Imaging of acute stroke

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Learning objectives

• Become familiar with findings of acute infarction on “routine” CT and MR
• Acquire knowledge of current options for treatment of acute infarction
• Understand the role of imaging in treatment decisions
  – Perfusion (CT and MR) imaging
• Discuss new controversies
“Stroke”

• 700,000 new stroke per year
• #3 cause of death
• Non-specific term – any acute neurologic deficit
  – Cerebral Infarction (85%)
  – Spontaneous cerebral hemorrhage (15%)
Imaging goals

• Exclude non-ischemic causes of acute neurologic dysfunction
  – Hemorrhage
    • Hypertensive, Cerebral Amyloid Angiopathy, AVM, aneurysm, trauma
  – Venous thrombosis
  – Tumor
  – Infection

• Identify infarct

• Determine if treatment can improve outcome
3 P’s

• Parenchyma
  – Changes seen in brain CT and MR

• Pipes
  – Vessels – CTA and MRA

• Penumbra
  – Perfusion CT and MR
3 P’s + C

• Parenchyma
  – Changes seen in brain CT and MR

• Pipes
  – Vessels – CTA and MRA

• Penumbra
  – Perfusion CT and MR

• Collaterals
Pathophysiology of acute infarction

- Vascular insufficiency
  - Hyperacute - < 6 hrs
- Cytotoxic edema
  - Hyperacute < 6 hrs
- Vasogenic edema
  - Acute 6-72 hrs
Cytotoxic Edema
Ischemic cascade

- Circulatory collapse > 5 minutes leads to anaerobic glycolysis
- Membrane damage leads to sodium pump failure
  - Sodium enters cell and potassium leaves
- Water passively follows sodium due to osmotic gradient
- Intracellular space expands and extracellular space shrinks
- Calcium follows sodium and activates intra-cellular enzymes that destroy organelles and produce cell lysis
- Excitatory amino acids (Glutamate) & vasoactive substances released that further damage cells in region of hypoperfusion
CT of hyperacute infarction
<6 hrs

• Clot in major artery
  – “Dense MCA or Basilar artery”

• Loss of contrast between gray and white matter
  – Due to loss of normal cortical density
  – Gray matter isodense to white matter
    • Cytotoxic edema v. decreased Cerebral Blood Volume

• Mass effect minimal or absent

• Findings are subtle
  – Expertise/experience necessary for accurate interpretation
MR of hyperacute stroke
< 6 hrs

• Hyperintensity on Diffusion Weighted Imaging
  – “The magic bullet of infarct detection”
• Subtle hyperintensity on T2 weighted and FLAIR sequences
• Absent or minimal mass effect
• Intravascular hyperintensity in arteries on FLAIR (slow flow)
• Clot in major artery
  – Marked intraluminal hypointensity on susceptibility weighted scans
• Findings obvious – little experience or expertise needed
Wake up stroke

• Time of onset cannot be determined clinically
  – Can’t treat

• Often occurs in early AM
  – 4:00 – 6:00 AM

• FLAIR/Diffusion mismatch
  – Ratio of infarcted region to contralateral hemisphere <1.5
  – Stroke < 4.5 hours
  – However ~ 45% of strokes < 4.5 hours demonstrated some FLAIR Hyperintensity
  – Emeriau et. al. Stroke 2013;44: 1651
Where is the infarct?

3 hours post-ictus
Flow effects and clot
Flow effects and clot
Acute Infarction Detection—MR vs CT

Two studies confirm superiority of MR over CT

  - 691 patients studied within 24 hours
  - Sensitivity: DWI 97%; conventional MR 58%; CT 40%
  - DWI least sensitive in the 12- to 16-hour period (80%)

  - 50 patients studied within 6 hours of symptom onset
  - Randomized to CT or MRI first exam
  - Sensitivity experts: DWI 91%; CT 61%
  - Sensitivity novices: DWI 81%; CT 46%
  - Greater inter-observer variation with CT for detection and determination of extent of infarction
Acute lacunar infarct
False Negative DWI

- 3-10% of infarcts will initially have a negative DWI (no hyperintensity)
- 75% will be sub-cm lesions in the stem or cerebellum.
- Small size, susceptibility artifact from skull base, and reader error account for most of these cases.
- Rarely, false negative DWI may be due to initial imaging during period of transient resolution (pseudo-normalization) of diffusion abnormalities.
6:00 AM
Reversible DWI changes

• < 5% complete reversal
• ADC reduction < 30%
• Typically see recurrence of DWI abnormality within 24 hours
  – Persistent reversal (<1%)
  – Apoptosis?
  – Freeman et al Stroke 2013;44: 1622

• Acute clot lysis
  – Endovascular < 2 hours
  – 30% demonstrated some reversal (>10 cc)
  – However final stroke volume correlated with initial DWI volume and reversal did not correlate with good outcome
    • Manabu et al. Stroke 2014;45:1024
Acute infarction
6-72 hours
Vasogenic edema

- Cytotoxic edema increases - progressive cell death
- After approximately 30 minutes endothelial cell damage occurs resulting in disruption of the blood brain barrier
- Fluid exudation from vessels produces vasogenic edema
- Increase in brain volume produces swelling beginning at around 6-8 hour
- Extent of vasogenic edema variable
  - When blood supply to a portion of the brain is completely cut off there may be very little edema in the first day
Detection of Hemorrhagic Infarction

- T2*W MR (Susceptibility weighted) > than CT for detecting hemorrhagic components of acute infarction
  - Linfante et. al. Stroke 1999;30:2263-2267
  - Schellinger et. al. Stroke 1999;30:765-768
- Gradient Echo T2*W > b_0 T2*W for detection of hemorrhagic component of infarct
- SWI > GrE
- Microbleeds more easily detected visible on Gr Echo
  - Lin et. al. AJNR 2001;22:1275-1281
Hemorrhagic conversion
CT vs MR
Current Treatment Options—Clot Lysis

- Intravenous recombinant tPA
  - FDA approved in 1996
  - Must be given within 4.5 hours
  - Less than 1/3 of middle cerebral artery distribution
  - No hemorrhage (CT)
  - No “T” occlusion (distal internal carotid/proximal MCA)
- Mechanical clot remover—MERCI catheter
  - FDA approved in 2004
  - Proximal MCA occlusions
- Off-label treatments
  - Intraarterial tPA
    - Effective up to 6 hours in MCA and up to 24 hours in basilar artery
    - No distal ICA or extensive proximal MCA occlusions
  - IV tPA–IA tPA combinations
Limitations of IV tPA

• Only 4% of acute strokes receive tPA
  (Kleindorfer et al, Stroke 2004; 35: e27-e29)
• Only 22% of patients present within 3 hours
  • 51% of these ineligible due to
    – Mild severity
    – Medical or surgical history
    – Blood tests
• Protocol violations are common
• Concern for hemorrhage
• tPA potentiates apoptotic injury to both neurons and endothelial cells
Figure 2 Distribution of modified Rankin scores by OTT interval OTT=onset to start of treatment. Definitions of scores: 0=no symptoms at all. 1=no significant disability despite symptoms; able to carry out all usual duties and activities. 2=slight disabl...

Kennedy R Lees, Erich Bluhmk, Rüdiger von Kummer, Thomas G Brott, Danilo Toni, James C Grotta, Gregory W A...

Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials


http://dx.doi.org/10.1016/S0140-6736(10)60491-6
tPA Thrombolysis

• Current treatment criteria are based on population derived statistics from all stroke patients.
• Improves outcome occurs when:
  – There is salvageable brain
  – Hemorrhage does not occur.
Maximizing therapeutic success

- Aim of imaging is to “individualize” therapeutic decisions and therefore extend the therapeutic window
  - Identify patients with brain at risk (ischemic but not infarcted)
  - Identify patients with hemorrhage or at risk for hemorrhage
  - Identify the site of arterial occlusion
  - Identify extent and type of collateral supply to brain at risk
- Routine CT and MR do not provide sufficient information
3 hours
SPOILER ALERT!

- Every thing I am about to say about use of “advanced” imaging to determine treatment may be untrue
Multi-modal infarct imaging

• 1) Anatomic imaging (Parenchyma)
  – NECT or MR with DWI
    • Detect extent of permanently infarcted brain (MR>>CT)
    • Detect hemorrhage and/or non-ischemic cause of “stroke”

• 2) Angiography (CTA or MRA) (Pipes)
  – Identify location and nature of occlusion or stenosis
  – Assess collaterals
  – CTA head
    • Evaluate source images for better delineation of acute

• 3) Perfusion (Penumbra)
  – Identify viable brain at risk

• 4) Collaterals
Vascular imaging

- CTA, MRA and Catheter angiography all equivalent in accuracy
- Look for major vascular occlusion
  - ICA, MCA M1, MCA M2, Vertebral, Basilar, PCA
- Assess collaterals
CS system: 0 = absent collaterals >50% of an M2 territory; 1 = diminished collaterals >50% M2 territory; 2 = diminished collaterals <50% M2 territory; 3 = collaterals equal to contralateral side; 4 = increased collaterals.
Distribution of mRS scores according to the leptomeningeal collateral scores.
Brain at risk
The “Ischemic Penumbra”

• Portions of the brain surrounding acutely infarcted tissue with decreased blood supply (perfusion) that are at risk for subsequent infarction

• Viable tissue with or without clinical evidence of dysfunction
The ischemic penumbra.
Overview: CT and MR Perfusion Methods

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<tr>
<th>INJECT</th>
<th>SCAN</th>
<th>MODEL</th>
<th>PARAMETER MAPS</th>
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**CT**
- I

**MR**
- Gd

**INJECT**

**SCAN**

**MODEL**

**PARAMETER MAPS**

- MTT
- CBV
- CBF

Courtesy H. Rowley
Overview: Bolus tracking perfusion (CT & MR)

<table>
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<tr>
<th>INJECT</th>
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<th>DENSITY/INTENSITY CURVES</th>
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CT

MR

Courtesy H. Rowley
MRI Perfusion
Gadolinium Bolus Tracking

T2* Image

SI vs Time Curve
MRI Perfusion
Gadolinium Bolus Tracking

T2* Image

SI vs Time Curve
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SI vs Time Curve
MRI Perfusion Parameters

CBV

MTT
CT Perfusion Parameters

- **Mean Transit Time (MTT)**
  - Units: Seconds
  - Capillary transit time (artery to vein)
  - *MTT elevation is earliest indicator of ischemia*

- **Cerebral Blood Flow (CBF)**
  - Units: ml/100 gm/min
  - Delivery of blood to tissue/unit time
  - *Bottom line for infarct volume*

- **Cerebral Blood Volume (CBV)**
  - Units: ml/100 gm
  - *Measure of autoregulation*
Equivalent Perfusion Parameters

Mean Transit Time (MTT)

Mean Time to Enhance (MTE)

Cerebral Blood Volume (CBV)

Negative Enhancement Integral (NEI)

Cerebral Blood Flow (CBF)

Maximum Slope of Decrease (MSD)
Central Volume Principle

• In the setting of arterial occlusion or severe stenosis, cerebral perfusion pressure (CPP) ↓
  • MTT ↑
    – Collateral vessels provide flow to brain “distal” to occlusion
  • CBV ↑
    – Maintains CBF
      • Cerebrovascular reserve
        – CBV increase is finite
• Continued ↓ in CPP leads to a ↓ in CBF
• CBF ↓ and infarction ensues

\[ CBF = \frac{CBV}{MTT} \]
Pathophysiology of Ischemic Injury:
Duration and Degree of ↓ CBF

Normal neuronal function

Reversible injury (penumbra)

Infarction

Time (hrs)

Courtesy of Howard Rowley
Normal brain
CBF > 50 ml/100 gm/min

Ischemic penumbra
Brain at risk for infarction
CBF 10-30 ml/100 gm/min

Core
Irreversible infarction
DWI +
or
CBF < 10 ml/100 gm/min

Oligemic region
Brain not at acute risk for infarction
CBF 30-50 ml/100 gm/min
**Perfusion/Diffusion Mismatch**

- **DWI + CBF < 10 ml/100 gm/ min**
  - Core irreversible infarct
  - >20% mismatch
  - **Treat**

- **DWI – CBF 10-30 ml/100 gm/min**
  - **No mismatch**
  - **Don’t Treat**
Diffusion-Perfusion Mismatch

3 hrs

DWI

MTE (MTT)

24 hrs

DWI
No Diffusion-Perfusion Mismatch

DWI  MTE (MTT)  NEI (CBV)

Courtesy H. Rowley
Whom to treat

• Time
  – < 4.5 hours IVtPA
  – ?? Up to 6 hours IA and combined IA/IV
  – ?? Up to 24 hours basilar occlusion

• Volume of infarct
  – <1/3 MCA

• Penumbra mismatch > 20%

• Collateral score of 3 or higher
Infarct volume quantification

• >1/3 involvement of the MCA territory has an increased risk of hemorrhage and poor outcome
• Poorly quantified by observation
• ASPECTS divided the MCA into 10 regions giving each 1 point
  • 10 = normal MCA
  • 0 = stroke of entire MCA
  • < 7 poor outcome even with successful recanalization

Perfusion parameters

MTT or Tmax best for determination of mismatch
CBV or CBF best for predicting final stroke volume
Elevation of CBV indicative of compensatory hyperfusion

Often temporary
Mismatch

FLAIR

DWI

rCBF

Infarct 12 hours
Acute infarct 2 days S/P embolectomy
Malignant mismatch

- Tmax or MTT > 8 with volume > 100 cc
- Even with successful lysis likely to go on to develop massive acute infarct with marked swelling
  - Mlynash et. al. Stroke 2011;42:1275
Figure 4. A, Venn diagram demonstrating prediction of good outcome with a clinical threshold of NIHSS <8 and an imaging threshold of MTT <47 mL.

Yoo A J et al. *Stroke*. 2010;41:1728-1735
Controversies
Evidence based medicine

• DEFUSE and EPITHET trials did not show statistical differences in results based on perfusion data
  – Both demonstrated improved outcome with IV treatment.

• Recent studies did not show benefit of IA over IV treatment or value of use of penumbra
  – NEJM 2013;368:904
  – NEJM 2013; 368:914

• Hot off the press: Good outcomes with IA thrombolysis
  – 536 patient
  – Abilleira et al. Stroke 2014;45:1046
New strategies
ACR/ASNR/SNIS

- Goal minimize time to treatment
  - Every minute “wasted” correlated with 1.8 days of healthy life
    - Meretoja et al. Stroke 2014;45:1054

- NCT to exclude hemorrhage and identify infarct and major vascular occlusion
  - If negative go direct to ivtPA
  - If positive for clot either CTA (+/- perfusion) or directly to catheter angio

- Can substitute MR/MRA if available
- For TIA MR not CT
Classification algorithm.

ICA, Prox MCA, Basilar Occluded?

- Yes
  - Major Stroke By Imaging

- No
  - Significant CT/DWI Lesion?
    - Yes
      - Minor Stroke By Imaging
    - No
Contra-indications for treatment
1) No hemorrhage
2) No T occlusion
3) Less than 1/3 of MCA territory
Conclusion

• We can now accurately and quickly identify hyperacute infarcts, and can determine if there is potentially viable brain tissue.
• Lots of controversy about how to work up stroke
• Treatment options remain limited
• Bummer