Disclosure:
Soterix Medical Inc. produces tDCS and High-Definition tDCS. Marom Bikson is founder and has shares in Soterix Medical. Some of the clinical data presented may be supported by Soterix Medical. Marom Bikson serves on the scientific advisory board of Boston Scientific Inc.

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**tDCS electrode position on the head determines which regions are stimulated**

- Current flows from one electrode to the other
- Extra-cephalic electrode won’t solve the issue of diffuse bi-directional flow
- tDCS is deep

Truong et al. Clinician accessible tools for GUI computational models. “BONSAI” and “SPHERES”. *Brain Stimulation* 2014

Datta et al. Electrode montage for tDCS: Role of return electrode. *Clinical Neurophysiology* 2010
Extra-cephalic electrode won’t solve the issue of diffuse bi-directional flow!

✓ tDCS is deep

Datta et al. Electrode montage for tDCS: Role of return electrode. Clinical Neurophysiology 2010

✓ Allows targeting of selected cortical regions


✓ Deep tDCS

“4x1” montage of High-Definition tDCS
“4x1” montage of High-Definition tDCS

✓ Total of 5 small “HD” electrodes (4+1)
✓ Center electrode over target determines polarity 4 return electrodes - Ring radius determines modulation area

Center electrode: CATHODE
Center electrode: ANODE

Outward current (inhibitory)
Inward current (excitatory)

“4x1” montage of High-Definition tDCS

✓ 2006-2008 Gyri-precise brain models
✓ 2008 3rd International Brain Stimulation Conference
✓ 2008-09 Publications on Theory
✓ 2008-10 Safety (Caparelli-Daquer et al.)
✓ 2012: Experimental Pain (George et al.)
✓ 2012 Fibromyalgia (Fregni et al.)
✓ 2013 Neuro-plasticity (Nitsche et al.)
✓ 2013 Focality Physiology (Edwards et al.)
✓ 2015 Cognitive Performance (Loo et al.)

Datta et al. Gyri-precise model of tDCS: Improved spatial focality using a ring versus conventional pad. *Brain Stimulation* 2009
It won’t work because:

- **The skull is resistive**
- Current is diffused in the skin and CSF, not skull, and can be controlled inside ring
- Prior efforts limited by use of large pads, not by physics

Minhas et al. Electrodes for High-Definition transcutaneous DC. J Neuroscience Methods 2010

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High-Definition tDCS uses arrays of electrodes to focus current to targets

- Without need for “search” there is a single solution given a target (2009-11)


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It won’t work because:

- **The skull is resistive**
- Current is diffused in the skin and CSF, not skull, and can be controlled inside ring
- Prior efforts limited by use of large pads, not by physics
- **DC can’t be applied through little electrodes**
- 2008-10 design of High-Definition Electrodes
- 3cm$^2$ electrode-electrolyte contact area, Ag/AgCl electrodes, high-capacity gel (e.g. Signa), rated 2 mA + 22 minutes

Minhas et al. Electrodes for High-Definition transcutaneous DC. J Neuroscience Methods 2010
• Comparable tolerability using HD electrodes
• 10 minutes of 2 mA 4x1 HD-tDCS produces >2 hour of after-effects

Kuo et al. Comparing cortical plasticity induced by conventional and HD-tDCS 4x1. *Brain Stimulation* 2013

Clinical Neurophysiology
Transcranial Electrical Stimulation (TES): Short high-intensity pulse that triggers MEPs

4x1 montage used to localize current on or off motor region

Edwards et al. Physiological and modeling evidence for focal transcranial electrical stimulation: HD-tDCS. Neuroimage 2013

Left: TES intensity increased to threshold for each subject
Right: Fixed TES intensity for each subject

>2x inter-individual difference captured by anatomical models

Edwards et al. Physiological and modeling evidence for focal transcranial electrical stimulation: HD-tDCS. Neuroimage 2013

Transcranial Electrical Stimulation (TES): Short high-intensity pulse that triggers MEPs

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Edwards et al. Physiological and modeling evidence for focal transcranial electrical stimulation: HD-tDCS. Neuroimage 2013

Pain
• 2 mA 4x1 (center anode) HD-tDCS over motor hot-spot (TMS)
• “Marginal” analgesic effect on experimental pain

Figure 5. Mean (standard) heat sensing thresholds before and after real versus sham HD-tDCS (Time x Condition interaction F(1, 444) = 1.29; p > .40).


**Saaverda, Fregni et al. Clinically effective treatment of fibromyalgia with HD-tDCS. In Review 2015**

• Phase-2 Harvard/Saulding + Elminda (Fregni, Geva):
• Open-label “survival” design, End-point 50% reduction in pain: Adaptive therapy
• Thermode (pain evoked potential) -> EEG
• Phase 2a: 4x1 (anode) HD-tDCS over motor
• Phase 2b: Custom HD-tDCS
• Principle of both anatomical and functional targeting
• End-point met in >50% (including drop-outs)
  ✓ All electrographic responders
• Data-base (“cloud”) on brain response
  ✓ Informs future treatment
• Molecular (u-opicd) imaging (DaSilva)
• Double-blind (Caparelli-Daquer)

**Datta, Fridriksson et al. Individualized model predicts brain current flow during tDCS in responsive stroke patient. *Brain Stim* 2011**

• Conventional pad tDCS with anode “over” target

Brain and CSF Current Density

Dmochowski, Datta, Fridriksson et al. Targeted tDCS for Rehabilitation after Stroke. *Neuroimage* 2013

HD-tDCS for stroke rehabilitation

4x2 HD-tDCS

Dmochowski, Datta, Fridriksson et al. Targeted tDCS for Rehabilitation after Stroke. *Neuroimage* 2013

Epilepsy
Cathodal 4x1 HD-tDCS applied at 1 mA for 20 min
EEG accessed before, during, after HD-tDCS

Clinical trial for HD-tDCS for focal epilepsy. Ongoing at Boston Children’s (PI Rotenberg) and NYU (PI Liu)
Epilepsia partialis continua
- Severity of epilepsy approximate animal models
- Conspicuous marker
- Target and montage well defined – superficial
- Occur every day

Simple partial, flashing lights on the left side, most frequent seizure type. Occurs many times per hour.

Complex partial, picking behaviors and confusion, mumbling, occurring daily

Atonic seizure, will fall to the side, can occur every day

Generalized tonic clonic, rare.

High-Definition tDCS trial for focal status epilepticus
Clinical trial for HD-tDCS for focal epilepsy. Ongoing at Boston Children’s (PI Rotenberg) and NYU (PI Liu)
Epilepsia partialis continua

NYU1P01

Clinical trial for HD-tDCS, 1 mA, 20 min
EEG accessed before, during, after HD-tDCS

Source “localization”

Brain Current Flow
Scalp voltage by HD-tDCS

P4 Spectrogram PRE - POST

Average Interictal Discharge Frequency
Tinnitus

Shekhawat, Searchfield et al. Intensity, duration, and location of HD-tDCS for tinnitus relief. Neuro rehab and Neural Repair 2015