

ACUPUNCTURE FOR WOUND HEALING: A REVIEW OF EVIDENCE AND ITS BIOLOGICAL BASIS

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Evidence on acupuncture for wound healing:

- ◆ As predicted by the growth control model of acupuncture [1], acupuncture enhances growth control factors and wound healing accelerators such as fibroblast growth factor (FGF) and platelet-derived growth factor (PDGF) [2,3].
- ◆ A literature search of PubMed using keywords acupuncture AND wound healing yielded 375 publications. Further filtering with RCT, meta-analysis and systematic review yielded 22 articles. A similar research in Google scholar yielded similar results.
- ◆ The results of the randomized controlled trials and systematic reviews showed that acupuncture related modality such as electroacupuncture, moxibustion were more effective than controls in promoting wound healing of arteriosclerotic wounds (effective size 1.7 for 50% wound closure in 6 wks) [4], diabetic foot ulcers (effect size for healing time 1.1, 1.7, 5.3)[5] except for 1 negative RCT on dogs in which only one session of substandard acupuncture was given lasting 5 to 15 minutes [6].

Biological basis of acupuncture

- ◆ In growth control, the fate of a larger region is frequently controlled by a small group of cells, which is termed an organizer. [7]
- ◆ Growth control is an essential function both during and after embryogenesis. Multi-cellular organisms maintain regular form and function despite constant replacement of cells, intracellular components and extracellular matrix. Without growth control, this constant renewal process is prone to structural disintegration, degeneration and cancer. [8,9]
- ◆ The growth control signal transduction is embedded in various physiological functions as well as pathological inflammatory, degenerative and neoplastic diseases. Many physiological processes are regulated through growth control mechanisms such as hypertrophy, hyperplasia, atrophy, apoptosis and signal transduction pathways involving growth control genes such as proto-oncogenes. [8,9]
- ◆ A model of growth control system suggests that a growth control system originates from a network of organizers which distribute at extreme points of structural surface or interface curvature, e.g. the locally most concave, convex or saddle points at body surface or interface between muscles, bones and other structures.[7,8] The growth control in adult is not limited to humoral factors such as growth hormone, but also involves the continuous function of the organizer network exerting both local control and cross-talk among organs and body parts. The growth control system is involved in the pathophysiology of various disorders.

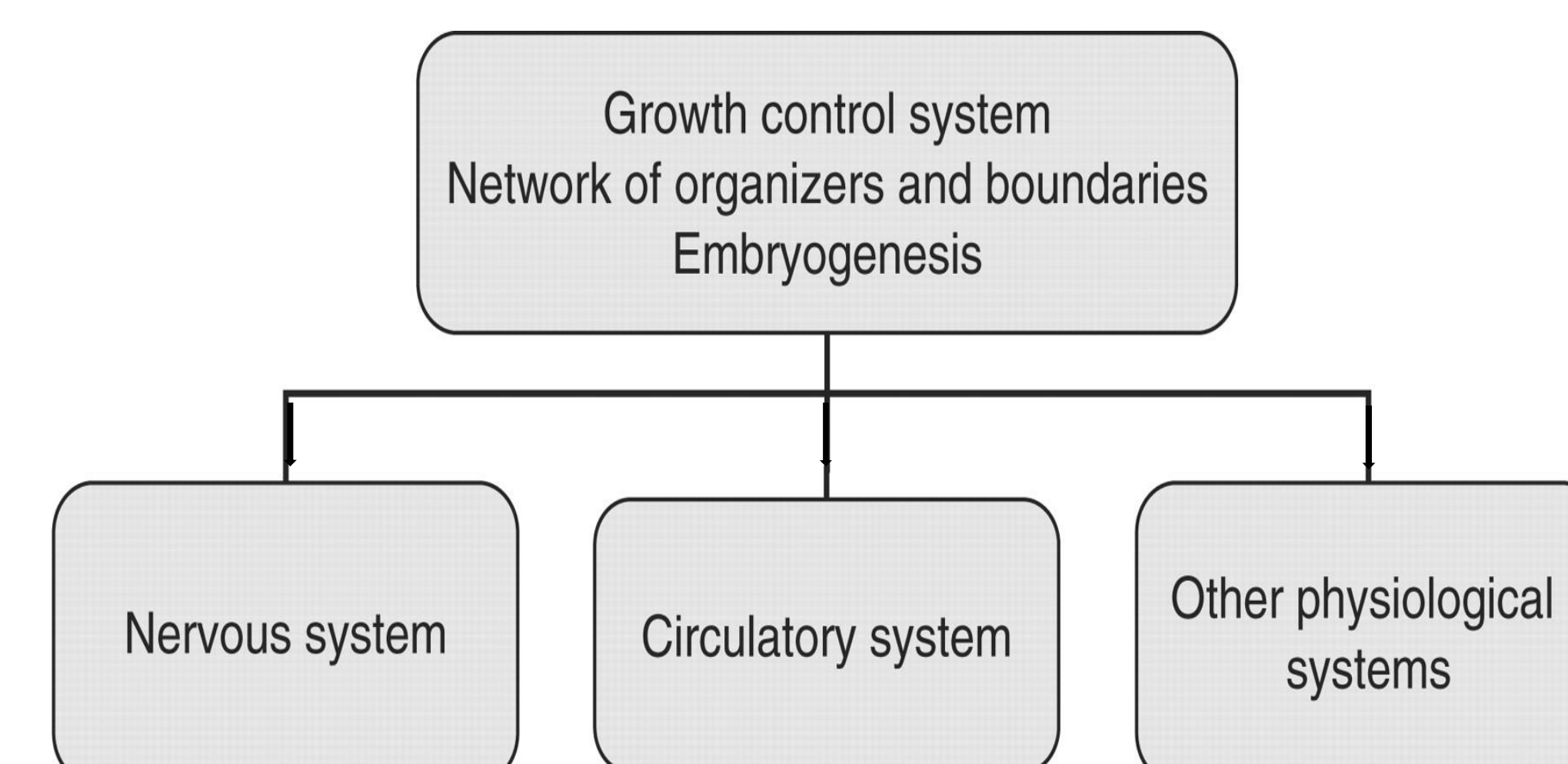


Figure 1. The role of the growth control system. In embryogenesis, the development of organizers precedes the development of other physiological systems. The formation, maintenance and regulation of all the physiological systems are dependent on the activity of the growth control system both during and after embryogenesis.

- ◆ Organizers are singular points of bioelectric field and morphogen gradient field. A singular point is a point of discontinuity. It indicates abrupt transition from one state to another. Due to their nature of singularity, they are prone to subtle, nonspecific perturbations which can cause long lasting systemic changes related to growth control activities.[1,7,8]
- ◆ As both organizers and acupuncture points are related to bioelectric field and prone to nonspecific perturbations [7,8], the growth control model suggests that acupuncture points originate from a network of under-differentiated organizers with high density of stem cells [8] in embryogenesis and the meridians originate from growth control boundaries which are associated with high density of gap junctions and therefore high electric conductance. This explains the distribution and non-specific activation of organizers and acupuncture points, the distribution of meridians, the origin and physiological function of the meridian system, the long term effects, and the origin of neurohumoral effects of acupuncture. [1,8]

Prospective tests on the model of growth control system:

The gold standard of validating a scientific theory is independent confirmation of its predictions by multiple research groups.[11] The growth control model has met this standard:

Confirmed prediction #1: Organizers have local maximum electric conductance and electric current density. It is a macroscopic singular point of abrupt change in electric current flow facilitated by high density of gap junctions. [12-15]

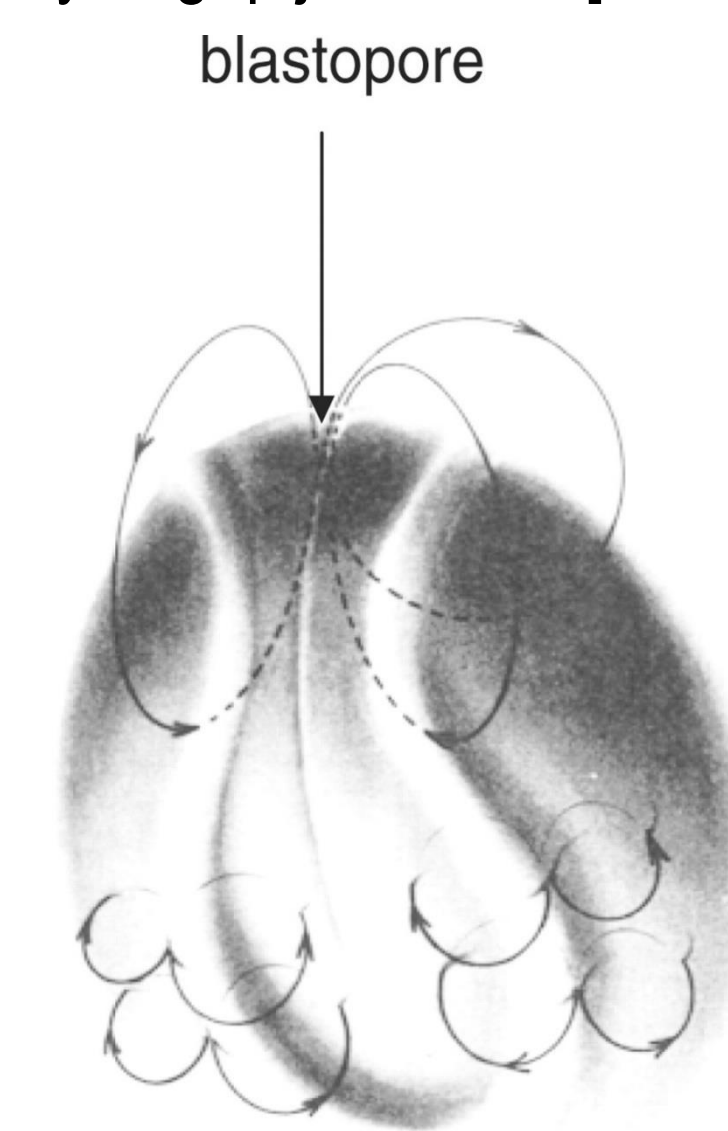


Figure 2. Electric currents traversing an embryo (Shi and Borgens, *Dev Dynamics* 1996;202:102. Courtesy of John Wiley & Sons). The blastopore, a classic organizer, has high electric conductance and current density. A steady blastopore current persists after early embryogenesis. The electric fields polarize the embryo and serve as cues for morphogenesis. These results confirmed earlier predictions. (Shang, *Am J Chin Med* 1989;17:119-27).

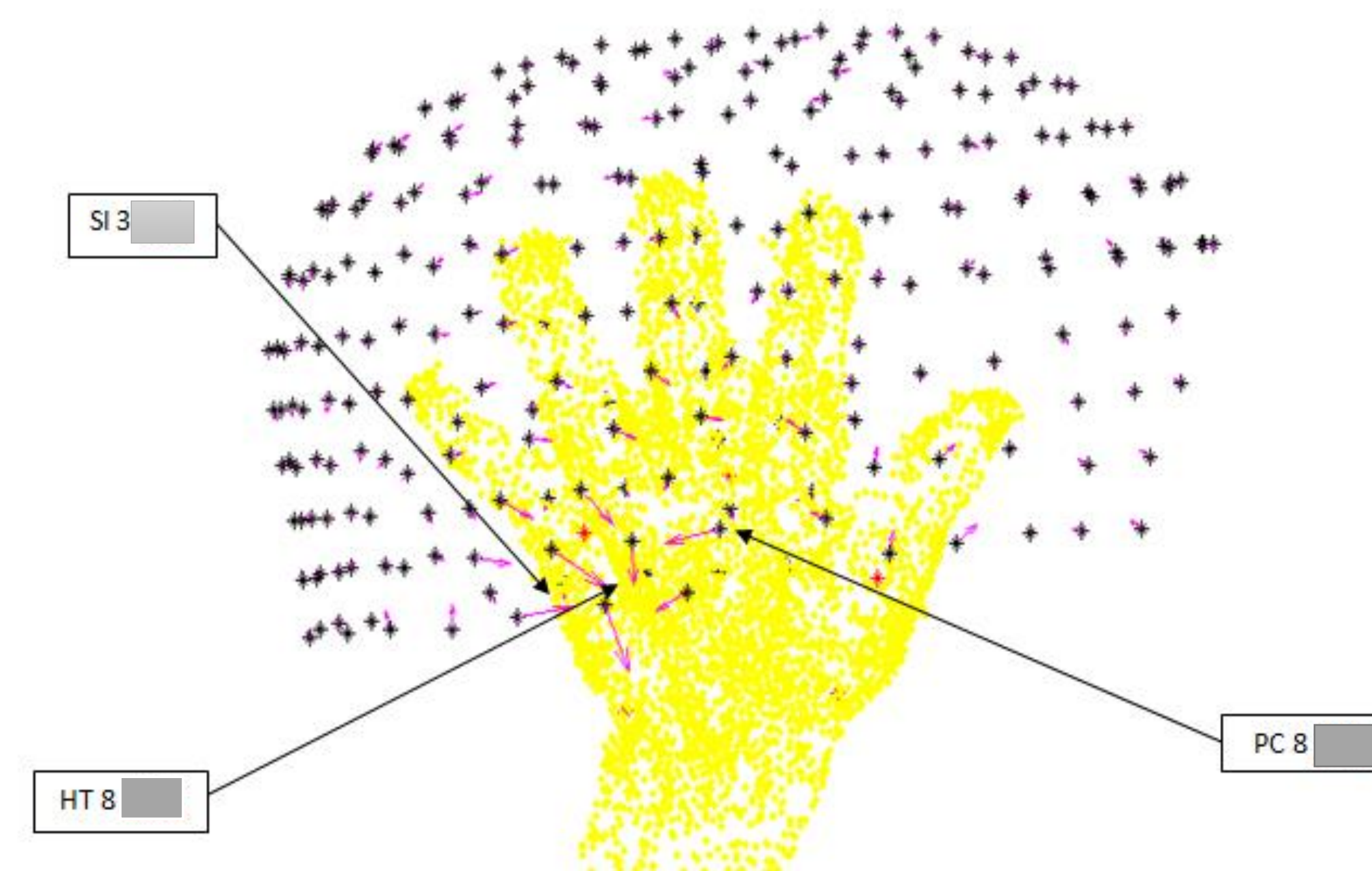


Figure 3: Similar patterns of singular points in DC bioelectromagnetic field have been detected on human palm using superconducting quantum interference device (SQUID) with 0.1Hz Lowpass filter. These patterns are correlated with acupuncture points – supporting the growth control model:

- ◆ **Confirmed prediction #2:** Boundaries in growth control have high electric conductance: High density of gap junctions become restricted at discrete boundaries during development, leading to the subdivision of the embryo into communication compartment domains. [9] The growth control boundaries are the separatrices of morphogen gradient and bioelectric field.
- ◆ **Confirmed prediction #3:** Singularity and separatrix exist in morphogenesis [16, 17]
- ◆ **Confirmed prediction #4:** Some morphogens and organizers continue to function after embryogenesis [18-20]
- ◆ **Confirmed prediction #5:** Acupuncture has extensive growth control effects: Acupuncture regulates various growth factors such as retinoic acid[21], NGF[22], TGF-beta1, IL-6, and the expression of various growth control genes such as c-fos,[23] Bcl-2, Bax, fas and FasL[10]. Acupuncture regulates apoptosis,[10] regeneration,[21] differentiation and cell proliferation[22] of various tissues. The 'classic' neuro-humoral factors induced by acupuncture such as serotonin and endorphin also have growth-control effects.[24,25] In randomized controlled trials, acupuncture has shown efficacy in treating growth control related disorders such as inflammatory bowel disease,[26]spinal cord injuries[27] and low sperm quality[28,29].
- ◆ **Confirmed prediction #6:** The efficacy of acupuncture is negatively correlated with patients' age [8]
- ◆ **Confirmed prediction #7:** Acupuncture points tend to distribute at boundaries between body domains and therefore overlap with connective tissue. [8]

Conclusion

- Acupuncture related modalities can be effective for wound healing with large effect sizes in randomized controlled trials by activating the organizers of growth control and increasing the wound healing response.
- Further research is needed to fully understand the mechanisms by which acupuncture promotes wound healing and to determine the optimal therapeutic parameters for wound healing. The development of wearable medical devices with low intensity transcutaneous acupoint stimulation can improve the cost effectiveness of wound healing.

The growth control model as biological basis of acupuncture

- ◆ Outlines the structure, function of a new physiological system.
- ◆ Has been prospectively tested with multiple independently confirmed predictions
- ◆ Has shed light on the distribution and non-specific activation of organizers and acupuncture points, the distribution of meridians, the origin and physiological function of the meridian system, the long term effects, and the origin of neurohumoral effects of acupuncture. [1,8]
- ◆ As Maxwell observed: 'Every existence above a certain rank has its singular points: the higher the rank, the more of them. At these points, influences whose physical magnitude is too small to be taken account of by a finite being, may produce results of the greatest importance. All great results produced by human endeavour depend on taking advantage of these singular states when they occur.' [30] The existence of singularity in growth control system offers a convenient and potentially cost-effective way of manipulating the growth control system, stem cells and related pathophysiology for wound healing.

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