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(54) **Title:** Electrophysiology Device with Ion-Selective Electrodes

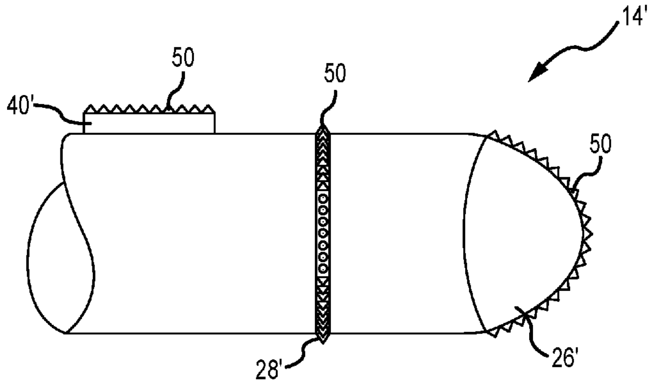

FIG.5

(57) **Abstract:** An electrophysiology catheter includes a body and at least one electrode disposed thereon. The electrode includes an ion-selective coating, such as a crown ether, a zeolite, and/or ethylenediaminetetraacetic acid (EDTA), that is selective for one or more ions relative to cardiomyocyte membrane potentials, such as potassium, sodium, calcium, and/or chlorine. The ion-selective coating can be applied uniformly over the electrodes or can cover only a portion of the electrodes. The electrodes can also include a tissue-penetrating texture.

WO 2018/226334 A1

ELECTROPHYSIOLOGY DEVICE WITH ION-SELECTIVE ELECTRODES

CROSS-REFERNCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of United States provisional application no. 62/515,778, filed 6 June 2017, which is hereby incorporated by reference as though fully set forth herein.

BACKGROUND

[0002] The instant disclosure relates to catheters for use in medical procedures, such as electrophysiology studies. In particular, the instant disclosure relates to electrophysiology catheters that include ion-specific electrodes.

[0003] Catheters are used for an ever-growing number of procedures, such as diagnostic, therapeutic, and ablative procedures, to name just a few examples. Typically, the catheter is manipulated through the patient's vasculature and to the intended site, for example, a site within the patient's heart.

[0004] A typical electrophysiology catheter includes an elongate shaft and one or more electrodes on the distal end of the shaft. The electrodes may be used for ablation, diagnosis, or the like. Oftentimes, these electrodes include ring electrodes that extend about the entire circumference of the catheter shaft, as well as a tip electrode.

[0005] For endocardial electroanatomical mapping, the measured voltage of a measurement electrode in contact with myocardium generally includes two components. A first component is related to the local electric field generated by the membrane potential of the cardiomyocytes, versus a distant reference electrode. A second component is an electrochemical potential related to the difference in local chemical/ion concentration between the measurement electrode and the reference electrode. The second component (*e.g.*, electrochemical potential) may be dependent on the surface chemical composition of the measurement electrode.

[0006] Extant measurement electrodes, such as those utilized in the diagnosis and treatment of atrial fibrillation, are typically made of relatively inert platinum iridium alloys and thus exhibit little chemical specificity. Instead, they measure primarily on the first component described above, which can result in susceptibility to far-field noise, *e.g.*, from the left ventricle.

BRIEF SUMMARY

[0007] Disclosed herein is an electrophysiology catheter including: a body; and at least one electrode disposed on the body, wherein the at least one electrode includes an ion-selective coating. The ion-selective coating can be applied uniformly over the at least one electrode or can cover only a portion of the at least one electrode.

[0008] According to aspects of the disclosure, the at least one electrode also includes a tissue-penetrating texture. The tissue-penetrating texture can extend between about 0.1 μm and about 20 μm from a surface of the at least one electrode.

[0009] The ion-selective coating can include one or more of a bound form of an ionic chelating agent; a non-ionic compound with an ability to complex with a specific ion; a material that binds ions through specific surface interactions; and a material that binds ions through three-dimensional topology. For example, the ion-selective coating can include a crown ether, a zeolite, and/or ethylenediaminetetraacetic acid (EDTA).

[0010] According to aspects of the instant disclosure, the ion-selective coating is selective for one or more ions relative to cardiomyocyte membrane potentials, such as potassium, sodium, calcium, and/or chlorine.

[0011] It is contemplated that the ion-selective coating can have a thickness between 0.005 μm and 10 μm.

[0012] Also disclosed herein is a method of manufacturing an electrophysiology catheter, including the steps of: forming a catheter body; forming at least one electrode on the catheter body; and coating the at least one electrode with an ion-selective coating.

[0013] The method optionally also includes forming a tissue-penetrating texture on a surface of the at least one electrode. The tissue-penetrating texture can be formed by plating the tissue-penetrating texture onto the surface of the at least one electrode; by vacuum depositing the tissue-penetrating texture on the surface of the at least one electrode; and/or by laser sintering the tissue-penetrating texture into the surface of the at least one electrode.

[0014] The ion-selective coating is selective for one or more ions relative to cardiomyocyte membrane potentials, such as one or more of potassium, sodium, calcium, and chlorine. The ion-selective coating can be selected from the group consisting of ethylenediaminetetraacetic acid (EDTA), crown ethers, and zeolites.

[0015] The foregoing and other aspects, features, details, utilities, and advantages of the present invention will be apparent from reading the following description and claims, and from reviewing the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] Figure 1 schematically depicts an electrophysiology catheter and associated systems.

[0017] Figure 2 is a close-up view of the distal region of the catheter shown in Figure 1.

[0018] Figure 3 is a transverse cross-section taken along line 3-3 in Figure 2.

[0019] Figure 4 depicts the application of an ion-specific coating to a flat electrode.

[0020] Figure 5 is a close-up view of an alternative embodiment of the distal region of the catheter shown in Figure 1.

[0021] Figures 6A-6C depict configurations of tissue penetrating textures and the application of ion-specific coatings thereto according to various aspects of the disclosure.

DETAILED DESCRIPTION

[0022] For purposes of illustration, the present teachings will be described in connection with a multi-electrode mapping and ablation catheter 10, such as illustrated in Figure 1. As shown in Figure 1, catheter 10 generally includes an elongate catheter body 12 having a distal region 14 and a proximal end 16. A handle 18 is shown coupled to proximal end 16. Figure 1 also shows connectors 20. Connectors 20 are configured to be connected to a source of ablation energy (schematically illustrated as RF source 22, which can be, for example, the Ampere™ RF ablation generator of Abbott Laboratories), an electrophysiology mapping device (schematically illustrated as 24, which can be, for example, the EnSite Precision™ cardiac mapping system, also of Abbott Laboratories), and a programmable electrical stimulator (schematically illustrated as 25, which can be, for example the EP-4™ cardiac stimulator, also of Abbott Laboratories). Although Figure 1 depicts three separate connectors 20, it is within the scope of the instant disclosure to have a combined connector 20 that is configured for connection to two or more of RF source 22, electrophysiology mapping device 24, and programmable electrical stimulator 25.

[0023] Various additional aspects of the construction of catheter 10 will be familiar to those of ordinary skill in the art. For example, the person of ordinary skill in the art will recognize that catheter 10 can be made steerable, for example by incorporating an actuator into handle 18 that is coupled to one or more steering wires that extend through elongate catheter body 12 and that terminate in one or more pull rings within distal region 14. Likewise, the ordinarily skilled artisan will appreciate that catheter 10 can be an irrigated catheter, such that it can also be coupled to a suitable supply of irrigation fluid and/or an irrigation pump. As a further example, those of ordinary skill in the art will appreciate that catheter 10 can be equipped with force feedback capabilities.

[0024] Insofar as such features are not necessary to an understanding of the instant disclosure, they are neither illustrated in the drawings nor explained in detail herein. By way of example only, however, catheter 10 can incorporate various aspects and features the following catheters, all from Abbott Laboratories: the EnSite™ Array™ catheter; the FlexAbility™ ablation catheter; the Safire™ BLU™ ablation catheter; the Therapy™ Cool Path™ irrigated ablation catheter; the Livewire™ TC ablation catheter; and the TactiCath™ Quartz irrigated ablation catheter.

[0025] Figure 2 is a close-up of distal region 14 of catheter 10. Distal region 14 of catheter 10 includes a tip electrode 26 positioned at its distal end and a plurality of additional electrodes 28 proximal of tip electrode 26. In particular, Figure 2 depicts five ring electrodes 28. The person of ordinary skill in the art will understand and appreciate, however, that by varying the size (*e.g.*, width) and spacing of electrodes 28, different diagnostic and/or therapeutic objectives and/or outcomes can be achieved. For example, the ordinarily skilled artisan will appreciate that, as electrodes 28 become smaller and closer together, the electrograms collected thereby will become sharper and more localized evidencing better depiction of local, near-field depolarization of the cardiac tissue in contact with the electrodes. Thus, it should be understood that distal region 14 can include any number of such electrodes 28 (*e.g.*, 9 electrodes 28 for a decapolar catheter 10) and that the inter-electrode spacing can vary along the length of distal region 14.

[0026] Electrodes 28 may include any metal capable of detecting and conducting the local electrical signal. Suitable materials for electrodes 28 include, without limitation, platinum-iridium alloys and gold.

[0027] Electrodes 28 can also be of various physical configurations. These include, by way of example only, ring electrodes, segmented ring electrodes, partial ring electrodes, flexible circuit electrodes, balloon electrodes, and spot electrodes. Various configurations of electrodes 28 (as well as electrode 26) are disclosed in International Publication No. WO 2016/182876, which is hereby incorporated by reference as though fully set forth herein.

[0028] The instant disclosure provides ion-selective or ion-specific electrodes. Figure 3 is a transverse cross section of electrode 28, taken along line 3-3 in Figure 2, according to a first embodiment of the instant disclosure. As shown in Figure 3, electrode 28 includes an ion-selective coating 30.

[0029] Figure 4 depicts an ion-selective electrode 40 according to another aspect of the instant disclosure. More particularly, Figure 4 depicts a flat electrode 40, such as a flex circuit electrode, with an ion-selective coating 30 thereon.

[0030] The relative thicknesses of catheter body 12, electrode 28 or electrode 40, and ion-selective coating 30 are not to scale in Figures 3 and 4. In particular, the thickness of ion-selective coating 30 is exaggerated for visibility. According to aspects of the disclosure, however, ion-selective coating 30 can be between about 0.005 microns and about 10 microns in thickness.

[0031] Ion-selective coatings for electrodes will be familiar to those of skill in the art. *See, e.g.*, Mikhelson, *Ion Selective Electrodes* (Springer-Verlag Berlin Heidelberg, 2013), which is hereby incorporated by reference as though fully set forth herein. Those of ordinary skill in the art will also be familiar with cardiac voltage map optical imaging using ion-sensitive chromophores. *See, e.g.*, Herron et al., *Optical Imaging of Voltage and Calcium in Cardiac Cells & Tissues*, Circulation Research (2012), which is hereby incorporated by reference as though fully set forth herein. Further, the ordinarily skilled artisan will appreciate that electrodes with ion-selective coatings can be used for the characterization of neural electrical activity. *See, e.g.*, Haack et al., *Double-barreled and Concentric Microelectrodes for Measurement of Extracellular Ion Signals in Brain Tissue*, J. Visualized Experiments (2015), which is hereby incorporated by reference as though fully set forth herein. Indeed, signal amplifications from calcium-specific functionalized electrodes, including super-Nernstian response, on the order of 100 mV have been reported. *See, e.g.*, Konopka et al., *Factors Affecting the Potentiometric Response of All-Solid-State Solvent Polymeric Membrane Calcium-Selective Electrode for Low-*

Level Measurements, Anal. Chem. (2004), which is hereby incorporated by reference as though fully set forth herein.

[0032] According to aspects of the instant disclosure, ion-selective coating 30 can be sensitive to any combination of ions relative to cardiomyocyte membrane potentials, including, without limitation, potassium, sodium, calcium, and chlorine. For example, insofar as it is understood that the local extracellular calcium concentration exhibits a relatively pronounced fractional change during the cardiac cycle (*see, e.g.*, Hrabcova et al., *Effect of Ion Concentration Changes in the Limited Extracellular Spaces on Sarcolemnal Ion Transport and Ca2+ Turnover in a Model of Human Ventricular Cardiomyocyte*, Int. J. Mol. Sci. (2013), which is hereby incorporated by reference as though fully set forth herein), it is desirable for ion-selective coating 30 to be sensitive to calcium.

[0033] Ion-selective coating 30 can include any material that affects the electrode surface voltage through specific chemical interaction with the local ion milieu. Suitable materials for ion-selective coating 30 include, without limitation, bound forms of ionic chelating agents (*e.g.*, ethylenediaminetetraacetic acid (EDTA)); non-ionic compounds with the ability to complex with specific ions (*e.g.*, crown ethers); and materials that bind ions through specific surface interactions or three-dimensional topology (*e.g.*, zeolites).

[0034] Figure 5 is a close-up of an alternative embodiment of the distal region of catheter 10, designated 14', that illustrates additional aspects of the instant disclosure. Figure 5 shows an alternative tip electrode 26', an alternative ring electrode 28', and an alternative flat electrode 40'. Each of tip electrode 26', ring electrode 28', and flat electrode 40' includes a tissue-penetrating texture 50. Tissue penetrating texture 50 allows electrodes 26', 28', and 40' to penetrate through the endothelium layer of the endocardium in order to facilitate the detection of ion variability.

[0035] According to aspects of the instant disclosure, tissue penetrating texture 50 extends between about 0.1 μm and about 20 μm from the surface of electrodes 26', 28', and 40'. Tissue penetrating texture 50 can be formed, for example, by plating, by vacuum deposition, by laser sintering, or by any other suitable manufacturing method.

[0036] Although tissue penetrating texture 50 is depicted in Figure 5 as a sawtooth feature, other configurations, such as a series of plateaus (*see, e.g.*, Figure 6C) are regarded as within the scope of the instant disclosure.

[0037] Figures 6A through 6C depict various approaches to applying ion-selective coating 30 to tissue penetrating texture 50. For example, as shown in Figure 6A, ion-selective coating 30 covers substantially all of tissue penetrating texture 50, as well as substantially the entire surface of the underlying electrode (*e.g.*, electrode 26', 28', and/or 40').

[0038] As another example, Figure 6B depicts ion-selective coating 30 covering only a tip of a sawtooth-shaped tissue penetrating texture 50. Thus, in the embodiment of the disclosure depicted in Figure 6B, ion-selective coating 30 covers only a portion of the underlying electrode (*e.g.*, electrode 26', 28', and/or 40').

[0039] Figure 6C similarly depicts ion-selective coating 30 covering only a portion of tissue penetrating texture 50, and therefore only a portion of the underlying electrode. More particularly, Figure 6C depicts an embodiment where ion-selective coating 30 covers the plateau of a plateau-shaped tissue penetrating texture.

[0040] In use, electrodes with ion-selective coatings as disclosed herein advantageously offer improved sensitivity to the true localized action potential sequence, allowing for an increased reliance on the second component of voltage signals measured by intracardiac electrodes. This, in turn, results in less susceptibility to far-field noise when measuring intracardiac electrograms.

[0041] Although several embodiments have been described above with a certain degree of particularity, those skilled in the art could make numerous alterations to the disclosed embodiments without departing from the spirit or scope of this disclosure.

[0042] All directional references (*e.g.*, upper, lower, upward, downward, left, right, leftward, rightward, top, bottom, above, below, vertical, horizontal, clockwise, and counterclockwise) are only used for identification purposes to aid the reader's understanding of the present invention, and do not create limitations, particularly as to the position, orientation, or use of the invention. Joinder references (*e.g.*, attached, coupled, connected, and the like) are to be construed broadly and may include intermediate members between a connection of elements and relative movement between elements. As such, joinder references do not necessarily infer that two elements are directly connected and in fixed relation to each other.

[0043] It is intended that all matter contained in the above description or shown in the accompanying drawings shall be interpreted as illustrative only and not limiting. Changes in detail or structure may be made without departing from the spirit of the invention as defined in the appended claims.

CLAIMS

What is claimed is:

1. An electrophysiology catheter, comprising:

a body; and

at least one electrode disposed on the body, wherein the at least one electrode comprises an ion-selective coating.

2. The electrophysiology catheter according to claim 1, wherein the ion-selective coating is applied uniformly over the at least one electrode.

3. The electrophysiology catheter according to claim 1, wherein the ion-selective coating covers only a portion of the at least one electrode.

4. The electrophysiology catheter according to claim 1, wherein the at least one electrode further comprises a tissue-penetrating texture.

5. The electrophysiology catheter according to claim 4, wherein the tissue-penetrating textured extends between 0.1 μm and 20 μm from a surface of the at least one electrode.

6. The electrophysiology catheter according to claim 1, wherein the ion-selective coating comprises one or more of a bound form of an ionic chelating agent; a non-ionic compound with an ability to complex with a specific ion; a material that binds ions through specific surface interactions; and a material that binds ions through three-dimensional topology.

7. The electrophysiology catheter according to claim 6, wherein the ion-selective coating comprises a crown ether.

8. The electrophysiology catheter according to claim 6, wherein the ion-selective coating comprises a zeolite.

9. The electrophysiology catheter according to claim 6, wherein the ion-selective coating comprises ethylenediaminetetraacetic acid (EDTA).

10. The electrophysiology catheter according to claim 1, wherein the ion-selective coating is selective for one or more ions relative to cardiomyocyte membrane potentials.

11. The electrophysiology catheter according to claim 10, wherein the ion-selective coating is selective for one or more of potassium, sodium, calcium, and chlorine.

12. The electrophysiology catheter according to claim 1, wherein the ion-selective coating has a thickness between 0.005 μm and 10 μm.

13. A method of manufacturing an electrophysiology catheter, comprising:

forming a catheter body;

forming at least one electrode on the catheter body; and

coating the at least one electrode with an ion-selective coating.

14. The method according to claim 13, further comprising forming a tissue-penetrating texture on a surface of the at least one electrode.

15. The method according to claim 14, wherein forming a tissue-penetrating texture on a surface of the at least one electrode comprises plating the tissue-penetrating texture onto the surface of the at least one electrode.

16. The method according to claim 14, wherein forming a tissue-penetrating texture on a surface of the at least one electrode comprises vacuum depositing the tissue-penetrating texture on the surface of the at least one electrode.

17. The method according to claim 14, wherein forming a tissue-penetrating texture on a surface of the at least one electrode comprises laser sintering the tissue-penetrating texture into the surface of the at least one electrode.

18. The method according to claim 13, wherein the ion-selective coating is selective for one or more ions relative to cardiomyocyte membrane potentials.

19. The method according to claim 13, wherein the ion-selective coating is selective for one or more of potassium, sodium, calcium, and chlorine.

20. The method according to claim 13, wherein the ion-selective coating is selected from the group consisting of ethylenediaminetetraacetic acid (EDTA), crown ethers, and zeolites.

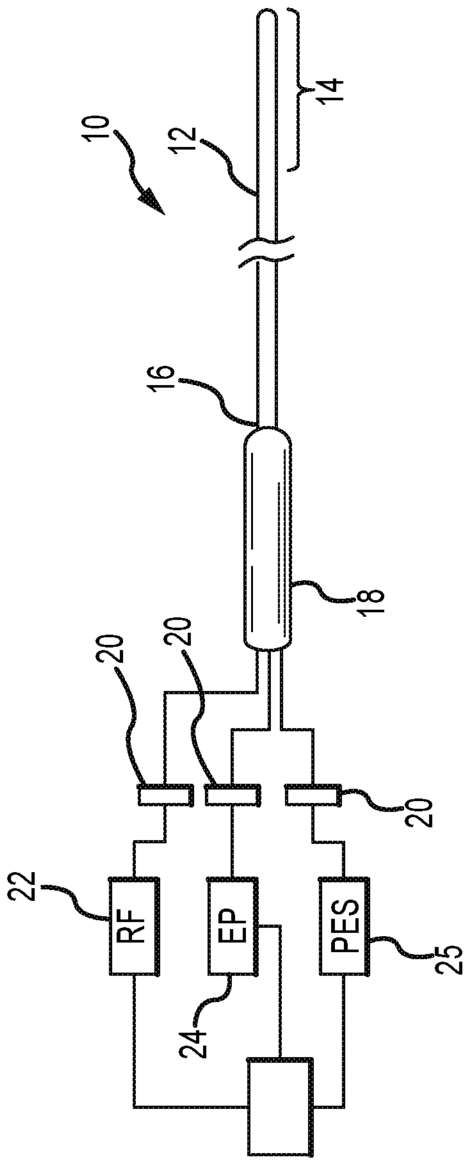

FIG.1

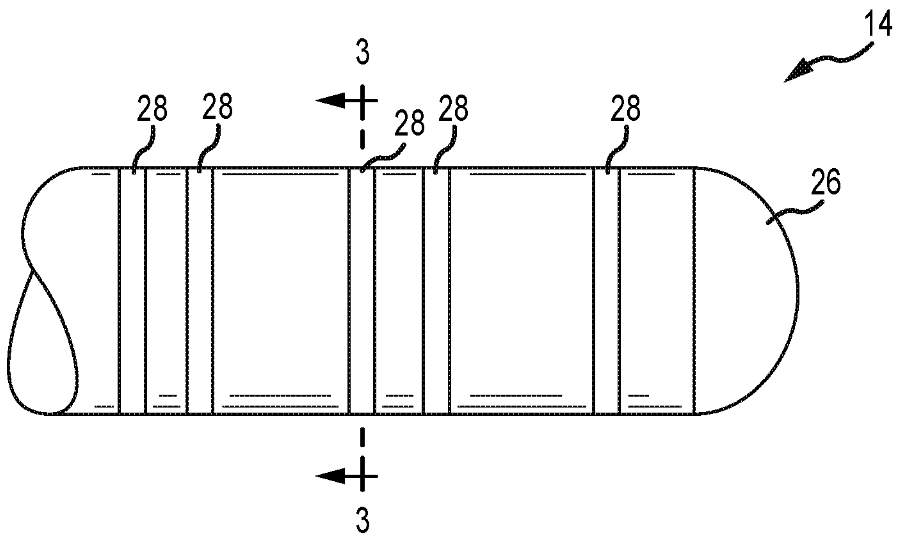

FIG.2

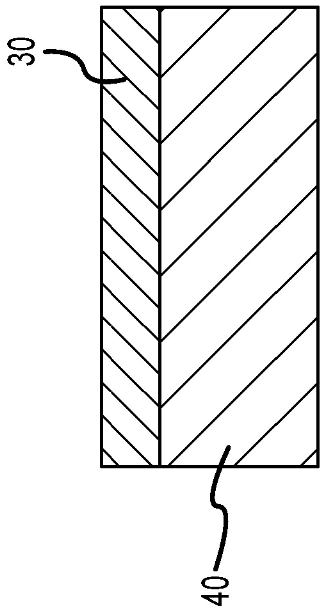

FIG.4

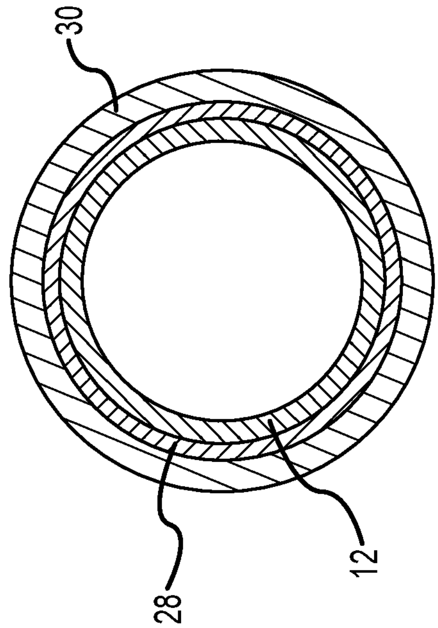

FIG.3

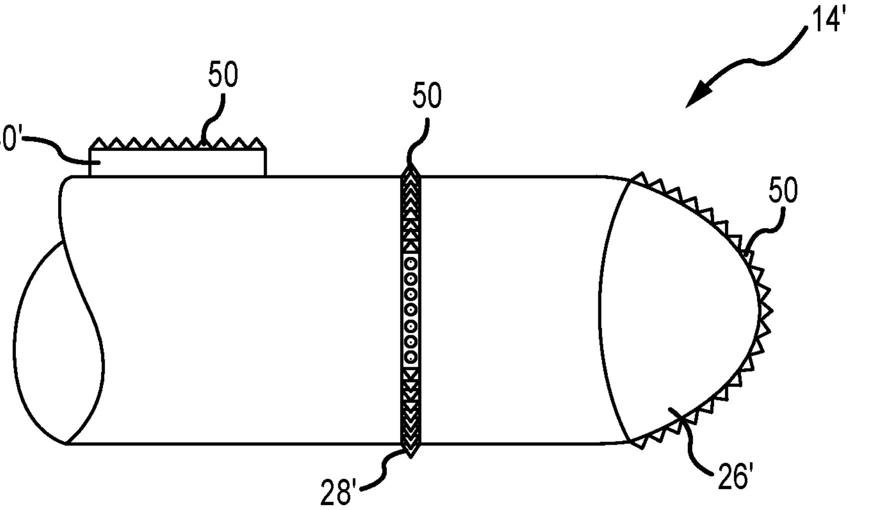

FIG.5

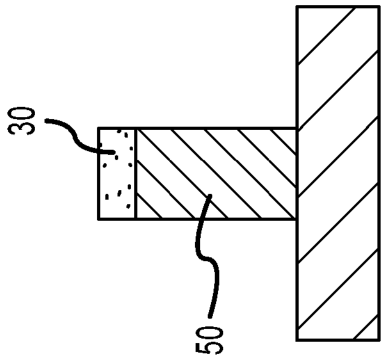

FIG.6C

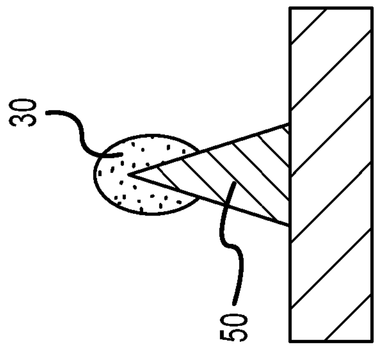

FIG.6B

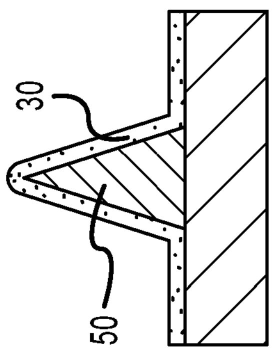

FIG.6A

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2018/031052

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B18/14 A61L29/08
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98/58681 A2 (EP TECHNOLOGIES [US]) 30 December 1998 (1998-12-30)	1-4,6, 10-15, 18,19
Y	page 4, line 26 - page 10, line 24; figures 1-10 page 11, line 30 - page 13, line 23 -----	5,7-9, 16,17,20
Y	US 2014/172010 A1 (VEZZU GUIDO [CH]) 19 June 2014 (2014-06-19) paragraph [0037]; figures 1-2 -----	5
Y	WO 2007/005910 A2 (MC3 INC [US]; UNIV MICHIGAN [US]; MERZ SCOTT I [US]; REYNOLDS MELISSA) 11 January 2007 (2007-01-11) paragraphs [0071] - [0075] paragraphs [0124] - [0126] ----- -/--	7,16,20

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 August 2018	17/08/2018

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Schnurbusch, Daniel

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2018/031052

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 02/18003 A1 (BIOCOAT INC [US]; AGION TECHNOLOGIES LLC [US]) 7 March 2002 (2002-03-07) pages 10-13	8
Y	WO 94/10838 A1 (UNIV TEXAS [US]) 26 May 1994 (1994-05-26) page 6, line 19 - page 8, line 32	9
Y	WO 2015/138360 A1 (MASSON STEPHEN C [US]; CUCHIARA MICHAEL [US]; MIRANDA EFRAIN A [US]; G) 17 September 2015 (2015-09-17) page 14, line 21 - page 15, line 6	17

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
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