7,001,422	B2	2/2006	Escamilla et al.	
7,004,954	B1	2/2006	Voss et al.	
7,004,955	B2	2/2006	Shen et al.	
7,004,956	B2	2/2006	Palmer et al.	
7,018,401	B1	3/2006	Hyodoh et al.	
7,029,688	B2	4/2006	Hubbell et al.	
7,037,329	B2	5/2006	Martin	
7,037,331	B2	5/2006	Mitelberg et al.	
7,041,116	B2	5/2006	Goto et al.	
7,048,014	B2	5/2006	Hyodoh et al.	
7,052,500	B2	5/2006	Bashiri et al.	
7,056,328	B2	6/2006	Arnott	
7,056,336	B2	6/2006	Armstrong et al.	
7,058,456	B2	6/2006	Pierce	
7,060,091	B2	6/2006	Killion et al.	
7,089,218	B1	8/2006	Visel	
7,097,653	B2	8/2006	Freudenthal et al.	
7,101,380	B2	9/2006	Khachin et al.	
7,112,217	B1	9/2006	Kugler et al.	
7,118,600	B2	10/2006	Dua et al.	
7,125,419	B2	10/2006	Sequin et al.	
7,128,073	B1	10/2006	van der Burg et al.	
7,128,736	B1	10/2006	Abrams et al.	
7,144,421	B2	12/2006	Carpenter et al.	
7,147,655	B2	12/2006	Chermoni	
7,147,659	B2	12/2006	Jones	
7,147,660	B2	12/2006	Chobotov et al.	
7,156,869	B1	1/2007	Pacetti	
7,156,871	B2	1/2007	Jones et al.	
7,160,317	B2	1/2007	McHale et al.	
7,169,165	B2	1/2007	Belef et al.	
7,172,575	B2	2/2007	El-Nounou et al.	
7,172,617	B2	2/2007	Colgan et al.	
7,175,607	B2	2/2007	Lim et al.	
7,179,273	B1	2/2007	Palmer et al.	
7,179,276	B2	2/2007	Barry et al.	
7,179,284	B2	2/2007	Khosravi et al.	
7,182,774	B2	2/2007	Barry et al.	
7,195,648	B2	3/2007	Jones et al.	
7,201,769	B2	4/2007	Jones et al.	
7,201,770	B2	4/2007	Johnson et al.	
7,223,284	B2	5/2007	Khosravi et al.	
7,232,432	B2	6/2007	Fulton, III et al.	
7,238,197	B2	7/2007	Sequin et al.	
7,240,516	B2	7/2007	Pryor	
7,241,301	B2	7/2007	Thramann et al.	
7,264,628	B2	9/2007	Jones et al.	
7,270,674	B2	9/2007	Jones et al.	
7,279,003	B2	10/2007	Berra et al.	
7,279,292	B2	10/2007	Imam et al.	
7,285,126	B2	10/2007	Sepetka et al.	
7,294,123	B2	11/2007	Jones et al.	
7,294,147	B2	11/2007	Hartley	
7,300,458	B2	11/2007	Henkes et al.	
7,303,572	B2	12/2007	Melsheimer et al.	
7,306,619	B1	12/2007	Palmer	
7,306,622	B2	12/2007	Jones et al.	
7,309,345	B2	12/2007	Wallace	
7,309,351	B2	12/2007	Escamilla et al.	
7,311,726	B2	12/2007	Mitelberg et al.	
7,323,000	B2	1/2008	Monstdt et al.	
7,323,005	B2	1/2008	Wallace et al.	
7,323,006	B2	1/2008	Andreas et al.	
7,326,240	B1	2/2008	Caro et al.	
7,344,550	B2	3/2008	Carrison et al.	
7,344,556	B2	3/2008	Seguin et al.	
7,344,558	B2	3/2008	Lorenzo et al.	
7,351,255	B2	4/2008	Andreas	
7,354,455	B2	4/2008	Stinson	
7,357,809	B2	4/2008	Jones et al.	
7,367,987	B2	5/2008	Balgobin et al.	
7,371,251	B2	5/2008	Mitelberg et al.	
7,371,252	B2	5/2008	Balgobin et al.	
7,377,932	B2	5/2008	Mitelberg et al.	
7,402,169	B2	7/2008	Killion et al.	
7,407,509	B2	8/2008	Greenberg	
7,435,254	B2	10/2008	Chouinard et al.	
7,438,720	B2	10/2008	Shaked	
7,455,646	B2	11/2008	Richardson et al.	
7,473,272	B2	1/2009	Pryor	
7,481,821	B2	1/2009	Fogarty et al.	
7,485,122	B2	2/2009	Teoh	
7,494,474	B2	2/2009	Richardson et al.	
7,510,565	B2	3/2009	Gilson et al.	
7,517,352	B2	4/2009	Evans et al.	
7,524,319	B2	4/2009	Dubrul	
7,534,252	B2	5/2009	Sepetka et al.	
7,549,974	B2	6/2009	Nayak	
7,553,314	B2	6/2009	Khachin et al.	
7,553,321	B2	6/2009	Litzenberg et al.	
7,582,101	B2	9/2009	Jones et al.	
7,618,434	B2	11/2009	Santra et al.	
7,640,952	B2	1/2010	Khachin et al.	
7,691,122	B2	4/2010	Dieck et al.	
7,727,242	B2	6/2010	Sepetka et al.	
7,727,243	B2	6/2010	Sepetka et al.	
7,749,243	B2	7/2010	Phung et al.	
7,780,694	B2	8/2010	Palmer et al.	
7,833,240	B2	11/2010	Okushi et al.	
7,972,342	B2	7/2011	Gandhi et al.	
7,976,560	B2	7/2011	Denison et al.	
8,052,640	B2	11/2011	Fiorella et al.	
8,062,307	B2	11/2011	Sepetka et al.	
8,066,757	B2	11/2011	Ferrera et al.	
8,070,791	B2	12/2011	Ferrera et al.	
8,088,140	B2	1/2012	Ferrera et al.	
8,100,918	B2	1/2012	Gandhi et al.	
8,100,935	B2	1/2012	Rosenbluth et al.	
8,105,333	B2	1/2012	Sepetka et al.	
8,197,493	B2	6/2012	Ferrera et al.	
8,357,179	B2	1/2013	Grandfield et al.	
8,425,549	B2	4/2013	Lenker et al.	
8,679,142	B2	3/2014	Slee et al.	
8,926,680	B2 *	1/2015	Ferrara	A61B 17/12022 623/1.11
8,940,003	B2	1/2015	Slee et al.	

(56) **References Cited**

U.S. PATENT DOCUMENTS

9,078,682	B2	7/2015	Lenker et al.
9,161,766	B2	10/2015	Slee et al.
2001/0000797	A1	5/2001	Mazzocchi
2001/0003801	A1	6/2001	Strecker
2001/0004705	A1	6/2001	Killion et al.
2001/0010013	A1	7/2001	Cox et al.
2001/0031981	A1	10/2001	Evans et al.
2001/0034531	A1	10/2001	Ho et al.
2001/0041899	A1	11/2001	Foster
2001/0044633	A1	11/2001	Klint
2001/0044647	A1	11/2001	Pinchuk et al.
2001/0044649	A1	11/2001	Vallana et al.
2001/0047202	A1	11/2001	Slaikeu et al.
2001/0051823	A1	12/2001	Khosravi et al.
2001/0053929	A1	12/2001	Vonesh et al.
2002/0004681	A1	1/2002	Teoh et al.
2002/0007210	A1	1/2002	Chouinard et al.
2002/0016564	A1	2/2002	Courtney et al.
2002/0016624	A1	2/2002	Patterson et al.
2002/0032479	A1	3/2002	Hankh et al.
2002/0038142	A1	3/2002	Khosravi et al.
2002/0038146	A1	3/2002	Harry
2002/0052643	A1	5/2002	Wholey et al.
2002/0068968	A1	6/2002	Hupp
2002/0072790	A1	6/2002	McGuckin et al.
2002/0087209	A1	7/2002	Edwin et al.
2002/0091355	A1	7/2002	Hayden
2002/0095141	A1	7/2002	Belef et al.
2002/0143387	A1	10/2002	Soetikno et al.
2002/0161377	A1	10/2002	Rabkin
2002/0169458	A1	11/2002	Connors
2002/0183831	A1	12/2002	Rolando et al.
2002/0193868	A1	12/2002	Mitelberg et al.
2002/0198588	A1	12/2002	Armstrong et al.
2003/0004536	A1	1/2003	Boylan et al.
2003/0023230	A1	1/2003	Lewis et al.
2003/0023299	A1	1/2003	Amplatz et al.
2003/0032941	A1	2/2003	Boyle et al.
2003/0032977	A1	2/2003	Brady
2003/0040771	A1	2/2003	Hyodoh et al.
2003/0040772	A1	2/2003	Hyodoh et al.
2003/0055440	A1	3/2003	Jones et al.
2003/0055451	A1	3/2003	Jones et al.
2003/0074056	A1	4/2003	Killion et al.
2003/0078605	A1	4/2003	Bashiri et al.
2003/0097114	A1	5/2003	Ouriel et al.
2003/0105484	A1	6/2003	Boyle et al.
2003/0125791	A1	7/2003	Sequin et al.
2003/0125798	A1	7/2003	Martin
2003/0130719	A1	7/2003	Martin
2003/0139796	A1	7/2003	Sequin et al.
2003/0139803	A1	7/2003	Sequin et al.
2003/0149475	A1	8/2003	Hyodoh et al.
2003/0153944	A1	8/2003	Phung et al.
2003/0176914	A1	9/2003	Rabkin et al.
2003/0199921	A1	10/2003	Palmer et al.
2003/0204202	A1	10/2003	Palmer et al.
2003/0212430	A1	11/2003	Bose et al.
2004/0002752	A1	1/2004	Griffin et al.
2004/0006306	A1	1/2004	Evans et al.
2004/0006381	A1	1/2004	Sequin et al.
2004/0010308	A1	1/2004	Zafrir-Pachter et al.
2004/0019322	A1	1/2004	Hoffmann
2004/0026942	A1	2/2004	Kessler et al.
2004/0030378	A1	2/2004	Khosravi et al.
2004/0034386	A1	2/2004	Fulton et al.
2004/0049258	A1	3/2004	Khosravi et al.
2004/0054367	A1	3/2004	Jimenez et al.
2004/0059259	A1	3/2004	Cornish et al.
2004/0059407	A1	3/2004	Escamilla et al.
2004/0068288	A1	4/2004	Palmer et al.
2004/0073300	A1	4/2004	Chouinard et al.
2004/0078050	A1	4/2004	Monstadt et al.
2004/0078071	A1	4/2004	Escamilla et al.
2004/0079429	A1	4/2004	Miller et al.
2004/0088002	A1	5/2004	Boyle et al.
2004/0098025	A1	5/2004	Sepetka et al.
2004/0102838	A1	5/2004	Killion et al.
2004/0106979	A1	6/2004	Goicoechea et al.
2004/0114912	A1	6/2004	Okamoto et al.
2004/0117003	A1	6/2004	Ouriel et al.
2004/0147939	A1	7/2004	Rabkin et al.
2004/0153117	A1	8/2004	Clubb et al.
2004/0158307	A1	8/2004	Jones et al.
2004/0158312	A1	8/2004	Chouinard et al.
2004/0186562	A1	9/2004	Cox
2004/0193246	A1	9/2004	Ferrera
2004/0199201	A1	10/2004	Kellett et al.
2004/0215312	A1	10/2004	Andreas
2004/0215319	A1	10/2004	Berra et al.
2004/0249439	A1	12/2004	Richter et al.
2004/0254628	A1	12/2004	Nazzaro et al.
2004/0260385	A1	12/2004	Jones et al.
2005/0021125	A1	1/2005	Stack et al.
2005/0033334	A1	2/2005	Santra et al.
2005/0033348	A1	2/2005	Sepetka et al.
2005/0033349	A1	2/2005	Jones et al.
2005/0033409	A1	2/2005	Burke et al.
2005/0038447	A1	2/2005	Huffmaster
2005/0038468	A1	2/2005	Panetta et al.
2005/0038496	A1	2/2005	Jones et al.
2005/0049676	A1	3/2005	Nazzaro et al.
2005/0055047	A1	3/2005	Greenhalgh
2005/0060017	A1	3/2005	Fischell et al.
2005/0075715	A1	4/2005	Borges et al.
2005/0080480	A1	4/2005	Bolea et al.
2005/0090857	A1	4/2005	Kusleika et al.
2005/0090888	A1	4/2005	Hines et al.
2005/0096726	A1	5/2005	Sequin et al.
2005/0102018	A1	5/2005	Carpenter et al.
2005/0107823	A1	5/2005	Leone et al.
2005/0119684	A1	6/2005	Guterman et al.
2005/0125023	A1	6/2005	Bates et al.
2005/0126979	A1	6/2005	Lowe et al.
2005/0131515	A1	6/2005	Cully et al.
2005/0131516	A1	6/2005	Greenhalgh
2005/0159774	A1	7/2005	Belef
2005/0165441	A1	7/2005	McGuckin et al.
2005/0165442	A1	7/2005	Thinnes et al.
2005/0177228	A1	8/2005	Solem et al.
2005/0187612	A1	8/2005	Edwin
2005/0192661	A1	9/2005	Griffen et al.
2005/0209673	A1	9/2005	Shaked
2005/0209675	A1	9/2005	Ton et al.
2005/0209678	A1	9/2005	Henkes et al.
2005/0216050	A1	9/2005	Sepetka et al.
2005/0222583	A1	10/2005	Cano et al.
2005/0222607	A1	10/2005	Palmer et al.
2005/0222676	A1	10/2005	Shanley et al.
2005/0267570	A1	12/2005	Shadduck
2005/0277978	A1	12/2005	Greenhalgh
2006/0020285	A1	1/2006	Niermann
2006/0020321	A1	1/2006	Parker
2006/0025845	A1	2/2006	Escamilla et al.
2006/0025850	A1	2/2006	Feller et al.
2006/0030865	A1	2/2006	Balg
2006/0036281	A1	2/2006	Patterson et al.
2006/0052797	A1	3/2006	Kanamaru
2006/0052816	A1	3/2006	Bates et al.
2006/0058833	A1	3/2006	VanCamp et al.
2006/0058836	A1	3/2006	Bose et al.
2006/0058838	A1	3/2006	Bose et al.
2006/0074480	A1	4/2006	Bales et al.
2006/0085065	A1	4/2006	Krause et al.
2006/0089703	A1	4/2006	Escamilla et al.
2006/0100663	A1	5/2006	Palmer et al.
2006/0106421	A1	5/2006	Teoh
2006/0106448	A1	5/2006	Shaked
2006/0122643	A1	6/2006	Wasicek
2006/0122685	A1	6/2006	Bonsignore
2006/0135947	A1	6/2006	Soltesz et al.
2006/0142841	A1	6/2006	Khosravi et al.
2006/0142849	A1	6/2006	Killion et al.
2006/0195118	A1	8/2006	Richardson

(56) **References Cited**

U.S. PATENT DOCUMENTS

2006/0195172 A1 8/2006 Luo et al.
2006/0200048 A1 9/2006 Furst et al.
2006/0200221 A1 9/2006 Malewicz
2006/0224179 A1 10/2006 Kucharczyk et al.
2006/0224180 A1 10/2006 Anderson et al.
2006/0229645 A1 10/2006 Bonnette et al.
2006/0259119 A1 11/2006 Rucker
2006/0265054 A1 11/2006 Greenhalgh et al.
2006/0271090 A1 11/2006 Shaked et al.
2006/0276883 A1 12/2006 Greenberg et al.
2006/0287701 A1 12/2006 Pal
2006/0287704 A1 12/2006 Hartley et al.
2007/0032852 A1 2/2007 Machek et al.
2007/0043424 A1 2/2007 Pryor
2007/0043425 A1 2/2007 Hartley et al.
2007/0055299 A1 3/2007 Ishimaru et al.
2007/0055358 A1 3/2007 Krolik et al.
2007/0055360 A1 3/2007 Hanson et al.
2007/0055365 A1 3/2007 Greenberg et al.
2007/0067011 A1 3/2007 Krolik et al.
2007/0073376 A1 3/2007 Krolik et al.
2007/0088387 A1 4/2007 Eskridge et al.
2007/0100425 A1 5/2007 Sequin et al.
2007/0118205 A1 5/2007 Davidson et al.
2007/0123972 A1 5/2007 Greenberg et al.
2007/0135826 A1 6/2007 Zaver et al.
2007/0135888 A1 6/2007 Khosravi et al.
2007/0141036 A1 6/2007 Gorrochategui Barrueta et al.
2007/0142896 A1 6/2007 Anderson et al.
2007/0156170 A1 7/2007 Hancock et al.
2007/0156228 A1 7/2007 Majercak et al.
2007/0162109 A1 7/2007 Davila et al.
2007/0179513 A1 8/2007 Deutsch
2007/0185501 A1 8/2007 Martin et al.
2007/0191866 A1 8/2007 Palmer et al.
2007/0191884 A1 8/2007 Eskridge et al.
2007/0191924 A1 8/2007 Rudakov
2007/0198028 A1 8/2007 Miloslavski et al.
2007/0198029 A1 8/2007 Martin et al.
2007/0198030 A1 8/2007 Martin et al.
2007/0198075 A1 8/2007 Levy
2007/0203452 A1 8/2007 Mehta
2007/0203559 A1 8/2007 Freudenthal et al.
2007/0208367 A1 9/2007 Fiorella
2007/0208371 A1 9/2007 French et al.
2007/0219621 A1 9/2007 Hartley et al.
2007/0225749 A1 9/2007 Martin et al.
2007/0225794 A1 9/2007 Thramann et al.
2007/0233236 A1 10/2007 Pryor
2007/0250040 A1 10/2007 Provost et al.
2007/0266542 A1 11/2007 Melsheimer
2007/0270932 A1 11/2007 Headley et al.
2007/0288034 A1 12/2007 MacCollum et al.
2007/0288037 A1 12/2007 Cheng et al.
2007/0288038 A1 12/2007 Bimbo
2007/0288054 A1 12/2007 Tanaka et al.
2007/0288080 A1 12/2007 Maccollum et al.
2007/0288083 A1 12/2007 Hines
2007/0293846 A1 12/2007 von Oepen et al.
2007/0299503 A1 12/2007 Berra et al.
2008/0001333 A1 1/2008 Kleine et al.
2008/0015558 A1 1/2008 Harlan
2008/0015682 A1 1/2008 Majercak et al.
2008/0033528 A1 2/2008 Satasiya et al.
2008/0039926 A1 2/2008 Majercak et al.
2008/0039930 A1 2/2008 Jones et al.
2008/0045995 A1 2/2008 Guterman et al.
2008/0046064 A1 2/2008 Sequin et al.
2008/0046072 A1 2/2008 Laborde et al.
2008/0051803 A1 2/2008 Monjtadt et al.
2008/0058724 A1 3/2008 Wallace
2008/0071178 A1 3/2008 Greenland et al.
2008/0077175 A1 3/2008 Palmer
2008/0082107 A1 4/2008 Miller et al.
2008/0082159 A1 4/2008 Tseng et al.
2008/0086196 A1 4/2008 Truckai et al.
2008/0097495 A1 4/2008 Feller, III et al.
2008/0103477 A1 5/2008 Jones
2008/0103585 A1 5/2008 Monstadt et al.
2008/0109063 A1 5/2008 Hancock et al.
2008/0109067 A1 5/2008 Caro et al.
2008/0114439 A1 5/2008 Ramaiah et al.
2008/0114445 A1 5/2008 Melsheimer et al.
2008/0119888 A1 5/2008 Huffmaster
2008/0125855 A1 5/2008 Henkes et al.
2008/0140107 A1 6/2008 Bei et al.
2008/0140181 A1 6/2008 Reynolds et al.
2008/0147100 A1 6/2008 Wallace
2008/0161903 A1 7/2008 Sequin et al.
2008/0161936 A1 7/2008 Feller et al.
2008/0167708 A1 7/2008 Molland et al.
2008/0183185 A1 7/2008 Miller et al.
2008/0183198 A1 7/2008 Sepetka et al.
2008/0188865 A1 8/2008 Miller et al.
2008/0195140 A1 8/2008 Myla et al.
2008/0200946 A1 8/2008 Braun et al.
2008/0208319 A1 8/2008 Rabkin et al.
2008/0221554 A1 9/2008 O'Connor et al.
2008/0221600 A1 9/2008 Dieck et al.
2008/0221664 A1 9/2008 Bales et al.
2008/0221671 A1 9/2008 Chouinard et al.
2008/0228216 A1 9/2008 Strauss et al.
2008/0234795 A1 9/2008 Snow et al.
2008/0243229 A1 10/2008 Wallace et al.
2008/0243232 A1 10/2008 Hegg et al.
2008/0247943 A1 10/2008 Lanza et al.
2008/0249598 A1 10/2008 Sherry
2008/0255678 A1 10/2008 Cully et al.
2008/0262506 A1 10/2008 Griffin et al.
2008/0262528 A1 10/2008 Martin
2008/0262532 A1 10/2008 Martin
2008/0262592 A1 10/2008 Jordan et al.
2008/0269774 A1 10/2008 Garcia et al.
2008/0269868 A1 10/2008 Bei et al.
2008/0275497 A1 11/2008 Palmer et al.
2008/0275498 A1 11/2008 Palmer et al.
2008/0275536 A1 11/2008 Zarins et al.
2008/0281302 A1 11/2008 Murphy et al.
2008/0281350 A1 11/2008 Sepetka et al.
2008/0281393 A1 11/2008 Armstrong et al.
2008/0281397 A1 11/2008 Killion et al.
2008/0281403 A1 11/2008 Kavteladze
2008/0306503 A1 12/2008 Que et al.
2008/0306504 A1 12/2008 Win et al.
2008/0312732 A1 12/2008 Hartley et al.
2008/0319525 A1 12/2008 Tieu et al.
2008/0319533 A1 12/2008 Lehe
2009/0018633 A1 1/2009 Lindquist et al.
2009/0018634 A1 1/2009 State
2009/0018640 A1 1/2009 State
2009/0024157 A1 1/2009 Anukhin
2009/0025820 A1 1/2009 Adams
2009/0030502 A1 1/2009 Sun et al.
2009/0036968 A1 2/2009 Hepworth et al.
2009/0036977 A1 2/2009 Rassat et al.
2009/0062726 A1 3/2009 Ford et al.
2009/0062773 A1 3/2009 Cornish et al.
2009/0062834 A1 3/2009 Moftakhar et al.
2009/0068097 A1 3/2009 Sevrain
2009/0069828 A1 3/2009 Martin et al.
2009/0069836 A1 3/2009 Labdag et al.
2009/0076450 A1 3/2009 Caizza et al.
2009/0082800 A1 3/2009 Janardhan
2009/0093822 A1 4/2009 Ducharme
2009/0105644 A1 4/2009 Leonard et al.
2009/0105722 A1 4/2009 Fulkerson et al.
2009/0105737 A1 4/2009 Fulkerson et al.
2009/0105747 A1 4/2009 Chanduszko et al.
2009/0125053 A1 5/2009 Ferrera et al.
2009/0163851 A1 6/2009 Holloway et al.
2009/0192455 A1 7/2009 Ferrera et al.
2009/0275974 A1 11/2009 Marchand et al.
2009/0292297 A1 11/2009 Ferrere
2009/0299393 A1 12/2009 Martin et al.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2010/0022951	A1	1/2010	Ferrera et al.
2010/0100106	A1	4/2010	Ferrera
2010/0114017	A1	5/2010	Lenker et al.
2010/0114135	A1	5/2010	Wilson et al.
2010/0137892	A1	6/2010	Krolik et al.
2010/0152766	A1	6/2010	Dieck et al.
2010/0174309	A1	7/2010	Fulkerson et al.
2010/0217187	A1	8/2010	Fulkerson et al.
2010/0256600	A1	10/2010	Ferrera
2010/0299911	A1	12/2010	Gianotti et al.
2010/0318097	A1	12/2010	Ferrera et al.
2011/0009875	A1	1/2011	Grandfield et al.
2011/0009941	A1	1/2011	Grandfield et al.
2011/0060212	A1	3/2011	Slee et al.
2011/0152920	A1	6/2011	Eckhouse et al.
2011/0160742	A1	6/2011	Ferrera et al.
2011/0160757	A1	6/2011	Ferrera et al.
2011/0160760	A1	6/2011	Ferrera et al.
2011/0160761	A1	6/2011	Ferrera et al.
2011/0160763	A1	6/2011	Ferrera et al.
2011/0166586	A1	7/2011	Sepetka et al.
2011/0172699	A1	7/2011	Miller et al.
2011/0184456	A1	7/2011	Grandfield et al.
2011/0190797	A1	8/2011	Fulkerson et al.
2011/0202088	A1	8/2011	Eckhouse et al.
2011/0238106	A1	9/2011	Ferrera et al.
2011/0270178	A1	11/2011	Fiorella et al.
2011/0288572	A1	11/2011	Martin
2011/0301686	A1	12/2011	Bowman et al.
2011/0319917	A1	12/2011	Ferrera et al.
2012/0016396	A1	1/2012	Dehnad
2012/0016406	A1	1/2012	Ferrera et al.
2012/0022576	A1	1/2012	Ferrera et al.
2012/0022581	A1	1/2012	Wilson et al.
2012/0035648	A1	2/2012	Wilson et al.
2012/0041411	A1	2/2012	Horton et al.
2012/0041449	A1	2/2012	Eckhouse et al.
2012/0041459	A1	2/2012	Fiorella et al.
2012/0041460	A1	2/2012	Ferrera et al.
2012/0041464	A1	2/2012	Monetti et al.
2012/0041474	A1	2/2012	Eckhouse et al.
2012/0041475	A1	2/2012	Ferrera et al.
2012/0046686	A1	2/2012	Wilson et al.
2012/0065600	A1	3/2012	Ashmead et al.
2012/0065660	A1	3/2012	Ferrera et al.
2012/0071964	A1	3/2012	Cattaneo et al.
2012/0078140	A1	3/2012	Nita
2012/0078285	A1	3/2012	Griffin
2012/0083868	A1	4/2012	Shrivastava et al.
2012/0089216	A1	4/2012	Rapaport et al.
2012/0116443	A1	5/2012	Ferrera et al.
2014/0343596	A1	11/2014	Slee et al.
2015/0157346	A1	6/2015	Ferrera et al.
2015/0359549	A1	12/2015	Lenker et al.

FOREIGN PATENT DOCUMENTS

CN	101061970	A	10/2007
DE	2804058	A1	8/1978
DE	2821048	B1	11/1979
DE	8435489	U1	8/1986
DE	19703482	A1	8/1998
DE	10010840	A1	9/2001
EP	201466	A2	11/1986
EP	484468	A1	5/1992
EP	629125	A1	12/1994
EP	0321912	B1	2/1995
EP	707830	A1	4/1996
EP	719522	A1	7/1996
EP	726745	A1	8/1996
EP	737450	A1	10/1996
EP	739606	A1	10/1996
EP	750886	A1	1/1997
EP	752236	A1	1/1997
EP	800790	A2	10/1997
EP	803230	A2	10/1997
EP	804904	A1	11/1997
EP	804905	A1	11/1997
EP	804906	A2	11/1997
EP	807410	A2	11/1997
EP	820729	A1	1/1998
EP	826341	A1	3/1998
EP	826342	A1	3/1998
EP	832606	A1	4/1998
EP	861634	A2	9/1998
EP	914803	A1	5/1999
EP	964659	A1	12/1999
EP	1000590	A1	5/2000
EP	1005837	A2	6/2000
EP	1009295	A1	6/2000
EP	1009296	A1	6/2000
EP	1225844	A2	7/2002
EP	1266639	A2	12/2002
EP	1266640	A2	12/2002
EP	1323385	A2	7/2003
EP	1329196	A1	7/2003
EP	1351626	A2	10/2003
EP	1366720	A1	12/2003
EP	1400219	A1	3/2004
EP	1437097	A1	7/2004
EP	2257248	B1	10/2011
EP	2301450	B1	11/2011
EP	2417919	A2	2/2012
EP	2254485	B1	8/2017
FR	2343488	A1	10/1977
GB	2020557	A	11/1979
JP	2095359		4/1990
JP	02255157	A	10/1990
JP	6-246004		9/1994
JP	8-033719	A	2/1996
JP	2975584	B2	11/1999
JP	2001-190686	A	7/2001
JP	2001178830	A	7/2001
JP	2003-033359	A	2/2003
JP	2004016668	A	1/2004
JP	2005532887	A	11/2005
JP	2006026423	A	2/2006
JP	2006-075233	A	3/2006
JP	2006-094876	A	4/2006
JP	2006095095	A	4/2006
JP	2007-185363	A	7/2007
JP	2007-222658	A	9/2007
JP	2007-236471	A	9/2007
WO	WO-94/03127	A1	2/1994
WO	WO-96/17634	A2	6/1996
WO	WO-96/28116	A1	9/1996
WO	WO-97/04711	A1	2/1997
WO	WO-98/25656	A3	10/1998
WO	WO-98/55173	A1	12/1998
WO	WO-98/55175	A1	12/1998
WO	WO-99/16382	A2	4/1999
WO	WO-99/23976	A1	5/1999
WO	WO-99/25252	A1	5/1999
WO	WO-99/29264	A1	6/1999
WO	WO-99/44542	A2	9/1999
WO	WO-99/48429	A1	9/1999
WO	WO-99/48440	A1	9/1999
WO	WO-00/012166	A1	3/2000
WO	WO-2000/32265	A1	6/2000
WO	WO-2000/53120		9/2000
WO	WO-00/59405	A1	10/2000
WO	WO-2001/008743	A1	2/2001
WO	WO-2001/36034	A2	2/2001
WO	WO-01/32099	A2	5/2001
WO	WO-2001/034041		5/2001
WO	WO-01/45566	A1	6/2001
WO	WO-2001/45569	A1	6/2001
WO	WO-01/72240	A1	10/2001
WO	WO-01/93780	A2	12/2001
WO	WO-02/54980	A2	7/2002
WO	WO-2003/017823	A2	3/2003
WO	WO-2004008991	A1	1/2004
WO	WO-2003/011188	A9	7/2004
WO	WO-2004/093696	A1	11/2004

(56) **References Cited**

FOREIGN PATENT DOCUMENTS

WO	WO-2006/052439	A1	5/2006
WO	WO-2007/089897		8/2007
WO	WO-2007/121005	A1	10/2007
WO	WO-2008/117256	A2	5/2008
WO	WO-2008063156	A2	5/2008
WO	WO-2008/117257	A2	10/2008
WO	WO-2008/124728	A1	10/2008
WO	WO-2009/067629	A2	5/2009
WO	WO-2009/086154	A2	7/2009
WO	WO-2009/105710	A1	8/2009
WO	WO-2009/114046	A2	9/2009
WO	WO-2009/124288	A1	10/2009
WO	WO-2009/126747	A1	10/2009
WO	WO-2010/010545	A1	1/2010
WO	WO-2010/023671	A2	3/2010
WO	WO-2010/046897	A1	4/2010
WO	WO-2010/049121	A2	5/2010
WO	WO-2010/062363	A1	6/2010
WO	WO-2010/102307	A1	9/2010
WO	WO-2010/115642	A1	10/2010
WO	WO-2010/121037	A1	10/2010
WO	WO-2010/121049	A2	10/2010
WO	WO-2011/054531	A2	5/2011
WO	WO-2011/095352	A1	8/2011
WO	WO-2011/133486	A1	10/2011
WO	WO-2011/135556		11/2011
WO	WO-2011/144336		11/2011
WO	WO-2011/147567		12/2011
WO	WO-2012/009675		1/2012
WO	WO-2012/025245		3/2012
WO	WO-2012/025247		3/2012

OTHER PUBLICATIONS

"Penumbra, Inc Enrolls First Patients in PULSE Clinical Trial to Evaluate a Fully Retrievable, Dense Mesh Temporary Stent for Immediate Flow Restoration in Interventional Acute Ischemic Stroke Treatment," Business Wire, Nov. 1, 2010, <http://wwwbusinesswirecom/news/home/d0101101006991/en/Penumbra-Enrolls-Patients-PULSE-Clinical-Trial-Evaluate>.

Doerfler, et al, "A Novel Flexible, Retrievable Endovascular Stent System for Small-Vessel Anatomy: Preliminary in Vivo Data," Am J Neuroradiol vol. 26, pp. 862-868 (Apr. 2005).

Duerig, et al An Overview of Superelastic Stent Design Min Invas Ther & Allied Technol 2000: 9(3/4) 235-246.

Henkes, et al, "A Microcatheter-Delivered Highly-Flexible and Fully-Retrievable Stent, Specifically Designed for Intracranial Use," Interventional Neuroradiology, vol. 9, pp. 391-393 (Dec. 2003).

Kelly, et al, Recanalization of an Acute Cerebral Artery Occlusion Using a Self-Expanding, Reconstrainable, Intracranial Microstent as a Temporary Endovascular Bypass; AHA Journal, Jun. 2008 edition.

Lavallee, et al, Stent-Assisted Endovascular Thrombolysis Versus Intravenous Thrombolysis in Internal Carotid Artery Dissection with Tandem Internal Carotid and Middle Cerebral Artery Occlusion, AHA 2007.

Levy, et al, Self-Expanding Stents for Recanalization of Acute Cerebrovascular Occulsions; AJNR May 28, 2007.

Liebig, et al, "A novel self-expanding fully retrievable intracranial stent (SOLO): experience in nine procedures of stent-assisted aneurysm coil occlusion," Neuroradiology vol. 48, pp. 471-478 (Jul. 2006).

Micro Therapeutics, Inc, DBA EV3 Neurovascular, Inc, Fully deployable Completely retrievable, Solitaire AB, Neurovascular Remodeling Device Mar. 2008.

Micro Therapeutics, Inc, DBA EV3 Neurovascular, Inc, Solitaire FR Revascularization Device, Instructions for Use, Rev Mar. 2009.

Pelz, et al, Advances in Interventional Neuroradiology 2007; American Heart Association Journal, Nov. 2007 edition.

Robertson, Stroke device startup lands National Science Foundation grant, Sacramento Business Journal, Oct. 23, 2009, Sacramento, California.

Sauvegeau, et al Middle Cerebral Artery Stenting for Acute Ischemic Stroke After Unsuccessful Merci Retrieval; Special Technical Report; Neurosurgery 60:701-706, 2007.

Wakhloo, et al, "Retrievable Closed Cell Intracranial Stent for Foreign Body and Clot Removal," Neurosurgery, May 5, 2008.

Yavuz, et al, "Immediate and midterm follow-up results of using an electrodetachable, fully retrievable SOLO stent system in the endovascular coil occlusion of wide-necked cerebral aneurysms," J Neurosurg vol. 107, pp. 49-55 (Jul. 2007).

Schumacher, H, "Endovascular Mechanical Thrombectomy of an Occluded Superior Division Branch of the Left MCA for Acute Cardioembolic Stroke," Cardiovascular and Interventional Radiology, Jun. 2003 26(3) pp. 305-308.

Nesbit, G, "New and Future Endovascular Treatment Strategies for Acute Ischemic Stroke," Journal of Vascular and Interventional Radiology, Jan. 2004 15(1) pp. S103-S110.

Imai, K, "Clot Removal Therapy by Aspiration and Extraction for Acute Embolic Carotid Occlusion," American Journal of Neuroradiology, Aug. 2006, vol. 27, pp. 1521-1527.

Wildberger, J, "Percutaneous Venous Thrombectomy Using the Arrow-Trerotola Percutaneous Thrombolytic Device (PTD) with Temporary Caval Filtration: In Vitro Investigations," Cardiovascular and Interventional Radiology, Mar. 2005 28(2) pp. 221-227.

Castano, C, "Use of the New Solitaire (TM) AB Device for Mechanical Thrombectomy when Merci Clot Retriever Has Failed to Remove the Clot A Case Report," Interventional Neuroradiology, Jul. 2009 15(2) pp. 209-214.

Ev3 Solitaire Brochure R2 dated Jan. 12, 2009.

Ev3 Solitaire AB Instructions for Use (IFU) dated Dec. 2007 The first commercial sale of the products numbered SAB-4-15 and SAB 4 20, referenced in the ev3 Solitaire AB IFU dated Dec. 2007, occurred on Jan. 4, 2008.

J Gralla, et al, "A Dedicated Animal Model for Mechanical Thrombectomy in Acute Stroke," ANJR 27:1357-61, Jun.-Jul. 2006.

J Gralla, et al, "Mechanical Thrombectomy for Acute Ischemic Stroke," Stroke 37:3019-3024, Dec. 2006.

V Marder, et al, "Analysis of Thrombi Retrieved From Cerebral Arteries of Patients With Acute Ischemic Stroke," Stroke 37:2086-2093, Aug. 2006.

T Massoud, et al, "Histopathologic Characteristics of a Chronic Arteriovenous Malformation in a Swine Model: Preliminary Study," AJNR 21:1268-1276, Aug. 2000.

Thomas Liebig, et al (p. 5) and "Multimodal endovascular treatment of ischemic stroke by mechanical thrombectomy; a two center / two years experience" Z Vajda, et al (p. 6).

H Henkes, et al, "Endovascular acute ischemic stroke treatment using the self-expanding and fully retrievable Solitaire stent", poster exhibition displayed on one or both of Feb. 18 and 19, 2009, at the International Stroke Conference, San Diego, California.

Abstracts from the 2009 International Stroke Conference, Stroke, 2009; 40, pp. e247-e248, originally published online Feb. 16, 2009.

Opposition Filed in EP 2254485.

Opposition (English Translation) in European Patent 2254485, dated May 30, 2018.

Reply to Opposition in European Patent 2254485, dated Oct. 29, 2018.

File History in Australian Patent Application No. 2016277687.

Summons to attend oral proceedings pursuant to Rule 115(1) EPC dated Mar. 1, 2019 in EP Application No. 09711843.4.

* cited by examiner

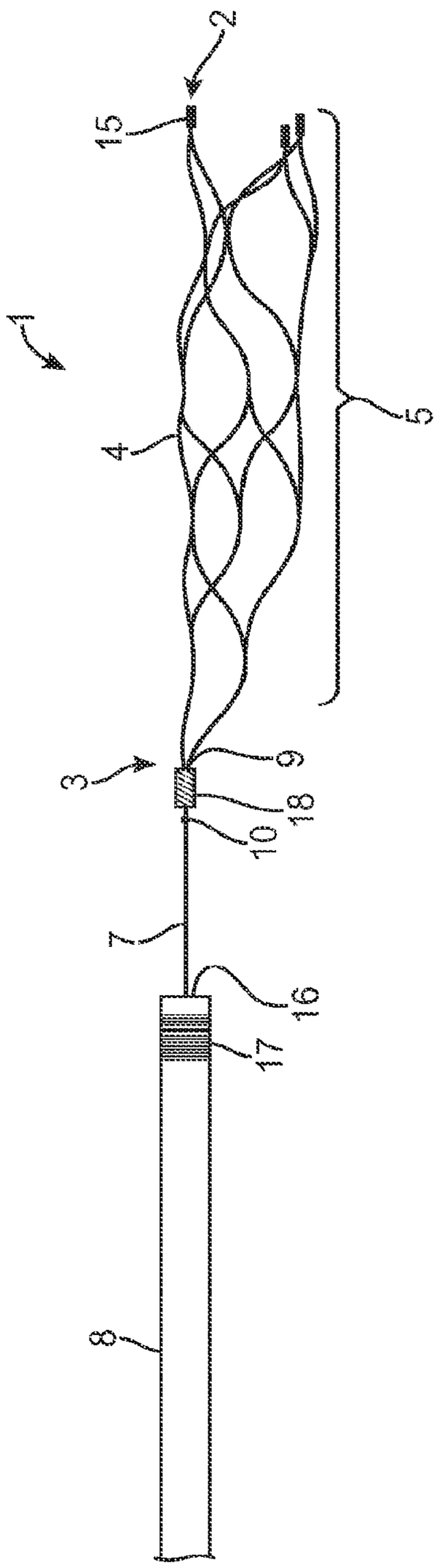


FIG. 1

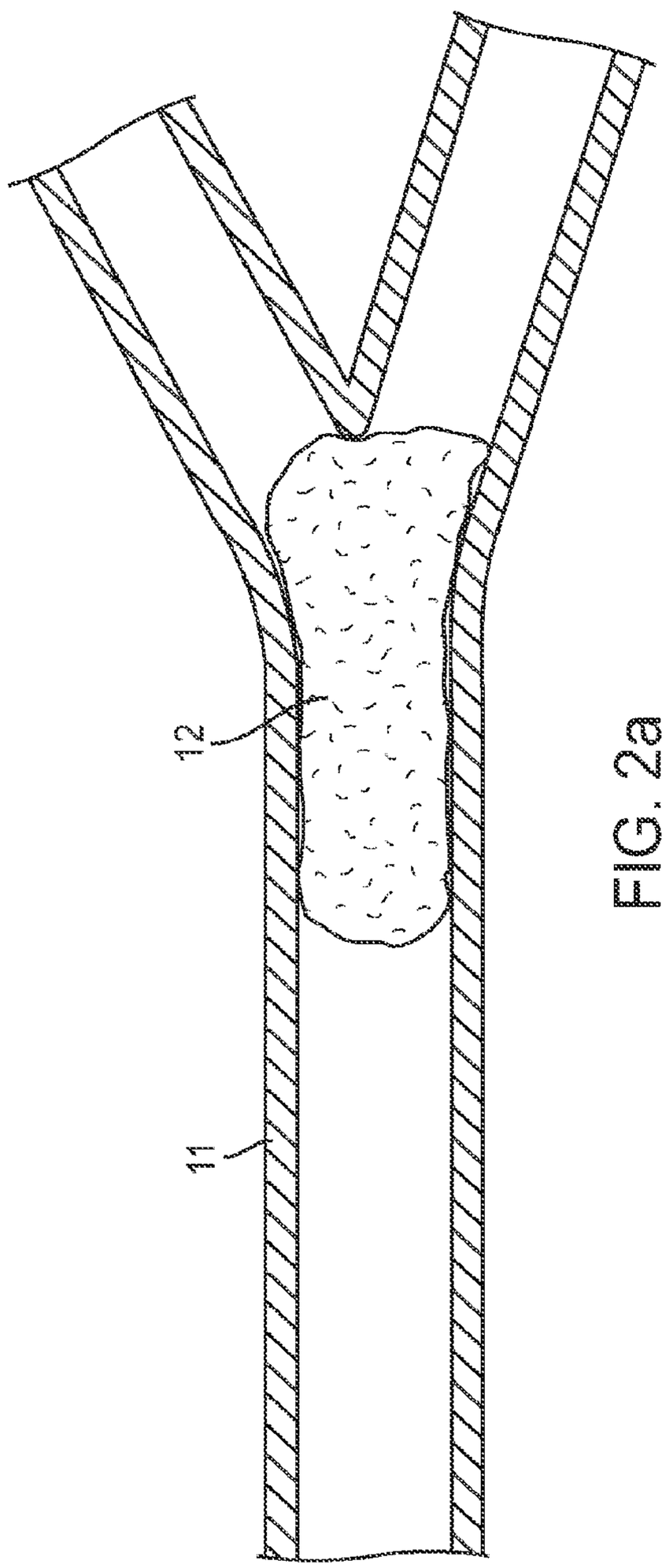


FIG. 2a

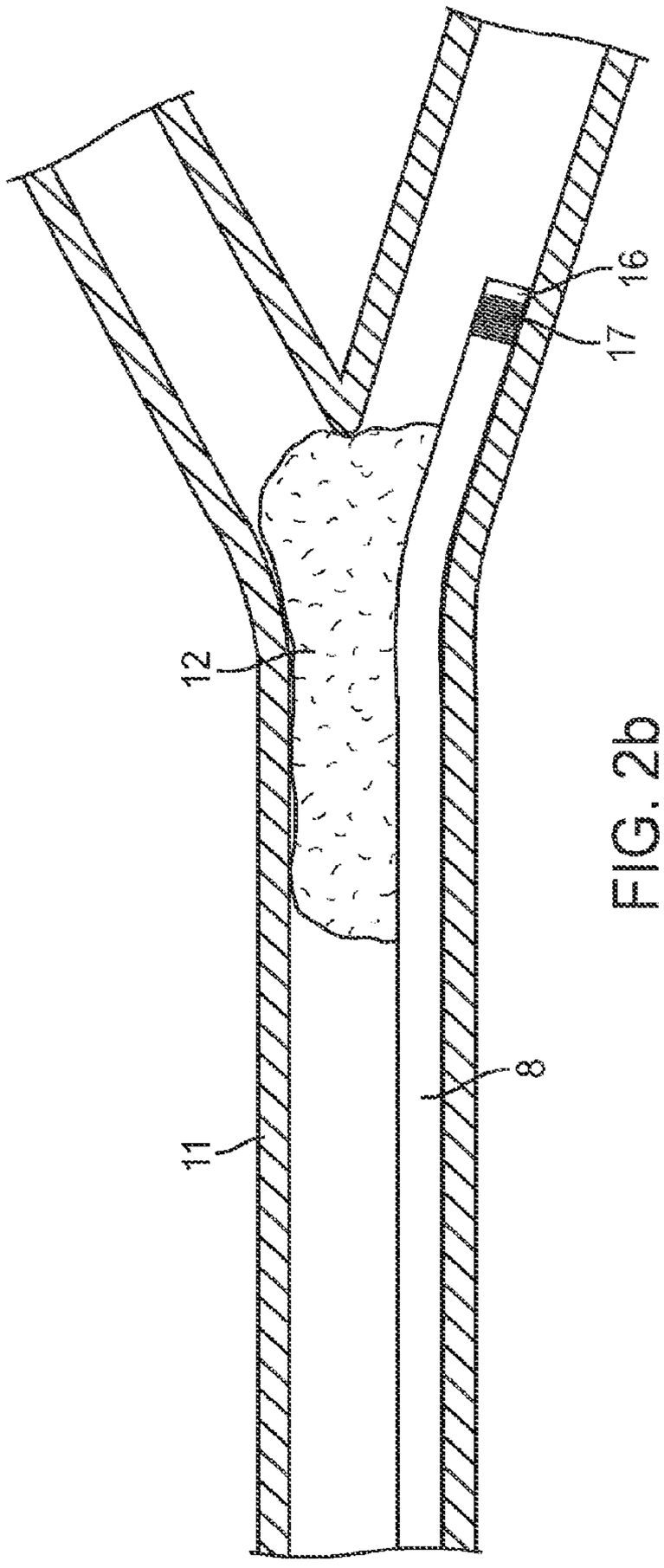


FIG. 2b

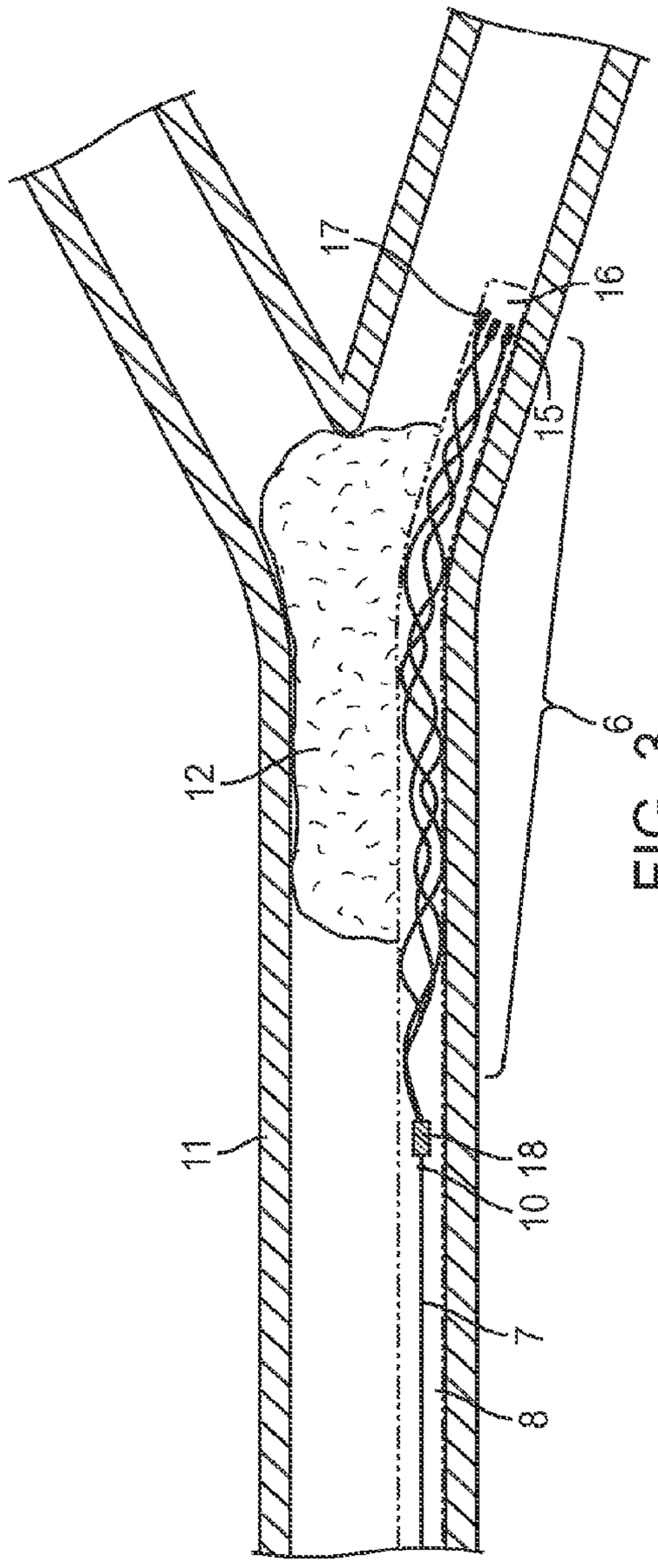


FIG. 3

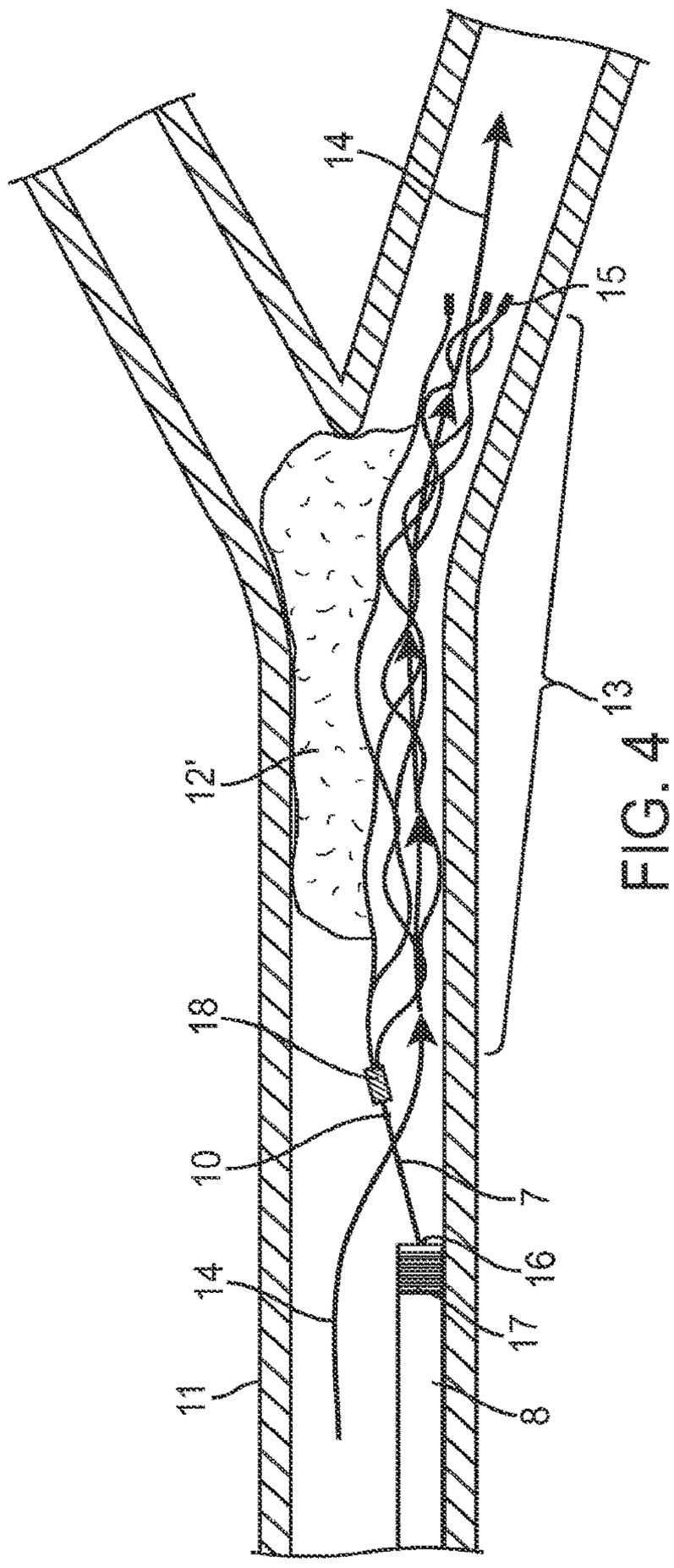


FIG. 4

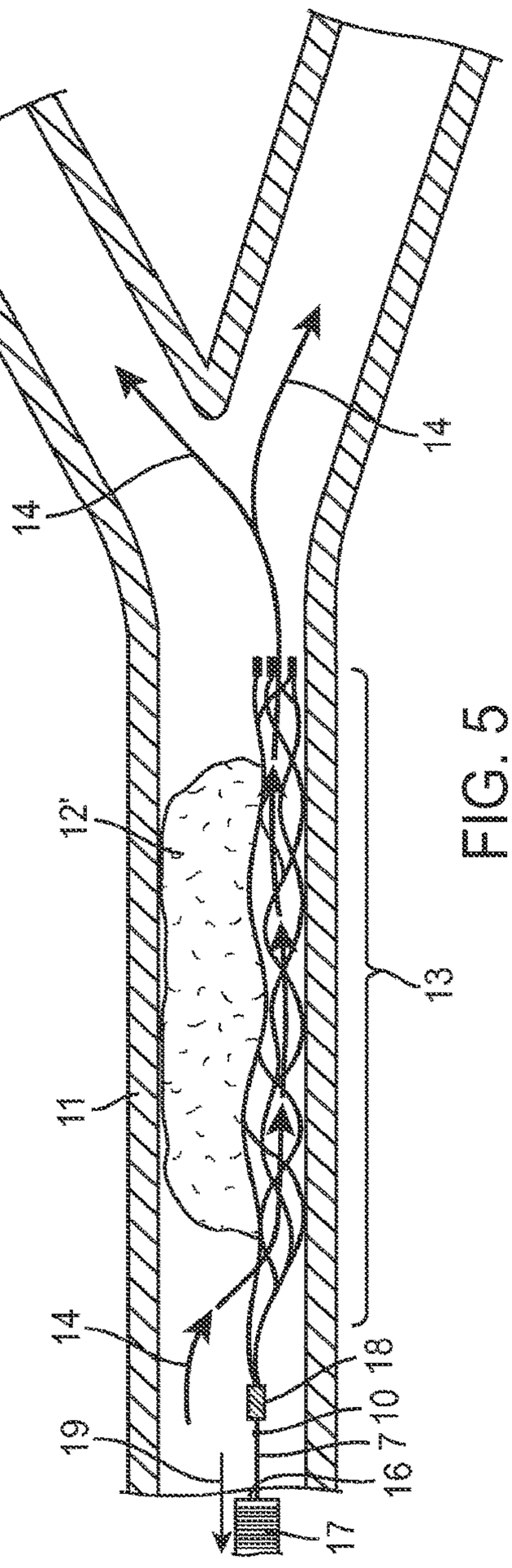


FIG. 5

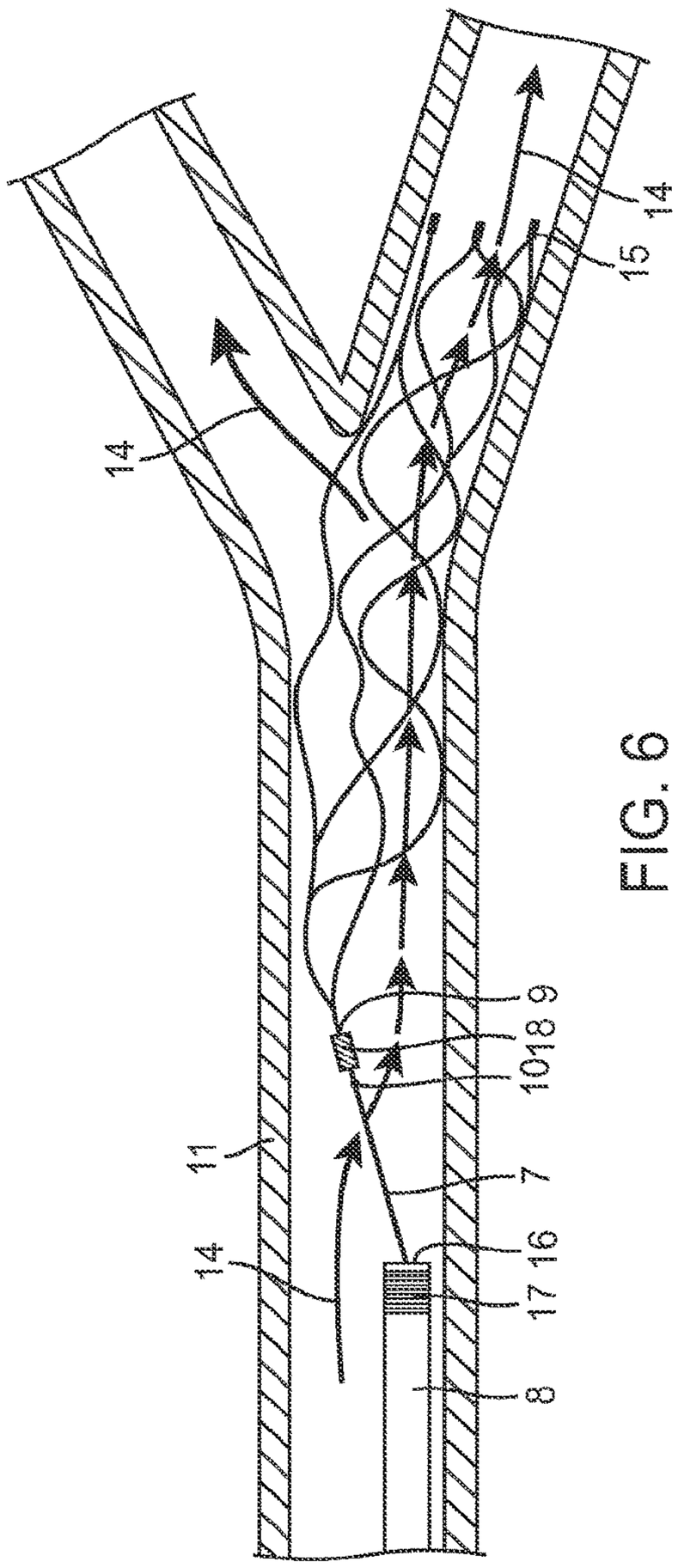


FIG. 6

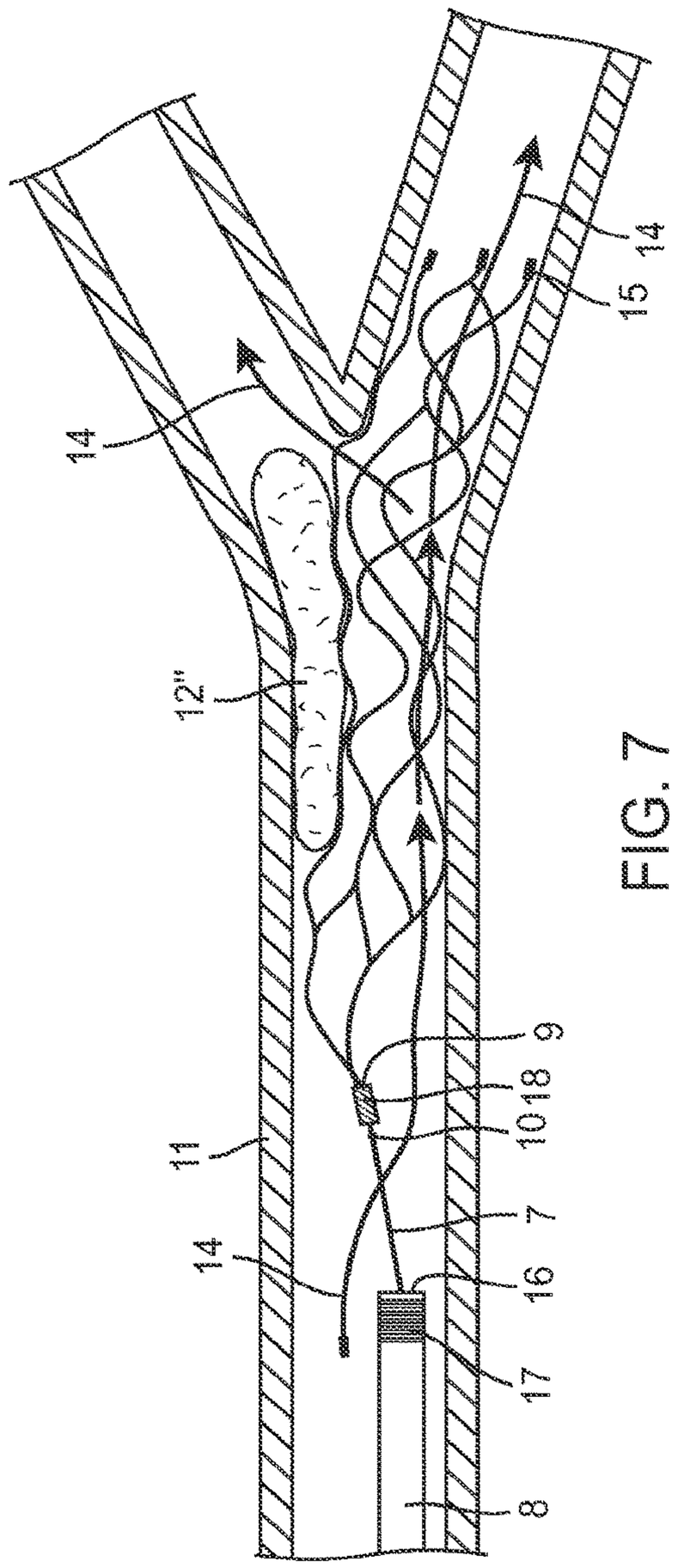


FIG. 7

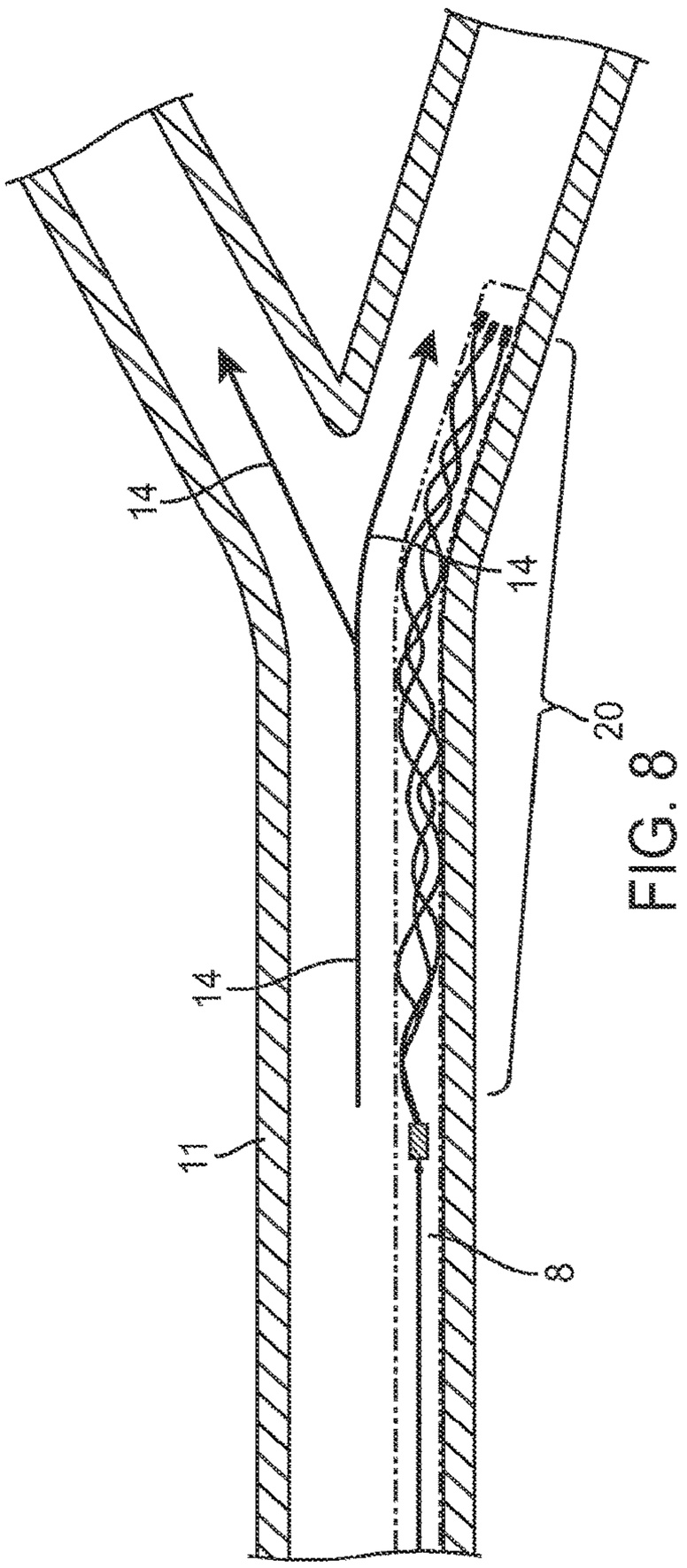


FIG. 8

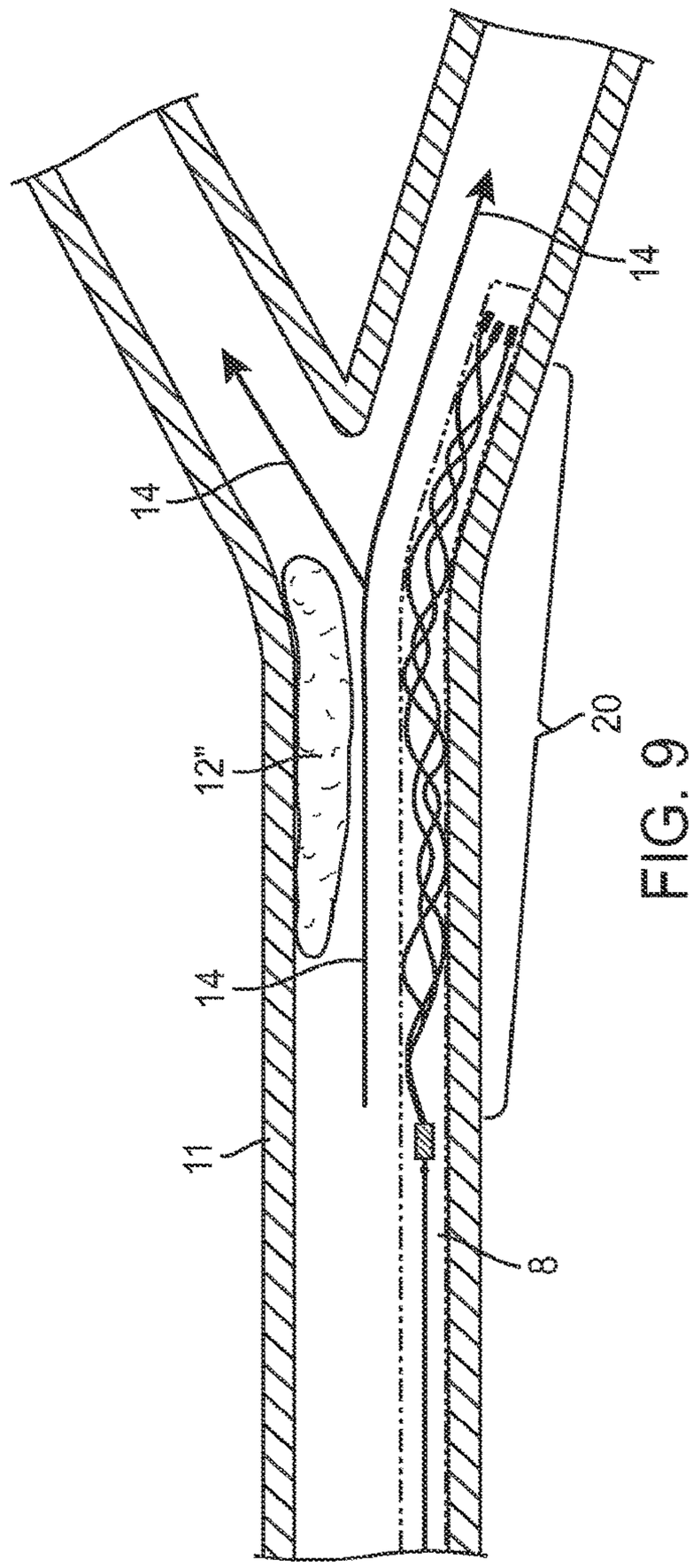


FIG. 9

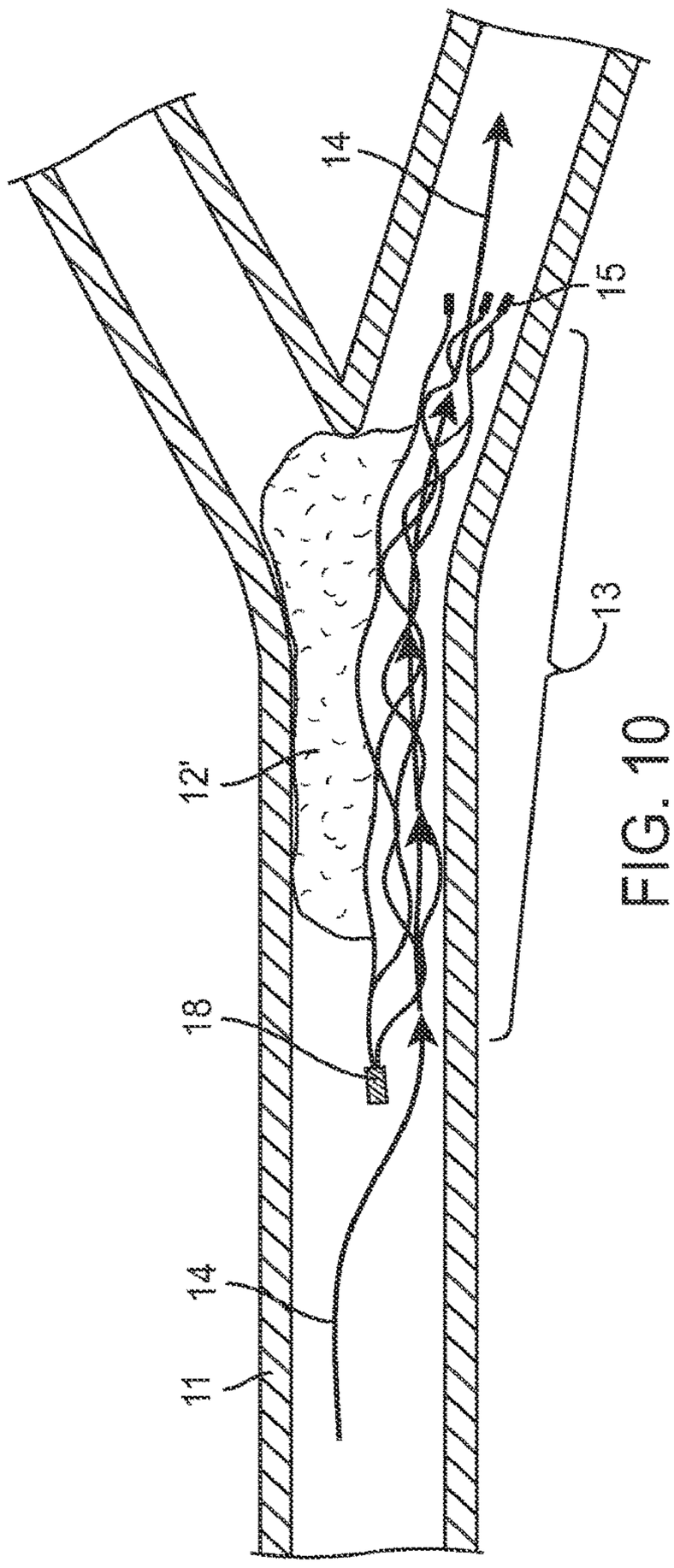


FIG. 10

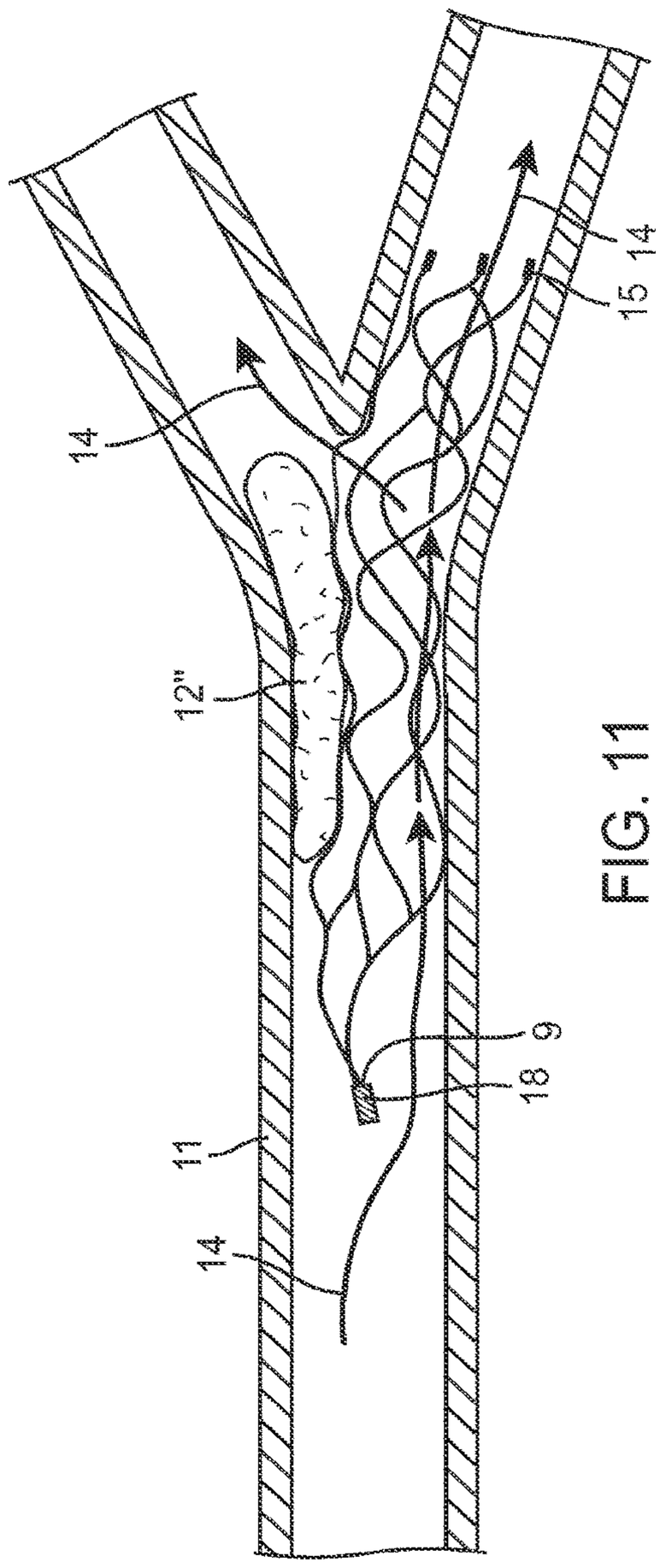


FIG. 11

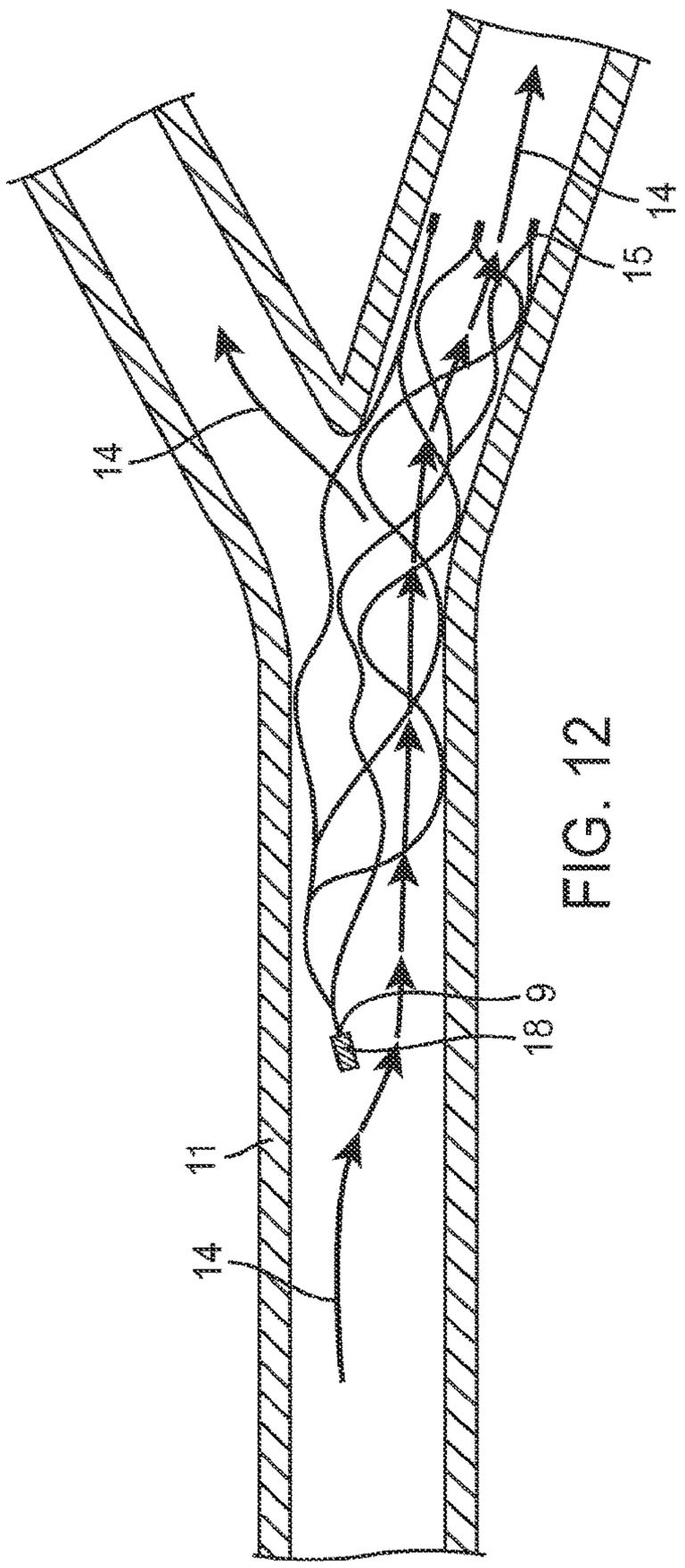


FIG. 12

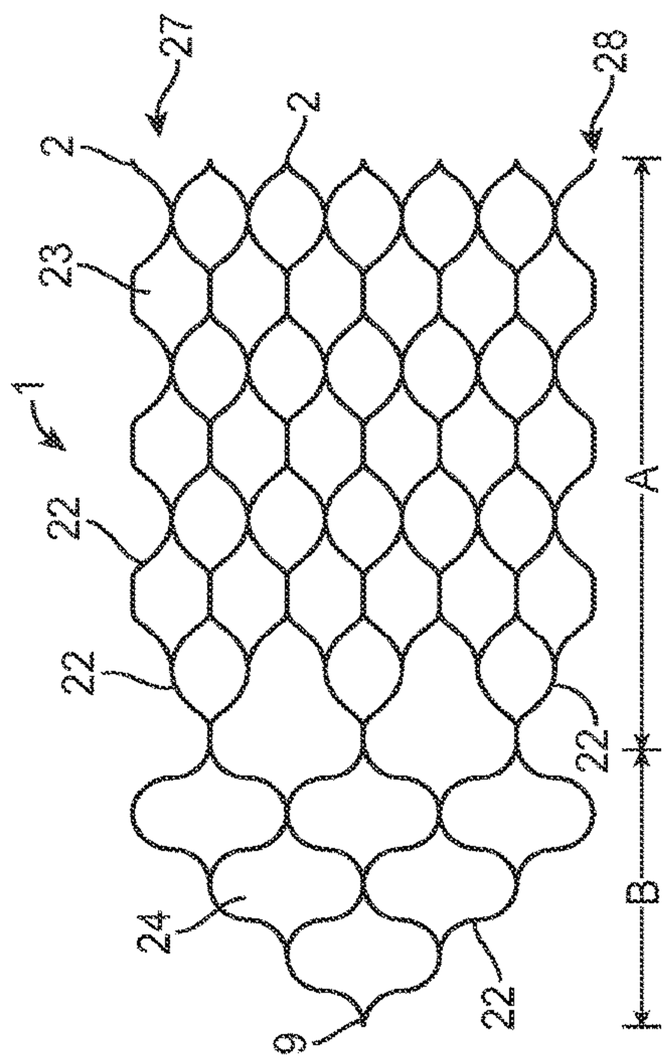


FIG. 13

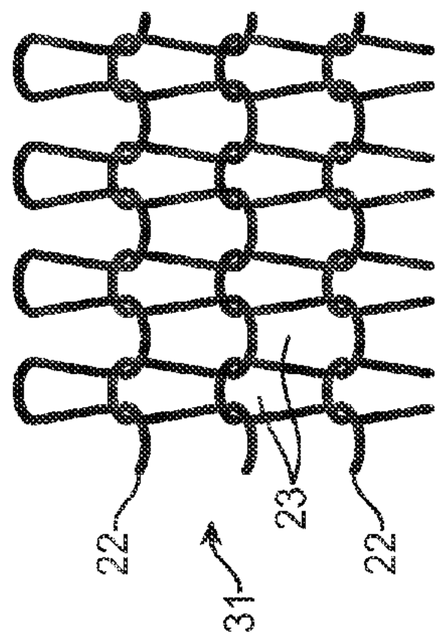


FIG. 16

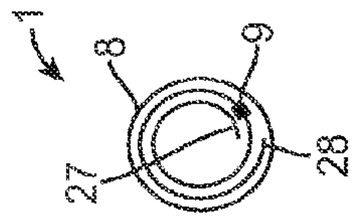


FIG. 17b

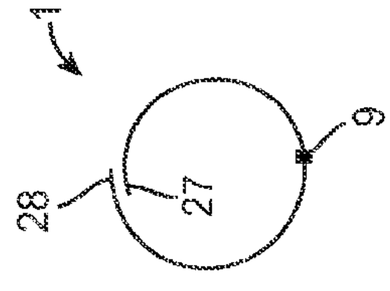


FIG. 17a

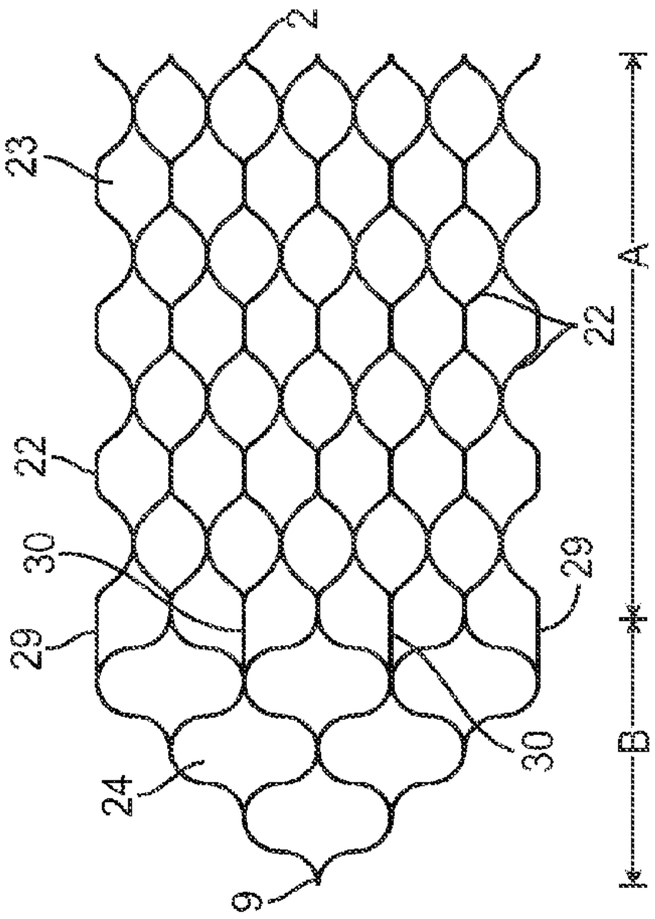


FIG. 14

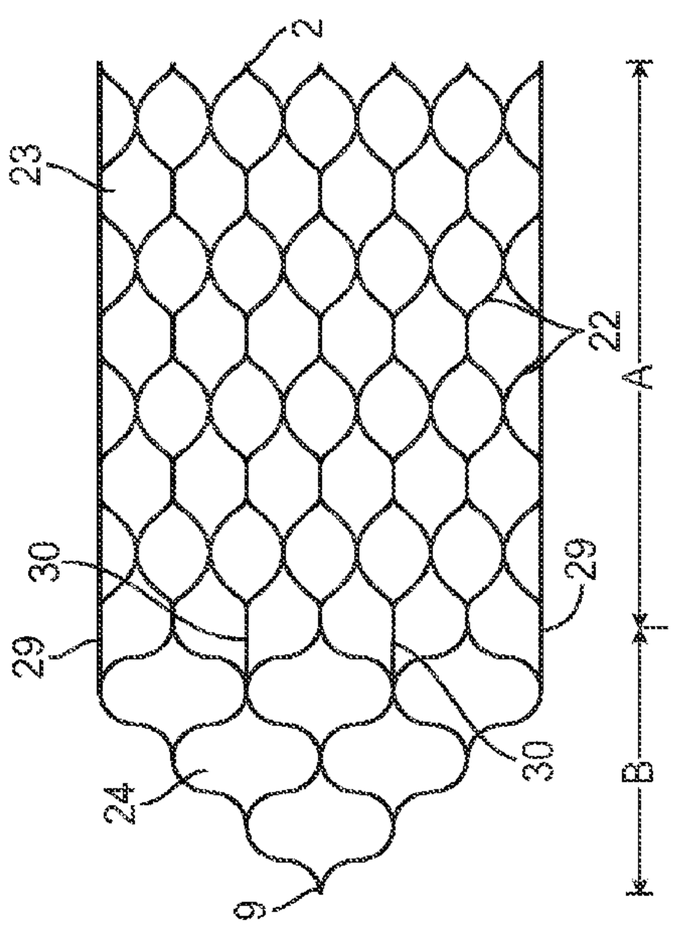


FIG. 15

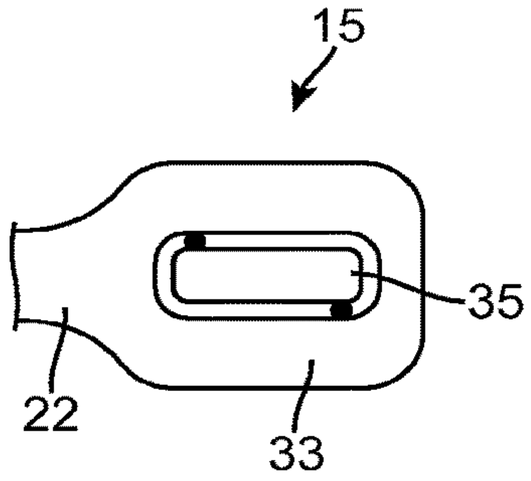


FIG. 18a

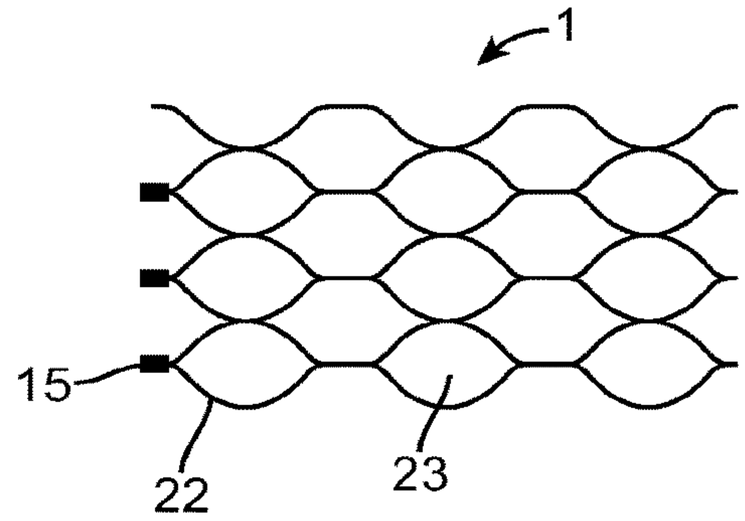


FIG. 18b

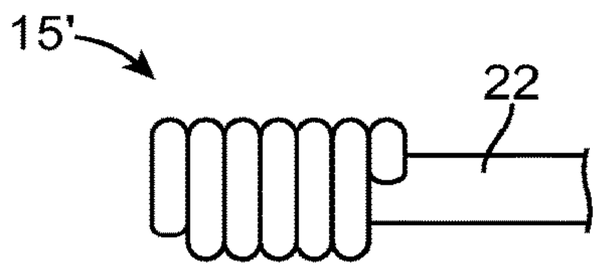


FIG. 18c

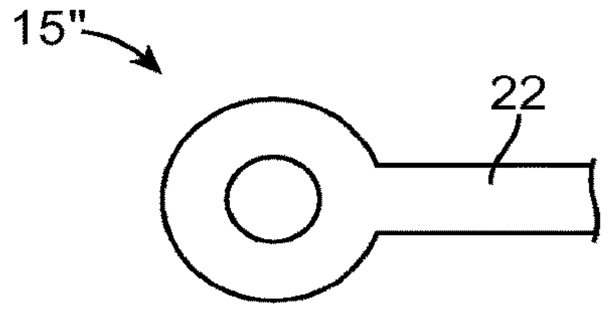


FIG. 18d

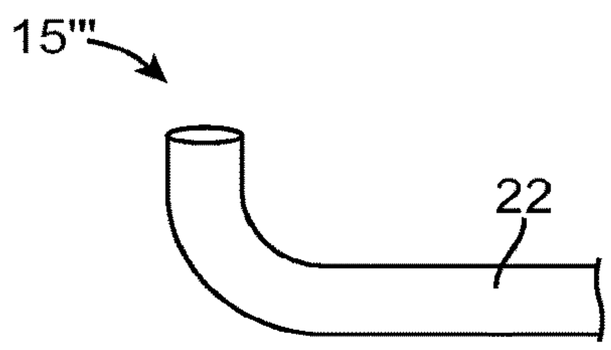


FIG. 18e

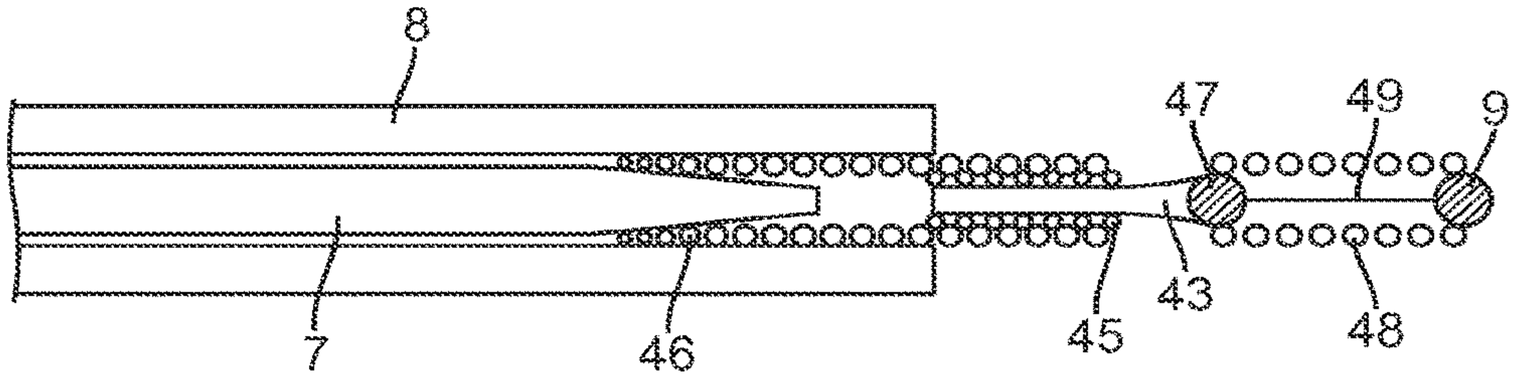


FIG. 19a

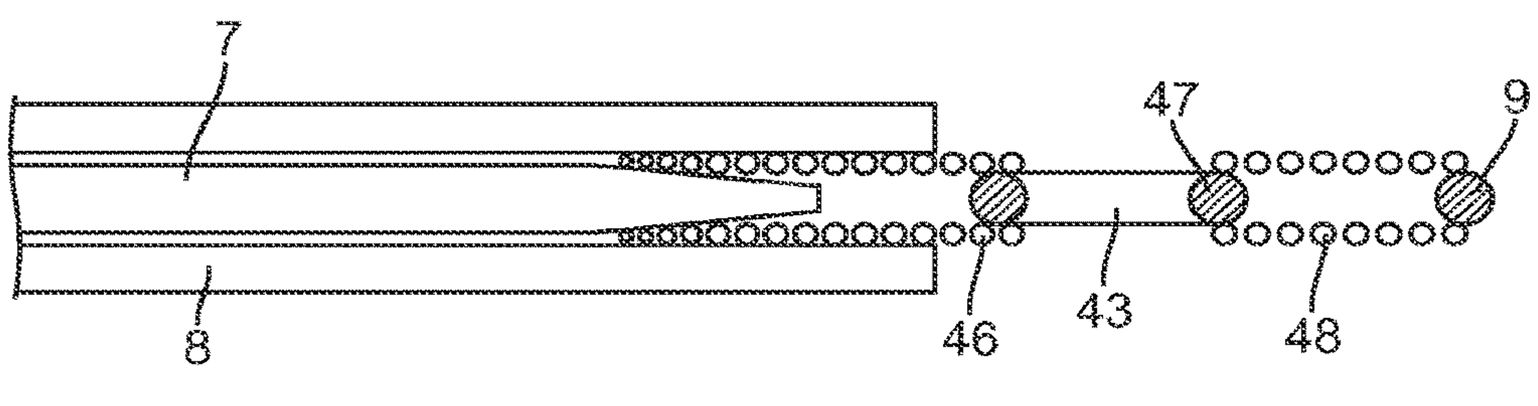


FIG. 19b

METHODS AND APPARATUS FOR FLOW RESTORATION

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 14/136,252, filed on Dec. 20, 2013, which is a continuation of U.S. patent application Ser. No. 13/678,464, filed on Nov. 15, 2012, which is a continuation of U.S. patent application Ser. No. 12/918,795, filed on Nov. 22, 2010, which is a U.S. National Phase under 35 U.S.C. § 371 of International Application No. PCT/US2009/034774, filed on Feb. 20, 2009, which claims the benefit under 35 U.S.C. § 119(e) of U.S. Provisional Application Ser. No. 61/030,838, filed on Feb. 22, 2008, each of which is hereby incorporated by reference in its entirety.

FIELD OF THE INVENTION

The present invention relates to methods and apparatus for quickly or immediately restoring blood flow in occluded blood vessels, particularly occluded cerebral arteries. Furthermore, the present invention relates to the application of such apparatus for thrombus removal and/or thrombus dissolution.

BACKGROUND OF THE INVENTION

Current technology for treating cerebral arteries occluded by thrombus may take hours to reestablish flow in the artery. Furthermore, known apparatus and methods for treating cerebral thrombus may be ineffective or only partially effective at resolving thrombus, and may additionally result in distal embolization or embolization of uninvolved arteries. The risk and degree of permanent neurological deficit increases rapidly with increased time from onset of symptoms to blood flow restoration.

SUMMARY OF THE INVENTION

The invention is directed to methods of restoring localized blood flow in a vascular site occluded with a thrombus. It is contemplated that the methods of the invention improve the speed and effectiveness of revascularization of cerebral arteries occluded by a thrombus.

In one embodiment, methods and apparatus are provided to create immediate (or restore) blood flow in the occluded artery upon deployment of the apparatus. In one aspect, a self-expandable apparatus is delivered to a site that is radially adjacent to the thrombus and the apparatus is expanded thereby restoring flow.

In another embodiment, the invention is directed to methods and apparatus that restore blood flow in the blood vessel that is occluded with a thrombus, with an associated increased efficiency in dislodging the thrombus from the vessel and removing the thrombus. In this embodiment, a self-expandable apparatus is delivered to a site that is radially adjacent to the thrombus and then expanded. The expanded apparatus then restores flow, which flow assists in disloding the thrombus from the vessel wall. In one embodiment, the apparatus enages the thrombus and the thrombus can then be removed from the site of occlusion.

In yet another embodiment, the invention is directed to methods and apparatus that restore blood flow in the occluded artery, with an associated increased efficiency in dissolving part or all of the thrombus from the vessel and optionally retrieval of the apparatus. In this embodiment, a self-expandable apparatus is delivered to a site that is radially adjacent to the thrombus and then expanded. Once expanded, the apparatus then restores flow to the occluded site and this increased flow may dissolve or partially or substantially dissolve the thrombus and the apparatus-thrombus mass is then removed from the formerly occluded site.

In still yet another embodiment, the invention is directed to methods and apparatus that restore blood flow in the occluded artery, with an associated increased efficiency in dissolving part or all of the thrombus from the vessel and implantation of a portion of the apparatus. In this embodiment, the apparatus engages (or implants in or integrates with) at least a portion of the thrombus providing a removable, integrated apparatus-thrombus mass. The removable, integrated apparatus-thrombus is removed from the site of occlusion.

In some embodiments, the method of the invention is directed to a method for imaging restoration of blood flow in a blood vessel occluded with a thrombus. This method comprises: a) acquiring an image of a self-expandable apparatus placed radially adjacent to a thrombus; and b) acquiring an image of expanding the apparatus thereby restoring blood flow.

In another embodiment, the method of the invention is directed to a method for imaging partially or substantially dissolving a thrombus lodged in a blood vessel. This method comprises: a) acquiring an image of a self-expandable apparatus placed radially adjacent to a thrombus; and b) acquiring an image of expanding the apparatus thereby increasing blood through the vessel wherein the increased blood flow partially or substantially dissolves the thrombus.

In still yet another embodiment, the method of invention is directed to a method for imaging dislodging a thrombus lodged in a blood vessel. This method comprises: a) acquiring an image of a self-expandable apparatus placed radially adjacent to a thrombus; b) acquiring an image of expanding the apparatus thereby engaging at least a portion of the thrombus; and c) acquiring an image of moving the apparatus distally or proximally thereby dislodging the thrombus.

A number of self-expandable apparatus are contemplated to be useful in the methods of the invention. In one embodiment, the apparatus is reversibly self-expandable. In another embodiment, the apparatus is fully retrievable or retractable. In one embodiment, the self-expandable apparatus comprises a mesh structure comprising a first plurality of mesh cells, the mesh structure having a proximal end and a distal end; a tapering portion comprising a second plurality of mesh cells, the tapering portion disposed toward the proximal end of the mesh structure; and a connection point, at which the tapering portion converges, located at a proximal end of the tapering portion, wherein the apparatus is preformed to assume a volume-enlarged form and, in the volume-enlarged form, takes the form of a longitudinally open tube tapering toward the connection point.

Another embodiment of the invention is a self-expandable apparatus for removal of a thrombus in a blood vessel, comprising: a mesh structure comprising a first plurality of mesh cells, the mesh structure having a proximal end and a distal end wherein said distal end of the mesh structure is configured to engage at least a portion of the thrombus to form a removable, integrated apparatus-thrombus mass; a tapering portion comprising a second plurality of mesh cells, the tapering portion disposed toward the proximal end of the mesh structure; and a connection point, at which the tapering portion converges, located at a proximal end of the tapering

portion, wherein the apparatus is pre-formed to assume a volume-enlarged form and, in the volume-enlarged form, takes the form of a longitudinally open tube tapering toward the connection point.

It is contemplated that the distal end of the mesh structure is configured to assist in thrombus retrieval by providing increasing support to the mesh structure and by increasing thrombus retention.

In another embodiment of the invention is provided a removable, integrated apparatus-thrombus mass, comprising a thrombus at least partially engaged with an apparatus, wherein the apparatus comprises a mesh structure comprising a first plurality of mesh cells, the mesh structure having a proximal end and a distal end wherein said distal end of the mesh structure is configured to engage at least a portion of the thrombus; a tapering portion comprising a second plurality of mesh cells, the tapering portion disposed toward the proximal end of the mesh structure; and a connection point, at which the tapering portion converges, located at a proximal end of the tapering portion, wherein the apparatus is pre-formed to assume a volume-enlarged form and, in the volume-enlarged form, takes the form of a longitudinally open tube tapering toward the connection point.

BRIEF DESCRIPTION OF THE DRAWINGS

The accompanying drawings, which are incorporated herein and constitute part of this specification, illustrate exemplary embodiments of the invention, and, together with the general description given above and the detailed description given below, serve to explain the features of the invention.

FIG. **1** shows an apparatus useful for the methods of the present invention.

FIG. **2***a* shows a target occlusion or thrombus to be treated by the present invention.

FIGS. **2***b*, **3**, and **4** show placement methods according to the present invention. FIG. **3** is shown with the microcatheter **8** in phantom.

FIG. **5** shows thrombus dislodgement and mobilization according to the present invention.

FIGS. **6** and **7** show thrombus dissolution methods according to the present invention.

FIGS. **8** and **9** show apparatus retrieval methods according to the present invention, with the microcatheter shown in phantom.

FIGS. **10**, **11**, and **12** show apparatus implantation methods according to the present invention.

FIG. **13** is an apparatus according to one embodiment of the present invention having a honeycomb structure.

FIG. **14** is another embodiment of a stent according to the present invention having a honeycomb structure.

FIG. **15** is a third embodiment of a stent according to the present invention having a honeycomb structure.

FIG. **16** is a warp-knitted structure as can be used for an apparatus according to the invention.

FIG. **17***a* and FIG. **17***b* is a schematic representation of an apparatus according to an embodiment of the present invention shown in its superimposed and in its volume-reduced shape.

FIG. **18***a*, FIG. **18***b*, FIG. **18***c*, FIG. **18***d*, and FIG. **18***e* are embodiments, including marker elements, that can be employed in the most distal segment of the apparatus according to the present invention.

FIG. **19***a* and FIG. **19***b* are schematic representations of two detachment locations by which the apparatus, according to the present invention, can be detachably linked to a guide wire.

DETAILED DESCRIPTION OF THE INVENTION

Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods, devices, and materials are now described. All publications and patent applications cited herein are incorporated herein by reference in their entirety. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention.

It must be noted that as used herein and in the appended claims, the singular forms "a," "an," and "the" include plural references unless the context clearly dictates otherwise.

Methods

The invention is directed to methods of restoring localized flow to an occluded vascular site. The vascular site, or blood vessel, can be occluded by a thrombus. The apparatus employed in the methods of the invention may be positioned at the vascular site with a microcatheter and optionally a guide catheter. The methods of the invention may employ a fully retrievable apparatus which is an improvement over the art which methods required the apparatus to be implanted permanently into the patient. When the apparatus is permanently placed in the patient, lifelong anticoagulant therapy for the patient is required. Therefore, it is contemplaed that by using a retrievable apparatus, lifelong anticoagulant therapy may be avoided.

Methods and apparatus are provided to restore blood flow in cerebral arteries **11** occluded with thrombus **12** (FIG. **2***a*). Such methods utilize an apparatus having a self-expandable, optionally reversibly self-expandable, distal segment **1** including distal end **2**, proximal end **3**, and body portion **4** that is pre-formed to assume a superimposed structure **5** in an unconstrained condition but can be made to take on a volume-reduced form **6** making it possible to introduce it with a push wire **7** attached at the proximal end **3** and a microcatheter **8**, with the distal segment **1** in its superimposed structure **5** assuming the form of a longitudinally open tube and having a mesh structure of interconnected strings or filaments or struts (FIGS. **1** and **3**). In one embodiment, the distal segment **1** has a tapering structure at its proximal end **3** where the strings or filaments or struts converge at a connection point **9**. The push wire **7** is preferably attached at or adjacent to the connection point **9**. Such attachment **10** may be permanent or a releasable mechanism. The methods disclosed herein can be performed with the medical distal segment **1** (or apparatus or stent, of which all terms are used interchangeably) described in U.S. Pat. No. 7,300,458, which is incorporated herein in its entirety.

According to the present invention, the self-expandable distal segment **1** of the apparatus is positioned within a blood vessel **11** occluded by thrombus **12** in a volume-reduced form **6** by advancing it with the push wire **7** within a microcatheter **8** such that its proximal end **3** is upstream of the thrombus and its distal end **2** and is downstream of the

thrombus and the body portion **4** is located radially adjacent to the thrombus **12** (FIGS. **1** and **3**). As shown in FIG. **3**, the distal end **2** of the distal segment **1** is positioned distal to the distal thrombus boundary and the proximal end **3** of the distal segment is positioned proximal of the proximal thrombus boundary. The distal segment **1** is held in a fixed position by holding the push wire **7** stationary while the distal segment **1** is released from its volume-reduced form **6** by withdrawing the microcatheter **8** proximally of the distal segment **1** (FIG. **4**). The distal segment **1** assumes at least a portion of its superimposed structure **5** in its unconstrained condition **13** thereby expanding to bring at least part of the body portion into penetrating contact with the thrombus **12'**, exerting an outward radial force on the thrombus **12'**, reducing the cross-sectional area of the thrombus **12'**, and immediately re-establishing blood flow **14** through the blood vessel **11** past the thrombus **12'**.

Also contemplated by this invention is administration of an effective amount of a clot-busting drug, such as, for example tissue plasminogen activator (tPA), to the site of the thrombus. Administration of this drug will act to further enhance dissolution of the clot.

This placement methodology expands the population of patients eligible for treatment over apparatus that require intravascular space distal to the reach of a microcatheter as the methodology of this invention places the distal segment **1** beyond the distal end of the thrombus **12**. Additionally, this placement methodology expands the population of physicians that can successfully practice the method, as it is delivered with microcatheter technology already familiar to the user, and facilitates rapid placement of the apparatus. Immediately restoring blood flow **14** is a significant advantage over known apparatus and methods for treating cerebral arteries **11** occluded by thrombus **12** because known apparatus and methods may take hours to re-establish flow **14**, and it is well established that the risk and degree of permanent neurological deficit increases rapidly with increased time from onset of symptoms to blood flow restoration.

In one embodiment thrombus removal methods and apparatus are provided that restore blood flow **14** in the occluded artery **11**, with an increased efficiency in dislodging the thrombus **12'** from the vessel coupled with removal of the thrombus **12'** and apparatus from the patient. In a preferred embodiment, restoring blood flow **14** in the occluded artery **11** involves placing a microcatheter **8** such that the distal tip **16** of the microcatheter is beyond the distal end of the thrombus **12**, wherein the distal tip **16** is from greater than about 0 millimeter (mm) to about 10 mm or more, or about 3 mm to about 5 mm (FIG. **2***b*) beyond the distal end of the thrombus **12**. The self-expandable distal segment **1** is advanced within the microcatheter **8** in its reduced volume form **6** by the push wire **7** until its distal end **2** is just beyond the distal end of the thrombus **12** (FIG. **3**).

Visualization of proper placement may be done by fluoroscopy. Specifically, this may be accomplished by aligning radiopaque markers **15** on the distal end of the distal segment with a distal radiopaque microcatheter marker **17** (FIG. **3**). As mentioned above, this invention is also directed to various methods of acquiring images of the process. The method of imaging typically employed is fluoroscopy (which can confirm proper placement of the apparatus) or contrast injection (which can confirm blood flow restoration). However, a number of imaging methods known by those of skill in the art are also contemplated.

The distal segment **1** is then deployed within and across the thrombus **12'** by holding the push wire **7** fixed while withdrawing the microcatheter **8** proximally until the distal segment **1** is released **13** (FIG. **4**). One indication of full deployment is the visualization by the clinician that a radiopaque marker **18** defining the proximal end **3** of the distal segment **1** is aligned with, or distal of, the distal radiopaque microcatheter marker **17**. Alternatively, the microcatheter **8** can be completely removed from the patient. Immediately upon distal segment **1** deployment **13**, blood flow **14** is restored across the thrombus **12'** and confirmation can be visualized via contrast injection. This is an indication of proper distal segment position relative to the thrombus **12'** and vascular anatomy.

The apparatus can be used to remove the thrombus **12'** after one of the following: a fixed amount of time has elapsed after deployment **13** of the distal segment **1**, which may be from about 0 minutes to about 120 minutes or more; blood flow **14** across the thrombus **12'** is observed to stop; a predetermined maximum amount of flow time has elapsed, whichever occurs first.

Removing the thrombus **12'** may be accomplished by any number of variations (FIG. **5**). For example, as the distal tip of volume-reduced form **6** is moved beyond the thrombus, it will encounter less resistance to expansion and provide a greater radial force as compared to that portion engaging the thrombus as shown in FIG. **5**. Thus distal tip **2** may expand beyond the thrombus **12'** creating a distal tip **2** having a larger diameter than the diameter of the distal segment that is engaged by at least a portion of the thrombus. In some embodiments, this can be a hook-like distal configuration. Further structural modifications are described below that could be used to further aid in thrombus engagement and removal. Using the push wire **7**, a pull force **19** of the deployed distal segment **13** will retract the thrombus back to the catheter as the hook-like configuration acts to snag the thrombus. Subsequent removal of the catheter will result in removal of the thrombus from the site of occlusion.

Prior to pulling the apparatus back, the microcatheter **8** can be manipulated in any of the following ways: the distal radiopaque microcatheter marker **17** can be left at or proximal to distal segment proximal radiopaque marker **18** or completely removed from patient; microcatheter **8** can be moved forward to a predetermined point relative to the distal segment **1**, which may be: when the distal radiopaque microcatheter marker **17** is desirably aligned with the distal segment of proximal radiopaque marker **18**; when the distal radiopaque microcatheter marker **17** is desirably aligned distal of the distal segment of proximal radiopaque marker **18**, for example about 0.5 mm to about 10 mm or about 5 mm to about 10 mm; when significant resistance to microcatheter **8** advancement is encountered as evidenced by buckling of the microcatheter **8**; or whichever of desired-alignment or significant resistance occurs first. While moving the deployed distal segment **13** toward or into the guide catheter, any of the following may occur: proximal guide lumen communicates with pressure bag or other positive pressure fluid source; proximal guide lumen communicates with atmosphere; or proximal guide lumen communicates with aspiration source or other negative pressure.

Thrombus removal methods of the present invention have unique advantages over known thrombus removal methods. When deployed accross a thrombus, the distal segment **1** creates intra-procedural flow **14** by creating a fluid path across the thrombus **12'** (FIG. **4**). In this way, the distal segment **13** significantly reduces the pressure drop across the thrombus **12'**, and accordingly significantly reduces the pressure related forces which would otherwise resist removal of the thrombus **12** (FIG. **5**). Further, the fluid path is created by the deployed distal segment **13** separating a

significant portion of the thrombus **12'** circumference away from the vessel wall. In addition, expansion of volume-reduced form **6** creates an integrated mass where the mesh is embedded within the thrombus. As above, the distal portion of volume-reduced form **6** can produce a greater radial force (and may be in a hook-like configuration upon expansion) thereby facilitating removal of the thrombus.

It is estimated that about 10% to about 60% of the original thrombus **12** circumference is separated from the vessel wall after the distal segment **1** is deployed **13**, and the ability of the post deployment thrombus **12'** to hang onto the vessel wall via adhesion and friction is accordingly reduced. Still further, the cross sectional area of the original thrombus **12** is significantly reduced by the deployed distal segment **13**, resulting in a thrombus **12'** having about 30% to about 95% of its original cross sectional area, but more typically about 50% to about 80% of its original cross sectional area. All of this results in a more effective revascularization procedure as a result of lower thrombus dislodgement and mobilization force and more effective thrombus mobilzation **19**, as demonstrated by the functions later described herein. Of further benefit, the lower thrombus mobilization force is distributed along the entire length of the thrombus **12'**, or at least along the entire length of the distal segment **13**, reducing the chances of the apparatus slipping past or through the thrombus or fragmenting the thrombus, which could result in residual thrombus, distal embolization, or embolization of uninvolved territories.

A target occlusion is represented by an original thrombus **12** having cross sectional area A (FIG. **2***a*), creating an associated pressure drop across the thrombus of P, having circumferential vessel contact area C, and f is a quantity proportional to a ratio of the thrombus adhesive and frictional forces/contact area. The force required to dislodge or mobilize this thrombus by known methods that do not establish intra-procedural flow across the thrombus and do not separate a significant portion of the thrombus circumference away from the vessel wall can be described by the function:

$$(A*P)+C*f$$

For the thrombus removal methods of the present invention, that is when the distal segment **1** is deployed **13** within the thrombus **12'** (FIG. **4**), the thrombus **12'** has reduced cross sectional area "a" where a<A, reduced pressure drop across the thrombus "p" where p<P, significantly reduced circumferential vessel contact area "c" where c<C, and f is a quantity proportional to a ratio of the thrombus adhesive and frictional forces/contact area. The force required to dislodge and mobilize the thrombus **12'** according to the methods described herein will be significantly lower than forces required to dislodge and mobilized original thrombus **12** by known methods (FIG. **5**), and can be described by the function:

$$(a*p)+c*f$$

Also contemplated by the present invention are thrombus dissolution methods and apparatus that restore blood flow **14** in the occluded artery, with an increased efficiency in dissolving part (FIG. **7**) or all (FIG. **6**) of the thrombus from the vessel and retreival of the apparatus (FIGS. **8** and **9**). As previously described, the distal segment is deployed within and across a thrombus **12'** to restore blood flow **14** in the occluded artery (FIG. **4**). Immediately reestablishing blood flow **14** is a significant advantage over know apparatus and methods for treating cerebral arteries occluded by thrombus because known apparatus and methods may take hours to reestablish flow. Specific benefits include reestablishing antegrade flow distal of the original occlusion to perfuse ischemic tissue and help break up emboli that may be present distal of the original occlusion. Additional benefit is derived from increasing the surface area of the thrombus **12'** exposed to the blood flow, thereby improving the effectivity of natural lysing action of the blood on the thrombus **12'** and improving the effectivity of the thrombolytic, anticoagulant, anti-platelet, or other pharmacological agents introduced by the physician, all of which facilitates thrombus dissolution. When the thrombus has been completely dissolved (FIG. **6**), or sufficiently reduced **12"** such that reocclusion is not likely (FIG. **7**), the distal segment **1** is retrieved **20** by advancing the microcatheter **8** over the entire distal segment **1** while holding the push wire **7** in a fixed position such that the distal segment **1** is not moved axially within the artery (FIGS. **8** and **9**). The apparatus may then be removed through the microcatheter **8** or alternatively the microcatheter **8** can be removed with the distal segment **1** of the apparatus still inside of it.

Additionally, it is contemplated that the methods of the present invention can restore blood flow in the occluded artery, with an increased efficiency in dissolving part or all of the thrombus from the vessel and implantation of the distal segment **1**. Methods that include implantation of the distal segment **1** require the use of an apparatus with a releasable attachment mechanism between the distal segment **1** and push wire **7**. As previously described, the distal segment **1** is deployed within and across **13** a thrombus **12'** to restore blood flow **14** in the occluded artery (FIG. **4**). The distal segment **1** can then be released from the push wire via a releasable attachment mechanism. Such release may occur immediately upon reestablishing blood flow (FIG. **10**), when the thrombus **12"** has been sufficiently reduced such that reocclusion is not likely (FIG. **11**), or when the thrombus is completely dissolved (FIG. **12**).

In another embodiment of the invention, the thrombus removal or dissolution is assisted by aspirating the microcatheter and/or the guide catheter.

Utility derived from a releasable mechanism between the distal segment and push wire includes suitability of one apparatus for all of the methods disclosed herein, providing procedural options for the user. Of futher benefit, a releasable mechanism enables the user to release the unconstrained distal segment if it is determined that removal from the patient is not possible.

Certain embodiments of the invention include methods of restoring blood flow and then detaching the apparatus and leaving the apparatus in situ (FIG. **12**). This can be done when it is determined by the clinician that either the apparatus is no longer retrievable. In this embodiment, it is contemplated that the apparatus would be coated or otherwise embedded with anticoagulant or antiplatelet drugs. This is more thoroughly discussed below.

Apparatus

As mentioned above, any suitable self-expandable apparatus may be employed by the methods of the invention. Various embodiments of the apparatus may be found in U.S. Pat. No. 7,300,458, which is incorporated by reference in its entirety.

A distal segment **1**, according to FIG. **13**, consists of a mesh or honeycomb structure that, in one embodiment, comprises a multitude of filaments interconnected by a laser welding technique. The distal segment **1** can be subdivided into a functional structure A and a tapering proximal struc-

ture B, the two structures being distinguishable, inter alia, by a different mesh size. To enable the functional structure A to perform its function, its mesh cells **23** are held relatively narrow so that they lend themselves to the implantation into the thrombus **12**. In general, the mesh width is in the range of 0.5 to 4 mm and may vary within the segment.

In one aspect of the present invention, the distal segment **1** is a flat or two-dimensional structure that is rolled up to form a longitudinally open object capable of establishing close contact with the wall of the vessel into which it is introduced.

In the tapering proximal structure B of the distal segment **1**, there is provided a wider mesh cell **24** structure which has been optimized towards having a minimum expansion effect. In the area of the tapering structure **22**, the filaments have a greater thickness and/or width to be able to better transfer to the functional structure A the thrust and tensile forces of the guide wire exerted at a connection point **9** when the distal segment **1** is introduced and placed in position. In the area of the tapering structure it is normally not necessary to provide support for, and coverage of, the vessel wall, but on the other hand requirements as to tensile and thrust strength increase. The filament thickness in the functional structure A generally ranges between 0.02 and 0.076 mm, and in proximal structure part B, the filament thickness is greater than 0.076 mm.

The proximal structure forms an angle from 45 degrees to 120 degrees at the connection point **9**, in particular an angle of about 90 degrees. The filament thickness (or string width) is the same as the mesh size and its shape may vary over a great range to suit varying requirements as to stability, flexibility and the like. It is understood that the proximal structure B, as well, contacts the vessel wall and thus does not interfere with the flow of blood within the vessel.

At a distal end, the filaments **22** end in a series of tails **2** that are of suitable kind to carry platinum markers that facilitate the positioning of the distal segment **1**.

The distal segment **1** is curled up in such a way that edges **27** and **28** are at least closely positioned to each other and may overlap in the area of the edges. In this volume-reduced form, the distal segment **1**, similar to a wire mesh roll, has curled up to such an extent that the roll so formed can be introduced into a microcatheter and moved within the catheter. Having been released from the microcatheter, the curled-up structure springs open and attempts to assume the superimposed structure previously impressed on it and in doing so closely leans to the inner wall of the vessel to be treated, thus superficially covering a thrombus and then implanting into the thrombus that exists in that location. In this case the extent of the "curl up" is governed by the vessel volume. In narrower vessels a greater overlap of the edges **27** and **28** of the distal segment **1** will occur whereas in wider vessels the overlap will be smaller or even "underlap," will be encountered, and due care must be exercised to make sure the distal segment **1** still exhibits a residual tension.

Suitable materials that can be employed in the device include alloys having shape-memory properties. The finished product is subjected to a tempering treatment at temperatures customarily applied to the material so that the impressed structure is permanently established.

The distal segment **1** has a mesh-like structure consisting of strings or filaments connected with each other. Strings occur if the distal segment **1** comprises cut structures as, for example, are frequently put to use in coronary stents, a mesh-like structure consisting of filaments is found if the distal segment **1** is present in the form of mats having knitted or braided structures or in the form of individual filaments that are welded to one another.

FIG. **14** shows another embodiment of a distal segment **1** according to the invention having the above described honeycomb structure where the tapering proximal structure B is connected with the functional structure part A by additional filaments **29** in a peripheral area **30** as well as in the central area. The additional filaments **29** and **30** bring about a more uniform transmission of the tensile and thrust forces from the proximal structure B to the functional structure A. As a result, the tensile forces can be better transmitted, especially if the stent might have to be repositioned by having to be retracted into the microcatheter. The additional filaments **29**, **30** facilitate the renewed curling up of the stent. Similarly, the transmission of thrust forces occurring when the stent is moved out and placed in position is facilitated so that the stent can be gently applied.

FIG. **15** shows another embodiment of a distal segment **1** according to the invention having a honeycomb structure with the edges **27** and **28** being formed of straight filaments **29**. According to this embodiment, the thrust or pressure exerted by the guide wire at the connection point **9** is directly transmitted to the edges **27** and **28** of the functional structure part A which further increases the effect described with reference to FIG. **14**.

The embodiment as per FIG. **15**, similar to those depicted in FIGS. **13** and **14**, may be based on a cut foil, i.e., the individual filaments **22**, **29** and **30** are substituted by individual strings being the remaining elements of a foil processed with the help of a cutting technique. Laser cutting techniques for the production of stents having a tubular structure are known. The processing of a foil for the production of a pattern suitable for a stent is performed analogously. The impression of the superimposed structure is carried out in the same way as is used for the filament design.

In one embodiment, expanded metal foil may be used with the respective string widths being of the same magnitude. In one embodiment, it is envisioned to subsequently smooth the foil to make sure all strings are arranged on the same plane. The thickness of the foil usually ranges between 0.02 and 0.2 mm. Foils of greater thickness also permit the stent to be used in other fields of application, for example, as coronary stents or in other regions of the body including, for instance, the bile duct or ureter.

Foils worked with the help of a cutting technique are finished by electrochemical means to eliminate burrs and other irregularities to achieve a smooth surface and round edges. One of ordinary skill in the art will understand these electrochemical processes as these processes already are in use in medical technology. In this context, it is to be noted that the stents according to the invention that are based on a two-dimensional geometry and on which a three-dimensional structure is impressed subsequently can be manufactured and processed more easily than the conventional "tubular" stents that already, during manufacture, have a three-dimensional structure and necessitate sophisticated and costly working processes and equipment.

As pointed out above, the mesh structure of the distal segment **1** according to the invention may consist of a braiding of individual filaments. Such a knitted structure is shown in FIG. **16** where the individual filaments **22** are interwoven in the form of a "single jersey fabric" having individual loops **23** forming a mesh-like structure **31**. Single jersey goods of this type are produced in a known manner from a row of needles. The single jersey goods have two fabric sides of different appearance, i.e., the right and left

side of the stitches. A single jersey fabric material features minor flexibility in a transverse direction and is very light.

Filaments consisting of a braid of individual strands and formed into a rope can also be employed. Braids comprising twelve to fourteen strands having a total thickness of 0.02 mm can be used. Platinum, platinum alloys, gold and stainless steel can be used as materials for the filaments. Generally speaking, all permanent distal segment **1** materials known in medical technology can be employed that satisfy the relevant requirements.

In one embodiment, it is advantageous to have the fabric rims of such a knitted structure curling up as is known, for example, from the so-called "Fluse" fabric, a German term, which is of benefit with respect to the superimposed structure and application dealt with here. In this case, the superimposed structure can be impressed by means of the knitting process. However, the use of shape-memory alloys in this case as well is feasible and useful.

For the production of such knitted structures, known knitting processes and techniques can be employed. However, since the distal segments according to the invention are of extremely small size—for example, a size of 2 by 1 cm—it has turned out to be beneficial to produce the distal segments in the framework of a conventional warp or weft knitting fabric of textile, non-metallic filaments, for example, in the form of a rim consisting of the respective metallic filaments from which the weft or warp knitting fabric either starts out or that extends from such a fabric. The arrangement of the metallic part of the weft or warp knitting fabric at the rim achieves the aforementioned curling effect. The non-metallic portions of the knitted fabric are finally removed by incineration, chemical destruction or dissolution using suitable solvents.

FIG. **1** shows a combination of a guide wire **7** with the distal segment **1** attached to it that consists of filaments connected to each other by welding. The distal ends **2** and the connection point **9** where the filaments of the distal segment **1** converge in a tapering structure and that simultaneously represents the joining location with guide wire **7** are shown. The guide wire **7** is introduced into a microcatheter **8** which is of customary make.

Shifting the guide wire **7** within the catheter **8** will cause the distal segment **1** to be pushed out of or drawn into the catheter. Upon the stent being pushed out of the microcatheter **8** the mesh-like structure attempts to assume the superimposed shape impressed on it, and when being drawn in, the mesh structure folds back into the microcatheter **8** adapting to the space available inside.

As a result of the stiffness of its mesh structure, the distal segment **1** can be moved to and fro virtually without restriction via the guide wire **7** until it has been optimally positioned within the vessel system.

As mentioned earlier, customary microcatheters can be used. One advantage of the distal segment **1** according to the invention and of the combination of distal segment **1** and guide wire according to the invention is, however, that after having placed the microcatheter in position with a customary guide wire/marker system, the combination of guide wire **7** and distal segment **1** according to the invention can be introduced into the microcatheter, moved through it towards the implantation site and then moved out and applied in that position. Alternatively, it will be possible to have a second microcatheter of smaller caliber accommodate guide wire **7** and distal segment **1** and with this second microcatheter within the firstly positioned microcatheter shift them to the implantation site. In any case, the distal segment **1** can be easily guided in both directions.

FIG. **17** shows a schematic representation of an distal segment **1** according to the invention in its superimposed or volume-expanded shape and in its volume-reduced shape. In its expanded shape, as illustrated in FIG. **17***a*, the distal segment **1** forms a ring-shaped structure with slightly overlapping edges **27** and **28**. In FIG. **17***a* the distal segment **1** is viewed from its proximal end as a top view with the connection point **9** being approximately positioned opposite to the edges **27** and **28**. In the combination according to the invention, the guide wire **7** is affixed at the connection point **9**.

FIG. **17***b* shows the same distal segment **1** in its volume-reduced form **6** as it is arranged, for example, in a microcatheter in a curled up condition. In the case illustrated there is a total of two windings of the curled-up distal segment **1** with the connection point **9** being located at the proximal side and the two lateral edges **27** and **28** being the starting and final points of the roll or spiral. The structure is held in its volume-reduced form by the microcatheter **8** and when the distal segment **1** is pushed out of the microcatheter **8** it springs into its expanded shape, as illustrated by FIG. **17***a*, similar to a spiral spring.

FIG. **18***a* shows a marker element **15** suitable for the distal segment **1** according to the invention with the marker element **15** being capable of being arranged at the distal end of the distal segment **1**. The marker element **15** consists of a lug **33** provided with a small marker plate **35** levelly arranged inside it, i.e., flush with the plane of the distal segment **1** without any projecting elements. The plate **35** is made of an X-ray reflecting material, for example, platinum or platinum-iridium. The marker plate **35** may be connected to the surrounding distal segment **1** structure by known laser welding techniques. As shown in FIG. **18***b*, the marker elements **15** are arranged at the distal end of the distal segment **1**.

As mentioned above, in one embodiment, the apparatus is configured to so as to provided a removable, integrated thrombus apparatus-mass. This configuration can be done in a variety of ways. For example, as can be seen in FIG. **18***c*, marker element **15'** can be provided in a spiral thereby increasing the support of the distal end of the mesh structure and aiding in the thrombus retrieval. Also, as seen in FIG. **18***d*, the marker element **15'** can be provided as an eyelet shape functioning in a manner similar to the spiral marker **15'**. FIG. **18***e* shows a marker element **15"** shown in the shape of a hook or a peg which can be added to provide additional retention of the thrombus during removal. Marker element **15'** is optionally radiopaque or may be made from the same shape memory alloy as the mesh structure.

Additional structural configurations contemplated to provide a removal, integrated thrombus apparatus-mass include: 1) a greater diameter of the mesh structure in the most distal location of the distal segment **1** compared to the proximal end of the mesh structure (or a widening-taper on the distal end of the distal segment **1**); 2) a third plurality of mesh cells located in the most distally in the distal segment **1**, wherein the this third plurality of mesh cells have smaller mesh size compared to the first plurality of mesh cells; 3) adding synthetic polymers or polymeric fibers to the mesh structure; and 4) heating the distal end of the distal segment **1** for a time sufficient to impart increased radial strength for better thrombus retention.

As mentioned above, fibers may be added to the mesh structure. Fibers may be wrapped or wound around the mesh structure. They may have loose ends or may be fully braided throughout the distal segment **1**.

Suitable fibers are taught in US Publication 2006/0036281, which is incorporated by reference in its entirety. In certain embodiments, the fibers may be comprised of polymeric materials. The polymeric materials may include materials approved for use as implants in the body or which could be so approved. They may be nonbiodegradable polymers such as polyethylene, polyacrylics, polypropylene, polyvinylchloride, polyamides such as nylon, e.g., Nylon 6.6, polyurethanes, polyvinylpyrrolidone, polyvinyl alcohols, polyvinylacetate, cellulose acetate, polystyrene, polytetrafluoroethylene, polyesters such as polyethylene terephthalate (Dacron), silk, cotton, and the like. In certain specific embodiments the nonbiodegradable materials for the polymer component may comprise polyesters, polyethers, polyamides and polyfluorocarbons.

The polymers can be biodegradable as well. Representative biodegradable polymers include: polyglycolic acid/polylactic acid (PGLA), polycaprolactone (PCL), polyhydroxybutyrate valerate (PHBV), polyorthoester (POE), polyethyleneoxide/polybutylene terephthalate (PEO/PBTP), polylactic acid (PLA), polyglycolic acid (PGA), poly (p-dioxanone), poly (valetolactone), poly (tartronic acid), poly (β malonic acid), poly (propylene fumarate), poly (anhydrides); and tyrosine-based polycarbonates. Additional polymers contemplated include polyglycolide and poly-L-lactide.

Other equivalent materials, including but not limited to stereoisomers of any of the aforementioned, may be used as well.

FIGS. **19***a* and **19***b* are representations, respectively, of two variations of a separating arrangement by which the distal segment **1** according to the invention is detachably connected to a guide wire **7**. In each case, a separating arrangement consists of a dumb-bell shaped element **43** that dissolves under the influence of electrical energy when in contact with an electrolyte. At the proximal (guidewire side) end of the dumb-bell shaped separating element **43**, as per FIG. **19***a*, a spiral structure **45** is located that interacts with a strengthening spiral **46** of the guide wire **7**. At the distal end, a ball-shaped element **47** is arranged that, with the help of a laser welding technique, is connected to a platinum spiral **48** which, in turn, is linked with the connection point **9** situated at the proximal end of the distal segment **1**. The platinum spiral **48** also serves as an X-ray reflecting proximal marker of the distal segment **1**.

To strengthen the joint between the ball-shaped element **47** and the connection point **9**, a reinforcement wire **49** may be provided. Alternatively, the platinum spiral **48** may also be designed in such a manner that it withstands the tensile and thrust forces imposed on it.

The separating element **43** can include a steel material that is susceptible to corrosion in an electrolyte under the influence of electrical energy. To accelerate corrosion and shorten the separating time span, a structural or chemical weakening of the dumb-bell shaped element **43** may be beneficial, for example, by applying grinding methods or thermal treatment.

Generally, the portion of the dumb-bell **43** accessible to the electrolyte has a length of 0.1 to 0.5 mm, particularly 0.3 mm.

The spiral structure **45** is secured via welding both to the dumb-bell shaped element **43** and the reinforcement spiral **46** of the guide wire **7**. The guide wire **7** itself is slidably accommodated within the microcatheter **8**.

FIG. **19***b* shows a second embodiment that differs from the one described with respect to FIG. **19***a*, in that the dumb-bell shaped element **43** has a ball-shaped element **47** at each end. The ball shaped elements **47** are connected distally to the connection point **9** of the distal segment **1** and proximally to the guide wire **7** via spirals **48**, **46**, respectively.

It is of course also provided that other separating principles may be applied, for example, those that are based on mechanical principles or melting off plastic connecting elements.

Coated Apparatus

This invention also contemplates coating the apparatus with anticoagulant and/or an antiplatelet agent or drug. It is contemplated that a drug may be used alone or in combination with another drug.

Anticoagulant agents or anticoagulants are agents that prevent blood clot formation. Examples of anticoagulant agents include, but are not limited to, specific inhibitors of thrombin, factor IXa, factor Xa, factor XI, factor XIa, factor XIIa or factor VIIa, heparin and derivatives, vitamin K antagonists, and anti-tissue factor antibodies, as well as inhibitors of P-selectin and PSGL-1. Examples of specific inhibitors of thrombin include hirudin, bivalirudin (Angiomax®), argatroban, ximelagatran (Exanta®,), dabigatran, and lepirudin (Refludan®). Examples of heparin and derivatives include unfractionated heparin (UFH), low molecular weight heparin (LMWH), such as enoxaparin (Lovenox®), dalteparin (Fragmin®), and danaparoid (Orgaran®); and synthetic pentasaccharide, such as fondaparinux (Arixtra®), idraparinux and biotinylated idraparinux. Examples of vitamin K antagonists include warfarin (Coumadin®), phenocoumarol, acenocoumarol (Sintrom®), clorindione, dicumarol, diphenadione, ethyl biscoumacetate, phenprocoumon, phenindione, and tioclomarol.

Antiplatelet agents or platelet inhibitors are agents that block the formation of blood clots by preventing the aggregation of platelets. There are several classes of antiplatelet agents based on their activities, including, GP IIb/IIIa antagonists, such as abciximab (ReoPro®), eptifibatide (Integrilin®), and tirofiban (Aggrastat®); P2Y12 receptor antagonists, such as clopidogrel (Plavix®), ticlopidine (Ticlid®), cangrelor, ticagrelor, and prasugrel; phosphodiesterase III (PDE III) inhibitors, such as cilostazol (Pletal®), dipyridamole (Persantine®) and Aggrenox® (aspirin/extended-release dipyridamole); thromboxane synthase inhibitors, such as furegrelate, ozagrel, ridogrel and isbogrel; thromboxane A2 receptor antagonists (TP antagonist), such as ifetroban, ramatroban, terbogrel, (3-{6-[(4-chlorophenylsulfonyl)amino]-2-methyl-5,6,7,8-tetrahydronaphth-1-yl}propionic acid (also known as Servier S 18886, by de Recherches Internationales Servier, Courbevoie, France); thrombin receptor antagonists, such as SCH530348 (having the chemical name of ethyl (1R,3aR,4aR,6R, 8aR, 9S, 9aS)-9-((E)-2-(5-(3 fluorophenyl)pyridin-2-yl)vinyl)-1-methyl-3-oxododecahydronaphtho[2,3-C] furan-6-ylcarbamate, by Schering Plough Corp., New Jersey, USA, described in US2004/0192753A1 and US2004/0176418A1 and studied in clinical trials, such as A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety of SCH 530348 in Subjects Undergoing Non-Emergent Percutaneous Coronary Intervention with ClinicalTrials.gov Identifier: NCT00132912); P-selectin inhibitors, such as 2-(4-chlorobenzyl)-3-hydroxy-7,8,9,10-tetrahydrobenzo[H]quinoline-4-carboxylic acid (also known as PSI-697, by Wyeth, New Jersey, USA); and non-steroidal anti-inflammatory drugs (NSAIDS), such as acetylsalicylic acid (Aspirin®), resveratrol, ibuprofen (Advil®, Motrin®),

naproxen (Aleve®, Naprosyn®), sulindac (Clinoril®), indomethacin (Indocin®), mefenamate, droxicam, diclofenac (Cataflam®, Voltaren®), sulfinpyrazone (Anturane®), and piroxicam (Feldene®). Among the NSAIDS, acetylsalicylic acid (ASA), resveratrol and piroxicam are preferred. Some NSAIDS inhibit both cyclooxygenase-1 (cox-1) and cyclooxygenase-2 (cox-2), such as aspirin and ibuprofen. Some selectively inhibit cox-1, such as resveratrol, which is a reversible cox-1 inhibitor that only weakly inhibits cox-2.

In one embodiment, a controlled delivery of the drug can control the lytic effect of the drug and treat ischemic stroke and many other vascular diseases. The release rate can be controlled such that about 50% of the drug can be delivered to the thrombus in from about 1 to about 120 minutes. This controlled delivery can be accomplished in one or more of the following ways. First, the drug and polymer mixture may be applied to the stent and the amount of polymer may be increased or the combination may be applied in a thicker layer. Second, the stent may be first coated with polymer, then coated with a layer of drug and polymer, and then a topcoat of polymer can be applied. The release rates of the drug can be altered by adjusting the thickness of each of the layers. Third, the stent can be manufactured to provide reservoirs to hold the drug. In this embodiment, the drug is filled in small reservoirs made on the stent surface. Reservoirs can be made by laser cutting, machine electro-chemical, mechanical or chemical processing.

In the embodiments just described the polymer is biocompatible and biodegradable. These polymers are well known in the art.

Additionally, stents can be coated with a drug-eluting coating such as a combination of a polymer and a pharmaceutical agent. Such coatings can be applied using methods well established in the art, such as dipping, spraying, painting, and brushing. See, U.S. Pat. Nos. 6,214,115; 6,153,252; U.S. patent application No. 2002/0082679; U.S. Pat. Nos. 6,306,166; 6,517,889; 6,358,556; 7,318,945; 7,438,925.

For example, Chudzik et al. (U.S. Pat. No. 6,344,035) teaches a method wherein a pharmaceutical agent or drug is applied in combination with a mixture of polymers such as poly(butyl methacrylate) and poly(ethylene-co-vinyl acetate). Guruwaiya et al. discloses a method for coating a stent wherein a pharmacological agent is applied to a stent in dry, micronized form over a sticky base coating (U.S. Pat. No. 6,251,136). Ding et al. teaches a method of applying drug-release polymer coatings that uses solvents (U.S. Pat. No. 5,980,972) wherein the solutions are applied either sequentially or simultaneously onto the devices by spraying or dipping to form a substantially homogenous composite layer of the polymer and the pharmaceutical agent.

Although various exemplary embodiments of the present invention have been disclosed, it will be apparent to those skilled in the art that changes and modifications can be made which will achieve some of the advantages of the invention without departing from the spirit and scope of the invention. It will be apparent to those reasonably skilled in the art that other components performing the same functions may be suitably substituted.

What is claimed is:

1. A removable, integrated apparatus-thrombus mass, comprising a thrombus at least partially engaged with an apparatus, wherein the apparatus comprises:

a self-expandable structure comprising a first plurality of cells, the structure having a proximal end and a distal end, the proximal end and the distal end being open, and the first plurality of cells being expanded into at least a portion of the thrombus;

a tapering portion comprising a second plurality of cells, the tapering portion disposed toward the proximal end of the structure;

a connection portion, at which the tapering portion converges, located at a proximal end of the tapering portion; and

a push or guide wire, wherein a distal end of the push or guide wire is non-releasably attached at or adjacent to the connection portion,

wherein the apparatus is self-expandable and pre-formed to assume a volume-enlarged form and, in the volume-enlarged form, takes the form of a longitudinally open tube tapering toward the connection portion.

2. The removable, integrated apparatus-thrombus mass of claim **1**, wherein a mesh size of the second plurality of cells is larger than a mesh size of the first plurality of cells.

3. The removable, integrated apparatus-thrombus mass of claim **2**, wherein the structure has a distal portion comprising a third plurality of cells distal to the first plurality of cells, the third plurality of cells having a mesh size smaller than the mesh size of the first plurality of cells.

4. The removable, integrated apparatus-thrombus mass of claim **1**, wherein the distal end of the structure is heated for a sufficient time to provide increased radial strength.

5. The removable, integrated apparatus-thrombus mass of claim **1**, wherein the distal end of the structure comprises fibers.

6. The removable, integrated apparatus-thrombus mass of claim **1**, wherein the distal end of the structure comprises one or more pegs and/or hooks.

7. The removable, integrated apparatus-thrombus mass of claim **1**, wherein the structure is coated with an anticoagulant or antiplatelet drug.

8. The removable, integrated apparatus-thrombus mass of claim **7**, wherein the structure is further coated with a biodegradable, biocompatible polymer to provide for sustained release of the anticoagulant or antiplatelet drug.

9. The removable, integrated apparatus-thrombus mass of claim **1**, wherein the structure comprises reservoirs to hold an anticoagulant or antiplatelet drug.

10. The removable, integrated apparatus-thrombus mass of claim **1**, wherein the apparatus can take a volume-reduced form, and the structure forms edges and is curled up such that the edges overlap in the volume-reduced form, and wherein in the volume-enlarged form the edges overlap less than in the volume-reduced form.

11. The removable, integrated apparatus-thrombus mass of claim **1**, further comprising radiopaque markers on the distal end of the structure.

12. The removable, integrated apparatus-thrombus mass of claim **11**, wherein the radiopaque markers are attached to distal tails at the distal end of the structure.

13. The removable, integrated apparatus-thrombus mass of claim **1**, further comprising a radiopaque marker at a proximal end of the tapering portion.

14. The removable, integrated apparatus-thrombus mass of claim **1**, further comprising fibers wrapped or wound around the structure.

15. The removable, integrated apparatus-thrombus mass of claim **1**, wherein the integrated apparatus-thrombus mass is removable by retracting the push or guidewire through a blood vessel.

16. The removable, integrated apparatus-thrombus mass of claim **1**, wherein the first plurality of cells are embedded within the thrombus.

17. The removable, integrated apparatus-thrombus mass of claim 1, wherein the first plurality of cells are implanted into the thrombus.

18. A removable, integrated apparatus-thrombus mass, comprising a thrombus at least partially engaged with a self-expandable apparatus, wherein the apparatus comprises:

a self-expandable structure comprising a first plurality of cells, the structure having a proximal end and a distal end, the proximal end and the distal end being open, and the first plurality of cells being expanded into and interlocked with at least a portion of the thrombus;

a tapering portion comprising a second plurality of cells, the tapering portion disposed toward the proximal end of the structure; and

a connection member, toward which the tapering portion converges, located at a proximal end of the tapering portion; and

a push or guide wire, and wherein a distal end of the push or guide wire is non-releasably attached to the tapering portion at or adjacent to the connection member,

wherein the self-expandable apparatus is configured to assume a volume-enlarged form and, in the volume-enlarged form, to take the form of a longitudinally open tube; and

wherein the thrombus extends outside of the structure.

19. The removable, integrated apparatus-thrombus mass of claim 18, wherein a mesh size of the second plurality of cells is larger than a mesh size of the first plurality of cells.

20. The removable, integrated apparatus-thrombus mass of claim 19, wherein the structure has a distal portion comprising a third plurality of cells distal to the first plurality of cells, the third plurality of cells having a mesh size smaller than the mesh size of the first plurality of cells.

21. The removable, integrated apparatus-thrombus mass of claim 18, wherein the distal end of the structure is heated for a sufficient time to provide increased radial strength.

22. The removable, integrated apparatus-thrombus mass of claim 18, wherein the distal end of the structure comprises fibers.

23. The removable, integrated apparatus-thrombus mass of claim 18, wherein the distal end of the structure comprises one or more pegs and/or hooks.

24. The removable, integrated apparatus-thrombus mass of claim 18, wherein the structure is coated with an anticoagulant or antiplatelet drug.

25. The removable, integrated apparatus-thrombus mass of claim 24, wherein the structure is further coated with a biodegradable, biocompatible polymer to provide for sustained release of the anticoagulant or antiplatelet drug.

26. The removable, integrated apparatus-thrombus mass of claim 18, wherein the structure comprises reservoirs to hold an anticoagulant or antiplatelet drug.

27. The removable, integrated apparatus-thrombus mass of claim 18, wherein the apparatus can take a volume-reduced form, and the structure forms edges and is curled up such that the edges overlap in the volume-reduced form, and wherein in the volume-enlarged form the edges overlap less than in the volume-reduced form.

28. The removable, integrated apparatus-thrombus mass of claim 18, further comprising radiopaque markers on the distal end of the structure.

29. The removable, integrated apparatus-thrombus mass of claim 28, wherein the radiopaque markers are attached to distal tails at the distal end of the structure.

30. The removable, integrated apparatus-thrombus mass of claim 18, further comprising a radiopaque marker at a proximal end of tapering portion.

31. The removable, integrated apparatus-thrombus mass of claim 18, further comprising fibers wrapped or wound around the structure.

32. The removable, integrated apparatus-thrombus mass of claim 18, wherein the integrated apparatus-thrombus mass is removable by retracting the push or guidewire through a blood vessel.

33. The removable, integrated apparatus-thrombus mass of claim 18, wherein the first plurality of cells are embedded within the thrombus.

34. The removable, integrated apparatus-thrombus mass of claim 18, wherein the first plurality of cells are implanted into the thrombus.

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