

Mechanisms of action: two principal pathways

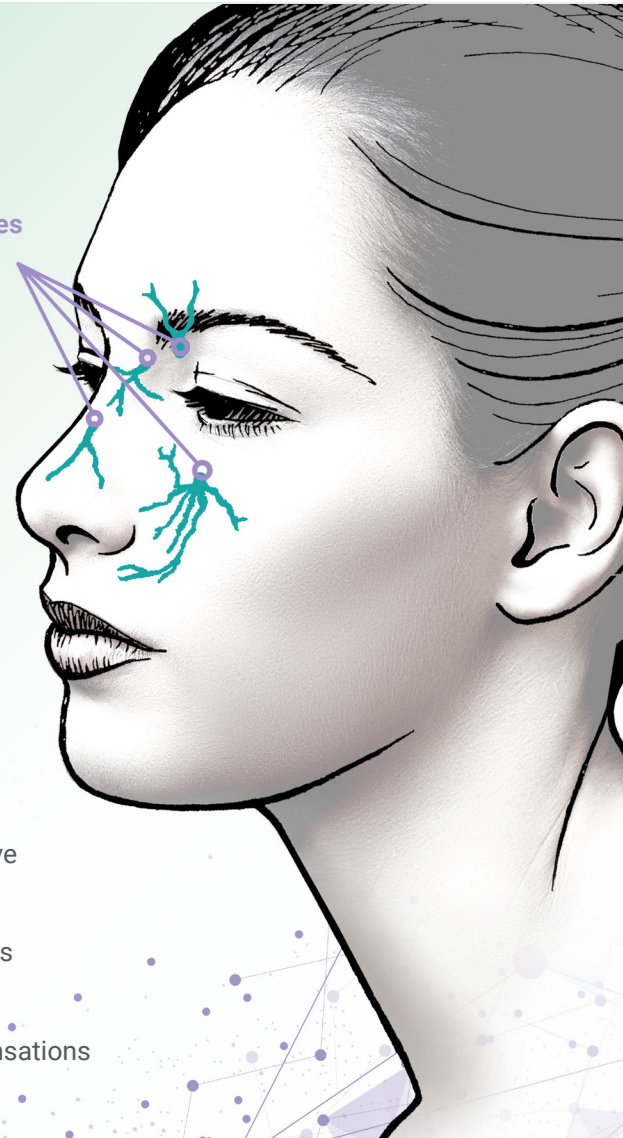
1. Vasoconstriction

- The blood vessels that supply the sinus and nasal mucosa are surrounded by sympathetic nerve fibers.
- Electrical stimulation of sympathetic nerve fibers has been shown to promote release of norepinephrine.¹⁻³
- Norepinephrine facilitates smooth muscle contraction around the blood vessels, leading to vasoconstriction.⁴
- Vasoconstriction of arterioles and venous vessels, in the context of sinonasal inflammation, results in smaller vessel diameter, relieving pressure on the nerves and reducing resistance to air flow.
- Over time, repeated vasoconstriction can reduce edema and extravasation of inflammatory immune cells, contributing to reduced symptom severity.

2. Trigeminal Nerve Stimulation

- The trigeminal nerve – the ophthalmic nerve (V₁) and maxillary nerve (V₂) – is responsible for relaying sensory information to the brain.
- Electrical microcurrent delivered in the periorbital regions stimulates subcutaneous fibers of these branches.
- Neuromodulation of the trigeminal nerve pathway may alleviate sensations of pain and pressure.

Trigeminal
Nerve Branches
(V₁, V₂)



Resources

¹ Mandel, Yossi, et al. "Vasoconstriction by electrical stimulation: new approach to control of non-compressible hemorrhage." *Scientific Reports* 3 (2013)

² Franco, O.S., et al. "Effects of different frequencies of transcutaneous electrical nerve stimulation on venous vascular reactivity." *Brazilian Journal of Medical and Biological Research* 47.5 (2014): 411-418.

³ Malm, L. "Stimulation of sympathetic nerve fibres to the nose in cats." *Acta otolaryngologica* 75.2-6 (1973): 519-526.

⁴ Fischer, Laurent, et al. "Adrenergic and non-adrenergic vasoconstrictor mechanisms in the human nasal mucosa." *Rhinology* 31.1 (1993): 11-15.

ClearUP® as a drug-free treatment option

For more information about ClearUP Sinus Pain Relief as an option for your patients to relieve sinus pain from allergic rhinitis, or to place an order, visit ClearUPsinus.com



About Tivic Health Systems Inc.

Tivic Health Systems Inc. is a neuromodulation medical device company dedicated to developing microcurrent therapy solutions for chronic diseases and conditions. Founded in 2016, Tivic Health is part of a \$6.2B global industry and is dedicated to harnessing the power of neuromodulation for home use products and to empowering people to improve their health and quality of life.



TIVIC HEALTH™

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Menlo Park, CA 94025

ClearUPsinus.com

SPECIFICATIONS: Output current: AC-coupled square wave. Maximum current density at 500 ohms is 3.2 mA/cm². Maximum voltage at 500 ohms +/-3V. Power source: Rechargeable lithium-ion AAA cell, +3.7V @ .3AH, safety PCB. Dimensions: Approximately L 3.3 x W 1.8 x H 1 (inch). Weight: Approximately 55 grams.

IMPORTANT SAFETY INFORMATION:

Warnings and Precautions (For Specific Populations)

- Do not use if patient has an implanted metallic device or electrostimulation device, including a pacemaker, a DBS (Deep Brain Stimulation device) or a cochlear implant.
- Do not use if patient has an abnormal cranial nerve or other neurological findings or symptoms.
- Do not use on pregnant women because the safety of electrical nerve stimulation during pregnancy or delivery has not been established.
- Do not use if the patient has suspected or diagnosed heart disease.
- Do not use on broken skin or a wound of any kind.

Warnings and Precautions (For Specific Medical Environments)

- Do not have patient apply stimulation in the presence of electronic monitoring equipment (e.g. cardiac monitors, ECG alarms) because it may disrupt the proper operation of the equipment.
- Do not use near active HF surgical equipment or in the RF-shielded room of an MRI scanner or near RF-emitting equipment such as diathermy and electrocautery & RFID because it could result in improper operation.

Adverse Events: A minority of subjects (<3% in clinical studies) experienced temporary skin irritation.

Drug Interactions: Can be taken with sinus medications safely.

Indications and Usage: ClearUP Sinus Pain Relief is for the temporary relief of sinus pain associated with allergic rhinitis in adults 18 years and older. Recommended usage is 1-4 times per day as needed. Relief lasts up to 6 hours.

Let's make one thing clear.

There's a new, drug-free way to treat the sinus pain of **allergic rhinitis**.

Learn
more at
booth 104



ClearUP™
Sinus Pain Relief

FDA cleared microcurrent
waveform treatment for
adults 18+ years old

Introducing ClearUP® Sinus Pain Relief

ClearUP Sinus Pain Relief is a drug-free, highly effective microcurrent treatment for the temporary relief of sinus pain associated with allergic rhinitis.

As a physician who treats allergic rhinitis, you know how common this condition is. In fact, 40 to 60 million Americans live with allergic rhinitis. The symptoms of sinus pain can negatively impact your patients' daily life.



ClearUP is a handheld peripheral nerve neuromodulation device that is applied to the bilateral periorbital regions and emits weak (microampere) levels of current.



FDA cleared as a drug-free option for allergic rhinitis.



Chemical-free and non-invasive, with minimal side effects.



Over the counter, no prescription required.

ClearUP as a drug-free treatment option

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How ClearUP works to reduce sinus pain

Although ClearUP's microcurrent technology should be self-administered by patients, physicians can provide an introduction to how the device is used and offer guidance in a clinical setting.

The patient places the device's electrode tip on the skin of the cheek and follows a treatment path along the cheek and nose, and below the brow ridge.

When the device vibrates, a treatment point has been identified where the microampere current can pass more easily. The patient keeps the device in place until it stops vibrating after 7 seconds.

ClearUP takes about 5 minutes total to administer (2.5 minutes on each side of the face). Recommended treatment is up to four times a day.



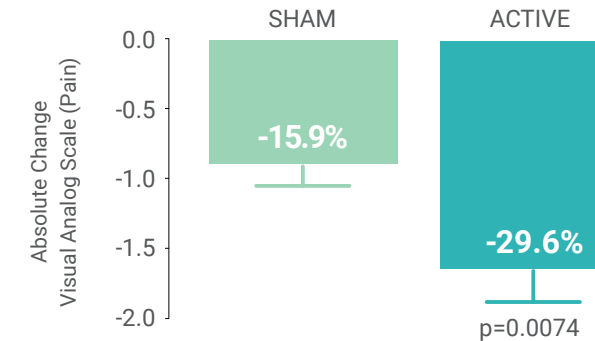
Two Microcurrent Clinical Trials have been conducted to assess ClearUP's safety and efficacy.

In the first trial[^], participants using an active ClearUP device vs. a sham treatment reported significant improvement in sinus pain.

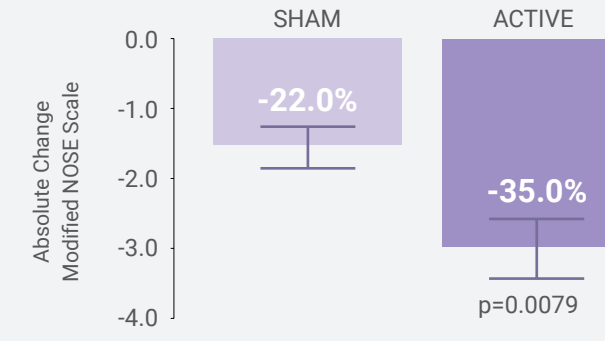
74%
success

► ClearUP was proven to reduce sinus pain in almost 3 out of 4 participants.

► Subjects reported a rapid reduction (-29.6%) in sinus pain.



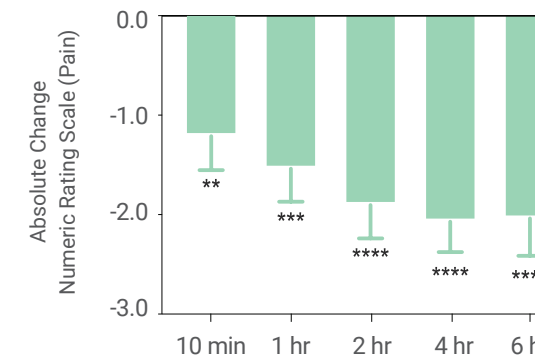
► Subjects reported a rapid reduction (-35%) in congestion.



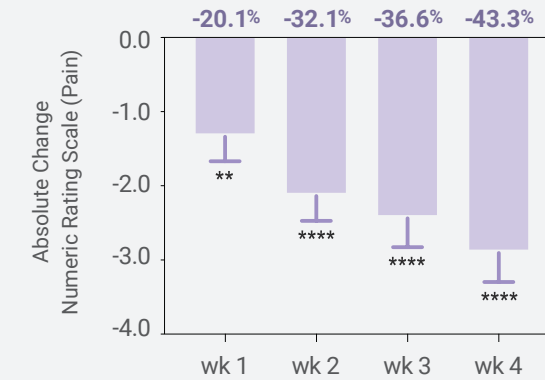
82%
preferred ClearUP to other allergy treatments.

In the second trial^{^^}, subjects receiving a 5-minute treatment in office followed by 4 weeks of at-home use also saw marked improvements.

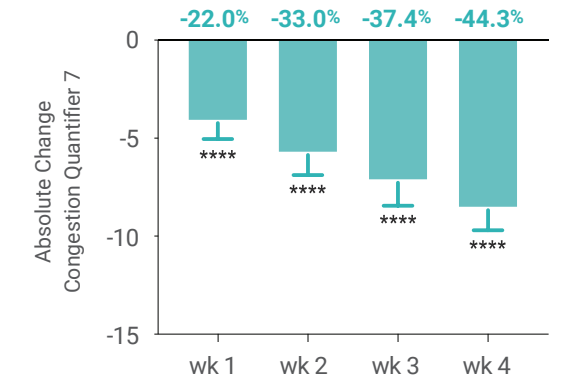
► ClearUP provided sinus pain relief for up to 6 hours.



► Subjects reported a significant reduction in sinus pain over 4 weeks.



► Subjects reported a significant reduction in congestion over 4 weeks.



77%
would recommend ClearUP to treat sinus symptoms.

[^] At Stanford Sinus Center, Palo Alto, Calif. | Publication: Maul, X.A., Borchard, N.A., Hwang, P.H., and Nayak, J.V. (2019, April). Microcurrent technology for rapid relief of sinus pain: a randomized, placebo-controlled, double-blinded clinical trial in International Forum of Allergy and Rhinology (IFAR) (Vol. 9, No. 4, Pp. 352-356) | Principal investigator: Jayakar Nayak, MD, PhD, Associate Professor and Director of Rhinology Research, Stanford University

^{^^} At Allergy and Asthma Associates of Santa Clara Valley Research Center, Santa Clara, Calif. | Publication: In preparation for peer review | Principal investigator: Alan Goldsobel, MD, Adjunct Associate Professor, Stanford University
Note: Congestion data has not been reviewed by the FDA.