未來的技術

Future technologies

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Research and development in the area of body composition has undergone considerable changes in the last decade. These changes have resulted in part from the improvement of established techniques — but also from the introduction of methods based upon principles new to body composition studies.

One can observe in recent developments a trend towards less invasive techniques, and cheaper, more portable instrumentation. There has also been a move towards improving the efficacy of the information obtained. The trend towards less invasive techniques, which includes lower dose, is particularly important when considering applications involving children.

The question of 'future technologies' needs to be considered against the background of these developments if one is to propose the direction of future research.

This paper considers possible new and modified technologies which may find application in the measurement of body composition. In addition, currently emerging technologies which need further research and development will be discussed. Examples of technologies examined in this paper include:

- a possible new approach to measurement of bone mineral density in neonates using laser beam transmission,
- possible modification of dual-energy X-ray absorption (DEXA) techniques for improved precision in the measurement of the relative lean/fat component, and
- the research required to validate the use of multifrequency bio-electrical impedance analysis for measurement of extracellular and total body water.

Introduction

There is continued development in the technology used for measurement of body composition resulting from either modifications to established techniques or from the introduction of methods based upon principles new to the area. The development of less- or non-invasive methods has been a major goal of research and with the acceptance that ionizing radiation is invasive there has been a move towards techniques involving less or no radiation dose. Development has also been influenced by the constraints imposed by the requirement of greater accountability of the research and health industry budget. These constraints have resulted in some emphasis being placed on the investigation of techniques which might provide cheaper alternatives to existing, possibly expensive, 'gold standards' of measurement of body composition. Greater portability of instruments is also an aim of research and development. This is important to allow for the more widespread use of body composition techniques outside major hospitals and research institutions so that the benefits of body composition measurements may become a more integral part of the management of patients.

However, concomitant with the above is the need to ensure the efficacy of the measurements obtained. This paper considers possible new technologies and modifications to existing technologies which might impact upon the area of body composition measurement. The discussion is divided into consideration of possible developments to measure three of the major components of body composition: bone mineral, water and fat.

Measurement of bone mineral and bone quality

The precision, accuracy and diagnostic efficacy of bone mineral measurements have improved significantly in the last two decades. Greenfield[1] recently reviewed the methods used to measure the skeleton and concluded that 'no one method includes all the features required to be entirely satisfactory'. His criteria were precision, accuracy, the measurement of volumetric density ($g\ cm^{-3}$) and the ability to predict fracture risk. The trend in bone mineral measurement has been towards lower dose and better precision. However, as Greenfield commented, there is a need for development of techniques to measure bone quality.

Technologies which may be used in the future to measure bone mineral density and quality may reduce the radiation dose employed even further and perhaps use non-ionizing radiation so that bone mineral measurements can be performed more routinely on neonates and young children. The use of laser beam transillumination and ultrasound measurements are being investigated and technologies based on these principles may find application in the future.

Transillumination, using differential spectroscopy of infra-red and near infra-red wavelengths is a technique which, although in the early stages of investigation, may find application in bone mineral measurements. Jarry et al.[5] investigated the use of transillumination to 'image' the adult hand. They were not concerned with measurements of bone mineral but did demonstrate the second to fifth metacarpals in their transillumination 'images'. van Doorn and Kleinschmidt[6] are investigating transillumination as a possible method of measurement of bone mineral content of the radius and ulna, particularly in neonates. Major difficulties with application of transillumination for the measurement of bone mineral are associated with the significant absorption of the laser beam by even thin samples of bone and the magnitude of scattering by soft tissue in the forward direction. Wilpizeski[7] compiled data on the transmission of 633 nm and 694 nm wavelengths through bone. He reported only 20% transmission through 0.5 mm sections of femoral bone with an increase in incident spot size from 0.3 mm to 0.5mm diameter (this latter observation implying significant scattering). These result are, however, encouraging when considering the possible application of transillumination to measure bone mineral in neonates. Fast time-of-flight techniques employing pulsed laser beams need to be used to reduce the effect of scattered radiation in the detected signal. Current time-of-flight measurements allow differentiation to about 1 ps which is the equivalent of less than 0.5 mm of path length and together with pin hole collimation of the laser beam may be adequate to permit the use of transillumination for the measurement of bone mineral content. Considerable work is being done to develop this technique for other applications, for example the detection of breast cancer, and it will be of interest to observe the improvements expected over the next few years and whether these improvements will permit the use of transillumination to the determination of bone mineral content. Assuming that the problems associated with absorption and scatter can be overcome it is not difficult to consider a rectilinear scanning system to allow measurements on an area of bone and the use of non-ionizing radiation would make transillumination an attractive alternative for the measurement of bone mineral, particularly in the young.

The measurement of both attenuation and velocity of ultrasound by bone have been investigated by a number of groups with the aim of characterization of bone. The Broadband Ultrasonic Attenuation (BUA) method developed by Langton et al[2] is one approach which shows promise as an indicator of bone quality. The indicator used by Langton and colleagues is the slope (in dB MHz^{-1}) of the attenuation/frequency relationship for the heel (Os Calcaneus). The technique compares the attenuation of an ultrasound beam measured when the heel is placed in a water bath with that for water alone and the difference is used to determine the attenuation by the bone. Comparison of the results of BUA with bone mineral density measured in the same subjects by more established techniques has resulted in relatively poor correlation with r-values ranging from 0.36 (BUA versus single Photon absorption (SPA), or Quantitative computed tomography (CT), in osteoporotic patients[3] to 0.8 (BUA versus SPA)[4] in rheumatoid patients. However, the poor correlations may be attributed in part to the different sites and in part to the different physical quantities measured. Further work is needed to evaluate the potential role of BUA in bone measurements.

The velocity of sound in bone is another parameter which has been shown to correlate with bone density and it is perhaps a combination of the measurement of both attenuation and velocity which may provide the best ultrasonic characterization of bone.

The measurement of body fat (and fat/lean ratio)

The measurement of whole body fat has perhaps proven to be the most difficult of the four components of body composition. The more established methods of measuring whole body fat involve exposure to ionizing radiation and in some cases fairly specialized equipment, eg a 14 MeV neutron generator. Spot measurements of fat thickness using ultrasound or other methods suffer from the problem of extrapolation of the measurements to whole body fat content. Dual-energy X-ray absorption (DEXA) is also currently used to measure body fat (and lean tissue) and it is possible that relatively minor modifications to the current technique can be employed to improve the efficacy of the measurement.

The precision of DEXA for the measurement of fat is quoted as 6–9% and 2–4%, respectively. The application has been developed somewhat secondary to the use of DEXA for measurement of bone mineral density (BMD) and hence the available devices are optimized for the measurement of BMD and not fat/lean tissue.

The measurement of fat and lean tissue using DEXA is based upon the principle of differential absorption by these two components assuming that no bone is present in the region being measured. The parameter used to determine the fat/lean ratio through a section of the soft tissue is the R-value (ratio of low to high energy attenuation in soft tissue). The R-value varies linearly with the % of lean in soft tissue and is relatively independent of the thickness of the soft tissues. The greater the magnitude of the difference in the R-value at the low and high energies used, the better will the fat/lean fractions be determined. This difference increases as the energy of the photon low energy beam decreases for a fixed high energy and hence better precision in the determination of the fat/lean ratio is possible if the two energies of photon beam used are as different as possible taking into consideration the need for adequate transmission of the beam. Current DEXA units utilizing cerium filters and 80 kVp produce dual-energy X-ray spectra with effective energies of 40 and 70 keV. These effective energies are appropriate when considering the measurement of BMD, however, for determination of fat/lean fractions a somewhat lower energy then 40 keV is to be preferred. A reduction to even 30 keV may result in improvement of precision. The measurement at 30 keV effective energy may be accomplished by using an alternative filter or by using information contained in the spectrum of transmitted photons.

Ultrasound is another technology with potential for use in determining fat/lean ratios. The percentage transmission of ultrasound through tissue is primarily determined by reflection (at interfaces) and absorption. Like ionizing radiation, the attenuation of an ultrasound beam by a thickness, x, of a homogeneous material may be described by an equation of the form:

$$I_x = I_0 e^{-\mu x},$$

where I_x and I_0 are the transmitted and incident intensities, respectively, and μ is the fraction of energy removed from the beam per unit path length.

The important feature in the potential application of ultrasound to fat/lean ratio measurements is that the attenuation of an ultrasound beam is tissue type and frequency dependent, whereas the reflection is essentially independent of frequency. Hence, if the relative transmitted intensities through a section of soft tissue is measured at two different frequencies of ultrasound, eg 1 MHz and 2 MHz, then the ratio of transmitted intensity at the two frequencies provides an indicator of fat/muscle ratio in that section. For 1 MHz and 2 MHz beams the ratio of relative transmitted intensities I (1 MHz)/I(2 MHz) decreases by about 3% for each 1% increase in the proportion of fat.

The use of attenuation of ultrasound by soft tissue certainly warrants further study particularly as it is thought that absorption in soft tissue occurs primarily in the protein macromolecule.

Body water

The measurement of total body water (TBW) has traditionally been performed using either isotope dilution, bioelectrical impedance or total body electrical conductivity (TOBEC). Of these techniques, bio-electrical impedance warrants further investigation due to its relative simplicity and cost and because of the potentially greater utility of the measurement following the relatively recent development of multi frequency or swept frequency bioelectrical impedance monitoring (SFBIM)[8,9]. The principle of bio-electrical impedance has been discussed by a number of authors (eg Kushner[10]). Briefly, the body is considered as containing two alternative paths of conduction for an applied alternating current, the one through the extracellular fluid and the second through the intracellular fluid and cell membrane. The fluids behave as resistors and the cell membranes as imperfect capacitors. At zero frequency (dc) an applied current passes entirely through the extracellular pathway and as the frequency increases the current distributes between the intracellular and extracellular pathways. The volume of conducting fluid, V, is obtained from prediction equations developed from consideration of the body as a conducting cylinder for which:

$$V = \frac{\rho L^2}{Z},$$

where:

ρ is the resistivity, L the distance between electrodes (generally taken as the height in human measurements) and Z the measured impedance.

The swept frequency approach measures bioimpedance at as many as 496 discrete frequencies between approximately 4 kHz and 1 MHz and the analysis of the data extracts the resistance of the body at zero frequency as well as the impedance at the characteristic frequency, Z_c[11]. Cornish et al.[8] have shown that L^2/R_0 and L^2/Z_c are the best predictors of extracellular and TBW in rats by correlation of the results of bioimpedance measurements with isotope dilution measures of these same quantities. Perhaps the most significant problem of the application of SFBIM is that the equations used to predict the water compartments are somewhat dependent upon the patient group measured. This dependence may be associated with differences in measured impedance due to different instruments used by the various groups[12,13] or due to the use of electrodes placed on wrist and ankle to measure whole body impedance (and hence body water). The resistance (or impedance) measured between wrist and ankle is due primarily (~80%) to the resistance of the arms and legs whereas the major part (~70%) of body water is in the trunk. Thus predictive equations developed using a normal healthy group may not be appropriate for a patient group with a different distribution of body water between the limbs and trunk. This difficulty may be overcome by measuring the impedance (and hence water content) of the limbs and trunk separately[15]. This modification to technique although under study needs to be investigated for a range of patient groups.

Extension of the technique of bio-electrical impedance to imaging of body tissues (electrical impedance tomography, EIT) is also being investigated although there has been relatively little work done in relation to its use in the measurement of body composition. Variations in tissue resistivity/permittivity with frequency may be of use in differentiating tissue types using EIT. This technology is in an early stage of development. However, like SFBIM it offers the attraction of relatively low cost and portable instrumentation.

Conclusion

The measurement of body composition has progressed steadily in the last few decades. Technologies have been improved and replaced as developments overtook them. The principles employed in the area are varied and the application of techniques demanding if one is to ensure the precision, accuracy and diagnostic efficacy required. Which technologies will find use in the future is uncertain although history indicates that new and modified technologies will certainly replace some of the existing techniques.

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