Stroke – CNS Ischemia

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Stroke

• An acute alteration in neurologic function/mental status/sensorium

• Stroke (discussed by us today) is assumed to represent an ischemic cerebral event
  – Result is a fixed neurologic deficit

Other relevant terms

• Transient ischemic attack (TIA)
  – Less than 5 minutes typically (<24 hours)

• Reversible ischemic neurologic deficit (RIND)
  – 24 – 72 hours of duration
Gross Pathologic Changes

- Day 0-2 (acute)
- Day 2-10 (subacute)
- Chronic

- Appears normal
- Swelling & softening
- Encephalomalacia & cystic change
Microscopic Pathologic Changes
Normal Brain and Acute Infarction
Microscopic Pathologic Changes
Subacute Infarction and Chronic Infarction
Imaging Correlates of Injury

• Cytotoxic edema (early)
  – Altered CBV with disproportionate oligemia in cortex
  – Decreased density of gray matter (CT)
  – Increased signal intensity of gray matter (MR)
  – Restricted diffusion (MR)

• Vascular changes (In situ thrombosis)
  – Increased density (CT)
  – Increased signal intensity (MR)
  – Loss of flow (CTA or MRA)
CT or MR for Acute Stroke Evaluation?

- Depends on who you ask
  - Good literature support for both
- Imaging choice often based on external factors
  - CT/MR availability
  - Neurologist preference
  - Patient factors (stability, pacemaker, contrast allergies)
Acute Stroke Imaging Goals

• Past
  – Exclusion of infarction mimics

• Present
  – Depict acute stroke
  – Identify regions at risk for infarction
  – Monitor success and complications

• Future
  – Atherosclerotic plaque imaging
  – Improved prognostic information
Acute Stroke Imaging Goals

- Detection of hemorrhage
  - NCCT
  - MR (FLAIR, GRE, SWI)
- Evaluate vessel status
  - CTA/MRA
- Determine extent of core infarction
  - CTA source images/DWI/Blood flow
- Estimate brain at risk and select patients for thrombolysis
  - CTP/MRP
Acute Stroke Imaging

• The 4 P’s of stroke evaluation
  – Pipes
    • CTA or MRA
  – Perfusion
    • MRP or CTP
  – Parenchyma
    • DWI or CTP
  – Penumbra
    • Perfusion-diffusion mis-match
    • Perfusion CBV vs. MTT or CBF mis-match
Diagnosis of Ischemic Stroke Mechanism

- Embolism
  - Cardiac
  - Aortic
  - Artery-to-artery

- Decreased perfusion
  - Large or small vessel disease
    - Atherosclerosis
    - Vasculitis

- Thrombosis
  - Increased risk in stenotic vessels

Adapted from Albers, et al. Chest 2004
PARENCHYMA (BRAIN)
Parenchymal Evaluation

• CT and MR are useful at onset
  – Extent of infarction
  – Hemorrhage or mass masquerading as infarction?

• MR DWI is single most useful study
Acute Ischemia

- **NCCT**
  - Loss of gray/white junction in first 3 hours (50-70%)
  - Parenchymal low density
Acute Ischemia

• MRI
  – Gyral swelling (~75%)
  – Abnormal cortical signal intensity
Acute Ischemia

- MRI DWI
  - Gold standard for acute stroke evaluation
DWI in Stroke

- Sensitivity nearly 95%
- DWI abnormal in minutes
- Resolves by 10-14 days
  - “Pseudonormalization” of ADC occurs somewhere around 7-10 days
- DWI hyperintensity can persist >50 days
- ADC is more specific than DWI
DWI in Infarction

- Cytotoxic edema causes water shift
  - Na/K pump failure, loss of membrane integrity
  - Bulk movement from fast extra-cellular space to slow intra-cellular space

- DWI is direct window into cell death
Pseudonormalization of ADC

First phase (decreasing rADC):
\[ rADC(t) = 1 + \frac{t}{t_t} (rADC(t_t) - 1) \]

Second phase (increasing rADC):
\[ rADC(t) = rADC(t_t) + s\log\left(\frac{t}{t_t}\right) \]

Copen W A et al. Radiology 2001;221:27-34
DWI in Brain

• Normal brain has two compartments:
  – Extracellular compartment where diffusion is fast
    • 20% of brain volume
  – Intracellular compartment where diffusion is restricted
    (barriers such as organelles and membranes)
    • 80% of brain volume

• Diffusion measurement is mixture of two compartments
Vascular Changes in Acute Ischemia

• In situ thrombosis or clot in affected vessel
  – Classic “hyperdense MCA” sign
  – Use other vessels for internal controls
  – REMEMBER:
    • Hyperdense basilar, PCA and ACA can also occur
  – MR SWI or GRE may show susceptibility in thrombosis

• Review more distal vessels also
• MR images also may reveal slow flow phenomenon as well as thrombosis
In Situ Thrombosis
Slow Flow or Occlusion
The Whole Package
Acute Ischemia
Cortical Laminar Necrosis

- Infarction pattern with selective injury to neurons in cortical layer (layer 3 most sensitive followed by layer 5 and 6)
- Can be seen in focal or diffuse infarction
- Can be missed if not aware of pattern
  - Swelling
  - Abnormal cortical T2 hyperintensity
  - “Supernormal” pattern on DWI with accentuated gray-white junction
Subacute Ischemia

- 2 days – 2 weeks
- Stroke becomes more conspicuous
- Necrosis and fluid
- Petechial cortical hemorrhage common
- Gyral enhancement, occasional hemorrhagic transformation
Subacute Ischemia

• Mass effect maximal 3 - 5 days
  – Herniation
  – Decompression

• Mass effect decreases at 7 – 10 days
Subacute Ischemia

- CECT or CE MRI
  - Patchy or gyral enhancement
    - Begins as early as 2 days
    - Peaks at 2 weeks
    - Disappears by 2 months
Ischemic Cerebrovascular Disease

- 5 major subtypes*
  - Large artery atherosclerosis
  - Cardioembolic
  - Small vessel/lacunar
  - Other known etiology
  - Etiology unknown

*Trial of the drug Org 10172 in Acute Stroke Treatment (TOAST)
Large Artery

- Thrombosis at site or plaque or emboli from plaque (artery-to-artery)
- Etiologies other than atherosclerosis:
  - Vasculopathy/vasculitis
  - Dissection
  - Hypercoagulable states
Atherosclerosis and Cerebral Vasculature

• NOT randomly distributed
• Carotid system
  – Bifurcation > siphon > M1 segment of MCA
• Vertebrobasilar system
  – V1 > V4 > proximal basilar artery
• Stenoses > 70% linearly associated with stroke risk
Inflammatory CNS Vasculitides

• Non-infectious
  – Drugs
  – Primary angiitis of central nervous system (PACNS)
  – Immune related diseases

• Infectious
  – Bacterial
  – Viral
  – Fungal
Vasculitides

- Inflammatory disease affects walls of muscular cerebral arteries
- Weakens muscle – vessel dilatation
- Fibrotic or inflammatory thickening – vessel narrowing
Mucormycosis
Arterial Dissection

- Consider in young adult with infarction
- Predisposing factors:
  - Fibromuscular dysplasia
  - Collagen vascular diseases
  - Blunt or penetrating trauma
Fibromuscular Dysplasia

Large Artery
Cardioembolic

- Relative stasis
  - Myocardial infarction
  - Ventricular aneurysm
  - Atrial fibrillation
  - Cardiomyopathy

- Valvular heart disease
- Cardiac tumors
- Right-to-left shunt
- 20-40% of strokes
Cardioembolic
Septic Embolism

- May lead to:
  - Cerebrovascular occlusions
  - Intracerebral abscesses
  - Arterial mycotic aneurysms
- May present with seizure

Cardioembolic

Abscess

CECT

Mycotic Aneurysm
Small Vessel or Lacunar

- Generally involve perforating arteries
- Common locations:
  - Basal ganglia
  - Internal capsule
  - Brainstem
  - Deep white matter of hemispheres
- Small! < than 1.5 cm
- Hypertension
Small Vessel or Lacunar

- Atherosclerotic
- Infectious or non-infectious vasculitides
- Meningitis
- Vasculopathies associated with collagen vascular disease
- Cerebral autosomal dominant arteriopathy with subcortical infarction & leukoencephalopathy (CADASIL)
CADASIL

- Familial, non-amyloid microangiopathy
  - Mutation of Notch 3 gene on chromosome 19
  - Early onset ischemic stroke (40-50s)
- Multi-infarct dementia
- Affects frontal lobes, temporal lobes, & insula
- Subcortical U Fiber involvement
CADASIL

Small Vessel
Other Known Etiology
Fat Embolism

- Fat emboli pass through pulmonary vasculature → systemic embolization
- Hypoxia, deteriorating mental status & petechiae
- CT usually negative
- MRI: Multiple, small, scattered ↑T2; DWI “star field”
- SWI also characteristic
“Negative Star Field”
SWI exam in fat emboli
Fat Embolism

Other Known Etiology
Venous Infarction

- Wide range of etiologies
  - Risk factors
    - Acquired: dehydration, sepsis, traumatic occlusion
    - Genetic: Factor V Leiden, Protein C, Protein S
- Symptoms often non-specific
  - Sudden deficit
  - Often heralded by seizure
- Typically hemorrhage
Venous Infarction: Imaging Patterns

- May be bilateral &/or multifocal
- Do not conform to arterial territory
  - Superior sagittal sinus → cortical veins → parasagittal convexity
  - Vein of Labbe → temporal lobe
  - Straight sinus → thalamostriate veins → thalamus
Prothrombotic States

• Antithrombins, heparin cofactor II, proteins C and S, and fibrinolytic system derangements
• Antiphospholipid antibodies (aPL) are associated with thrombosis, thrombocytopenia, and variety of neurological manifestations
  – Specially important with respect to recurrent cerebrovascular disease
PERFUSION AND PENUMBRA

CT and MR Perfusion
Cerebral Blood Flow (CBF) Values

- Normal range 55-110 ml/100 gm/min
- Oligemia 23-44 ml/100 gm/min
- Ischemia 10-22 ml/100 gm/min
- Infarction <10 ml/100 gm/min
Overview: CT and MR Perfusion Methods

<table>
<thead>
<tr>
<th>INJECT</th>
<th>SCAN</th>
<th>MODEL</th>
<th>DENSITY/INTENSITY CURVES</th>
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CT

MR

Courtesy H. Rowley
Overview: CT and MR Perfusion Methods

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<th>PARAMETER MAPS</th>
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<tbody>
<tr>
<td>CT</td>
<td>![CT Images]</td>
<td>![CT Models]</td>
<td>MTT, CBV, CBF</td>
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Courtesy H. Rowley
Central Volume Principle

• In 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 ↓ in CBF
• CBF ↓ and infarction ensues

\[ CBF = \frac{CBV}{MTT} \]
CT and MR Perfusion Parameters

- **Mean Transit Time (MTT)**
  - Capillary transit time (artery to vein)

- **Cerebral Blood Flow (CBF)**
  - Delivery of blood to tissue/unit time

- **Cerebral Blood Volume (CBV)**
  - Measure of autoregulation
CT Perfusion

• Qualitative Interpretation
  – TTP / MTT most sensitive
  – CBF indicates ischemia
    • Too low CBF is infarction
  – CBV correlates with infarct
  – Mismatch:
    \[\text{CBF} - \text{CBV} = \text{penumbra}\]
Normal brain
CBF > 50 ml/100 gm/min

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

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

Core
Irreversible infarction
DWI +
or
CBF < 10 ml/100 gm/min
Diffusion-Perfusion Mismatch

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

>20% mismatch

Penumbra
DWI –
CBF 10-30 ml/100 gm/min

TREAT
Diffusion-Perfusion Mismatch

5 hrs

24 hrs

DWI

MTE (MTT)

Post IA TPA

DWI
Territorial Infarction

- rCBF
- rCBV
- TTP
No Diffusion-Perfusion Mismatch

**Core irreversible infarction**
- DWI +
- CBF < 10 ml/100 gm/min

**Penumbra**
- DWI –
- CBF 10-30 ml/100 gm/min

**DO NOT TREAT**
No Diffusion-Perfusion Mismatch

DWI  MTE (MTT)  NEI (CBV)
Indications for Thrombolysis

• Rapid diagnosis
  – 3 hours post-ictus to beginning therapy

• Accurate means of depicting core infarction and potential ischemic penumbra

• Evaluation of vasculature
  – Define exclusion site
  – Exclude dissection
  – Grade collateral blood flow

• Exclude hemorrhage
Exclusions

- ASPECT scores are utilized at some centers
- < 1/3 of MCA territory is reasonable criteria
- Hemorrhage
ASPECT Score

10 - 8 = 2
CT or MR?

- Both are quite adequate examinations if well performed
- CT, CTA and CTP do less well at depicting brainstem, distal embolic and lacunar strokes
Summary

• Pathophysiology of cerebral infarction
• Role of imaging in infarction
  – Confirm diagnosis & rule out mimics
  – Location, size and acuity
  – Etiology
  – Determine appropriateness of therapy