Ischemic Stroke Imaging

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I own stock in Neuralstem, Johnson and Johnson, Medtronic, Esperion, Gilead, Mannkind, and Northwest Biotherapeutics
- The Ischemic Penumbra
- The role of Imaging
- CT and MRI
- Perfusion Techniques
- CTA/MRA
So what happens to brain tissue deprived of blood flow

After arterial occlusion, survival of brain tissue is dependent on the depth and duration of ischemia as well as the presence of collateral flow.

Animal data and PET studies in humans demonstrate existence of ischemic penumbra, non-functional (not electrically active) but viable brain tissue (Lassen NA 1990, Baron 1999).

Penumbral tissue may persist up to 24 hrs (Darby DG Stroke 1999).
The Ischemic Penumbra Physiologic Basis

First defined in 1981


A separate threshold for irreversible cell death (measured by measurement of extracellular potassium, as a marker for pump failure) was also reported (Branston NM Exp Neurol. 1974).

The condition of ischemic brain between the two thresholds was called the ischemic penumbra.

J Astrup, BK Siesjo, and L Symon (Stroke 1981 12: 723- 725)
The Ischemic Penumbra
Physiologic Basis

Progression to irreversible damage dependent on both the depth and duration of ischemia. (Jones TH J Neuro. Surg 1981).

Established that time is brain, and originated the time dependent concept of a dynamic penumbra that guides all modern stroke intervention.

The Penumbra is an electrophysiologic phenomenon. Imaging surrogates may provide an operational penumbra that is clinically useful.
Goals of Imaging

Establish Diagnosis: Hemorrhage versus ischemic, location of stroke, stroke size, exclude stroke mimics.

Guide Acute Treatment: Should an intervention be performed, and if so what. Determine presence of viable tissue, vascular anatomy, and site of occlusion. Exclude hemorrhage or a large completed infarct. Large vessel occlusions do better with endovascular treatment in addition to iv t-PA alone.

Secondary stroke prevention.

Monitor for complications/progression.
Modalities

Non-contrast head CT: x-ray based modality that is very fast and readily available. Based on attenuation (density) differences between tissues.

MRI: Takes advantage of magnetic properties of protons in different tissues. Most sensitive imaging modality to detect stroke, determine extent.
CT/MR Perfusion: Used to determine tissue viability. Clinically primarily use first pass contrast enhanced techniques.

CTA/MRA: Evaluate vasculature for cause of stroke, determine site of occlusion.
Hyperdense MCA, early left MCA stroke signs, disappearing basal ganglia
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Clinical Role of CT in ischemic stroke:

Exclude Hemorrhage, mimics (tumor) and large infarct core

Greater than 1/3\textsuperscript{rd} MCA distribution infarct is considered a relative contraindication to iv t-PA (ECASS Stroke 1999, Schellinger Stroke 2003).

ASPECTS scoring (Alberta Stroke Program Early CT Scores). 10 points for normal MCA. (Barber et al Lancet 2000)

Lose one point for each abnormal territory. Better interobserver reliability than determination of 1/3 rd MCA.
ASPECTS CT has good correlation with diffusion MRI ASPECTS for acute strokes to determine large area of infarct (Barber JNNP 2005, Nezu et al Stroke 2011). Trade off of accuracy for availability and speed.

Non Contrast CT has been shown to be an effective triage tool for stroke treatment with iv t-PA (NINDS, ECASS 3)
CTA/CT Perfusion

CT Angiography and CT Perfusion are new imaging methods that provide information in a rapid fashion that may be very useful in the management of patient’s with cerebrovascular disease.

CTA is able to determine the site of arterial occlusion in patient’s with acute stroke, which is useful in triaging patient’s to endovascular therapy. Endovascular treatment of large vessel occlusions is now the standard of care.
Clinical Trial Data for CT and CTA

MR CLEAN trial used non contrast CT (to exclude hemorrhage) and CTA for patient selection (within 6 hrs). NIHSS>2

ESCAPE trial used ASPECTS (>6) scoring of non contrast CT, CTA to document proximal vessel occlusion, and presence of collaterals on multiphase CTA (out to 12 hrs). NIHSS >5

REVASCAT Trial also used CT (ASPECTS >7) or MRI (ASPECTS>6) with CTA, MRA or DSA out to 8 hrs. NIHSS >6
Does NIHSS and proximal vessel occlusion select patients with large at risk tissue (correlates with large area electrically inactive)?

Does non contrast Head CT alone identify infarct core well enough? With ASPECTS?
Perfusion Imaging

Goal is to image the operational penumbra

Cerebral Blood Flow (amount of blood passing through a given region of brain per unit time measured in ml/100g/min).

Cerebral Blood Volume (amount of blood in a given region of brain tissue measured in ml/100 g)

Mean Transit Time (average amount of time it takes blood to pass through a region of the brain).

Tmax : time to peak of deconvoluted tissue residue function

CBF= CBV/MTT Central Volume Principal

Currently CT with a first pass contrast bolus tracking technique and MRI with a similar technique are used most frequently clinically .

Multiple post processing methods
CT Perfusion

CBF and CBV measurements with CT have the potential to identify an ischemic penumbra (Eastwood AJNR 2003).

Ischemia determined by reduced CBF and increased MTT.

Classically infarct core regions thought to have reduced CBV. MRI diffusion is gold standard for core infarct. CBV will be normal or even increased in areas that are potentially reversible.

Many different definitions of how penumbra and core are now defined. RAPID technique uses CBF <30% (core) and Tmax delay >6 s (penumbra). Validated with DWI MRI. CTP method used in both successful endovascular stroke trials.

Goal is to image the operational penumbra
Penumbra

CBF

CBV

MTT
Infarct

CBF

CBV

MTT
Infarct
Clinical Trial Data with Perfusion Imaging

SWIFT PRIME and EXTEND IA both used perfusion (CT or MRI) imaging with RAPID software (Tmax delay > 6 seconds for penumbra, CBF <30% of normal tissue for core) in iv t-PA eligible patients
MRI Findings of Acute Ischemic Stroke

MRI is the gold standard for the diagnosis of ischemic stroke.

Diffusion weighted imaging is the most sensitive method of detecting an infarct, with changes visible in 30 minutes. FLAIR sensitive within a few hours.

Diagnosis of stroke now includes anyone with MRI changes.

30% of previously classified TIAs have diffusion changes. Predicts increased risk of recurrent events. These events are now classified as strokes.
Left Internal Capsule stroke
Left Internal Capsule stroke
MRI Findings of Acute Ischemic Stroke

Late MRI evolution:
Contrast enhancement can start in a few hours, and last 6-8 weeks.
Diffusion weighted images “pseudo-normalize” in 7-10 days.
Clinical Pearl: Look at ADC map for diffusion images, otherwise may be fooled by T2 shine through
MRA: Rapid non-invasive imaging techniques that can give a good picture of vascular anatomy to help patient triage (large vessel occlusion, small vessel occlusion, aortic arch).

MRA techniques can use gadolinium based contrast but can also use flow sensitive techniques (time of flight versus phase contrast).
Summary

Non-contrast Head CT used to exclude hemorrhage or other lesions (non-ischemic) and large infarct. Alone sufficient for iv t-PA.

CTA to demonstrate a large vessel occlusion and non contrast head CT (ASPECTS>6) are sufficient for triage to endovascular therapy.

Strong physiologic basis for the existence of ischemic penumbra, which provides the basis for revascularization strategies.

Current imaging methods act as physiologic surrogates. Endovascular stroke trials have shown a benefit with and without penumbral imaging. More trials needed to elucidate.

Ability to rapidly non-invasively image the cerebrovascular tree is useful for stroke acute decision making and secondary prevention.
Thank You