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(54) METHOD AND APPARATUS FOR DETECTION OF RIGHT TO LEFT SHUNTING IN THE CARDIOPULMONARY VASCULATURE

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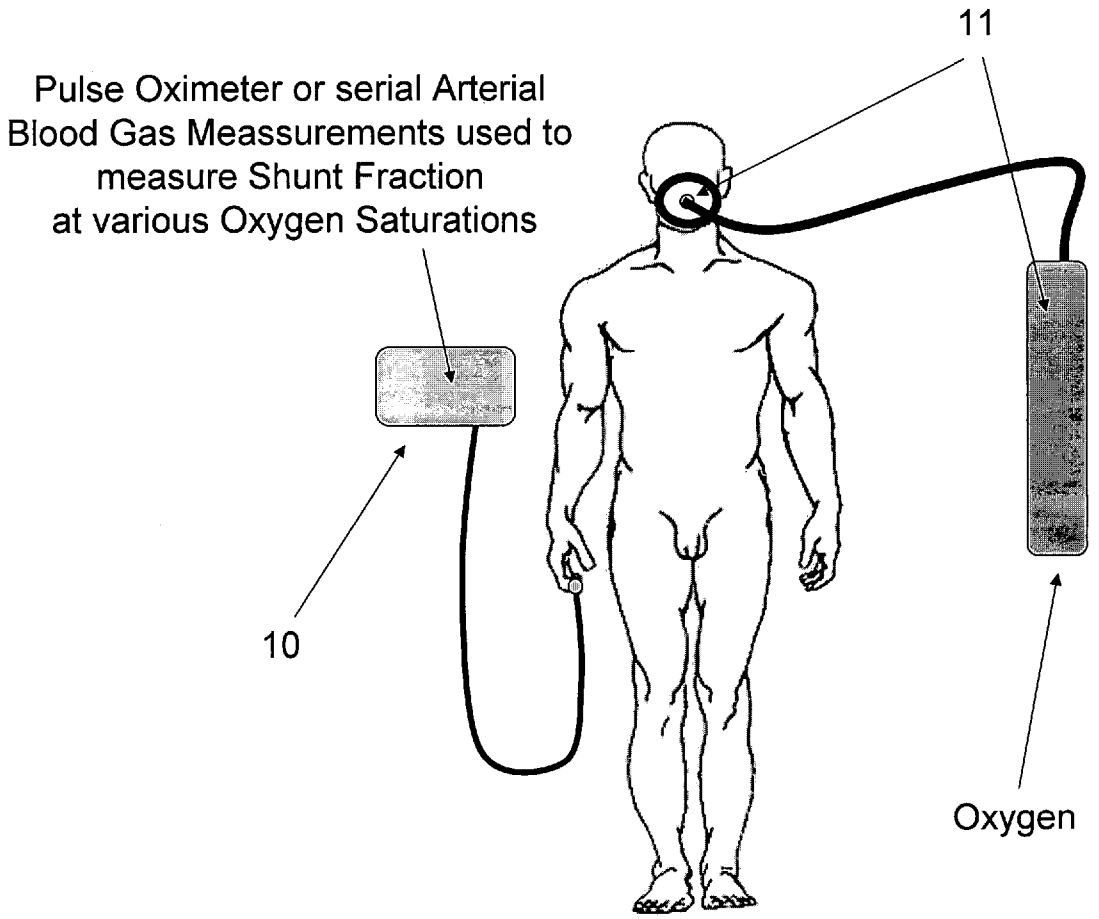
(52) **U.S. Cl.** **600/309**

(57) **ABSTRACT**

The present invention provides a rapid, economical test for the detection of a right to left shunt applicable to the population at large due to its safety and noninvasiveness. The intended procedure involves gaining access to the circulatory system, injecting a measurable substance, ideally during prolonged and/or repeated Valsalva maneuvers, and then rapidly and repeatedly, ideally continuously, assaying for the substance. Through the determination of the appearance of a small amount of the substance prior to the subsequent high concentrations generated by the remainder of the bolus, one may safely diagnose a meaningful communication between the right and left heart, or other right to left shunt bypassing the lungs.



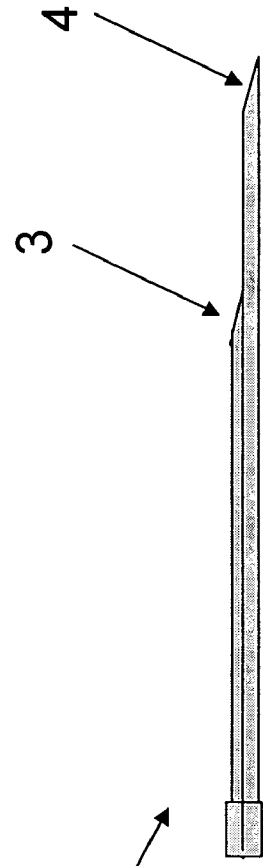


Fig 1A

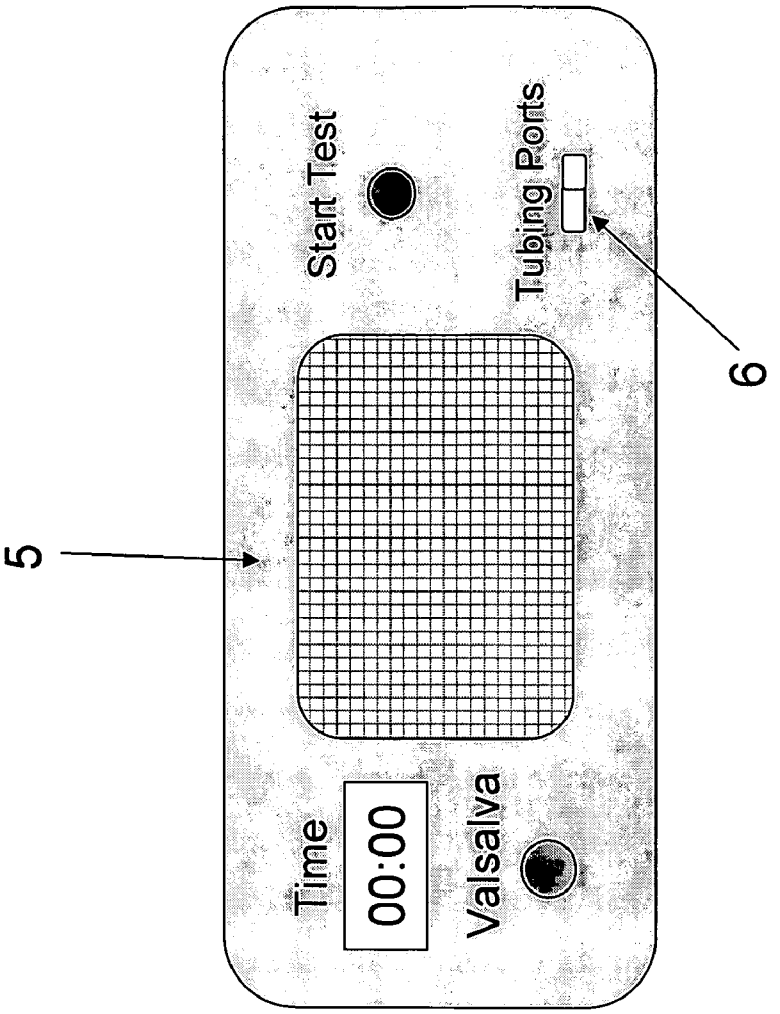


Fig 1B

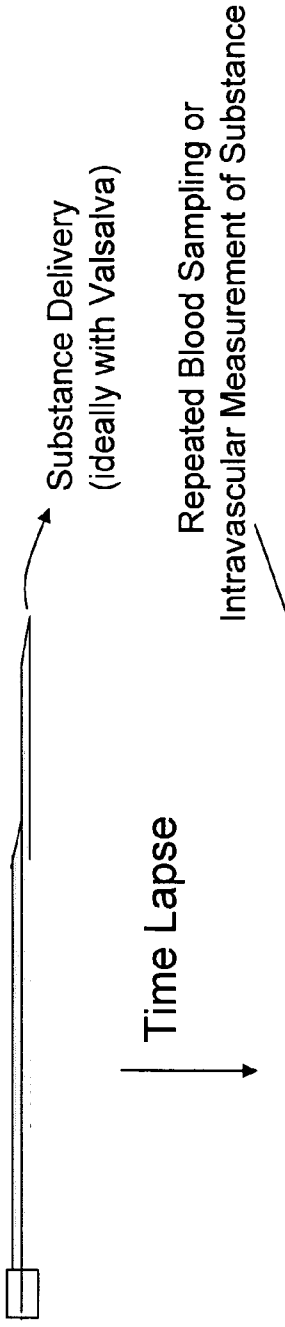
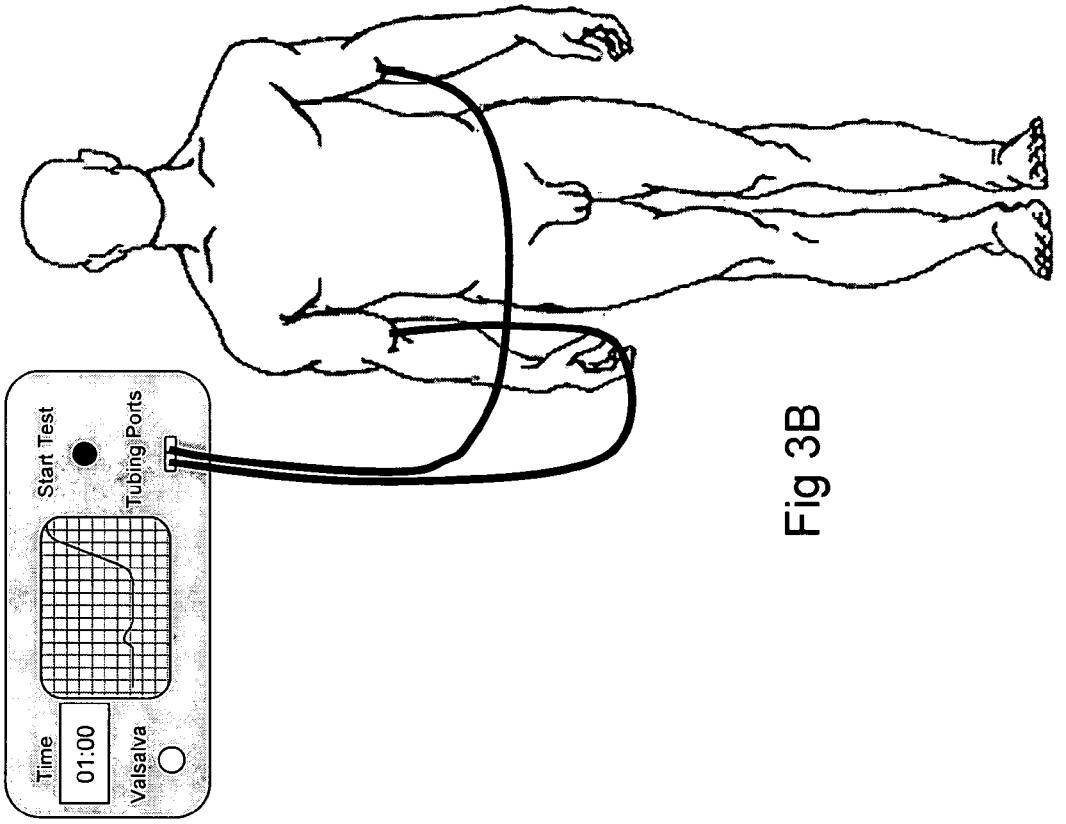


Fig 2A

Fig 2B

Fig 2C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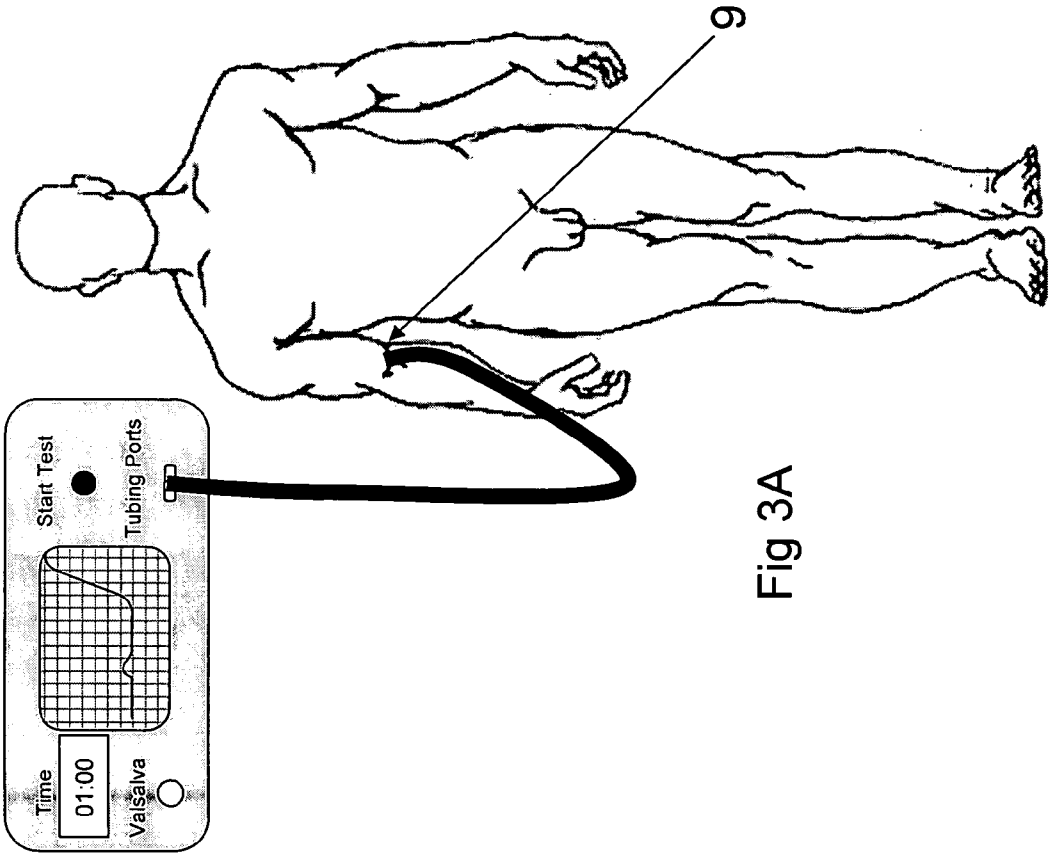
Tubing Ports
Time
01:00
Valsalva

Fig 3B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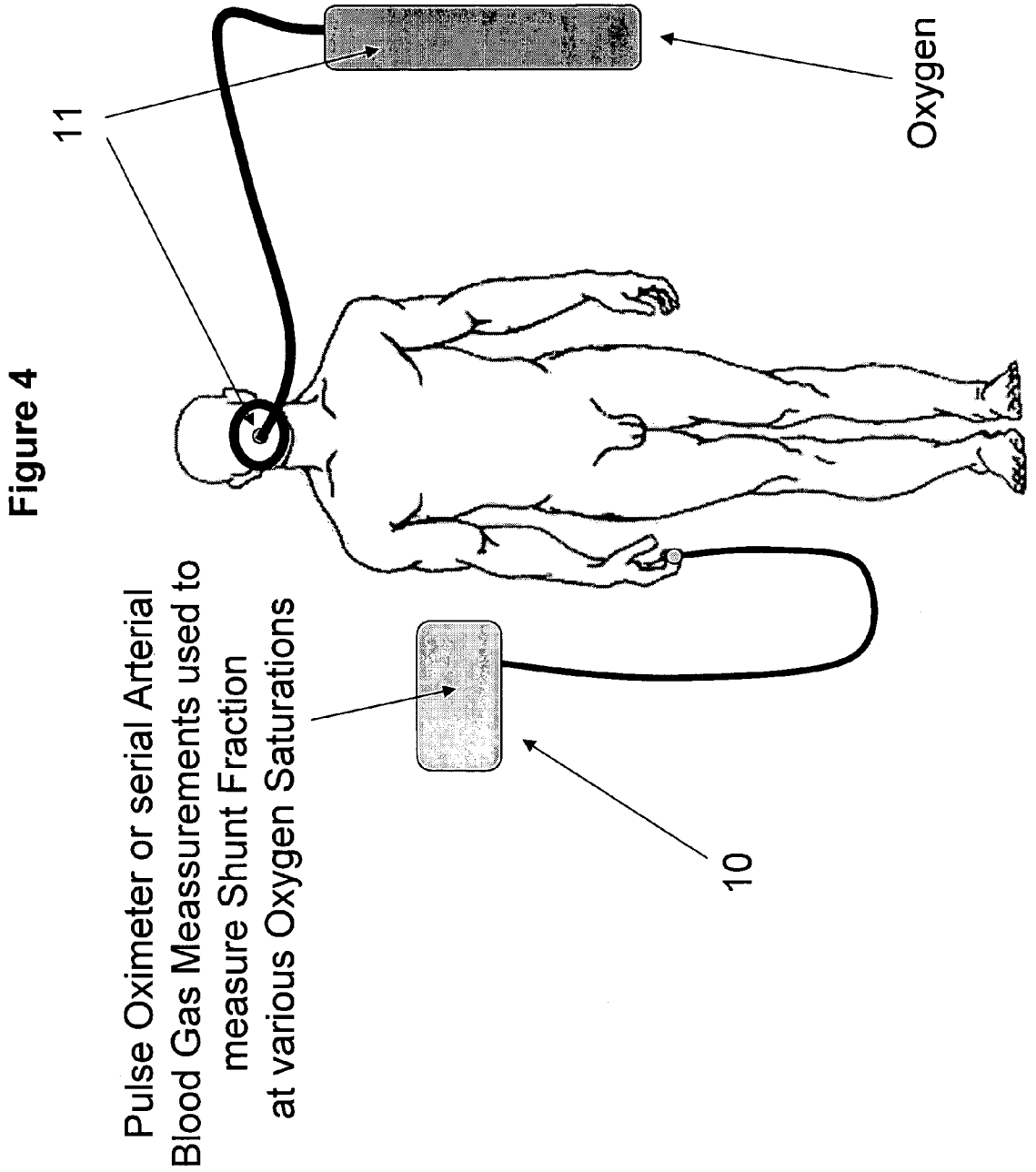
Start Test
Tubing Ports
Time
01:00
Valsalva

Fig 3A

Figure 4


11
Oxygen
Pulse Oximeter or serial Arterial Blood Gas Meassurements used to measure Shunt Fraction at various Oxygen Saturations
10

METHOD AND APPARATUS FOR DETECTION OF RIGHT TO LEFT SHUNTING IN THE CARDIOPULMONARY VASCULATURE

CROSS-REFERENCES TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Patent Application Ser. No. 60/613,205, filed Sep. 27, 2004, U.S. Provisional Patent Application Ser. No. 60/643,145, filed Jan. 12, 2005 and U.S. Provisional Patent Application Ser. No. 60/728,785, filed Oct. 21, 2005. The relevant disclosures of the applications cited in this paragraph is hereby incorporated by reference.

BACKGROUND OF THE INVENTION

[0002] A patent foramen ovale (PFO) is a defect in the septum (wall) between the two upper (atrial) chambers of the heart. Specifically, the defect is an incomplete closure of the atrial septum that results in the creation of a flap or a valve-like opening in the atrial septal wall (see illustration). A PFO is frequent in everyone before birth but seals shut in about 80% of people.

[0003] When a person with this defect creates pressure inside his or her chest—such as when coughing, sneezing, or straining during a bowel movement—the flap can open, and blood can flow in either direction directly between the right and left atrium. When blood moves directly from the right atrium to the left atrium, this blood bypasses the filtering system of the lungs. If debris is present in the blood, such as small blood clots, it can pass through the left atrium and lodge in the brain, causing a stroke, or another organ, such as the heart, eyes, or kidneys.

[0004] PFOs are not uncommon and usually cause no symptoms at all. One in five people have a PFO but less than 1% have a stroke or other cause to have the PFO closed. A PFO is congenital, meaning it is a defect that is inborn or exists at birth. Stated another way, the defect is an abnormality, not a disease. The septum between the two atrium of the heart developed normally before birth but the flap did not seal completely after birth.

[0005] While there is a plethora of prior art surrounding the closure of PFOs including, among others, US Pat. App. Nos. 20050080406, 20050216054, 20050209636, 20050192654, 20050192627, 20050187568, 20030225421 and U.S. Pat. Nos. 5,846,261, 5,718,725, little work has been done to assist in the diagnosis of PFOs. The ideal procedure would be accurate and inexpensive as the optimal use of such a technology would allow for the screening of patients for PFOs, or other right to left shunts, prior to the onset of stroke or migraine symptoms. Currently, diagnosis of a PFO is accomplished through the use of an air-filled contrast agent and ultrasound, either Transesophageal or Transthoracic. This procedure is both expensive and involves risks associated with contrast usage, namely if there is a communication between the right and left heart bypassing the lungs, said air-filled contrast agent will instead become trapped in the cerebral or peripheral vasculature, potentially resulting in morbidity or mortality.

SUMMARY OF THE INVENTION

[0006] The present invention provides a rapid, economical test for the detection of a right to left shunt applicable to the population at large due to its safety and noninvasiveness. The intended procedure involves gaining access to the circulatory system, injecting a measurable substance, ideally during prolonged and/or repeated Valsalva maneuvers, and then rapidly and repeatedly, ideally continuously, assaying for the substance. Through the determination of the appearance of a small amount of the substance prior to the subsequent high concentrations generated by the remainder of the bolus, one may safely diagnose a meaningful communication between the right and left heart, or other right to left shunt bypassing the lungs.

[0007] The device may consist of one or two access sites (arterial or venous), a pump or syringe for delivering the substance and a discrete and repeatable sampling or measuring mechanism linked to a timer. The sampling mechanism, alternatively, could be a continuous mechanism and the diagnosis of a PFO could be based on the qualitative or quantitative appearance of the substance at key time points. In the preferred embodiment, the delivery of the substance and the acquisition of samples will be completely automated and the device will consist of an indicator panel to signal the beginning and the end of the required Valsalva. The substance may be any substance which is safe for use in the bloodstream and easily detectable and may be assayed for externally via blood sampling or may be assayed for via an intravascular sensor, in the instances where such a sensor may be miniaturized enough to be placed on a catheter. Possible substances include, but are not limited to: ammonia, ethanol, indocyanine green, lithium, radiolabled plasma or any other indicator capable of being injected and rapidly detected.

[0008] Due to the requirement for sensitivity in measuring the substance, the ideal embodiment of the device involving a single access site will consist of a dual-lumen catheter where the sampling port is proximal to the site of substance delivery and the two lumens do not communicate. In this way, the delivery will not interfere with the sampling for the substance.

[0009] Alternatively, a substance can be used which is completely, or nearly completely, removed from the bloodstream by the lungs. A simple assay for the substance can then be used and any blood concentration above a certain threshold can be considered diagnostic of a communication between the right and left heart. Either embodiment may involve one or two points of access, most likely a venous and/or arterial access.

[0010] In yet another embodiment, the device may consist of a controlled source of oxygen delivered to the patient during which arterial blood gases or pulse oximetry is performed. By varying the oxygen level that is inhaled, the corresponding decrease or increase in arterial or venous oxygen can then be used to measure shunt fraction, or percent of the blood that is not being passed through the lungs. This will allow for the quick, easy determination of the amount of blood that is being shunted from right to left.

[0011] This device and method will create a PFO screening test that can be widely applicable to all patients due to the ease and inexpensiveness of the test. In addition the device could provide an economical, minimally invasive test for any right to left shunt, including PFOs, ventricular septal defects, atrial septal defects, patent ductus arteriosus, arte-

riovenous malformation in the pulmonary bed and any other condition allowing blood to bypass the capillary bed of the lungs.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] FIGS. 1A-B—A frontal view of an example of an access catheter FIG. 1A and the logic controller FIG. 1B.

[0013] FIGS. 2A-C—Frontal views of the access catheter FIGS. 2A-B in action delivering the measurable substance FIG. 2A and then acquiring the appearance data FIG. 2B with all functions controlled, and the data analyzed, by the logic controller FIG. 2C.

[0014] FIGS. 3A-B—Frontal views of the system attached to the patient while delivering, and recording the appearance of, the measurable substance. FIG. 3A illustrates the system utilizing a single access site utilizing a multi-function catheter.

[0015] FIG. 4—Frontal view of the system in which injection is not required due to use of oxygen at varying concentrations of inhalation as the measurable substance.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0016] FIGS. 1A-B—A frontal view of an example of an access catheter FIG. 1A and the logic controller FIG. 1B. The needle 1 is shown with two ports, an intake port 3 and an outflow port 4. The logic controller 2 is shown with the tubing ports 6 and other controls 5.

[0017] FIGS. 2A-C—Frontal views of the access catheter FIGS. 2A-B in action delivering the measurable substance FIG. 2A and then acquiring the appearance data FIG. 2B with all functions controlled, and the data analyzed, by the logic controller FIG. 2C. The logic controller is shown with possible graphical data analyzer 7 and controls 8. Controls 8 include start button, time indicator and possible indicator to begin Valsalva maneuver, etc.

[0018] FIGS. 3A-B—Frontal views of the system attached to the patient while delivering, and recording the appearance of, the measurable substance. FIG. 3A illustrates the system utilizing a single access site 9 utilizing a multi-function catheter 1. FIG. 3B illustrates the multi-catheter system.

[0019] FIG. 4—Frontal view of the system in which injection is not required due to use of oxygen at varying concentrations of inhalation as the measurable substance. The logic controller 10 is used to analyze the fluctuation in oxygen concentration while the oxygen delivery system 11 controls the oxygen levels. In the ideal embodiment, the oxygen delivery system 11 and the logic controller 12 are integrated to allow for automated delivery of pulmonary oxygen and recording of blood oxygen levels. The blood oxygen levels can be recorded using pulse oximetry, arterial blood gases, venous blood gases, etc.

We claim:

1. A method providing for the detection of cardiovascular shunting and/or bypassing of the pulmonary capillary bed comprising:

Intravascular injection of a measurable substance, and

Assaying for said measurable substance, and

Interpreting the appearance and/or disappearance of the measurable substance to determine if said shunting or bypassing is present

2. The method of claim 1 in which the measurable substance may be ethanol, indocyanine green, lithium, radiolabled plasma, ammonia or any other indicator capable of being injected and rapidly detected

3. The method of claim 1 in which said injection is accomplished by an automated mechanism to provide reliability of infusion

4. The method of claim 1 in which said assaying may be conducted repeatedly or on a continuous basis

5. The method of claim 4 in which the curve associated with said appearance of the substance is use to conduct said interpretation of the presence of shunting or bypassing

6. The method of claim 5 in which abnormal shape of the curve or appearance of measurable substance earlier than anticipated is interpreted as a the presence of shunting or bypassing

7. The method of claim 1 in which said assaying for said measurable substance occurs intravascularly

8. The method of claim 7 in which said intravascular measurement is accomplished at the site of injection of the measurable substance

9. The method of claim 8 in which a single multi-function catheter is used to inject the measurable substance and to assay for said measurable substance

10. The method of claim 1 in which said assaying for said measurable substance occurs external to the patient

11. The method of claim 1 in which injecting the measurable substance, assaying for said measurable substance and interpreting the acquired data may be fully automated

12. A method providing for the detection of cardiovascular shunting and/or bypassing of the pulmonary capillary bed comprising:

Varying concentrations of inhaled oxygen, and

Measurement of blood oxygen content

13. The method of claim 12 in which inhaled oxygen and blood oxygen are used to directly measure cardiovascular shunting and/or bypassing of the pulmonary capillary bed

14. The method of claim 12 in which inhaled oxygen and blood gas measurements may be coordinated via a single instrument

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