Neuroimaging Selection for Intravenous Thrombolysis and Endovascular Thrombectomy

Bryan Y. Yoo, MD
Associate Clinical Professor
Section of Diagnostic Neuroradiology
David Geffen School of Medicine at UCLA
Financial Disclosures

• None.
Objectives

• Using neuroimaging to evaluate the acutely ischemic brain
  • Exclude hemorrhage
  • Evaluation and quantification of the infarct core
  • Identification of intravascular thrombus
  • Penumbral imaging

• Imaging criteria in standard treatment windows for intravenous and endovascular therapies

• Imaging criteria in late or unknown treatment windows for intravenous and endovascular therapies
Endovascular Therapy for Stroke

• 0-6 hours: MR CLEAN¹, EXTEND-IA², ESCAPE³, SWIFT-PRIME⁴, REVASCAT⁵
  • Absolute benefit of endovascular therapy compared to IV-TPA alone for functional independence (MRS ≤2) ranged from 13.5 to 31%

• 6-24 hours: DAWN⁶, DEFUSE-3⁷
  • 28-35% increase in functional independence (mRS score of 0-2) over medical therapy
  • IV-TPA was not administered

• Neuroimaging plays critical role in determining eligibility for mechanical thrombectomy

---

Intravenous Therapy for Stroke: IV-TPa

- Intravenous tPA has been demonstrated to be beneficial up to 4.5 hours after symptom onset (Lancet 2010; 375:1695-1703)
  - NCCT remains sufficient to treat with IV-TPa in the 0-4.5 hr window
  - Exclude hemorrhage, large infarction
- Recent clinical trials IVT may be beneficial in unknown LKW (WAKE-UP\(^1\)) or LKW between 4.5-9 hrs (EXTEND\(^2\))
  - Favorable outcome (MRS 0-1): WAKE UP 11.5%, EXTEND 6% over placebo
  - Higher rates of symptomatic hemorrhage, mortality
  - Excluded patients who underwent MT - adjunct treatment role unknown
  - Advanced imaging techniques (MRI, CTP) to assess tissue status in unknown or late LKW

Evaluation of Hemorrhage: CT and MR

• NCCT: Imaging standard for acute intracranial hemorrhage

• MRI: GRE/SWI
  - 100% sensitivity and 100% accuracy in detection of acute hemorrhage compared to NCCT (Stroke 2004; 35:502-6)
  - GRE pitfalls: Calcification, fat, air
  - MRI superior in detection of chronic microhemorrhages (JAMA 2004; 292:1823-30)
IV-tPA and Cerebral Microhemorrhages

• Cerebral microhemorrhages (CMH) may be a marker of hemorrhagic prone state due to microangiopathy (hypertension vs amyloid)

• Risk of ICH in thrombolysis in patients with CMHs conflicting
  • Two meta-analyses reported sICH more common with baseline CMH, two meta-analyses and multicenter trial did not

• CMH on MRI **should not** be considered a contraindication to IV- tPA in otherwise eligible patients (Class 1, LOE B; AHA 2019 AIS guidelines)
Imaging the Infarct Core

- Infarct core imaging: NCCT, DWI, CTP
- Final infarct size critical determinant of clinical outcome
- Pre-treatment core volume for MT patient selection: Small core
- Rapid recanalization to prevent infarct growth

Associations between 90-day modified Rankin Scale (mRS) and 27-h infarct volume.

Gregory W. Albers et al. Stroke. 2015;46:2786-2794
Infarct Core: NCCT and ASPECTS

- NCCT remains dominant modality for stroke evaluation
  - Low sensitivity (39%), high specificity (100%)  
    ([AJNR 1994; 32: 9-15; Neuroradiology 1996; 38:31-33])
- Quantification of infarct size challenging on NCCT
- ASPECTS: Systematic approach to assess and quantify early infarct change on NCCT

ASPECTS

= 8

http://www.aspectsinstroke.com/
ASPECTS

ASPECTS = 5

http://www.aspectsinstroke.com/
Patient Selection MT < 6 hrs: ASPECTS

• Pooled data from 5 endovascular trials (<6 hrs) (HERMES; Lancet 2016; 387: 1723–310)
  • ASPECTS 9-10 and 6-8: Both strongly associated with improved functional outcome
    • Similar benefit conferred between ASPECTS 9-10 and 6-8
  • ASPECTS 0-5: No statistically significant benefit for functional outcomes
    • Majority of trials excluded ASPECTS <5 – low sample size
    • Ongoing clinical trials evaluating low ASPECTS in MT

• 2018 AHA/ASA Guidelines for Management of Acute Stroke
  (Stroke. 2018 Mar;49(3):e46-e110)
  • Patients with ASPECTS of 6 or greater should be offered endovascular therapy within 6 hrs after symptom onset (Class I, LOE A)
Infarct Core: Diffusion Weighted Imaging

- Imaging surrogate for cytotoxic edema
- Delineate core with high precision and reproducibility
- Initial DWI lesion closely correlates to final infarct volume with recanalization
Infarct Core: CT Perfusion

- Estimate of infarct core using CTP
- No accepted consensus on most accurate parameter or thresholds: CBF vs CBV
- ET Clinical trials: 70% relative reduction CBF threshold for infarct core
- Measure of blood flow, not metabolic activity (unlike DWI)

Limitations of CT Perfusion to Identify Core
Patient Selection MT < 6 HRs: Core Volume DWI/CTP

- **DWI/CTP**: more precise measurement of core volume than NCCT
- Automated, volumetric assessment
- **Target**: *Small baseline core*
  - SWIFT PRIME (<6hr), DAWN (>6hr):
    Core vol < 50 cc
  - EXTEND IA (<6hr), DEFUSE3 (>6hr):
    Core vol < 70 cc

ADC<620 volume: 10 ml
Identification of Intravascular Thrombus: NCCT and MRI

- NCCT: Hyperdense MCA sign
- MRI: GRE artery susceptibility sign

  - GRE (82%) is more sensitive than NCCT (54%) for detection of acute thromboembolism (Radiology.2000;215:476–482.)
Length of Clot as Predictor of Recanalization by IV-tPA Alone

- IV-tPA is unlikely to recanalize thrombus > 8 mm in length based on hyperdense MCA sign on NCCT

Stroke. 2011;42:1775-1777
Detection of Intravascular Thrombus: CTA and MRA

• **CTA**
  - Rapid acquisition, high sens/spec

• **Time-of-flight MRA**
  - Susceptible to flow related artifacts
  - Long scan times (~7 min)

• **CE-MRA**
  - Rapid acquisition (~1 min)
  - Less susceptible to flow related artifacts compared to TOF
  - Lower spatial resolution
Thrombus Location and Outcomes

- All thrombectomy trials used CTA/MRA - Class 1 rec AHA
- Pooled analysis from 5 positive endovascular trials (HERMES; Lancet 2016; 387: 1723–310)
  - Clear benefit for ICA and M1 occlusions
  - Unclear benefit for M2 occlusions

![Diagram of cerebrovascular anatomy with annotations]

Stroke location (pinteraction = 0.17)

<table>
<thead>
<tr>
<th>Location</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>274</td>
</tr>
<tr>
<td>M1</td>
<td>887</td>
</tr>
<tr>
<td>M2</td>
<td>94</td>
</tr>
</tbody>
</table>

Favours control: 3.96 (1.65-9.48)
Favours intervention: 2.29 (1.73-3.04)
M1 MCA: 1.28 (0.51-3.21)

Imaging of Penumbra: CTP / MRP

- Penumbral imaging currently based on perfusion techniques
- Various parameters and thresholds used to define penumbra
  - **Penumbra: Tmax > 6s**
- Distinguishing between oligemia and true penumbra limited by perfusion
Day 8 MRI
Limitations of Imaging Penumbra

• Challenges of defining penumbra using perfusion
  • Sensitive to delay in antegrade flow from LVO, but may not distinguish from delayed retrograde flow from pial collaterals
  • Perfusion parameter thresholds may not be generalizable from patient to patient

• Alternatives to perfusion imaging
  • "Penumbra" can be inferred from presence of LVO and small core
  • Clinical/core mismatch based on small core and large clinical deficit
Extending Treatment Windows Beyond 6 Hours: Tissue-based selection

• Clear benefit for MT in late presenting patients: DAWN and DEFUSE3
  • MT within 6-16 hr LKW incorporated into 2019 AHA guidelines (Class 1, LOE A)
• Possible benefit of IV-TPA in unknown LKW or late presenting patients
  • IV TPA for unknown LKW included 2019 AHA guidelines (Class 2a, LOE B)
  • Confirmatory trials, benefit/safety of adjunct IV-TPA prior to MT unanswered
  • May consider in patients lacking target LVO, otherwise ineligible for MT
• Tissue-based patient selection in later windows: Advanced imaging (DWI, CTP) recommended
Infarct Growth Rates are Highly Variable: Tissue-based Approach to Patient Selection

Poor collaterals – large core, rapid progressors despite early times

Good collaterals - small core, slow progressors with later times

Imaging Selection Criteria for Mechanical Thrombectomy: > 6 hrs

**DAWN**
- LVO by CTA or MRA
- **Core/Clinical mismatch**
  - Core (DWI or CTP): 0-50 cc
  - Penumbra: NIHSS ≥ 10

**DEFUSE 3**
- LVO by CTA or MRA
- **Core/Perfusion Target mismatch**
  - Core (DWI or CTP): 0-70cc
  - Penumbra (Tmax>6s): mismatch ratio >1.8, mismatch vol >15 cc

Identify slow progressors: Good collaterals, small core, large penumbra – Tissue-based selection
61 F R sided weakness, facial droop, aphasia
LKW 9 hrs prior: NIHSS 12, L M1 occlusion

Core<50 cc, NIHSS>10; Mismatch ratio >1.8, Mismatch volume >15 cc:
Meets DAWN and DEFUSE 3 criteria
Thrombectomy: TICI 2B recanalization, no infarct expansion
Imaging Selection Criteria for IV-TPA: Undetermined LKW or Wake Up Stroke

• Using MR signature as “clock”
  • DWI: minutes after occlusion
  • FLAIR: ~ 6 hrs after occlusion
  • DWI/FLAIR mismatch: 78% to 93% spec, 65% sens for stroke onset within 4.5 hours (Lancet Neurol 2011; 10:978 and Radiology 2010; 257:782).

• Eligibility for IV TPA (WAKE-UP: NEJM 2018; 379:611-622)
  • (+) DWI, (-) FLAIR: IV TPA eligible
  • (+) DWI, (+) FLAIR: IV TPA ineligible
Imaging Selection Criteria for IV-TPA: 4.5 -9 Hour Window (EXTEND)

- MRI/CTP core/hypoperfusion mismatch
  - Core: DWI, CTP (CBF<70%)
  - Penumbra (Tmax <6 sec)
- Eligibility criteria (EXTEND; N Engl J Med 2019; 380:1795-1803)
  - Mismatch ratio > 1.2
  - Absolute difference >10 cc
  - Core < 70 cc
Conclusions

• IV TPA < 4.5 hr: Clock + NCCT
  • Exclude hemorrhage, large established infarct

• IV TPA unknown, > 4.5 hr
  LKW: MRI, CTP
  • DWI/FLAIR mismatch
  • Core/perfusion mismatch
  • May consider in late or unknown LKW, careful evaluation pt and imaging required

• MT < 6 hrs: LVO + small core
  • LVO on CTA/MRA
  • NCCT: ASPECTS 6-10
  • DWI/CTP: 50-70 cc or less

• MT > 6 hrs: DAWN/DEFUSE 3 criteria
  • LVO on CTA/MRA
  • DWI/CTP: 50-70 cc or less
  • Core/clinical (NIHSS) mismatch
  • Core/perfusion mismatch
Thank you for your attention!

• byoo@mednet.ucla.edu