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Current Standards for Treatment of Stroke: Management of Acute Ischemic Stroke

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Current Standards for Treatment of Stroke

Management of Acute Ischemic Stroke

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Acute Ischemic Stroke

- How big and how bad a problem is it?
- How good are the treatment options?
  - Why don't we use them more often?
- What are the risks of good therapies?
  - Who should receive these therapies?
- How should we move forward to obtain best practice for our communities?

Cerebrovascular Disease: Pathogenesis

Ischemic Stroke (83%)

Atherothrombotic Cerebrovascular Disease (30%)

Cardio embolic (30%)

Lacunar (25%)
(small vessel disease)

Other (vasculitis, dissection, hypercoagulable, Etc. (10%)

Cryptogenic (5%)

Hemorrhagic Stroke (17%)

Intracerebral Hemorrhage (70%)

Subarachnoid Hemorrhage (30%)

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How Big and How Bad a Problem is Acute Ischemic Stroke?

Stroke is Very Big and Very Bad

- Happens a lot
- Kills many
- Disables most
- Costs a ton
- Happens fast

- 800,000/year
- 1 every 3 minutes
- Leading US cause
- $50,000,000,000/year
- 2 million neurons
- 14 billion synapses
- 7.5 miles of axons/ min

- Window of RX small

- Under 4.5 hours/onset

How Good are the Treatment Options?

Preventive and Acute Intervention Therapies Work Well (But ….)

- Antihypertensive RX
- Blood glucose control
- Afib anticoagulation
- Antiplatelet Rx
- Anti hyperlipidemia Rx
- Life Style Change
- Smoking Cessation
- tPA

- Costs
- Commitment
- Time
- Effort
- Reimbursement
- Compliance
- Culture
- Not fun

Why Don’t More AIS Patients Receive Early Restorative Treatment?

Patients Arrive Late

- Mean 155 minutes
- Mean 380 minutes
- 40%
- 66%
- 5%
- Only 25%
- If using 911
- If first call PCP
- Arrive within 90min
- Arrive within 4hrs
- Actually get tPA
- Know stroke signs

Stroke Specialists are Rare

- Neurologists / USA
- Vascular boarded
- Hospitals USA
- Total Beds
- JC Primary Stroke Centers
- BAC Comprehensive
- Telestroke spoke.hub
- tPA administration

- 13,400
- 345
- 5795
- 944,000
- 800
- 200 anticipated
- Vascular neuro only
- Rare by ED physician

Tissue Plasminogen Activator (tPA)

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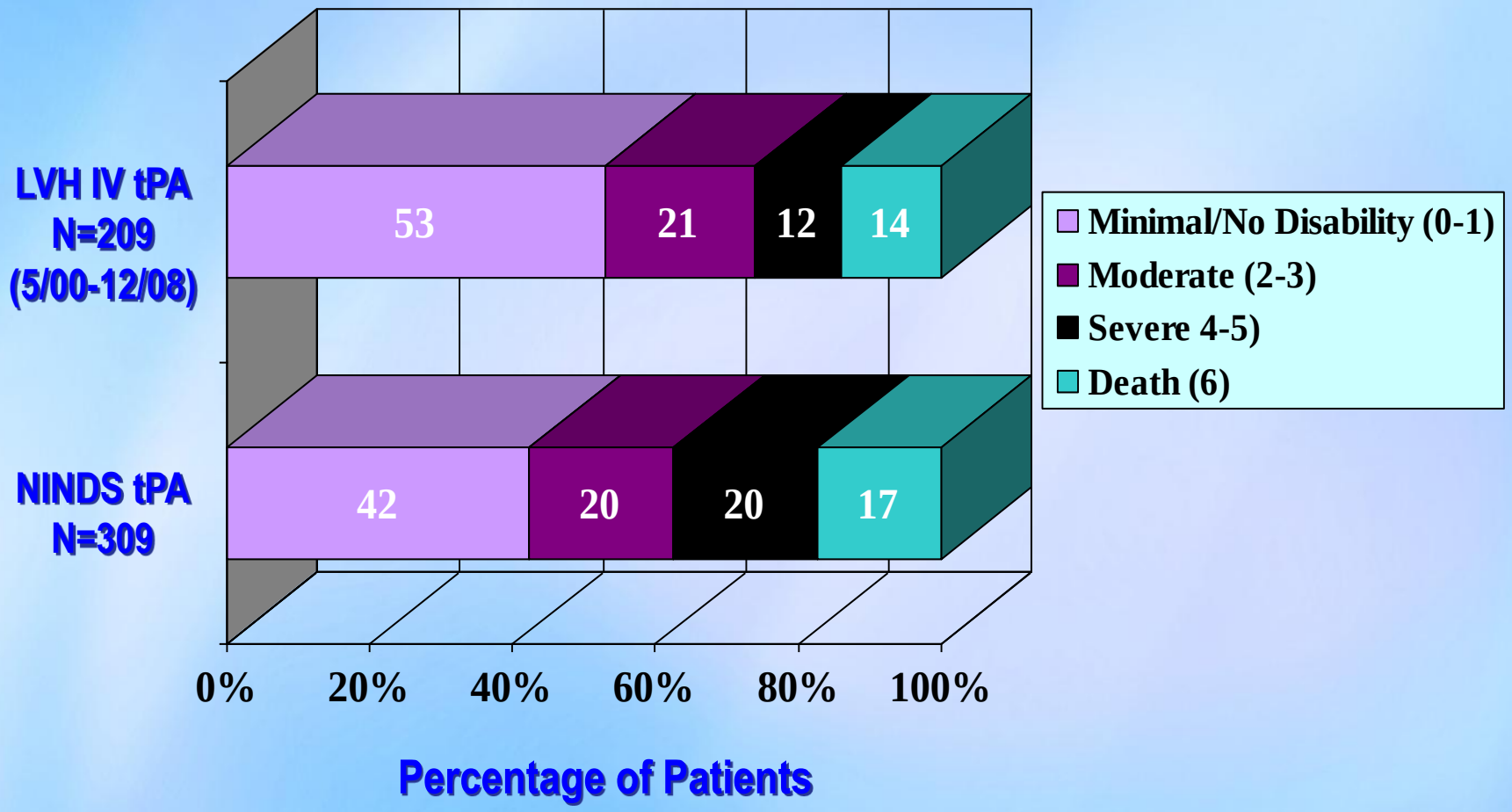
How Safe and How Effective is tPA Anyway?

How good is tPA in Stroke ?

- Roughly 50% of patients who receive tPA within time window leave hospital with minimal disability (ranking 0-1)
- Roughly 85% of patients who don't receive tPA are disabled, 15% are dead

Comparison 90 Day Outcomes tPA Treated LVH to NINDS Study

Modified Rankin Scale @ 90 Days



IV tPA - Is Safe and It Works

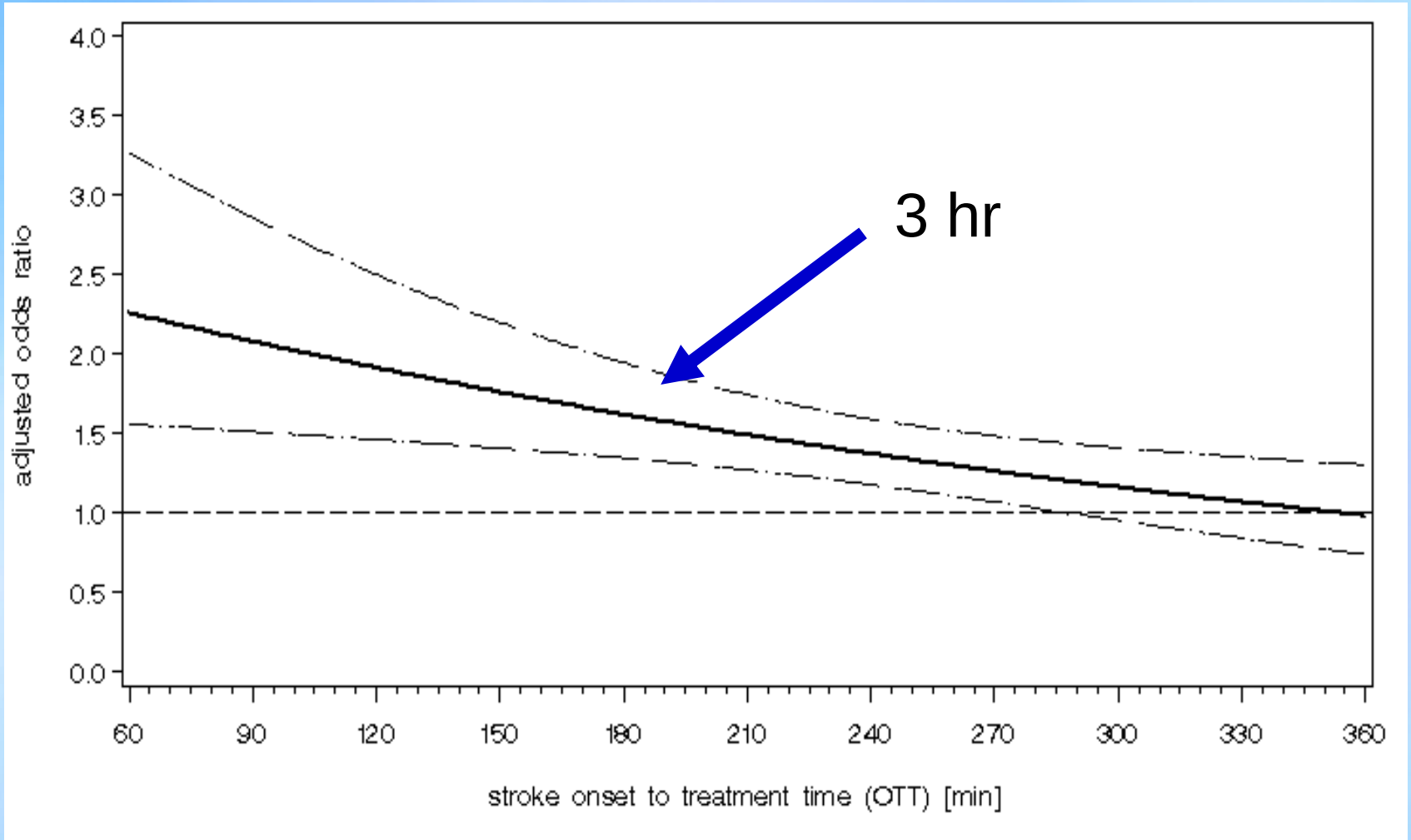
- If
- Pt recognizes signs
- Pt calls 911
- Arrives at a PCS
- Stroke team in place
- Neurologist on scene

- But
- Few do
- Many call PCP
- Ambulance don’t divert
- 24/7 hard to muster

Using tPA in Routine Clinical Practice

- Overall only about 3%-4% of stroke patients receive tPA—mostly due to time delays
- Efficacy similar to NINDS trial at most centers
- Rate of ICH: 4%-6%
- Risk of ICH increases with protocol violations
  - Time > 4.5 hours
  - Poor blood pressure control
  - INR > 1.7
  - Recent prior stroke
  - Wrong dose
    - 0.9 mg/kg
    - Maximum dose: 90 mg
  - Elevated age and blood sugar also increases risk

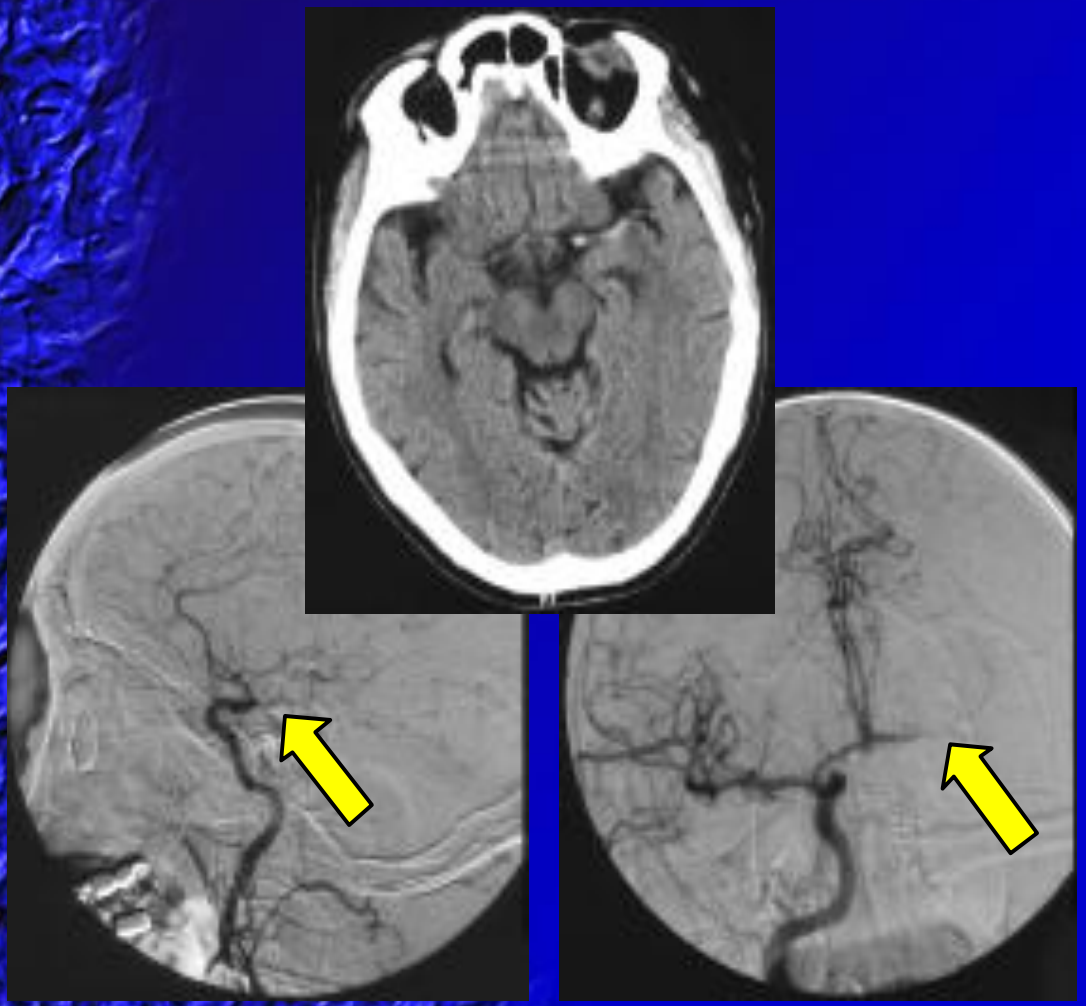
Time is Brain:
Benefits of IV tPA Diminish Rapidly

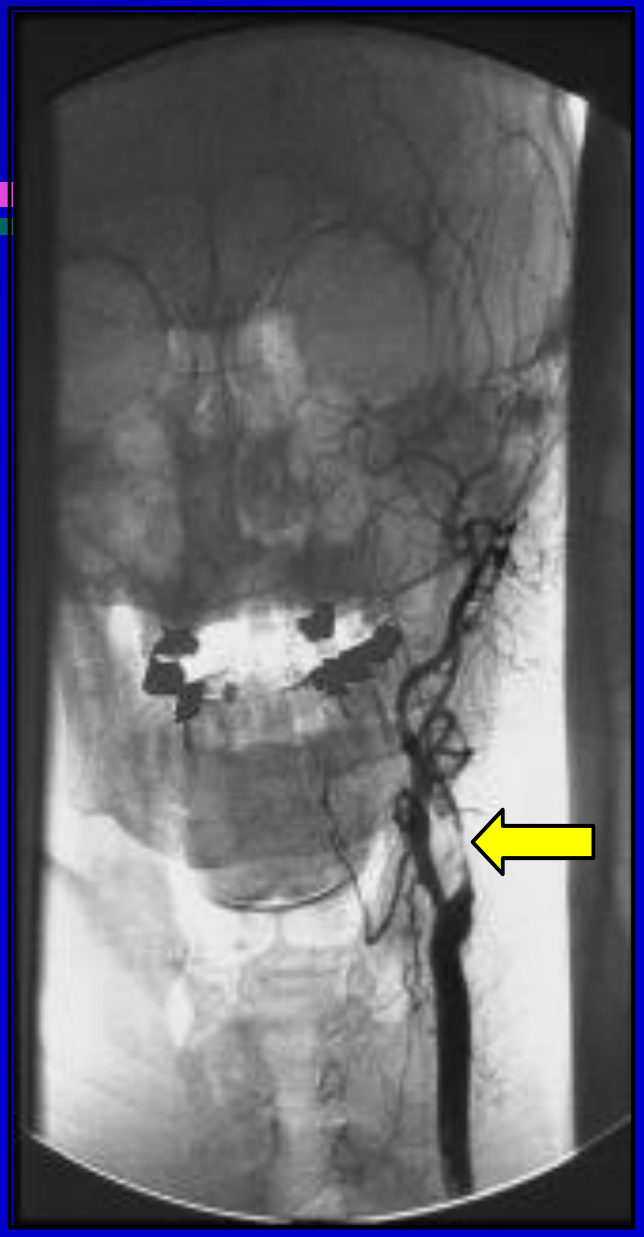


Influence of Interval Response to tPA: Odds Ratio for Favorable Outcomes

Time (min)	Odds Ratio
<90	2.81
91–180	1.55
181–270	1.40
>270	1.15

Acute Carotid Stroke





Post Stent and tPA ICA Stenosis

Who Should Receive tPA?

Questions to Ask Before Initiating Thrombolytic Therapy

- Did the stroke start within the last 3 hours?
- Any recent illness associated with bleeding risk?
- Is patient taking anticoagulants?
- Are the baseline coagulation tests normal?
- Any medical contraindication for treatment?
- Any neurologic contraindication for treatment?
- What are the findings on CT?
- Are patient and family aware of risks for bleeding?
- What is the blood pressure?

ACCP 2008 Recommendations: Thrombolytic Therapy in AIS

- For eligible patients, we recommend IV tPA 0.9 mg/kg (maximum of 90 mg), provided that treatment is initiated within 3 hours of clearly defined symptom onset (Grade 1A)

- For patients with extensive (greater than 1/3 of the MCA territory) and clearly identifiable hypo density on CT, we recommend against thrombolytic therapy (Grade 1B)

Treatment of Hypertension During and Following Administration of IV tPA

- SBP 180–230 mm Hg or DBP 105–120 mm Hg
  - Labetalol—10 mg IV over 1–2 min
    - Repeat every 10–20 min; maximum dose 300 mg; or
  - Labetalol—10 mg IV followed by infusion 2–8 mg/min
- SBP >230 mm Hg or DBP 121–140 mm Hg
  - Labetalol as above; or
  - Nicardipine—IV infusion at 5 mg/hr
    - Titrate up to desired effect by 2.5 mg/hr every 5 min; maximum rate 15 mg/hr
- DBP >140 mm Hg
  - Nitroprusside infusion 0.5 µg/kg/min; titrate to desired effect

Goals of Antihypertensive Treatment (in search of the Goldilocks BP)

- Too high is bad and may cause bleeding
- Too low may decompensate collaterals and extend infarct size
- Lowering too fast is worse than not lowering blood pressure at all (unless considering tPA)
- In general target 140-180/90-105
- Start with Nicardipene for best results

What Does Best Practice for AIS Look Like in the Age of tPA?

AIS Treatment: Other Options

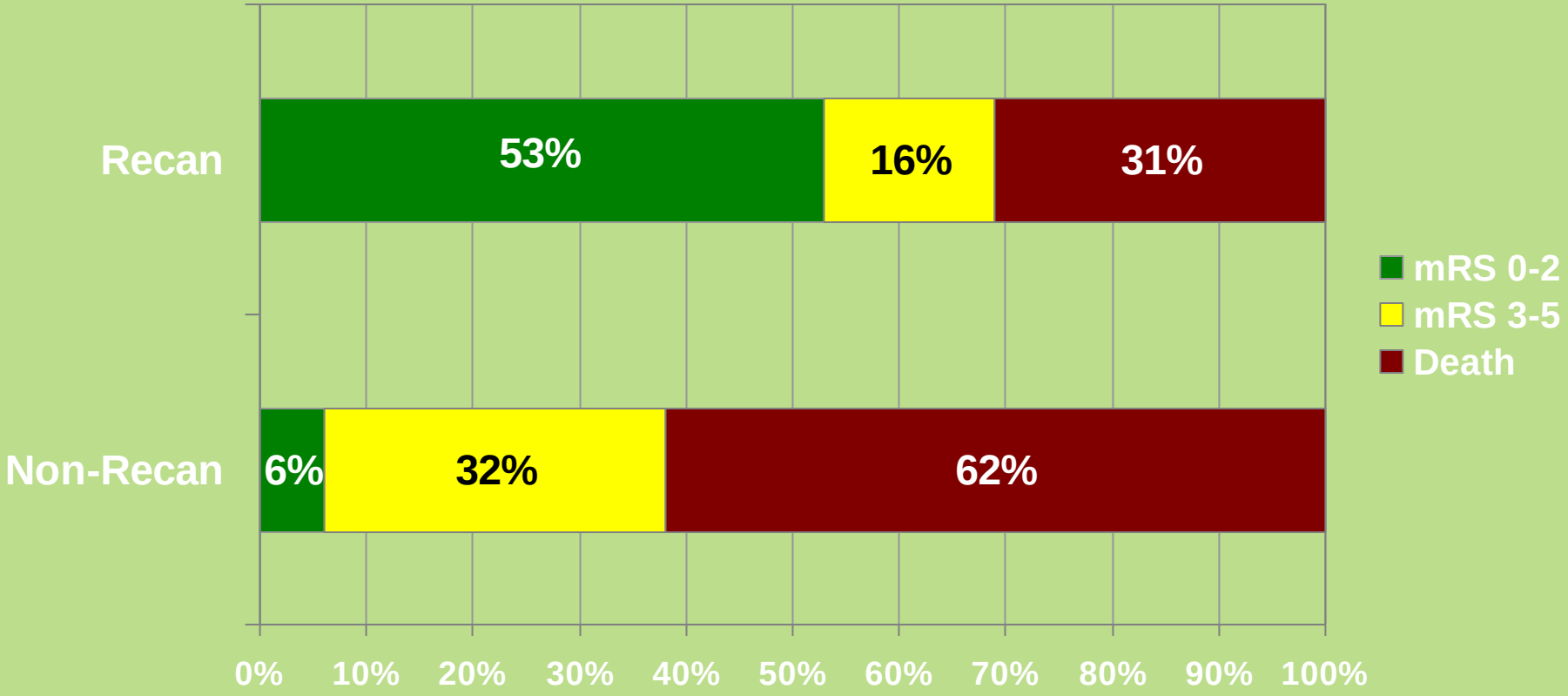
- IA administration
- Mechanical thrombolysis
- IA and IV administration
- New thrombolytic agents
- Combination with other antithrombotic agents
- Combination with neuroprotective agents

Thrombolysis: IV or IA Approach?

- An IA approach to recanalization allows for titrated and potentially more effective recanalization vs. IV alone
- But takes longer and time is brain
- Requires Neuro Interventionalist with experience
- Delays or eliminates window for IV tPA which may be fleeting
- Complications

90-Day Modified Rankin Score

Revascularized vs. Unrevascularized



Antiplatelet Therapy

- ACCP 2008 Guidelines for Use of Antiplatelet Therapy in Ischemic Stroke
  - In patients not eligible for thrombolytic therapy, early Aspirin therapy (160–325 mg/day) is recommended (Grade 1A)
  - Delay Aspirin for at least 24 hours after tPA
  - Aspirin can be used safely in combination with low doses of subcutaneous Heparin

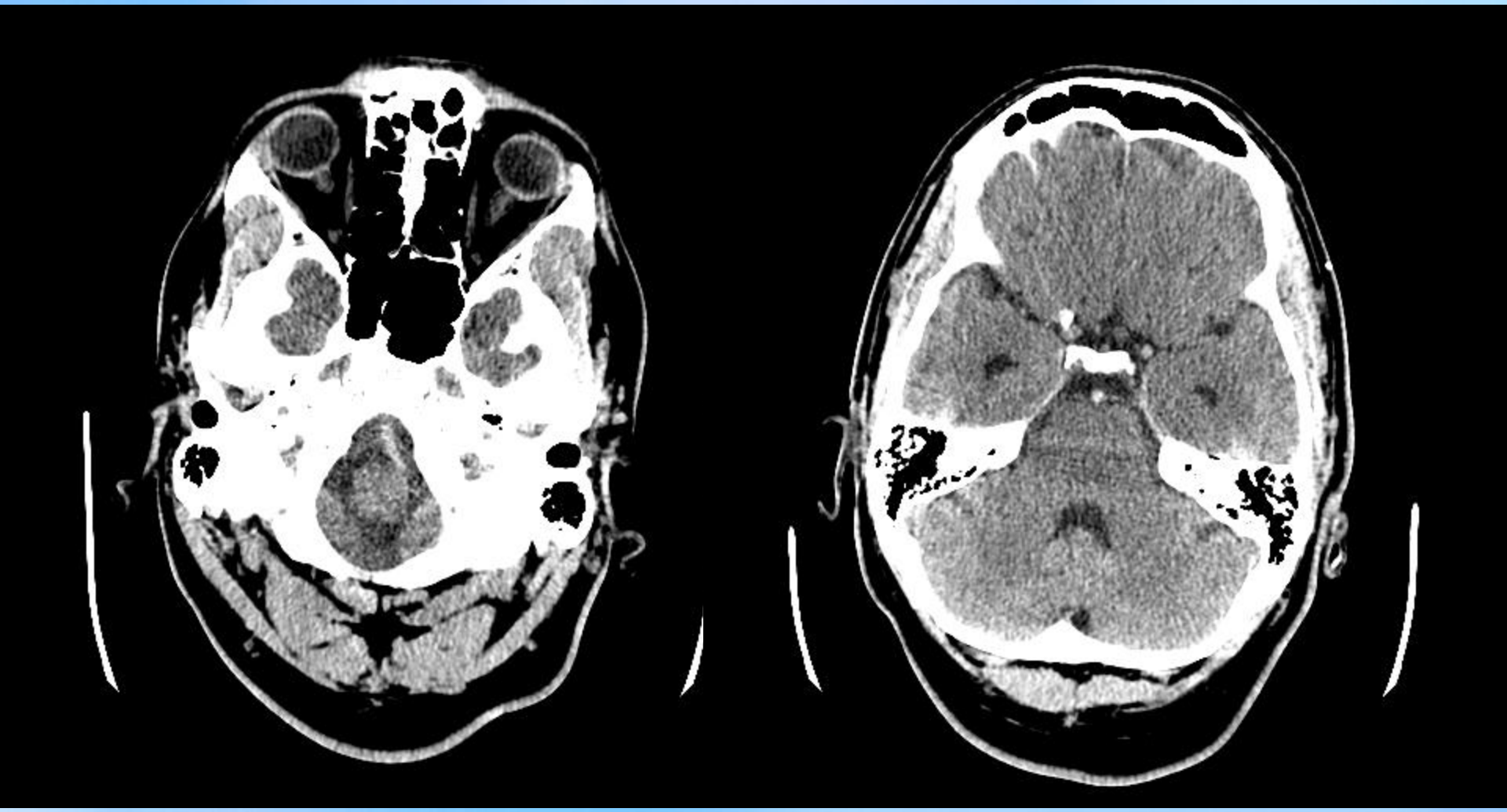
Early Anticoagulation

- Urgent anticoagulation is not recommended
  - Does more harm than good in all studies
- Should not be given at all unless imaging has excluded hemorrhage
- Requires slow initial administration and continuous monitoring of anticoagulation and adjustments in dose

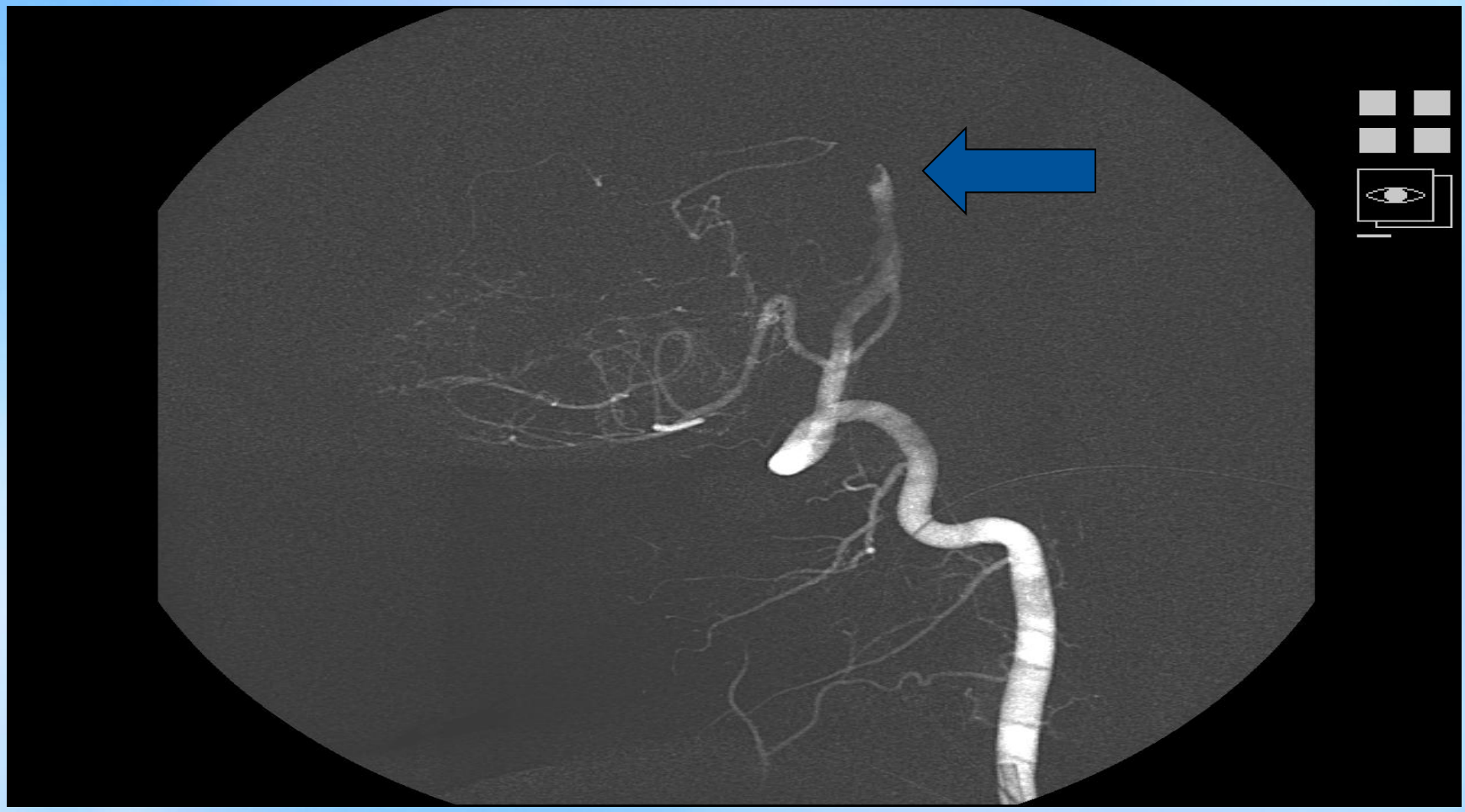
Case Presentation (BM)

- 36yo man found down in a pile of mulch
- LVH ED 30 minutes out from discovery
- Stroke Alert : Flaccid quadriplegia, sluggish pupils, absent gag, respiratory arrest
- Toes Up going bilaterally

BM
Found down unresponsive



Distal Basilar Artery Occlusion



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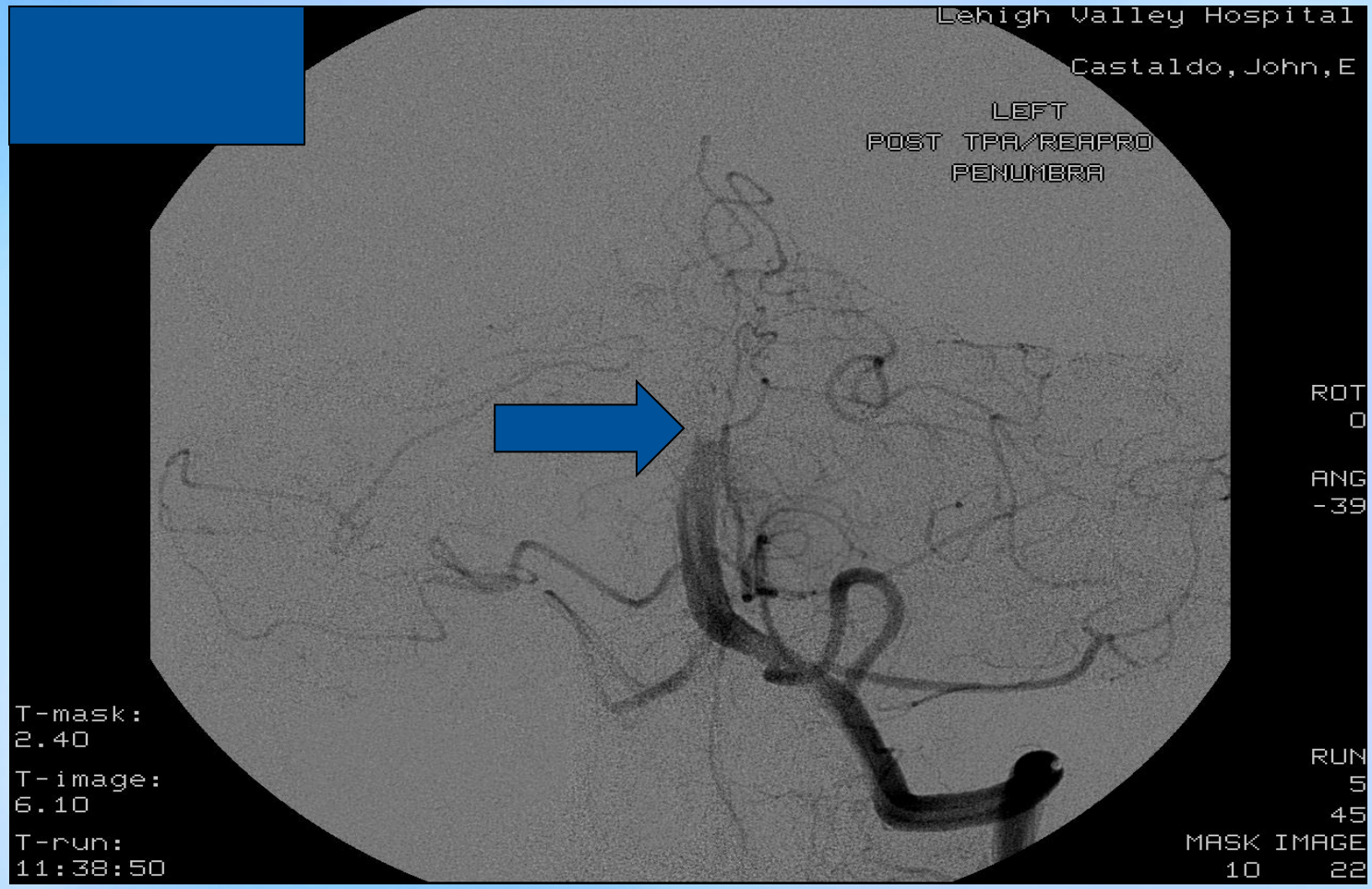

Interventional Catheter Clot Penetration of Basilar Clot

Basilar Clot Extracted with Penumbra Device:

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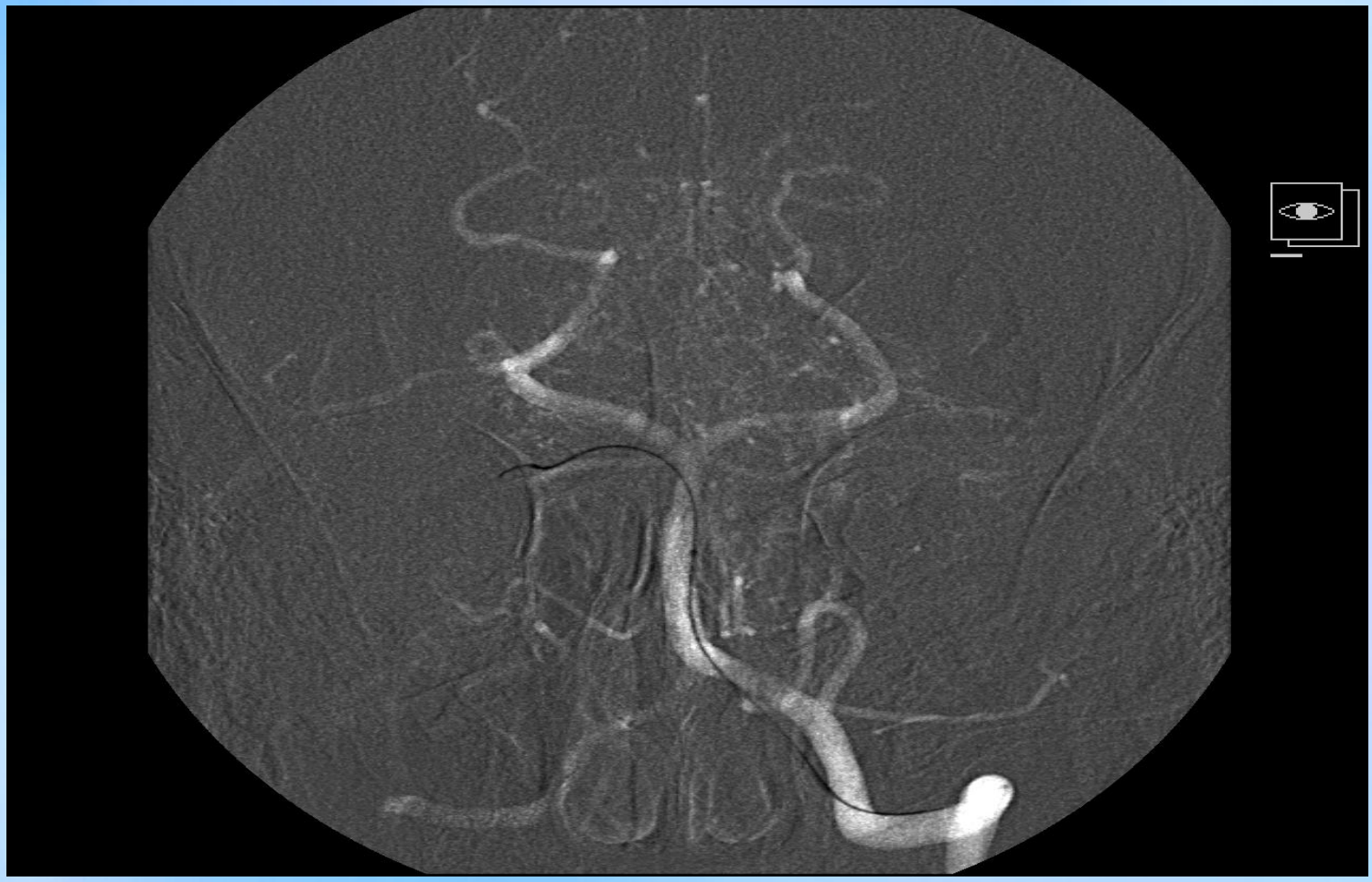
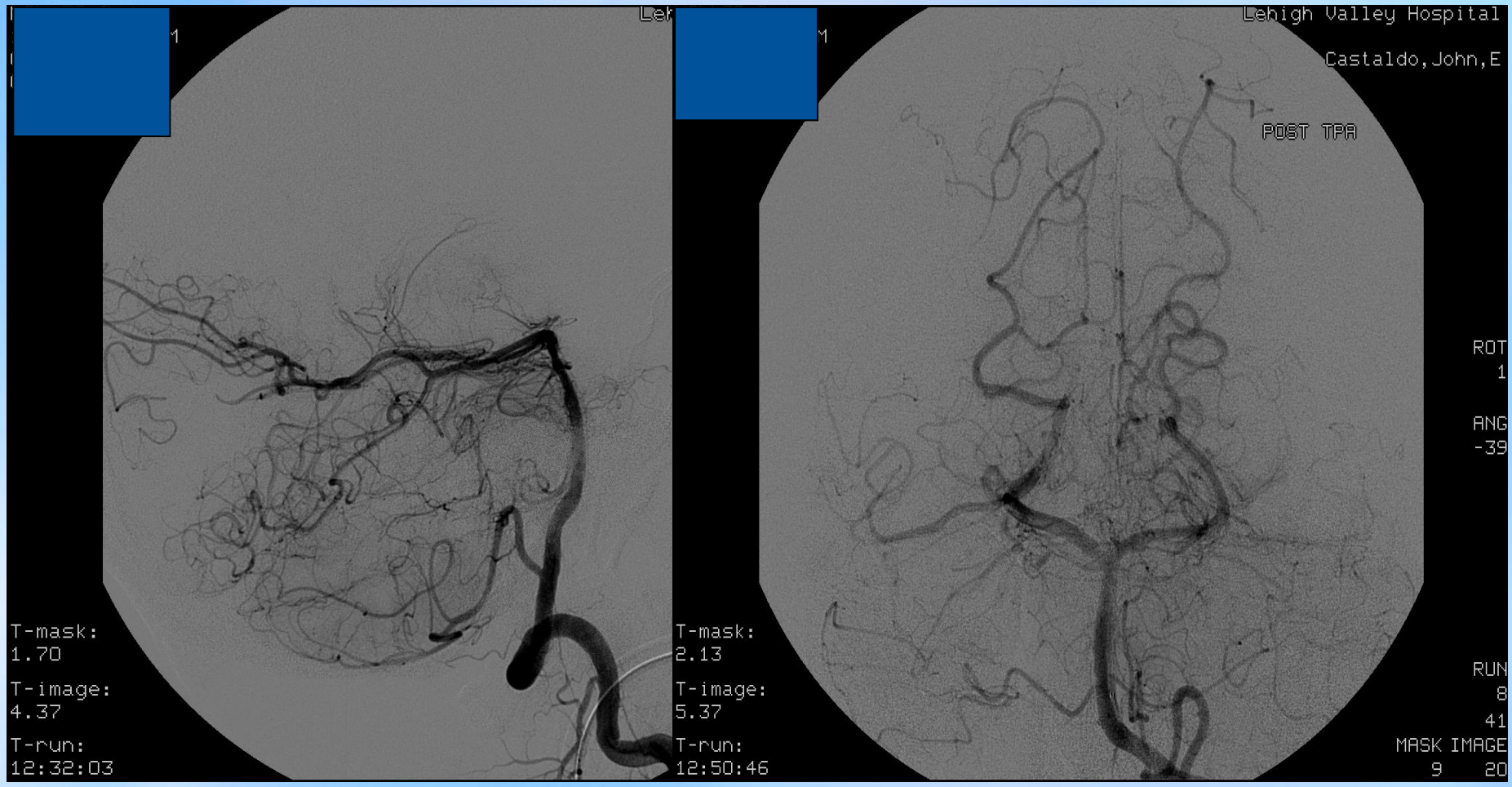
Basilar Occlusion After TPA and Reopro

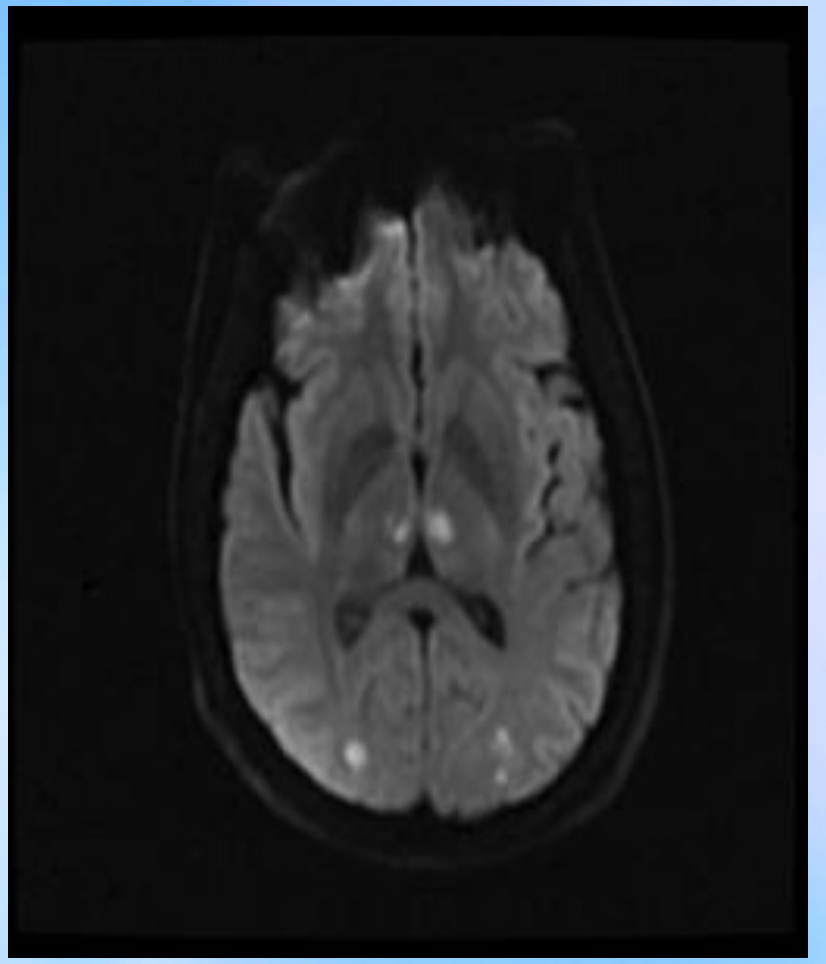
Re-cannalization after tPA Cath in SCA

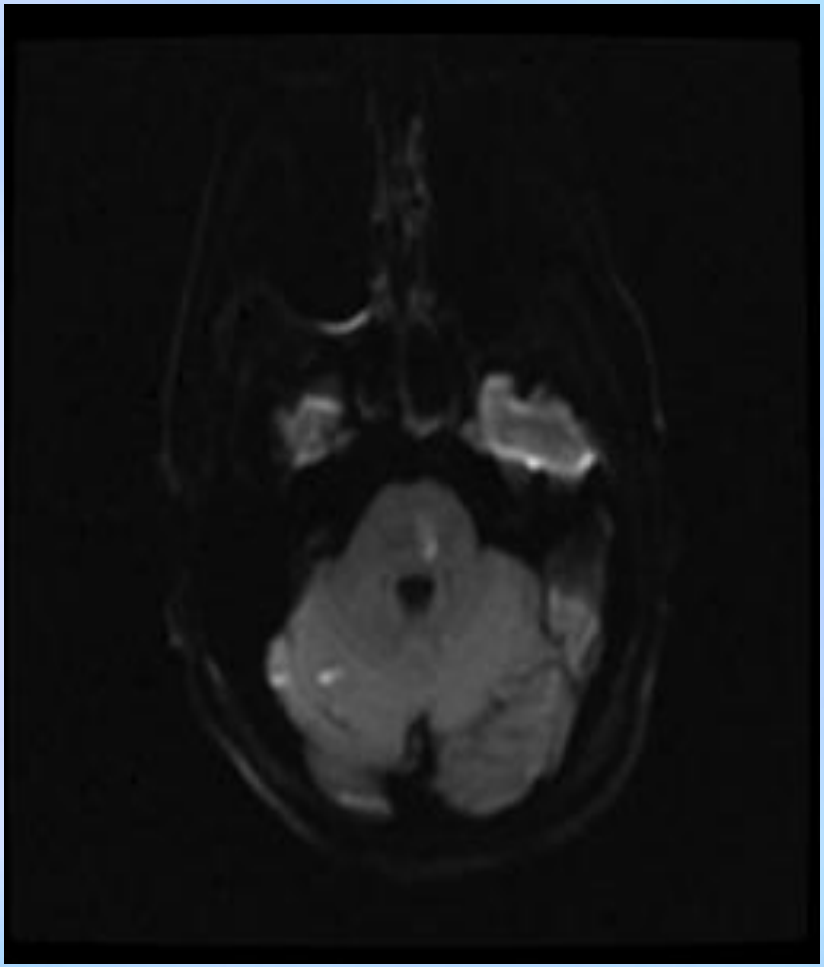


Basilar Artery: Final Interventional Results

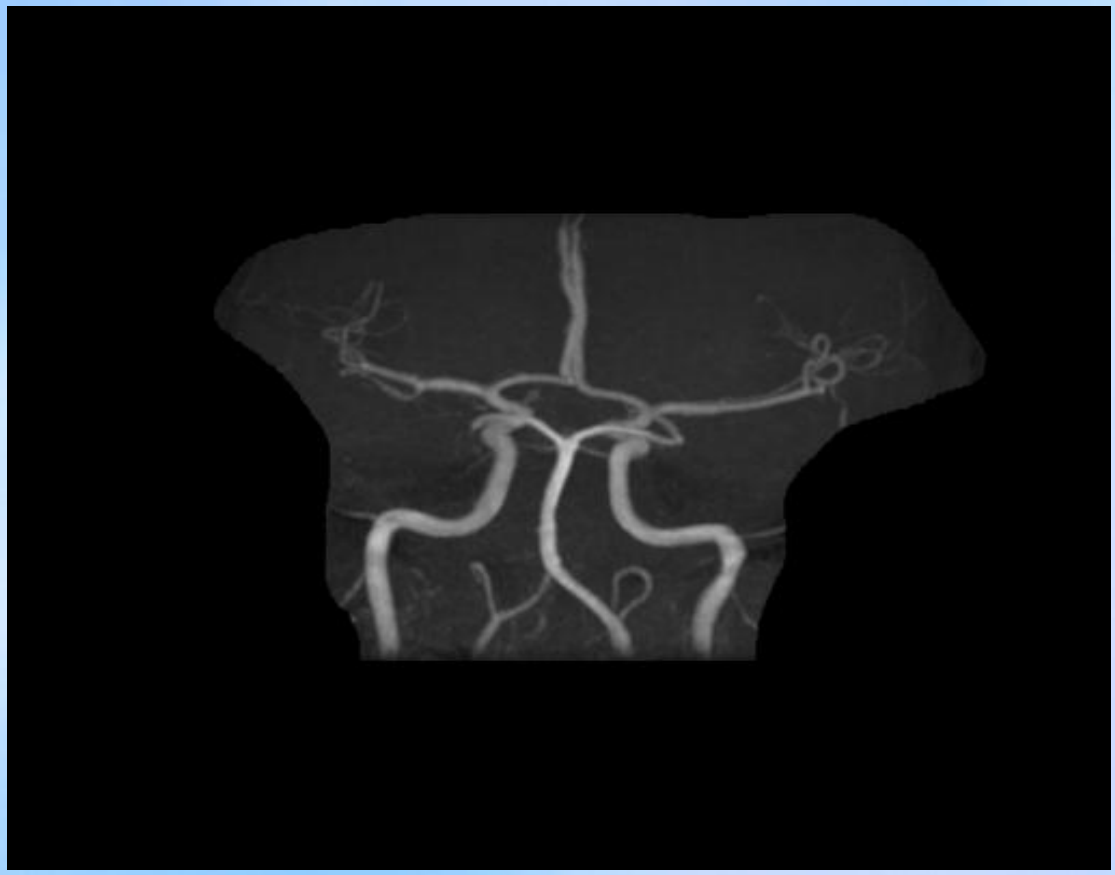


MRI Day 2 Stroke Alert





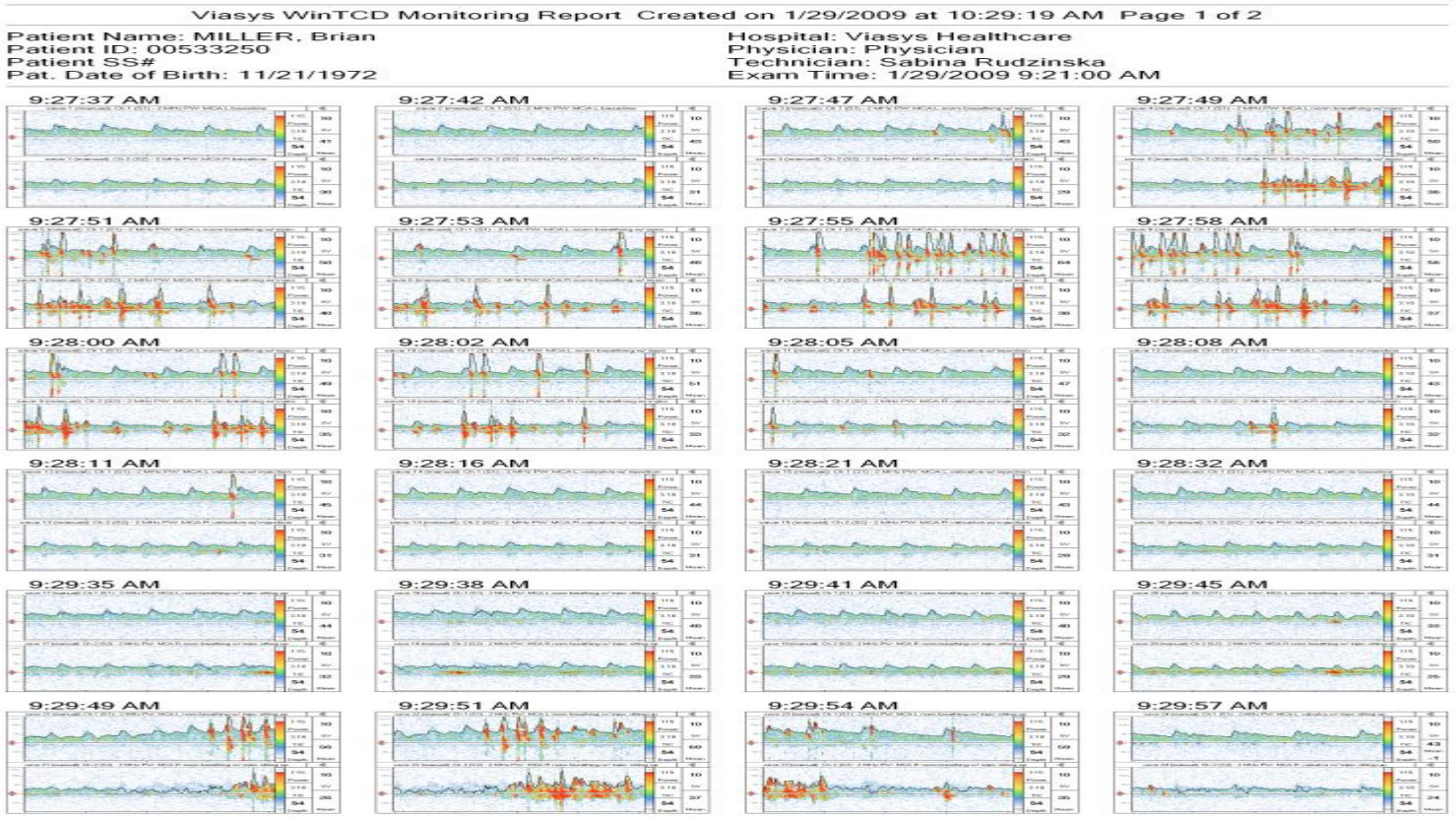
MRA Day 2



Outcome

- NIHSS 0
- Walking the hospital floor unaware of any neurological deficits
- Discharged home

TCD Bubble Study with Valsalva (BM)



On Follow-up

- TEE showed small PFO
- TCD showed aggressive bubble emboli
- Randomized to RESPECT
- Amplatzer device deployed
- Patient has remained free of neurological deficits for 2 years

In a typical acute ischemic stroke, every minute the brain loses

- 1.9 million neurons
- 14 billion synapses
- 7.5 miles myelinated fibers

-- Saver, Stroke 2006

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Summary AIS Optimal Medical Management 2013

- Rapid diagnosis and treatment is crucial to outcome: Time is Brain!
- Different strategies are necessary for different time windows for IV and IA tPA
- Neuroimaging is opening better understanding of tissue at risk/therapeutic outcome with aggressive therapy
- Early Risk Factor Modification and Stroke Unit improves outcomes substantially