Body water measurement in growth disorders:
a comparison of bioelectrical impedance and
skinfold thickness techniques with isotope dilution

J W Gregory, S A Greene, C M Scrimgeour, M J Rennie

Abstract
Total body water was estimated as part of the
assessment of body composition in children with
growth disorders, using the newly commercially available method of bioelectrical
impedance. This was undertaken to compare
the precision and accuracy of the results with
those derived from skinfold thickness against
measurement of stable isotopically labelled
water (H$_2$O) dilution as a standard. The
comparisons were carried out to see to what
extent the impedance method could be
applied with confidence to assessment of chil-
dren with growth disorders. Total body water
was derived from impedance (I) using an asso-
ciation with height (Ht/I). Impedance and
skinfold thickness estimates of total body
water were equally precise when compared
with values obtained from H$_2$O dilution
(limits of agreement -1.9 to +1.3 and -1.7 to
+2.0% respectively). The mean intraob-
server coefficient of variation for repeat mea-
surements of impedance was 0-9% compared
with 4-6% for skinfold thickness with an
interobserver coefficient of variation for
impedance of 2.8%. Bioelectrical impedance
estimation of body composition is likely to be
of value in the growth clinic when expertise
in measurement of skinfold thickness is
limited or repeated measurements are to be
undertaken by different observers.

Body composition measurement is useful in the
diagnosis of pathology, assessment of disease
progress and response to treatment. Techni-
ques currently in use are mostly indirect, often
expensive, difficult, and time consuming.
Furthermore, the original reference data for
body composition was based on the chemical
analysis of the cadavers of six adults, several of
whom died of illnesses likely to make their body
composition unrepresentative. Values for body
composition of children have often been derived
by extrapolation from those values together
with those obtained from the chemical analysis
of a 4.5 year old boy and newborn infants.

Densitometric analysis of body fat content by
the underwater weighing technique is not
widely applicable in the clinical context and is
based on uncheckable assumptions concerning
the density of fat and lean tissues. Skinfold
thickness measurement is a standard method
of body composition assessment in clinical
paediatric practice. Regression equations
derived from underwater weighing and deuter-
ium oxide dilution methods for the calcu-
lation of body density and thus body fat from
the sum of four skinfold thicknesses have been pub-
lished for use in adolescents and prepuberal
children. The method of skinfold thicknesses
may, however, be unreliable because distribu-
tion of fat within the body may vary with sex,
age, and race. There is considerable variabil-
ity between measurements made by different
observers on the same individual and the techni-
ique requires practice to reduce the error to the
minimum possible with a single observer.

The present ‘gold standard’ for body water
measurement from which body composition
may be estimated depends on the dilution of iso-
topically labelled water tracer. This assumes
that the tracer is uniformly distributed through-
out the body water compartments and excreted
like native water. Tritium is radioactive and
thus ethically unacceptable for use in children
but both deuterium (H$^2$) and H$_2$O are stable iso-
topes that may be used as tracers of water with-
out radiation hazard. H$_2$O is expensive and in
short supply but the H$_2$O dilution space is a
more accurate measure of total body water,
usually about 3% less than the H$_2$O space
because of greater exchange of H$^2$O with non-
aqueous components. However, isotopic analy-
sis of H$_2$O requires expensive mass spectromet-
ric facilities and expertise in their use.

The measurement of impedance is a techni-
que for the indirect estimation of total body
water and has recently been evaluated in several
clinical situations. It is based on the associa-
tion between the physical dimensions and electrical
properties of a conductor. The impedance to the
passage of a current through a conductor varies
directly with the product of its volume resistiv-
ity and the length squared and inversely with its
volume. Hoffer et al. have confirmed that in the
human body, assuming water to be the electrical
conductor, total body water is related closely to
height$^2$/impedance (Ht$^2$/I). The technique has
been validated in adults but there is little
information on its use in children. Given that
the technique is quick, safe, and non-invasive,
it should be of particular value in the assess-
ment of body composition in children.

We have therefore undertaken a preliminary
study in children with growth disorders to
assess how well bioelectrical impedance predicts
total body water determined by H$_2$O dilution
in those circumstances. We have compared the
results with those from measurements of skin-
fold thickness to identify the relative utility of
each of the simple indirect methods.

Patients and methods
Thirty four children (28 boys, six girls) under-
Body water measurement in growth disorders: a comparison of bioelectrical impedance and skinfold thickness techniques with isotope dilution

Table 1 Details of patients and measurements

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>12.0 (2.5)</td>
<td>7.4 to 15.7</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>132.4 (13.6)</td>
<td>106.5 to 151.7</td>
</tr>
<tr>
<td>Height SDS</td>
<td>-2.56 (1.08)</td>
<td>-4.60 to 1.06</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>29.9 (8.1)</td>
<td>15.7 to 49.8</td>
</tr>
<tr>
<td>Total body water</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(H218O dilution) (kg)</td>
<td>17.3 (4.3)</td>
<td>9.3 to 25.1</td>
</tr>
<tr>
<td>Total skinfolds (mm)</td>
<td>33.5 (16.0)</td>
<td>17.0 to 78.0</td>
</tr>
<tr>
<td>Resistance (ohms)</td>
<td>608 (71)</td>
<td>489 to 742</td>
</tr>
</tbody>
</table>

SDS = growth measurement expressed as standard deviation score for chronological age.10

The going investigation of growth disorders were assessed. Of these, 19 had constitutionally delayed puberty (height <3rd centile, bone age delay >1.5 years), nine had growth hormone deficiency (growth hormone <10 μg/l in response to a standard insulin stress test),11 and six had normal variant short stature (height <3rd centile, growth hormone >10 μg/l in response to a standard insulin stress test). Details of the subjects are shown in table 1 and these children are representative of the referral pattern to our clinic. Height was measured using a Holtain stadiometer and weight with a beam balance.

Total body water was measured from H218O dilution after giving 0.3 g H218O/kg estimated total body water by mouth after an overnight fast (18O was 10-4 atom % from Isotec Inc). Urine specimens for analysis were taken before and five hours after the dose. Urine aliquots of 400 μl were equilibrated with 5% carbon dioxide in 20 ml Vacutainers (Becton Dickinson) for three days before analysis of the carbon dioxide for 18O ratio using a Finnigan MAT Delta D gas isotope ratio mass spectrometer fitted with an automated dual gas analysis system.12 Standard corrections for fractionation and dilution of the label by the added carbon dioxide were applied.13 Total body water was calculated by the method of Schoeller et al after standardising the enrichment of the given tracer by analysis of suitable dilutions with tap water.6

Bioelectrical impedance measurements were made using Holtain body composition analyser (Holtain Limited). The technique is simple to perform and highly acceptable to patients. Electrodes are applied for a few seconds to the dorsum of the right wrist and to the flexor surface of the right ankle through which a harmless 800 μA, 50 khz high frequency alternating current is passed allowing the impedance to be measured.

Skinfold measurements were made by a single observer (JWG) using a Holtain skinfold caliper from the triceps, biceps, subcapular and suprailiac sites as described previously.3 Separate regression equations were used for converting the sum of the four skinfold thicknesses into body density for prepubertal4 and adolescent5 children. Fat mass was calculated5 and for comparative purposes total body water was deduced (assuming that fat mass is anhydrous and fat free mass contains 730 g water/kg weight14) using the equation, total body water = 0.73×(weight−fat mass).

Comparison of the values for total body water obtained from impedance and skinfold techniques with those obtained by isotope dilution were made using the method of Bland and Altman.15 This entails comparing the difference between the methods against the mean of the two methods, with results expressed as the bias (mean of the differences) together with its limits of agreement (mean (2 SD) difference) and the 95% confidence intervals for the lower and upper limits.

Results

Subject details and measurements by each technique are shown in table 1. The association for H2/I and total body water derived from H218O dilution produced the regression equation: total body water=0.79+0.55 (H2/I) (figure). Statistical analysis of the variance involved in prediction of total body water by values derived from impedance and skinfold thickness measurements suggests both methods are of similar precision when compared with the H218O dilution method (table 2).15

Repeated measurements of impedance by the same observer at the same time of day resulted in a mean coefficient of variation for the measurement of 0.9%. When repeat measurements were made at different times throughout the day regardless of mealtime or a full bladder, the coefficient of variation only increased to 2.4%. Repeat measurements on the same occasion by different observers resulted in a coefficient of

Table 2 Total body water (kg) derived from H218O dilution compared with that from skinfold thickness and impedance (H2/I).

<table>
<thead>
<tr>
<th>Skinfold thickness</th>
<th>H2/I (this study)</th>
<th>H2/I (Davies et al13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>r</td>
<td>0.98</td>
<td>0.98</td>
</tr>
<tr>
<td>Bias</td>
<td>-0.3</td>
<td>-0.1</td>
</tr>
<tr>
<td>Limits of agreement</td>
<td>-1.9 to 1.3</td>
<td>-1.7 to 2.0</td>
</tr>
<tr>
<td>95% Confidence interval:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower limit</td>
<td>-2.4 to -1.4</td>
<td>-2.3 to -1.2</td>
</tr>
<tr>
<td>Upper limit</td>
<td>0.8 to 1.8</td>
<td>1.4 to 2.5</td>
</tr>
</tbody>
</table>

The association between height/impedance (H2/I) and total body water measured by H218O dilution. Total body water=0.79+0.55 (H2/I).
variation of 2.8%. In contrast, the coefficient of variation for repeat skinfold measurements taken by a single experienced observer was 4.6%.

The application of skin electrodes in the use of the impedance technique was perceived as less threatening and thus better tolerated than the use of skinfold calipers in children under the age of 8 and in our experience may be used without difficulty in children as young as 3 years old (unpublished data).

Discussion
The principles of bioelectrical impedance were described nearly 30 years ago, but only in the last five years have instruments suitable for clinical measurement become available. Our study confirms the results of Davies et al who derived total body water from impedance in 26 children and adolescents with a variety of disorders (inflammatory bowel disease, growth hormone deficiency, diabetes, and obesity). We found a mathematical association very similar to their findings (total body water = 0.5 + 0.6 x H̄/L). The study of Davies et al involved children with a variety of illnesses and it is reassuring that in our own study, focusing on children with growth disorders in whom fat content may be abnormal, that the above association holds. Together these results suggest that impedance may be reliably used for the assessment of body composition in paediatric practice, although clearly much larger studies are necessary to confirm the precision of the technique in girls and in disorders other than those affecting growth.

Our results (table 2) comparing both impedance and the established technique of skinfold thickness estimation with $H_2^{18}O$ dilution show concordance of estimates of the bias and extent of agreement of the indirect methods in predicting total body water, although the confidence intervals for the limits of agreement are wide, reflecting the small size of our sample and the inherent imprecision of indirect measurements of total body water. The concordance holds even when estimates of total body water based only on published equations are compared.

This avoids the minimisation of prediction error that is introduced when our equation for deriving total body water from impedance is compared with total body water derived from isotope dilution, the former having previously been derived from the latter. Impedance and skinfold techniques, when used by a single experienced observer, are of comparable precision in the assessment of total body water, though the coefficient of variation for repeat measurements by the former method is considerably less.

In summary, bioelectrical impedance appears to be at least as accurate and precise a method for the measurement of total body water as the skinfold thickness technique performed by a single experienced observer. The impedance method is of advantage with younger children or when the clinician has limited expertise in skinfold measurement. It is also of value when different observers are undertaking serial measurements; this is because of the smaller variation in values obtained by one or more than one observer and so is the preferred choice when monitoring patients’ response to treatment.

This work was supported by grants from the Biomedical Research Council of the Scottish Home and Health Department, Novo-Nordisk A/S, and Organon Laboratories.

17 Thomasen I. Body electric properties of tissues. Estimation by measurement of impedance of extracellular ion strength and intracellular ion strength in the clinic. Lyon Medical 1963;209:1325-52.