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(54) DEVICE AND METHOD FOR MONITORING BODY FLUID AND ELECTROLYTE DISORDERS

VORRICHTUNG UND VERFAHREN ZUR ÜBERWACHUNG VON KÖRPERFLÜSSIGKEIT UND ELEKTROLYTENSTÖRUNGEN

DISPOSITIF ET PROCEDE PERMETTANT DE SURVEILLER DES TROUBLES RELATIFS AUX FLUIDES CORPORELS ET AUX ELECROLYTES

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Description

[0001] The maintenance of body fluid balance is of foremost concern in the care and treatment of critically ill patients, yet physicians have access to few diagnostic tools to assist them in this vital task. Patients with congestive heart failure, for example, frequently suffer from chronic systemic edema, which must be controlled within tight limits to ensure adequate tissue perfusion and prevent dangerous electrolyte disturbances. Dehydration of infants and children suffering from diarrhea can be life-threatening if not recognized and treated promptly.

[0002] The most common method for judging the severity of edema or dehydration is based on the interpretation of subjective clinical signs (e.g., swelling of limbs, dry mucous membranes), with additional information provided by measurements of the frequency of urination, heart rate, serum urea nitrogen SUN/creatinine ratios, and blood electrolyte levels. None of these variables alone, however, is a direct and quantitative measure of water retention or loss.

[0003] The indicator-dilution technique, which provides the most accurate direct measure of water in body tissues, is the present de facto standard for assessment of body fluid distribution. It is, however, an invasive technique that requires blood sampling. Additionally, a number of patents have disclosed designs of electrical impedance monitors for measurement of total body water. The electrical-impedance technique is based on measuring changes in the high-frequency (typically 10 KHz - 1 MHz) electrical impedance of a portion of the body. Mixed results have been obtained with the electrical-impedance technique in clinical studies of body fluid disturbances as reported by various investigators. The rather poor accuracy of the technique seen in many studies points to unresolved deficiencies of these designs when applied in a clinical setting. Document US 2001/020 122 discloses a device as described in the preambule of claim 1.

[0004] Therefore, there exists a need for methods and devices for monitoring body water fractions which do not suffer from problems due to their being invasive, subjective, inaccurate and difficult to interpret for the purpose of clinical diagnosis and intervention. This object can be achieved by the device and method as defined in the independent claims. Further enhancements are characterized in the dependent claims.

[0005] Embodiments of the present invention provide devices and methods that measure body fluid-related metrics using spectrophotometry that may be used to facilitate diagnosis and therapeutic interventions aimed at restoring body fluid balance. The disclosed invention facilitates rapid, non-invasive, and continuous measurement of fractional tissue water, f_w. Additional embodiments facilitate intermittent measurement of f_w. The specifications of source-detector spacings, wavelength ranges of optical measurement, and algorithms for combining the measurements, provide highly accurate and reproducible methods for determination of f_w.

[0006] In one embodiment, the present invention provides a device for measuring a body-tissue water content metric as a fraction of the fat-free tissue content of a patient using optical spectrophotometry. The device includes a probe housing configured to be placed near a tissue location which is being monitored; light emission optics connected to the housing and configured to direct radiation at the tissue location; light detection optics connected to the housing and configured to receive radiation from the tissue location; and a processing device configured to process radiation from the light emission optics and the light detection optics to compute the metric where the metric includes a ratio of the water content of a portion of patient's tissue in relation to the lean or fat-free content of a portion of patient's tissue.

[0007] In another embodiment, the present invention provides a device for measuring a body-tissue metric using optical spectrophotometry. The device includes a probe housing configured to be placed near a tissue location which is being monitored; light emission optics connected to the housing and configured to direct radiation at the tissue location; light detection optics connected to the housing and configured to receive radiation from the tissue location; and a processing device configured to process radiation from the light emission optics and the light detection optics to compute the metric where the body tissue metric includes a quantified measure of a ratio of a difference between the water fraction in the blood and the water fraction in the extravascular tissue over the fractional volume concentration of hemoglobin in the blood.

[0008] In another aspect, the present invention provides a method for measuring a body-tissue water content metric in a human tissue location as a fraction of the fat-free tissue content of a patient using optical spectrophotometry. The method includes placing a probe housing near the tissue location; emitting radiation at the tissue location using light emission optics that are configured to direct radiation at the tissue location. The method also includes detecting radiation using light detection optics that are configured to receive radiation from the tissue location; and processing the radiation from the light emission optics and the light detection optics; and computing the water content metric, where the water content metric, f_w^1 is determined such that

$$f_w^l = \frac{\left[\sum_{n=1}^{N} p_n \log\{R(\lambda_n)\}\right] - \left[\sum_{n=1}^{N} p_n\right] \log\{R(\lambda_{N+1})\}}{\left[\sum_{m=1}^{M} q_m \log\{R(\lambda_m)\}\right] - \left[\sum_{m=1}^{M} q_m\right] \log\{R(\lambda_{M+1})\}},$$

and where:

p_n and q_m are calibration coefficients;
$R(\lambda)$ is a measure of a received radiation at a wavelength;
n=1-N and m=1-M represent indexes for a plurality of wavelengths which may consist of the same or different combinations of wavelengths. The method may also include displaying the volume fraction of water on a display device.

[0009] In another embodiment, the present invention provides a method for measuring a body-tissue metric in a human tissue location using optical spectrophotometry. The method includes emitting and detecting radiation using light emission and detection optics. In addition, the method includes processing the radiation from light emission and detection optics to compute the metric where the body fluid-related metric is related to a quantified measure of a ratio of a difference between the water fraction in the blood and the water fraction in the extravascular tissue over the fractional volume concentration of hemoglobin in the blood. In one aspect, the metric is a water balance index Q, such that:

$$Q = \frac{f_w^{IV} - f_w^{EV}}{f_h^{IV}} = a_1 \frac{(\Delta R / R)_{\lambda_1}}{(\Delta R / R)_{\lambda_2}} + a_0$$

where f_w^{IV} and f_w^{EV} are the fractional volume concentrations of water in blood and tissue, respectively, f_h^{IV} is the fractional volume concentration of hemoglobin in the blood, $(\Delta R/R)_\lambda$ is the fractional change in reflectance at wavelength λ, due to a blood volume change in the tissue, and a_0 and a_1 are calibration coefficients.

[0010] In another embodiment, the present invention provides a method for measuring a physiological parameter in a human tissue location. The method includes emitting radiation at the tissue location using light emission optics and detecting radiation using light detection optics. Furthermore, the method includes processing the radiation from the light emission optics and the light detection optics and computing the physiological parameter, where the parameter is determined such that it is equal to

$$\frac{\left[\sum_{n=1}^{N} p_n \log\{R(\lambda_n)\}\right] - \left[\sum_{n=1}^{N} p_n\right] \log\{R(\lambda_{N+1})\}}{\left[\sum_{m=1}^{M} q_m \log\{R(\lambda_m)\}\right] - \left[\sum_{m=1}^{M} q_m\right] \log\{R(\lambda_{M+1})\}},$$

and where:

p_n and q_m are calibration coefficients,; $R(\lambda)$ is a measure of a received radiation at a wavelength; n=1-N and m=1-M represent indexes for a plurality of wavelengths which may be the same or different combinations of wavelengths. In one aspect, the physiological parameter is a an oxygen saturation values. In another aspect, the physiological parameter is a fractional hemoglobin concentration.

[0011] In yet another embodiment, the present invention provides a method of assessing changes in volume and osmolarity of body fluids near a tissue location. The method includes emitting radiation at a tissue location using light emission optics and detecting radiation using light detection optics that are configured to receive radiation from the tissue location. The method also includes processing the radiation from the light emission optics and the light detection

optics; determining a water balance index using the processed radiation; determining a tissue water concentration and analyzing in combination the water balance index and the tissue water concentration to assess changes in volume and osmolarity of body fluids near the tissue location.

[0012] For a fuller understanding of the nature and advantages of the embodiments of the present invention, reference should be made to the following detailed description taken in conjunction with the accompanying drawings.

[0013] Fig. 1 is a graph showing tissue water fraction measured on the ear of a pig during an experiment using reflectance measurements at two wavelengths.

[0014] Fig. 2 is a graph showing an example regression for prediction of water from reflectances measured at three wavelengths.

[0015] Fig. 3 is a graph showing an example regression of a two-wavelength algorithm for determination of the difference between the intravascular and extravascular water fraction from pulsatile reflectances measured at two wavelengths.

[0016] Fig. 4 is a diagram of an intermittent-mode version of a fluid monitor.

[0017] Fig. 5 is a diagram of a continuous-mode version of a fluid monitor.

[0018] Fig. 6 is a block diagram of a handheld apparatus for noninvasive measurement and display of tissue water.

[0019] Fig. 7 is a bar graph of water content as a percentage of total and lean mass for men and women between the ages of 20 and 79.

[0020] Fig. 8 is a bar graph of water content as a percentage of fat-free and fat-free-bone-free mass for men and women between the ages of 20 and 79.

[0021] Fig. 9 is a graph of the correlation between separate fat-free or lean volume water fraction ("f_w^l") measurements on the same patient.

[0022] Embodiments of the present invention overcome the problems of invasiveness, subjectivity, inaccuracy, and difficulty of interpretation for the purpose of clinical diagnosis and intervention, from which previous methods for body fluid assessment have suffered. The method of diffuse reflectance near-infrared ("NIR") spectroscopy is employed to measure the fraction of water in skin. An increase or decrease in the water content of the skin produces unique alterations of its NIR reflectance spectrum in three primary bands of wavelengths (950 - 1400 nm, 1500 -1800 nm, and 2000 - 2300 nm) in which none-heme proteins (primarily collagen and elastin), lipids, hemoglobin, and water absorb. According to the results of numerical simulations and experimental studies carried out by the inventors, the tissue water fraction, f_w, defined spectroscopically as the ratio of the absorbance of water and the sum of the absorbances of water and other constituents of the tissue, can be measured accurately in the presence of nonspecific scattering variation, temperature, and other interfering variables.

[0023] Various constituents of tissue, other than water, are included in the denominator of the ratio used to compute the tissue water fraction according to the embodiments of the present invention. In one embodiment, all of the other major tissue constituents, such as non-heme protein, lipid ("fat"), and hemoglobin, are included, resulting in the computation of the total tissue water fraction, f_w^T. In other embodiments, certain constituents of the tissue are specifically excluded from the measured tissue water fraction. Spectroscopic methods for the removal of certain tissue constituents from the computation of tissue water fraction are disclosed, either by choosing spectral regions where the absorbance contribution due to these tissue constituents is small, or by appropriately combining spectroscopic measurements made at multiple wavelengths to cancel the absorbance contribution due to these tissue constituents. The use of such spectroscopic methods for removing the absorbance contribution due to lipid from the measurement, thereby providing fractional water in fat-free or lean tissue, f_w^l, are described. Spectroscopic methods for the exclusion of hemoglobin from the fractional water measurement are also disclosed.

[0024] In addition to these spectroscopic methods, physical methods for including and excluding certain tissue constituents are also described in the present invention. By disclosing source-detector separations in the range of 1-5 mm, the present invention targets the dermis, simultaneously avoiding shallow penetration that would be indicative only of the outer dead layer of the skin as well as avoiding deep penetration into the underlying, high fat-content layer, or even further into bone-containing layers. Additional disclosures include the application of pressure at the tissue site of the optical measurement allowing various mobile constituents of the tissue to be included or excluded from the fractional water measurement. In one embodiment, the fractional water is measured before and after the application of pressure at the tissue site, allowing the mobile intravascular portion of the tissue to be included or excluded from the measurement. By this means, measurements of the fractional water content in the intravascular space, f_w^{IV}, extravascular space, f_w^{EV}, and a difference between the two $f_w^{IV} - f_w^{EV}$, is accomplished. In additional embodiments, these measurements are accomplished by photoplethysmography, taking advantage of the natural arterial pulsation of blood through tissue.

[0025] In the following detailed descriptions of the embodiments of the invention, the terms "fractional tissue water", "tissue water fraction", "water fraction", and "f_w" all have equivalent meanings and are meant as general terms that include all of the more specific measurements outlined above, including, but not limited to, total tissue water fraction (f_w^T), lean tissue water fraction (f_w^l), intravascular water fraction (f_w^{IV}), and extravascular water fraction (f_w^{EV}).

[0026] In embodiments of the present invention, the apparatus and its associated measurement algorithm are designed according to the following guidelines:

1. To avoid the shunting of light through the superficial layers of the epidermis, the light source and detector in optical reflectance probe have low numerical apertures, typically less than 0.3.
2. The spacing between the source and detector in the probe is in the range of 1-5 mm to confine the light primarily to the dermis.
3. The reflectances are measured at wavelengths greater than approximately 1150 nm to reduce the influence of hemoglobin absorption. Alternatively, reflectances are measured at wavelengths as short as 950 nm, but the influence of hemoglobin absorbance is reduced by appropriately combining measurements of reflectance at multiple wavelengths. Or as a further alternative, the absorbance of hemoglobin is intentionally included in the denominator of the ratio used to compute tissue water fraction.
4. To ensure that the expression that relates the measured reflectances and water content yields estimates of water fraction that are insensitive to scattering variations, the lengths of the optical paths through the dermis at the wavelengths at which the reflectances are measured are matched as closely as possible. This matching is achieved by judicious selection of wavelength sets that have similar water absorption characteristics. Such wavelength sets may be selected from any one of the three primary wavelength bands (950-1400 nm, 1500-1800 nm, and 2000-2300 nm) discussed above. Wavelength pairs or sets are chosen from within one of these three primary bands, and not from across the bands. More particularly the wavelength pair of 1180 and 1300 nm is one such wavelength set where the lengths of the optical paths through the dermis at these wavelengths are matched as closely as possible.
5. To ensure that the expression that relates the measured reflectances and water fractions yields estimates of water fraction that are insensitive to temperature variations, the wavelengths at which the reflectances are measured are chosen to be either close to temperature isosbestic wavelengths in the water absorption spectrum or the reflectances are combined in a way that cancels the temperature dependencies of the individual reflectances. Typically, absorption peaks of various biological tissue constituents may shift with variations in temperature. Here, wavelengths are selected at points in the absorption spectrum where no significant temperature shift occurs. Alternately, by knowing the value of this temperature shift, wavelength sets may be chosen such that any temperature shift is mathematically canceled out when optical measurements are combined to compute the value of a tissue water metric. Such wavelength sets may be selected from any one of the three primary wavelength bands (950-1400 nm, 1500-1800 nm, and 2000-2300 nm) discussed above. Wavelength pairs or sets are chosen from within one of these three primary bands, and not from across the bands. More particularly the wavelength pair of 1180 and 1300 nm are one such pair of temperature isosbestic wavelengths in the water absorption spectrum.
6. The reflectances measured at two or more wavelengths are combined to form either a single ratio, a sum of ratios, a ratio of ratios of the form $\log[R(\lambda_1)/R(\lambda_2)]$, or a ratio of weighted sums of $\log[R(\lambda)]$ terms, in which the numerator depends primarily on the absorbance of water and the denominator depends primarily on the sum of the volume fractions of water and other specific tissue constituents, such that the denominator is equally sensitive to a change in the concentration of any of these specific constituents and water.

[0027] Thus, in one embodiment of the present invention the water fraction, f_w is estimated according to the following equation, based on the measurement of reflectances, $R(\lambda)$ at two wavelengths and the empirically chosen calibration constants c_0 and c_1:

$$f_w = c_1 \log\left[R(\lambda_1)/R(\lambda_2)\right] + c_0 \qquad (1)$$

[0028] Numerical simulations and *in vitro* experiments indicate that the total tissue water fraction, f_w^T, can be estimated with an accuracy of approximately +/-2 % over a range of water contents between 50 and 80% using Equation (1), with reflectances $R(\lambda)$ measured at two wavelengths and the calibration constants c_0 and c_1 chosen empirically. Examples of suitable wavelength pairs are λ_1 =1300 nm, λ_2 =1168 nm, and λ_1 =1230 nm, λ_2 =1168 nm.

[0029] The ability to measure changes in the total tissue water content in the ear of a pig using two-wavelength NIR

reflectometry was demonstrated experimentally in a study in which a massive hemorrhage was induced in a pig and the lost blood was replaced with lactated Ringer's solution over a period of several hours. Ringer's solution is a well-known solution of salts in boiled and purified water. Fig. 1 shows the total water fraction in the skin of the ear of a pig, measured using Equation (1) with λ_1 =1300 nm and λ_2 =1168 nm. Referring to Fig. 1, it should be noted that experimental observations of concern to this embodiment commence when the lactated Ringer's solution was infused 120 minutes after the start of the experiment. It should also be noted that the drift in the total water fraction from approximately 77.5% to 75% before the infusion is not related to this infusion experiment, but is related to the base-line hemorrhage portion of the experiment. The results show that the method of the present embodiment correctly reflects the effect of the infusion by showing an increase in total tissue water fraction from approximately 75% to 79% while the infusion is continuing. These data suggest that the disclosed embodiment has a clear value as a monitor of rehydration therapy in a critical care setting.

[0030] In another embodiment of the present invention the water fraction, f_w is estimated according to Equation (2) below, based on the measurement of reflectances, $R(\lambda)$ at three wavelengths and the empirically chosen calibration constants c_0, c_1 and c_2 :

$$f_w = c_2 \log[R(\lambda_1)/R(\lambda_2)] + c_1 \log[R(\lambda_2)/R(\lambda_3)] + c_0 \qquad (2)$$

[0031] Better absolute accuracy can be attained using Equation (2) which incorporates reflectance measurements at an additional wavelength. The results of *in vitro* experiments on excised skin indicate that the wavelength triple (λ_1 =1190 nm, λ_2 =1170 nm, λ_3 =1274 nm) yields accurate estimates of total tissue water content based on Equation (2).

[0032] In yet another embodiment of the present invention the water fraction, f_w is estimated according to Equation (3) below, based on the measurement of reflectances, $R(\lambda)$ at three wavelengths and the empirically chosen calibration constants c_0 and c_1:

$$f_w = c_1 \frac{\log[R(\lambda_1)/R(\lambda_2)]}{\log[R(\lambda_3)/R(\lambda_2)]} + c_0 \qquad (3)$$

[0033] Better absolute accuracy can be attained using Equations (3), as is attained using Equations (2), which also incorporates reflectance measurements at an additional wavelength. Numerical simulations as shown in Fig. 2 indicate that total tissue water accuracy better than +/-0.5% can be achieved using Equation (3), with reflectances measured at three closely spaced wavelengths: λ_1 =1710nm, λ_2 =1730 nm, and λ_3 =1740 nm. Additional numerical simulations indicate that accurate measurement of the lean tissue water content, f_w^l, can be accomplished using Equation (3), by combining reflectance measurements at 1125, 1185, and 1250 nm.

[0034] An additional embodiment of the present invention is directed towards the measurement of water content as a fraction of fat-free or lean tissue content, f_w^l.

[0035] Preferably, a tissue water monitor provides the clinician with an indication of whether the patient requires more, less, or no water to achieve a normo-hydrated state. Such a measurement may be less universally applicable than clinically desired when it is determined using an instrument that reports fractional water relative to either total body weight or total tissue content, due to the high variability of fat content across the human population. Fat contains very little water, so variations in the fractional fat content of the body lead directly to variations in the fractional water content of the body. When averaged across many patients, gender and age-related differences in fat content, result in systematic variations in water content, a fact that has been well-documented in the literature, as is shown for example in Fig. 7. Values shown in Fig. 7 are computed from Tables II-III of Cohn et al., J. Lab. Clin. Med. (1985) 105(3), 305-311.

[0036] In contrast, when fat is excluded from the calculation, the fractional water content, f_w^l, in healthy subjects, is consistent across both gender and age, as is shown, for example, in Fig. 7. This suggests that f_w^l, can be a more clinically useful measurement than f_w for certain conditions. An additional reduction in the subject-to-subject variation in the "normal" level of fractional water content may observed if bone mass is excluded from the calculation, as may be seen in Fig. 8. This may be due to the fact that the bone content of the body tends to decrease with age (such as by osteoporosis). Due to the specified source-detector separations (e.g., 1-5 mm), wavelength ranges, and algorithms, the

measurement of f_w^l in tissue according to the embodiments of the present invention will be closely related to the whole body water content as a fraction of the fat-free-bone-free body content.

[0037] In yet another embodiment of the present invention, tissue water fraction, f_w, is estimated according to the following equation, based on the measurement of reflectances, $R(\lambda)$, at a plurality of wavelengths:

$$f_w = \frac{\left[\sum_{n=1}^{N} p_n \log\{R(\lambda_n)\}\right] - \left[\sum_{n=1}^{N} p_n\right] \log\{R(\lambda_{N+1})\}}{\left[\sum_{m=1}^{M} q_m \log\{R(\lambda_m)\}\right] - \left[\sum_{m=1}^{M} q_m\right] \log\{R(\lambda_{M+1})\}} \qquad (4)$$

where p_n and q_m are calibration coefficients.

[0038] An obstacle to the quantification of tissue analytes is the high subject-to-subject variability of the scattering coefficient of tissue. Determination of the fractional tissue water in accordance with Equation (4) provides similar advantage as that of Equation (3) above, in that scattering variation is automatically cancelled, especially as long as the N+1 wavelengths are chosen from within the same wavelength band (950-1400 nm, 1500-1800 nm, or 2000-2300 mn). An explanation of the manner in which Equation (4) automatically cancels scattering variations is provided below.

[0039] Tissue reflectance can be modeled according to a modified form of the Beer-Lambert equation:

$$\log\{R(\lambda)\} = -l(\lambda)\sum_{j=1}^{J} c_j \varepsilon_j(\lambda) - \log\{I_0(\lambda)\} \qquad (5)$$

[0040] where R is the tissue reflectance, l is the mean pathlength of light at wavelength λ, εj and c_j are the extinction coefficient and concentration of constituent j in the tissue, and $\log\{I_0(\lambda)\}$ is a scattering offset term. According to this model, the scattering dependence of tissue reflectance is due to the offset term, $\log\{I_0(\lambda)\}$, and the pathlength variation term, $l(\lambda)$. Since the scattering coefficient varies slowly with wavelength, by selecting all of the wavelengths from within the same wavelength band, the wavelength dependence of the scattering coefficient can be ignored to a good approximation. Under these conditions, by multiplying the log of the reflectance at wavelength N+1 (or M+1) by the negative of the sum of the coefficients used to multiply the log of the reflectances at the N (or M) other wavelengths, the scattering offset terms are cancelled in both the numerator and denominator of Equation (4). This can be seen, for example, by substituting Equation (5) into the numerator of Equation (4):

$$\left[\sum_{n=1}^{N} p_n \log\{R(\lambda_n)\}\right] - \left[\sum_{n=1}^{N} p_n\right] \log\{R(\lambda_{N+1})\} = -l\sum_{n=1}^{N}\left[p_n \sum_{j=1}^{J} c_j \varepsilon_j(\lambda_n)\right] + l\left[\sum_{n=1}^{N} p_n\right]\sum_{j=1}^{J} c_j \varepsilon_j(\lambda_{N+1}) \qquad (6)$$

[0041] A review of Equation (6) shows that the scattering offset term has been cancelled, but the scattering dependent pathlength variation term, l, remains. When the numerator and denominator of Equation (4) are combined, the pathlength variation term is also cancelled, as shown in Equation (7):

$$f_w = \frac{-\sum_{n=1}^{N}\left[p_n \sum_{j=1}^{J} c_j \varepsilon_j(\lambda_n)\right] + \left[\sum_{n=1}^{N} p_n\right]\sum_{j=1}^{J} c_j \varepsilon_j(\lambda_{N+1})}{-\sum_{m=1}^{M}\left[q_m \sum_{j=1}^{J} c_j \varepsilon_j(\lambda_m)\right] + \left[\sum_{m=1}^{M} q_m\right]\sum_{j=1}^{J} c_j \varepsilon_j(\lambda_{M+1})} \qquad (7)$$

[0042] A review of Equation (7) shows that Equation (7) depends only on the concentrations and extinction coefficients of the constituents of tissue and on the calibration coefficients p_n and q_m.

[0043] In addition to providing for variable scattering compensation, the methods using Equation (4) allow a more general implementation by relaxing some of the constraints that are imposed by the use of Equation (3), above. For

example:

[0044] (a) In order to provide a certain level of accuracy for measurement of f_w, the numerator in Equation (3) may need to be sensitive to changes in water concentration but insensitive to changes in all other tissue constituents. For example, Equation (3) may require that the absorbance of all tissue constituents besides water (e.g. lipid, non-heme protein, hemoglobin) are nearly equal at wavelengths 1 and 2. This constraint is removed in Equation (4), where the coefficients p_n are chosen to cancel out absorbance by all tissue constituents other than water.

[0045] (b) In order to provide a certain level accuracy for measurement of f_w, the denominator in Equation (3) may need to be equally sensitive to concentration changes of all tissue constituents to which the water fraction is to be normalized. In addition, Equation (3) may require that the absorbance be equal at wavelengths 2 and 3 for all tissue constituents to be excluded from the water fraction normalization. This constraint is removed in Equation (4), where the coefficients, q_m, can be chosen to cancel the absorbance contribution due to certain constituents, while equalizing the absorbance sensitivity to the remaining tissue constituents.

[0046] In the case of measurement of the water fraction in lean tissue, f_w^l, the coefficients, p_n, in the numerator of Equation (4) are chosen to cancel the contribution from all of the major light-absorbing constituents of tissue, except water. Similarly, the coefficients, q_m, in the denominator of Equation (4) are chosen to cancel the contribution from all tissue constituents other than water and protein. In addition, the coefficients, q_m, are chosen to equalize the sensitivity of the denominator to changes in water and protein on a volume fractional basis. By computing the ratio of these two terms, the result is a fractional volume measurement of water concentration in lean tissue.

[0047] In addition, application of Equation (4) to the measurement of fractional water content in total tissue volume, f_w^T, is accomplished by choosing the coefficients in the denominator of Equation (4), q_m, so that all tissue constituents (including lipid) are equalized on a fractional volume basis.

[0048] By relaxing some of the constraints imposed by Equation (3), the use of Equation (4) can be expected to produce a more accurate prediction of fractional tissue water content, for the reasons set forth above. Various wavelength combinations may be used based on the criteria disclosed above. In order to select one wavelength combination for use with Equation (4) for the purpose of measuring fractional water content in lean tissue, f_w^l, extinction coefficients of the major absorbing constituents of tissue (water, non-heme protein, lipid, and hemoglobin) were experimentally measured and various wavelength combinations of these were applied to a numerical model of tissue absorbance. The reproducibility of the algorithms incorporating the most promising of these wavelength combinations were then compared using real tissue data. The real tissue data were collected from 37 different volunteers at a local hospital, with Institutional Review Board (IRB) approval. The sensor measured reflected light from the pad of the finger, with a source-detector spacing of approximately 2.5 mm. The sensor was completely removed from the tissue between each pair of measurements. One such preferred algorithm combines measurements at 4 wavelengths, namely: 1180, 1245, 1275, and 1330 nm. Using this selection of wavelengths, the measurement-to-measurement reproducibility, as shown in Fig. 9, is 0.37%, indicating high reproducibility of the tissue water measurements using the methods disclosed herein.

[0049] In addition to providing a method for measuring tissue water fraction, the method in accordance with Equation (4) above, also has general utility for the fractional quantification of analytes in tissue. In general, by appropriate choice of wavelengths and coefficients, Equation (4) is extendible to the fractional concentration measurement of any tissue constituent or combination of constituents in tissue with respect to any other constituent or combination of constituents. For example, this equation is also applicable for the determination of the fractional hemoglobin content in tissue.

[0050] Thus, in one embodiment of the present invention, the fractional volume of total hemoglobin in tissue is determined using Equation (4) by combining reflectance measurements at wavelengths where hemoglobin is strongly absorbing with reflectance measurements where the remaining tissue constituents (such as water, lipid, and non-protein) are strongly absorbing. The coefficients, p_n, in the numerator of Equation (4) are chosen to cancel the absorbance contributions from all tissue constituents except total hemoglobin. The coeffients, q_m, in the denominator of Equation (4) are chose to equalize the absorbance contributions of all major tissue constituents, on a volume fractional basis. One specific wavelength combination for accomplishing this measurement is 805 nm, 1185 nm, and 1310 nm. At 805 nm the absorbance by the oxy- and deoxyhemoglobin are approximately equal. At 1185 nm, the absorbance of water, non-heme protein, and lipid, are nearly equal on a fractional volume basis. At 1300 nm the tissue absorbance will be dominated by water.

[0051] In another embodiment of the present invention, measurement of fractional concentrations of different species of hemoglobin in tissue is performed. In general, the method provides a means of measuring the fractional concentration of hemoglobin in a first set comprised of one or more species of hemoglobin with respect to the concentration of hemoglobin in a second set comprised of one or more hemoglobin species in tissue. The coefficients, p_n, in the numerator of Equation (4) are chosen to cancel the absorbance contributions from all tissue constituents except the hemoglobin species included in set 1. The coeffients, q_m, in the denominator of Equation (4) are chose to equalize the absorbance

contributions from all tissue constituents except the hemoglobin species included in set 2. Sets 1 and 2 are subsets of hemoglobin species that are present in the body tissue or blood. For example, such hemoglobin species include oxyhemoglobin, deoxyhemoglobin, carboxyhemoglobin, methemoglobin, sulfhemoglobin and, so on. And in general, as used herein, other physiological parameters have other subsets of constituents each being capable of absorbing at different wavelengths. In the case where set 1 is comprised of oxyhemoglobin and set 2 is comprised of oxy- and deoxyhemoglobin, a specific wavelength combination for accomplishing the measurement is 735, 760, and 805 nm.

[0052] Individuals skilled in the art of near-infrared spectroscopy would recognize that, provided that the aforementioned guidelines are followed, additional terms can be added to Equations (1) - (4) and which may be used to incorporate reflectance measurements made at additional wavelengths and thus improve accuracy further.

[0053] An additional embodiment of the disclosed invention provides the ability to quantify shifts of fluid into and out of the bloodstream through a novel application of pulse spectrophotometry. This additional embodiment takes advantage of the observation that pulsations caused by expansion of blood vessels in the skin as the heart beats produce changes in the reflectance at a particular wavelength that are proportional to the difference between the effective absorption of light in the blood and the surrounding interstitial tissues. Numerical simulation indicate that, if wavelengths are chosen at which water absorption is sufficiently strong, the difference between the fractions of water in the blood, f_w^{IV} and surrounding tissue, f_w^{EV} is proportional to the ratio of the dc-normalized reflectance changes ($\Delta R/R$) measured at two wavelengths, according to Equation (8) below:

$$f_w^{EV} - f_w^{IV} = c_1 \frac{(\Delta R/R)_{\lambda_1}}{(\Delta R/R)_{\lambda_2}} + c_0, \qquad (8)$$

where c_0 and c_1 are empirically determined calibration constants. This difference, integrated over time, provides a measure of the quantity of fluid that shifts into and out of the capillaries. Fig. 3 shows the prediction accuracy expected for the wavelength pair λ_1 = 1320 nm and λ_2 = 1160 nm.

[0054] An additional embodiment of the present invention is directed towards the measurement of water balance index, Q, such that:

$$Q = \frac{f_w^{IV} - f_w^{EV}}{f_h^{IV}} = a_1 \frac{(\Delta R/R)_{\lambda_1}}{(\Delta R/R)_{\lambda_2}} + a_0 \qquad (9)$$

[0055] where f_h^{IV} is the fractional volume concentration of hemoglobin in the blood, and a_o and a_1 are calibration coefficients. The use of Equation (9) to determine a water balance is equivalent to using Equation (8) above, where f_h^{IV} is set equal to 1. However, using Equation (9) provides for a more accurate determination by not neglecting the influence f_h^{IV} of on the derived result. The effect of this omission can be understood by allowing total hemoglobin to vary over the normal physiological range and computing the difference between the results provided by Equation (9) when f_h^{IV} is fixed or allowed to vary. For example, when calculations were performed with f_w^{EV} fixed at 0.65, f_w^{IV} varying between 0.75 and 0.80, and f_h^{IV} varying between 0.09 and 0.135 or held fixed at 0.112, the resulting error was as large as +/-20%. In situations of extreme blood loss or vascular fluid overload (hypo- or hypervolemia) the error could be larger.

[0056] The quantity Q, provided by Equation (9) may be combined with a separate measurement of fractional hemoglobin concentration in blood, f_h^{IV}, (such as may be provided by standard clinical measurements of hematocrit or total hemoglobin) in order to provide a measure of the difference between the intravascular and extravascular water content, f_w^{IV} - f_w^{EV}. Alternatively, the quantity Q, may have clinical utility without further manipulation. For example, by providing a simultaneous measurement of both Q and fractional tissue water (either f_w or f_w^l), the embodiments of the present invention enable the provision of a clinical indication of changes in both volume and osmolarity of body fluids.

Table 1 lists the 6 combinations of volume and osmolarity changes in body fluids that are clinically observed (from Physiology, 2nd Edition, Linda S. Costanzo, Williams and Wilkins, Baltimore, 1998, pg. 156), and the expected direction and magnitude of the resultant change in fractional volume of water in blood (f_w^{IV}), the fractional volume of water in tissue (f_w^{EV}), the fractional volume of hemoglobin in blood (f_h^{IV}), the numerator of Q (Q_n), the inverse of the denominator of Q ($1/Q_d$), the combined result ($Q_n / Q_d = Q$), and the fractional volume of water in lean tissue, f_w^l. Taking the first row of Table 1 as an example, the result of isosmotic volume expansion, such as may be brought about by infusion with isotonic saline, would result in an increase in the fraction of water in blood (f_w^{IV}), a small increase in the extravascular water fraction (f_w^{EV}), and a large decrease in the fractional concentration of hemoglobin in the blood (f_h^{IV}). The combined effect of these 3 factors would result in a large increase in Q. A small increase in the fraction of water in the lean tissue, f_w^l, would also be expected. Notice that when Q and f_w^l are viewed in combination, they provide unique signatures for each of the 6 types of fluid balance change listed in Table 1. An instrument providing these measurements in a non-invasive and continuous fashion is thus able to provide a powerful tool for the monitoring of tissue water balance.

Table 1. Expected changes in Q and f_w^l resulting from changes in body fluid volume and osmolarity

Type	Example	f_w^{IV}	f_w^{EV}	f_h^{IV}	Q_n	$1/Q_d$	Q	f_w^l
Isosmotic volume expansion	Isotonic NaCl Infusion	↑	↑	↓	↑	↑	↑	↑
Isosmotic volume contraction	Diarrhea	↓	↓	↑	↓	↓	↓	↑
Hyperosmotic volume expansion	High NaCl intake	↑	↓	↓	↑	↑	↑	0
Hyperosmotic volume contraction	Sweating, Fever	↓	↓	↑	0	↓	↓	↓
Hyposmotic volume contraction	SIADH	↑	↑	↓	0	↑	↑	↑
Hyposmotic volume contraction	Adrenal Insufficiency	↓	↑	↑	↓	↓	↓	0

[0057] Figs. 4 and 5 show diagrams of two different versions of an instrument for measuring the amount of water in body tissues. The simplest version of the instrument 400 shown in Fig. 4 is designed for handheld operation and functions as a spot checker. Pressing the spring-loaded probe head 410 against the skin 412 automatically activates the display of percent tissue water 414. The use of the spring-loaded probe head provides the advantages of automatically activating the display device when needed and turning the device off when not in use, thereby extending device and battery life. Moreover, this unique use of a spring-loaded probe also provides the variable force needed to improve the reliability of measurements. Percent tissue water represents the absolute percentage of water in the skin beneath the probe (typically in the range 0.6 - 0.9). In one embodiment of the present invention, the force exerted by a spring or hydraulic mechanism (not shown) inside the probe head 410 is minimized, so that the fluid content of the tissue beneath the probe is not perturbed by its presence. In this manner, the tissue water fraction, including both intravascular and extravascular fluid fractions is measured. In another embodiment of the invention, the force exerted by the probe head is sufficient to push out most of the blood in the skin below the probe to allow measurement of only the extravascular fluid fraction. A pressure transducer (not shown) within the probe head 410 measures the compressibility of the skin for deriving an index of the fraction of free (mobile) water.

[0058] The more advanced version of the fluid monitor 500 shown in Fig. 5 is designed for use as a critical-care monitor. In addition to providing a continuous display of the volume fraction of water 510 at the site of measurement 512, it also provides a trend display of the time-averaged difference between the intravascular fluid volume ("IFV") and extravascular fluid volume ("EFV") fractions (e.g., $\text{IFV-EFV} = f_w^{IV} - f_w^{EV}$) 514 or the quantity Q (as defined above with reference to Equation (9), updated every few seconds. This latter feature would give the physician immediate

feedback on the net movement of water into or out of the blood and permit rapid evaluation of the effectiveness of diuretic or rehydration therapy. To measure the IFV-EFV difference or *Q*, the monitor records blood pulses in a manner similar to a pulse oximeter. Therefore, placement of the probe on the finger or other well-perfused area of the body would be required. In cases in which perfusion is too poor to obtain reliable pulse signals, the IFV-EFV or *Q* display would be blanked, but the tissue water fraction (f_w) would continue to be displayed. A mechanism for mechanically inducing the pulse is built into the probe to improve the reliability of the measurement of IFV-EFV or *Q* under weak-pulse conditions.

[0059] Fig 6. is a block diagram of a handheld device 600 for measuring tissue water fraction, as well as shifts in water between the IFV and EFV compartments, or a measurement of *Q*, with a pulse inducing mechanism. Using this device 600, patient places his/her finger 610 in the probe housing. Rotary solenoid 612 acting through linkage 614 and collar 616 induces a mechanical pulse to improve the reliability of the measurement of IFV-EFV or *Q*. LEDs 618 emit light at selected wavelengths and photodiode 620 measure the transmitted light. Alternately, the photodiode 620 can be placed adjacent to the LEDs to allow for the measurement of the reflectance of the emitted light. Preamplifier 622 magnifies the detected signal for processing by the microprocessor 624. Microprocessor 624, using algorithms described above, determines the tissue water fraction (f_w) (such as in the total tissue volume (f_w^T), within the lean tissue volume (f_w^l), and/or within the IFV (f_w^{IV}) and the EFV (f_w^{EV})), as well as shifts in water between the IFV and EFV (such as IFV-EFV or *Q*), and prepares this information for display on display device 626. Microprocessor 624 is also programmed to handle the appropriate timing between the rotary solenoid's operation and the signal acquisition and processing. In one embodiment, a means is provided for the user to input the fractional hemoglobin concentration (f_h^{IV}) or a quantity proportional to f_h^{IV} (such as hematocrit or total hemoglobin) in order to convert *Q* into IFV-EFV. The design of the device and the microprocessor integrates the method and apparatus for reducing the effect of noise on measuring physiological parameters as described in U.S. Pat. No. 5,853,364, assigned to Nellcor Puritan Bennett, Inc. Additionally, the design of the device and the microprocessor also integrates the electronic processor as described in U.S. Pat. No. 5,348,004, assigned to Nellcor Incorporated.

[0060] As will be understood by those skilled in the art, other equivalent or alternative methods for the measurement of the water fraction within tissue (f_w), as well as shifts in water between the intravascular and extravascular compartments, IVF-EVF or *Q*, according to the embodiments of the present invention can be envisioned without departing from the essential characteristics thereof. For example, the device can be operated in either a handheld or a tabletop mode, and it can be operated intermittently or continuously. Moreover, individuals skilled in the art of near-infrared spectroscopy would recognize that additional terms can be added to the algorithms used herein to incorporate reflectance measurements made at additional wavelengths and thus improve accuracy further. Also, light sources or light emission optics other then LED's including and not limited to incandescent light and narrowband light sources appropriately tuned to the desired wavelengths and associated light detection optics may be placed within the probe housing which is placed near the tissue location or may be positioned within a remote unit; and which deliver light to and receive light from the probe location via optical fibers. Additionally, although the specification describes embodiments functioning in a back-scattering or a reflection mode to make optical measurements of reflectances, other embodiments can be working in a forward-scattering or a transmission mode to make these measurements. These equivalents and alternatives along with obvious changes and modifications are intended to be included within the scope of the present invention.

Claims

1. A device for measuring a body-tissue metric using optical spectrophotometry, comprising:

a probe housing (400, 500, 600) configured to be placed proximal to a tissue location (412, 512) which is being monitored;

light emission optics (618) adapted to emit two different wavelengths connected to said housing (400, 500, 600) and configured to direct radiation at said tissue location (412, 512);

light detection optics (620) connected to said housing (400, 500, 600) and configured to receive radiation from said tissue location (412, 512); and

a processing device (624) configured to process radiation from said light emission optics (618) and said light detection optics (620) to compute said body-tissue metric, wherein said body tissue metric comprises a ratio of the water content of a portion of patient's tissue in relation to the water content of a lean or fat-free portion of patient's tissue or a ratio of a difference between the water fraction in the blood and the water fraction in the extravascular tissue over the fractional volume concentration of hemoglobin in the blood, **characterized in that**

the processing device (624) is further configured to receive and compare at least two sets of optical spectrophotometry measurements from at least two different wavelengths, wherein light at the at least two different wavelengths is primarily absorbable due to water which is in the vascular blood and in the extravascular tissue, and the processing device (624) is adapted to calculate a ratio of the at least two measurements provides a measure proportional to said difference between the fractions of water in the blood and surrounding tissue location.

2. The device of claim 1, wherein said body-tissue water content metric is computed as a fraction of bone-free-fat-free tissue content.

3. The device of claim 1, further comprising a display device (414, 514, 626) connected to said probe housing (400, 500, 600) and configured to display said water content.

4. The device of claim 1, wherein said light emission optics (618) and said light detection optics (620) are spaced between 1 and 5 mm from one another at said tissue location.

5. The device of claim 1, wherein said body-tissue metric is monitored intermittently or continuously.

6. The device of claim 1, wherein the probe housing (400) further comprises a spring-loaded probe (410) configured to automatically activate a display device (414) connected to said probe housing (400) when said spring-loaded probe (410) is pressed against and near a tissue location (414) which is being monitored.

7. The device of claim 1, wherein the probe housing (400, 500, 600) further comprises a pressure transducer to measure the compressibility of tissue for deriving an index of a fraction of free water within said tissue.

8. The device of claim 1, wherein the probe housing (400, 500, 600) further comprises a mechanism for mechanically inducing a pulse within said tissue location to permit measurements related to the differences between an intravascular fluid volume and an extravascular fluid volume fractions under weak-pulse conditions.

9. The device of claim 1, wherein the probe housing (400, 500, 600) further comprises a mechanism for mechanically minimizing the pressure at said tissue location to permit measurements related to the unperturbed fluid volume fraction in the tissue.

10. The device of claim 1, wherein the probe housing (600) further comprises a mechanism (612, 614, 616) for mechanically inducing pressure at said tissue location to permit measurement of the extravascular fluid fraction in the absence of the intravascular fluid fraction.

11. The device of claim 1, wherein the probe housing (400, 500, 600) further comprises a mechanism 612, 614, 616) for mechanically varying pressure at said tissue location to permit measurement of both the intravascular and extravascular water fraction.

12. The device of claim 1, wherein said light emission optics (618) are tuned to emit radiation at a plurality of narrow spectral wavelengths chosen so that the biological compound of interest will absorb light at said plurality of narrow spectral wavelengths and so that absorption by interfering species will be at a minimum, where a minimum absorption is an absorption by an interfering species which is less than 10% of the absorption of the biological compound of interest.

13. The device of claim 1, wherein said light emission optics (618) are tuned to emit radiation at a plurality of narrow spectral wavelengths chosen to be preferentially absorbed by tissue water, non-heme proteins and lipids, where preferentially absorbed wavelengths are wavelengths whose absorption is substantially independent of the individual concentrations of non-heme proteins and lipids, and is substantially dependent on the sum of the individual concentrations of non-heme proteins and water.

14. The device of claim 1, wherein said light emission optics (618) are tuned to emit radiation at a plurality of narrow spectral wavelengths chosen to ensure that measured received radiation are substantially insensitive to scattering variations and such that the optical path lengths through the dermis at said wavelengths are substantially equal.

15. The device of claim 1, wherein said light emission optics (618) are tuned to emit radiation at a plurality of narrow

spectral wavelengths chosen to ensure that measured received radiation from said tissue location are insensitive to temperature variations, where said wavelengths are temperature isosbestic in the water absorption spectrum or said received radiation are combined in a way that substantially cancel temperature dependencies of said individual received radiation when computing tissue water fractions.

16. The device of claim 1, wherein said light emission optics (618) are tuned to emit radiation at a plurality of narrow spectral wavelengths chosen from one of three primary bands of wavelengths of approximately 950-1400 nm, approximately 1500-1800 nm and approximately 2000-2300 nm.

17. The device of claim 1, wherein said light emission optics (618) and said light detection optics (620) are mounted within said probe housing (600) and positioned with appropriate alignment to enable detection in a transmissive mode.

18. The device of claim 1, wherein said light emission optics (618) and said light detection optics (620) are mounted within said probe housing (400, 500, 600) and positioned with appropriate alignment to enable detection in a reflective mode.

19. The device of claim 1, wherein said light emission optics (618) and said light detection optics (620) are placed within a remote unit and which deliver light to and receive light from said probe housing via optical fibers.

20. The device of claim 1, wherein said light emission optics (618) comprise at least one of a (a) incandescent light source, (b) white light source, and (c) light emitting diode ("LED").

21. The device of claim 1, wherein said processing device (624) receives and compares said at least two sets of optical measurements, where the at least first set of optical measurements corresponds to the detection of light whose absorption is primarily due to water and non-heme proteins, and where the at least second set of optical measurements corresponds to the detection of light whose absorption is primary due to water, and where a comparison of said at least two optical measurements provides a measure of a fat-free or lean water fraction within said tissue location.

22. The device of claim 1, wherein said processing device (624) receives and compares said at least two sets of optical measurements, where said at least two sets of optical measurements are based on received radiation from at least two wavelengths and which are combined to form a ratio of combinations of said received radiation.

23. The device of claim 22, wherein said processing device (624) forms a weighted summation of said combinations.

24. The device of claim 1, wherein said water content metric, f_w^1 is determined such that,

$$f_w^1 = \frac{\left[\sum_{n=1}^{N} P_n \log\{R(\lambda_n)\}\right] - \left[\sum_{n=1}^{N} p_n\right] \log\{R(\lambda_{N+1})\}}{\left[\sum_{m=1}^{M} q_m \log\{R(\lambda_m)\}\right] - \left[\sum_{m=1}^{M} q_m\right] \log\{R(\lambda_{M+1})\}}$$

and where:

p_n and q_m are calibration coefficients;
$R(\lambda)$ is a measure of a received radiation at a wavelength; and
n=1-N and m=1-M represent indices for a plurality of wavelengths which may comprise of the same or different combinations of wavelengths.

25. The device of claim 24, wherein M and N are both equal to 3, the wavelengths indexed by m and n comprise of the same combination of wavelengths, and said first, second, third and fourth wavelengths are approximately 1180, 1245, 1275 and 1330 nm respectively.

26. The device of claim 1, wherein said metric is a water balance index Q, such that

$$Q = \frac{f_w^{IV} - f_w^{EV}}{f_h^{IV}} = a_1 \frac{(\Delta R/R)_{\lambda_1}}{(\Delta R/R)_{\lambda_2}} + a_0$$

where f_w^{IV} and f_w^{EV} are the fractional volume concentrations of water in blood and tissue, respectively, f_h^{IV} is the fractional volume concentration of hemoglobin in the blood, $(\Delta R/R)\lambda$ is the fractional change in reflectance at wavelength λ, due to a blood volume change in the tissue, and a_0 and a_1 are calibration coefficients.

27. The device of claim 1, further comprising an input device configured to enable a user to input a fractional hemoglobin concentration in blood for use by said processing device (624).

28. The device of claim 27 wherein said processing device (624) is further configured to compute a measure of the change in water content between the intravascular fluid volume ("IFV") and extravascular fluid volume ("EFV") using said water index.

29. The device of claim 26, wherein said first and second wavelengths are approximately 1320 nm and approximately 1160 nm respectively.

30. The device of claim 1, wherein said body-tissue metric further comprises an integral of said difference to provide a measure of the water that shifts into and out of the capillaries.

31. A method for measuring a body-tissue metric in a human tissue (412, 512) location using optical spectrophotometry, comprising:

placing a probe housing (400, 500, 600) proximal to said tissue location (412, 512);
emitting radiation using light emission optics (618) configured to direct radiation at said tissue location (412, 512);
detecting radiation using light detection optics (620) configured to receive radiation from said tissue location (412, 512);
processing said radiation from said light emission optics (618) and said light detection optics (620) to compute said body-tissue metric wherein said body-tissue metric comprises a ratio of the water content of a portion of patient's tissue in relation to the water content of a lean or fat-free portion of patient's tissue or a ratio of a difference between the water fraction in the blood and the water fraction in the extravascular tissue over the fractional volume concentration of hemoglobin in the blood, wherein at least two sets of optical spectrophotometry measurements from at least two different wavelengths are received and compared, wherein light at the at least two different wavelengths is primarily absorbable due to water which is in the vascular blood and in the extravascular tissue, and wherein a ratio of the at least two measurements provides a measure proportional to the difference between the fractions of water in the blood and surrounding tissue location; and
displaying said body-tissue metric or a quantity derived from said metric on a display device (414, 510, 626).

32. The method of claim 31 wherein said body-tissue metric is a water balance index Q, such that:

$$Q = \frac{f_w^{IV} - f_w^{EV}}{f_h^{IV}} = a_1 \frac{(\Delta R/R)_{\lambda_1}}{(\Delta R/R)_{\lambda_2}} + a_0$$

where f_w^{IV} and f_w^{EV} are the fractional volume concentrations of water in blood and tissue, respectively, f_h^{IV}

is the fractional volume concentration of hemoglobin in the blood, $(\Delta R/R)\lambda$ is the fractional change in reflectance at wavelength λ, due to a blood volume change in the tissue, and a_0 and a_1 are calibration coefficients.

33. The method of claim 31, wherein a physiological parameter f_w^1 is determined such that,

$$f_w^1 = \frac{\left[\sum_{n=1}^{N} P_n \log\{R(\lambda_n)\}\right] - \left[\sum_{n=1}^{N} p_n\right] \log\{R(\lambda_{N+1})\}}{\left[\sum_{m=1}^{M} q_m \log\{R(\lambda_m)\}\right] - \left[\sum_{m=1}^{M} q_m\right] \log\{R(\lambda_{M+1})\}}$$

and where:

p_n and q_m are calibration coefficients;
$R(\lambda)$ is a measure of a received radiation at a wavelength; and
n=1-N and m=1-M represent indices for a plurality of wavelengths which may comprise of the same or different combinations of wavelengths.

34. The method of claim 33, wherein said physiological parameter is the tissue water fraction in said tissue location.

35. The method of claim 33, wherein said physiological parameter is an oxygen saturation value in said tissue location.

36. The method of claim 33, wherein said physiological parameter is a fractional hemoglobin concentration in said tissue location.

37. The method of claim 33, wherein said physiological parameter is the fractional concentration of hemoglobin in a first set comprised of one or more species of hemoglobin with respect to the concentration of hemoglobin in a second set comprised of one or more hemoglobin species in tissue.

38. The method of claim 37, wherein the coefficients, p_n, are chosen to cancel the absorbance contributions from all tissue constituents except the hemoglobin species included in set 1 and the coefficents, q_m, are chosen to cancel the absorbance contributions from all tissue constituents except the hemoglobin species included in set 2.

Patentansprüche

1. Vorrichtung zum Messen eines Körpergewebemaßes mittels optischer Spektrophotometrie, mit:

- einem Sondengehäuse (400, 500, 600), das dazu ausgelegt ist, nahe einer überwachten Gewebestelle (412, 512) platziert zu werden,
- einer mit dem Gehäuse (400, 500, 600) verbundenen Lichtemissionsoptik (618), die zwei unterschiedliche Wellenlängen zu emittieren vermag und dazu ausgestaltet ist, Strahlung auf die Gewebestelle (412, 512) zu lenken,
- einer mit dem Gehäuse (400, 500, 600) verbundenen Lichtdetektionsoptik (620), die Strahlung von der Gewebestelle (412, 512) zu empfangen vermag, und
- eine Verarbeitungseinrichtung (624), die Strahlung von der Lichtemissionsoptik (618) und der Lichtdetektionsoptik (620) zu verarbeiten vermag, um das Körpergewebemaß zu berechnen, wobei das Körpergewebemaß ein Verhältnis des Wassergehalts eines Teils des Patientengewebes in Bezug auf den Wassergehalt eines fettarmen oder fettfreien Teils eines Patientengewebes oder ein Verhältnis einer Differenz zwischen dem Wasseranteil im Blut und dem Wasseranteil im extravasalen Gewebe über der anteiligen Volumenkonzentration von Hämoglobin im Blut umfasst,

dadurch gekennzeichnet, dass die Verarbeitungseinrichtung (624) ferner dazu konfiguriert ist, wenigstens zwei Sätze optischer Spektrophotometriemessungen zumindest zweier unterschiedlicher Wellenlängen zu empfangen

und zu vergleichen, wobei Licht mit den zumindest zwei unterschiedlichen Wellenlängen hauptsächlich aufgrund des Wassers absorbierbar ist, das sich im vaskulären Blut und im extravasalen Gewebe befindet, und dass die Verarbeitungseinrichtung (624) ein Verhältnis der wenigstens zwei Messungen zu berechnen vermag, das ein zu der Differenz zwischen den Wasseranteilen im Blut und in der umgebenden Gewebestelle proportionales Maß angibt.

2. Vorrichtung nach Anspruch 1,
bei der das Körpergewebe-Wassergehalt-Maß als Anteil eines knochenfreien, fettfreien Gewebegehalts berechnet wird.

3. Vorrichtung nach Anspruch 1,
die ferner eine Anzeigeeinrichtung (414, 514, 626) umfasst, die mit dem Sondengehäuse (400, 500, 600) verbunden und dazu ausgelegt ist, den Wassergehalt anzuzeigen.

4. Vorrichtung nach Anspruch 1,
bei der die Lichtemissionsoptik (618) und die Lichtdetektionsoptik (620) unter einem Abstand von 1 bis 5 mm voneinander an der Gewebestelle angeordnet sind.

5. Vorrichtung nach Anspruch 1,
bei der das Körpergewebemaß intermittierend oder kontinuierlich überwacht wird.

6. Vorrichtung nach Anspruch 1,
bei der das Sondengehäuse (400) ferner eine unter Federspannung stehende Sonde (410) umfasst, die dazu ausgestaltet ist, eine mit dem Sondengehäuse (400) verbundene Anzeigeeinrichtung (414) automatisch zu aktivieren, wenn die unter Federspannung stehende Sonde (410) nahe einer überwachten Gewebestelle (414) gegen diese gedrückt wird.

7. Vorrichtung nach Anspruch 1,
bei der das Sondengehäuse (400, 500, 600) ferner einen Druckwandler umfasst, um die Komprimierbarkeit des Gewebes zu messen, um einen Index eines Anteils freien Wassers im Gewebe abzuleiten.

8. Vorrichtung nach Anspruch 1,
bei der das Sondengehäuse (400, 500, 600) ferner einen Mechanismus zum mechanischen Induzieren eines Pulses in der Gewebestelle umfasst, um Messungen bezüglich der Unterschiede zwischen einem intravasalen Flüssigkeitsvolumenanteil und einem extravasalen Flüssigkeitsvolumenanteil unter Kleinpulsbedingungen zu ermöglichen.

9. Vorrichtung nach Anspruch 1,
bei der das Sondengehäuse (400, 500, 600) ferner einen Mechanismus zum mechanischen Minimieren des Druckes an der Gewebestelle umfasst, um Messungen bezüglich des unbeeinträchtigten Flüssigkeitsvolumenanteils im Gewebe zu ermöglichen.

10. Vorrichtung nach Anspruch 1,
bei der das Sondengehäuse (600) ferner einen Mechanismus (612, 614, 616) zum mechanischen Induzieren von Druck an der Gewebestelle umfasst, um Messungen des extravasalen Flüssigkeitsanteils in Abwesenheit des intravasalen Flüssigkeitsanteils zu ermöglichen.

11. Vorrichtung nach Anspruch 1,
bei der das Sondengehäuse (400, 500, 600) ferner einen Mechanismus (612, 614, 616) zum mechanischen Variieren des Druckes an der Gewebestelle umfasst, um Messungen sowohl des intravasalen als auch des extravasalen Wasseranteils zu ermöglichen.

12. Vorrichtung nach Anspruch 1,
bei der die Lichtemissionsoptik (618) darauf eingestellt ist, Strahlung mit einer Mehrzahl eng beieinander liegender spektraler Wellenlängen zu emittieren, die so gewählt werden, dass die interessierende biologische Verbindung Licht mit der Mehrzahl eng beieinander liegender spektraler Wellenlängen absorbiert, und dass eine Absorption durch interferierende Arten auf ein Minimum beschränkt ist, wobei eine minimale Absorption eine Absorption durch eine interferierende Art ist, die kleiner als 10 % der Absorption der interessierenden biologischen Verbindung ist.

13. Vorrichtung nach Anspruch 1,

bei der die Lichtemissionsoptik (618) darauf eingestellt ist, Strahlung mit einer Mehrzahl eng beieinander liegender spektraler Wellenlängen zu emittieren, die so gewählt werden, dass sie bevorzugt von Gewebewasser, Nicht-Häm-Proteinen und Lipiden absorbiert werden, wobei bevorzugt absorbierte Wellenlängen Wellenlängen sind, deren Absorption im Wesentlichen von den individuellen Konzentrationen von Nicht-Häm-Proteinen und Lipiden unabhängig und im Wesentlichen von der Summe der individuellen Konzentrationen von Nicht-Häm-Proteinen und Wasser abhängig ist.

14. Vorrichtung nach Anspruch 1,
bei der die Lichtemissionsoptik (618) darauf eingestellt ist, Strahlung mit einer Mehrzahl eng beieinander liegender spektraler Wellenlängen zu emittieren, die so gewählt werden, dass sichergestellt ist, dass gemessene, empfangene Strahlung im Wesentlichen unempfindlich gegenüber Streuungsabweichungen ist, und dass die optischen Weglängen durch die Dermis bei den Wellenlängen im Wesentlichen gleich sind.

15. Vorrichtung nach Anspruch 1,
bei der die Lichtemissionsoptik (618) darauf eingestellt ist, Strahlung mit einer Mehrzahl eng beieinander liegender spektraler Wellenlängen zu emittieren, die so gewählt werden, dass sichergestellt ist, dass gemessene, empfangene Strahlung von der Gewebestelle unempfindlich gegenüber Temperaturschwankungen ist, wobei die Wellenlängen im Wasserabsorptionsspekturm temperaturisosbestisch sind, oder die empfangene Strahlung derart kombiniert wird, dass Temperaturabhängigkeiten der individuellen empfangenen Strahlung bei der Berechnung der Gewebewasseranteile im Wesentlichen aufgehoben sind.

16. Vorrichtung nach Anspruch 1,
bei der die Lichtemissionsoptik (618) darauf eingestellt ist, Strahlung mit einer Mehrzahl eng beieinander liegender spektraler Wellenlängen zu emittieren, die aus einem von drei Primärbändern mit Wellenlängen von ungefähr 950 bis 1.400 nm, ungefähr 1.500 bis 1.800 nm und ungefähr 2.000 bis 2.3000 nm ausgewählt sind.

17. Vorrichtung nach Anspruch 1,
bei der die Lichtemissionsoptik (618) und die Lichtdetektionsoptik (620) im Sondengehäuse (600) montiert und geeignet ausgerichtet positioniert sind, um eine Detektion in einem transmissiven Modus zu ermöglichen.

18. Vorrichtung nach Anspruch 1,
bei der die Lichtemissionsoptik (618) und die Lichtdetektionsoptik (620) im Sondengehäuse (400, 500, 600) montiert und geeignet ausgerichtet positioniert sind, um eine Detektion in einem reflektierenden Modus zu ermöglichen.

19. Vorrichtung nach Anspruch 1,
bei der die Lichtemissionsoptik (618) und die Lichtdetektionsoptik (620) in einer entfernten Einheit angeordnet sind und dem Sondengehäuse über Glasfasern Licht zuführen und von diesem empfangen.

20. Vorrichtung nach Anspruch 1,
bei der die Lichtemissionsoptik (618) umfasst: (a) eine Glühlichtquelle und/oder (b) eine Weißlichtquelle und/oder (c) eine Lichtemissionsdiode ("LED").

21. Vorrichtung nach Anspruch 1,
bei der die Verarbeitungseinrichtung (624) die wenigstens zwei Sätze optischer Messungen empfängt und vergleicht, wobei der wenigstens eine erste Satz optischer Messungen der Detektion von Licht entspricht, dessen Absorption hauptsächlich auf Wasser und Nicht-Häm-Proteine zurückzuführen ist, und wobei der wenigstens eine zweite Satz optischer Messungen der Detektion von Licht entspricht, dessen Absorption hauptsächlich auf Wasser zurückzuführen ist, und wobei ein Vergleich der wenigstens zwei optischen Messungen ein Maß eines fettfreien oder fettarmen Wasseranteils in der Gewebestelle bereitstellt.

22. Vorrichtung nach Anspruch 1,
bei der die Verarbeitungseinrichtung (624) die wenigstens zwei Sätze optischer Messungen empfängt und vergleicht, wobei die wenigstens zwei Sätze optischer Messungen auf empfangener Strahlung zumindest zweier Wellenlängen basieren, die kombiniert werden, um ein Verhältnis von Kombinationen der empfangenen Strahlung zu bilden.

23. Vorrichtung nach Anspruch 22,
bei der die Verarbeitungseinrichtung (624) eine gewichtete Summierung der Kombinationen bildet.

24. Vorrichtung nach Anspruch 1,
bei der das Wassergehaltmaß, $f_w{}^1$, derart bestimmt wird, dass:

$$f_w{}^1 = \frac{\left[\sum_{n=1}^{N} P_n \log\{R(\lambda_n)\}\right] - \left[\sum_{n=1}^{N} p_n\right] \log\{R(\lambda_{N+1})\}}{\left[\sum_{m=1}^{M} q_m \log\{R(\lambda_m)\}\right] - \left[\sum_{m-1}^{M} q_m\right] \log\{R(\lambda_{M+1})\}}$$

und wobei:

- p_n und q_m Kalibrierungskoeffizienten sind,
- R(λ) ein Maß einer empfangenen Strahlung mit einer Wellenlänge ist, und
- n=1-N und m=1-M Indizes für eine Mehrzahl von Wellenlängen darstellen, die dieselben oder unterschiedliche Wellenlängenkombinationen umfassen können.

25. Vorrichtung nach Anspruch 24,
bei der sowohl M als auch N gleich 3 sind, die durch m und n indizierten Wellenlängen dieselbe Wellenlängekombination umfassen und die erste, zweite, dritte und vierte Wellenlänge ungefähr 1.180, 1.245, 1.275 bzw. 1.330 nm betragen.

26. Vorrichtung nach Anspruch 1,
bei der das Maß ein Wasserhaushaltsindex Q ist, so dass:

$$Q = \frac{f_w^{IV} - f_w^{EV}}{f_h^{IV}} = a_1 \frac{(\Delta R/R)_{\lambda_1}}{(\Delta R/R)_{\lambda_2}} + a_0$$

wobei f_w^{IV} und f_w^{EV} die anteiligen Volumenkonzentrationen von Wasser im Blut bzw. Gewebe sind, f_h^{IV} die anteilige Volumenkonzentration von Hämoglobin im Blut ist, (ΔR/R)λ die anteilige Reflexionsänderung bei der Wellenlängen λ aufgrund einer Blutvolumenänderung im Gewebe ist, und a_0 und a_1 Kalibrierungskoeffizienten sind.

27. Vorrichtung nach Anspruch 1,
die ferner eine Eingabeeinrichtung umfasst, die dafür konfiguriert ist, es einem Benutzer zu ermöglichen, eine anteilige Hämoglobinkonzentration im Blut zur Verwendung durch die Verarbeitungseinrichtung (624) einzugeben.

28. Vorrichtung nach Anspruch 27,
bei der die Verarbeitungseinrichtung (624) ferner dafür konfiguriert ist, ein Maß der Veränderung des Wassergehalts zwischen dem intravasalen Flüssigkeitsvolumen ("IFV") und dem extravasalen Flüssigkeitsvolumen ("EFV") unter Verwendung des Wasserindex zu berechnen.

29. Vorrichtung nach Anspruch 26,
bei der die erste und zweite Wellenlänge ungefähr 1.320 nm bzw. ungefähr 1.160 nm betragen.

30. Vorrichtung nach Anspruch 1,
bei der das Körpergewebemaß ferner ein Integral der Differenz umfasst, um ein Maß des Wassers bereitzustellen, das sich in die und aus den Kapillaren verlagert.

31. Verfahren zum Messen eines Körpergewebemaßes in einer menschlichen Gewebestelle (412, 512) mittels optischer Spektrophotometrie, das umfasst:

- Platzieren eines Sondengehäuses (400, 500, 600) nahe der Gewebestelle (412, 512),

- Emittieren von Strahlung unter Verwendung einer Lichtemissionsoptik (618), die dazu ausgelegt ist, Strahlung auf die Gewebestelle (412, 512) zu lenken,
- Detektieren von Strahlung unter Verwendung einer Lichtdetektionsoptik (620), die dazu ausgelegt ist, Strahlung von der Gewebestelle (412, 512) zu empfangen, und
- Verarbeiten der Strahlung von der Lichtemissionsoptik (618) und der Lichtdetektionsoptik (620), um das Körpergewebemaß zu berechnen, wobei das Körpergewebemaß ein Verhältnis des Wassergehalts eines Teils eines Patientengewebes in Bezug auf den Wassergehalt eines fettarmen oder fettfreien Teils eines Patientengewebes oder ein Verhältnis einer Differenz zwischen dem Wasseranteil im Blut und dem Wasseranteil im extravasalen Gewebe über der anteiligen Volumenkonzentration von Hämoglobin im Blut umfasst, wobei wenigstens zwei Sätze optischer Spektrophotometriemessungen zumindest zweier unterschiedlicher Wellenlängen empfangen und verglichen werden, wobei Licht mit den zumindest zwei unterschiedlichen Wellenlängen hauptsächlich aufgrund des Wassers absorbierbar ist, das sich im vaskulären Blut und im extravasalen Gewebe befindet, und wobei ein Verhältnis der wenigstens zwei Messungen ein zu der Differenz zwischen den Wasseranteilen im Blut und in der umgebenden Gewebestelle proportionales Maß angibt, und
- Anzeigen des Körpergewebemaßes oder einer von dem Maß abgeleiteten Größe auf einer Anzeigeeinrichtung (414, 510, 626).

32. Verfahren nach Anspruch 31,
bei dem das Körpergewebemaß ein Wasserhaushaltsindex Q ist, so dass:

$$Q=\frac{f_w^{IV}-f_w^{EV}}{f_h^{IV}}=a_1\frac{(\Delta R/R)_{\lambda_1}}{(\Delta R/R)_{\lambda_2}}+a_0$$

wobei f_w^{IV} und f_w^{EV} die anteiligen Volumenkonzentrationen von Wasser im Blut bzw. Gewebe sind, f_h^{IV} die anteilige Volumenkonzentration von Hämoglobin im Blut ist, $(\Delta R/R)\lambda$ die anteilige Reflexionsänderung bei der Wellenlängen λ aufgrund einer Blutvolumenänderung im Gewebe ist, und a_0 und a_1 Kalibrierungskoeffizienten sind.

33. Verfahren nach Anspruch 31,
bei dem ein physiologischer Parameter, $f_w{}^1$, derart bestimmt wird, dass:

$$f_w{}^1=\frac{\left[\sum_{n=1}^{N}P_n\log\{R(\lambda_n)\}\right]-\left[\sum_{n=1}^{N}p_n\right]\log\{R(\lambda_{N+1})\}}{\left[\sum_{m=1}^{M}q_m\log\{R(\lambda_m)\}\right]-\left[\sum_{m-1}^{M}q_m\right]\log\{R(\lambda_{M+1})\}}$$

und wobei:

- p_n und qm Kalibrierungskoeffizienten sind,
- $R(\lambda)$ ein Maß einer empfangenen Strahlung mit einer Wellenlänge ist, und
- n=1-N und m=1-M Indizes für eine Mehrzahl von Wellenlängen darstellen, die dieselben oder unterschiedliche Wellenlängenkombinationen umfassen können.

34. Verfahren nach Anspruch 33,
bei dem der physiologische Parameter der Gewebewasseranteil in der Gewebestelle ist.

35. Verfahren nach Anspruch 33,
bei dem der physiologische Parameter ein Sauerstoffsättigungswert in der Gewebestelle ist.

36. Verfahren nach Anspruch 33,

bei dem der physiologische Parameter eine anteilige Hämoglobinkonzentration in der Gewebestelle ist.

37. Verfahren nach Anspruch 33,
bei dem der physiologische Parameter die anteilige Hämoglobinkonzentration in einem aus einer oder mehreren Hämoglobinarten bestehenden ersten Satz bezogen auf die Hämoglobinkonzentration in einem aus einer oder mehreren Hämoglobinarten im Gewebe bestehenden zweiten Satz ist.

38. Verfahren nach Anspruch 37,
bei dem die Koeffizienten, p_n, so gewählt werden, dass die Absorbanzbeiträge von allen Gewebebestandteilen außer den im Satz 1 enthaltenen Hämoglobinarten aufgehoben werden, und die Koeffizienten, q_m, so gewählt werden, dass die Absorbanzbeiträge von allen Gewebebestandteilen außer den im Satz 2 enthaltenen Hämoglobinarten aufgehoben werden.

Revendications

1. Dispositif pour mesurer une valeur de tissu corporel en utilisant une spectrophotométrie optique, comprenant :

un logement (400, 500, 600) de sonde configuré pour être placé à proximité d'un emplacement tissulaire (412, 512) qui est surveillé ;
une optique d'émission de lumière (618) adaptée à émettre deux longueurs d'ondes différentes connectée audit logement (400, 500, 600) et configurée pour diriger un rayonnement sur ledit emplacement tissulaire (412, 512) ;
une optique de détection de lumière (620) connectée audit logement (400, 500, 600) et configurée pour recevoir des rayonnements dudit emplacement tissulaire (412, 512) ; et
un dispositif de traitement (624) configuré pour traiter les rayonnements de ladite optique d'émission de lumière (618) et de ladite optique de détection de lumière (620) pour calculer ladite valeur de tissu corporel, dans lequel ladite valeur de tissu corporel comprend un rapport de la teneur en eau d'une partie d'un tissu du patient en relation à la teneur en eau d'une partie pauvre en ou exempte de graisse du tissu du patient ou un rapport d'une différence entre la fraction d'eau dans le sang et la fraction d'eau dans le tissu extravasculaire sur la concentration volumique fractionnelle d'hémoglobine dans le sang,
caractérisé en ce que le dispositif de traitement (624) est en outre configuré pour recevoir et comparer au moins deux ensembles de mesures de spectrophotométrie optique ayant au moins deux longueurs d'onde différentes, dans lequel la lumière aux au moins deux longueurs d'onde différentes est essentiellement absorbable du fait de l'eau qui est dans le sang vasculaire et dans le tissu extravasculaire, et le dispositif de traitement (624) est adapté à calculer un rapport des au moins deux mesures donnant une mesure proportionnelle à ladite différence entre les fractions d'eau dans le sang et l'emplacement tissulaire environnant.

2. Dispositif selon la revendication 1, dans lequel ladite valeur de teneur en eau du tissu corporel est calculée comme une fraction de teneur en tissu exempt d'os et exempt de graisse.

3. Dispositif selon la revendication 1, comprenant en outre un dispositif d'affichage (414, 514, 626) connecté audit logement (400, 500, 600) de sonde et configuré pour afficher ladite teneur en eau.

4. Dispositif selon la revendication 1, dans lequel ladite optique d'émission de lumière (618) et ladite optique de détection de lumière (620) sont espacées de 1 à 5 mm l'une de l'autre au niveau dudit emplacement tissulaire.

5. Dispositif selon la revendication 1, dans lequel ladite valeur de tissu corporel est surveillée de façon intermittente ou continue.

6. Dispositif selon la revendication 1, dans lequel le logement (400) de sonde comprend en outre une sonde à ressort de rappel (410) configurée pour activer automatiquement un dispositif d'affichage (414) connecté audit logement (400) de sonde lorsque ladite sonde à ressort de rappel (410) est pressée contre et à proximité d'un emplacement tissulaire (414) qui est surveillé.

7. Dispositif selon la revendication 1, dans lequel le logement (400, 500, 600) de sonde comprend en outre un transducteur de pression pour mesurer la compressibilité du tissu pour obtenir un indice d'une fraction d'eau libre au sein dudit tissu.

8. Dispositif selon la revendication 1, dans lequel le logement (400, 500, 600) de sonde comprend en outre un mécanisme pour induire mécaniquement une impulsion au sein dudit emplacement tissulaire pour permettre des mesures se rapportant aux différences entre des fractions volumiques de fluide intravasculaire et de fluide extravasculaire sous des conditions de faible impulsion.

9. Dispositif selon la revendication 1, dans lequel le logement (400, 500, 600) de sonde comprend en outre un mécanisme pour minimiser mécaniquement la pression au niveau dudit emplacement tissulaire pour permettre des mesures se rapportant à la fraction volumique de fluide non perturbé dans le tissu.

10. Dispositif selon la revendication 1, dans lequel le logement (600) de sonde comprend en outre un mécanisme (612, 614, 616) pour induire mécaniquement une pression au niveau dudit emplacement tissulaire pour permettre une mesure de la fraction de fluide extravasculaire en l'absence de la fraction de fluide intravasculaire.

11. Dispositif selon la revendication 1, dans lequel le logement (400, 500, 600) de sonde comprend en outre un mécanisme (612, 614, 616) pour faire mécaniquement varier une pression au niveau dudit emplacement tissulaire pour permettre une mesure de la fraction d'eau à la fois intravasculaire et extravasculaire.

12. Dispositif selon la revendication 1, dans lequel ladite optique d'émission de lumière (618) est réglée pour émettre des rayonnements à une pluralité de longueurs d'ondes spectrales étroites choisies de façon à ce que le composé biologique d'intérêt absorbe la lumière à ladite pluralité de longueurs d'ondes spectrales étroites et que l'absorption par une espèce interférente soit réduite au minimum, où une absorption minimum est une absorption par une espèce interférente qui est inférieure à 10 % de l'absorption du composé biologique d'intérêt.

13. Dispositif selon la revendication 1, dans lequel ladite optique d'émission de lumière (618) est réglée pour émettre des rayonnements à une pluralité de longueurs d'ondes spectrales étroites choisies de façon à être préférentiellement absorbées par l'eau du tissu, les protéines non hèmes et les lipides, où des longueurs d'ondes préférentiellement absorbées sont des longueurs d'ondes dont l'absorption est sensiblement indépendante des concentrations individuelles de protéines non hèmes et de lipides, et est sensiblement dépendante de la somme des concentrations individuelles de protéines non hèmes et d'eau.

14. Dispositif selon la revendication 1, dans lequel ladite optique d'émission de lumière (618) est réglée pour émettre des rayonnements à une pluralité de longueurs d'ondes spectrales étroites choisies de façon à assurer que les rayonnements mesurés reçus soient sensiblement insensibles à des variations par éparpillement et de façon à ce que les longueurs de chemins optiques à travers le derme auxdites longueurs d'ondes soient sensiblement égales.

15. Dispositif selon la revendication 1, dans lequel ladite optique d'émission de lumière (618) est réglée pour émettre des rayonnements à une pluralité de longueurs d'ondes spectrales étroites choisies de façon à assurer que les rayonnements mesurés reçus dudit emplacement tissulaire soient insensibles à des variations de température, où lesdites longueurs d'ondes sont isobestiques pour la température dans le spectre d'absorption de l'eau ou lesdits rayonnements reçus sont combinés d'une manière qui annule sensiblement les dépendances à la température desdits rayonnements reçus individuels lors du calcul des fractions d'eau du tissu.

16. Dispositif selon la revendication 1, dans lequel ladite optique d'émission de lumière (618) est réglée pour émettre des rayonnements à une pluralité de longueurs d'ondes spectrales étroites choisies parmi l'une de trois bandes primaires de longueurs d'ondes d'approximativement 950 à 1 400 nm, approximativement 1 500 à 1 800 nm et approximativement 2 000 à 2 300 nm.

17. Dispositif selon la revendication 1, dans lequel ladite optique d'émission de lumière (618) et ladite optique de détection de lumière (620) sont montées à l'intérieur dudit logement (600) de sonde et positionnées avec un alignement approprié pour permettre une détection dans un mode transmissif.

18. Dispositif selon la revendication 1, dans lequel ladite optique d'émission de lumière (618) et ladite optique de détection de lumière (620) sont montées à l'intérieur dudit logement (400, 500, 600) de sonde et positionnées avec un alignement approprié pour permettre une détection dans un mode réflectif.

19. Dispositif selon la revendication 1, dans lequel ladite optique d'émission de lumière (618) et ladite optique de détection de lumière (620) sont placées à l'intérieur d'une unité distante et qui délivre une lumière audit et reçoit une lumière dudit logement de sonde par l'intermédiaire de fibres optiques.

20. Dispositif selon la revendication 1 dans lequel ladite optique d'émission de lumière (618) comprend au moins l'une (a) d'une source de lumière à incandescence, (b) d'une source de lumière blanche et (c) d'une diode électroluminescente (« LED »).

21. Dispositif selon la revendication 1, dans lequel ledit dispositif de traitement (624) reçoit et compare lesdits au moins deux ensembles de mesures optiques, où au moins le premier ensemble de mesures optiques correspond à la détection de la lumière dont l'absorption est essentiellement due à l'eau et aux protéines non hèmes, et où au moins le deuxième ensemble de mesures optiques correspond à la détection de la lumière dont l'absorption est essentiellement due à l'eau, et où une comparaison desdites au moins deux mesures optiques donne une mesure d'une fraction d'eau exempte de ou pauvre en graisse au sein dudit emplacement tissulaire.

22. Dispositif selon la revendication 1, dans lequel ledit dispositif de traitement (624) reçoit et compare lesdits au moins deux ensembles de mesures optiques, où lesdits au moins deux ensembles de mesures optiques sont basés sur des rayonnements reçus à au moins deux longueurs d'ondes et qui sont combinés pour former un rapport de combinaisons desdits rayonnements reçus.

23. Dispositif selon la revendication 22, dans lequel ledit dispositif de traitement (624) forme une somme pondérée desdites combinaisons.

24. Dispositif selon la revendication 1, dans lequel ladite valeur de teneur en eau, f_w^1, est déterminée de telle façon que

$$f_w^1 = \frac{\left[\sum_{n=1}^{N} p_n \log\{R(\lambda_n)\}\right] - \left[\sum_{n=1}^{N} p_n\right] \log\{R(\lambda_{N+1})\}}{\left[\sum_{m=1}^{M} q_m \log\{R(\lambda_m)\}\right] - \left[\sum_{m=1}^{M} q_m\right] \log\{R(\lambda_{M+1})\}}$$

et où :

p_n et q_m sont des coefficients d'étalonnage ;
R(λ) est une mesure d'un rayonnement reçu à une certaine longueur d'onde ; et
n=1-N et m=1-M représentent des indices pour une pluralité de longueurs d'ondes qui peuvent être constituées de combinaisons identiques ou différentes de longueurs d'ondes.

25. Dispositif selon la revendication 24, dans lequel M et N sont tous les deux égaux à 3, les longueurs d'ondes indexées par m et n sont constituées de la même combinaison de longueurs d'ondes, et lesdites première, deuxième, troisième et quatrième longueurs d'ondes sont approximativement 1 180, 1 245, 1 275 et 1 330 nm respectivement.

26. Dispositif selon la revendication 1, dans lequel ladite valeur est un indice d'équilibre hydrique Q, tel que

$$Q = \frac{f_w^{IV} - f_w^{EV}}{f_h^{IV}} = a_1 \frac{\left(\Delta R/R\right)_{\lambda_1}}{\left(\Delta R/R\right)_{\lambda_2}} + a_o$$

où f_w^{IV} et f_w^{EV} sont les concentrations volumiques fractionnelles d'eau dans le sang et le tissu, respectivement, f_h^{IV} est la concentration volumique fractionnelle d'hémoglobine dans le sang, $(\Delta R/R)\lambda$ est le changement fractionnel de facteur de réflexion à la longueur d'onde λ, dû à un changement de volume sanguin dans le tissu, et a_0 et a_1 sont des coefficients d'étalonnage.

27. Dispositif selon la revendication 1, comprenant en outre un dispositif d'entrée configuré pour permettre à un utilisateur d'entrer une concentration fractionnelle d'hémoglobine dans le sang destinée à une utilisation par ledit dispositif de traitement (624).

28. Dispositif selon la revendication 27, dans lequel ledit dispositif de traitement (624) est en outre configuré pour calculer une mesure du changement de la teneur en eau entre le volume fluidique intravasculaire (« IFV ») et le volume fluidique extravasculaire (« EFV ») en utilisant ledit indice d'eau.

29. Dispositif selon la revendication 26, dans lequel lesdites première et deuxième longueurs d'onde sont approximativement 1 320 nm et approximativement 1 160 nm respectivement.

30. Dispositif selon la revendication 1, dans lequel ladite valeur de tissu corporel comprend en outre une intégrale de ladite différence pour donner une mesure de l'eau qui entre dans les et sort des capillaires.

31. Procédé pour mesurer une valeur de tissu corporel dans un emplacement tissulaire (412, 512) humain en utilisant une spectrophotométrie optique, comprenant :

la mise en place d'un logement (400, 500, 600) de sonde à proximité dudit emplacement tissulaire (412, 512) ;
l'émission d'un rayonnement en utilisant une optique d'émission de lumière (618) configurée pour diriger un rayonnement sur ledit emplacement tissulaire (412, 512) ;
la détection d'un rayonnement en utilisant une optique de détection de lumière (620) configurée pour recevoir un rayonnement dudit emplacement tissulaire (412, 512) ;
le traitement desdits rayonnements de ladite optique d'émission de lumière (618) et de ladite optique de détection de lumière (620) pour calculer ladite mesure de tissu corporel, dans lequel ladite mesure de tissu corporel comprend un rapport de la teneur en eau d'une partie d'un tissu du patient en relation à la teneur en eau d'une partie pauvre en ou exempte de graisse du tissu du patient ou un rapport d'une différence entre la fraction d'eau dans le sang et la fraction d'eau dans le tissu extravasculaire sur la concentration volumique fractionnelle d'hémoglobine dans le sang, dans lequel au moins deux ensembles de mesures de spectrophotométrie optique ayant au moins deux longueurs d'onde différentes sont reçus et comparés, dans lequel la lumière aux au moins deux longueurs d'onde différentes est essentiellement absorbable du fait de l'eau qui est dans le sang vasculaire et dans le tissu extravasculaire, et dans lequel un rapport des au moins deux mesures donne une mesure proportionnelle à la différence entre les fractions d'eau dans le sang et l'emplacement tissulaire environnant ; et
l'affichage de ladite valeur de tissu corporel ou d'une quantité dérivée de ladite valeur sur un dispositif d'affichage (414, 510, 626).

32. Procédé selon la revendication 31, dans lequel ladite valeur de tissu corporel est un indice d'équilibre hydrique Q, tel que

$$Q = \frac{f_w^{IV} - f_w^{EV}}{f_h^{IV}} = a_1 \frac{\left(\Delta R/R\right)_{\lambda_1}}{\left(\Delta R/R\right)_{\lambda_2}} + a_o$$

où f_w^{IV} et f_w^{EV} sont les concentrations volumiques fractionnelles d'eau dans le sang et le tissu, respectivement, f_h^{IV}est la concentration volumique fractionnelle d'hémoglobine dans le sang, $(\Delta R/R)\lambda$ est le changement fractionnel de facteur de réflexion à la longueur d'onde λ, dû à un changement de volume sanguin dans le tissu, et a_0 et a_1 sont des coefficients d'étalonnage.

33. Procédé selon la revendication 31, dans lequel un paramètre physiologique f_w^1 est déterminé de telle façon que

$$f_w^1 = \frac{\left[\sum_{n=1}^{N} p_n \log\{R(\lambda_n)\}\right] - \left[\sum_{n=1}^{N} p_n\right] \log\{R(\lambda_{N+1})\}}{\left[\sum_{m=1}^{M} q_m \log\{R(\lambda_m)\}\right] - \left[\sum_{m=1}^{M} q_m\right] \log\{R(\lambda_{M+1})\}}$$

et ou :

p_n et q_m sont des coefficients d'étalonnage ;
R(λ) est une mesure d'un rayonnement reçu à une certaine longueur d'onde ; et
n=1-N et m=1-M représentent des indices pour une pluralité de longueurs d'ondes qui peuvent être constituées de combinaisons identiques ou différentes de longueurs d'ondes.

34. Procédé selon la revendication 33, dans lequel ledit paramètre physiologique est la fraction d'eau tissulaire dans ledit emplacement tissulaire.

35. Procédé selon la revendication 33, dans lequel ledit paramètre physiologique est une valeur de saturation en oxygène dans ledit emplacement tissulaire.

36. Procédé selon la revendication 33, dans lequel ledit paramètre physiologique est une concentration fractionnelle d'hémoglobine dans ledit emplacement tissulaire.

37. Procédé selon la revendication 33, dans lequel ledit paramètre physiologique est la concentration fractionnelle d'hémoglobine dans un premier ensemble constitué d'une ou plusieurs espèces d'hémoglobine par rapport à la concentration d'hémoglobine dans un deuxième ensemble constitué d'une ou plusieurs espèces d'hémoglobine dans le tissu.

38. Procédé selon la revendication 37, dans lequel les coefficients, p_n, sont choisis pour annuler les contributions à l'absorbance de tous les constituants tissulaires à l'exception des espèces d'hémoglobine incluses dans l'ensemble 1 et les coefficients, q_m, sont choisis pour annuler les contributions à l'absorbance de tous les constituants tissulaires à l'exception des espèces d'hémoglobine incluses dans l'ensemble 2.

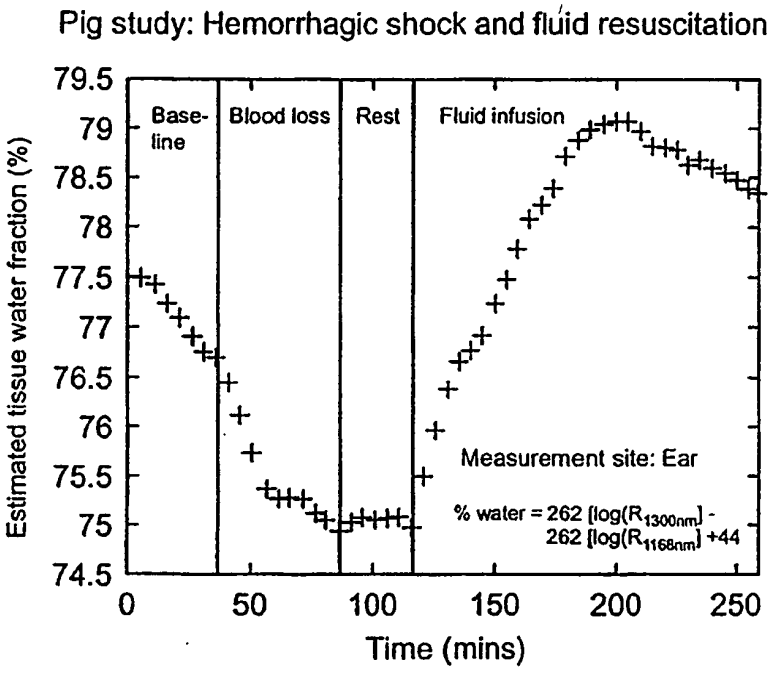
Pig study: Hemorrhagic shock and fluid resuscitation
Estimated tissue water fraction (%)
79.5
79
78.5
78
77.5
77
76.5
76
75.5
75
74.5
Base-line
Blood loss
Rest
Fluid infusion
Measurement site: Ear
% water = 262 [log(R1300nm] -
262 [log(R1168nm] +44
0
50
100
150
200
250
Time (mins)

FIG. 1

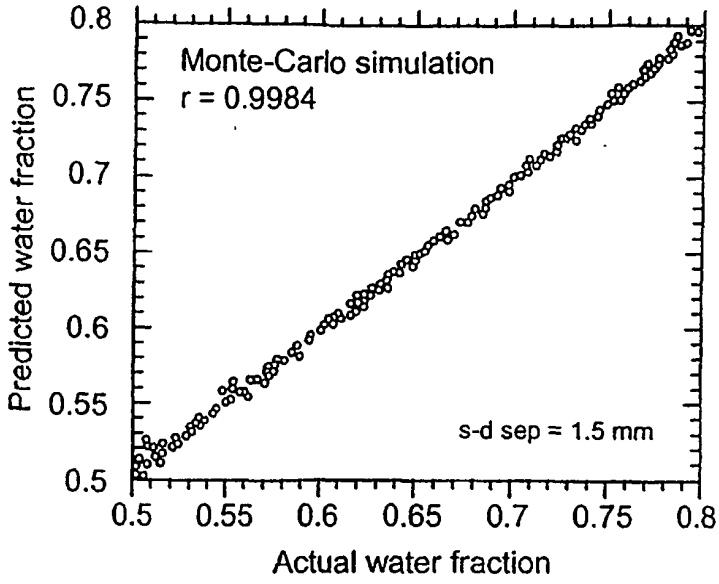
Monte-Carlo simulation
r = 0.9984
s-d sep = 1.5 mm
Predicted water fraction
Actual water fraction
0.5
0.55
0.6
0.65
0.7
0.75
0.8

FIG. 2

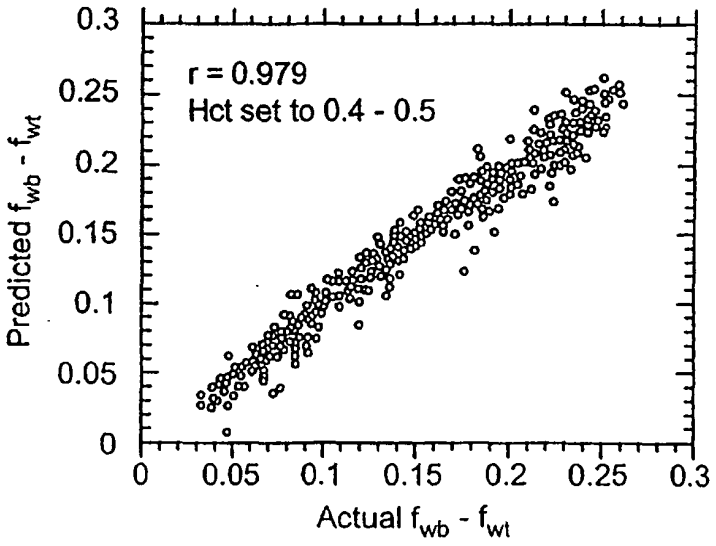
r = 0.979
Hct set to 0.4 - 0.5
Predicted $f_{wb} - f_{wt}$
Actual $f_{wb} - f_{wt}$
0
0.05
0.1
0.15
0.2
0.25
0.3

FIG. 3

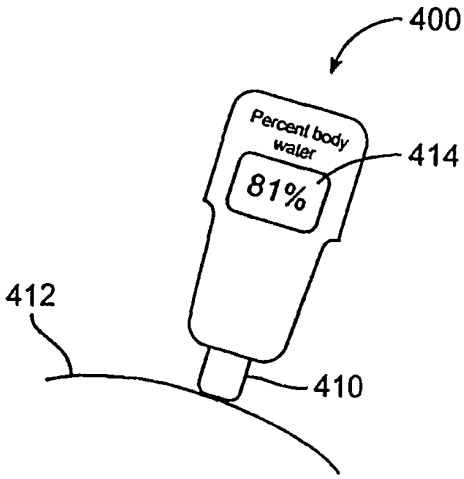
400
Percent body water
81%
414
412
410

FIG. 4

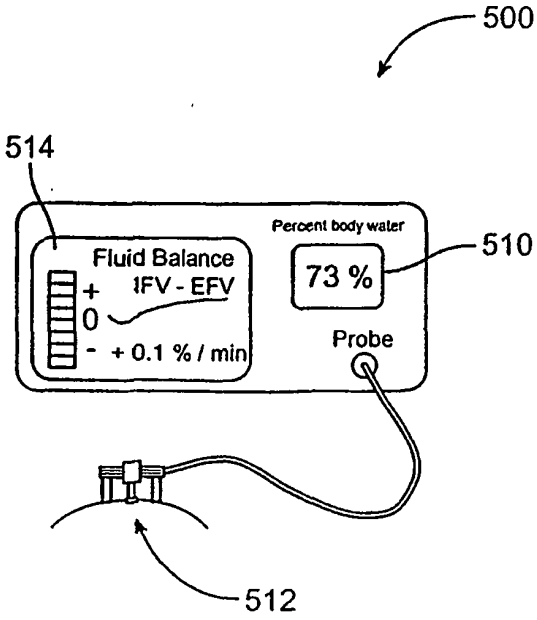
500
514
Percent body water
Fluid Balance
+
0
-
IFV - EFV
+ 0.1 % / min
73 %
510
Probe
512

FIG. 5

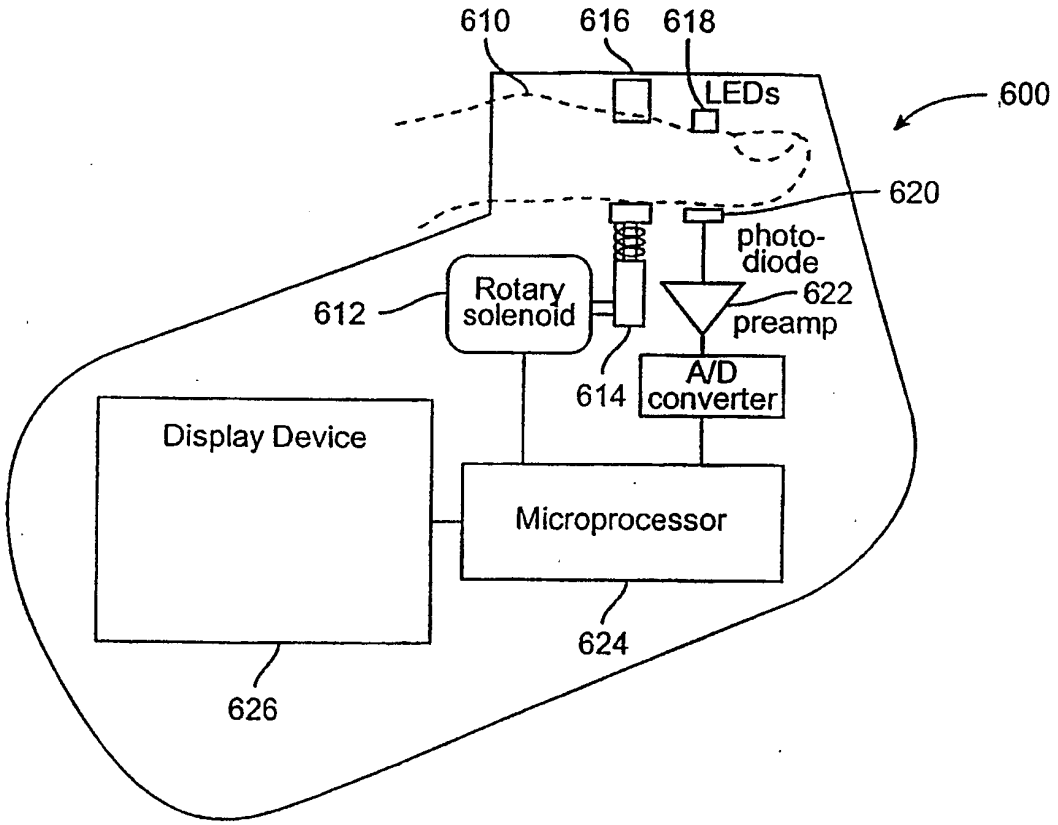
610
616
618
LEDs
600
620
photo-
diode
622
preamp
612
Rotary
solenoid
614
A/D
converter
Display Device
Microprocessor
624
626

FIG. 6

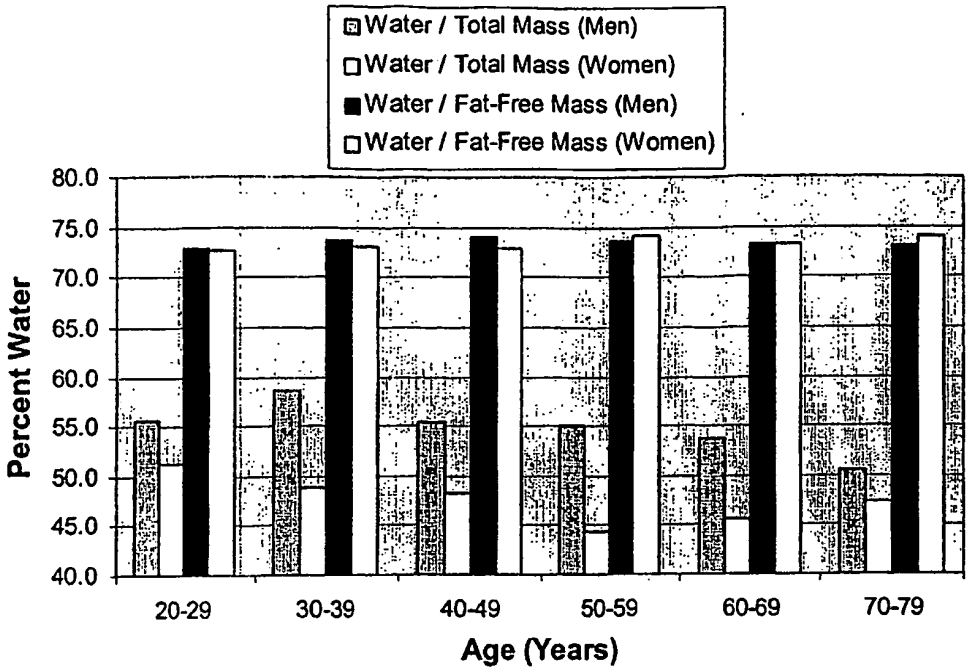
Water / Total Mass (Men)
Water / Total Mass (Women)
Water / Fat-Free Mass (Men)
Water / Fat-Free Mass (Women)
80.0
75.0
70.0
65.0
60.0
55.0
50.0
45.0
40.0
Percent Water
20-29
30-39
40-49
50-59
60-69
70-79
Age (Years)

Fig. 7

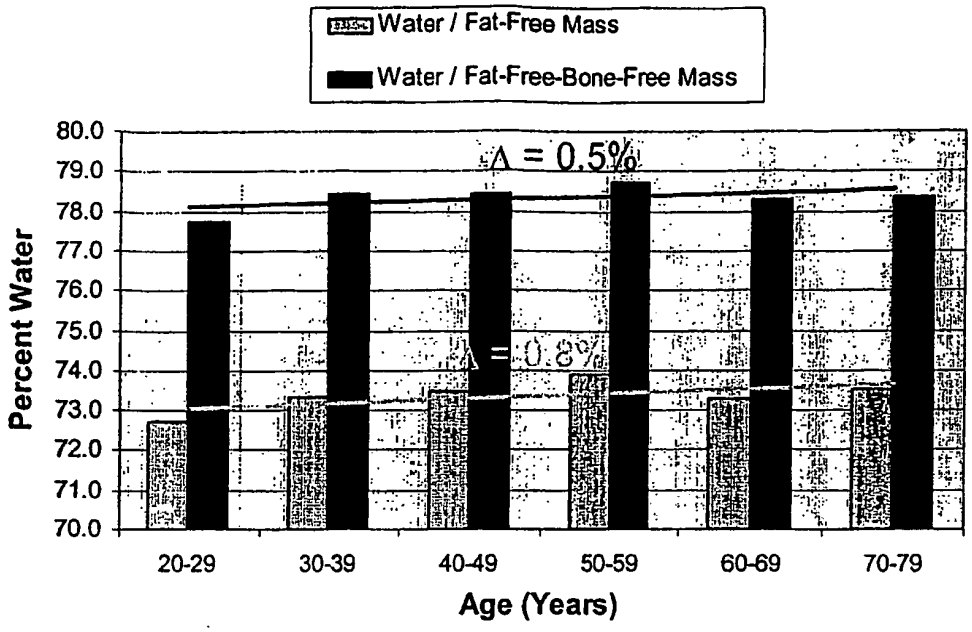
Water / Fat-Free Mass
Water / Fat-Free-Bone-Free Mass
80.0
79.0
78.0
77.0
76.0
75.0
74.0
73.0
72.0
71.0
70.0
Percent Water
Δ = 0.5%
Δ = 0.8%
20-29
30-39
40-49
50-59
60-69
70-79
Age (Years)

Fig. 8

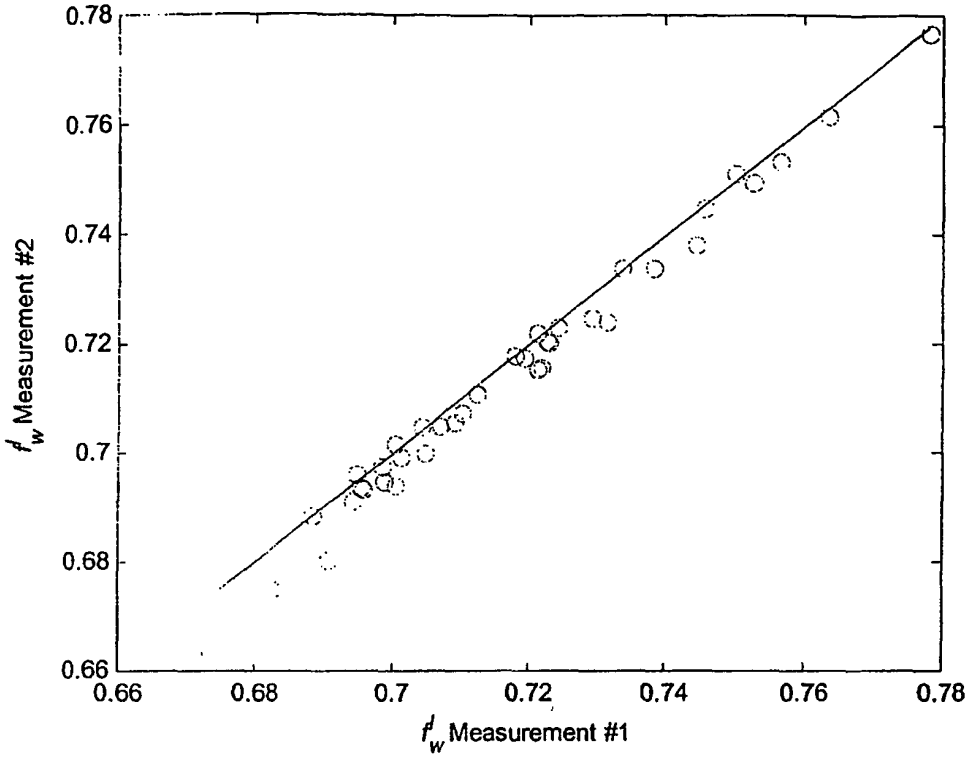
0.78
0.76
0.74
0.72
0.7
0.68
0.66
0.66
0.68
0.7
0.72
0.74
0.76
0.78
f_w Measurement #2
f_w Measurement #1

Fig. 9

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- US 2001020122 A **[0003]**
- US 5853364 A **[0059]**
- US 5348004 A **[0059]**

Non-patent literature cited in the description

- **Cohn et al.** *J. Lab. Clin. Med.,* 1985, vol. 105 (3), 305-311 **[0035]**
- **Linda S. Costanzo.** Physiology. Williams and Wilkins, 1998, 156 **[0056]**

专利名称(译)	用于监测体液和电解质紊乱的装置和方法		
公开(公告)号	EP1701653B1	公开(公告)日	2011-02-09
申请号	EP2004796817	申请日	2004-10-28
[标]申请(专利权)人(译)	内尔科尔普里坦贝内特公司		
申请(专利权)人(译)	NELLCOR PURITAN BENNETT INCORPORATED		
当前申请(专利权)人(译)	NELLCOR PURITAN BENNETT LLC		
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发明人	SCHMITT, JOSEPH, M. DEBRECZENY, MARTIN		
IPC分类号	A61B5/00 A61B5/024 G01N21/35		
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代理机构(译)	拜尔，ANDREAS		
优先权	10/699610 2003-10-30 US		
其他公开文献	EP1701653A1		
外部链接	Espacenet		

摘要(译)

使用分光光度法测量体液相关度量的装置和方法，其可用于促进旨在恢复体液平衡的诊断和治疗干预。在一个实施例中，本发明提供了一种用于使用光学分光光度法测量身体组织水含量度量作为患者的无脂肪组织含量的一部分的装置。该装置包括探头壳体，该探头壳体被配置成放置在正被监测的组织位置附近;发光光学器件连接到壳体并配置成将辐射引导到组织位置;光检测光学器件，连接到壳体并配置成接收来自组织位置的辐射;处理装置，被配置为处理来自光发射光学系统和光检测光学系统的辐射，以计算度量，其中度量包括患者组织的一部分的水含量相对于a的瘦肉或无脂肪含量的比率。患者组织的一部分。