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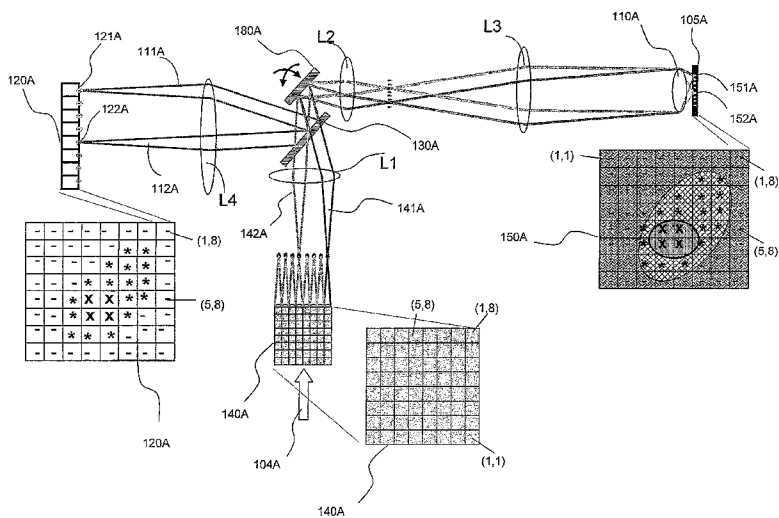
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- Declarations under Rule 4.17:**
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))
  - of inventorship (Rule 4.17(iv))

[Continued on next page]

(54) Title: MULTIFOCAL SCANNING MICROSCOPY SYSTEMS AND METHODS



(57) Abstract: In the systems and methods of the present invention a multifocal multiphoton imaging system has a signal to noise ratio (SNR) that is reduced by over an order of magnitude at imaging depth equal to twice the mean free path scattering length of the specimen. An MMM (multi-photon multi-focal microscopy) system based on an area detector (120A) such as a multianode photomultiplier tube (MAPMT) that is optimized for high- speed tissue imaging. The specimen (105A) is raster- scanned with an array (151A,152A) of excitation light beams. The emission photons from the array of excitation foci are collected simultaneously by a MAPMT and the signals from each anode are detected using high sensitivity, low noise single photon counting circuits. An image is formed by the temporal encoding of the integrated signal with a raster scanning pattern. A deconvolution procedure taking account of the spatial distribution and the raster temporal encoding of collected photons can be used to improve decay coefficient . We demonstrate MAPMT-based MMM can provide significantly better contrast than CCD- based existing systems.

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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

**INTERNATIONAL SEARCH REPORT**

International application No  
PCT/US2006/020372

**A. CLASSIFICATION OF SUBJECT MATTER**  
INV. G02B21/00  
ADD. G01N21/64

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)  
G02B

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 practical, search terms used)

EPO-Internal, COMPENDEX, INSPEC, IBM-TDB, 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	US 6 028 306 A (HAYASHI SHINICHI [JP]) 22 February 2000 (2000-02-22) abstract; figure 3 column 5, lines 19-33 column 5, line 66 - column 6, line 11 column 6, line 37 - column 7, line 22 column 7, lines 56-61 column 8, line 63 - column 9, line 11 column 9, lines 41-56 column 12, line 22 - column 13, line 65	1,81, 151,156
X	US 2004/125372 A1 (WALLA PETER JOMO [DE] ET AL) 1 July 2004 (2004-07-01) abstract; figure 1 paragraph [0051] - paragraph [0063]	1,81, 151,156

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 document 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

27 October 2006

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13/11/2006

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## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/020372

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LEVEQUE-FORT S ET AL: "Time-resolved multifocal multiphoton microscopy" PROC SPIE INT SOC OPT ENG; PROCEEDINGS OF SPIE - THE INTERNATIONAL SOCIETY FOR OPTICAL ENGINEERING 2003, vol. 5139, 2003, pages 173-179, XP002403956 * p.173, item 2.; p.175, item 4.; Fig.4 *	1,81, 151,156
X	LEVEQUE-FORT S ET AL: "Fluorescence lifetime imaging with a multifocal two-photon microscope" PROCEEDINGS OF THE SPIE - THE INTERNATIONAL SOCIETY FOR OPTICAL ENGINEERING SPIE-INT. SOC. OPT. ENG USA, vol. 5323, no. 1, 2004, pages 99-107, XP002403957 ISSN: 0277-786X * p.101, item 4.; Fig.3,4 *	1,81, 151,156
X	KIM DAEKEUN ET AL.: "Optical biopsy in high-speed handheld miniaturized multifocal multiphoton microscopy" PROGR. BIOMED. OPT. IMAGING PROC. SPIE; PROGRESS IN BIOMEDICAL OPTICS AND IMAGING - PROCEEDINGS OF SPIE; MULTIPHOTON MICROSCOPY IN THE BIOMEDICAL SCIENCES V 2005, vol. 5700, March 2005 (2005-03), pages 14-22, XP002403958 * p.15, item 2.; Fig.1 *	1,81, 151,156
X	KIM DAEKEUN ET AL: "High speed handheld multiphoton multifoci microscopy" PROC SPIE INT SOC OPT ENG; PROCEEDINGS OF SPIE - THE INTERNATIONAL SOCIETY FOR OPTICAL ENGINEERING; PROGRESS IN BIOMEDICAL OPTICS AND IMAGING - MULTIPHOTON MICROSCOPY IN THE BIOMEDICAL SCIENCES IV 2004, vol. 5323, 2004, pages 267-272, XP002403959 * p.268, item 2 - p.269, item 3.2; figure 1 *	1,81, 151,156

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2006/020372

## Box 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.: 2-80, 82-150, 152-155, 157-160  
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:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
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 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 an additional fee, this Authority did not invite payment of any additional fee.
  
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.
- No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 2-80, 82-150, 152-155, 157-160

The application comprises 4 independent claims (1,81,151 and 156) that lack novelty (see the documents cited in the Search Report). Moreover, at least some of the independent claims lack essential features resulting in an unjustified broad scope in view of the description and its examples. The number of dependent claims directly dependent on one of the four anticipated claims is so high that they are not in compliance with the provisions of clarity and conciseness (Art.6 PCT), as they erect a "smoke screen" in front of the skilled reader when trying to assess what should be the new and inventive subject-matter to be protected. The non-compliance with the substantive provisions is to such an extent that a non-unity objection (Rule 13 PCT) could not be properly detailed in view of the huge variety of different technical features in the dependent claims, most of them being not so linked as to form a single general inventive concept.

The search was directed to multi-focus multi-photon microscopy devices and methods without particular emphasis on features of the dependent claims. If amended claims are filed, additional searches may be necessary in the national/regional phases.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/020372

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 6028306	A	22-02-2000	JP 3816632 B2 JP 10311950 A	30-08-2006 24-11-1998
US 2004125372	A1	01-07-2004	NONE	