Advanced Neuroimaging for Acute Stroke

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Disclosures

FERNE – Board member
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Genentech – Consultant, Speaker
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

- Normal Blood Flow
  - 40-60cc/100g/min
- Neurons stop firing; Membrane integrity is maintained
- Membrane failure
- < 10cc/100g/min
- Cell death occurs
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

Progression of Ischemic Stroke
Definition of Ischemic Penumbra:
Salvageable Neuronal Tissue

Hyperdense MCA Sign

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

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

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<th>Parameters</th>
<th>Definition of Penumbra</th>
<th>Advantages</th>
<th>Limitations</th>
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<tr>
<td><strong>CTPerfusion</strong></td>
<td>CBF, CBV, MTT, TTP</td>
<td>Relative CBF &lt;46%, CBV &gt;2.5 mL/200g, TTP delay ≥45s and normal DWI</td>
<td>- Combined with plain CT &lt;br&gt;- Available &lt;br&gt;- Fast</td>
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<tr>
<td><strong>DWI-PWI MRI</strong></td>
<td>CBF, CBV, MTT, TTP</td>
<td>Relative TTP (or MTT) delay, DWI abnormal, and normal PWI</td>
<td>- Sensitive &lt;br&gt;- No radiation &lt;br&gt;- Directly visualizes core</td>
</tr>
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</table>
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

**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

Definitions

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Changes in Cerebral Vascular Physiology with Worsening Circulatory Impairment

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<tr>
<td>Salvageable Penumbra</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
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<tr>
<td>Irretrievable Infarct</td>
<td>↓</td>
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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

MTT = Blood Flow / Blood Volume

Time to Peak
Figure 4. Perfusion CT Scan 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

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

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

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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