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Blood Flow Volume as an Indicator of the Effectiveness of Traditional Medicine

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1. Introduction

In pulse diagnosis, an important diagnostic technique in traditional medicine (TM), treatment plans for traditional therapies are adjusted according to a patient’s observed pulse. Use of this approach suggests that blood flow can be an ideal indicator of the effectiveness of TM in humans.

To our knowledge, few studies have examined the relationship between peripheral artery haemodynamics and traditional therapies in humans.

We must overcome some difficulties to confirm this hypothesis. First, it is necessary to use a very simple intervention in the study to investigate its effect and add reproducibility. Second, we need to use a quantitative indicator to evaluate the effect of traditional interventions such as acupuncture, moxibustion, and herbal medicine. Acupuncture and moxibustion therapies are complex interventions, and this complexity causes a loss of objectivity for the study. In our recent studies, we employed a simple or standardised acupuncture technique and a moxibustion simulator to ensure reproducible results. On the other hand, blood flow volume (BFV) is known to be an important index to demonstrate the condition of organs and tissues. Thus, we employed BFV as a quantitative indicator to show the effects of traditional interventions on the human body.

We would like to summarise our 4 recent studies: first, a study of the effect of simple acupuncture on the BFV of extremities (Takayama et al., 2010); second, a study on the effect of the moxibustion simulator on the BFV of the abdominal organs and extremities (Takayama et al., 2009); third, a comparison study on the effects of herbal medicine and the moxibustion simulator on the BFV of abdominal organs (Takayama et al., 2010); and fourth, a study on the effects of standardised acupuncture in a patient with open angle glaucoma (Takayama et al., 2011).

2. TEAM theory and intervention characteristics

TM developed differently than modern biomedicine did in that it was based on many years of experience rather than experiments. Many TM theories are considered unproven by the modern biomedical concept. Traditional East Asian Medicine (TEAM) practiced in China, Japan, Korea, Mongolia, Tibet, and Vietnam originated in ancient China and spread throughout history. For instance, it came to Japan about 1,500 years ago and developed in its own way in Japan. It continues to exist as Kampo medicine (Traditional Japanese Medicine;
TJM) and uses different terminologies, interventions, and acupuncture points (acupoints) than does today’s traditional Chinese medicine (TCM). It can be said that TM develops differently depending on the natural environment and culture and, thus, has different interventions.

2.1 TEAM meridians and organs
The TEAM theory states that meridians are connected to the organs and that acupoints on meridians affect organ function. It was historically very difficult to verify the meridian or acupoint structure and the connection between the organs and meridians.

According to TEAM, the main physiological functions of the stomach include receiving, digesting, transforming food and water, and taking charge of sending down food contents (Liu et al., 2006). Zusanli (ST36) and Tianshu (ST25) are located on the stomach meridian (Figure 1A). Zusanli is on outer side of just below the knee. Tianshu is located on the outside of the belly bottom on both sides. Those acupoints are known to be effective in the treatment of digestive system diseases, improving digestive function and decreasing abdominal pain (Liu et al., 2006). One of the functions of the liver is to regulate the free movement of Qi. Stagnation of liver Qi may impede blood circulation (Liu et al., 2006) and cause habitual limb chills. Taichong (LR3) is the source point of the liver meridian (Figure 1B) and stimulation on this point can regulate liver function (Liu et al., 2006).

However, the evidence of the functions explained above remains intangible.

Fig. 1. (A) Stomach meridian. (B) Liver meridian. Modified from Liu et al., 2006.

2.2 Complexity of TEAM interventions
Acupuncture and moxibustion therapy are major TEAM interventions, and each has a wide range of treatment methods. This variation is due to the treatment method in clinical experiments, including acupuncture point; needle number, gauge, length, manufacturer, and materials; insertion depth; needle retention time and insertion technique; stimulation intent and duration; and the specific needling response be elicited (e.g., the de qi sensation in traditional acupuncture, the muscle twitch in trigger point treatment, or muscle contraction in
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In order to standardise therapy methods, the STandards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA), which was organised by a group of British and American magazine editors, encourages practitioners to record needling data. In addition, for moxibustion therapy, therapy types, processing method, amount of moxa, and handling can vary. Due to the nature of the therapies that require treatment method variation, it is extremely challenging to ensure result reproducibility.

3. Reproducible simple or standardised intervention for the acupuncture and moxibustion therapy study

We reported some clinical experiments using simple or standardised acupuncture methods rather than using the method that is equivalent to actual acupuncture treatments. The report indicated that the results concluded that by the use of a simple acupuncture method, which involves inserting the needle perpendicularly into the skin surface on the acupoints, no additional stimulation with certain needle retention times was required. Example findings include improved swallowing in patients with swallowing problems and improved ambulatory function in patients with gait disorders (Seki et al., 2003; Seki et al., 2004; Seki et al., 2005). Intraocular pressure (IOP) changes in patients with glaucoma before and after 1 month of standardised acupuncture have also been reported (Kurusu et al., 2005). Clinical research conducted using the simple acupuncture method is a helpful tool for simplifying the complexity of clinical experiments for acupuncture treatments. Standardised acupuncture is a new treatment measure for some diseases. We used a simple or standardised acupuncture method with simple or no manipulation for the research shown below to investigate the effect of acupuncture.

Simple acupuncture employed in the studies is as follows:
A disposable fine stainless-steel needle (diameter, 0.16 mm; length, 40 mm; Seirin Co., Ltd., Shizuoka, Japan) was inserted bilaterally on an acupoint and maintained at a depth of 10 mm during the test. After insertion, stimulation (rotating the needles manually within an angle of 90°) was performed for 18 s.

Standardised acupuncture employed in the glaucoma study is as follows:
The acupoints were selected on the basis of the principles of TCM (Kurusu et al., 2005). Acupuncture was performed bilaterally for 15 min using disposable stainless-steel needles (0.16 mm or 0.20 mm × 40 mm; Seirin Co. Ltd., Shizuoka, Japan) at acupoints Cuanzhu (BL2), Taiyang (M-HN9), Sibai (ST2), Zusanli (ST36), Sanyinjiao (SP6), Taixi (KI3), and Taichong (LR3) while the patient was in the supine position, and bilaterally for 15 min at acupoints Fengchi (GB20), Ganshu (BL18), and Shenshu (BL23) while the patient was in the prone position. Each needle was simply inserted without any intention of eliciting specific responses (e.g., de-qi feelings) to a depth of approximately 20 mm at acupoints ST36, SP6, K13, GB20, BL18, and BL23. The needles were inserted to a depth of approximately 3–10 mm for the BL2, M-HN9, ST2, and LR3 acupoints. Neither needle manipulation techniques nor other auxiliary interventions were used.

As stated above, reproducibility is the challenge for this type of moxibustion experiment. Several studies have assessed the effect of moxibustion (Freire et al., 2005; Joos et al., 2004; Joos et al., 2006; Yun et al., 2007), but controlling the temperature achieved by burning moxa has been difficult. The actual temperature depends on the practitioner’s experience, and the temperature distribution in the target area is not uniform, making quantification of the effects of moxibustion difficult.
Moxibustion is a way of heating a local area in which moxa is burned at acupoints on the skin. Because the direct burning of moxa on the skin can cause burns, materials such as salt, ginger, or garlic may be used as a buffer between the skin and the moxa. To overcome such a challenge, we developed a heat transfer control device (HTCD) for local thermal stimulation that can be used to simulate the heat and mechanical pressure effects of moxibustion through collaboration with Prof. Shigenao Maruyama from the Institute of Fluid Science at Tohoku University (Figure 2) (Maruyama et al., 2009; Okajima et al., 2009; Takashima et al., 2007; Takashima et al., 2008). This device consists of a heating disk (10 cm in diameter) that can be set at a certain temperature with a precision of 0.1 °C that heats a small area to a uniform temperature, thus allowing us to quantify the effects of moxibustion. There are several acupoints located at the paraumbilical region. In particular, Shenque (CV8) and ST25 are considered by TEAM to influence the stomach, spleen, and intestines (Chen, 1981). This size of the disk can cover the important acupoints CV8 and ST25 for the treatment of digestive diseases. It also provides consistent area and temperature, both of which are crucial in this type of clinical research.

Fig. 2. (A) The heat transfer control device consists of a heating disk, a temperature sensor, and a heat controller. (B) Thermal stimulation to the paraumbilical region with the device for 20 min at 40 °C.

4. Haemodynamic evaluation method

Blood pressure, electrocardiogram, impedance cardiography (ICG), and ultrasound were employed to evaluate the haemodynamic changes in the study.

4.1 Blood pressure, electrocardiogram, and ICG

Blood pressure was measured using an oscillometer on the subjects’ left upper arms. Three monitoring electrocardiographic electrodes were attached to the anterior chest. ICG is a non-invasive monitoring method that allows for cardiac output measurements based on the thoracic resistance changes that result from variations in intrathoracic BFV (Albert et al., 2004; Perrino et al., 1994). Four ICG electrodes (BioZ ICG Module, Dash 3000®, GE Healthcare, Milwaukee, USA) were placed at the base of the neck and at the level of the xiphoid process in the midaxillary line.
4.2 Ultrasound system
Blood flow changes rapidly in the arteries of the extremities, especially in the peripheral arteries (Nimura et al., 1974). Pulse Doppler ultrasound is a non-invasive method for evaluating blood flow velocity. High-resolution ultrasound combined with pulsed Doppler ultrasound is useful for investigating small vessels such as the coronary, splenic, adrenal, and superior mesenteric artery (SMA) (Gembruch, 1996).
A Prosound α10® ultrasound system (Aloka Co., Ltd., Tokyo, Japan) was employed for measuring the haemodynamics of radial artery (RA), brachial artery (BA), and SMA. The haemodynamics of the retrobulbar vessels was assessed using a LOGIQ e® ultrasound system (GE Healthcare, Tokyo, Japan).

4.2.1 Measurements to compare RA and BA haemodynamics
Although the RA can be easily visualised by ultrasound, its diameter is far smaller than that of the BA. To compare the changes of haemodynamics in the RA and BA, we employed an e-Tracking system® (Aloka Co., Ltd., Tokyo, Japan) built into the Prosound α10® to obtain more minute data with a high-resolution linear array transducer (13 MHz). The e-Tracking system® is a computer-assisted analysis software developed for the measurement of flow-mediated vasodilatation, which is usually measured at the BA (Corretti et al., 2002; Deanfield et al., 2005). The software could automatically detect the vessel edge and continuously measure the vessel diameter and BFV with a precision of 0.01 mm (Soga et al., 2007).
Making the correct assessment of haemodynamics is more difficult and requires some skill. Fixing the probe at the optimal position and preventing upper-limb movement are crucial. The transducer was fixed with a special probe holder (MP-PH0001, Aloka Co., Ltd.) throughout the test at the site where the clearest B-mode image of the anterior and posterior vessel wall was obtained (Figures 3A and 3B). Compression of the artery was carefully avoided. The RA or BA diameter was automatically monitored when the tracking gate was placed on the intima of the vessel. The waveform of the vessel diameter changes over the cardiac cycle was displayed in real time using the e-Tracking system (Figure 3C). A Doppler angle of ≤60° was maintained to ensure accurate measurement. BFV was calculated automatically as the Doppler flow velocity (corrected for the angle) multiplied by the heart rate and the vessel cross-sectional area (Burns & Jaffe, 1985; Gill, 1985; Taylor & Holland, 1990). The use of this system avoids operator bias, increases reproducibility, and improves accuracy.
It is reported that changes in venous return due to respiration cause oscillation of the stroke volume and blood pressure (Hsieh et al., 2003). Thus, the arterial pulse should be modified by breathing (Korpas et al., 2006). The subjects were asked to breathe every 6 s during the test, and the haemodynamic parameters were calculated as average values for each 6-s period to minimise the influence of respiration in the present study.

4.2.2 Haemodynamic measurements to evaluate the effects of simple acupuncture in the SMA and BA and the effects of thermal stimulation and herbal medicine in SMA
A 5-MHz convex transducer was used to measure SMA haemodynamics and a 13-MHz linear transducer was used for the BA haemodynamics. The cross-sectional areas (CSAs) of the SMA and BA were calculated using the vessel diameter (VD) value, the distance from the anterior to the posterior intima (Figures 4A and 4C).
Fig. 3. (A) Ultrasound measurement of the radial artery with a special probe holder. (B) Brachial artery measurement. (C) Left, the vessel image and the position of the tracking gate of the artery; Right, the changes in the vessel diameter, Doppler flow, and flow velocity determined using an automated edge detection device and computer analysis software (e-Tracking system®, Aloka Co., Ltd., Tokyo, Japan).

SMA measurements were acquired within 2–3 cm of the arterial origin (Figure 4B) (Gill, 1985; Van Bel et al., 1990). Pulsed Doppler signals were obtained at the same site. The BA was monitored at a site above the elbow (Figure 4D).

To ensure accurate measurements, a Doppler angle of ≤60° was employed. Each Doppler waveform was drawn automatically and calculated using the ultrasound system software. The following haemodynamic parameters were determined.

Haemodynamic parameters: VD, CSA \((VD/2)^2 \times \pi\), peak systolic velocity (PSV), end-diastolic velocity (EDV), resistive index \((RI = (PSV-EDV)/PSV)\), pulsatility index \((PI = (PSV-EDV)/mean flow velocity (MV))\), MV, and blood flow volume \((CSA \times MV)\) (Gill, 1985; Van Bel et al., 1990).

Each parameter was recorded 3 times in 3 different cardiac cycles and averaged for each subject in an effort to minimise random errors (Gill, 1985).
4.2.3 Haemodynamic measurement of the retrobulbar arteries

Real-time and non-invasive haemodynamic measurement using colour Doppler imaging (CDI) has been applied for measuring retrobulbar vessel haemodynamics, and its reproducibility has already been demonstrated (Matthiessen et al., 2004). Ultrasound measurements were performed carefully to avoid any pressure on the eye. CDI was performed using a 13-MHz linear transducer for retrobulbar vessels such as the ophthalmic artery (OA), central retinal artery (CRA), and short posterior ciliary artery (SPCA). The OA was examined approximately 20 mm behind the globe (Figure 5A). The CRA was examined within 5 mm of the retrolaminar portion of the optic nerve (Figure 5B). The temporal SPCA was examined approximately 5–10 mm behind the globe (Figure 5C). All blood flow velocity waveforms were measured at the corrected Doppler angle. Resistive index (RI = (PDV-EDV)/PSV) was also measured in each retrobulbar vessel.

Fig. 4. Haemodynamic data obtained by ultrasound. Vessel diameter of the superior mesenteric artery (SMA) (A) and the brachial artery (BA) (C) were measured in B-mode. Blood flow velocity of the SMA (B) and the BA (D) were obtained by pulsed Doppler.
Fig. 5. Horizontal scans collected using colour Doppler imaging through the globe showing the (A) ophthalmic artery, (B) central retinal artery, and (C) short posterior ciliary artery.

5. Short-term effect of acupuncture on the peripheral arterial system of the upper limb and systemic haemodynamics

The radial, carotid, fibular, and posterotibial arteries have been used in pulse diagnosis. However, the radial pulse is more common in clinical pulse diagnosis. There have been some reports about the haemodynamic influences of acupuncture using a single acupoint (Haker et al., 2000; Syuu et al., 2001; Wan et al., 2000), but its effects on BFV changes in the peripheral artery have not been demonstrated. We reported the only preliminary study on the effects of simple acupuncture on the RA BFV (Takayama et al., 2010). Furthermore, the relationship between peripheral artery blood flow and the cardiac index with regard to acupuncture has not been studied in human subjects.

We hypothesised that LR3, the primary acupoint in the liver meridian, could affect the peripheral artery BFV and the cardiac index. Blood flow to the RA is supplied via the BA. The aim of this study is to clarify the effect of acupuncture on BFV of the RA and BA and the cardiac index in healthy subjects.

5.1 Methods
5.1.1 Subjects
Eighteen healthy volunteers (age, 32 ± 5 years; range, 24–40 years; 14 men and 4 women) were enrolled in the study. The study protocol was approved by the Ethics Committee of Tohoku University Graduate School of Medicine. Written informed consent was given by all the subjects prior to participation.
5.1.2 Setting
All subjects were examined in the morning after an overnight fast. They were placed in a quiet, air-conditioned room (25–26 °C) and told to rest in the supine position. Each subject’s right arm was fixed and the right RA or BA was scanned longitudinally at a position in which the vessel diameter and Doppler wave readings were stable.

5.1.3 Protocol
An outline of the study is shown in Figure 6. Each subject underwent the test on the RA first followed by the BA at 7-day intervals. We performed acupuncture bilaterally on the LR3 and measured the haemodynamics of the RA or BA from rest to 180 s after acupuncture. Cardiac index was measured and the BA test was performed at same time.

After 10 min of resting in the supine position, haemodynamic measurements of blood pressure using the right RA or BA were taken (Corretti et al., 2002; Deanfield et al., 2005). Simple acupuncture was performed by a licensed acupuncturist. We measured RA or BA haemodynamics before and during acupuncture and at 30, 60, and 180 s after acupuncture (Figure 6). The haemodynamic parameters, including vessel diameter, BFV, cardiac index, and heart rate, were continuously recorded. Haemodynamic parameter values were calculated as averages for each 6-s period. Blood pressure was measured under resting conditions and 180 s after acupuncture.

Fig. 6. Outline of the test. Ultrasound measurements were performed before, during, and 30, 60, and 180 s after acupuncture. Acupuncture consists of needle insertion and stimulation. An impedance cardiography monitor was used in the brachial artery test.

5.1.4 Statistical methods
Statistical analysis was performed using SPSS software (version 16.0; SPSS Japan Inc., Tokyo, Japan). Repeated-measure analysis of variance followed by Dunnett’s post hoc test was used for statistical comparison between the measure points. Results are presented as the mean (SD) and $P < 0.05$ indicated significance for all statistical analysis.

5.2 Results
5.2.1 RA and BA haemodynamics
Neither the systolic nor the diastolic diameter of the RA or BA significantly changed in the test. The BFV was determined as millilitres per second per square metre and the percent
change at each time was calculated in relation to before acupuncture. BFV in the RA decreased significantly during acupuncture (mean (SD); 0.24 (0.23) mL/(s·m²), \( P < 0.01 \)) but increased significantly at 60 s (0.62 (0.41) mL/(s·m²), \( P < 0.05 \)) and 180 s after acupuncture (0.61 (0.31) mL/(s·m²), \( P < 0.05 \)) compared with before acupuncture (0.51 (0.31) mL/(s·m²)). BFV in the BA also decreased significantly during acupuncture (0.56 (0.33) mL/(s·m²), \( P < 0.05 \)) and increased significantly at 180 s after acupuncture (0.87 (0.36) mL/(s·m²), \( P < 0.05 \)) compared with before acupuncture (0.73 (0.38) mL/(s·m²)). Figure 7 illustrates the profile of the percent changes in RA and BA BFV. BFV in the RA decreased significantly during acupuncture \( (P < 0.01) \) but increased significantly at 180 s after acupuncture \( (P < 0.05) \). BFV in the BA also increased significantly at 180 s after acupuncture \( (P < 0.05) \).

![Figure 7](image_url)

**Fig. 7.** Percent change in blood flow volume in the radial and brachial arteries. Each variable is relative to the 6-s period before acupuncture. Values represent the mean (SD). AP, acupuncture. **\( P < 0.01 \) versus before acupuncture.

### 5.2.2 Systemic haemodynamics

The percent change in cardiac index did not significantly change during acupuncture or at 30, 60, or 180 s after acupuncture compared with the values before acupuncture. Heart rate significantly decreased during acupuncture relative to that before acupuncture \( (P < 0.01) \). However, these values returned to before acupuncture levels 30 s after acupuncture. Neither systolic nor diastolic blood pressure changed significantly after acupuncture compared with before acupuncture. Systemic vascular resistance was calculated using the cardiac index and the mean blood pressure. The percent change in the systemic vascular resistance index decreased significantly after acupuncture compared with the value before acupuncture \( (P < 0.05) \).

### 5.2.3 Adverse events

There were no local complications such as bleeding, haematoma, or infection.
5.3 Discussion
To our knowledge, this is the first report to provide physiological evidence that acupuncture at only 1 acupoint has an effect on the peripheral and systemic haemodynamics in human subjects. The present result demonstrated that RA and BA BFV decreased immediately during acupuncture at LR3 and increased 180 s after acupuncture. While the cardiac index did not change significantly, the systemic vascular resistance index decreased significantly after acupuncture. We showed a decrease in BFV of the RA and BA during acupuncture and an increase in volume 180 s after acupuncture. We speculate that the response of acupuncture on peripheral artery haemodynamics during acupuncture was due to an increase in sympathetic tone as an extreme rapid response to the intervention caused by needle insertion.

These results suggest that the mechanism of increased blood flow by acupuncture is mainly due to decreased peripheral vascular resistance rather than to an increase in the cardiac index. The present findings also indicate that acupuncture at a single point increases peripheral blood flow without increasing the cardiac index, suggesting that acupuncture treatment can affect sympathetic tone in the upper limbs.

In conclusion, we measured the effect of acupuncture on the haemodynamics of the upper limb using high-resolution ultrasound.

5.3.1 Study limitations
This study had 2 primary limitations. The e-Tracking system cannot simultaneously show the pulsatility or resistive index, both of which reveal distal vascular resistance. However, continuous recording using this system showed that the blood flow velocity patterns changed gradually starting 60 s after acupuncture.

The test duration was <15 min, which may be insufficient for evaluating the effects of acupuncture. We attempted a longer test duration in a preliminary study, but fixing the right upper limb for more than 15 min was difficult due to muscle strain and cramps.

The present findings suggest that acupuncture at a single acupoint can alter both RA and BA haemodynamics in healthy subjects. However, these results should be treated with caution considering that this is a pilot study with no control intervention and with a limited sample size.

5.3.2 Future studies
In future studies, we plan to compare changes in peripheral BFV and cardiac index with control conditions (e.g., another acupoint).

6. BFV changes in the SMA and BA with abdominal thermal stimulation
In TEAM, a local thermal therapy known as moxibustion is widely used for conditions such as pain, nausea, vomiting, neurodegenerative diseases, inflammatory bowel diseases, and cerebrovascular and cardiovascular diseases (Giovanni, 1994; Cheng & Cheng, 2008; Wu et al., 2006).

Under normal conditions, SMA blood flow pattern and velocity show large variations due to the metabolic activity of the bowel (Kjeldsen & Schaffalitzky de Muckadell, 1993; Moneta et al., 1988; Perko, 2001). SMA BFV also changes in several diseases (Byrne et al., 2001; Erden et al., 1997; Sigirici et al., 2001). BFV is also strongly related to mesenteric ischaemia, especially chronic mesenteric ischaemia (Dietrich et al., 2007). To date, no reports have examined SMA blood flow changes in relation to moxibustion therapy.
The aim of this study was to evaluate SMA BFV changes in healthy subjects using abdominal ultrasound after thermal stimulation with an HTCD.

6.1 Methods
6.1.1 Subjects
Twenty-four healthy men (age, 31 ± 7 years; range, 21–44 years) were enrolled in the study. The study protocol was approved by the Ethics Committee of Tohoku University Graduate School of Medicine. Written informed consent was given by all subjects prior to participation.

6.1.2 Setting
All subjects were examined in the morning after an overnight fast (at least 8 h). They were placed in a quiet, air-conditioned room (temperature: 25–26 °C) and told to rest in the supine position.

To quantify the heat delivered, we developed an HTCD instead of moxibustion for local thermal stimulation (Figure 2) (Takashima et al., 2008). The temperature of the heating disk could be increased incrementally to the target without exceeding it. Thermal damage occurs when the tissue temperature rises above 44 °C (Jiang et al., 2002; Ng & Chua, 2002). As a result, the disk temperature was set at 40–41 °C for safety. A patent for this device is pending in Japan.

6.1.3 Protocol
An outline of the study is shown in Figure 8. This is a prospective observational study. We performed abdominal thermal stimulation at the paraumbilical region using an HTCD for 20 min and measured SMA haemodynamics by ultrasound from rest until 40 min after thermal stimulation. To compare intestinal and peripheral BFV, we measured the haemodynamics of the BA simultaneously.

After the ultrasound system was positioned, the subjects rested in the supine position for 10 min. Abdominal thermal stimulation was done for 20 min at the paraumbilical region using the HTCD to a temperature of 40 °C. After 5 min, if the subjects were used to the heat, the temperature was increased to 41 °C. After thermal stimulation for 20 min, the device was removed. We measured the SMA and BA haemodynamics, heart rate, and blood pressure at rest (baseline), after 15 min of thermal stimulation, and at 10, 20, 30, and 40 min after the end of thermal stimulation (Figure 8).

Fig. 8. Outline of the study. Thermal stimulation was applied to the paraumbilical region using a heat transfer control device for 20 min. Haemodynamics were measured at rest (baseline), during thermal stimulation (after 15 min), and at 10, 20, 30, and 40 min after the completion of thermal stimulation.
6.1.4 Statistical analysis
Statistical analysis was performed using SPSS software (version 16.0; SPSS Japan Inc.). Repeated measures analysis of variance with a Tukey post hoc test was used for statistical comparison with baseline. Although 24 subjects were enrolled in our study, data of 3 subjects were excluded because their examinations were technically unsuccessful (the SMA could not be identified clearly due to intestinal gas). As a result, data of 21 subjects were included in the final analysis. Results are presented as the medians and quartile (first and third), the mean and SEM, and 95% confidence intervals. $P < 0.05$ was used to indicate significance in all statistical tests.

6.2 Results
6.2.1 SMA and BA haemodynamics
The SMA diameter significantly increased during thermal stimulation ($P < 0.01$), as well as at 10 ($P < 0.01$), 20 ($P < 0.01$), and 30 min ($P < 0.05$) after thermal stimulation. The BA diameter also increased significantly during thermal stimulation ($P < 0.01$) and at 20 min ($P < 0.05$) after thermal stimulation. The MV in the SMA increased significantly during thermal stimulation ($P < 0.01$) as well as at 10 ($P < 0.01$) and 20 min ($P < 0.01$) after the end of thermal stimulation, but the MV in the BA decreased significantly at 30 ($P < 0.01$) and 40 min ($P < 0.01$) after thermal stimulation. The BFV in the SMA increased significantly during thermal stimulation ($P < 0.01$) as well as at 10 ($P < 0.01$) and 20 min ($P < 0.05$) after thermal stimulation (Figure 9A). In the BA, however, BFV decreased at 40 min after the end of thermal stimulation ($P < 0.01$) (Figure 9B).
PSV in the SMA increased significantly during thermal stimulation ($P < 0.01$) but it decreased significantly in the BA at 30 ($P < 0.05$) and 40 min ($P < 0.01$) after thermal stimulation. EDV did not change in the SMA, but it decreased significantly in the BA at 30 ($P < 0.01$) and 40 min ($P < 0.01$) after the end of thermal stimulation. RI in the SMA did not change, but it increased significantly in the BA at 40 min after the end of thermal stimulation ($P < 0.01$). However, the PI did not change significantly in either the SMA or the BA compared with baseline.

Fig. 9. Blood flow volume changes in the superior mesenteric artery (SMA) (A) and in the brachial artery (BA) (B). Values represent the mean and SEM. *$P < 0.05$, **$P < 0.01$ versus baseline.
6.2.2 Systemic haemodynamics
There were no significant changes in heart rate compared with baseline. Systolic blood pressure showed a significant increase at 40 min after the end of thermal stimulation \((P < 0.05)\), but no significant changes in diastolic blood pressure was observed between baseline and 40 min after thermal stimulation.

6.2.3 Adverse events
There were no complications such as local burns, pain, or discomfort that required treatment.

6.3 Discussion
To our knowledge, this is the first report to examine BFV changes in the SMA or BA after local thermal stimulation using an ultrasound system. The present study showed that BFV in the SMA increased significantly during thermal stimulation and at 10 and 20 min after stimulation. BFV decreased significantly in the BA 40 min after stimulation. The thermal stimulation and pressure applied to the skin by the present method influences somatic afferent fibres. We speculate that the present method of stimulation increases SMA blood flow mediated by somatic group II, III, and IV afferent fibres and parasympathetic cholinergic nerves. Moxibustion is often combined with acupuncture; however, in Western countries, it is not often used because of the odour of the burning moxa. HTCD can heat the target area uniformly without any odour or fire-associated danger. Thus, abdominal thermal therapy using HTCD may be useful in place of moxibustion for patients with intestinal disorders. In conclusion, we quantitatively measured the effect of local thermal stimulation using an HTCD and high-resolution ultrasound. Thermal stimulation of the paraumbilical region in healthy subjects increased blood flow in the SMA 20 min after stimulation.

6.3.1 Study limitations
This trial was a pilot study with a small sample size and no controls or randomisation. All subjects were men.

6.3.2 Future studies
In future studies, we plan to recruit men and women and use a larger sample size, a control group, and randomisation. We hope to study the effect of thermal stimulation on patients with disorders. We would also like to undertake further studies to clarify the effect of local thermal stimulation, for not only the abdomen but also other areas.

7. Effect of abdominal warming and herbal medicine on SMA blood flow
In TEAM, warming of the abdomen is performed to dispel cold and help Yang recovery via the use of moxibustion or warming herbal medicines (Liu et al., 2006). However, their physiological effect on abdominal blood flow has never been investigated. Daikenchu-to is one of the warming herbal medicines that is used in TEAM to treat coldness in the Middle Jiao and abdominal pain (Liu et al., 2004). Daikenchu-to has traditionally been used in Japan for the treatment of intestinal obstruction and cold feeling in the abdomen. It is reported that Daikenchu-to stimulates colonic motility and increases portal blood flow in humans (Kawahara & Yanaga, 2009; Ogasawara et al., 2008).
The SMA supplies blood to the entire small intestine except for the superior duodenum, and it also supplies the caecum, ascending colon, and most of the transverse colon (Williams & Warwick, 1980). Our preliminary report was the first to show the effect of Daikenchu-to on the BFV of the SMA in humans (Takayama et al., 2009).

The aim of this partly randomised control study was to clarify the physiological effects of warming the abdomen in moxibustion-like stimulation and herbal medicine on SMA BFV in healthy subjects.

7.1 Methods
7.1.1 Subjects
Twenty-eight healthy men were randomly assigned to intervention groups A (age, 33 ± 7 years) and B (age, 35 ± 8 years). As a control group, another 14 healthy men (age, 33 ± 8 years) were assigned to group C. Since randomisation was performed in groups A and B, the study design was a partly randomised trial. We enrolled 42 subjects in this study. The study protocol was approved by the Ethics Committee of Tohoku University Graduate School of Medicine. Written informed consent was given by all subjects prior to participation.

7.1.2 Setting
All subjects were examined in the morning after an overnight fast.

The herbal medicine Daikenchu-to (TJ-100; Tsumura, Co., Tokyo, Japan) was made in the form of a dry powder but is manufactured as an aqueous extract containing processed ginger (*Zingiber officinale*), ginseng (*Panax ginseng*), and zanthoxylum fruit (*Zanthoxylum piperitum*) in the ratio 5:3:2. These plants are all registered in the Pharmacopoeia of Japan. The 3 herbal medicines were extracted with purified water at 95 °C for 1 h and then spray-dried to produce a powder. TJ-100 was made by mixing Daikenchu-to extract powder and maltose syrup powder (Tsumura Co., Tokyo, Japan) in the ratio 1:8 (Tokita Y et al., 2007).

7.1.3 Protocol
An outline of the study is shown in Figure 10. Group A (n = 14) underwent abdominal thermal stimulation at the paraumbilical region using a HTCD for 20 min at 40 °C. Group B (n = 14) took 5.0 g of TJ-100 (Tsumura, Co., Tokyo, Japan) orally with 50 mL of distilled water (37 °C). As a control, group C (n = 14) took 50 mL of distilled water (37 °C) alone. Abdominal ultrasound was performed at rest and at 10, 20, 30, 40, and 50 min after the starting thermal stimulation, after oral administration of TJ-100, or after oral administration of water alone.

7.1.4 Statistical methods
Statistical analysis was performed using SPSS software (version 16.0; SPSS Japan Inc.). Characteristics and BFV changes between groups were compared using ANOVA. Repeated-measures ANOVA with a post-hoc Dunnett’s test was used for statistical comparison to the resting state; *P* < 0.05 was considered significant.

7.2 Results
There were no significant differences in baseline characteristics between groups. SMA BFV increased significantly at 10, 20, 30 min (*P* < 0.01), and 40 min (*P* < 0.05) after the start of local thermal stimulation in group A compared to the resting value. SMA BFV also increased significantly at 10, 20, 30, 40, and 50 min after administration of TJ-100 (*P* < 0.01) in
Fig. 10. Outline of the study. Group A: Thermal stimulation was applied to the paraumbilical region using the heat transfer control device for 20 min. Group B: Daikenchuto (TJ-100; 5.0 g) in distilled water (37 °C; 50 mL) was administered orally. Group C: Distilled water (37 °C; 50 mL) alone was administered orally. Ultrasound measurements were performed at rest and at 10, 20, 30, 40, and 50 min after the start of thermal stimulation, oral administration of TJ-100, or oral administration of water alone.

Fig. 11. Percent changes in superior mesenteric artery blood flow volume from the resting value. Values represent the mean (SD). Repeated-measures ANOVA with a post-hoc Dunnett’s test was used for statistical comparison with the resting state. *P < 0.05, **P < 0.01 vs. the resting value in group A. ††P < 0.01 vs. the resting value in group B.
group B; however, it did not change significantly after administration of water alone in group C. There were significant differences between groups A and C \((P < 0.01)\) and groups B and C \((P < 0.05)\); however, no significant differences were observed between groups A and B \((P = 0.96)\) with respect to BFV changes. Figure 11 displays the percent changes in SMA BFV.

No adverse events were observed in the study.

7.3 Discussion
To our knowledge, this is the first report to examine the physiological effects of warming the abdomen in moxibustion-like stimulation compared with an herbal medicine on SMA BFV in healthy subjects.

The present study showed that SMA BFV was increased by local thermal stimulation of the abdomen and by oral administration of TJ-100 compared with oral administration of water alone. The pattern of blood flow increase was similar in local thermal stimulation on the abdomen and oral administration of TJ-100.

The present findings indicate that warming the abdomen by thermal stimulation or the herbal medicine of Daikenchu-to has a physiological effect in increasing BFV in the SMA.

In conclusion, we evaluated the difference between thermal stimulation with HTCD and herbal medicine on the haemodynamics of SMA using a high-resolution ultrasound system.

7.3.1 Study limitations
Limitations of this study were as follows:
This was a partly randomised control study with a small sample size and enrolled only men. HTCD was developed to simulate the heat and mechanical pressure effects of moxibustion. However, it does not simulate the smell of moxa or the smoke of moxibustion.

The subjects could identify the Daikenchu-to because this medicine is spicy and a little sweet. Thus, the test was not perfect, even though the examiners and subjects were blinded to the treatment.

Intake of food prior to the study was controlled by asking the subjects not to eat before the study. However, the patients fasted at home and were not monitored. Thus, there is a very small chance that an increase in SMA BFV could have occurred due to the subject’s diet.

7.3.2 Future studies
Evaluation of the clinical effects of these therapies in patients with SMA or IMA ischaemia is required. In future studies, we would like to include both genders and patients with low SMA blood flow.

8. Short-term effects of acupuncture on open-angle glaucoma in retrobulbar circulation: additional therapy to standard medication
Glaucoma is one of the causes of blindness (K. Nakae et al., 2005). The main treatment strategy for glaucoma is to control IOP (Weinreb & Khaw, 2004). Although IOP reduction is currently the main target for the treatment of glaucoma, treatment modalities that enhance retrobulbar haemodynamics in addition to reducing IOP may have a beneficial effect on glaucoma therapy. It has been reported that glaucoma is associated with reduced blood flow velocity and elevated RI in the retrobulbar vessels (Akarsu & Bilgili, 2004; Costa et al., 2003;
Kaiser et al., 1997; Rankin, 1999). Impaired ocular circulation contributes to the progression of glaucomatous damage (Satilmis et al., 2003; Schumann et al., 2000; Yamazaki & Drance, 1997). Acupuncture has also been used for the treatment of ocular diseases, including glaucoma, in TEAM (Li, 1999).

The aim of this study was to evaluate haemodynamic changes in the retrobulbar vessels using CDI to investigate the effect of acupuncture on open-angle glaucoma (OAG) eyes.

8.1 Methods
8.1.1 Subjects
Eleven patients with OAG (20 eyes with OAG; 1 man and 10 women; mean age, 63 ± 11 years) were enrolled in the study. Each underwent standard medical treatment for at least 3 months. Patients who underwent laser trabeculoplasty, any ocular surgery, or inflammation within the past year were excluded from the present study. The study protocol was approved by the Ethics Committee of Tohoku University Graduate School of Medicine. Written informed consent was given by all the subjects prior to participation.

8.1.2 Setting
The ultrasound measurements were performed in an air-conditioned room with the patients in the supine position. On the trial days, patients arrived having taken their regular medications.

Each patient received standardised acupuncture therapy in the morning as described above. Five licensed acupuncturists and 1 physician-acupuncturist with >5 years of acupuncture experience administered the acupuncture treatment.

8.1.3 Protocol
An outline of the study is shown in Figure 12. To minimise the effects of diurnal variation, all measurements were recorded at the same time of day (10–11 AM) for each patient by the same examiner. As a control, subjects underwent measurements of the systemic haemodynamics, retrobulbar vessel haemodynamics, and IOP that were performed at rest and 1 hour after rest. One month later, each patient underwent the same measurements before and after acupuncture treatment.

Fig. 12. Outline of the study. Standardised acupuncture was applied at the second visit more than 1 month after the first visit.

8.1.4 Statistical methods
Statistical analysis was performed using SPSS software (version 16.0; SPSS Japan Inc.). The parameters between before and after acupuncture or between control and acupuncture were compared by paired t-test.
8.2 Result
The blood pressure and heart rate did not change significantly by acupuncture. The IOP level significantly decreased by acupuncture compared with before acupuncture ($P < 0.05$). The $\Delta$ value of IOP also significantly decreased by acupuncture compared with control ($P < 0.01$).

Retrobulbar vessel RI in the OA, CRA, and SPCA is shown in Table 1. The RI in the CRA and SPCA decreased significantly by acupuncture compared with that before acupuncture ($P < 0.05$). The $\Delta$ value of RI in the SPCA also decreased significantly by acupuncture compared with that of the control ($P < 0.01$) (Table 1).

No adverse events were observed in the study.

Table 1. Resistive index in the ophthalmic artery, central retinal artery, and short posterior ciliary artery. The values represent the mean and SD. *$P < 0.05$ versus before acupuncture. ††$P < 0.01$ versus control.

8.3 Discussion
To our knowledge, this is the first report to examine haemodynamic changes in retrobulbar vessels related to acupuncture in OAG eyes.

The present findings suggest that acupuncture can alter vessel resistance in the SPCA despite treatment with standard medications. Decreased distal vascular resistance in the SPCA indicates increased blood flow in the choroid. It has been reported that the blood flow in the eye is controlled by sympathetic and parasympathetic nerves and is related to the release of nitric oxide or calcitonin gene-related peptide (Shimura et al., 2002; Wiencke et al., 1994). It has also been reported that the regulation of regional blood flow by somatic afferent stimulation is based on somatoautonomic reflex mechanisms in the choroidal blood flow of the eyeball (Shimura et al., 2002). Haemodynamic changes in the SPCA induced by acupuncture may be related to these mechanisms. Acupuncture may be applied as an additional therapy to treat OAG.

In conclusion, we measured the effect of standardised acupuncture on the retrobulbar haemodynamics in OAG eyes using high-resolution ultrasound.

8.3.1 Study limitations
We should interpret these results cautiously because the present study was a case series study in which intervention was provided only once.

8.3.2 Future studies
Longer observation of acupuncture therapy in future studies is needed to investigate the progression of glaucomatous damage associated with impaired ocular circulation.
9. Conclusion

TM therapies affect the autonomic nervous system and the human body. Invasive measurement methods may also affect the autonomic nervous system. As a result, invasive measurement methods might not accurately evaluate the effect of TM therapies. These studies suggest that use of non-invasive and real-time methods like blood pressure, ECG, ICG, and ultrasound to evaluate haemodynamics could assess the effects of TM therapies on various organs in humans in detail. This type of method may be an ideal indicator for the assessment of the effects of TM therapies in humans.

10. Acknowledgment

The authors would like to thank all of the participants and Mr. Tetsuharu Kamiya, Ms. Ayane Matsuda, and Mr. Souichiro Kaneko (acupuncturists in Department of Acupuncture Therapy, Tohoku University Hospital) for their technical assistance. We also would like to thank Mr. Atsushi Hirano for drawing the figures. The authors would like to thank Prof. Shigenao Maruyama, Prof. Makoto Yoshizawa, Prof. Tomoyuki Yambe, Dr. Satoshi Konno, Prof. Nobuo Yaegashi and Prof. Shinmichi Nitta of Tohoku University for their academic support. These works were supported by Special Coordination Funds for Promoting Science and Technology from the Japanese Ministry of Education, Culture, Sports, Science and Technology; a Grant-in-Aid for Scientific Research (C)(21590753) from the Japanese Ministry of Education, Culture, Sports, Science and Technology; and Health and Labour Sciences Research Grants for Clinical Research from the Japanese Ministry of Health, Labour and Welfare.

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Acupuncture and related techniques are useful tools for treating a spectrum of diseases. However, there are still many areas of controversy surrounding it. We hope this book can contribute to guide the advance of this ancient medical art. In the present work, the reader will find texts written by authors from different parts of the world. The chapters cover strategic areas to collaborate with the consolidation of the knowledge in acupuncture. The book doesn’t intend to solve all the questions regarding this issue but the main objective is to share elements to make acupuncture more and better understood at health systems worldwide.

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