Resonant Cavity Perturbation: a promising new method for the assessment of total body water in children

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Short title: "Resonant cavity perturbation for assessment of total body water in children"

Abstract

The accurate measurement of total body water (TBW) in children has important clinical and nutritional applications. Resonant cavity perturbation (RCP) is a new method for estimating TBW. This method measures the dielectric properties of the body which are related to body water. For RCP measurements, each subject lay supine on a bed inside a screened room which acts as a resonant cavity. A network analyser measures the frequencies of two low-order cavity resonances of the room, with electric-field vectors that were respectively vertical and horizontal,

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the resonant frequency shifts relative to the empty room are then derived. These frequency shifts correlates with TBW. The aims of this present study were to a) develop TBW_{RCP} predictive equations for children using TBW_{dil} as the criterion method, b) cross-validate the derived equations, c) determine precision of the TBW_{RCP} method, and d) compare the criterion method TBW_{dil} with three methods of estimating TBW: RCP, MFBIS and Anthropometry.

Predictive equations, independent of sex, were developed with linear regression in a group of 36 children. The relationship between combined RCP frequency shifts and TBWdilution had an $r^2=0.90$ and standard error of the estimate (SEE) =1.42kg. Multiple regression analysis, that included a term for body mass index, only had a small effect on $r^2=0.93$ and SEE=1.25kg. In-vivo TBW precision for the vertical, horizontal and combined frequency modes ranged from 0.7 to 3.4%. Bland Altman analysis indicated close agreement between the criterion method TBWdil and the three other methods of TBW estimation. Mean differences were $TBW_{RCP(2)} = 0.01+/-1.34kg$, $TBW_{MFBIS} = 0.45+/-1.35kg$, $TBW_{Anthropometry} = 0.29+/-1.29kg$.

Currently the RCP method does not significantly improve the prediction of TBW compared to MFBIS and anthropometry in this initial study. However the derived equation was independent of sex and body size had only a small effect.

1. Introduction

Knowledge of total body water (TBW) is important for the evaluation of nutritional status in health and disease and for monitoring treatment. Accurate measurement of body water volumes has critical importance in particular for parenteral fluid therapy in acute care and for conditions such as peritoneal dialysis, for clinical decision-making on dialysis dose (Morgenstern et al, 2001). Water retention is a common outcome of response to injury and trauma or critical illness (Jacobs, 1996). With paediatric care in particular, determining an accurate and timely measurement of whole body fluid volumes in patients can be problematic. Existing body water assessment methods in children include isotope dilution, equations based on anthropometry and

single frequency (50KHz) bioimpedance (SF-BIA) (Horlick et al 2002) – multi-frequency bio-electrical impedance (MFBIA) at 5,50,100 and 200KHz (Mehta et al 2014) – multi-frequency (50 frequencies from 5KHz to 1MHz) bio-impedance spectroscopy (MFBIS) (Scharfetter et al 1997, Zhu et al 2006). TBW has been measured isotopically using dilution measurements of deuterium oxide (TBW_{dil}). This is regarded as the criterion method, but is time consuming and expensive, and therefore not ideal for clinical practice. With anthropometry, published equations from earlier years have overestimated TBW with biases from 4 to 11% (Wells et al, 2005). The most appropriate equation reported has used weight, height, age and sex, with a standard error of estimation of 7.8% (Wells et al, 2005). Whole-body BIA represents an index of TBW through the electrical conducting properties of tissues and is commonly used in practice due to its ease of use and affordability. However, BIA estimates of body water may be erroneous for individual children and subject to significant bias for groups, depending on the equation used (Wells et al, 1999). In a recent report, Elia et al (2013) stated that BIA in combination with weight and height had failed to demonstrate that it was superior to simple anthropometry measurements in predicting body composition. Accuracy has been reported to be limited due to a disproportionate whole body resistance that is dominated by the limbs due to their smaller cross-sectional area compared to the trunk. Hence, the trunk has only a small contribution to whole body impedance (Fuller et al, 2002) and will be insensitive to fluid changes (Woodrow et al, 1996). Numerous studies have reported large discrepancies between BIA and TBW_{dil} in children (Sen et al, 2010; Bell et al, 2013; Montugnese et al, 2013).

There is an ongoing need to improve current or to develop new techniques suitable for measuring body water in children. Resonant cavity perturbation (RCP) is a novel, electromagnetic method that can determine TBW from the dielectric properties of the body, which alter the resonances of a large screened room (TBW_{RCP}) (Robinson et al 2003; Stone et al 2004; Robinson et al 2005). The advantages of TBW_{RCP} are that measurements are rapid, non-invasive and relatively inexpensive and compare favourably with TBW_{dil} in adults (Robinson et al 2005).

Although the perturbations can be calculated theoretically for simple shapes such as discs and cylinders, this is not feasible for the complex geometry of the human body, and so an empirical approach is more appropriate. The RCP method has not yet been validated in children and development of predictive equations are needed, which consider the variables that can impact on body water measurements in children such as body size.

Therefore, the aims of this present study were to a) develop TBW_{RCP} predictive equations for children using TBW_{dil} as the criterion method, b) statistically cross-validate the derived equations, c) determine in-vivo and in-vitro precision of the TBW_{RCP} method, and d) compare the criterion method TBW_{dil} with three methods of estimating TBW: RCP, MFBIS and anthropometry.

2. Methods

A small study group of thirty six children (14 female, 22 male), recruited from the Leeds area, participated in the study which was reviewed and approved by the Leeds Hospitals Research Ethics Committee, UK. The inclusion criteria were children between the ages of 5 and 14 years, free from known disease. For all measurements, children wore a hospital gown and the bladder was voided before measurement. Body weight (Wt) was measured to the nearest 0.1kg using a SECA 880 digital weighing scale (SECA, Birmingham, UK) and height (Ht) measured to within 0.1cm with a wall mounted digital stadiometer (Holtain, Dyfed, UK). Body mass index (BMI) was calculated as body weight (kg) / height $(m)^2$. The study group physical parameters are shown in Table 1. The age matched Z-scores for height (ZHt), weight (ZWt) and BMI (ZBMI) were derived from the UK reference data 1990 (Freeman et al, 1995; Cole et al, 1995). Z-scores express the number of standard deviations (sd) below or above the reference mean value for gender and age

Table 1. Physical characteristics of study group

	Females (n=14)		Males (n=22)	
	Mean (sd)	Range	Mean (sd)	Range
Age(yr)	9.9(2.4)	6.2 to 14.5	10.0(2.0)	6.5 to 13.6
Height (cm)	139.0(12.1)	122.2 to 164.0	139.4(12.3)	111.5 to 169.3
Weight(kg)	33.7(7.8)	24.4 to 50.4	33.0(8.9)	19.8 to 58.6
BMI(kg/m^2)	17.3(1.9)	14.9 to 21.8	16.6(1.9)	13.6 to 20.4
ZHt	0.30(0.74)	-1.34 to 1.20	0.17(1.02)	-1.65 to 1.82
ZWt	0.22(0.54)	-0.66 to 1.12	0.10(0.80)	-1.62 to 2.02
ZBMI	0.04(0.80)	-1.53 to 1.04	-0.04(0.85)	-2.29 to 1.28

Mean(sd)   sd = standard deviation   ZHt, ZWt, ZBMI = Z-scores for height, weight and BMI

2.1 Resonant cavity perturbation (RCP)

The principle of the RCP method is to measure the lower-order resonances of a large metal enclosure acting as a resonant cavity and to determine TBW$_{RCP}$ from the changes in these electromagnetic standing-wave patterns, which are related to the dielectric properties of body water in a human subject.

The only physiological effect at RCP frequencies (tens of MHz) is heating due to the conversion of electromagnetic energy into thermal energy. The maximum power supplied to the cavity was 0.01W. This ensured that exposure was within the ICNIRP (International Commission on Non-Ionising Radiation Protection) guidelines (ICNIRP 1998), which recommend that the Specific Absorption Rate (SAR) should be less than 0.4 W/kg. For subjects weighing between 10 and 50kg, SAR values for RCP are at most 0.001 and 0.002W/kg respectively. None of the subjects in this study reported any negative effects from RCP.

A network analyzer (Agilent, Stockport, UK) is connected to a pair of antennas that are mounted in the cavity and automatically measures the power transmitted between them in order to find the resonant frequencies of the cavity. In this study, the cavity was a screened room (Rainford EMC Systems, St Helens, UK), 2.94m (width) x 2.32m (height) x 4.60m (length)

(Figure 1). Advancing from our previous model (Robinson et al 2005), the earlier monopole antennas were replaced with a capacitor-loaded or 'top hat' design (Figure 2), which improved impedance-matching and hence gave a better signal-to-noise ratio. Measurements with a test phantom showed that this change did not significantly affect the resonant frequencies. Two pairs of antennas, located on the ceiling and side walls, enabled two separate resonances frequencies to be measured for the empty room: 60MHz in the vertical mode (Vm) and 72MHz in the horizontal mode (Hm). The dielectric constants of water, fat, cancellous and cortical bone at these frequencies are approximately, 74, 6.5, 17 and 30 respectively (Stogryn 1971, Gabriel 1996).

The temperature of the room is monitored and the daily variation is approx 18 to 25°C. This temperature variation results in a change in the vertical resonant frequency of 0.004061MHz (0.007%) and a change in the resonant horizontal frequency of 0.005522MHz (0.008%) for the empty room. To reduce any effect of temperature the empty room is measured immediately prior to the subject measurement.

Subjects are asked to remove all metal objects before the measurement. However, studies on phantoms have revealed that watches, earings, chains, rings, piercings and even joint replacements and cardiac pacemakers do not significantly affect the frequency shifts. Possible effects of tattoos have also been considered. The amount of ink is quite small – at most 1.2mg/cm^2 of skin (Prior 2014). As the surface area for a typical adult is 16,000 to 18,000cm^2 (ICRP 1974), total mass of tattoo ink would be no more than 20g, which is insignificant compared to the mass of the body.

With a subject present, there are negative frequency shifts of the order of 0.5MHz. It is generally recommended that for RCP measurements the sample volume should be less than 1% of the cavity (Robinson and Stone, 2003). The volume of our room was 31.4 m^3 and a normal adult patient's volume is less than 0.1m^3, which equates to 0.3% of the room. Given the smaller body volume of children, the percentage of the room volume would be even lower, making non-linear effects unlikely.

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2.2 RCP measurement protocol

The resonant frequencies of the empty room in both modes were determined immediately prior to each subject measurement. Subjects lay supine on a thin mattress on a polystyrene block in the centre of the room with palms of the hands placed on the thighs. The material of the block is chosen for its low permittivity and low loss, to minimise any effect on the field patterns.

Figure 1. Resonant cavity perturbation equipment: screened room, network analyser, switching unit and RF cables
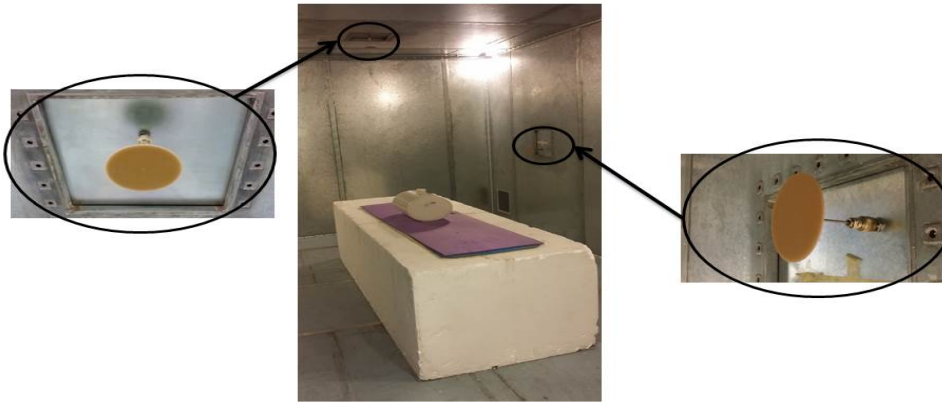
Figure 2. Interior of screened room showing dialysis-fluid test object on polystyrene bed, and details of 'top-hat' antennas.

A camera monitored all measurements. Five measurements were performed per subject, in each mode, taking approximately 8 minutes in total. An automated computer program evaluated the mean of the five measured values of the 'vertical' and 'horizontal' resonant frequencies for both the 'empty' and 'loaded' room. The differences between the mean values were the resultant vertical mode (Vm) and horizontal mode (Hm) resonant frequency shifts. The combined (Vm+Hm) resonant frequency shift was also derived, by summing the vertical and horizontal shifts. We have previously shown that the measured response of these parameters enables the determination of TBW in adults. (Robinson et al 2003, Stone et al 2004).

To monitor quality control of the RCP method a polythene elliptical trunk (length = 43cm, width = 34cm and height = 24 cm) filled with 16 litres of dialysis fluid was measured over the study period to monitor the frequency shift in the Vm, Hm and combined (Vm+Hm) modes. Dialysis fluid was preferred to distilled water as a better representation of body fluids.

2.3 Deuterium dilution measurement of TBW

Subjects consumed 100 ml of water containing 7% deuterium solution. Urine samples of 7ml were collected daily, from pre (evening before dosing) to 4 days post dosing (each evening), and were frozen until analysis for deuterium decay curve. The value for TBW_{dil} was divided by a factor of 1.04 to correct for exchange of deuterium with non-aqueous hydrogen in the body (Racette et al, 1994) .TBW_{dil} was divided by 0.9937, the density of water at body temperature, to convert from litres to kg. The mean (SD) for TBW_{dil} of the study group was 19.4 (4.5) kg. Analysis was performed by the Medical Research Council (MRC) Human Nutrition Unit, Cambridge, UK, where the laboratory precision for TBW is 1%.

2.4 Multi-frequency bio-impedance spectroscopy (MFBIS)

Bio-impedance monitoring can provide quick, inexpensive, non invasive measurements of body composition and fluid status at the bedside with good reproducibility. The Fresenius Body Composition Monitor (BCM) (Fresenius Medical Care, Bad Homburg, Germany) is a whole body MFBIS, operating at 50 frequencies between 5 kHz and 1 MHz. It extrapolates impedance values at zero and infinity using the Cole-Cole model. Additionally, it uses Hanai emulsion theory equations to estimate TBW (Moissl et al, 2006). Electrodes were attached to the left hand and foot of the body and measurements were taken by a trained nurse after participants had been supine for 5 minutes. Two measurements were also made on the right side of the body and the mean values were used to estimate TBW_{mfbis}.

2.5 Anthropometric equations

Anthropometry is a simple method of estimating TBW. Two sex specific anthropometric equations for predicting TBW(kg) from Wt(kg), Ht(cm), Age(yr) and sex, derived from UK children (Wells 2005), were applied.

Males :   ln TBW(kg) = -2.952+0.551lnWt(kg)+0.796lnHt(cm)+0.008Age(yr)

Females : ln TBW(kg) = -2.952+0.551lnWt(kg)+0.796lnHt(cm)+0.008Age(yr)-0.047

ln = natural log

3. Statistics

Statistical analyses were performed using SPSS Version 22. Descriptive statistics for all variable were calculated and expressed as the mean (SD). Normality of the variables was examined using Shapiro-Wilk test. Linear regression analysis investigated the relationship between TBW_{dil} as the dependent variable and the shift of frequency in the vertical, horizontal and combined modes as the independent variables when the room was loaded with a subject. Stepwise multiple regression analysis was used to determine potential effects of independent variables sex, age, height, weight and BMI and frequency shifts on TBW_{dil}. The standard error of the estimate (SEE) was calculated for each relationship to indicate the accuracy of the estimate. Multicollinearity diagnostics for multiple regression analysis were performed using the variance inflation factor (VIF) for the data. Homoscedasticity was estimated from residual plots of the data. For statistical significance, $p<0.05$.

The selected preliminary predictive equations determined in this study were validated using the PRESS (prediction of sum of squares) method. In this procedure each subject in the group is excluded one at a time and a regression analysis is performed on the remaining data. This regression equation is then applied to the excluded subject and a predicted value determined. The differences between the measured and predictive values are called the PRESS residuals. This method of validation is similar to applying the equation to a cross-validation group because the PRESS residuals are obtained from observations that are not included in the group when deriving the predictive equation. (Sun et al 2003, Chumlea et al 2005).

The in-vivo precision of the TBW_{RCP} method was derived from paired measurements. The root mean square error standard deviation (RMS-SD) was derived from the equation:

$$\text{RMS SD} = \sqrt{\left[\sum (x_i - y_i)^2 / 2n \right]} \qquad (3)$$

Where n = number of subjects and x_i and y_i are paired measurements for i = 1 to n

The %CV is derived from the equation:

$$\%CV = (RMS\ SD/mean\ value) \qquad (4)$$

To establish the association and level of agreement between the estimates of TBW and the criterion method, Bland Altman analyses were performed, and the mean differences (bias) in measurements were plotted against the mean value of the measurements to determine if a systematic bias exists. Significance was attained if the 95% confidence intervals (CI) of the mean difference did not include zero. Limits of Agreement (LOA, 95%), were used to indicate the range of random error, and were derived from the standard deviation (SD) of the mean difference as follows:

$$LOA = +/-1.96*SD \qquad (5)$$

The correlations of the differences and mean values were derived to determine if the observed differences were dependent on the magnitude of the measurement and to determine if the bias was proportional (Bland Altman1986).

4. Results

Normality was not indicated for the following variables weight, horizontal and combined frequency shift and TBW_{dil} ($p<0.05$). From the linear regression analysis between TBW_{dil} and the three resonant frequency shift modes similar r^2 values (0.87 to 0.91) and SEE (1.41 to 1.65 kg) were observed (Table 2). Only the Vm frequency shift had a regression with zero intercept. The selected predictive equation was;

$$TBW_{RCP(1)}(kg) = 1.37 + 26.96*(Vm + Hm)MHz \qquad (6)$$

The resultant PRESS statistic was 1.46 comparable to the SEE of 1.42. The relationship between TBW_{dil} and (Vm + Hm) frequency shift is shown in Figure 3.

Table 2. Linear Regression Equations for Total Body Water (TBW) from Resonant Frequency

Shifts

	Linear Regression Equation (95% CI)	r^2	SEE (kg)	Press
TBW(kg)	78.60(69.87 to 87.33)*(Vm)MHz	0.91	1.41	
TBW(kg)	2.69(0.41 to 4.97)+39.58(34.30 to 44.80)*(Hm)MHz	0.87	1.65	
TBW(kg)	1.37(0.7 to3.40)+26.96(23.9 to 29.99)*(Vm+Hm)MHz	0.90	1.42	1.46

Vm, Hm and (Vm+Hm) = vertical, horizontal and combined resonant frequency shifts, MHz = Mega Hertz

CI = Confidence interval ; SEE = standard error of estimate   r = correlation coefficient
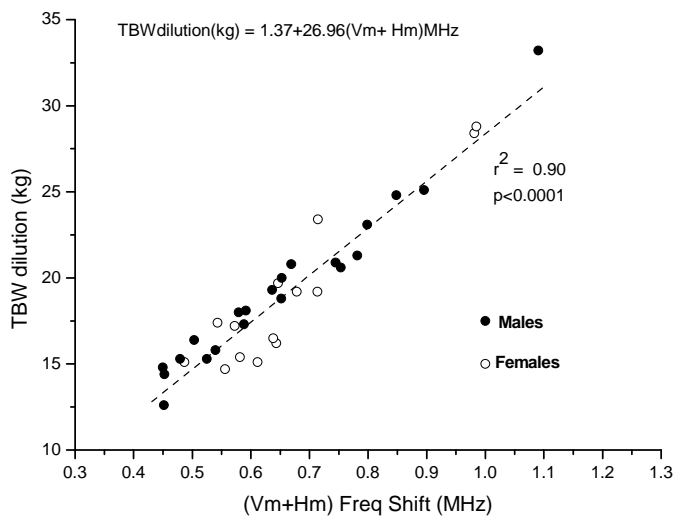
Press = Prediction of sum of squares

Figure 3. Linear regression of TBW by dilution against combined vertical and horizontal

frequency shifts

4.1 TBW_{RCP} : Body size predictive equations

Multiple stepwise regression analysis with TBW_{dil} as the dependent value and the resonant

frequency shifts, age, sex, height, weight and BMI as independent variables, was performed. Age

and sex were not predictive variables. The highest r^2 =0.93 and lowest SEE =1.25kg was observed for the (Vm+Hm) combined frequency shift mode and BMI and this was the selected predictive equation (Table 3). The addition of BMI to the predictive equation for Vm+Hm frequency shift only increased r^2 from 0.90 to 0.93 and reduced SEE from 1.42 to 1.25kg.

$$TBW_{RCP(2)} \text{ (kg)} = 7.55 + 32.47*(Vm+Hm)MHz - 0.58*BMI \text{ (kg/m}^2) \tag{7}$$

The relationship between TBW_{dil} and $TBW_{RCP (2)}$ is shown in Figure 4. All values lay on or close to the identity line indicated an excellent fit. The plot of residuals versus predicted values show the residuals randomly scattered around zero (Figure 5). The PRESS method validated the predictive equation and the PRESS statistic of 1.33 was comparable to the SEE of 1.25kg for the TBW_{RCP} predictive equation. No collinearity was observed with regression analyses in the study.

Table 3. Multiple regression predictive equations for Total Body water (TBW) from resonant frequency shifts and BMI

	Multiple Regression Equation (95% CI)	r^2	SEE (kg)	SEE (%)	PRESS
TBW (kg)	3.95(-0.38to8.30)+88.69(75.87to101.56)*Vm -0.38 (-0.74to -0.01)*BMI	0.92	1.34	6.9	
TBW (kg)	8.14(2.76to13.53)+46.63(38.54to54.72)*Hm-0.50(-0.94to-0.05)*BMI	0.89	1.56	8.0	
TBW (kg)	7.55(3.31to11.80)+32.47(28.13to36.80)*(Vm+Hm)-0.58(-0.94to-0.22)*BMI	0.93	1.25	6.5	1.33

Vm,Hm and (Vm+Hm) = vertical, horizontal and combined resonant frequency shifts (MHz): BMI=kg/m^2

MHz = Megahertz : CI= Confidence interval ; SEE = standard error of estimate   r = correlation coefficient

PRESS = Prediction of sum of squares

Correlations between TBWdil and the three methods of estimating TBW are given in Table 4. All methods had similar correlation coefficients for sex and their combination.

Table 4   Correlation coefficients r between TBWdilution and the three study methods of
estimating TBW : TBW$_{RCP(2)}$, TBW$_{MFBIS}$ and TBW$_{Anthropometry}$

	Males (r)	Females (r)	Combined (r)
TBW$_{RCP(2)}$	0.96	0.95	0.96
TBW$_{MFBIS}$	0.97	0.95	0.95
TBW$_{Anthropometry}$	0.96	0.94	0.96

RCP = resonant cavity perturbation   MFBIS = multi frequency bio-impedance spectroscopy

r = correlation coefficient

4.2 TBW$_{RCP}$ reproducibility

The RCP quality control and in-vitro precision for the three resonant frequency shifts modes over the study period using the 16 litres dialysis fluid trunk are shown in Table 5. The magnitude of the frequency shift mode was greater in the Hm compared to the Vm. The observed in-vitro precision (SD/mean) was 0.15 to 0.25 %CV, indicating excellent stability in the measurement method.

Table 5. RCR Quality Control of the Dialysis Trunk Resonant Frequency shift : in-vitro precision

	n	Vertical Resonant Frequency (MHz)	Horizontal Resonant Frequency (MHz)	Combined
Empty room	33	60.200115 (0.002952)	72.202314 (0.003138)	
"Loaded room" Dialysis Trunk	14	60.089095 (0.002019)	72.012416 (0.001758)	
Resonant Frequency shift		-0.111934 (0.000281)	-0.191312 (0.000324)	-0.303246 (0.000465)
Precision %CV		0.25%	0.16%	0.15%

Mean (sd)

MHz = Megahertz; CV = coefficient of variation

Table 6   Resonant Frequencies shift : In-vivo precision

Shift in Resonant Frequency (MHz)			
	Vertical	Horizontal	Combined
Measurement 1 (sd)	0.248573 (0.058501)	0.423089 (0.113731)	0.671662 (0.170522)
Measurement 2 (sd)	0.248311 (0.057531)	0.426794 (0.115146)	0.675105 (0.170685)
Mean (sd)	0.248442 (0.058005)	0.424941 (0.114438)	0.673383 (0.170603)
RMS - SD	0.001950	0.009639	0.009993
%CV	0.8	2.4	1.6

sd = standard deviation   RMS-SD = root mean square standard deviation

MHz = Megahertz; CV = coefficient of variation

The precision of the in-vivo resonant frequency shifts and TBW for RCP were derived from paired measurements with reposition. Precision calculated as %CV varied between 0.8 to 2.4 % for the resonant frequency shift modes (Table 6). For in-vivo precision TBW was predicted for each mode using the derived predictive equation for the particular frequency mode, the in-vivo precision ranged from 0.7 to 3.4% (Table 7). Vm for both in-vitro and in-vivo was the most precise measurement.

Table 7. Resonant Cavity Perturbation Total Body Water (TBW$_{RCP}$) in-vivo precision measurements

	TBW$_{RCP}$ Measurement Mode		
	Vertical	Horizontal	Combined
Measurement 1 (kg)	19.41(4.32)	19.23(4.11)	19.25(4.26)
Measurement 2 (kg)	19.36(4.25)	19.55(4.37)	19.45(4.40)
Mean (sd)	19.38(4.28)	19.39(4.24)	19.35(4.33)
RMS-SD (kg)	0.13	0.67	0.47
%CV	0.7	3.4	2.4

sd = standard deviation   RMS-SD = root mean square standard deviation

CV = coefficient of variation

4.3 Bland Altman Analysis

The Bland Altman analysis by sex of the three methods of estimating TBW are shown in Table 8. The highest mean difference observed was 0.75kg for TBW$_{MFBIS}$ in females but was not significant (p=0.09). The LOA observed between the methods indicated that the predictive errors for all three methods were comparable. There was only a small decrease in the mean difference and LOA when BMI was included in the RCP predictive equation. No systematic or proportional biases were observed between the magnitude of measurement and the differences.

Table 8. Bland Altman analysis of three methods of estimating TBW with the dilution method as the criterion method

TBW Method	Females (n=14)			Males (n=22)		
	Mean (sd)	Mean Difference (sd)	LOA	Mean (sd)	Mean Difference (sd)	LOA
Dilution (kg)	19.02(4.69)			19.48(4.59)		
MFBIS (kg)	19.77(4.03)	0.75(1.56)	-2.37 to 3.87	19.74(4.60)	0.26(1.19)	-2.12 to 2.64
Predictive Equations						
RCP(1) (kg)	19.37(3.95)	0.35(1.73)	-3.11 to 3.81	19.22(4.61)	-0.26(1.32)	-2.90 to 2.38
RCP(2) (kg)	19.19(4.11)	0.17(1.54)	-2.91 to 3.25	19.38(4.64)	-0.09(1.23)	-2.55 to 2.37
Anthropometry (kg)	19.10(4.04)	0.08(1.58)	-3.08 to 3.24	19.84(4.53)	0.36(1.11)	-1.86 to 2.58

sd = standard deviation   RCP = Resonant Cavity Perturbation

MFBIS = multifrequency bio-impedance spectroscopy   LOA = Limits of Agreement

Data from boys and girls were combined and re-analysed (Figures 6 to 8). The mean differences were not significant and no significant correlations were observed.
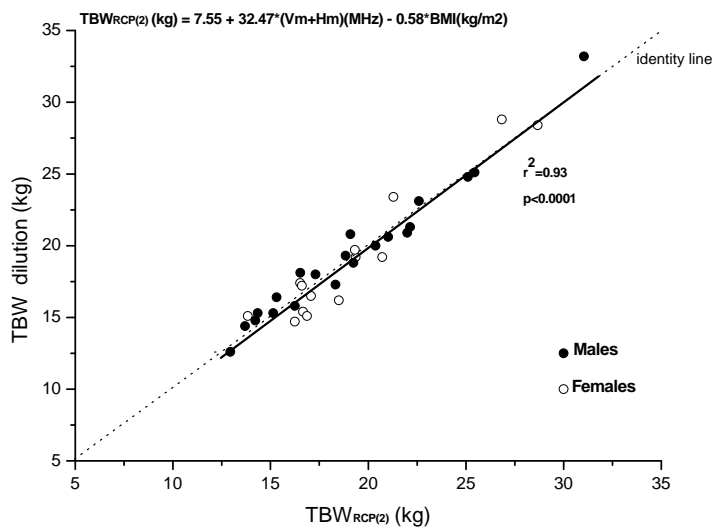

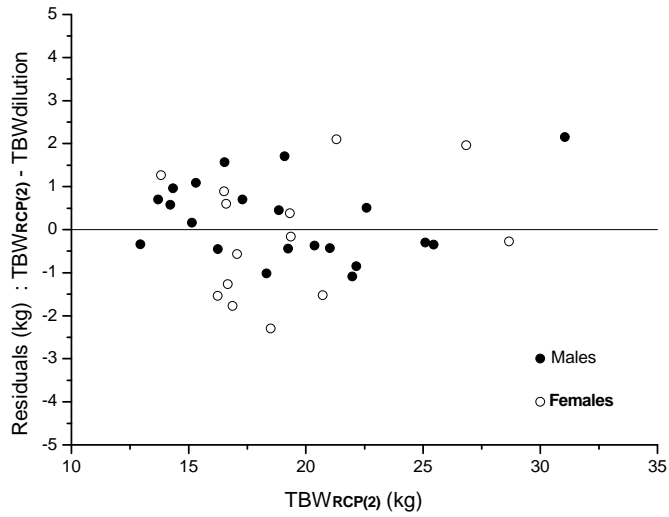Figure 4. Multiple regression of TBW by dilution against TBW predicted by RCP

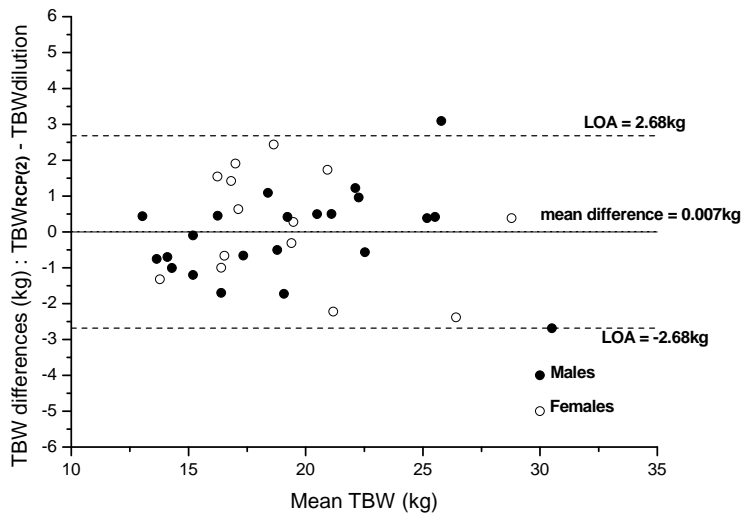Figure 5. Residuals plot for TBW by RCP

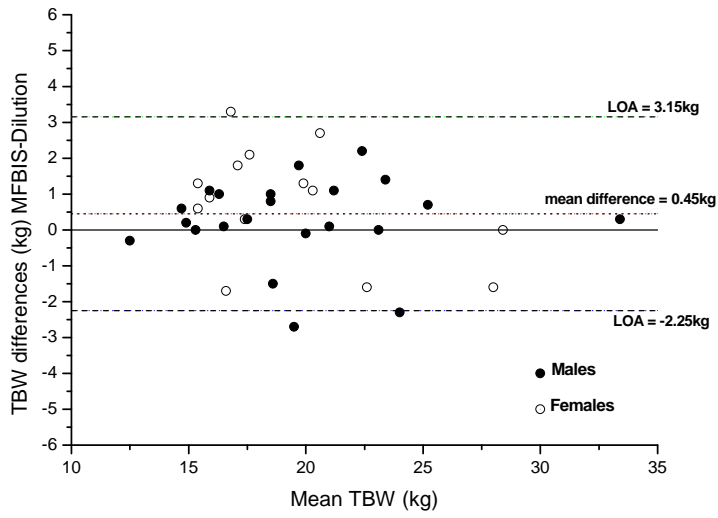Figure 6. Bland-Altman analysis of TBW by dilution and by RCP

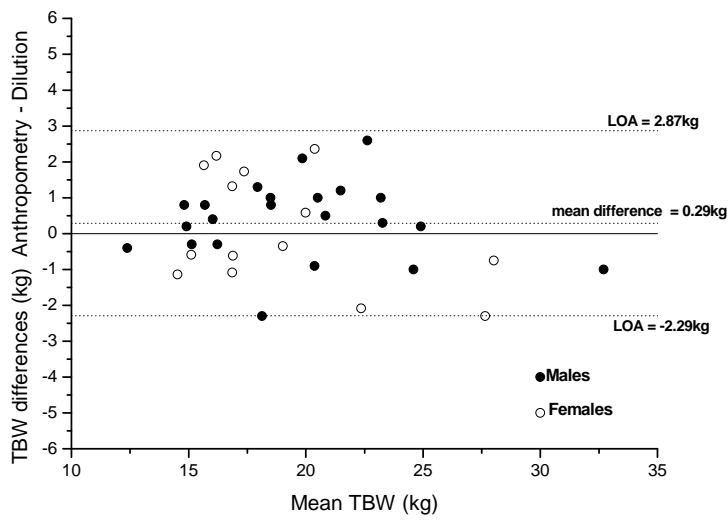Figure 7.   Bland-Altman analysis of TBW by dilution and by MFBIS

Figure 8   Bland–Altman analysis of TBW by dilution and by anthropometry

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5. Discussion

Resonant cavity perturbation (RCP) is a novel, electromagnetic method which can determine TBW from the dielectric properties of the body. This study is the first to develop and validate RCP equations that are predictive of TBW status in healthy children and compare them with the dilution reference method, MFBIS and anthropometry.

The ideal TBW predictive equation should be independent of sex, age and disease state. In this study sex and age were not significant variables in regression analysis, and two predictive equations for TBW were developed with (Vm +Hm) Freq shift as the main variable and BMI as an additional variable. The addition of BMI to the predictive equation only increased r^2 from 0.90 to 0.93 and reduced SEE from 1.42 to 1.25kg.

The Bland Altman analysis of the three methods of estimating TBW compared to the criterion method, indicated that all three methods had comparable prediction errors in the study group. The comparison of the two RCP predictive equations indicated that the inclusion of BMI resulted in only a small reduction in the prediction error.

Reproducibility of TBW measurements is fundamental for surveillance of response to interventions and of recovery or disease trajectories. We report high precision for paediatric TBW_{RCP} assessments performed in all modes, particularly in vertical mode. The in-vivo precision results reflect our in vitro study findings, and collectively offer confidence for the use of this method for monitoring change. It was also observed that in both in-vitro and in-vivo RCP measurements the Hm frequency shift was greater than Vm. This may reflect that for the subject position on the bed, the body width is greater than the body thickness. Similarly, with the elliptical dialysis trunk, the width is greater than the height.

A limitation of the study was the small number of children with a limited age range. We recommend further evaluation of the predictive equations in children with a wider age and BMI range to possibly develop a single predictive equation for TBW in children using this method. Also clinical populations of children, including dialysis patients and malnourished and obese

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patients need to be studied. However it is the ability to accurately measure change in TBW which is important and further research is required to determine whether the RCP method is superior to BIA/MFBIS in accurately measuring change in TBW.

Benefits of the RCP method are that it is fast, non-invasive and comfortable for the subject. Although the eqiupment is bulky, the screened room can be dismantled and reassembled at another location – the authors have done this and found that the resonant frequencies were not affected by this procedure. In future, it should be possible to design a cavity that folds up when not in use. A further advantage is that the applied electric field is approximately uniform over the body, so the resonant frequencies respond to water at any location.

The regression coefficients depend on the size and shape of the cavity. A smaller chamber would give a larger, more easily measurable perturbation for a particular subject, and would also be cheaper and take up less space. However if it were too small the variation of frequency shift with TBW would become non-linear, and also it would no longer be valid to assume uniform field at the centre of the chamber. A much smaller cavity would become more like a sensor, potentially allowing segmental or tomographic measurements of hydration. Some of the technical issues with this approach are discussed by Robinson et al. (2010)

Research is required on the effect of body size parameters body thickness, width and waist circumference on the RCP method. We are currently investigating relationships with body surface area and thickness of subcutaneous fat. Further research is required on the ability of the RCP method to predict fat free mass, and also the effect on the RCP method of variation of body composition needs to be determined. Deviation from average composition at the same water content (e.g. more bone, less fat) should not greatly affect the resonant cavity measurements, because bone and fat have similar dielectric constants, both of which are much lower than that of water (Gabriel et al. 1996).

Although a pacemaker does not affect the resonant cavity perturbation and it is unlikely that the low power radio waves would interfere with the operation of implanted devices, for

safety, subjects fitted with pacemakers and other electronic implants should be excluded from studies until the effect of radio waves on such electronic implants has been resolved.

We conclude that the equations based on the combined frequency mode with and without BMI give reliable predictions of TBW in healthy children using the RCP method. In this study the TBW_{RCP} predictive equations were not an improvement on TBW_{MFBIS} or the $TBW_{Anthropometry}$ equations. However the derived equations were independent of gender and body size had only a small effect.

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Conflict of Interest Statement

The authors declare no conflict of interest.

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