



Non-invasive Hypertension & Migraine Therapy Devices

PhysioCue Devices & Health Monitoring App



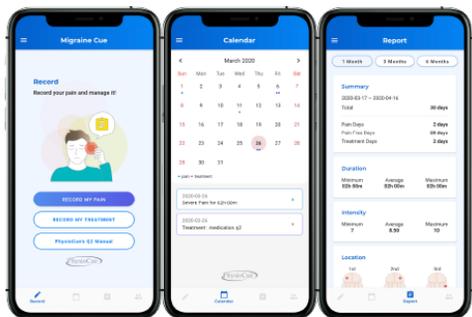
Hypertension Therapy



Migraine & Headache Therapy



Hypertension Therapy & BP Monitor



MigraineCue Mobile App



Hypertension BP Monitoring Q3 Device

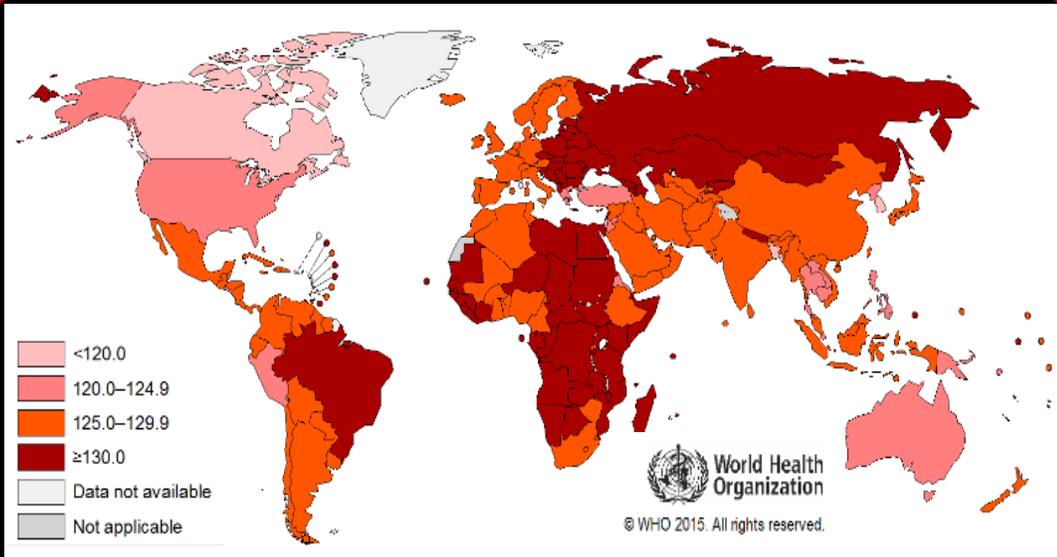


Hypertension Mobile App

Hypertension – Silent Killer: 1.4 B People



1.4 Billion Worldwide



Mean Systolic BP (mmHg)– Males, age 18+ (2014)



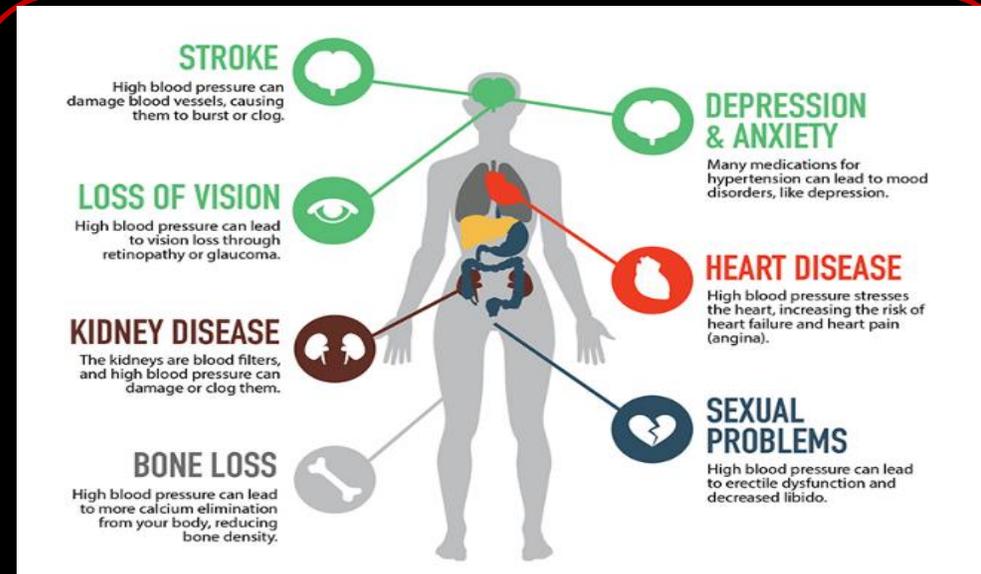
- 1B people → 1.5B by 2025
- \$1 trillion in direct healthcare cost, WW
- \$3.6 trillion in indirect costs, WW
- \$48.6B in direct & indirect, US

Over **50%** are not under control

- Treated but not controlled
- Unaware
- Aware but not treated



Silent Killer



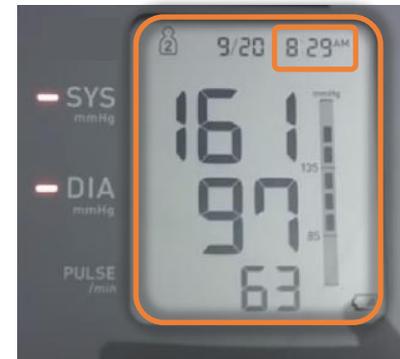
- WW death due to hypertension complications: 9.4M per year
- Hypertension is responsible for 45% of deaths due to heart disease and 51% of deaths due to stroke, WW.



PhysioCue Q1 works with throughout all ages, ethnicity, gender, and regardless of your blood pressure level, or your current medication.



Jose Bolanos M.D.



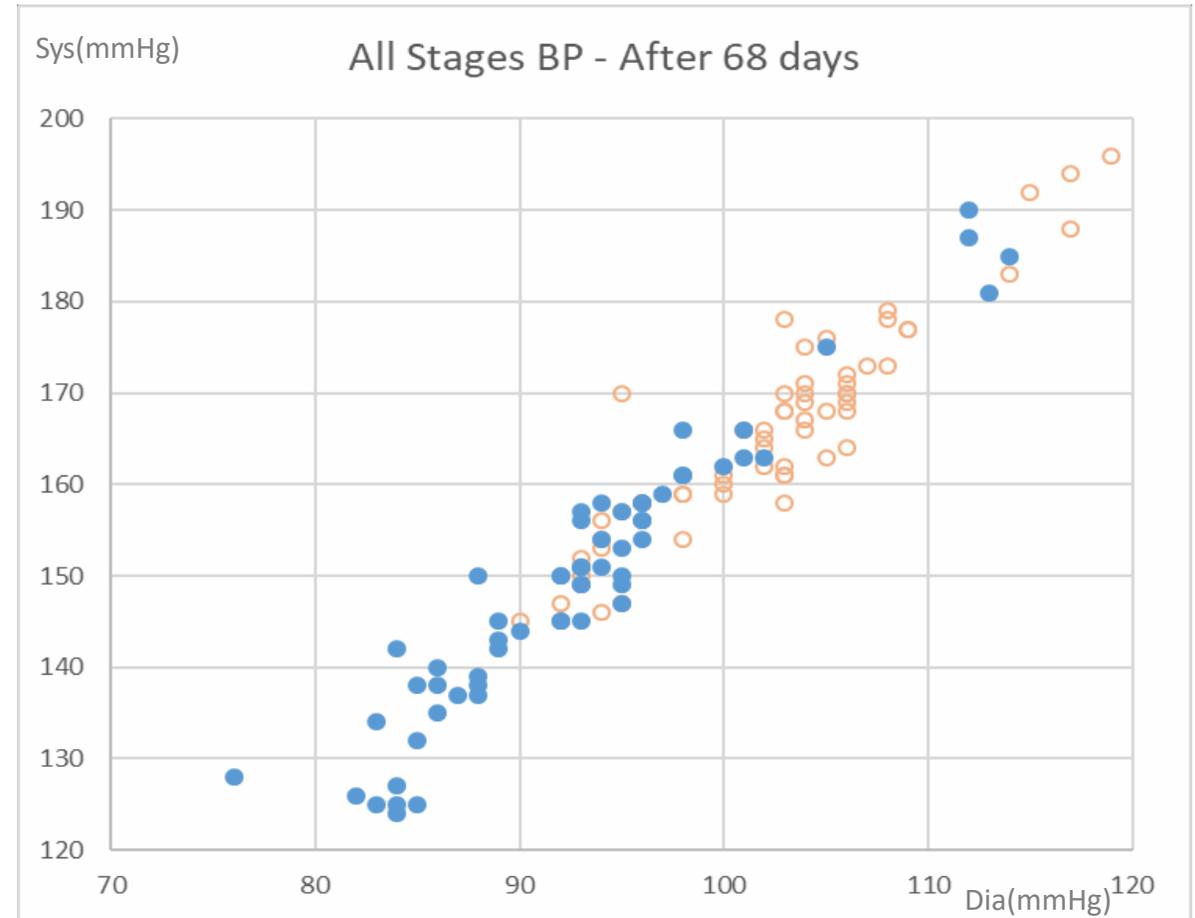
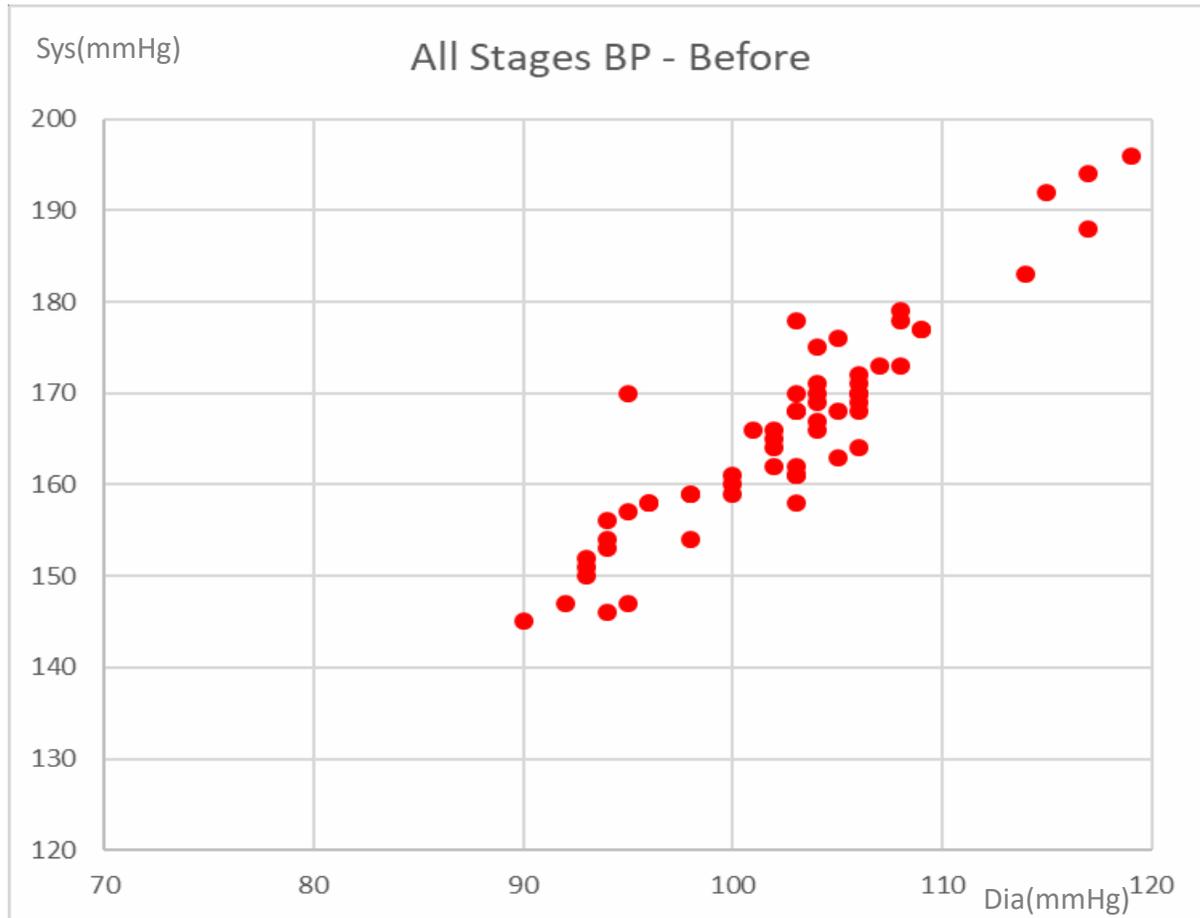
- Safe
- Non-Invasive
- Easy to use
- 5 minutes!

Demo PhysioCue Hypertension Therapy Device



Our devices work for all ages, ethnicity, and gender regardless of your blood pressure level, or your current medication

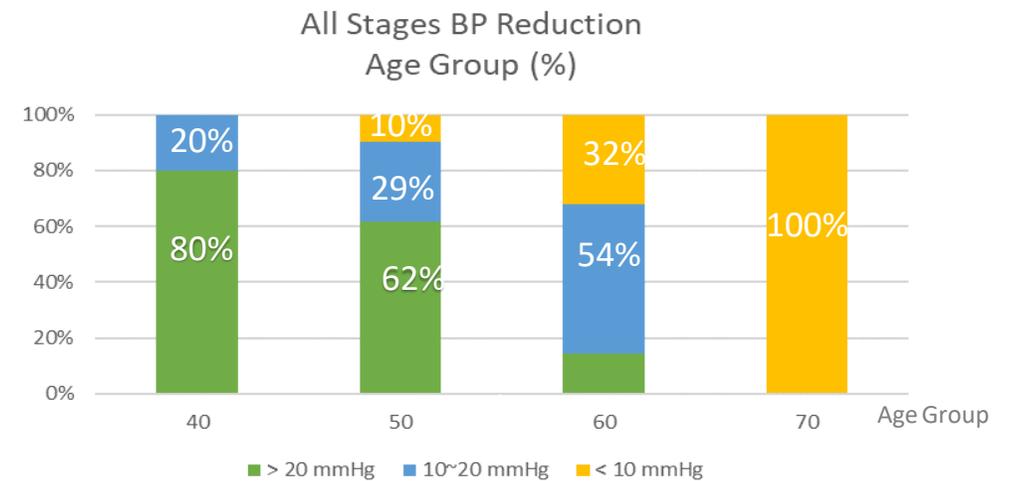
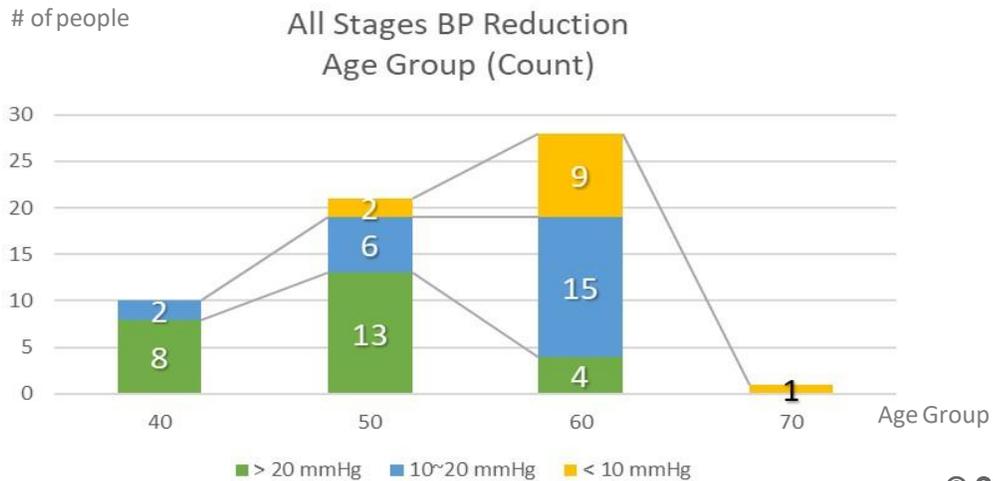
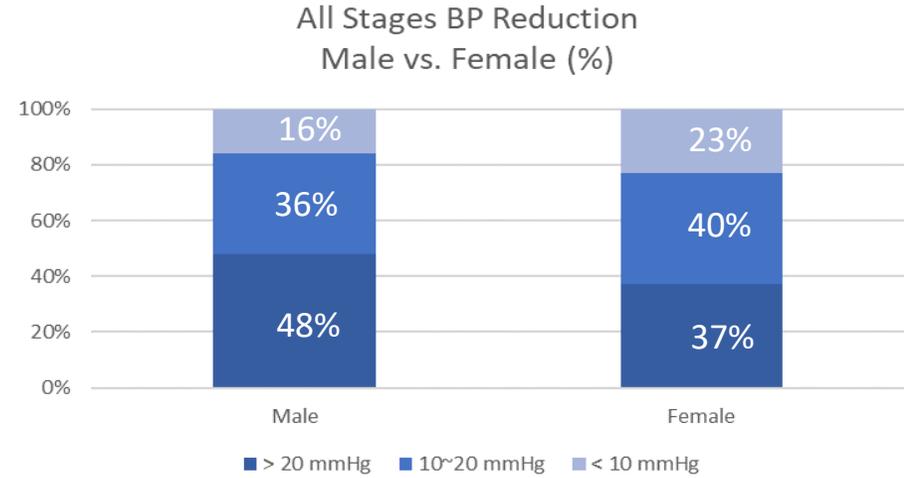
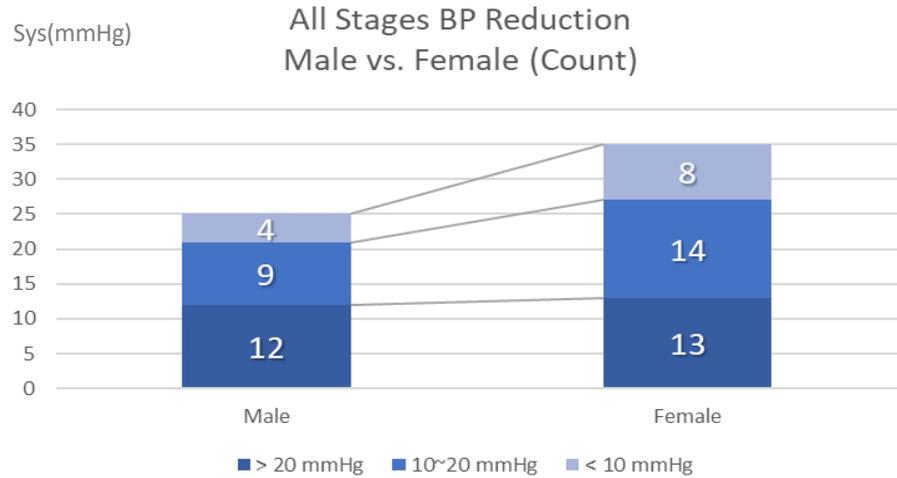
60 Patients net result of Therapy Group after 68 days, Before vs. After



60 patients used the device **once a day at the hospital**

- **83% of Stage 2 people became Stage 1**
- **78% of Stage 3 people became Stage 2**
- **20% of Stage 4 people became Stage 3**

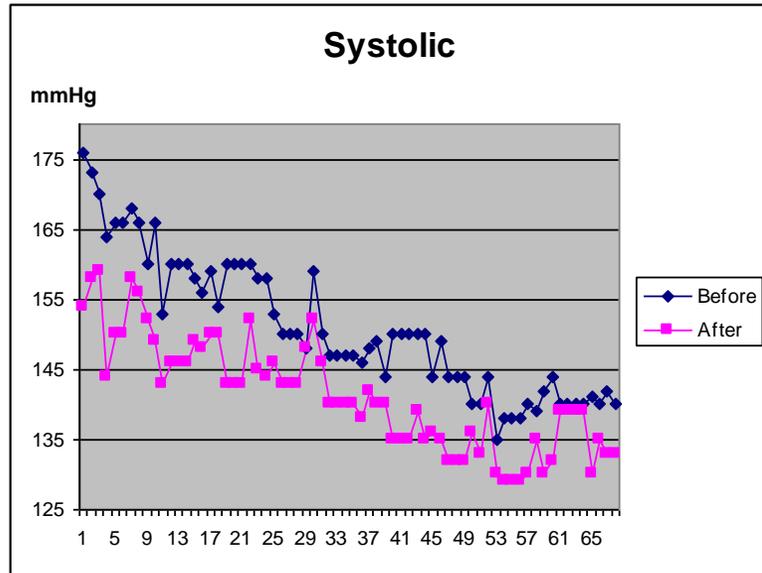
60 Patients net result of Therapy Group after 68 days, Male vs. Female, and Per age group



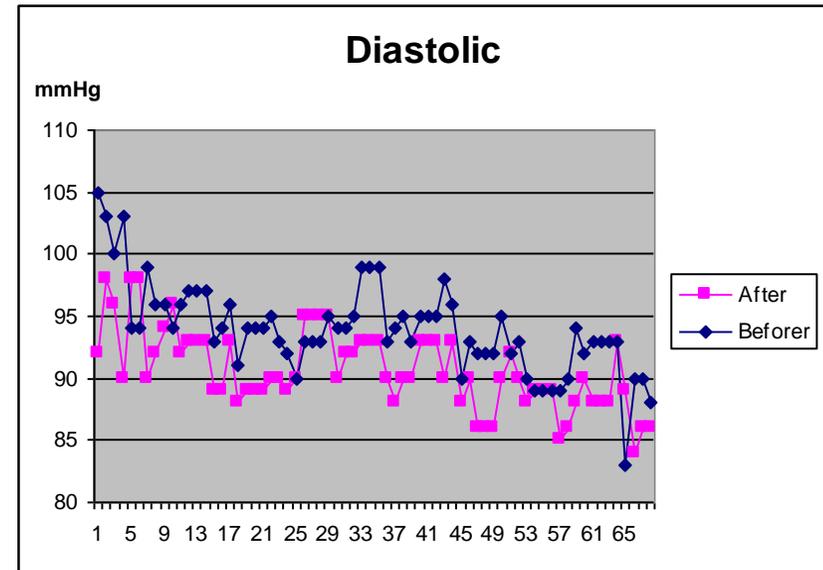
Beneficial Cumulative Effects of Therapy



- 58 years old male case
- Diagnosed with Stage 2 initially
- BP measured “Before” and “After” use of PhysioCue for 5 minutes
- No medication during 68 days:



After: BP reading taken 20-30 minutes after treatment



Daily treatment administered at the hospital once a day over a period of 68 days excluding weekends (plotted as Friday)

➤ BP Reduction

➤ Gap  between daily “Before” and “After” is **diminishing**

Rest BP, Prior Daily Treatment

mmHg	Systolic	Diastolic
Day 1	176	105
Day 68	140	88
Lowest	129	84

Users' Feedback w/ Medication



67 year old male

I have been healthy and disciplined daily swimming and exercise regime all my life. Then, 6 months ago, I was diagnosed with high blood pressure and was depressed about it. My blood pressure was about **160/96** over the last few months. After I used PhysioCue device, I could feel an immediate drop and the blood pressure was **130/79!**

Now, it has been over 2 weeks and my blood pressure is hovering around 120/75 in any day.



65 year old male

I have been taking multiple prescribed anti-hypertensive medications for the past 6 years. My blood pressure prior to beginning medications was usually in the area of **175/105** When I used PhysioCue therapy device, my blood pressure dropped from 176/100 to 155/90 after 5 minute therapy. my blood pressure and pulse became **consistently steadier.**

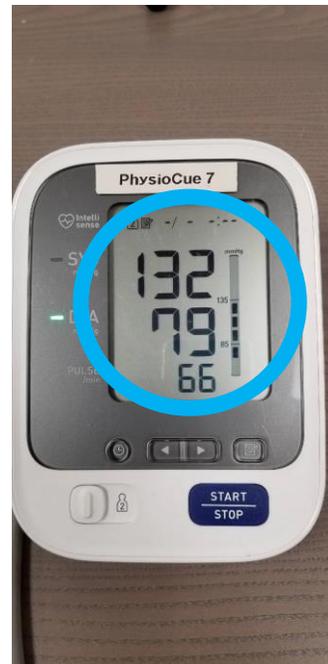
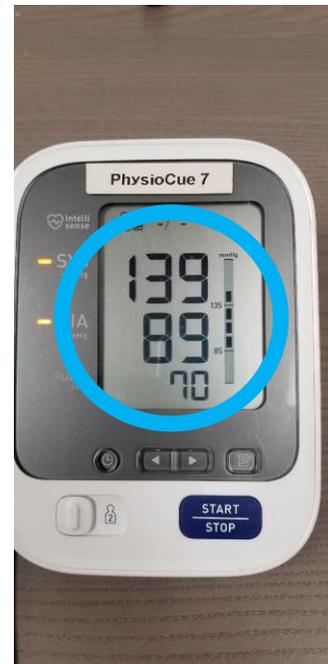
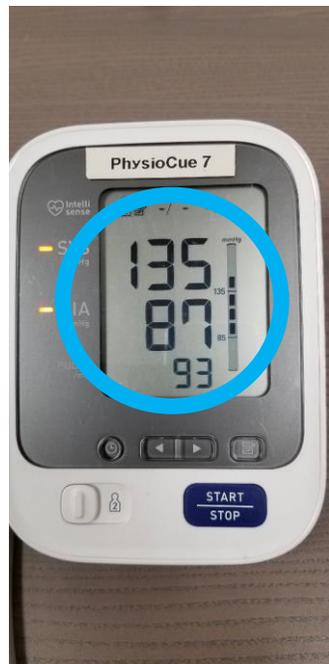
My overall blood pressure is less erratic, consistently recoding in the 130/85 range, which is a big improvement.



And many more!



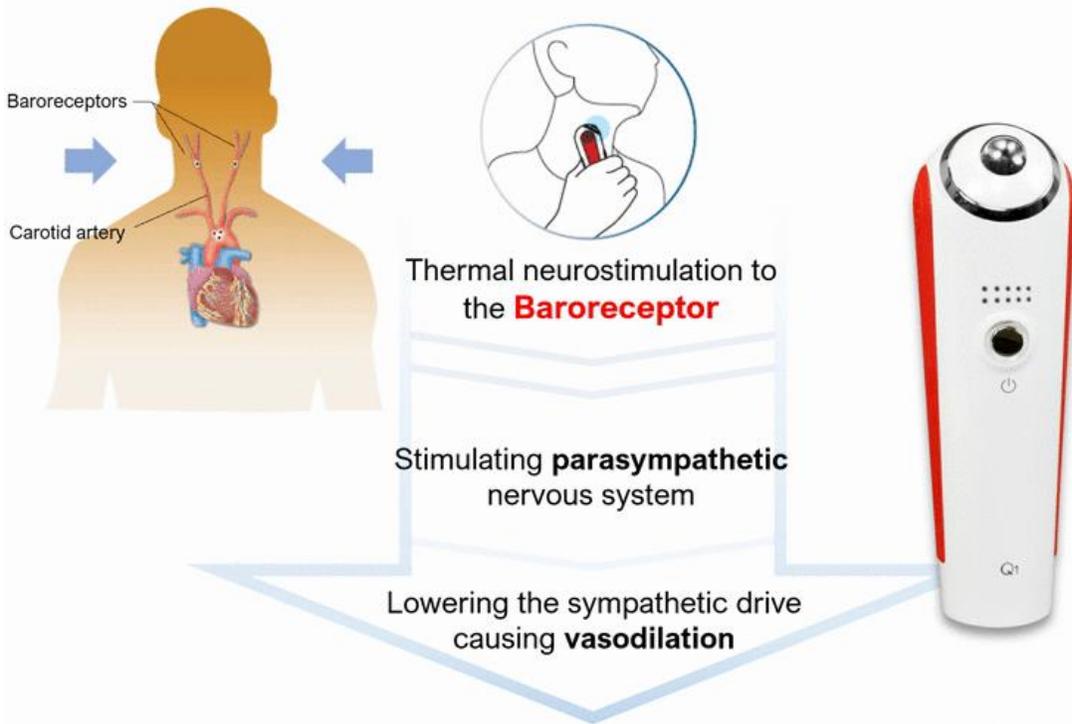
5 MINUTES



How It Works - Mechanism of Action “ Baroreflex”



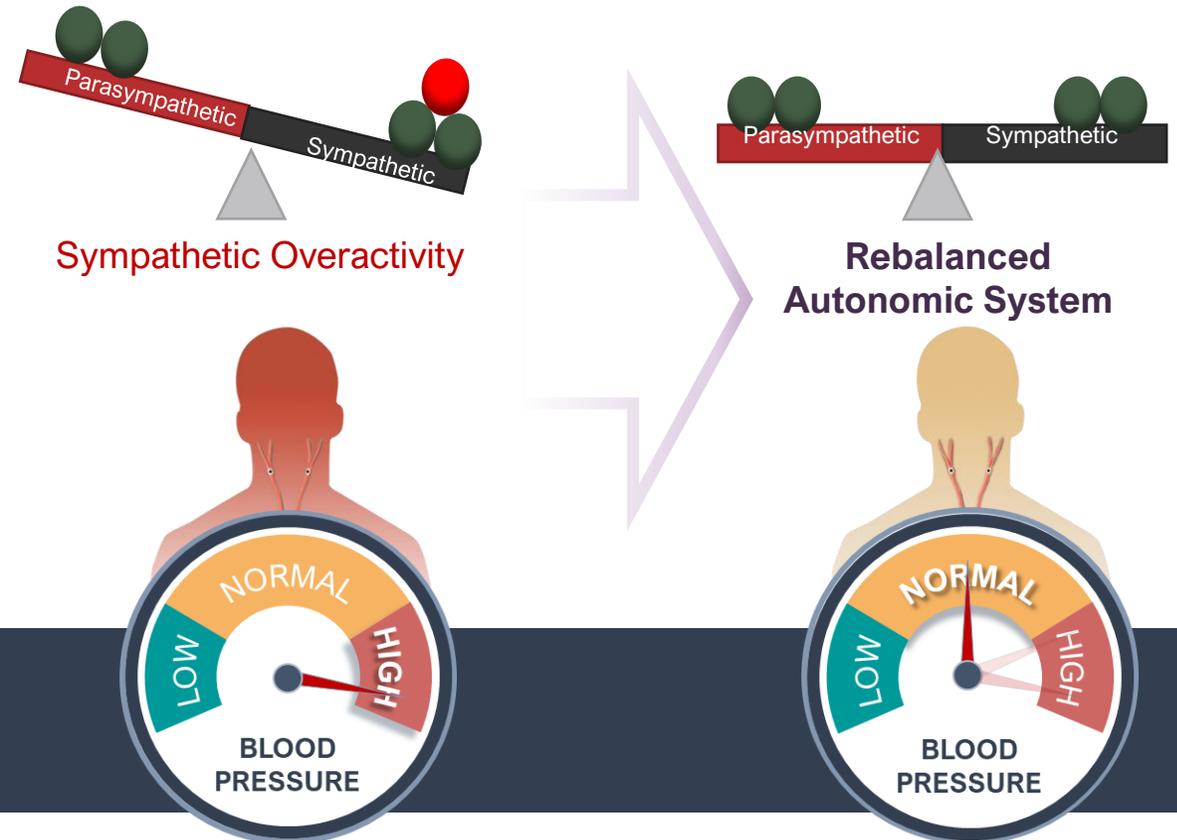
① Patented Thermal Neurostimulation Technology



**Decrease
Blood Pressure & Heart Rate**

② Autonomic System Balance

Continuous therapy results conditioning baroreceptor to **regain proper balance in autonomic system**



Biosensor BP Monitor Mobile Service



Mobile Application



Blood Pressure Biosensors



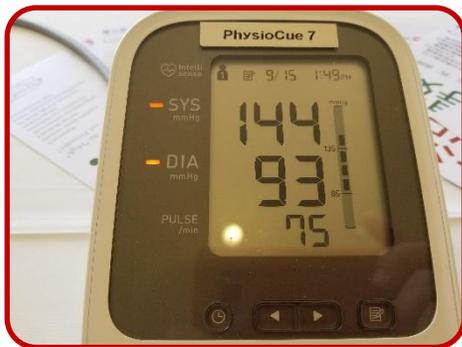
Bluetooth®



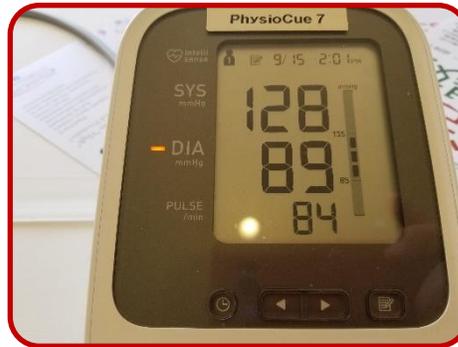
Data Collection & Distribution



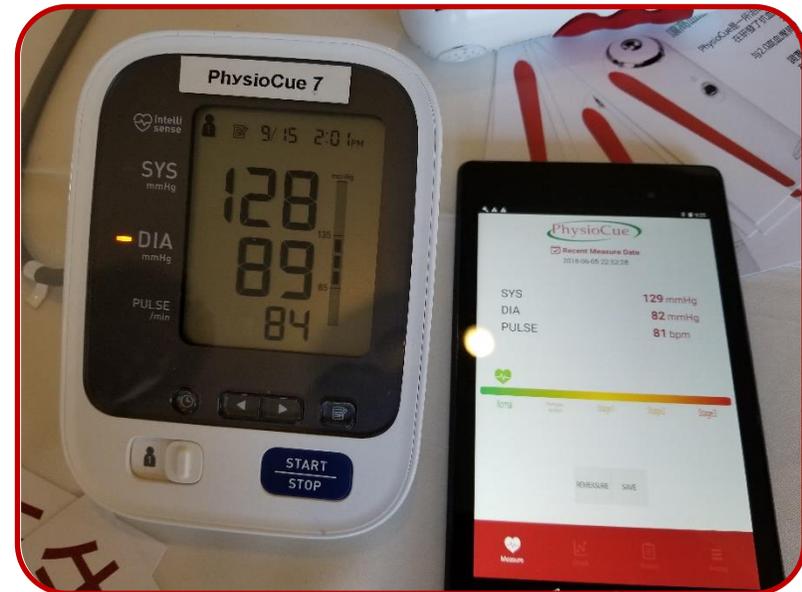
Biosensor BP Monitoring vs Omron BP Monitor



Before



After



Bio sensor measuring vs Omron BP Monitor



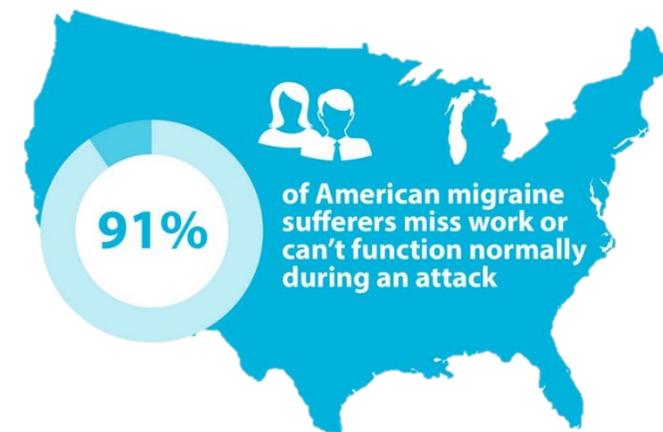
Migraine and Headache Problem



- 1B WW, 39M US
 - 3rd most common disease in the world
 - 25% US household
 - Women suffers 3 times more than man
 - \$20B in Lost Productivity (US)



- No Cure
 - \$4,619/yr direct cost
 - Not under control
 - Near 50% of patients
 - Often lead to opioid overdose
 - Hard to describe the symptoms to doctors
 - : Triggers (food, environment, stress, etc),
 - Pain area, time occurred, etc





Our Approach

- Non-Invasive and Safe**
- 5 minutes**
- No side-effects No pain**
- Affordable**



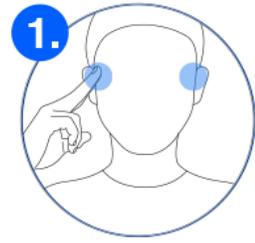
Q4 Bio-Sensor BP Monitor



Q3 Hypertension Therapy & BP Monitor Combo with APP

Q1 Hypertension Therapy

MigraineCue Mobile Diary



Find your temples



Turn it ON



Wait for solid green with beep



Apply the device 2~2.5 minutes



Repeat on the other side



Pilot Study



Cold Temperature Therapy in Migraine Patients: Pilot Study

Brajesh Agrawal, MD, Verity Medical Group

Abstract

An estimated 45 million Americans are believed to suffer from recurrent headaches per the National Headache Foundation (1). Among these headaches, tension-type is the most common, it is a nonspecific, benign headache, experienced by approximately 78% of adults. It is not vascular or migrainous, and not related to organic disease. Some patients with headache report that they have frequently used physical therapies such as application of cold temperature to relieve their headache. There are only a few reported studies related to cold temperature therapies in patients with migraine. In this study, we investigated the effect of cold temperature application on migraine patients. Fifteen migraine patients were included. Cold temperature therapy was administered to them by PhysioCue device. Patients used PhysioCue device during their migraine attacks. Before and after the cold temperature therapy, headache severity was recorded by using visual analogue scale (VAS). Patients used PhysioCue device for 5 min in each application. They recorded their VAS score just after the therapy and 5 min, 1 h, 2 h and 3 h later. Five minutes after treatment of the attack, VAS score was decreased from 7.78 ± 1.84 to 5.45 ± 2.45 ($P < 0.01$). Cold temperature application alone may be effective in patients suffering from migraine attacks. Its combination with conventional drugs should be investigated in future studies.

Introduction

An estimated 45 million Americans are believed to suffer from recurrent headaches per the National Headache Foundation (1). The pain is pressing or tightening, of mild to moderate intensity, and occurs on both sides of the head. This tension-type headache is generally divided into three categories, based on the frequency of attacks, as follows:

1. Episodic headache (which occurs less than once a month) is triggered by stress, anxiety, fatigue or anger.
2. Frequent headache (which occurs 1-15 days per month) is triggered by the same factors as above.
3. Chronic headache (which occurs 15 or more days per month) sufferer usually requires professional help.¹

The other two major types of headaches are as follows. (1) **Migraine** – affecting 6% of American men and 18% of American women for a total of almost 29 million people. See the next paragraph for more details on the migraine headache. (2) **Cluster type**- it is the least common type of headache, suffered by an estimated one million Americans, mostly males. These headaches occur in a group or cluster of attacks. Each period of attacks can last several weeks or months, and then disappear for months or years. Most sufferers get one to four headaches per day during a cluster period. The pain is of short duration, generally 30 to 45 minutes. (2)

Exclusion Criteria

We excluded patients who had more than one type of headache (menstrual migraine was also excluded), took prophylactic treatment and patients with analgesic or ergotamine overuse. We reasoned that menstrual migraine may have different clinical characteristics and it can be more resistant than non-menstrual migraine. Patients using prophylactic treatment were deemed to be the possible cause of confusion when evaluating the responses of migraine patients. Fifteen migraine patients were included in this study. All patients were evaluated by a neurologist.

Cold Temperature Administration

All patients kept a diary for migraine attacks (before and after the treatment). The diary included the time patients used the PhysioCue cold temperature device, visual analogue scale (VAS) of patients (before the treatment and 25 min, 1 h, 2 h, 3 h post-treatment), associated symptoms (i.e. nausea and vomiting) and side effects.

Cold temperature therapy was administered to the patients by PhysioCue cold temperature device (Fig. 1) during both migraine attacks. At the onset of the migraine attacks, patients used it for 5 min. Headache severity was measured by VAS (0: no pain to 10: severe pain) and pain relief was measured on a similar scale. They recorded their headache severity before the using and then 5 min, 1 h, 2 h and 3 h after the cold temperature therapy. Analgesic treatment was not taken within 5 min after the onset of cold therapy. If patients did not experience adequate relief from the headache, we allowed them to use analgesics 5 min after the onset of cold therapy.



Figure 1

The picture of PhysioCue device used in the study. Application of the device to the temporal area of the head.

In this study, we did not evaluate the patients beyond 3 h. This is a pilot study to determine the short-term effect of the treatment.

be significantly lower compared to VAS scores before treatment ($P < 0.01$) (Fig. 2). In patients with a clinical benefit, the mean number of attacks was 3.30 ± 1.37 , the mean pretherapy VAS score was 8.00 ± 2.04 and the duration of migraine attack was 21.23 ± 6.75 h. In patients who did not have any clinical benefit, mean attack number was 3.07 ± 1.03 , mean VAS score before the therapy was 7.69 ± 2.01 and duration of migraine attack was 19.00 ± 7.95 h. These were not significantly different between patients with or without clinical benefit ($P > 0.05$).

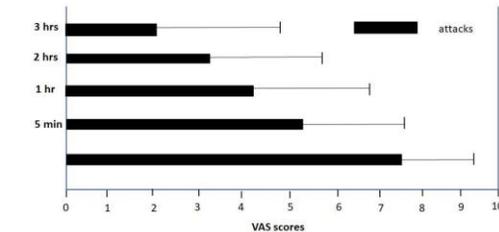


Figure 2

VAS scores before and after the treatment of attacks.

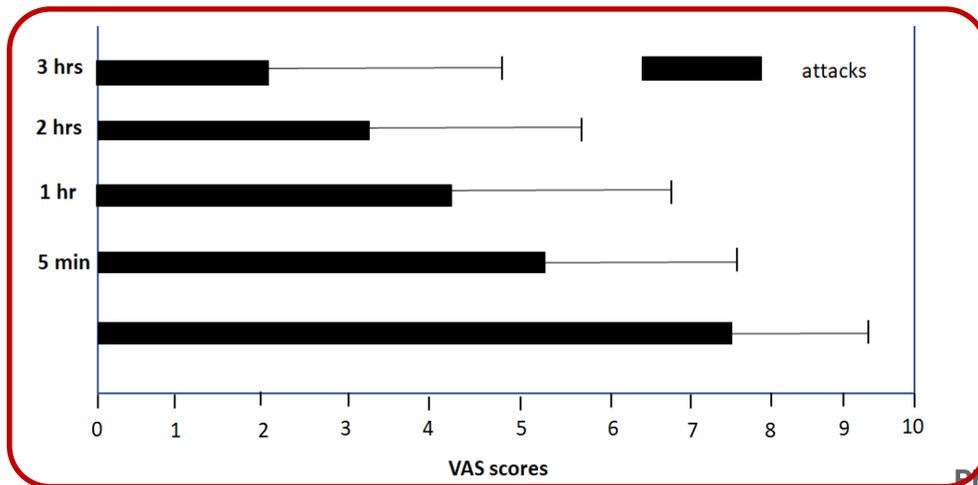
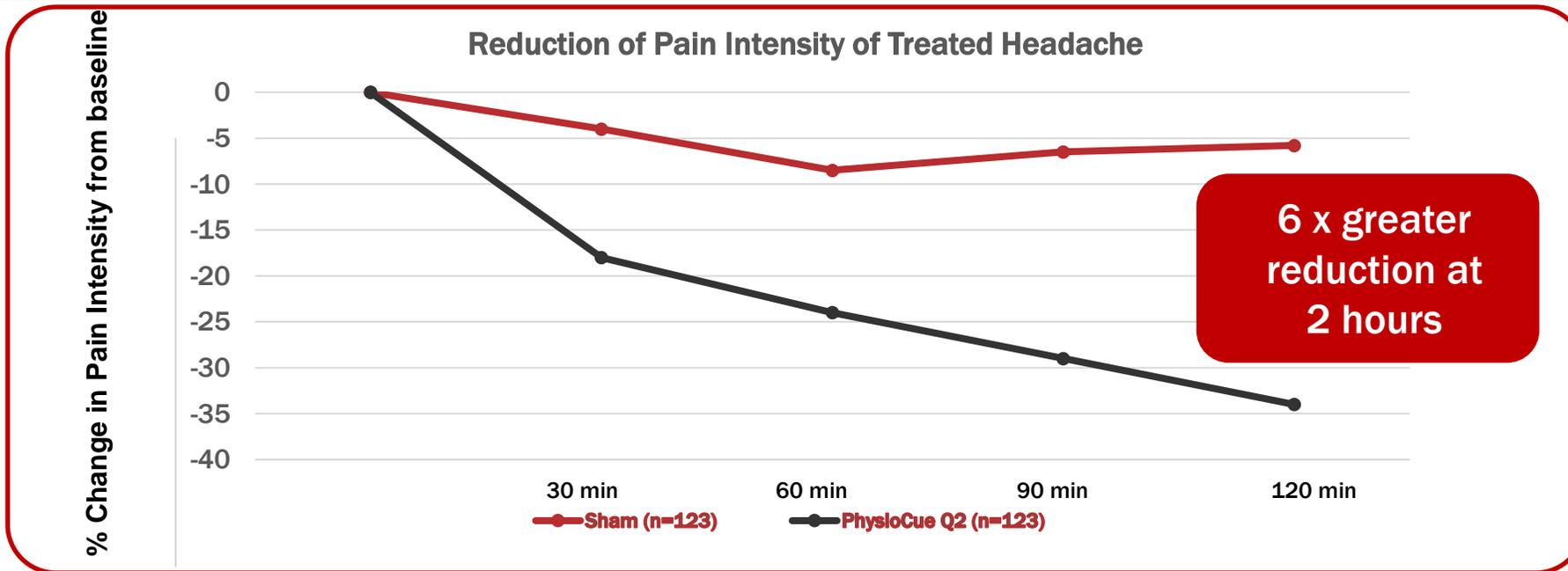
Discussion

Headache and Migraine are a chronic disease characterized by frequent attacks, high levels of pain and disability during attacks, causing reduced quality of life between attacks (20). It is a widespread disorder in the world, affecting ~10–15% of general population (22). There are four types of therapeutic choice for migraine patients as follows: general measures, abortive therapy, pain relief measures and prophylactic therapy. Abortive therapy is commonly employed to eliminate head pain and other symptoms associated with acute migraine headache (5). A variety of drugs are known to be effective in the treatment of migraine. Their side effects, however, may restrict their use in some patients and the medications used in these patients may worsen the present headache or even create a new kind of headache known as a drug abuse headache. It is well known that evidence-based complementary and alternative medical therapies have shown remarkable success in healing acute as well as chronic diseases. Therefore, non-pharmacological methods are worthy of investigation.

Various non-pharmacological methods have been investigated in the past to control the pain of acute migraine attacks. Application of an ice pack is a frequently used procedure. However, there are only a few reported studies in the literature regarding this non-pharmacological therapy (10-12). Since the potential benefits of cold temperature application in headache patients have not yet been clearly understood, we decided to investigate the benefits of cold temperature application on migraine patients.



Migraine & headache device case study



PhysioCue, Inc.



Migraine & Headache Therapy Device Users' Feedback



“It has been a great pleasure to experience your marvelous products first hand
**My headache disappeared in less than four minutes and never came back.
WOW!**” ---- Dr. Mariana Bozesan (AQAL Group)



“My sister finally used the PhysioCue for her headache and she said it worked.
She is really happy with it.” ---- Carol Gillespie



"It worked! I woke up with a really bad headache, the kind that could have easily turned into a migraine. I used the machine on my temple just like you said, 2.5 minutes on each side. **Headache went away!**” ---- Valeta Rodgers





**It has been a great pleasure
to experience your
marvelous products
firsthand.**

**My headache disappeared in
less than four minutes and
never came back. WOW!**

**---- Dr. Mariana Bozesan
(AQAL Group)**



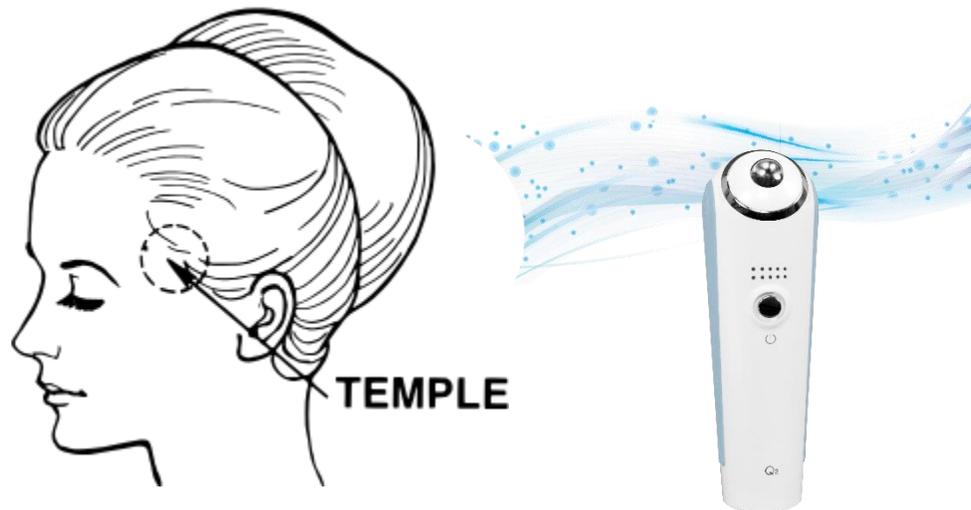
<https://aqalgroup.com/portfolio/#gsc.tab=0>

How it works? Migraine/Headache

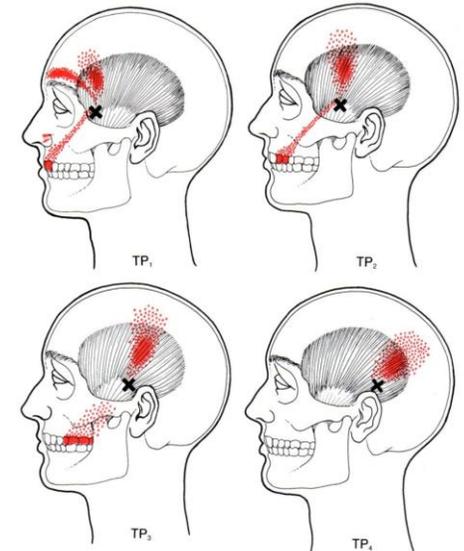
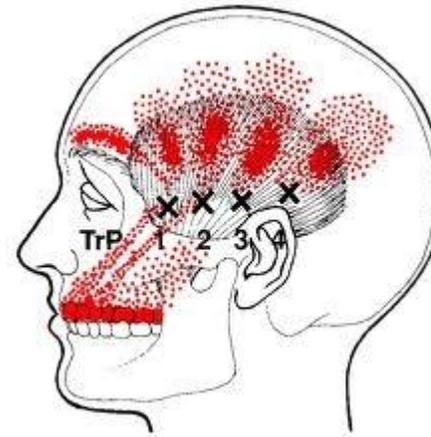


1. Fundamental & Immediate effect

Coldness and vibration with light massage with patented thermal neurostimulation technology on temple area (temporalis).

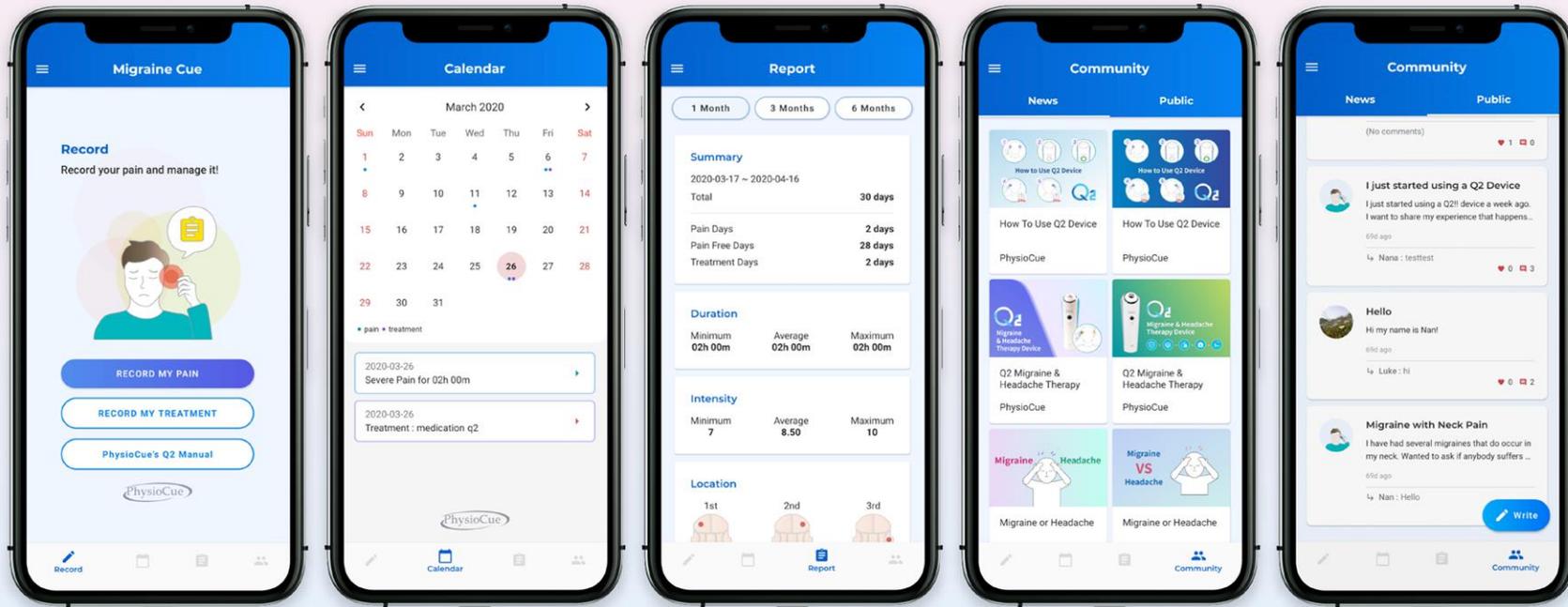


2. Stimulate active Myofascial Trigger Points (MTrPs) which will decrease referred pains of headaches and migraine by desensitizing or modulating the release of nociceptive and inflammatory mediators within deep temporal nerves of temporalis.



3. Migraines is considered vascular headaches, triggered by increased blood flow. Some suffers have experienced increased efficacy of the therapy by using PhysioCue Q1 Hypertension Therapy together.

Migraine & Headache Pain Monitoring Mobile App



TRIGGER

1st	Salty food	4 Times
2nd	Stress Event	3 Times
3rd	Sinus	1 Times

MIDAS

(Migraine Disability Assessment)

MIDAS GRADE III
Moderate Disability

Score: 11

If your MIDAS grade is 6 or more, please discuss with your doctor.

TREATMENT

Medication Days	5 days
Q2 Therapy Days	11 days

INTENSITY





gammaCore

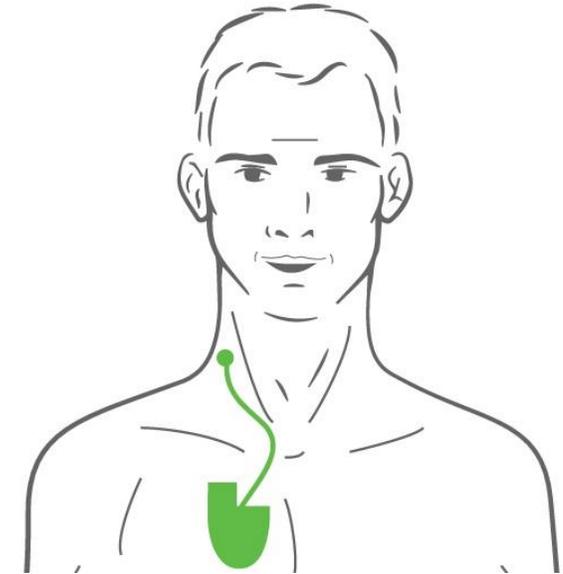
electroCore : gammaCore (nVNS)

<https://www.electrocore.com/>

CVRx[®]



<https://www.youtube.com/watch?v=1R5YDxyzjeU&t=191s>



Vagus nerve stimulator for headache & Migraine
With SoC, $\geq 50\%$ pain reduction, 40% patients (45 total) MSRP \$500/mon.

(electroCore) Merck, Core Ventures, Gakasa(Knoll Capital), American Investment Holdings, Vinik Family, \$150M

Carotid Sinus Lead:

A 2mm electrode is attached to the carotid artery and connected to the IPG, with the design to electrically activate the baroreceptors.

Implantable Pulse Generator (IPG) Device:

An implantable pulse generator is inserted under the skin, below the collar bone, delivering an electrical stimulation through the lead.

Competitors



Neurolief: CE approved

\$ 500/number of treatment
Need to purchase extra electrodes



eNeura: CE/FDA approved

\$ 2,250 (\$250/month)
User not friendly device
SIM card



Cefaly: FDA approved

\$ 499
20 mins/day
Electrodes



MigraineCue &Q
2
FDA Class 1

\$ 299
5 Minutes/ Easy to use

	PhysioCue Q2 & MigraineCue	Neurolief - Relivion	eNeura - Cerena	Cefaly
Technology	Thermal Neural Stimulation	<ul style="list-style-type: none"> TMS - 6 nerve branch stimulation via electrodes for trigeminal & occipital. Wearable 	<ul style="list-style-type: none"> TMS - Single pulse TMS, magnet Back of the head placement 	<ul style="list-style-type: none"> TMS - Electric TMS (eTMS) Forehead, directs a mild frequency directly into the end of the trigeminal nerve
Treatment	5m, as needed	1h	≈ 1m~1.5m, up to 3 times a day	20m/day
Price	\$299 to purchase (V)	<ul style="list-style-type: none"> ≈ \$500/x number of treatment Recharge treatment via mobile App Electrode pack purchase 	<ul style="list-style-type: none"> \$250/month. (\$2,250) Recharge treatment via prepaid SIM card 	<ul style="list-style-type: none"> \$499 to purchase \$25, 3 pack electrodes
Efficacy	<ul style="list-style-type: none"> 70% of patients reduce pain within 5 mins Easy to use (V) 	Based on Pain VAS, 55 patient study; <ul style="list-style-type: none"> 76% mild pain relieved after 1 treatment 43% with severe or moderate pain relieved after 1 treatment 	164 patients, 2 group study; 39% pain free after 2h (vs. sham 22%)	Pain reduction by; 57.1% @ 1h 52.8% @ 2h → 34.6% used rescue medication @ 24h
Side-effects	None (V)	N/A (no data), claim none.	<ul style="list-style-type: none"> Increased Headache Worsening of migraines Scalp discomfort Facial twitching Dizziness Tingling sensations Sleepiness during treatment Rare seizure Mood disturbances 	<ul style="list-style-type: none"> Tension headache Buzzing sensation or pain Insomnia Sleepiness during use Skin irritation Allergic reaction
etc	FDA (I) No restriction nor limitation for the application regardless of the patient's condition.	CE Can't use if; <ul style="list-style-type: none"> Allodynia: intolerance to supraorbital and/or occipital neurostimulation Supraorbital or occipital nerve blocks Drug/alcohol abusers Pregnancy/lactation brain/facial trauma 	FDA Can't use if; <ul style="list-style-type: none"> Cardiac pacemaker, VNS or other implanted neurostimulator Implanted cardioverter defibrillator (ICD) Others: stents, staples, facial tattoos with metallic ink, aneurysm clips/coil, etc. 6ft clearance from other people with metal objects and phones 	FDA

PhysioCue Devices



Competitive Advantages



- Addressing the **root causes**: nervous systems
- Highest **efficacy**
- Sustaining & Residual effect



- Non-Invasive
- Safe



- No side-effects
- No pain



- Affordable
- One time investment



- 5 minutes a day
- Easy to use



Q1



Q2



- No more cuff
- 2 thumbs in 30 sec.



- Personalized data
- Mobile & Web App



- Share data in real-time



Q3



Q4



- Higher insurance premium
- Higher direct costs
- Pills for life
- Overdose, Side-effects
- or, inferior effective device with more \$\$



Marketing Strategy & Potential Marketing Partners



Sales through indirect distribution and white-labeling

- QVC & HSN distribution for current sub-\$299 product with limited claims
- GSK, J&J, Medtronic and others, OSIM, DNR, Century Medical etc.

Co-marketing & Sponsoring

- AARP & other associations
- Combination therapies with drugs, blood pressure reading devices

Pricing

- Current manufacturing cost in China: ~\$120
- Target FOB ~\$80
- MSRP from \$299 - \$350
- Equipment leasing and/or annual service plan for recurring revenues

GSK (GlaxoSmithKline)

DNR-Indonesia

We are seeking strategic investors and partners

Executive Team & BoD



Johnathan Leong
(CEO)



Simon Yi
(President & COO)



Reza Kazemipour
(BoD)



Terrence Tormey
(BoA)



Wasim Malik
(BoA)



Hugh Sharkey
(CRO)



Rosh Vora
(VP of Clinical Affairs)



James Choi
(VP of Marketing)



Medical Advisory Team & Board of Directors also bring their impressive experiences from following prestigious backgrounds

UCSF Medical Center



Medical Advisory Team



Bruce T. Adornato, M.D., Medical Advisor, is Neurologist, Physician Stanford Hospital, Palo Alto Veterans Hospital, Clinical Professor of Neurology, Stanford School of Medicine, President, Palo Alto Neurology. UCSD School of Medicine, UCSF, National Institutes of Health,



Waldo Concepcion, M.D., Medical Advisor, is Professor of Surgery and Chief of Clinical Transplantation at Stanford University Medical Center, a Senator at the Faculty Senate of the School of Medicine, and Chair, PPEC and Quality Committee, for the Multi-Organ Transplantation Division.



Clifton Watt, M.D. Medical Advisor, is cardiologist UCSF Medical Center, Berkeley Cardiovascular Medical Center, UC Davis cardiology fellowship, University of Illinois at Chicago.



Jose R Bolanos, M.D, Medical Advisor, Managing Director, Venture-Med Angel Investment Group. He trained at Stanford Medical Center as an Ob/Gyn specialist and served in clinical practice for over 20 years. He is currently an advisor to multiple healthcare companies.



Elena Rios, M.D. MSPH, FACP, Medical Advisor is President and CEO of the National Hispanic Medical Association, National Hispanic Health Foundation, U.S. Department of Health and Human Services.



Glen A. Lutchman M.D. MHSc, Medical Advisor, completed a research fellowship in the Liver Disease Branch at the National Institutes of Health and a Masters in Clinical Research at Duke before moving to the University of California at San Francisco. Since 2008 he has been Clinical Assistant Professor in the Division of Gastroenterology and Hepatology at Stanford University Medical School.



PhysioCue Ecosystem



\$3.5M in seed round from



- TEEC Angels
- Danen Ventures
- Jiyou Fund
- NewDo Ventures
- Anda Asset Management
- WS Investments
- ENV
- AQAL Capital GmbH
- keiretsu Forum

Strategic alliances for clinical trial with IRB approvals



Clinical Trial Partners

- University of Texas Health Science Center
- South Texas Veterans Healthcare System
- Hypertension Clinic at Loma Linda University
- King Faisal Specialist Hospital (Saudi Arabia, Riyadh)

Series A (Use of Funds)



Preferred Financing:

Pre-money Valuation of \$15 M

Aggregate Proceeds of \$7M

**With this investment, we
expect to create a fast-
growing business high
potential ROI**

Use of Funds:

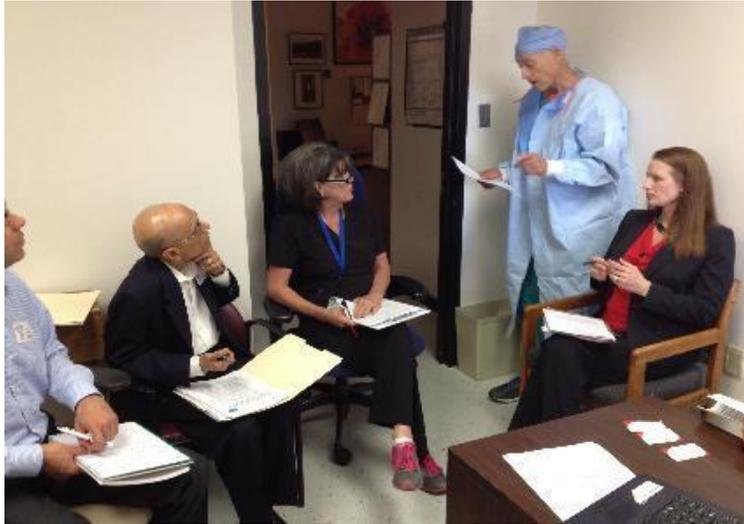
- 1. Certification for UL, CE, FDA 510 (K) Approval, Additional Clinical trials**
- 2. Dedicated Sales & Marketing, Develop EU & Asia distribution channel**
- 3. Independent database & software interface / Migraine Mobile App / BP Monitoring App**
- 4. Final Stage R&D for Model Q3 & Q4**
- 5. Legal expenses relating to additional IP & Licensing**
- 6. Complete mass production capabilities & Operations Expenses**

Live Healthier, Happier & Longer Lives



Contact: Simon Yi
syi@physiocue.com

Clinical Trial Partner



**Clinical partnership with VA
Hospital, San Antonio, TX**

Clinical Trial Partner



Partnership meeting with Loma Linda Hospital Staff, Douglas Hegstad, MD, Ramin Assadi, MD, Bryant Nguyen, MD, Ken Jutzy, MD, Jose Bolanos, MD, Waldo Concepcison, MD (Stanford Hospital)

Hypertension Competitors



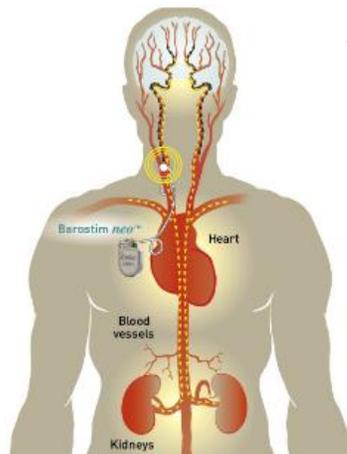
\$12.9M in 3 round from Longitude Capital and Versant Ventures.

Sympara describes its device as being positioned near a dermal bone to selectively activate baroreceptors or nerves to reduce blood pressure and alter the sympathetic nervous system.



Cibiem is a medical device company leveraging its proprietary, minimally invasive, catheter-based approach focused on Carotid Body Modulation (CBM) for the treatment of sympathetic nervous system-mediated diseases such as hypertension, heart failure, diabetes and renal failure.

CVRx



**SV Life Sciences and Third Rock Ventures Launch Transformative Medical Device Company
Cibiem with \$10 Million Series A**

CVRx received > \$200 M from New Enterprise Associates, Inc. (NEA) and Johnson & Johnson ,BBT Fund L.P. and SightLine Partners.