Will these new devices fill the gap between drug therapy and surgery?

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Therapeutic Devices for Epilepsy

What’s the State of the Art Seizure “Quantification”?

a) Patients failed to report 55.5% of all recorded seizures
   (Hoppe et al. Arch Neurol 2007; 64:1595-9)

b) Only 26% of patients were always aware and 30% never aware of their seizures
   (Blum et al. Neurology 1996; 47:260-4)

c) Accuracy of seizure descriptions is low and inconsistent
   (Mannan & Whiesmann Seizure 2003;12:444-7)

Do seizure diaries make for evidence-based Epileptology?
   NO!
Epileptology has no “Accounting” Department
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Q: How to address this fundamental limitation without which progress would be limited?

1. Introduction of Relevant Seizure “Metrics”

Severity (Intensity; Duration and Extent of Spread
Inter-seizure interval
Frequency

2. Adoption of “Novel” Statistical Analyses

Regression Analyses
Principal Component Analysis

3. Systems-Dynamical Approach

Look at the forest, not just a tree and keep in mind the forest’s history!
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25 hours of continuous seizure monitoring
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Local: Frequency: mean -55% [3/4 responders: -86% (-100 to -59%)]

Remote: Frequency: mean - 41% [2/4 responders -74.3%]

(Osorio et al. Ann Neurol 2005; 57:258-68)

**High Frequency electrical stimulation in these subjects significantly:**

- Decreased severity in 2/8 and increased inter-seizure interval in 1/8 subjects
- Increased severity in 1/8 subjects in the secondary EZs and decreased it in the primary zone
- Had a beneficial and detrimental effect on severity and inter-seizure intervals in the remainder. These effects were immediate and also outlasted the duration of stimulation (“carry-over).

(Osorio, Manly, Sunderam, Manuscript in preparation)
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Will these new therapy modalities and devices fill the gap between drug therapy and surgery?

1. Efficacy vs. Side effects? Yes, provided........

All relevant seizures variables are quantified

The spatio-temporal behavior of seizures at short and long time scales is better understood

Statistical analyses of efficacy conform to and address the multi-dimensional, complex nature of seizures
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Will these new therapy modalities and devices fill the gap between drug therapy and surgery?

2. Capacity to cost effectively decrease disease burden globally?  **No, unless.....**

Cost-effectiveness will be demonstrable especially if they fully replace drugs, decrease accidents/injuries through advanced warning and foster re-integration into society’s streamline

Disruptive (revolutionary) conceptual and technological approaches and social entrepreneurship come to the rescue
(T,D) choices and detection time relative to Clinical Onset:

- (1.30,0): 0.44s after
- (1.25,0): 0.25 before
- (1.20,0): 0.93s before
- (1.15,0): 1.63s before
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- Cost-effectiveness will be demonstrable especially if they fully replace drugs, decrease accidents/injuries through advanced warning and foster re-integration into society’s streamline

- **Disruptive** (revolutionary) conceptual and technological approaches and social entrepreneurship will be required to address the disease burden at a global scale

Devices will likely have an evolutionary positive impact on epilepsy therapies, increasing their efficacy and decreasing adverse events. This advance may be enhanced by the introduction of concepts from systems biology and dynamical theory among others
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NEUROSYSTEMS

Pharmaco-resistant seizures: self-triggering capacity, scale-free properties and predictability?

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(A) ECoG Signal

(B) Output of Algorithm