

Ischemic Stroke Time is Brain: *Or Is It?*

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Key Clinical Questions

- What is the best imaging study for diagnosing an evolving ischemic stroke?
- What therapies exist in 2007 for the treatment of ischemic stroke?
- What new therapies are on the horizon and how will they impact the EM management of stroke?

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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

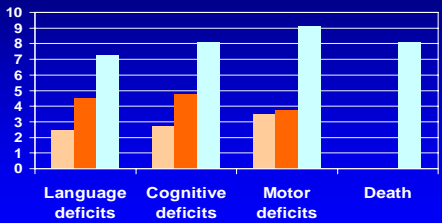
- Glucose = 97
- Not pregnant
- CBC, electrolytes, coagulation all normal
- CT head = normal
- Differential Diagnosis:
 - Stroke
 - Multiple Sclerosis
 - Hysteria
 - Conversion Reaction
 - Intoxicant

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Stroke in Perspective:

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Patient Aversion to Various Stroke Outcomes



Outcome	Mild	Moderate	Severe
Language deficits	2.5	4.5	7.5
Cognitive deficits	3.0	5.0	8.0
Motor deficits	3.5	4.5	9.0
Death	8.0	8.5	9.0


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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

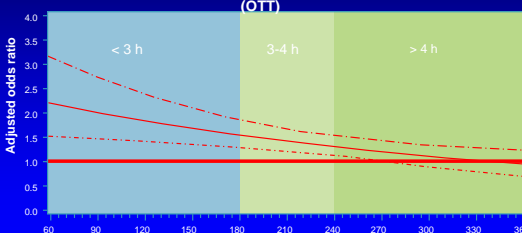
- 14% absolute increase for the best clinical outcomes as measured by an NIHSS of 0-1.
- **Benefit** = Need to treat **8** patients with t-PA in order to have one additional patient with this best outcome.
- 6% absolute increase in the number of symptomatic ICH.
- **Harm** = Will have one symptomatic 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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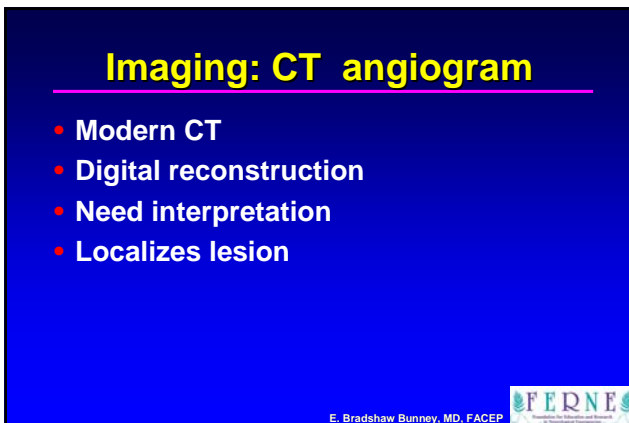
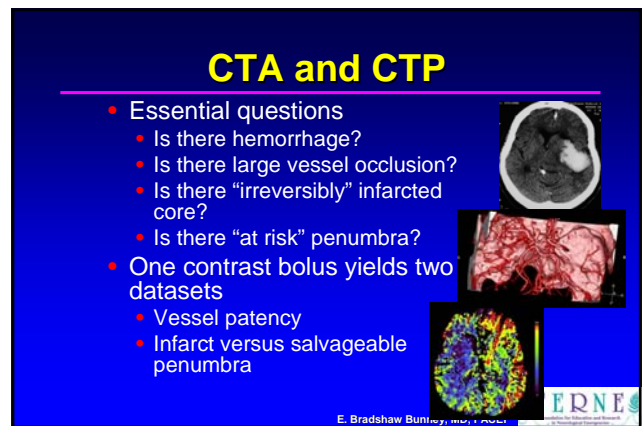
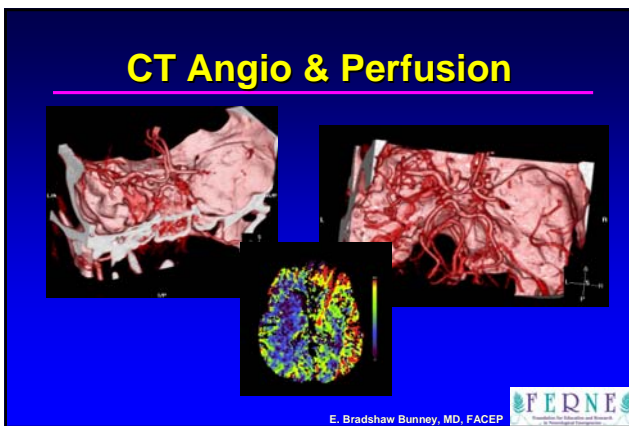
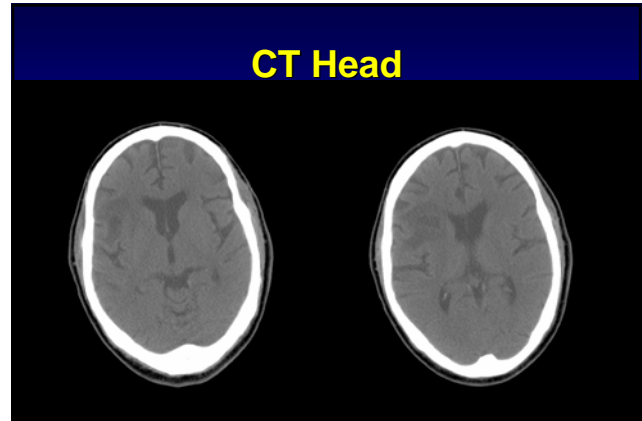
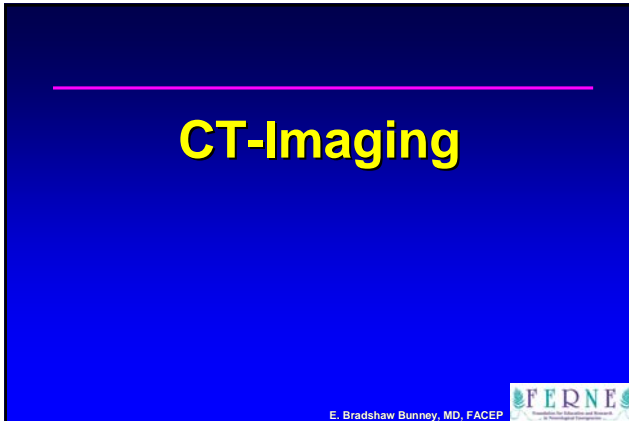
Time to Treatment and tPA Benefit

Brott et al. NINDS, ECASS I and II and ATLANTIS
 mRS 0-1 at day 90

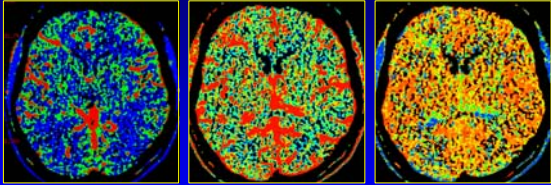
Adjusted odds ratio with 95 % confidence interval by stroke onset to treatment time (OTT)



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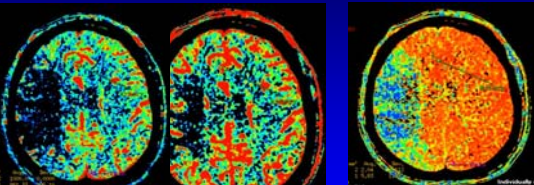
CT Perfusion Terminology



Blood Flow Blood Volume Mean Transit Time
 or
 Time to Peak

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Relationship between CBV, CBF, and MTT



Blood Flow Blood Volume Mean Transit Time
 or
 Time to Peak

$MTT = \text{Blood Volume} / \text{Blood Flow}$


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MR-Imaging

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Diffusion-Weighted Imaging

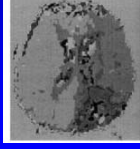
- Ischemia decreases the diffusion of water into the brain
- Extracellular water accumulates
- DWI detects this as hyperintense signal
- Delineates areas of irreversible damage
- Present within mins



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Perfusion-Weighted Imaging

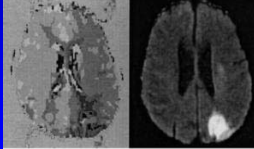
- Tracks a bolus of gadolinium through the brain
- PWI detects areas of hypoperfusion
 - infarct core
 - penumbra



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DWI/PWI Mismatch

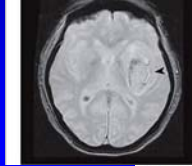
- Subtract DWI hyperintense signal area from the PWI hypoperfused area = DWI/PWI mismatch
 - Hypoperfused area that is still viable (penumbra)
 - Target area for reperfusion



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Gradient Recalled Echo (GRE) Pulse Sequence

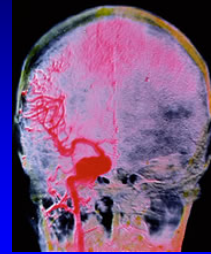
- Core of heterogeneous signal intensity reflecting recently extravasated blood with significant amounts of oxyhgb
- Rim of hypointensity reflecting blood that is fully deoxygenated



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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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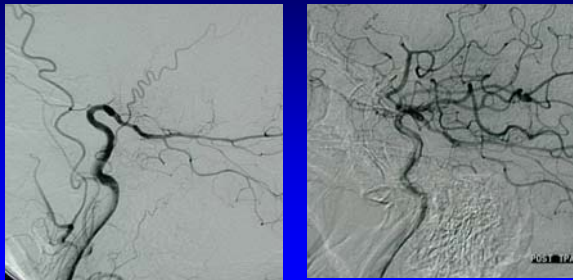
IA Clinical Practice

- 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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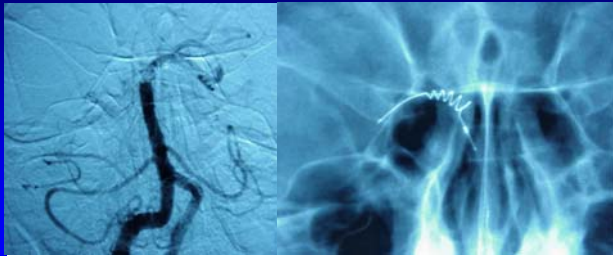
Multi MERCI Trial

- 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

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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 assoc. with poor outcome
- 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

- CT remains the gold standard for the diagnosis of ischemic stroke
- Thrombolytics are currently the only therapy that can be initiated in the ED
- Mechanical clot removal provides an alternative at institutions able to use it
- CTA and CT perfusion may become routine
- 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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