Advanced Neuroimaging for Acute Stroke

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Disclosures

FERNE – Board member
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Objectives

- The role of MR in the emergent management of patients
- Describe the emergent use of CTA/CTP
- Discuss how advanced imaging can help difficult neurological diagnoses

Case

- 59 year old male is found by his wife at 6:30 am unable to speak and not moving the right side of his body.
- He had the symptoms upon awakening
- He is brought to the ED around 9:45 am by his family.
- PMHx: HTN, DM

Case

- BP 140/85, HR 75, RR 18, T 98.2
- Heart, lungs and abdomen are normal
- Neuro exam: he is aphasic. He does follow verbal commands. He has right facial droop, only trace movement in the right arm, and 4/5 right leg weakness NIHSS 16
- A non-contrast head CT demonstrates “no acute lesion”

Advanced Neurological Imaging

- "Four P's"
- Parenchyma, Pipes, Perfusion, and Penumbra
  - *Parenchymal* evaluation will detect early signs of acute stroke and rule out hemorrhage.
  - *Pipes* assesses intracranial and extracranial circulation for evidence of intravascular thrombus, dissection or leak.
  - *Perfusion* = cerebral blood flow, blood volume, and mean transit time measurements, which will ultimately yield assessment of penumbra.
  - *Penumbra* refers to tissue at risk of dying if a lack of perfusion continues.

Pathophysiology

Pathophysiology

40-60cc/100g/min
Normal Blood Flow

< 20cc/100g/min
Neurons stop firing; Membrane integrity is maintained

< 10cc/100g/min
Membrane failure

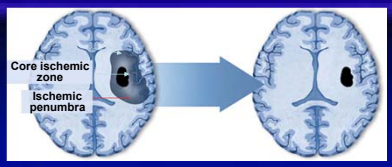
Circulation

Collateral circulation leaves a large area with 10-20cc/100g/min

< 3hrs of ischemia: neuro deficits are reversible

> 6hrs of ischemia: neuro deficits are irreversible

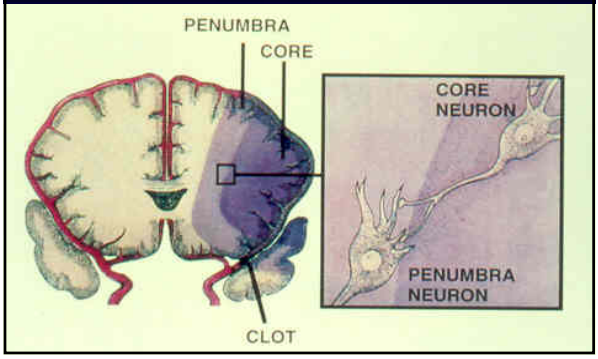
"Time Is Brain"



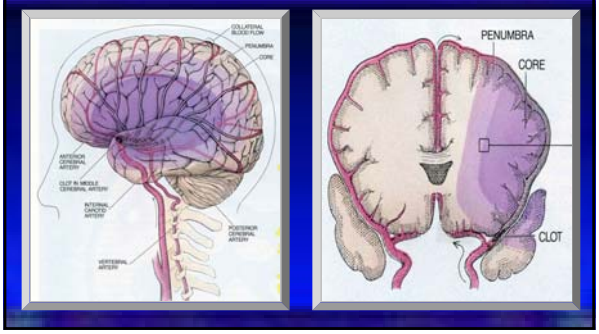
- Reperfusion of the ischemic penumbra may reduce the extent of damage and improve recovery of function
- Timing is critical
  - The average patient with large vessel, acute ischemic stroke loses 32,000 brain cells/second
  - Fast response is essential

Thomas SH, et al. *N Engl J Med.* 2006;354:2263-2271; Heiss WD. *J Cereb Blood Flow Metab.* 2000;20:1276-1293; Saver JL. *Stroke.* 2006;37:263-266.

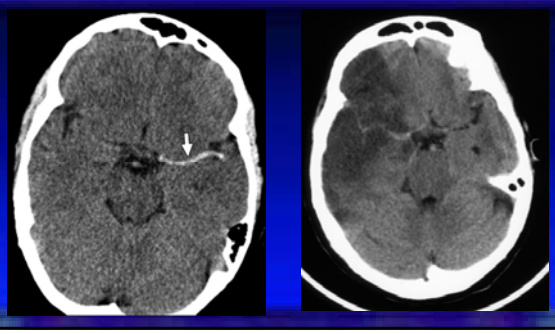
Progression of Ischemic Stroke



Definition of Ischemic Penumbra: Salvageable Neuronal Tissue



Hyperdense MCA Sign



Hyperdense MCA Sign

- Size matters
- IV tPA may not dissolve clot
- < 10mm 86% recanalized
- > 10mm 37% recanalized
- > 20mm none recanalized

Shobha N et al. *J Neuroimaging 2013;20:1-4*

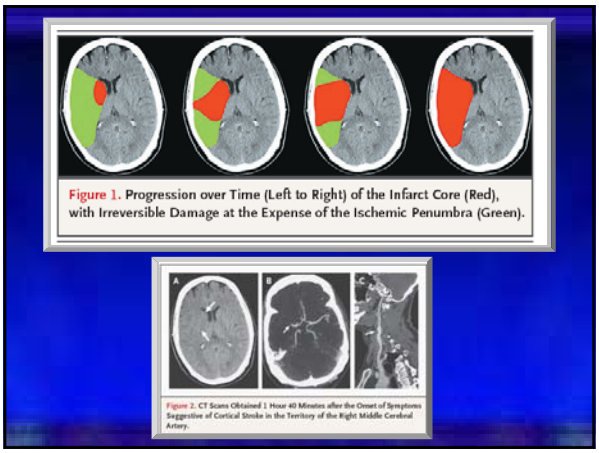


Figure 1. Progression over Time (Left to Right) of the Infarct Core (Red), with Irreversible Damage at the Expense of the Ischemic Penumbra (Green).

Figure 2. CT Scans Obtained 1 Hour 40 Minutes after the Onset of Symptoms Suggestive of Cortical Stroke in the Territory of the Right Middle Cerebral Artery.

Definitions

Perfusion	The steady-state delivery of blood to cerebral tissue through the capillaries
Cerebral Blood Flow (CBF)	Volume flow rate of blood through the cerebral vasculature per unit time
Cerebral Blood Volume (CBV)	Amount of blood in a given amount of tissue at any time
Mean Transit Time (MTT)	Average time it takes for blood to traverse from the arterial to the venous side of the cerebral vasculature

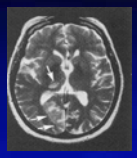
Advanced CT Imaging for Acute Stroke: CTP versus MRI

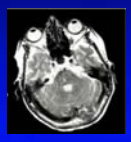
	Parameters	Definition of Penumbra	Advantages	Limitations
CT Perfusion	CBF, CBV, MTT, TTP	Relative CBF <66%; CBV >2.5 mL/200g	➢Combined with plain CT ➢Available ➢Fast	➢Limited brain coverage ➢Poorly sensitive to posterior circulation ➢Indirect core visualization ➢Iodinated contrast
DWI-PWI MRI	CBF, CBV, MTT, TTP	Relative TTP (or MTT) delay >45s and normal DWI	➢Sensitive ➢No radiation ➢Directly visualizes core	➢Limited availability ➢CBF and CBV values not accurate ➢Patient cooperation required ➢Frequent contraindications

Muir KW et al. *Lancet Neurology* 2006; 5:755-768

MRI: T1 & T2 Weighted Pulse Sequences

- Sensitive for subacute and chronic blood
- Less sensitive for hyperacute parenchymal hemorrhage



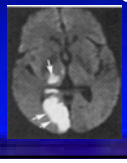


Imaging: MRI

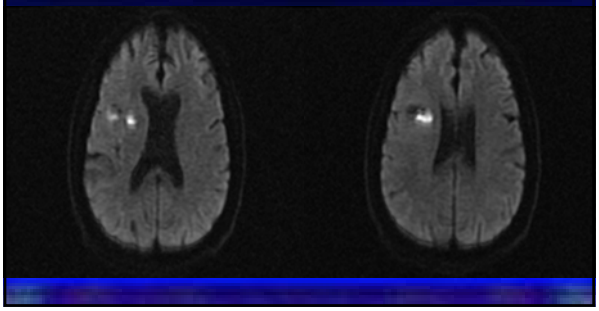
- Diffusion weighted (DWI) = Core
- Extracellular water collection
- Perfusion weighted (PWI) = Penumbra (P=P)
- Hypoperfusion of gadolinium

Diffusion-Weighted Imaging

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

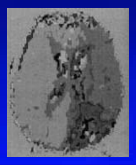


Diffusion Weighted Image



Perfusion-Weighted Imaging

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

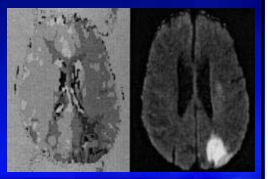


Digital Subtraction: MRI

- Digital subtraction of DWI from PWI = area of mismatch
- Mismatch = Viable tissue
- No mismatch = no viable tissue

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
  - If no mismatch, no benefit to thrombolytic therapy

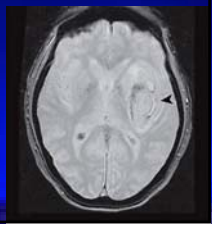


Imaging: Gradient Recalled Echo (GRE)

- Increased signal intensity = recent extravasated blood
  - Detects oxyhemoglobin levels
  - Allows for detection of hyperacute cerebral hemorrhages

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



MR Diffusion/Perfusion Imaging Advantages

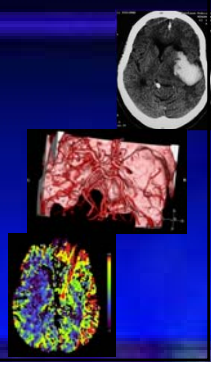
- Well defined brain parenchyma
- Provides early detection of ischemic changes
- Does not expose patient to ionizing radiation
- More effective than CT for identifying small ischemic strokes

MR Diffusion/Perfusion Imaging Disadvantages

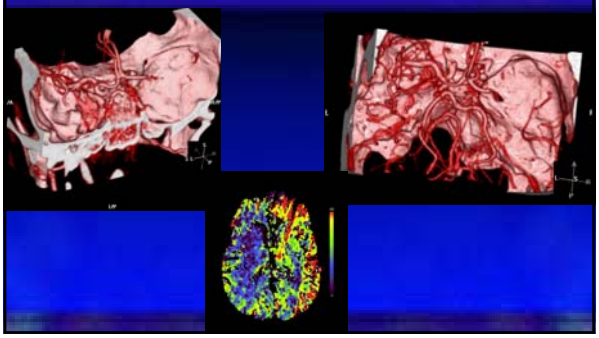
- Limited availability compared with CT and after hours
- Patient contraindications such as claustrophobia, metal implants, and pacemakers.
- Examination is lengthy (up to 60 minutes)
- Risk of gadolinium reaction

CTA and CTP

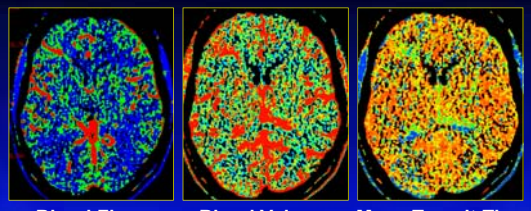
- Essential questions
  - Is there hemorrhage?
  - Is there large vessel occlusion?
  - Is there “irreversibly” infarcted core?
  - Is there “at risk” penumbra?
- One contrast bolus yields two datasets
  - Vessel patency
  - Infarct versus salvageable penumbra



CT Angio & Perfusion



CT Perfusion Terminology



Blood Flow | Blood Volume | Mean Transit Time or Time to Peak

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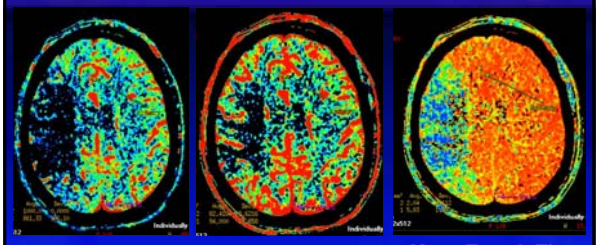
Changes in Cerebral Vascular Physiology with Worsening Circulatory Impairment

	CBF	CBV	MTT
Salvageable Penumbra	↓	↑	↑
Irretrievable Infarct	↓	↓	↑↑

CT Perfusion (CTP) and CT Angiography (CTA)

- An absolute CBV threshold < 2.0 ml/100 g = acute infarct core
- MTT threshold at 145%, and where normal is 100%, = penumbra

Relationship between CBV, CBF, and MTT



Blood Flow | Blood Volume | Mean Transit Time or Time to Peak

MTT= Blood Flow / Blood Volume

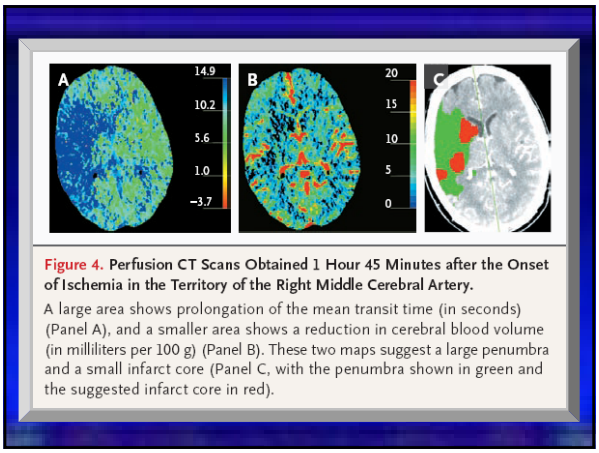
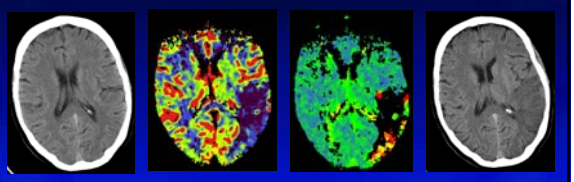


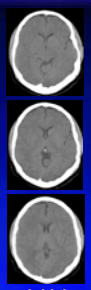
Figure 4. Perfusion CT Scans Obtained 1 Hour 45 Minutes after the Onset of Ischemia in the Territory of the Right Middle Cerebral Artery.

A large area shows prolongation of the mean transit time (in seconds) (Panel A), and a smaller area shows a reduction in cerebral blood volume (in milliliters per 100 g) (Panel B). These two maps suggest a large penumbra and a small infarct core (Panel C, with the penumbra shown in green and the suggested infarct core in red).

Value of Perfusion Scanning



Case: Value of CTA/CTP within 3 hour window



Initial

- 50 yo male
- CT within hour of symptom onset
- Awake, alert, dysarthric
- Fixed right sided gaze
- Left sided weakness

Case:
Value of CTA/CTP within 3 hour window

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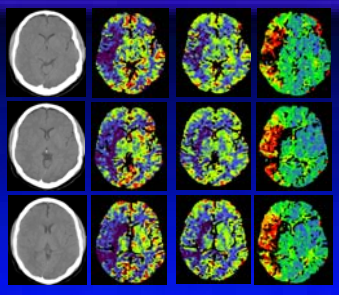
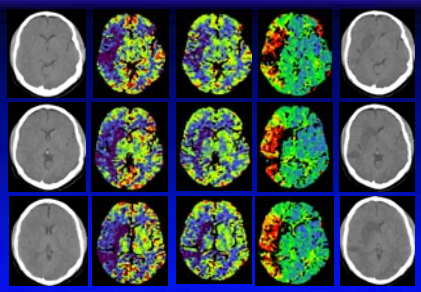
Value of CTA/CTP within 3 hour window



Case:
Value of CTA/CTP within 3 hour window



CT Perfusion Advantages

- Produces fewer motion artifacts than with MR imaging.
- Can be completed in 5 to 10 minutes.
- Provides good visualization of major structures.
- Uniformly available.

CT Perfusion Advantages

- Provides information on salvageable penumbra.
- Has overall accuracy of 90% to 100%
- Can be used in patients with pacemakers, defibrillator, or claustrophobia

CT Perfusion Disadvantages

- Exposes patient to ionizing radiation
- Low resolution for small parenchymal abnormalities
- Risk of contrast reactions
- Technician training

Using CTP/CTA and MRI/MRA

- DIAS and DEDAS enrolled from 3-6 hours only if there is at least a 20% penumbra
- "Time is brain" to "physiology is brain"
- DEFUSE study
  - Found MRI profiles that identify patients likely to benefit from reperfusion therapies
  - Patients unlikely to benefit or who may be harmed

CTP: Not all good

- 2009 FDA warning
- California radiation problem
- Annual back ground 2 mSv
- CXR 0.1 mSv, CTP 4 mSv
- One institution 32 mSv for several pts
- Hair loss, nausea
- Warning to check radiation parameters

CTP used to predict bad outcomes

- Malignant profile
  - Volume > 85 ml
  - Tmax > 8 sec
- 42 patients, 5 with malignant profile
- All 5 had poor outcomes
- 100% specific, 67% sensitive
- sICH rate 40%, compared to 5.6%

Inoue, *Stroke* 2012;43:00-00

Europeans using CTP to push the window

- < 1/3 middle cerebral artery infarct and > 20% penumbra
- 172 pts < 4.5 h, 43 > 4.5 h
- Mean onset times 143 min, 509 min (8.5 h)
- Mean NIHSS 11 vs 9
- Good outcomes (mRS ≤ 2) 64% vs 60%
- sICH 2.9% vs 2.3 %
- More cardioembolic in > 4.5 h
- How many with NIHSS = 9 would be mRS 2 with nothing?

Garcia-Bermjo Cerebrovasc Dis 2012;34:31–37

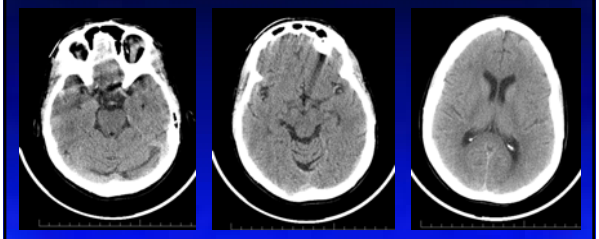
Using CTP/CTA and MRI/MRA

- NOT standard of care
- ASA Stroke Guidelines 2007
- "Multimodal CT and MRI may provide additional information that will improve diagnosis of ischemic stroke. . . Vascular imaging should not delay treatment of patients whose symptoms started <3 hours ago…"

Case Conclusion

- Non-contrast head CT scanning demonstrated no acute lesion
- Three dimensional reconstructions of the CTA demonstrated absence of left MCA flow
- CTP showed a blood flow/blood volume mismatch in the distribution of the left MCA = penumbra present
- Diagnosis: Acute left MCA distribution ischemic stroke

Case: "Wake up" Stroke



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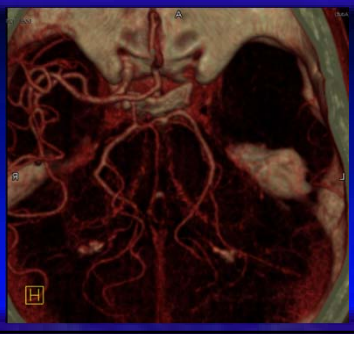

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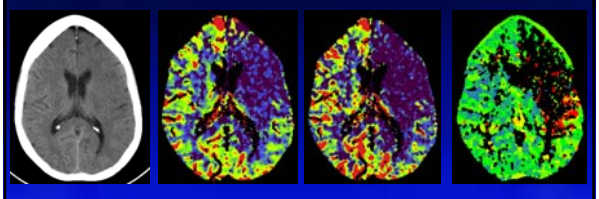

10:30 at stroke center

Case Conclusion

- Risks and benefits of an endovascular procedure were discussed with the patient and his family
- Clot in the left ICA, as well as the left MCA were identified
- The left ICA was opened with balloon angioplasty, and a carotid stent was placed
- The MCA was opened with the combination of the Merci retriever device, intra-arterial t-PA, and balloon angioplasty
- Six month follow-up: his speech was clear, although he had some hesitation with speech. He had 4/5 strength on the right side

Conclusion

- MRI/MRA provides good detail but may not be available or is difficult to utilize. Vague or transient symptoms may reveal lesions on MRI
- CTP/CTA provide good detail but are not without problems
  - Formatting difficulty
  - Radiation exposure
- CTP can be used to rule out candidates for treatment
- CTP may be helpful in extending the window of treatment, or for treating wake up strokes

Questions?

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