“Energetic signaling mechanisms such as electromagnetic frequencies are a hundred times more efficient in relaying environmental information than physical signals such as hormones, neurotransmitters, growth factors, etc”. Shared by James Oschman C.W.F McClare in “Resonance in Bioenergetics 1974 from Lipton Biology of Belief 2005
Transpalpebral Frequency Specific Microcurrent Stimulation in the Treatment of Macular Degeneration

Laurie Chaikin OD, Kellen Kashiwa OD, Walter Gregory, PhD, George Papastergiou MD, PhD and Michael Bennett MD

Thank you to the Retina Institute of Hawaii

Purpose: to determine the safety and efficacy of transcutaneous (transpalpebral) frequency specific microcurrent stimulation to slow progression of or improve vision in dry & wet macular degeneration
The Story

2011 met Kellen Kashiwa, OD from Retina Institute of Hawaii; working with CentraSight program: the Implantable Miniature Telescope; for whom I consult. Shared my interest in MCS & shared my recently developed FSM protocol for AMD with him. We decided to run a safety & efficacy study and ......
We presented our results in a poster session at ARVO in 2013:

As a result of the supportive responses we got, I decided it was worthwhile to write up into a paper.

Here’s the poster:
**Transcutaneous Microcurrent Electrical Stimulation (MCS) in the therapy of Previously Untreatable Retinal Diseases**

**Kellen Kashiwa OD, Laurie Chaikin OD, Michael Bennett MD, Fayssal El-Jabali DO, and George Papastergiou MD**

**Purpose**
To determine the safety and efficacy of the application of transcutaneous (trans-palpebral) microcurrent stimulation (MCS) to slow progression of or improve vision in a variety of retinal conditions including dry & wet macular degeneration, diabetic retinopathy, retinitis pigmentosa, cystoid macular edema, cone dystrophy and others.

**Background**
Trans-retinal MCS was demonstrated in 2011 to both increase visual fields by 20% and improve visual acuity by 1 line of letters in patients with RP.

Adaptability trans-conjunctival MCS stimulation showed improvements in a number of functional parameters. The question was could a trans-palpebral approach of MCS application provide similar efficacy, with improved safety.

Frequency Specific Microcurrent was chosen for its demonstrated ability to selectively target both a tissue and a condition using dual channel frequency-modulated microamperage current. Published animal research demonstrated that when a mouse’s ear painted with arachidonic acid to create inflammation was treated with 40Hz/16Hz, for 4 minutes, there was a 92% reduction of COX mediated inflammation and 30% reduction of COX mediated inflammation. This was compared to other Hz combinations which had no effect. A case study of herpes zoster virus on ophthalmic branch CN V was treated with 230/430 Hz for a period of 35 minutes per treatment. The frequency sets selected were based on the understanding that specific frequencies would target a particular tissue and condition as described by the literature produced by Frequency Specific MCS technology, and was based on assumptions and current understanding of the pathophysiology of the condition.

Current was alternating, amplitude was 150 uA. EDTRS visual acuity by I line of letters in patients with RP was pain free in one hour with no return of pain. In a clinical study of pain in 77 fibromyalgia patients statistically significant subjective improvements were associated with reductions in inflammatory cytokines by a factor of 10 to 20 times in 90 minutes: Interleukin 1 β by a factor of 10 to 20 times in 90 minutes: Interleukin 6 from 204 pg/ml to 15 pg/ml and IL-6 from 204 pg/ml to 15 pg/ml and COX-2.

**Methods**
Patients with dry and wet age-related macular degeneration, diabetic retinopathy, retinitis pigmentosa, cystoid macular edema were screened for inclusion after providing written informed consent.

Inclusion criteria were: greater than 50 years of age, diagnosis of dry or wet macular degeneration, diabetes vision in a variety of retinal conditions including dry & wet macular degeneration, diabetic retinopathy, retinitis pigmentosa, cystoid macular edema, cone dystrophy and others; Anti-VEGF treatments for at least 3 months prior to study; no Anti-VEGF treatments for at least 6 months prior to study.

**Methods (cont.)**
Screening procedures included standard of care: best-corrected visual acuity, ophthalmic examination, intracocular pressure measurement, fluorescein angiography, fundus photography, and OCT; these tests were performed no earlier than 14 days prior to initiation of the treatment.

After initial screening, patients returned for regular clinic visits and diagnostic testing per standard of care. These visits were conducted depending on the type and severity of the retinal disease condition per standard of care.

Vitals, visual acuity, intraocular pressure measurements, OCT and dilated eye exams were performed at each visit. Fundus photos, Fluorescein angiograms, and Microperimetry were obtained based on standard of care and severity of disease.

**Treatment**
Subjects received weekly treatments of microcurrent. One moist pad holding carbon electrodes was placed over the closed eyes and another was placed at the back of the neck for a period of 35 minutes per treatment. The frequency sets selected were based on the understanding that specific frequencies would target a particular tissue and condition as described by the literature produced by Frequency Specific MCS technology, and was based on assumptions and current understanding of the pathophysiology of the condition.

Current was alternating, amplitude was 150 uA. EDTRS visual acuity by I line of letters in patients with RP was pain free in one hour with no return of pain. The use of microcurrent is FDA approved for treatment of pain. A physician may use an instrument for off label use following a physician’s diagnosis, a patient’s consent and under ethical supervision.

**Results**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Pre txs VA OD/OS</th>
<th>Post txs VA OD/OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>DAMD</td>
<td>20/50</td>
<td>20/25</td>
</tr>
<tr>
<td>Patient 2</td>
<td>RP</td>
<td>20/100</td>
<td>20/25</td>
</tr>
<tr>
<td>Patient 3</td>
<td>CME</td>
<td>20/100</td>
<td>20/50</td>
</tr>
<tr>
<td>Patient 4</td>
<td>PDR</td>
<td>20/50</td>
<td>20/40</td>
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<tr>
<td>Patient 5</td>
<td>DAMD</td>
<td>20/100</td>
<td>20/50</td>
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<tr>
<td>Patient 6</td>
<td>DAMD</td>
<td>20/100</td>
<td>20/40</td>
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<tr>
<td>Patient 7</td>
<td>WAMD</td>
<td>20/50</td>
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<td>Patient 8</td>
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<td>Patient 9</td>
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<tr>
<td>Patient 10</td>
<td>PDR</td>
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<td>20/40</td>
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<tr>
<td>Patient 11</td>
<td>PDR</td>
<td>20/50</td>
<td>20/40</td>
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<tr>
<td>Patient 12</td>
<td>WET/DRY</td>
<td>20/50</td>
<td>20/40</td>
</tr>
<tr>
<td>Patient 13</td>
<td>POAG</td>
<td>20/50</td>
<td>20/40</td>
</tr>
<tr>
<td>Patient 14</td>
<td>ERMD</td>
<td>20/50</td>
<td>20/50</td>
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<tr>
<td>Patient 15</td>
<td>DAMD</td>
<td>20/50</td>
<td>20/50</td>
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<tr>
<td>Patient 16</td>
<td>Cone Dys</td>
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<tr>
<td>Patient 17</td>
<td>CSR</td>
<td>20/50</td>
<td>20/50</td>
</tr>
<tr>
<td>Patient 18</td>
<td>DAMD</td>
<td>20/50</td>
<td>20/50</td>
</tr>
</tbody>
</table>

**Disclosures**
No funding was received for this research project.

The use of microcurrents is FDA approved for treatment of pain. A physician may use an instrument for off label use as determined by their medical judgment.

**Conclusions**
In this study, dual channel frequency specific microcurrent stimulation (FSM) therapy was used in a non-invasive procedure, involving transcutaneous electrical current with very low intensity. It is hypothesized that FSM’s mechanism of action is to increase intracellular adenosine triphosphate (ATP), thereby enhancing protein synthesis and modulating neural group polarizing response. Although the majority of the patients demonstrated both subjective and objective improvement, the effect was short lived and determination of efficacy is limited. Those patients who continued treatment once a month maintained their VA gains. This pilot study suggests that MCS can be safely administered to this population, however longer-term controlled trials are indicated.

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Laurie Chaikin, OD laurie.chaikin@gmail.com

**Microperimetry Results**

For further details on the treatment, please refer to the original study published in the Transcutaneous Microcurrent Electrical Stimulation (MCS) in the therapy of Previously Untreatable Retinal Diseases.
After taking a course on how to do research from the NIH.....

With lots of help from friends, editors and statisticians (Carol McMakin, Gloria St. John and Walter Gregory)......

Rejected by Journal of Optometry & Visual Science.....

Accepted for publication in the international Journal of Clinical Ophthalmology!
History of MCS use and the eye

• 1873 Henry Dor, ophthalmologist applied MCS to amblyopia, glaucoma and optic atrophy

• 1983 Grace Halloran applied it to herself for treatment of retinitis pigmentosa (Amazing Grace published 1993)

• 1993 Drs Michael and Allen: MCS plus nutritional supplementation

• 1994 Larry Wallace, OD patent for MCS device
History of microcurrent and vision

- MCS use had fallen into disfavor until the 1970’s; suprathreshold stimulation for phosphene perception which led to eventual development of retinal prosthesis implant.

- Video camera transmits signals to processor which wirelessly sends electrical stimulation signals to retina. Retina perceives as vision.

- Key finding: sub-threshold stimulation in inactive implants led to unexpected improvements in vision in RP subjects.

ARGUS II FDA APPROVED 2013
Animal research: transcorneal stimulation

- Neuro-protective effects on rats following light induced retinal damage: altered gene expression: upregulation of neurotrophic factors (protects mature neurons), and of genes which produce anti-apoptotic factors, simultaneous down regulation of pro-apoptotic factors such as BAX

- Following crushed optic nerves of rats; enhanced and increased survival of retinal ganglion cells as well as significant delay of post-traumatic cell death; increased amplitude of visual evoked potential.

- Amelioration of progressive photoreceptor degeneration following light induced retinal damage measured on ERG;

- Neuroprotection is thought to occur through pro-inflammatory effects; inhibitive effect on the secretion of interleukin (il)-1β and tumor necrosis factor (tnf)-α in microglia and upregulation of BDNF and CNTF in müller cells.
Human Studies

• Transcorneal microcurrent delivery (TES)
• A thin thread electrode is placed across the front surface of the eye
• All studies are non frequency specific
Human Research

- Two cases of non-arteritic anterior ischemic optic neuropathy and four cases of traumatic optic neuropathy had improvements in visual acuity\textsuperscript{17}.

- Two cases of branch retinal artery occlusion of long duration and three cases of short duration showed significantly improved ERG and improved visual fields\textsuperscript{8}.

- 12 Stargharts patients (genetic AMD) received TES at three levels of phosphene stimulation threshold (0 or sham, 66\% or 150\% of threshold). No significant changes in ganzfeld, mferg, visual field or OCT\textsuperscript{19}.

- 24 patients with retinitis pigmentosa were given TES in the same 3 groups as described above. Statistically significant improvements in both visual field and ERG\textsuperscript{20}.

- One case of Best vitelliform macular dystrophy had visual acuity improvement over six months from 20/200 to 20/25 after two monthly TES sessions, with small changes in visual field and ERG.

- Chorioretinal blood flow measures of ten healthy subjects following TES showed that there was statistically significant increase in blood flow in the macular zone and may account for the improvements in patients with ischemia\textsuperscript{22}.
Transpalpebral microcurrent delivery

- 2008 Shinoda: 27 eyes with WAMD, 7 eyes with DAMD. 800 uA, 20 min 4x day at 290 Hz, 31 Hz, 8.9 Hz, 0.28 Hz. Ave VA improved from 39.8 to 42.9 $p=0.0401$ in DAMD and from 29.5 to 31.8 $p=0.0407$ in WAMD (letters improved)

- 2013 Anastassiou: 22 DAMD; 12 treated; 10 sham. Single blind randomized; treated with TheraMac a variable current 150-220 uA & variable Hz 5-80 Hz on 8 points around the eye 40 sec per point 2x/day for 5 days
  - On average 5.7 letter VA increase in treatment group, no significant VA change in sham

- 2015 Chaikin et al: 1st FSM research with dual channel. Details to follow.
Current study: selection

17 patients between the ages of 67 and 95 with an average age of 83 were tested and treated in two eye care centers. There were 25 eyes with dry age-related macular degeneration (DAMD) and 6 eyes with wet age-related macular degeneration (WAMD).
Inclusion criteria

- Inclusion criteria were: greater than 45 years of age, male and female, history of retinal disease involvement; no anti-vegf treatments for at least 3 months prior to study; no new antioxidant/vitamin supplementation for at least 6 months prior to study.
- All subjects signed an informed consent and an IRB was filed.
Study Objectives

• Change in visual acuity from baseline to three month
• Changes in retinal thickness as measured by optical coherence tomography (OCT)
• Changes in microperimetry, as measured by Nidek MP-3 microperimeter. Not all subjects were able to complete the microperimetry testing.
METHOD

• FSM was applied in a trans-palpebral manner, with flat carbon electrodes placed into chamois type fabric which was moistened with water and placed over the closed eyes; another was placed at the base of the skull.

• Two custom care units were programmed with the FSM protocol.

• Treatment time was 35 minutes once a week for 3-12 weeks

• ETDRS visual acuity was measured before and after each treatment session
Protocol design is based on understanding of pathophysiology of AMD

• **Oxidative stress**: reduced digestive rate of photoreceptors in the outer segment by the RPE causes lipofuscin formation

• **Chronic vascular disease**: slow degradation of choroidal blood vessels leads to blockages. These blockages cause increased capillary resistance elevating pressure causing release of proteins and lipids extracellularly forming deposits and drusen. Note: AMD just now being recognized as a manifestation of chronic systemic disease

• **Deterioration of elastin and collagen** in Bruch’s membrane causing calcification and fragmentation. Increase in the protein VEGF (vascular endothelial growth factor) leads to neovascularization, blood vessel leakage, bleeding and scarring (wet AMD)

• **Inflammation and injury** to the RPE and choroid alters diffusion of nutrients to the retina and RPE causing further RPE injury. Oxidative stress induced injury to the RPE can lead to an immune mediated chronic inflammatory response, drusen formation and RPE atrophy with increased levels of C reactive protein.
FSM Protocol

- "The basics" with arteries, connective tissue, eye, retina, vitreous
- Inflammation, chronic inflammation with arteries, connective tissue, eye, retina, vitreous
- Organic toxicity in the eye and retina
- Emotional component and, frustration, grief, restore joy
- Calcium deposits and eye, retina
- Scarring in arteries, veins, eye and retina
- Hypoxia
- Increase secretion in the immune system
- Increase vitality in the immune system, blood, eye, retina and vitreous

- 294,321.9/62,77,42,95,495
- 40, 284/62,77,42,95,495
- 900,920/42,95
- 970/200,71,17,33
- 91/42,95
- 3,13/62,79,42,95
- 880/7.4
- 81/116
- 49/116,103,42,95,495
Range of improvement was -3 to +34 letters, ave. +6.68 letters
16 improved (64%) p=0.012
8 stayed the same
2 worse: 1 letter & 3 letter

Visual acuity results dry AMD, 25 eyes

<table>
<thead>
<tr>
<th>Eye #</th>
<th>Pre txs VA</th>
<th>Post txs VA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20/40</td>
<td>20/20-</td>
</tr>
<tr>
<td>2</td>
<td>20/50</td>
<td>20/25-2</td>
</tr>
<tr>
<td>3</td>
<td>20/200</td>
<td>20/200</td>
</tr>
<tr>
<td>4</td>
<td>HM 1'</td>
<td>HM 1'</td>
</tr>
<tr>
<td>5</td>
<td>20/800+</td>
<td>20/640-</td>
</tr>
<tr>
<td>6</td>
<td>20/320+</td>
<td>20/160+</td>
</tr>
<tr>
<td>7</td>
<td>20/125+</td>
<td>20/63-</td>
</tr>
<tr>
<td>8</td>
<td>20/25-</td>
<td>20/30+</td>
</tr>
<tr>
<td>9</td>
<td>20/80</td>
<td>20/80-</td>
</tr>
<tr>
<td>10</td>
<td>20/200-</td>
<td>20/80-</td>
</tr>
<tr>
<td>11</td>
<td>20/20</td>
<td>20/20+</td>
</tr>
<tr>
<td>12</td>
<td>20/40-</td>
<td>20/32+</td>
</tr>
<tr>
<td>13</td>
<td>20/100-</td>
<td>20/70+</td>
</tr>
<tr>
<td>14</td>
<td>CF @ 4'</td>
<td>CF @ 4'</td>
</tr>
<tr>
<td>15</td>
<td>20/50-</td>
<td>20/50</td>
</tr>
<tr>
<td>16</td>
<td>20/200</td>
<td>20/200</td>
</tr>
<tr>
<td>17</td>
<td>20/60</td>
<td>20/50</td>
</tr>
<tr>
<td>18</td>
<td>20/100</td>
<td>20/30-</td>
</tr>
<tr>
<td>19</td>
<td>20/250+</td>
<td>20/50-</td>
</tr>
<tr>
<td>20</td>
<td>20/80+</td>
<td>20/60-</td>
</tr>
<tr>
<td>21</td>
<td>20/125-</td>
<td>20/125-</td>
</tr>
<tr>
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<tr>
<td>25</td>
<td>20/1000</td>
<td>20/1000+</td>
</tr>
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</table>
Visual acuity results wet AMD
All 6 eyes improved

<table>
<thead>
<tr>
<th>Eye #</th>
<th>Wet AMD</th>
<th>Pre-Txs VA</th>
<th>Post-Txs VA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20/160-1</td>
<td>20/100+1</td>
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</tr>
<tr>
<td>2</td>
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<tr>
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<td>20/1000+</td>
<td>20/800</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>20/100-</td>
<td>20/80-</td>
<td></td>
</tr>
</tbody>
</table>

• Range of improvement was +2 to +19 letters
• Average improvement was +8.5 letters
• All improved but did not reach significance (p=0.059) probably due to small sample size
Use of logMAR VA over Snellen chart; data converted

• Equal number of letters per line
• Regular spacing between lines and letters
• Uniform progression in letter size
• Final score based precisely on the total of all letters read
• Finer grading scale allows for greater accuracy and improved test/retest reliability
Dry AMD eyes: absolute LOGMAR differences from starting values for each patient - plotted over first 3 months only.
Wet AMD eyes: absolute LOGMAR differences from starting values for each patient - plotted over first 3 months only.
OCT and Microperimetry changes

• There were no changes in OCT findings

• Of the patients who had microperimetry testing done, there was an increased retinal sensitivity across the board.

• Patients with large areas of geographic atrophy tended to increase their sensitivity in areas of their preferred retinal locus.

• Patients with smaller to no areas of geographic atrophy increased their sensitivity in their fovea.
Conclusions

• The normal course of the disease is worsening vision, so same or improving VA is positive; for DAMD significance was $p=0.012$ and WAMD was $0.059$ (small sample size)

• When treatment was discontinued progression of disease continued.

• For patients with no improvement VA was very poor: HM, CF, 20/200, 20/800; so likely geographic atrophy (big blind spot): cant put tissue back that isn’t there.

• Likely best results at beginning stages of disease

• Likely more frequent treatments (3x week or daily) would be optimal
Critique: study weaknesses

• No control group, no double blinding randomization.
• Is there a learning effect from repeated visual acuity measures?
• Long term effects? 1 year, 2 year…
Considerations

• AMD is a systemic disease, therefore the whole body should be treated

• The only treatment applied was microcurrent. Very important to look at:
  • Nutrition
  • Toxicity testing and chelation therapies
  • Oxidative therapies (ozone, hyperbaric)
  • Light therapy (syntonics) for ANS balance
  • Emotional aspects
Some interesting reviewer questions re DC system

• What is the nature of the electrical stimulus? It cannot be a DC system because DC does not alternate polarity (originally described as “DC system with alternating polarity at 150 microamps”). Also if the stimulus had alternating polarity, it would be important to know what the frequency was.

• Description of the electrical stimulus: thank you to Ning Wu and an electrical engineer friend! The instrument is powered by a DC source but delivers a square wave pulse train at a specific rate; frequency is the number of times that a square wave passes a point in one second. The pulse train can be delivered polarized positive or alternating polarity. Running the current in one direction is usually reserved for nerve injuries, so the current was run with alternating polarity.
Also...Where do the frequencies come from????

Reviewer response to statement: "the frequencies selected were based on the understanding that particular tissues are affected by conditions created by the pathophysiology of the disease." Does not help in replicating the procedure by others, nor does it specify which frequencies are specific for the retina or AMD and how the authors know these specificities (whether it is from the literature, personal communication or from previous own experience).

It is known that low powered electrical stimulation can have positive biological effects. It is less well known that there can be a positive tissue response to specific frequencies. Molecular bonds are known to have resonant frequencies which respond to an externally delivered signal. A gross example is the response of crystal lead glass to a particular note delivered by a singer. When the singer hits the resonant frequency of the lead crystal molecule the bond is dissolved and the glass shatters. It is suggested that both tissues and degenerative processes have a specific resonant frequency which the microcurrent is attempting to target. My revision attempts to explain this.
FSM protocols have been developed for the following eye conditions:

- Minimally tested; some of the results will be presented tomorrow
- Retinitis pigmentosa
- Diabetic retinopathy
- Glaucoma
- Iritis
- Dry eye; not tried
- Hemianopsia
- Cataracts
- Eye muscle paresis
Opportunity....

• Post cataract extraction, wound healing, anterior segment inflammatory conditions

• Study group for eye protocol development?

• Currently revising protocol

• Better understanding of responders vs non-responders; what is interfering: blockage of VGCC?
Thank you

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Laurie Chaikin, OD, OTR/L, FCOVD
www.optorehab.com
Office: 888-551-9991
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