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(54) Title: SYSTEM FOR EX-VIVO NMR INSPECTION OF REMOVED TISSUE

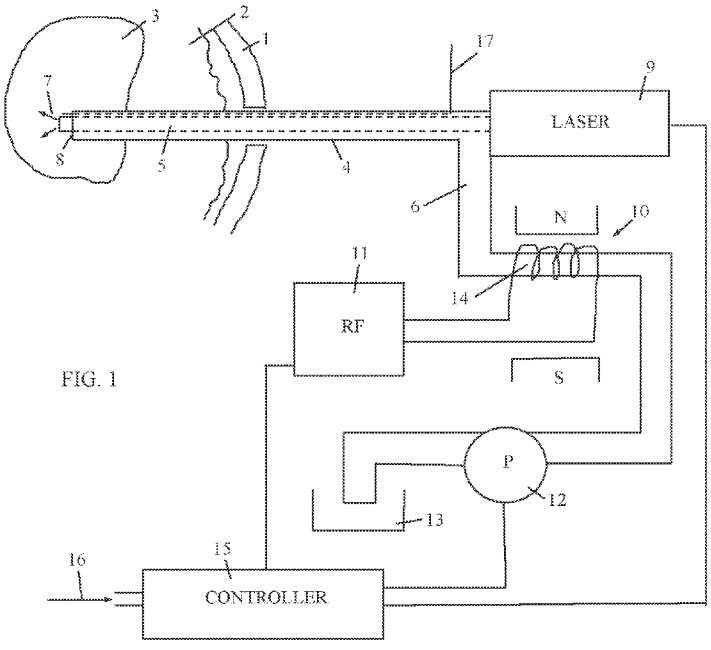

FIG. 1

(57) Abstract: A system and method are described for ex-vivo, real-time NMR analysis of tissue removed either for purposes of biopsy or tissue removed during an ablation procedure.

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SYSTEM FOR EX-VIVO NMR INSPECTION OF REMOVED TISSUE

FIELD OF THE INVENTION

The present invention relates generally to a system and a method for ex-vivo inspection of tissue removed by minimally invasive tools, in which NMR is used to analyze the removed tissue.

BACKGROUND OF THE INVENTION

In minimally invasive processes tissue is either removed from an organ of a patient for further investigation (biopsy) or destroyed in a targeted manner (various ablation methods exist to destroy malignant tumors, among them cryo-ablation, RF ablation and laser ablation). However, in the prior art, there is no real-time feedback to the operator indicating whether the excised or destroyed tissue is cancerous or non-cancerous.

In the case of biopsy sampling, a real-time feedback can be useful to establish that the sample removed contains the targeted tissue type at all, or enough of that targeted tissue for diagnosis. For example, navigation with a bronchoscope down the bronchi in order to reach a specific location and remove suspicious tissue is very difficult and may need to be repeated if there is doubt that tissue removed actually comes from the targeted location.

In the case of tumor ablation there is uncertainty with regard to the precise tumor boundary. There is need for a reliable, real-time way to stop ablative processes at the margin between cancerous and healthy tissue. Today ablation is done based in pre-operative planning based on CT or MRI images, but the information obtained is only partially relevant at the time of intervention. Both registration, that is, the tumor location, and even more so tumor size, are usually not consistently preserved when going from planning to intervention.

Monitoring of minimally invasive, interventional procedures with a regular imaging device (CT, MR) is in principle possible, but only for coarse navigational purposes. Margin assessment in situ would require a very expensive, high resolution device in a dedicated interventional suite. There is no routine deployment of such technology today.

SUMMARY OF THE INVENTION

The present invention seeks to provide improved systems and methods for ex-vivo inspection of tissue removed by minimally invasive tools, in which NMR is used to analyze the removed tissue, as is described more in detail below.

The invention may be used for real-time margin assessment in tumor removal or ablation. The NMR analysis can be used to determine the ratio between cancerous and non-cancerous tissue in the excised sample. This serves to indicate how close the ablation or tissue removal tool has come to the edge of the tumor. Once there is little or no cancerous tissue left in the analyzed samples, ablation (or other removal) can be stopped in that direction. Thus, the invention solves the problems of the prior art by providing a good real-time feedback to achieve more precise tissue ablation or removal.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will be understood and appreciated more fully from the following detailed description, taken in conjunction with the drawings in which:

Fig. 1 is a simplified illustration of a system and method for ex-vivo NMR analysis of tissue removed either for purposes of biopsy or tissue removed during an ablation procedure, constructed and operative in accordance with a non-limiting embodiment of the present invention; and

Fig. 2 is a simplified illustration of a system and method similar to Fig. 1, with the addition of a carrier liquid in order to transport a specific tissue sample quickly from the point of removal, in accordance with a non-limiting embodiment of the present invention.

DETAILED DESCRIPTION OF EMBODIMENTS

Reference is now made to Fig. 1, which illustrates a system and method for ex-vivo, real-time NMR analysis of tissue removed either for purposes of biopsy or tissue removed during an ablation procedure, constructed and operative in accordance with a non-limiting embodiment of the present invention.

The system may include a catheter or tube 4, which can be introduced into tissue. In the non-limiting illustrated embodiment, catheter 4 enters an aperture formed in a skull 1 (small aperture for minimally invasive access), passes into a brain 2 and enters a tumor 3. A laser unit 9 is coupled to an optical fiber 5, which passes through a portion of catheter 4 and exits a distal end 8 of catheter 4. The laser emits photons 7 via fiber 5 to the tumor 3. The entry of fiber 5 into catheter 4 may be sealed by a seal (not shown).

The laser unit 9, in the example of ablating a brain tumor, may be, without limitation, a CO_2 or Nd:YAG laser.

A tissue manipulation tool 17 (such as, but not limited to, scissors, pliers, knife, or ablation head, etc.) may be introduced through catheter 4 for excising a piece of tissue for NMR analysis. Tool 17 may be manipulated by the surgeon, as is known.

Catheter 4 is fluidly coupled to a tube 6 (alternatively the tube 4 may be continuous and serve as tube 6, without the need for a separate catheter 4 and another tube 6) passes through an NMR unit 10, which, as is well known in the art, includes, among other components, magnets for generating a magnetic field, and an RF transceiver 11 for tissue excitation through an RF coil 14.

Tube 6 (or in the alternative, catheter 4) continues proximally and is coupled to a suction pump 12. Suction pump 12 is configured to draw tissue and other material excised from the tumor. The tissue and other material are deposited by pump 12 into a storage container 13. The storage container 13 may increment and store each sample and groups of samples separately, if desired. The pump 12 and tubing (catheter 4 and/or tube 6) are also referred to as a tissue remover.

A controller 15 is coupled to the laser unit 9, the pump 12 and the RF transceiver 11 or other components of the NMR unit 10. Controller 15 may receive a signal input 16, such as an acoustic signal 16 (as in the example below). Controller 15 is used to synchronize laser ablation pulses with pump action and RF excitation as well as signal collection.

The system of Fig. 1 performs NMR/MRI analysis on the tissue *removed* from the body during biopsy, while also performing ablation therapy or any other minimally invasive processes. This approach avoids the cost and complexity of trying to do this with a conventional medical imaging device, like CT or MR, and at the same time allows higher signal-to-noise ratio (SNR) and tissue contrast because of the proximity of tissue sample and sensing coils.

In order to have minimal lag between the tissue sample removal and the analysis, the tissue to be inspected is sucked or flushed (or both) down the flexible tube (4 and 6, or alternatively, just 4) until it reaches the center of the magnetic field generated by the permanent magnet (or electromagnet or superconductive magnet) of NMR unit 10. At that point the tube goes through the long axis of RF coil 14 used to excite the magnetized tissue sample and receive the echo from that tissue. For the purpose of the NMR measurement the flow may be stopped momentarily, synchronized with the tissue removal process at the top end of the catheter, establishing a “stop and go, stop and go”-like process. The process may also be continuous, using a gradient/coil configuration

making the measurement insensitive to the flow direction, but very sensitive in the lateral direction.

The NMR method used to detect cancerous tissue in the sample removed can be any sequence: pure T1 or T2 measurement, such measurements enhanced with contrast material, or diffusion-weighted measurement, all with or without fat suppression sequences employed before the actual measurement.

Since the removed tissue sample retains a cellular structure, diffusion-weighted measurements are especially useful to distinguish between cancerous and non-cancerous tissue. Much of the hardware and software of the existing CLEARSIGHT system (commercially available from ClearCut Medical Ltd., Israel) can be used to do such measurement. For example, without limitation, a CLEARPACK container (commercially available from ClearCut Medical Ltd., Israel) may be exchanged with a replaceable, one-time-use tube 6 from the end of the catheter 4 to the magnet/coil section of NMR unit 10 (such as that of the CLEARSIGHT system) and from there to pump 12 and tissue storage container 13. Although a coil configuration symmetrical around the tube 6 may be superior in terms of signal-to-noise ratio, one can also use the current configuration of the CLEARSIGHT system, in which coil(s) would sit on the tube surface (like a saddle on a horse).

The result of the measurement can be a ratio between cancerous and non-cancerous tissue in the last sample measured, displayed as a numerical ratio on a screen or an acoustic signal, so that the catheter operator does not have to take his/her eyes off the screen visualizing the procedure.

For example, in an ablation procedure, an acoustic signal 16 of a certain frequency would be audible initially and change gradually as the ablation probe reaches the boundaries of the tumor and the tissue sucked from the treatment volume contains less and less tumor tissue.

It is important to note that today ablation procedures do not require removing the ablated tissue from the treated volume. In contrast to the prior art, the present invention adds tissue fragment removal as part of the ablation procedure as well as to the NMR/MRI-based, real-time analysis of the removed fragments.

Reference is now made to Fig. 2, which illustrates a system similar to Fig. 1, with like elements being designated by like numerals. The system of Fig. 2 differs from that of Fig. 1 by having the addition of a carrier liquid 21, which helps to transport the specific tissue sample quickly from the point of removal all the way to the NMR analysis point

without the need to remove more tissue in order to keep the tube filled. The carrier liquid 21 (e.g., water or saline), may be pumped from a reservoir 22 by a pump 24 through a fluid conduit 25 to a sleeve 26 that surrounds catheter 4.

CLAIMS

What is claimed is:

1. A system comprising:

a tissue manipulation tool (17) configured to perform a biopsy or ablation procedure on tissue in a body;

a tissue remover (4, 6, 12) configured to move a removed tissue away from said tissue manipulation tool (17);

an NMR unit (10) in communication with said tissue remover (4, 6, 12) and operative to perform an NMR analysis of said removed tissue during the biopsy or ablation procedure.

2. The system according to claim 1, wherein said tissue remover (4, 6, 12) comprises a suction pump (12) and a tube (4, 6), said tube (4, 6) configured to convey said removed tissue to said NMR device (10).

3. The system according to claim 2, wherein said tube goes through a long axis of a RF coil used to excite said removed tissue for NMR analysis and receive an echo from said removed tissue.

4. The system according to claim 1, wherein said NMR device (10) uses T1 or T2 measurement, T1 or T2 measurements enhanced with contrast material, diffusion-weighted measurement, or a combination thereof.

5. The system according to claim 2, further comprising a carrier liquid (21) in said tube (4, 6) for transporting said removed tissue in said tube (4, 6).

6. A method for real-time margin assessment in tumor removal or ablation comprising:

removing tissue during a biopsy or ablation procedure;

performing an NMR analysis of the tissue removed during the biopsy or ablation procedure; and

using the NMR analysis to determine a ratio between cancerous and non-cancerous cells in the tissue removed to indicate how close the biopsy or ablation procedure has come to an edge of a tumor.

7. The method according to claim 6, comprising repeating the steps of claim 6 and stopping the biopsy or ablation procedure once little or no cancerous tissue is left in tissue which is removed for the NMR analysis.

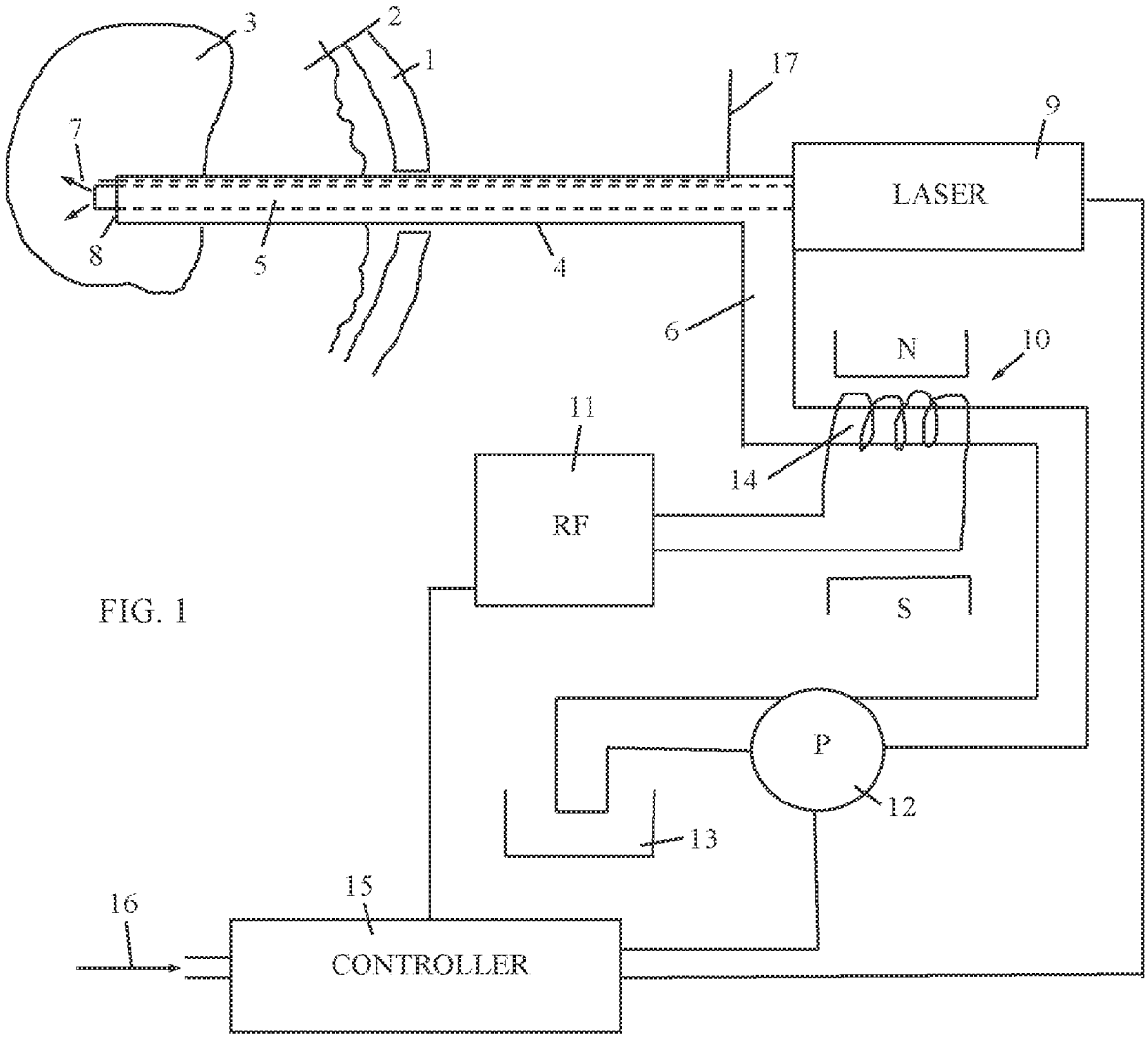
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FIG. 1

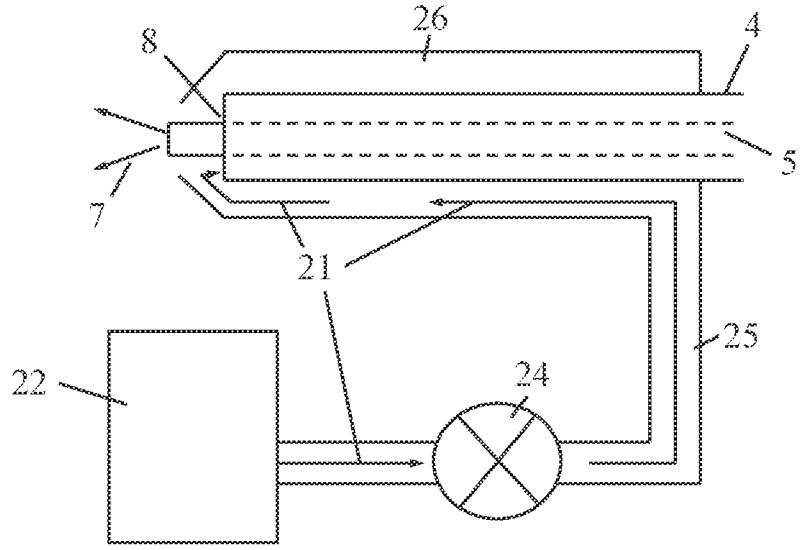
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FIG. 2

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2018/050381

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01R33/30 A61B5/06
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)
G01R A61B

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	PAPA MOSHE ET AL: "An intraoperative MRI system for margin assessment in breast conserving surgery: Initial results from a novel technique.", JOURNAL OF SURGICAL ONCOLOGY JUL 2016, vol. 114, no. 1, July 2016 (2016-07), pages 22-26, XP002780844, ISSN: 1096-9098 (p 23, col 1, para 2)(p 23, col 1-2, bridging para); abstract (p 23, col 2, para 2)	1-7
X	US 2005/000525 A1 (KLIMBERG V SUZANNE [US] ET AL) 6 January 2005 (2005-01-06) [0053]; claims 18,20,26	1-7

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[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

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
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Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2018/050381

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 3 075 321 A1 (RYAN MAXIMILLIAN FREDERICK [IE]) 5 October 2016 (2016-10-05) [0010]; claims 1,12 -----	1-7
X	TORCUATOR ROY G ET AL: "Intraoperative real-time MRI-guided stereotactic biopsy followed by laser thermal ablation for progressive brain metastases after radiosurgery", JOURNAL OF CLINICAL NEUROSCIENCE, CHURCHILL LIVINGSTONE, GB, vol. 24, 16 November 2015 (2015-11-16), pages 68-73, XP029382422, ISSN: 0967-5868, DOI: 10.1016/J.JOCN.2015.09.008 (p 69, col 1, para 3)(p 69, col 2, para 2) -----	1-7
X	WO 2011/094659 A2 (CLEAR CUT MEDICAL LTD [IL]; GOLAN EREZ [IL]; KLEIN DAVID [IL]) 4 August 2011 (2011-08-04) claims 1, 5,7, 13, 15 -----	1-7

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2018/050381

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