Stroke: diagnosis and therapy

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• Stroke is a rapidly developing focal or global brain dysfunction of vascular origin lasting more than 24 hours

**Ischemic stroke (80%)**
**Intracerebral hemorrhage (15%)**
**Cerebral venous sinus thrombosis**
**Subarachnoid hemorrhage**
Ischemic stroke

New therapeutic options: intravenous thrombolysis (rtPA) and intraarterial or interventional thrombolysis.

Severe side effects: intracranial hemorrhage.

Selection of patients that benefit within 4.5 hours.
Time is brain

Physiology is brain
Normal blood flow in gray matter (Cerebral Blood Flow=CBF): 50-60 ml / 100gr / min

CBF < 35 ml / 100gr / min (50-60% of normal values): **BENIGN OLIGEMIA**

CBF < 20 ml / 100gr / min (30-40% of normal values): **tissue at risk** (PENUMBRA)

CBF < 10 ml / 100gr / min (20% of normal values): **IRREVERSIBLE CELL DEATH**
Volumes of cortical penumbra decline over time.

The initial perfusion threshold of the ischemic core rises progressively to reach the penumbra threshold.

Baron 1999
CBF < 10 ml / 100gr / min: DEPLETION OF ENERGY METABOLITES

**CELLS**
efflux of K+, influx of NA+, CA++, water

**CYTOTOXIC EDEMA**
(from the first minutes)

**VESSELS**
Blood Brain Barrier damage

**VASOGENIC EDEMA**
(after the first 6-8 hours)
Goals of Stroke Imaging

**PARENCHYMA**
- Exclude hematoma
- Show ischemia
- Assess hemodynamic changes
- Detect tissue at risk (penumbra)

**VESSELS**
- Intracranial circulation
- Extracranial circulation
Stroke Imaging

Computed Tomography
- Non-contrast CT
- CT Perfusion
- CT Angiography

Magnetic Resonance Imaging
- Conventional MRI
- Diffusion weighted imaging (DWI)
- MR Perfusion
- MRA
EXCLUDE HEMATOMA
EXCLUDE HEMATOMA
CT versus MRI

CT

EPI-GRE T2*

Stroke MRI is accurate in hyperacute intracerebral hemorrhage

Fiedbach JB et al. Stroke 2004
Early CT signs of ischemic infarction

• Dense artery sign

• Hypodensity of gray matter structures:
  Insular ribbon sign
  Disappearing basal ganglia sign

• Mass effect

Early CT signs are associated with worse prognosis, but are not contraindication for treatment
Dense artery sign

Visualization of the thrombus

The most early sign
35-67% of acute stroke (common in MCA)
32% positive predictive value for fatal outcome

Von Cumber et al AJNR 1996

Dot sign
Thrombus within the branch vessel
- MCA M2 and/or M3
Dense artery sign

Disappears within a few days or after thrombolysis – recanalisation in 50%

Calcified atherosclerosis
Higher density, persists in follow-up CT

False-positive cases
Calcified atherosclerosis
High hematocrit levels

BE CAREFUL!!
Hypodensity of gray matter structures

- Early hypodensity reflects **cytotoxic edema**
- Attenuation in HU is directly proportional to **degree of edema**
- Increase in tissue water content by 1% $\rightarrow$ decrease in parenchymal attenuation by 2-3 HU
Mass effect

Loss of cortical sulci

38% of cases
70% PPV for fatal outcome

Narrowing of Sylvian fissure
Enhancing visibility on CT

1. Setting narrower window width to enhance the gray–white matter contrast

   - Window width 70 HU, center level 30 HU
   - Window width 20 HU, center level 30 HU

2. Using CTA-source images

   - CTA source images with narrow window width >> NCCT in detection of early irreversible ischemia

   - Source CTA images
   - Lovblad 2010
EARLY DETECTION OF ISCHEMIA
conventional MRI

TIME

- Vascular changes
  - Absence of flow
  - Arterial enhancement
  - Increased signal intensity on FLAIR

- Parenchymal morphologic changes on T1 2-4 h
- Signal intensity (SI) changes
  - Increased SI on T2 6-8 h
  - Decreased SI on T1 16-24 h
Vascular changes

Absence of flow

Increased signal intensity on FLAIR

Arterial enhancement

T2 TSE

T1 MPRAGE
Parenchymal morphologic changes on T1

Signal intensity (SI) changes on T1

Signal intensity (SI) changes on T2
EARLY DETECTION OF ISCHEMIA
CT- conventional MRI

VASCULAR CHANGES (after mins)

PARENCHYMAL CHANGES (after hours)

MORPHOLOGICAL CHANGES

DENSITY (CT) SIGNAL INTENSITY (MR) CHANGES

LIMITATIONS

Early detection of cytotoxic edema
Assessment of hemodynamic changes
Distinguish between penumbra and infarct core
EARLY DETECTION OF ISCHEMIA
Diffusion-Weighted Imaging

Apparent Diffusion Coefficient (ADC) map
EARLY DETECTION OF ISCHEMIA
Diffusion-Weighted Imaging

CYTOTOXIC EDEMA

ATP-depletion
Na+-K+ pump failure
Increased intracellular viscosity
Decreased extracellular space

ADC ↓  DWI ↑

VASOGENIC EDEMA

Brain blood barrier damage
Cell destruction
Increased extracellular space

ADC ↑ variable DWI
EARLY DETECTION OF ISCHEMIA
Diffusion-Weighted Imaging

4 hours

T2TSE

DWI

ADC map

DWI >> Non-Contrast CT and conventional MRI in detecting acute ischemia

Sensitivity: CT: 16-70%
            DWI: 80-100%
BE CAREFUL!!

DWI and ADC map must be interpreted TOGETHER

T2 shine-through effect
ASSESS HEMODYNAMIC CHANGES
perfusion imaging

Measure tracer concentration

- at input (artery)
- in tissue (brain)
- at output (vein)

- Cerebral Blood Volume (CBV)
- Cerebral Blood Flow (CBF)
- Mean Transit Time (MTT)
- relative CBV, CBF, MTT, TTP

CT Perfusion
MR perfusion

T2* weighted imaging (GE DSC MRI)

Signal Intensity

0 200 400 600 800 1000

Time / s

0 200 400 600 800 1000

Gd-DTPA conc.

0 0.005 0.01 0.015 0.02

Cerebral Blood Volume (CBV)
Cerebral Blood Flow (CBF)
Mean Transit Time (MTT)

CBF = CBV / MTT

CBV map

CBF map

MTT map
CT perfusion

Non ionic contrast agent concentration.

Hounsfield units

Hoeffner et al., 2004
DETECT TISSUE AT RISK WITH MRI

PWI > DWI → MISMATCH (PENUMBRA) → THROMBOLYSIS

PWI = DWI → MATCH → NO TISSUE AT RISK → NO THROMBOLYSIS

PWI < DWI → REPERFUSION
3 hours after the onset of the symptoms

NCCT  
T1SE  
T2TSE  

FLAIR  
DWI  
ADC map
TIME WINDOW: 3 hours

THROMBOLYSIS
1 DAY AFTER INTRAVENOUS THROMBOLYSIS

T2TSE

FLAIR

T1SE

DWI

ADC map
1 DAY AFTER INTRAVENOUS THROMBOLYSIS
## Detect Tissue at Risk with CT Perfusion Parameters on Stroke

<table>
<thead>
<tr>
<th>Condition</th>
<th>CBV</th>
<th>CBF</th>
<th>MTT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benign Oligemia</strong></td>
<td>Normal or elevated</td>
<td>Moderately reduced</td>
<td>Prolonged</td>
</tr>
<tr>
<td><strong>Penumbra</strong></td>
<td>Normal or elevated or mildly decreased</td>
<td>Markedly reduced</td>
<td>Prolonged (&gt;145%)</td>
</tr>
<tr>
<td><strong>Infarct Core</strong></td>
<td>Severely reduced (&lt;2ml/100gr)</td>
<td>Severely reduced</td>
<td>Strong prolongation or not measurable</td>
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</table>
Threshold values for CT Perfusion

**CBV/MMT mismatch (penumbra)**

CBV <2ml/100gr = core infarct

MTT> 145% = ischemic area

Wintermark et al, 2008

Definite thresholds are not still available

High correlation between CTP and MRP

Schaefer et al, 2008
4 hours after onset

CT PERFUSION

NON CONTRAST CT

CBV/MTT mismatch (penumbra)

THROMBOLYSIS

1 day after thrombolysis
Assess the intracranial and extracranial vessels: CT Angiography, MR Angiography

Site of artery occlusion
Origin of infarction
Collateral blood flow
Thrombolytic therapy control
Magnetic Resonance Angiography (MRA)

3DTOF source images

CEMRA

DSA
RT Internal Carotid Artery dissection

Suspect dissection: use T1SE+Fat Saturation
Computed Tomography Angiography (CTA)

CTA source images

CTA-MIP

RT Internal Carotid Artery occlusion

CTA-VRT
STROKE CT PROTOCOL

• NCCT
  Exclude hemorrhage, or stroke mimics
  Early ischemic signs

• CT Perfusion
  MTT, CBV, CBF maps

• CT Angiography
  MIP images
  Source images with narrow window
STROKE MRI PROTOCOL

- DWI
- T2/FLAIR/T1
- T2*
- 3D-TOF-MRA
- PERFUSION
  - optional
- T1FS (neck)
- Contrast-enhanced MRA (neck)
Acute ischemic stroke: CT or MRI?

**CT**
- Widespread access
- Greater acquisition speed
- Highly sensitive for hemorrhage
- CTP (CBV), CTA (source images) correlate with DWI
- Multimodal CT (NCCT, CTP, CTA) as sensitive as MRI, CTP mismatch
- Radiation dose

**MRI**
- Less widely available
- Contraindications: Electronic implants, patient intolerance, medical instability
- T2*GE imaging > CT for acute hemorrhage
- DWI >>> NCCT
- MRI more sensitive than NCCT (Small infarctions, chronic infarctions, TIA) PWI/DWI mismatch
- No radiation dose
In May 2009, the American Heart Association/American Stroke Association (AHA/ASA) guidelines for the administration of rt-PA following acute stroke were revised to expand the window of treatment from 3 hours to 4.5 hours.

Patients with evidence of low attenuation involving more than a third of the distribution of the middle cerebral artery (MCA) on their initial noncontrast CT (NCCT) scan are thought to be at higher risk for hemorrhagic transformation of their ischemic stroke and must be excluded.
CONCLUSIONS

• Optimal time for stroke imaging: AS SOON AS POSSIBLE

• Optimal modality for stroke imaging: AVAILABLE (usually CT)

• Selection criteria for thrombolysis:
  - Current time window for intravenous thrombolysis: within 4,5 hours from symptoms onset
  - Current tissue window: < 1/3 MCA on NCCT
CONCLUSIONS

• Non conventional MRI (DWI, MRP) and CT techniques (CTP) offer new concepts for stroke pathophysiology (penumbra) and therapeutics.

• Ongoing clinical trials with new imaging techniques may further change the selection criteria for thrombolysis.