practice and associated with angiogenesis and accelerated wound healing. This experimental model evaluated topical negative pressure as a mechanism for non-invasive preconditioning for perforator flap microvasculature and perfusion.

**METHODS:** Two gluteal perforator flaps (matched control and intervention) were designed on sixteen 400g Sprague-Dawley male rats. NPWT was applied to the flap area directly continuously at -125mmHg for 7 days, after which the rats were divided into two principal groups. Group A (n=8) underwent 4D computed tomographic and angiography (CTA) with a body volume perfusion protocol after NPWT and euthanized. Group B (n=8), control and intervention flaps were raised, isolated on a single pedicle and laid back down and monitored for a further 7 days. Group B flaps were assessed using laser-assisted indocyanine fluorescence angiography before surgery, following flap harvest and at 7 days prior to euthanasia. Half of all rats in each group were analyzed with Micro-CT to assess the microvasculature. All paired specimens were assessed histologically with H&E and immunohistochemistry (IHC).

**RESULTS:** There was a 17% increase in CT tissue perfusion in skin treated with NPWT versus matched controls (P=0.001). LA-ICGFA demonstrated higher perfusion following NPWT treatment (P=0.006), however no significant difference immediate post flap harvest (P=0.19) but a difference was seen 7 days postoperatively (P=0.03). Micro-CT evaluation showed an increase in average vessel volume (%) from 0.005 in control to 0.009 in the NPWT flaps (P=0.04). H&E analysis showed significant difference in the epidermal thickness (P<0.001), but comparable dermal thickness (P=0.34). Quantitative analysis of CD31 IHC demonstrated a mean area fraction percentage of 4.30 and 2.68 in the NPWT and control flaps respectively (P=0.002). There was partial necrosis in the control (n=3) and NPWT flaps (N=1), however this was <5% in the NPWT flap.

**CONCLUSION:** We present novel multimodal approaches using static and dynamic imaging and histological assessment to provide a proof of concept on the use of NPWT for non-invasive conditioning of flaps. The study provides the basis for further investigation and clinical studies with potential for direct translation into clinical practice.

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**Ex Vivo Normothermic Limb Perfusion and Limb Specific Monitoring Evaluation of Perfusion Quality**

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**PURPOSE:** Ischemia time represents a significant limitation for successful extremity reimplantation and transplantation because of the rapid deterioration of ischemic muscle. Static cold storage (SCS) of the limb is the standard clinical practice. Normothermic ex vivo perfusion system has the potential to prolong viability providing oxygen and metabolites after limb amputation. The aim of our study was to establish a perfusion protocol with limb specific diagnostic tools to evaluate the quality and uniformity of perfusion in an ex vivo model.

**METHODS:** A total of 18 swine limbs were perfused, five of them followed the final, optimized protocol. Limbs were perfused at 39°C for twelve hours using an oxygenated colloid solution with packed red blood cells. Glucose and electrolytes were kept within physiologic range by the addition of hypertonic solution or by partial hypotonic perfusate exchanges. Limb specific perfusion quality was assessed by muscle contractility upon electrical nerve stimulation, compartment pressure, creatine kinase (CK) and myoglobin concentrations, tissue oxygen saturation (near infrared spectroscopy), indocyanine green (ICG) angiography, and infrared radiation emission by thermographic imaging.

**RESULTS:** All five limbs reached the 12 hour perfusion target maintaining normal compartment pressure (16.23 ± 7.94 mmHg), minimal weight increase (0.54%±0.07), mean muscle temperature of 33.54 ± 1.5°C, and tissue oximetry readings of 59.67%±10.21. Average values of final myoglobin and CK were 875 ± 291.4 ng/mL, and 53344 ± 14850.34 U/L, respectively. Muscle movement was present in all limbs until cessation of perfusion. Differences in uniformity and quality of distal perfusion were demonstrated using thermography and angiography imaging after 12 hours of perfusion. Colder areas on Thermographic imaging correlated to mal perfused areas on ICG angiography.
CONCLUSIONS: Ex-vivo normothermic limb perfusion preserves limb physiology and function for at least 12 hours. Thermography and ICG angiography are valuable tools in the assessment of limb perfusion quality with the advantage of providing an immediate evaluation which allows for the visual identification of perfusion gradients and regions of mal-perfusion. Muscle contraction upon nerve stimulation, a uniform physiologic temperature and tissue oxygenation, and the distal dye distribution on angiography identify a successful perfusion. These methods may have important future implications on the decision to transplant or replant a perfused limb. Myoglobin and CK concentration increased in all limbs during ex vivo perfusion, but the functional significance of this is still to be determined.

Topical Application of Nitrosonifedipine, a Novel Free Radical Scavenger, Ameliorate the Ischemic Skin Flap Necrosis

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INTRODUCTION: Ischemic flap necrosis is often occurred by insufficient blood supply, which prolongs the treatment period and occasionally requires an additional surgery. Ischemic flaps generate an excess amount of free radicals which is regarded as a major factor of ischemic skin necrosis. Thus free-radical scavengers would be an effective drugs in improvement of flap survival. In our previous studies, we have reported nitrosonifedipine (NO-NIF), which is a photolytic compound of nifedipine, possesses a potent radical scavenging activity, and shows the favorable effects against vascular endothelial dysfunction and type 2 diabetic nephropathy. In this study, we evaluated the ameliorating effect of NO-NIF on the ischemic flap model mice.

MATERIAL AND METHODS: 9–10 weeks old Male C57BL/6 mice were divided into 2 groups, NO-NIF or control (n=6 in each group), respectively. A 1.0 × 3.0 cm cranially based random pattern flap was elevated on the dorsum of mice. NO-NIF 30 mg/kg or vehicle was injected subcutaneously immediate after the operation and once a day until evaluation. Seven days after surgery, the survival area was calculated as a percentage of the total flap area. To detect the oxidative stress, malondialdehyde (MDA) in the distal part of the flap at post-operative day 1 and 3 was measured by thiobarbituric acid reactive substances assay. Protein expression of p22phox, an essential component of NADPH-oxidase, in the flap was measured by western blotting.

RESULTS: At post-operative day 7, the flap survival area was significantly larger in the NO-NIF-treated mice than controls (78.29 ± 7.04% vs. 51.81 ± 6.85%, p=0.021). The amount of MDA significantly decreased in the NO-NIF-treated mice at post-operative day 3 (2.31 ± 0.28 µmol/g protein vs. 4.21 ± 0.32 µmol/g protein, p=0.001), whereas MDA was same level in the both groups at the post-operative day 1 (2.77 ± 0.61 µmol/g protein vs. 2.96 ± 0.51 µmol/g protein). In a manner consistent with MDA levels, protein expression level of p22phox was decreased in the NO-NIF-treated mice at post-operative day 3 (p=0.002).

CONCLUSIONS: We present the ameliorating effect of NO-NIF on ischemic flap survival. MDA and p22phox protein was decreased by NO-NIF treatment, which suggests the ameliorating effect was exerted via free radical scavenging. This investigation indicates that free-radical scavengers including NO-NIF are effective drugs in improvement of flap survival.

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Safety and Efficacy of Sufentanil Sublingual 30 mcg Tablets for the Treatment of Acute Pain following Outpatient Abdominoplasty

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INTRODUCTION: The sufentanil sublingual tablet system is a non-invasive, patient-controlled analgesia (PCA) drug/device product recently approved by the European Medicines Agency for treatment of acute moderate-to-severe post-operative pain in a hospital setting. A second sufentanil product, a 30 mcg tablet (ST) dispensed sublingually by a healthcare professional via a single-dose applicator, is