Title: INTERPRETATION OF GAS LEVELS MEASURED VIA BREATH, BLOOD AND SKIN AFTER DIFFERENT BREATH-HOLDING TIMES

Abstract: A method or device for assaying physiological gas levels in a human, comprising: repeatedly measuring a gas in samples of breath or blood, or continuously measuring the gas through the skin or fingernail, while he or she holds his or her breath for a specified time interval (BHT) before each measurement, wherein these time intervals are selected from the group consisting of BHT = 0, 4 - 6, 20 - 25 and 35 - 40 seconds, and recording the results to form a series of values including at least one measurement at BHT = 35-40 which is treated as representing the average gas level in all the tissues of the body (T) at that time, to determine if the individual is net inhaling, net exhaling or in equilibrium with the gas.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 5/08, A61B 5/083, A61B 5/087 (2014.01)
CPC - A61B 5/08, A61B 5/0803, A61B 5/087

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)

IPC(8): A61B 5/08, A61B 5/083, A61B 5/087 (2014.01)
CPC: A61B 5/08, A61B 5/0803, A61B 5/087

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

CPC: A61B 5/082 (keyword limited; terms below)

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
PatBase, PubWEST, Google Scholar, Google Patents: gas level, breath, blood, physiological, breath holding time or Bht, end-tidal or ET, gas sensing device, oximeter, blood gas analyzer, 02, C02, NO, N02, SO2, 03, H2, H2S, ethanol, carbon monoxide

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y</td>
<td>SASSE et al., Arterial blood gas changes during breath-holding from functional residual capacity, CHEST, October 1996, Vol 110, p 958-964; p 961, col 1 para 2</td>
<td>1-14, 18-19</td>
</tr>
<tr>
<td>Y</td>
<td>US 8,417,305 B2 (DIXON) 09 April 2013 (09.04.2013); abstract</td>
<td>3, 10, 13</td>
</tr>
<tr>
<td>Y</td>
<td>US 5,293,875 A (STONE) 15 March 1994 (15.03.1994); abstract; col 2, in 46-52</td>
<td>9-11</td>
</tr>
<tr>
<td>Y</td>
<td>US 5,603,332 A (O’CONNOR) 18 February 1997 (18.02.1997); abstract</td>
<td>19</td>
</tr>
</tbody>
</table>

Further documents are listed in the continuation of Box C.

* 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

Date of the actual completion of the international search
05 January 2015 (05.01.2015)

Date of mailing of the international search report
16 JAN 2015

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-3201

Authorized officer: Lee W. Young
PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774
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).

This International Searching Authority found multiple inventions in this international application, as follows:

Group 1: Claims 1-14, 18, 19. Drawn to a method for assaying physiological gas levels, and a device suitable for said measurement comprising: a) repeatedly measuring a gas level in a human who has held his or her breath for a specified time interval (BH) before each measurement, wherein at least two and up to four time intervals are selected from the group consisting of BH = 0, 4, 6, 20 - 25 and 35 - 40 seconds, b) recording the results to form a series of values including at least one measurement at BH = 35 - 40, which is treated as the average gas level in all tissues of the body, including the lungs, arteries and veins, c) calculating differences between recorded results that represent relative estimates of the level of the gas in lungs minus tissues, arteries minus veins, arteries minus tissues, and/or veins minus tissues, d) interpreting the recorded and calculated results to determine if the gas is being net inhaled or absorbed versus net exhaled or excreted, and at what relative rate.

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.: 1-14, 18, 19

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.
Continuation of Box No. III:
Group II: Claims 15-17, drawn to a method for assaying physiological gas levels, comprising: a. measuring O2 and CO gas levels in a human with a device that continuously measures and displays both the arterial and venous levels of %O2Hb (or SpO2) and %COHb (or SpCO), b. simultaneously calculating and displaying the difference between the venous and arterial levels of each measure (A-V gaps).

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.2 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features

Group I requires the method steps of repeatedly measuring a gas level in a human who has held his or her breath for a specified time interval (BHt) before each measurement, wherein at least two and up to four time intervals are selected from the group consisting of BHt = 0, 4 - 6, 20 - 25 and 35 - 40 seconds, recording results, calculating results, and interpreting the results to determine if the gas is being net inhaled or absorbed versus net exhaled or excreted, not required by Group II.

Group II requires using a device that continuously measures and displays both the arterial and venous levels of %O2Hb (or SpO2) and %COHb (or SpCO) for measuring O2 and CO gas levels, and simultaneously calculating and displaying the difference between the venous and arterial levels of each measure (A-V gaps), not required by Group I.

Common Technical Features

The feature shared by Groups I and II is a method of assaying physiological gas levels by measuring gas levels in a human and calculating the difference between the venous and arterial levels or A-V gaps. However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is taught by US 2007/0149891 A1 to George et al. (hereinafter ‘George’) in view of the article entitled "Arterial blood gas changes during breath-holding from functional residual capacity" by Sasse et al. (Chest, October 1996, Vol 110, No 4, pp 958-64) (hereinafter ‘Sasse’).

George discloses a method of assaying physiological gas levels after a series of breath holds (abstract "an apparatus and method to characterize NO gas exchange dynamics in human lungs comprising the steps of: (1) performing a series of breath hold maneuvers of progressively increasingly breath hold times, each breath hold maneuver comprising a) inhaling a gas, b) holding a breath for a selected time duration, and c) exhaling at a flow rate which is uncontrolled but which is effective to ensure evacuation of the airway space and (2) measuring airway NO parameters during consecutive breath hold maneuvers. As a result disease states of the lungs are diagnosed using the measured airway NO parameters."; para [0013]). George does not teach calculating the difference between the venous and arterial levels or A-V gaps.

However, Sasse teaches determining blood gas levels during breath holding by a method that requires patients to hold their breath for a breath holding time of about 35 (+/- 10) s while arterial blood gas measurements are obtained at 5 second intervals (abstract). Sasse further teaches that arterial partial pressure of oxygen (P02) showed a decline during the first 35 s of breath holding (p 961, col 1, para 3 - "our results showed a marked decline of 50 mm Hg in the arterial P02 during the first 35 s of breath-holding.") while venous P02 remains constant during the 35 s breath-hold (p 961, col 1, para 2 to col 2, para 1 - "venous P02 remains constant (as is true early in the breath-hold), the arterial P02 decline (as a function of time) can be described by a rapidly declining inverse exponential function such as the inverse logistic function. Due to the wide gradient between the alveolar and mixed venous P02, the arterial P02 does not have sufficient time to reach its true minimum asymptotic value (mixed venous P02) during a 35-s breath-hold."). Sasse also teaches that the difference in arterial and venous oxygen content relates to the rate at which oxygen leaves the oxygen gas reservoir (ie, lung volume) and the rate at which gas leaves the reservoir (ie, arterial and venous oxygen content difference and cardiac output or rate of oxygen consumption9). Thus in view of Sasse, one of ordinary skill in the art would have found it obvious to calculate the difference between the venous and arterial gas levels (A-V gap) in order to determine the rate at which gas leaves a gas reservoir in a subject. One of ordinary skill in the art would have found it obvious to modify the method of George to include the method step taught by Sasse, since both relate to methods of determining gas levels from breath holding maneuvers. As the technical feature was known in the art at the time of the invention, it cannot be considered a special technical feature that would otherwise unify the groups.

Groups I and II therefore lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature.