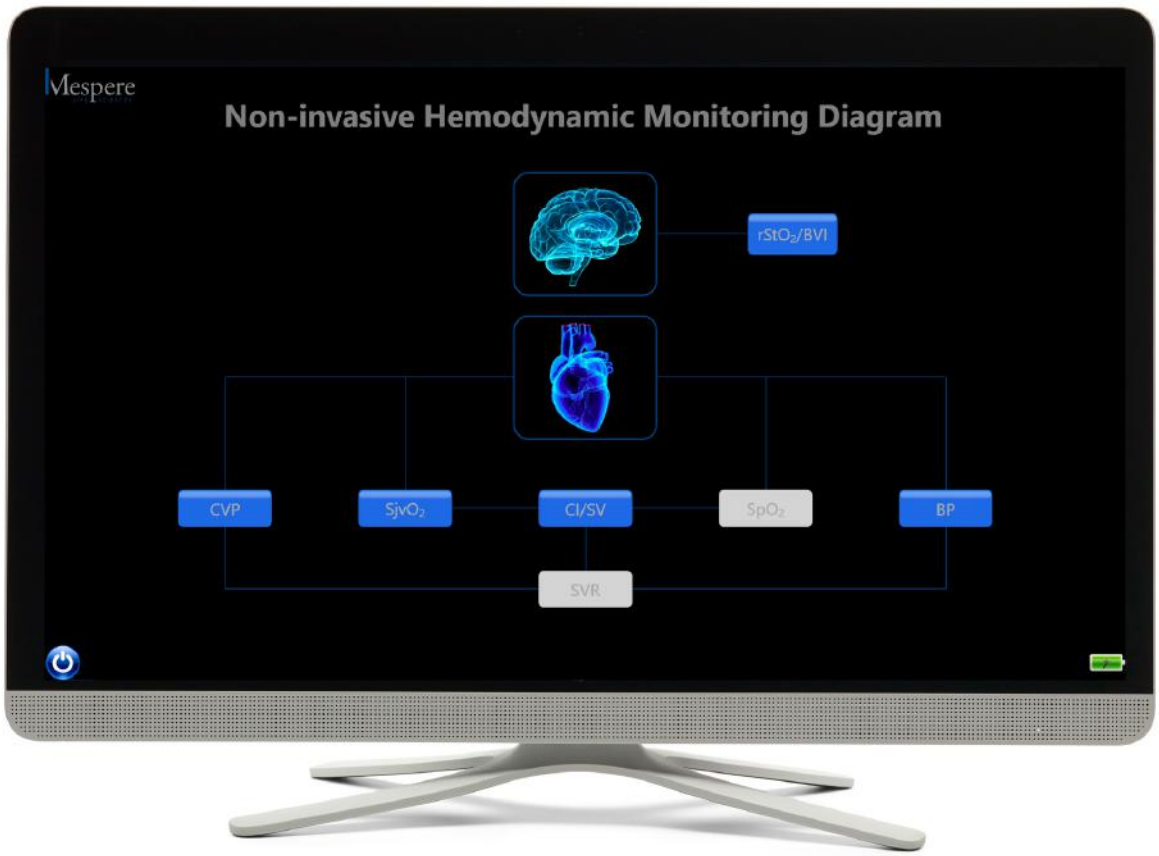
Mespere
LIFE SCIENCES



NON-INVASIVE & CONTINUOUS HEMODYNAMIC MONITORING

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Mespere LIFE SCIENCES

Mespere LifeSciences is a high tech medical company located in Waterloo, Ontario, Canada. Mespere is devoted to developing non-invasive solutions to reduce invasive clinical procedures. The company has successfully developed a number of breakthrough products in the field of cardiac and cerebral hemodynamic monitoring such as, the world's first non-invasive and continuous central venous pressure (VENUS 2000 CVP), jugular venous oximetry (VO 100), and cerebral oximetry with blood volume (NeurOs Cerebral Oximetry) monitoring systems. Currently, these measurements can only be obtained through highly invasive catheters. Other products that Mespere has developed include cardiac output, stroke volume, cerebral perfusion, muscle oxygenation, brain imaging etc.

Mespere's products have significant advantages over the traditional invasive methods in that they are; non-invasive, infection free, easy to use, lower cost etc. Mespere LifeSciences products have a wide range of clinical applications in hospital and at-home settings. The products can be applied to patients with chronic diseases such as congestive heart failure and early stage renal failure to help improve the quality of life and reduce the cost of medical care.

Mespere is ISO 13485 certified, with more than 30 US and international patents. The products have obtained CE mark, FDA, and Health Canada approval. The company is at the early stage of market development and has established distribution and clinical partnerships in over 20 countries. Mespere's key team consists of entrepreneurs with successful track records, world renowned doctors and research scientists.

PRODUCTS

SENSORS & CORRESPONDING SOFTWARE

OVERVIEW

Sensor Placement

Key Clinical Applications

Heart Failure Management - Early Venous Congestion Detection
Heart Clinics, LTC, ED, and ICU

Cardiac and Vascular Surgery - monitor oxygen saturation and blood flow
OR, ICU, and Heart Clinics

Cardiac Function Management - Cardiac Hemodynamics during surgery and critical care
ICU and OR

Cerebral and Tissue Hypoxia
OR, ICU, and Rehabilitation

Sepsis Management - Fluid Overload and Tissue Reperfusion
LTC, ED, and ICU

Beach Chair Position Surgery - orthopedic shoulder surgery
OR, ICU, and Rehabilitation

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VENUS 2000 CVP

Central Venous Pressure Monitoring System

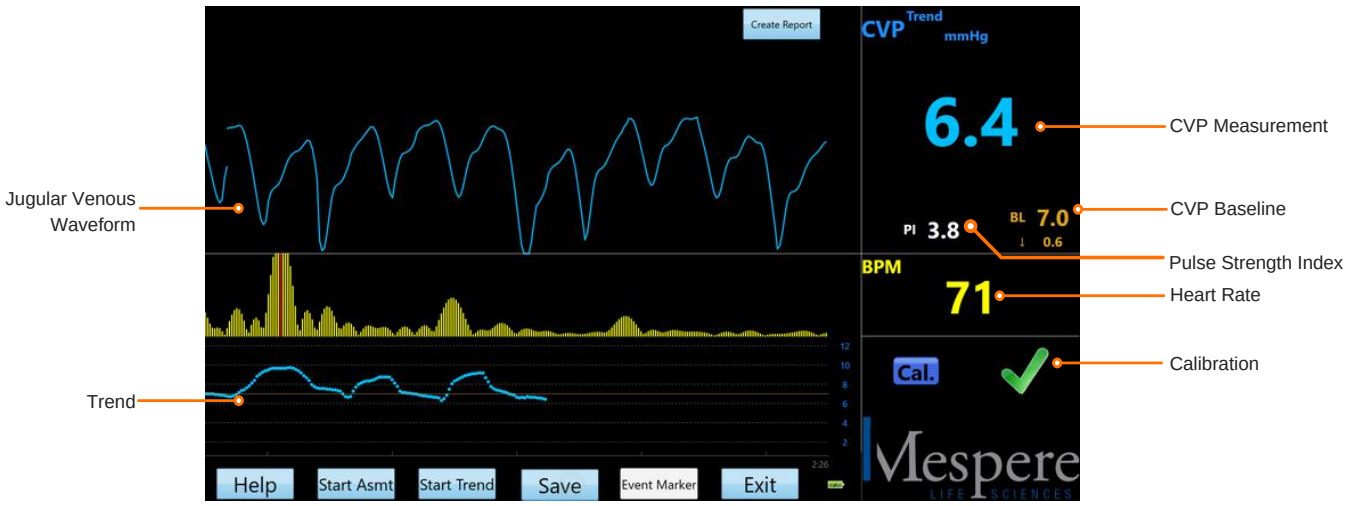
- High accuracy and precision of ± 2.94 cmH2O or ±2.16 mmHg
- Efficient: Measurements achieved in minutes versus hours
- Completely Non-Invasive: Infection Free
- Operates on either tablet, laptop, computer, or any third-party monitors of the customers choice

Key Clinical Applications

Heart Failure Management - Early Venous Congestion Detection
Heart Clinics, LTC, ED, and ICU

Sepsis Management - Fluid Overload and Tissue Reperfusion
LTC, ED, and ICU

VENUS 2000 Display



VENUS 2000 Sensor

MESPERE
VO 100 JUGULAR VENOUS OXIMETRY

Jugular Venous Oximetry Monitoring System

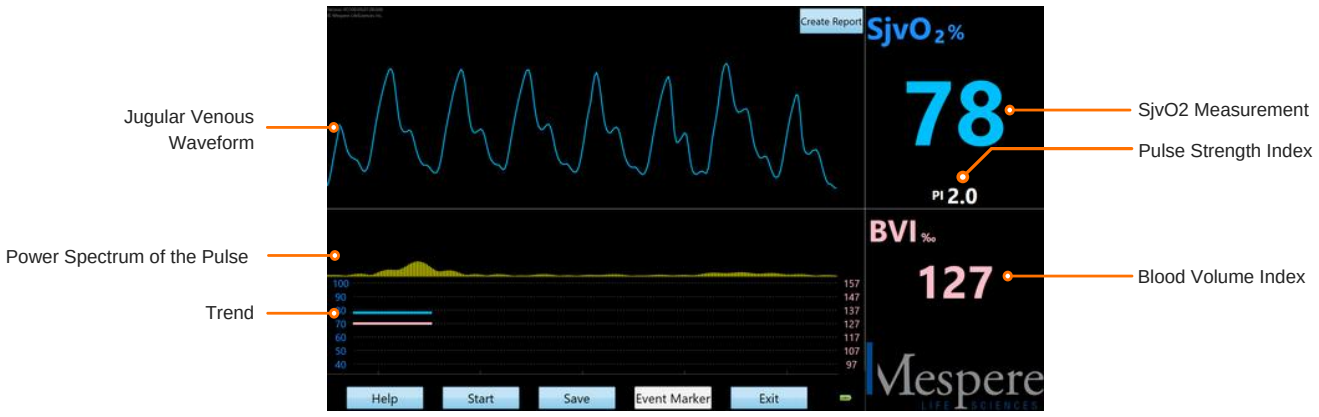
- High accuracy and precision of ±2.00%
- Completely Non-Invasive: Infection Free
- Efficient: Measurements achieved in minutes versus hours
- Operates on either tablet, laptop, computer, or any third-party monitors of the customers choice
- Placement: Right or left, internal or external jugular vein

Key Clinical Applications

Post Cardiac Surgery Management - Cardiac Hemodynamics
ICU

Sepsis Management - Fluid Overload and Tissue Reperfusion
LTC, ED, and ICU

VO 100 Display



VO 100 Sensor

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VENART DUAL PULSE OXIMETRY

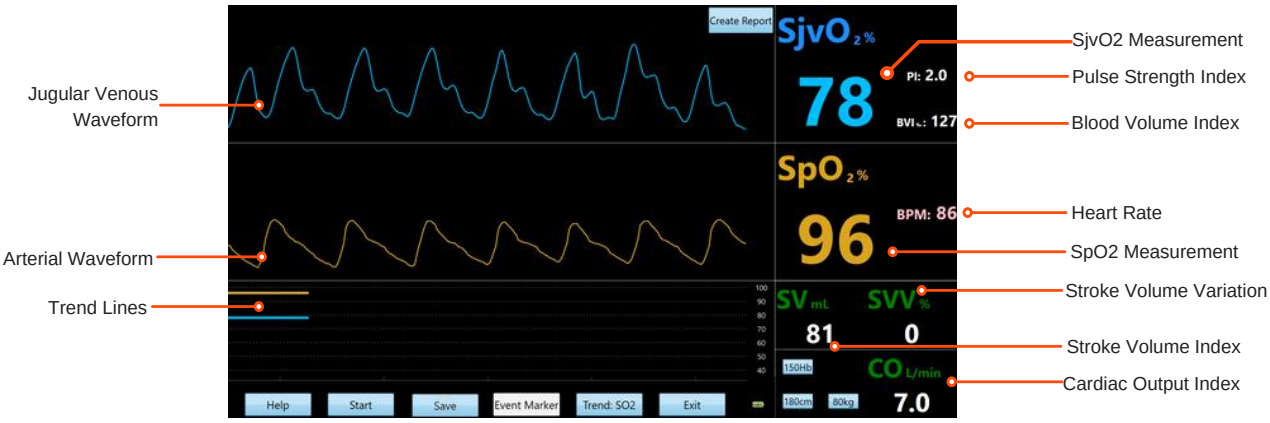
Arterial and Venous Oximetry with Cardiac Index and Stroke Volume

- Beat by Beat Fick's Principle Calculation of Cardiac Output & Stroke Volume
- Completely Non-Invasive: Infection Free
- Placement: VO100 sensor on jugular vein and pulse oximeter on index finger

Key Clinical Applications

Cardiac Function Management -
Fluid Optimization during surgery and critical care
ICU and OR

VenArt Display



VenArt Sensors

Reusable Sensors

Single-Use Adhesive

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NEUROS CEREBRAL OXIMETRY

Cerebral Tissue Oximetry System

- Highest absolute trending accuracy ± 1.5% of tissue oxygenation
- New Blood Volume Index which correlates closely with blood vessel dilation/opening and constriction/collapsing
- Reusable sensors with the best signal quality at a fraction of the cost compared to the existing one time use sensors
- Placement: NeurOs sensor on forehead

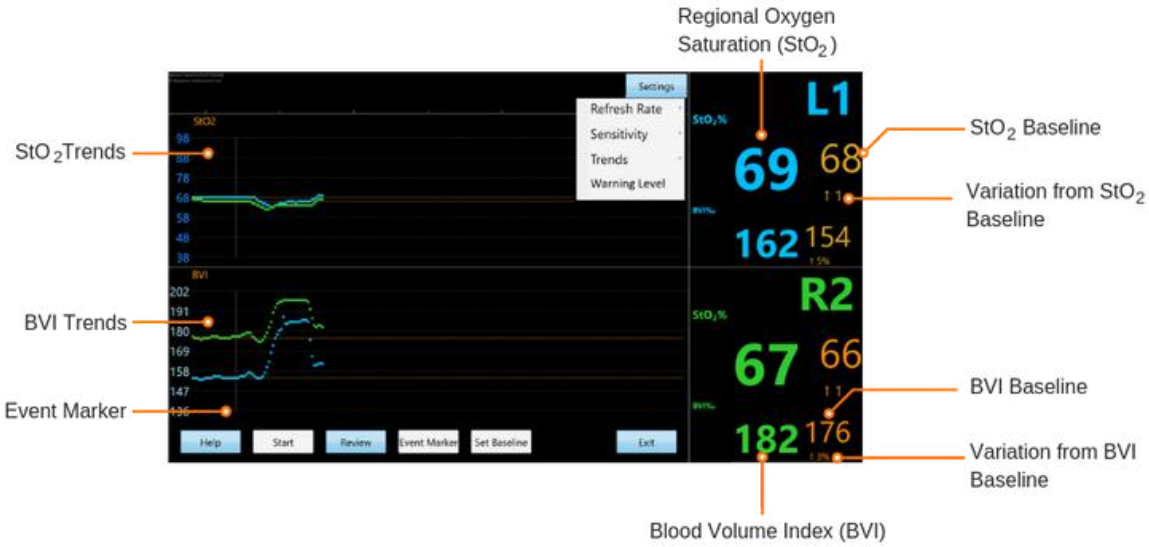
Key Clinical Applications

Cardiac and Vascular Surgery - monitor oxygen saturation and blood flow
OR, ICU, and Heart Clinics

Cerebral and Tissue Hypoxia
OR, ICU, and Rehabilitation

Beach Chair Position Surgery - orthopedic shoulder surgery
OR, ICU, and Rehabilitation

NeurOs Display



NeurOs Sensor

CLINICAL EDUCATION

CENTRAL VENOUS PRESSURE

CVP Physiology

Central Venous Pressure (CVP) is the clinical measurement of right atrial pressure. It is used to evaluate the adequacy of circulating blood volume and cardiac preload. Central venous pressure is comprised of the pressure generated by the volume of blood returning to the right atrium and the pressure adjacent to the heart, called juxta-cardiac pressure. The gradient between mean systemic filling pressure and CVP creates venous return and cardiac output [1].

Venous return is the rate that blood returns to the heart. Mean systemic filling pressure, right atrial pressure, and vascular resistance all play a key role in venous return. Cardiac output correlates with the function and performance of the heart. Ventricular afterload, autonomic tone, and many intrinsic factors affect cardiac output.

Any factor that causes a change in venous return and/or cardiac output can greatly influence CVP. An elevated CVP may be due to an impediment to venous return, hyperinflation, venous return has exceeded the limit of cardiac accommodation, dysfunction in the right heart or obstruction to right ventricular outflow - causing retention of blood, renal failure, or hepatic dysfunction. A lower CVP could be a response to venodilation - causing low venous return, volume loss, sympatholysis, or from any cardiac function that encourages the ejection of blood [1-4].

Due to the fact that CVP is very responsive to any change in venous return or cardiac output, it has shown to be an important measurement to integrate with other monitoring techniques, to better evaluate the patient's hemodynamic instability and to confirm a preliminary diagnosis. It has been used in the ICU for hemodynamic intervention, and bedside for interpretation of a bedside echocardiogram [4].

Current Methods

Currently the common practiced method for attaining CVP is by invasive central venous catheter. Many risks and complications are associated with central venous catheters therefore it would be an attractive option to have a non-invasive technique. Mespere LifeSciences has developed a novel device to continuously monitor CVP non-invasively.

The Mespere VENUS 2000 CVP system will help make the physical examination of CVP an easier and reliable process for the physician. In addition, the VENUS 2000 CVP system will have the additional benefits of allowing physicians to continuously asses CVP over a period of time and to observe the plethysmographic waveform, a feature not available with physical examination.

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CENTRAL VENOUS PRESSURE

Accuracy of Mespere LifeSciences VENUS 2000 CVP Compared to Catheters

Current risks involved with taking continuous CVP measurements, are catheter placement and maintenance. Catheters are susceptible to conflicting results due to, the rate that fluids are introduced, head positioning, and correct tip placement [5]. The current precision for commonly used catheters is -0.1±3.5 cmH2O [6]. Contrary to catheters, the Mespere VENUS 2000 CVP is not susceptible to these risks since it is non-invasive, and there is no placement or insertion of a catheter. The accuracy and precision of the Mespere VENUS 2000 CVP is ± 1.35 cmH2O or ±1 mmHg, therefore it is more precise than the current traditionally practiced method for attaining CVP.

Interpreting a Change in CVP Measurement

Normal range for CVP is between 4-12 cmH2O or 3-8 mmHg. A CVP reading outside of this range should be monitored, and appropriate measures should be taken to get the CVP back into the normal range.

Clinical Applications of Non-Invasive CVP

The Mespere VENUS 2000 CVP system is indicated for individuals to measure hemodynamic cardiac pressures in the human body to allow physicians to better understand cardiovascular health. The Mespere VENUS 2000 CVP system should be used by health care professionals as a non-invasive, spot-checking and/or continuous monitoring tool for physical assessment of central venous pressure (CVP) of an individual. This is done via an adhesive neck patch placed over the external jugular vein. The device is intended for use in hospital and clinical environments.

VENUS 2000 CVP is ideal for preload and volume status assessment and monitoring for patients with congestive heart failure, sepsis, renal failure, congenital heart disease etc. It can be used in a variety of settings such as; Emergency Department, Heart Failure Clinics, and Long Term Care Facilities.

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JUGULAR VENOUS OXIMETRY

Physiology and Venous Oxygen Saturation

Venous oxygen saturation (SvO2) is a measurement used to describe the balance between oxygen delivery and consumption in the brain. SvO2 has been studied comprehensively, since it has shown to be an improved measurement over the traditional methods (heart rate, blood pressure and central venous pressure). Monitoring jugular venous oxygen saturation (SjvO2) has been occurring for many decades and has shown to have useful clinical applications for neurosurgical procedures, cardiovascular procedures, head injuries, and sepsis patients.

Monitoring jugular venous oximetry allows clinicians to make more accurate adjustments, in order to improve the patient's wellbeing and will result in better long term outcomes.

Current Methods

Monitoring in the past, has occurred with the use of co-oximetry laboratory analysis and fiber optic technology. Currently the most common device used are fiber optic catheters. Fiber optic catheters are an invasive method. The Mespere VO 100 is a noninvasive continuous jugular venous oxygenation monitoring system, which uses near infrared spectroscopy to measure venous hemodynamics without the need for invasive catheterization.

Accuracy of Mespere LifeSciences VO 100 Jugular Venous Oximetry Compared to Catheters

Current risks involved with taking a SjvO2 reading, are catheter placement and maintenance. Catheters are susceptible to conflicting results due to, the rate that the blood is withdrawn, head positioning, and correct tip placement [1]. The current precision for commonly used fiber optic catheters, is ±4.41% [2]. Contrary to fiber optic catheters, the Mespere VO 100 Jugular Venous Oximetry is not susceptible to these risks since it is non-invasive, blood is not withdrawn and there is no placement or insertion of a catheter. The accuracy and precision of the Mespere VO 100 is ±2.00%, therefore it is more precise than the current SjvO2 continuous monitoring methods.

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JUGULAR VENOUS OXIMETRY

Interpreting a Change in Venous Oxygen Saturation

The normal range for SjvO2 is 60-80%, below 60% usually indicates that there is a low oxygen delivery, and above 80% indicates that there is low consumption. When monitoring a patient, clinicians should look for changes of ±5-10% for a period of 5 minutes of longer. If this occurs, that it is an indication of a change in oxygen consumption or demand [3]. Jugular desaturation commonly occurs in patients with traumatic brain injury [4], cardiac surgery patients [5], and patients that are comatose.

Clinical Applications of Non-Invasive VO 100 Jugular Venous Oximetry

Monitoring jugular venous oxygen saturation (SjvO2) has been occurring for many decades and has useful clinical application for neurosurgical procedures, cardiovascular procedures, head injuries, and sepsis patients. Continuous monitoring of venous oxygenation, has shown to be a valuable measurement for clinicians. It allows them to monitor the balance between oxygen delivery and consumption. The Mespere VO 100 is a non-invasive continuous jugular venous oxygenation monitoring system that is more accurate, precise, and has far less risks than most commonly used fiber optic catheters.

VO 100 Jugular Venous Oximetry is ideal for use in Emergency Department, Intensive Care Units and in Anesthesia.

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CARDIAC OUTPUT

CI Physiology

Cardiac Output (CO) is an important hemodynamic parameter that explains the volume of blood being pumped out of the heart per minute. Fick's Principle, states that the volume of the oxygen consumed per unit of time (VO2) is proportional to the difference in oxygen content between arterial (Ca) and venous (Cv) blood. Cardiac Output has the units of L/min.

$$CO = {}^{VO_2}/_{C_a - C_v}$$

CO = Cardiac Output
VO2 = Oxygen Consumption, mL of gas per minute
Ca = concentration of arterial (oxygenated) blood
Cv = concentration of venous (deoxygenated) blood

Cardiac Index (CI) is a hemodynamic parameter that expresses the volume of blood pumped by the heart in a minute (CO) divided by the body surface area (BSA). It is used to evaluate the performance of the heart to the size of the individual. Cardiac Index has the units of L/min/m2.

$$CI = {}^{CO}/_{BSA}$$

CI = Cardiac Index
CO = Cardiac Output
BSA = Body Surface Aread

Current Method

Currently there are numerous methods to measure cardiac output, both invasive and non-invasive, but none are considered the "gold standard". Invasive methods are more commonly accepted but evidence has proven that they are not necessarily effective in managing therapy, therefore there is a growing need for the development of non-invasive methods.
The Mespere Cardiac Index system is a non-invasive and continuous solutions that can help healthcare professionals make an easy and reliable cardiac index assessment.

Interpreting a Change in CI Measurement

Normal range of CI is between 2.6-4.2 L/min/m2. A CI reading outside of this range should be monitored, and appropriate measures should be taken to get the CI back into the normal range.

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Mespere LifeSciences Solution for CI

Based upon assumed Fick determination, the Mespere Cardiac Index (CI) system is able to non-invasively assess cardiac index. Because it is very difficult to monitor and measure gas concentrations a common value for VO2 consumption at rest is used, 125mL O2 per minute per meter of body surface area. It is also a known fact that each gram of hemoglobin can carry 1.34 mL of O2 and that there is a hemoglobin concentration of 150 grams of hemoglobin per liter of blood. Using these assumptions, the oxygen content can then be calculated with the following formula:

Clinical Validation of Mespere NeurOs against Invasive Blood Sample Analysis By Co-Oximeter

Methods

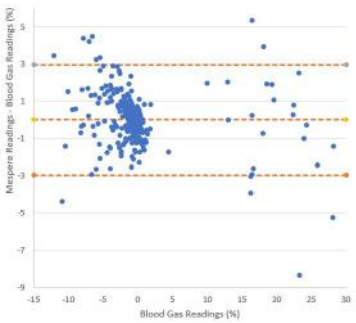
A peripheral IV was placed in the patient's hand or arm vein. An ultrasound-guided small diameter catheter was then inserted in the right upper internal jugular vein. A radial arterial line was inserted into a radial artery on the left arm. Two standard pulse oximeters were attached to the patient's fingers to help guide the hypoxia state plateau levels. The Mespere Cerebral Oximetry sensor was placed on the forehead. Blood gas analysis to determine oxyhemoglobin saturation was performed using a Co-Oximeter. Each subject had control data taken at the beginning of each experiment, with two control blood samples drawn while breathing room air. Hypoxia was induced to different levels of oxyhemoglobin saturation (between 70-100% SpO2) by having subjects breathe mixtures of nitrogen, room air, and carbon dioxide. Once a steady state level of hypoxia is achieved, a 1.0ml sample of blood are obtained simultaneously from the jugular line and radial arterial line. A second blood pair of samples, at the same steady-state saturation, is taken 30 seconds later. The VO200 - NeurOs Cerebral Oximetry samples were recorded simultaneously to the blood samples. The blood samples were immediately analyzed by the Co-Oximeter. Up to 27 paired samples were obtained on the plateaus across this span for each subject.

Results

A total of 284 paired venous and arterial blood sample readings, and 284 Mespere VO 200-NeurOs Cerebral Oximetry System readings were used to perform the comparison and statistical analysis.

The calculated statistical results from the study are as follows:

Absolute Trending Accuracy	**± 1.5%**
Pearson Coefficient	**0.973**



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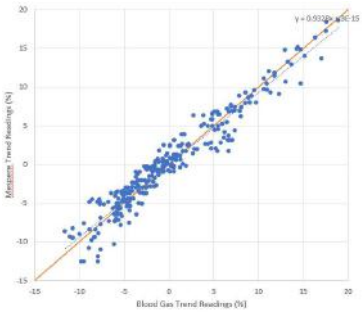

Pearson Coefficient

HEART FAILURE

Facts about Heart Failure[1]

- There are approximately 600,000 Canadians living with heart failure and 50,000 new cases diagnosed every year.
- Upon diagnosis, 50% will die within 5 years and the remaining 50% will die within 10 years.
- Heart Failure is the third most common reason for hospitalization in Canada.
- 25% of patients will be readmitted within 30 days of discharge.
- Heart Failure patients cost $2.8 billion annually

What is Heart Failure?

Heart Failure is a very complex and incurable disease that causes patients to frequently visit the Emergency Department requiring urgent medical care. Heart Failure is a disease that develops after the heart has been damaged or weakened. It occurs when the pumping action of their heart is not strong enough to move blood around to fulfill the body's needs. The damage of the heart function can cause fluid to back up into the patient's lungs or in other parts of the body. The congestion of fluid will cause a lack of oxygen and will cause the patient to have a shortness of breath and feel tired much quicker.

Patients with congestive heart failure typically present with fluid overload and require diuresis or other measures to reduce the pulmonary congestion that results from increased preload. For heart failure patients, venous congestion is the primary reason for hospital readmission. Venous congestion is apparent 1-2 weeks prior to decompensation occurring.[2]

Current Common Practice

Following heart failure hospitalization, patients are in a vulnerable state. Heart disease management programs have been established which provide some form of nursing-intensive interventions that are focusing on ensuring the delivery of guideline-based medical therapy (therapeutic modification), enhancing patient self-efficacy through education regarding adherence and self-management (education), and regular surveillance for early signs of clinical deterioration (monitoring)[3]. Patients will need to adjust their lifestyle, monitor their weight daily, and record how they are feeling.

There is a need for new technologies to reduce the number of costly hospitalization and improve the quality of life of these patients.

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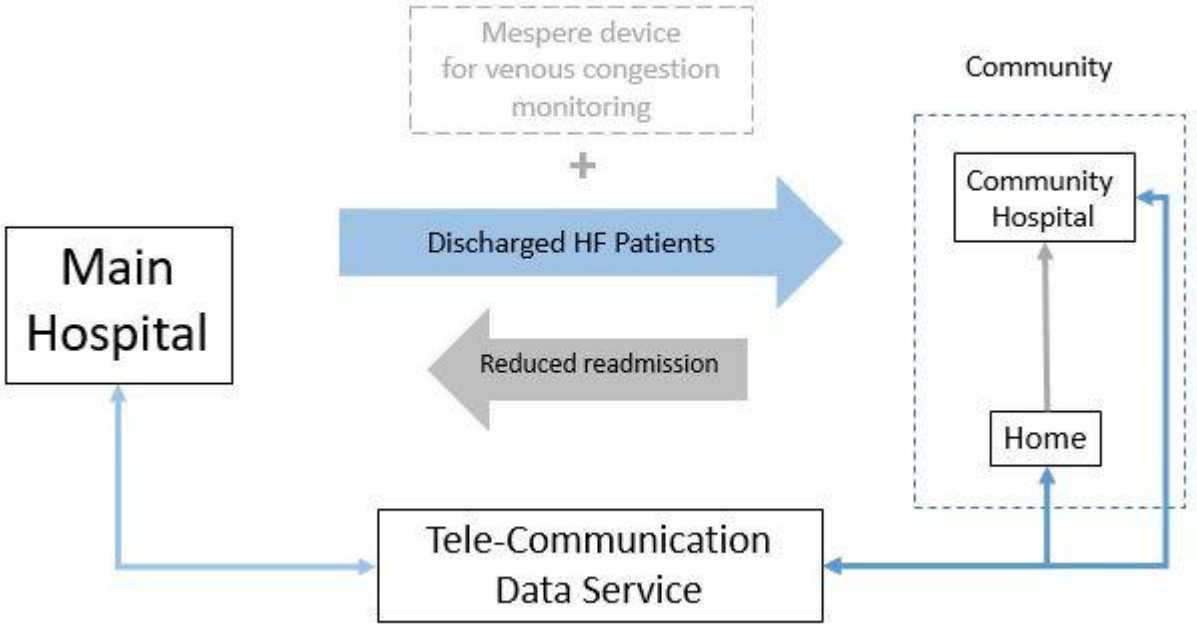
Mespere LifeSciences Solution

The Mespere monitoring system has the best of all features given it is non-invasive application, continuous monitoring capabilities, and tele-monitoring feature. The Mespere monitoring system can monitor venous congestion in a home setting. However, to have meaningful impact on patient care, the information provided by the device has to be monitored by physicians. Heart failure patients will conduct daily monitoring, and physicians can utilize the information provided by a non-invasive venous congestion monitoring device to assist in the management of their heart failure patients.



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SEPSIS SOLUTIONS

Facts about Sepsis[1-5]

- Worldwide incidence of sepsis is estimated to be 19 million cases per year.[1]
- Between 28-50% of people diagnosed with sepsis die.
- Most expensive condition treated in U.S. hospitals, costing $20 billion in 2011 and increase on average annually by 11.9%.[2]
- Mortality from sepsis increases 8% for every hour that treatment is delayed.[4] As many as 80% of sepsis deaths could be prevented with rapid diagnosis and treatment.
- 80% of patients diagnosed with sepsis developed the condition outside the hospital.

What is Sepsis?

Sepsis is a life-threatening illness caused when the body's response to an infection damages its own tissues and organs. Sepsis can be broken down into three core stages:

1. Sepsis: chemicals of the immune system reach the bloodstream and cause inflammation throughout the body
2. Severe Sepsis: infection disrupts blood flow to the brain or kidneys, leading to organ failure
3. Septic Shock: patient's blood pressure drops significantly causing respiratory, heart, or organ failure which could result in mortality[6]

Current Common Practice

Sepsis must be treated as an emergency. Aggressive fluid resuscitation must be performed to restore tissue perfusion in order to prevent organ dysfunction.

- **Within 3 Hours:** aggressive fluid resuscitation by administering antibiotics and intravenous fluids to the patient, approximately 30mL/kg
- **Within 6 Hours:** In the case of blood pressure remaining low despite initial fluid resuscitation, central venous pressure and central venous oxygen saturation should be measured
- **Within 12 Hours:** essential to diagnose or exclude any source of infection

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SEPSIS SOLUTIONS

Fluid Overload

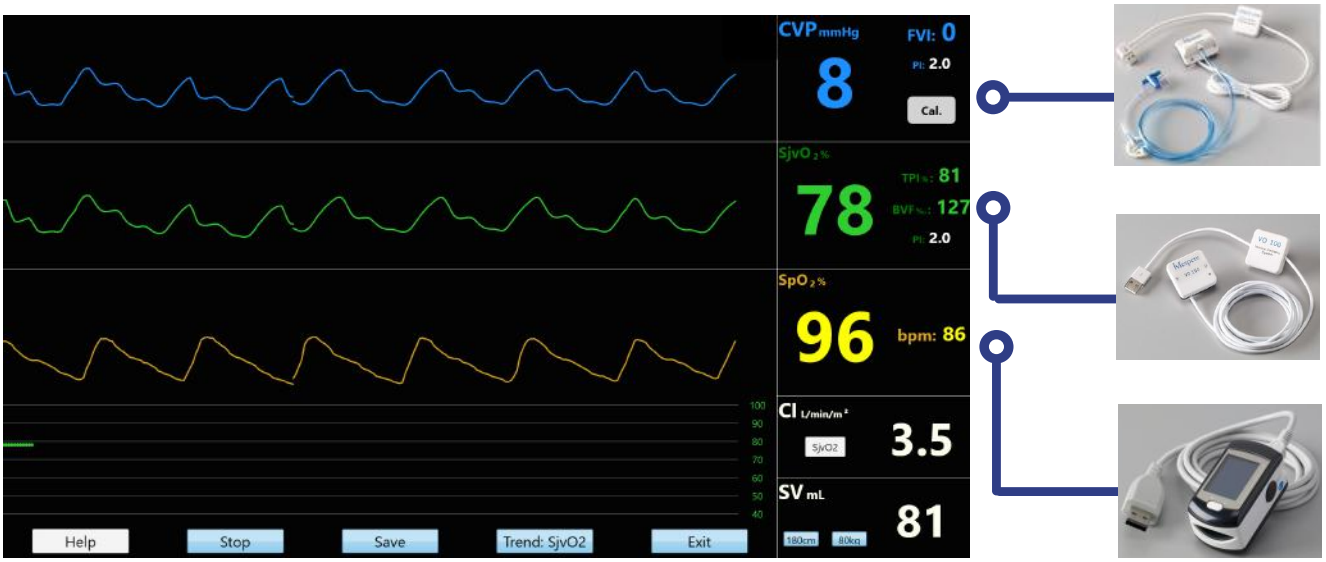
If too much fluid is administered, then fluid overload can occur and cause further complications. Clinical studies have shown that fluid overload can lead to hypertension, peripheral edema, pulmonary edema, respiratory failure, and increased cardiac demand.[7,8]

Mespere LifeSciences Solution

Mespere LifeSciences introduces the first-ever monitoring systems that use near infrared spectroscopy to accurately measure venous hemodynamics without the need for invasive catheterization. Our innovative and cost-effective solutions can be used to ensure that patients are receiving the appropriate fluids in a timely manner.

VENUS 2000 CVP - Mespere LifeSciences VENUS 2000 CVP is a non-invasive and continuous central venous pressure (CVP) monitoring system. With the use of our product, healthcare professionals can now easily and efficiently monitor fluid levels during resuscitation to avoid overload.

VO 100 Jugular Venous Oximetry - Mespere LifeSciences VO 100 Jugular Venous Oximetry is a non-invasive and continuous monitoring system for jugular venous oxygen saturation (SjvO2). Our product allows healthcare workers to monitor the effectiveness of fluid resuscitation for tissue re-perfusion and make sure that the appropriate treatment is being provided to the patient.



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