METHOD FOR RAPID IDENTIFICATION OF INFECTIONS AND/OR RISK SITUATIONS RELATED TO GASTRODUODENAL PATHOLOGIES AND MACHINE FOR PERFORMING THE METHOD

Abstract: A method for immediate identification and rapid comparative assessment of indicators of the presence of infections and/or risk situations related to gastroduodenal pathologies, comprising the steps of: aspirating, during an endoscopy, a preset quantity of gastric juices, and sending at least part of the aspirated gastric juices to a control unit, where it is subjected to at least one analysis, the outcome of which is provided before the endoscopy ends.
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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.
METHOD FOR RAPID IDENTIFICATION OF INFECTIONS AND/OR RISK SITUATIONS RELATED TO GASTRODUODENAL PATHOLOGIES AND MACHINE FOR PERFORMING THE METHOD

Technical Field

The present invention relates to a method for rapid identification of infections and/or risk situations related to gastroduodenal pathologies and to a machine for performing the method.

Background Art

It is known that esophagogastroduodenoscopy is currently the main diagnostic technique for pathologies of the upper digestive tract: it also allows to obtain biopsy specimens for possible complementary tests.

While providing excellent macroscopic visualization of the explored viscera, endoscopy alone does not achieve a satisfactory diagnostic sensitivity, since several pathologies do not produce macroscopically detectable changes in the affected organs.

Pathologies frequently associated with normal endoscopic findings are infection with Helicobacter pylori (H. pylori) and fundal atrophic gastritis. Both conditions are important from the clinical and pathological standpoint: the former (H. pylori infection) because in addition to being widespread in the general population (20-90%) it is involved in determining the pathogenesis of many gastroduodenal disorders (ulcer, gastritis, lymphoma, et cetera), and the latter (atrophic gastritis) because it is a neoplastic risk factor.

In order to increase diagnostic possibilities, endoscopy is usually complemented by complementary tests performed on biopsy samples taken during endoscopy. These tests are usually the urease test and histological examination.

Actually, performing these tests does not provide full protection against possible diagnostic errors or omissions. The spot distribution of these pathologies can in fact cause falsely negative results due to the fact
that the biopsy samples were taken in areas not affected by the disease. Moreover, falsely positive results are also possible.

The problem worsens if one considers that a substantial percentage of patients subjected to endoscopy is found to have neither H. pylori infection nor histological evidence of simple or atrophic gastritis. For these patients, performing the complementary tests leads to an unnecessary increase of the duration of the test (and therefore to greater invasiveness), to consumption of materials (biopsy forceps, test tubes, et cetera) and most of all to a considerable financial expenditure.

The problem could be solved if one could, in some way, predict atrophy and H. pylori-status in individuals with normal endoscopic findings. In this manner, complementary diagnostic tests would be performed only in patients who are potentially affected by these pathologies and would be avoided in the others. Such a prediction might also allow a better and more suitable biopsy screening program (with many biopsy samples in the areas most at risk), so as to greatly contain the problem of lesion focality.

Disclosure of the Invention

The aim of the present invention is to obviate the cited drawbacks and meet the mentioned requirements, by providing a method that can be performed with an electromedical machine connected to an ordinary endoscopic apparatus, which allows to determine the H. pylori-status and detect any fundal atrophic gastritis.

Within this aim, an object of the present invention is to provide a method that is simple, relatively easy to provide in practice, safe in use, effective in operation, and has a relatively low cost.

This aim and this and other objects that will become better apparent hereinafter are achieved with the present method for immediate identification and rapid comparative assessment of indicators of the presence of infections and/or risk situations related to gastroduodenal pathologies, characterized in that it comprises the steps of: during an
endoscopic test, aspirating a preset quantity of gastric juices; sending at least part of said aspirated gastric juices to a control unit, where it is subjected to at least one analysis, the outcome of which is provided before said endoscopic test ends.

This method is performed by means of a machine that is characterized in that it comprises a measurement unit that is constituted by a container that is fed by a gastric juice suction pump in which an agitator for agitating the mixture of gastric juice, reagents and water operates, and at least one probe for detecting the values of the analyses, a hydraulic section that comprises a set of tanks for the reagents required for the analyses and for the water, which are connected to respective feed pumps of said measurement unit and to a pump for sending water into the stomach of the patient, a generator of heating air at a low temperature that is connected to said container, and an electrical section, which comprises a programmable control unit for operating and controlling said pumps and said measurement unit, which is suitable to determine the times and methods of execution of the analyses.

Brief description of the Drawings

Further characteristics and advantages of the present invention will become better apparent from the following detailed description of a preferred but not exclusive embodiment of a method for rapid identification of infections and/or risk situations related to gastroduodenal pathologies and of the machine for performing the method according to the invention, illustrated by way of non-limiting example in the accompanying drawings, wherein:

Figure 1 is an installation diagram of a machine that performs the method according to the invention with respect to the endoscopic unit and to the vessel for collecting the aspirated material;

Figure 2 is a schematic view of a possible embodiment of the machine that performs the method according to the invention;

Figure 3 is an exploded view of the container in which the process for
analysis of the gastric juices occurs;

Figure 4 is a diagram of the electrical and electronic connections of the units assigned to the management, control and user interface of the machine that performs the method according to the invention;

Figure 5 is a functional block diagram of the machine that performs the method according to the invention.

Ways of carrying out the Invention

The machine M according to the invention is arranged between an endoscopy unit, designated by U, and a vessel R for collecting the aspirated liquids; in practice, the suction duct of the endoscopy unit U is connected to the inlet of the machine M and the outlet thereof is connected to the collection vessel R (which in turn is connected to the suction unit).

The machine M can be divided schematically into four sections: a measurement unit A, a hydraulic section B, an electrical section C, and a constant-temperature air generator D.

Figure 2 illustrates the measurement unit A, the hydraulic section B and the constant-temperature air pump D. The measurement unit A consists of a normally-open two-way electric valve 1, which blocks (when activated) the suction on a line 2 for the intake of the gastric juice on the part of a general suction duct 3; a second normally-closed two-way electric valve 4, which allows (when activated) to empty a measurement container 8, a pH measurement probe 5, an ammonia measurement probe 6 (the probe is an ammonia measurement probe; ammonium is measured indirectly by converting it into ammonia (gas) by adding ISA), a supporting panel 7 and a measurement container 8 inside which (measurement chamber) the analysis of the gastric juice occurs. This container, as shown in the exploded view of Figure 3, is constituted by a cylinder 9 that is advantageously made of a material such as plexiglass, which is closed at its lower end by a thin disk 10 of a material such as polyvinyl chloride, referenced hereinafter with the abbreviation PVC, and at its upper end by a plug 11, also made of PVC,
which is crossed by seven ducts for introducing liquids 12, two supporting
guides 13 for the probes 5 and 6, a duct 14 for introducing air at a constant
temperature of 30-35 °C (depending on the type of probes used), and a
venting hole 15. At the intersection between the bottom and the side wall of
the container there is an emptying hole 16, which is connected to the suction
system (which is not shown and is located downstream of the vessel R); just
below the upper plug 11, in an internal point of the cylinder 9, there is
instead a temperature sensor 17. At the level that corresponds to the internal
volumes of 5 ml and 10 ml there are two electronic level sensors 18 and 19.

The supporting base of the container 8 is constituted by a small PVC
cylinder 20, inside which there is a receptacle for an agitator 21. The
agitator 21 is constituted by a small DC motor 22, on the rotating shaft of
which a base 23 is mounted; said base supports a permanently magnetized
bar 24, the rotation of which is transmitted, by magnetic coupling, to an
armature 25 (also permanently magnetized), which rests above the bottom
10 of the container 8.

All the components of the measurement unit A are fixed to an upper
face of the supporting panel 7, which in addition to providing mechanical
support also provides (by means of an electric circuit with conducting tracks
formed on the surface of the panel 7) the connections between the various
electrical components of the unit A and a connector 26 for connection to the
electrical section C; an alarm sensor 27 also acts on the panel 7, is suitable
to detect and indicate the presence of liquids on the panel 7, and is
constituted by two parallel and closely spaced conducting tracks.

The hydraulic section B is substantially constituted by six tanks for
liquids, eight peristaltic pumps and a network of ducts that connects the
hydraulic section to the measurement unit and to the pneumatic-hydraulic
input and output connectors of the machine. Each tank is connected to a
specific pump: a tank 28 for the max pH buffer solution is connected to a
pump 29, a tank 30 for the max NH4 calibration solution is connected to a
pump 31, a tank 32 for the min NH4 calibration solution is connected to a pump 33, a tank 34 for the ISA (ionic strength adaptation) solution is connected to a pump 35, a tank 36 for the min pH buffer solution is connected to a pump 37, and a water tank 38 is connected to two pumps 39 and 40: the first of these two pumps, i.e., the pump 39, is designed to feed water into the measurement container 8, and the second pump 40 is instead designed to pump water into the endoscope U (in order to wash mucous regions covered by mucus, blood or clots, ingested material, et cetera) or into the echoendoscope (for filling the viscera to be explored). The reference numeral 41 designates a pump that introduces the gastric juice in the measurement container 8.

The constant-temperature air generator D is designed to maintain a substantially constant temperature inside the measurement container 8. The generator D consists of an actual air pump 42, which produces a low-pressure air stream, a controlled heating unit 43, which warms (30-35 °C) the generated air, and a temperature sensor 17, which is arranged inside the measurement container 8 and constantly informs the heating unit 43 regarding the temperature inside the measurement container 8.

The electrical section C is summarized schematically in Figure 4 and consists of a power supply unit 44 that supplies current to the entire section C. The various power supply lines are guided on a motherboard 45 and distributed from there to the various user devices. The motherboard 45 is the core of the entire section C; by way of suitable multipolar connectors, it is connected to electrical boards and to the various electromechanical devices (agitator 21, electric valves 1 and 4, pumps 29, 31, 33, 35, 37, 39, 40 and 41) and manages all the functions of the machine M by means of a microprocessor 46. By way of a probe interface board 47, the motherboard 45 receives the information acquired by the probes related to pH and NH3 concentration sensing. The signals emitted by the probes are processed by the board 47 and are sent to the microprocessor 46 of the motherboard 45.
From the measurement unit supporting panel 7, the motherboard 45 instead receives the indications related to the movement of the liquids inside the measurement container 8 (detected by the level sensors 18 and 19), and is informed, by way of six further level sensors 48, regarding the filling status of the liquid tanks (28, 30, 32, 34, 36 and 38). The only information it receives from the human operator is: power-on of the machine M (by means of the power-on button 49), start of test (by means of the start button 50), and power-off of the machine M (by means of the power-off button 51). The activation of the electromechanical devices (agitator 21, electric valves 1 and 4, pumps 29, 31, 33, 35, 37, 39, 40 and 41) is managed by means of a driver board 52; all the electromechanical devices are controlled by the microprocessor 46, except for the pump 40, which is activated directly by a pedal 53 that is controlled by the operator. A sound card 54, a display card 55 and a card with luminous indicators 56 are instead used by the machine M to communicate with the outside world. The sound card 54 is provided with a voice synthesis chip 54a on which the messages are prerecorded digitally, an electronic integrated-circuit device 54b, which acts as an intermediary between the microprocessor 46 and the voice synthesis chip, and an amplifier 54c, which is connected to a loudspeaker 57. The display card 55 comprises two display devices 55c and 55d (7-segment bands), on which the microprocessor 46 shows the value of the pH and the value of the ammonium (in ppm), and two millivoltmeters 55a and 55b, which display continuously the operating conditions (signal sent to the microprocessor 46) of the pH measurement probe 5 and of the ammonium concentration measurement probe 6. The card with luminous indicators 56 instead comprises a system of eight two-color light-emitting diodes (known by the acronym LED), which informs the operator regarding the filling condition of the liquid tanks (28, 30, 32, 34, 36 and 38), the suitability for operation of the probes 5 and 6, and the operational status of the machine M.

Figure 5 illustrates the block diagram of the operation of the device.
After power-on (by means of the button 49), the microprocessor 46 performs a self-test to check that the electromechanical devices (agitator 21, electric valves 1 and 4, pumps 29, 31, 33, 35, 37, 39, 40 and 41) are suitable for operation, to check the level of the liquids in the various tanks (28, 30, 32, 34, 36 and 38), and to detect any abnormal losses of liquids inside the machine M. If there are anomalies that are incompatible with correct execution of the tests, or if any loss of liquids is detected, the machine M reports verbally the faulty component or reports the loss of liquids and shuts down automatically. If instead the levels in the tanks (28, 30, 32, 34, 36 and 38) are found to be nearly empty, the machine M reports this shortage verbally to the operator, switches (from green to red) the LED that corresponds to the nearly empty tank on the display card 56, and continues the sequence; in this case, the detected anomaly is in fact compatible with the regular operation of the machine M.

After the self-test, the microprocessor 46 empties (by activating the electric valve 4) and washes with water (deactivation of the electric valve 4 and activation of the water pump 39) the measurement container 8, using the level sensors 18 and 19 as a reference for the movement of the liquids inside the container 8. The microprocessor then calibrates the probes 5 and 6 by introducing sequentially therein the max and min pH buffer solutions (for pH calibration) and the min and max NH4Cl solutions (for ammonium calibration), separating the various steps with a washing cycle and activating the agitator 21 at each measurement. Ammonium measurement is performed after converting said ammonium into ammonia by means of the ISA (ionic strength adaptation) solution, which is added every time ammonium is to be measured; the function of the ISA solution is to increase the pH of the solution to be measured, so as to facilitate the conversion of ammonium into ammonia (gas), which can accordingly be detected by the ammonia probe 6. The resulting ammonium and pH calibration values are compared with reference parameters (suggested by the probe manufacturer);
if the operation of the probes 5 and 6 is found to be normal, the values are stored by the microprocessor 46, which will then use them in calculating the measurements of the samples; if the comparison instead shows that one or both probes are not operating correctly, the device reports the anomaly to the operator, specifying that further operations are not possible (on penalty of inaccurate measurements), washes the measurement container 8, introduces the preservation solution therein and shuts down automatically. If instead the resulting values indicate an initial alteration of the probe or probes 5 and 6, the machine M warns the operator of the drop in the performance of the probe or probes 5 and 6, switches (from green to red) the corresponding LED on the display card 56, stores the values and continues the sequence.

After calibration, the microprocessor 46 again washes the measurement container 8 and introduces the solution, whose composition is related to the type of pH and ammonium probe used. The microprocessor then enters a standby condition (warning the operator of its "ready" condition) and cyclically monitors the start button 50 and the power-off button 51.

The testing procedure begins when the operator presses the start button 50 (a few seconds before beginning the gastroscopy). When the button is pressed, the microprocessor 46 produces the suction of the solution and a cycle for washing the container 8; then it activates the electric valve 1 and the pump 41, so that the aspirated material (gastric juice) is diverted into the measurement container. At this point, the operator merely has to aspirate at least 10 ml of gastric juice from the stomach of the patient. When the level of the gastric juice inside the measurement container reaches the level sensor 19, the microprocessor deactivates the electric valve 1 and the pump 41, so that any further aspirated material is guided toward the suction duct and then toward the container for collecting the aspirated material R. After this, the microprocessor activates the agitator 21 and
records the value detected by the pH probe 5; it then adds the ISA and, after
110 seconds of agitation, measures the value of the ammonia with the probe
6. Then, on the basis of the previously stored calibration parameters, the
microprocessor calculates the value of pH and ammonium (in ppm) of the
sample of gastric juice being tested and displays them on the specific
displays of the card 56; it then compares these values with preset reference
values and reports to the operator the results of the comparison, informing
him as to the presence/absence of H. pylori infection and as to the acidity
condition (normo-, hypo- achlorhydria) of the patient being tested, allowing
to deduce in each instance the diagnostic procedure that is most suitable for
the particular case. All this occurs in no more than 2 minutes, i.e., before the
operator has ended the endoscopic test. During the testing procedure, no
visual monitoring on the part of the operator is required; the reaching of the
10-ml level of suitably aspirated gastric juice, the acidity condition, the
presence/absence of H. pylori and the diagnostic procedure to be followed
are all reported verbally by the microprocessor 46 by way of the sound card
54 and the loudspeaker 57.

Analysis of the data and their reporting by way of voice messages is
followed by the emptying of the measurement container 8, by its washing
and then by the reintroduction of the solution. After this, the device is again
ready for a new test (start button 50) or for shutdown (button 51). If the 10-
ml level is not reached (due to insufficient availability of gastric juice in the
stomach of the patient), the operator presses the start button 50 again. At
this point, the microprocessor checks the level sensor 18, and if it finds it to
be activated (i.e., there are at least 5 ml of juice), it conducts the test,
warning the operator that the procedure is performed on a reduced sample.
If instead the level indicator 18 is not activated (i.e., there are less than 5 ml
of juice), the device warns the operator that the test cannot be performed
and prepares itself for a new test.

When the operator has ended the session of tests, he presses the
power-off button 51. The microprocessor 46 activates the suction of the
solution, washes the measurement container 8, introduces therein the
preservation solution, and switches off the machine M. The preservation
solution can be constituted by one of the four liquids (suitably modified)
used for calibration or by a mixture thereof (in relation to the type of pH and
NH3 probe used).

During any step of the test, and even outside of said test, the operator
can take advantage of the possibility to infuse water into the gastroscope or
echoendoscope, in order to cleanse or fill the affected viscera. To do so, he
merely has to press the pedal 53 that manages the water pump 40 and
connect the water outlet duct to the instrument.

It has thus been shown that the invention achieves the intended aim
and object.

The invention thus conceived is susceptible of numerous
modifications and variations, all of which are within the scope of the
appended claims.

All the details may further be replaced with other technically
equivalent ones.

In the embodiments cited above, individual characteristics, given in
relation to specific examples, may actually be interchanged with other
different characteristics that exist in other embodiments.

Moreover, it is noted that anything found to be already known during
the patenting process is understood not to be claimed and to be the subject
of a disclaimer.

In practice, the materials used, as well as the shapes and dimensions,
may be any according to requirements without thereby abandoning the
scope of the protection of the appended claims.

The disclosures in Italian Patent Application No. BO2003A000091
from which this application claims priority are incorporated herein by
reference.
CLAIMS

1. A method for immediate identification and rapid comparative assessment of indicators of the presence of infections and/or risk situations related to gastroduodenal pathologies, characterized in that it comprises the steps of: during an endoscopic test, aspirating a preset quantity of gastric juices and sending at least part of said aspirated gastric juices to a control unit, where it is subjected to at least one analysis, the outcome of which is provided before said endoscopic test ends.

2. The method according to claim 1, characterized in that said analysis identifies the presence of Helicobacter pylori.

3. The method according to claim 2, characterized in that said analysis determines the concentration of ammonium.

4. The method according to claim 3, characterized in that said analysis is a measurement of the quantity of ammonia that is present and is preceded by the addition of an ISA solution to the gastric juices to convert the ammonium into ammonia.

5. The method according to claim 1, characterized in that said analysis identifies fundal atrophic gastritis.

6. The method according to claim 5, characterized in that said analysis is a measurement of the pH of gastric juice.

7. A machine for performing the method of claims 1-6, characterized in that it comprises a measurement unit (A) that is constituted by a container (8) supplied by means (3) for aspirating gastric juices in which an agitator (21) of the mixture of gastric juice, reagents and water operates, and at least one probe for sensing the values of the analyses, a hydraulic section (B) that comprises a set of tanks for the reagents required for the analyses and for the water, which are connected to respective apparatuses for feeding said measurement unit (A) and to a pump for feeding water into the stomach of the patient, an apparatus (D) for controlling the temperature of said container (8), and an electrical section (C), which comprises a
programmable control unit (46) for actuating and controlling said feeder apparatuses and said measurement unit (A) and is suitable to determine the test execution methods.

8. The machine according to claim 7, characterized in that said means (3) for aspirating gastric juices comprise at least one pump.

9. The machine according to claim 7, characterized in that said means for feeding fluids for the measurement unit (A) comprise at least one pump for sending said reagents and water and/or air.

10. The machine according to claim 7, characterized in that said apparatus (D) for controlling the temperature of said container (8) is a generator of heating air at an adjustable temperature.

11. The machine according to one or more of claims 7 to 10, characterized in that said container (8) of said measurement unit (A) is of a substantially closed type and is provided with connections for a plurality of ducts (12) for the flow of liquids and/or air and for the access of probes (5, 6).

12. The machine according to claim 11, characterized in that said container (8) is substantially cylindrical and comprises at least one temperature sensor (17) and at least one level sensor (18, 19) suitable to indicate the presence of certain volumes of liquids within said container (8).

13. The machine according to claim 11, characterized in that said container (8) comprises, on its side wall, an emptying hole (16) to which an intake is connected.

14. The machine according to claim 11, characterized in that said container (8) contains at least one temperature sensor (17) and a plurality of level sensors (18, 19) that are suitable to indicate the presence of certain volumes of liquids within the container (8).

15. The machine according to one or more of claims 7 to 10, characterized in that said agitator (21) comprises a driving motor (22) to the shaft of which a disk (23) is rigidly coupled, said disk supporting a
permanently magnetized bar (24), and an armature (25), which is also permanently magnetized and rests above the bottom (10) of said container (8).
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B10/00  G01N1/14  G01N33/483

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 7 A61B  G01N

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, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
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<td>Y</td>
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Date of the actual completion of the international search
23 July 2004

Date of mailing of the international search report
02/08/2004

Name and mailing address of the ISA
European Patent Office, P.B. 5816 Patentlaan 2 NL-2280 HV - Hilversum
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Form PCT/IB/10 (second sheet) (August 2004)
### 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. **X** Claims Nos.: 1-6
   - because they relate to subject matter not required to be searched by this Authority, namely:
     - Rule 39.1(iv) PCT – Diagnostic method practised on the human or animal body

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 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.
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