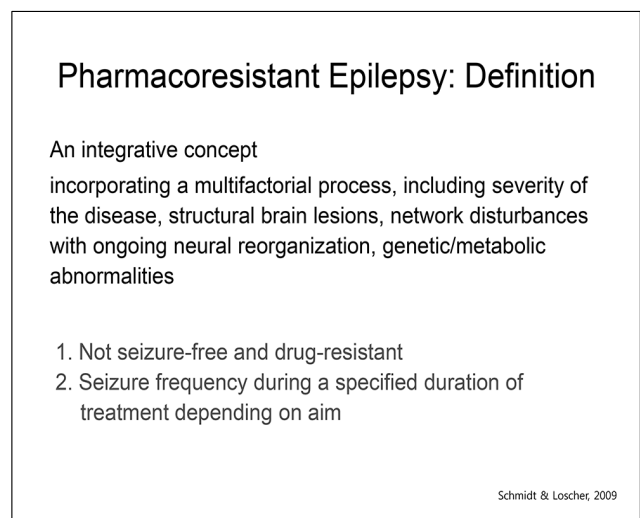
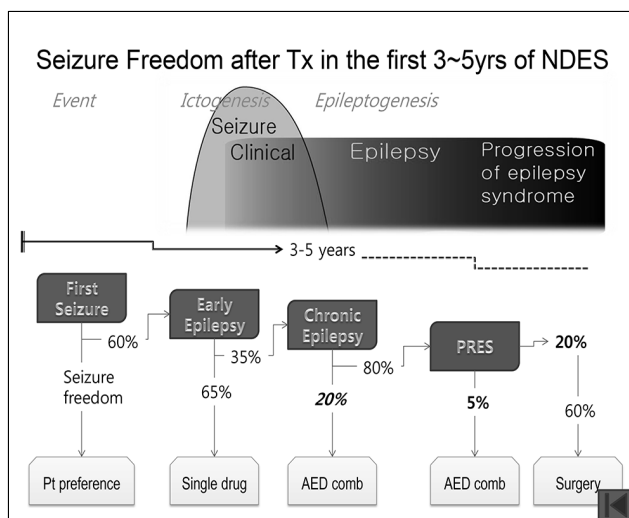
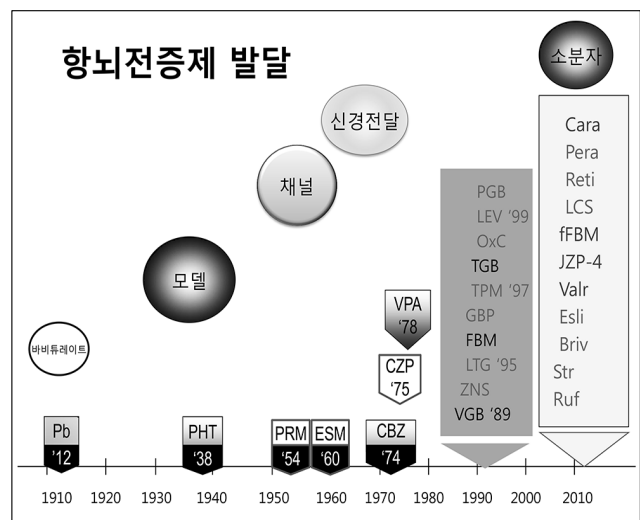
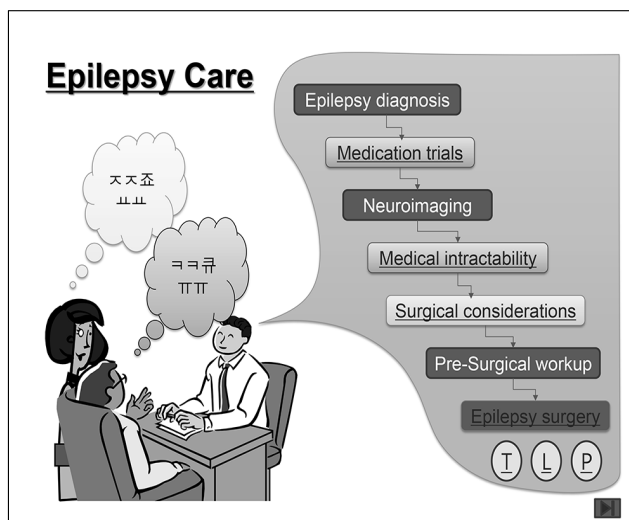


# Selection for epilepsy surgery candidates and seizure outcomes



서대원  
성균관대의대



## Predictor of PRES

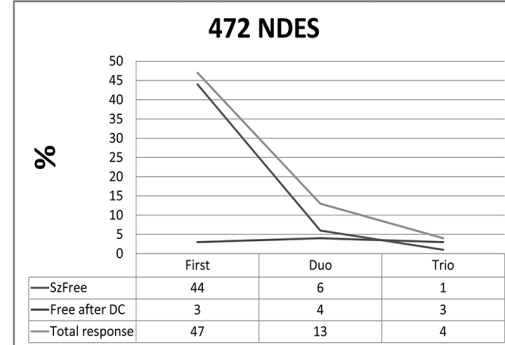
- Early onset of seizures
- Multiple seizures prior to treatment
- Inadequate response to initial treatment
- Long history of poor seizure control by AED
- FHx of epilepsy or PMHx of SE, TBI, febrile seizures
- Causes: structural abnormalities [cortical dysplasia]
- Seizures: mixed seizure types aw developmental delay
- Comorbidity: cognitive disability
- Others:
  - Certain abnormalities on EEG
  - Remote symptomatic etiology [head trauma]
  - Prior or current psychiatric comorbidity [depression]

Loscher & Schmidt, 2011

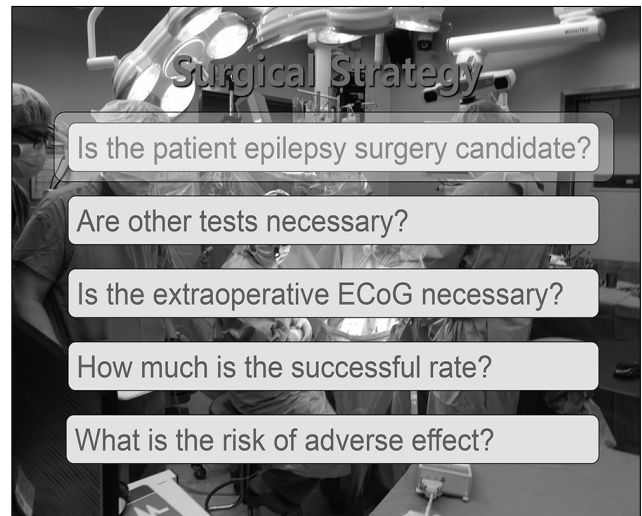
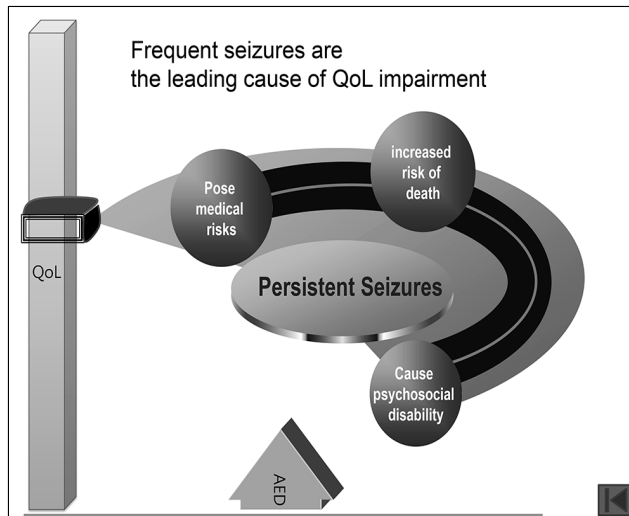
The New England Journal of Medicine 2000;342:314-319

## EARLY IDENTIFICATION OF REFRACTORY EPILEPSY

PATRICK KWAN, M.D., AND MARTIN J. BRODIE, M.D.



→ Patients who have inadequate response to initial treatment with AED are likely to have refractory epilepsy.



## Candidates for Epilepsy Surgery

**Persistent seizures** despite appropriate pharmacotherapy  
usu.  $\geq$  two drugs  
at adequate doses  
with adequate compliance  
appropriate to seizure types

**Impairment of quality of life** due to ongoing seizures  
loss of driving privileges & employment opportunities  
dependence on others, social stigma  
adverse effects of medications  
memory & attention deficit  
injuries & accidents

## Recommendation of Surgical Treatment

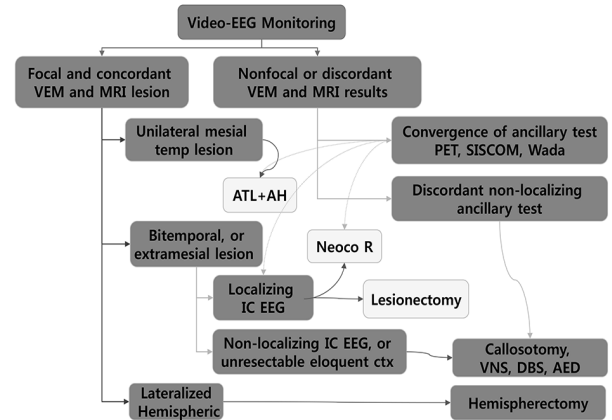
- Surgically remediable epilepsy syndrome
  - Mesial temporal lobe epilepsy
- NE caused by discrete, easily resectable lesions
  - Lesional neocortical epilepsy
- The most refractory to pharmacotherapy
  - Pharmacoresistance epilepsy
- Catastrophic seizures (gen or unilateral) in infants or children
  - Hemimegalencephaly, Sturge-Weber SD
  - large porencephalic cysts, Rasmussen's SD
- Pts with secondarily generalized epilepsy
  - Lennox-Gastaut SD (disabling drop attacks)

Engel et al. Neurology 2006

## Surgical Procedure

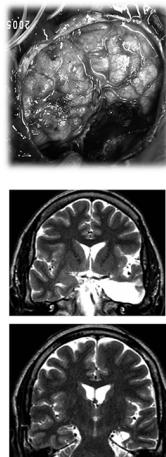
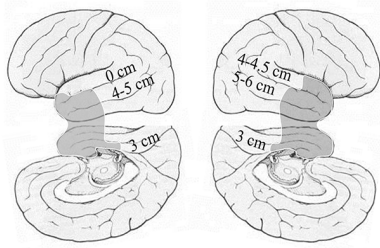
- Anteromesial temporal resection
- Lesionectomy
- Neocortical resection
- Multilobar resection
- Multiple subpial transection
- Hemispherectomy (functional)
- Corpus callosotomy (total, partial)
- Neurostimulation (VNS, DBS, RNS)
- Laser-/ Radio-surgery

Suggested Algorithm for Evaluation of Potential Surgical Candidates:  
Failure of Two or Three adequate trials of AED



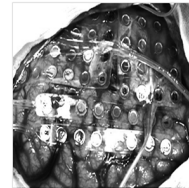
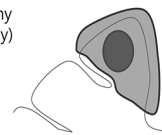
## Epilepsy Surgery-1

- Anterior temporal lobectomy + amygdalohippocampectomy

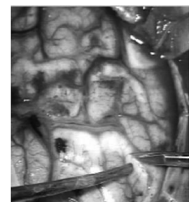
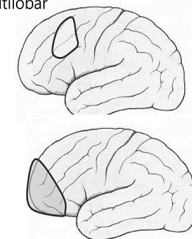


## Epilepsy Surgery-2

Lesionectomy  
(Topectomy)



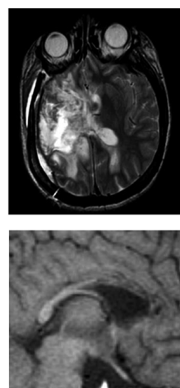
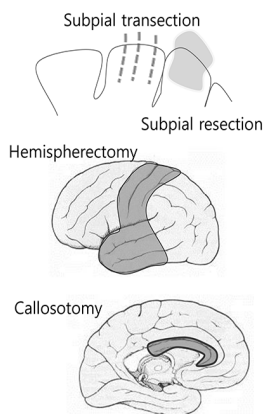
Resection  
Lobar, Multilobar  
Tailored



Lobectomy



## Epilepsy Surgery-Palliative



## Epilepsy Surgery-Neurostimulation

DBS

VNS



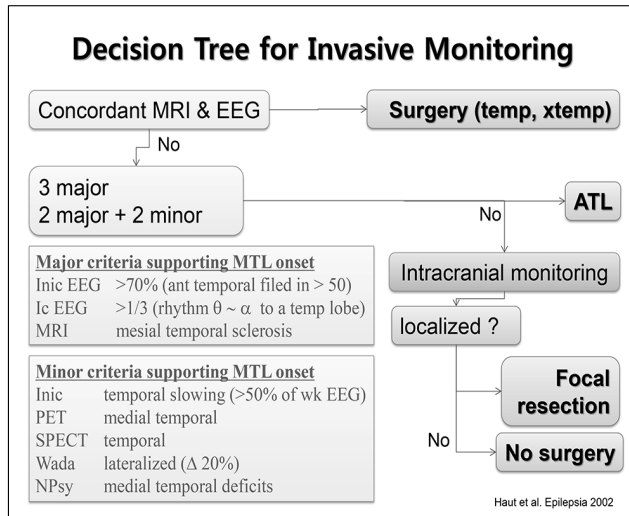
RNS



Responsive Neurostimulation



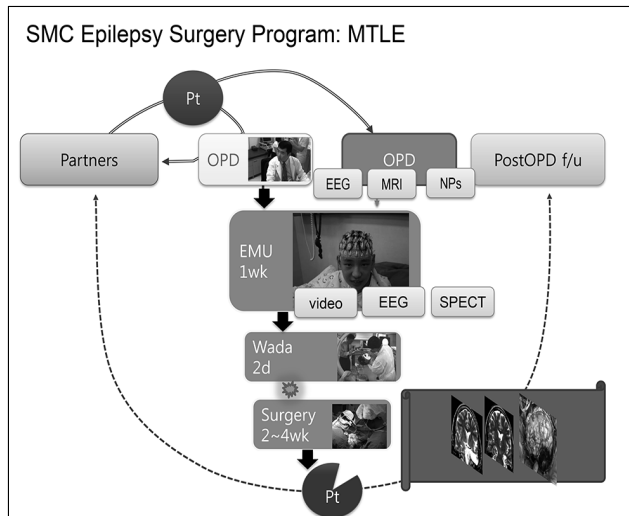
Deep Brain stimulation



## Surgical Candidate: Optimal Timing

- Pharmacoresistance
- Progression
- How long to become intractable? → 9 yr Berg et al. Neurol 2003
- Shorter duration with better result → < 1yr, < 5yr  
Luyken et al. Epilepsia 2003

Early detection of pharmacoresistance  
 Early surgery of mTLE and Lesional epilepsy



## The Syndrome of Mesial Temporal-lobe Epilepsy

Epilepsia 45(6):665-714, 2004  
 Blackwell Publishing, Inc.  
 © 2004 International League Against Epilepsy

### ILAE Commission Report

### Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis

Compiled by Heinz-Gregor Wieser for the ILAE Commission on Neurosurgery of Epilepsy

Department of Neurology, University Hospital Zurich, Zurich, Switzerland

**Summary:** Experts discussed the definition, natural history, pathologic features, pathogenesis, electroclinical, neuropsychological, structural and functional imaging findings, as well as surgical outcome in mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS). After a long-lasting consensus process the ILAE Commission Neurosurgery of epilepsy accepted the resulting conclusions as state-of-the-art report on MTLE-HS. The major-

ity of contributors considered MTLE-HS to represent a sufficient cluster of signs and symptoms to make up a syndromic diagnostic entity. **Key Words:** Definition—natural history—pathologic features—pathogenesis—electroclinical—neuropsychological—neurophysiological—structural and functional imaging—surgical outcome of mesial temporal lobe epilepsy with hippocampal sclerosis—Istanbul Workshop on mesial temporal lobe epilepsy with hippocampal sclerosis.

Engel. NEJM 1996  
 ILAE. Epilepsia 2004

## The Syndrome of Mesial Temporal-lobe Epilepsy

Hx FS, onset, rare SGS, remit/resist, depression, FHx  
 Ex Normal [except for memory deficit]

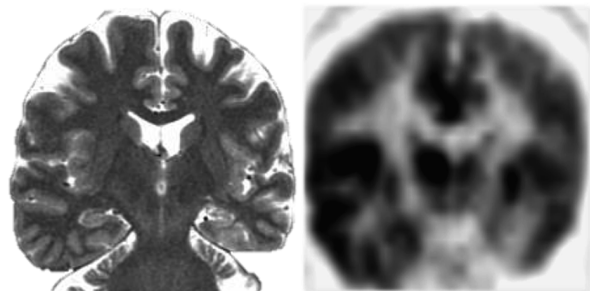
Sz Aura epigastric, autonomic, psychic, (olfac/gust)  
 Motor stare/arrest, automatism, posturing (contralat)  
 Postic disorientation, memory deficit, dysphasia

Lab EEG (in) temp spikes [max in ant. basal (uni/bi independent)]  
 EEG (ic) focal rhythmic onset of 5~7 Hz. (basal temp max)  
 MRI hippocampal atrophy  
 PET temporal hypometabolism (+ ipsi-thalamus and BG)  
 SPECT (in/ic) temporal hypoperfusion/hyperperfusion  
 Npsy memory dysfunction specific to involved temporal  
 Wada amnesia with con-ICA injection of amytal

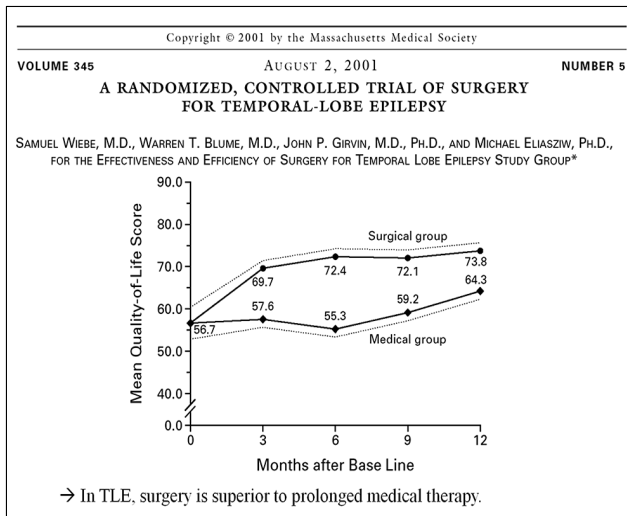
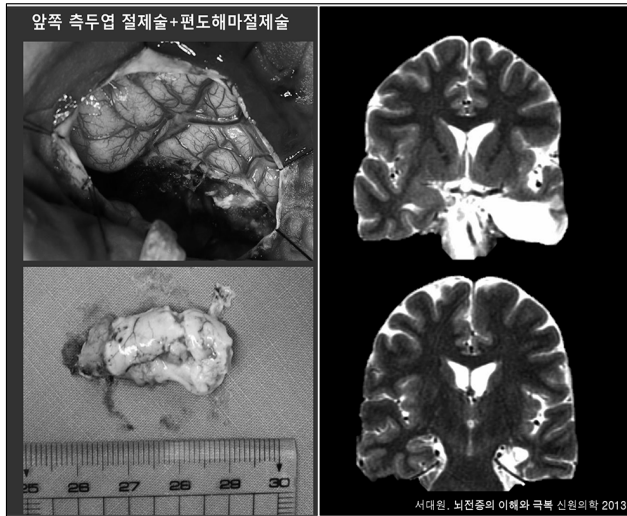
Engel. NEJM 1996

F/36 since 7y 고졸/청주/주부/우측

IPI Febrile seizure at 3 yo  
 Sz SPS (7-8/m), CPS (2-3/m), SGS (1)  
 SE (1997, >20/day for 2-3d)  
 AED CBZ 3T, TPM 125mg bid

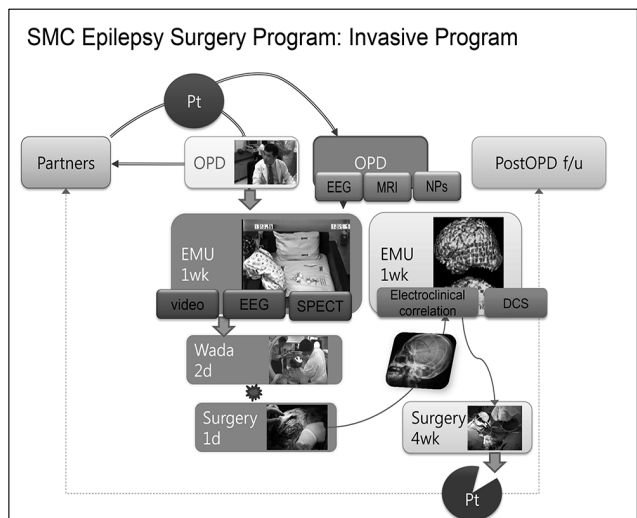






- ### Independent Predictors of Sz Control after AMTR
- Hippocampal atrophy (+ concordant EEG localization)
  - Temporal lobe hypometabolism
  - Lateralization of memory function
  - Presence of an early risk factor
  - Absence of GS or immediate postoperative seizures
- ? → FS
  - Not → Epilepsy duration, Resection extent
- Spencer. Lancet Neurol 2002

- ### Considerations in MTLE
- Normal MRI
  - Bitemporal lobe epilepsy
  - Extrahippocampal focus
  - Dual pathology
- The concept of MTLE does not imply that the onset of seizures is always and exclusively confined to the sole of a sclerotic hippocampus



### Predicting Response to Medical Treatment

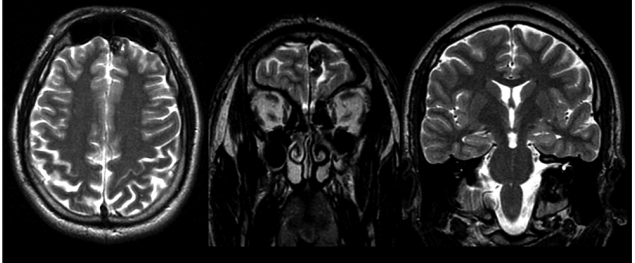
	Seizure free (%)
Newly diagnosed patients	40
MCD	24-54
Dual Pathology of MTS and MCD	4
Tumor, VM, Infarct	46-78
Calcification, Granuloma	?

Spencer. Lancet Neurol 2002

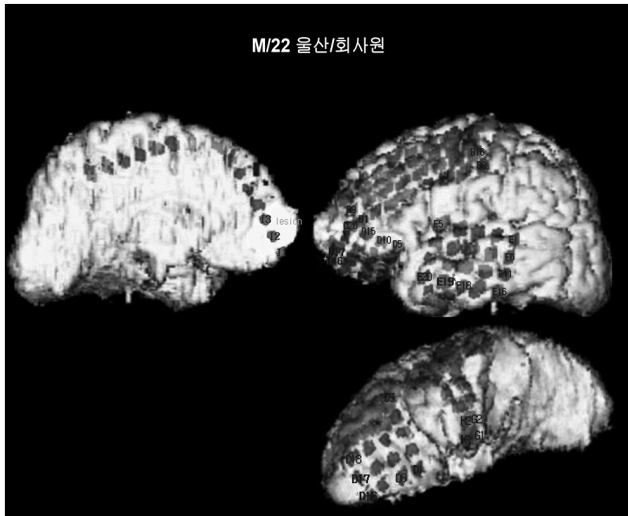
### M/22 since 5y 울산/회사원

IPI none  
5 y-o Sz, seizure free with med for 10yr  
SPS 1-5/d, CPS 1-2/3m, SGS rare

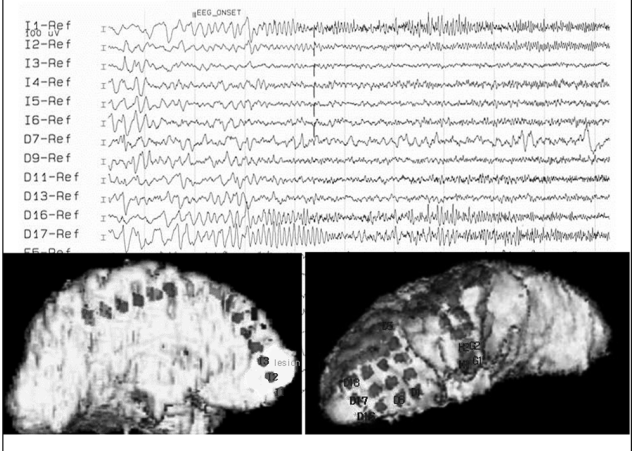
AED DPH 2.5T+CBZCR 2.5T+VPA 600mg bid  
Level DPH 9.0 CBZ 8.6 VPA 61.3 mg/L



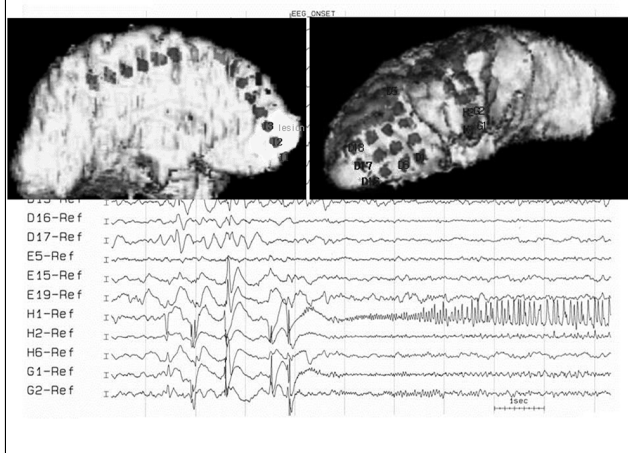
### M/22 울산/회사원



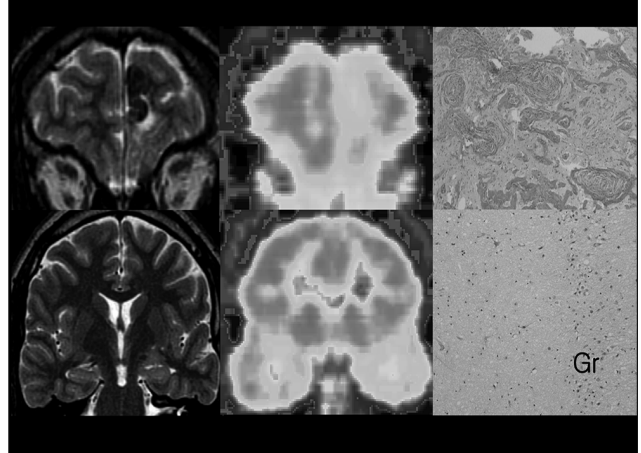
### M/22 울산/회사원



### M/22 울산/회사원



### M/22 울산/회사원



## Practice parameter: Temporal lobe and localized neocortical resections for epilepsy

Report of the Quality Standards Subcommittee of the American Academy of Neurology, in Association with the American Epilepsy Society and the American Association of Neurological Surgeons

J. Engel, Jr., MD, PhD; S. Wiebe, MD; J. French, MD; M. Sperling, MD; P. Williamson, MD; D. Spencer, MD; R. Gumnit, MD; C. Zahn, MD; E. Westbrook, MD; and B. Enos, MD, PhD

**Abstract—Objectives/Methods:** To examine evidence for effectiveness of anteromedial temporal lobe and localized neocortical resections for disabling complex partial seizures by systematic review and analysis of the literature since 1990. **Results:** One intention-to-treat Class I randomized, controlled trial of surgery for mesial temporal lobe epilepsy found that 50% of patients randomized to be evaluated for surgical therapy (54% of those who received surgery) were free of disabling seizures and 10 to 15% were unimpaired at the end of 1 year, compared with 8% free of disabling seizures in the group randomized to continued medical therapy. There was a significant improvement in quantitative quality-of-life scores and a trend toward better social function at the end of 1 year for patients in the surgical group; no surgical mortality, and infrequent morbidity. Twenty-four Class IV series of temporal lobe resections yielded essentially identical results. There are similar Class IV results for localized neocortical resections; no Class I or II studies are available. **Conclusions:** A single Class I study and 24 Class IV studies indicate that the benefits of anteromedial temporal lobe resection for disabling complex partial seizures is greater than continued treatment with antiepileptic drugs, and the risks are at least comparable. For patients who are compromised by such seizures, referral to an epilepsy surgery center should be strongly considered. Further studies are needed to determine if neocortical seizure benefit from surgery, and whether early surgical intervention should be the treatment of choice for certain surgically remediable epileptic syndromes.

NEUROLOGY 2001;56:338-347

27/M since 26y

Handedness) Rt.

SHx) Guard, University, Single

Onset) 1YA (late 2000)

Seizure) smiling, blank stare, amnesia

for 20-30sec, 2-3/d

Nocturnal tendency

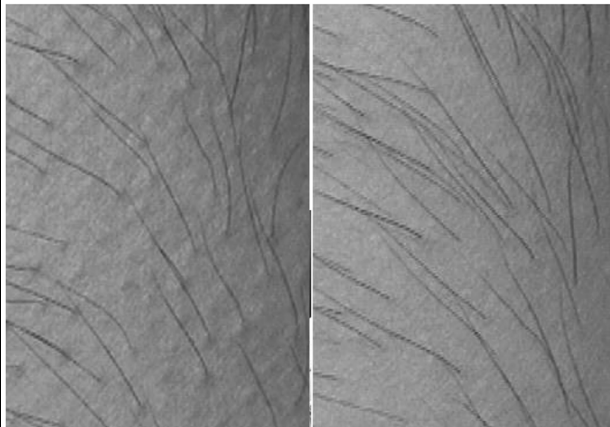
N/E) free

Med) OXC+VPA+TPM+CLB

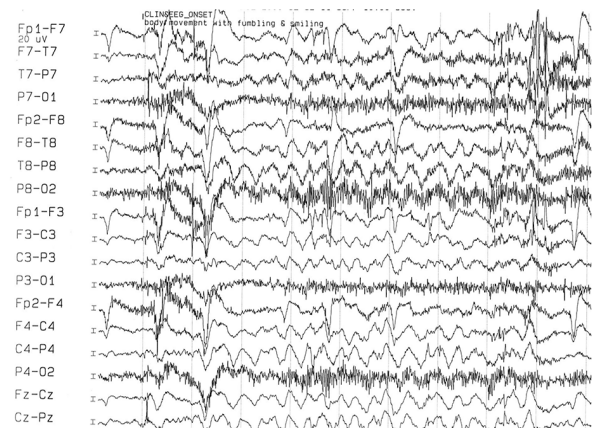
W/U) EEG and MRI: normal

Early 2001, VEM

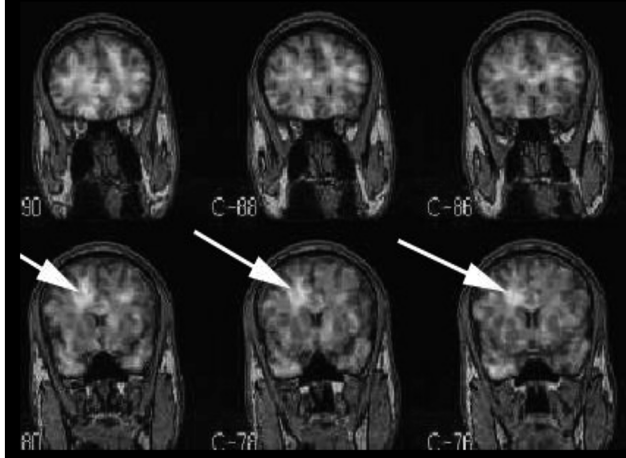
## Piloerection during his seizures



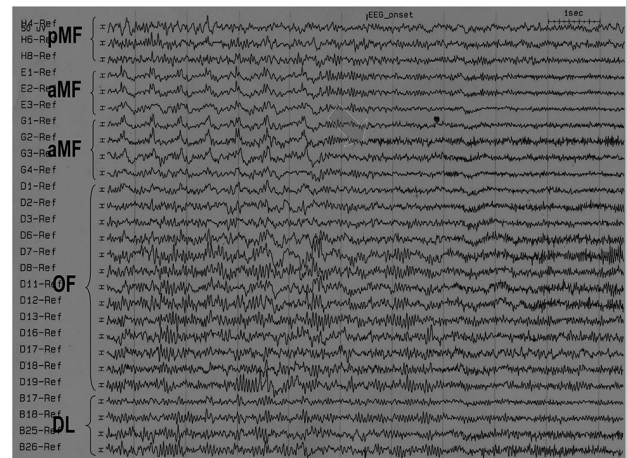
## Ictal EEG



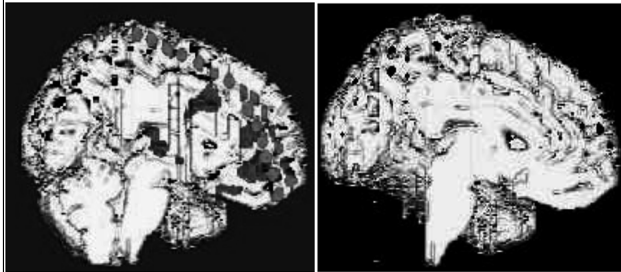
## SISCOM



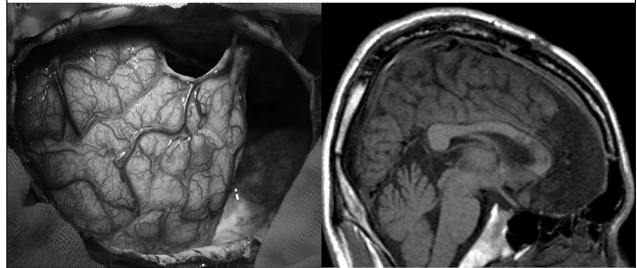
## Ictal ECoG



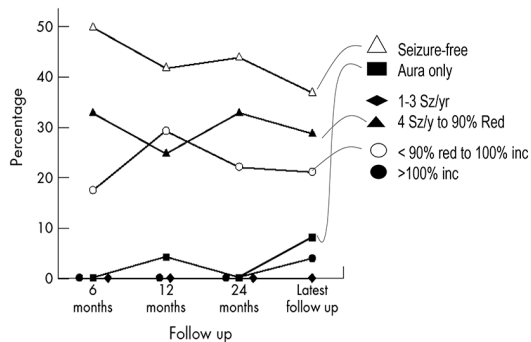
## Subtracted ictal SPECT on 3-D MRI



## Resection of Rt. ant. frontal area



## Seizure Outcome in Nonlesional Neocortical Epilepsy



Chapman et al. JNNP 2005

## Pooled seizure outcome

- Anteromesial temporal resection
  - 24 centers 66.8 (64-68)
  - 4 European centers 62.1 (58-66)
  - 3 Asian centers 67.0 (61-73)
  - 2-5 yr f/u (9 centers) 63.2 (60-66)
  - All after 1985 (15 centers) 68.2 (65-71)
- Neocortical resection
  - 8 centers 49.7 (44-55)

Engel, et al. Epilepsia 2003

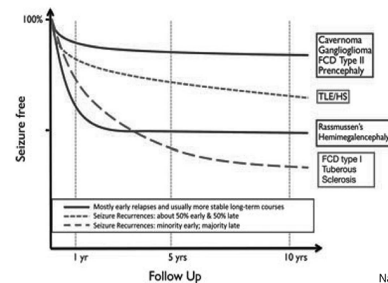
## Efficacy and Complications

- Seizure control
  - ATL
    - 60~70% free
    - 10~15% unimproved
  - NCR
    - 50% free
    - 15% unimproved
- Surgical complications
  - Morbidity 11%
    - 3% permanent
  - Cognitive 6%
    - 3% permanent

Engel et al. Epilepsia 2003

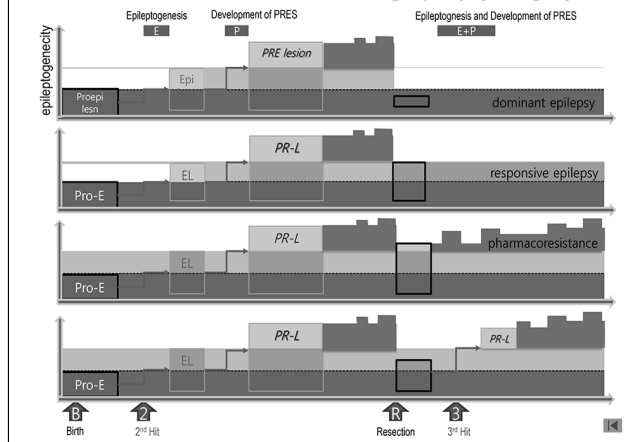
## Epilepsy Surgery Failure

- Failure to define/resect the epileptogenic zone
- Non-static nature of epilepsy as a disease through the persistence of preepileptic cortical pathology

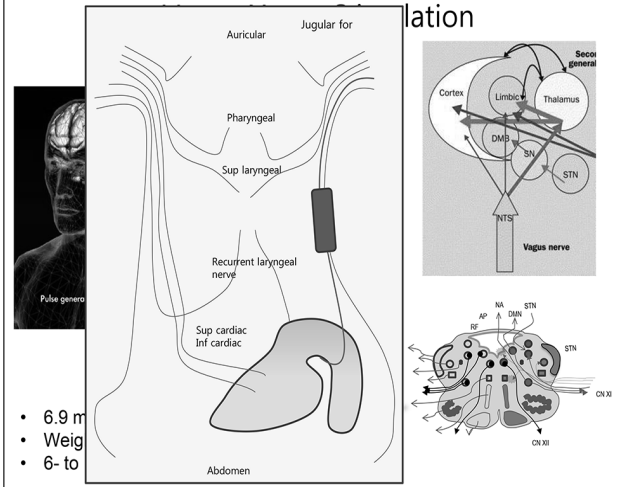


Najm I et al. Epilepsia 2013

### Schematic representations of the possible outcomes and their determinants following epilepsy surgery



## lation



## Epilepsy &amp; Behavior

journal homepage: [www.elsevier.com/locate/yebeh](http://www.elsevier.com/locate/yebeh)

#### Efficacy of vagus nerve stimulation over time: Review of 65 consecutive patients with treatment-resistant epilepsy treated with VNS > 10 years

Robert E. Elliott<sup>a,\*</sup>, Amr Morsi<sup>a</sup>, Omar Tanweer<sup>a</sup>, Bartosz Grobelny<sup>a</sup>, Eric Geller<sup>b</sup>, Chad Carlson<sup>c</sup>,  
Orrin Devinsky<sup>b,c,d</sup>, Werner K. Doyle<sup>a,b</sup>

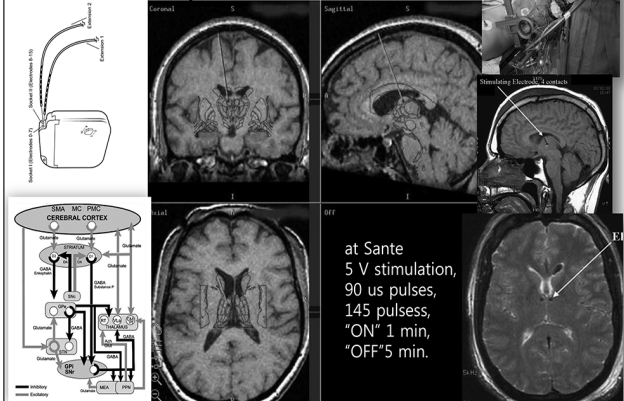
**Table 3**  
Seizure control outcomes by modified Engel and McHugh outcome classifications for 65 patients who underwent VNS therapy >10 years for treatment-resistant epilepsy.

Class	Modified Engel description	Number (%)	McHugh description	Number (%)
I	Seizure free Rare, nondisabling simple partial seizures	16 (24.6%)	80–100% reduction in seizure frequency	36 (55.4%)
II	>90% reduction in seizure frequency Rare complex partial seizures	10 (15.4%)	50–79% reduction in seizure frequency	20 (30.8%)
III	50–90% reduction in seizure frequency	30 (46.2%)	<50% reduction in seizure frequency	6 (9.2%)
IV	<50% reduction in seizure frequency	9 (35.1%)	Magnet benefit only	0 (0%)
V	—	—	No improvement	3 (4.6%)

Fig. 1. Histogram illustrating mean percentage seizure reduction (gray bars), with 95% confidence intervals of the mean (vertical black lines), at serial follow-up visits after initiation of VNS therapy.

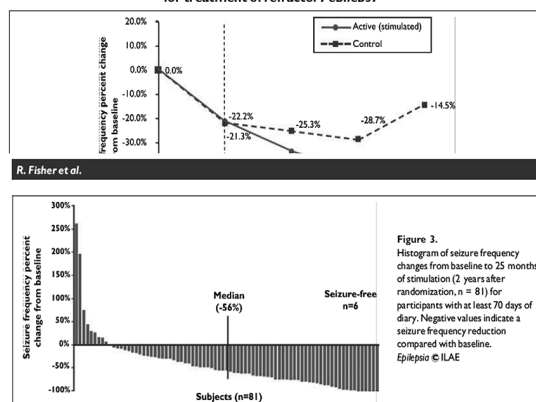
Elliott RE, et al, Efficacy of vagus nerve stimulation over time: Review of 65 consecutive patients with treatment-resistant epilepsy treated with VNS N10 years, *Epilepsy Behav* (2011), doi:10.1016/j.yebeh.2010.12.042

## Deep Brain Stimulation



**FULL-LENGTH ORIGINAL RESEARCH**

## Electrical stimulation of the anterior nucleus of thalamus for treatment of refractory epilepsy



**Figure 3.** Histogram of seizure frequency changes from baseline to 25 months of stimulation (2 years after randomization,  $n = 81$ ) for participants with at least 70 days of diary. Negative values indicate a seizure frequency reduction compared with baseline.

Epilepsy Res. 2010 May;89(2-3):310-8.

# Surgical outcomes in lesional and non-lesional epilepsy: A systematic review and meta-analysis

José F. Téllez-Zenteno<sup>a,\*</sup>, Lizbeth Hernández Ronquillo<sup>a</sup>,  
Farzad Moien-Afshari<sup>a</sup>, Samuel Wiebe<sup>b</sup>

Surgical outcomes in lesional and non-lesional epilepsy: A systematic review and meta-analysis

313

Table 1 Results by surgical topography, including all age groups.

Categories (n of studies)	Non-lesional			Lesional		
	Total N patients	Seizure-free %	95%CI	Total N patients	Seizure-free %	95%CI
<i>Temporal and extratemporal</i>						
Overall (n = 35)	697	43	39–46	2860	68	66–70
Using MRI (n = 19)	398	46	41–51	965	70	68–73
Using histopathology (n = 17)	302	39	34–44	1953	67	65–69
<i>Temporal lobe</i>						
Overall (n = 20)			SF rate			66–70
Using MRI (n = 12)			non-les 51, 35			71–89
Using histopathology (n = 8)	TLE		non-les 32, 35	les 75, 65		63–68
	XTLE		non-les 32, 35	les 60, 74		
<i>Extratemporal</i>						
Overall (n = 13)	156	34	27–41	350	66	61–70
Using MRI (n = 9)	124	35	27–42	225	60	54–66
Using histopathology (n = 4)	35	32	18–47	125	74	67–82

Numbers in "Overall" category do not represent the sum of MRI and histopathology because studies reported different numbers of patients for each category. Some articles contributed more than one study (see text).

### When to Consider Referral for Presurgical Investigation of Epilepsy?

- ❑ Disabling seizures
- ❑ Uncontrolled seizures for  $\geq 2$  yr
- ❑ Failure of adequate trials of  $\geq 2$  AED
- ❑ Controlled seizure with unacceptable AE
- ❑ Focal abnormalities on EEG or brain MRI
- ❑ Partial symptoms or signs of seizure semiology

Engel et al. Epilepsia 2003  
Bruneo and McLachlan. CMAJ 2005

### Summary

- PRES is caused by a multifactorial process, determined by seizure frequency during a specified duration of treatment depending on aim, and predicted by several factors including initial AED responsiveness.
- Mesial temporal lobe epilepsy syndrome, lesional epilepsy, and pharmacoresistant epilepsy syndrome are commonly considered as surgical candidates.
- Timely epilepsy surgery and adequate surgical procedures should be decided deliberately.