


**FERNE / MEMC IV Brain Illness and Injury Course:  
Acute Ischemic Stroke  
E. Bradshaw Bunney, MD, FACEP**

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**Acute  
Ischemic Stroke  
Update**

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**FERNE**  
Foundation for Education and Research  
in Neurological Emergencies

**FERNE Brain Illness  
and Injury Course**

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The Fourth  
Mediterranean Brain and Acute Care Course (MEMC IV)  
Sorrento, Italy  
15-19 September 2007



**4<sup>th</sup> Mediterranean  
Emergency Medicine  
Congress  
Sorrento, Italy  
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E. Bradshaw Bunney, MD 

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**E. Bradshaw Bunney  
Associate Professor**

Department of Emergency Medicine  
University of Illinois College of Medicine  
Chicago, IL


E. Bradshaw Bunney, MD 

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**Attending Physician  
Emergency Medicine**

**University of Illinois Hospital  
Our Lady of the Resurrection Hospital**

**Chicago, IL**

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**Board Member**

**FERNE**

**Chicago, IL**

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## Disclosures

- Genentech, AstraZeneca advisory group
- ACEP Scientific Review Committee
- Executive Board, FERNE
- FERNE support by Abbott, Eisai, Pfizer, UCB

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The logo for the Foundation for Education and Research in Neurological Emergencies (FERNE), featuring the acronym in purple and green letters with decorative flourishes.

www.ferne.org

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The logo for the Foundation for Education and Research in Neurological Emergencies (FERNE), featuring the acronym in purple and green letters with decorative flourishes.

## Key Clinical Questions

- What is primary stroke center designation?
- What stroke surveillance systems currently exist?
- How are patients not at stroke centers treated?
- How are telemedicine systems utilized in these stroke systems?

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## Key Clinical Questions

- What therapies exist in 2007 for the treatment of ischemic stroke after 3 hours?
- What new therapies are on the horizon and how will they impact the EM management of stroke?
- What is new in the 2007 ASA Guidelines?

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## Case

- 19 yo female collapsed a work on Super Bowl Sunday 2006
- EMS found her not moving her right side, aphasic, eyes deviated to the left
- Onset time 20 minutes prior to EMS arrival
- BP 120/62, HR 84, RR 14

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## Case


- In ED – Friend confirms onset time
- Friend states no PMHx, no drug or alcohol use
- PE - R arm 0/5 strength, R leg 3/5, aphasic, eyes deviated to L
- No family available

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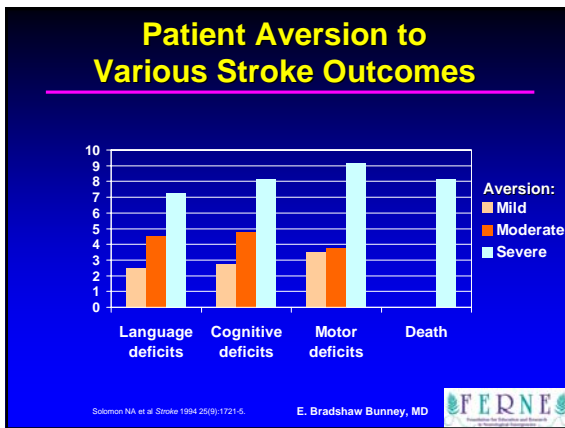
## Case

- Glucose = 97
- Not pregnant
- CBC, electrolytes, coagulation all normal
- CT head = normal
- Differential Diagnosis:
  - Stroke
  - Multiple Sclerosis
  - Hysteria
  - Conversion Reaction
  - Intoxicant

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## Stroke in Perspective

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### Primary Stroke Centers

- Patient care areas
  - Acute stroke teams
  - Written care protocols
  - Emergency medical services
  - Emergency department
  - Stroke unit
  - Neurosurgical services
- Support services
  - Stroke center director
  - Neuroimaging services
  - Laboratory services
  - Outcome and quality improvement activities
  - Continuing medical education

Alberts MJ, et al. JAMA. 2000;283:3102-3109. E. Bradshaw Bunney, MD 


### Primary Stroke Centers

- Approximately 5,000 hospitals in the US
- As of June 2007 there are 352 certified Stroke Centers
- 94 more in the pipeline
- 40 states
- State certification in several states

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### Stroke Registries

- Senator Paul Coverdell from Georgia
- Died July 2000
- CDC awarding grants to states to establish registries
- National link

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### **Coverdell Stroke Registry**

- 6867 stroke admissions at 98 hospitals
- 4 states (MI, GA, OH, MA)
- Less than 2/3 had documented onset times.
- Less than 50% had:
  - dysphagia screening (45%)
  - lipid testing (34%)
  - smoking cessation counseling (21%)
- 3% received tPA in MI, GA, OH, while 8% received tPA in MA.
- Conclusion: only a minority of acute stroke patients are treated according to established guidelines.
- Protocols will be redesigned to improve compliance with the established guidelines which may reveal outcomes benefit.

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### **Stroke Networks**

- Consultation agreements
- Rotating call between institutions
- Consolidating resources among a network of hospitals
- Uniform protocol usage
- Maximize therapy usage

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### **Rural Nevada**

- One designated stroke center
- 25 rural EDs
- One protocol agreed to by all hospitals
- Central stroke team
- Site visits to confirm protocol adherence and promote team approach
- Help to raise the treatment of stroke patients to a common norm

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### **Telemedicine Systems**

- Two-way videoconferencing to connect a treating physician with a remote consultant
- Management option for the treatment of acute stroke patients in hospitals without the resources to provide acute stroke care.

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### **Telemedicine Systems**

- Telemedicine consultation on 24 acute stroke patients
- 6 (25%) received tPA
  - door to needle time of 106 (+/- 22) minutes
  - consult to needle time of 36 (+/- 15) minutes.
- No protocol violations
- May increase the number of stroke patients receiving therapy
- May assist in delineating a group of patients that can receive optimal treatment at the originating hospital thus improving the utilization of scarce resources.

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### **Ischemic Stroke Treatment**

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### Treatment: Thrombolysis

- NINDS 1995, 3 hour window
- 30 day: absolute benefit toward favorable outcome 14% (relative 30%) (OR 1.7)
- Symptomatic ICH 6.4% vs 0.6%
- Mortality the same

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### Treatment: Thrombolysis

- 14% absolute increase for the best clinical outcomes as measured by an NIHSS of 0-1.
- **Benefit** = Need to treat **8** patients with t-PA in order to have **1** additional patient with this best outcome.
- 6% absolute increase in the number of symptomatic ICH.
- **Harm** = Will have one symptomatic ICH for every **16** patients treated with t-PA.
- 2 patients will have a minimal or no deficit for everyone patient with a symptomatic ICH

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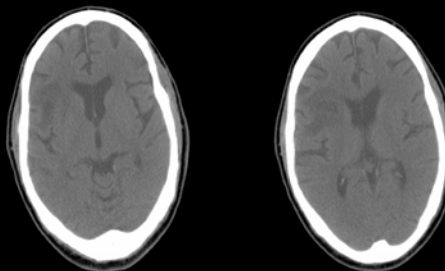


### CT Imaging

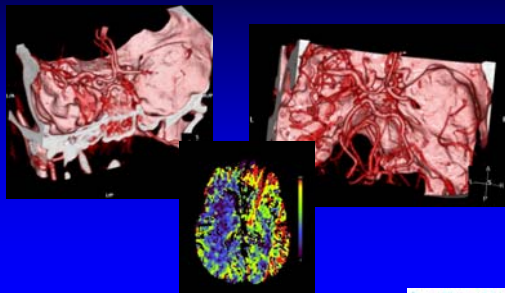
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### CT Head



### CT Angio & Perfusion

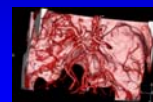
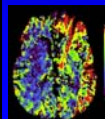
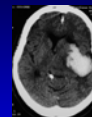


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### CTA and CTP

- Essential questions
  - Is there hemorrhage?
  - Is there large vessel occlusion?
  - Is there "irreversibly" infarcted core?
  - Is there "at risk" penumbra?
- One contrast bolus yields two datasets
  - Vessel patency
  - Infarct versus salvageable penumbra



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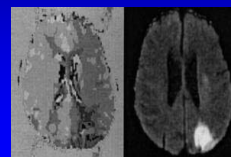
## MR Imaging

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## DWI/PWI Mismatch

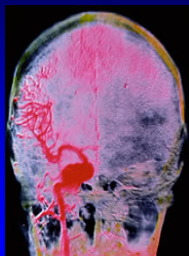
- Subtract DWI hyperintense signal area from the PWI hypoperfused area = DWI/PWI mismatch
- Hypoperfused area that is still viable (penumbra)
- Target area for reperfusion



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## New Therapies



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## Intra-Arterial Thrombolysis

- Two randomized trials – PROACT 1 & 2
- Tested prourokinase vs. heparin <6 hours
- MCA occlusions only
- Recanalization improved with IA
- Mortality identical
- Relative risk reduction for outcome – 60%
- Risk of invasive procedure

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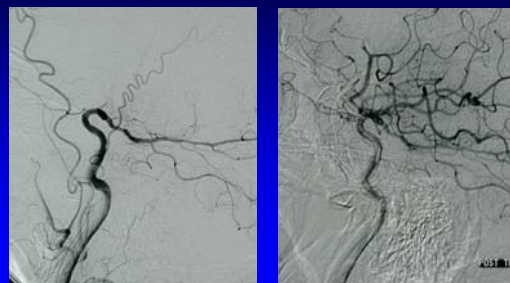
## IA in Clinical Practice

- Numerous clinical series published
- Basilar artery thrombosis series suggest benefit
- Benefit with basilar may be late (12-24 hrs)
- MRI diffusion/perfusion may aid selection

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## Pre- and Post IA t-PA



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## Mechanical Clot Removal

- Invasive neuroradiologist/neurosurgeon
- Window extended to 8 to 12 hours
- Intra-arterial thrombolysis may be given after clot removal

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## Multi MERCI Trial

- N = 164
- Baseline NIHSS = 19.3
- Revascularization = 68%
- Good Outcome (90-day mRS < 2) = 36%
- SICH = 9.8%
- Mortality at 90 days = 33%

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## Multi MERCI Trial

- Subgroup of 29% (48/164) that failed IV t-PA
- Revascularization = 73%
- mRS < 2 at 90 days = 38%
- SICH 10.4%

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## MERCI Clot Retriever



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## MERCI Clot Retriever



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## Desmoteplase

- DIAS, DEDAS studies
- More fibrin specific, longer half life
- MRI diffusion / perfusion mismatch >20%
- NIHSS 4-20
- 3-9 hours after onset

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## Desmoteplase

- N = 37
- No symptomatic ICH
- Reperfusion:
  - Placebo 37%
  - 125 ug/kg 53%
- Good clinical outcome (composite):
  - Placebo 25%
  - 125 ug/kg 60%

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## ASA Guidelines 2007

- New EMS Section
  - Educate the public
  - EMS use of scales
  - “Closest institution that can provide emergency stroke care”
- New Stroke Center Section
  - Creation of Primary Stroke Center strongly recommended
  - Develop Comprehensive Stroke Centers
  - Bypass hospitals that do not have the resources to treat stroke

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## ASA Guidelines 2007

- ED Evaluation Section (Not Changed)
  - Develop strict protocol
  - Use stroke scale
- Imaging Section
  - CT provides the information needed to treat
  - Dense artery sign assoc. with poor outcome
  - CTA and MR provide additional information
  - Insufficient data to say that other signs on CT should stop therapy
  - Do not delay treatment for other images

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## ASA Guidelines 2007

- Management Section
  - Management of HTN is controversial
  - No good data to guide selection of BP meds, NTG paste??
  - If treat must maintain BP at 180/105 for 24 h
  - Glucose >140 mg/dl: poor outcome seen
- TPA Section
  - Caution should be exercised in treating pts with major deficits, NIHSS > 20
  - Aware of side effect of angioedema
  - Seizure is not a contraindication

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## Case Outcome

- Small hospital, no neurologist interested in seeing the patient
- Called 2 Universities before finding one to accept the patient
- Family arrived, patient not improving

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## Case Outcome

- Stroke neurologist = “Give IV t-PA”
- t-PA given at 2 hours 15 minutes from onset
- R arm movement and aphasia improving prior to transfer

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## Case Outcome

- MRI at University = small infarct
- ECHO cardiogram = Patent foramen ovale, likely embolic stroke
- Outcome = normal except small vision loss.

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## Conclusions

- Stroke center certification provides a method of measuring quality improvement in stroke patient care
- Stroke networks allow a region to achieve a particular quality standard
- Outcomes measurement needs to be continued to establish the role of stroke systems as well as therapies

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## Conclusions

- IA thrombolysis and mechanical clot removal provide an alternative at institutions able to use it
- CTA and CT perfusion may become routine
- “Time is brain” may be replaced by “Physiology is brain”

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## Conclusions

- Accurate measurement of the penumbra may surpass the strict time nature of treatment
- New therapies based on the percent of penumbra remaining may allow for time to be relatively unimportant

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## Questions?

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bbunney@uic.edu  
312 413 7484

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