Neural network technology to predict intracellular water volume

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SUMMARY

Artificial neural network (ANN) is increasingly applied in clinical medicine. We therefore constructed an ANN to predict intracellular water (ICW) volume in 44 healthy Taiwaners. Demographic and anthropometric data were recorded as predictors, and ICW volume measured by bioelectrical impedance analysis (ICW-BIA) was the reference. ICW volume predicted by ANN (ICW-ANN) was compared with ICW-BIA. ICW-BIA (21.26 ± 0.58 l) and ICW-ANN (21.25 ± 0.57 l) was insignificantly different ($p = 0.76$). ICW-BIA and ICW-ANN were strongly correlated ($r = 0.94$, $p < 0.0001$) with a significant agreement (mean difference, 0.01; lower and upper limits of agreement, −2.31 and 2.33) in Bland–Altman plot. Passing–Bablok regression was described as ICW-BIA = 1.04 × ICW-ANN − 0.49, with 95% confidence interval for slope 0.94–1.14 and for intercept −2.76–1.49, indicating that both methods were interchangeable. ANN provided an excellent alternative of BIA to predict ICW volume in healthy subjects.

Keywords: Neural network; anthropometry; intracellular water; bioelectrical impedance

INTRODUCTION

Estimating intracellular water (ICW) volume has important implications in clinical care. It can influence the determination of body cell mass, nutritional condition, renal function, electrolytes balance and drug pharmacokinetics. Accurate measurement of ICW volume is thus necessary in either healthy subjects or patients with malnutrition, cardiac dysfunction, renal impairment or sepsis. Dilution of radioactive ^{42}potassium or whole-body counting of radionuclide ^{40}potassium can measure ICW volume in a direct manner (1). However, it is impractical in most hospitals due to requirement of complex equipment with a specialised team, radiation exposure and high cost. Although there are increasingly studies using multifrequency bioelectrical impedance analysis (MF-BIA) to measure body compositions as a substitute for complex techniques of nuclear medicine (2,3), MF-BIA is not widely available and the time of measurement is also concerned. By contrast, MF-BIA is not convenient in subjects with illness and the procedure will bother patients every time if physicians want to evaluate hydrational or nutritional status frequently to make decisions for following medical plans. Therefore, mathematical equations for predicting ICW volume are commonly used by physicians and nutritionists (4,5).

With the assistance of advances in computer-aided analysis, it is easy to use the software for prediction tasks. The representation of flexible model is artificial neural network (ANN) which is a computational simulation of biologic nervous system (6). Every processing element ('neuron') is interconnected through a set of weighted signals similar to biologic synaptic connections in a way to memorise, learn and predict the response with least bias (7). The purpose of the present study was to evaluate the feasibility of ANN in quantitatively predicting ICW volume for a population of healthy Taiwaners in comparison with the measurement by using MF-BIA as reference method to avoid healthy subjects exposing to additional radiation.

RESEARCH DESIGN AND METHODS

Subjects

The Ethics Committee on Human Studies of Tri-Service General Hospital (Taipei City, Taiwan) approved the study protocol. All subjects provided signed informed consent prior to enrolment in the study. Subjects were excluded if they had any systemic illness such as hypertension, diabetes, cardiac, hepatic or renal diseases. Subjects were also excluded if they were taking any medication or had a history of oedema formation or oedema on careful physical examinations. The final study population consisted of 44 healthy Taiwaners (17 male and 27 female).

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ANN was applied to the training set and cross-validated using leave-one-out resampling technique. Among the common cross-validation techniques, leave-one-out cross-validation generates the most accurate estimation of the predictive performance for ANN (8). In short, ANN was trained on 43 cases, and the trained model was then used to test the case that had been left out. This process was repeated until every case in the dataset had been used once as an unseen test case. The results were averaged across the 44 test cases to estimate the predictive performance. This technique is useful to enable all the available subjects to be used in training process and gives a significant validation of the generalising ability of the trained model.

Measurements

Demographic and anthropometric data recorded for all patients included age, gender, weight and height. All anthropometric measurements were performed by the same operator. All patients were clothed in underwear with bare feet for measurements, with weight measured to the nearest 0.1 kg using a digital scale and height measured to the nearest 0.1 cm using a linear height scale. Mean values from two measurements were employed as data.

MF-BIA is based on the basic principle that resistance of the body to an electrical current applied at low frequencies reflect extracellular water space, whereas at high frequencies the current is conducted in both extracellular and intracellular spaces, reflecting the total body water (TBW) space. The direction of the electricity can be changed when the frequency of the electrical signal is changed. Normally, MF-BIA is carried on at frequencies from 1 KHz to 1 MHz. At our institute, segmental resistances of arms, trunk and legs were measured by a MF bioelectrical impedance analyser (Inbody 3.0, Biospace Co. Ltd, Seoul, Korea) with all patients standing upright. The instrument uses eight-polar tactile electrodes: two in contact with the palm and thumb of each hand and two with the anterior and posterior aspects of the sole of each foot. The patient stands with soles in contact with foot electrodes and grasps hand electrodes (9). These electrodes are connected to the current and voltage supply of the device. Before the measurement procedure, the demographic (age and gender) and anthropometric (weight and height) data are input to the built-in software of the instrument. Impedance is then measured through on and off switches regulated by microprocessor of the instrument. By regulation of these switches in a proper order, the impedance from different body segments can be accordingly detected. The measured body segments are left and right arms, trunk and left and right legs. The MF measurement is conducted by using multiple frequencies at 5, 50, 250 and 500 kHz. This analyser calculates TBW as $\mathrm{TBW} = A_1 \times \mathrm{height}^2/R_{arm} + A_2 \times \mathrm{height}^2/R_{trunk} + A_3 \times \mathrm{height}^2/R_{leg} + C$, where R_{arm}, R_{trunk} and R_{leg} are resistances of the arm, trunk and leg, respectively; A_1, A_2 and A_3 are coefficients and C is a constant, based on the theory proposed by K. Cha et al. (10). ICW volume is also calculated through the same analyser by body resistances at high and low frequency as $\mathrm{ICW} = \mathrm{TBW} \times (R_5/R_{500})$, where R_5 and R_{500} are resistances at 5 and 500 kHz, respectively.

In all subjects, the study was performed in the fasting state and after urination. The procedure was performed in 3 min or less. To analyse the repeatability of the study, we performed MF-BIA five times at intervals of 3 min in nine subjects. The mean of the standard deviation and the coefficient of variation of each set of readings were 0.10 and 0.29%.

ANN Construction

The configuration of ANN, including number of hidden layers, number of nodes in each hidden layer or activation function, is constructed by the designer at the beginning. No any protocol is standardised to decide these parameters, and the best practice seems to be based on trial and error (11). Some commercial programs provide automatic optimisation of networks to find better architectures (12,13). In our study, the software NEUROSOLUTIONS 4.32 (NeuroDimension Inc., Gainesville, FL, USA) was used to build our topological network. According to our experience, we selected the most popular and generally acknowledged multilayer perceptron architecture. We adopted the default values of network parameters provided by the NEUROSOLUTIONS. Multilayer perceptron is a layered feed forward network typically trained with back propagation. It is easy to approximate any input-output ontology. We used demographic variables (age and gender) and anthropometric variables (weight and height) to feed ANN as input variables. This model had one hidden layer with five processing elements based on the TanhAxon transfer function with hyperbolic tangent (Figure 1). We set up the momentum at 0.7 and step size at 1.0 as the learning rule. In output layer, the transfer function was also TanhAxon with hyperbolic tangent; the momentum and step size of learning rule were 0.7 and 0.1, respectively.

We used the standard approach to randomly divide the dataset into three parts: a training set, a selection set and a test set. The training set is used to fit the model; the selection set is used to estimate prediction error for model selection; the test set is used for assessment of the generation error of the final chosen model. Besides using leave-one-out cross-validation technique, to determine the training set and validation set in our study, we randomly selected 15% of training set as selection set which was a method for stopping network training. This step monitors the error on an independent set of data and stops training when this error begins to increase. In simulation control, the stop criteria for the

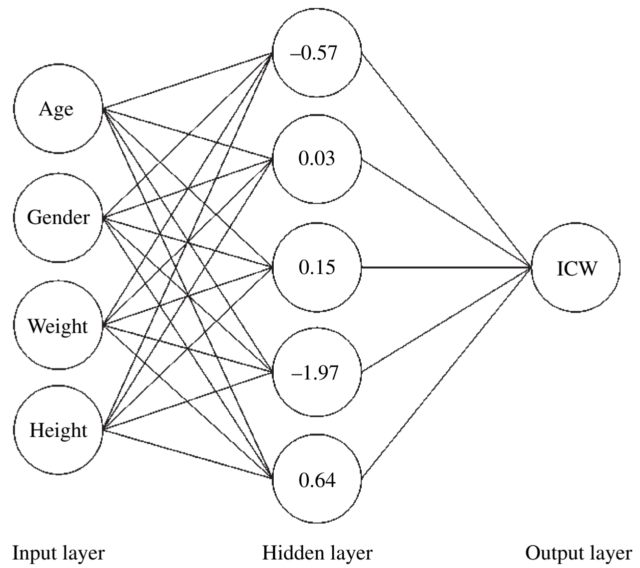

Figure 1 Graphical representation of our multilayer perceptron artificial neural network model. The number in each processing element of hidden layer stands for the mean value of corresponding weights

supervised training of the network were specified. The maximum epochs over the training set was set to 1000 iterations. The mean squared error was used to terminate the training process and supervised learning. The mean squared error termination is to base the stop criteria on the selection set instead of the training set. This will tend to be a good indicator of the level of best generalisation that the network has achieved (14). We also used the 'increase' function when using the selection set for mean squared error termination. This stops the network when the mean squared error of the selection set begins to increase. This is an indication that the network has begun to overtrading. The weights of the best network (the one with the lowest mean squared error) are automatically saved by default. The mean values of processing elements in the hidden layer were also calculated and presented in Figure 1. By loading best on test, these weights will automatically be loaded into the network before the test set is fed through the network. Therefore, we used fine adjustments to achieve the optimised architecture to monitor ANN training and overcome the problems of overtraining and overfitting. In 44 training processes, all iterations stop before maximal 1000 epochs, and the numbers of iterations were from 700 to 800 actually.

Anthropometric Equation Construction

For comparison with ANN, we used the software MEDCALC 8.0 (MedCalc Software, Mariakerke, Belgium) to develop our anthropometric equation in calculating ICW volume-Taiwan (ICW-TWN). The input variables were the same as in ANN, and multiple stepwise linear regression (variable entered if $p < 0.05$ and variable removed if $p > 0.1$) was carried out. Due to the limitation in linear regression analysis, we transferred the categorical variable 'gender' into numerical type (i.e. male and female as 1 and 0, respectively). The leave-one-out resampling technique was also applied for each set, using the mean value of each parameter as the final choice. Besides, another anthropometric equation developed by R.N. Pierson et al. (4) was also used to calculate ICW volume-Pierson as follows: $\text{ICW-PSN} = (0.470 - 0.0014 \times \text{age}) \times \text{weight}$ in male and $\text{ICW} = (0.451 - 0.0021 \times \text{age}) \times \text{weight}$ in female.

Statistical Analysis

Data were analysed using the MEDCALC 8.0 AND expressed as mean ± standard error. Correlations between each input variable and ICW volume derived from MF-BIA were analysed by Spearman's rank correlation coefficient (R_s) with 95% confidence interval (CI). ICW volumes derived from Pierson formula (ICW-PSN), our anthropometric equation (ICW-TWN) and ANN (ICW-ANN) were compared with BIA-measured ICW volume (ICW-BIA) by using Wilcoxon test. The statistical association between ICW-BIA and each predictive ICW volume was also expressed in terms of R_s with 95% CI. High correlation means that the measurements by the two methods are linearly related. However, this high correlation does not mean that the two methods agree. Bland–Altman plot, which calculates differences between of the measurements of the two methods against averages, is a useful graphical analysis to reveal a relationship between the differences and the average, to look for any systematic bias (15). The graph displays a scatter diagram of the differences plotted against the averages of the two measurements. Horizontal lines are drawn at the mean difference, and at the mean difference plus and minus 1.96 times, the standard deviation of the differences. Although Bland–Altman plot can be used as an indication of bias for a new model to compare with a reference method, a poor goodness-of-fit can occur in a lesser bias model. To alleviate this problem, we use root mean square error (RMSE) as a measure of goodness-of-fit for models comparison. The model with smaller RMSE value will have better fit if there is more than one model to fit the data. The equation used for RMSE is as follows, $\sqrt{\sum_{1}^{n}(\text{ICW}_{\text{model}} - \text{ICW}_{\text{BIA}})^2/n}$, where n is the sample size. To evaluate the interchangeability of two methods, it was found the Passing–Bablok regression describes a linear regression procedure with no special assumptions regarding the distribution of the samples and the measurement errors (16). The result does not depend on the assignment of the methods to variables X and Y. The slope B and intercept A are calculated with their 95% CI. These CIs are

Table 1 The characteristics of 44 healthy subjects

Characteristics	*Value or ratio*	*R_s (95% confidence interval)*	*P value**
Age (years)	48.16 ± 1.95	−0.25 (−0.51–0.05)	0.10
Gender (male/female)	17/27	0.83 (0.70–0.90)	<0.0001
Height (cm)	161.18 ± 1.16	0.83 (0.70–0.90)	<0.0001
Weight (kg)	63.15 ± 1.41	0.84 (0.73–0.91)	<0.0001

*The *P* value denotes that each variable correlated with intracellular water-bioelectrical impedance analysis using Spearman's correlation coefficient (R_s) with 95% confidence interval.

used to determine whether there is only a chance difference between B and 1 and between A and 0.

RESULTS

The characteristics of study subjects are presented in Table 1. Their age ranged from 22 to 78 years old and male to female ratio was 0.63. Among these input variables, gender, height and weight were strongly correlated with ICW-BIA statistically ($p < 0.0001$). Although age was not statistically correlated, the R_s value showed the negative correlation which was different with other variables. Our anthropometry-based equation after stepwise processes was ICW-TWN = 3.13 × gender + 0.09 × height + 0.19 × weight − 0.04 × age − 5.05, where gender = 1 if male and 0 if female ($r = 0.92$, $p < 0.001$). The p values of gender, height, weight and age in formula ICW-TWN were <0.0001, 0.03, <0.0001 and 0.0081, respectively.

Figure 1 is the diagram of our ANN model which shows the number of processing elements in each of the three layers, and it illustrates the fact that the network was fully connected in that each processing element in a given layer was connected to every processing element in the adjacent layer. The number in each processing element of hidden layer represents the mean value of corresponding weights. The magnitudes of the weights were determined during the training period on the training set, and they were not changed during the time that the network was applied to the selection set and test set.

Table 2 presents results of measured ICW volume by MF-BIA (21.26 ± 0.58l) and predictive ICW volumes by anthropometric equations and ANN. ICW volume derived from Pierson formula (ICW-PSN) was significantly higher than ICW volume measured by MF-BIA (ICW-BIA). No statistical difference was found between ICW-BIA and ICW-TWN or ICW-ANN. All estimates of ICW volumes (ICW-PSN, ICW-TWN and ICW-ANN) significantly correlated with ICW-BIA ($R_s = 0.94$, 95% CI 0.89–0.97, $p < 0.001$). Nevertheless, Bland–Altman plot shows a proportional bias between ICW-BIA and ICW-PSN (Figure 2A); its mean difference was −2.24, with a largest absolute interval of agreement 7.27 (−5.87 to 1.40) which represented more bias than ICW-TWN or ICW-ANN compared with ICW-BIA. In contrast, the mean difference either between ICW-BIA and ICW-TWN or ICW-ANN is −0.01 and 0.01, respectively, according to the representation of Bland–Altman plot which shows that their differences are randomly scattered around a mean of approximately zero (Figure 2B,C); no significant bias was found in the predictions of our anthropometric equation or ANN compared with MF-BIA. In addition, the absolute interval of agreement between ICW-BIA and ICW-ANN was 4.64 (−2.31 to 2.33) which was smaller than the value 4.69 (−2.35 to 2.34) between ICW-BIA and ICW-TWN despite they were comparable. The RMSE value between ICW-BIA and ICW-ANN was also smallest than the value either between ICW-BIA and ICW-PSN or ICW-TWN. This represented that ANN had better fit to MF-BIA than other two calculation-based equations (Table 3).

Table 2 Results of ICW volumes by MF-BIA, anthropometric equations and ANN

	ICW (l)	*P value**
ICW-BIA	21.26 ± 0.58	–
ICW-PSN	23.50 ± 0.75	<0.0001
ICW-TWN	21.27 ± 0.56	0.81
ICW-ANN	21.25 ± 0.57	0.76

ANN, artificial neural network; BIA, bioelectrical impedance analysis; ICW, intracellular water; MF, multifrequency; PSN, Pierson; TWN, Taiwan. *The p value denotes that each predictive ICW volume was compared with ICW-BIA using Wilcoxon test.

Using Passing–Bablok regression analysis for method comparison, the functions were as follows: ICW-BIA =0.77 × ICW-PSN − 3.29 (Figure 3A), ICW-BIA = 1.05 × ICW-TWN − 1.15 (Figure 3B) and ICW-BIA =1.04 ×ICW-ANN − 0.49 (Figure 3C). All their 95% CIs of three methods proved the corresponding slopes and intercepts to be not statistically different from one and zero without statistically significant deviation ($p > 0.10$), indicating that these three methods are interchangeable with MF-BIA. However, only Passing–Bablok regression between ICW-BIA and ICW-ANN with simultaneously narrowest 95% CIs for slope 0.94–1.14 includes one and for intercept −2.76 to 1.49 includes zero could truly reflect the best interchangeability for ICW-ANN and ICW-BIA (Table 3).

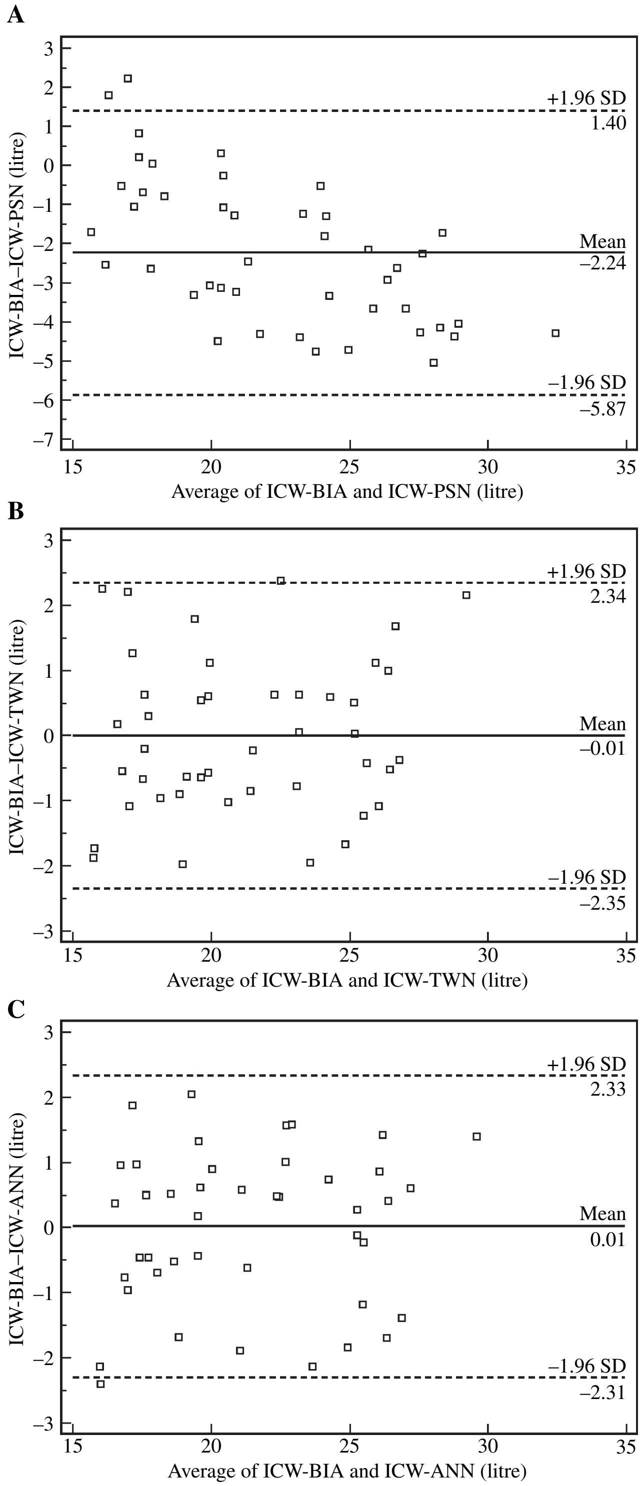

Figure 2 Comparison of intracellular water-bioelectrical impedance analysis (ICW-BIA) and each predictive model according to the graphical representation of Bland–Altman plot with indication of the mean difference between the values and of the limits of agreement. (A) ICW-PSN, (B) ICW-TWN and (C) ICW-ANN

DISCUSSION

MF-BIA has been used to measure ICW volume with ease by many clinical researchers because of its portable, inexpensive, non-invasive technique without radiation exposure. Although MF-BIA can not measure ICW volume directly as do radiotracer techniques, several investigations support its reliability (17–19). Herein, we designed such an investigation to explore other possible model for predicting ICW volume in healthy subjects without using radiotracers or MF-BIA.

From the perspective view of practice, several anthropometric equations are available for estimating TBW volume including TBW volume as 58% of body weight, the Watson formula (20) and the Hume formula (21). It is reasonable to use demographic data (gender and age) and anthropometric measurements (weight and height) as predictors to construct a model in predicting ICW volume. For any forecasting model to be applicable in making clinical decisions, a most valuable meaning is that only data that are readily and easily available to the physicians at the time of triage are used (12). Because many variables in body compartment study have an optimal estimate (e.g. body mass index), they correlate with output in a nonlinear pattern (22). Because a nonlinear phenomenon seems to be essential in medicine, ANN has an advantage to recognise complex underlying relationships of biological processes between independent and dependent variables in a nonlinear pattern by learning algorithms and containing more or less processing elements in hidden layers. Furthermore, ANN approach can make use of combinations of categorical and continuous variables. No assumption of variable distribution is necessary, and correlative interactions among inputs are pruned during the network's training process. The performance of ANN will continuously improve over time because ANN can be constantly retrained as more cases accumulate. Such advantages make ANN a more robust application in the real world setting. Before initiating one predictive model into the clinical application for ill subjects, the model in predicting ICW volume for healthy subjects should be studied as the baseline first. Therefore, we tried to develop an ANN to predict ICW volume and increase the efficiency of health-care resource usage.

Unlike more equations for TBW volume prediction (20,21,23), there are limited anthropometry-based equations for ICW volume prediction. We used Pierson formula for comparison with our ANN. Pierson formula was derived from 58 normal North American (30 males and 28 females) whose gender proportion was not statistically different with ours ($p = 0.27$). Their age range was 19–80 years old that was also similar with our subjects (aged from 22 to 78 years old). In our study, the predictive ICW volume derived from Pierson formula was significantly higher than the actual measurement of ICW volume by MF-BIA through the direct comparison using nonparametric paired Wilcoxon test, but the difference was not statistically significant from our anthropometric equation and ANN forecasting. In addition to body compositions related to racial difference, other justifications might contribute to this discrepancy. The predictors used in

Table 3 Spearman's rank correlation coefficient with 95% CI, RMSE and Passing–Bablok regression for anthropometric equations and ANN compared with MF-BIA

	ICW-PSN	*ICW-TWN*	*ICW-ANN*
Spearman's rank correlation coefficient	0.94	0.94	0.94
95% CI	0.89–0.97	0.89–0.97	0.89–0.97
RMSE	2.89	1.19	1.16
Passing–Bablok regression			
Slope	0.77	1.05	1.04
95% CI	0.68–0.86	0.95–1.17	0.94–1.14
Intercept	−3.29	−1.15	−0.49
95% CI	0.76–5.63	−3.91–0.98	−2.76–1.49

ANN, artificial neural network; CI, confidence interval; ICW, intracellular water; MF, multifrequency; RMSE, root mean square error; PSN, Pierson; TWN, Taiwan.

Pierson formula were limited to weight and age. In contrast, ANN may identify input variables that are most valuable with regard to accuracy of prediction. Our ANN model did not prune any input variable (age, gender, weight and height) and adopted all these four fundamental anthropometric predictors into constructing architecture which lead to more accurate prediction of ICW volume. Even though age was statistically insignificant in our univariate correlation analysis, multiple stepwise linear regression analysis still selected these four predictors to build our anthropometric equation. These findings suggest that applying variables in clinical medicine should not be easily neglected and explained as linear relationship, especially for biological phenomenon. Although input variables selected in ANN should not be depicted as independent predictors as discerned by clinicians, they could be interpreted as a framework of multiple local models or as part of global function of ANN, in which different mathematical functions are developed and applied in different clusters within the problem space, expressing the multidimensional nature of interconnections among clinical factors (24).

In our study, all predictive methods strongly correlated with ICW volume measured by MF-BIA using Spearman's rank correlation coefficient, Bland–Altman plots predominately revealed the distributed pattern of proportional error and wider absolute interval of agreement for Pierson formula calculation which means that Pierson formula may be not the appropriate method to predict ICW volume in healthy subjects. By contrast, Bland–Altman graphical approach to compare two methods of measurements of a given biological value, ICW-TWN vs. ICW-BIA or ICW-ANN vs. ICW-BIA, does not tell if the interchangeability found between these two methods is good or not; this qualification depends on the error magnitude that is, arbitrarily, considered clinically acceptable. When looking at Figure 3A–C, it can be seen that for many of the 44 data points, the two methods (ICW-

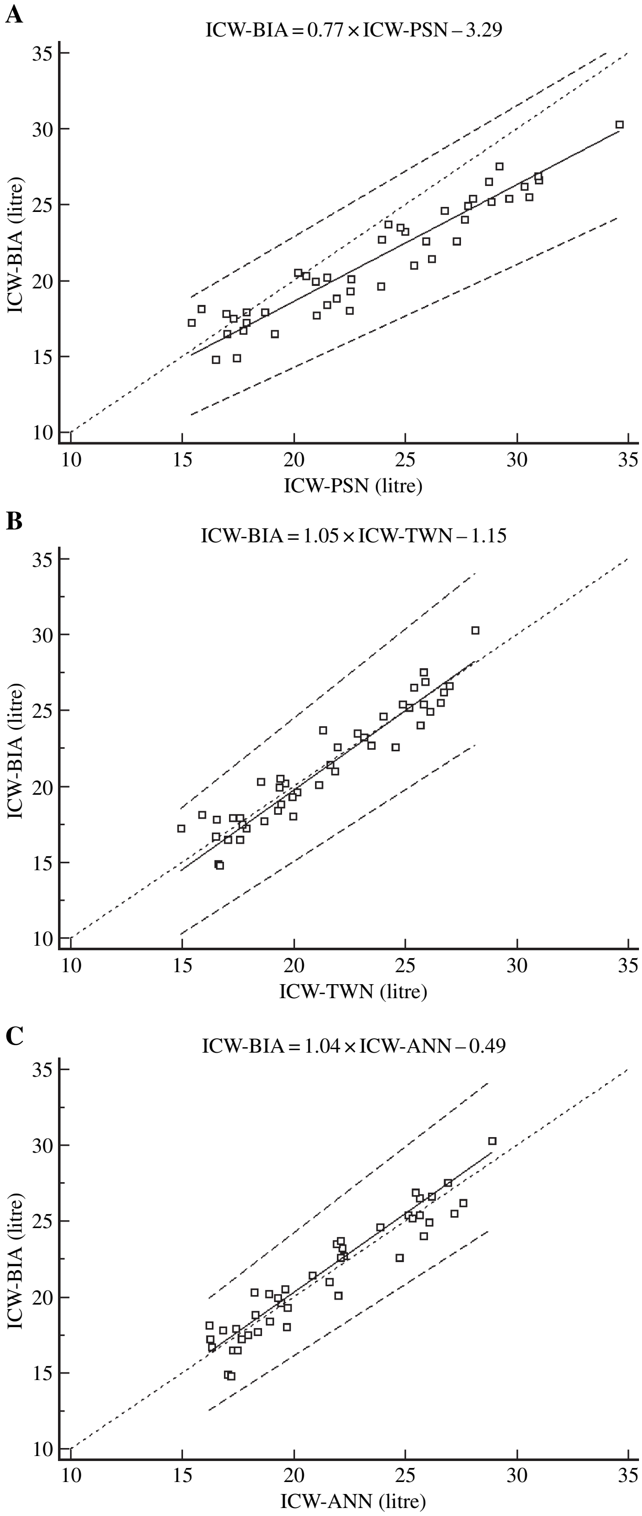

Figure 3 Passing–Bablok regression shows a scatter diagram with regression line (solid line), the 95% confidence interval for the regression line (dashed lines), and identity line (X = Y, dotted line). (A) ICW-PSN vs. ICW-BIA, (B) ICW-TWN vs. ICW-BIA and (C) ICW-ANN vs. ICW-BIA

BIA vs. ICW-ANN) yielded values most close to identity than other two comparisons (ICW-BIA vs. ICW-PSN and ICW-BIA vs. ICW-TWN). Moreover, our ANN had the lowest

RMSE value, an index of goodness-of-fit for a model, than other two calculation-based equations. Despite both our anthropometric equation and ANN did a similarly excellent task to predict ICW volume, our ANN proved to have better performance in predicting ICW volume based on MF-BIA.

Although the number of study population were relatively limited in our study, we utilised the leave-one-out cross-validation technique, a kind of resampling method, to overwhelm this difficulty and it performed the superior results. Nevertheless, we must make plans for more subjects to participate in our following study. There are also some potential limitations in our study. Actually, no clearly direct cause-and-effect relation has been shown between input and output variables and this 'black box' phenomenon remains an obstacle to the acceptance in clinical use. The restriction of ANN approach is that statistical importance to each input variable could not be easily computed and offered as they are in linear regression analysis. Although weights and values of processing elements are produced in ANN process, their interpretation is difficult and can not be though as standardised coefficient of each predictor. This deficiency of interpretability at the level of individual predictors is the most unfavourable characteristics in ANN analysis. Conversely, supporters of ANN claim that discovering a good enough solution is worthy of acceptance and better than conventional calculation-based approaches. The existing exchange between being able to model nonlinear functions favours ANN for applications where its principal purpose is to acquire a dependable forecasting rather than to earn an understandability of the contribution of individual predictors (25). ANN is an alternative approach to algebraic equations for problem solving in medical research and routine clinical practice. Nevertheless, in those cases where the purpose of the analysis is examination of possible causal relationships or explanation of interactions among predictors rather than prediction, traditional multivariate methods are probably favoured; hence, we also offered one algebraic equation to examine the causality.

Meanwhile, some designs incorporating structures of both conventional linear regression and ANN might lead to the optimum of predictive models (6). Conventional linear regression as a tool of feature selection helps the researchers recognise those input variables that may be significant predictors and helps to taper the numbers of dimensional variables included in ANN approach. Conventional linear regression also permits the researchers to put confidence around model outputs and parameters estimates after the underlying structure of relationships among predictors is recognised (anatomic analysis). Clinical predictive performance may be intensified through the benefit of ANN process that is able to inspect nonlinear interactions among predictors (functional analysis). As a new development of medical technology combing the utilisation of positive emission tomography and X-ray computed tomography, this epochal evolution of functional (ANN approach) and anatomic (traditional multivariate statistics) integrations will eventually take best advantage to the medical progression if applying these information technologies properly.

Algebraic equations indeed could be produced by anyone with papers and pens whereas ANN needs a computer with appropriate software; we herein provide an anthropometry-based equation which has similar performance closely to ANN whilst there are no computers and/or ANN software available. If ANN can improve the effectiveness in patient care, many physicians will accept such a tool as an assistant in clinical use. Sometimes, ANN is thought to be too difficult to manage by physicians, but the bioengineering of ANN into tools of medical practice is not difficult as many medical devices already have such systems embedded in them such as electrocardiography (26). At the present time, with the help of graphical user interface by friendly software, ANN is actually comfortable to use without loosing its flexibility and accuracy. Also given the rapid advances in ANN software and in computer hardware, it is likely that sophisticated ANN programs, such as the one used in our study, could be made available to clinical facilities and could save time and resources by supporting the physicians towards a quick and accurate prediction. Future studies may concentrate on developing the web-based platform using our ANN as kernel engine to help the physicians to evaluate ICW volume in real time.

In conclusion, ANN can be used as a feasible alternative to predict ICW volume in healthy subjects on the basis of MF-BIA. With the assistance of friendly software in evolutional era of information technology, it is easy to use artificial intelligent model without any difficulty. We deeply believe that our study using ANN in predicting ICW volume will be a foundation for further investigation in illness status. Therefore, further research need to be programmed for various diseases status in the future.

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