Forearm skin tissue dielectric constant measured at 300 MHz: effect of changes in skin vascular volume and blood flow

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Summary

Skin tissue dielectric constant (TDC) values measured via the open-ended coaxial probe method are useful non-invasive indices of local skin tissue water. However, the effect of skin blood flow (SBF) or skin blood volume (SBV) on TDC values is unknown. To determine the magnitude of such effects, we decreased forearm SBV via vertical arm raising for 5 min (test 1) and increased SBV by bicep cuff compression to 50 mmHg for 5 min (test 2) in 20 healthy supine subjects (10 men). TDC values were measured to a depth of 1·5 mm on anterior forearm, and SBF was measured with laser-Doppler system simultaneously on forearm and finger. Results indicate that decreasing vascular volume (test 1) was associated with a small but statistically significant reduction in TDC (3·0 ± 4·3%, P = 0·003) and increasing vascular volume (test 2) was associated with a slight but statistically significant increase in TDC (3·5 ± 3·0%, P<0·001). SBF changes depended on test and measurement site. For forearm, test 1 significantly increased SBF (102·6 ± 156·2%, P<0·001) and test 2 significantly decreased it (39·5 ± 13·1%, P<0·001). In finger, SBF was significantly reduced by both tests: in test 1 by 55·3 ± 32·1%, P<0·001 and in test 2 by 53·3 ± 27·6%, P<0·001. We conclude that the small percentage changes in TDC values (3·0–3·5%) over the wide range of induced SBV and SBF changes suggest a minor effect on clinically determined TDC values because of SBV or SBF changes or differences when comparing TDC longitudinally over time or among individuals of different groups in a research setting.

Introduction

Previous work has established the measurement of tissue dielectric constant (TDC) of human skin at a frequency of 300 MHz as a useful index of local skin-to-fat tissue water (Nuutinen et al., 2004). The TDC measurement is based on the open-ended coaxial probe method (Stuchly et al., 1981; Alanen et al., 1998a,b) that is sensitive to both free and bound water contained within volume that is measured. Subsequently, the method was used in a variety of clinically related applications including the assessment of lymphoedema (Mayrovitz, 2007, 2009; Mayrovitz et al., 2007a, 2008a) and quantification of lymphoedema changes following treatments such as pneumatic compression therapy (Fife et al., 2012), laser therapy (Mayrovitz & Davey, 2011) and manual lymphatic drainage therapy (Mayrovitz et al., 2008b). Other aspects of its application have included the characterization of arm tissue water in women with breast cancer prior to their treatment (Mayrovitz et al., 2009), in women with fully developed lymphoedema (Mayrovitz, 2007) and changes accompanying weight loss (Laaksonen et al., 2003), postoperative cardiac surgery (Petaja et al., 2003), skin irradiation (Nuutinen et al., 1998), skin irritation (Miettinen et al., 2006) and during the menstrual cycle (Mayrovitz et al., 2007b). However, because measured TDC values depend on water content within the measurement volume of the probe, typically 0·5–5·0 mm, it is unclear as to the possible impact of skin blood volume (SBV) and skin blood flow (SBF) per se on the measured value of TDC. If TDC values are to be of optimal use in tracking localized skin water changes, then it is important to know the potential effect of both blood flow and volume. Thus, the purpose of this study was to evaluate the magnitude of these effects by measuring TDC before, during and after induced changes in arm SBV and SBF.

Methods

Subjects

Twenty adult volunteer subjects participated in this study (10 men and 10 women). They were evaluated after signing a University Institutional Review Board approved informed consent. Requirements for participation included that subjects (i) be at least 21 years of age; (ii) had self-reported normal upper extremity function with no history of serious trauma, vascular issues, implanted wires or electronic medical devices; (iii) reported no current pregnancies; (iv) had no evidence of any abnormal arm skin condition at the time of the study. All subjects were asked not to apply any skin cream or lotions on the day of their scheduled experiment. Group age (mean ± SD) was 26 ± 3·3 years (range of 23–36 years) and a median age of 26 years. The group body mass index (BMI) was 23 ± 3·1 kg m^{-2} (range 18–32 kg m^{-2}) and a median of 23 kg m^{-2}. With respect to the BMI classification, one subject (5%) was underweight (BMI < 18·5 kg m^{-2}), 14 subjects (70%) had a BMI in the normal range (BMI 18·5–24·9 kg m^{-2}), four subjects (20%) were overweight (BMI 25 –29·9 kg m^{-2}), and one subject (5%) would be classified as obese (BMI > 30 kg m^{-2}). The right hand was the self-reported dominant hand in all 20 subjects. Forearm girths were measured on the right arm 8 cm distal to the antecubital fossa with a calibrated tape at uniform tension. Girth values were 24 ± 2.2 cm with a range of 20-28 cm and a median value of 24 ± 2.2 cm. Blood pressures determined with a mercury sphygmomanometer at the end of the measurement sequence showed no subject to be hypertensive with group systolic pressures of 111·9 ± 8·5 mmHg (range 106–120 mmHg) and diastolic pressures of 71·6 ± 6·2 mmHg (range 64–82 mmHg). Tests were carried out in a quiet experimental room with average room temperature and relative humidity of 22·9 ± 1·6°C and 51·1 ± 6·0%, respectively.

Preliminary skin biophysical measurements

To help insure that the subsequent measurements of TDC values would be made on skin with normal barrier function and epidermal moisture, each subject had their stratum corneum (SC) moisturization and transepidermal water loss (TEWL) measured while in the supine position at the specific forearm site that would subsequently be used for TDC measurements. The relative SC moisturization was based on the SC capacitance (Alanen *et al.*, 2004) and was measured using the MoistureMeter SC-2 (Delfin Technologies Ltd, Kuopio, Finland). TEWL is a measure of the non-sweat-related passive water loss through the skin and is an index of skin barrier function (Fluhr *et al.*, 2006; Machado *et al.*, 2010). TEWL was measured using the VapoMeter SWL-2 (Delfin Technologies Ltd). The VapoMeter (Nuutinen *et al.*, 2003) is battery-operated and contains a humidity sensor housed in a closed chamber within a cylindrical probe that contacts the skin for about 10 s for a TEWL measurement that is reported in water flux units of g m^{-2} h^{-1}. Its use in comparison with open chamber devices has been determined (De Paepe *et al.*, 2005; Steiner *et al.*, 2011). TEWL and SC values obtained for the present subjects were, respectively, 9·1 ± 3·1 g m^{-2} h^{-1} (range 5·4–17·2) and 16·7 ± 5·0 (range 10–30) with both parameters being within normal ranges previously measured for TEWL (Nuutinen *et al.*, 2003; De Paepe *et al.*, 2005) and for SC (Zioni *et al.*, 2010), suggesting that the subsequent TDC and SBF determinations are representative of normal hydrated skin.

Tissue dielectric constant measurement method

The device used to measure TDC was the MoistureMeter-D (unit number D3N014, Delfin Technologies Ltd). It consists of a cylindrical probe connected to a control unit that displays the TDC value when the probe is placed in contact with the skin as illustrated in Fig. 1. The physics and principle of operation have been well described (Stuchly *et al.*, 1981; Alanen *et al.*, 1998a,b; Alanen *et al.*, 1999; Nuutinen *et al.*, 2004). In brief, a 300-MHz signal is generated within the control unit and is transmitted to the tissue via the probe that is in contact with the skin. The probe acts as an open-ended coaxial transmission line (Alanen *et al.*, 1998a). A portion of the incident electromagnetic wave is reflected that depends on the dielectric constant of the tissue, which itself depends on the amount of free and bound water in the tissue volume through which the wave passes. Reflected wave information is processed within a control unit, and the dielectric constant is displayed. For reference, pure water has a value of about 78·5, and the display scale range is 1–80. The effective measurement depth depends on the probe dimensions, with larger spacing between inner and outer conductors corresponding to greater penetration depths. In this study, a probe with an effective measurement depth of 1·5 mm was used as this depth approximates the anterior forearm skin thickness. This probe used has an outside diameter of 20 mm with 3-mm spacing between the inner and outer concentric conductors.

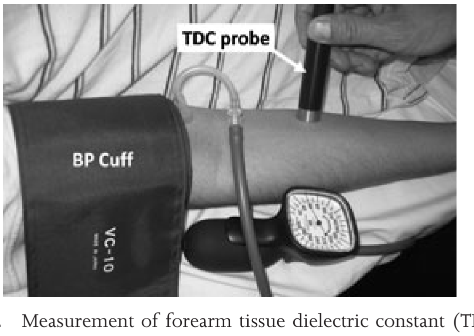

Figure 1 Measurement of forearm tissue dielectric constant (TDC). TDC is measured on the anterior forearm by touching the skin with the shown probe for about 10 s. The BP cuff is used for a later manoeuvre to cause venous congestion by elevating the cuff pressure to 50 mmHg.

Tissue dielectric constant measurement procedure

TDC measurements were started after a subject was lying supine for 5 min on a padded examination table with arms at his or her side with hands positioned palm up to expose the anterior surface of both forearms. A standardized measurement site, along the right forearm midline located 8 cm distal to the antecubital fossa, was marked with a dot using a surgical pen. The dot served as a reference centre point for probe placement. A single measurement was obtained by placing the probe in contact with the skin of the right forearm and held in position using gentle pressure (Fig. 1). After about 10 s, an audible signal indicated completion of the measurement. A baseline measurement set consisting of 10 values were collected by continuing in this fashion and obtaining TDC values every 20 s for 3 min. The subject's arm was then gently raised by the investigator to 90°. After 2 min with the arm raised, another set of 10 measurements were collected by obtaining values every 20 s for 3 min. The total arm raise time was 600 s (5 min). The subject's arm was then slowly lowered back to the horizontal position. After the arm had been resting for 2 min, a 2nd baseline TDC measurement sequence of 10 measurements was taken, and then, the cuff around the bicep of the right arm was inflated to 50 mmHg. After 2 min of cuff inflation, TDC measurements were again taken every 20 s for 3 min after which the cuff pressure was released. This completed the TDC measurements sequence. The average value of the 10 TDC values taken with the arm at 0° and the cuff not inflated was calculated and subsequently compared to the average value of the 10 TDC values taken with the arm cuff inflated to 50 mmHg.

Skin blood flow measurement method

Skin blood flow (SBF) was measured using a dual-channel laser-Doppler system (Moor Instruments model MBF3D, Wilmington, DE, USA) with one probe (Model MP11sc) affixed with paper tape to the right anterior forearm 8 cm distal to the antecubital crease and one probe affixed to the palmer surface of the 3rd finger as shown in Fig. 2. The probe is made of flexible silicon rubber tape with a thickness of 2 mm. Flow outputs of the monitoring system underwent A/D conversion (DataQ model 720B) at 100 samples s^{-1} and were recorded at a standardized gain on a dedicated laptop.

Principles and applications of laser-Doppler flow measurements have been previously published (Nilsson *et al.*, 1980; Kastrup *et al.*, 1987; Rendell *et al.*, 1992; Bornmyr *et al.*, 1998; Mayrovitz, 1998). Briefly, a low-intensity laser light signal is transmitted into the skin to a depth of about 1–2 mm, and the reflected light is used to measure local blood flow. The Doppler-shifted signal contains information about the speed and number density of moving red blood cells in a tissue region to a depth of about 1–2 mm (Jakobsson & Nilsson, 1993). Speed and number density information is processed to yield a parameter that is proportional to blood flow and usually expressed in arbitrary units (a.u.). The probe, which was directly attached to the skin with tape, received blood flow data from a surface area of about 2 mm^2 and transmitted this data via a fibre optic bundle to the central processor. Response time resolution was 0·1 s. Basal SBF values of the finger are typically much lesser than that on the forearm but because forearm and finger values were scaled for convenience of recording display, comparisons of absolute differences between these sites are not appropriate.

Skin blood flow measurement procedure

After TDC values were obtained, subjects remained comfortably in the supine position while laser-Doppler probes were placed at the previous site of TDC measurement and also on the palmer aspect of the 3rd finger (Fig. 2). SBF was recorded from both sites continuously during a horizontal resting interval, an arm raise interval, an arm lowering interval and a cuff compression interval as illustrated for one subject's finger SBF in Fig. 3. For 5 min, the arm was kept in a horizontal

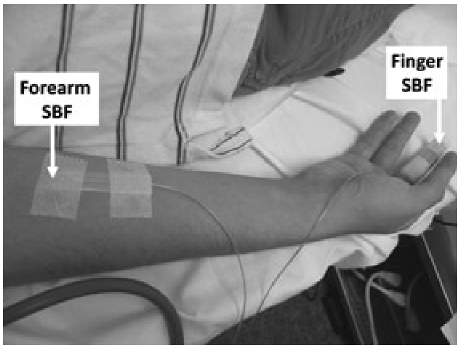

Figure 2 Measurement of skin blood flow (SBF). Laser Doppler flat probes are positioned on the anterior forearm and on the palmer surface of the third finger of the right arm. SBF is measured continuously at both sites with the arm horizontal (as shown) and while elevated vertically (not shown).

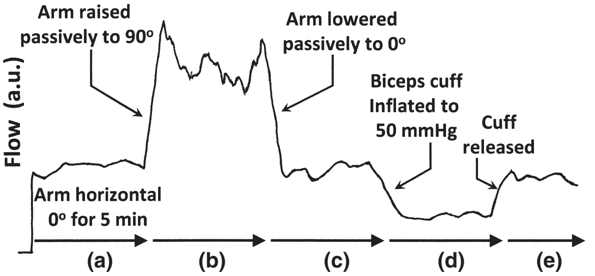

Figure 3 Experimental manoeuvres for the SBF sequence. The experimental procedure can be divided into five segments, each segment lasting 5 min. Continuous SBF recordings are obtained throughout this sequence. [A] the right arm is lying horizontally (0°) on the table, and the biceps cuff is not inflated; [B] the subject's arm is raised passively by the experimenter to 90°, and the subject is instructed to maintain this position; [C] the subject's arm is passively lowered back to 0°; [D] after 5 min, the biceps cuff is inflated to 50 mmHg and is maintained at this pressure for 5 min; [E] the pressure in the cuff is returned to 0 mmHg. A similar pattern of manoeuvres is also used for the TDC measurement series.

position before being raised slowly to a vertical position for an additional 5 min. Thereafter, the arm was returned to the horizontal position, and another 5 min, data set was recorded. Then, the arm cuff was inflated to 50 mmHg and SBF continued to be monitored for 5 min. The cuff pressure was then released.

Vascular perturbations in skin blood volume and skin blood flow

Changes in SBV and SBF were accomplished with two test manoeuvres. Test 1 consisted of changing the arm position from a horizontal position resting on the examination table surface to a self-supported vertical position approximately 90° to the bed surface. Test 2 consisted of a 50 mmHg compression of the upper arm on the tested side via a blood pressure cuff connected to a sphygmomanometer. These manoeuvres were performed in association with the TDC and SBF measurements described below and illustrated for an SBF measurement in Fig. 3.

Analysis

All statistical analyses were performed using SPSS version 13 (IBM, Armonk, NY, USA). TDC and SBF values were first tested for normality using the Shapiro–Wilk test. Results showed that TDC values were not distributed significantly different from normality with Shapiro–Wilk's significance values ranging from 0·12 to 0·33. Contrastingly, all SBF values were not normally distributed as judged by the significance values of the Shapiro–Wilk test, which were all less than 0·05. Accordingly, changes in TDC values were analysed using paired t-tests, and changes in SBF values were analysed using the Wilcoxon signed rank procedure using the Fisher's exact test.

Results

Changes in TDC values with changes in time, arm position and cuff pressure

For each test condition, the 10 sequential TDC values measured at 20 s intervals are shown in Fig. 4. Except for the measurements taken with the arm horizontal prior to the arm raise manoeuvre, there was no detectible trend in the sequential TDC values as assessed by regression analysis. For the arm in the horizontal position (Fig. 4a), there was a slight but significant increase ($P<0·01$) in TDC values from the first TDC value (mean ± SD) of 28·4 ± 2·6–29·0 ± 3·0 for the last measurement ($r = 0·797$). This minor increase had little effect on the average calculated value used for assessing changes in TDC accompanying arm elevation.

Moving the arm from the horizontal position (0°) to the vertical position (90°) was associated with a small but statistically significant reduction in the measured TDC value (Fig. 5). The TDC average value in the horizontal position

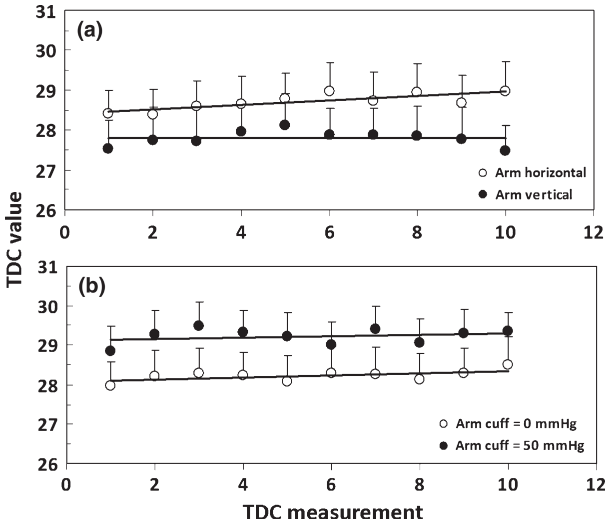

Figure 4 Sequential TDC values. Ten sequential TDC values were measured at 20-s intervals during each manoeuvre. Values (circles) are mean and bars are SEM for the 20 subjects evaluated. (a) Arm positional manoeuvre; (b) arm compression manoeuvre. In (a), a slight trend (from 1st to 10th measurement) is noted for TDC values obtained with the arm in the horizontal position.

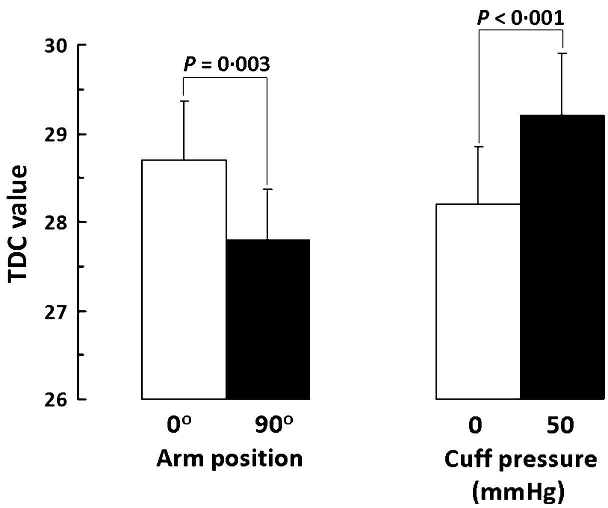

Figure 5 Tissue dielectric constant values for Arm Position and Compression Pressures. Left: TDC values measured with and without arm elevation to 90° with respect to horizontal; Right: TDC values measured with and without application of 50 mmHg of pressure around the biceps proximal to the site of measurement. Data are the mean TDC values of 20 subjects measured to a depth of 1·5 mm. Bars are +1 SD. TDC values measured with elevation of the arm to 90° is, on average, significantly lower than control ($P = 0·003$), and TDC values measured with application of 50 mmHg of pressure is significantly higher than control ($P<0·001$).

(mean ± SD) was 28·7 ± 2·9 and was reduced to 27·8 ± 2·5 ($P = 0·003$) with the average reduction amounting to 3·0 ± 4·3%. Contrastingly, inflation of the cuff around the upper arm to 50 mmHg with the arm in a horizontal position was associated with a slight but statistically significant increase in

TDC value as also shown in Fig. 5. The TDC average value for the arm in the resting horizontal position prior to cuff inflation was 28·2 ± 2·8 and was increased to 29·2 ± 3·1 (P<0·001) after 5 min of cuff inflation. This change corresponded to a percentage increase of 3·5 ± 3·0%.

Changes in skin blood flow associated with arm position and cuff pressure

Forearm

Moving the arm from the 0° to 90° position was associated with a significant increase in the forearm SBF (Fig. 6). The SBF average value in the horizontal position (mean ± SD) was 0·26 ± 0·13 a.u. and was increased to 0·47 ± 0·33 a.u. (P<0·001) with the average increase amounting to 102·6 ± 156·2% as calculated from the mean and SD of the changes measured in each of the 20 subjects. Contrastingly, inflation of the cuff around the upper arm to 50 mmHg with the arm in a horizontal position was associated with a significant decrease in SBF. The SBF average value for the arm in the resting horizontal position prior to cuff inflation was 0·29 ± 0·22 a.u. that decreased to 0·15 ± 0·07 a.u. (P<0·001) after 5 min of cuff inflation. This change corresponded to a percentage decrease of 39·5 ± 13·1%.

Finger

Moving the arm from the 0° to 90° position was associated with a significant decrease in the finger SBF (Fig. 7). The SBF average value in the horizontal position was 0·38 ± 0·24 a.u. and was decreased to 0·16 ± 0·13 a.u. (P<0·001) with the average decrease equal to 55·3 ± 32·1%. Similarly, inflation of the cuff around the upper arm to 50 mmHg with the arm in a horizontal position was also associated with a significant decrease in SBF. The SBF average value for the arm in the resting horizontal position prior to cuff inflation was 0·35 ± 0·29 a.u. that decreased to 0·16 ± 0·18 a.u. (P<0·001) after 5 min of cuff inflation. This change corresponded to a percentage decrease of 53·3 ± 27·6%.

Discussion

The main new findings of the present study relate to the determination of the extent to which changes in skin blood volume (SBV) and skin blood flow (SBF) impact the measured value of skin tissue dielectric constant, TDC. The findings indicate that changes in SBV, induced by volume reductions associated with arm elevation and volume increases associated with cuff compressions to 50 mmHg, cause anticipated directional changes in TDC values; TDC decreases with arm elevation, and its associated blood volume reduction and TDC increases with arm compression and its associated reduction in venous outflow from the arm. Although both manoeuvres induced statistically significant changes in measured TDC values, the changes were functionally small amounting to an average of a 3·0% reduction on arm elevation and a 3·5% increase associated with the SBV increase induced by arm cuff inflation. Tests of the associated blood flow changes induced by these two manoeuvres showed a nearly twofold increase in forearm SBF with arm elevation and a nearly 40% decrease in SBF with cuff compression. Despite these large changes in SBF, only minor changes in TDC values occurred. These data suggest that for most clinical evaluation and tracking purposes,

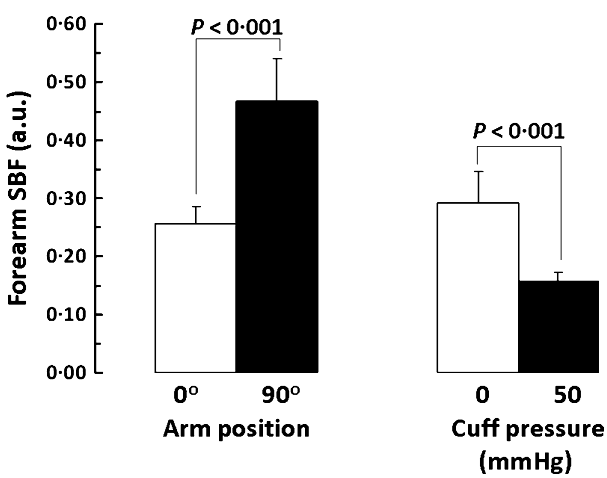

Figure 6 Forearm SBF values for Arm Position and Compression Pressures. Left: Forearm skin blood flow (SBF) with and without arm elevation to 90°; Right: SBF with and without application of 50 mmHg cuff pressure. Data are mean SBF values (flow units, pu) of 20 subjects. Bars are +1 SD. Mean SBF value measured with 90° arm elevation is significantly greater than with the arm at 0° (P<0·001), and SBF measured with 50 mmHg of cuff pressure is significantly less than at 0 mmHg (P<0·001).

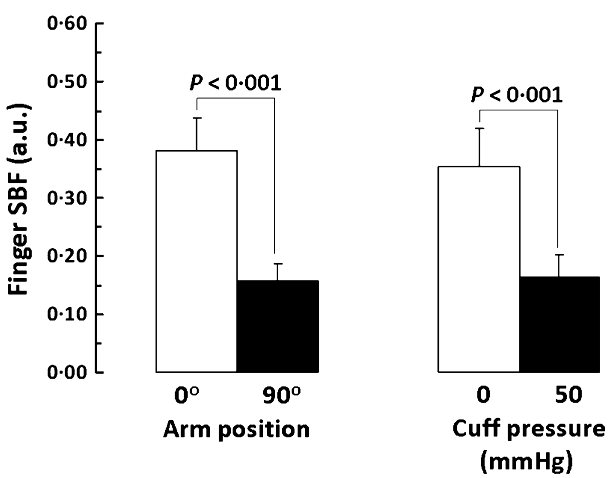

Figure 7 Finger SBF values for Arm Position and Compression Pressures. Left: Finger skin blood flow (SBF) with and without arm elevation to 90°; Right: SBF with and without application of 50 mmHg cuff pressure. Data are mean SBF values (expressed in arbitrary units) of 20 subjects. Bars are +1 SD. Mean SBF value measured with 90° arm elevation is significantly less than with the arm at 0° (P<0·001), and SBF measured with 50 mmHg of cuff pressure is significantly less than at 0 mmHg (P<0·001).

any potential confounding effects of variations in blood volume or blood flow changes are minimal with respect to effects on measured TDC values. This is important because it impacts the way in which TDC values may be interpreted when used to measure persons in different groups or the same persons over time. As in general these persons will have unknown but possible differences or changes in their vascular volumes or flows at sites of TDC measurements, the present findings help define an upper bound on the potential variance attributable to changes in either SBV or SBF. Thus, a reasonable working estimate would be to assume that individual changes (or group differences) greater than ±3% would not likely be related to vascular changes.

Additional findings of interest in the present study relate to the observed changes in SBF. Although it was anticipated that cuff inflation would reduce SBF as a consequence of the reduction in the effective perfusion pressure distal to the upper arm cuff, the oppositely directed effects of arm elevation on forearm versus finger SBF were not anticipated. Elevation of the arm from the horizontal to vertical position was associated with the anticipated gravity-dependent blood volume drainage and a reduction in the finger SBF. Contrastingly, however, the forearm SBF was noted to significantly increase during the arm elevation. Although the present study was not designed to investigate the mechanism responsible for this increase, it is notable that an increase in forearm blood flow during arm elevation was observed in a prior study (Tschakovsky & Hughson, 2000). These authors used Doppler ultrasound to determine brachial artery blood flow in the elevated arm under two conditions: (i) when venous drainage was allowed and (ii) when drainage was prevented via cuff compressions to pressures above venous levels. They found that compared to the horizontal position, 2 min of arm elevation to the vertical position resulted in a 24% increase in blood flow only when venous drainage was allowed during the arm elevation interval. The authors concluded that this flow increase was attributable to a venous emptying–related arteriolar vasodilatation. However, the responsible mechanism for such a venous–arteriolar coupling is unclear although the present findings of a skin blood flow increase would be consistent with their prior observation of brachial artery blood flow increase.

In summary, TDC changes accompanying wide variations in skin blood volume and skin blood flow ranged from −3% to +3·5%. These values may be used as reasonable upper bound estimates on potential TDC variations attributable to volume or flow changes in individuals tracked over time or comparisons between groups.

Conflict of interest

The authors declare that they have no conflict of interests.

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