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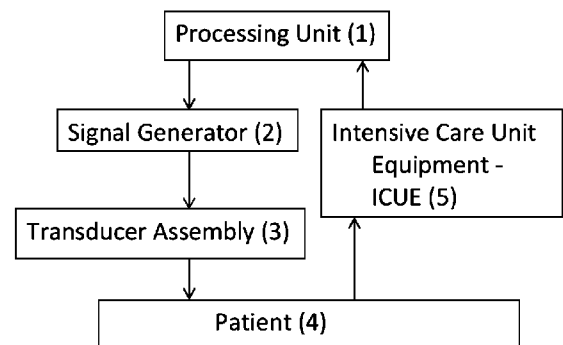
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(54) Title **SYSTEM AND METHOD FOR THE REMOVAL OF ALVEOLAR (THORAX) FLUIDS IN PATIENTS WITH INFECTIOUS AND/OR VIRUS DISEASES (COVID-19)**

(57) Abstract

A system for providing acoustic energy into a human body includes a processing unit with a processor and a memory, an ultrasound signal generator, an ultrasound probe having at least one transducer, the ultrasound signal generator generating actuating signals for the at least one transducer, and intensive care unit equipment (ICUE) including equipment and devices that are locally or remotely connected together to monitor and control a target environment of a patient, in real time. The processor runs a program stored in the memory and causes the system to perform the steps providing input signals to the signal generator causing the signal generator to actuate the ultrasound probe to transmit an ultrasound beam to the patient at a frequency and intensity that remove fluid from alveoli in a lung of the patient; and monitoring, by the ICUE, parameters of the patient or equipment connected to the patient, including real time temperature measurements within the airway, and lung/bronchial or alveoli system(s). One preferred application is to treat patients infected with the SARS-CoV-2 virus and the subsequent disease COVID-19.



Field of the Invention

The present invention relates to systems and optimized procedures for non-invasive removal of fluids in the lungs, bronchial and alveolar organs by the application of ultrasound.

Background of the Invention

WO2018126322 provides an apparatus, method, and use for ultrasound mediated micro bubble delivery of pharmaceutically active molecule(s) to the pulmonary tissue.

WO2017126753 describes an apparatus to which the ultrasound probe is connected, and a server connected to the ultrasound monitoring apparatus, wherein a B-line of the lungs is measured by the ultrasound probe and the ultrasound monitoring apparatus, enabling to monitor the state of the lungs of intensive care patients.

US2011142837 provides methods for treating and/or alleviating acute respiratory distress syndrome in an individual. The methods comprise administering a therapeutically effective amount of a complement thereby treating the ARDS, or delaying or preventing onset of ARDS.

US2015068526 describes a ventilator for use by a clinician in supporting a patient presenting pulmonary distress. A controller operates a positive or negative pressure gas source that communicates with the intubated or negative pressure configured patient through valved supply and exhaust ports.

Patients with preexisting diseases such as, for example, diabetes, chronic obstructive pulmonary disease (COPD), kidney dysfunctions, coronary heart disease have worst clinical outcomes when infected with the virus SARS-CoV-2. The only current treatment of the subsequent disease COVID-19 is supportive.

The pathological features of COVID-19 resemble those of SARS and MERS. The early stages of an infection reveal the presence of pneumonia, edema, proteinaceous exudate with globules and focal hyperplasia of alveolar epithelial cells associated with patchy inflammatory infiltrates. At later stages, diffuse alveolar damage (DAD) is observed in addition to hemorrhage and some areas of interstitial fibrosis.

<https://journals.physiology.org/doi/pdf/10.1152/physrev.00013.2020> (Physiol Rev 100:1065-1075, 2020)

Lethality of Covid-19 is critically driven by disruption of the alveolar-capillary barrier of the lung, leading to lung edema as a direct consequence of SARS-CoV-2 infection, and/or cause acute respiratory distress syndrome (ARDS). See fig. 1 for an illustration of alveolar edema and ARDS. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3558887

Successful drainage of alveolar fluids can restore the alveolar-capillary barrier and provide adequate O₂ and CO₂ exchange, thus reduce COVID-19 lethality.

Brief Summary of the Invention

An objective of the present invention is to provide an ultrasound system and method for non-invasive removal of fluids in the lungs, bronchial and alveolar organs by the application of ultrasound.

According to an embodiment of the invention, the system includes a processing unit (1), an ultrasound signal generator (2), ultrasound probe(s) (3), and Intensive Care Unit Equipment - ICUE (5). The processor (1) includes a memory and runs a program stored in the memory causing the system to perform steps of measuring and/or monitoring input parameters from the ICUE (5) and/or controlling devices represented by the ICUE (5). The system is suitable for Machine learning and/or Artificial Intelligence. One preferred application is to treat patients infected with the SARS-CoV-2 virus and the subsequent disease COVID-19.

An alveolar has typically a diameter of 200 μm . By applying the right frequencies and adequate ultrasound energy intensity, alveoli and/or bronchial tracts come in, one or several modes related to harmonic vibrations, reach one of several natural frequencies, being exposed to pressure waves or shear waves, of a system of such organs, thus displacing alveoli and/or bronchial fluids.

The system operates in real time or in an approximate real time modus. ICUE (5) represents a group of electronic, electric, and mechanical equipment and devices that are locally or remotely connected together to monitor and control a target environment, i.e., a patient (4). In this application, this represents to monitor the restoring of an adequate respiratory capability of the patient.

In general, the target environment is inevitably associated with hardware devices that are sensors, actuators, and valves. Real-time control system means that the control system must provide the control responses or actions to the stimulus or requests within specific times, which therefore depend not just on what the system does but also on how fast it reacts. In software, each of the stimulus handlers requires a process (or task). A real-time control system normally consists of these three types of processes: (1) Sensor control processes that collect information from sensors and may buffer information collected in response to a sensor stimulus. (2) Data processor carrying out processing of collected information and computing the system response. (3) Actuator control processes that generate control signals for actuators.

Real-time control systems are usually designed in the software as cooperating processes with an executive concurrently controlling of these processes. (Industrial control technology: a handbook for engineers and researchers, Peng Zhang, William Andrew Inc, 2008.)

The provided systems can have forecasting, self-learning and/or intelligent capabilities. Machine learning (ML) is a way of development which enables an algorithm to evolve. In this case “learning” means feeding the algorithm with a massive amount of data so that it can adjust itself and continually improve.

Artificial Intelligence (AI) is linked to the concept of mimicking human decision making processes, and the performance of complex tasks in a more human-like way.

It involves machines that have the ability to carry out tasks characteristic of human intelligence. It’s a much broader concept than machine learning. These tasks include: planning, problem-solving, learning, and can include understanding languages and to recognize voices and images. Some relevant IA languages or platforms are; Python, R, Wolfram Language and MATLAB.

An intensive care unit (ICU), also known as an intensive therapy unit or intensive treatment unit (ITU) or critical care unit (CCU), is a special department of a hospital or health care facility that provides intensive treatment medicine. Intensive care unit equipment includes, but are not limited to, patient monitoring, life support and emergency resuscitation devices, and diagnostic devices. Intensive care equipment for life support and emergency resuscitation includes in this context, but are not limited to, the following:

- acute care physiologic monitoring system, i.e., comprehensive patient monitoring systems that can be configured to continuously measure and display a number of parameters via electrodes and sensors that are connected to the patient (these may include the electrical activity of the heart via an EKG, respiration rate, blood pressure, body temperature, cardiac output, amount of O₂ and CO₂ in the blood),

- pulse oximeter, which monitors the arterial hemoglobin oxygen saturation of the patient's blood with a sensor clipped over the finger or toe,

- an intracranial pressure monitor that measures the pressure of fluid in the brain in patients with head trauma or other conditions affecting the brain (such as tumors, edema, or hemorrhage) (these devices warn of elevated pressure and record or display pressure trends),

- an apnea monitor, which continuously monitors breathing via electrodes or sensors placed on the patient,

ventilators (respirators) which regulate the volume, pressure, and flow of patient respiration (ventilator monitors and alarms may interface with a central monitoring system or information system),

infusion pumps that deliver fluids intravenously or epidurally through a catheter (infusion pumps employ automatic, programmable pumping mechanisms to deliver continuous anesthesia, drugs, and blood infusions to the patient),

resuscitation or code cart containing emergency resuscitation equipment for patients who are "coding", i.e., their vital signs are in a dangerous range (the emergency equipment includes a defibrillator, airway intubation devices, a resuscitation bag/mask, and medication box),

intraaortic balloon pump that helps reduce the heart's workload and helps blood flow to the coronary arteries for patients with unstable angina, myocardial infarction (heart attack), or patients awaiting organ transplants (intraaortic balloon pumps use a balloon placed in the patient's aorta, the balloon being arranged on the end of a catheter that is connected to the pump's console, which displays heart rate, pressure, and electrocardiogram (ECG) readings (<https://www.surgeryencyclopedia.com/Fi-La/Intensive-Care-Unit-Equipment.html>, See also e.g. <https://adonyss.com> and <https://www.narang-usa.com>)),

a suction catheter and suction machines or aspirators, which are tracheostomy-care devices used for removing obstructions from a person's airway using suction to pull out mucus, saliva, blood, secretions or other fluids clearing the airway (See e.g.: <https://dir.indiamart.com/impcat/suction-machine.html>, and <https://www.healthproductsforyou.com/c-suction-machinesaspirators.html>).

The ICUE (5) includes at least one of the above listed features, elements or functionalities.

An ultrasound signal generator (2) provides energy to an ultrasound transmitter (3). The ultrasound transmitter may be combinations of single transducers, an array of transducers or a phase array of transducers. Single transducers may be focused by shaping the transducer. Arrays of transducers allow beam forming and focusing techniques. The arrays and elements can be of a general type, for example annular arrays, phased or switched arrays, matrix arrays, linear arrays with division in both azimuth and elevation direction.

The at least one transducer can transmit at least one therapy beam based on at least one set of transmit parameters, where said transmit parameters comprises at least one of i) a transmit focus, ii) a transmit frequency, iii) a transmit pulse amplitude, iv) a transmit pulse length, v) a transmit pulse repetition frequency, vi) a treatment beam transmit duration. The

signal generator sets up the transmit parameters and the transducer transmits the at least one therapy beam across the region of the body (thorax) to be treated.

Other objects and features of the present invention will become apparent from the following detailed description considered in conjunction with the accompanying drawings. It is to be understood, however, that the drawings are designed solely for purposes of illustration and not as a definition of the limits of the invention, for which reference should be made to the appended claims. It should be further understood that the drawings are not necessarily drawn to scale and that, unless otherwise indicated, they are merely intended to conceptually illustrate the structures and procedures described herein.

Brief Description of the Drawings

In the drawings:

Fig. 1 is a cross sectional view showing a normal alveolus on the left side and an injured alveolus suffering acute respiratory distress syndrome on the right side; and

Fig. 2 is a block diagram of a system according to an embodiment of the present invention; and

Preferred embodiments of the invention

A system according to an embodiment of the present invention includes processing unit (1), which may include ML and/or AI, provides input to a signal generator (2), which provide a frequency signal and energy input to a transducer assembly, i.e., an ultrasound probe (3) having at least one transducer. The at least one transducer can be attached with a fluid or gel padding (not shown) to maximize acoustic contact. A gel can be added between the patient and the padding. The ultrasound probe (3) can be placed on the chest or the back of the patient (4), but not necessarily. The input signal from the generator (2) to the at least one transducer of the ultrasound probe (3) can represent combinations of a fixed or variable energy intensity and a fixed or variable frequency. The system also includes Intensive Care Unit Equipment (ICUE) (5) a group of electronic, electric, and mechanical equipment and devices that are locally or remotely connected together to monitor and control a target environment of a patient (4).

The energy intensity level I meets the following: $0 < I < 500 \text{ W/cm}^2$, preferably in the range: $0 < I < 25 \text{ W/cm}^2$.

The frequencies f : $0 < f < 15 \text{ MHz}$, preferably in the range: $0 < f < 500 \text{ kHz}$.

Pulse duration, if applied, is 1 to 5000 cycles.

To prevent excess heating in thorax/lung system/alveoli, human thermocouple or temperature sensors could be applied. The thermocouple sensors can be incorporated with a suction catheter, by a separate probe for insertion into the airway, placed on (outside) the body (e.g. chest or combinations of these modes). Temperature sensors are an integral part of the ICUE (5).

The ICUE (5) measures and monitors in real time, preferable, but not limited to, the amount of O₂ and CO₂ in the blood. The increase of O₂ and/or decrease of CO₂ in the blood, positive changes in respiratory rate, cardiac activity or any other parameters measured by the ICUE (5), is interpreted as a drainage of fluid in the alveolar and/or bronchial system, thus providing increased O₂ influx over the alveolar membrane.

The processing unit (1), with input from the ICUE (5) can adjust the signal generator (2) to control the at least one transducer of the ultrasound probe (3) to provide a combination of a fixed or variable energy intensity and a fixed or variable frequency which maximized the increase of O₂ and/or decrease of CO₂ in the blood.

If the temperature in the airway, lung/bronchial or alveoli system of the patient (4) exceeds a predetermined level, e.g., 41 degrees Celsius, the processing unit (1) will send a command to the signal generator (2) to reduce the intensity from the at least one transducer (3), ensuring the temperature within the airway, lung/bronchial or alveoli system stays at or below the maximum predetermined temperature level. In addition, the at least one transducer of the ultrasound probe is subject to active cooling by an appropriate medium. The active cooling can be controlled in response to the temperature in the airway, lung/bronchial or alveoli system of the patient (4) or in response to a temperature of the ultrasound probe (3).

The output signal from the processing unit (1) can be manually fixed, thus overriding the closed feedback or the intelligence of the system.

The processing unit (1) can include ML and/or AI capabilities, thus the system (1-5) can evolve as a function of time and according to the improvements of the patient(s).

A pharmaceutical substance is a substance (including a mixture or compound of substances) for therapeutic use whose application involves a chemical interaction and/or a physicochemical interaction with a human physiological system.

Micro bubbles are small spherical type of bubbles which consists of a gas. They have a size range usually in the range 1-100 micrometer. They are capable of penetrating even into the smallest blood capillaries and releasing drugs or genes, incorporated on their surface, under the action of ultrasound, *International Journal of Pharmaceutical Sciences and Research* 20(3):3058-3063, 2012.”

The system (1-5) can be operated in conjunction with pharmaceutical substances and/or micro bubbles which are injected into the patient.

In preferred embodiments a system for providing acoustic energy into a human body includes a processing unit (1), an ultrasound signal generator (2), an ultrasound probe (3), and an ICUE (5). The processor (1) includes a memory, and the processor (1) runs a program stored in the memory causing the system to perform the steps of:

providing input signals to the signal generator (2) and ultrasound probe (3),

the processor (1) running the program stored in the memory further causes the system to perform the steps of:

measuring and/or monitoring input parameters from the ICUE (5) unit and/or controlling units represented by the ICUE (5) represented by:

activity of the heart, respiratory rate, blood pressure, body temperature, cardiac output, amount of O₂ and CO₂ in the blood, the arterial hemoglobin oxygen saturation of the patient's blood, the pressure of fluid in the brain, ventilators (respirators), infusion pumps, intraaortic balloon pump, suction catheter(s) and suction machines, and temperature measurements of the thorax/lung/bronchial/ alveoli system.

The present invention is not limited to the described apparatus, system or algorithms, thus all devices and the use thereof that are functionally equivalent are included by the scope of the invention. Modifications of the patent claims are within the scope of the invention.

Drawings and figures are to be interpreted illustratively and not in a limiting context. It is further presupposed that all the claims shall be interpreted to cover all generic and specific characteristics of the invention which are described, and that all aspects related to the invention, no matter the specific use of language, shall be included. Thus, the whole document and the stated references have to be interpreted to be included as part of this invention's basis, methodology, mode of operation and apparatus or system.

CLAIMS

What is claimed is:

1. A system for providing acoustic energy into a human body, the system comprising:
a processing unit including a processor and a memory,
an ultrasound signal generator,
an ultrasound probe having at least one transducer, the ultrasound signal generator generating actuating signals for the at least one transducer,
intensive care unit equipment (ICUE) including equipment and devices that monitor and control a target environment of a patient,
wherein the processor, running a program stored in the memory, causes the system to perform the following steps:
actuating, by the signal generator, the ultrasound probe to transmit an ultrasound beam to the patient at a frequency and intensity that remove fluid from alveoli in a lung of the patient;
monitoring, by the ICUE, parameters of the patient or equipment connected to the patient; and
determining, by the processing unit, whether the ultrasound beam produces a drainage of fluid in the alveolar and/or bronchial system based on the parameters monitored by the ICUE.
2. The system of claim 1, wherein the processor further performs the step of:
controlling equipment of the ICUE.
3. The system of claim 1, wherein the processor further performs the step of:
adjusting the input signals to the signal generator based on the parameters monitored by the ICUE.
4. The system of claim 3, wherein the parameters relate to at least one parameter of the group consisting of activity of the heart, respiratory rate, blood pressure, body temperature, cardiac output, amount of O₂ and CO₂ in the blood, the arterial hemoglobin oxygen saturation of the patient's blood, the pressure of fluid in the brain, ventilators (respirators), infusion pumps, intraaortic balloon pump, suction catheter(s) and suction machines, temperature measurements within the airway, and lung/bronchial or alveoli system(s).

5. The system of claim 1, wherein the intensity is in the range including 0 to 500 W/cm².
6. The system of claim 5, wherein the intensity is in the range including 0 to 25 W/cm².
7. The system of claim 1, wherein the frequency is in the range including 0 to 15 MHz.
8. The system of claim 7, wherein the frequency is in the range including 0 to 500 kHz.
9. The system of claim 3, wherein the adjusting includes lowering the intensity of the ultrasound beam when a temperature of in an airway, a lung, a bronchial system or an alveoli system of the patient exceeds a predetermined threshold.
10. The system of claim 1, wherein the processor further performs the steps of adjusting at least one of frequency and intensity of the ultrasound beam until the parameters monitored by the ICUE indicate an improvement in respiratory function.
11. The system of claim 10, wherein the processor has AI or ML capabilities and further performs the step of:

learning effective treatment parameters by storing intensity and frequency levels that results in the improvement in respiratory function.
12. The system of claim 1, wherein operated in conjunction with pharmaceutical substances and/or micro bubbles which are injected into the patient.
13. A method for providing acoustic energy into a human body, the method comprising:

providing, by a processor, input signals to a signal generator causing the signal generator to actuate at least one transducer of an ultrasound probe to transmit an ultrasound beam to a patient at a frequency and intensity that remove fluid from alveoli in a lung of the patient;

monitoring, by an ICUE, parameters of the patient or equipment connected to the patient, the ICUE including equipment and devices that are locally or remotely connected together to monitor and control a target environment of the patient; and

determining, by the processing unit, whether the ultrasound beam produces a drainage of fluid in the alveolar and/or bronchial system based on the parameters monitored by the ICUE.

14. The method of claim 13, further comprising the step of:
adjusting the input signals to the signal generator based on the parameters monitored by the ICUE.

15. The method of claim 14, wherein the parameters relate to at least one parameter of the group consisting of activity of the heart, respiratory rate, blood pressure, body temperature, cardiac output, amount of O₂ and CO₂ in the blood, the arterial hemoglobin oxygen saturation of the patient's blood, the pressure of fluid in the brain, ventilators (respirators), infusion pumps, intraaortic balloon pump, suction catheter(s) and suction machines, temperature measurements within the airway, and lung/bronchial or alveoli system(s).

16. The method of claim 14, wherein the step of adjusting includes lowering the intensity of the ultrasound beam when a temperature of in an airway, a lung, a bronchial system or an alveoli system of the patient exceeds a predetermined threshold.

17. The method of claim 13, further comprising the step of adjusting at least one of frequency and intensity of the ultrasound beam until the parameters monitored by the ICUE indicate an improvement in respiratory function.

18. The method of claim 17, wherein the processor has AI or ML capabilities and the method further comprises the step of:

learning effective treatment parameters by storing intensity and frequency levels that results in the improvement in respiratory function.

19. The method of claim 1, wherein the step of providing input signals is performed in conjunction with the injection of pharmaceutical substances and/or micro bubbles into the patient.

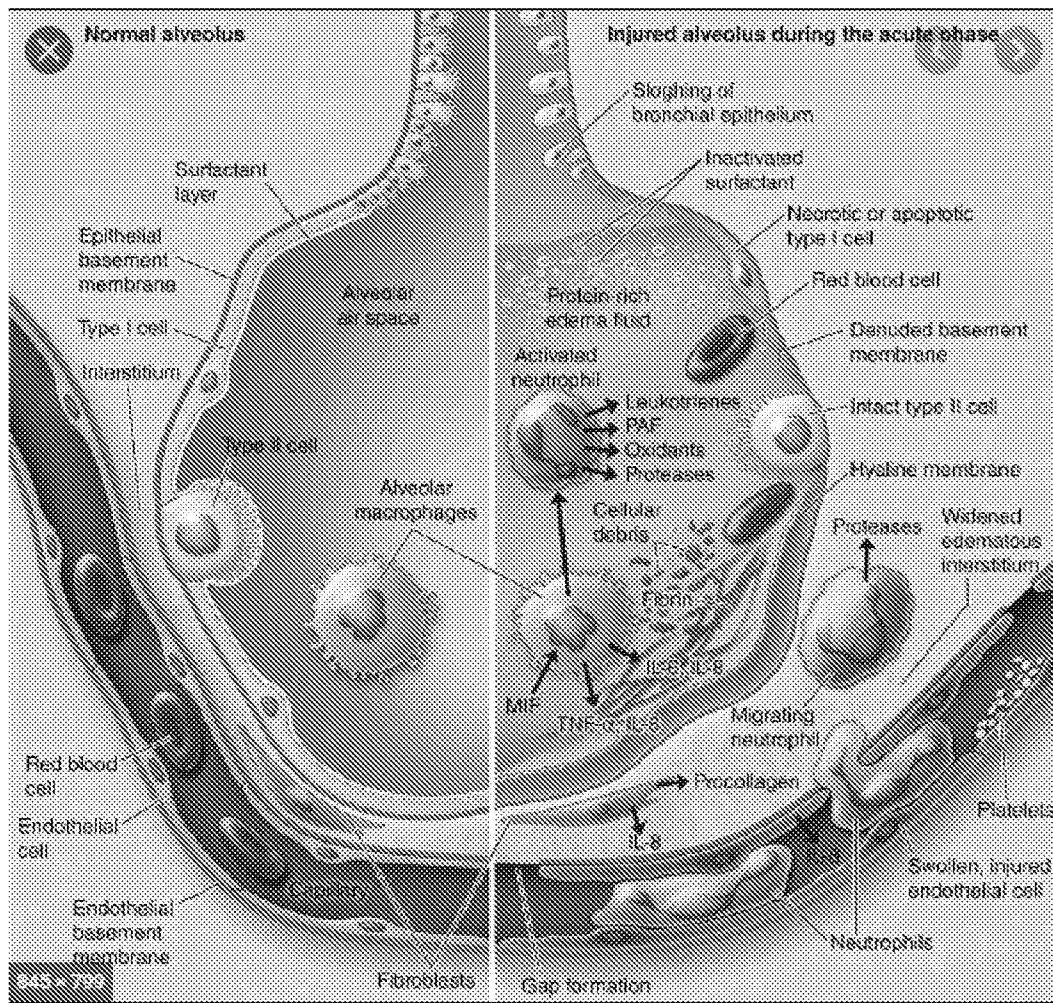


Fig. 1

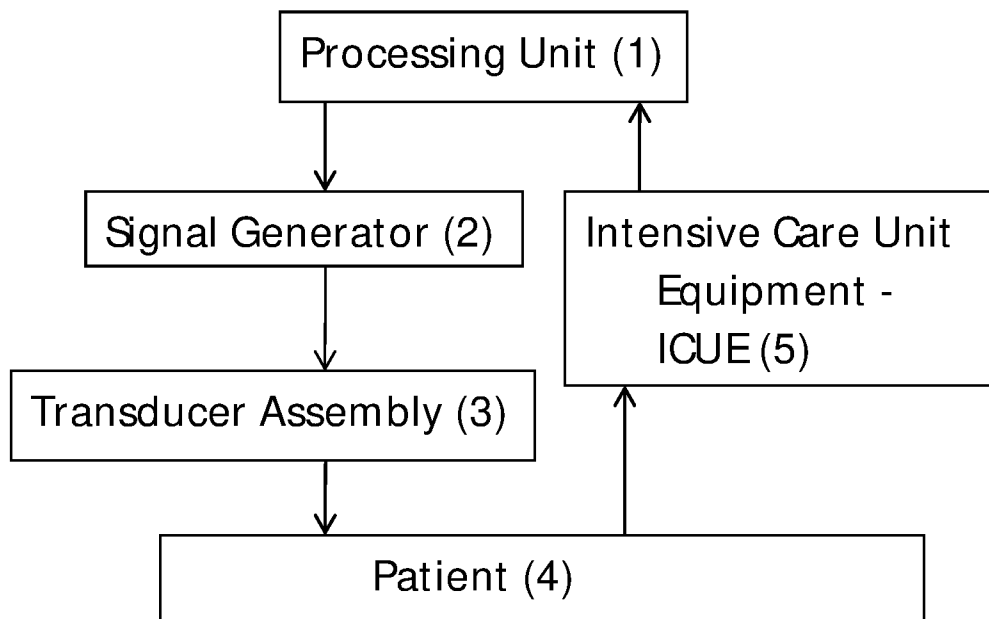


Fig. 2