In the 1970s, Behan and Wilson introduced the angiotome concept that culminated in the key- stone island flap design. An emerging body of basic science research and published clinical series suggest that keystone island flaps are robust and versatile with superior clinical outcomes due at least partially to its island design. Based on his clinical observations including the “red dot sign” and hyperemic flare, Behan has advocated the superior vascularity of the island flap design for at least 2 decades. Despite increasing interest and popularity of the keystone island flap in the current era of evidence-based medicine, his clinical observations and interpretations need to be further substantiated.

**AIM/HYPOTHESIS**

The aim of this study is to determine (1) whether surgical islanding of a flap alters the vascularity or blood supply of the flap and (2) whether these changes in blood supply explain Behan’s clinical observations of “red dot sign” and hyperemic flare.

**Background:** Based on his clinical observations the “red dot sign” and hyperemic flare, Behan has advocated the superior vascularity of the island flap design for at least 2 decades. The aim of this study was to determine whether (1) surgical islanding of a flap alters the vascularity or blood supply of the flap and (2) these changes in blood supply explain Behan’s clinical observations of “red dot sign” and hyperemic flare.

**Methods:** Patients undergoing local island fasciocutaneous flaps or anterolateral thigh fasciocutaneous free flaps were recruited for this trial from a single institution over a 10-month period (September 2013 to July 2014). Three adjacent specimens of skin and subcutaneous fat (control, non-island, and island) were harvested from each patient at various stages of their surgery for histological assessment. A pathologist reviewed randomized specimens for microvascular variables, including arteriole wall thickness, arteriole diameter, venule wall thickness, and venule diameter.

**Results:** Thirteen patients (with 14 sets of specimen) were recruited for this study. When compared with the control state, both arteriole diameter and venule diameter in island flaps were significantly increased.

**Conclusions:** These results validate Behan’s clinical observations of “red dot sign” and hyperemic flare. Further studies are required to directly compare island and non-island flap designs.
changes in blood supply explain Behan’s clinical observations of “red dot sign” and hyperemic flare.

METHODS

This study was approved by Human Research and Ethics Committee on September 6, 2013 (reference: 131 93B). Subjects for this study were recruited by the first author from patients undergoing local island fasciocutaneous flap or anterolateral thigh fasciocutaneous free flap reconstructions over a 10-month period from September 2013 to July 2014 at a single institution. Every subject provided oral and written consent via a Participant Information Sheet and Consent Form approved by the Human Research and Ethics Committee. Data collected include patient demographics, clinical details, outcomes including complications, and follow-up period.

Collection of Histological Specimens

Each specimen consisted of 10 mm³ blocks of soft tissue (skin and subcutaneous tissue) removed from the patient at specified times. After a traumatic harvest, each specimen was placed in containers with 4% buffered formaldehyde. Vasoconstrictive or vasodilating agents, such as local anesthesia and adrenaline, were not used, and diathermy and electrocautery were avoided to minimize tissue damage in the specimens.

After flap design and skin markings made as per normal routine, 3 adjacent specimens were collected from each patient during their surgery. First, a control specimen was taken (Fig. 1). Then a flap was raised to simulate a transposition flap with at least 25% of the skin bridge remaining intact. The second specimen was then harvested from the tip of the transposition flap (non-island flap specimen). The remaining skin bridge was then divided and the islanding completed. Last, the third specimen (island flap specimen) was harvested from the island flap, from an area adjacent to the first 2 specimens.

Randomization

For each patient, 3 specimen containers were labeled with a square, triangle, and circle, respectively, and were placed in a plastic bag. As each specimen (control, non-island, or island) was harvested, a theater nurse chose a labeled container at random to receive the specimen, with the final specimen going into the remaining container in the plastic bag. As records of the specimen and corresponding containers were made available only to the first author, the pathologist assessing the vasculature of the specimens was completely masked to the specimen type.

Histological Analyses

For each specimen, multiple sections were performed (minimum of 2 sections). After routine hematoxylin and eosin (H&E) staining, the histopathologist
examined arteriolar wall thickness, intraluminal arteriolar diameter, venule wall thickness, and intraluminal venule diameter (in μM using an eyepiece reticule at 400× total magnification). Ten separate fields were assessed for each of these variables; consequently each specimen, for each patient, had 10 measurements for each of the 4 microvascular variables being studied.

**Statistical Analyses**

Data were available from 13 patients, and the data from all patients were aggregated according to the type of specimen (control, non-island, and island), and the 4 microvascular variables being assessed. The raw data were retained, and in addition, we created a parallel database with log-transformed data as the distribution of the raw data was not normal.

Statistical analyses and graphing were done using Prism version 6.0 for Mac OS X. Categorical data were analyzed by the $\chi^2$ test. Nonparametric analog data from all 3 stages were assessed using the Kruskal–Wallis nonparametric test, and the log-transformed (normalized) data were tested by one-way ANOVA. Secondary comparisons between 2 of the 3 specimens used the Mann–Whitney test for non-parametric data and $t$ tests for normalized data. All comparisons used $P < 0.05$ as indicating significance.

**RESULTS AND DISCUSSION**

To our knowledge, this is the first histological study comparing non-island and island flaps. Thirteen patients (with 14 sets of specimens) were initially recruited for this study (Table 1). One patient was excluded from further analysis due to inadvertent departure from protocol during collection of the specimens. Twelve patients (with 13 sets of specimens) were analyzed histologically (Table 2).

**Table 2. Types of Flap Each Patient Had and Their Outcomes**

| Patient No. | Flap                  | Local or Free Flap | Flap-Related Complications |
|-------------|-----------------------|--------------------|----------------------------|
| 1           | ALT                   | Free               | None                       |
| 2           | Left VY advancement island | Local               | None                       |
| 3           | ALT                   | Free               | None                       |
| 4           | ALT                   | Free               | None                       |
| 5           | ALT                   | Free               | None                       |
| 6           | ALT                   | Free               | None                       |
| 7           | ALT                   | Free               | None                       |
| 8*          | ALT                   | Free               | None                       |
| 9           | ALT                   | Free               | None                       |
| 10          | Keystone island       | Local               | None                       |
| 11          | Keystone island       | Local               | None                       |
| 12          | VY advancement island | Local               | None                       |
| 13          | ALT                   | Free               | None                       |

*Patient excluded from histological analyses. ALT, anterolateral thigh fasciocutaneous free flaps.

Overall, there were significant changes in arteriolar diameter and venule diameter as the plastic surgical procedure progressed from control to non-island and then on to island (Fig. 2). The big change in arteriolar diameter was an increase from control to the non-island state, with a nonsignificant ($P = 0.18$) decrease from non-island to island. Venule diameter increased gradually and reached a plateau during progression from non-island to island flaps.

Interestingly, the change in arteriolar wall thickness was only a trend, and the change in venular wall thickness was not significant. Arteriolar wall thickness increased from control to the non-island state but then regressed to the control value in the island specimen.

These results were consistent with Behan’s clinical observations of “red dot sign” and hyperemic flare of more than 2 decades. He noted that island flaps were relatively pink or vascular in complexion (hyperemic flare). While insetting island flaps, they almost always bled from the site where the suture needle pierced the flap, an observation not replicated by the opposite skin edge (red dot sign). The histological findings of the increased arteriolar and venule diameter in the island flaps support these observations of increased vascularity in the island flap.

The high venule diameter in the non-island and island states (relative to the control) is likely associated with increased venous perfusion pressure and some degree of venous congestion. However, islanding led to decreased arteriolar diameter and presumably decreased inflow, potentially helping to ease congestion and improve flap survival.

Retention of a dermal pedicle, as is the case in the design of a transposition flap as opposed to an is-

**Table 1. Summary of Patients Recruited for the Study**

| Patient No. | Age (yr) | ASA | Pathology               | Follow-up (wk) |
|-------------|----------|-----|-------------------------|----------------|
| 1           | 80       | 3   | Parotid SCC metastases  | 49             |
| 2           | 74       | 3   | Vulva recurrent Paget’s disease | 21  |
| 3           | 82       | 3   | Preauricular invasive SCC | 42             |
| 4           | 58       | 2   | Ankle open fracture     | 4              |
| 5           | 37       | 2   | Foot open fracture      | 46             |
| 6           | 62       | 3   | Parotid SCC metastases  | 2              |
| 7           | 60       | 2   | Oropharyngeal recurrent SCC | 1              |
| 8*          | 79       | 3   | Sublingual adenocarcinoma | 28            |
| 9           | 29       | 1   | Ankle open fracture     | 27             |
| 10          | 75       | 3   | Upper back melanoma     | 1              |
| 11          | 59       | 1   | Upper back BCC          | 18             |
| 12          | 87       | 2   | Vulva SCC               | 8              |
| 13          | 56       | 1   | Lower leg open fracture | 3              |

*Patient excluded from histological analyses. ASA, American Society of Anaesthesiologist score; SCC, squamous cell carcinoma.
land flap, may alleviate anxiety. However, it has been previously demonstrated that island flaps survive to at least the same length as those with a cutaneous pedicle, which contains segmental vessels. More recently, it was shown that conversion of a perforator flap with a skin bridge into an island perforator flap prevented “hemodynamic steal” and increased peripheral tissue perfusion. This may form the basis for improved survival of island flaps relative to dermal pedicled flaps. Based on studies and clinical impressions past and present (ours), retention of a skin bridge brings no added advantage. In addition, we concur with the suggestion of incorporating named or segmental underlying vessels, and hence, our principle of designing keystone flaps was based on the angiotome concept.

The sequence of vasoconstriction and the coagulation cascade following trauma may be well documented, but the control of blood supply to the skin is yet to be fully understood. Cutaneous blood flow is the result of a complex interplay of reflex (whole body) and local control mechanisms. Reflex sympathetic innervation of cutaneous circulation has 2 branches; sympathetic noradrenergic vasoconstrictor system and non-noradrenergic active vasodilator system. Sympathetic noradrenergic vasoconstrictor nerves provide tonic innervation. Interruption of this sympathetic noradrenergic innervation causes a passive vasodilatation due to withdrawal of the tonic activity of vasoconstrictor nerves. The active vasodilator system does not exhibit resting tone and is only activated by increases in body temperature (heat exposure and exercise). A role also exists for afferent or sensory nerves.

Observations similar to Figure 2 were made when data from the subgroups of local island flaps and anterolateral free flaps were analyzed separately. These findings confirm our assumption that the vascular changes occurring in both subgroups occur along the same spectrum with the raising of these flaps.

This study involves histological assessment of specimens harvested in the early intraoperative period. Although the small number of patients could be considered a limitation of this study, the highly significant differences suggest that a much larger study would be unlikely to arrive to a different outcome. To investigate intraflap differences, specimens need to be harvested from the base and the tip of the transposition flap. To verify permanence of these vascular changes, and ultimately impact on flap survival, a long-term study is necessary. The effect of flap mobility, flap insetting, and tension on flaps with altered vascularity remains outside the scope of this study.

CONCLUSIONS

The histological findings of increased arteriole and venule diameter in the island flap were entirely consistent with Behan’s clinical observations of red dot sign and hyperemic flare. Further studies are required to directly compare island and non-island flap designs.

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