Regression models for near-infrared measurement of subcutaneous adipose tissue thickness

Yu Wang[1, 2], Dongmei Hao[*1], Jingbin Shi[1], Zeqiang Yang[1], Liu Jin[1], Song Zhang[1], Yimin Yang[1], Guangyu Bin[1], Yanjun Zeng[1], Dingchang Zheng[*3]

1: College of Life Science and Bioengineering, Beijing University of Technology, Beijing 100124, China;

2: China-Japan Friendship Hospital, Beijing 100029, China;

3: Health and Wellbeing Academy, Faculty of Medical Science, Anglia Ruskin University, Chelmsford, CM1 1SQ, UK

Abstract: Obesity is often associated with the risks of diabetes and cardiovascular disease, and there is a need to measure the subcutaneous adipose tissue (SAT) thickness for acquiring the distribution of body fat. The present study aimed to develop and evaluate different model-based methods for SAT thickness measurement using a SATmeter developed in our lab. Near infrared signals backscattered from body surface were recorded from 40 subjects at 20 body sites each. Linear regression (LR) and support vector regression (SVR) models were established to predict SAT thickness on different body sites. The measurement accuracy was evaluated by ultrasound, and compared with mechanical skinfold caliper (MSC) and body composition balance monitor (BCBM). The results showed that both LR and SVR based measurement produced better accuracy than MSC and BCBM. It has also been concluded that using the regression models specifically designed for certain local parts of human body, higher measurement accuracy could be achieved than using the general model for the whole body. Our results demonstrated that SATmeter is a feasible method, which can be applied at home and community for its portability and convenience.

Keywords: Subcutaneous adipose tissue (SAT), Near-Infrared (NIR), Linear regression (LR), Support vector regression (SVR)

1. Introduction

With the development of the social economy and the improvement of the people's living standard, the proportion of overweight or obese people continues to rise. Obesity is often accompanied by a variety of chronic diseases such as metabolic syndrome and cardiovascular diseases, which seriously affects people’s health and quality of life [1, 2]. Not only the amount of total adipose tissue, but also its distribution is of special importance in the healthcare [3-5].

Subcutaneous adipose tissue (SAT) is accepted as a body fat indicator because about 40–60 % of total body fat is in the subcutaneous regions [6]. Many techniques have been used to measure the lean body mass and subcutaneous fat distribution to evaluate the nutritional status and the sectoral distribution of adipose tissue, including the magnetic resonance imaging (MRI) [7], computed tomography (CT) [8], dual energy X-ray absorptionmetry (DEXA) [9] and ultrasound imaging [10, 11]. But these methods either have radiation hazard or are high cost, which are only available in hospitals. Therefore, there is a need to develop a simple and low-cost technique for the measurement of SAT thickness for home use by the general public.

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[*] Corresponding authors: Dongmei Hao and Dingchang Zheng
E-mail：haodongmei@bjut.edu.cn & dingchang.zheng@anglia.ac.uk
[*] Corresponding authors: Dongmei Hao and Dingchang Zheng
E-mail：haodongmei@bjut.edu.cn & dingchang.zheng@anglia.ac.uk

It is widely accepted that mechanical skinfold caliper (MSC) is an inexpensive and noninvasive way to assess SAT layer thickness. However, it is not easy to palpate the fat/muscle interface in some parts of body, and it even causes pain [12]. SAT thickness can also be measured based on bioelectrical impedance analysis (BIA) [13]. However, impedance does not measure fat, it estimates fat-free mass from which fat mass is computed, and the body's hydration and electrolyte level might influence the prediction of impedance-derived indices of fat [14]. Measuring SAT thickness by near-infrared (NIR) light is another noninvasive and convenient approach. Previous work investigated the reflected intensity as a function of fat thickness, from which the fat thickness measurement could be derived with curve fitting procedure [15, 16]. Several studies using the optical device named Lipometer (from Medical University Graz, Austria) indicated that there were close relationships between thickness of SAT-layers and body fat measured by DXA [17] and BIA [18]. Our research group previously reported a SATmeter to determine SAT thickness at any given part of the human body and investigated the effect of contact pressure and skin colour on the measurement. Principal component analysis (PCA) and support vector regression (SVR) were combined for predicting the SAT thickness [19].

Although the NIR based technique is a prospective method, its measurement accuracy still needs to be improved. Therefore, an appropriate regression model for SAT thickness has to be investigated with its input variables carefully selected. Linear and nonlinear functions are often used in the regression analysis. Some studies included anthropometric parameters such as weight, height and abdomen circumference as independent variables in multiple linear regression analysis [20-22]. Artificial neural network (ANN) trained by error back propagation has also been implemented, which provided high correlation coefficients and measurement agreement with CT [23, 24]. However, the architecture of ANN is usually decided by experience and multiple trials, and the training algorithm is prone to local minima in the process. Therefore, the selection of model and its inputs plays a key role in the measurement technique development.

The aim of this study was to develop and evaluate different regression model-based methods for SAT thickness measurement using a SATmeter previously developed in our lab. The linear regression (LR) and support vector regression (SVR) models will be used with their inputs investigated. The measurement accuracy will also be evaluated by ultrasound technique, and compared with two conventional techniques, including the MSC and body composition balance monitor (BCBM).

2. Material and Method

2.1 Subjects

Forty subjects (20 men and 20 women, aged 23.7 ± 1.1 years) were recruited in this experiment. Among them, 26 had normal BMI (body mass index is defined as the body mass divided by the square of the body height in kg/m^2) of 18.5 to 24, 7 were over weighted with BMI above 24, and 7 were obese with BMI above 28. None of them had suffered from a photoallergy. The subjects were measured lying in bed with supine or prone position depending on the measurement sites. The study protocol was designed under the Code of Ethics of the World Medical Association (Declaration of Helsinki) and approved by the Research Ethics Committee of College of Life Science and Bioengineering, Beijing University of Technology.

2.2 SATmeter design

Body surface consists of epidermis, subcutaneous fat and muscle. It has been widely accepted that the epidermis features good near-infrared penetration, while subcutaneous fat is characterized by low absorption and high backward scattering. Muscle, under the fat, demonstrates high absorption and high forward scattering properties [25]. Thus, SAT thickness can be measured from calibrated NIR backscattered light.

We have previously developed a SATmeter to measure the SAT thickness, as shown in Fig.1. It was composed of a sensor head, detection circuit, single chip microcontroller (SCM), liquid crystal display and power circuit. The sensor head consisted of a set of light emitting diodes (LEDs) and one photodetector. The wavelength of the LED was 845.1nm with the half-wave width of 38.6nm. The LEDs driven by the pulse signals controlled by the SCM, generated four light patterns in succession by illuminating the measured SAT layer with different LEDs.

Pattern1: one LED (15 mm from the photodetector) was on, while the others were off;

Pattern2: one LED (20 mm from the photodetector) was on, while the others were off;

Pattern3: two LEDs (25 mm from the photodetector) were on, while the others were off;

Pattern4: three LEDs (30 mm from the photodetector) were on, while the others were off.

The corresponding backscattered light was detected by the photodetector. The photoelectric signal was then amplified, filtered and digitized under the control of SCM. SCM was also programmed to remove the ambient light interference, acquire, integrate and average the sampled signals, and then calculate the SAT thickness with the regression models proposed in this study.

Fig.1 SATmeter prototype device developed in our lab.

2.3 Measurement procedure

SAT thickness was measured at 20 body sites, including calf (front and back), thigh (front and back), 4 cm above iliac crest, waist, subscapular protrusion, biceps, triceps and 5 cm to navel on the left and right sides of the body, by SATmeter, MSC (China Institute of Sport Science), Body Composition Balance Monitor (BCBM, EW-FA70, Panasonic Electric Works, Beijing Co., Ltd., China) and SSI-3000 color ultrasound Doppler system (SonoScape CO., LTD, China） separately. MSC measured the SAT thickness using a pair of clamp, and BCBM includes a pair of LED (NIR) and a photodetector. Three repeated measurements were performed from each method. It took about 60 minutes to complete all the measurements for each subject. Ultrasound measurement performed by an experienced physician was used to obtain the reference SAT thickness, which was considered as the golden criterion. MSC and BCBM were used for technique comparison.

2.4 Regression model development

2.4.1 Dataset creation

800 sample data from 20 sites in 40 subjects were obtained by the SATmeter. Four datasets were created based on the different measurement sites. Dataset1 composed of all the samples from the whole body, which was used to build the whole body model. Dataset2 and dataset3 both consisted of 234 samples collected from the upper and lower limb and was used to build the upper and lower limb model, respectively. Dataset4 contained 226 samples from the abdomen and was used to build the abdomen model.

2.4.2 Selection of input variables to the regression model of SATmeter

Each data contained 4 light patterns (P1, P2, P3 and P4) acquired by the photodetector. Supposed P5 is for the skin color. According to the Beer-Lambert law, which states that there is a logarithmic dependence between the transmitted and incident light, the natural logarithms of light pattern values were selected as input variables. Meanwhile, the differences and ratios between light pattern values were also selected in order to reduce the interference from non-fat tissue such as skin and ambient light. Therefore, the light pattern values, their transformations and skin color Pi , Pi-Pj, Pi/Pj, lnPi, (lnPi-lnPj), (lnPi/lnPj) (i，j =1…4，i≠j) and P5 provided 33 candidate variables in total for the regression models. Stepwise method was adopted to select the most relevant input variables and reduce the computational complexity. In statistics, stepwise regression includes regression models in which the choice of predictive variables is carried out by an automatic procedure. The main selection approaches include forward selection, backward elimination and bidirectional elimination. Backward elimination was used in this study, which involved starting with all candidate variables, testing the deletion of each variable using a chosen model comparison criterion, deleting the variable (if any) that improved the model the most by being deleted, and repeating this process until no further improvement was possible.

2.4.3 Regression models for SATmeter

In this study, both the LR and SVR models were used. The LR analysis in formula (1) was utilized to fit the absolute SAT thickness.

$$Y = b_0 + b_1X_1 + \ldots + b_iX_i \tag{1}$$

Where b_0 is constant; X_1, $X_2 \ldots X_i$ are independent input variables; b_i is the coefficient of X_i. Y is the reference SAT thickness obtained from the ultrasound measurement. Least-squares estimation technique was used to obtain the coefficients.

The nonlinear SVR model was used to minimize the generalization error bound so as to achieve generalized performance. The principle of SVR is based on the computation of a linear regression function in a high dimensional feature space where the input data are mapped via a nonlinear function. The most commonly used kernel functions are linear, radial basis, polynomial and cubic spline data interpolation. Different forms of kernel functions can generate different support vector machines. In our study, radial basis function was adopted as a kernel function after the initial comparison of the regression accuracy with linear and polynomial functions. Support vector machine or support vector network is showed in Fig. 2.

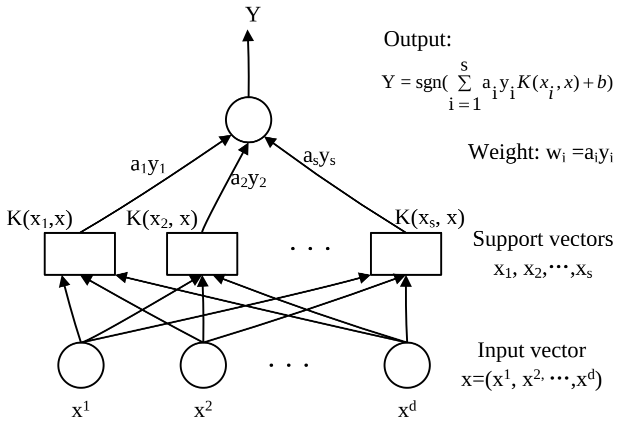

Fig. 2 The architecture of support vector machine for SVR implementation.

2.4.4 Measurement accuracy assessment

Three-fold cross-validation was applied to each of the four datasets (dataset1, dataset2, dataset3 and dataset4) to evaluate the measurement accuracy of the SAT thickness from the LR and SVR models in comparison with the ultrasound technique. Each dataset was randomly partitioned into three subsets. One subset was retained as the validation data to test the model, and the remaining two subsets were employed as training data. The cross-validation process was then repeated three times, with each of the three subsets used once as the validation data. The results from the repeated cross-validation were then averaged to produce estimation. The advantage of this method over repeated random sub-sampling was that all observations were used for both training and validation, and each observation was used for validation for only once.

Besides, the Bland-Altman analysis [26] was utilized to assess the agreement between SATmeter-LR, SATmeter-SVR, MSC, BCBM and ultrasound, respectively. The scatterplot, regression line and correlation coefficient were then provided for these methods. The measurement accuracy of SATmeter-LR, SATmeter-SVR, MSC and BCBM referred to ultrasound technique was also calculated respectively.

All the statistical analysis was performed using IBM SPSS statistics (IBM Corporation, New York, United States). Coefficient of variation (CV) was calculated to assess the measurement repeatability. ANOVA analysis with post-hoc multiple comparisons was then used to determine the gender effect, the measurement repeatability for each technique and whether there was significant difference between SATmeter-LR, SATmeter-SVR, MSC, BCBM and ultrasound.

3. Results

3.1 Regression models

The SATmeter-LR models for dataset1 to dataset4 are expressed in formula (2) to (5).

Mode1 $$TK=|-99.949-0.017P_4+20.983\ln P_4-0.008(P_1-P_2)| \quad (2)$$

Mode2 $$TK=|-447.647-40.615\ln P_1+72.197\ln P_4+268.404(\ln P_1/\ln P_4)+2.488(P_1/P_2) -0.016(P_1-P_3)+0.02(P_2-P_4)| \quad (3)$$

Mode3 $$TK=| -57.499-0.306P_5+12.7\ln P_4-0.005(P_1-P_2)| \quad (4)$$

Mode4 $$TK=|97.62-71.434(\ln P_1/\ln P_4)+0.009(P_2-P_4)| \quad (5)$$

where TK is the SAT thickness in mm. | | is a sign for absolute value. P_1, P_2, P_3 and P_4 represent the four light patterns. P_5 is the skin color.

It was noticed that the coefficients of P_4, $\ln P_4$, $\ln P_1/\ln P_4$ and $\ln P_1$ were much larger than the other coefficients in these models. As the distance between the LED and photodetector increased, the detected light intensity rapidly decreased. However, the backward scattering light carried more fat information with more LEDs, which improved the resolution and signal to noise ratio [15]. Therefore, it could be inferred that P_1 and P_4 were the two major factors in the models and skin color P_5 did not influence the measurement distinctly.

The connecting weights and support vectors in SATmeter-SVR models were determined after training with dataset1 to dataset4.

3.2 SAT thickness measurement from different techniques

Fig.3 shows the SAT thicknesses (mean+/-SD) estimated by SATmeter-LR, SATmeter-SVR, and measured by MSC, BCBM and ultrasound. The SD in Fig.3 represents between-subject variability. It can be seen that the SAT thickness varied a lot between-subjects. However, for the measurement repeatability, the CV for all the techniques used in this study were all less than 5%. Besides, ANOVA analysis showed that there was no significant difference ($p<0.01$) between the three repeats for all the techniques used in our study. Therefore, the average values from the three repeats were used to for further analysis.

Overall, there were no significant differences between SATmeter-LR and ultrasound ($p>0.05$) except for the dataset3. SATmeter-SVR was different from ultrasound in dataset1 and dataset4 (both $p<0.05$), but not in dataset2 and dataset3. Both MSC and BCBM had significant differences when compared with ultrasound (all $p<0.01$) in all the four datasets.

ANOVA analysis also showed that there was no significant difference between males and females for all the datasets (all $p>0.05$).

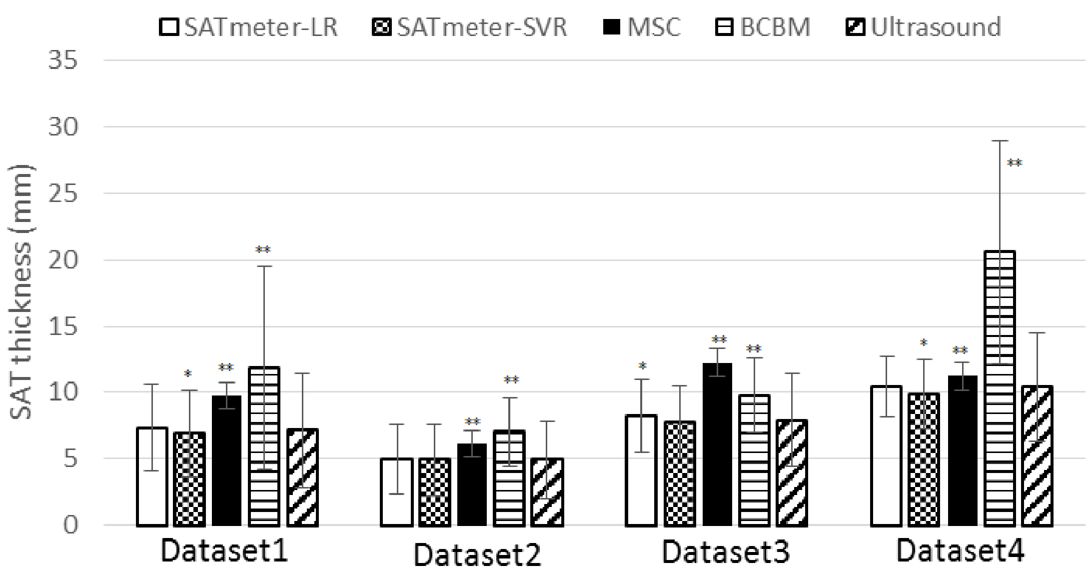

Fig.3 SAT thickness of Dataset1 to Dataset 4 measured with SATmeter-LR, SATmeter-SVR, MSC, BCBM and ultrasound. Dataset1: whole body; Deteset2: upper limb; Dataset3: lower limb; Dataset4: abdomen.

Note: *p<0.05, **p<0.01 significant difference in comparsion with the reference ultrasound technique.

3.3 Bland-Altman analysis

Fig.4 shows the mean difference and 95% limits of agreement between SATmeter-LR, SATmeter-SVR, MSC, BCBM and ultrasound for dataset2. We need highlight that, for figure 4 (a) and (b), the 'zero' line is overlapped with the mean difference line since there is no significantly difference between our proposed techniques and reference ultrasound technique. Bland-Altman results (mean±1.96SD) for dataset1 to dataset4 are summarized in Table 1. They indicate that SATmeter-LR and SATmeter-SVR have smaller mean and SD of difference than MSC and BCBM, and therefore better agreement with ultrasound for all datasets.

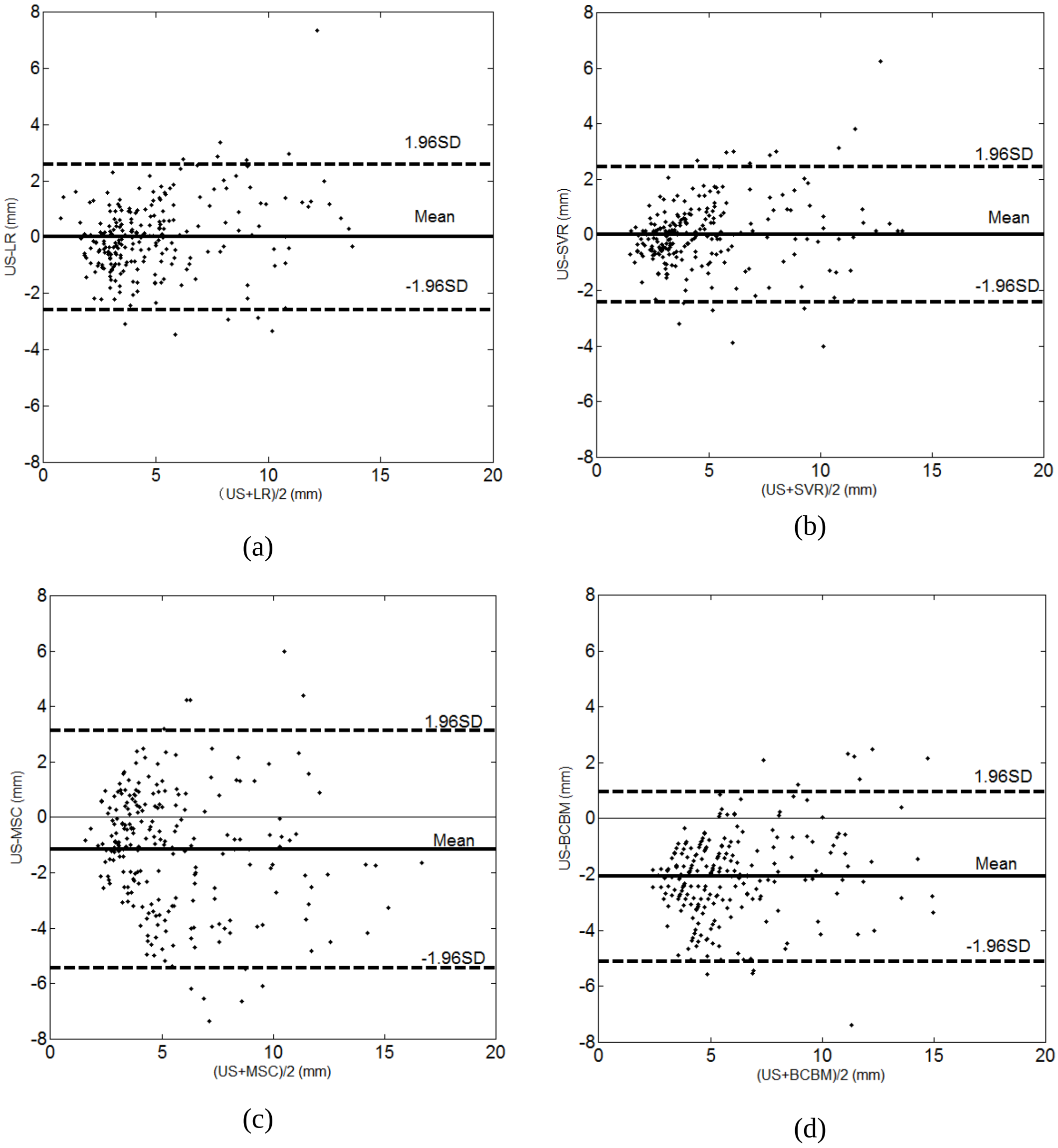

Fig.4 Bland-Altman analysis plots between (a) SATmeter-LR (LR) vs ultrasound (US); (b) SATmeter-SVR (SVR) vs US; (c) MSC vs US; (d) BCBM vs US

Table 1 Mean±1.96SD (in mm) difference between the four methods (SATmeter-LR, SATmeter-SVR, MSC and BCBM) and the ultrasound measurement

Dataset	SATmeter-LR	SATmeter-SVR	MSC	BCBM
1(whole body)	-0.19±5.74	0.23±5.55*	-2.62±7.08**	-4.69±10.42**

2 (upper limb)	0.0015±2.58	0.016±2.43	-1.15±4.30**	-2.08±3.04**
3 (lower limb)	-0.34±4.33*	0.15±3.64	-4.35±6.94**	-1.90±3.62**
4 (abdomen)	0.14±3.68	0.34±4.33*	-4.32±6.92**	-1.88±3.61**

Note: *p<0.05, **p<0.01 significant difference in comparison with the reference ultrasound technique.

3.4 Correlation between techniques

Fig.5 gives an example results for the regression analysis between the measurement on the upper limb from SATmeter-LR, SATmeter-SVR, MSC and BCBM and ultrasound using dataset2. Table 2 and Table 3 summarize the correlation coefficients and measurement accuracy relative to ultrasound for all the datasets. There were all significantly correlated (all $p<0.001$).

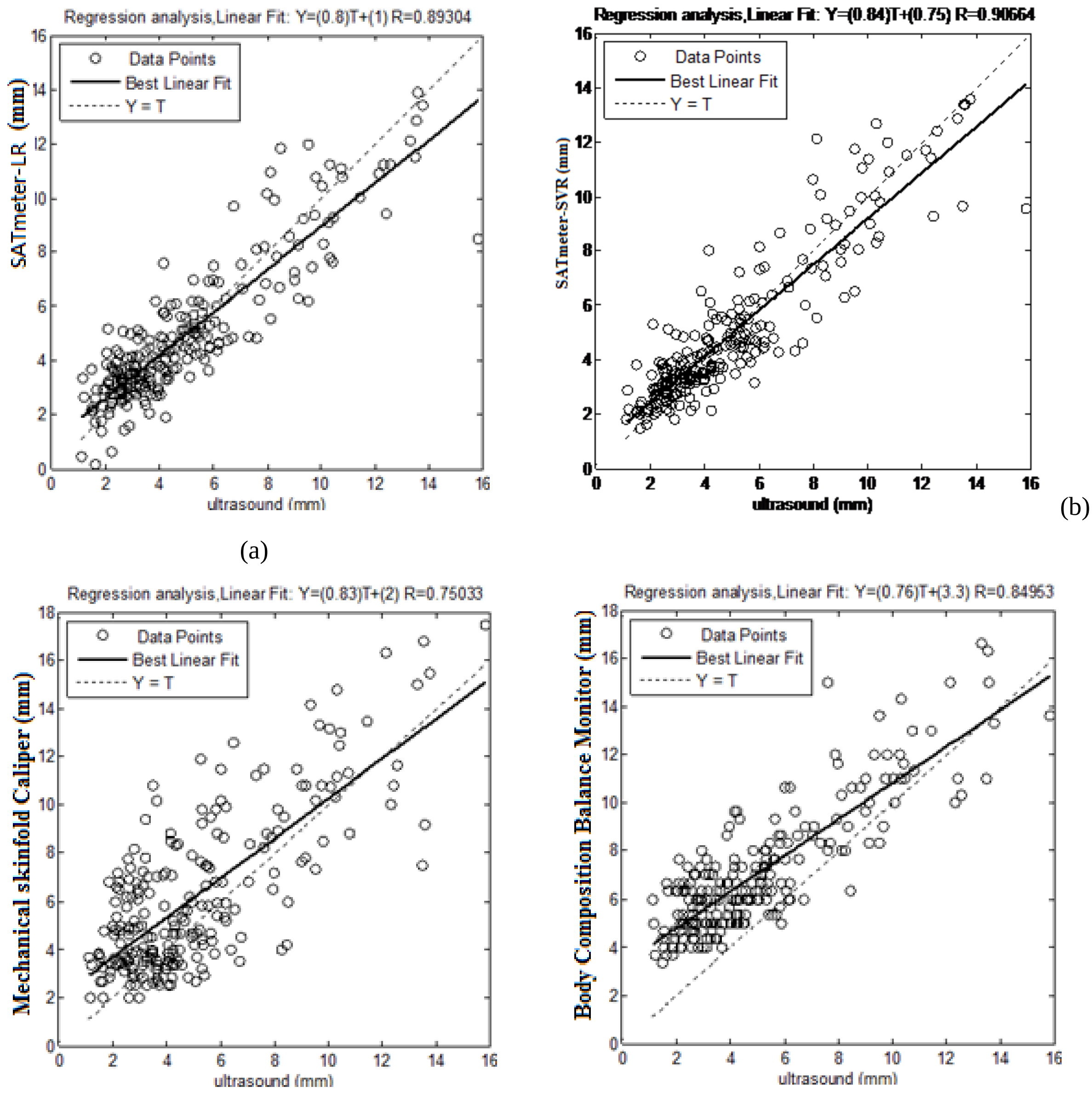

Fig.5 Regression analysis of the SAT thickness on the upper limb between SATmeter-LR (a), SATmeter-SVR (b), MSC (c) and BCBM (d) and ultrasound.

Table 2 Correlation coefficient between SATmeter-LR, SATmeter-SVR, MSC and BCBM and ultrasound measurement.

Dataset	SATmeter-LR	SATmeter-SVR	MSC	BCBM
1(whole body)	0.74	0.76	0.62	0.74
2 (upper limb)	0.90	0.91	0.75	0.85
3 (lower limb)	0.77	0.85	0.34	0.85
4 (abdomen)	0.56	0.58	0.66	0.62

Table 3 Average measurement accuracy of SATmeter-LR, SATmeter-SVR, MSC and BCBM relative to ultrasound

Dataset	SATmeter-LR	SATmeter-SVR	MSC	BCBM
1(whole body)	74.3%	76.1%	70.3%	74.3%
2 (upper limb)	86.3%	96.6%	81.5%	86.9%
3 (lower limb)	84.4%	90.2%	56.9%	85.4%
4 (abdomen)	67.2%	67.7%	68.5%	70.7%

It can be seen that SATmeter-LR was better than MSC for dataset1 to dataset3. SATmeter-SVR was better than SATmeter-LR in dataset1 to dataset4 and better than both MSC and BCBM in dataset1 to dataset3. MSC had the lowest correlation and accuracy because it was hard to pick up the adipose tissue by MSC especially on the lower limb (dataset3). It is also observed that, for the comparison between the four datasets, all the techniques have relatively lower accuracy and correlation for the measurement on the abdomen (dataset4). Both the measurement on the upper limb provided higher correlation and better accuracy than other locations.

Discussion and conclusion

In this study both LR and SVR models for the measurement of SAT thickness using SATmeter have been investigated, with the accuracy compared with MSC, BCBM and ultrasound techniques. In general, SATmeter presented better accuracy than MSC and BCBM, especially at the upper and lower limb. It was also concluded that using different models from the specific body parts could achieve better accuracy than using one general model for the whole body. SATmeter could be more suitable for Chinese population because of its regression models based on Chinese database although further research needs to be followed.

The SATmeter developed in our lab was designed based on the same principle as the Lipometer, but it employed different regression models. Lipometer used backpropagation neural networks with light pattern values as inputs. However, SVR in our SATmeter was easier to design its architecture with better generalization ability. Besides, the natural logarithm transformation of light pattern values and their ratios were introduced to reduce the interference from non-fat tissue. In addition, the Lipometer measured SAT thickness at any body sites using the same regression model, while SATmeter applied the specific model taking the different fat compactness into consideration.

Regarding the measurement accuracy between different body parts, for the SATmeter-LR, SATmeter-SVR and BCBM techniques, the best measurement was from the upper limb and the worst from the abdomen. The reason may be due to the thinner fat on upper limb and the thicker fat on abdomen, and NIR penetrating capability is limited in the thicker SAT layer.

The predictive power of the regression approaches is markedly determined by breadth of sample variability and the size of the sample. 20 body sites were used in this study to generate relatively large dataset for validating the measurement accuracy. This also allowed the comparison of measurement performance between different sites.

It is noted that the range of fat thickness was not large enough to cover obese subjects. In order to extend the measurement range, in a future study, more subjects at different ages with different BMI should be recruited. We also recognize that the proposed method could be improved further by using CT or MRI as alternative reference to achieve better measurement accuracy for clinical use. Other advanced correlation analysis method, such as the concordance regression [27] could be investigated. Next, a full clinical trial on some of the main clinical sites (biceps, triceps etc) will be our next step to comprehensively explore its clinical value and the variability allowed for clinical significance.

Nevertheless, our proposed method performed better than the existing technologies such as MSC and BCBM. Furthermore, our technique is much simpler than the ultrasound measurement, providing great potential for home care use.

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