Green Plasma Disappearance Rate in Critically Ill Patients." Chest 122: 1715-20, 2002.

A number of public domain systems exist that utilize a single irradiation source, such as a fiber optic cable connected to a laser and an associated separate detector, such as a CCD camera or spectrophotometer. The laser emitter and fluorescence detector have been further associated with endoscopic devices. Even simpler densitometric systems have likewise existed for some time, with such systems relying on the absorption of ICG in the 805-810 nm range. An ear densitometer produced by the Waters Co. of Rochester, Minnesota is advertised as being capable of in vivo measurement of ICG absorbance, but in the aforementioned higher doses.

In light of the marginally useful devices available for continuous monitoring of liver or other organ function using a circulating analyte, the present disclosure provides the advantages of a useful non-invasive system. Thus, in application for United States Patent Serial No. 12/418,866, to which priority is claimed, a generally non-invasive technique for screening for measuring the concentration of a circulating analyte is disclosed. The present disclosure provides advantages that will be apparent. This results in one or more intensity versus time curves, representing an analyte concentration resulting from metabolism of the indicator through the circulatory system, i.e. by the lungs, brain, kidney or other organs.

Implementation of the transcutaneous detection system for accurate detection of a circulating indicator allows monitoring of the decay of a circulating indicator in the blood, and thus allows for monitoring of organ function with relatively low doses of indicator.

BRIEF SUMMARY

According to a first aspect of the present invention, there is a system for measuring the concentration of a liver activity analyte that is predominantly removed from the circulating blood by the liver and that contains a fluorescent moiety that can be excited to emit fluorescence through irradiation by excitation photons in wavelength range known to induce fluorescence in said fluorescent moiety of a liver activity indicator analyte, comprising providing an indicator delivery system having an outlet located in a blood vessel of the patient in blood flow communication with the heart; providing at surface of the skin of a human subject one or more sources of excitation photons in wavelength range known to induce fluorescence in said fluorescent component of liver activity indicator; providing at the surface of the skin of a human subject and in alignment with a fraction of the emitted fluorescence photons excited by the source of excitation photons one or more detectors to measure the intensity of emitted fluorescence photons from the liver activity indicator; and providing a monitor/controller responsive to said one or more detectors to record the time-varying relative concentration of the

liver activity indicator by recording the time-varying fluorescence signal level. a sensor comprising a photodiode emitter energizable to generate light at the excitation radiation wavelength and a photodetector which is filtered for response substantially only to the fluorescence emission. providing a transmissive sensor positionable to sense the presence of at least a portion of the blood-borne indicator flowing within a blood vessel at arterial vasculature of one or more symmetrically paired distal locations of the patient and having one or more outputs corresponding with the instantaneous concentration of indicator at such blood vessel vasculature; providing a monitor/controller having a display and responsive to said actuation to commence measuring the relative concentration of blood concentration of a liver activity indicator in the blood, responsive to a sensor output to display one or more metrics reflecting indicator concentrations to determine the nature of liver function.

According to the second aspect of the present invention, there is a sensing array apparatus comprising (a) a plurality of sources of excitation photons and photodetector pairs for measuring the fluorescence emitted by a fluorescent moiety of a liver activity indicator analyte; b) said sources of excitation photons providing an excitation light source emitting a first wavelength for excitation of a liver activity indicator within the tissues of a patient body, said emitters transmitting the excitation light through a collimator lens having a collimating channel aligned with an optical path interference filter, said collimating channel and interference filter located intermediate between said sources of excitation photons and photodetector; and (c) said photodetectors providing for measuring the intensity of the fluorescent light emitted at a second wavelength from the fluorescent moiety of the liver activity indicator analyte; and, (d) a support system of a plurality of array support arms; wherein the array support arms of the support system allow positioning of the sensing array apparatus on the exterior of the patient body, whereupon activation of one or more of the sources of excitation photons transmit excitation light through tissue of the patient, thereby exciting liver activity indicator analyte present in said tissue, said photodetectors thereby measuring the intensity of light emitted by excited liver activity indicator analyte.

According to the third aspect of the present invention, there is a kit supplying consumable materials necessary for quantifying liver function comprising: a) an indicator delivery tubing system providing a valve, syringe connectors, a flow sensor and sterile intravenous injector; b) one or more doses of liver activity indicator reagent as a shelf stable material; c) a diluent for preparing the dose of liver activity indicator reagent for injection or for delivering an indicator bolus; and d) a dose of nonreactive blood compatible clearing reagent for completing the injection.

According to the fourth aspect of the present invention, there is a method for measuring the relative concentration over time of a liver activity indicator in the circulating blood stream, comprising the steps: a) selecting a liver activity indicator analyte that is predominantly removed from circulating blood by the liver said analyte further comprising a fluorescent moiety that can be excited to emit fluorescence through irradiation by excitation photons in wavelength range known to induce fluorescence in said analyte; b) positioning about the skin of a human subject one or more emitter/detector arrays for emitting excitation photons in a given wavelength range known to induce fluorescence in said fluorescent moiety of the liver activity indicator analyte, said emitter in alignment with one or more detectors configured to measure the intensity of emitted fluorescence photons from the liver activity indicator analyte; c) recording the relative concentration over time of the liver activity indicator analyte that has been injected into the blood stream of a human subject, by recording time-varying fluorescence signal level; and d) calculating a liver activity metric according to Formula 1, whereby the relative liver activity of the patient is displayed in a report.

The present system discloses using a transcutaneous detection system to measure the quantity of a circulating detection agent in the blood, and thereby measure the decay of concentration due to liver function. The present system utilizes a variation of the previously disclosed system, method and apparatus for detecting and quantifying right-to-left pulmonary shunts. The preferred indicator, which is employed, is indocyanine green (ICG) dye, which will fluoresce when exposed to an appropriate wavelength of higher energy light, for example, a laser in the near infrared region. The procedure is under the control of a monitor/controller having a visual display and capable of providing a cue to the operator. A vein access catheter is employed in connection with a peripheral vein

associated photodetectors, with the monitor controller collecting said data signal and calculating a organ function metric.

The disclosure is further embodied in a kit supplying consumable materials necessary for quantifying liver function comprising an indicator delivery tubing system providing a valve, syringe connectors, a flow sensor and sterile intravenous injector, one or more doses of liver activity indicator reagent as a shelf stable material, a diluent for preparing the dose of liver activity indicator reagent for injection or for delivering an indicator bolus and a dose of nonreactive blood compatible clearing reagent for completing the injection. The kit may further be embodied in a flow initiation sensor that further comprises an initiation sensor with a circuit that in communication with a monitor-controller responds to a query determining the number of injections a flow initiation sensor has cued and that is disabled for repeated use after a testing procedure time period. The kit further comprises a sealed tray containing the kit contents maintained in a sterile condition until opened.

~~Yet another embodiment of the discloure is a method for measuring the relative concentration over time of a liver activity indicator in the circulating blood stream, comprising the steps a) selecting a liver activity indicator analyte that is predominantly removed from circulating blood by the liver said analyte further comprising a fluorescent moiety that can be excited to emit fluorescence through irradiation by excitation photons in wavelength range known to induce fluorescence in said analyte; b) positioning about the skin of a human subject one or more emitter/detector arrays for emitting excitation photons in a given wavelength range known to induce fluorescence in said fluorescent moiety of the liver activity indicator analyte, said emitter in alignment with one or more detectors configured to measure the intensity of emitted fluorescence photons from the liver activity indicator analyte; c) injecting said liver activity indicator analyte into the blood stream of a human subject; d) recording the relative concentration over time of the liver activity indicator analyte by recording time-varying fluorescence signal level; and e) calculating a liver activity metric according to Formula 1, whereby the relative liver activity of the patient is displayed in a report.~~

Other ~~objects~~embodiments of the invention will, in part, be obvious and will, in part, appear hereinafter. The various embodiments of the invention, accordingly, comprises the method, apparatus and system possessing the construction, combination of elements, arrangement of parts and steps which are exemplified

19. The kit of claim 18 further comprising a flow initiation sensor that further comprises an initiation sensor with a circuit that in communication with a monitor-controller responds to a query determining the number of injections a flow initiation sensor has cued and that is disabled for repeat use after a testing procedure time period.

20. A method for measuring the relative concentration over time of a liver activity indicator in the circulating blood stream, comprising the steps:

a) selecting a liver activity indicator analyte that is predominantly removed from circulating blood by the liver said analyte further comprising a fluorescent moiety that can be excited to emit fluorescence through irradiation by excitation photons in wavelength range known to induce fluorescence in said analyte;

b) positioning about the skin of a human subject one or more emitter/detector arrays for emitting excitation photons in a given wavelength range known to induce fluorescence in said fluorescent moiety of the liver activity indicator analyte, said emitter in alignment with one or more detectors configured to measure the intensity of emitted fluorescence photons from the liver activity indicator analyte;

~~c) injecting said liver activity indicator analyte into the blood stream of a human subject;~~

~~d~~c) recording the relative concentration over time of the liver activity indicator analyte that has been injected into the blood stream of a human subject, by recording time-varying fluorescence signal level; and

~~e~~d) calculating a liver activity metric according to Formula 1,

whereby the relative liver activity of the patient is displayed in a report.