Stroke Diagnosis & Interventional Therapy:

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Neuroradiology Clinical Fellow

Stroke Statistics

- 97% of all stroke patients get no therapy.
- 97% of all stroke lawsuits:
  - are for nontreatment.
- True middle cerebral artery stroke:
  - kills 1/3 of patients within 1–6 months.
- 80% of survivors: left with severe disabilities.

JJ Connors, Reviews in CV Medicine
S2, Vol 2, Suppl 2, 2002,

Stroke Epidemiology

- # 3 adults cause of death in the U.S.
- # 1 adults cause of disability in the U.S.
- Incidence: 600-700.000 cases/year
- Mortality: 160.000 deaths/year
- Prevalence: 4.5 million stroke survivors
- Cost: > 30 billion dollars/year

Rafael Llinas, Stroke Director JH Sch. of Medicine Carotid Intervention Workshop, ASITN, Wash DC May/2003.

Stroke Pathophysiology

Ischemia => ↓ O2 & Glucose = metabolism is affected

↓

If prolonged => cell death

Cellular metabolism ⟶ from aerobic to anaerobic:

- ↑ intracell lactate
- ↓ intracell ATP

} Disrupted local homeostasis

↓

Cell death

When blood flow ↓ to 20-30 ml/100g/min (N: 50-60):

-neurons stop functioning => producing observable clinical symptoms

-but have not undergone cell death (may be reversible)

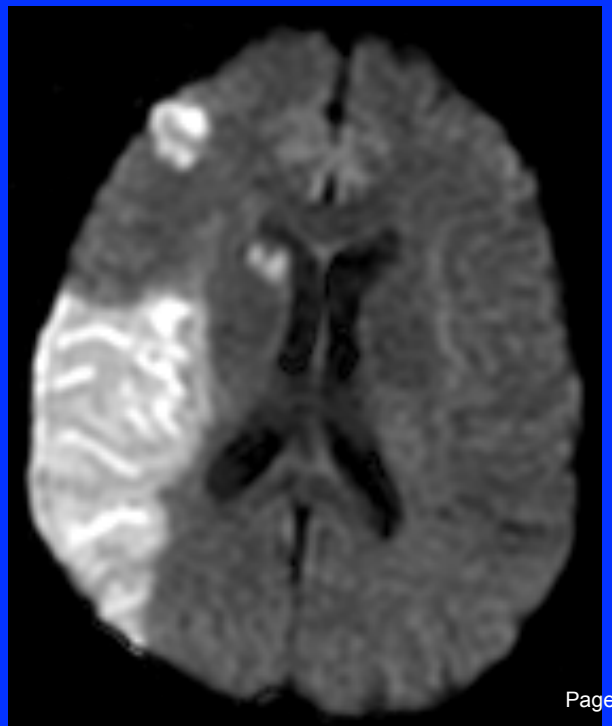
Ischemic Penumbra: cells may be salvageable by intervention

Dx: DWI

- Free diffusion:
  - molecules move in a random fashion
- Totally free diffusion: does not occur due to:
  - Cell membranes
  - Molecular boundaries
- In ischemia:
  - Alteration in membrane imposed restrictions
  - & thus → changes in the ADC of water

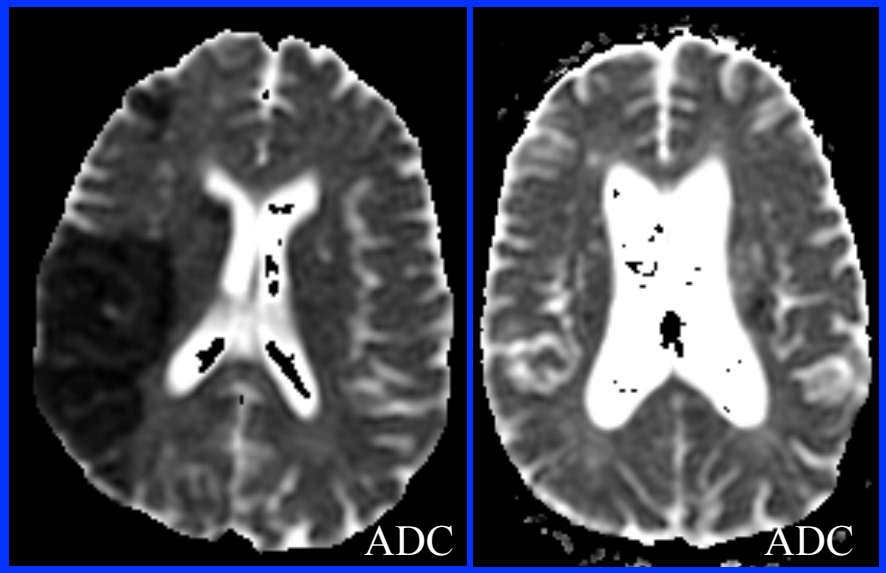
DWI

- Increased water motion ➔ "diffusional motion" ➔ signal loss = CSF
- Acute Infarction areas: water motion is constrained
  - < signal loss than normal areas on DWI
  - Infarct: hyperintense relative to unaffected parenchyma
- Chronic Infarct areas:
  - Increased diffusional motion
  - Thus: decreased SI on DWI



ADC Maps

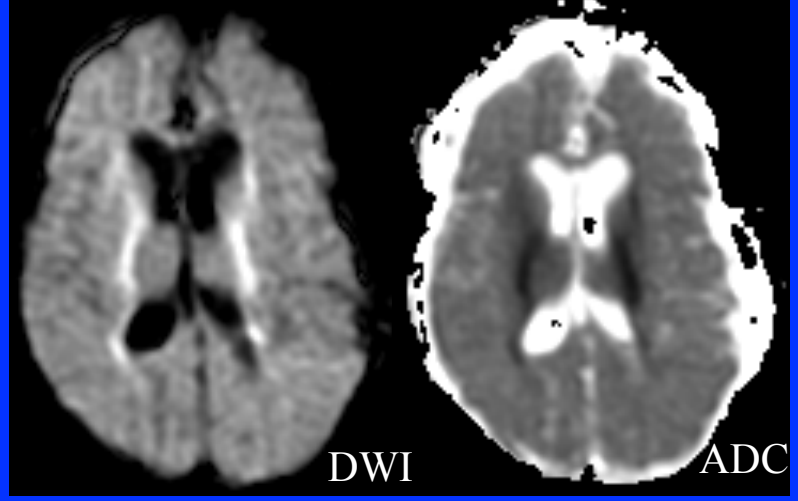
- Generated from DWI images
- Apparent diffusion is anisotropic
  - Normal WM: > parallel to nervous tracts
- ADC: quantitative measure of diffusion
  - High diffusion areas: hyperintense on ADC
  - Restricted diffusion areas: hypointense on ADC



Acute Infarct Old Infarct

http://sisbib.unmsm.edu.pe/BVRevistas/neurologia/Vol7_N1-2_2001/Imagenes-Infarto.htm
Radiology 2000; 217: 331-345

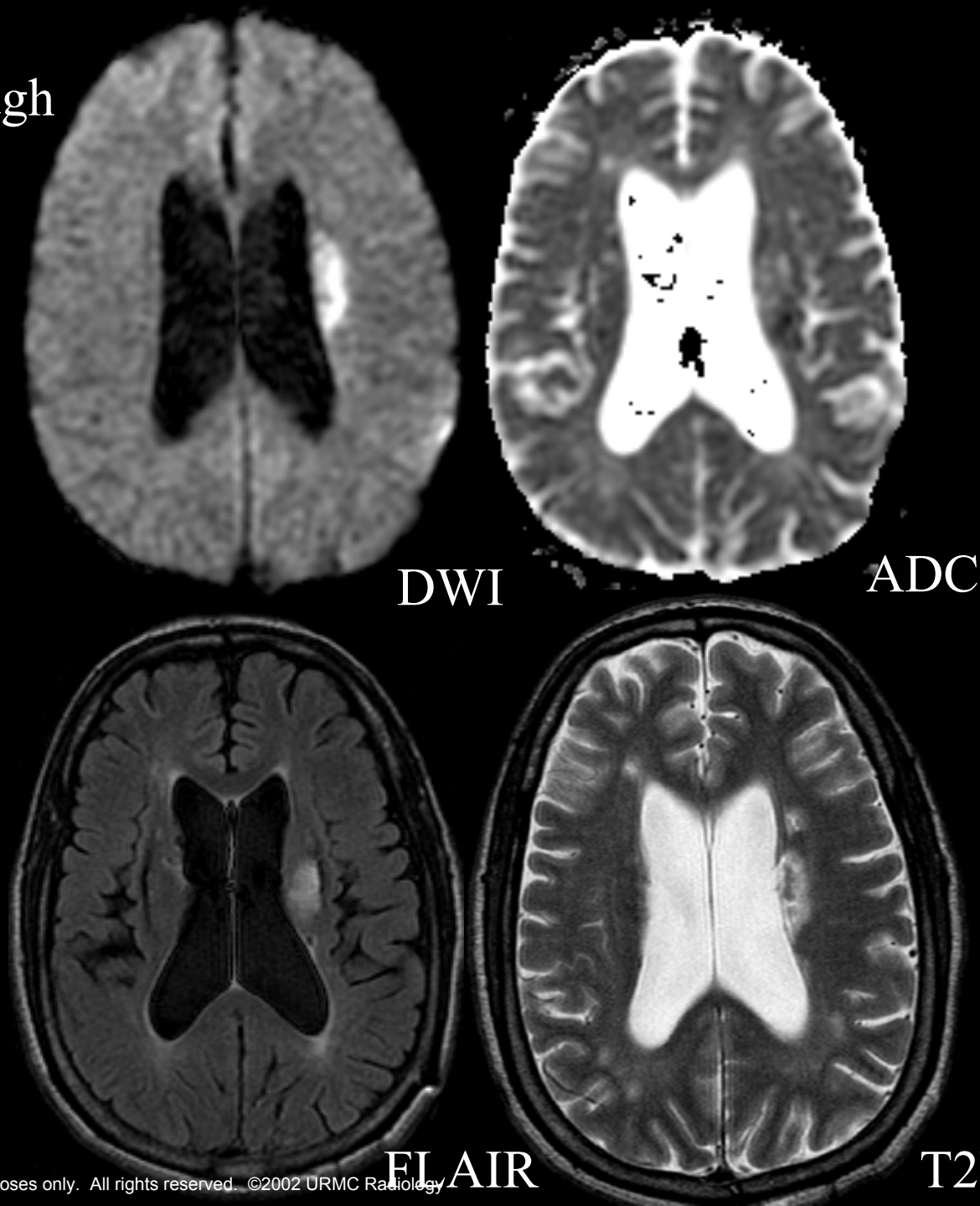
ADC Maps



- DWI used clinically > ADC because:
  - Lesions are easier to see
- ADC maps: used to exclude "T2 shine thorough"
  - DWI have a T2 contribution: means =
    - hyperintensity due to T2 effect
    - & not due to real restricted diffusion
      - Chronic infarcts, MS plaques, tumors etc

http://sisbib.unmsm.edu.pe/BVRevistas/neurologia/Vol7_N1-2_2001/Imagenes-Infarto.htm

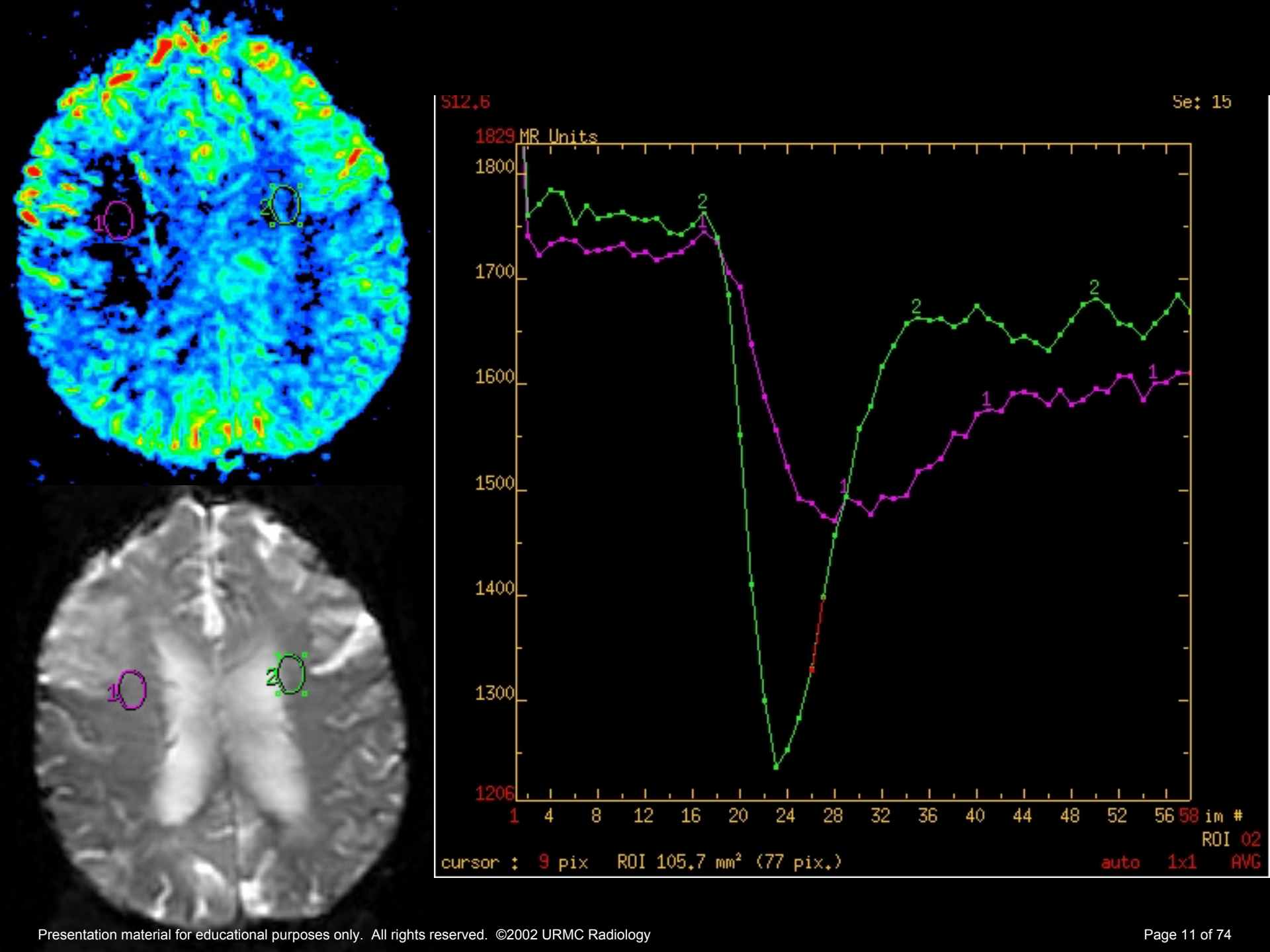
T2 Shine Thorough



Perfusion (PWI):

- PWI:
  - depends on effects of the first passage of Gd bolus
  - For specific regions of the brain:
    - It determines the time it takes for the bolus to reach that region
    - Compares to an analogous region, usually contralateral
  - rCBV: best predictor of final infarct size
  - TTP & MTT:
    - greatest sensitivity for any area of ischemic risk

Radiology 1999; 210 (2): 519-527,
Cerebral MR Perfusion Imaging, Sorensen/Reimer, Thieme 2000



Perfusion parameters :

- MTT: time between arterial inflow & venous inflow
- TTP: time from the beginning of ct injection to maximum peak of enhancement within a ROI
- CBV: volume of blood/unit of brain mass at any time
  - Normal: 4-5 mL/100 g
- CBF: amount of blood moving through a given amount of tissue per unit time.

RadioGraphics, Vol 23, #3, May-June 2003

Brain Perfusion

- Normal CBF: 50-60 mL/100g/min
- 35 (55%):
  - protein synthesis within neurons ceases completely
- 20 (35%):
  - synaptic transmission between neurons is disturbed => loss of fx of still viable neurons
- 10 (<20%):
  - irreversible cell death

Hyperacute Stroke

- Ischemic Penumbra (PWI – DWI) =
  - potentially salvageable tissue
- Perfusion perturbation:
  - total area of tissue at risk from ischemic stress
- Diffusion abnormality:
  - areas most likely destined to die as an infarct core

Perfusion maps compared with DWI:

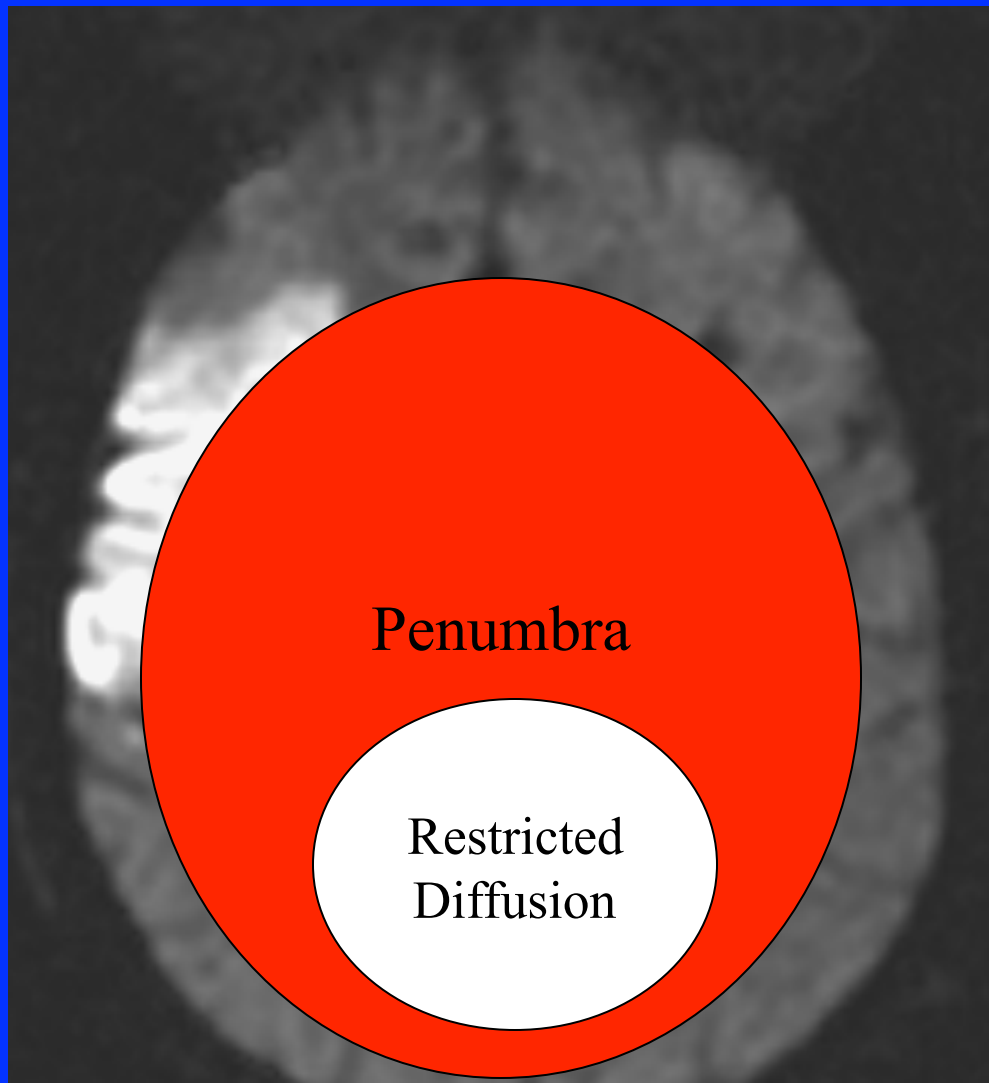
- DWI:
  - sensitive in acute stroke: 12 or > hrs
  - Hyperacute stage (<12 hrs): can be falsely negative in a significant minority
  - Fades away within 10-14 days

AJNR 2001; 22 (5): 915-921

- DWI alone: not enough
  - Incomplete ischemia + adequate collateral circulation:
    - May cause symptoms
    - Not necessarily undergoes irreversible damage
- PWI alone:
  - Smallest infarcts are beyond its spatial resolution
- Ideally: combine DWI & PWI!

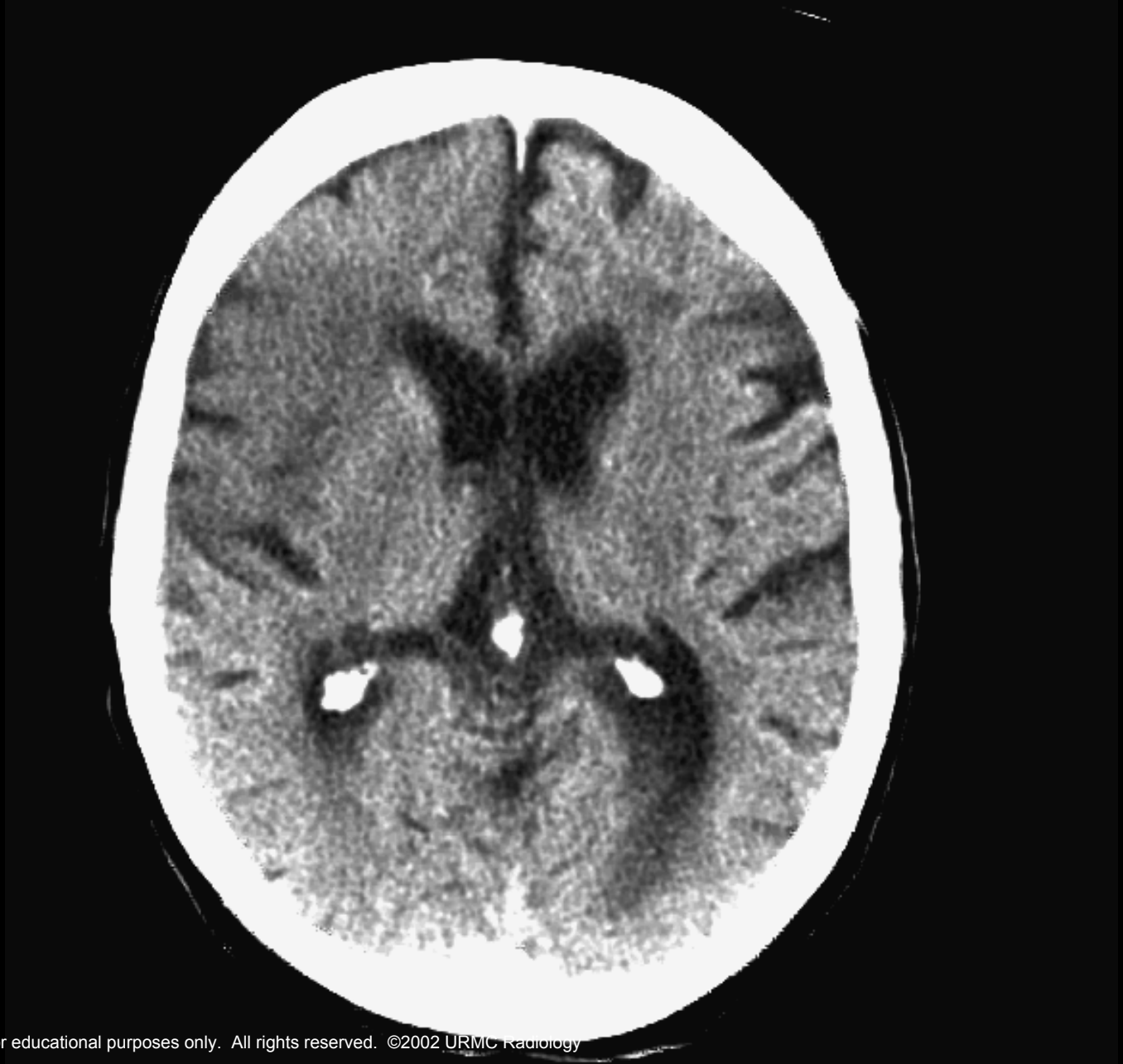
Patient selection for stroke ttx:

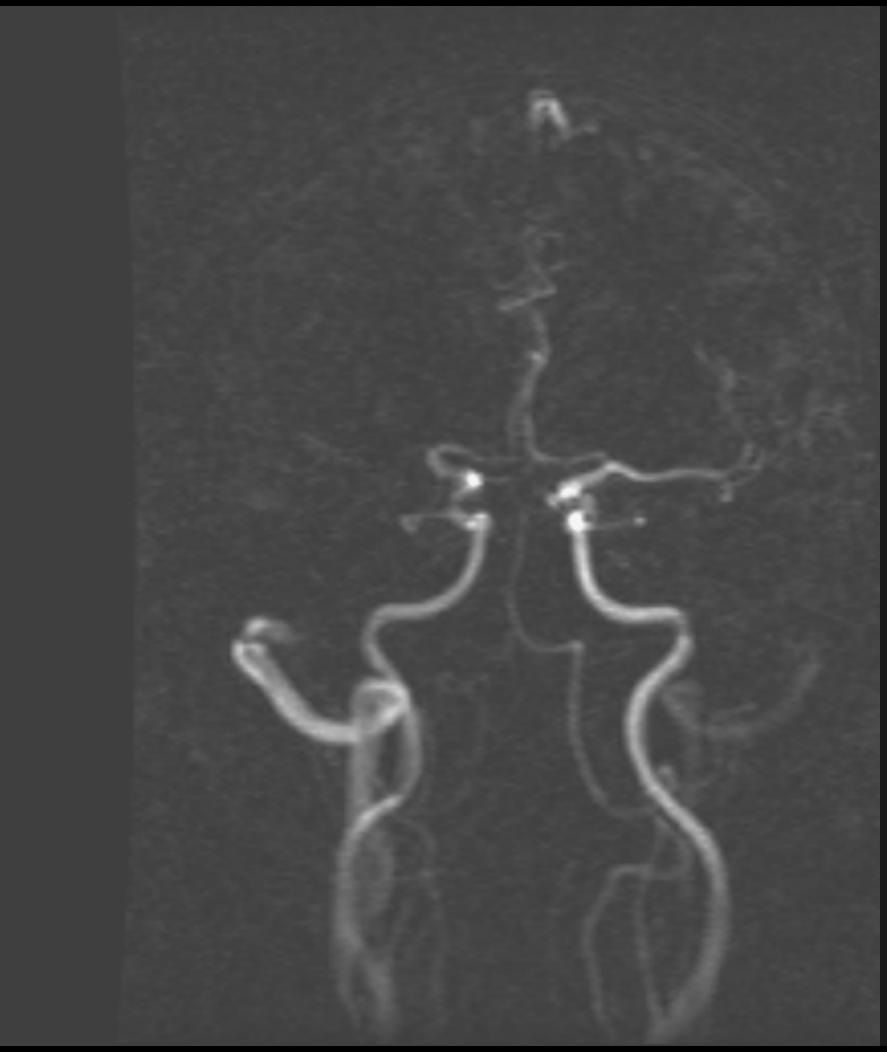
- Ideal Pt:
  - Core: quick death
  - Penumbra: slow death

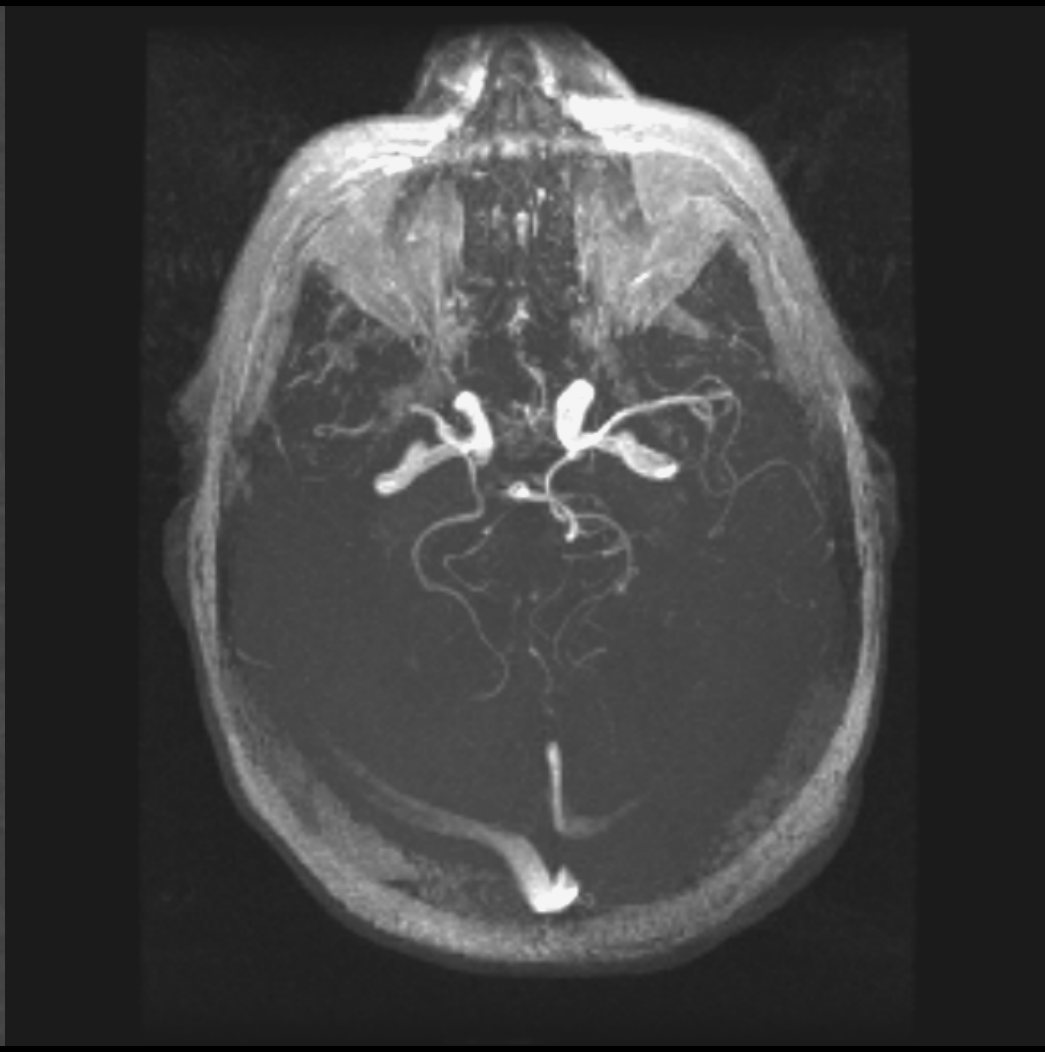


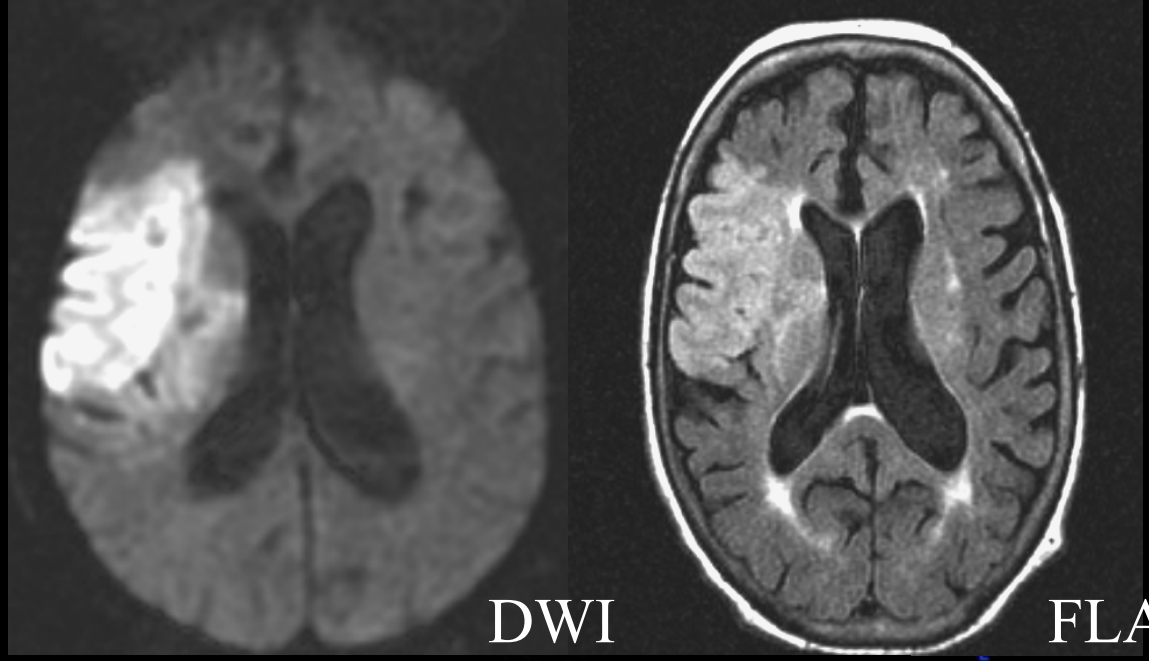
Modified from www.science.smith.edu/departments/Geology/Rhodes/dwi_5a.ppt

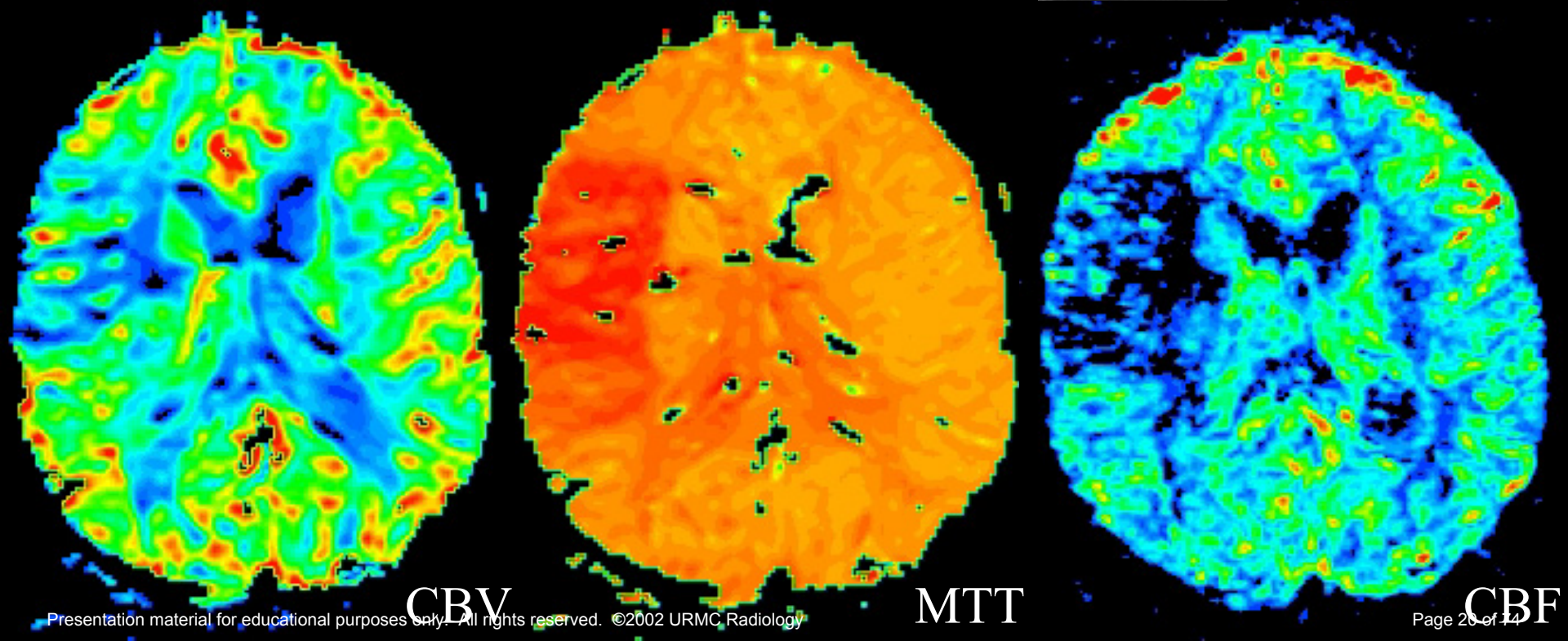
88 y old female with left hemiparesis & slurred speech after found down

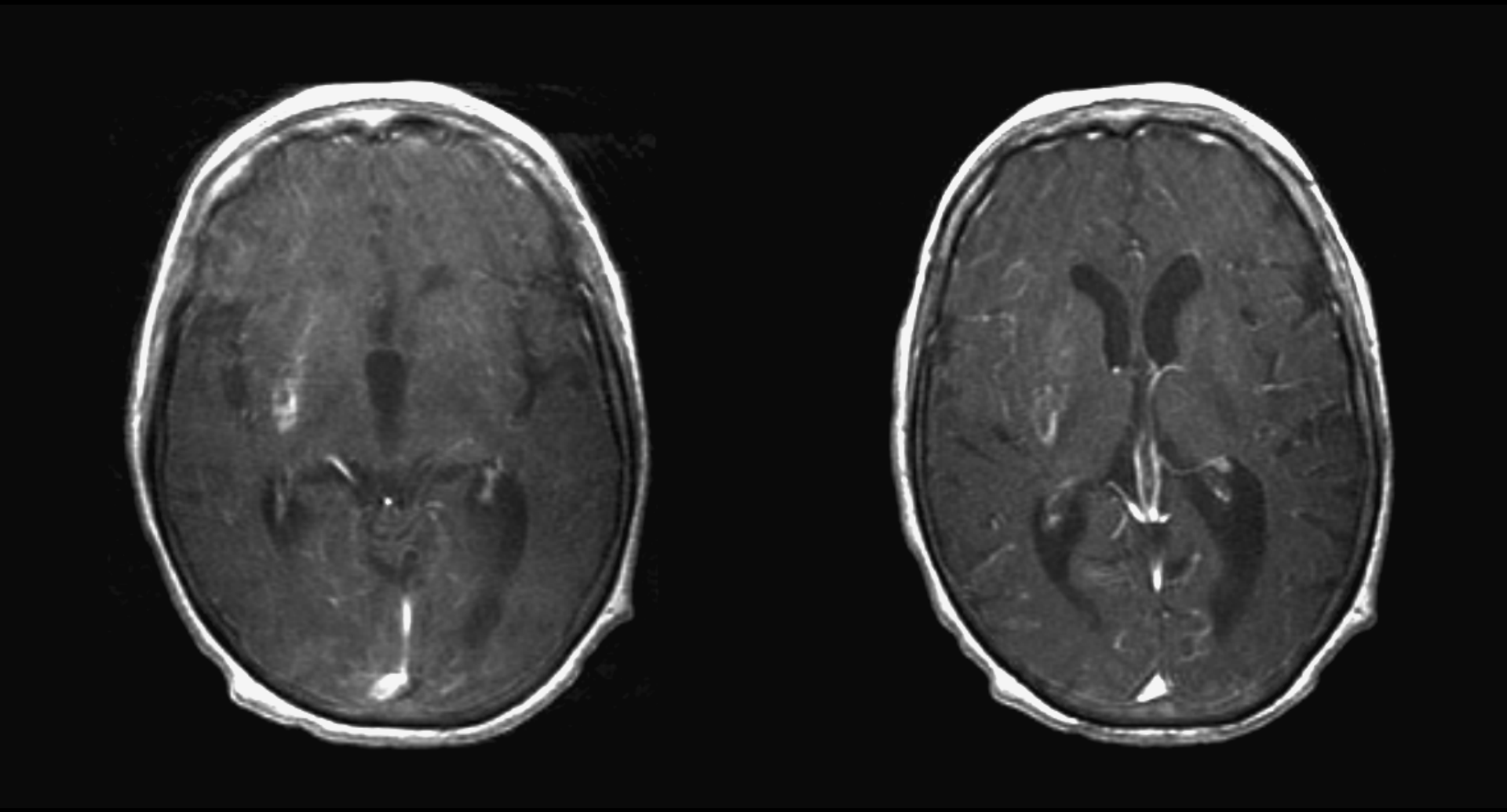




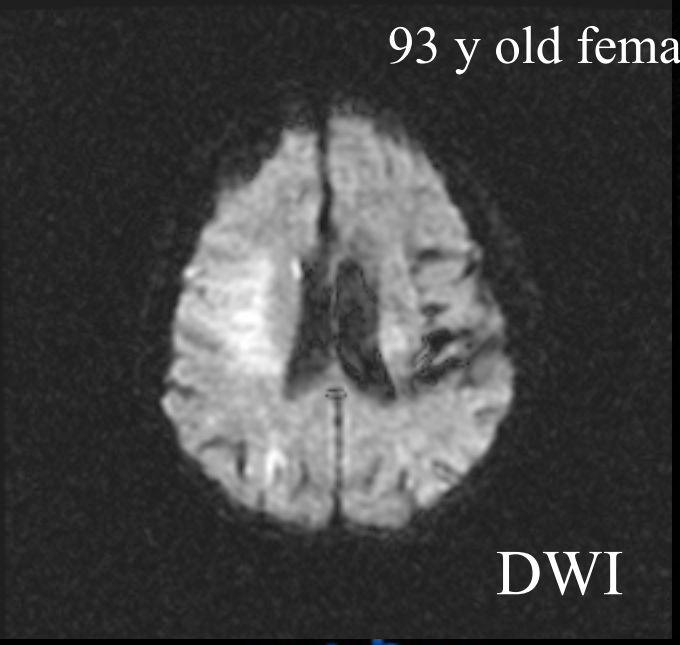




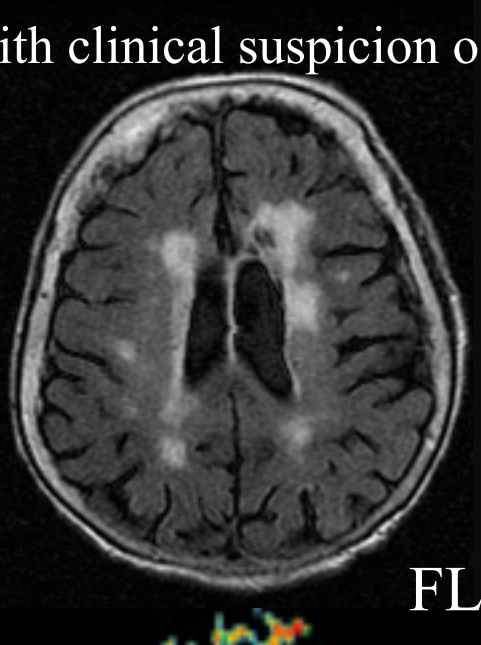




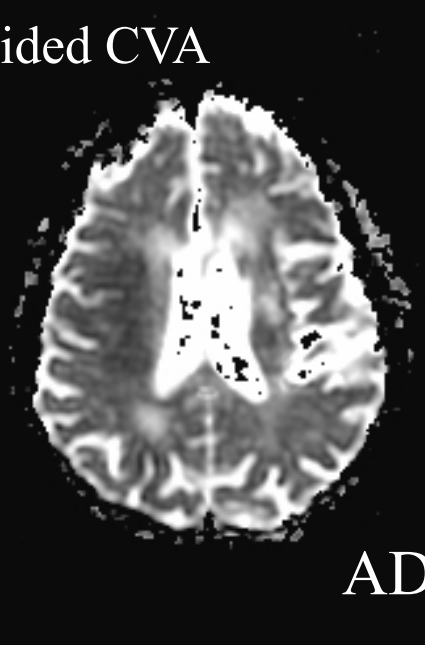
93 y old female with clinical suspicion of Rt sided CVA



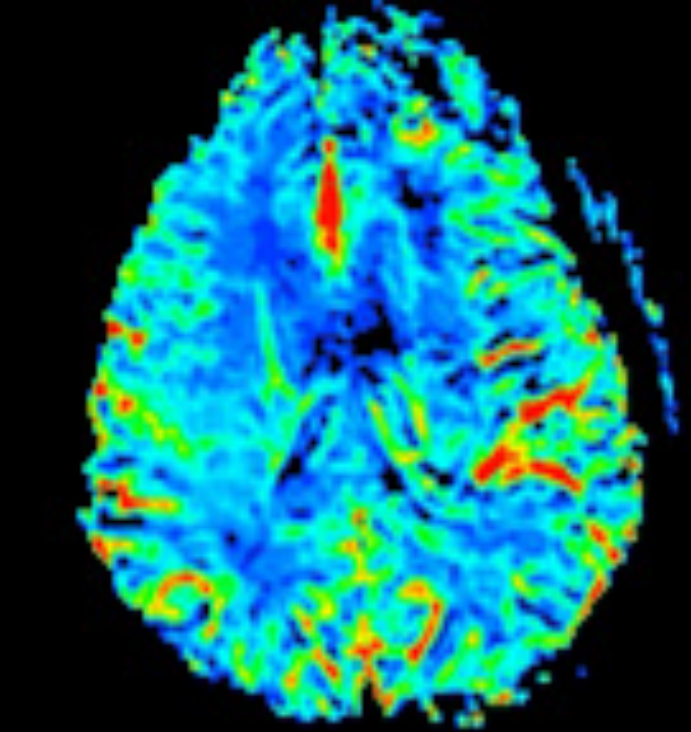
DWI



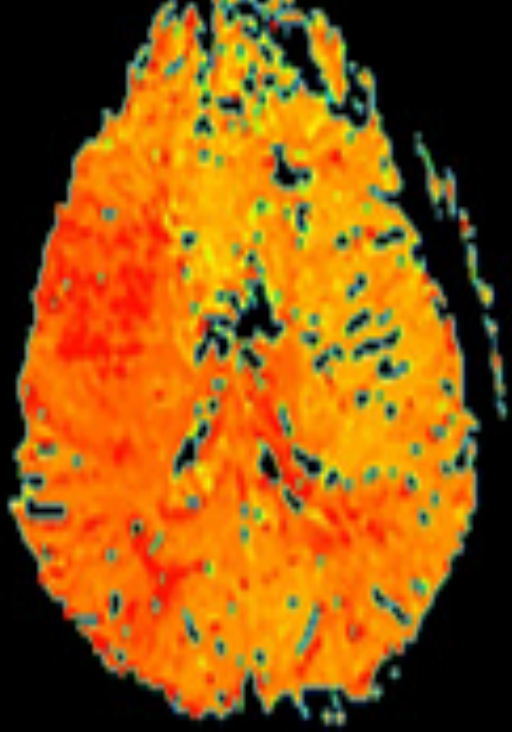
FLAIR



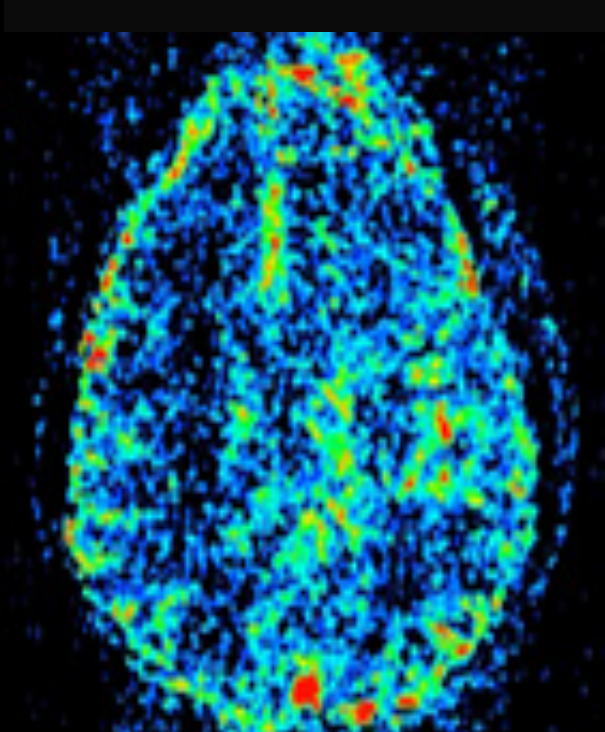
ADC



CBV



MTT



CBF

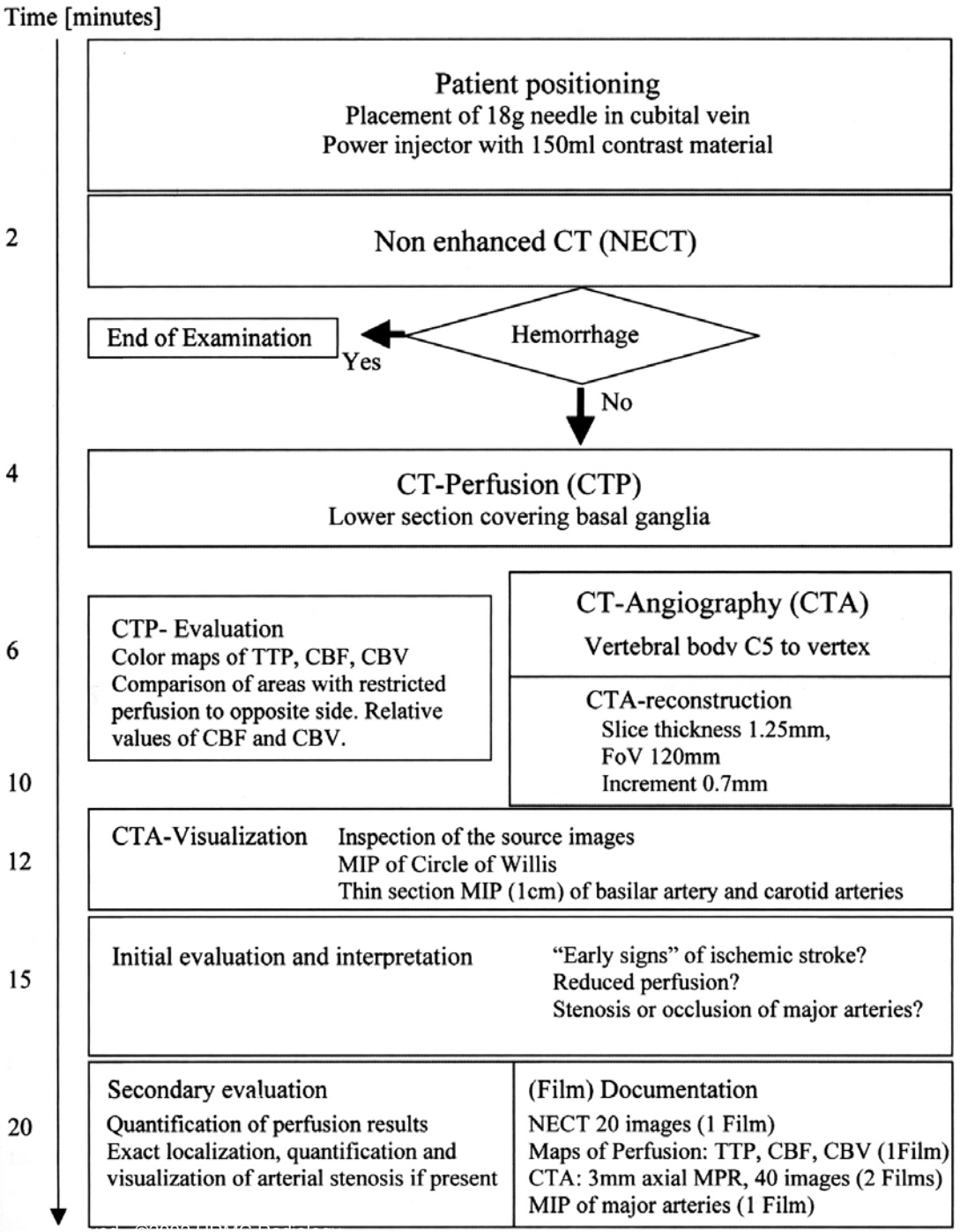
CT:

- Multisection CT:
  - Time-optimized stroke protocol:
    - Nonenhanced CT
    - Perfusion CT
    - CTA

    } -Decisions reg lysis can be taken in < 15 min

- More readily available than MRI
- CT Perfusion main disadvantage:
  - Limitation to a 2-3 cm section of brain tissue (4 row detector CT scanner)

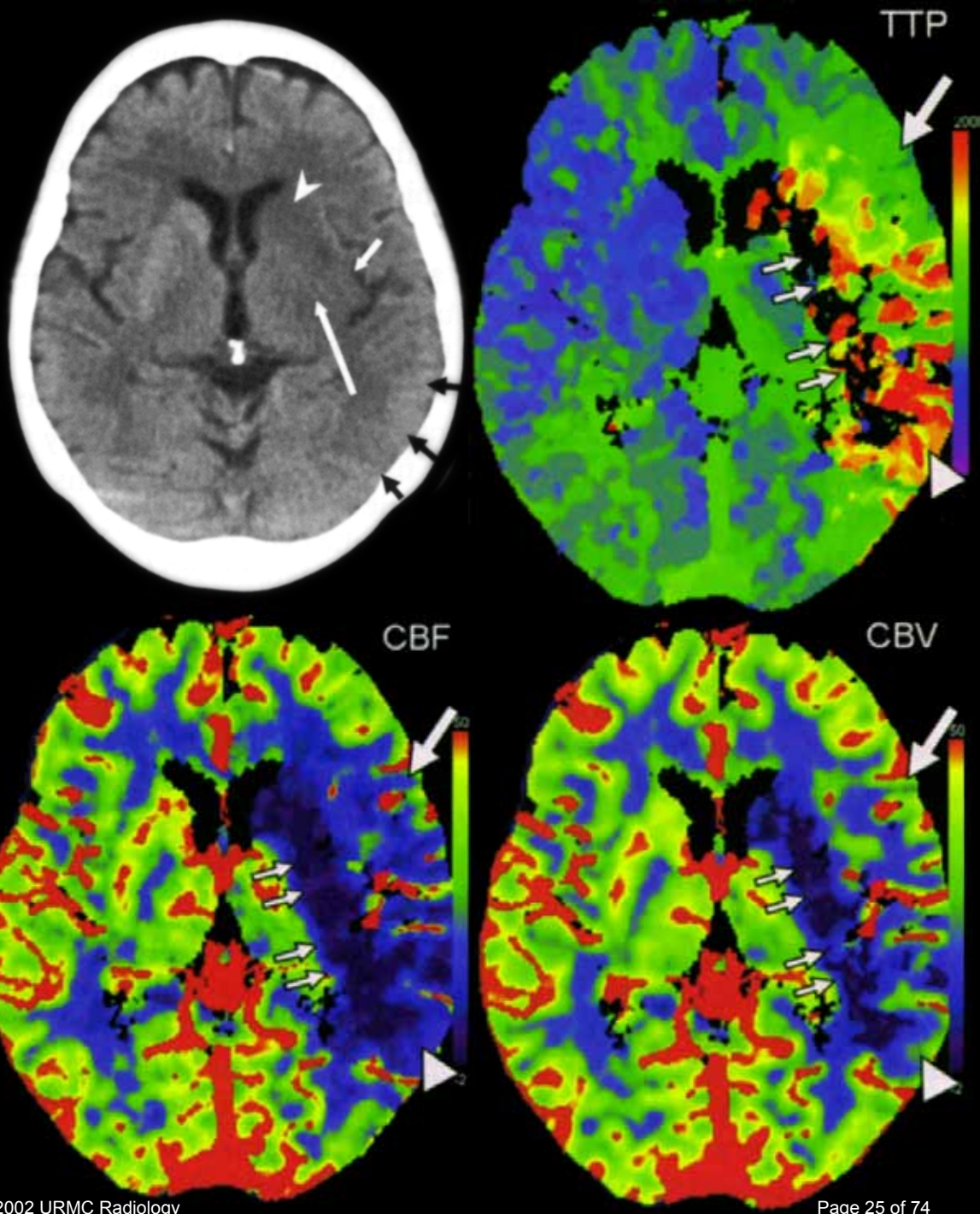
Radiographics, May-June 2003, Vol 23 #3, p565-592



RadioGraphics, Vol 23 #3, May-June2003, p 565-592

CT Perfusion

65 y old male with Lt MCA occlusion
5 h after stroke onset



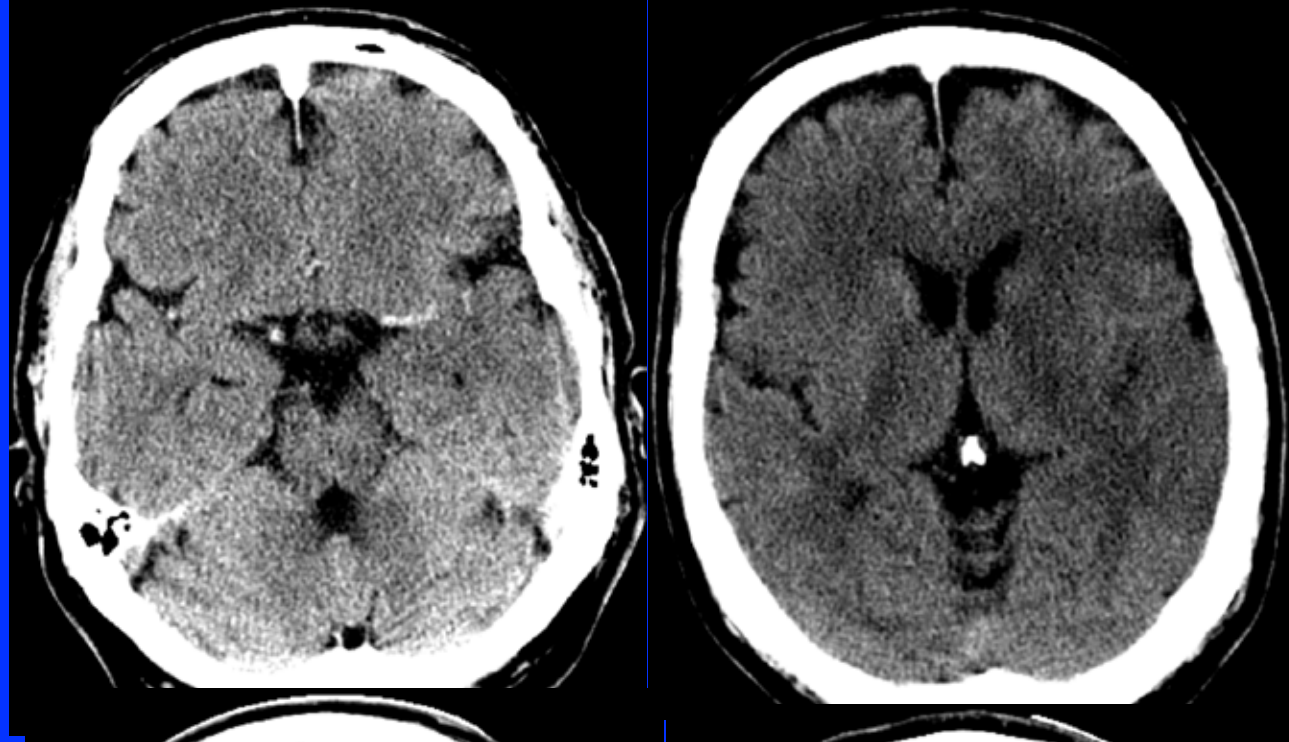
RadioGraphics, Vol 23 #3, May-June 2003, p 565-592

Nonenhanced CT:

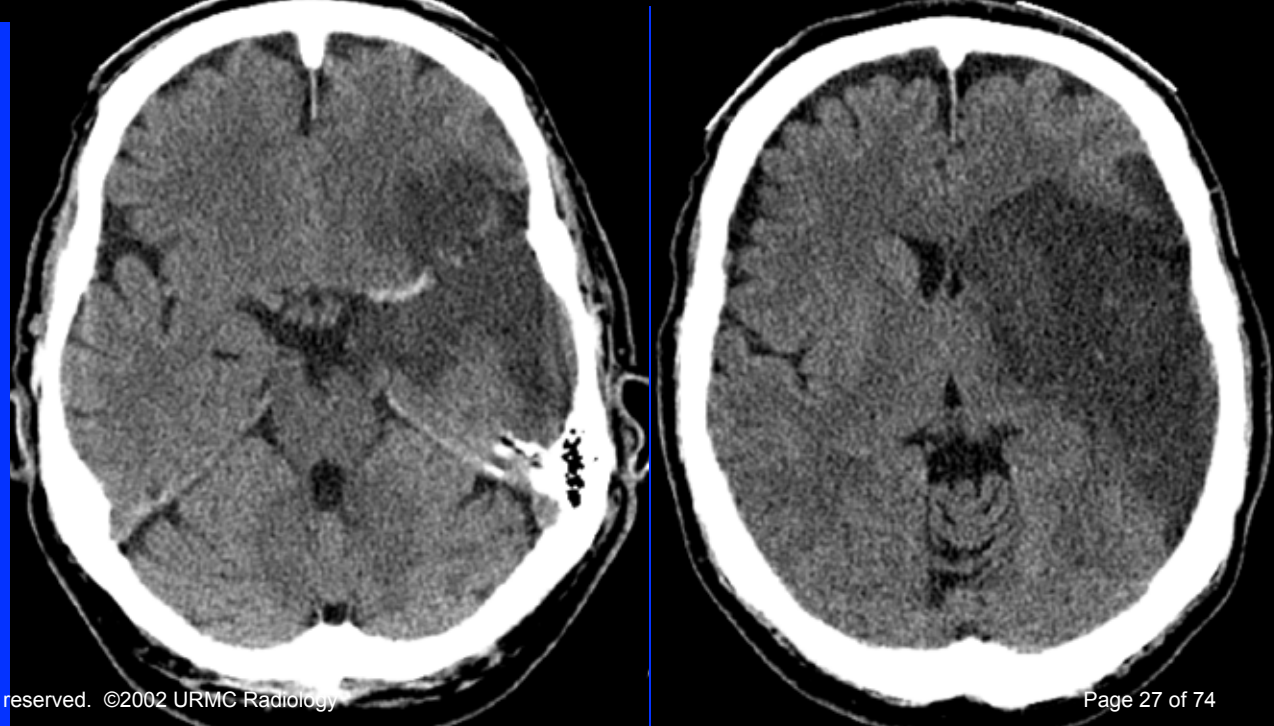
- If IC hemorrhage is excluded:
  - Ischemic lesion must be assumed
- CT early signs of MCA territory infarct:
  - Obscuration of lentiform nucleus: seen within 2 hrs
  - Insular Ribbon sign
  - Hyperdense MCA sign: can be seen within 90 min after the acute event
  - Normal findings within 2-3 hrs after onset of symptoms

RadioGraphics, Vol 23, #3, May-June 2003, p565-592

At presentation: ➔



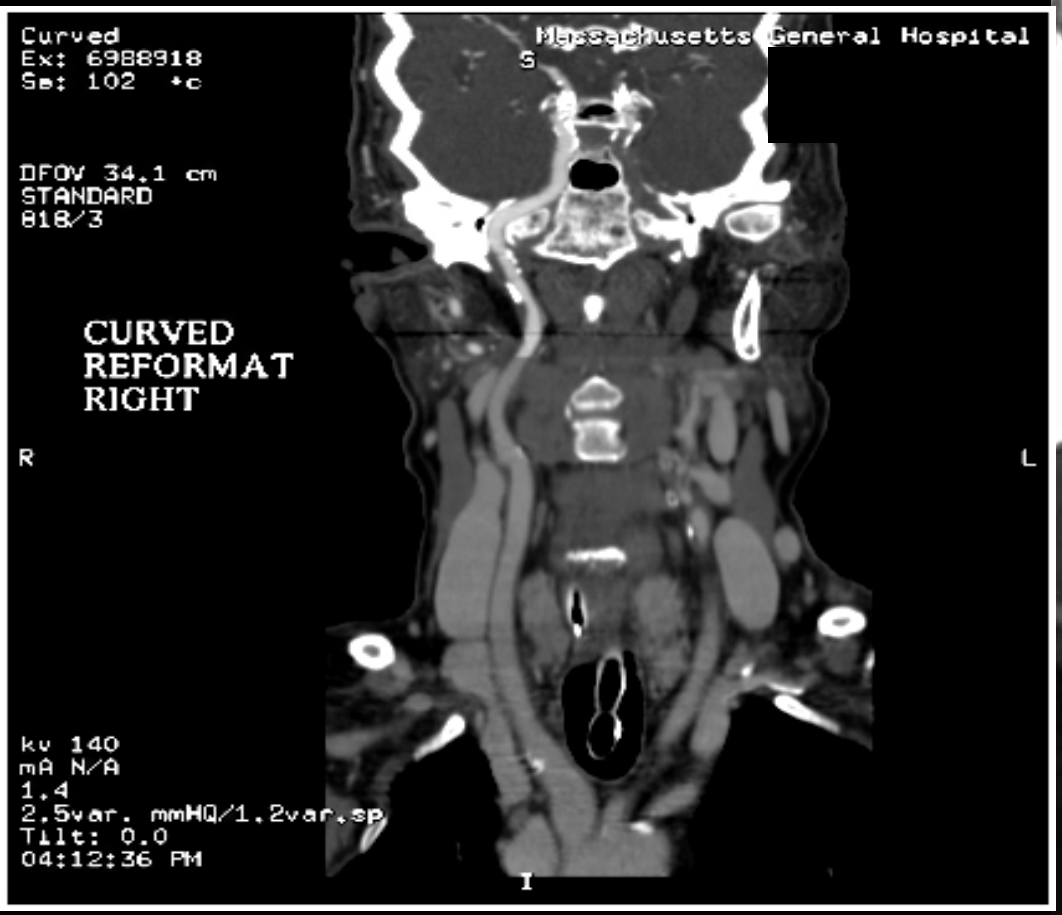
2 days later: ➔



CTA:

- For a comprehensive dx w/u in stroke pts:
  - Essential to know:
    - site of intracranial vessel occlusion/stenosis
    - Thrombosis/occlusion of the carotids as the underlying cause of the dz
- With multidetector CTs:
  - Entire region from CCAs to circle of Willis can be covered in a single data acquisition (<20secs)

RadioGraphics, Vol 23 #3, May-June 2003, p565-592



Common Methods of 3D Imaging:

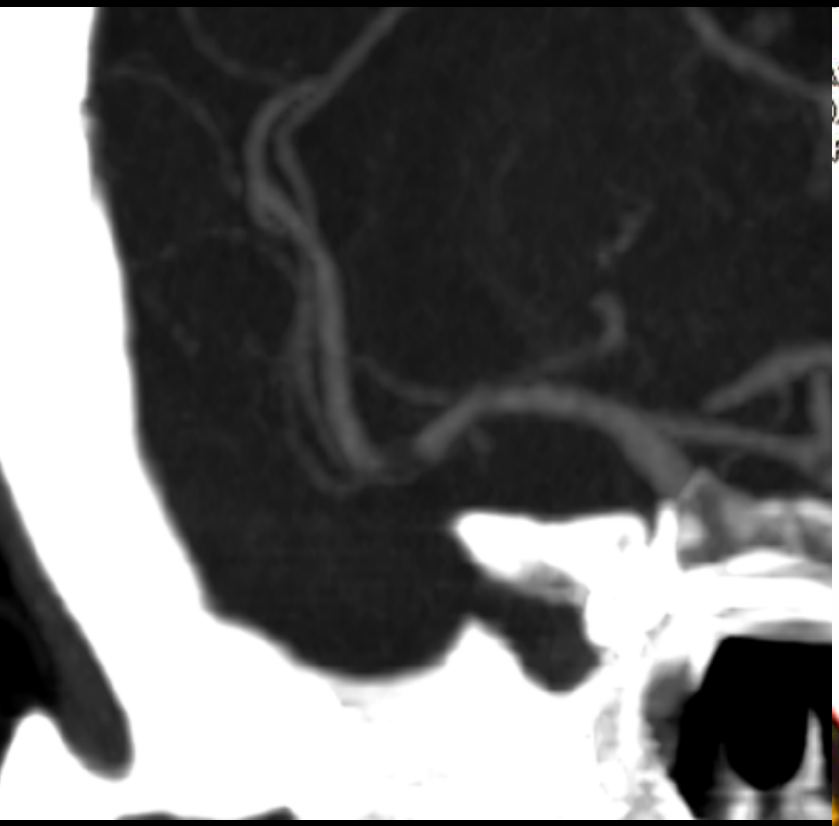
- Knowledge necessary to ensure extraction of the optimal spatial info about vascular structures from the volume data w/o eliminating important anatomic structures

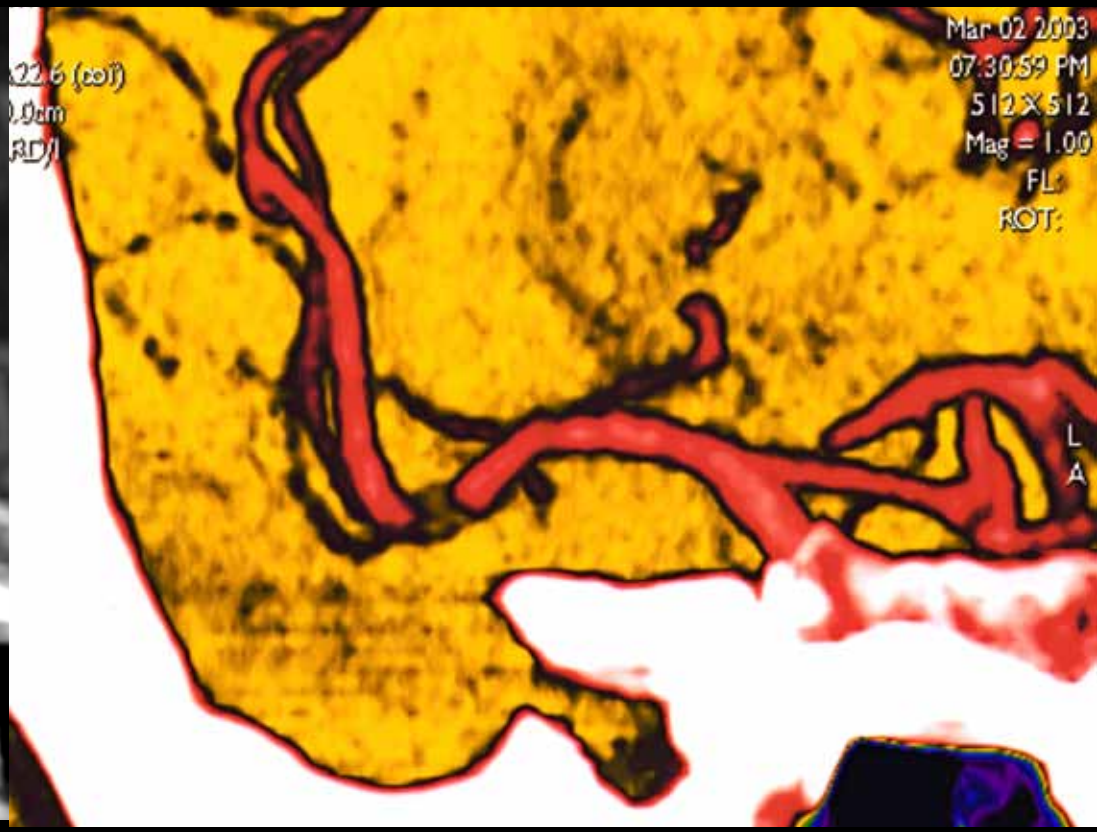
- None substitutes evaluation of source images!

RadioGraphics, Vol 23 #3, May-June 2003, p565-592

MIP

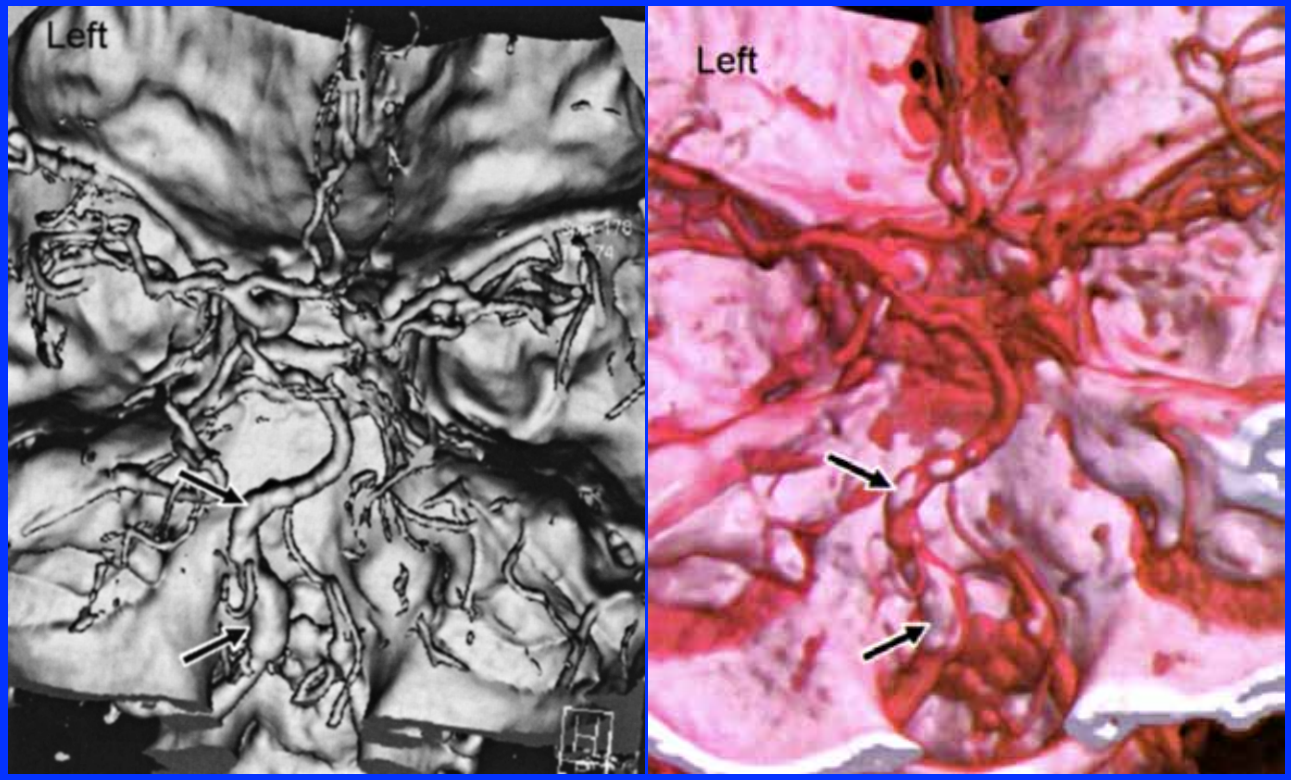
- Useful for:
  - Rapid detection of vascular discontinuities
- Fails to:
  - Accurately depict stenosis due to overlying calcifications





SSD

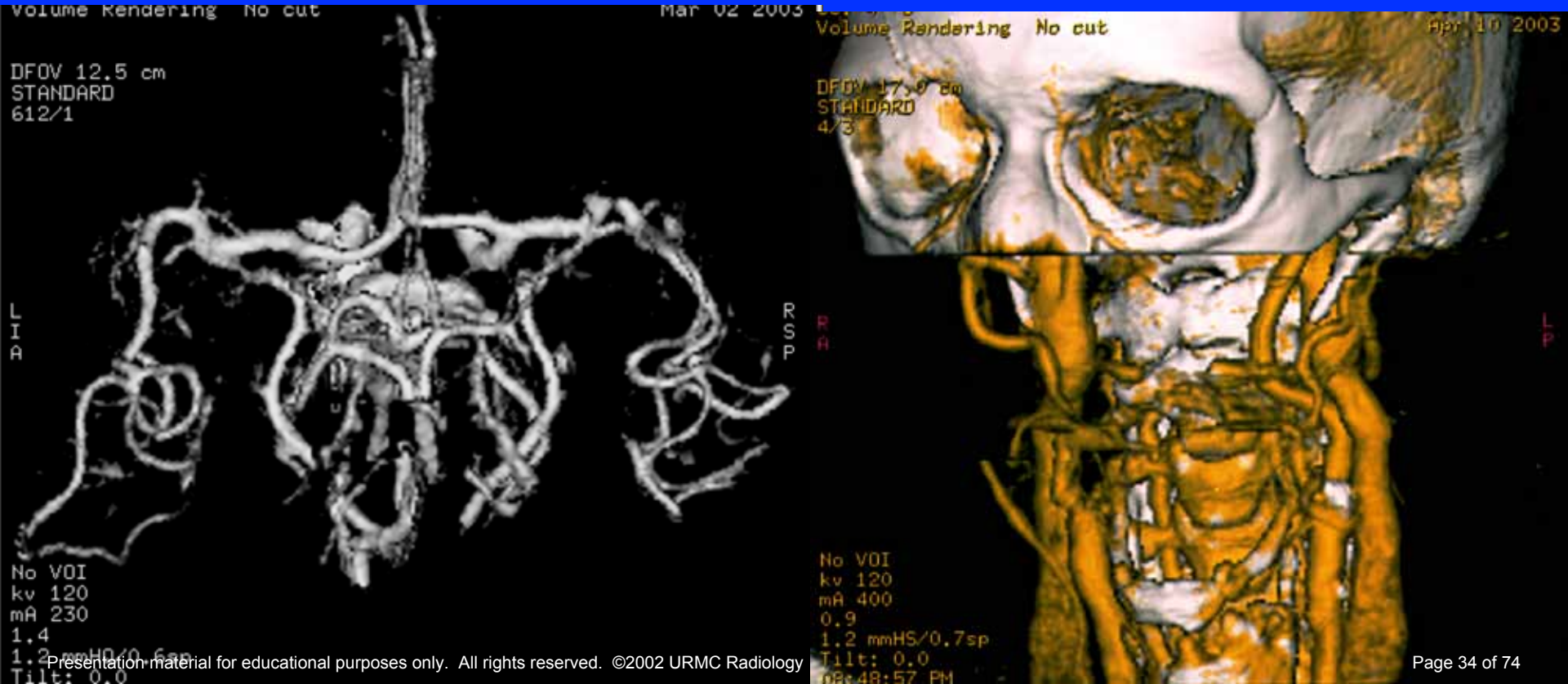
- The 1st layer of voxels within defined thresholds is used for display ➔ leading to visualization of the surface of all structures that fulfill the threshold



RadioGraphics, Vol 23, #3, May-June 2003

VR: Volume Rendering

- Groups of voxels within defined attenuation thresholds are selected & a color is assigned



NIH Stroke Scale (NIHSS)

- Standardized, fast and easy neurologic exam
- 13 areas:
  - Level of consciousness, vision, motor, ataxia, sensory, speech, neglect etc..
- 0 – 42 points
- More points = worse function

NIHSS

- < 4: not treated endovascularly
- 4-10:
  - may have SVDz rather than large vessel dz
  - May respond well to IV therapy only
- > 20:
  - correlate with a poorer outcome despite therapy
  - but can yield the most dramatic recovery when treated IA

Reviews in CV Medicine, JJ Connors III, Vol 3 Suppl 2, S92, 2002

Acute Stroke Therapy

- Goal of acute stroke therapy:
  - Preservation of acutely ischemic tissue
- Reperfusion strategy:
  - Only treatment that have yielded positive results
- To date:
  - Emergent IV revascularization: only FDA-approved therapy
- Intra-arterial revascularization:
  - Also been shown to improve outcomes

Reviews in CV Medicine, JJ Connors S92, Vol 3, suppl 2, 2002

Ideal tto

- Removal of vascular obstruction
- Protection of the injured brain
- Restoration of function

- Irreversible brain injury:
  - Begins 5 min after onset of complete ischemia

Interventional & EV Therapy of the Nervous System, P. Morris, Springer-Verlag 2002

ECASS

- IV tpA within 6 hrs of onset
- Results:
  - statistically nonsignificant
  - trend toward efficacy on the part of the drug

NINDS rt-PA Stroke Trial:

- IV tpA administered within 3 hrs of onset
- 30% relative enhancement of outcomes in rt-PA group vs control ($p<.001$) ➔ **FDA Approval**

- Symptomatic intracranial hemorrhage:
  - more common in rt-PA group (6.4% vs 0.6%, $P<.001$)

Limitations of IV Therapy from NINDS

- short time window for therapy[1].
- Large doses of IV rt-PA: ➔ risk of hemorrhage
- Earlier treatment (<90 min): better response
- Near 3 hours: poorer response[2]

- Emergency Managmt of Stroke (EMS) Bridging Trial:
  - Pts with NIHSS scores (>10): have large vessel occlusion
  - IV rt-PA alone does not open major arterial occlusions during the first few hours

1. The NINDS rt-PA Stroke Study Group. *Stroke*. 1997;28:2119–2125.
2. Marler et al. *Neurology*. 2000;55:1649–1655.

Retrospective analysis of NINDS data:

- ??? efficacy of IV tto in pts with large vessel occlusions, like[1] :
  - patients with dense MCA sign on CT
    - poor response to IV therapy (1 of 18 with positive outcome).
- Clot in MCA means high NIH stroke scale score
  - Odds of IV t-PAs working plummet with higher scores
    - NIHSS <10: 73% success rate[2]
    - NIHSS >20: 6% success rate

1. Tomsick et al. *Am J Neuroradiol*. 1996;17:79–85.
2. The National Institutes of Health Stroke Scale (NIHSS)

Efficacy of IV Lytics: Time From Onset of Symptoms to Treatment.

- Up to 90 minutes:
  - 2.8 times better outcomes than placebo
- 90–180 minutes:
  - 1.5 times better outcomes than placebo
- Over 180 minutes:
  - multiple failed trials

Marler et al. *Neurology*. 2000;55:1649–1655.

Efficacy of IV Lytics for Stroke: Angiographic Proof

- All angiographic trials of IV rt-PA lytic efficacy indicate:
  - no more than ~20% effectiveness for large-vessel emboli
  - EMS, IMS, TTATTS

Emergency Management of Stroke Bridging Trial (EMS)

Can we extend the time window?

IV tpA: NO

- Atlantis Trial:
  - 3-6 hrs window
  - No benefit in outcome
  - ICH rate: 7.2 %
- ECASS II Trial:
  - 0-6 hr window
  - No benefit in outcome beyond 3 hrs
  - ICH rate: 8.8 %

ASITN Carotid Workshop, Wash DC, May 2003

IA t-PA: May Be

- Current John Hopkins Hospital protocols:
  - Anterior circulation: < 6 hrs
  - Post circulation: < 12 hrs (or more)
  - Central retinal A Occlusion: < 12 hrs
  - Can be used POP

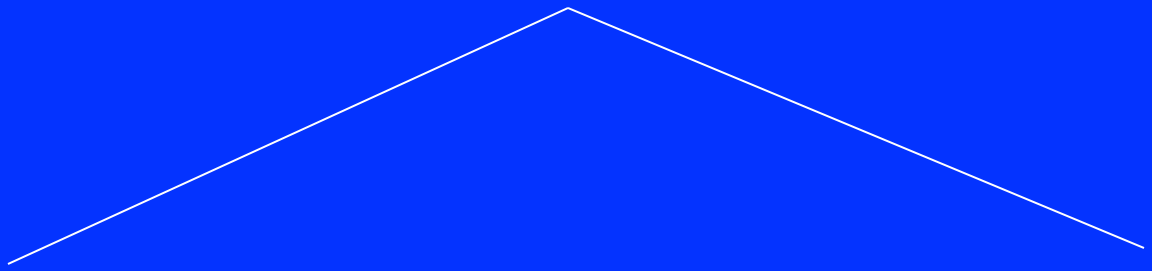
ASITN Carotid intervention Workshop, Wash DC, May 2003

Intra-Arterial Thrombolysis

- Early experience: urokinase!
- Though no randomized trial has been performed:
  - urokinase has an acceptable safety and efficacy profile
- Other thrombolytic agents also been used for intra-arterial fibrinolysis:
  - (rt-PA, scu-PA, r-proUK, SK, APSAC, TNK)

Single-Chain Urokinase Plasminogen Activator (scu-PA)
Recombinant Prourokinase (r-proUK), Streptokinase (SK)
Anisoylated Plasminogen Streptokinase Activator Complex (APSAC)
Tenecteplase (TNK)

PROACT II Trial of Acute MCA Stroke



- IA r-proUK + IV heparin
- IA placebo + IV heparin
- Results not powerful enough for FDA approval
- PROACT II: favorable outcome:
  - 66% recanalization with r-proUK infusion
  - 18 % with placebo (control group)
- Revascularization of acute stroke can work as late as 6 hours after the acute insult

Interventional Therapy of the NS, P Morris 2002

Symptomatic Hemorrhagic Transformation:

- PROACT: 10.2 %.
- IV tpA trials:
  - NINDS: 6.4%
  - ATLANTIS: 7.2%
  - ECASS II: 8.8%

Strategic Considerations based on Location

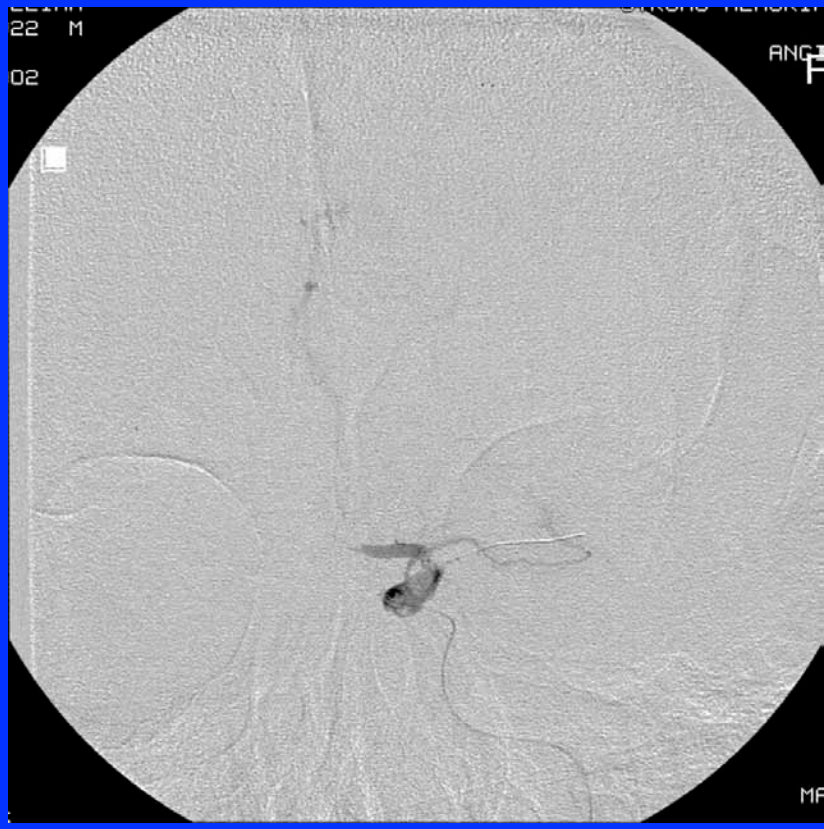
- Anterior Circulation Occlusions:
  - Typically embolic:
    - Mostly cardiogenic
    - Also: aorta & cervical vessels
    - 5-10%: intrinsic atherosclerotic stenosis of major intracranial vessels

Reviews in CV Medicine, JJ Connors III, Vol 3 Suppl 2, S92, 2002

Pial-pial collaterals & lenticulostriate As

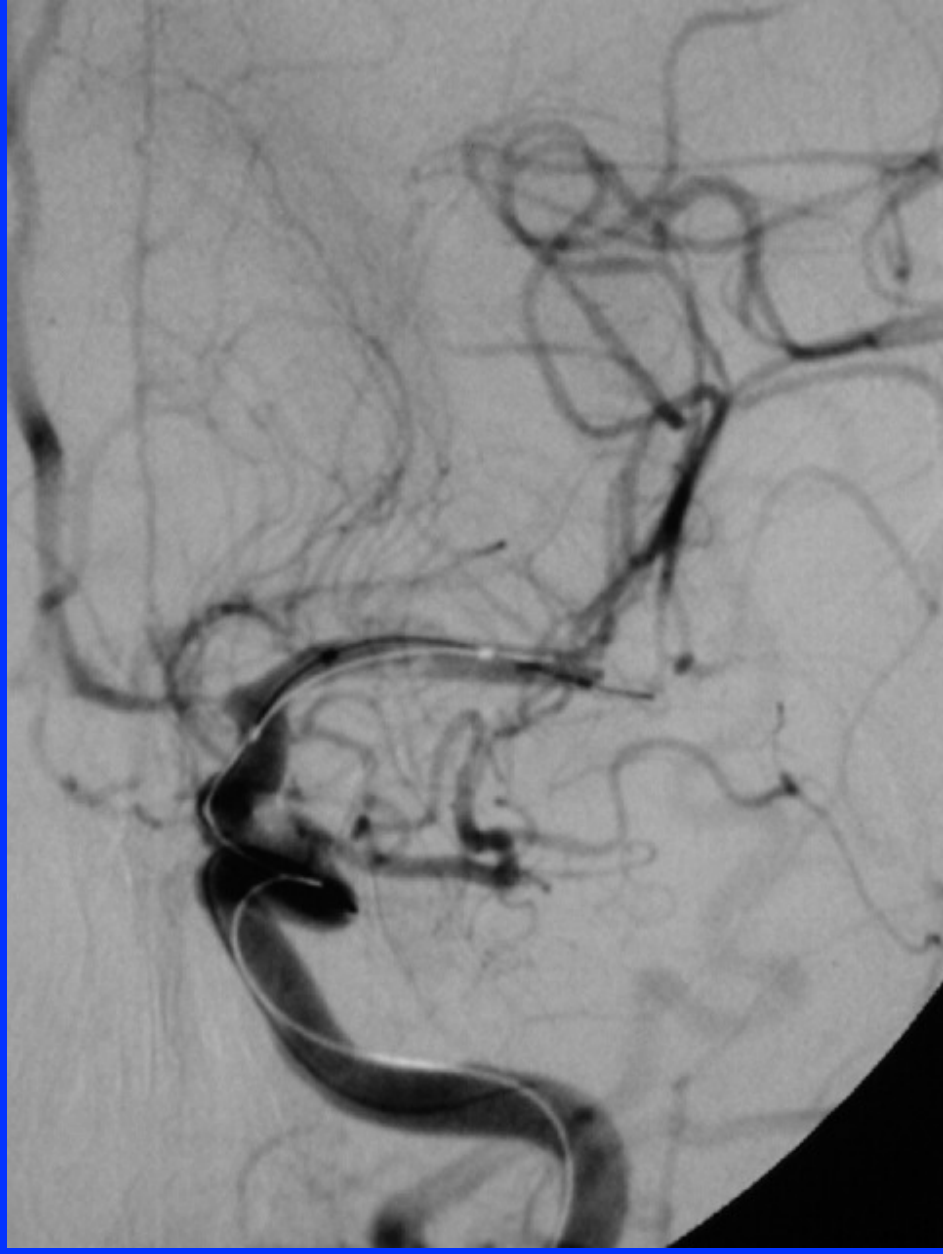
- Collateral filling of ischemic MCA territory:
  - Anastomosis between pial branches of:
    - MCA
    - ACA
    - PCA
- Lenticulostriate As: End As! (no collateral supply)

  ↓
- Main MCA trunk occlusion => direct lent/str occlusion with profound & rapid ischemia
  - Low likelihood of a good functional result



Lenticulostriate As Supply:

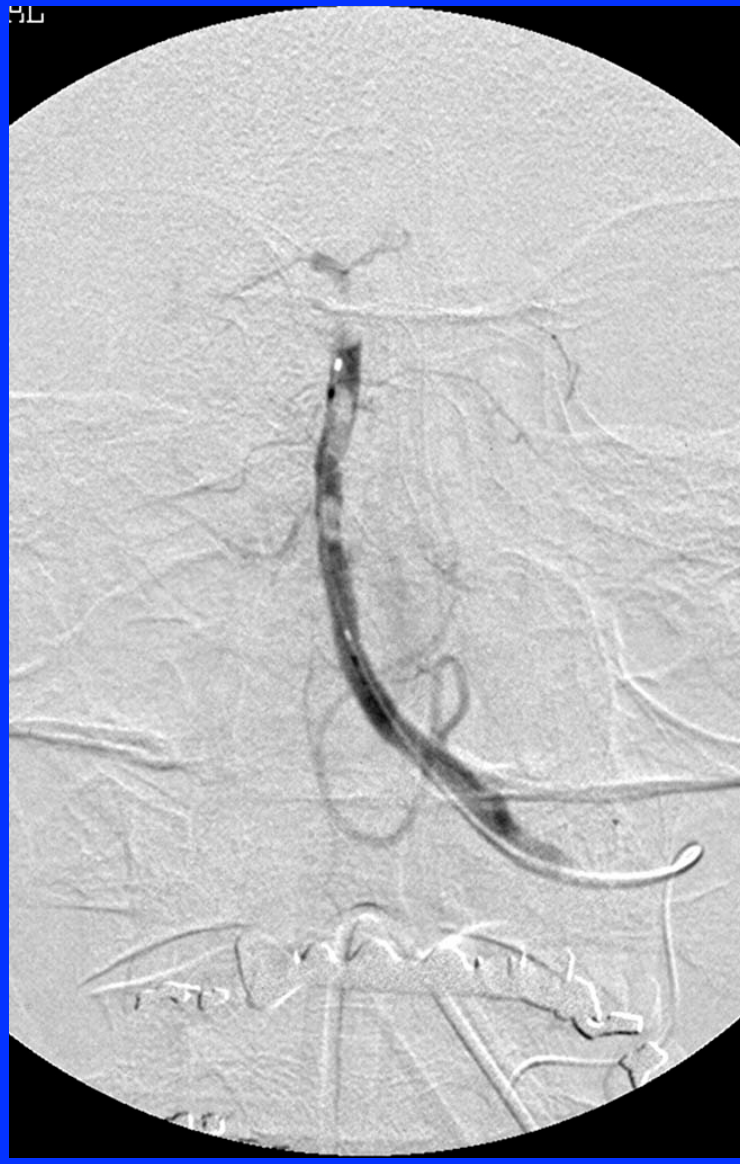
- Basal ganglia
- Radiating fibers from the cortex
- Deep WM of the frontal & parietal lobes, including:
  - Internal: carries motor & sensory fibers from the cortex
  - & external capsules



Reviews in CV Medicine, JJ Connors III, Vol 3 Suppl 2, S92, 2002

Posterior Circulation Occlusions:

- Occlusion more often due to:
  - Intrinsic thrombus formation & occlusion associated with an underlying stenosis
- Embolus origins:
  - Heart: largest source
  - VA origin or proximal brachiocephalic vessels



Reviews in CV Medicine, JJ Connors III, Vol 3 Suppl 2, S92, 2002

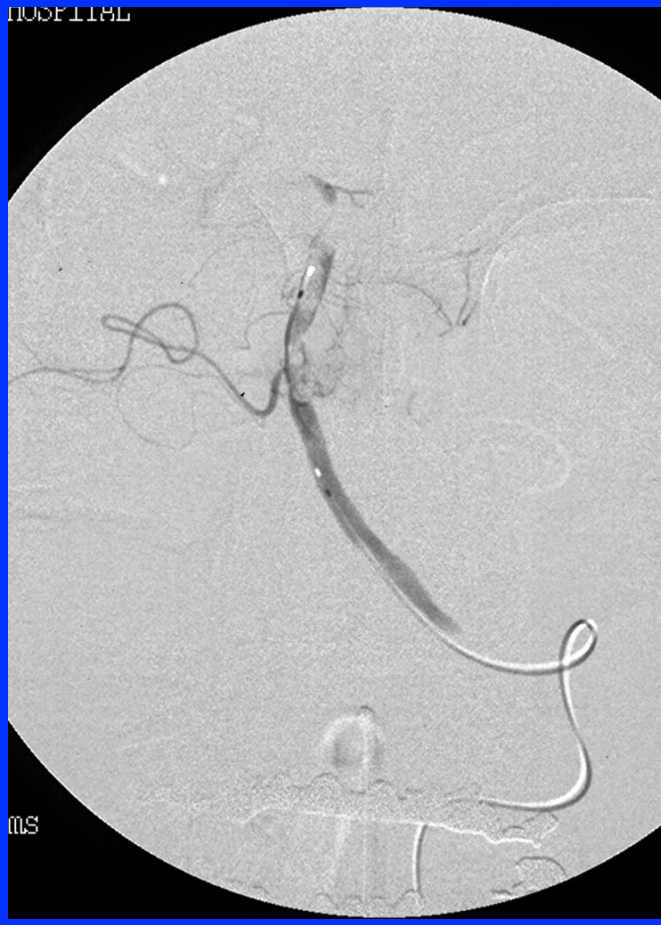
Prognosis of Post Circul Infarcts

- Acute symptomatic occlusion of the Basilar trunk or both VAs:
  - Death sentence! => unless the vessel can be reopened.
  - Underlying stenosis => needs Angioplasty after lysis to achieve success

Reviews in CV Medicine, JJ Connors III, Vol 3 Suppl 2, S92, 2002

Basilar Trunk Occlusions:

- Distal better than proximal:
  - Main trunk is still perfused
  - PICA & AICA can supply entire cerebellum and brainstem
  - PICA to SCA collateral flow: helps supplying distal basilar trunk past an occlusion
  - More likely due to an embolus implying lack of vertebrobasilar dz



Reviews in CV Medicine, JJ Connors III, Vol 3 Suppl 2, S92, 2002

Prognosis of Post Circul Infarcts

- As opposed to MCA occlusions:
  - The downstream structures:
    - Occipital lobe, distal pons, basilar apex

  - Are not in immediate jeopardy because of collateral supply from:
    - PComms
    - Pial collaterals from MCA to PCA
    - PICA to SCA collaterals

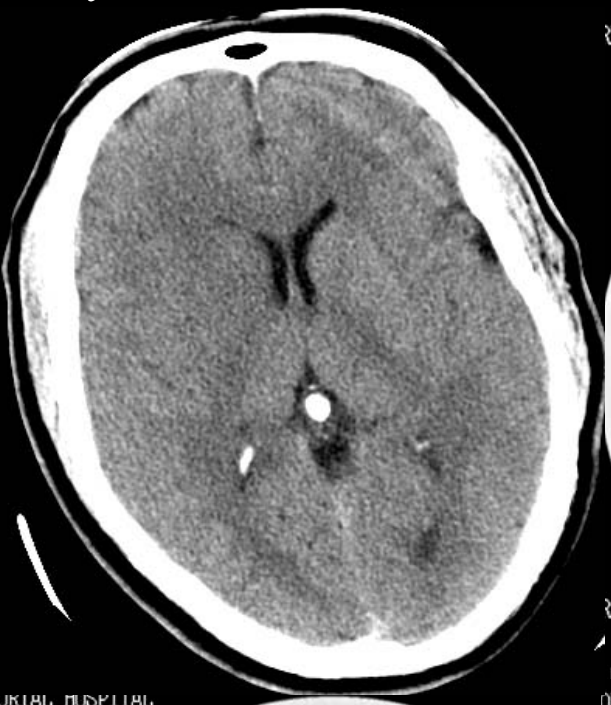
Reviews in CV Medicine, JJ Connors III, Vol 3 Suppl 2, S92, 2002

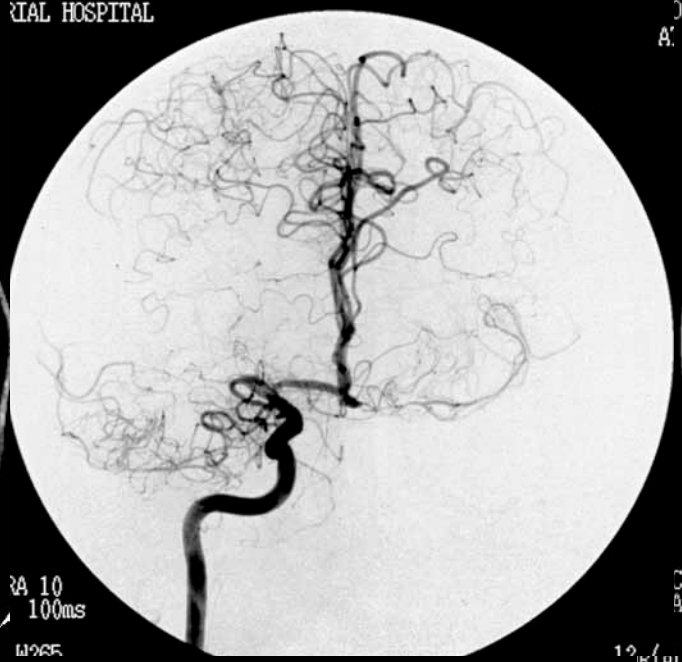
Technique & Procedure

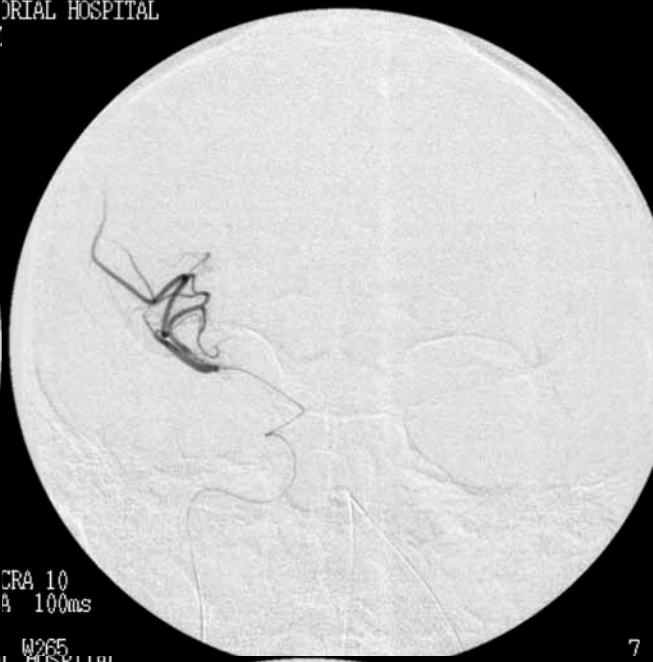
- Stroke team leadered by neurologist
- Time is brain!
- Communication
- Dose:
  - UK: 1-1.2 million U (up to 2 million U) delivered over 1 hour
  - tpA: solution: 1mg/ml, administered IA 1mg/min up to 20 mg commonly used
    - Up to 40 mg: > efficacy & reasonable risk

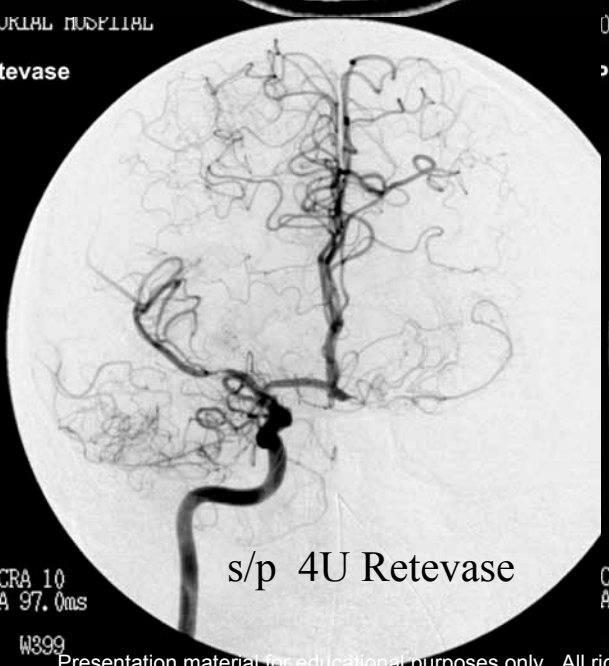
Interv & EV Therapy of the NS, P Morris 2002

43 y old male with acute dense lt hemiparesis

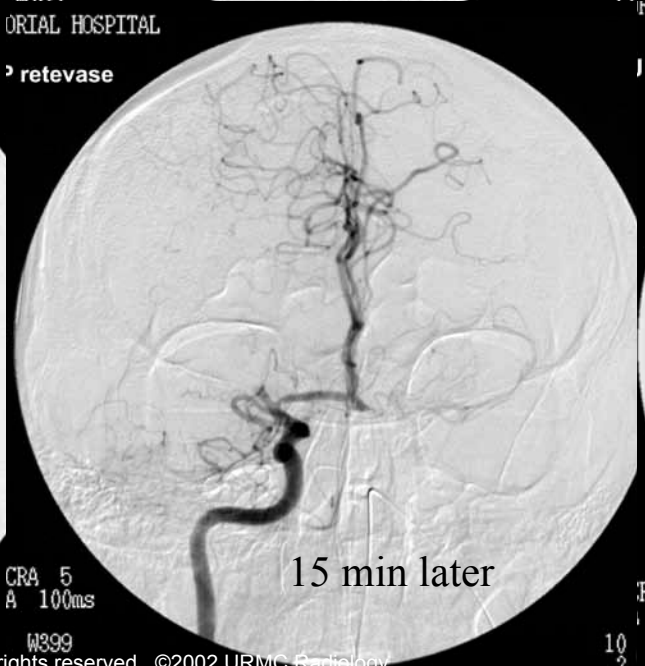




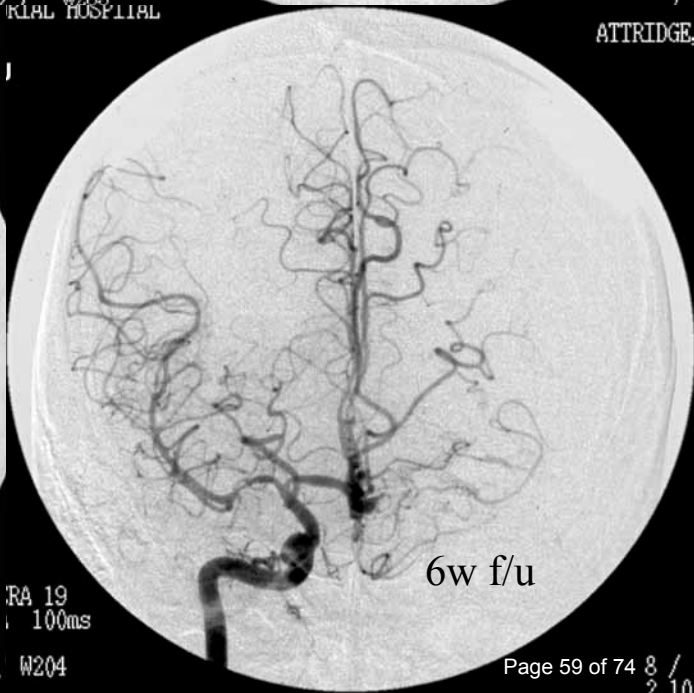




s/p 4U Retevase



15 min later



6w f/u

GPIIb/IIIa Plts Inhibitors

Favorable experience in acute infarct

IND:

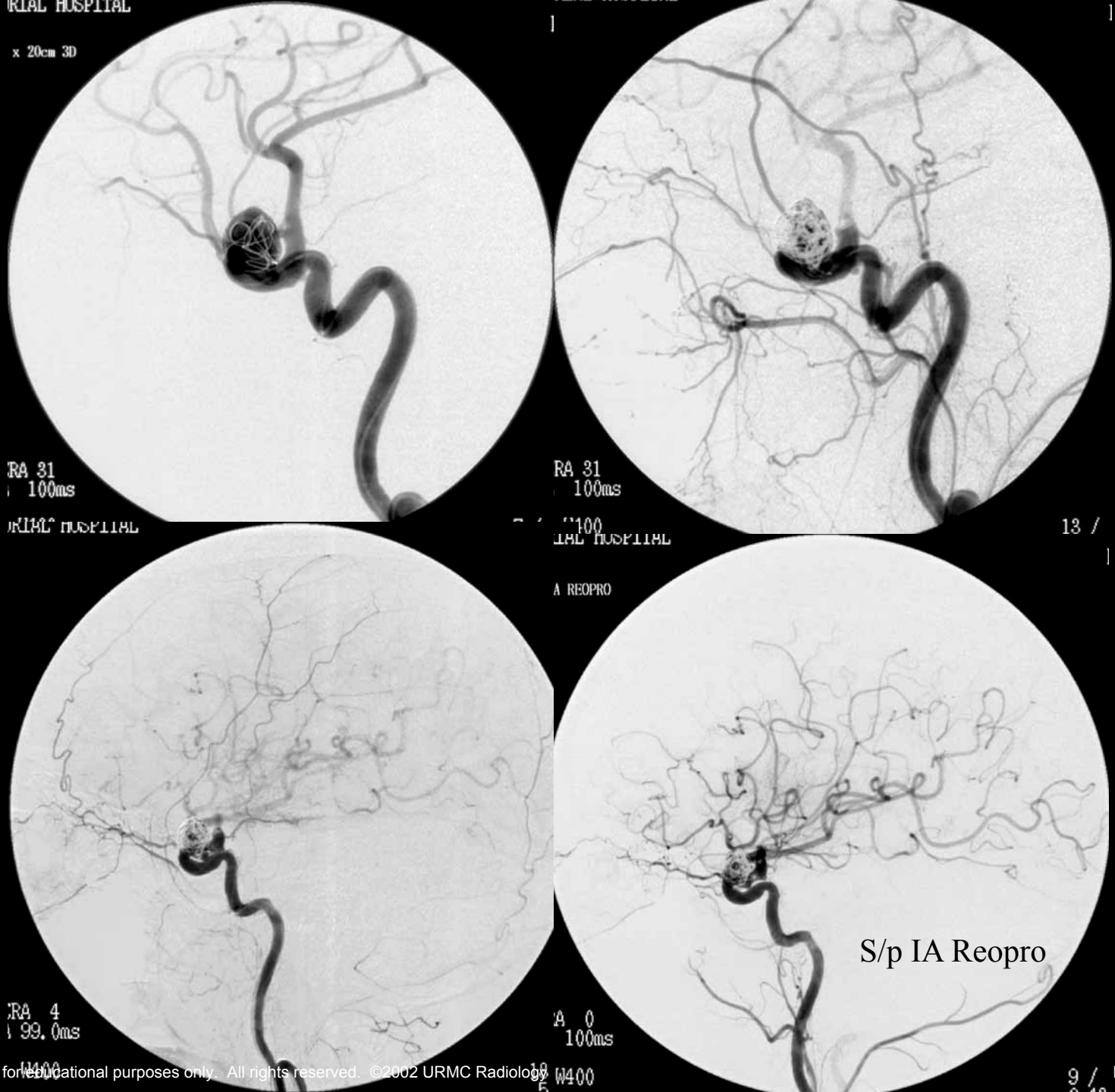
Acute Thrombolysis
Acute in-stent thrombosis

Eptifibatide
Tirofiban

} Less potent than Reopro, so theoretically < hemorrhagic complications

Abciximab (Reopro)

– Interventional & EV Therapy of the Nervous System, P. Morris, Springer-Verlag 2002, p269-280.

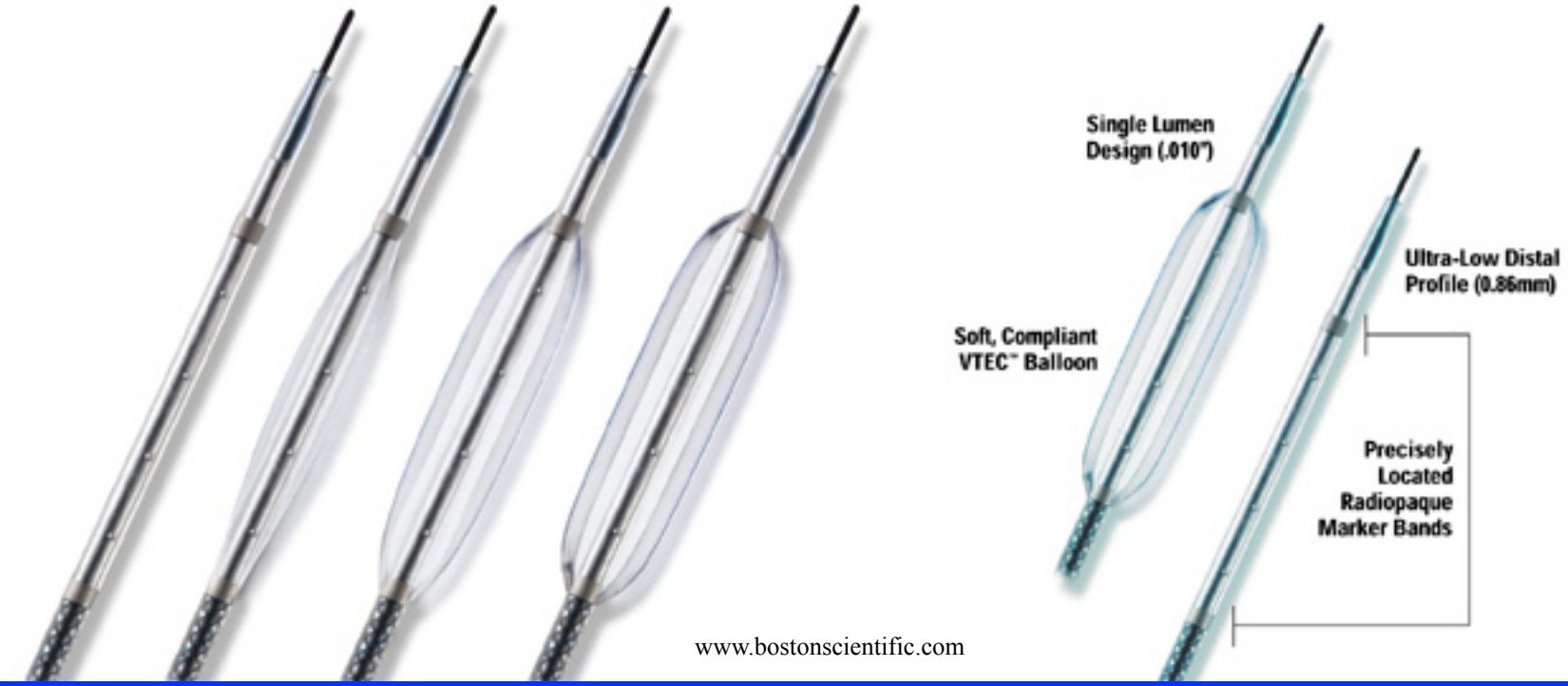


Technique & Procedure

- Puncture:
  - Single wall, micropuncture
- 6-8 Fr guiding catheter
- Arterial closure device
- Mechanical Clot Disruption:
  - Increases the surface area of clot exposed to the thrombolytic agent

Interv & EV Thearpy of NS, P. Morris 2002

- Balloons:
  - Soft compliant: Endeavor (Boston Scientific)
  - Wire-directed:
    - Commodore (Cordis)
    - Sentry (Target)
    - Equinox (MTI)



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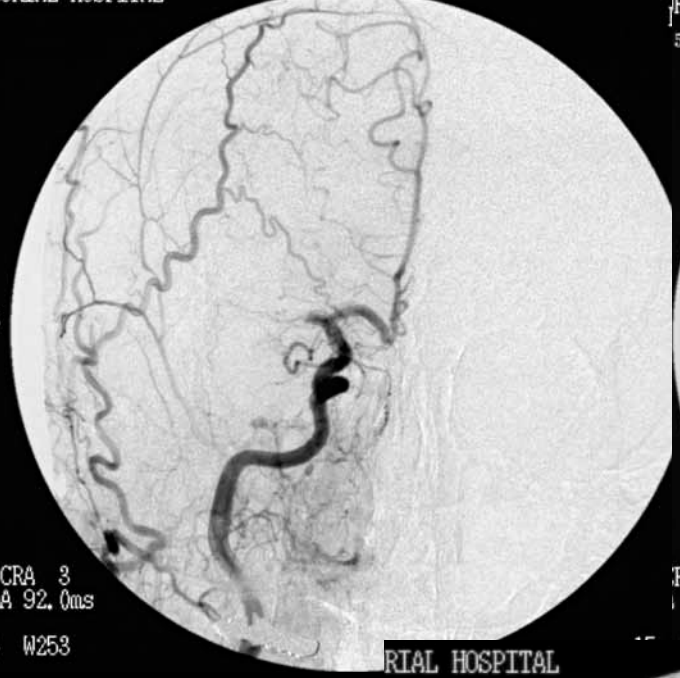
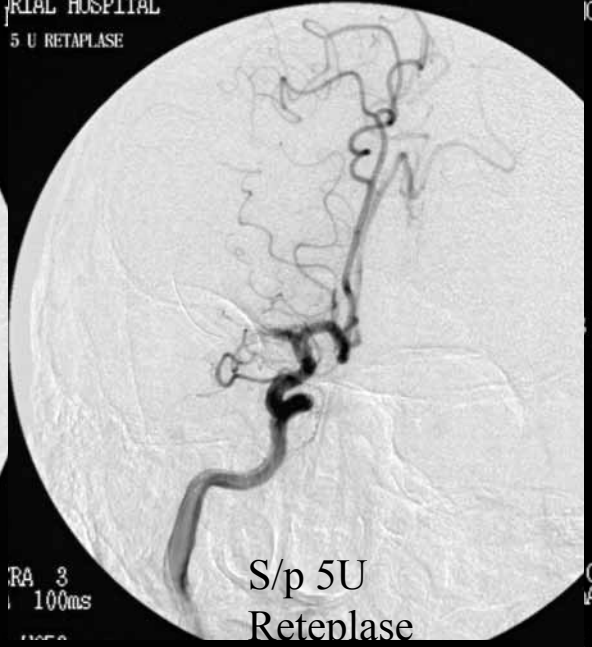
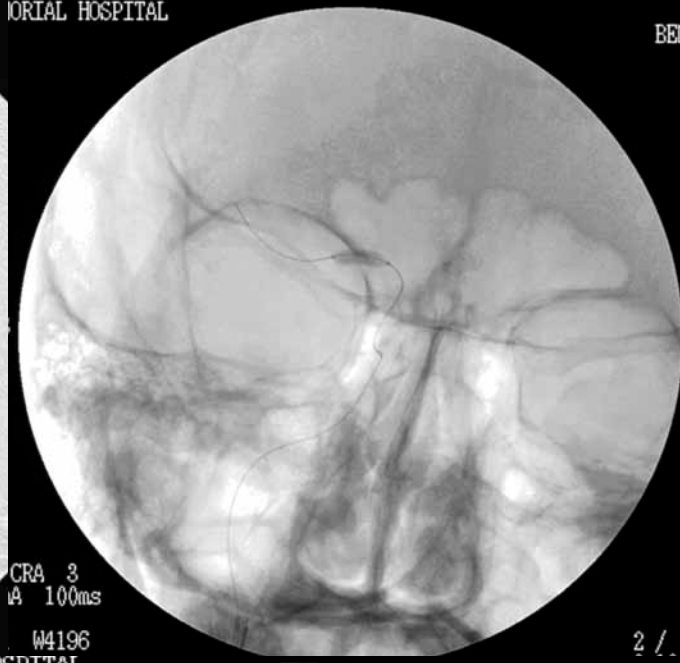
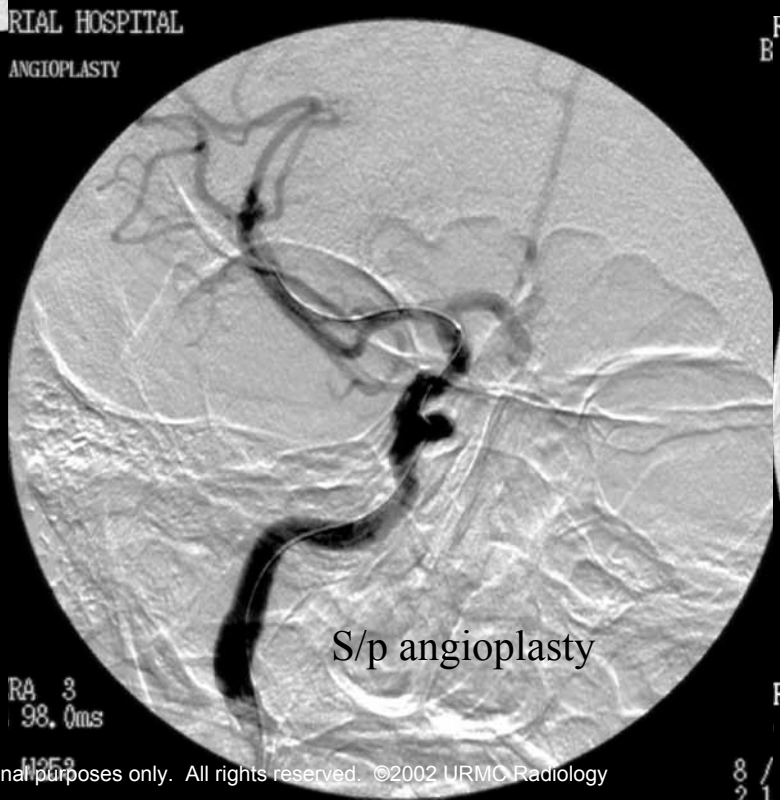




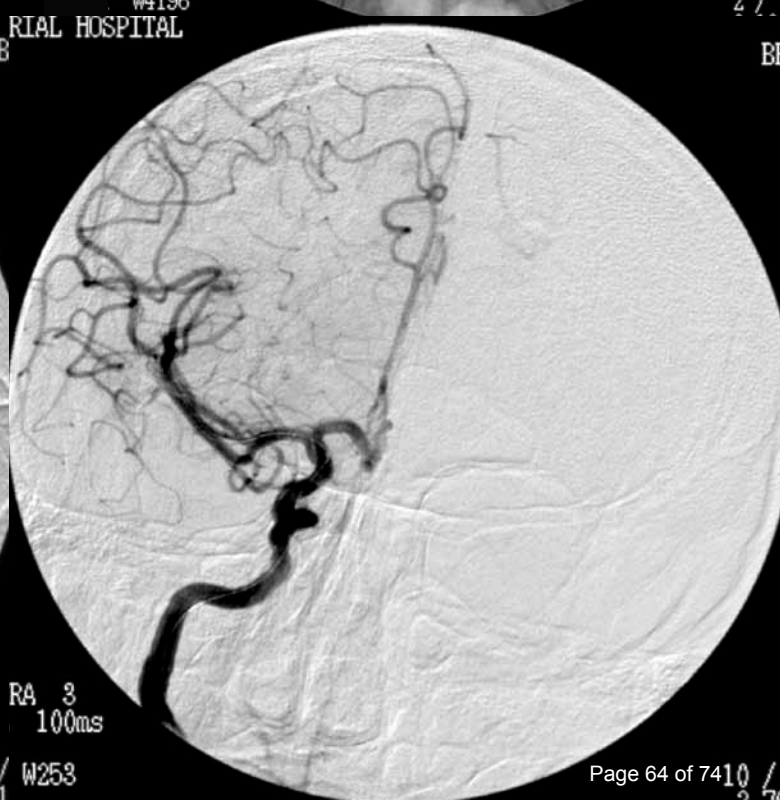
S/p 5U Reteplase



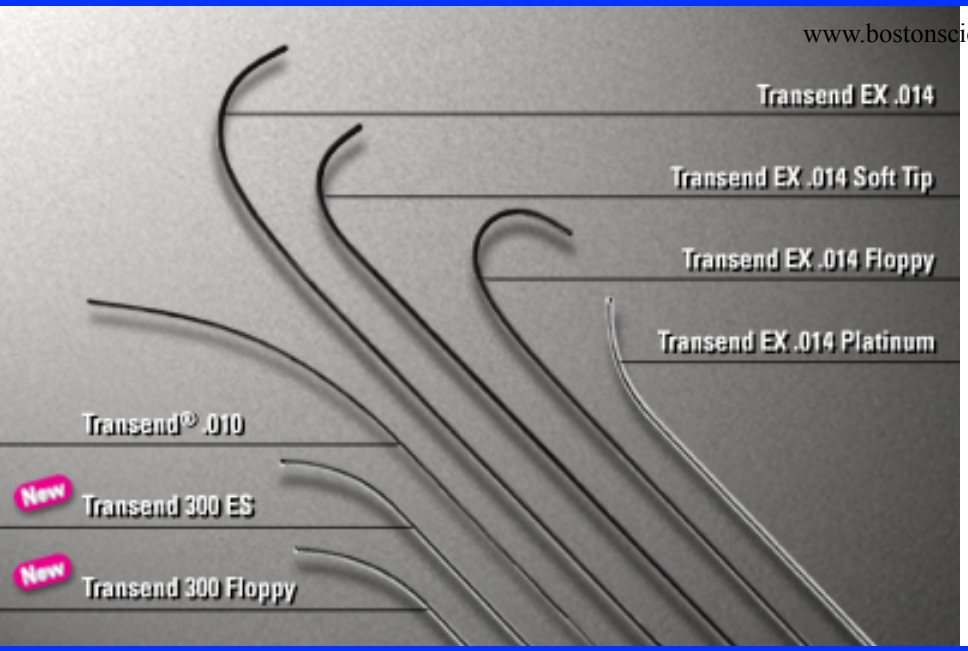
53 y old male with dense lt hemiparesis, 3-6 hrs after onset



S/p angioplasty



- Wires:
  - Used to probe & fragment intraluminal clot
    - (careful: avoid dissection or perforation!)
  - Safer with a J curve at the tip, to avoid:
    - Opht A, PComm, Ant Choroidal A.



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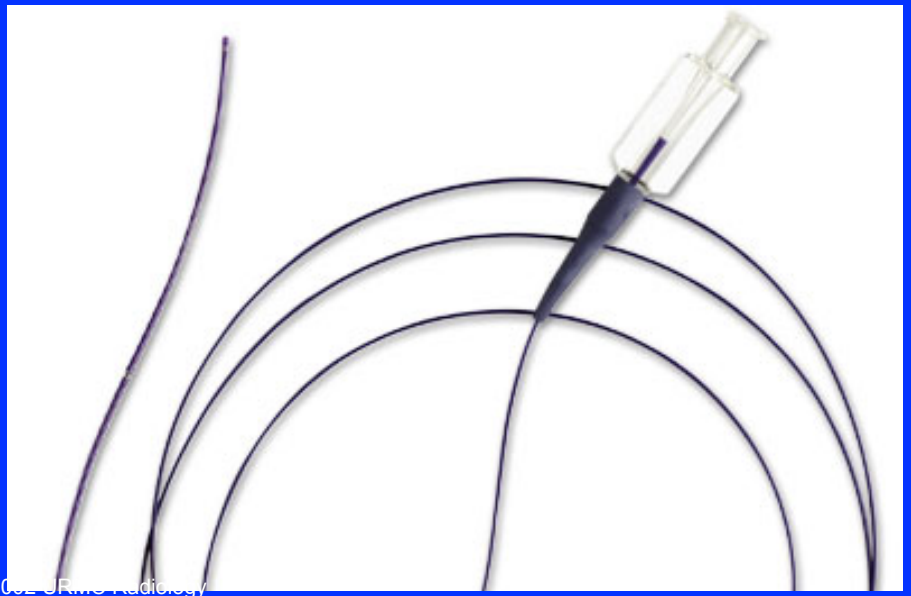
- Microcatheters:
  - Passing it over the wire through the thrombus aids in clot fragmentation & formation of channels
  - Inject heparinized saline into the clot at high speed, with a 1 cc syringe
    - Very effective as long as it is not wedged in a small branch

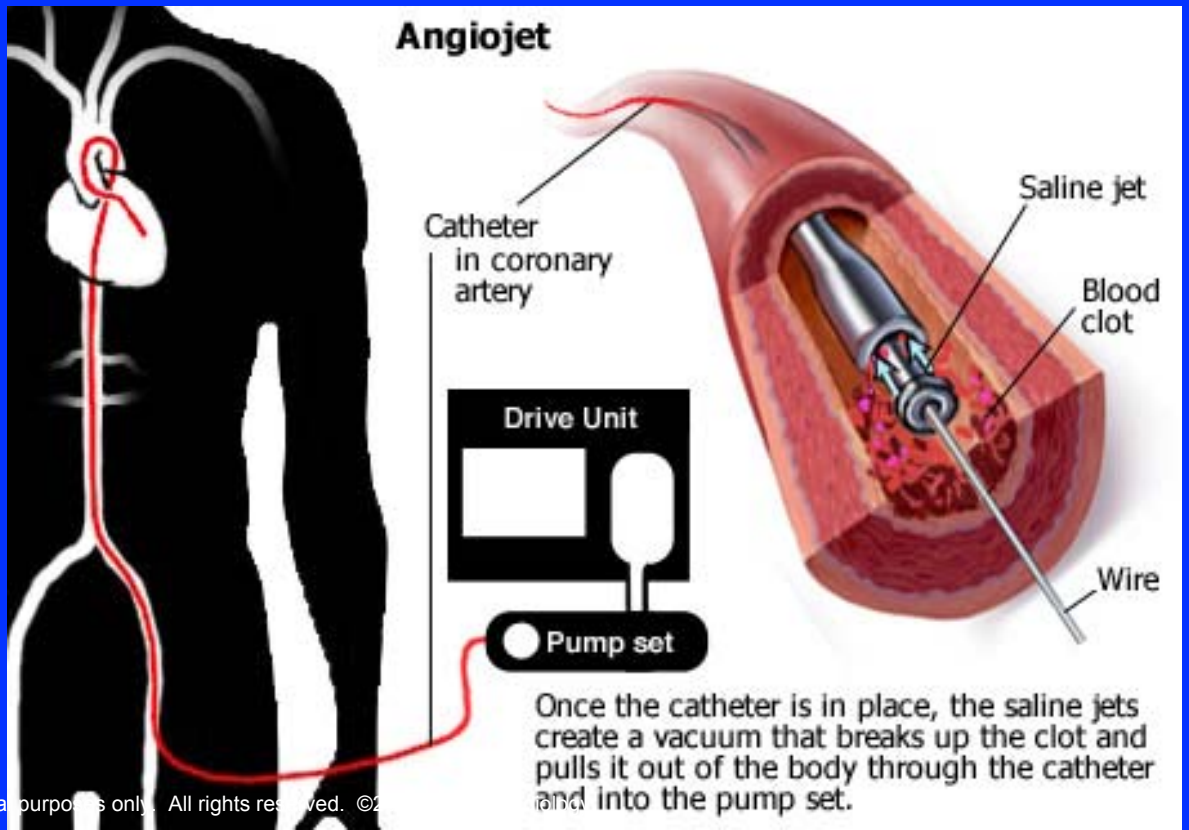


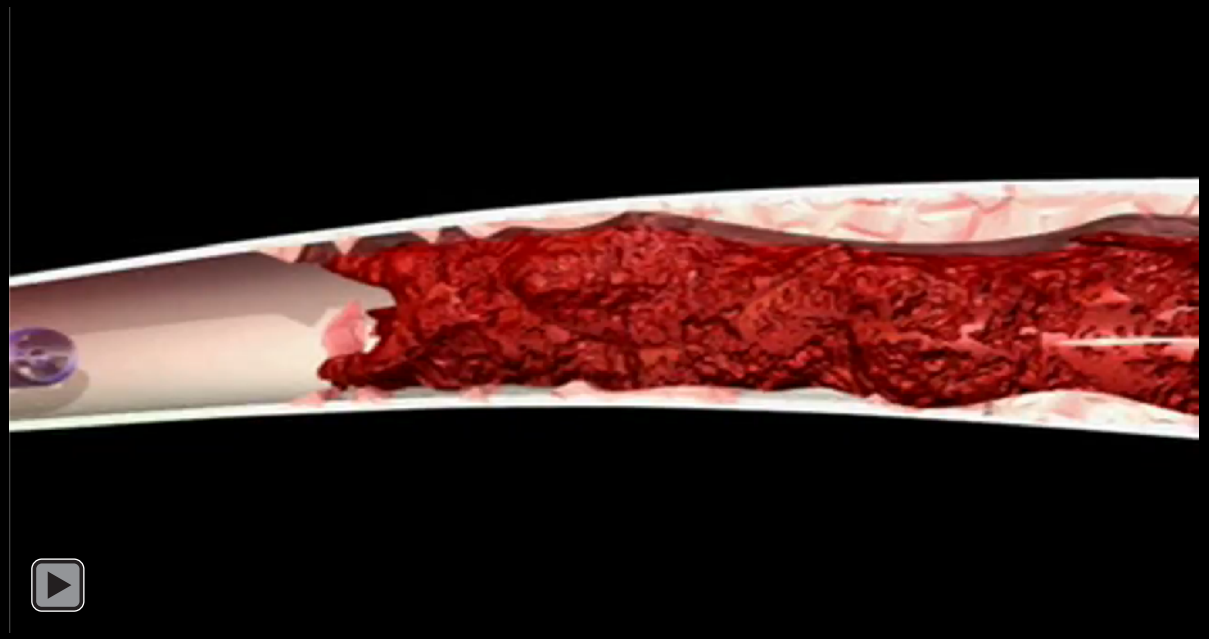
Interventional & EV Therapy of the NS, P. Morris, 2002
www.bostonscientific.com

- Snares (Microvena, Target):
  - If trawled repeatedly through the clot can break it up.
  - May extract intact emboli of hard clot when not responding to lysis

www.microvena.com

- Rheolytic Devices:
  - High velocity jet of saline at the tip directed back into the shaft of the catheter
  - Suction effect causes thrombus to be drawn and macerated by the high speed saline jet



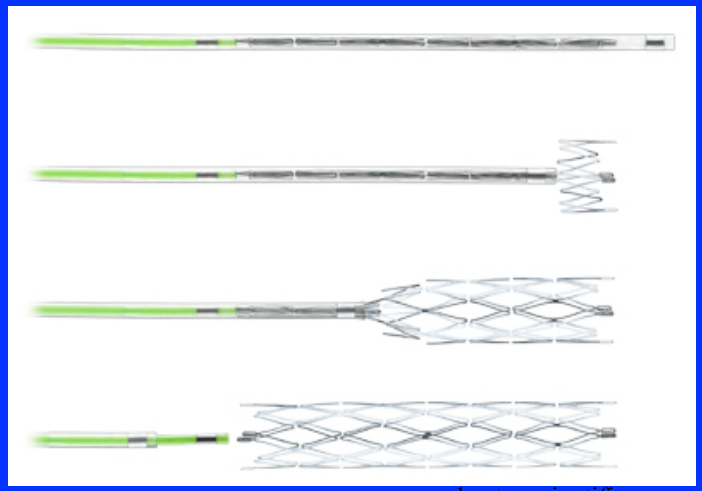


macerate

Intra/extracranial stenosis:

- Commonly discovered during thrombolysis
- Angioplasty/stenting can be performed with a reasonable risk
  - IV aspirin if available
  - IV Plavix
  - Heparinization

Interv & EV Therapy of the NS, P. Morris 2002



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Patient Selection for Intra-Arterial Fibrinolysis:

- No prior neurologic event that would obscure interpretation of neurological deficits
- Onset of new neurological signs of stroke:
  - within 6 hours of the time to fibrinolytic therapy
- Clinical signs consistent with diagnosis of acute ischemic stroke
  - Impairment of language
  - Impairment of cognition
  - Impairment of gaze, vision or neglect

Patient Selection:

- Signal stroke must be:
  - Acute
  - The most recent significant, acute worsening of serial neurologic events
  - Related to radiographic procedures
- Minimum NIHSS score of 4 except for:
  - isolated aphasia or isolated hemianopia

CT Scan Exclusions for Intra-Arterial Fibrinolysis

- Early CT scan changes of stroke:
  - Hemorrhage of any degree.
  - Significant mass effect with midline shift due to large infarct.

ContraIND to IA Thrombolysis

- Established neurological damage
- Recent surgery or trauma:
  - Calculated risk can be individually taken with fully informed family consent
  - Use common sense
- Pregnancy & other "absolute contraInd":
  - Post circul occlusions: bad prx ➔ all absolute contraInd become relative, even pregnancy
  - "locked-in" ➔ may be worse than death!

Interventional & EV Therapy of the NS, P Morris, 2002