MRI Scanning in Epilepsy

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CT Scanning

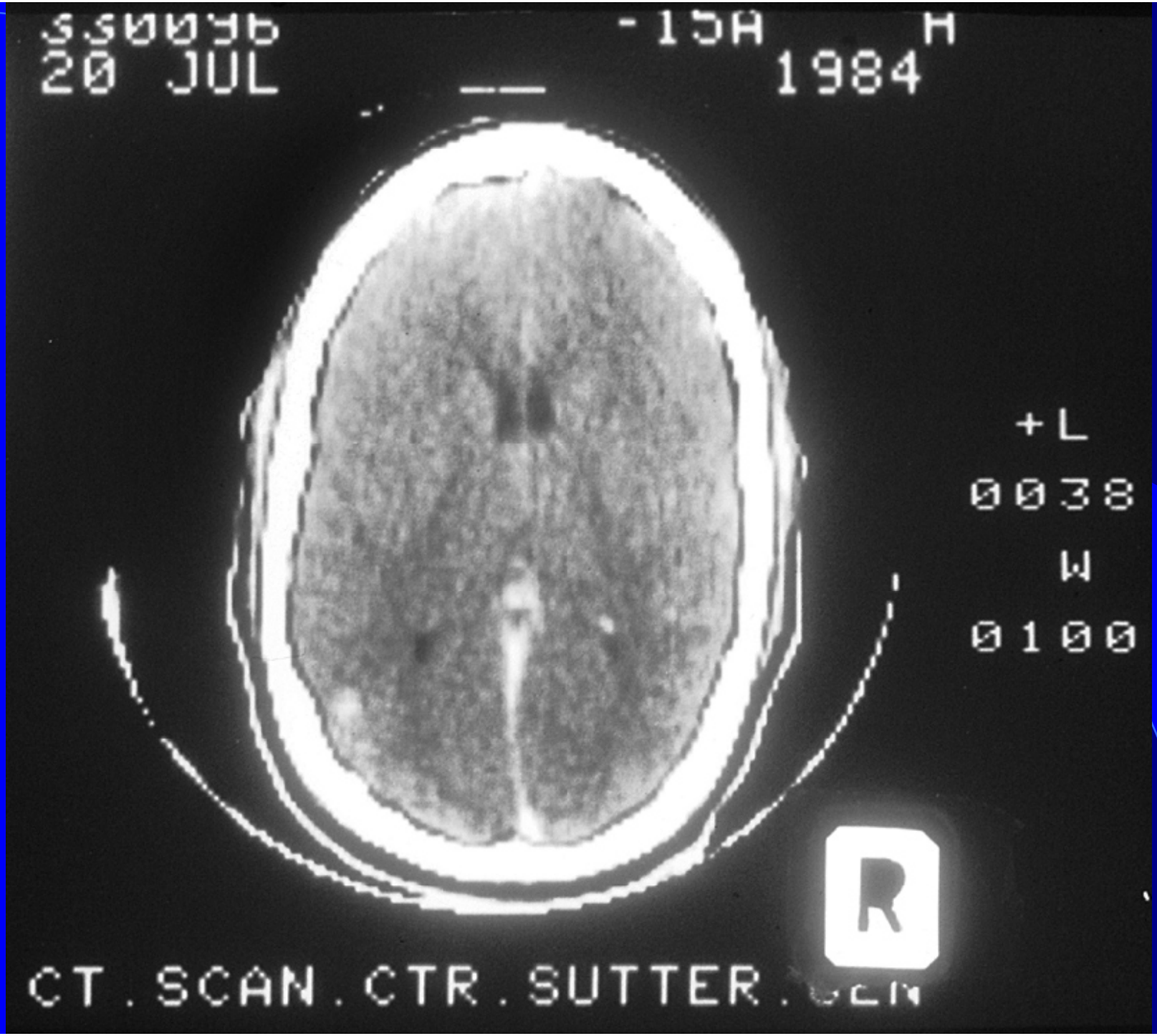
- Advantages
  - Intracranial calcification
  - Skull fracture
  - Acute bleeding into or around the brain
- Disadvantages
  - Lack of high spatial resolution
  - Poor contrast between gray and white matter
- Generally not useful in the evaluation of epilepsy

MRI Scanning: Qualitative Imaging

- MRI scanning is now the imaging study of choice in the initial evaluation of patients with epilepsy
- Small structural lesions
- Neuronal migration disorders (NMD)
- Hippocampal sclerosis
- Correlation with surgical outcome after anterior temporal lobectomy (ATL)

Small Structural Lesions

- MRI is superior to CT scanning in the detection of a variety of small structural lesions
  - Gliosis or sclerosis
  - Tumors
  - Vascular malformations
  - Focal atrophy
  - Infections
- Gadolinium enhancement is useful in some settings, but is usually not necessary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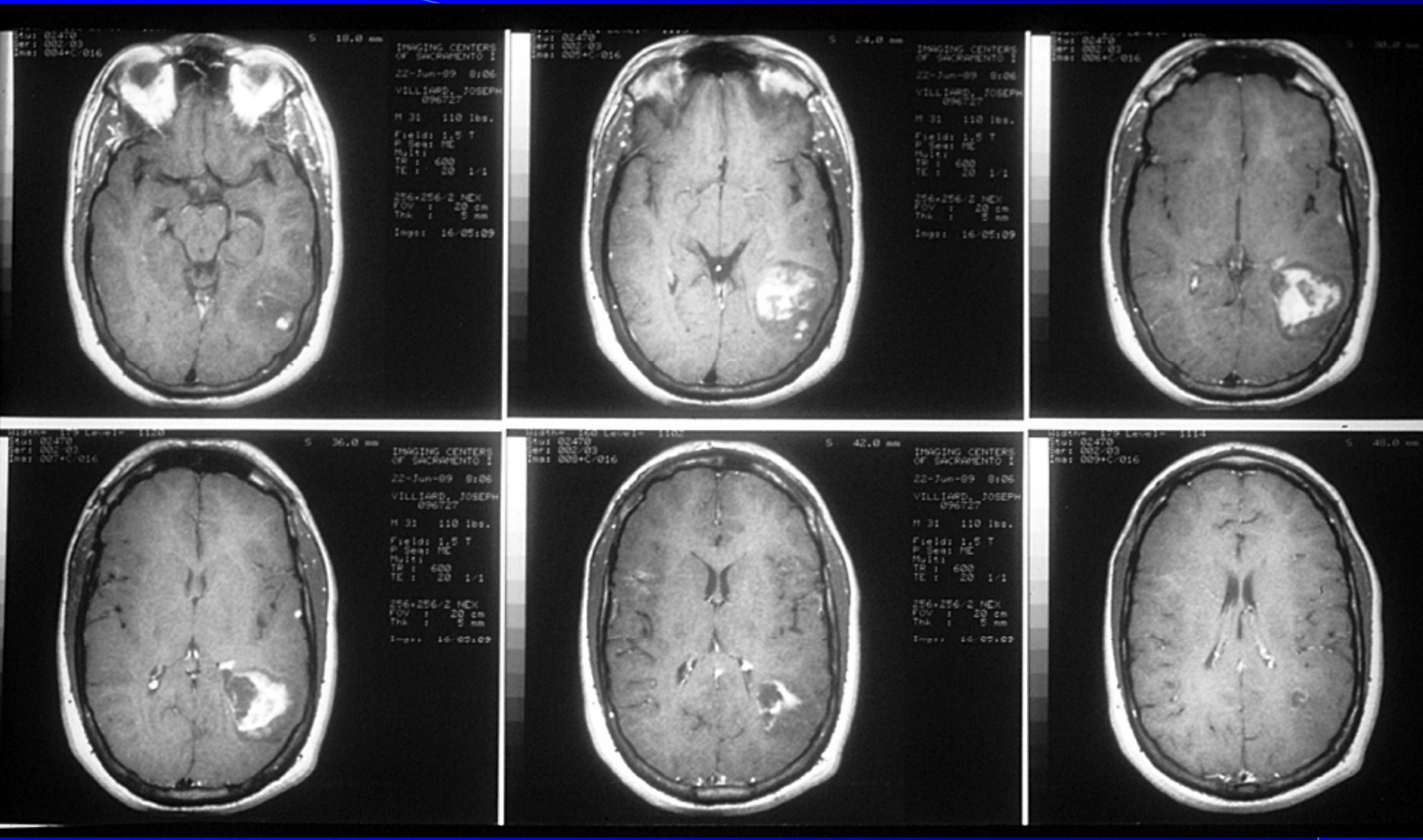
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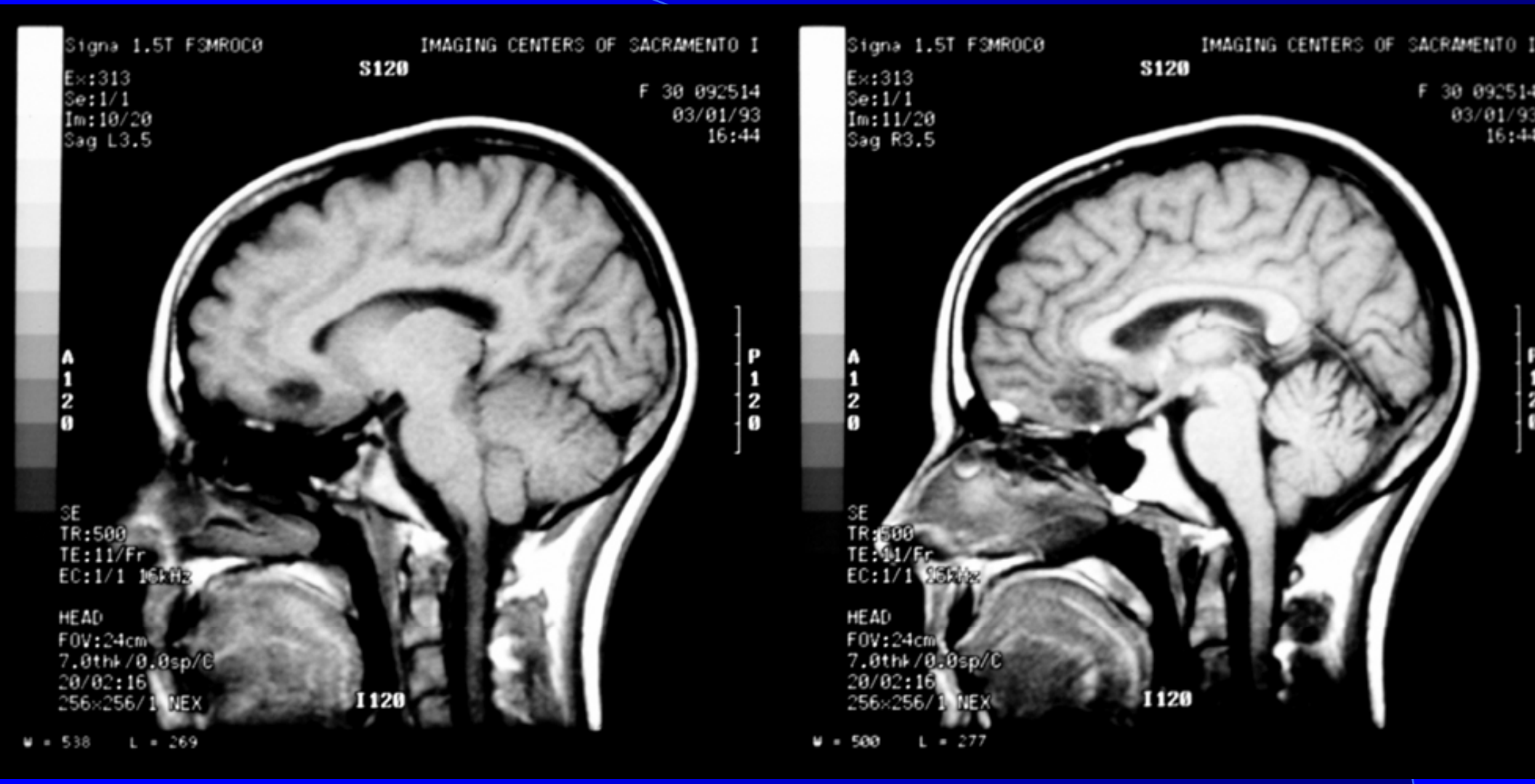
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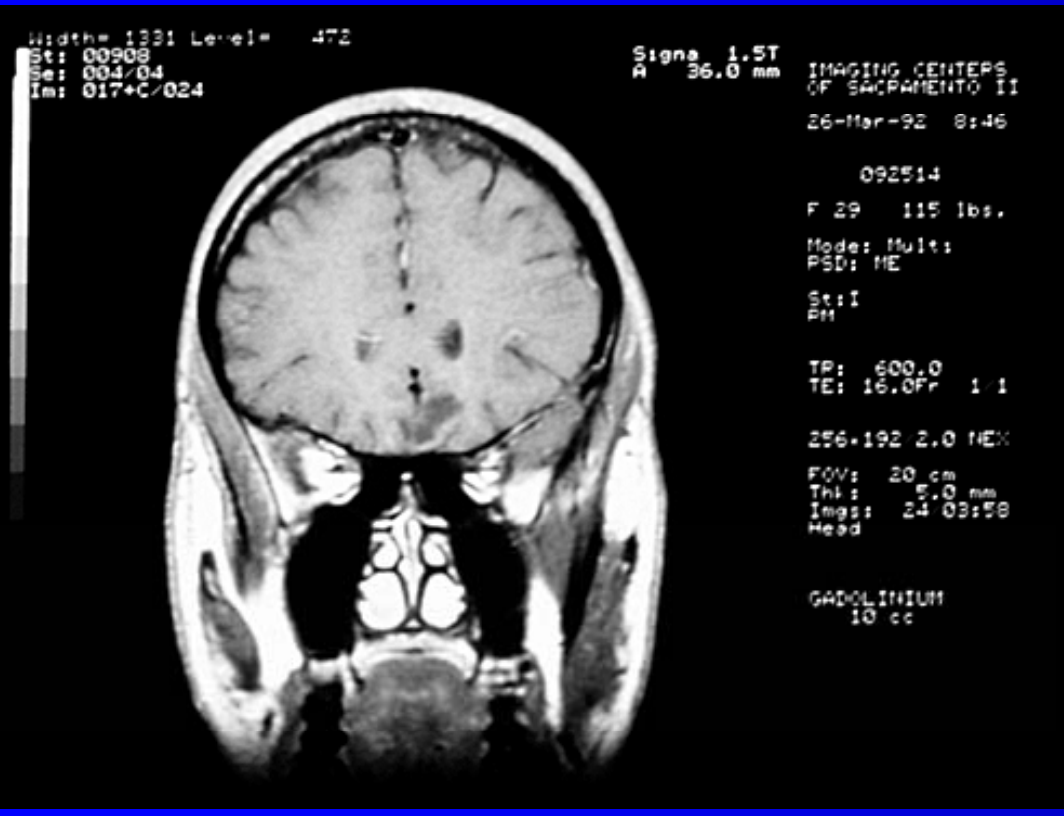
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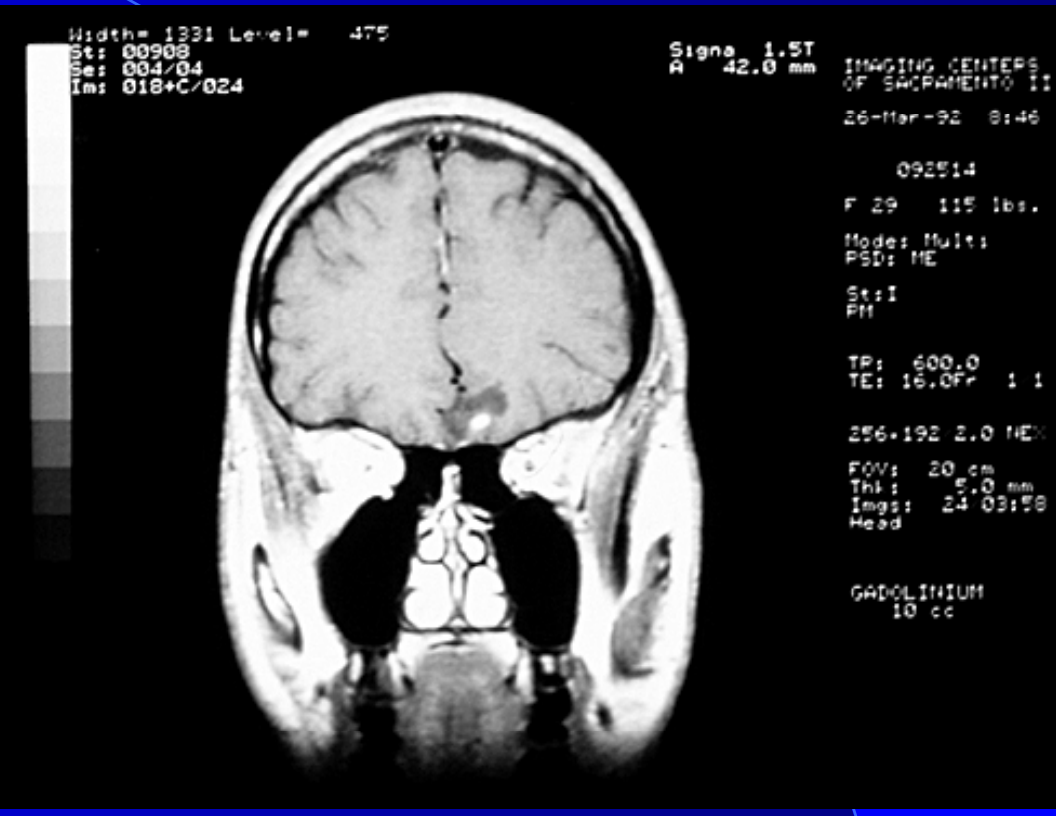
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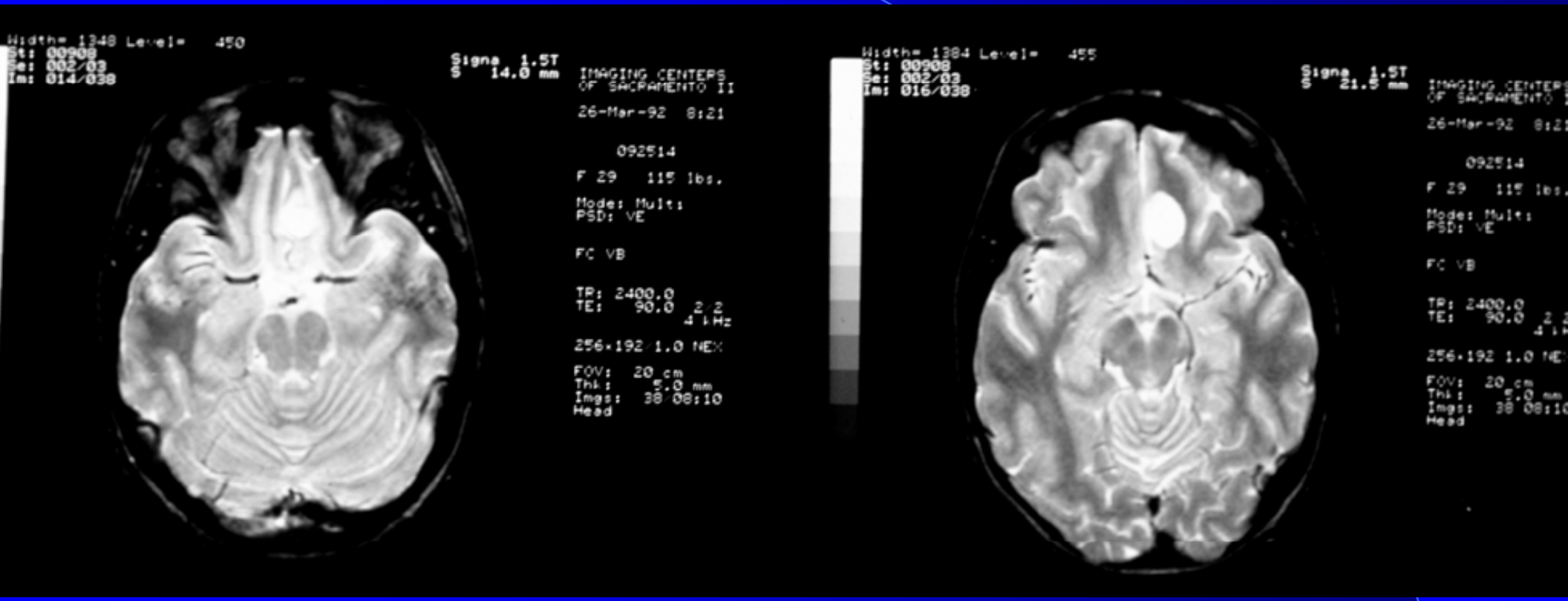
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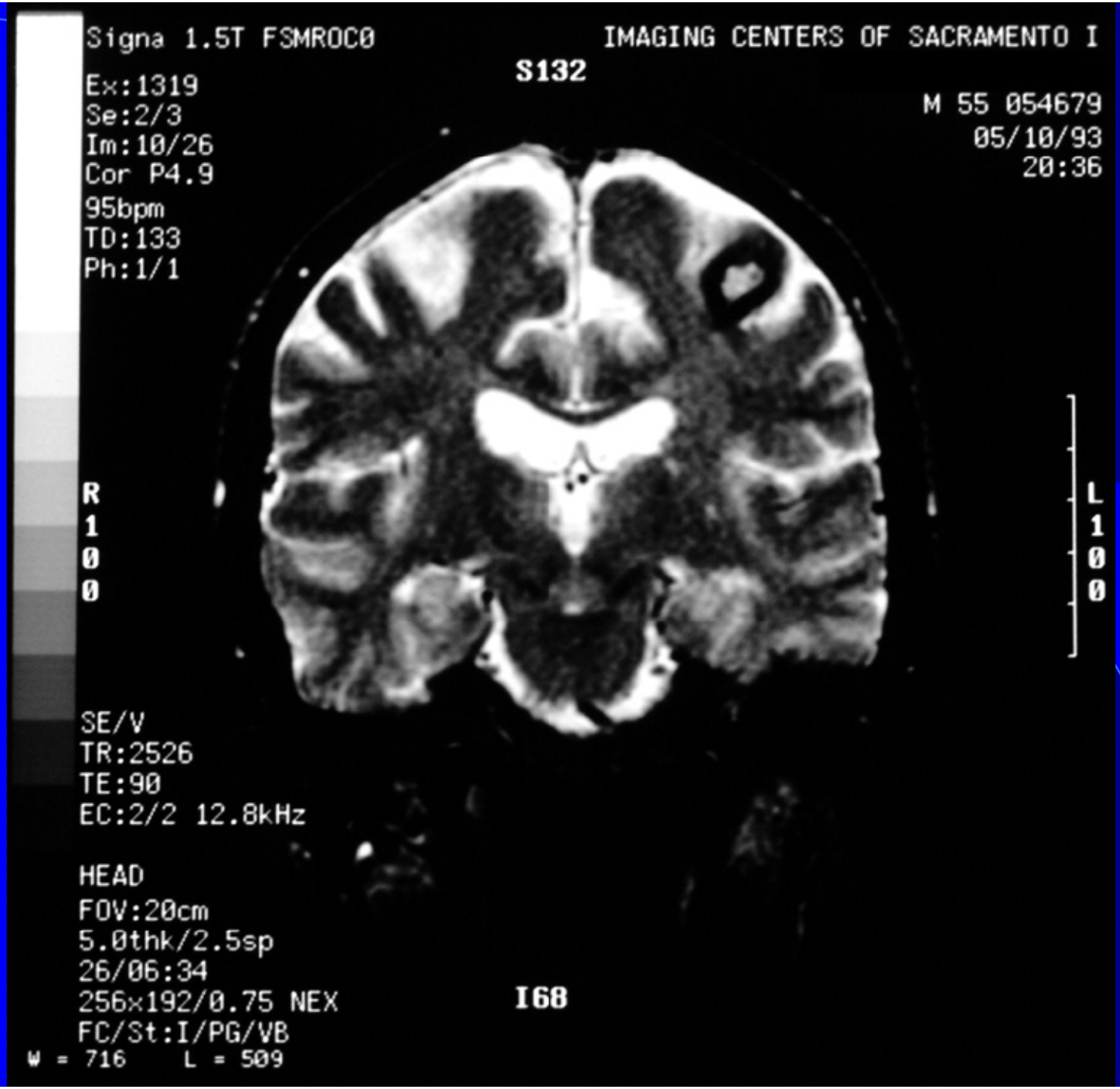
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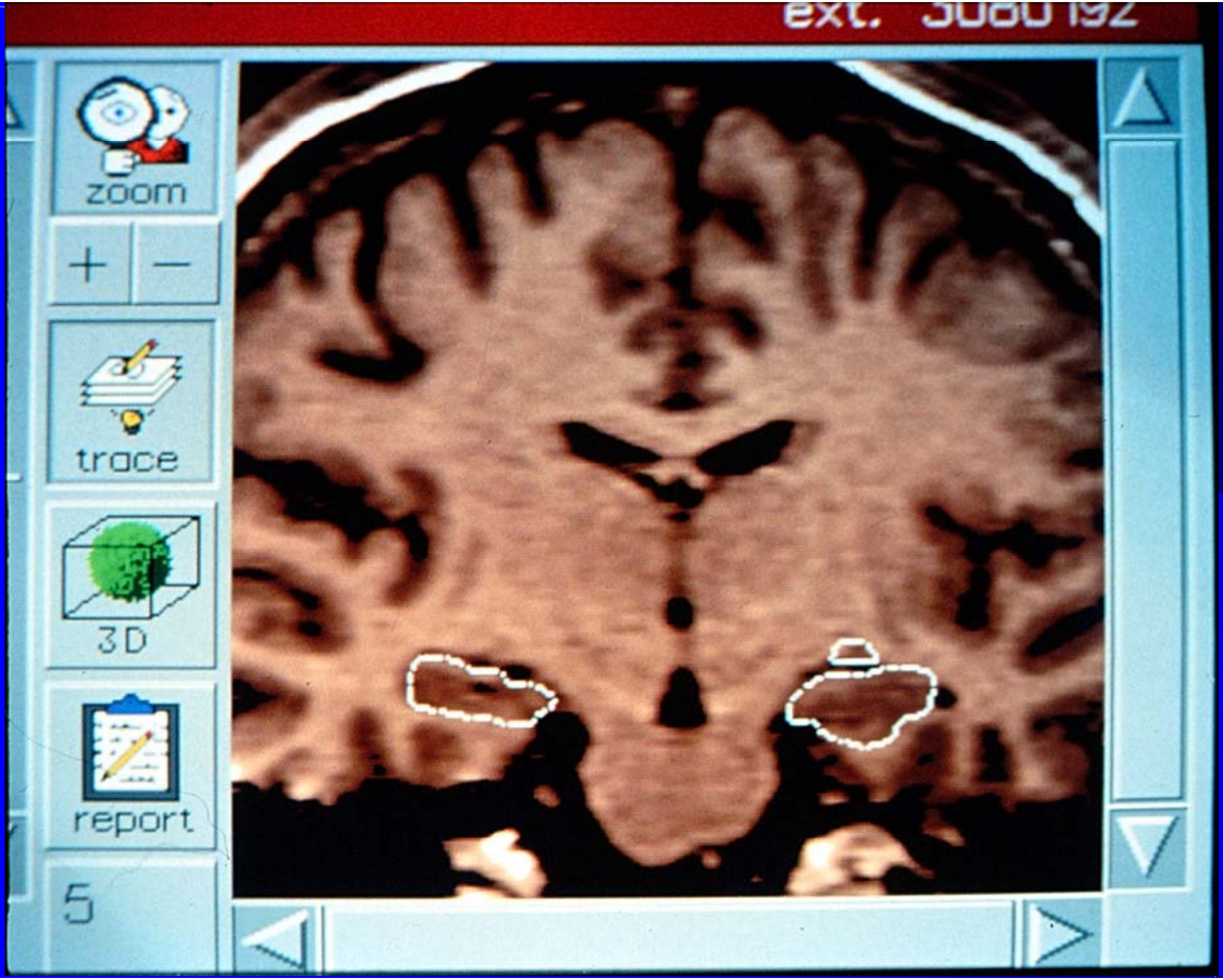
Neuronal Migration Disorders (NMD)

- MRI is clearly superior to CT scanning in the detection of a variety of NMDs that are often associated with epilepsy
  - Microdysgenesis
  - Focal cortical dysplasia
  - Heterotopia
  - Developmental anomalies of the cerebral cortex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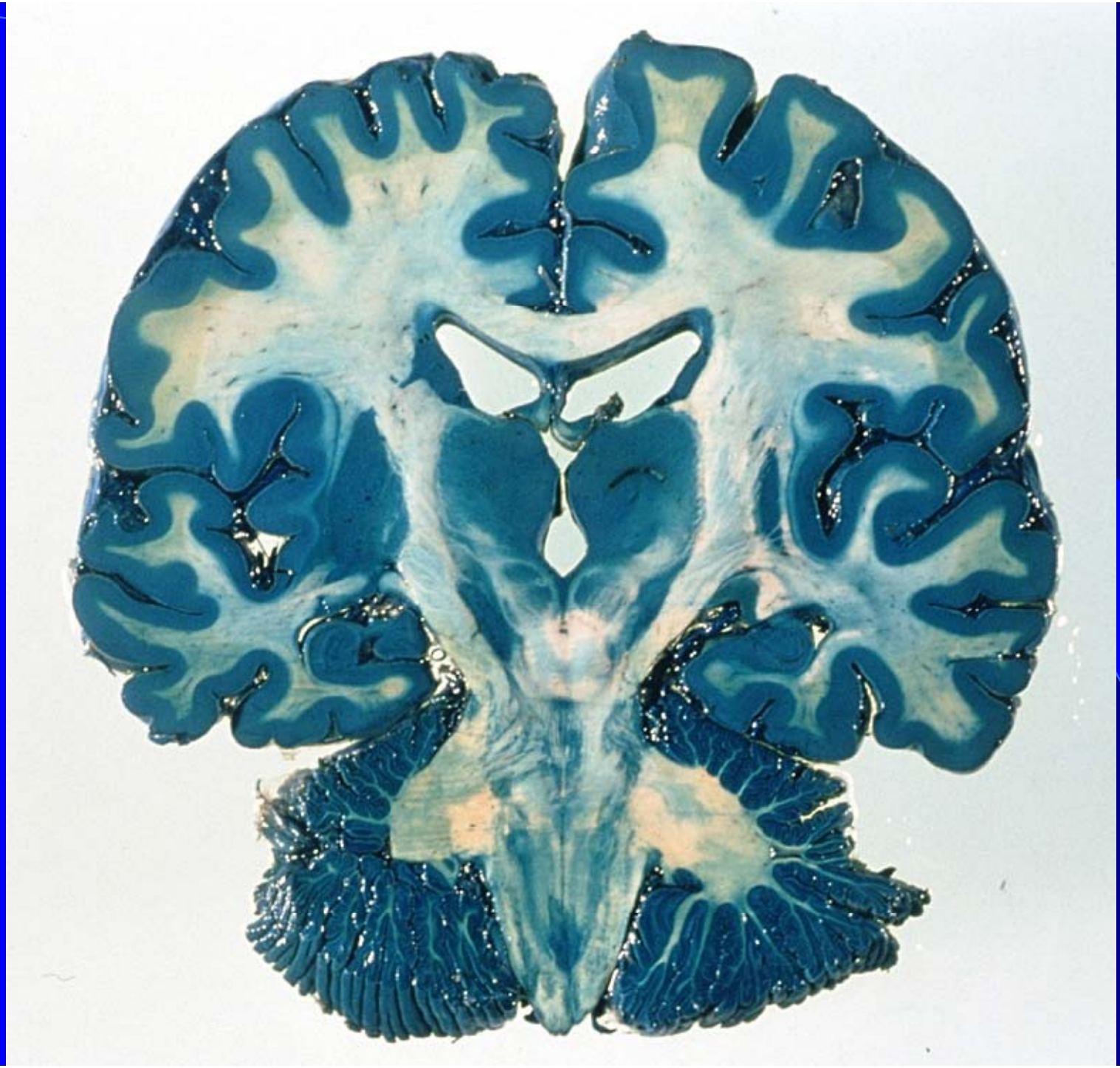
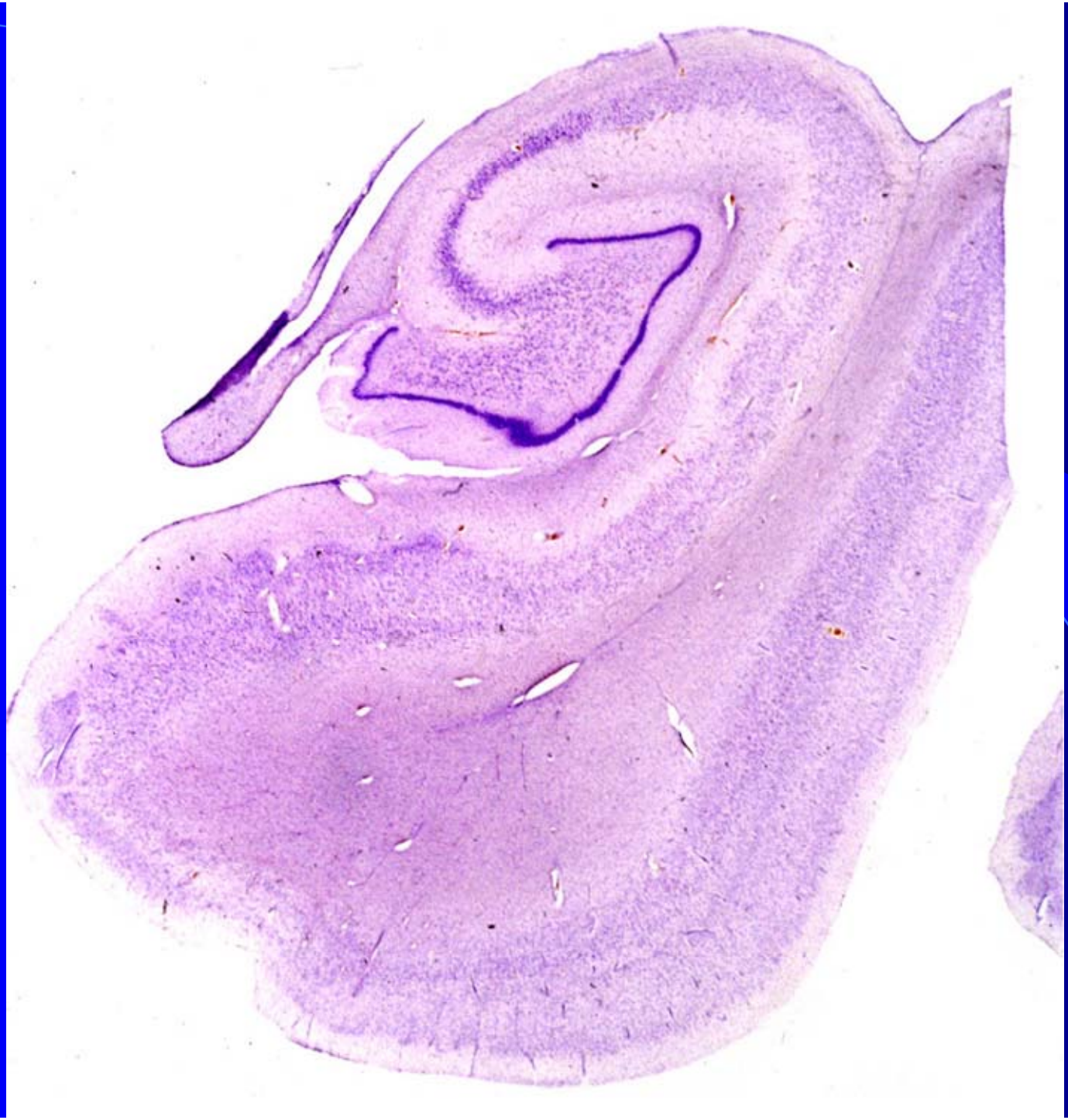
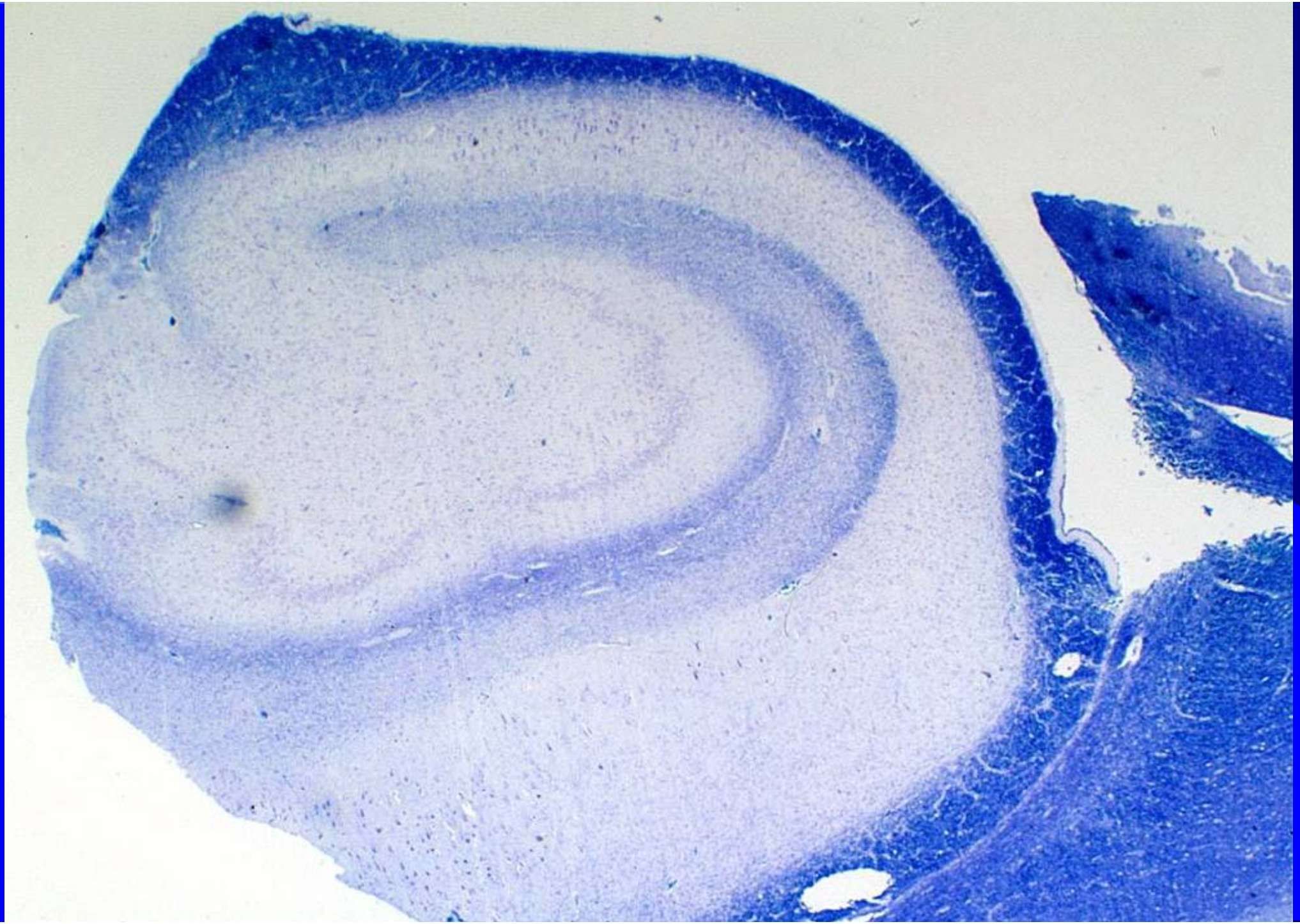
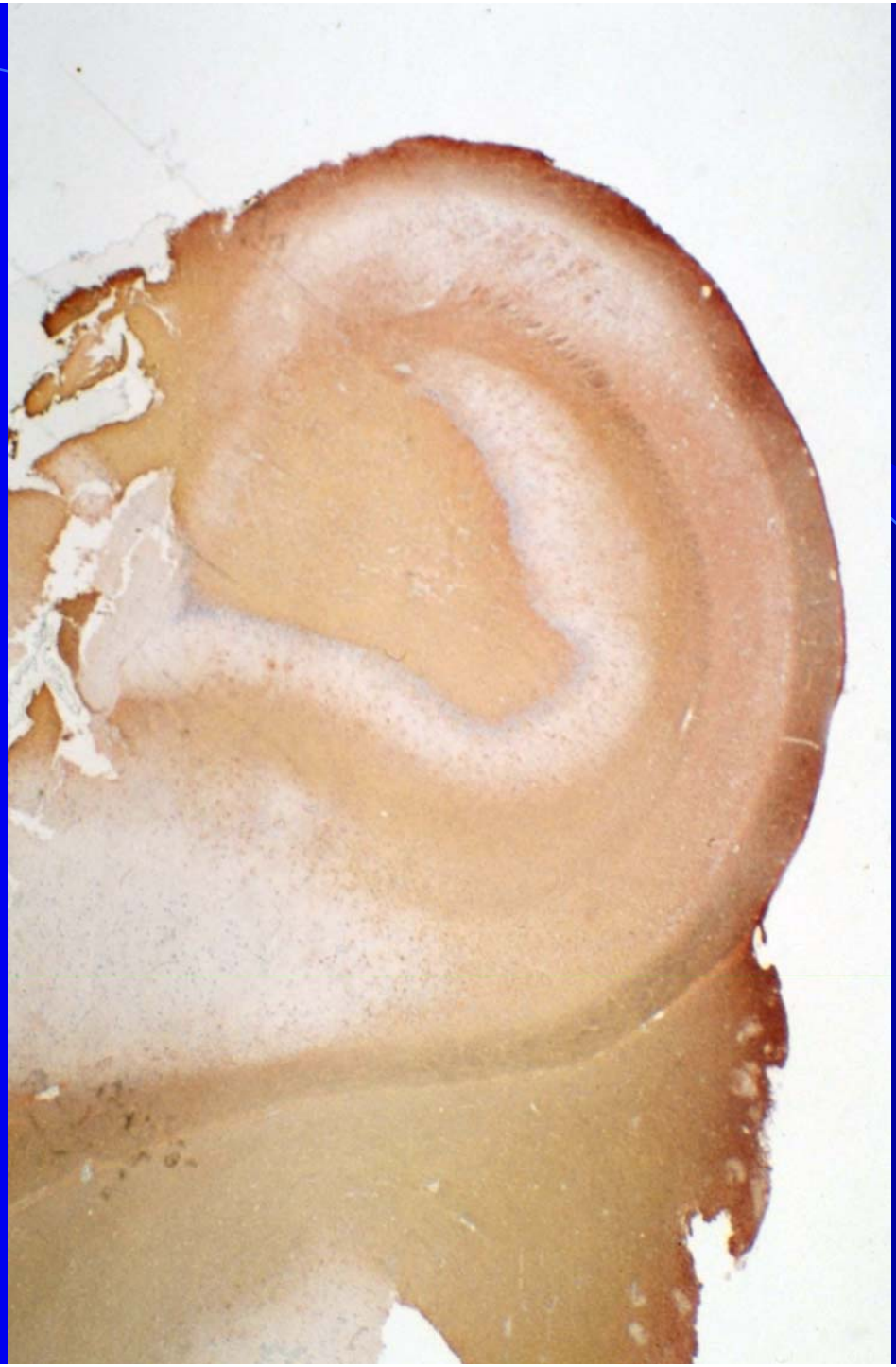
Etiology of Temporal Lobe Epilepsy

- Most common lesion is Hippocampal Sclerosis (60-75%)
  - Neuronal cell loss and gliosis in CA1,CA3,CA4 with occasional wider involvement (CA2, DG, PHG, AM)
- Symmetry of lesions
  - 80% bilateral and asymmetric
  - 10% bilateral and symmetric
  - 10% unilateral only
- Approximately 50% (40-80%) of patients with hippocampal sclerosis experience a prolonged febrile convulsion(s) between the ages of 6 months and 6 years



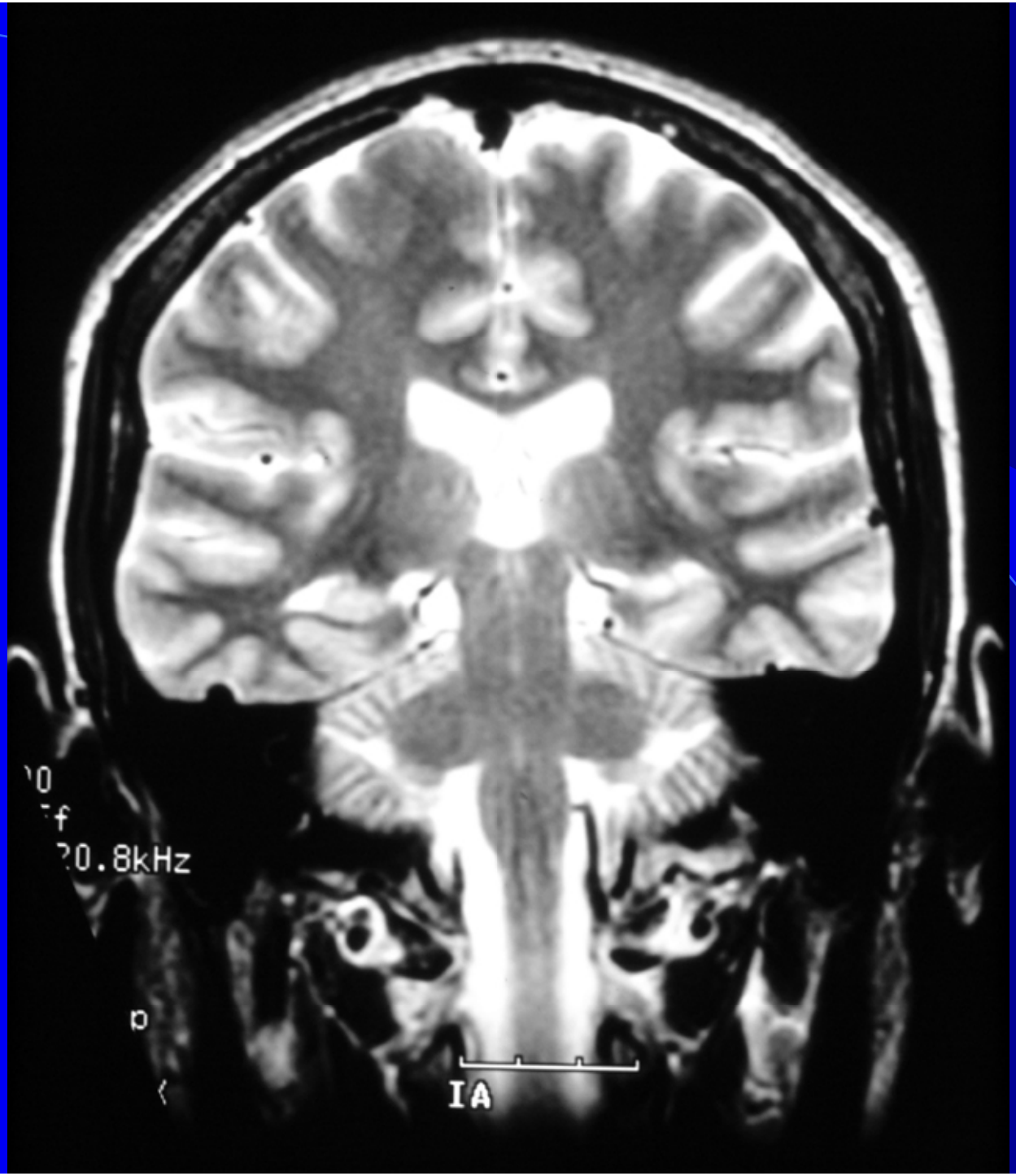






Hippocampal Sclerosis (HS)

- Success of qualitative MRI in detecting HS has varied
- Thin (3-5 mm), coronal images are mandatory
- Increased signal intensity in hippocampus on T2, proton density, or FLAIR images
- Atrophy of hippocampus on T1-weighted images
- Decreased signal in hippocampus on T1-weighted images
- Disruption of internal hippocampal structure
- Enlargement of the inferior horn of the lateral ventricle
- 70-85% accurate in lateralizing side of seizure onset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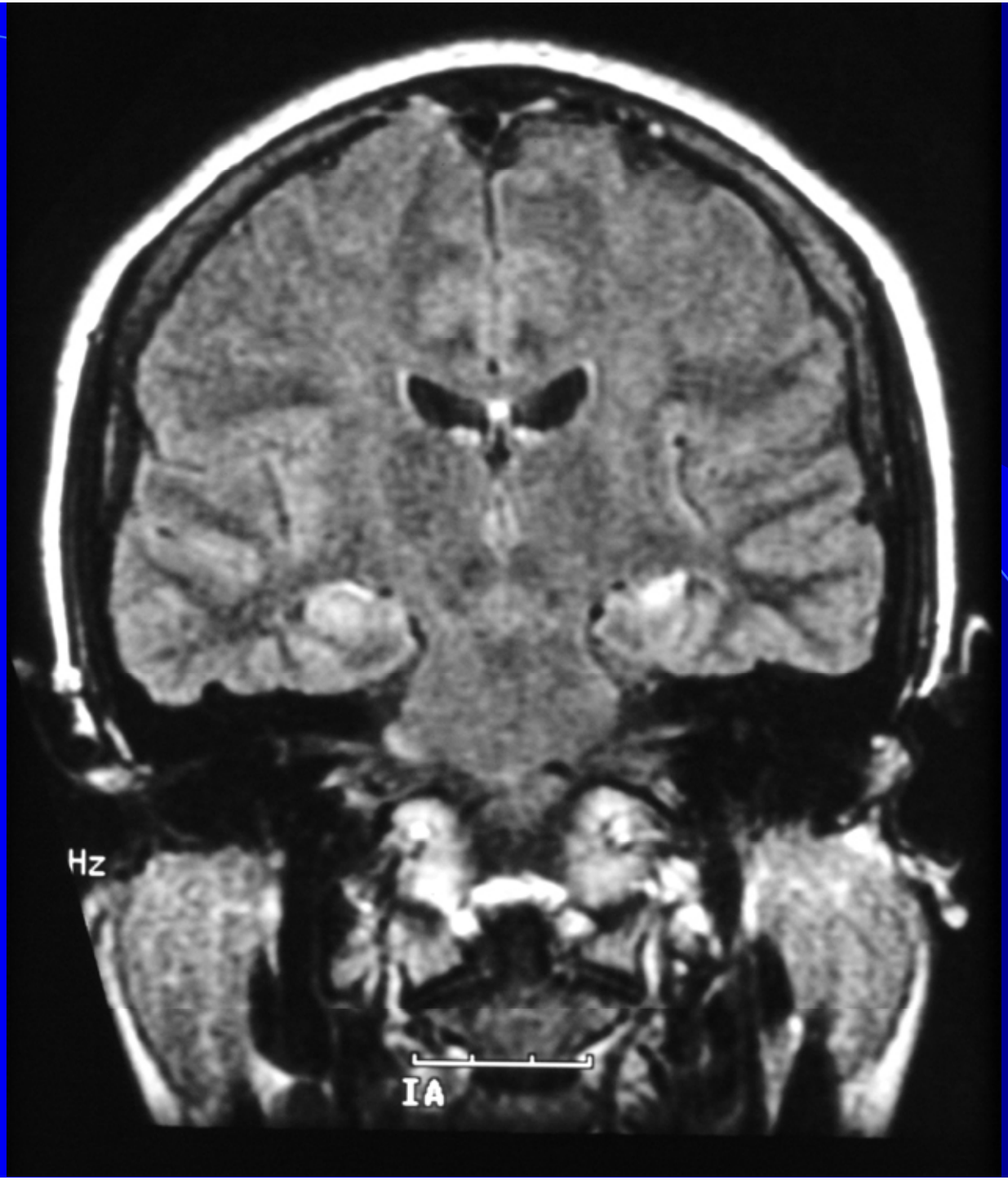
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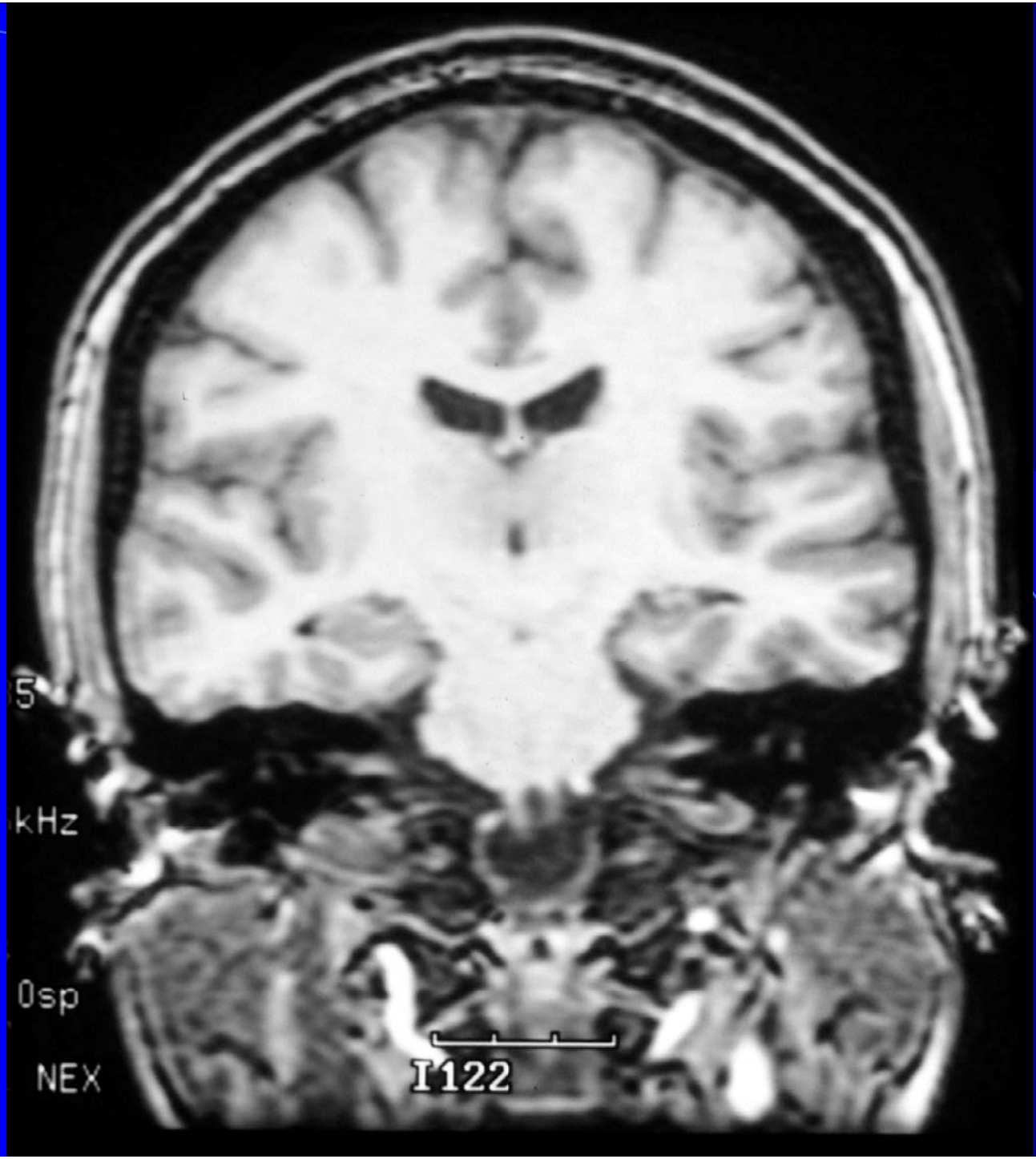
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Correlation with Surgical Outcome after ATL

- Presence of a structural lesion or hippocampal atrophy on MRI
  - Seizure-free or nearly seizure-free outcome in 62-87% of cases
- Normal MRI scan
  - Seizure-free or nearly seizure-free outcome in only 21-56% of cases

MRI Scanning: Quantitative Imaging

- Volumetric MRI has proven useful in preoperative evaluation of patients with TLE due to unilateral hippocampal sclerosis (HS)
- Significantly reduced hippocampal, and sometimes amygdaloid, volumes correlate with neurophysiologic, neuropathologic, and neuropsychologic studies, as well as outcome after temporal lobectomy

Jack et al, 1990
Cascino et al, 1991
Ashtari et al, 1991
Watson et al, 1991
Jack et al, 1992
Lencz et al, 1992
Cendes et al, 1992
Cendes et al, 1993

Quantitative Volumetric MRI: Technique

- High resolution, thin coronal sections
  - 1.5 mm, contiguous sections
  - Angled sections, perpendicular to the plane of the lateral sulcus
  - T1-weighted, inversion recovery, or gradient echo sequences
- Transfer images to computer work station
- Manually outline the hippocampus and amygdala
- Computer calculates the volumes of the HF and AM
- Compare volumes and ratios (smaller/larger) to controls

Watson et al, 1992

Quantitative Volumetric MRI: Interpretation

- Hippocampal or amygdaloid sclerosis is diagnosed if the volumes are 2 SDs smaller than the control population or the ratios are less than 0.90
- 87% accurate if HF volumes alone are used
- 93% accurate if HF and AM volumes are used
- Probably useful in patients with bilateral, independent, temporal seizure onsets

Watson et al, 1992
Cendes et al, 1993

"Normalization" of Volumetric MRI Measurements

- Obtain the **mean** **"Total Intracranial Volume (TIV)" of the normal control group**
- **"Normalize" the volume of each of the structures measured (e.g., HF or AM) for individual variation in head size, using the formula:**
  - "Normalized" HF Volume = R x HF Volume
  - Where, $R = \frac{\text{mean TIV of the controls}}{\text{patient's TIV}}$

Volumetric MRI in Temporal Lobe Epilepsy (TLE): EEG

- 30 patients with intractable TLE
  - 18 with left-sided TLE
  - 12 with right-sided TLE
- Lateralization was determined by interictal and ictal EEG evaluation (6 patients with depth electrodes)
- Volumetric MRI lateralization, when present, agreed with EEG lateralization

Cendes et al, 1992
Cendes et al, 1993

Temporal Lobe Epilepsy: Results

- Our results corroborate those of others: Volumetric studies of the hippocampus help lateralize the epileptogenic region
- Hippocampal volumes were more helpful than amygdaloid volumes (87% vs 67%)
- Hippocampal volumes plus amygdaloid volumes were even more helpful (93%)

Cendes et al, 1992
Cendes et al, 1993

Correlation with Pathology

- Strong relationship exists between the degree of hippocampal volume loss and the severity of hippocampal sclerosis
- These findings have been consistent in qualitative, semiquantitative, and quantitative neuropathological studies
- Thus, the severity of HS can be predicted preoperatively with volumetric MRI

Cascino et al, 1991

Watson et al, 1996

Lencz et al, 1992

Correlation with Outcome after ATL

- Significant relationship exists between hippocampal volumes and outcome after ATL
- EEG lateralization is same as hippocampal atrophy
  - 97% of patients had good outcome
- Hippocampal volumes are not lateralizing
  - 42% of patients had good outcome
- Hippocampal volumes are abnormal on side opposite side of surgery
  - 33% of patients had good outcome

Jack et al, 1992

Specificity of Volumetric MRI Findings I

- Some authors suggest that atrophy of medial temporal lobe structures is common in CPS, and
  - Atrophy is also present in other seizure types
  - Atrophy can even occur in patients without epilepsy
- Do seizures originating at extrahippocampal sites cause cell loss, gliosis, and atrophy of medial temporal structures?

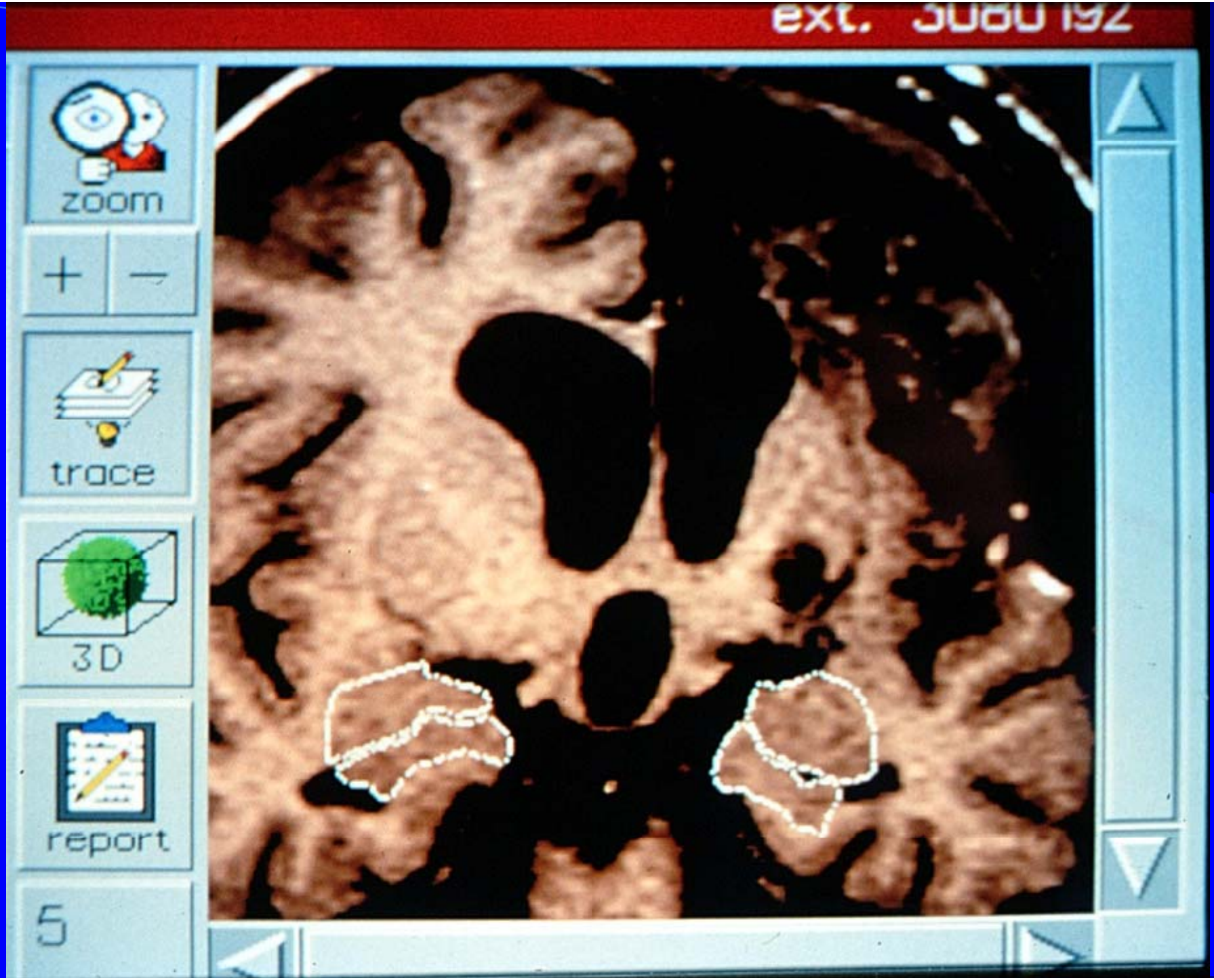
Diaz-Arrastia et al, 1992
Adam et al, 1994

Specificity of Volumetric MRI Findings II

- Extratemporal lesional epilepsy (Cook et al, 1992; Cascino et al, 1993; Cendes et al, 1993; Watson, 1993; Watson et al, 1994; Cendes et al, 1995)
- Extrahippocampal lesional temporal lobe epilepsy (Cendes et al, 1993; Watson et al, 1994; Cendes et al, 1995)
- Primary generalized epilepsy (Watson et al, 1994; Watson et al, 1995)
- Secondary generalized epilepsy (Watson et al, 1995; Watson et al, 1996)

Specificity of Volumetric MRI Findings III: Patient Groups

- 114 patients with chronic epilepsy were studied using MRI-based volumetric measurements of the hippocampus and amygdala
  - Extratemporal lesional epilepsy — 30 patients
  - Extrahippocampal lesional temporal lobe epilepsy (TLE) — 15 patients
  - Primary generalized epilepsy — 30 patients
  - Secondary generalized epilepsy — 22 patients
  - TLE due to hippocampal sclerosis — 17 patients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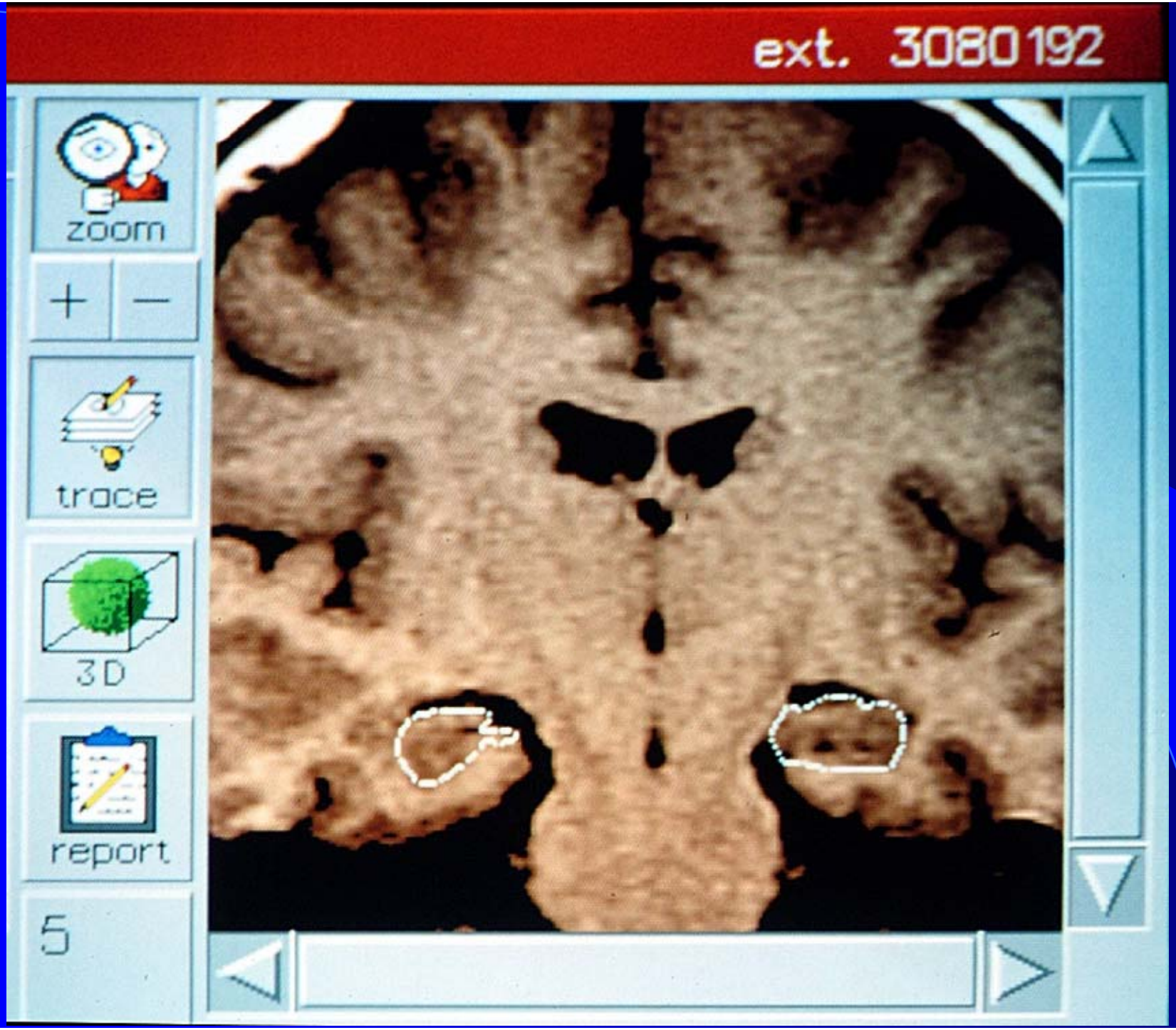
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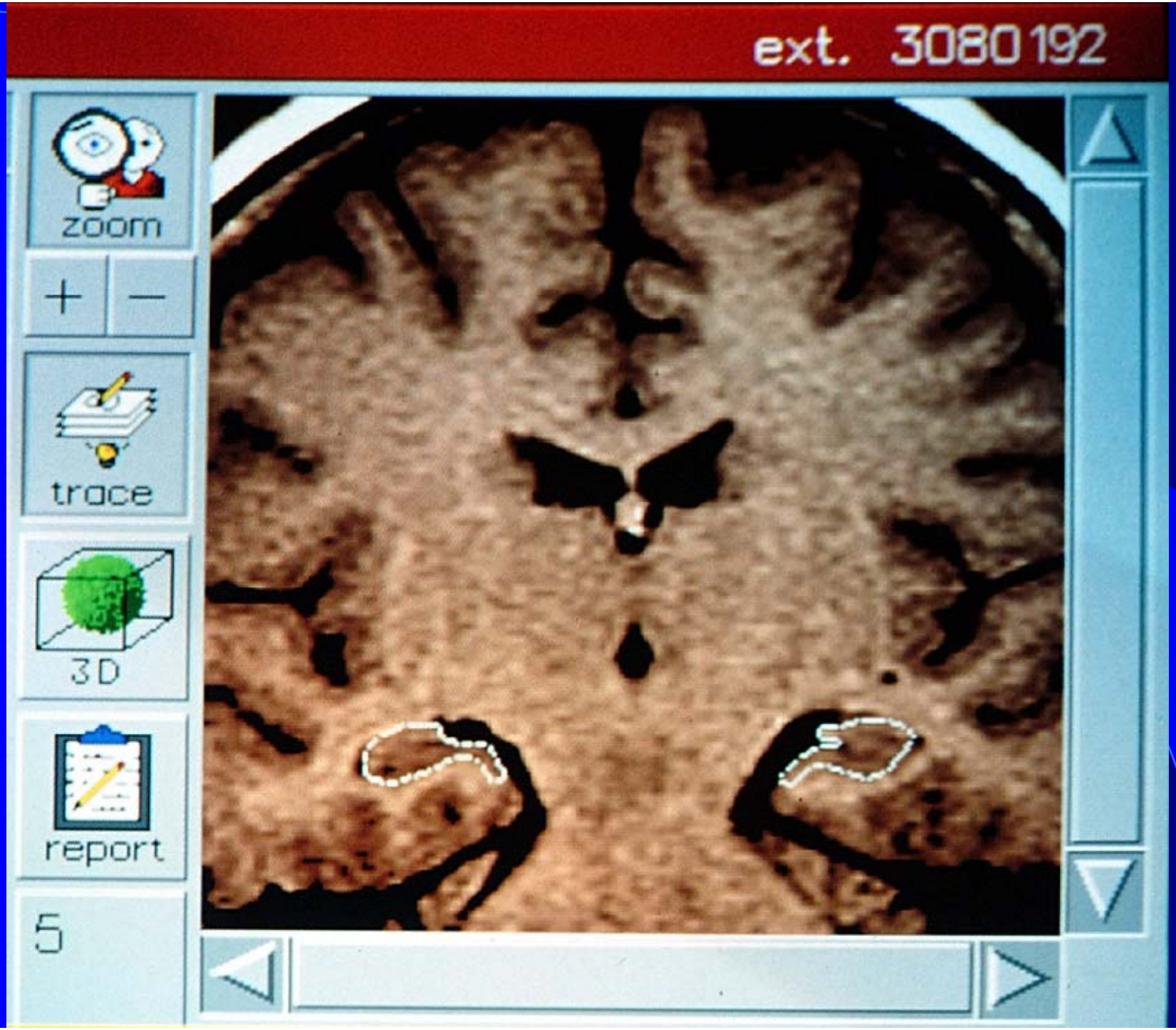
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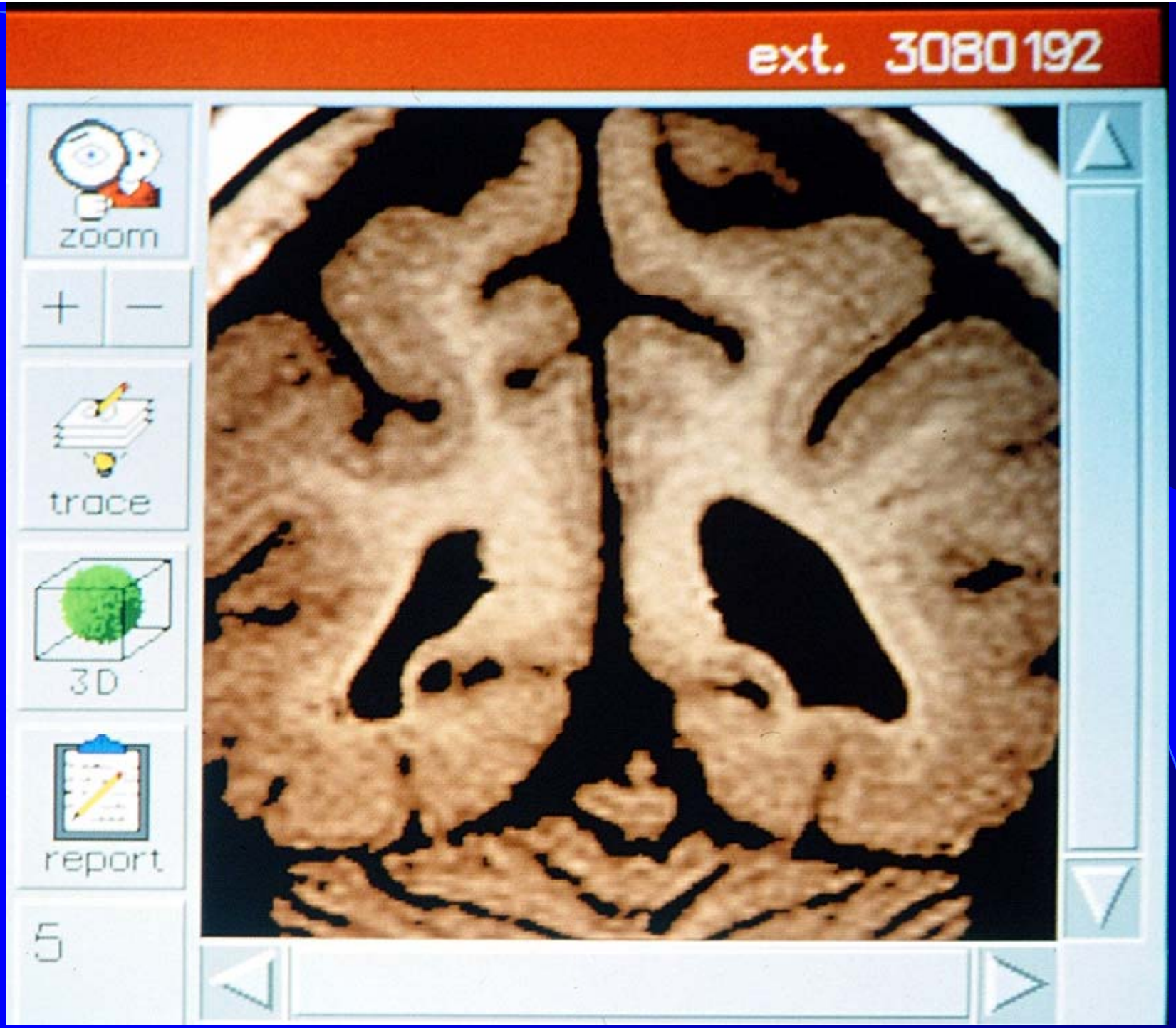
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HIPPOCAMPAL SCLEROSIS (HS):
Pathologic Grading Schema

GRADE	DESCRIPTION
0	Normal
I	Gliosis with slight (<10%) or no neuronal cell loss in CA1, CA3, and/or CA4.
II	Gliosis with 10-50% neuronal cell loss in CA1 and CA3/CA4.
III	Gliosis with >50% neuronal cell loss in CA1 and 10-50% cell loss in CA3/CA4. Sparing of CA2.
IV	Gliosis with >50% neuronal cell loss in CA1 and CA3/CA4. Sparing of CA2.
V	Gliosis with >50% neuronal cell loss in CA1-CA4. DG, Subiculum, PHG may be involved.

Hippocampal Sclerosis (HS): MRI Findings

- All 17 patients had decreased hippocampal volumes of > 2 SDs below the mean values of the control group
- All 17 patients had hippocampal ratios (smaller/larger) of < 0.90
  - Mild hippocampal atrophy (0.85-0.89) - 2 patients
  - Moderate-marked hippocampal atrophy (0.60-0.80) - 12 patients
  - Severe hippocampal atrophy (< 0.60) - 3 patients
- 7 patients (41%) had amygdaloid ratios of < 0.90

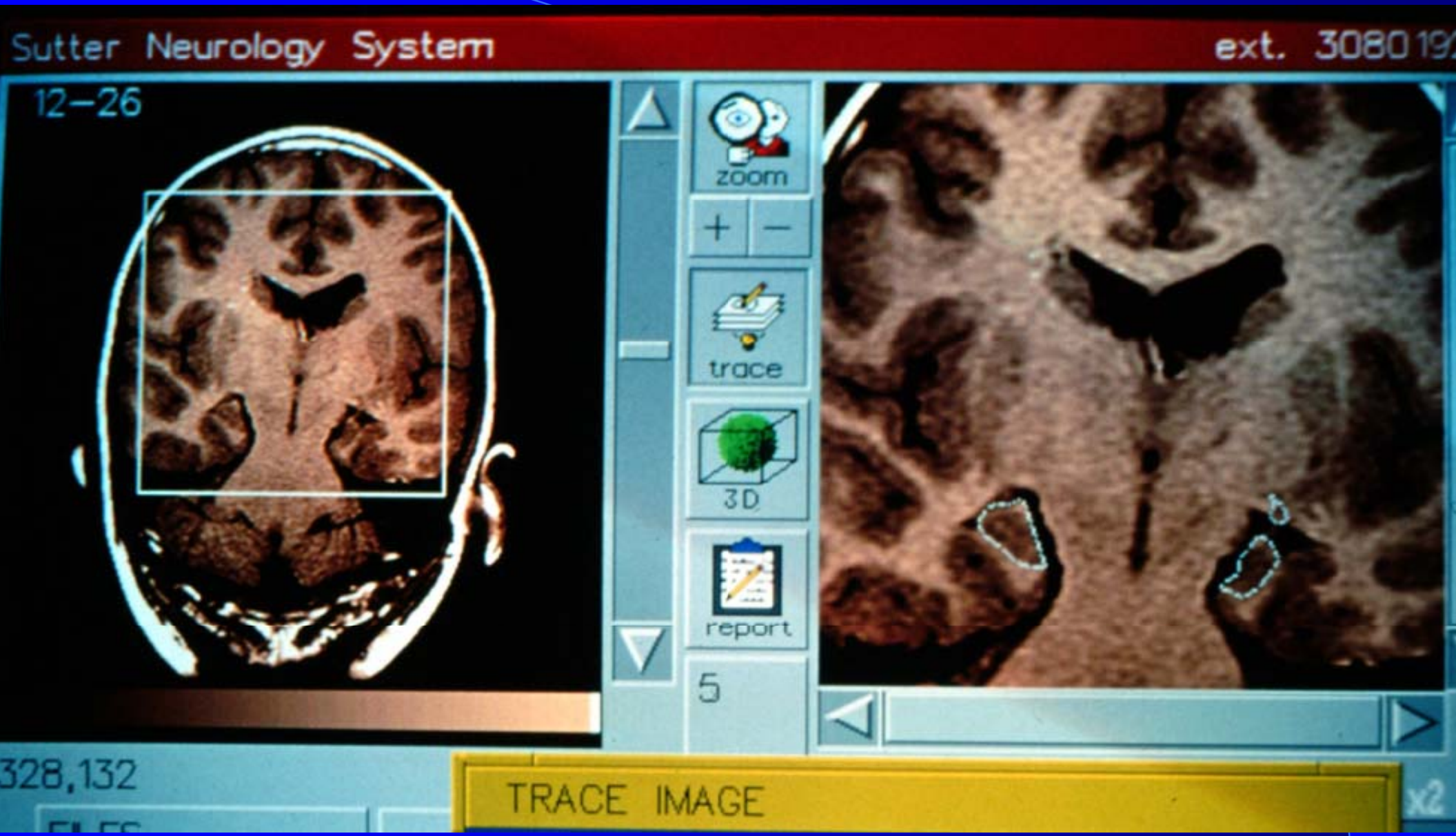
Watson et al, 1995, 1996

Hippocampal Sclerosis (HS): Pathology - MRI Correlation

- All 17 patients with hippocampal ratios of < 0.90 had pathologically proven HS
  - Minimal-mild HS (I, II) - 2 patients
  - Moderate-marked HS (III, IV) - 12 patients
  - Severe HS (V) - 3 patients
- Degree of hippocampal atrophy on MRI correlated well with the severity of HS on pathological evaluation

Watson et al, 1995

Watson et al, 1996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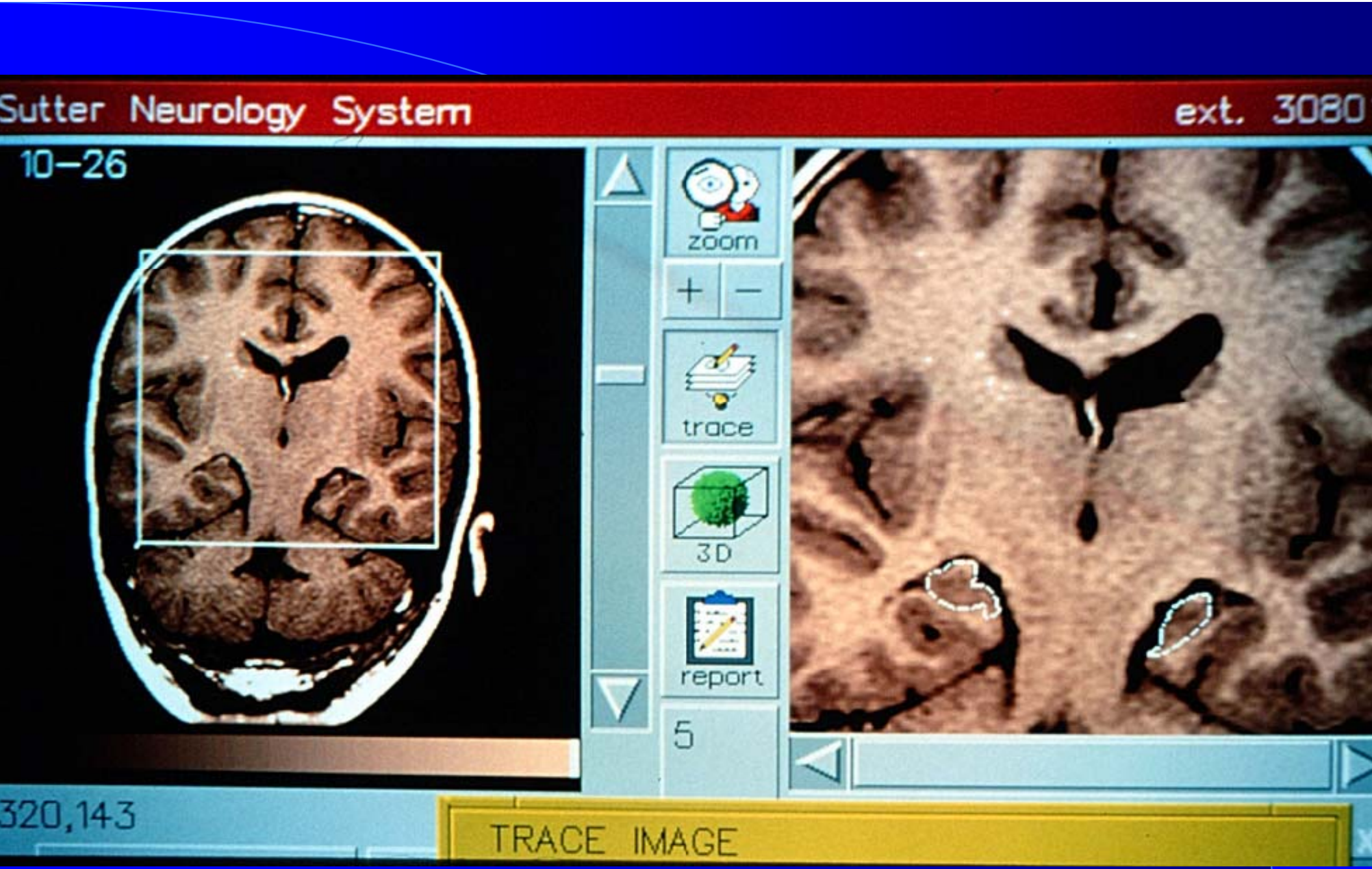
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Conclusions I

- Patients with epilepsy due to extrahippocampal temporal lobe lesions, extratemporal lesions, primary generalized epilepsy, and secondary generalized epilepsy do not have reductions in hippocampal and amygdaloid volumes
- Patients with TLE due to HS do have significant reductions in hippocampal, and sometimes amygdaloid, volumes

Conclusions II

- Seizures originating at extrahippocampal sites do not cause cell loss, gliosis, and atrophy of medial temporal structures
- Reduction of hippocampal and amygdaloid volumes is a specific marker for hippocampal and amygdaloid sclerosis

Watson et al, 1995

Watson et al, 1996

MRI of the Hippocampus: Qualitative vs Quantitative

- Studies have shown quantitative volumetric MRI to be more sensitive than visual inspection alone
- Degree of increased sensitivity has varied in different studies
  - 76% vs 71% -- Jack et al, 1990
  - 92% vs 56% -- Cendes et al, 1993
  - Volumetric=20% more sensitive -- Reutens et al, 1993
- However, volumetric MRI is more time consuming and must be done correctly to be reliable and accurate

Extratemporal Lesional Epilepsy: Patient Characteristics

- 30 patients with epilepsy and extratemporal lesions
  - 17 females with mean age of 36 years (range, 16-62)
  - 13 males with mean age of 40 years (range, 14-71)
- Seizure types
  - SPS - 22 patients
  - CPS - 12 patients
  - GTCS - 15 patients
  - Atonic - 2 patients
- Age of seizure onset - 3 months to 70 years
- Duration of seizures - 1 day to 43 years

Watson et al, 1993 & 1994

Extratemporal Lesional Epilepsy: MRI Findings

- MRI lesion location
  - Frontal lobe - 19 patients
  - Parietal lobe - 11 patients
  - Occipital lobe - 4 patients
  - Intraventricular - 1 patient
  - Multifocal - 1 patient
- Type of MRI lesion
  - Tumor - 8 patients
  - Developmental anomaly - 8 patients
  - Atrophic - 6 patients
  - Vascular malformation - 4 patients
  - Cystic, traumatic, gliotic, ischemic - 1 each

Extratemporal Lesional Epilepsy: Results

- Total hippocampal and amygdaloid volumes were in normal range for all 30 patients
- Hippocampal and amygdaloid ratios were symmetric
- Mean values for patient groups were comparable to those of control groups

Watson, 1993
Watson et al, 1994

Extratemporal Lesional Epilepsy: Summary

- Patients with epilepsy and extratemporal lesions do not have reduction in hippocampal and amygdaloid volumes
- Reduction of hippocampal and amygdaloid volumes is a specific marker for hippocampal and amygdaloid sclerosis

Watson, 1993
Watson et al, 1994

Extrahippocampal Temporal Lobe Lesions: Patient Characteristics

- 15 patients with epilepsy and extrahippocampal temporal lobe lesions
  - 9 females with mean age of 50 years (range, 28-70)
  - 6 males with mean age of 45 years (range, 17-73)
- Seizure types
  - SPS - 11 patients
  - CPS - 10 patients
  - GTCS - 10 patients
- Age of seizure onset - 10 to 64 years
- Duration of seizures - 6 months to 43 years

Watson et al, 1994

Extrahippocampal Temporal Lobe Lesions: MRI Findings

- MRI lesion location
  - Medial - 7 patients
  - Posterior - 4 patients
  - Lateral - 4 patients
  - Inferior - 2 patients
  - Anterior - 1 patient
- Type of MRI lesion
  - Tumor - 6 patients
  - Cysts - 4 patients
  - Vascular malformations - 3 patients
  - Developmental anomaly - 2 patients
  - Traumatic and infectious - 1 each

Extrahippocampal Temporal Lobe Lesions: Results

- Total hippocampal and amygdaloid volumes and ratios were in normal range for all 15 patients except for one patient
  - This patient was studied with intracranial electrodes
  - All of her seizures began in her atrophic hippocampus, which was subsequently found to exhibit marked hippocampal sclerosis
  - None of her seizures began in her post-traumatic atrophic lesion
- Mean values for patient groups were comparable to those of control groups

Watson et al, 1994

Extrahippocampal Temporal Lobe Lesions: Summary

- Patients with epilepsy and extrahippocampal temporal lobe lesions do not have reduction in hippocampal and amygdaloid volumes
- Reduction of hippocampal and amygdaloid volumes is a specific marker for hippocampal and amygdaloid sclerosis

Watson, 1993
Watson et al, 1994

Extrahippocampal Lesional Epilepsy:
Patient Characteristics

- 167 patients with epilepsy and extrahippocampal structural lesions
  - 80 males
  - 87 females
  - Mean age of 33 years (range, 10-67)
- Mean age of seizure onset - 16 years (SD=12)
- Mean duration of seizures - 15 years (SD=12)
- Febrile seizures during childhood
  - Patients with hippocampal atrophy (N=25) - 5 (20%) ($p<0.01$)
  - Patients without hippocampal atrophy (N=142) - 4 (3%)

Cendes et al, 1995

Extrahippocampal Lesional Epilepsy:
MRI Findings

- Neuronal migration disorders (NMD) - 48 patients
  - Heterotopia (nodular or band) - 35 patients
  - Pachygyria and/or polymicrogyria - 13 patients
- Tumors - 53 patients
  - Low grade gliomas - 29 patients
  - DNT - 11 patients
  - Meningiomas - 10 patients
  - Epidermoid cysts - 3 patients
- Vascular malformations - 34 patients
- Porencephalic cysts - 15 patients
- Reactive gliosis - 17 patients

Cendes et al, 1995

Extrahippocampal Lesional Epilepsy: Results I

- Total hippocampal volumes and ratios were in the normal range in 142 patients (85%)
- 25 patients (15%) had unilateral hippocampal atrophy ***plus*** a structural lesion ("dual pathology")
  - NMD - 12 patients (25%) with dual pathology
  - Tumors - 2 patients (4%) with dual pathology
  - Vascular malformations - 3 patients (9%) with dual pathology
  - Porencephalic cysts - 4 patients (27%) with dual pathology
  - Gliosis - 4 patients (23%) with dual pathology

Cendes et al, 1995

Extrahippocampal Lesional Epilepsy:
Results II

- Dual pathology was present both in patients whose lesions involved the temporal lobe (17%) and extratemporal areas (14%)
- Age of seizure onset and duration of epilepsy did not influence the presence of dual pathology
- Febrile seizures in childhood were found more frequently in patients with hippocampal atrophy ($p<0.01$)

Cendes et al, 1995

Extrahippocampal Lesional Epilepsy:
Summary

- Patients with epilepsy and extrahippocampal lesions have a low incidence (15%) of hippocampal atrophy (“dual pathology”)
- Dual pathology is more common in patients with NMD, porencephaly, and gliosis, and it is independent of the distance of the lesion from the hippocampus in these entities
- Tumors and AVMs cause dual pathology only when the lesion is close to the hippocampus
- A common pathogenic mechanism during pre or perinatal development is more likely to cause concomitant hippocampal sclerosis and extrahippocampal lesions (dual pathology) than is secondary epileptogenesis

Cendes et al, 1995

Primary Generalized Epilepsy: Patient Characteristics

- 30 patients with primary generalized epilepsies
  - 17 females with mean age of 27 years (range, 10-62)
  - 13 males with mean age of 26 years (range, 11-41)
- Age of seizure onset - 6 months to 46 years
- Duration of seizures - 1 to 26 years
- Family history of seizures - 14 patients (67%)
- No patients had febrile seizures during childhood

Watson et al, 1994
Watson et al, 1995

Primary Generalized Epilepsy: Epilepsy Types

- Juvenile myoclonic epilepsy (JME) - 9 patients
- Primary generalized tonic-clonic seizures - 4 patients
- Childhood absence epilepsy (CAE) - 3 patients
- Juvenile absence epilepsy (JAE) - 2 patients
- Unclassified primary generalized epilepsy - 2 patients
- Photosensitive epilepsy - 1 patient

Watson et al, 1994
Watson et al, 1995

Primary Generalized Epilepsy: Seizure Types

- GTCS - 14 patients
- Absence - 9 patients
- Myoclonic - 7 patients
- Atypical absence - 6 patients
- Atonic - 2 patients

Watson et al, 1994
Watson et al, 1995

Primary Generalized Epilepsy: EEG Findings

- Bursts of generalized spike and wave and/or polyspike and wave activity (2-6 Hz)
  - Interictal - 19 patients
  - Ictal - 8 patients

Watson et al, 1994
Watson et al, 1995

Primary Generalized Epilepsy: Results

- Total hippocampal and amygdaloid volumes were in normal range for all 21 patients
- Hippocampal and amygdaloid ratios were symmetric
- Mean values for patient groups were comparable to those of control groups

Watson et al, 1994
Watson et al, 1995

Primary Generalized Epilepsy: Summary

- Patients with primary generalized epilepsy do not have reduction in hippocampal and amygdaloid volumes
- Reduction of hippocampal and amygdaloid volumes is a specific marker for hippocampal and amygdaloid sclerosis

Watson et al, 1994
Watson et al, 1995

Secondary Generalized Epilepsy: Patient Characteristics

- 22 patients with secondary generalized epilepsy
  - 13 females with mean age of 25 years (range, 8-55)
  - 9 males with mean age of 28 years (range, 16-36)
- Age of seizure onset - 3 months to 12 years
- Duration of seizures - 5 to 43 years
- Family history of seizures - 3 patients (14%)
- Mental retardation - 17 patients (77%)

Watson et al, 1995
Watson et al, 1996

Secondary Generalized Epilepsy: Seizure Types

- GTCS or GTS - 21 patients
- CPS - 14 patients
- Atonic - 12 patients
- Absence - 5 patients
- Myoclonic - 2 patients
- SPS - 1 patient

Watson et al, 1995
Watson et al, 1996

Secondary Generalized Epilepsy: EEG Findings

- Bilateral, generalized and/or multifocal, spike and wave and/or polyspike and wave activity
  - Interictal - 22 patients
  - Ictal - 15 patients

Watson et al, 1995
Watson et al, 1996

Secondary Generalized Epilepsy: MRI Findings

- Diffuse cortical atrophy - 8 patients
- BPPS - 3 patients
- UPPS - 2 patients
- Heterotopias - 2 patients
- Double cortex, pachygyria, tuberous sclerosis - 1 each
- Normal - 6 patients

Watson et al, 1995
Watson et al, 1996

Secondary Generalized Epilepsy: Results

- Total hippocampal and amygdaloid volumes were in normal range for all 22 patients
- Hippocampal and amygdaloid ratios were symmetric
- Mean values for patient groups were comparable to those of control groups

Watson et al, 1995
Watson et al, 1996

Secondary Generalized Epilepsy: Summary

- Patients with secondary generalized epilepsy do not have reduction in hippocampal and amygdaloid volumes
- Reduction of hippocampal and amygdaloid volumes is a specific marker for hippocampal and amygdaloid sclerosis

Watson et al, 1995
Watson et al, 1996

Hippocampal Sclerosis (HS): Patient Characteristics

- 17 patients with pathologically proven hippocampal sclerosis - mean age of 33 years (range, 6 to 52)
  - 8 with left-sided HS
  - 9 with right-sided HS
- Mean age of seizure onset - 12 years (range, 0.5 to 23)
- Mean duration of seizures - 22 years (range, 2 to 38)
- 10 patients (59%) had febrile seizures during childhood
- 4 patients had other early risk factors (trauma, meningitis)

Watson et al, 1995, 1996

Hippocampal Sclerosis (HS): Seizure Types

- SPS - 17 patients
- CPS - 17 patients
- GTCS - 12 patients

Watson et al, 1995

Watson et al, 1996

Hippocampal Sclerosis (HS): Pathology

- Hippocampal Sclerosis - 17 patients
  - Grade I - 1 patient
  - Grade II - 1 patient
  - Grade III - 4 patients
  - Grade IV - 8 patients
  - Grade V - 3 patients
- Dual Pathology - 4 patients
  - Heterotopia + HS - 2 patients
  - Cortical dysplasia + HS - 2 patients
  - Hemispheric atrophy + HS - 1 patient

Watson et al, 1995, 1996

Hippocampal Sclerosis (HS): Summary

- Patients with TLE due to HS have significantly reduced (> 2 SDs) hippocampal volumes
- Patients with TLE due to HS have hippocampal ratios (smaller/larger) of < 0.90
- Reduction of hippocampal volume is a specific marker of hippocampal sclerosis

Watson et al, 1995

Watson et al, 1996

"Normalization" of Volumetric MRI Measurements

- Obtain the **mean** **"Total Intracranial Volume (TIV)" of the normal control group**
- **"Normalize" the volume of each of the structures measured (e.g., HF or AM) for individual variation in head size, using the formula:**
  - "Normalized" HF Volume = R x HF Volume
  - Where, $R = \frac{\text{mean TIV of the controls}}{\text{patient's TIV}}$