Effects of tissue component volumes on vascular resistance in free flaps

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Abstract

Background: A successful free flap transfer is achieved, in part, by having a thorough understanding of vascular anatomy and blood flow dynamics. We previously reported that vascular resistance differs by type of free flap. To test the hypothesis that the difference reflects the proportion of tissue components within free flaps, we calculated blood flow and vascular resistance for free flaps in which we determined the volume of each tissue component.

Methods: Measurements and calculations were made for 40 free flap transfers carried out at our hospital: 7 radial forearm flaps, 14 anterolateral thigh flaps, and 19 rectus abdominis myocutaneous flaps.

Results: The vascular resistance of free flaps was inversely related to the volume of each tissue component. Univariate regression analysis revealed that muscle volume correlated most closely with resistance ($r = 0.881$), followed by skin ($r = 0.622$), and fat ($r = 0.577$). Multiple regression analysis confirmed the relationship between combined muscle and fat volume and resistance ($R^2 = 0.865$).

Conclusions: A strong inverse correlation exists between vascular resistance and combined muscle and fat tissue volume in flaps. It may be helpful to consider these relationships when making decisions regarding choice of free flap and recipient vessels.

Introduction

Successful free flap transfer depends greatly on a thorough understanding of flap anatomy and physiology, especially vascular anatomy and blood flow dynamics.[1] Blood flow within the flap is an important determinant for the patency of the microvascular anastomosis. Flaps with abundant blood flow have been shown to exhibit high patency of anastomosed vessels [2,3], result in large flap survival areas,[4] and relate to high resistance to local infection[5] in both clinical studies and experimental animal models. Surgeons often require flaps with particularly high blood flow when treating wounds complicated by infection [5] or irradiation.[6]

Considering such needs, minimizing vascular resistance in flaps can help to achieve better outcomes in reconstructive surgery. Various techniques have been used to assess blood flow in transferred free or pedicle flaps. Extracorporeal ultrasonographic imaging techniques such as laser Doppler [7] or color Doppler [8-11] are noninvasive and convenient, providing blood flow information without exposing the vessels. They highlight postoperative time-dependent hemodynamic change in blood flow. However, signals obtained from the skin surface often include nonspecific, potentially confounding components.[12] To minimize such problems, some reconstructive surgical teams prefer transit-time ultrasonographic flowmetry [12,13] to assess blood flow in free flap transfer. In this method, the probe is applied directly to the vessels. Although this technique can measure blood flow only when access to the vascular pedicle is available, it yields values more specific to blood flow than those obtained by extracorporeal ultrasonographic devices. This study is based on transit-time ultrasonographic flowmetry.

Our previous study showed that vascular resistance differed among flap types. The intra-abdominal flap had the lowest vascular resistance, followed by the myocutaneous flap, with the fasciocutaneous flap having the highest vascular resistance.[13] We believe that this difference reflects the proportion of tissue components (skin, fat, and muscle) comprising free flaps since the different tissue types differ in vascular anatomy and distribution (both of which are important determinants of vascular resistance). In the present study, we analyzed the relationship between the vascular resistance of a flap and the volumes of each tissue type included in the flap.

Patients and Methods

Patient characteristics

We analyzed vascular blood flow in 40 consecutive free flaps that were witnessed by a single observer (KT) between September 2004 and July 2014 at Nagoya

University Hospital. The flaps included myocutaneous and fasciocutaneous flaps and excluded osteocutaneous flaps and intraperitoneal flaps in order to avoid focusing on bone or intraperitoneal organs. Among the 40 patients, 23 were male and 17 were female. Ages ranged from 8 to 79 years old (mean, 59). Indications for surgery were squamous cell carcinoma in 19 patients, adenocarcinoma in 5, invasive ductal carcinoma in 6, non-invasive ductal carcinoma in 2, dysplasia of the hypopharynx in 2, olfactory neuroblastoma in 1, verrucous carcinoma in 1, sarcoma of the lower the limb in 1, osteomyelitis of the mandible in 1, and thoracic empyema in 2. The flaps studied included 7 radial forearm (RF) flaps, 14 anterolateral thigh (ALT) flaps, 8 transverse rectus abdominis myocutaneous (TRAM) flaps and 11 vertical rectus abdominis myocutaneous (VRAM) flaps. Due to the wide age range of participants in the study, one-way analysis of variance (ANOVA) was employed to assess the existence of confounding factors in the group. However, mean age did not differ among each flap type ($p = 0.496$). All VRAM flaps contained the full width of the rectus abdominis muscle, whereas TRAM flaps included the muscle sparing flaps; DIEP flaps were not included. Information on patient characteristics, indication, and flap types were retrospectively collected from medical records. Patient characteristics included age, gender, and factors that may affect vascular condition (hypertension, diabetes mellitus, and smoking history).

Measurement of blood flow

The flap was completely isolated on a single pedicle and the 1-cm segment of vessel that required probe application was dissected free. Lidocaine (4%) was applied to the vascular pedicle to prevent vasospasm. After waiting at least 30 minutes for blood flow stabilization, blood flow volume was measured using transit-time ultrasound flowmetry (HT323 surgical flowmeter; Transonic Systems, NY). A hook-shaped probe of the size appropriate to vessel diameter (1.5, 2, or 3 mm) was applied to the vessel being assessed. Blood flow was recorded for two minutes to ensure accuracy. The quantity of flow was computed from the difference between the upward and downward deflections in the ultrasonographic tracing produced using output from the two transducers at the tip of the probe applied to the vessels.

Calculation of the vascular resistance of the flap

We calculated vascular resistance as milliliters of mercury per milliliter per minute of flow using a previously reported formula [14]:

$$\mathrm{Res}_{\mathrm{uncorrected}} = \triangle P/Q \ (\mathrm{mmHg/ml/min})$$

where $\triangle P$ (change in blood pressure) = ABP (arterial blood pressure)-VBP (venous blood pressure), Res = vessel resistance, and Q = amount of blood flow.[4]

We set the values for arterial blood pressure (ABP) to equal mean arterial blood pressure (MAP).

MAP was calculated using the formula:

$$MAP = (SBP+2\times DBP)/3$$

where SBP = systolic blood pressure and DBP = diastolic blood pressure. Venous blood pressure was estimated to be 0.

Vascular resistance was adjusted further for hematocrit (Hct) and body temperature (T) by the formula:

$$Res_{corrected}=Res_{uncorrected}\times 1.025^{(T-T0)}\times(1+0.025\times Hct_0+0.00735\times Hct_0^2)/(1+0.025\times Hct+0.00735\times Hct^2)$$

where T_0=37℃, and Hct_0=40%.

Thus, each flap's resistance was standardized to a hematocrit of 40% and a temperature of 37℃, as reported previously.[3, 15]

Measurement of volumes in flaps

Photographs of the flap alongside a ruler were taken superficial, deep and lateral sides. Volumes of each tissue component (skin, fat, and muscle) were calculated by multiplying area by thickness **(Figure 1)**. Area and thickness of each component of the flap were calculated using NIH Image J version 1.48r (US National Institutes of Health, Bethesda, MD).

Statistical analysis

All data are shown as the mean ± standard deviation (SD). One-way analysis of variance (ANOVA) was performed, followed by Tukey's multiple comparison. The relationship of vascular resistance to total volume of the flap and to volume of each tissue component were assessed by univariate regression analysis. Since these analyses are univariate, each influential factor is not adjusted and potentially confounds the others. Thus, relationships between vascular resistance and each tissue component volume were further assessed by multiple regression analysis with adjustments for factors including age, gender, diabetes mellitus, hypertension and smoking history. All statistical analyses were performed utilizing Dr. SPSS Ⅱ for Windows (release 11.0.1J, IBM Japan, Tokyo, Japan). A p-value below 0.05 was considered to indicate statistical significance.

Results

Statistical background

Before initialing the statistical analysis, we considered multiple patient factors **(Table 1)**. The mean age was 56.6 ±14.2 years, and the number of men and woman were nearly equal. Hypertension was present in 3 patients, diabetes mellitus in 4, and a smoking history in 17. The mean volume of skin was 18.3 ± 10.7 cm^3; fat, 133 ±115 cm^3; and muscle, 55.6 ±73.5 cm^3. The mean vascular resistance (Res) of the flaps was 15.3±13.2. Assuming an inverse relationship between the volume of each tissue component in the flaps and vascular resistance of the flaps, we used the reciprocal of the vascular resistance value for univariate and multiple regression analyses. The mean reciprocal of vascular resistance (1/Res) in the 40 flaps was 0.113 ± 0.094.

Vascular resistance and flap type

Differences in vascular resistance between flap types were analyzed statistically. The mean vascular resistance for RF was 29.1 mmHg/min/mL; ALT, 16.0

mmHg/min/mL; TRAM, 12.9 mmHg/min/mL; and VRAM, 7.31 mmHg/min/mL. Statistically significant differences were found between RF and TRAM and between RF and VRAM ($p<0.05$; **Figure 2**).

Volume of each tissue component and flap type

The mean vascular resistance, total volume of flaps, and volume of each component in each flap type were calculated **(Table 2)**. The mean total volume of RF was 39.0 cm^3; ALT, 109 cm^3; VRAM, 341 cm^3; and TRAM, 344 cm^3.

Univariate regression analysis

Vascular resistance of the flap was plotted against total volume **(Figure 3A),** and also against the volume of each flap component **(Figure 3B to D)**. Vascular resistance tended to decrease as flap volume increased in each scatter plot. This tendency was present in all plots; muscle volume showed the strongest correlation with vascular resistance. Muscle volume was related to resistance as follows: $1/Res= 1.1\times10^{-3} V_1+ 0.050$, with V_1 representing volume (cm^3) of muscle tissue.

Multiple regression analysis

A multiple regression analysis was performed. We first considered the relationships between each tissue component volume on line orientation scatter diagrams **(Figure 4).** Colinearity was evident between volumes of skin and fat. This relationship is reflective of operative technique; when we elevate a free flap, skin and fat are elevated together. Values for skin and fat correlate strongly, r= 0.825; **(Table 3).** It was easier to obtain a precise calculation of fat volume than it was of skin volume since adipose tissue is thicker than skin. We determined that skin volume was not an independent variable.

Next, we adjusted for factors likely to affect vascular health, such as diabetes mellitus, hypertension, and smoking history.**(Table 4).** Age, hypertension and diabetes did not influence the formula, but gender and smoking did show a possible influence. Multiple regression analysis revealed that the strongest correlation was between vascular resistance and volume of muscle (plus fat combined) (R^2 = 0.865).

Finally, we derived a formula in which the volume of muscle and fat was related to resistance as follows: the coefficient of the muscle volume (V_1) was 9.19×10^{-4} and that of the fat volume (V_2) was 3.04×10^{-4}. An increase in muscle volume has greater influence than an increase in the fat volume **(Table 5).**

Discussion

We previously showed that blood flow volume and vascular resistance of free flaps differ among flap types.[13] Fasciocutaneous and osteocutaneous flaps were associated with the highest vascular resistance, followed by myocutaneous flaps, and finally, intraperitoneal flaps. Each flap has various tissue components such as skin, fat, muscle, and bone; each tissue component contributes different vascular resistance. The vascular network of the intraperitoneal flap differs from that of the other flap types, perhaps because intraperitoneal flaps have dense vascular anastomosis and arteriovenous shunts. Regarding flap size and flap resistance, there is a report that as the weight of a muscle flap increases, resistance of the flap decreases.[3] A relationship of blood flow to flap weight also was described in a dog study.[16] One might speculate that as the mass of a flap increases, its blood vessel content would increase, consequently decreasing resistance. Type of tissue components present and tissue volumes are both considered to affect the vascular resistance of flaps.

In the present study, according to univariate regression analysis for each tissue component in the flaps, muscle volume was strongly related to vascular resistance. Although the result was obtained from univariative analysis and potentially affected by confounding factors, it was consistent with the multivariative analysis and was similar to previously reported research on muscle flaps.[3] This finding may reflect the vascular anatomy of the flaps.

Veins and venules (except blood vessels) include the aorta, main arteries, small arteries, arterioles, and capillaries. The aorta, main artery, and small artery repiefent a series arrangement until they branch into arterioles and capillaries within each tissue **(Figure 5)**. In the case of free flaps, tissue components receive blood from arterioles and capillaries that branch out in a parallel fashion, predominantly from a perforator or small artery. Vascular resistance of a flap is considered to be inversely proportional to the total cross-sectional area of its vascular networks, regardless of the distance from the heart to the pedicle vessels. Blood pressure drops progressively to approximately 0 mm Hg as the blood flows through the systemic circulation. Within the systemic circulation, arterioles and capillaries are the main contributors to vascular resistance, since these are responsible for the greatest blood pressure drop.[17] When the vascular network in different tissues consists of components arranged in parallel, total resistance is calculated as follows from each tissue component: $1/Res_{total} = 1/Res_1 + 1/Res_2 + 1/Res_3 \ldots$, where Res_n is the vascular resistance in each tissue. The volume within arterioles and capillaries in each tissue is related to the volume of the respective tissue (V_n), and is related to each $1/Res_n$ value.

Regarding the density of arterioles and capillaries in the respective tissue, Kim et al. assessed microvessels in muscle and fat according to ultrasonographic findings using a contrast medium, concluding that muscle tissue contains a richer vascular network than those in other tissue types.[18] Nasir S et al. found that muscle flaps have higher blood flow than skin flaps (similar to our results). Resistance indexes were lower in muscle flaps compared with skin flaps, something that may be due to the rich vascular network in muscle.

When a free flap is intraoperatively harvested with its blood supply, tissue consistency varies among flaps: some have extensive muscle tissue, while others do not. In some instances, flaps contain no muscle (i.e. perforator flaps). Clinically, the flap design and the content of the flap are primarily determined by the content and size of the defect. However, there is some controversy as to whether the flap should contain muscle for the recipient site in the case of poor blood supply (such as an infected wound or irradiated site). It was thus important that we investigate the resistance of each tissue component and then determine to what extent each tissue type contributes to flap resistance. We performed multiple regression, which gave us the opportunity to assess the effect of each tissue component. This analysis revealed that muscle and fat are two important factors that determine vascular resistance of the flap, with muscle volume showing a stronger correlation with vascular resistance than fat volume. Given the collinearity between skin and fat volumes, the skin volume was eliminated from the potentially independent variables. This was technically inevitable because the surgical flap is typically designed such that skin and fat are included in the same area. Finally, we determined the extent to which muscle and fat contribute to the vascular resistance of the flap (**Table 5.**). Interestingly, the vascular resistance of flaps did not differ significantly among individuals and seemed largely dependent on the content of the flap.

Knowledge concerning free-flap vascular resistance should reduce microvascular complications and improve outcomes.[11] For successful reconstruction using free tissue transfer, we chose flaps with a high quality blood supply. [3,5,6] Flaps that contain rich muscle tissue are preferred when treating intractable ulcers. On the other hand, for procedures such as breast reconstruction, we use flaps that primarily contain fat tissue (for volume augmentation) because the muscle tissue volume decreases over time. We also use flap with relatively poor blood supply such as the radial forearm flap when thin flap is needed.

This study is clinically relevant in another way. Niranjan et al. reported on the efficacy of a supercharged anastomosis in TRAM flaps as a means of providing improved blood supply for the flap.[19] Tsao et al. claimed adequate venous drainage to be the most important factor in minimizing venous congestion in a free jejunal transfer.[20] It is thought that flaps containing abundant blood flow require a recipient vein capable of accepting substantial venous drainage from the flaps. Our data may aid in the intraoperative selection of a recipient vessel and in decisions concerning additional anastomosis of vessels.

Certain limitations of this study should be mentioned. The degree to which comorbidities such as hypertension, diabetes, and smoking might affect vascular resistance of flaps could not be considered due to small sample size. Ideally, additional samples could be added to provide a more detailed analysis. Since our data arose from patients requiring surgery, the population was somewhat elderly. Also, flap size and tissue components were determined based on clinical need and do not cover all the possible values. While an animal study with a uniform flap size and composition could decrease variability within the sample, animal vascular systems might not be entirely comparable to those of humans. A paper by Nasir a time-dependent decrease of blood flow in transferred flap.[11] All of our data were obtained intraoperatively and time-dependant data may provide more interesting information if the patient experiences postoperative problems.

Conclusions

As volumes of each tissue component increase in a flap, vascular resistance decreases. Moreover, we found that vascular resistance correlated strongly with the combination of muscle and fat volume in flaps. The volume of each tissue component influences the vascularity of the flaps.

We have demonstrated that it is possible to improve blood flow within free flaps by optimizing the combined volume of muscle and fat. Choice of a recipient vein should be carefully matched with potential venous drainage from the flap. Venous supercharge anastomosis might be utilized if necessary.

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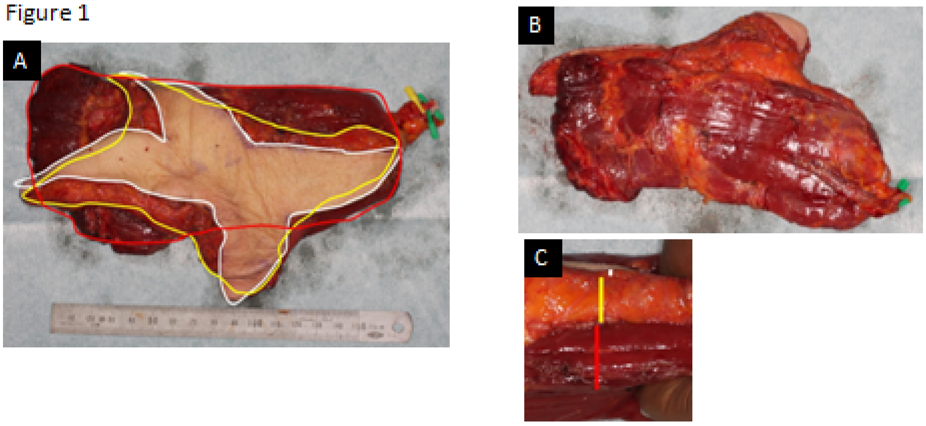
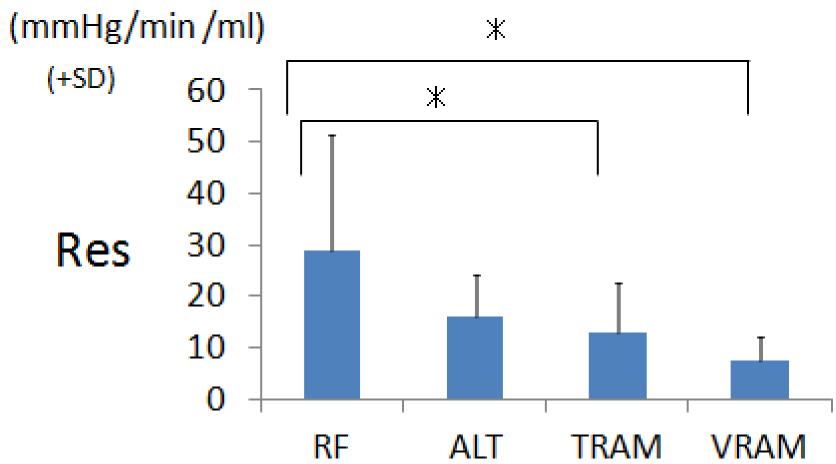
Figure 1



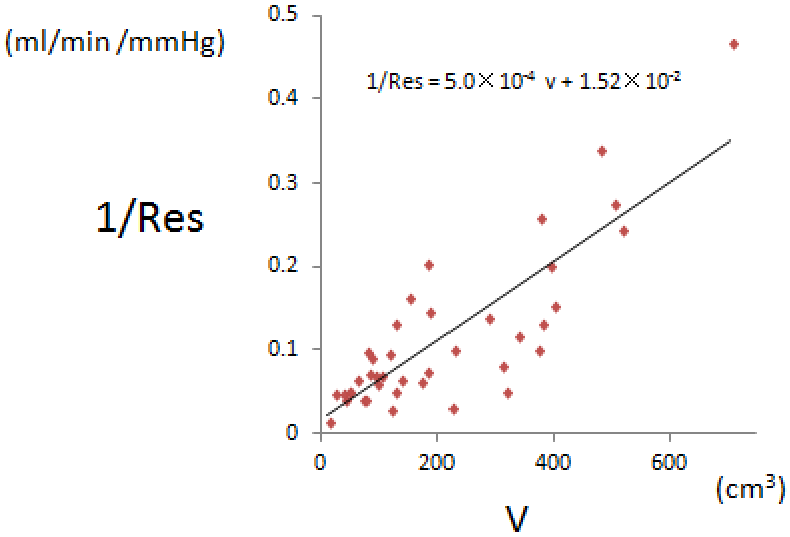
Photographs of a flap to illustrate tissue volume measurement
A) superficial view. The white outline is drawn to calculate the square measure of the skin area. The yellow outline represents the fat area. The red outline represents the muscle area, superimposed from the deep aspect B).
C) Lateral view of flap used to determine thicknesses of skin (white), fat (yellow), and muscle (red).

Figure 2



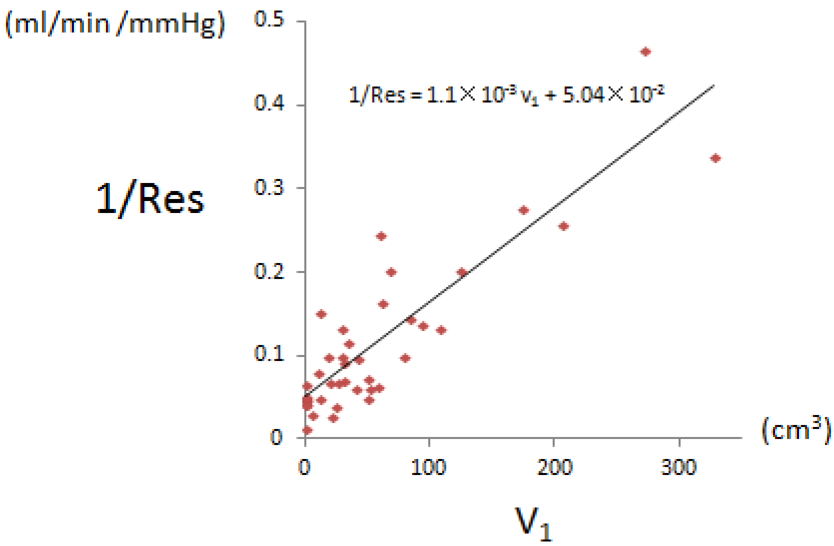
Type of flap and mean resistance (Res). RF, radial forearm flap; ALT, anterolateral thigh flap; TRAM, transverse rectus abdominis myocutaneous flap; VRAM, vertical rectus abdominis myocutaneous flap
Mean Res differed significantly between RF and VRAM.
* $p < 0.05$ (Tukey's multiple comparison).

Figure 3A



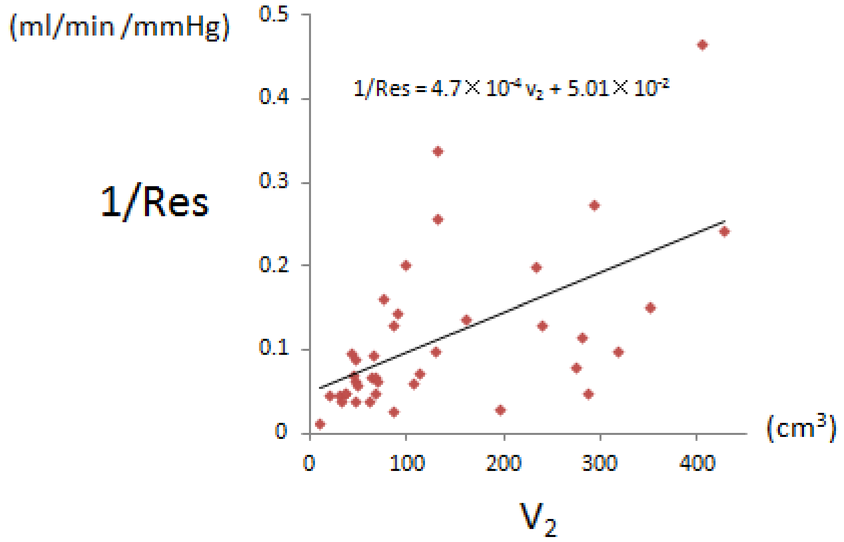
A, single regression analysis between total volume (V) and reciprocal of the vascular resistance (1/Res). Pearson correlation, r = 0.83.

Figure 3B



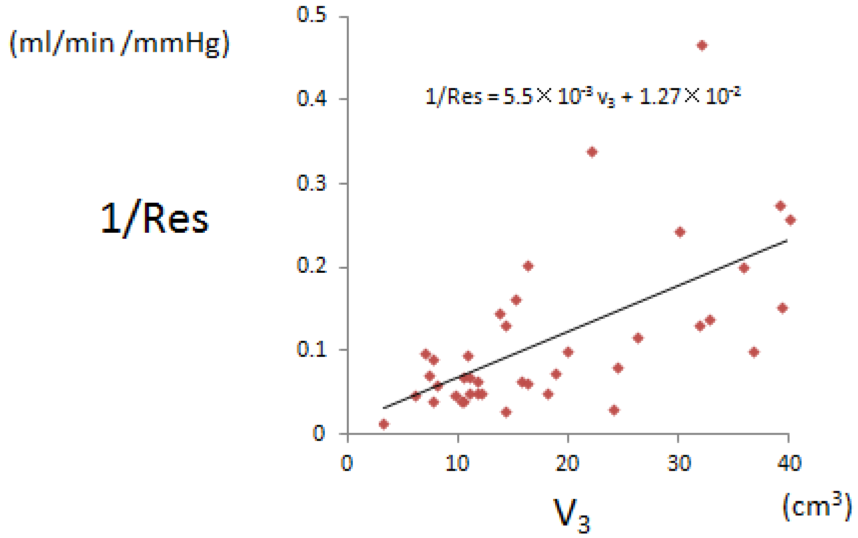
B, single regression analysis between muscle volume (V_1) and 1/Res. Pearson correlation, r = 0.88.

Figure 3C



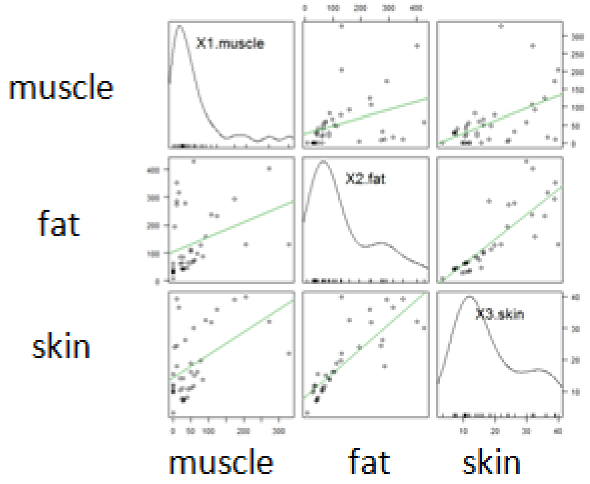
C, single regression analysis between fat volume (V_2) and 1/Res. Pearson correlation, r = 0.58.

Figure 3D



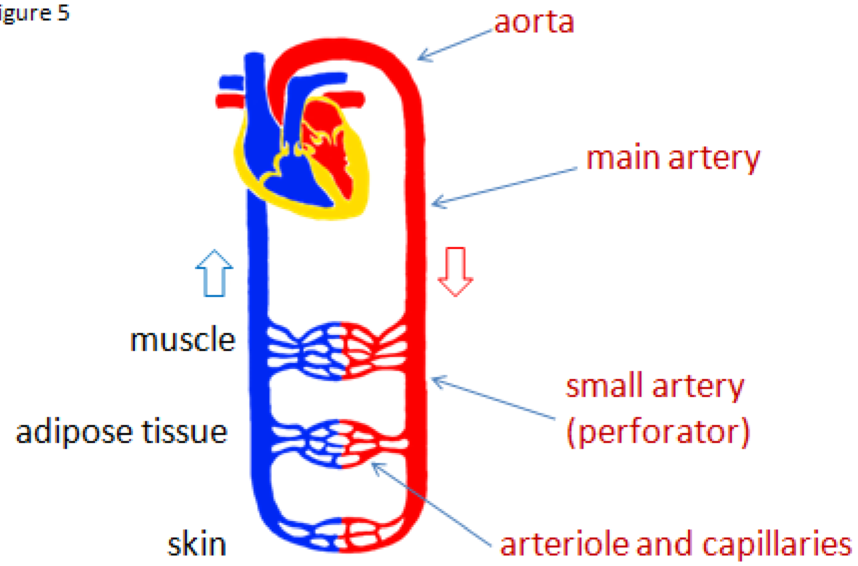
D, single regression analysis between skin volume (V_3) and 1/Res. Pearson correlation, r = 0.62.

Figure 4



Scatter-plot matrix with regression alignment.
colinearity is present between volumes of skin and fat.

Figure 5



Vascular network of the free flap.
Blood supply of tissue components is distributed in parallel
via arterioles and capillaries from a small artery (perforator).

Table 1. Characteristics of 40 Patients and their free flaps

Res, resistance.

Variables	Total N = 40
Demographics and comorbidities	
Age	56.6 (±14.2)
Male/gender	21 /40 (52.5%)
Hypertension	9 /40 (22.5%)
Diabetes	4 /40 (10.0%)
Smoking	17 /40 (47.5%)
Flap volumes by component	
Skin	18.3 cm^3 (±10.67)
Fat	132.9cm^3 (±114.6)
Muscle	55.6cm^3 (±73.5)
Vascular resistance	
Res	15.27 (±13.22)
1/Res	0.113 (±0.094)

Table 2. Total and tissue component volumes of flaps

Values are mean ± SD. RF, radial forearm flap; ALT, anterolateral thigh flap; TRAM, transverse rectus abdominis myocutaneous flap; VRAM, vertical rectus abdominis myocutaneous flap

The mean total volume of RF was least, followed by ALT, VRAM, and TRAM.

	Total volume (cm^3)	Muscle (cm^3)	Fat (cm^3)	Skin (cm^3)
RF	39.0 ± 16.3	0.0 ± 0.0	29.3 ± 12.2	9.8 ± 4.08
ALT	109.3 ± 35.6	32.3 ± 16.3	66.1 ± 21.8	11.0 ± 3.63
TRAM	344.4 ± 87.7	29.2 ± 30.9	286.3 ± 84.1	28.9 ± 7.07
VRAM	337.0 ± 181.1	140.0 ± 93.7	172.2 ± 106.1	29.5 ± 10.75

Table 3. Pearson correlations showing relationships between skin, fat, and muscle volumes

	Skin	Fat
Skin	-	-
Fat	0.82593	-
Muscle	0.50972	0.3514

Table 4. Univariate regression analysis in relation to vascular resistance (1/Res)

Gender and smoking possibly were related to 1/Res.

Variable	Coefficient	95% Confidence interval		p value
Patient factors				
Age	-4.00×10^{-5}	-2.22×10^{-3}	2.24×10^{-3}	0.971
Gender	4.36×10^{-2}	-1.60×10^{-2}	10.32×10^{-2}	**0.147**
Hypertension	2.43×10^{-2}	-4.85×10^{-2}	9.72×10^{-2}	0.503
Diabetes	4.73×10^{-2}	-5.36×10^{-2}	14.8×10^{-2}	0.349
Smoking	4.24×10^{-2}	-1.78×10^{-2}	10.28×10^{-2}	**0.162**
Flap tissue Volumes				
Muscle	11.34×10^{-4}	9.34×10^{-4}	13.33×10^{-4}	**<0.01**
Fat	4.76×10^{-4}	2.55×10^{-4}	6.97×10^{-4}	**<0.01**

Table 5. Multiple regression analysis in relation to vascular resistance (1/Res)

Volume of muscle plus fat was identified as an independent predictor.
Adjustment for smoking and gender, $R^2 = 0.865$.

	Coefficient	95% Confidential interval		p value
Intercept (V_0)	6.69×10^{-3}	-1.66×10^{-2}	3.00×10^{-2}	0.564
Muscle (V_1)	9.19×10^{-4}	7.41×10^{-4}	10.96×10^{-3}	< 0.05
Fat (V_2)	3.04×10^{-4}	1.90×10^{-4}	4.18×10^{-4}	< 0.05