‘Real Angiosome’ Assessment from Peripheral Tissue Perfusion Using Tissue Oxygen Saturation Foot-mapping in Patients with Critical Limb Ischemia

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WHAT THIS PAPER ADDS
This article describes a new method of StO2 foot-mapping for the assessment of peripheral tissue perfusion in critical limb ischemia, and presents a new concept, namely the “real angiosome,” which is compared with the conventional angiosome model. StO2 foot-mapping can non-invasively detect the actual distribution of peripheral tissue perfusion (real angiosome) in the CLI patient’s foot more appropriately than the assessment based on angiography and the angiosome model.

Objectives: The “tissue oxygen saturation (StO2) foot-mapping” method was developed using a non-invasive near-infrared tissue oximeter monitor to classify the foot regions as ischemic and non-ischemic areas. The purpose of this study was to evaluate StO2 foot-mapping as a reliable method to detect ischemic areas in the feet of patients with critical limb ischemia (CLI), and to compare the results with assessments from the angiosome model.

Methods: The foot areas of 20 CLI patients and 20 healthy controls were classified into four regions: (1) 0 ≤ StO2 < 30%, (2) 30 ≤ StO2 < 50%, (3) 50 ≤ StO2 < 70%, and (4) 70 ≤ StO2 ≤ 100% to perform StO2 foot-mapping. Each area occupancy rate was compared between the two groups, and the threshold StO2 value for detecting ischemia was set. Next, the locations of ulcers (in 16 patients) were compared to the predicted ischemic regions by the StO2 foot-mapping and by the angiosome model and angiography.

Results: In regions (1) and (2) (StO2 < 50%), the area occupancy rate was significantly higher in the CLI group and almost zero in the control group, so that the threshold StO2 value for detecting ischemia was set at 50%. The locations of ulcers were compatible with StO2 foot-mapping in 87.5% of the cases (14/16), while they were compatible with the assessment from the angiosome model in 68.8% of the cases (11/16).

Conclusions: This study suggests that StO2 foot-mapping can successfully and non-invasively detect ischemic areas in the peripheral tissue of the foot, and also more appropriately than the assessment provided by the angiosome model. StO2 foot-mapping can be used to evaluate the real angiosome: the real distribution of the peripheral tissue perfusion in the CLI patient’s foot, which is determined by the peripheral microvascular blood flow, rather than the main arterial blood flow.

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INTRODUCTION
For the appropriate treatment of critical limb ischemia (CLI), it is necessary to evaluate peripheral tissue perfusion and understand the distribution of ischemic and non-ischemic areas in a CLI patient’s foot.

Recently, the angiosome concept has been an essential idea for both the evaluation of tissue perfusion in CLI patients’ feet and in the treatment of CLI. The angiosome is a model of five or six distinct three-dimensional blocks of tissue fed by three main source arteries and their branches to the foot and ankle. Angiography can visualize the main arterial blood flow and the branches, but cannot visualize the microvascular blood flow that directly feeds peripheral tissue, so the angiosome model has been used to predict the peripheral tissue perfusion from the main arterial blood flow. However, discrepancies sometimes occur between the predicted ischemic region from angiography using the angiosome model and the actual ulcerated region in a CLI patient’s foot.

We developed a new method of “tissue oxygen saturation (StO2) foot-mapping” utilizing a near-infrared tissue oximeter monitor to non-invasively evaluate the peripheral tissue perfusion and detect the ischemic areas in the entire...
foot of a CLI patient. We measure the StO2 of many points on the foot using the near-infrared tissue oximeter monitor, and make a map by classifying the foot regions into low and high StO2 areas.

In order to evaluate the appropriateness of StO2 foot-mapping as a reliable method to detect ischemic areas in CLI, the results of StO2 foot-mapping were compared for CLI patients and healthy controls. Furthermore, in order to assess the validity of StO2 foot-mapping to locate ischemic regions in CLI patients’ feet, the locations of ulcers in the feet were compared with the predicted ischemic regions using StO2 foot-mapping and using the angiosome model.

MATERIALS AND METHODS

Subjects

We performed a prospective study on 20 CLI patients (20 limbs) with chronic symptomatic peripheral arterial disease (PAD) in Rutherford clinical categories 4/5/6 (ischemic rest pain or ischemic ulceration) prior to revascularization, between January 2012 and September 2012. There were 14 males and six females, with a mean age of 71.2 ± 10.1 years (55–88 years). There were four Rutherford 4, 13 Rutherford 5 and three Rutherford 6 cases. Co-morbidity included nine diabetics on insulin and 15 with chronic kidney disease on hemodialysis.

Angiography was carried out on all CLI patients within 6.40 ± 5.72 days (0–21 days) after StO2 measurement, and revascularization therapies were performed on all patients (endovascular therapies in 18 cases and distal bypass operations in 2 cases).

In contrast, 20 healthy volunteers (20 limbs; 5 males, 15 females) with no ischemic symptoms and no past history of PAD, with a mean age of 32.5 ± 6.88 years (24–52 years), were included as the control group. The dorsalis pedis artery and posterior tibial artery (PTA) pulses were checked in order to confirm normal circulation.

The study was conducted in accordance with the Declaration of Helsinki on investigations in humans and was approved by the institutional ethics committees at the participating institutions. Informed consent was obtained from all patients and volunteers.

StO2 measuring device

The near-infrared tissue oximeter monitor, OXY-2 (ViOptix Inc., Fremont, CA, USA), was used to measure the StO2 (Fig. 1). The OXY-2 is an optical measuring device using near-infrared rays to non-invasively measure the oxygen saturation of hemoglobin in soft tissue, which is located under the sensor probe. The StO2 can be measured in real time and recorded continuously by radiating near-infrared rays at two wavelengths (830 nm and 690 nm) that are specifically absorbed by oxyhemoglobin (HbO2) and deoxyhemoglobin (Hb), respectively, up to a depth of 0–10 mm, and by sensing diffuse light with four optical sensors inside the sensor probe. The StO2 is the percentage of saturated hemoglobin (StO2 (%) = 100 × HbO2/(HbO2 + Hb)). StO2 values can be measured within 10 seconds per point, by applying a sensor probe on the skin surface, while another approximately 10 seconds are required to stabilize the measurement values. Once the measurement values are obtained, the sensor probe can immediately be moved to the next measurement position, making speedy measurement possible.

StO2 foot-mapping

In order to assess the StO2 values of the entire foot, the boundary values of StO2 were set to 30%, 50%, and 70%, and about 60 points of StO2 on the foot surface were measured. After measuring the StO2, the StO2 value was classified as, (1) 0 ≤ StO2 < 30%, (2) 30 ≤ StO2 < 50%, (3) 50 ≤ StO2 < 70%, (4) 70 ≤ StO2 ≤ 100%, and that point on the foot was marked (four types of mark had been selected before the examination). In order to be able to rapidly perform the measurements, it was sometimes necessary to measure several points consecutively, and if the adjacent points were classified in the same StO2 range, a single mark was made in the region. In the boundary region detailed measurements were made to determine its precise position. After all the measurements had been carried out, boundary lines were drawn according to the
markings of the four StO2 value areas to complete a StO2 foot-map (Fig. 2). After finishing the mapping, some markings were erased to make the map easier to see. The number of measurement points per patient varied according to the complexity of the peripheral tissue perfusion, but the average number of measurements was approximately 60 per foot, and the average time required for each foot was approximately 15 minutes.

The mapped foot was photographed with a digital camera from two directions (dorsal and plantar sides of the foot) for recording. With respect to the scope of mapping, the dorsal region included the area from the metacarpophalangeal (MP) joint to the distal edge of the medial and lateral malleolus, excluding the toes, while the planter regions included the area from the MP joint to the calcaneal region, excluding the toes. Measurement in the toes was excluded because the proximity of the bones to the skin made accurate measurement impossible.

The photographs were processed, and the four territories from (1) to (4) were classified by color, using the Photoshop software program (Adobe Systems Inc., San Jose, CA, USA) in a bmp file format. The areas of the four territories were measured in pixel counts, to calculate the occupancy rate defined as the surface ratio between each region and the entire area (Fig. 2).

The same physician in charge of the examination measured the StO2 at outpatient clinics or in the hospital wards. The subjects were supine during measurement, with the foot horizontal after setting a soft cushion under the lower leg in order to avoid putting pressure on the heel.

**Items for assessment**

Comparison of the StO2 foot-mapping between the CLI group and the control group. The area occupancy rate of each StO2 value region, (1) $0 \leq \text{StO2} < 30\%$, (2) $30 \leq \text{StO2} < 50\%$, (3) $50 \leq \text{StO2} < 70\%$, and (4) $70 \leq \text{StO2} \leq 100\%$, was compared between the CLI group and the control group in order to evaluate the appropriateness of StO2 foot-mapping as a method to detect ischemic areas in a CLI patient’s foot.

Based on the results, the threshold StO2 value was set to detect ischemic areas.

**Figure 2.** Examples of StO2 foot-mapping. StO2 foot-maps of a patient with critical limb ischemia (CLI) (A) and a control (B) were made by directly recording with a pen onto the foot skin, with boundary StO2 values of 30%, 50%, and 70%. Four territories from (1) to (4) were classified by color, wherein (1) $0 \leq \text{StO2} < 30\%$ was black, (2) $30 \leq \text{StO2} < 50\%$ was gray, (3) $50 \leq \text{StO2} < 70\%$ was pink, and (4) $70 \leq \text{StO2} \leq 100\%$ was red. (A) The CLI patient: area (1) (black) occupancy rate of the territory was 63.9% (dorsal) and 47.8% (plantar), area (2) (gray) occupancy rate of the territory was 32.4% (dorsal) and 45.1% (plantar), area (3) (pink) occupancy rate of the territory was 3.7% (dorsal) and 7.2% (plantar), and area (4) (red) occupancy rate of the territory was 0% (dorsal) and 0% (plantar). (B) The control subject: area (1) (black) occupancy rate of the territory was 0% (dorsal) and 0% (plantar), area (2) (gray) occupancy rate of the territory was 8.3% (dorsal) and 30.5% (plantar), area (3) (pink) occupancy rate of the territory was 8.3% (dorsal) and 30.5% (plantar), and area (4) (red) occupancy rate of the territory was 91.7% (dorsal) and 69.5% (plantar).
Comparison of the locations of ulcers and the predicted ischemic regions by the StO2 foot-mapping and by the angiosome model. The 16 patients with Rutherford 5/6 status, who had ischemic ulcers, were included in the following evaluation.

**The location of the ulcer compared with the results of StO2 foot-mapping.** The area under the threshold StO2 value (described above) was considered to be an ischemic area, and foot regions of CLI patients were classified into low StO2 (ischemic) and high StO2 (non-ischemic) areas. The compatibility between the locations of ulcers and predicted ischemic areas in StO2 foot-mapping was evaluated. The findings were judged to be compatible if the ulcers were surrounded mostly (more than 90%) by low StO2 areas.

**The location of the ulcer compared with the results of the angiography and the angiosome model.** From the result of angiography, the distribution of ischemic and non-ischemic areas in a CLI patient’s foot was predicted utilizing the angiosome model. There were minor differences in the angiosome models used among past reports.1–3 We used the angiosome shown in Fig. 3 to predict the ischemic and non-ischemic areas in a CLI patient’s foot.

If the feeding arteries (anterior tibial artery, medial plantar artery, lateral plantar artery, calcaneal branch of the PTA, peroneal artery) were visualized to their own angiosome regions by angiography, even if by way of collateral vessels, the angiosomes of these arteries were predicted to be a non-ischemic.

The compatibility between the locations of the ulcers and predicted ischemic areas from the angiosome model was then evaluated.

**Statistical analysis**

The differences between the CLI group and the control group were reviewed using the Mann—Whitney test.

**RESULTS**

StO2 foot-mapping was possible in all cases in both the CLI group and the control group. Angiography was performed on all CLI patients within an average of 6.40 ± 5.72 days (0–21 days) from the date of StO2 measurements.

**Comparison of StO2 foot-mapping between the CLI and control groups**

The total StO2 foot-mapping data (area occupancy rate) of the dorsal and plantar regions are shown (Fig. 4A). The average (dorsal and plantar) area occupancy rate of the four regions, (1) 0% ≤ StO2 < 30%, (2) 30% ≤ StO2 < 50%, (3) 50% ≤ StO2 < 70% and (4) 70% ≤ StO2 ≤ 100%, was

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**Figure 3.** The angiosomes of the foot and ankle. The six angiosomes of the foot and ankle are fed by the three main arteries. The anterior tibial artery (ATA) becomes the dorsalis pedis artery supplying the dorsum of the foot. The PTA feeds the toes, the sole, and heel of the foot. The three main branches of the PTA supply distinct portions of the sole: the calcaneal branch to the heel, the medial plantar artery to the instep, and the lateral plantar artery to the lateral midfoot and the forefoot. The second to fifth toes are supplied by the lateral plantar artery. The first toe may be supplied by the medial plantar artery via the deep branch, by the lateral plantar artery via the plantar arch, and by the anterior circulation; as a result, the first toe is classified as an independent angiosome supplied by the three arteries. The peroneal artery supplies the lateral border of the ankle and heel.
compared between the CLI group and the control group (Fig. 4B). Significant differences were found in regions (1), (2), and (4) (significance level < 1%).

In regions (1) and (2) (StO2 < 50%), the area occupancy rate was significantly higher in the CLI group and almost zero in the control group, so that the threshold StO2 value was set at 50% for the detection of ischemic areas in a CLI patient’s foot. The threshold StO2 value of 50% was used for subsequent evaluations.

**Comparison of the locations of ulcers and the predicted ischemic regions by the StO2 foot-mapping and by the angiosome model**

Using the threshold StO2 value of 50% (set above), the foot regions of CLI patients were classified into low StO2 (StO2 < 50%, considered to be ischemic) and high StO2 (StO2 ≥ 50%, considered to be non-ischemic) areas. In 14 of the 16 patients (87.5%) the locations of ulcers were surrounded mostly by low StO2 areas, which were judged to be compatible cases (ulcer and StO2 foot-mapping). There were 11 cases among 16 patients (68.8%) in which the locations of the ulcers were in angiosomes that were considered to be ischemic, and were judged to be compatible cases (ulcer and the angiosome model).

Two representative cases are shown (Figs. 5 and 6). Fig. 5 shows a case where the locations of ulcers were compatible with both the angiosome model and StO2 foot-mapping. Fig. 6 shows a case where the locations of the ulcers were not compatible with the angiosome model, but were compatible with the StO2 foot-mapping.

**DISCUSSION**

The ‘StO2 foot-mapping’ by near-infrared spectroscopy

The near-infrared tissue oximeter monitor, OXY-2, can rapidly and non-invasively measure many points of StO2. Based on these features of StO2 measurement, foot-mapping can be prepared and blood flow evaluation of the entire CLI patient’s foot is possible. The technique has generally been called near-infrared spectroscopy (NIRS), and was first reported by Jöbsis. Various experimental and clinical studies about NIRS have since been reported, and it is believed that the StO2 measured by NIRS is an indicator that closely reflects the peripheral blood flow. In this study, the boundary StO2 values of foot-mapping were set to 30%, 50%, and 70%, taking into consideration past reports and the ease of measuring.

From the results of StO2 foot-mapping, the StO2 value of the CLI group was clearly lower than that of the control...
group, and almost all StO2 values of the control group were above 50% (Fig. 4). Even though the control group was not age and sex matched for the CLI group in this study, a clear difference was observed in the StO2 values between the two groups, indicating that the areas with a low StO2 value (under 50%) indicate the ischemic areas of CLI patients’ feet.

Comparison of the StO2 foot-mapping with the angiosome model. StO2 foot-mapping is considered to be able to detect the ischemic areas in CLI patients’ feet more appropriately than the angiosome model, based on the results of this study. The distribution of ischemic and non-ischemic areas in CLI patients’ feet noted by StO2 foot-mapping was complex and different from the angiosome model, suggesting that peripheral tissue perfusion in a CLI patient’s foot is determined by the branch, capillary, and microvascular blood flow more than by the five or six areas where the main arteries are supposed to feed separately, as proposed under the angiosome concept.

The angiosome model connects the main arteries to peripheral tissue, and has been considered useful for predicting the peripheral tissue perfusion by angiography. However, it is possible that the angiosome model cannot explain the actual distribution of peripheral tissue perfusion, especially in cases of severe CLI. Since in such cases the blood flow toward the peripheral tissue is complicated by such factors as the growth of collateral arteries, the diversity and atrophy of the capillary and microvascular plexus, and other abnormalities of the vessels or peripheral tissue, that peripheral tissue perfusion may not be related to the main arterial blood flow.

Comparison of StO2 foot-mapping with the other methods used to evaluate the peripheral tissue perfusion. In order to understand the actual blood supply to the peripheral tissue in a CLI patient’s foot, an evaluation of the peripheral tissue itself is considered to be necessary, but there have been limited methods available for this purpose. Transcutaneous oxygen tension (tcPO2)15–19 and skin perfusion pressure (SPP),15,16,18,20–25 have been used to indirectly and non-invasively evaluate the arterial blood supply to the peripheral tissue of CLI patients’ feet, and to detect ischemia.

These methods evaluate only a few points, because it takes a lot of time to evaluate each point, and because the measurements are easily affected by the patient’s motion and other factors. Sometimes a patient is unable to stand.
still during the measurement, and taking a measurement is then impossible.

StO2 measurement is totally non-invasive and requires a very short time for the evaluation of each point, so measurement is possible even if a patient cannot stand still for a long time. Although a direct comparison between StO2 foot-mapping and tcPO2 or SPP is impossible, in terms of being able to evaluate multiple points and the two-dimensional distribution of the ischemic region in a short time, and also the high success rate of performing a measurement itself, StO2 foot-mapping can be said to be superior to tcPO2 or SPP.

**The concept of the “real angiosome”**. This study indicates that StO2 foot-mapping can non-invasively evaluate from the peripheral tissue the actual blood flow in the entire foot of a CLI patient, and can detect the ischemic areas which cannot be determined by the angiosome concept.

We advocate the concept of the real angiosome: the real distribution of peripheral tissue perfusion in a CLI patient’s foot, which is determined by peripheral microvascular blood flow (Fig. 7). StO2 foot-mapping can detect the real angiosome, which can locate the ischemic area in a CLI patient’s foot more appropriately than the angiosome concept. The difference between the two methods is considered to be because the real angiosome assessment is based on the peripheral tissue, while the angiosome assessment is based on the main arterial blood flow of the foot region.

The near-infrared tissue oximeter monitor, the OXY-2, can evaluate the StO2 of peripheral tissue within 10 mm of the skin surface, so the subcutaneous blood flow is considered to be related to StO2 foot-mapping, that is the real angiosome. In most cases, a correlation was seen between StO2 foot-mapping results and the results of angiography.

The peripheral tissue is directly fed by microvascular blood flow, which cannot be visualized by angiography but is most likely distributed around the subcutaneous visualized blood flow. However, in some cases microvascular blood flow is considered to be independent of the visualized blood flow, and in other cases the microvascular plexus is considered to be atrophic even if a visualized flow is present. This explains why the results of StO2 foot-mapping sometimes did not agree with the subcutaneous visualized blood flow.

**Figure 6.** Case 2 (the locations of ulcers were not compatible with the angiosome model, but were compatible with the StO2 foot-mapping). This case had an ulcer comprising the entire first toe, for which debridement was performed, because the ulcer had an accompanying infection. Ulcers of the lateral heel region were also seen. The locations of ulcers are shown by arrows. The angiography study showed a relatively good flow of the three branches of the posterior tibial artery (PTA) and occlusions of the anterior tibial artery (ATA) and the peroneal artery. The ischemic ulcers of the lateral heel are explained by peroneal artery occlusion. The ulcer of the first toe corresponds to the occlusions of the dorsalis pedis artery, medial plantar artery, and lateral plantar artery from the angiosome model; however, the medial and lateral plantar arteries were patent on the basis of the angiography study. Hence, the distribution of the ulcers is not compatible with the angiosome model. The ulcers were seen mostly in low StO2 areas, so the locations of ulcers and StO2 foot-mapping results were compatible. High StO2 areas were mainly on the plantar aspect, and angiography showed that there was PTA-dominant blood flow. In addition, the partial high StO2 area of the distal dorsal aspect was considered to be around the perforator from the plantar to the dorsal side. Therefore, a correlation was seen between the StO2 foot-mapping results and the results of angiography.
It has been reported that usually angiography can detect a vessel whose diameter is larger than 500 μm. A high-resolution angiography system may successfully detect thinner vessels in the foot, but not to the extent of microvascular perfusion that directly feeds the peripheral tissue. Recently, some experimental studies about quantifying tissue perfusion of the foot using indocyanine green angiography have been reported. It is possible that this method can evaluate subcutaneous microvascular perfusion. The real angiosome assessment from StO₂ foot-mapping enabled us to easily image the ischemic and non-ischemic regions. As a practical application of StO₂ foot-mapping to the clinical setting, StO₂ foot-mapping can be used to detect ischemic areas when performing appropriate debridement or partial amputation, or to evaluate in which area and to what degree peripheral tissue perfusion improves just after revascularization therapy, adding a qualitative value to the surgical and revascularization strategy for CLI. The evaluation of peripheral tissue perfusion from StO₂ foot-mapping can inform the surgeon of a need for extra blood flow during or after revascularization therapy; however, further investigations will be required to understand the changes of StO₂ in a CLI patient’s foot after revascularization therapy and for utilizing StO₂ foot-mapping for the revascularization strategy.

CONCLUSION
This study suggests that StO₂ foot-mapping can successfully and non-invasively detect ischemic areas in peripheral tissue in the feet of CLI patients, and more appropriately than assessment using the angiosome model. StO₂ foot-mapping can be used to evaluate the real angiosome: the real distribution of peripheral tissue perfusion in a CLI patient’s foot, which is determined by the peripheral microvascular blood flow, rather than the main arterial blood flow.

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CONFLICT OF INTEREST
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