Brain Imaging: Multi-Modal Computed Tomography Workshop

MODULE 4: Brain Mapping for Translational Investigators
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General Strategy – Patient and managed care driven- Ideal is to use a minimum studies to perform:

- Detection
- Quantitation
- Characterization
- Treatment planning
- Non-invasive follow-up after intervention
Lecture Overview – Stroke

- Noncontrast CT
- CTA
- CTP
- CTV
- Dynamic imaging
CT Imaging: Goals of Emergent Evaluation of Acute Stroke

- Establish vascular etiology of neurologic deficit
- Rule-out stroke mimics
- Differentiate hemorrhagic from ischemic stroke
- Determine etiology or mechanism of the event
- Assess reversibility and eligibility for acute therapies
- Provide early prognostic information
Stroke Types

• Hemorrhagic
  – Bleeds
  – 15% of stroke
  – Blood vessel rupture
  – Around or into brain

• Ischemic
  – Clots
  – 87% of all stroke
  – Clots form or land in brain artery

www.strokeassociation.org
Stroke Symptoms

- **Right Brain**
  - Paralysis on the left side of the body
  - Vision problems
  - Personality change
  - Memory loss

- **Left Brain**
  - Paralysis on the right side of the body
  - Speech/language problems
  - Change in behavior
  - Memory loss

- **Brainstem**
  - Balance problems
  - Coordination
  - Breathing difficulty
Stroke Risk Factors

• **Age** — Third leading cause of death in US. Stroke affects one person every 45 seconds in the US. The probability of stroke doubles for each decade of life after age 55. Stroke is common among the elderly.

• **Heredity (family history) and race** — Your stroke risk is greater if a parent, grandparent, sister or brother has had a stroke. African Americans have a much higher risk of death from a stroke. This is partly because blacks have higher rates of high blood pressure, diabetes and obesity. Aneurysms predispose to hemorrhagic stroke if they rupture.

• **Sex (gender)** — Stroke is more common in men than in women. However, more than half of total stroke deaths occur in women, and more women than men die of stroke.

• **Prior stroke, TIA or heart attack** — The risk of stroke for someone with a prior stroke is much that of a person who has not. Transient ischemic attacks (TIAs) are "warning strokes" that produce stroke-like symptoms but no lasting damage. TIAs are strong predictors of future stroke. A person with one or more TIAs is almost 10 times more likely to have a stroke than someone of the same age and sex with no TIA. Recognizing and treating TIAs can reduce your risk of a major stroke. If you've had a heart attack, you're at higher risk of having a stroke, too. TIA should be considered a medical emergency and followed up immediately with a healthcare professional.
Ischemic Stroke: A blood clot in a brain artery causes injury to a core of brain tissue, with potential injury to additional surrounding brain if blood flow is not re-established quickly.

The Internet Stroke Center
During a stroke the cells of the brain stop sending electrical signals and will die if blood flow is not restored quickly.
Routine CT - Infarct Signs
Case #1

• 40 yo WM presents at 1 hour after symptom onset with left hemiplegia and neglect
• PMH: HTN, Paroxysmal Atrial Fibrillation, Hypercholesterolemia
• Medications: Coumadin, Enalapril, Zocor
Imaging Findings
Case Discussion – Late Infarct Signs

• Finding
  – Hypodensity throughout MCA territory – findings inconsistent with onset time
  – Hyperdense MCA Sign

• Clinical Consequence
  – History retaken – onset time clarified – patient actually last known well 5 hours prior to CT
  – Large MCA territory completed infarct
  – Therefore, IV tPA not given
  – Anticipate poor functional recovery
Case #2

- 66 yo WM presents at 2 hours after sudden onset of right hemiparesis and global aphasia
Imaging Findings
Case Discussion - Early Infarct Signs

• Finding:
  – Loss of gray-white differentiation
  – Sulcal Effacement
  – No hemorrhage

• Relevant Data:
  – In NINDS trials, early infarct signs not an exclusion criterion; patients with early infarct signs benefited from therapy

• Clinical Consequence
  – Patient treated with thrombolytics with improvement in NIHSS score from 14 to 3 at day 7
Current AHA Guidelines: Early CT Infarct Signs

- Patients with early infarct signs on CT (even if they involve greater than 1/3 of the middle cerebral artery territory) and with a well established stroke onset time < 4.5 hours are candidates for treatment with IV rtPA and may have a favorable response to thrombolytic therapy.
AHA Guidelines: Early CT Infarct Signs

• There are insufficient data to make a strong recommendation regarding the use of IV rt-PA treatment in the rare patient whose CT reveals extensive and clearly identifiable hypodensity yet show a well established stroke ictus onset time < 4.5 hours.

• While differences of opinion exist, some experts would recommend that thrombolytic therapy not be administered in these patients because a possibly unfavorable risk/benefit ratio.
Stroke Treatment

- Physical examination/conservative treatment
- Imaging study (CT or MRI) to determine if hemorrhagic (bleed) or ischemic (clot) type
- Intravenous clot dissolving drug (tPA) if within 4.5 hours of stroke onset
- Intra-arterial clot dissolving drug if within 4.5-6 hours of stroke onset
- Intra-arterial mechanical clot retrieval if within 6 hours of stroke onset
- Remember: Time is key!
Pre-Retriever

Neurointerventional Techniques

Concentric Retriever Deployed

Post Retriever
Multimodal CT - Ischemia, Acute Stroke and Completed Stroke: NECT, CTA and CT Perfusion

NECT

PCT

CTA
Case #3

• 39 yo RH WM with history of hyperlipidemia presents with recurrent episodes of left hemiparesis while therapeutic on warfarin therapy
Sensitivity and PPV of CTA for intracranial stenosis (98% v. 70) and occlusion (100% v. 87%) is higher than 3D TOF-MRA using DSA as gold standard*

*Bash, et al. AJNR 2004
Perfusion CT - Findings
Perfusion CT - Findings

CBV

CBF
Quantitative CT Perfusion
Mean Transit Time Map (MTT)

Pre Diamox

Post Diamox

Note: Diamox (Acetazolamide) tests cerebrovascular reserve
CT Perfusion: Identification of The Ischemic Penumbra

<table>
<thead>
<tr>
<th>Tissue type</th>
<th>CBF</th>
<th>CBV</th>
<th>MTT</th>
<th>Tissue State</th>
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<tbody>
<tr>
<td>Normal tissue</td>
<td>→</td>
<td>→</td>
<td>→</td>
<td>Normal</td>
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<tr>
<td>Viable, oligemic</td>
<td>↓</td>
<td>→</td>
<td>→</td>
<td>Penumbral</td>
</tr>
<tr>
<td>Viable, ischemic</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>Penumbral</td>
</tr>
<tr>
<td>Infarcted – bland</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>Core</td>
</tr>
<tr>
<td>Infarcted, reperfused</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>Core</td>
</tr>
</tbody>
</table>

Wintermark, et.al, Ann Neurol. 2002;51:417-432
Case Discussion- CTP: Hypoperfusion and Impaired Cerebrovascular Reserve

• Finding
  – CTA: 83% MCA stenosis
  – Perfusion CT: resting perfusion deficit in MCA territory worsened following diamox
  – Indicates impaired cerebrovascular reserve

• Clinical Consequence
  – Pt treated with florinef for presumed hemodynamic events with resolution of symptoms
  – Consider EC-IC bypass
Quantitative and qualitative analysis of the size and position of the superficial temporal artery – 3D CTA and 2D MPR Images
Loss of Autoregulatory Control in Reperfused Infarct Zone - CT Hyperperfusion

CT and Perfusion CT scan performed 24 hr after thrombolysis for left MCA occlusion

Source image

CBF

CBV

MTT
Case Discussion- PCT and Risk of Hemorrhagic Transformation

• Finding
  – NCT: Small established infarct, MCA branch
  – Perfusion CT:
    – Flow re-established to most of left MCA territory.
    – Recanalization in area of completed branch MCA infarction with luxury perfusion.

• Clinical Consequence
  – Consider stopping hypervolemic, hypertensive therapy to avoid potentiation of hemorrhagic transformation and reperfusion injury.
Computed Tomography (CT): CT Perfusion – Whole Brain Blood Flow Analysis

Courtesy Toshiba – Aquilion 1 5 mSv, 50 cc contrast, 20 second exposure
## Detection Power of Perfusion CT

<table>
<thead>
<tr>
<th>Author</th>
<th>Territorial infarcts</th>
<th>Non-territorial infarcts</th>
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<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>Maruya, 2005</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Mayer, 2000</td>
<td>93%</td>
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CT Monitoring of Stroke Complications

Hemorrhagic transformation

Hemicraniectomy for malignant cerebral edema
## Comparative Evaluation of Imaging Modalities

<table>
<thead>
<tr>
<th>Feature</th>
<th>CTA</th>
<th>DSA</th>
<th>TOF-MRA</th>
<th>US</th>
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<tbody>
<tr>
<td>String sign</td>
<td>+</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Plaque characterization</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+/1</td>
</tr>
<tr>
<td>Tandem stenosis</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Ulcerations</td>
<td>+</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Arterial dissection</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Web stenosis</td>
<td>+/-</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Metallic stents</td>
<td>+</td>
<td>+</td>
<td>-</td>
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CT Perfusion – Current Limitations

Requires intact blood-brain barrier
Limited to 4-5 total slices (MR=7-15)
Motion sensitive
Ionizing radiation
Contrast allergy
Renal insufficiency
Carotid atherosclerosis and Stroke

Up to 83% of all stroke, TIA or amaurosis fugax believed to be due to carotid bifurcation atheromatous disease

Pharmacotherapy 1998;18:97s-93s.
Carotid Artery Source
Carotid Endarterectomy
NASCET: Endarterectomy Protects from Stroke

Graph plots proportion without stroke.
NASCET - Results

“CEA produces an absolute reduction of 17% in stroke at 2 years when compared to ASA in symptomatic patients with 70% or greater ICA stenosis. Risk of no treatment is 26%. Risk of CEA is 9%”.

CTA and Cervical Stenosis - Desirable Imaging Information

- High quality visualization
- Accurate quantitation
- Location relative to cervical column
- Eccentric stenosis
- Tandem stenosis
- Carotid and Vertebral artery stenosis
- Nonatherosclerotic stenosis
Helical CTA in Tandem stenosis
Non-atherosclerotic causes of arterial stenosis

Uncovertebral Joint osteophyte
Multidetector CT Angiography - Plaque Characterization

<table>
<thead>
<tr>
<th>Plaque Type (Coronary)</th>
<th>HU Density</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft¹</td>
<td>14 ± 26</td>
</tr>
<tr>
<td>Lipid rich²</td>
<td>50 ± 12</td>
</tr>
<tr>
<td>Intermediate/Fibrous¹,²</td>
<td>91 ± 21</td>
</tr>
<tr>
<td>Calcified¹</td>
<td>419 ± 194</td>
</tr>
</tbody>
</table>

¹ Schroeder S, et. al., J Am Coll Cardiol 2001;37:1430-1435
² Nikolau K, et.al., Radiology 2001;221:503
Multidetector CT Angiography-Plaque Characterization

“Further studies will be required to determine if MD-CTA of carotid atherosclerosis with noncalcified components can identify vulnerable plaque, or patients at risk of developing atheroembolic complications”

Fayad ZA, et.al., Circulation. 2002;106:2026-2046
Multidetector Protocol T4-Vertex

- GE LightSpeed
- Pitch 3.75 HQ
- Collimation 1.25 mm
- Recon interval 0.625
- FOV 180 mm
- Matrix 512 X 512
- Inj. Rate Min. 3-4 cc/sec
- Timing injection or SmartPrep
- 30-60 second exposure
- 120 kV, 300 mA

- Sensation 16
- Collimation 0.75 mm
- Recon interval 0.5
- mAs 350, kVp 120
- FOV 180 mm
- Matrix 512 X 512
- Inj. Rate 3-4 cc/sec.
- SmartPrep or hand inj
- <23 second exposure
- 6.8 mm/rotation feed
- H40f medium
CTA and Carotid Stenosis

- Accurate quantiation
- Anatomic localization
- Luminal and non-luminal information
- Tandem stenoses
- Longitudinal follow-up
- Endoluminal visualization
- 3D visualization
- Extended coverage
Multi-detector helical scanning =
Increased scan coverage
Visualization of vertebral arteries
CTA axial or axial oblique source images correlate more closely with DSA than do MIP or SSD images for all degrees of stenosis (Stroke 2000;31:2168-2174)
DSA may underestimate eccentric luminal stenosis.
Volume Rendered Helical CTA of Neck: Endoluminal Fly-Through Showing Calcific Left Carotid Plaque
CTA and Carotid Stenosis

“CTA has been shown to have a pooled sensitivity of 95% and a specificity of 98% for the detection of >70%, even if only single slice techniques are used”

3D and 2D MPR Helical CTA vs. DSA
CTA in Acute Carotid Dissection with complete occlusion
Subacute/chronic arterial dissection
70% of dissections heal spontaneously

Desfontaines P. Acta Neurol Belg. 1995;95:226-234

Dissection causes 0.4-2.5% of all strokes, and 5-20% of stroke in young

Proenzale J.M. AJR 1995;165:1099-1104
Type I Fibromuscular Dysplasia – Left Cervical Internal Carotid Artery
Aneurysm Rupture
Intraoperative Aneurysm Rupture
Correlation Between CTA and Intraoperative Findings

3D-CTA

Intraoperative Photo
3D CTA shows Ca++ at neck
Surgical Planning with CTA – Giant Partially Thrombosed Peripherally Calcified Fusiform Right MCA Aneurysm
Discordant findings

Helical 3D CTA shows left PComA aneurysm, long segment stenosis of left M1 segment.
Value of soft tissue windows

3D CTA with soft tissue window shows saccular aneurysm with large thrombosed component causing mass effect upon left M1
37 year-old female: 1.2 mm laterally projecting right SC-ICA aneurysm

2D-DSA

3D-CTA
Bone Subtracted CTV – Petrocavernous ICA Segments
Noninvasive Longitudinal Follow-up: ACOM Aneurysm

11/5/01  2/21/02  9/9/03

4.9 mm AP X 2.9 mm TR X 3.2 mm CC  
4.9 mm AP X 2.8 mm TR X 3.2 mm CC  
7.0 mm AP X 2.8 mm TR X 3.2 mm CC
Time Resolved CT Angiogram
Left Carotico Ophthalmic Aneurysm
Helical CTA: Artifacts and Limitations

- Gross patient motion artifacts
- Beam hardening artifacts: amalgam, hyperconcentrated contrast
- Simultaneous arterial and venous imaging
- Reconstruction artifacts
- Contrast gradient artifacts
- Stent blooming artifacts
- Contrast allergy
- Low ejection fraction (heart failure)
- Overestimation of stenosis in thick calcific plaque
Conclusion

CT is a flexible and powerful noninvasive tool to evaluate vascular causes of stroke due to cerebrovascular

CTA offers unique advantages over DSA and MRI
Relationship Between Plaque Rupture and Inflammation

• No measurable FDG uptake in normal carotids
• Autoradiography confirmed accumulation of deoxyglucose in macrophage rich areas of plaque
• Conclusion: Plaque rupture may be a consequence of inflammatory cell activation

The Role of Shear Stress in Atherogenesis

- An essential feature of atherogenesis
- Fluid drag force on vessel wall is mechanotransduced into biochemical signals
- The endothelium controls local arterial responses by transduction of shear stress
- Physiological laminar shear stress is crucial for normal vascular functioning
- Therefore, laminar shear stress is *atheroprotective* by inhibiting vascular proliferation, thrombosis and inflammation
Carotid Shear Stress – Normal Diastolic/Systolic Condition
Carotid Artery Pathology

• Carotid “string-sign” – critical stenosis
• Bifurcation ulcer crater
• Plaque characterization and stroke risk
3D TOF-MRA vs. DSA – Critical Stenosis

Possible flow gap with stenosis (>60%) or turbulent flow
CE-MRA vs TOF-MRA

• Advantages
  – Shorter scan time
  – Large coverage
  – More accurate stenosis, string sign and occlusion
  – Contrast independent of flow direction
  – Less contamination from short T1 materials
  – Better SNR vs. TOF-MRA
  – Less signal loss from slow/turbulent flow
  Willig DS, et al., 1996

• Disadvantages
  – Longer prep time
  – Lower spatial resolution vs. TOF-MRA
  – Stents and metallic artifact
  – T2* effects with bolus
  – Maki effect (k-space ordering)
  – May miss string sign
  – Vessel diameter varies during contrast bolus cycle
  – No calcifications
3D TOF-MRA vs 1.5T CE-MRA

In-plane flow saturation effects
Contrast Enhanced 3.0T MRA: Basilar tip Aneurysm – Volume Rendered Video Clip

20 sec breath hold, voxel size 0.7 x 0.7 x 0.9 mm³
Contrast Enhanced 3T MRA
Time-Resolved CE-MRA at 3.0T: Right Subclavian Steal

Phase Contrast MRA

Temp resolution 1.5s, In-plane resolution: 1 x 1.3mm², at 3.0T using GRAPPA x3

CE-MR Angiography* and Black Blood Techniques

Cross sectional MRA is accurate in predicting degree of stenosis vs. DSA**

MRA Limitations – 3D TOF and CE-MRA

Maki Effect
Arterial cycle
T2* Effect

Blood Products
Flow gap
Motion
CE-MR Angiography – Major Advantage over 2D-TOF

• Cross-sectional CE-MRA may be accurate in predicting stenosis severity vs. en-bloc endarterectomy specimen.¹

Summary: Advantages of CTA over TOF-and CE-MRA

• Provides information about vessel lumen and vessel wall in single study vs. contrast enhanced MRA (CE-MRA) and TOF-MRA.
• No vascular signal artifacts arising from slow/complex/turbulent/in-plane flow vs. TOF-MRA and black blood MRA techniques.
• Higher spatial resolution
• Easier to acquire
Disadvantages of CTA vs. TOF-MRA and CE-MRA

- Radiation
- Contrast allergy
- Less coverage vs. CE-MRA using single detector systems
- Longer processing time
- Renal insufficiency
Carotid Ulceration

- Known thromboembolic source
- May be a marker of unstable plaque
- Presence and location
- Size
- Number
- Response to therapy
CT and MR Imaging Findings

CT

MR- DWI
3D TOF- MRA
Discussion – Proximal Embolic Source

• Finding
  – DWI-positive TIA
  – DWI is positive in ~56% of TIA patients
  – Embolic appearing lesion
  – CTA showed left carotid stenosis with ulcer crater

• Radiologic facts
  – Sensitivity and specificity for the detection of >60% stenosis is 87% and 90%, respectively and high for ulcer crater detection¹

Carotid Dissection – Confirmation and Aging of Injury
Imaging Findings – DWI hyperintense, ADC hypointense, T2W and FLAIR hyperintense = watershed infarct
Carotid Dissection – Circumferential Intramural Hematoma

Coronal Oblique 2D MPR

Axial 2D MPR
Carotid Stenting – Intraluminal Analysis
Recurrent Atherosclerosis is generally eccentric and irregular.
Intimal Hyperplasia is generally concentric and smooth.
Fibromuscular Dysplasia

• String of beads appearance
• Alternating strictures and dilatations
• ICA, 2nd most common site
• Type I, 80-85% - segmental beading
• Type II, 6-12% - long tubular
• Type III, 4-6% - one side of artery
• DSA and CTA unable to differentiate between intimal, medial and subadventitial types
• Ischemia 20%, TIA 30%, thromboembolic stroke 6%, dissection 10-20%
• 33% also have renal FMD
• 10% also involve vertebral artery
Type II Fibromuscular Dysplasia.

Note smooth narrowing of long segment of cervical segment of the left internal carotid artery.
Short Segment FMD – Type III

Coronal 2D curved oblique MPR

Sagittal 2D curved oblique MPR
Rapid, Automated Post-Processing of Carotid CTA’s
Centerline segment with isolated volume rendered vessel and curved oblique reformatted image in single display.
Automated segmentation of smaller arteries with segments traveling close to bone
Helical CTA
Artifacts and Pitfalls:
Beam hardening artifacts and contrast entry phenomena
CTA Advantages

• High spatial resolution: >MRA, < DSA
• Accurate measurements
• Comprehensive
• Minimally invasive
• Widely available
• Low cost
• Large coverage with multidetector systems
CTA Limitations

• Limited direct hemodynamic information
• Radiation – equivalent to CT of brain performed with an without contrast
• Contrast reaction (1:30,000)
• Simultaneous arterial and venous imaging
• Renal insufficiency
• Gross motion in 3D images