Nirali Vora, MD
Clinical Associate Professor, Neurology
Director, Global Health Neurology
Stanford Stroke Center

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SLASH DISABILITY AND DEATH WITH PRECISION IN ACUTE STROKE CARE

stroke is deadly and disabling

stroke is preventable

stroke is <u>treatable</u>

only if you are prepared

65 yo with word finding difficulty

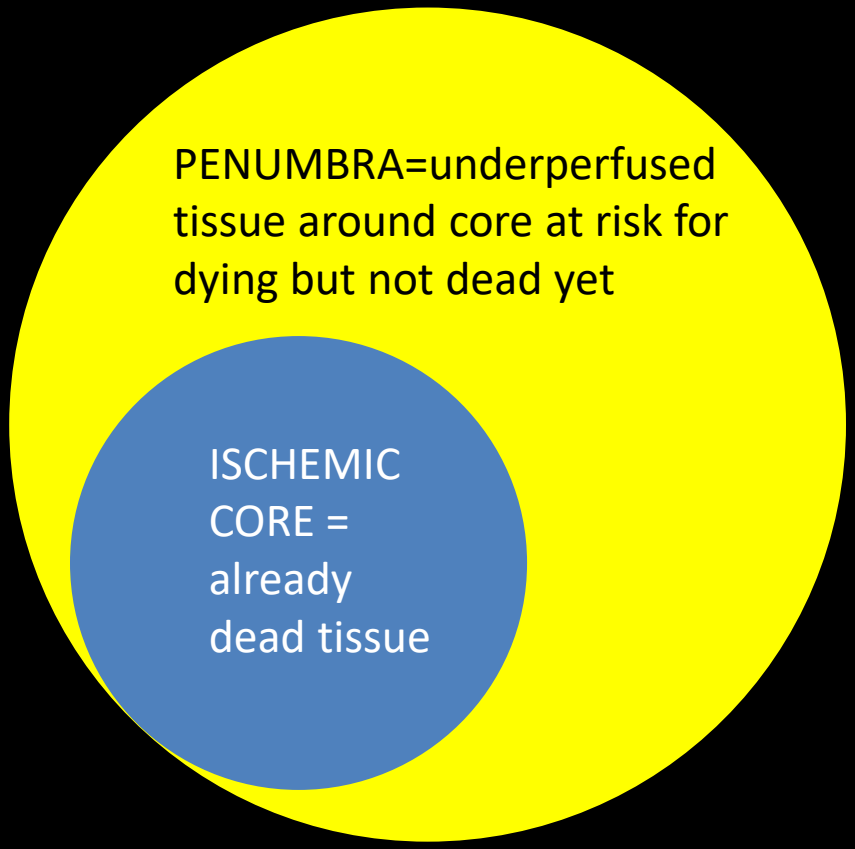
- The patient's partner calls your office 8am:
- *She understands me, but is substituting words and keeps pausing when trying to talk. It started after dinner at 8pm last night but she didn't improve after a good night's rest.*
- *She just had hip surgery and only wants to leave the house if something can be done*

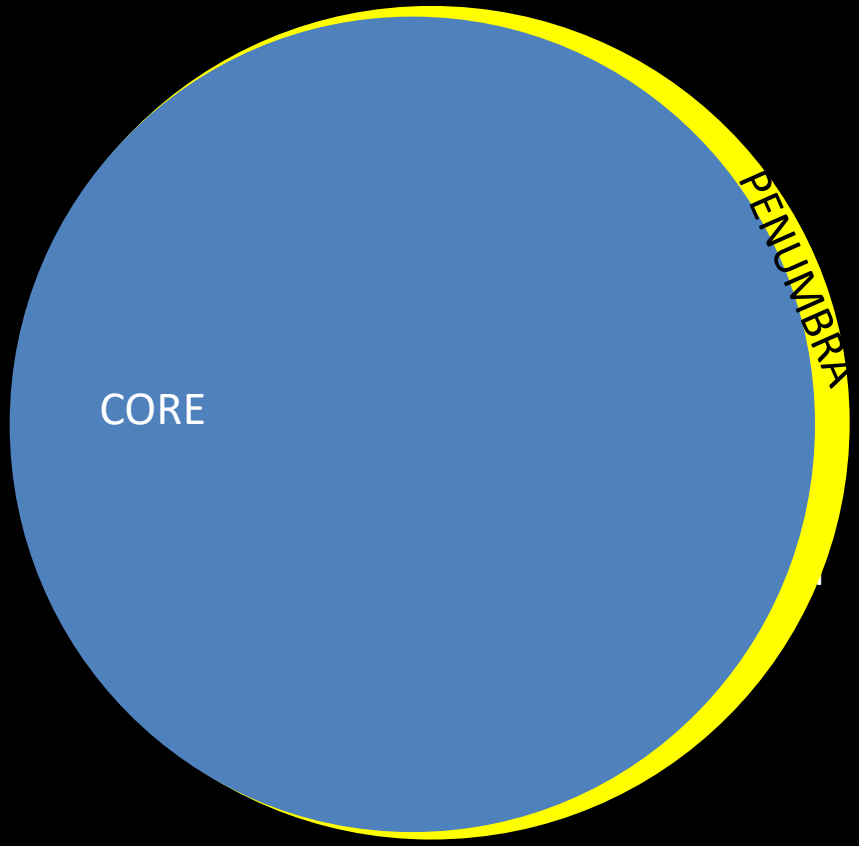
is the patient eligible for treatment?

step 1
eliminate outdated eligibility criteria

Therapy	Time from last normal
IV thrombolysis	0-4.5 hours
thrombectomy	0-6 hours

treat patients with penumbra

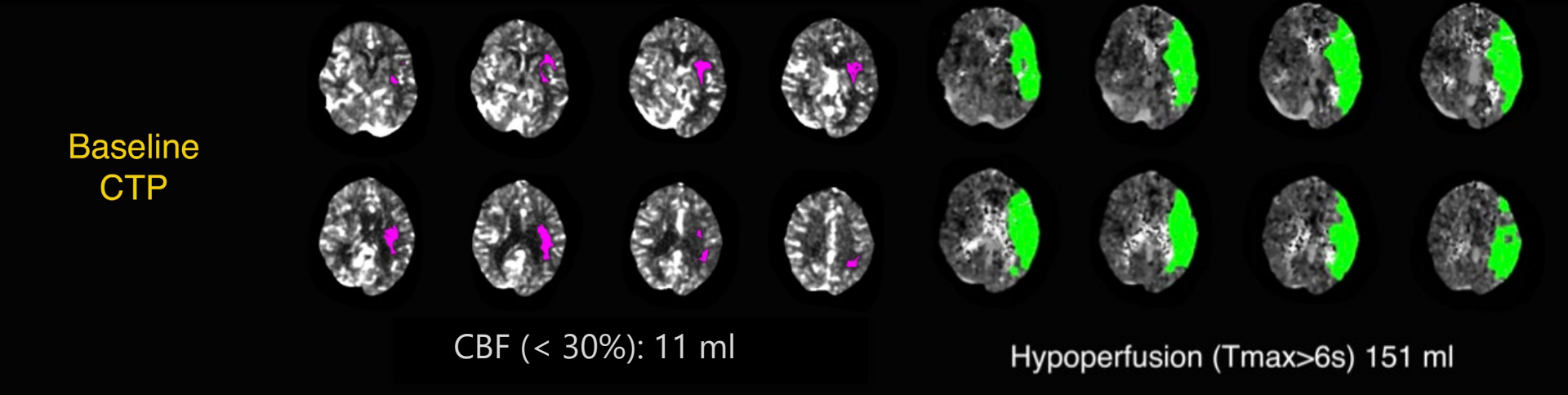




When there is a mismatch, there is an opportunity to save tissue

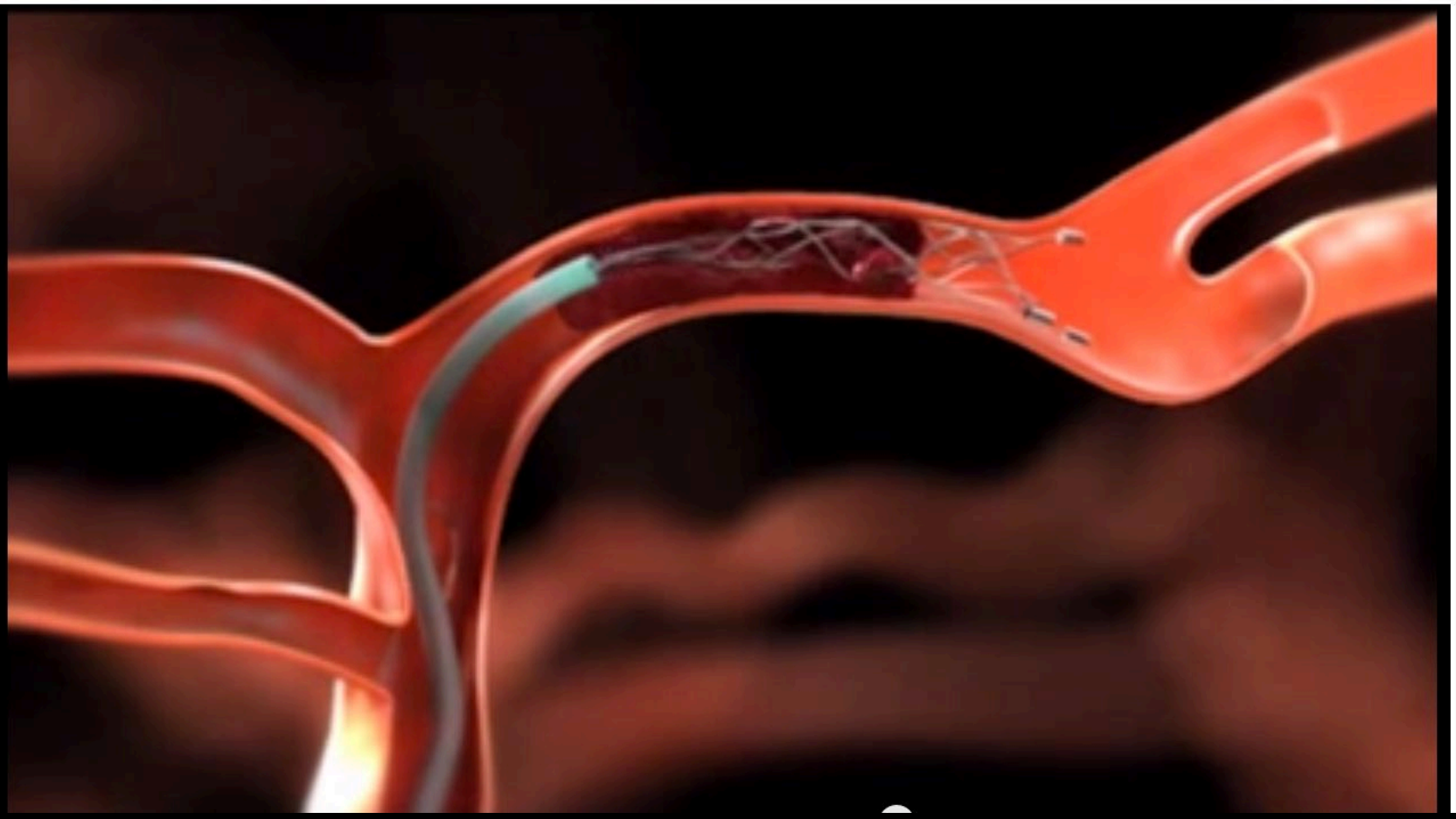
No mismatch = no acute therapy

mismatch identification with multimodal imaging

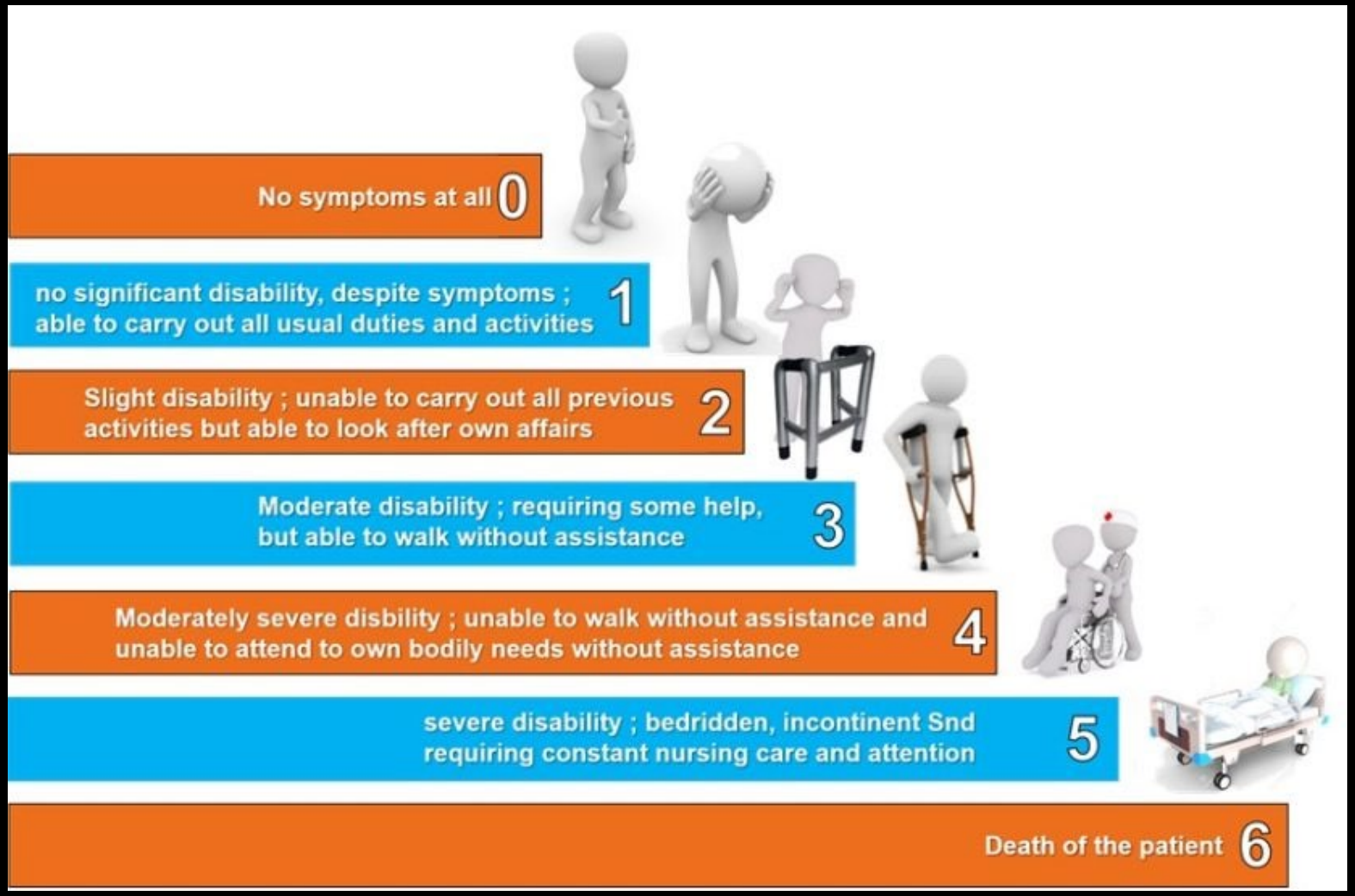


mechanical thrombectomy reliably reperfuses the brain in large vessel occlusions (LVOs)

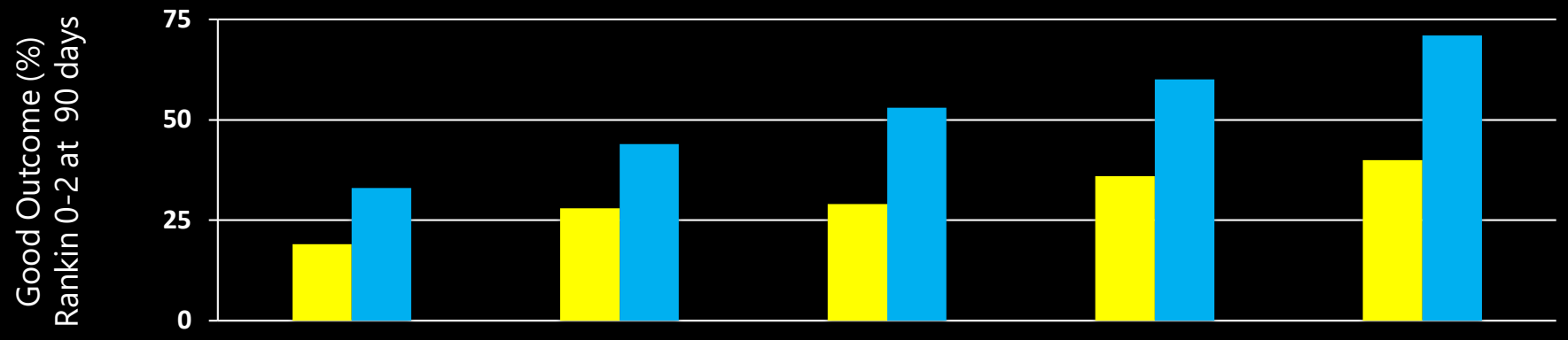
mechanical thrombectomy



modified Rankin Scale (mRS) measures function & independence



endovascular trials succeed with precision in patient selection & tech



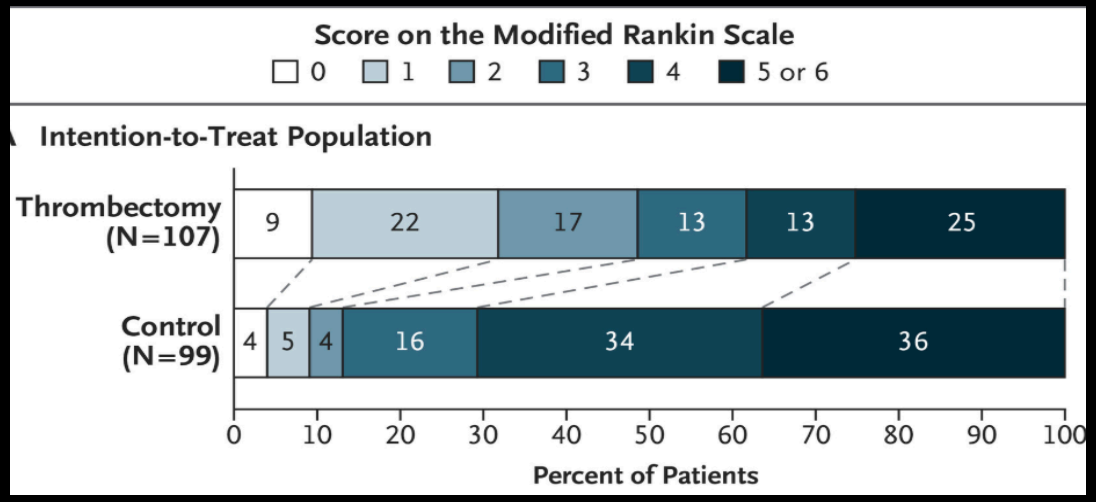
	MR CLEAN P<0.05 CT	REVASCAT P<0.05 ASPECTS	ESCAPE P<0.001 ASPECTS CTA Collaterals	SWIFT PRIME P<0.001 CTP/MRP 90% RAPID 80%	EXTEND-IA P<0.01 CTP 100% RAPID 100%
Endo- vascular	33%	44%	53%	60%	71%
Control	19%	28%	29%	35%	40%
ARR	14%	16%	24%	25%	31%
NNT	7	6	4	4	3

Trial	MR CLEAN	ESCAPE	EXTEND-IA	SWIFT PRIME	REVASCAT	THERAPY	THRACE[‖]
Key inclusion criteria	NIHSS ≥ 2, age ≥ 18	NIHSS > 5, ASPECTS > 5, moderate/good collaterals (CTA)	Eligible for IV-tPA < 4.5 hours from stroke onset, ischemic core < 70 cm^3, mismatch[†]	Eligible for IV-tPA < 4.5 hours from stroke onset, age 18-80, NIHSS 8-29, ASPECTS ≥ 6	[¶]Age 18-80, NIHSS ≥ 6, ASPECTS ≥ 7	Eligible for IV-tPA < 4.5 hours from stroke onset, age 18-85, NIHSS ≥ 8, Clot length ≥ 8 mm	Eligible for IV-tPA < 4.5 hours from stroke onset, age 18-80, NIHSS 10-25
Interventional arm	Intra-arterial therapy	Intra-arterial therapy	Endovascular thrombectomy with Solitaire FR stentriever	Endovascular thrombectomy with Solitaire FR stentriever	Endovascular thrombectomy with Solitaire FR stentriever	Endovascular thrombectomy with Penumbra aspiration system	Endovascular mechanical thrombectomy
Control arm	Best medical management (+/– IV-tPA)	Best medical management (+/- IV-tPA)	IV-tPA only	IV-tPA only	Best medical management (+/- IV-tPA)	IV-tPA only	IV-tPA only
Time window for intervention	< 6 hours from onset	< 12 hours from onset	< 6 hours from onset	< 6 hours from onset	< 8 hours from onset	< 4.5 hours from onset	< 5 hours from onset
Number of patients	500 (I: 233, C: 267)	315 (I: 165, C: 150)	70 (I: 35, C: 35)	196 (I: 98, C: 98)	206 (I: 103, C: 103)	108 (I: 54, C: 54)	385 (I: 190, C: 195)
Mean/median age (year)	I: 65.8, C: 65.7	I: 71, C: 70	I: 68.6, C: 70.2	I: 66.3, C: 65.0	I: 65.7, C: 67.2	NR	I: 62, C: 62
Median NIHSS	I: 17, C: 18	I: 16, C: 17	I: 17, C: 13	I: 17, C: 17	I: 17, C: 17	NR	I: 17, C: 17
Median ASPECTS	I: 9, C: 9	I: 9, C: 9	NR	I: 9, C: 9	I: 7, C: 8	NR	NR
Received IV-tPA	I: 87.1%, C: 90.6%	I: 72.7%, C: 78.7%	I: 100%, C: 100%	I: 100%, C: 100%	I: 68.0%, C: 77.7%	I: 100%, C: 100%	I: 100%, C: 100%
Median time from stroke onset to groin puncture (minute)	260	241[‡]	210	224	269	226	255[‡]
Intervention with stentriever device	81.5%	86.1%	100%	100%	100%	0%[§]	NR
Improvement in mRS 0-2 at 90 days	13.5%* (I: 32.6, C: 19.1%)	23.7%* (I: 53.0%, C: 29.3%)	31.4%* (I: 71.4%, C: 40.0%)	24.7%* (I: 60.2%, C: 35.5%)	15.5%* (I: 43.7%, C: 28.2%)	7.6% (I: 38.0%, C: 30.4%)	12.1%* (I: 54.2%, C: 42.1%)
Decrease in mortality at 90 days	1.1% (I: 21.0%, C: 22.1%)	8.6* (I: 10.4%, C: 19.0%)	11.4% (I: 8.6%, C: 20.0%)	3.2% (I: 9.2%, C: 12.4%)	-2.9% (I: 18.4%, C: 15.5%)	11.9% (I: 12.0%, C: 23.9%)	0.6% (I: 12.5%, C: 13.1%)
TICI grade 2b/3 recanalization	58.70%	72.40%	86.20%	88.00%	65.70%	NR	NR
Symptomatic ICH	I: 7.7%, C: 6.4%	I: 3.6%, C: 2.7%	I: 0%, C: 5.7%	I: 0%, C: 3.1%	I: 1.9%, C: 1.9%	I: 10.9%, C: 11.3%	NR

endovascular therapy extends to 24 hours in select patients

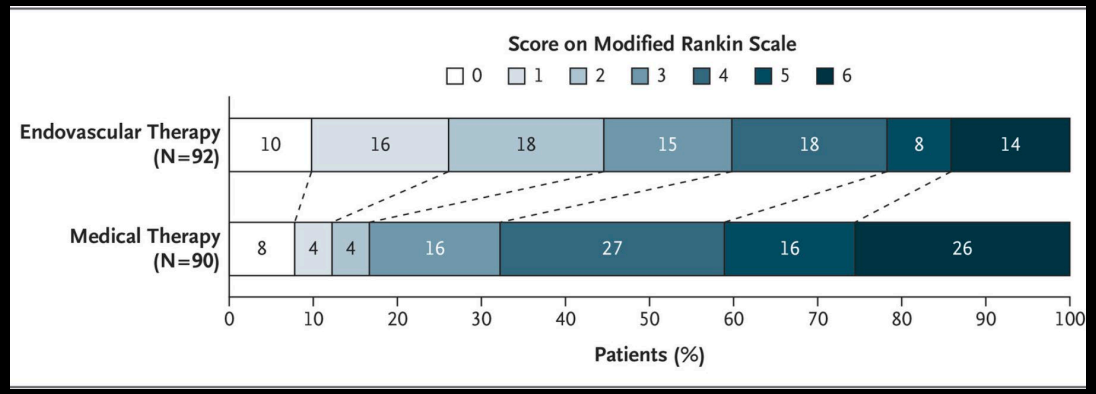
6 - 24 hours (median 12.5)

35% increase in functional independence



6 - 16 hours (median 11)

20% absolute reduction in death/severe disability



AHA guidelines 2018 & 2019 adopt new standard of care

3.7. Mechanical Thrombectomy (Continued)	COR	LOE
7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.	I	A
8. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.	IIa	B-R

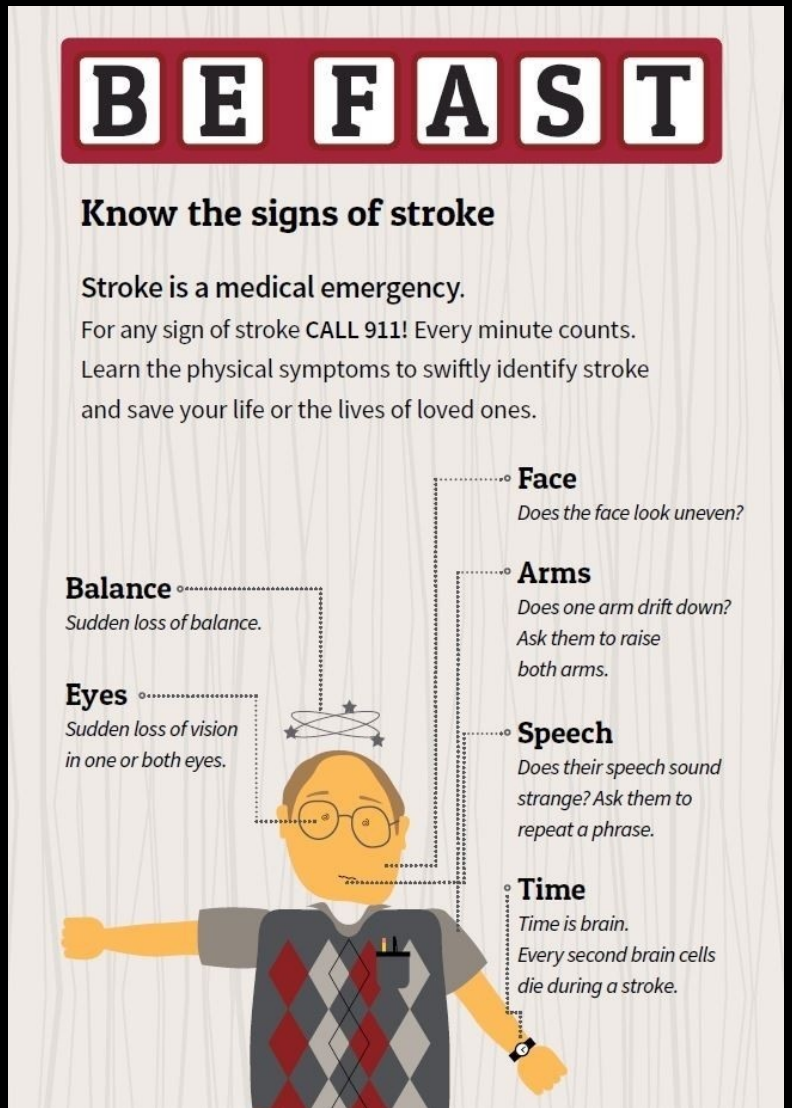
extending window with IV thrombolysis

WAKE-UP	IV tPA vs. placebo >4.5 hrs with MRI imaging (DWI-FLAIR) mismatch. ARR 11.5%.
EXTEND	IV tPA vs. placebo 4.5-9 hours (from sleep midpoint) with perfusion imaging mismatch. ARR 5.9% . ended early.
E-CASS 4	IV tPA vs. placebo 4.5-9 hours with perfusion imaging mismatch. No difference. ended early.
TIMELESS	IV tenecteplase (TNK) vs. placebo 0-24 hours with perfusion imaging mismatch
TEMPO-2	IV TNK vs. placebo 0-12 hours with perfusion imaging mismatch
TWIST	IV TNK vs. placebo <4.5 hours from “wake-up” stroke with noncom CT head

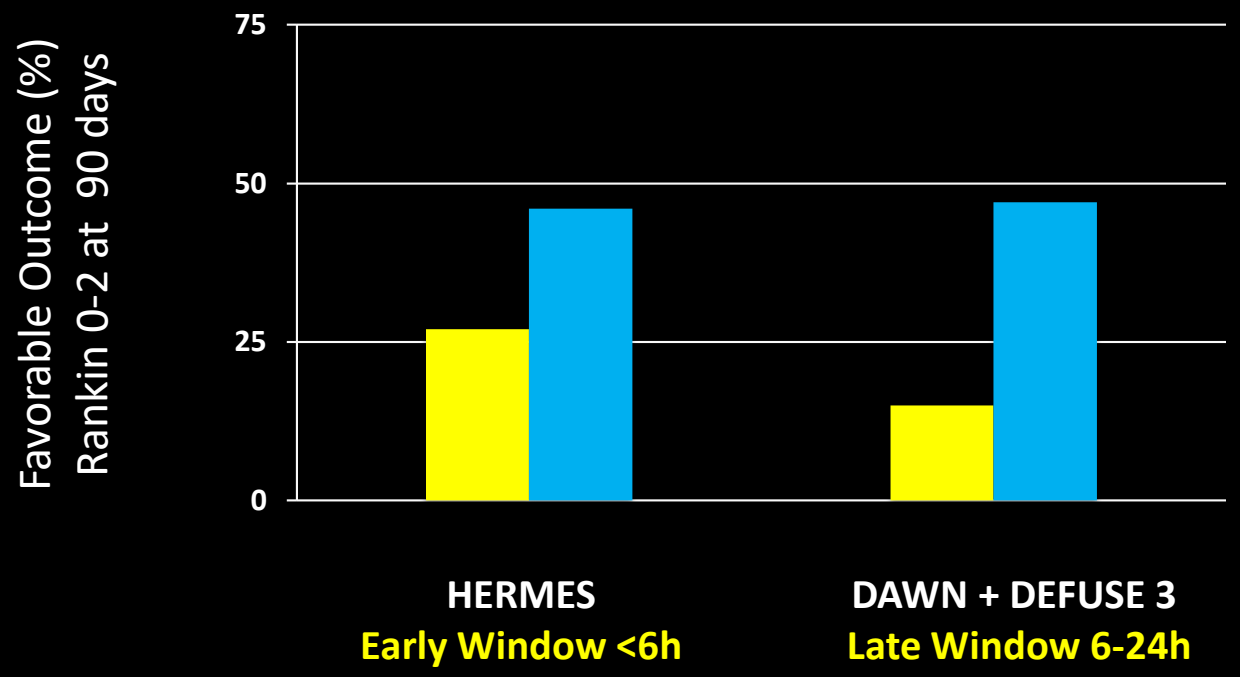
extended window for IV tPA not standard

Recommendations	COR	LOE
1. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is recommended for selected patients who can be treated within 3 hours of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined in Table 8 to determine patient eligibility.	I	A
2. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is also recommended for selected patients who can be treated within 3 and 4.5 hours of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined in Table 8 to determine patient eligibility.	I	B-R
3. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 min with initial 10% of dose given as bolus over 1 minute) administered within 4.5 hours of stroke symptom recognition can be beneficial in patients with AIS who awake with stroke symptoms or have unclear time of onset > 4.5 hours from last known well or at baseline state and who have a DW-MRI lesion smaller than one-third of the middle cerebral artery (MCA) territory and no visible signal change on FLAIR.	IIa	B-R

step 2
empower all to recognize stroke & call 911

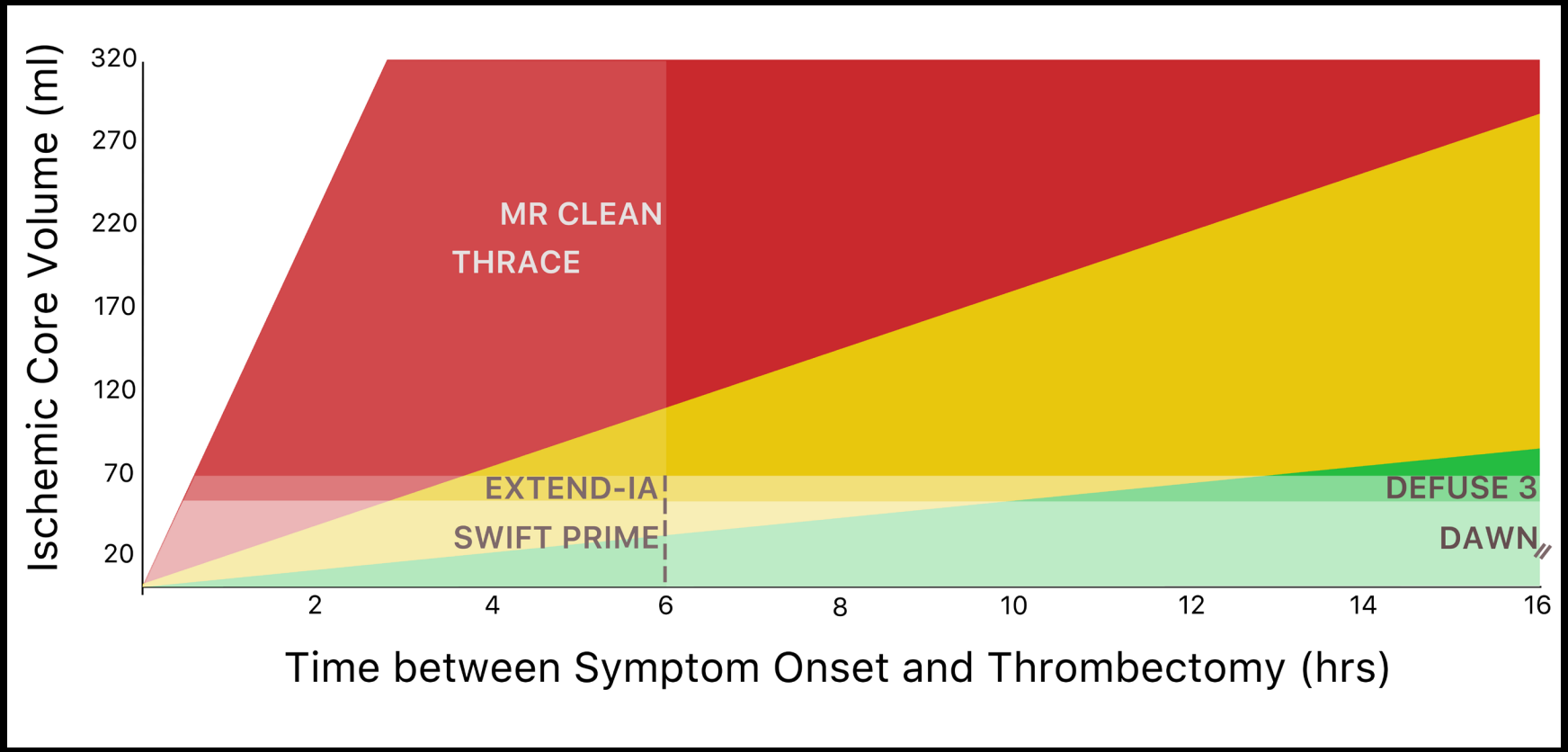


extended window did even better than the traditional 6 hour window



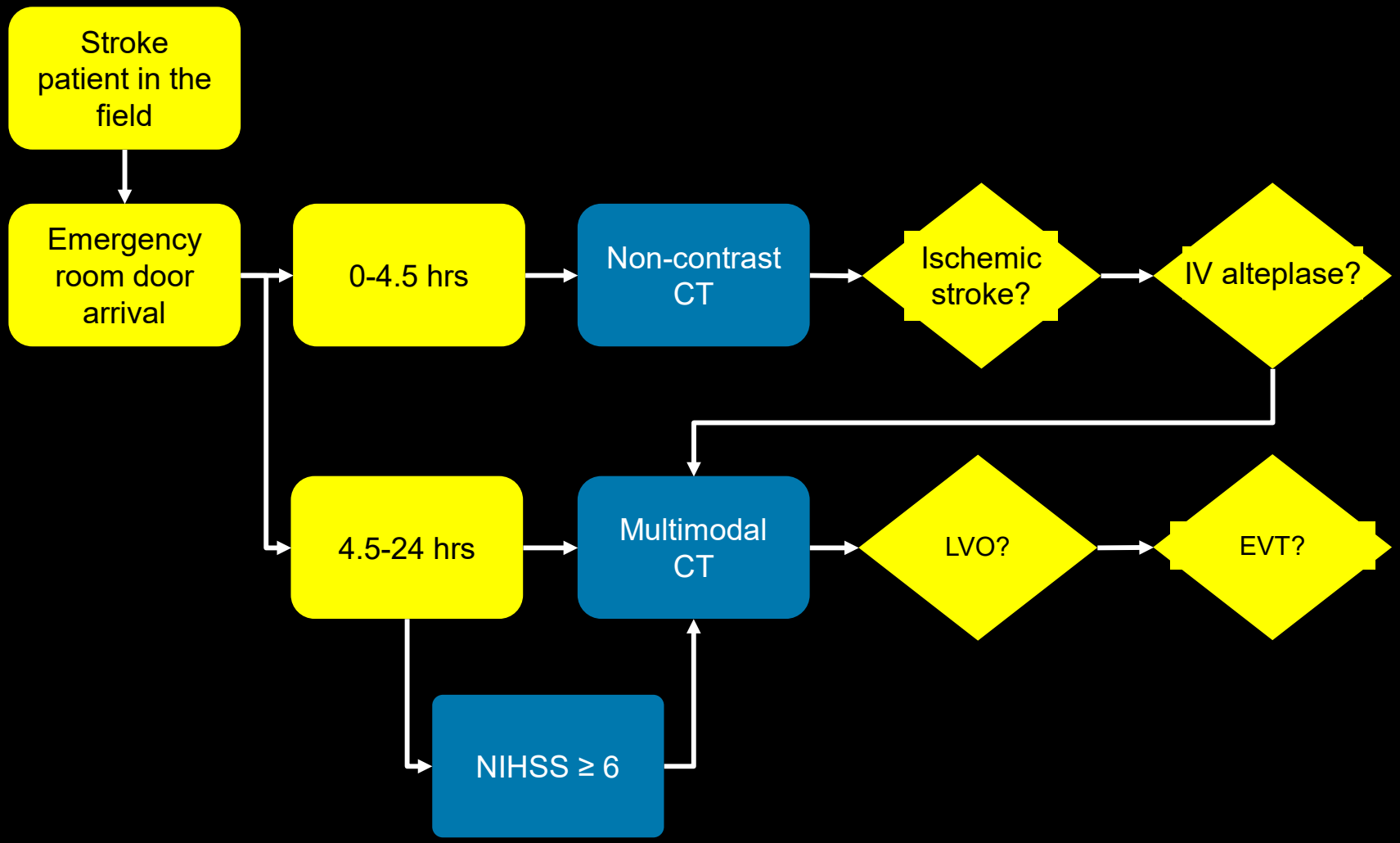
	HERMES Early Window <6h	DAWN + DEFUSE 3 Late Window 6-24h
Endovascular	**46%**	**47%**
Control	27%	15%
ARR / NNT	19% / 5	32% / 3

different rates of ischemic core growth



Late Window Paradox, Stroke, January 24, 2018

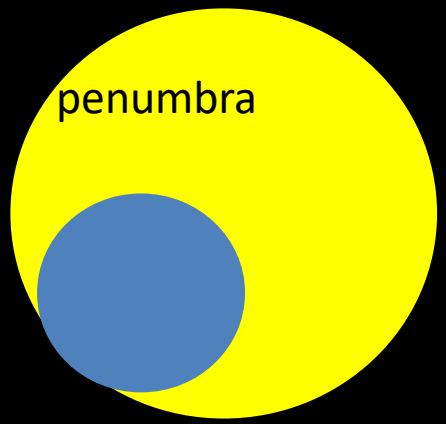
step 3
ensure system of care is ready for rapid triage and treatment



TIME IS BRAIN HAS EVOLVED…

TIME EVERY BRAIN PRECISELY WITH TISSUE PERFUSION

1



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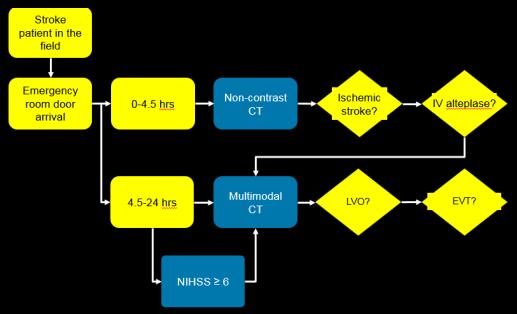

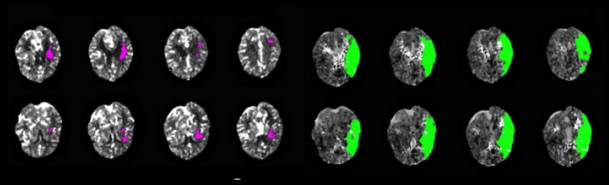

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