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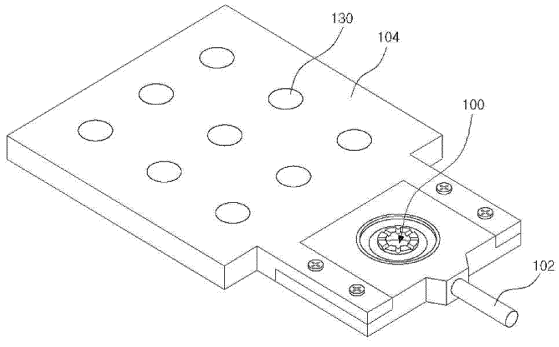
(54) MICROASPIRATION-BASED LUNG WINDOW APPARATUS FOR OBTAINING MICROSCOPIC IMAGE OF IN VIVO LUNG TISSUE AND METHOD FOR OBTAINING IMAGE USING SAME

(57) Disclosed are a microaspiration-based lung window apparatus for obtaining a microscopic image of in vivo lung tissue and a method for obtaining an image using same. The present invention provides a lung window apparatus comprising: an open window which has the upper part and lower part open, a cover glass placed over the upper part and lung tissue coming in contact with the lower part; an aspiration tube which extends from one side of the open window to an aspiration apparatus and enables the inside of the open window to be in a vacuum state; and a tilting mount placing unit which extends from one side of the open window and has placed thereon a tilting mount that enables the cover glass and an object lens of a confocal microscope system to stay parallel to each other. The present invention enables maintaining of physiological respiration and circulation of an animal without interference as well as stable acquisition of cell-level and molecular level microscopic images of in vivo lung tissue.

FIG. 1



EP 3 345 546 A1

Description

[0001] This application claims priority from Korean Patent Application No. 10-2015-0123216, filed on August 31, 2015, which is hereby incorporated by reference for all purposes as if fully set forth herein.

Technical Field

[0002] The present disclosure relates to a microaspiration-based lung window apparatus for obtaining a microscopic image of a lung tissue in vivo and a method for obtaining an image using the same.

Background Art

[0003] A confocal laser scanning microscope using fluorescent signals is used to observe cellular-level and molecular-level phenomenon.

[0004] Unlike other tissues, the pulmonary system periodically moves due to the respiration process and the beating of the heart close to it, thus due to such motion artifacts it is difficult to obtain accurate images when wishing to obtain microscopic images.

[0005] Due to this limit, most molecular biological studies are performed in the process of extracting, fixing, and then observing tissues. However, it is difficult to find out, in living animals, changes in blood vessels, or changes or interaction of blood vessels, tissue cells in lung parenchyma, and circulating cells including erythrocytes, leukocytes, and thrombocyte.

[0006] Accordingly, it became an important subject to find out interaction between cells and molecular-level structures while physiologically maintaining respiration and circulation of living animals.

[0007] To this end, it is required to develop an imaging window that allows for observing a molecular biological mechanism that occurs in a lung system and blood vessels in vivo, and can overcome a motion-artifact of microscopic images obtained through a confocal microscope.

Detailed Description of the Invention

Technical Problem

[0008] In order to solve these problems in the related art, the present disclosure provides a microaspiration-based lung window apparatus for obtaining a microscopic image of an in vivo lung tissue and a method for obtaining an image using the same, the apparatus and method being able to stably obtain cellular-level and molecular-level microscopic images of a lung tissue in vivo while physiologically maintaining and not interfering with respiration and circulation of an animal.

Technical Solution

[0009] According to an embodiment, there is provided a microaspiration-based lung window apparatus for obtaining a microscopic image of a lung tissue in vivo, the apparatus comprising: an open window configured to open in upper and lower parts thereof, have a cover glass placed on the upper part thereof, and have a lung tissue brought in contact with the lower part thereof;
a suction tube configured to extend to a suction device from a side of the open window and make the inside of the open window vacuum; and a tilting mount seat, configured to extend from a side of the open window, in which a tilting mount is placed to maintain the cover glass and an objective lens of a confocal microscope system in parallel.

[0010] According to an embodiment, there is provided a microaspiration-based lung window apparatus for obtaining a microscopic image of a lung tissue in vivo, the apparatus consisting of: an open window configured to open in upper and lower parts thereof, have a cover glass placed on the upper part thereof, and have a lung tissue brought in contact with the lower part thereof;
a suction tube configured to extend to a suction device from a side of the open window and make the inside of the open window vacuum; and a tilting mount seat, configured to extend from a side of the open window, in which a tilting mount is placed to maintain the cover glass and an objective lens of a confocal microscope system in parallel.

[0011] According to an embodiment, there is provided a microaspiration-based lung window apparatus for obtaining a microscopic image of a lung tissue in vivo, the apparatus essentially consisting of: an open window configured to open in upper and lower parts thereof, have a cover glass placed on the upper part thereof, and have a lung tissue brought in contact with the lower part thereof;
a suction tube configured to extend to a suction device from a side of the open window and make the inside of the open window vacuum; and a tilting mount seat, configured to extend from a side of the open window, in which a tilting mount is placed to maintain the cover glass and an objective lens of a confocal microscope system in parallel.

[0012] The open window may have a conical shape of which a diameter is increased from its upper part to its lower part.

[0013] The tilting mount seat may have a plurality of fastening holes for coupling the tilting mount.

[0014] The open window and the suction tube are formed in a first plate which has a first body and first protrusions having a step with respect to the first body and protrudes from sides of the first body, and
the tilting mount seat is formed in a second plate which has a second body and second protrusions having a step with respect to the second body and joining with the first protrusions.

[0015] According to another aspect, there is provided a microaspiration-based lung window apparatus for obtaining a microscopic image of an lung tissue in vivo, the apparatus comprising: a first plate in which an open window and a suction tube are formed, wherein the open window is configured to open in upper and lower parts thereof, have a cover glass placed on the upper part thereof, and have a lung tissue brought in contact with the lower part thereof, wherein the suction tube is configured to extend to a suction device from a side of the open window and make the inside of the open window vacuum; and a second plate, which is configured to join with the first plate, where there is formed a tilting mount seat in which a tilting mount is placed to maintain the cover glass and an objective lens of a confocal microscope system in parallel.

[0016] According to another aspect, there is provided a microaspiration-based lung window apparatus for obtaining a microscopic image of an lung tissue in vivo, the apparatus consisting of: a first plate in which an open window and a suction tube are formed, wherein the open window is configured to open in upper and lower parts thereof, have a cover glass placed on the upper part thereof, and have a lung tissue brought in contact with the lower part thereof, wherein the suction tube is configured to extend to a suction device from a side of the open window and make the inside of the open window vacuum; and a second plate, which is configured to join with the first plate, where there is formed a tilting mount seat in which a tilting mount is placed to maintain the cover glass and an objective lens of a confocal microscope system in parallel.

[0017] According to another aspect, there is provided a microaspiration-based lung window apparatus for obtaining a microscopic image of an lung tissue in vivo, the apparatus essentially consisting of: a first plate in which an open window and a suction tube are formed, wherein the open window is configured to open in upper and lower parts thereof, have a cover glass placed on the upper part thereof, and have a lung tissue brought in contact with the lower part thereof, wherein the suction tube is configured to extend to a suction device from a side of the open window and make the inside of the open window vacuum; and a second plate, which is configured to join with the first plate, where there is formed a tilting mount seat in which a tilting mount is placed to maintain the cover glass and an objective lens of a confocal microscope system in parallel.

[0018] According to another aspect, there is provided a method of obtaining an image using a confocal microscope system and a microscopic aspiration-based lung window apparatus, the method comprising: adjusting the angle of the lung window apparatus by using a tilting mount placed on a tilting mount seat of the lung window apparatus; radiating laser beams having a plurality of wavelengths to a lung tissue through an open window of the lung window apparatus, wherein a cover glass is placed over the upper part of the open window, the lung tissue is brought in contact with the lower part of the open window, a suction tube extending to a suction device is formed on a side of the open window, so as to keep the inside of the open window vacuum; and detecting a fluorescent signal excited in the lung tissue, wherein the cover glass placed over the open window and an objective lens of the confocal microscope system are maintained in parallel in a respiration or circulation process by adjusting the angle of the tilting mount.

[0019] According to another aspect, there is provided a method of obtaining an image using a confocal microscope system and a microscopic aspiration-based lung window apparatus, the method consisting of: adjusting the angle of the lung window apparatus by using a tilting mount placed on a tilting mount seat of the lung window apparatus; radiating laser beams having a plurality of wavelengths to a lung tissue through an open window of the lung window apparatus, wherein a cover glass is placed over the upper part of the open window, the lung tissue is brought in contact with the lower part of the open window, a suction tube extending to a suction device is formed on a side of the open window, so as to keep the inside of the open window vacuum; and detecting a fluorescent signal excited in the lung tissue, wherein the cover glass placed over the open window and an objective lens of the confocal microscope system are maintained in parallel in a respiration or circulation process by adjusting the angle of the tilting mount.

[0020] According to another aspect, there is provided a method of obtaining an image using a confocal microscope system and a microscopic aspiration-based lung window apparatus, the method essentially consisting of: adjusting the angle of the lung window apparatus by using a tilting mount placed on a tilting mount seat of the lung window apparatus; radiating laser beams having a plurality of wavelengths to a lung tissue through an open window of the lung window apparatus, wherein a cover glass is placed over the upper part of the open window, the lung tissue is brought in contact with the lower part of the open window, a suction tube extending to a suction device is formed on a side of the open window, so as to keep the inside of the open window vacuum; and detecting a fluorescent signal excited in the lung tissue, wherein the cover glass placed over the open window and an objective lens of the confocal microscope system are maintained in parallel in a respiration or circulation process by adjusting the angle of the tilting mount.

[0021] The term 'comprising' used herein have the same meaning as terms 'including' or 'characterized by', not excluding additional non-stated apparatuses, components, or steps in an apparatus or a method. The term 'consisting of' excludes additional elements, steps, or components not specifically stated. The term 'essentially consisting of' means including elements, components, or steps that do not actually influence basic characteristics in addition to stated elements, components, or steps in an apparatus or a method.

Advantageous Effects

[0022] According to the present disclosure, an open window that is attached to a lung tissue and placed close to an object lens and a seat that extends from the open window and on which a tilting mount is mounted are provided, and the open window and the objective lens can be maintained in parallel during respiration and circulation on an animal, so it is possible to obtain stable images.

Brief Description of the Drawings

[0023]

FIG. 1 is a perspective view showing a lung window apparatus according to a preferred embodiment of the present invention,
FIG. 2 is a view showing the lung window apparatus according to an embodiment of the present invention when it is separated,
FIG. 3 shows a front view and a bottom view of the lung window apparatus according to an embodiment,
FIG. 4 shows a vertical cross-sectional view of the lung window apparatus according to an embodiment,
FIG. 5 is a view showing arrangement of a confocal microscope system, the lung window apparatus, and an objective lens according to an embodiment,
FIG. 6 is a view showing a lung tissue image obtained using a microaspiration-based lung window apparatus and a confocal microscope system according to an embodiment,
FIG. 7 is a view showing an image obtained by continuously imaging movement of erythrocyte after injecting FITC-Dextran into a C57BL6/J mouse obtained using a microaspiration-based lung window apparatus and a confocal microscope system according to an embodiment, and
FIG. 8 is a view showing an image obtained by continuously imaging movement of leukocyte in the C57BL6/J mouse obtained using a microaspiration-based lung window apparatus and a confocal microscope system according to an embodiment.

Mode for Carrying Out the Invention

[0024] The present disclosure may be modified in various ways and implemented by various exemplary embodiments, so that specific exemplary embodiments are shown in the drawings and will be described in detail.

[0025] However, it is to be understood that the present disclosure is not limited to the specific exemplary embodiments, but includes all modifications, equivalents, and substitutions included in the spirit and the scope of the present disclosure. Reference numerals are assigned to reference components in the following description of drawings.

[0026] Hereinafter, exemplary embodiments will be described in detail with reference to the accompanying drawings.

[0027] FIG. 1 is a perspective view showing a long window apparatus according to an embodiment, FIG. 2 is a view showing the lung window apparatus according to an embodiment when it is separated, FIG. 3 shows a front view and a bottom view of the lung window apparatus according to an embodiment, and FIG. 4 shows a vertical cross-sectional view of the lung window apparatus according to an embodiment.

[0028] Referring to FIGS. 1 to 4, a lung window apparatus according to an embodiment may include an open window 100, a suction tube 102, and a tilting mount seat 104.

[0029] The open window has a conical shape with open top and bottom and a diameter is increased from its upper part to its lower part.

[0030] The open window 100 is brought in contact with a lung tissue on the bottom and a cover glass seat 106 is placed over the open window 100.

[0031] When an image is obtained, a cover glass 110 is placed on the cover glass seat 106 and an objective lens 120 is placed over the cover glass 110.

[0032] The suction tube 102 extends to a suction device (not shown) from a side of the open window 100.

[0033] A cross-section of a lung tissue is brought in contact with the bottom of the open window 100, the cover glass 110 is placed over the open window 100, and the suction tube 102 is placed on a side of the open window 100, so it is possible to keep the inside of the open window 100 vacuum when obtaining an image.

[0034] The tilting mount seat 104 extends from a side of the open window 100 and has a plurality of fastening holes 130, and a tilting mount 140 is coupled through at least some of the fastening holes 130.

[0035] In the embodiment, the tilting mount 140 is a kinematic tilting mount and maintains the lung window apparatus and the objective lens 120 in parallel by adjusting the angle of the lung window apparatus.

[0036] When the objective lent 120 and the cover glass 110 placed over the open window 100 are maintained in parallel by adjusting the angle of the lung window apparatus through the kinematic tilting mount 140, movement of the lung window apparatus can be restricted even with respiration and circulation physiologically maintained, so images can be stably obtained.

[0037] According to an embodiment, the lung window apparatus may be provided by combining first plate 200 and a second plate 202, which are individual parts, with each other.

[0038] Referring to FIG. 2, it is possible to provide the lung window apparatus comprising the tilting mount seat 104 and the open window 100 by putting the first plate 200 and the second plate 220 such that first protrusions 212 formed on a side of a first body 210 of the first plate 200 and second protrusions 222 formed on a side of a second body 220 of the second plate overlap each other,

and then fastening the plates with bolts 230.

[0039] The open window 100 is formed in the first body 210 and the tilting mount seat 104 is formed in the second body 220.

[0040] According to the embodiment, the first protrusions 212 are smaller in thickness than the first body 220 and the second protrusions 222 are smaller in thickness than the second body 220.

[0041] Preferably, the first body 210 and the second body 220 may be the same in thickness, and the entire thickness when the first protrusions 212 and the second protrusions 222 overlap each other may be the same as the thickness of the first body 210 and the second body 220.

[0042] The first plate 200 and the second plate 202 have steps, and when the first protrusions 212 and the second protrusion 222 overlap each other, the entire thickness is uniform.

[0043] FIG. 5 is a view showing the configuration of a confocal microscope system and arrangement of the lung window apparatus and the objective lens according to an embodiment.

[0044] A process of obtaining an image according to the embodiment is as follows.

(1) Adjustment of angle of lung window apparatus

[0045] The angle of the lung window apparatus is adjusted using the tilting mount 140 placed on the tilting mount seat 104 of the lung window apparatus.

(2) Emission of laser beam

[0046] As in FIG. 5, laser beams having a plurality of wavelengths are radiated to a lung tissue through the open window 100 of the lung window apparatus.

(3) Detection of fluorescent signal

[0047] A fluorescent signal excited in the lung tissue is detected through a detector.

[0048] Referring to FIG. 5, the confocal microscopic system according to the embodiment includes four laser sources 500-1 to 500-4 respectively four wavelengths of 405nm, 488nm, 561nm, and 640nm within the visible light band, a polygonal rotation mirror 502, and a galvanometer mirror 504, and generates an XY raster scanning pattern, using these components.

[0049] The confocal microscopic system may comprise a plurality of neutral density filters ND, mirrors M, and Dichroic beam splitters DBS, and beam pass filters BPF and photomultiplier tubes for detecting a fluorescent signal excited in a lung tissue.

[0050] Images of a lung tissue were obtained from an actual animal model, using the confocal optical microscope using the microaspiration-based lung window apparatus of the present disclosure.

[0051] An optical system was designed to have an observation view of $250\times250\ \mu m^2$ at the focus when using a $\times40$ objective lens (LUCPlanFL, NA0.6; Olympus) and a fluorescent signal was detected and processed by photomultiplier tubes individually and frame grabbers (Matrox, SOLIOS) that are provided for wavelengths such that 2D images having cellular-level resolution and being able to be sectioned in the Z-axial direction could be obtained at a speed of 30 sheets per second.

[0052] By attaching the lung window apparatus according to an embodiment to the confocal microscope system and radiating laser beams to a lung tissue through an objective lens, it is possible to obtaining cellular-level images in real time through excited fluorescent signals.

[0053] FIG. 6 is a view showing a lung tissue image obtained using a microaspiration-based lung window apparatus and a confocal microscope system according to an embodiment.

[0054] A lung tissue has a pulmonary alveolus and a capillary vessel surrounding the pulmonary alveolus and the capillary vessel has a vascular endothelial cell and a basement membrane covering the vascular endothelial cell.

[0055] In order to check first the structure of such a lung, observation was performed on the lungs of a Tie2-GFP mouse having a green fluorescent signal expressed in a Tie2 receptor and an Actin-DsRed & Histone-GFP having a red fluorescent signal expressed in an Actin filament and a green fluorescent signal expressed in Histone, using a confocal microscope system and the lung window apparatus according to the embodiment.

[0056] As described above, a black circular pulmonary alveoli and a capillary vessel (red in FIG. 6A and green in FIG. 6B) composed of vascular endothelial cells surrounding the lungs are found.

[0057] Further, in a lung tissue, nuclei (green in FIG. 6B) of type I pulmonary cells, type II pulmonary alveoli, and nuclei of macrophages around the pulmonary cells could be found.

[0058] FIG. 7 is a view showing an image obtained by continuously imaging movement of erythrocyte after injecting FITC-Dextran into a C57BL6/J mouse obtained using a microaspiration-based lung window apparatus and a confocal microscope system according to an embodiment.

[0059] An image for observing movement of erythrocyte and leukocyte was checked in consideration of influence on cells in a lung tissue due to microaspiration. An image of erythrocyte contrasted by black was obtained by injecting FITC-Dextran into a blood vessel of the C57BL6/J mouse, and as in FIG. 7, it was found that movement of the erythrocyte was continued and was not influenced by microaspiration.

[0060] FIG. 8 is a view showing an image obtained by continuously imaging movement of leukocyte in the LysM-GFP mouse obtained using a microaspiration-based lung window apparatus and a confocal microscope system according to an embodiment.

[0061] In order to observe movement of leukocyte, in-

jecting TMR-Dextran into a LysM-GFP mouse in which a green fluorescent signal was expressed in LysM protein to show blood vessels with red was performed and then tracing the movement path of the LysM in the blood vessels was performed. As shown in FIG. 8, it was found that movement of leukocyte was also continued and was not influenced by microaspiration.

[0062] As described above, by using the lung window apparatus according to the embodiment, it was found that the apparatus was useful for low-invasive and microscopic access to a lung tissue of an animal model without interfering with physiological circulation. Further, it was found that the apparatus was suitable for securing stable images of lung parenchyma and blood vessels and obtaining images for finding out interaction of cells and single cellular-level movement.

[0063] Hereinabove, although the present disclosure is described by specific matters such as concrete components, and the like, embodiments, and drawings, they are provided only for assisting in the entire understanding of the present disclosure. Therefore, the present disclosure is not limited to the embodiments. Various modifications and changes may be made by those skilled in the art to which the present disclosure pertains from this description. Therefore, the sprit of the present disclosure should not be limited to the above-described embodiments, and the following claims as well as all modified equally or equivalently to the claims are intended to fall within the scope and spirit of the disclosure.

Claims

1. A microaspiration-based lung window apparatus for obtaining a microscopic image of a lung tissue in vivo, the apparatus comprising:

   an open window configured to open in upper and lower parts thereof, have a cover glass placed on the upper part thereof, and have a lung tissue brought in contact with the lower part thereof;
   a suction tube configured to extend to a suction device from a side of the open window and make the inside of the open window vacuum; and
   a tilting mount seat, configured to extend from a side of the open window, in which a tilting mount is placed to maintain the cover glass and an objective lens of a confocal microscope system in parallel.

2. The apparatus of claim 1, wherein the open window has a conical shape of which a diameter is increased from its upper part to its lower part.

3. The apparatus of claim 1, wherein the tilting mount seat has a plurality of fastening holes for coupling the tilting mount.

4. The apparatus of claim 1, wherein the open window and the suction tube are formed in a first plate which has a first body and first protrusions having a step with respect to the first body and protrudes from sides of the first body, and
   the tilting mount seat is formed in a second plate which has a second body and second protrusions having a step with respect to the second body and joining with the first protrusions.

5. A microaspiration-based lung window apparatus for obtaining a microscopic image of a lung tissue in vivo, the apparatus comprising:

   a first plate in which an open window and a suction tube are formed, wherein the open window is configured to open in upper and lower parts thereof, have a cover glass placed on the upper part thereof, and have a lung tissue brought in contact with the lower part thereof, wherein the suction tube is configured to extend to a suction device from a side of the open window and make the inside of the open window vacuum; and
   a second plate, which is configured to join with the first plate, where there is formed a tilting mount seat in which a tilting mount is placed to maintain the cover glass and an objective lens of a confocal microscope system in parallel.

6. The apparatus of claim 5, wherein the first plate has a first body where the open window and the suction tube are formed and first protrusions having a step with respect to the first body and protruding from sides of the first body, and
   the second plate has a second body where the tilting mount seat is formed and second protrusions having a step with respect to the second body and joining with the first protrusions.

7. A method of obtaining an image using a confocal microscope system and a microscopic aspiration-based lung window apparatus, the method comprising:

   adjusting the angle of the lung window apparatus by using a tilting mount placed on a tilting mount seat of the lung window apparatus;
   radiating laser beams having a plurality of wavelengths to a lung tissue through an open window of the lung window apparatus, wherein a cover glass is placed over the upper part of the open window, the lung tissue is brought in contact with the lower part of the open window, a suction tube extending to a suction device is formed on a side of the open window, so as to keep the inside of the open window vacuum; and
   detecting a fluorescent signal excited in the lung tissue,

wherein the cover glass placed over the open window and an objective lens of the confocal microscope system are maintained in parallel in a respiration or circulation process by adjusting the angle of the tilting mount.

FIG. 1

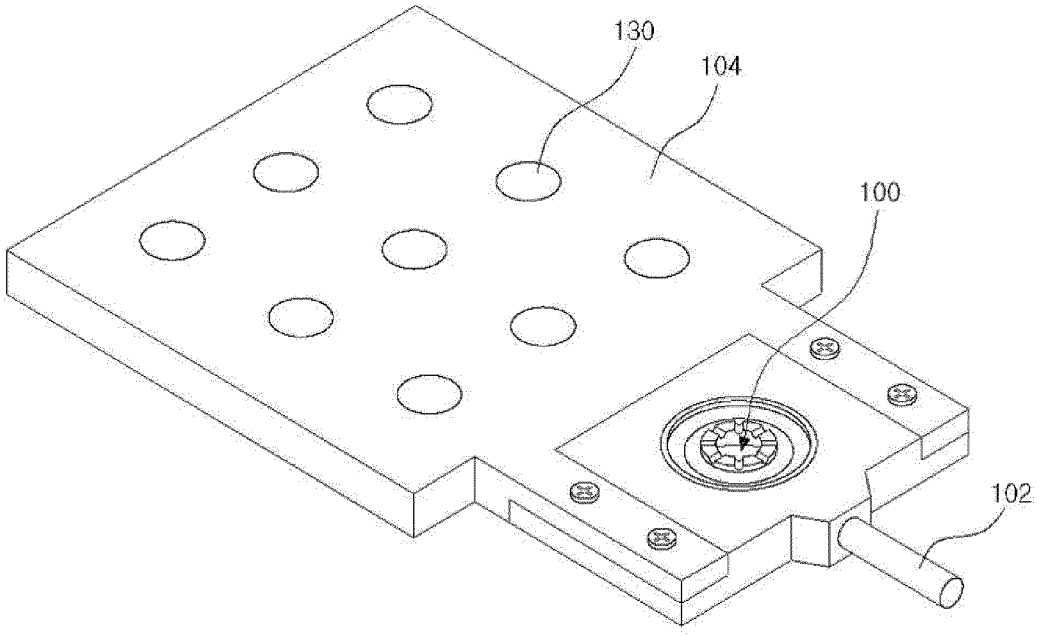


FIG. 2

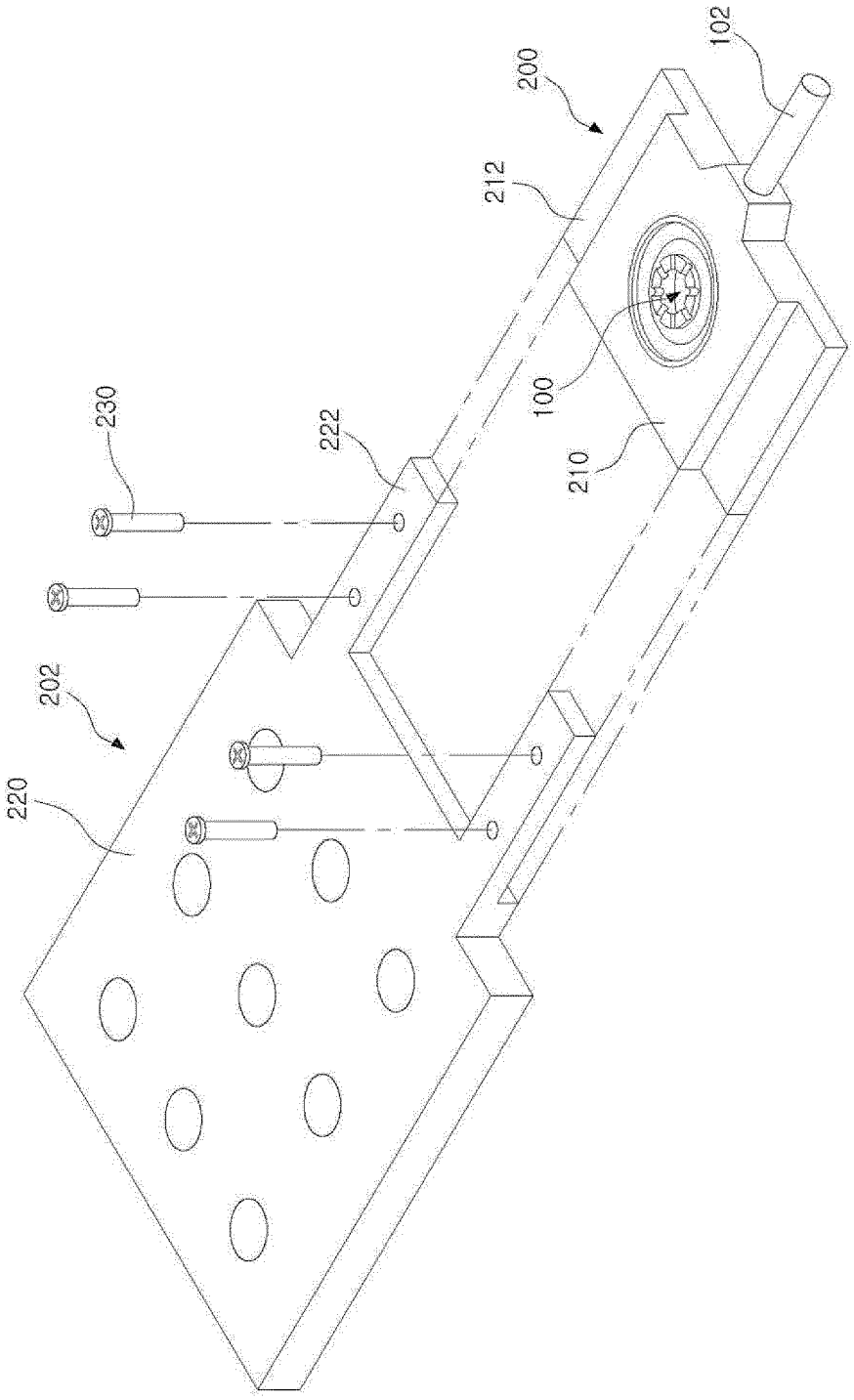


FIG. 3

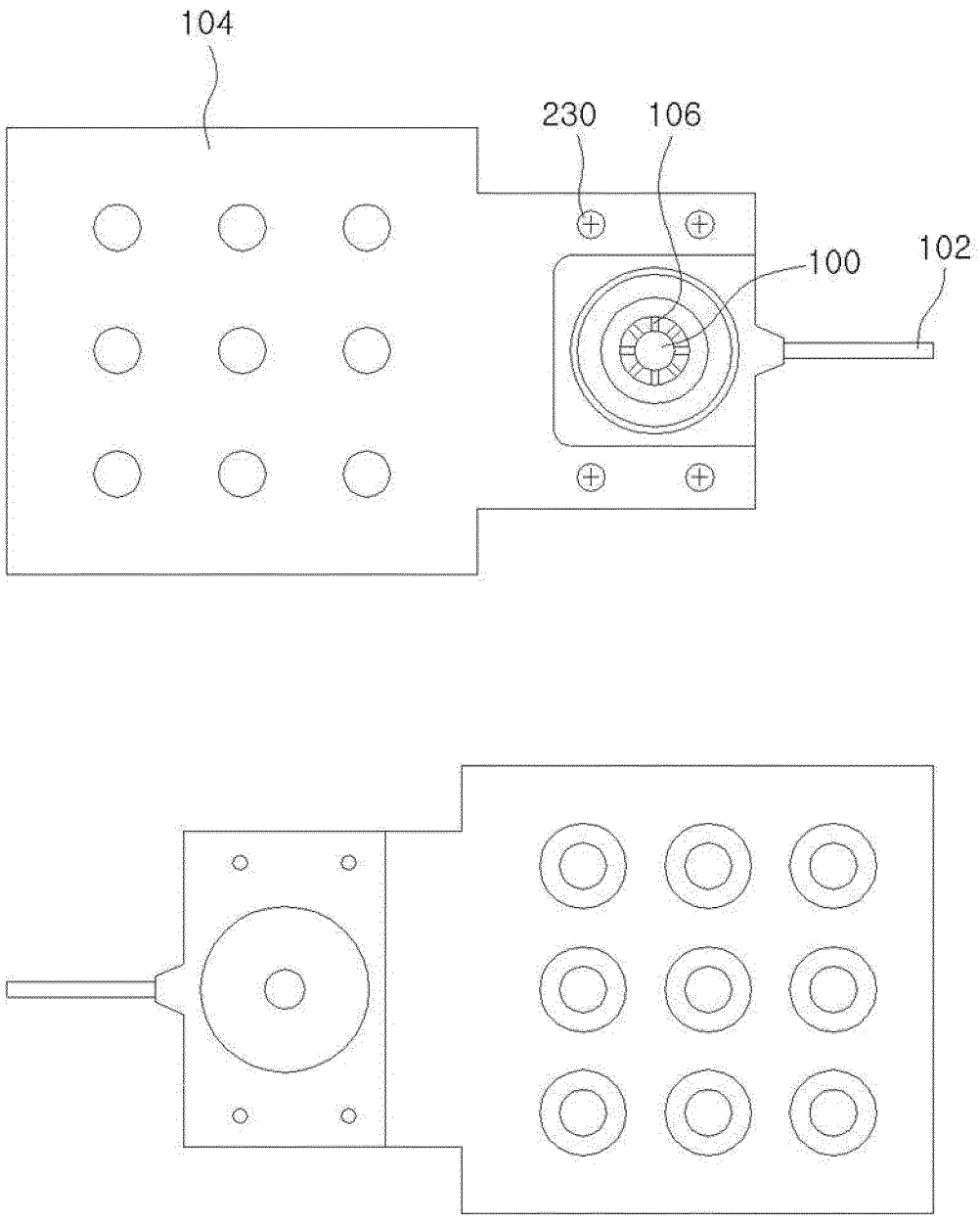


FIG. 4

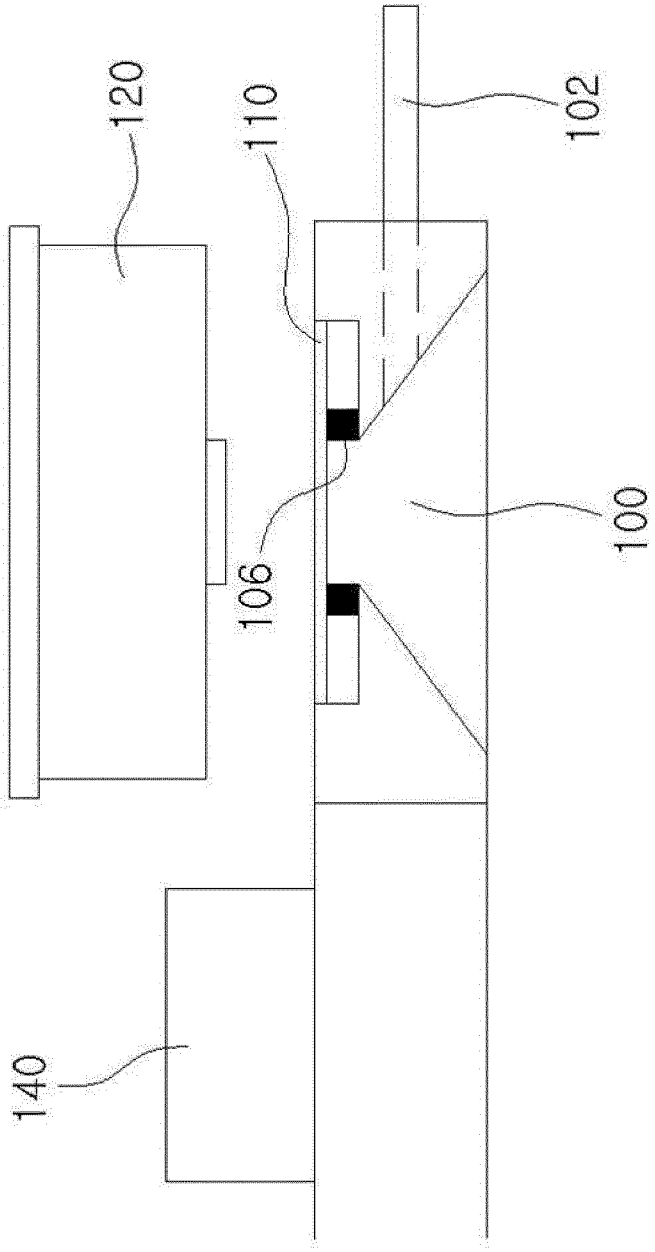


FIG. 5

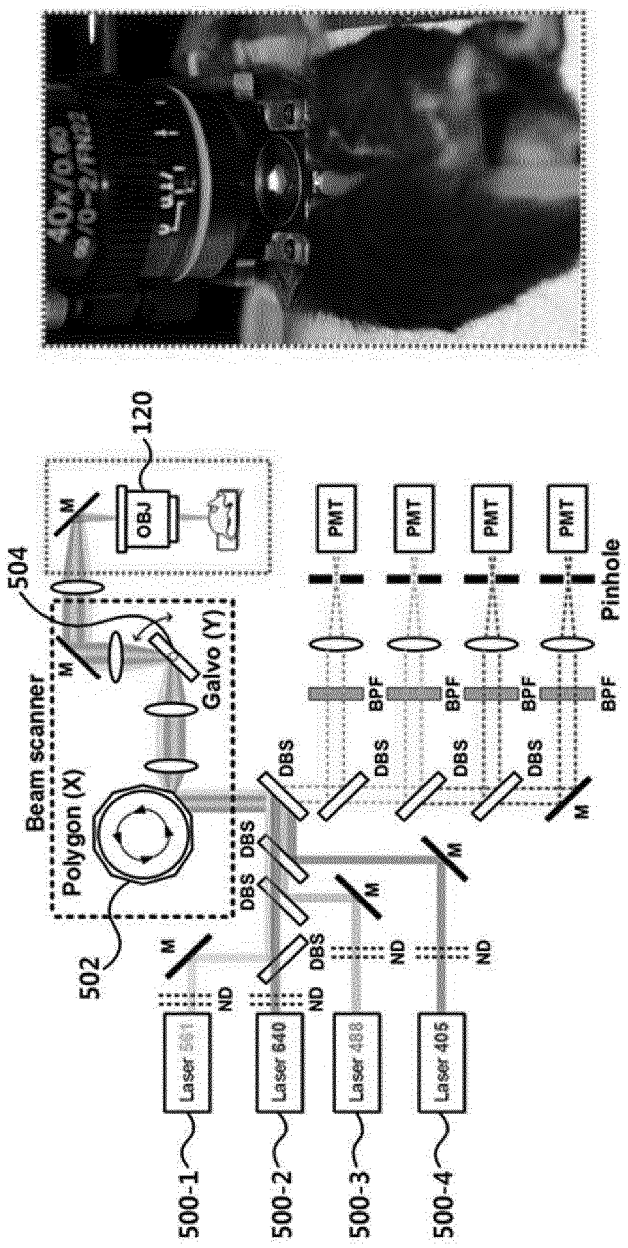

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FIG. 6

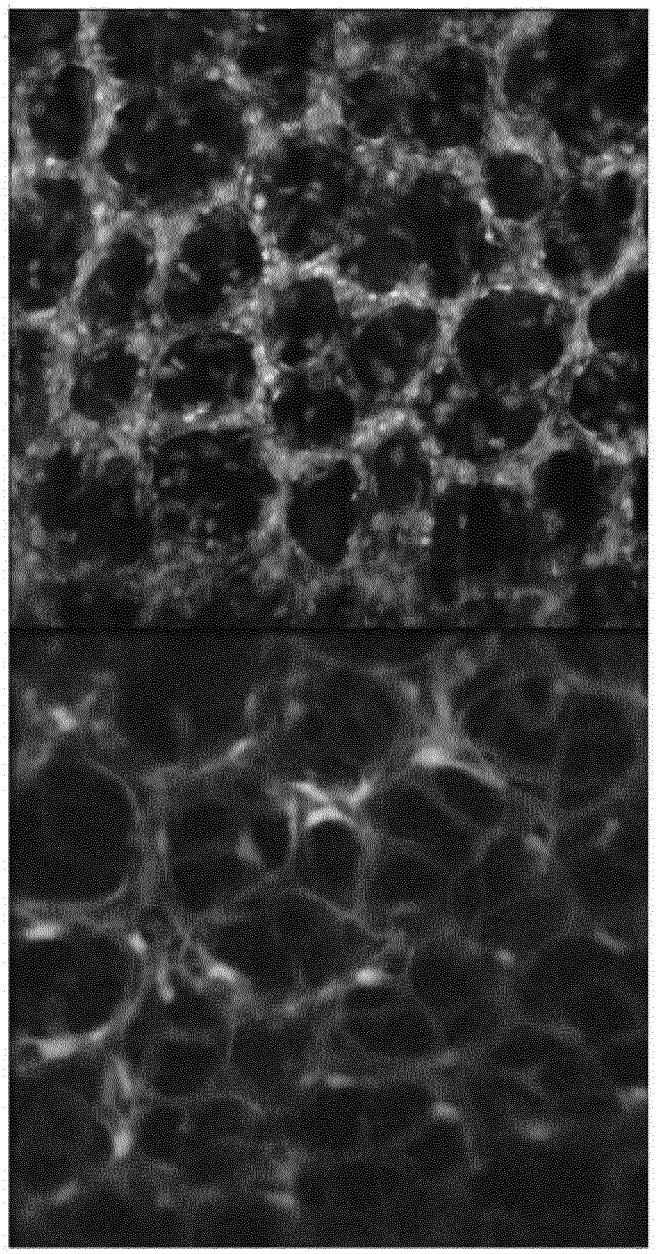
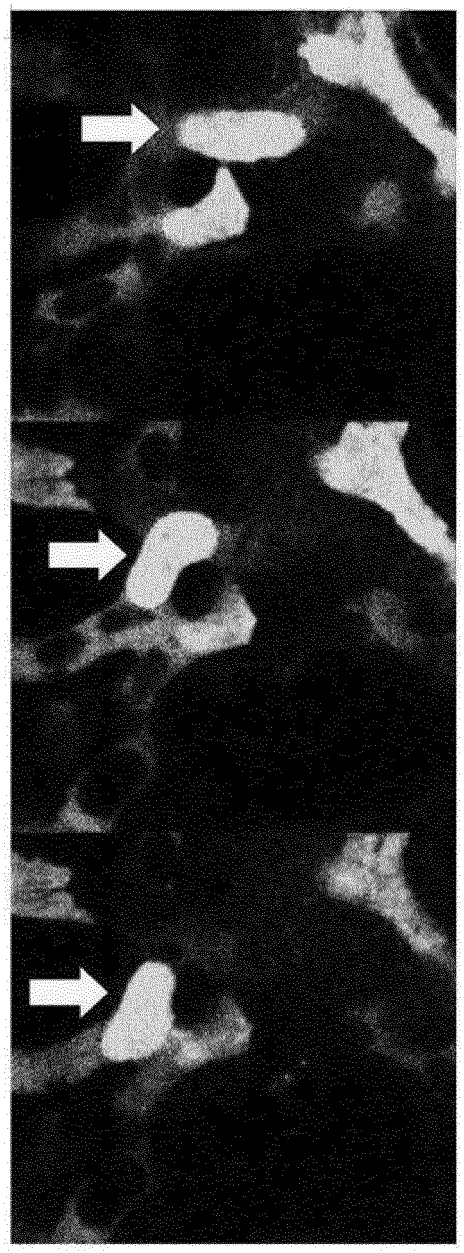


FIG. 7

FIG. 8



INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR2016/009720

A. CLASSIFICATION OF SUBJECT MATTER

A61B 5/08(2006.01)i, A61B 5/00(2006.01)i, G02B 21/00(2006.01)i, G02B 21/36(2006.01)i

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 5/08; G01N 1/36; A61B 10/00; A61B 5/1455; H01J 37/20; G02B 21/34; A61B 19/00; G11B 7/135; G02B 7/02; A61B 5/00; G02B 21/00; G02B 21/36

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean Utility models and applications for Utility models: IPC as above
Japanese Utility models and applications for Utility models: IPC as above

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

eKOMPASS (KIPO internal) & Keywords: microscopy, chamber, vacuum, window, lens, parallel, tilting, holder

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JP 2007-536969 A (KONINKLIJKE PHILIPS ELECTRONICS N.V.) 20 December 2007 See abstract, paragraphs [36]-[49], claim 1 and figures 1-4.	1-6
A	KR 10-2010-0063840 A (HYUNDAI STEEL COMPANY) 14 June 2010 See abstract, paragraph [28] and figures 1, 2.	1-6
A	KR 10-1990-0701215 A (LEVY, Walter J., Jr.) 01 December 1990 See abstract, claim 1 and figure 1.	1-6
A	JP 2002-537573 A (LUCID, INC.) 05 November 2002 See abstract, claims 1-22 and figures 1-3.	1-6
A	JP 09-035317 A (SHARP CORP.) 07 February 1997 See abstract, claims 1-6 and figure 1.	1-6

☐ 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
06 DECEMBER 2016 (06.12.2016)	**06 DECEMBER 2016 (06.12.2016)**

Name and mailing address of the ISA/KR	Authorized officer
Korean Intellectual Property Office Government Complex-Daejeon, 189 Seonsa-ro, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Telephone No.

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR2016/009720

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.: **7**
because they relate to subject matter not required to be searched by this Authority, namely:
Claim 7 pertains to a diagnostic method, and thus pertains to subject matter on which the International Searching Authority is not required to carry out an international search under the provisions of PCT Article 17(2)(a)(i) and PCT Rule 39.1(iv).

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:

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.:

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.

Form PCT/ISA/210 (continuation of first sheet (2)) (January 2015)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/KR2016/009720

Patent document cited in search report	Publication date	Patent family member	Publication date
JP 2007-536969 A	20/12/2007	CN 1950026 A	18/04/2007
		CN 1950026 B	20/06/2012
		EP 1748724 A1	07/02/2007
		JP 2012-101054 A	31/05/2012
		JP 4896874 B2	14/03/2012
		US 2008-0262324 A1	23/10/2008
		US 7761129 B2	20/07/2010
		WO 2005-107579 A1	17/11/2005
KR 10-2010-0063840 A	14/06/2010	NONE	
KR 10-1990-0701215 A	01/12/1990	CA 2002891 A1	14/05/1990
		WO 90-05481 A1	31/05/1990
JP 2002-537573 A	05/11/2002	AU 2000-34938 A1	04/09/2000
		EP 1169630 A1	09/01/2002
		EP 1169630 A4	24/10/2007
		JP 4564664 B2	20/10/2010
		US 2002-154399 A1	24/10/2002
		US 2013-182318 A1	18/07/2013
		US 2015-277094 A1	01/10/2015
		US 6411434 B1	25/06/2002
		US 8149506 B2	03/04/2012
		US 9052523 B2	09/06/2015
		WO 00-49392 A1	24/08/2000
		WO 00-49392 A9	20/06/2002
JP 09-035317 A	07/02/1997	JP 3214805 B2	02/10/2001

Form PCT/ISA/210 (patent family annex) (January 2015)

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- KR 1020150123216 **[0001]**

专利名称(译)	用于获得体内肺组织的显微图像的基于微气体的肺窗装置和使用其获得图像的方法		
公开(公告)号	EP3345546A4	公开(公告)日	2019-05-29
申请号	EP2016842282	申请日	2016-08-31
[标]申请(专利权)人(译)	医药生命融合研究团 韩国科学技术院		
申请(专利权)人(译)	药用BIOCONVERGENCE研究中心 韩国高等学院科技		
当前申请(专利权)人(译)	药用BIOCONVERGENCE研究中心 韩国高等学院科技		
[标]发明人	KIM PIL HAN PARK INWON KIM SUNGHOON		
发明人	KIM, PIL HAN PARK, INWON KIM, SUNGHOON		
IPC分类号	A61B5/08 A61B5/00 G02B21/00 G02B21/36		
CPC分类号	A61B5/0071 A61B5/0084 A61B5/6886 A61B5/00 A61B5/08 G02B21/00 G02B21/36 A61B5/0803 G02B21/0012 G02B21/361 G02B21/362		
优先权	1020150123216 2015-08-31 KR		
其他公开文献	EP3345546A1		
外部链接	Espacenet		

摘要(译)

公开了一种用于获得体内肺组织的显微图像的基于微气体的肺窗装置和使用该装置获得图像的方法。本发明提供一种肺窗装置，包括：开窗，其上部和下部开口，盖玻璃放置在上部，肺组织与下部接触;抽吸管，从打开的窗口的一侧延伸到抽吸装置，并使开窗的内部处于真空状态;倾斜安装件放置单元，其从打开的窗口的一侧延伸并且在其上放置有倾斜安装件，该倾斜安装件使得盖玻璃和共焦显微镜系统的物镜能够保持彼此平行。本发明能够在不干扰的情况下维持动物的生理呼吸和循环，以及稳定获取体内肺组织的细胞水平和分子水平的显微图像。