



Advancing Acute Stroke Treatment Using the S.M.A.R.T. Approach

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Thrombolysis use very low

- Only ~1.1%-5.0% of ALL ischemic stroke patients receive thrombolysis^{1,2,3}
 - 5-10% at stroke centers (15% highest reported)⁴
- Why?
 - Conservative treatment criteria?

1. Ann Emerg Med. May 2007
2. Stroke 32(8):2001
3. Stroke 2011; Online June 2
4. Arch Neurol 2001;58:2009-2013

Key Concepts

- We can increase thrombolysis treatment rates and improve outcomes
 - At least **25-30%** of ischemic stroke patients may be treatable
- Use **SMART** (Simplified Management of Acute stroke using Revised Treatment) criteria
 - Safe, effective
 - Increases patient treatment eligibility

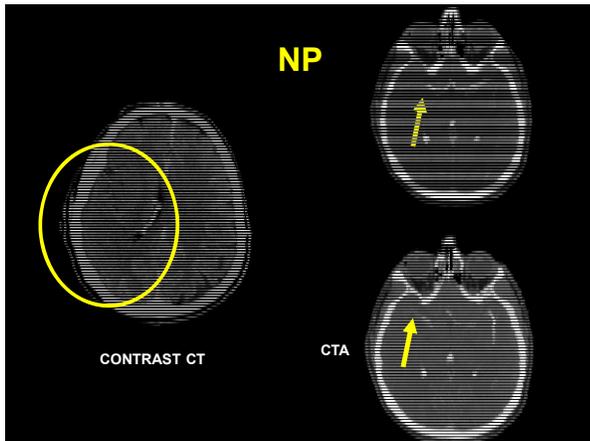
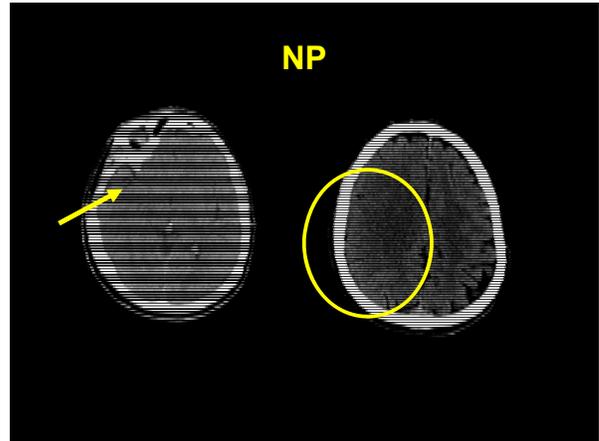
Case

NP

- 61 yo male carpenter
- PMH: hypertension, smoking
- Meds: none
- Allergy: Iodine, (Contrast) ?
- Usually goes to sleep at 21:00
- ? 3:30-4:00A next day L hemiplegia
 - Unwitnessed, found around 5:00 AM
- In ED 6:00 AM (2-2.5h?)
- Telemedicine consult 06:30 (2.5-3h)

NP

- Exam: 0/5 LUE/LLE, R gaze preference, L VF cut, L neglect (NIHSS=20)
- CT/CTA: Read as “normal”



NP: Rt-PA Contraindications

- Uncertain time of onset
- Early infarct signs
- Hyperdense MCA
- Large stroke
- Contrast Allergy?
- Inexperienced hospital

SMART
Simplified Management of Acute Stroke Using Revised Treatment Criteria

The SMART Premise

- Current IV rt-PA treatment criteria are too strict
 - Clinical trial ≠ clinical practice
 - Most rt-PA exclusion criteria are not evidence based
 - Many centers' exclusion criteria even more strict than guidelines and clinical trials
- Simplified Management of Acute Stroke using Revised Treatment Criteria (SMART)
 - Rethink exclusion criteria
 - Streamline management
 - Increase number of candidates for treatment

SMART: IV rt-PA Absolute Exclusion Criteria

- Acute hemorrhage that is the cause of the patient's symptoms

Common IV rt-PA Contraindications That Are NOT SMART Criteria

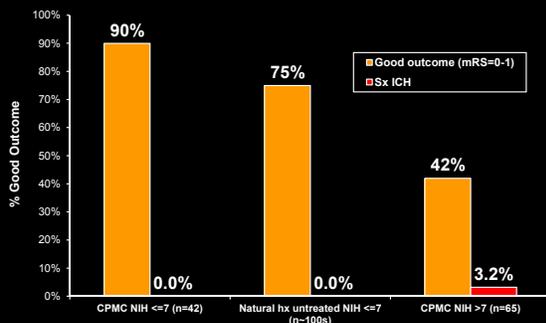
- Stroke severity (mild or severe)
- Older Age (≥ 80)
- Presence of other asymptomatic brain lesions (e.g. tumor, aneurysm, subdural hematoma etc.)
- Improving symptoms (if still disabling)
- Stroke, head trauma, surgery, other bleeding or arterial puncture < 3 months
- Seizure
- Blood sugar (low or high)
- Elevated PTT/INR (on warfarin, heparin, LMWH)
- Pregnancy
- Dementia
- Renal failure, recent MI (unless <1 wk), other co morbidity
- Early infarct signs on CT
- Clear cut onset time

SMART: Reduction of rt-PA Exclusions

- No NIHSS (stroke severity) cut offs
 - symptoms must be "disabling"
 - "mild strokes" cause significant morbidity/mortality
 - ~20-30% of "mild strokes" are disabling, especially if large artery occlusion present¹⁻³
 - Represent ~20-30% of acute stroke patients¹⁻³
 - Higher risk of subsequent deterioration¹⁻³
 - rt-PA effective in these patients⁴
 - Severe strokes also benefit from IV rt-PA⁶
- No age cut off
 - Older patients generally do worse, but still benefit from treatment⁵⁻⁹
 - IST 3/SITS/VISTA registries support this approach^{10,11}

1. Smith, Stroke, 2005 Nov;36(11):2497-9
 2. Hochmeister Stroke, 2007;38(23):2523-2528
 3. Barlow, Neurology 2001;58:1015-1020
 4. Der Kuyper, Stroke, 2007;38(26):2612-2618
 5. Stroke, 2007;38(26):2612-2618
 6. Eur Neurol, 2005;54(3):142-4
 7. BMJ, 2005;331(7616):1405
 8. Stroke, 2004;41:2840
 9. Wallis, N Engl J Med, 2004;251(16):1688-1694
 10. Lancet, 2012 Jun 23; 379 (9834): 2352-63

rt-PA in Mild Strokes (NIHSS ≤ 7): SMART Vs Natural History



Tong, et al. ASA International Stroke Conference: 2009

SMART: IV not IA Is Preferred Initial Treatment

- Rationale:
 - Time to reperfusion is likely more important than modality of reperfusion
 - IA treatment requires much more time to initiate compared with IV and is generally less available
 - No compelling data that IA is superior to IV, including in large artery occlusion or basilar occlusion
 - IA can always be added to IV (bridging/full dose)
 - IV first may "soften" clot, and make IA more effective
 - No good evidence that additional doses of rt-PA causes more bleeding, especially if delayed
 - Data supporting IA thrombolysis is lower quality than that supporting IV

IV vs. IA therapy myths^{1,2}

- IA better than IV due to higher recanalization rate
 - Not been conclusively shown
 - Difficult to make a fair comparison (timing/severity/location)
 - Clinical outcomes may not be significantly different
- IA better >3h
 - ECASS 3 refutes this
- IA better in VB stroke
 - Similar outcomes in meta analysis²
- IA superior if occlusion seen on CTA/MRA/CUS
 - See above, limited evidence
- DWI/PWI identifies good IA candidates
 - DEFUSE/EPITHET show IV rt-PA works in these patients

¹Stroke. 2007;38:2191-2195
²Stroke. 2006; 37: 922-928.

IV Rt-PA in Anticoagulated Patients

- No reports of increased harm in anticoagulated patients
 - In fact, some old IV rt-PA studies routinely used heparin after treatment
 - IA therapy often includes full anticoagulation
- Increased risk in anticoagulated patients is purely theoretical
 - Are anticoagulated stroke patients less likely to bleed?
 - Why do these patients experience clot formation despite anticoagulation?

Mechanical Devices vs. IV rt-PA

- Not an either/or question
- No reason why mechanical treatment cannot be used with IV rt-PA
- ~50% of patients in recent mechanical thrombectomy trials had IV rt-PA before device use
- No difference in ICH rate in these patients

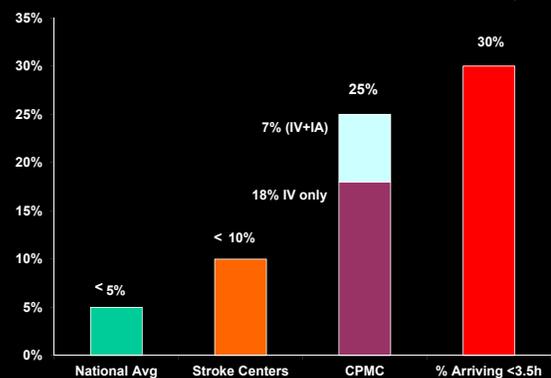
Stroke. 2012;43: Jul 31
 Lancet 2012; Aug 26

SMART RESULTS: CPMC

Using SMART Criteria: Our Hospital's Results

- Between 7/06 and 12/09, 178 patients received thrombolysis
 - Represents 25-30% of **ALL** acute ischemic stroke patients at our hospital during this time
- 135 patients (76%) treated with IV rt-PA alone using **SMART** criteria

% All Ischemic Stroke Patients Treated with Thrombolysis



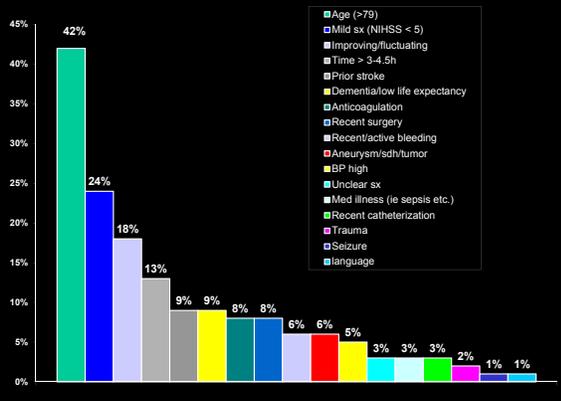
SMART IV rt-PA Stroke Patient Characteristics

- 49% male
- Mean NIHSS= 10
- Median age 76 years (NINDS age: 66-69)
 - 42% ≥ 80 years old
 - 13% ≥ 90 years old
- Median door to needle time: 58 minutes
- Median symptom onset time to treatment time:
 - 135 minutes (95% CI 65-195 minutes)
 - 21% >3h after symptom onset

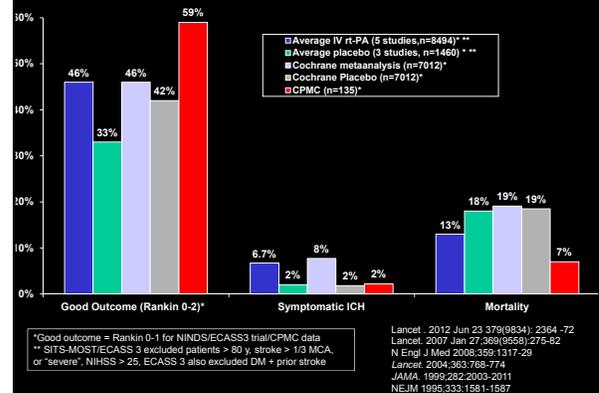
SMART: High Number of Relative Treatment Contraindications

- On the basis of common IV rt-PA exclusion criteria **89%** of these patients would NOT have qualified for thrombolysis
 - 42% age ≥ 80 (13% ≥ 90)
 - 24% NIHSS ≤ 5 (41% NIHSS ≤ 7)
 - Average # contraindications: 1.4, range 0-4
 - 45% had more than one relative contraindication

SMART: Frequency of Common Relative Contraindications



CPMC Versus Major IV rt-PA Studies



SMART: Dealing with Stroke MIMICS

- If unclear it is a stroke, should you treat?
 - Risk of hemorrhage is very small (<1%)¹⁻⁴
 - Repercussion of missing treatment may be high
 - Mimics may constitute 10-23% of acute stroke rt-PA cases at high volume centers¹
 - Risk of bleeding is 0% in these cases
 - If you have not treated a stroke mimic with rt-PA, you are likely under treating

1. Stroke. 2009 Apr;40(4):1622-5
 2. Chernyshev. International Stroke Conference 2009
 3. Stroke 2006; 37: 759-765
 4. Neurology. 1999; 52: 1784-1792

CPMC SMART: Rapid ED evaluation

- Door to CT completion: 15 minutes
- Door to needle: 62 minutes
- Symptom onset to needle: 135 minutes
- Requires strong commitment from hospital and staff
- Increases options for treatment

SMART: Streamlining the ED rt-PA Evaluation Process

- No labs required prior to initiation of therapy if clinically appropriate¹⁻³
- Stroke code alerts CT technologist to clear scanner
- No written consent required
- CT read by treating neurologist

1. Neurology 2006;67:1665-1667.
2. Stroke, Dec 2006; 37: 2935 – 2939.
3. Acad Emerg Med. 2007 May ;14 (5 Suppl 1):S33.

SMART: Conclusions

- A substantial proportion of stroke patients may be treated safely and effectively with IV rt-PA using SMART criteria
- Requires commitment of treating institution and staff
- We should strongly consider revising stroke protocols to reflect changing knowledge about stroke practice

Case

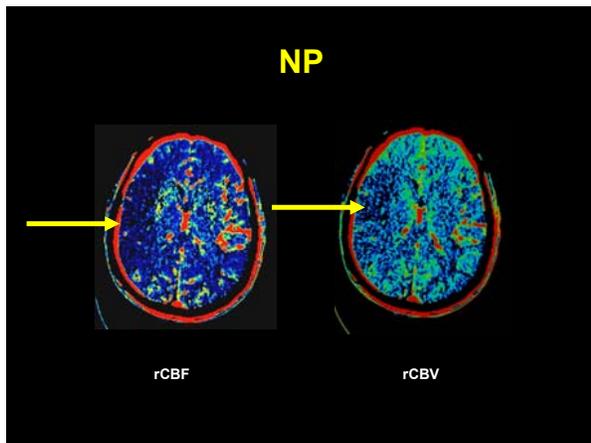
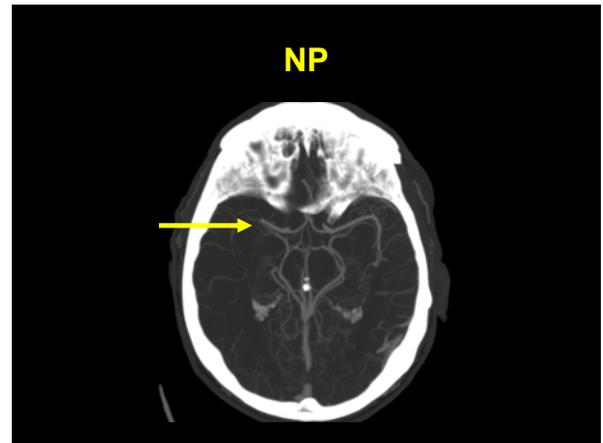
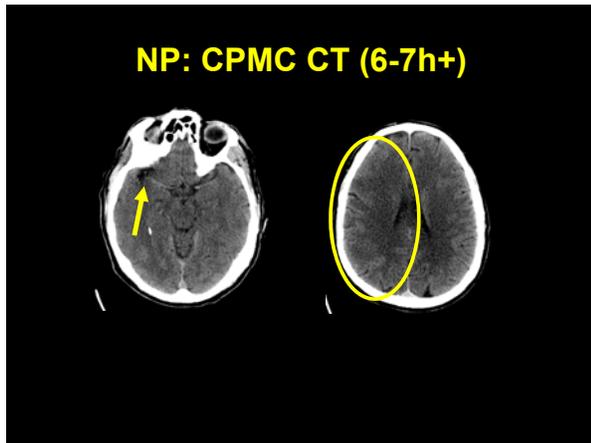
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- Patient treated with IV rt-PA at 7:25A (3.5h-6h+ after onset)
- Rationale:
 - The stroke is severe
 - Outcome likely to be poor without treatment
 - CT/CTA are not adequate predictors of tissue viability
 - Onset time could be within 4.5h
 - Patient/family accept risk
 - Patient is younger
- Most physicians would not treat
 - But we are “experts”

NP

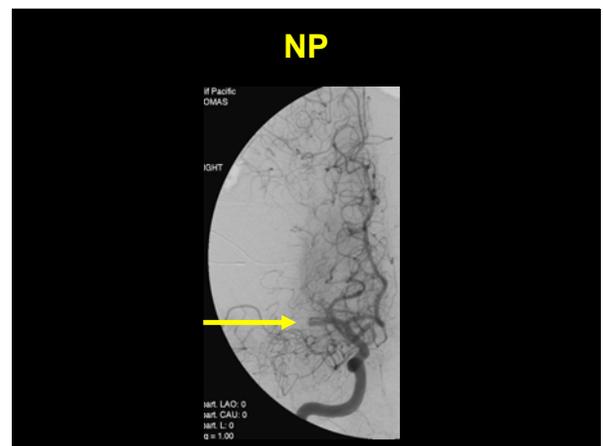
- Patient transferred to CPMC
- Arrived 10:00 AM (6-7h+)
- Exam: LUE/LLE 4/5, no visual field cut, dysarthria, L facial droop, r gaze preference
- NIHSS=9

What should we do?



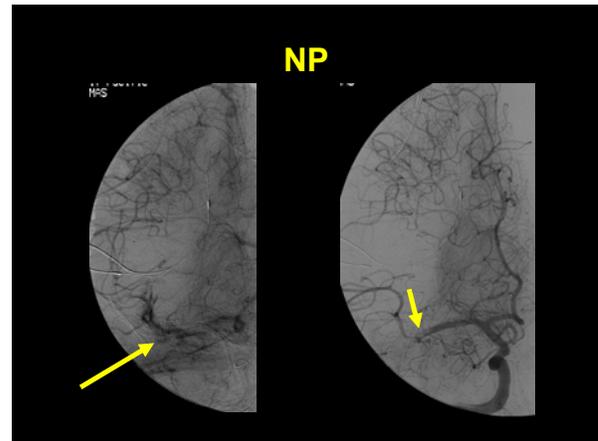
What should we do?

- Case**
- Due to significant mismatch, intra-arterial (IA) therapy offered:
 - Patient begins to deteriorate just before taken to angiography



NP

- Pretreated for possible contrast allergy
- 6 mg IA rt-PA infused: no change in occlusion
- Angioplasty of L MCA: Partially successful, but contrast extravasation consistent with vessel damage: procedure stopped
- Normal in SSEPs during procedure (i.e. motor pathways intact)



NP

- Post procedure: Normal arm and leg strength, NIHSS=3 (dysarthria, LUE sensation, L facial droop)



Wake up Strokes: Clinical Trials

- EXTEND: Extending the Time for Thrombolysis in Emergency Neurological Deficits (Australia)
- WAKEUP: Efficacy and Safety of MRI-based Thrombolysis in Wake-up Stroke (Europe)
- MR WITNESS: Multicenter Safety Trial of IV rt-PA in patients with unwitnessed stroke onset (USA)

SMART Conclusions

- We can increase thrombolysis treatment rates and improve outcomes
 - **25-30%** of ischemic stroke patients treatable
 - Use **SMART** criteria to increase treatment ra
- Neuroimaging:
 - CT perfusion (CTP)/CT angiography (CTA)
- Telemedicine
 - Increases treatment availability and accuracy

Do All IV rt-PA subgroups need to be studied with a formal clinical trial?

- Impractical: insufficient patients in most subgroups
 - IST-3 took >10 years and got 1/2 planned enrollment
- Expensive
- No subgroup has been identified where rt-PA is ineffective
 - ? Very large complete infarct on MRI > 3h?

Case

Case: DT

- 91 year old female at remote hospital
- Acute aphasia, right sided weakness
- Symptom onset time: 15:15
- Past Medical History:
 - congestive heart failure
 - atrial fibrillation
 - active bleeding hemorrhoids
- Receiving warfarin: INR 2.5

DT: Examination

- Telemedicine consultation using remote video equipment: 16:15 (60 minutes)
- Exam: NIHSS=27 (right hemiplegia, aphasia, neglect, visual field cut)
- Non-Contrast Head CT: negative



What should we do?

Thrombolysis Contraindications in this Case

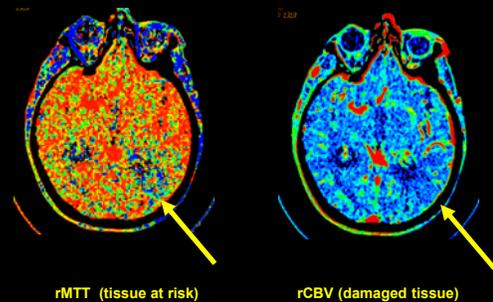
- Older Age (≥ 80)
- Large stroke (NIHSS >20)
- Anticoagulation (INR 2.5)
- Active Bleeding (hemorrhoids)

What should we do?

Case Management

- Half dose IV rt-PA (0.45 mg/kg) administered at 17:30 (2h:15m)
- Transferred
- Upon arrival (3 hours later): Aphasia improved, right side strength is better (3/5)
- CTA/CTP performed

CT Perfusion (CTP)

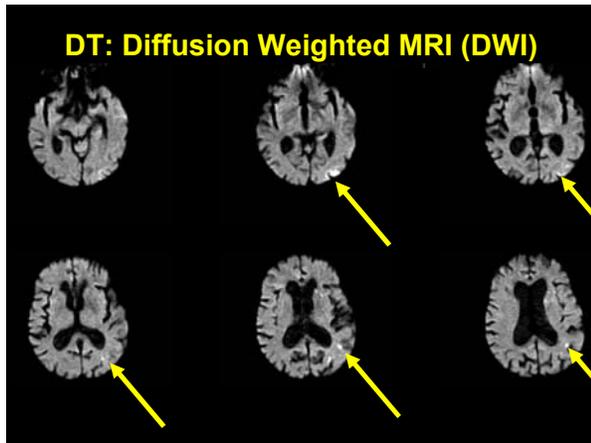


CT Angiogram (CTA)



Management and Outcome

- No further treatment
 - CTP: no tissue at risk
 - CTA: no large artery occlusion
- Patient experienced **full recovery**
- No bleeding
- MRI



**IV rt-PA and Anticoagulation:
CPMC Experience**

- 28 patients (INR > 1.7 or full dose LMWH)
- Received either full dose or half dose IV rt-PA
- No symptomatic intracranial hemorrhage
- Mean NIHSS reduced from 12 to 2

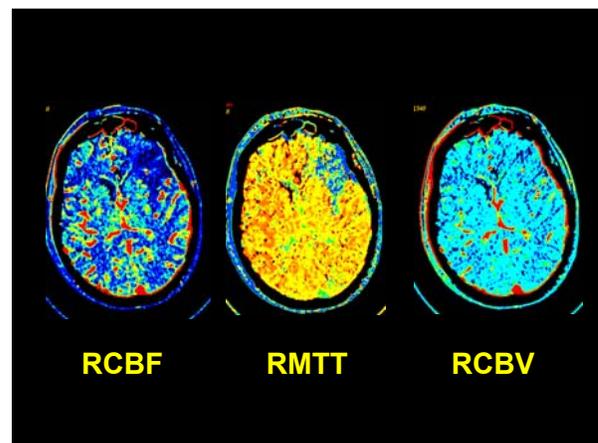
International Stroke Conference San Antonio Tx , 2010

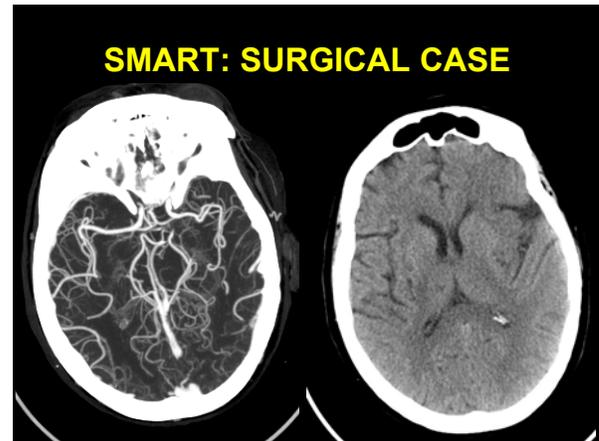
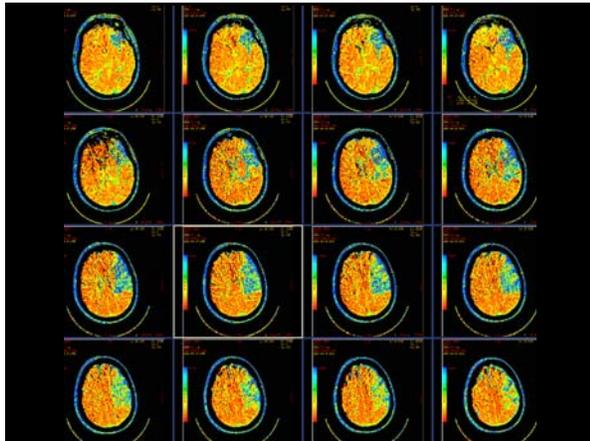
Conclusions

- IV rt-PA is **not** contraindicated in many patients who are frequently excluded from treatment including:
 - Age >80 (or >90)
 - Large strokes (NIHSS > 20)
 - Anticoagulated (INR >1.7)
 - Active bleeding (mild)
- CTP/CTA useful in management
- Criteria for IV rt-PA need revision
 - Many more patients can be treated safely and effectively
 - **Use SMART criteria!!**

SMART CASE STUDY

- 59 yo RH female, h/o Crohn's disease, superior mesenteric artery infarct
- Bowel resection/abscess drainage 4d prior
- Acute global aphasia, R facial droop, NIHSS=10
- Last well: 18:30
- Discovered: ~19:15 (0.75h)
- CT: 19:20





What would you do?

SMART CASE: POST SURGICAL

- IV therapy administered at 21:00 (2.5h)
 - Surgeon ok'ed treatment
- No bleeding complications
- Patient experienced complete recovery

S.M.A.R.T. Post Procedure Stroke

- Post-surgical patients should not automatically be excluded from treatment
 - Talk to you surgeon
 - Some patients may be candidates
 - There are varying degrees of surgical bleeding risk

Comments/Questions