

# AAPM 2018 Use of Physiologic Imaging in Acute Stroke Treatment

Kenneth V Snyder MD PhD FAANS FACS  
University at Buffalo Neurosurgery  
Canon Stroke and Vascular Research Center  
Jacobs Institute, Gates Vascular Institute, and Kaleida Health

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## Public Health Impact of Stroke

- 4<sup>th</sup> leading cause of death in US, #2 worldwide
- #1 cause of Disability! Most prevalent neurologic condition, most common discharge diagnosis to nursing homes and rehab
  - 5 million Americans currently living with the effects of stroke
  - > \$70 Billion Annually in US in 2012
- WHO (2002) 15.3 million stroke and 5.5 million deaths per year
- WNY is 25% higher than national rate with one regional zip code at 200%

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## Classification of Stroke

- Ischemic (80%)
  - ICAD
  - Lacunar
  - Carotid Occlusive disease (25%)
- Hemorrhagic (20%)
  - Intracerebral hemorrhage
  - Subarachnoid hemorrhage

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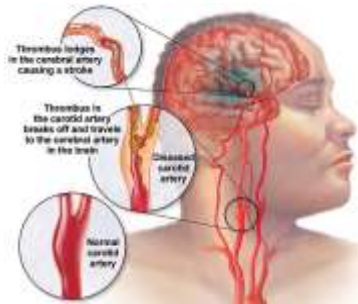
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### Stroke Treatment Options in 2013

- **ASA** within 24-48 hrs is recommended
- **IV rtPA** in appropriate patients (<3-4.5 hours)
- **IA thrombolysis** an option in major MCA stroke patients <6 hours if not IV rtPA candidates (dose not determined and NOT FDA approved)
- Mechanical thrombectomy devices can be offered in carefully selected patients and should continue to be studied in randomized trials

AHA/ASA Stroke Guidelines Stroke 2013

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### IV tPA and Large-Vessel Occlusion (35-40% of Ischemic Stroke)

- Clinical response to thrombolysis is influenced by the site of occlusion
- Rate of recovery from IV tPA by occlusion
  - 33% for distal MCA occlusion
  - 15% for proximal MCA occlusion
  - 0% with ICA-T occlusions
- Mortality of LVO

Vessel	Mortality Rate
ICA	53% <sup>1</sup>
MCA	27% <sup>2</sup>
Basilar Artery	89-90% <sup>3</sup>

Stroke. 2007;38:940-954  
 1. Jansen O, et al.  
 2. Fisher A et al: PROACT II Trial  
 3. Brückmann H et al.

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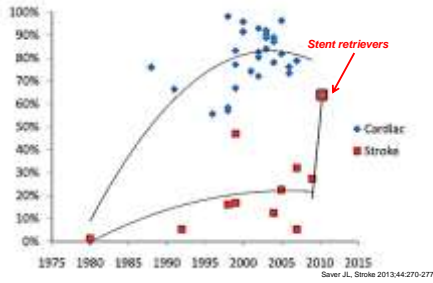
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### What's A Retrievable Stent?



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### 2015: Endovascular vs Best Medical Therapy

- 5 major studies evaluating the role of endovascular therapy in stroke treatment
  - MR CLEAN
  - EXTEND-IA
  - ESCAPE
  - SWIFT PRIME
  - REVASCAT
- Endovascular Therapy within 6 hours, NIHSS >7
- ALL 5 trials stopped because of significant benefit in the Endovascular arms

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THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

**Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke**

Jeffrey L. Saver, M.D., Michael Geysk, M.D., Brian Burchak, M.D., Hani Chaturvedi, M.D., Ph.D., David Levy, M.D., Vivek M. Pillay, M.D., Gregory W. Albers, M.D., Christopher Cognard, M.D., David J. Cohen, M.D., Werner Hacke, M.D., Ph.D., Olaf Jaimes, M.D., Ph.D., Raouf G. Jovin, M.D., Francisco P. Martin, M.D., Paul G. Nagel, M.D., Andre H. Schild, M.D., Ph.D., Christoph F. von der Lippe, M.D., Marco W. Sperling, M.D., Thomas G. Bockler, M.D., Ph.D., Deborah E. Laperle, M.D., Virek K. Bhatia, M.D., Richard du Mesnil de Genneville, M.D., Oliver E. Singer, M.D., and Peter Johnsrud, M.D., for the SWIFT PRIME Investigators\*

**SWIFT PRIME**

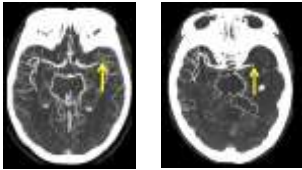
Medtronic- US



- Proximal anterior circulation occlusion
- Randomized patients who received IV-tPA to undergo endovascular therapy with Solitaire or continue receiving IV-tPA alone
- RESULTS:
- Endovascular showed improvement in mRS at 90 days
  - **60.2% vs 35.5% , P<0.001**
- No significant differences in mortality or the occurrence of symptomatic ICH
- **NNT = 4**

	NIHSS>=2 <6 hr not required	NIHSS (IPA) <6 hr, dual 1-12 hr-6	NIHSS>=6 <12 hr, consecutive 120min	NIHSS>=8 <6 hr SWIFT PRIME	NIHSS>=6 <8 hr RETRACT
Stroke care	Not required	NIHSS performed within 120 min, SWIFT<=30% Preemptive	ASPECTS score 9-10	ASPECTS score 9-10 or MRS2 or DWI, MRS0 performed within <=6 hr, SWIFT<=30% SWIFT<=30%	ASPECTS score 9-10 or MRS2, ASPECTS score 9-10 or DWI, SWIFT ASPECTS<=4 SWIFT<=40%
Pericatheter	Not required	Target hematoma: SWIFT performed within 120 min, SWIFT<=30% NIHSS<=4 Preemptive	Not required	Target hematoma: SWIFT performed within 120 min, SWIFT<=30% NIHSS<=4 Preemptive	Not required Catheterization hematoma SWISS-10
Coarctation	Not required	Not required	Aneurysm confirmed intracranial defined as being 100% of 10% or greater of the diameter, territory with circulation beyond occlusion on CT angiography or magnetic resonance CT angiography	Not required	Not required
mRS <=2	32.6% vs 19.1%	<b>71% vs 40%</b>	53% vs 29.3%	<b>60.2% vs 35.5%</b>	43.7% vs 28.2%

### CTA Collaterals



<http://www.aspectsinstroke.com>

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### Future of Stroke Imaging

The greatest challenge is to show that advanced neuroimaging, used as a biomarker to select patients for reperfusion therapy (in an extended time window), improves patient outcomes

The Future of Stroke Imaging: What Do You and How to Achieve It  
J Neuroimaging and Stroke 2015;4:1-11

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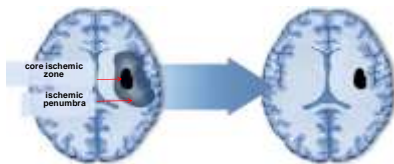
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### Advanced Imaging



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## Advanced Imaging

- Dynamic Studies capturing one cycle of the full transit of a contrast bolus through the tissue
- Physiologic Imaging: Transit Time, Blood Flow, Blood Volume
  - Parenchyma (Capillary phase NOT large vessels)
  - Intravascular surrogate for Intracellular process (not biological, Xenon)
- Ability to distinguish core (infarcted tissue) from penumbra (salvageable tissue)
- Individualize stroke treatment

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## Buffalo Protocol

- NIHSS and CTSS (CTA head and neck and CTP)
  - Intervention based on perfusion parameters, clinical exam, and Time of Onset
  - MRI if no obvious deficit on CTP
- Post intervention CT/ LCI /MRI GRE
- CTP POD #1, NIHSS at 24hrs
- MRI at 3-5 days
- Discharge disposition, NIHSS and mRS
- CT or MRI at 1-3 months, mRS and NIHSS
- All patients collected in prospective registry

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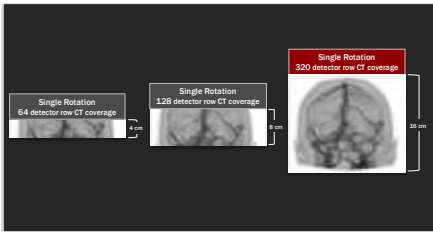
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### Neuro One Protocol

- Perfusion
  - 50 cc at 5cc/s 19 volumes
- Equivalent to 1.5 NCCT Rad Dose




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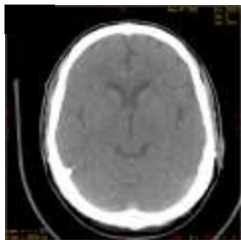
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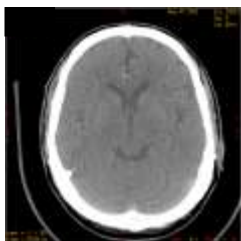
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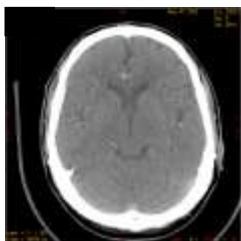
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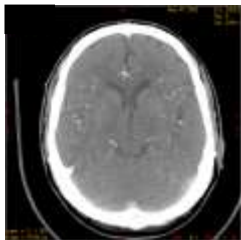
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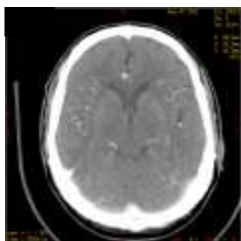
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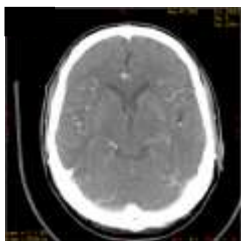
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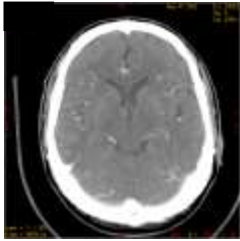
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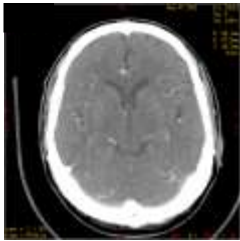
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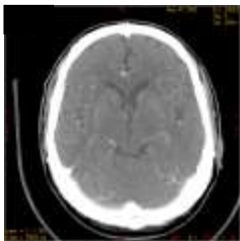
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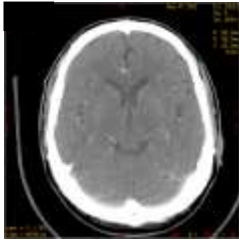
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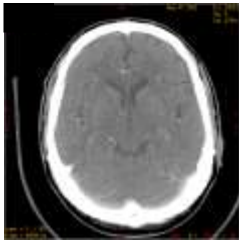
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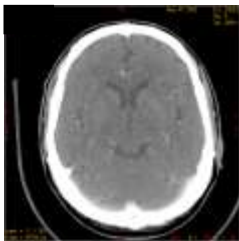
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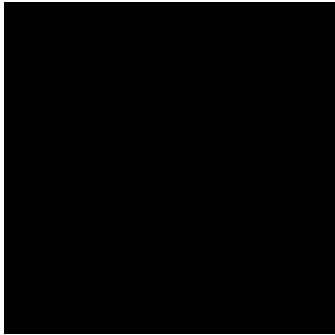
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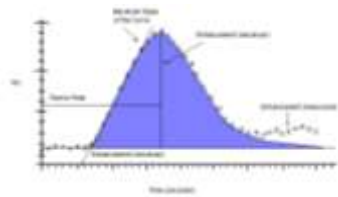
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Time/Tissue Attenuation Curve



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CT Perfusion Models (4 min processing time)

- Maximum Slope
- Deconvolution
  - Parametric  $R(t)$  has specific distribution
  - Non-parametric –  $R(t)$  is an unknown
    - Transform – Fourier
    - SVD
    - Delay Insensitive Deconvolution (SVD+)
- Bayesian

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## CT Perfusion Parameters

- CBF mL blood/100g brain tissue/min
- CBV mL blood/100g brain tissue
- Mean transit time (MTT)
- Time to peak (TTP)
- Delay Map

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Condition	rTTP	rCBF	rCBV
None	Normal	Normal	Normal
Art stenosis/ occl with comp	Prolonged	Normal	Normal
Oligemic	Prolonged	> 60%	> 80%
Tissue at risk	Prolonged	> 30%	> 60%
Dead tissue	Strong prolonged	< 30%	< 30-40%

Tomsand, 2002; Mayer 2000; Koening 2001

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## Cerebral Perfusion

- CBF = 50-60 mL/100 g/min, normal
- CBF = 35: protein synthesis ceases, oligemic stage, tissue can survive.
- CBF = 20: disturbance of synaptic transmission, loss of function (still viable)
- CBF = 10: irreversible cell death

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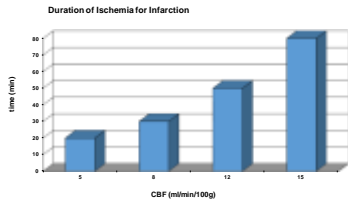
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Heiss and Rosner (1983)




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Reliability?



Radiology 254(1): Jan 2010

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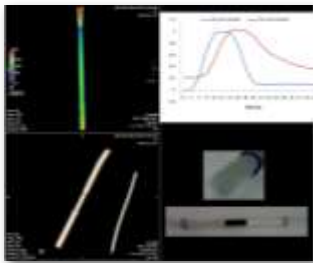
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- Penumbra/Core – volume mismatch
- Clinical Exam/Core – appropriate for patient selection

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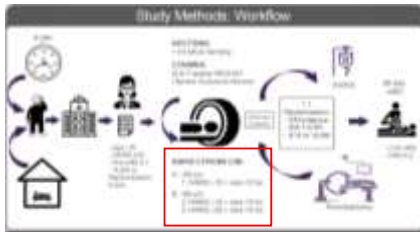
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Co-primary endpoints

	Stroke	MM	Treatment group (95% CI)	Response probability of superiority
Day 90 weighted ratio	5.0 x 3.0	3.4 x 3.1	2.1 (1.20, 3.18)	=0.0050*
Day 90 mRS 0-2	48.8%	12.1%	35.5% (23.8%, 47.0%)	=0.0050*

NNT for 90-day functional independence = 2.8

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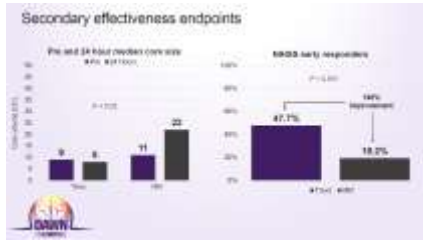
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**Defuse 3- Thrombectomy for Stroke at 6-16 hours with selection by Perfusion Imaging**

- NEJM 2018: 378:708-18
- Multicenter, randomized, MCA or ICA, Primary outcome mRS at 90 days
- Less than 70 cc core, and Ratio of >1.8
- RESULTS:
  - Terminated Early for efficacy (92 endo and 90 BMT)
  - mRS 0-2 (45% vs 17%)
  - 90 day mortality (14% vs 26%)
  - No sign difference in sICH (7% vs 4%)

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**DAWN**

- Age: > 18
- NIHSS: >= 10
- Vessel: ICA/M1
- LSN: 6-24
- CTP Core: <20, <30, <50
- CTP Ratio: none

**DEFUSE 3**

- 18-90
- >= 6
- ICA/M1
- 6-16
- < 70
- >1.8

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**AHA/ASA Guideline**

**2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke**

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

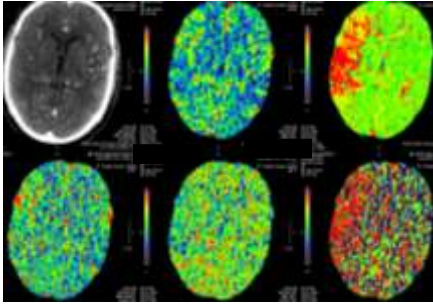
Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Endorsed by the Society for Academic Emergency Medicine

5. Although the benefits are uncertain, the use of mechanical thrombolysis with distal catheters may be reasonable for carefully selected patients with M1 or anterior/middle cerebellar artery stroke within 6 hours of symptom onset and who have contraindications of the anterior/middle cerebellar arteries, vertebral artery, basilar artery, or posterior cerebral arteries.	III	C-OR	Recommendation considered for study from 2015 Evidence-Based Stroke Guidelines. L2B. Consider to combine with ACC/AHA 2013 Recommendation Classification System (see Table 1.0000) in extra class (supplement) for ongoing writing.
6. Although the benefits are uncertain, the use of mechanical thrombolysis with distal catheters may be reasonable for patients with M1 or anterior/middle cerebellar artery stroke within 6 hours of symptom onset and who have posterior MCA stroke ± DPECTE, ±6, or SPECT stroke ±6, and consider resolution of the lateral carotid artery (LCA) or posterior MCA (PMCA) additional treatment and data are needed.	III	B-N	Recommendation considered from 2015 Evidence-Based Stroke Guidelines.
7. In selected patients with AIS within 6 to 16 hours of last known normal after hours (LKN) in the anterior/middle and most other (MCA) or (DPECTE) ± eligibility criteria, mechanical thrombolysis is recommended.	I	A	This recommendation.
8. In selected patients with AIS within 6 to 16 hours of last known normal after hours (LKN) in the anterior/middle and most other (MCA) eligibility criteria, mechanical thrombolysis is recommended.	IIa	B-N	This recommendation.
9. The technical goal of the thrombolysis procedure should be expansion to a modified Thrombolysis in Stroke (TIS) or (DPECTE) ± eligibility criteria to maximize the probability of a good functional clinical outcome.	I	A	Recommendation considered for study from 2015 Evidence-Based Stroke Guidelines. See Table 1.0000 in extra class (supplement) for ongoing writing.

Clinical History

- 50 yo who woke up with left hemiplegia, dysarthria, and facial droop.
- NIHSS = 16.
- PMH - Anxiety disorder, tobacco dependence, alcohol dependence



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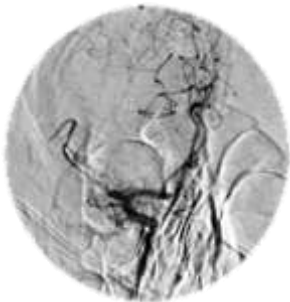
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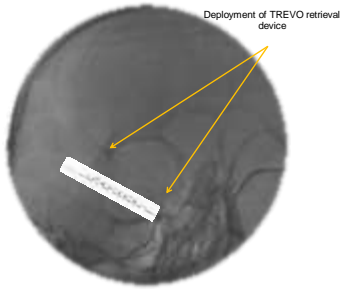
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1<sup>st</sup> pull of the microcatheter with the retrieval device  
Total intervention time ~20 min

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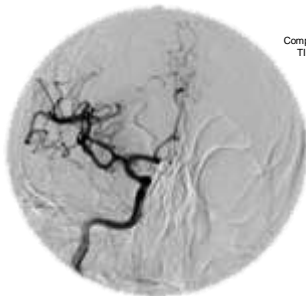
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Complete recanalization  
TIMI-3 after 1 pull

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- In the angio suite – the patient could lift his Rt arm antigravity, improved gaze, NIHSS 16 to 5 immediately
- POD#1 NIH -3
- POD#2– NIH -0

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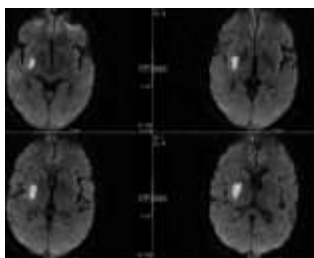
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### Clinical History

- 75 yo WM last seen normal at 10 pm,  
? Issues at 2 am, awoke thrashing at 4 am with Right gaze preference and left HP
- NIHSS 18

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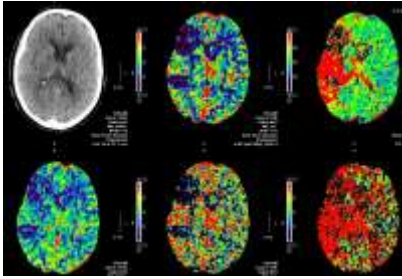
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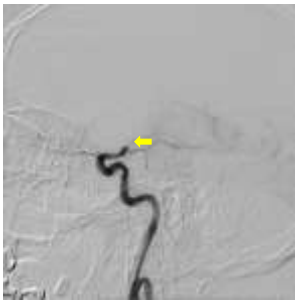
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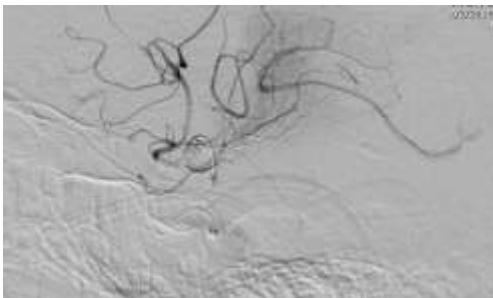
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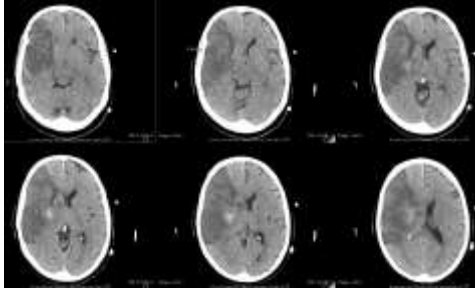
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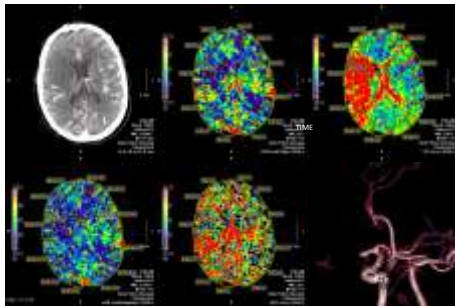
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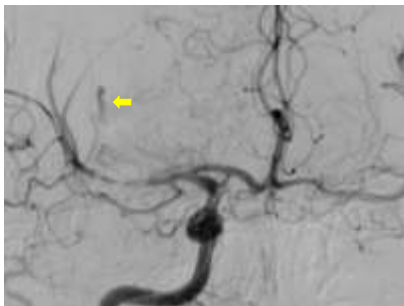
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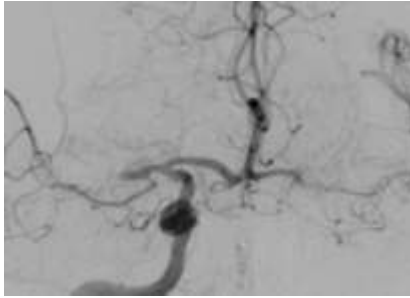
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### Future Advanced Imaging Considerations

- Improvements in validation studies and/or deterministic models (Xenon?)
- Define Futility Thresholds for grey and white matter
- Validation of Semi automated methods across vendor platforms and modalities
- Applications to other organ systems
- Generation of Physiologic Maps from Angiography

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### Speed to Reperfusion is Critical

- Even though physiologic imaging allows more people to be offered treatment at later time points, realize...
- IT IS STILL A RACE
  
- Streamlining Stroke triage from ambulance to CTP has helped tremendously

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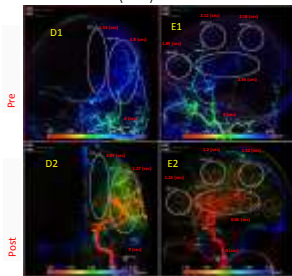
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Time To Peak (TTP)



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| *See. Diagnose. Treat.*



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Thank you!

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