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(54) Title: OPTICAL DEVICE, SYSTEM AND METHOD OF MONITORING THERMAL THERAPY IN SOFT TISSUE

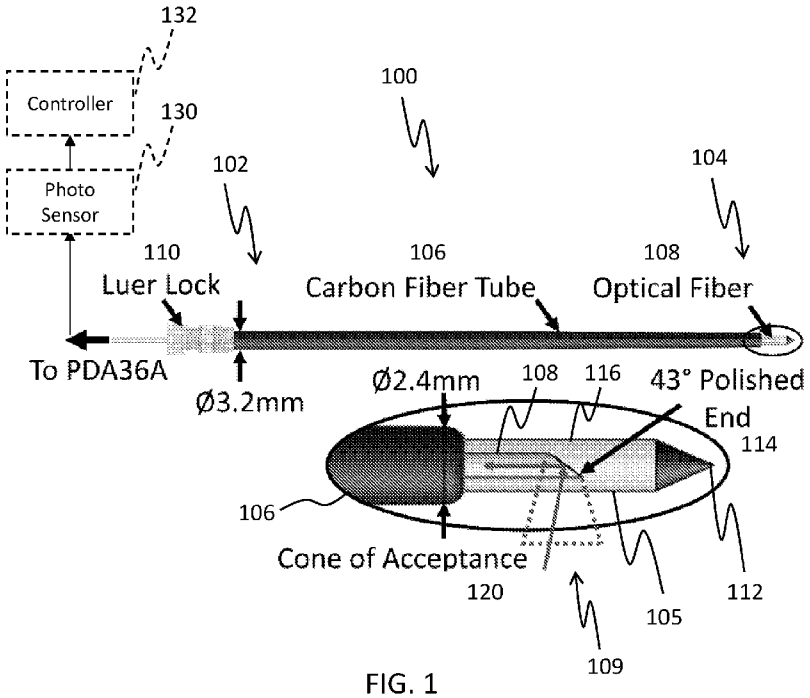

FIG. 1

(57) Abstract: An optical probe system includes an elongate rigid housing having a proximal end, a distal end, and an optically transparent portion near a distal tip of the housing. A photo sensing element includes a distal tip positioned within the optically transparent portion of the housing. A controller is configured to detect a coagulation boundary based on a photovoltage measured from the photo sensing element. An optical probe and a method for determining a coagulation boundary is also disclosed.

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[Continued on next page]

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OPTICAL DEVICE, SYSTEM AND METHOD OF MONITORING THERMAL THERAPY IN SOFT TISSUE

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Patent Application No. 62/699,064 filed July 17, 2018, the contents of which are incorporated by reference herein in their entirety.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

[0002] This invention was made with government support under Grant Number CA218547, awarded by the National Institutes of Health. The government has certain rights in the invention.

BACKGROUND OF THE INVENTION

[0003] Laser interstitial thermal therapy (LITT), also known as focal laser ablation (FLA), has been demonstrated to be a promising method of focal therapy for prostate cancer. The procedure includes inserting a laser fiber into a target tumor and raising the temperature above 60°C. A 980nm diode laser is commonly used. For a single laser ablation, exposure duration lies in the range of 1-10 minutes. The goal of the procedure is to induce coagulative necrosis within a desired region of interest (ROI)

while minimizing damage to surrounding healthy tissue. It is therefore necessary to monitor the growth of the induced coagulation zone in real time. Magnetic resonance thermometry (MRT) and interstitial thermal probes are conventionally used for monitoring the growth of the coagulation zone.

[0004] MRT facilitates quantification of thermal maps throughout the target organ. These thermal maps can be converted to damage maps using the Arrhenius damage model to determine the onset of coagulative necrosis. The resulting damage maps have been shown to be inaccurate due to motion artefact and errors inherent to the Arrhenius model due to incomplete characterization of tissue properties i.e. the frequency factor and activation energy barrier. Due to the problems inherent to this model, it is unlikely that such an approach will ever be capable of ensuring treatment success. Moreover, MRT is both time consuming and expensive.

[0005] There is a need in the art for an improved and minimally invasive method of monitoring thermal therapy, and an improved device, system and method for performing LITT without relying on MRT or the Arrhenius damage model. The device, system and method should also improve the time and cost associated with operating conventional devices, systems and methods for performing LITT.

SUMMARY OF THE INVENTION

[0006] In one embodiment, an optical probe system includes an elongate rigid housing having a proximal end, a distal end, and an optically transparent portion near a distal tip of the housing; a photo sensing element having a distal tip positioned within

the optically transparent portion of the housing; and a controller configured to detect a coagulation boundary based on a photovoltage measured from the photo sensing element. In one embodiment, the photo sensing element is an optical fiber, and wherein the distal tip has an angled edge. In one embodiment, the angled edge is a polished edge. In one embodiment, the angled edge is angled between 30 degrees and 45 degrees relative to a longitudinal axis of the probe. In one embodiment, the angled edge is angled at 43 degrees relative to a longitudinal axis of the probe. In one embodiment, a distal tip of the housing is optically opaque. In one embodiment, the optical fiber has a core diameter between 50 μm and 500 μm. In one embodiment, the entire elongate rigid housing comprises an optically transparent material and portions of the elongate rigid housing are coated with an optically opaque material. In one embodiment, the optically transparent portion is at least partially surrounded by an optically opaque portion to limit an optical cone of acceptance. In one embodiment, the photo sensing element is a diffuser. In one embodiment, the controller is configured to determine when a coagulation boundary reaches the probe based on a measured decrease and plateau in photovoltage detected. In one embodiment, the controller is configured to determine when the coagulation boundary reaches the probe based on a comparison to a previously measured baseline voltage.

[0007] In one embodiment, a method for determining a coagulation boundary includes the steps of advancing an optical probe to a target coagulation boundary within a patient; measuring photovoltage detected from the optical probe; and determining when the coagulation boundary reaches the probe based on a measured decrease and plateau in photovoltage detected. In one embodiment, the method includes the step of

orientating the optical probe such that the cone of acceptance is directed towards a light source within the patient. In one embodiment, the method includes the step of acquiring a baseline photovoltage. In one embodiment, the method includes determining when the coagulation boundary reaches the probe based on a comparison to the acquired baseline voltage.

[0008] In one embodiment, an optical probe includes an elongate rigid housing having a proximal end, a distal end, and an optically transparent portion near a distal tip of the housing; and an optical fiber having an angled distal tip positioned within an optically transparent portion of the housing. In one embodiment, the optically transparent portion is at least partially surrounded by an optically opaque portion to limit an optical cone of acceptance. In one embodiment, the angled edge is angled between 30 degrees and 45 degrees relative to a longitudinal axis of the probe.

[0009] In one embodiment, an optical probe includes an elongate rigid housing having a proximal end, a distal end, and an optically transparent portion near a distal tip of the housing; and a diffuser positioned within an optically transparent portion of the housing; where the optically transparent portion is at least partially surrounded by an optically opaque portion to limit an optical cone of acceptance.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] The foregoing purposes and features, as well as other purposes and features, will become apparent with reference to the description and accompanying figures

below, which are included to provide an understanding of the invention and constitute a part of the specification, in which like numerals represent like elements, and in which:

[0011] Figure 1 is side view of an optical probe and system according to one embodiment.

[0012] Figure 2 is a side view of a guide system utilizing the optical probe according to one embodiment.

[0013] Figure 3 is a flow chart of a method for determining a coagulation boundary according to one embodiment.

[0014] Figure 4 is an experimental setup according to one embodiment.

[0015] Figure 5 is a graph of experimental data illustrating the signal response according to the setup of Fig. 4 during thermal therapy according to one embodiment.

DETAILED DESCRIPTION OF THE INVENTION

[0016] It is to be understood that the figures and descriptions of the present invention have been simplified to illustrate elements that are relevant for a more clear comprehension of the present invention, while eliminating, for the purpose of clarity, many other elements found in systems and methods of monitoring thermal therapy in soft tissue. Those of ordinary skill in the art may recognize that other elements and/or steps are desirable and/or required in implementing the present invention. However, because such elements and steps are well known in the art, and because they do not facilitate a better understanding of the present invention, a discussion of such elements

and steps is not provided herein. The disclosure herein is directed to all such variations and modifications to such elements and methods known to those skilled in the art.

[0017] Unless defined otherwise, all technical and scientific terms used herein have the same meaning 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 and materials are described.

[0018] As used herein, each of the following terms has the meaning associated with it in this section.

[0019] The articles "a" and "an" are used herein to refer to one or to more than one (*i.e.*, to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

[0020] "About" as used herein when referring to a measurable value such as an amount, a temporal duration, and the like, is meant to encompass variations of ±20%, ±10%, ±5%, ±1%, and ±0.1% from the specified value, as such variations are appropriate.

[0021] Ranges: throughout this disclosure, various aspects of the invention can be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the invention. Where appropriate, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a

range such as from 1 to 6 should be considered to have specifically disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 2.7, 3, 4, 5, 5.3, and 6. This applies regardless of the breadth of the range.

[0022] Referring now in detail to the drawings, in which like reference numerals indicate like parts or elements throughout the several views, in various embodiments, presented herein is a device, system and method for monitoring thermal therapy in soft tissue.

[0023] Embodiments described herein take advantage of thermally induced changes in laser-tissue interaction, which present a method of assessing tissue coagulation in real time. The propagation of light in tissue is governed by the absorption coefficient (μ_a) and the reduced scattering coefficient (μ'_s). Thermal tissue damage can in certain instances cause up to a five-fold increase in total attenuation. This is predominantly due to increased scatter as a result of thermally induced protein coagulation. Embodiments described herein utilize an interstitial optical probe capable of identifying the LITT induced coagulation boundary based on thermally induced changes in laser-tissue interaction.

[0024] In one embodiment, the Interstitial Optical Monitoring System (IOMS) can be used to monitor laser, radiofrequency and microwave ablation of soft tissue. A primary component of the IOMS is an optical probe which facilitates interrogation of tissue optical properties in real-time. For laser ablation the probe collects photons emitted from the laser fiber during treatment. In radiofrequency and microwave ablation, the

transducer can be adapted to contain a near infrared light source. The light source would be used for monitoring only and could thus be low power. The optical probe is positioned at the desired coagulation boundary prior to ablation. Data from the probe is analyzed to provide feedback to the operator or direct control of the ablation system via a feedback loop.

[0025] With reference now to Fig. 1, according to one embodiment, an optical probe 100 has a proximal 102 and distal 104 end and includes an optical fiber 108 housed within a rigid tube 106 having a sharp point 112 to facilitate insertion into soft tissue. In one embodiment, the optical fiber 108 has a core diameter in the range 50-500μm. In one embodiment, the tip 114 of the optical fiber 108 is angled to enable collection of light from a constrained range of angles denoted as the cone of acceptance 120. The angle may be achieved by polishing the fiber 108. In one embodiment, the angle lies in the range of 30-45°. In one embodiment, the angle is 43°. In one embodiment the entire tube 106 is manufactured from an optically transparent material such as polycarbonate to ensure light transmission to the fiber 108. The transparent housing can be coated with an optically opaque material to further constrain the cone of acceptance 120. For example, in one embodiment, coating the tip 112 of the probe is necessary to ensure that the majority of light is collected from the cone of acceptance 120 defined by the angle of the fiber tip 114. In another embodiment, the housing is opaque with an optical window 105 positioned to facilitate light transmission to the tip of the sensor. The optical window 105 may be composed of polycarbonate, glass or other transparent material. In another embodiment, the optical fiber 108 contains a diffuser instead of an angled tip. In one embodiment, the length of the diffuser lies in the range

0.5-10mm. The diffuser can collect light from all angles but can be constrained based on the geometry of the optical window 105 in the probe housing.

[0026] The optical fiber 108 transmits light to a photosensor 130 such as an amplified photodiode (for example, a PDA36A by Thorlabs). The resulting signal is recorded using a controller 132, such as a microcontroller or other computing device (for example, an Arduino Due). In one embodiment, the signal is sampled in the range of 1-1000Hz. Data is analyzed and displayed on a GUI in real-time. In one embodiment a GUI is a python script running on a PC. In one embodiment, the GUI provides feedback to the operator indicating when the desired volume of tissue has been ablated. The operator can then manually adjust or cease ablation. In another embodiment, the GUI interfaces directly with the ablation system and automatically adjusts parameters such as power and coolant flowrate to achieve the predefined ablation volume.

[0027] In one embodiment, the probe 100 is designed to be MR safe, and thus is made from carbon fiber. A luer lock 110 is connected to a proximal end of the probe. The optical fiber 108 is held in place by the luer lock 100. Distally, the polycarbonate tip 112 is press fit into the carbon fiber tube 106. The enlargement of Fig. 1 shows the fiber optic 108 within the polycarbonate casing 116. The distal tip 112 of the polycarbonate has been coated with ink to prevent light from entering directly into the fiber 108 rather than reflecting off the polished edge 114 as illustrated by the cone of acceptance 120.

[0028] Fig. 2 illustrates a clinical setup of a system 200 according to one embodiment. The system 200 consists of a needle guide 204 placed on an ultrasound probe 202. The needle guide 204 contains a central channel 205 housing a laser fiber 208 within a catheter. The secondary channel 207 contains an optical probe 206. MR-US fusion guidance is used to place the laser fiber 208 within the target tumor (or a targeted "region of interest" ROI) 212. The secondary channel 207 ensures that the optical probe 206 is placed at the desired boundary of thermal coagulation 212. Although the setup shows laser ablation, it could be adapted for microwave or radiofrequency ablation. For microwave or radiofrequency modalities, a light source should be included. Multiple needle guides could be used to achieve various coagulation radii. In one embodiment, the typical range is 4-10mm.

[0029] In one embodiment, the optical probe consists of a single fiber optic, thus, permitting measurement at a single point. Due to the small size of the fiber, it is possible to bundle multiple fibers within the same probe. For example if the length of the ablation zone is in the range of 10-50mm, multiple measurements along this length may be desirable.

[0030] Successful treatment not only requires treatment of the target tissue, but also requires that nearby critical structures are not damaged. For example, when treating areas of the prostate, it is critical that the rectal wall remains intact. To ensure this, the sensing element at the tip of the laser fiber could be spaced along the probe trajectory such that at least one lies between the expected ablation zone and the rectal wall. The signal from this sensing element can be used to ensure the safety of the rectal wall.

[0031] In one embodiment, thermal probes (fluoroptic, thermistors, thermocouples etc.) can also be incorporated into the probe. By combining thermal and optical data, it is possible to modulate ablation parameters in real-time to ensure a successful treatment. In one operational example: An optical probe is directed towards the laser diffuser and a rapid decrease in optical signal observed. A slow rate of temperature increase recorded by thermal sensor. This suggests that tissue near the fiber is coagulating rapidly, thus trapping the light. Continuing the procedure is likely to result in a small ablation zone and damage to the laser fiber or laser fiber housing due to high temperatures. To counteract this, the flowarate of the coolant could be increased and/or the laser power reduced. Alternatively, the fiber could be repositioned to achieve multiple small ablation zones.

[0032] A method 300 of determining a coagulation boundary is shown in Fig. 3 according to one embodiment. The method includes the steps of advancing an optical probe to a target coagulation boundary 302, measuring photovoltage detected from the optical probe 304, and determining when the coagulation boundary reaches the probe based on a measured decrease and plateau in photovoltage detected 306. In one embodiment, the optical probe is orientated such that the cone of acceptance is directed towards the light source. In LITT, according to one embodiment, baseline photovoltage is acquired during the first 5 seconds of laser activation. In microwave and radiofrequency ablation, according to one embodiment, baseline photovoltage is typically acquired prior to ablation. During ablation, recorded photovoltage is compared to baseline photovoltage. As Figs. 4 and 5 demonstrate with regard to the experimental results, as the ablation zone advances towards the sensor, there is a decrease in

signal. This occurs because coagulation causes an increase in scatter thus decreasing light penetration and ultimately trapping light within the coagulation zone. A signal plateau is observed as the coagulation boundary reaches the sensor indicating that no further coagulation is possible between the probe and source. In one embodiment, once the plateau is observed, the GUI indicates to the user that the treatment is complete and the user may manually cease ablation. In a further embodiment, the GUI automatically terminates treatment without manual user input.

[0033] In a further embodiment, the probe is orientated such that the cone of acceptance is directed away from the light source. As before, a baseline signal is acquired. Once the probe has been encompassed by the coagulation zone an increase in signal is observed. This occurs as once the probe is encapsulated within the coagulation zone, trapped light scatters backwards causing an increase in signal. In one embodiment, once the signal rise is observed, the GUI indicates to the user that the treatment is complete and the user may manually cease ablation. In a further embodiment, the GUI automatically terminates treatment without manual user input.

EXPERIMENTAL EXAMPLES

[0034] The invention is now described with reference to the following Examples. These Examples are provided for the purpose of illustration only and the invention should in no way be construed as being limited to these Examples, but rather should be construed to encompass any and all variations which become evident as a result of the teaching provided herein.

[0035] Without further description, it is believed that one of ordinary skill in the art can, using the preceding description and the following illustrative examples, make and utilize the present invention and practice the claimed methods. The following working examples therefore, specifically point out the preferred embodiments of the present invention, and are not to be construed as limiting in any way the remainder of the disclosure.

[0036] In the experimental setup shown in Fig. 4, the IOMS consists of a 200μm optical fiber with a 43° tip. The fiber is connected to a photodiode (PDA36A, Thorlabs, NJ) and photovoltage (PV) is recorded using a microcontroller and software. The system was tested by mimicking clinical conditions in which patients underwent 980nm LITT at 13.75W for 3 min. The optical probe was orientated with the cone of acceptance directed towards the laser fiber. The coagulation zone was tracked in real-time using a 3T MRI scanner (Prisma, Siemens) with a T2-weighted turbo spin echo (TSE) cine sequence (TE = 15ms, TR = 390ms, resolution = 0.9*0.9*2mm3, acquisition time = 2s). The experiment was repeated for probe distances (r) of 4, 5, 6 & 7mm from the laser fiber.

[0037] Fig. 5 shows the relationship between the growth of the LITT induced coagulation zone and PV. The coagulation radius is derived from the MRI data using a custom Matlab script to track the coagulation boundary. PV is normalized by dividing each value by the reading at t = 1s. For each experiment, PV decreases as the coagulation boundary approaches the optical probe. The signal plateaus as the coagulation boundary reaches the sensor. This is the first time that this relationship has been empirically demonstrated. It is hypothesized that the signal plateau can be used

to achieve predefined coagulation zones by placing the optical probe at the desired boundary prior to laser activation. At r=4mm, PV increases after the plateau has been observed. This may be due to backscatter as the coagulation boundary extends beyond the probe.

[0038] The disclosures of each and every patent, patent application, and publication cited herein are hereby incorporated herein by reference in their entirety. While this invention has been disclosed with reference to specific embodiments, it is apparent that other embodiments and variations of this invention may be devised by others skilled in the art without departing from the true spirit and scope of the invention.

CLAIMS

What is claimed is:

1. An optical probe system comprising:

an elongate rigid housing having a proximal end, a distal end, and an optically transparent portion near a distal tip of the housing;

a photo sensing element having a distal tip positioned within the optically transparent portion of the housing; and

a controller configured to detect a coagulation boundary based on a photovoltage measured from the photo sensing element.

2. The optical probe system of claim 1, wherein the photo sensing element is an optical fiber, and wherein the distal tip has an angled edge.

3. The optical probe system of claim 2, wherein the angled edge is a polished edge.

4. The optical probe system of claim 2, wherein the angled edge is angled between 30 degrees and 45 degrees relative to a longitudinal axis of the probe.

5. The optical probe system of claim 2, wherein the angled edge is angled at 43 degrees relative to a longitudinal axis of the probe.

6. The optical probe system of claim 1, wherein a distal tip of the housing is optically opaque.

7. The optical probe system of claim 1, wherein the optical fiber has a core diameter between 50 μm and 500 μm.

8. The optical probe system of claim 1, wherein the entire elongate rigid housing comprises an optically transparent material and portions of the elongate rigid housing are coated with an optically opaque material.

9. The optical probe system of claim 1, wherein the optically transparent portion is at least partially surrounded by an optically opaque portion to limit an optical cone of acceptance.

10. The optical probe system of claim 1, wherein photo sensing element is a diffuser.

11. The optical probe system of claim 1, wherein the controller is configured to determine when a coagulation boundary reaches the probe based on a measured decrease and plateau in photovoltage detected.

12. The optical probe system of claim 11, wherein the controller is configured to determine when the coagulation boundary reaches the probe based on a comparison to a previously measured baseline voltage.

13. A method for determining a coagulation boundary comprising:
advancing an optical probe to a target coagulation boundary within a patient;
measuring photovoltage detected from the optical probe; and
determining when the coagulation boundary reaches the probe based on a measured decrease and plateau in photovoltage detected.

14. The method of claim 13 further comprising:
orientating the optical probe such that the cone of acceptance is directed towards a light source within the patient.

15. The method of claim 13 further comprising:
acquiring a baseline photovoltage.

16. The method of claim 15 further comprising:

determining when the coagulation boundary reaches the probe based on a comparison to the acquired baseline voltage.

17. An optical probe comprising:

an elongate rigid housing having a proximal end, a distal end, and an optically transparent portion near a distal tip of the housing; and

an optical fiber having an angled distal tip positioned within an optically transparent portion of the housing.

18. The optical probe of claim 17, wherein the optically transparent portion is at least partially surrounded by an optically opaque portion to limit an optical cone of acceptance.

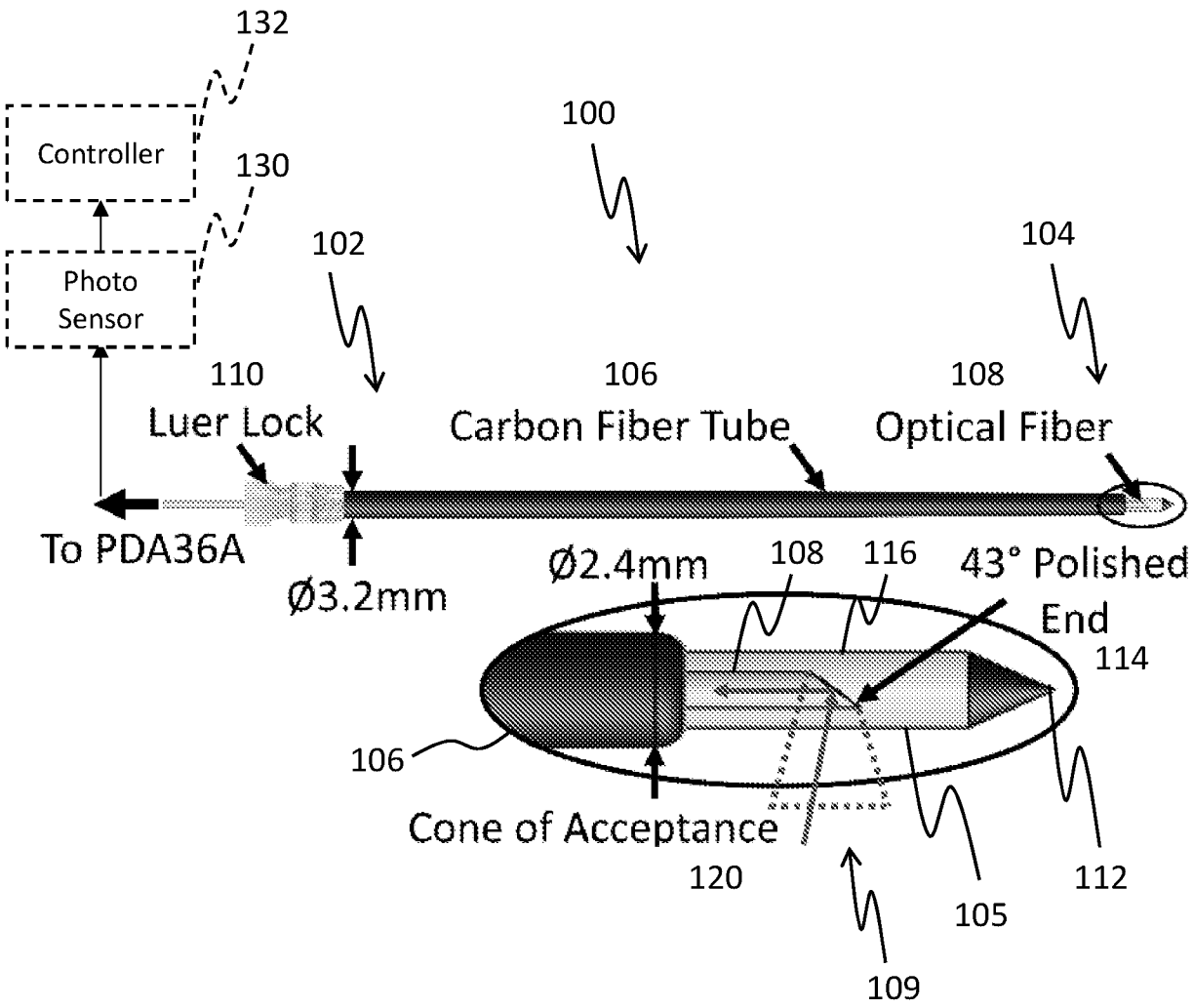
19. The optical probe of claim 17, wherein the angled edge is angled between 30 degrees and 45 degrees relative to a longitudinal axis of the probe.

20. An optical probe comprising:

an elongate rigid housing having a proximal end, a distal end, and an optically transparent portion near a distal tip of the housing; and

a diffuser positioned within an optically transparent portion of the housing;

wherein the optically transparent portion is at least partially surrounded by an optically opaque portion to limit an optical cone of acceptance.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114
106
Cone of Acceptance
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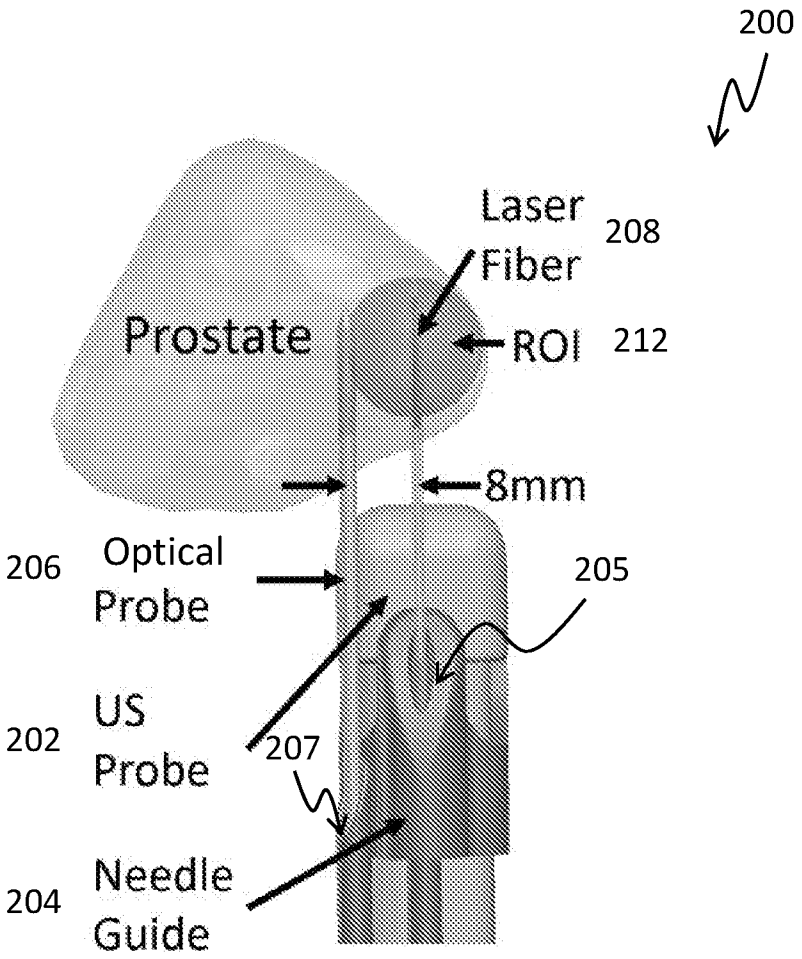
105
112
109

FIG. 1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Fiber
208
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ROI
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Optical
Probe
205
202
US
Probe
207
204
Needle
Guide

FIG. 2

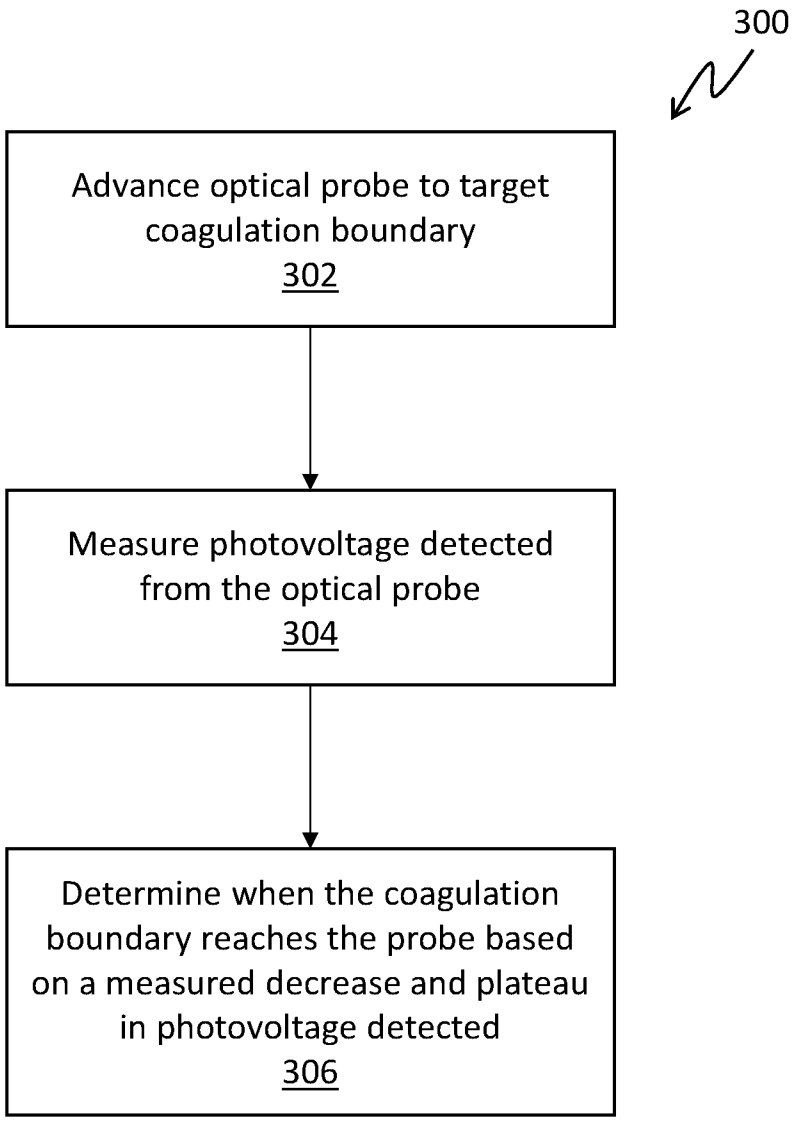
300
Advance optical probe to target coagulation boundary
302
Measure photovoltage detected from the optical probe
304
Determine when the coagulation boundary reaches the probe based on a measured decrease and plateau in photovoltage detected
306

FIG. 3

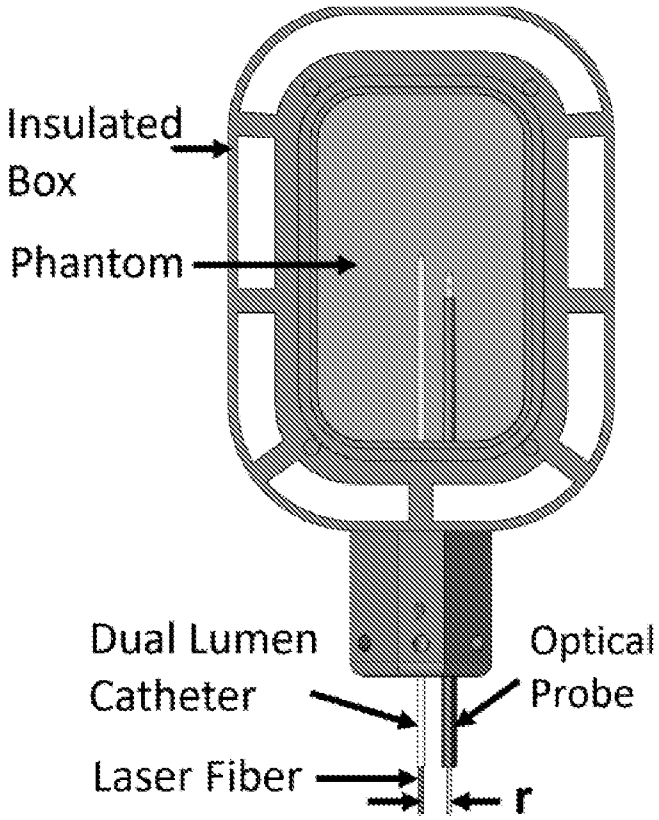
Insulated
Box
Phantom
Dual Lumen
Catheter
Optical
Probe
Laser Fiber
r

FIG. 4

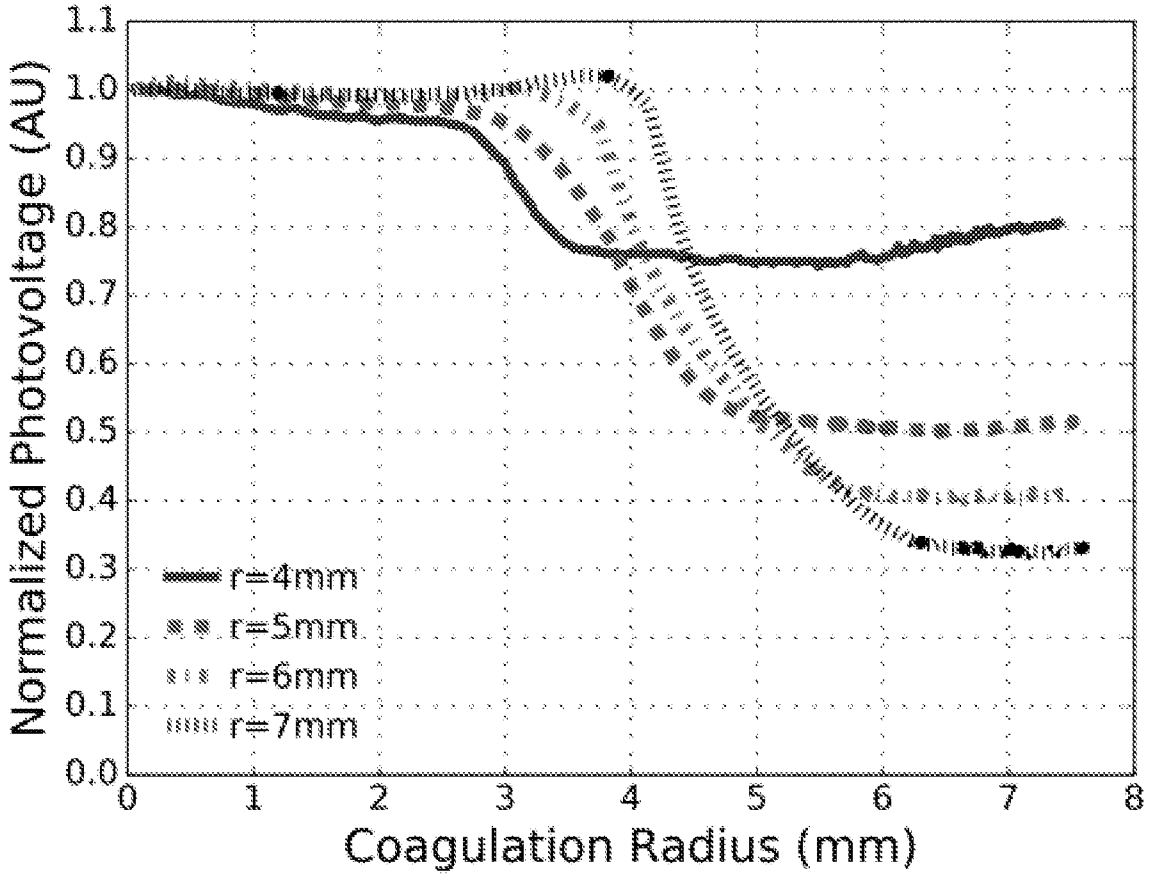
Normalized Photovoltage (AU)
Coagulation Radius (mm)
r=4mm
r=5mm
r=6mm
r=7mm
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
0
1
2
3
4
5
6
7
8

FIG. 5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/042291

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 1/05; A61B 1/012; A61B 1/018; A61B 1/07; A61B 6/12; A61N 5/06 (2019.01)
CPC - A61B 1/05; A61B 1/012; A61B 1/018; A61B 1/07; A61B 6/12; A61N 5/06 (2019.08)

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)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 606/1; 606/27; 607/1; 607/96 (keyword delimited)

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2017/132345 A1 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 03 August 2017 (03.08.2017) entire document	1-8, 10-12, 17, 19
Y	US 6,564,089 B2 (IZATT et al) 13 May 2003 (13.05.2003) entire document	1-8, 10-12, 17, 19
Y	US 2014/0187929 A1 (SCHMITT et al) 03 July 2014 (03.07.2014) entire document	4, 5, 7, 19
A	US 2008/0255461 A1 (WEERSINK et al) 16 October 2008 (16.10.2008) entire document	1-12, 17-20
A	US 2016/0287308 A1 (MONTERIS MEDICAL CORPORATION) 06 October 2016 (06.10.2016) entire document	1-12, 17-20

☐ Further documents are listed in the continuation of Box C. ☐ 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
21 October 2019	08 NOV 2019
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/042291

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
See extra sheet(s).

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-12, 17-20

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

Continued from Box No. III Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-12 and 17-20, are drawn to an optical probe system comprising: an elongate rigid housing having a proximal end, a distal end, and an optically transparent portion near a distal tip of the housing.

Group II, claims 13-16, are drawn to a method for determining a coagulation boundary comprising: advancing an optical probe to a target coagulation boundary within a patient.

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical feature of the Group I invention: an elongate rigid housing having a proximal end, a distal end, and an optically transparent portion near a distal tip of the housing; a photo sensing element having a distal tip positioned within the optically transparent portion of the housing; and a controller configured to detect a coagulation boundary based on a photo voltage measured from the photo sensing element as claimed therein is not present in the invention of Group II. The special technical feature of the Group II invention: advancing an optical probe to a target coagulation boundary within a patient; measuring photo voltage detected from the optical probe; and determining when the coagulation boundary reaches the probe based on a measured decrease and plateau in photo voltage detected as claimed therein is not present in the invention of Group I.

Groups I and II lack unity of invention because even though the inventions of these groups require the technical feature of an optical probe to determine a coagulation boundary, this technical feature is not a special technical feature as it does not make a contribution over the prior art.

Specifically, US 2008/0255461 to Weersink et al. teaches an optical probe to determine a coagulation boundary (Paras. [0014-0016], [0034]).

Since none of the special technical features of the Group I or II inventions are found in more than one of the inventions, unity of invention is lacking.