ABSTRACT

Problem Addressed
Angiogenic growth factors have the potential to improve skin flap survival; however, their sustained delivery to tissues remains challenging. This project describes an innovative modality for interstitial delivery of Vascular Endothelial Growth Factor (VEGF).

METHODS AND MATERIALS

Using the porcine model, 32 skin flaps (4 x 11 cm) were treated for flap survival and the flap diameter. This flap model allowed for dorsal placement of catheters for VEGF delivery. Treated flaps underwent infusion of 1 microgram of VEGF via the catheter over a period of seven days. Animals were sacrificed and flaps were analyzed for water content. Control animals had no treatment and no catheter placement. Survival was assessed by a blinded observer. Flaps with water content determined by the wet-dry method. Results

Water content was significantly lower in treated flaps (55.3 ± 9.7%) compared to the control group (61.9 ± 8.2%) by ANOVA for group, position, and interaction (all p < .001 df=31). There was no significant contraction of the control flap compared to the treated flaps (by 3.2%, p=.02). The posterior control flaps were noted to have very high survival (89%).

Conclusions
This pilot study demonstrates the feasibility of hollow fiber for sustained delivery of VEGF and removal of edema fluid from the skin flap. Further studies are needed to optimize these findings.

RESULTS

Water content
• Treated flaps had reduced water content which was significant by ANOVA for group, position, and interaction (all p < .001 df=31).

Contraction
• Control flaps had significantly more contraction by 3.2% compared to treated flaps (p<.02)

Survival
• Inter-rater reliability was high for rating the portions of the flap deemed to be alive and without necrosis. The posterior control flaps had 89% survival which is likely related to an inability to remove edema fluid from the skin flap. All animals had four identical 4 x 11 cm ventrally based skin flaps (see figure 3). Visible vessels at the base of the flaps were cauterized so as to create a random blood supply yet allow accessibility to the flaps while the animal was placed in a special harness (see figure 3). Control flaps had no further intervention.

• Treated flaps underwent infusion of one microgram of VEGF via a five cm hollow fiber (see figures 1 and 4) on preoperative day one and postoperative days one and three. Additionally, half of the treated flaps underwent simultaneous ultrafiltration via separate five cm hollow fibers to reduce edema. Multiple catheters were placed in each flap to serve both infusion and ultrafiltration functions. Infusion took approximately one hour while the ultrafiltration took place over four hours.

METHODS AND MATERIALS

• A porcine model was utilized with the eight total animals randomly divided into either the control or treated groups. All animals had four identical 4 x 11 cm ventrally based skin flaps (see figure 2). Visible vessels at the base of the flaps were cauterized so as to create a random blood supply yet allow accessibility to the flaps while the animal was placed in a special harness (see figure 3). Control flaps had no further intervention.

• Treated flaps underwent infusion of one microgram of VEGF via a five cm hollow fiber (see figures 1 and 4) on preoperative day one and postoperative days one and three. Additionally, half of the treated flaps underwent simultaneous ultrafiltration via separate five cm hollow fibers to reduce edema. Multiple catheters were placed in each flap to serve both infusion and ultrafiltration functions (see figure 4). Infusion took approximately one hour while the ultrafiltration took place over four hours.

• On postoperative day seven the flaps were analyzed and harvested. Photographs were taken and both the first author and a blinded observer graded them using a computerized system (BIOQUANT) to determine areas that were alive, dead or intermediate. Additionally, punch biopsies were taken at four intervals along the flap and these were analyzed for water content by weighing the specimen immediately after sacrifice and then again seven days later.

REFERENCES