

BioElectric Stimulation Therapy (BEST) in Wound Healing : How Does it Work?

Stimulation of Fibroblasts

BEST Mechanisms of Action

The fibroblast cell plays a crucial role in wound healing, particularly in the proliferative and maturing phases. It not only produces the new matrix needed to restore structure and function to injured tissue, but also collagen to provide strength and stability. In addition, fibroblasts are co-responsible for neovascularization through the secretion of bFGF (basic Fibroblast Growth Factor).

Several different effects of BEST on fibroblast function have been reported in the literature:

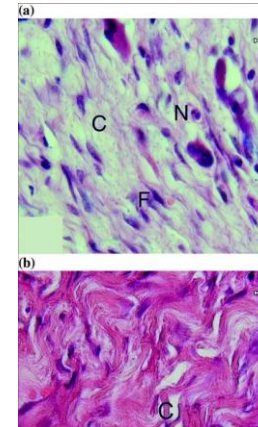
- In vitro
 - enhanced DNA and protein (collagen) synthesis, an increase in Ca^{++} uptake [Bourguignon 1987]
 - upregulation of TGF- β receptors (important in granulation tissue formation) [Falanga 1987]
- In vivo
 - fibroblast proliferation [Taskan 97]
 - increased collagen deposition [Canseven 96]
 - improved collagen fiber alignment [Bayat 2006]
 - increased tensile strength [Taskan 97, Bayat 2006]

All in all, there is a clear picture : BEST stimulates fibroblasts to proliferate and become metabolically active, with a resultant increase in their function, especially **granulation tissue formation** and **collagen production**.

Several authors reported on the senescence (early death) of fibroblasts as a significant factor in chronic or non-healing wounds.

References

- Bourguignon GJ. Electric stimulation of human fibroblasts causes an increase in Ca^{2+} influx and the exposure of additional insulin receptors. *J Cell Physiol* 140(2):379-85, 1989.
- Falanga M, Song B, Pu J et al. Electrical stimulation increases expression of fibroblast receptors for TGF- β . *J Invest Dermatol* 1987;88:488-92.
- Taskan A comparative study of the effect of ultrasound and electrostimulation on wound healing in rats. *Plast Reconstr Surg.* 1997;100(4):966-72.
- Bayat M et al. Experimental wound healing using microamperage electrical stimulation in rabbits. *J Rehabil Res Dev.* 2006;43(2):219-26.



From Bayat 2006
b) more mature fibroblasts and connective tissue fibers after BEST treatment

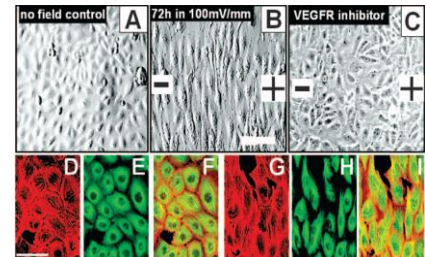
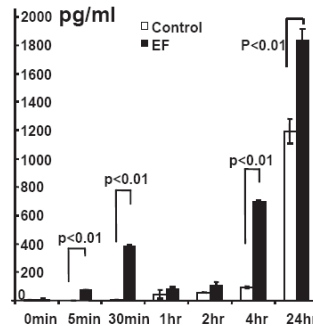
**BioElectric Stimulation Therapy (BEST) in Wound Healing :
How Does it Work?**

Angiogenesis

BEST Mechanisms of Action

Neovascularization is a key event in wound healing, particularly during the proliferative phase. In vitro experiments have shown that BEST induces a distinctive pre-angiogenic response by directing the **movement of human endothelial cells**, as well as fibroblast and vascular smooth muscle cells [Bai 2004].

In addition, BEST **stimulates VEGF production** by endothelial cells, and this growth factor directly promotes neovascularization, as elegantly demonstrated by Zhao [Zhao 2004]



cultured endothelial cells

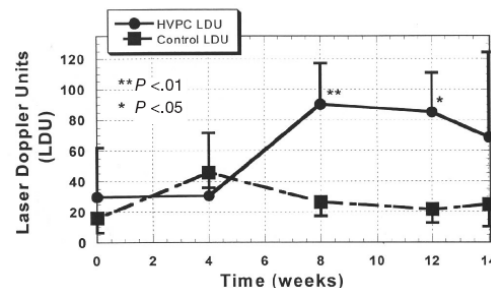
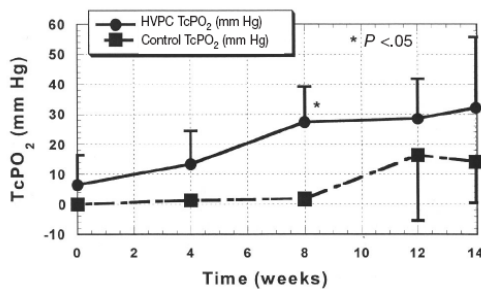
- A = control
- B = with EF, demonstrating early blood vessel formation
- C = small EF but with VEGF inhibitor
- G, H = EF causes elongation and reorientation of actin (red) and tubules (green)

VEGF production
white = control
black = with electric field

These in vitro effects provide an explanation for what have been observed in animal studies. Greenberg, for example, reported **prominent neovascularity** in burn wounds and earlier epithelialization [Greenberg 2000].

Importantly, it is also backed up by clinical evidence showing that BEST can **improve the microcirculation** and healing of ischemic wounds, as measured by:

TcPO₂ (transcutaneous oxygen pressure) and laser Doppler flow [Goldman 2004].



References

Bai H et al. DC Electric Fields Induce Distinct Preangiogenic Responses in Microvascular and Macrovascular Cells *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2004;24:1234.

Zhao M et al. Electrical stimulation directly induces pre-angiogenic responses in vascular endothelial cells by signaling through VEGF receptors, *J Cell Science* 2004;26(117):397-405.

Greenberg J et al. The effect of electrical stimulation on wound healing and angiogenesis in second degree burns. *Proceedings 13th Symposium on Adv Wound Care* 2000.

Goldman R et al. Electrotherapy Promotes Healing and Microcirculation of Infrapopliteal Ischemic Wounds: A Prospective Pilot Study. *Adv Skin Wound Care* 2004;17:284-90.