

FDA Workshop on Pediatric Clinical Trials for Devices

Neurologic Disorders: Epilepsy
Sudha Kilaru Kessler M.D.
Children's Hospital of Philadelphia
October 29th, 2009

Disclosures: none

Device Needs in Epilepsy Therapy

Brain Stimulation

existing: vagus nerve stimulation

deep brain stimulation

responsive neurostimulation

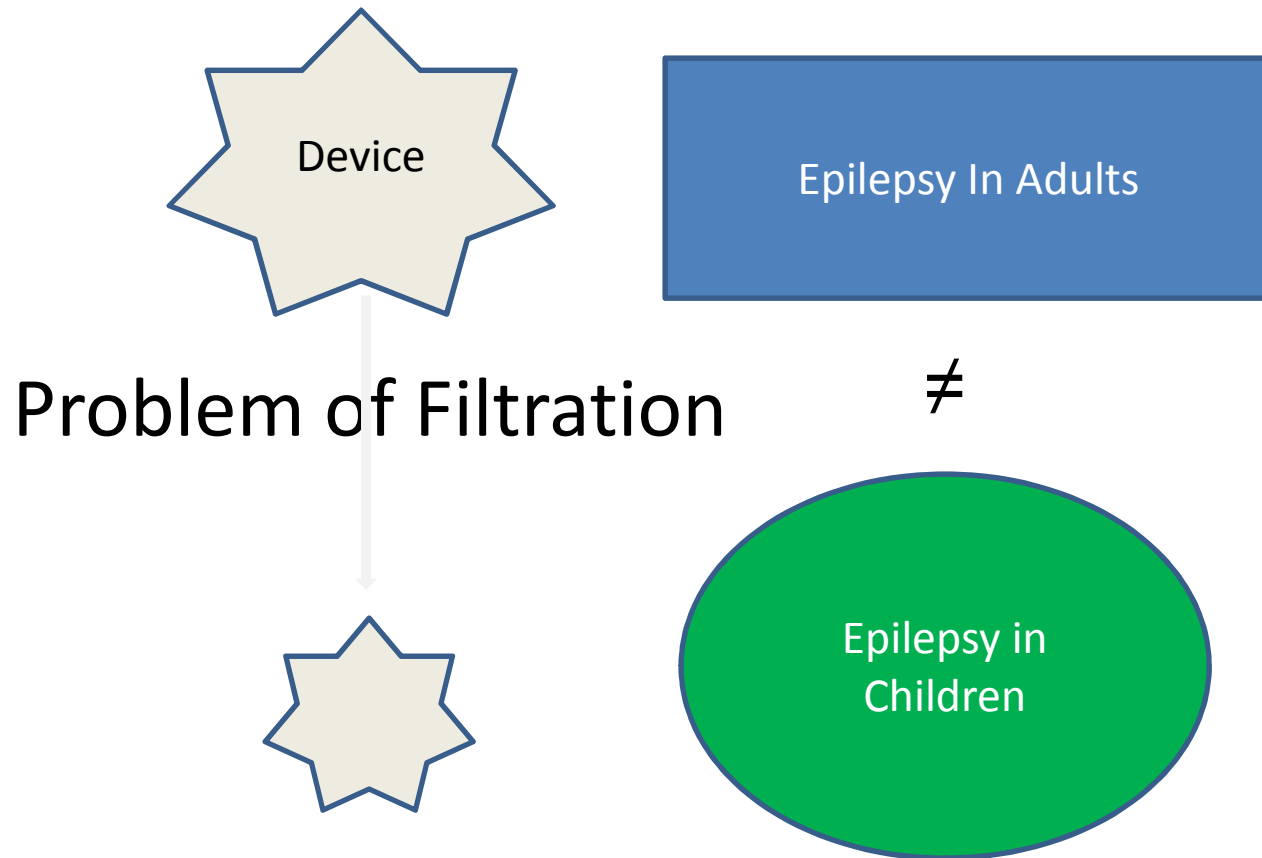
non-invasive stimulation

Targeted drug delivery devices

Prior Experience: Vagus Nerve Stimulation

Trial	Total Subjects	Children
International double blinded randomized active control trial	67	2 (age 12-18)
National multicenter double blind randomized active control trial	196	17 (age 12-18)
Compassionate use		41
Combined		60 Age range 3.6-18 Median age 13.5

Scientific and Clinical Barriers



Scientific and Clinical Barriers

Systems:

- Developing a culture of research participation

- Integration of research infrastructure

- Paucity of trained clinical investigators

Anticipating and measuring long term issues

- Life span of device in one child may be longer than life span of device in the market

Clinical Trial Design Issues

Randomized studies

- Sham controls

- Active controls (dose response)

- Cross-over studies

Observational studies

- Advance planning → best data, minimize bias

- Allows long term follow up

Parent input at the protocol planning stages on the feasibility/tolerability of procedures and visits

Preclinical and Animal Studies

Well developed rodent models of epilepsy
Some models in developing rodent brains

Assessing efficacy:

- seizure frequency

- threshold for inducing seizures

Obvious barriers to translation:

- choosing the appropriate model

 - heterogeneity in the clinical population versus animals

- physical constraints

- time line of assessment

- assessing adverse effects on development

Safety and Effectiveness

Outcome measures: Seizures versus Co-morbidities

Seizure frequency (parent assessment)

QOL measures

Neuropsychological assessments

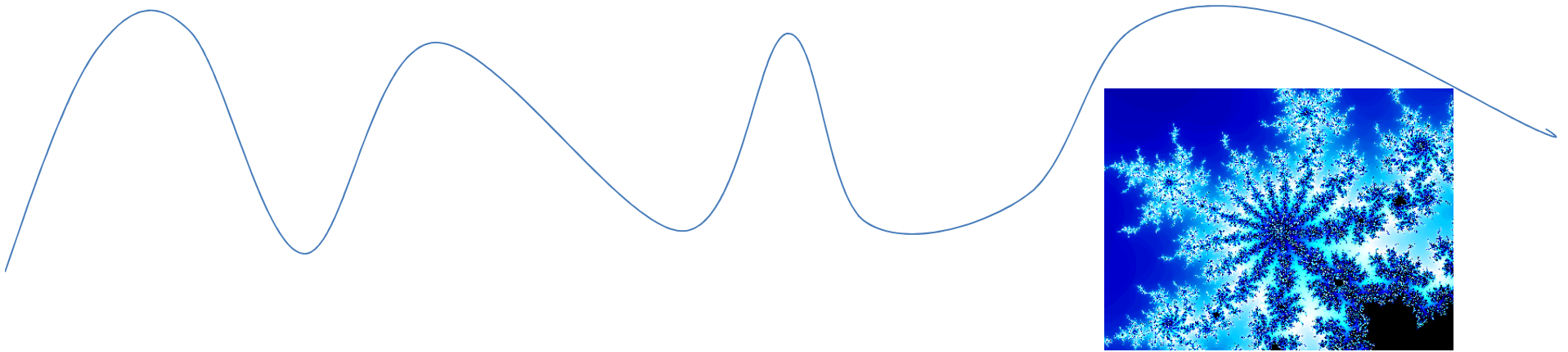
Adverse effects measures

What is needed:

Understanding the *clinically important difference*

Instruments to measure procedure tolerability

Study and Treatment Success



Short term goals
Intermediate goals
Long term goals