

# A study of the biological factors and wound healing of a skin flap model

## Author:

Henry Vasconez, Stephanie Edelmann (2), Betsy F. Fink (1), Sreenatha Kirakodu (3), Robert E.H. Ferguson (1), Karen F. Novak(3), M. John Novak (3), Wolfgang Schaden, C. William Balke (2)

## Institution:

- 1) University of Kentucky Chandler Medical Center Division of Plastic and Reconstructive Surgery
- 2) Department of Internal Medicine
- 3) College of Dentistry<sup>3</sup> Lexington, KY USA

## Device and producing company:

ESWT (VetWave 1400, NITS)

## Introduction:

This animal study was performed to assess the effectiveness of extracorporeal shock wave (ESWT) treatment to promote cell differentiation with neovascularization, thus minimizing the measurable area of necrosis and enhancing epigastric skin flap survival. In addition, we measured the expression level of the mRNAs of the growth factors known to play a major role during normal wound healing angiogenesis using Real-Time PCR. In particular, we studied the expression of basic fibroblast growth factor (bFGF), transforming growth factor beta, (TGF-(3), platelet derived growth factor (PDGF), epidermal growth factor (EGF) and vascular endothelial cell growth factor (VEGF) at several time points following the skin flap surgery. We studied the localized changes in expression as well as systemic changes that were initiated by the treatment with ESWT.

## Methods:

**Experimental Design:** This study was approved by our Institutional Animal Care and Use Committee. This study was conducted in two phases. Sprague-Dawley rats with a weight range of 400-500g were used for both phases. Phase I The rats were randomized into two groups of eight: a control group and an ESWT group. Immediately following surgery, while the animals were anesthetized, the flap area was treated with Level 1 (500 pulses at 0.15 mJ/mm<sup>2</sup>) in the EWST group. The control group underwent the same surgery but did not receive ESWT. On Day 7 post-op, the animals were euthanatized and clinical measurements of healing were collected post-mortem. The control group underwent the same surgery but did not receive ESWT. Phase II The rats were randomized into two groups of eight: a control group and an ESWT group. Immediately following surgery, while the animals were still anesthetized, the flap area was treated with Level 1 (500 pulses at 0.15 mJ/mm<sup>2</sup>) in the EWST group. Two rats from each group were euthanatized at 12 hours, 24 hours, 48 hours and 72 hours. The necrotic area plus 2-3 mm of adjacent healthy tissue was obtained postmortem and stored in liquid nitrogen for growth factor and stem cell marker analysis.

## Results:

When the area of necrosis was analyzed using the PictZar imaging software, we found that the area of skin flap necrosis for the control group (n=8) was an average of 11.7 cm<sup>2</sup>. In the treatment group (n=8) necrosis of the same flaps were an average of 3.8 cm<sup>2</sup>. Statistical analysis using the Mann Whitney t-test showed significance at P=0.0006. The expression of EGF, PDGF and VEGFG was detectable at 12, 24,48 and 72 hours in the control and shockwave treated animal on both, the treated and the untreated side of the flap. This was true when the expression was compared to actin as well as compared to GAPDH.

## Discussion:

The results of our animal study showed that the treatment of skin flaps with unfocused ESWT had a significant beneficial effect on survival and viability of the skin flaps. Additionally this effect appears similar with unfocused as compared to focused shockwaves. The area of necrosis on the

skin flap was significantly smaller in the treated group compared to the untreated group without apparent side effects. ( $p=0.0006$ ) The second phase of the study demonstrated local and systemic effects of various growth factors, which could prove to be of invaluable help in wound healing. Some of the groups who experimented with injection of growth factor or with gene therapy using growth factors remarked that, because growth factors expression is orchestrated in a specific way, it would be necessary to inject several factors over a specific time frame in order to mimic what is naturally happening in the body

**Conclusion:**

The range of applications of shockwave therapy is as yet undefined and is an area of active interest and research. Further work in the field of wound healing may result in establishing a painless, noninvasive, modality of therapy for wounds that have been up to now recalcitrant to other forms of established treatment.