Acute Ischemic Stroke Imaging Innovations

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Disclosures

Microvention – consultant
Covidien/Medtronic – consultant and proctor
Penumbra - Consultant
Surpass Medical/Surpass – shareholder
InNeuroCo, Inc – shareholder
Medina Medical - shareholder
Stroke Statistics

- Stroke is an important cause of death in the US
- 795,000 strokes/year in the US
- 25% death within 1 year after the initial stroke
- Near 50% of stroke victims will not regain functional independence
- Estimated costs: $68.9 billion in 2009

STROKE FUTURE

- Assuming no change in the age-specific rates of stroke, approximately 1.1 million Americans will suffer a stroke in 2025

STROKE TYPES

Total Stroke: 695,000

Ischemic Stroke (85%): 590,000
- As many as 40% due to large vessel occlusion
  - 236,000

Hemorrhagic Stroke (15%): 105,000

IV tPA Reperfusion Limitations

- Location
  - Vessel occlusion location prognostic of response*
    - Distal ICA  4.4%
    - M1-MCA  32.3%
    - M2-MCA  30.8%
    - Basilar  4.0%
  - Reperfusion most predictive of outcome (RR 2.7)

- Clot size (<8mm)**
  - Reperfusion remains strongly predictive
    - Mean discharge mRS
      - Reperfused  1.9
      - No reperfusion  4.4

*Bhatia Stroke. 2010;41:2254-2258, **Riedel, Stroke. 2011;42:1775-1777
Timing Is Critical – IMS I & II

Each 30 minutes = 10% loss!

(Khatri. Neurology, 2009)
Advances in Stroke Treatment
Therapy for acute ischemic stroke

“Standard” (…or old) imaging criteria

- Standard imaging: no hemorrhage or extensive infarction
- NINDS and ECASS III: IV tPA up to 3 or 4.5hs

Changing perspective

- A fixed time window is not physiologically based
- Functional imaging can identify patients who might benefit from “delayed” treatment
A NEW ERA
MR CLEAN

A Multicenter Randomized Clinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands
Imaging critical component for patient selection!
# Main Current AIS-LVO Trials

<table>
<thead>
<tr>
<th></th>
<th>Recanalization</th>
<th>90-day MRS 0-2 Interventional Arm</th>
<th>90-day MRS 0-2 Medical Arm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MR CLEAN</strong></td>
<td>58.7%</td>
<td>32.6%</td>
<td>19.1%</td>
</tr>
<tr>
<td><strong>ESCAPE</strong></td>
<td>72.4%</td>
<td>53%</td>
<td>29.3%</td>
</tr>
<tr>
<td><strong>EXTEND-IA</strong></td>
<td>86%</td>
<td>71%</td>
<td>40%</td>
</tr>
<tr>
<td><strong>SWIFT PRIME</strong></td>
<td>88%</td>
<td>60.2%</td>
<td>35.5%</td>
</tr>
</tbody>
</table>
CT role: evaluation of acute stroke

• Exclude hemorrhage and “stroke” mimics
  ■ Hemorrhage, tumor, etc.

• If ischemic:
  ■ Exclude massive infarction
  ■ ASPECT Score
    ■ Very large infarcts do not do well even with early recanalization
  ■ Determine site of occlusion

• Assess potential for reversibility
  ■ Differentiate dead from viable but still “at risk” tissue - “Ischemic penumbra” with functional neuroimaging
Infarct detection with CT: Early signs

- Hyperdense artery sign
  - Densest vessel visualized
- Loss of gray/white differentiation
  - Subtle but usually positive within 1-3 hours
  - Cortical band or insular ribbon sign
  - Obscuration of deep gray matter often the key - lentiform nucleus

CT sensitivity for detection of acute infarct in patients presenting in less than 6 hours after the onset is low (approximately 60%) - Horowitz SH. Stroke 1991
Examine all the images at the ganglionic and supra-ganglionic levels.

Take off 1 pt from 10 for every region that is affected.

**ASPECTS**

8-10 Small core.

6-7 Moderate core.

0-5 Large core.
24h post EVT NIHSS 1
Should we go ahead???

- 40yo M sudden onset of right sided hemiplegia during exercising
Should we go ahead???
Should we go ahead???
When not to intervene? Ex. 1
44F presented left facial and left UE and LE weakness

3PM

6:25PM
MR of Hyperacute Infarction: standard sequences

- Standard sequences usually negative for parenchymal changes
  - No vasogenic edema (or mass effect)
  - No parenchymal enhancement
- Absent or slow arterial flow
  - “Flow voids” missing
  - Intravascular enhancement
The four P’s
Systematic approach for stroke imaging

- Parenchyma: How much damage has occurred?
  - DWI or CTA-SI or CBV

- Pipes: What is the cause of stroke – MRA or CTA

- Perfusion: What is the status of hemodynamic compensatory mechanisms? – PWI or CTP

- Penumbra: How much tissue is still at risk?
  - PWI minus DWI or CBF minus CBV/CTA-SI
The four P’s: Parenchyma

Diffusion Weighted Imaging (DWI)

The most sensitive technique to identify the “core” of the infarct

- Water shifts to intracellular space – cytotoxic edema and increased viscosity
- Intracellular “cytotoxic edema” results in slow Brownian motion of water - “diffusion restriction”

Gonzalez RG, et al. Radiology 1999
65y F 2h after the onset
Reversible DWI Abnormalities

- Initial DWI abnormalities may resolve if occluded vessel is quickly reopened
- May see with other entities:
  - Post-ictal, Hemiplegic migraine, Transient global amnesia (TGA), venous hypertension, venous thrombosis, DAVF
Reversible DWI: Venous hypertension/ischemia

Patient with acute onset right sided weakness
Reversible DWI: arterial ischemia

4pm

8pm
Reversible DWI: Venous ischemia
Post-embolization LCCA injection
Follow-up imaging

No evidence of infarction on CT or MRI
The four P’s #2: **Pipes**

**CTA and MRA**

- Localization of vascular etiology is important
  - Source of emboli
  - Large vessel occlusions (ICA, M1, basilar) respond poorly to IV tPA
  - IA options defined by anatomy, collaterals
CTA source images for acute infarction

- NCCT and CTA source images compared (51 pts)
- Follow-up imaging to confirm infarct volume
- Results: 33 patients had an infarct
  - NCCT sensitivity: 48%
  - CTA source image sensitivity: 70%
- Conclusion: CTA source images more sensitive for early infarction and more accurate for prediction of final infarct volume

Goal: Evaluate capillary/tissue level hemodynamics in brain parenchyma

- CBF – measure of the volume of blood perfusing an area of tissue per unit time
  - Neurological dysfunction - <18-20 ml/100gm/min
    - Potentially salvageable
  - Neurological dysfunction - <10 ml/100gm/min
    - Cell death within minutes
Autoregulation

- Initial mechanism of autoregulation
  - Increasing oxygen extraction fraction (OEF)

- Primary mechanism of autoregulation
  - Vasodilatation
    - Decreases cerebral vascular resistance (CVR)
    - Increases cerebral blood volume (CBV)

\[
\text{CBV} \quad \text{CBF} = \frac{\text{MTT}}{\text{MTT}}
\]

The 4th “P”: Penumbra - Tissue at risk

Table 4
Perfusion CT Analysis of Hyperacute Ischemic Stroke

<table>
<thead>
<tr>
<th>Entity</th>
<th>MTT</th>
<th>CBF</th>
<th>CBV</th>
<th>Nonenhanced CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penumbra</td>
<td>Elevated (&gt;145%)</td>
<td>Decreased</td>
<td>Normal or mildly increased</td>
<td>Normal findings or brain swelling</td>
</tr>
<tr>
<td>Infarct core</td>
<td>Elevated</td>
<td>Markedly decreased (&lt;2.0 mL × 100 g⁻¹)</td>
<td>Hypoattenuating parenchyma</td>
<td></td>
</tr>
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</table>
Large Mismatch
Large penumbra
When not to intervene? Ex. 1
CT Perfusion: RAPID Processing

Auto Image Analysis:
- motion & time correction
- AIF & VOF selection
- deconvolution & map generation
- CTP or DWI and PWI lesion segmentation
- Lesion volume calculation

Images on PACS
00:05:00
auto-send via DICOM

RAPID image analysis complete
00:04:30

CT/MR tech pushes CTP/DWI & PWI to RAPID via DICOM

00:00:30
image arrival

Stroke MRI/CTP

00:00:30
image arrival

Courtesy Raul Nogueira, MD
RAPID for CT and MRI
Fast, standardized, fully automated, quantitative, thresholded mismatch

CT perfusion

CT relCBF
Diffusion MRI

RAPID
ischemic core
segmentation
CT relCBF<30%

Tmax

RAPID
Tmax>6sec
segmentation

Ischemic core: 6mL  Perfusion lesion: 58mL
Mismatch ratio = 9.7  Absolute mismatch = 52mL
→ Randomize patient

Ischemic core: 7mL  Perfusion lesion: 55mL
Mismatch ratio = 7.6  Absolute mismatch = 48mL
→ Randomize patient

Straka et al JMRI 2010
83 yo Man – NIHSS 14 – CTA Right M2 Cutoff – Not IV TPA Candidate – Patient/Family Declined IAT

RAPID: Prediction of Core and Penumbra

Estimated core 2 ml
Hypoperfusion (Tmax>6s) 57 ml
Mismatch volume: 55 ml
Mismatch ratio: 28.6

NOTE: Add volumes from BOTH slabs to determine eligibility:
Joint estimated core <= 50ml?
Joint mismatch volume > 15ml and ratio > 1.8?
Joint (Tmax>10s) <=100ml?

Courtesy Raul Nogueira, MD
RAPID: Lack of Reperfusion and Core Progression in to Predicted Penumbra

Core Progression: Follow-up DWI

Courtesy Raul Nogueira, MD
81 yo wake up stroke at 5am – last seen normal at 11pm
Aphasia, right hemiparesis NIHSS 20
69M partial lung resection 2 days prior; heavy smoker, HTN

- 15h after last seen normal
- Arrived at OSH at 1:30pm
- Aphasic, right hemiplegia; NIHSS - 24
- Not considered for IV tPA
- CT/CTA/CTP ordered
CTA/CTP @ 2:30pm
Stentretriever
6 x 30
CT 48h post procedure – NIHSS 4
Future Imaging in Acute Stroke???

- Mobile CT or Stroke Units may plan an important role in pre-hospital patient selection
- Improvements in Cone Beam CT imaging will create a paradigm shift

- ED
- Transfers
- Mobile Stroke Units

CBCT
CBCTA
CBCTP

EVT
Niu K, et al.
AJNR online
Feb 2016
Conclusions

- Therapeutic advances will require quantitative assessment of imaging data.
- Off hours availability of expertise must be developed.
- Functional imaging should be added to anatomical imaging for the assessment of acute stroke.
- The future is bright...
“We are what we repeatedly do. Excellence, then, is not an act, but a habit.”

Aristotle 384 BC-322 BC

Thank You!