

Is MRI helpful in guiding acute stroke therapies?

Brett Cucchiara, MD

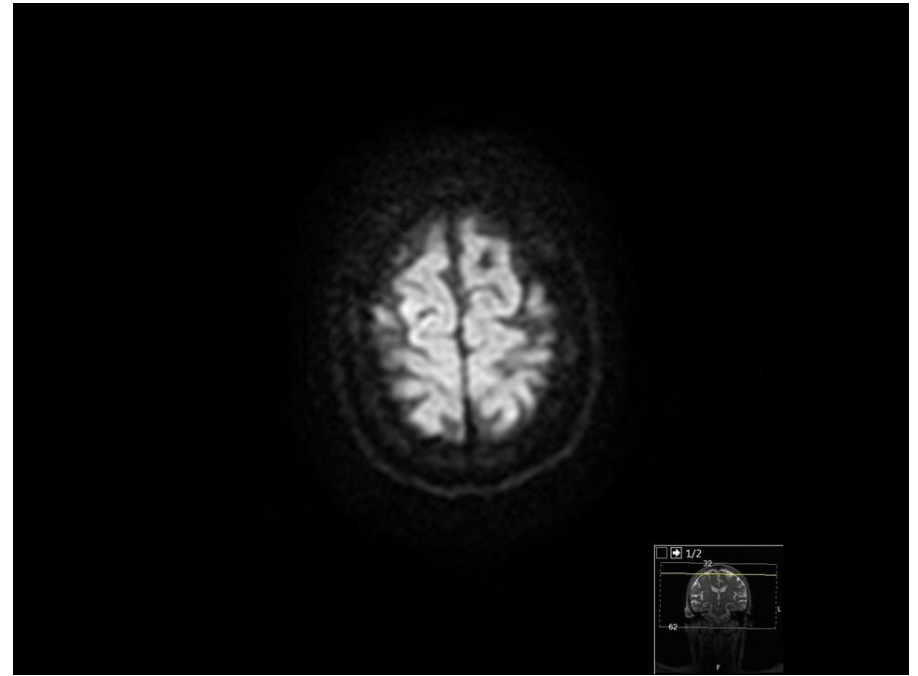
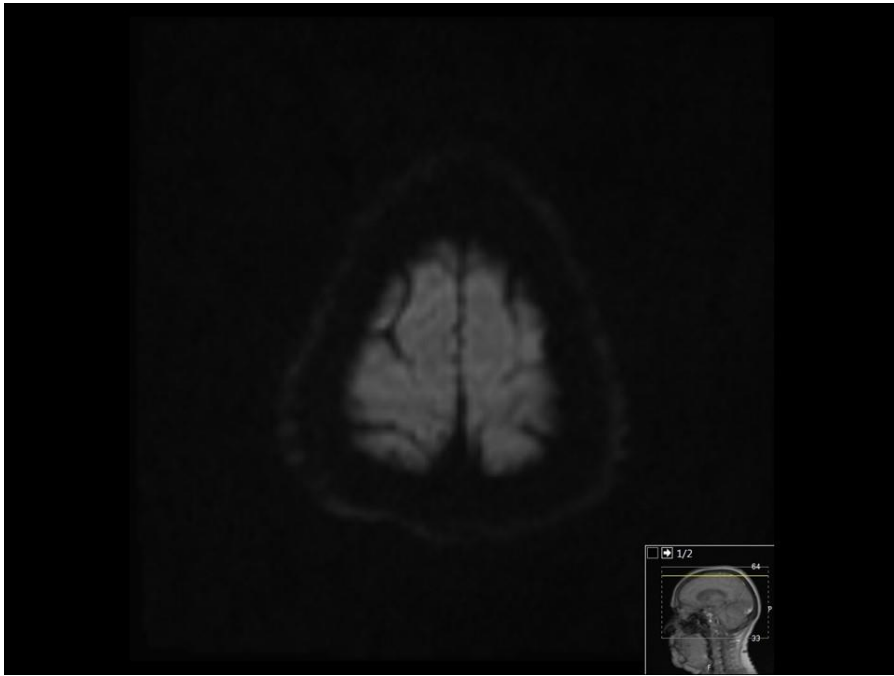
Associate Professor of Neurology

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Compared to what? Which therapies? Which patients?

- MRI vs. non-contrast HCT vs CTA/CTP
- IV tPA, mechanical thrombectomy
- Clinical presentation
 - Age, risk factors
 - Stroke severity
 - Anterior vs. posterior circulation suspected

Everyone knows MRI is better than CT...for diagnosis



CT vs. MRI for stroke diagnosis

Magnetic resonance imaging and computed tomography in emergency assessment of patients with suspected acute stroke: a prospective comparison

Julio A Chalela, Chelsea S Kidwell, Lauren M Nentwich, Marie Luby, John A Butman, Andrew M Demchuk, Michael D Hill, Nicholas Patronas, Lawrence Latour, Steven Warach

Summary

Background Although the use of magnetic resonance imaging (MRI) for the diagnosis of acute stroke is increasing, this method has not proved more effective than computed tomography (CT) in the emergency setting. We aimed to prospectively compare CT and MRI for emergency diagnosis of acute stroke.

Methods We did a single-centre, prospective, blind comparison of non-contrast CT and MRI (with diffusion-weighted and susceptibility weighted images) in a consecutive series of patients referred for emergency assessment of suspected acute stroke. Scans were independently interpreted by four experts, who were unaware of clinical information, MRI-CT pairings, and follow-up imaging.

Results 356 patients, 217 of whom had a final clinical diagnosis of acute stroke, were assessed. MRI detected acute stroke (ischaemic or haemorrhagic), acute ischaemic stroke, and chronic haemorrhage more frequently than did CT ($p < 0.0001$, for all comparisons). MRI was similar to CT for the detection of acute intracranial haemorrhage. MRI detected acute ischaemic stroke in 164 of 356 patients (46%; 95% CI 41–51%), compared with CT in 35 of 356 patients (10%; 7–14%). In the subset of patients scanned within 3 h of symptom onset, MRI detected acute ischaemic stroke in 41 of 90 patients (46%; 35–56%); CT in 6 of 90 (7%; 3–14%). Relative to the final clinical diagnosis, MRI had a sensitivity of 83% (181 of 217; 78–88%) and CT of 26% (56 of 217; 20–32%) for the diagnosis of any acute stroke.

Interpretation MRI is better than CT for detection of acute ischaemia, and can detect acute and chronic haemorrhage; therefore it should be the preferred test for accurate diagnosis of patients with suspected acute stroke. Because our patient sample encompassed the range of disease that is likely to be encountered in emergency cases of suspected stroke, our results are directly applicable to clinical practice.

Lancet 2007; 369: 293–98

See Comment page 252

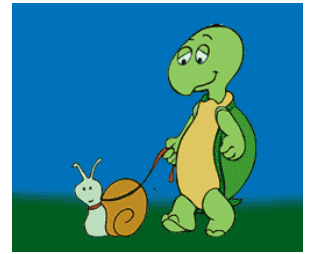
Medical University of South Carolina, Charleston, SC, USA (J A Chalela MD); Georgetown University, Washington Hospital Center, Washington DC, USA (C S Kidwell MD); Boston Medical Center, Boston, MA, USA (L M Nentwich MD); National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA (M Luby MS, L Latour PhD, S Warach MD); National Institutes of Health Clinical Center, Bethesda, MD, USA (J A Butman MD, N Patronas MD); and University of Calgary, Alberta, Canada (A M Demchuk MD, M D Hill MD)
Correspondence to: Dr Steven Warach, Section on Stroke Diagnostics and Therapeutics, National Institute

Chalela J, Lancet 2007


	n	Acute stroke		Acute ischaemic stroke	
		CT	MRI	CT	MRI
Sensitivity					
All	356	26% (20–32)	83% (78–88)	16% (12–23)	83% (77–88)
>12 h	135	22% (14–33)	91% (82–96)	16% (9–27)	92% (83–97)
3–12 h	131	29% (19–41)	81% (70–89)	20% (12–33)	81% (69–90)
<3 h	90	27% (17–40)	76% (64–86)	12% (5–24)	73% (59–84)
Specificity					
All	356	98% (93–99)	97% (92–99)	98% (94–99)	96% (92–99)
>12 h	135	98% (89–100)	96% (86–99)	98% (90–100)	97% (88–99)
3–12 h	131	97% (87–99)	98% (90–100)	96% (87–99)	99% (91–100)
<3 h	90	100% (85–100)	96% (79–100)	100% (89–100)	92% (78–98)

Data in parentheses are 95% CI.

Table 4: Sensitivity and specificity of blinded imaging diagnosis by time from onset to scan



MRI: The Dark Side

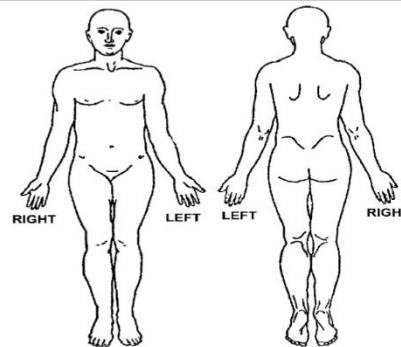


WARNING: Certain implants, devices, or objects may be hazardous to you and/or may interfere with the MR procedure (i.e., MRI, MR angiography, functional MRI, MR spectroscopy). Do not enter the MR system room or MR environment if you have any question or concern regarding an implant, device, or object. Consult the MRI Technologist or Radiologist **BEFORE** entering the MR system room. **The MR system magnet is ALWAYS on.**

Please indicate if you have any of the following:

- | | | |
|-----|----|--|
| Yes | No | Aneurysm clip(s) |
| Yes | No | Cardiac pacemaker |
| Yes | No | Implanted cardioverter defibrillator (ICD) |
| Yes | No | Electronic implant or device |
| Yes | No | Magnetically-activated implant or device |
| Yes | No | Neurostimulation system |
| Yes | No | Spinal cord stimulator |
| Yes | No | Internal electrodes or wires |
| Yes | No | Bone growth/bone fusion stimulator |
| Yes | No | Cochlear, otologic, or other ear implant |
| Yes | No | Insulin or other infusion pump |
| Yes | No | Implanted drug infusion device |
| Yes | No | Any type of prosthesis (eye, penile, etc.) |
| Yes | No | Heart valve prosthesis |
| Yes | No | Eyelid spring or wire |
| Yes | No | Artificial or prosthetic limb |
| Yes | No | Metallic stent, filter, or coil |
| Yes | No | Shunt (spinal or intraventricular) |
| Yes | No | Vascular access port and/or catheter |
| Yes | No | Radiation seeds or implants |
| Yes | No | Swan-Ganz or thermodilution catheter |
| Yes | No | Medication patch (Nicotine, Nitroglycerine) |
| Yes | No | Any metallic fragment or foreign body |
| Yes | No | Wire mesh implant |
| Yes | No | Tissue expander (e.g., breast) |
| Yes | No | Surgical staples, clips, or metallic sutures |
| Yes | No | Joint replacement (hip, knee, etc.) |
| Yes | No | Bone/joint pin, screw, nail, wire, plate, etc. |
| Yes | No | IUD, diaphragm, or pessary |
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| Yes | No | Other implant |
| Yes | No | Breathing problem or motion disorder |
| Yes | No | Claustrophobia |

Please mark on the figure(s) below the location of any implant or metal inside of or on your body.





IMPORTANT INSTRUCTIONS

Before entering the MR environment or MR system room, you must remove all metallic objects including hearing aids, dentures, partial plates, keys, beeper, cell phone, eyeglasses, hair pins, barrettes, jewelry, body piercing jewelry, watch, safety pins, paperclips, money clip, credit cards, bank cards, magnetic strip cards, coins, pens, pocket knife, nail clipper, tools, clothing with metal fasteners, & clothing with metallic threads.

Please consult the MRI Technologist or Radiologist if you have any questions or concerns BEFORE you enter the MR system room.

NOTE: You may be advised or required to wear earplugs or other hearing protection during the MR procedure to prevent possible problems or hazards related to acoustic noise.



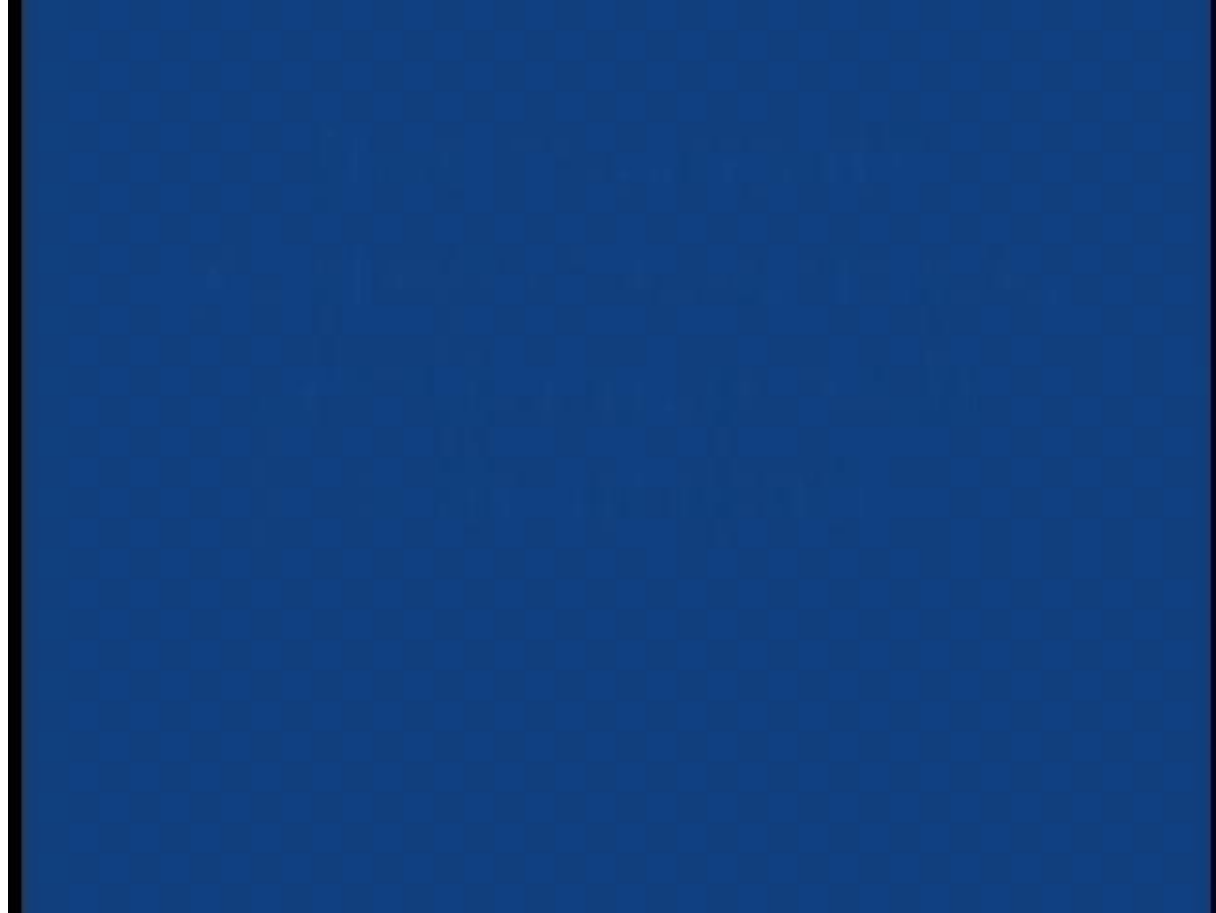
I attest that the above information is correct to the best of my knowledge. I read and understand the contents of this form and had the opportunity to ask questions regarding the information on this form and regarding the MR procedure that I am about to undergo.

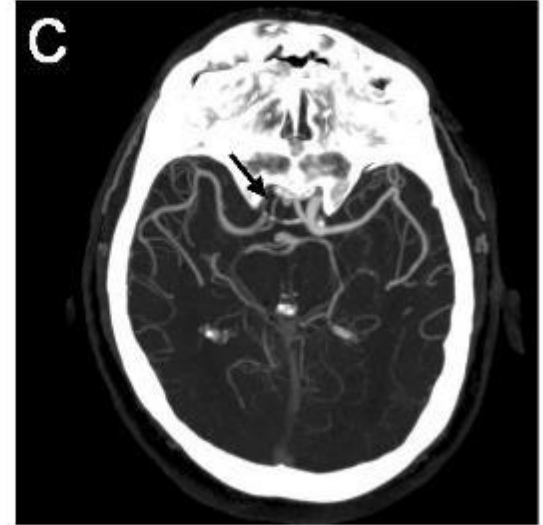
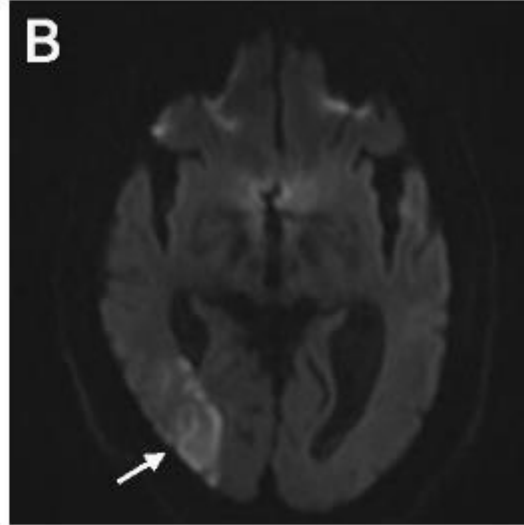
Signature of Person Completing Form: _____ Date ____/____/____
Signature

CT vs. MRI for diagnosis

- Pre-test probability of stroke is critical
 - Patient features: age, risk factors, stroke severity
- High pre-test probability, normal CT = treat as stroke
 - CTA improves diagnostic certainty, and is necessary when thrombectomy is a consideration
- Low pre-test probability, normal CT = ??? what to do – MRI has a role

Case example – 76 year old man





Selection for IV tPA: CT vs. MRI

Time is brain: faster tPA is better

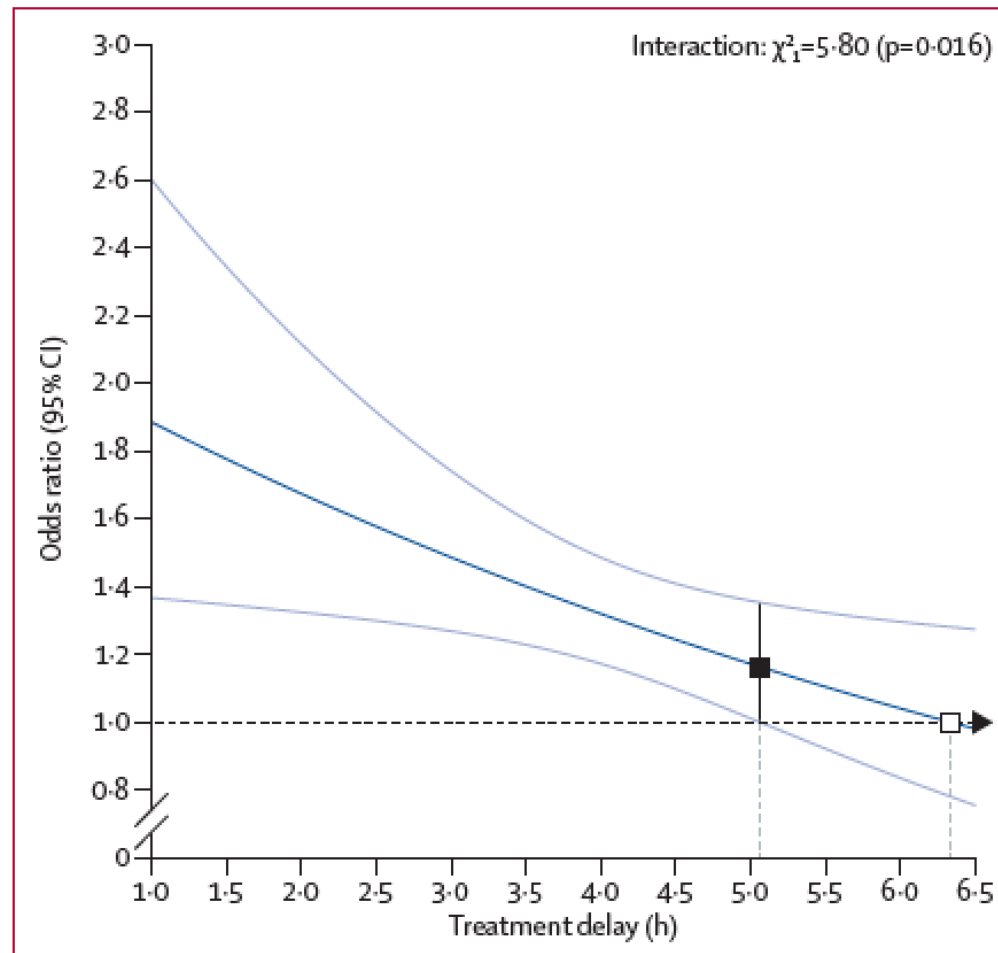


Figure 1: Effect of timing of alteplase treatment on good stroke outcome (mRS 0-1)

Emberson J, Lancet 2015

MRI is slower than CT

- SMART study – NIH MRI stroke group
- Highly organized acute stroke MRI pathway for all eligible patients
- Protocol includes limited MR brain, MRA brain, PWI
- Reported QI process to speed up imaging
- 157 tPA patients 2012-2013, 135 screened with MRI

MRI delays tPA compared to CT



Table 2 Changes in SMART metrics with the QI process

Characteristic	1st half of 2012	2nd half of 2012	1st half of 2013	2nd half of 2013	p Value
No. of patients treated with IV tPA (% of patients evaluated)	23 (9)	27 (12.2)	46 (16.0)	39 (12.8)	0.11
Patients with DTN time \leq 60 min, %	13.0	11.1	28.2	61.5	0.00001 ^a
Door-to-stroke team paging time, min ^b	6 (3-18)	12 (7-21.5)	6 (5-11)	3 (0-8.5)	0.001 ^a
Door-to-MRI start time, min ^b	49 (39-61.5)	52 (40.5-60)	44 (31.2-57)	24 (16.5-37)	<0.0001 ^a
MRI-to-needle time, min ^b	40 (29.5-52.5)	31 (23.5-39)	33.5 (21.7-40.7)	30.5 (25-38)	0.13
Door-to-needle time, min ^b	93 (77-103)	82 (71-92.5)	71 (58-92)	55 (46.5-76.5)	<0.0001 ^a
Last seen normal-to-needle time, min ^b	166 (150-195.5)	160 (114-219)	141.5 (109.7-191.7)	140 (96-201)	0.18

Compare to Helsinki model times: Door direct to CT <5 min, median CT to needle times <20-30 min

Compare to Coverdell registry: DTN<60 min achieved in 66% of patients, DTN <45 min in 40%

(Tong X, Circ Cardiovasc Qual Outcomes, 2018)

MRI for patient selection for tPA: WAKE-UP trial

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ESTABLISHED IN 1812

AUGUST 16, 2018

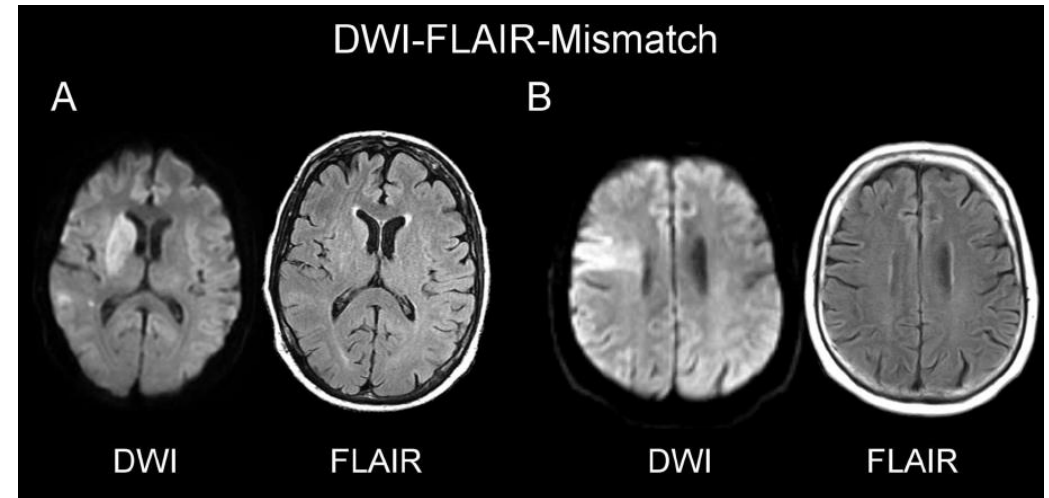
VOL. 379 NO. 7

MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

G. Thomalla, C.Z. Simonsen, F. Boutitie, G. Andersen, Y. Berthezene, B. Cheng, B. Cheripelli, T.-H. Cho, F. Fazekas, J. Fiehler, I. Ford, I. Galinovic, S. Gellissen, A. Golsari, J. Gregori, M. Günther, J. Guibernau, K.G. Häusler, M. Hennerici, A. Kemmling, J. Marstrand, B. Modrau, L. Neeb, N. Perez de la Ossa, J. Puig, P. Ringleb, P. Roy, E. Scheel, W. Schonewille, J. Serena, S. Sunaert, K. Villringer, A. Wouters, V. Thijs, M. Ebinger, M. Endres, J.B. Fiebach, R. Lemmens, K.W. Muir, N. Nighoghossian, S. Pedraza, and C. Gerloff, for the WAKE-UP Investigators*

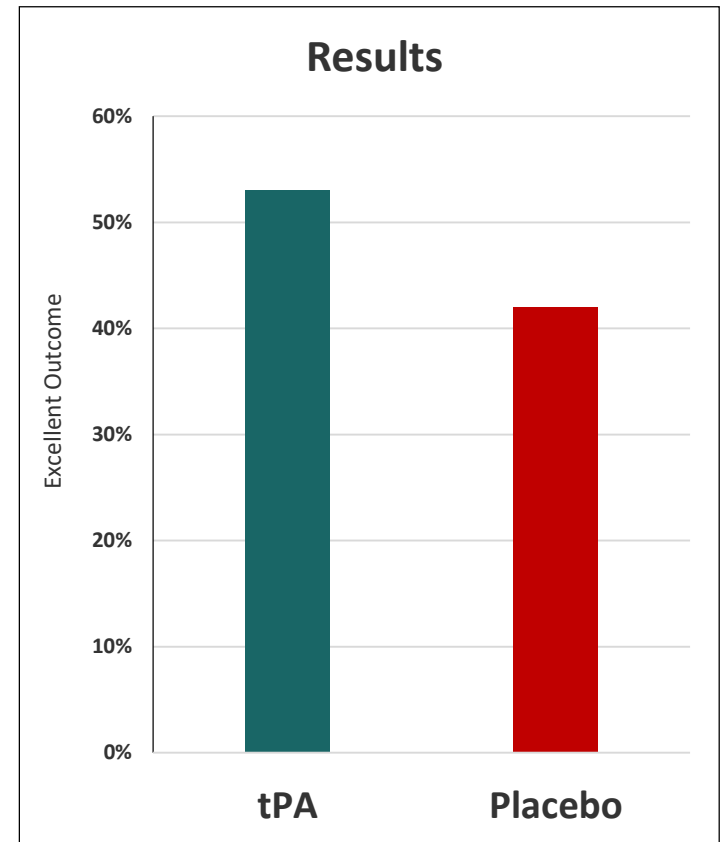
WAKE-UP Trial: MRI guided tPA

- Acute ischemic stroke and unknown time of onset
 - MRI used to select patients
 - Lesion on DWI but not FLAIR
- Excluded thrombectomy
- Randomized to tPA or placebo



WAKE-UP Trial: Results

- Stopped early due to lack of funding
- N=503
- Median NIHSS=6
- Excellent outcome:
 - 53% tPA vs. 42% placebo, $p=0.02$
- Safety concerns:
 - Death 4.1% vs 1.2%, $p=0.07$
 - sICH 2.0% vs. 0.4%, $p=0.15$



Selection for mechanical thrombectomy: CT vs. MRI

Mechanical thrombectomy (MT)

- Standard of care for acute major stroke with large vessel occlusion (LVO) within 6 hours of onset
- Therapeutic benefit HUGE (NNT=2-3)
- The field is moving towards asking who **SHOULDN'T** be treated, instead of who **SHOULD** be treated

What you need to proceed with MT

- 1) A large vessel that is occluded
- 2) An infarct core that is not gigantic
 - What does “gigantic” mean? Moving target...
 - Measured with ASPECTS, DWI MRI, or CTP
- 3) Some penumbral brain tissue that is salvageable
 - Presumed in patients < 6 h from onset

OR

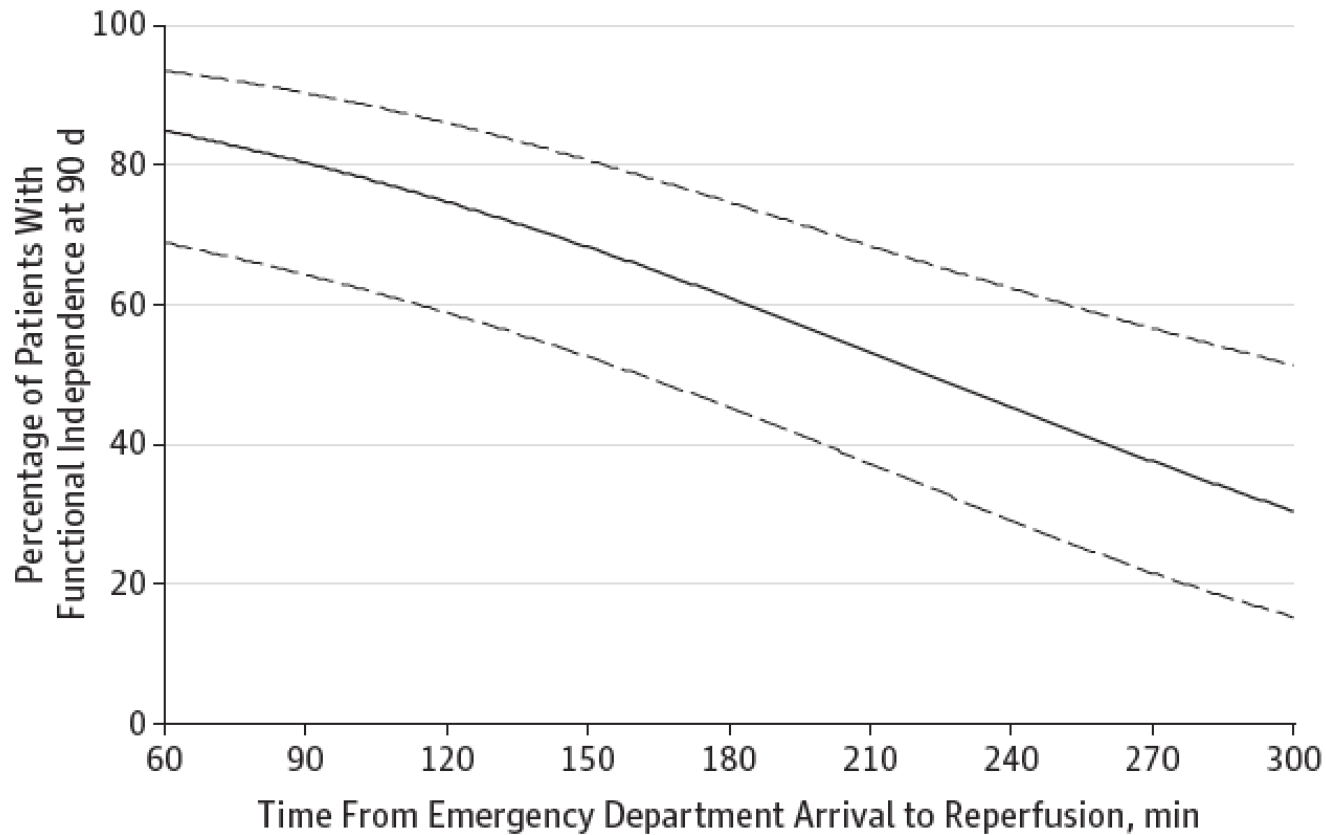
 - Perfusion imaging showing mismatch (i.e. core smaller than perfusion defect) in late time window

Mechanical thrombectomy: AHA guidelines 2018

3.7. Mechanical Thrombectomy (Continued)	COR	LOE	New, Revised, or Unchanged
<p>3. Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3) age \geq18 years; (4) NIHSS score of \geq6; (5) ASPECTS of \geq6; and (6) treatment can be initiated (groin puncture) within 6 hours of symptom onset.</p>	I	A	<p>Recommendation revised from 2015 Endovascular.</p>
<p>Results from 6 recent randomized trials of mechanical thrombectomy using predominantly stent retriever devices (MR CLEAN, SWIFT PRIME, EXTEND-IA, ESCAPE, REVASCAT, THRACE) support Class I, LOE A recommendations for a defined group of patients as described in the 2015 guidelines.^{102–107} A pooled, patient-level analysis from 5 of these studies reported by the HERMES collaboration showed treatment effect in the subgroup of 188 patients not treated with IV alteplase (cOR, 2.43; 95% CI, 1.30–4.55); therefore, pretreatment with IV alteplase has been removed from the prior recommendation. The HERMES pooled patient-level data also showed that mechanical thrombectomy had a favorable effect over standard care in patients >80 years</p>			<p>See Tables XXIII and XLI in online Data Supplement 1.</p>

Time is brain: faster thrombectomy is better

A Functional independence (mRS 0-2) by time from emergency department arrival to actual substantial reperfusion



Saver J, JAMA 2016

MRA is slower than CTA



Table 2. Comparisons of Workflow Time Metrics Between the CTA and MRI Groups in Patients With 6 Hours of OTA Time

Time Metrics	Overall Patients	CTA Group (N=273)	MRI Group (N=758)	P Value
Time metrics from onset (last well seen)				
OTA	94 (44–178)	85 (37–159)	98 (47–184)	0.004
OTI	142 (95–222)	113 (62–178)	154 (105–233)	<0.001
OTP	215 (160–291)	190 (135–260)	225 (168–305)	<0.001
OTR	289 (215–365)	250 (181–328)	297 (224–371)	<0.001
Time metrics from arrival				
ATI	43 (24–61)	21 (15–35)	49 (35–66)	<0.001
ATP	106 (84–133)	89 (63–127)	110 (91–135)	<0.001
ATR	164 (127–213)	135 (100–187)	169 (135–217)	<0.001
Time metrics from decision imaging				
ITP	61 (43–84)	65 (42–94)	60 (43–81)	0.014
ITR	119 (85–165)	113 (79–155)	121 (86–171)	0.234

Values are presented as median minutes (IQRs). *P* value for the comparison between the CTA and MRI groups. ATI indicates time from arrival to decision imaging; ATP, time from arrival to puncture; ATR, time from arrival to reperfusion; CTA, computed tomography angiography; IQRs, interquartile ranges; ITP, time from decision imaging to puncture; ITR, time from decision imaging to reperfusion; MRI, magnetic resonance imaging; OTA, time from onset to arrival; OTI, time from onset to decision imaging; OTP, time from onset to puncture; and OTR, time from onset to reperfusion.

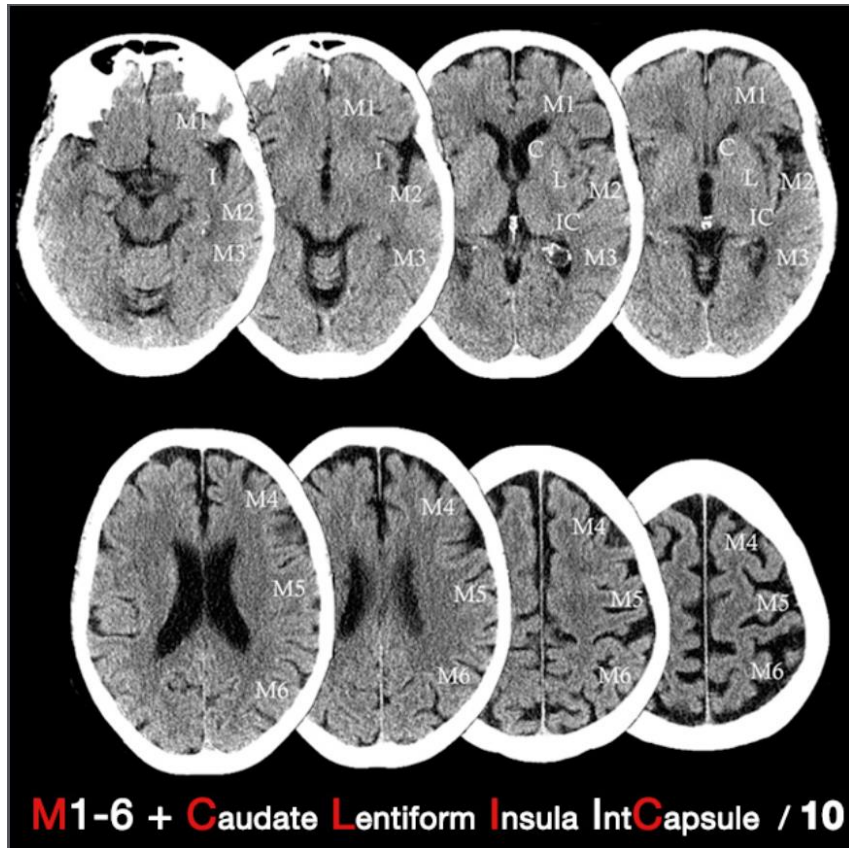
**MRA takes
20-30 min
longer than
CTA**



CTA also better for:

- Distal branch occlusions
- Near occlusions
- Intraluminal thrombus

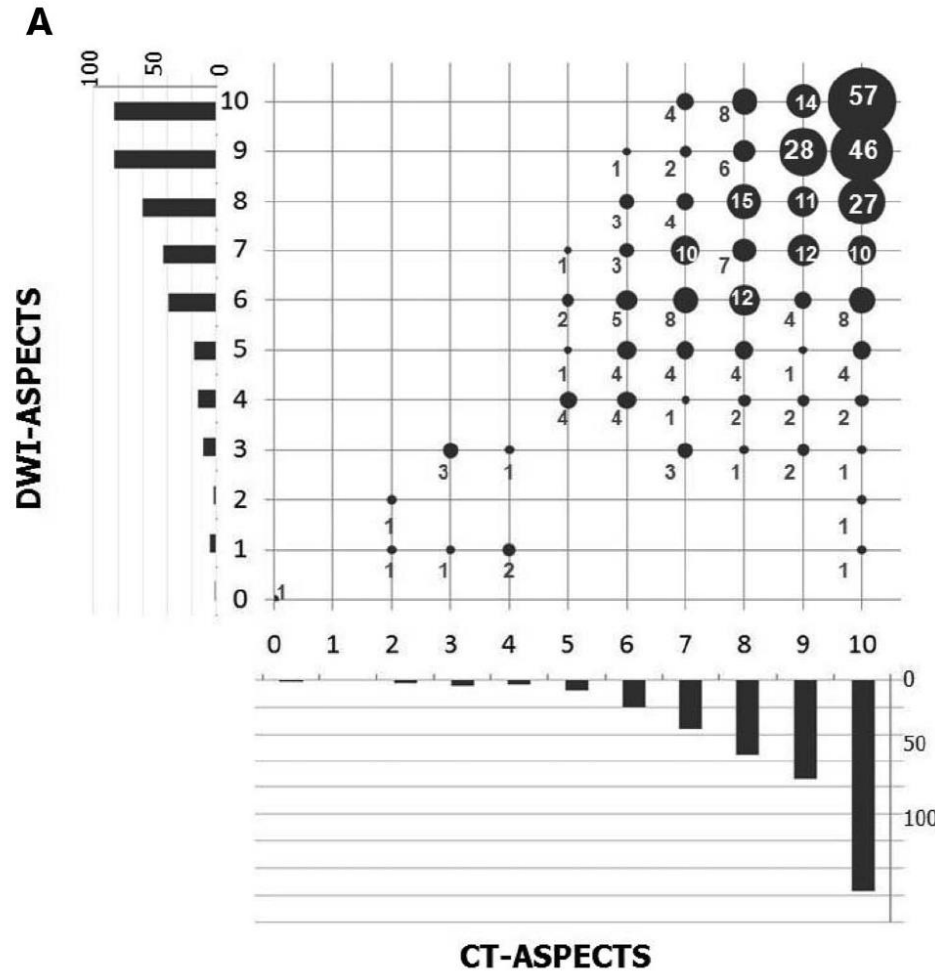
Alberta Stroke Program Early CT Score (ASPECTS)



- Quantitative score assessing early infarct signs in 10 brain regions
- 10 = normal
- 0 = large hemispheric infarction

ASPECTS:

Despite name, can score MRI as well



MRI more sensitive to early ischemia → ASPECTS scores lower on MRI vs CT

Selection for thrombectomy using ASPECTS to estimate infarct core

- HERMES meta-analysis of patient level data
- Included patients with vessel imaging
- 1764 patients with LVO randomized, 7 trials
 - MR CLEAN
 - EXTEND-IA
 - ESCAPE
 - SWIFT PRIME
 - REVASCAT
 - PISTE
 - THRACE

Baseline characteristics

	Endovascular thrombectomy group (n=871)	Control group (n=893)
Age, years	67.4 (57.0-76.0)	67.8 (58.0-76.0)
Sex		
Female	412 (47%)	421/891 (47%)
Male	459/871 (53%)	470/891 (53%)
NIHSS	17 (14-20)	17 (13-21)
Onset to randomisation, min	181 (141-241)	184 (140-250)
Intravenous alteplase	763/871 (88%)	809/893 (91%)
ASPECTS	8 (7-9)	8 (7-9)
Clot burden score	4 (3-6)	4 (3-6)
>33% involvement of middle cerebral artery territory	114/860 (13%)	119/876 (14%)
Hyperdense vessel sign	356/687 (52%)	330/701 (47%)
Thrombus location		
Internal carotid artery	215/818 (26%)	227/828 (27%)
Proximal M1 segment of middle cerebral artery	315/818 (39%)	327/828 (39%)
Distal M1 segment of middle cerebral artery	221/818 (27%)	210/828 (25%)
M2 segment of middle cerebral artery	67/818 (8%)	64/828 (8%)
Collateral circulation grade		
0	6/639 (1%)	8/651 (1%)
1	91/639 (14%)	108/651 (17%)
2	283/639 (44%)	275/651 (42%)
3	259/639 (41%)	260/651 (40%)

Data are median (IQR), n (%), and n/N (%). NIHSS=National Institutes of Health Stroke Scale. ASPECTS=Alberta Stroke Program Early CT Score.

Table 1: Baseline clinical and imaging variables by treatment groups

Selection for thrombectomy using ASPECTS

- Outcome improved with MT across a broad range of baseline characteristics
- Benefit similar across ASPECTS categories
- BUT....beware how ASPECTS determined – i.e. MR vs. CT
- Most ASPECTS 0-4 in this analysis used MRI!

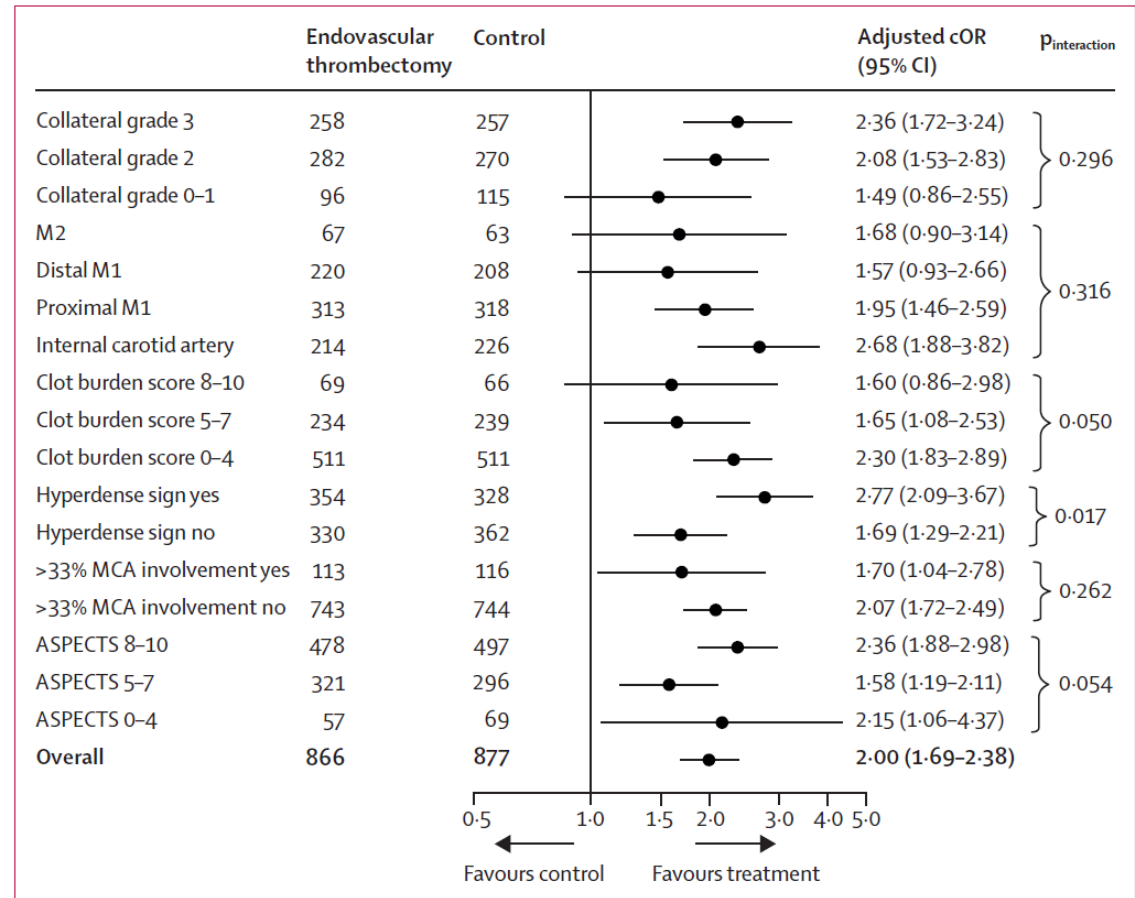


Figure 1: Forest plot of endovascular treatment effect on primary outcome (modified Rankin Scale shift at 90 days), by baseline imaging variable categories
 cOR=common odds ratio. M1=M1 segment of MCA. M2=M2 segment of MCA. MCA=middle cerebral artery.
 ASPECTS=Alberta Stroke Program Early CT Score.

Mechanical thrombectomy – selection based on core using CTP or DWI MR

- HERMES meta-analysis of patient level data
- Included patients with penumbral imaging data (CTP or MRI DWI)
- 900 patients, 7 trials
 - MR CLEAN
 - EXTEND-IA
 - ESCAPE
 - SWIFT PRIME
 - REVASCAT
 - PISTE
 - THRACE

Baseline characteristics

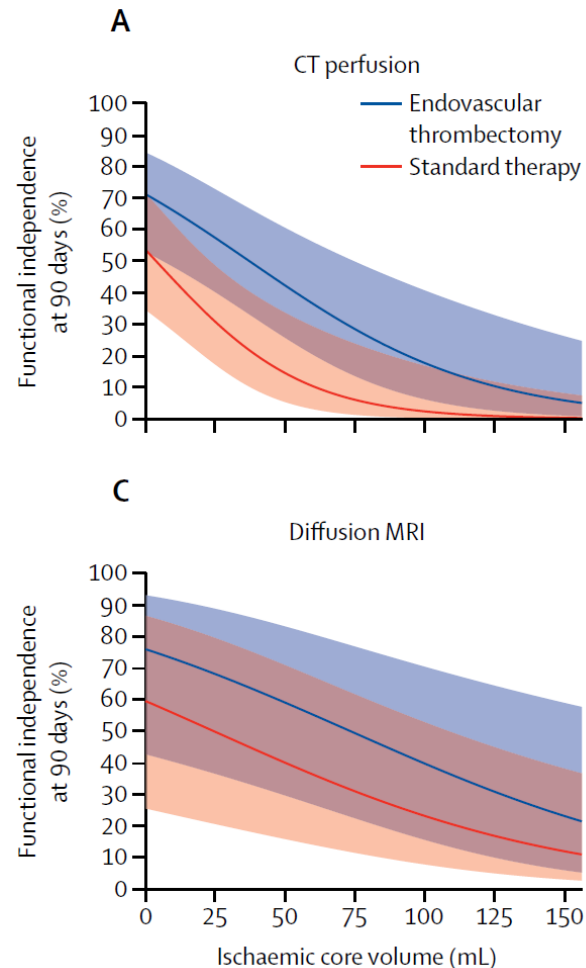
	CT perfusion		Diffusion MRI		All participants (n=1764)
	Endovascular thrombectomy group (n=289)	Standard therapy group (n=302)	Endovascular thrombectomy group (n=153)	Standard therapy group (n=156)	
Age, years	65.5 (13.7)	65.7 (13.0)	63.1 (13.1)	63.6 (14.0)	65.6 (13.5)
Sex					
Men	137 (47%)	168 (56%)	94 (61%)	73 (47%)	929 (53%)
Women	152 (53%)	134 (44%)	59 (39%)	83 (53%)	835 (47%)
NIHSS	17 (14–20)	17 (13–21)	18 (14–21)	17 (14–21)	17 (13–21)
ASPECTS	8 (7–9)	8 (7–9)	7 (6–8)	7 (5–8)	8 (7–9)
Site of arterial occlusion					
Internal carotid artery	79 (27%)	78 (26%)	25 (16%)	33 (21%)	442 (25%)
M1	171 (59%)	189 (63%)	112 (73%)	101 (65%)	1073 (61%)
M2	28 (10%)	24 (8%)	5 (3%)	8 (5%)	131 (7%)
Unknown	11 (4%)	11 (4%)	11 (7%)	14 (9%)	116 (7%)
Onset to emergency department, min	110 (57–183)	110 (54–197)	105 (75–139)	110 (80–159)	105 (60–180)
Emergency department to arterial access, min	103 (75–150)	NA	107 (85–140)	NA	115 (80–165)
Intravenous alteplase	248 (86%)	269 (89%)	145 (95%)	154 (99%)	1572 (89%)
Baseline ischaemic core volume, mL	10 (3–30)	9 (2.5–24)	18 (9–41)	23 (12–63)	NA
Baseline critical hypoperfusion volume, mL	122 (79–165)	123 (82–167)	NA	NA	NA

Data are mean (SD), median (IQR), or n (%). NIHSS is a standardised neurological examination for which the score ranges from normal (0) to death (42). ASPECTS reflects the extent of early ischaemic change on the CT brain: 10 is normal, 0 shows involvement of the entire middle cerebral artery territory. ASPECTS=Alberta Stroke Program Early CT Score. M1=first segment of middle cerebral artery (pre-bifurcation). M2=second segment of middle cerebral artery (from bifurcation to the circular sulcus of the insula in the Sylvian fissure). NA=not applicable. NIHSS=National Institutes of Health Stroke Scale.

Table 1: Baseline clinical and imaging characteristics of patients receiving endovascular thrombectomy or standard medical therapy

MT beneficial over broad range of core volumes

- Prognosis relative to core volume worse in patients assessed with CT vs. MRI
- CT probably underestimates “true core”
- MRI may overestimate “true core”



Late time window patients: DEFUSE 3

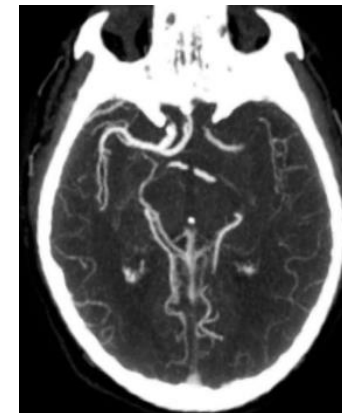
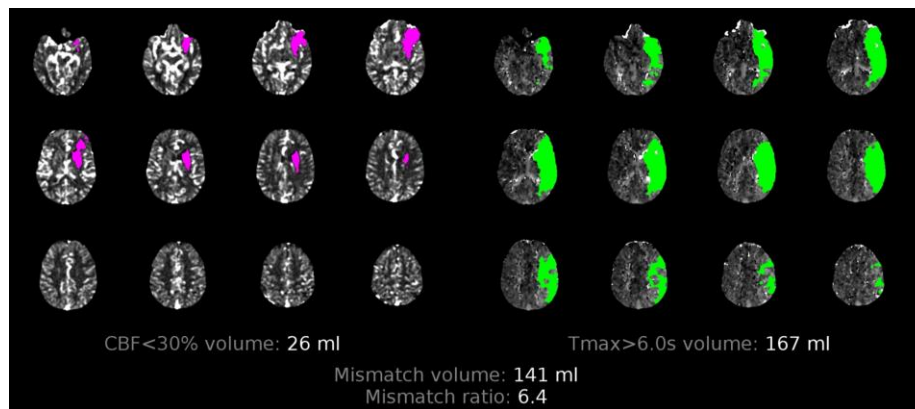
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

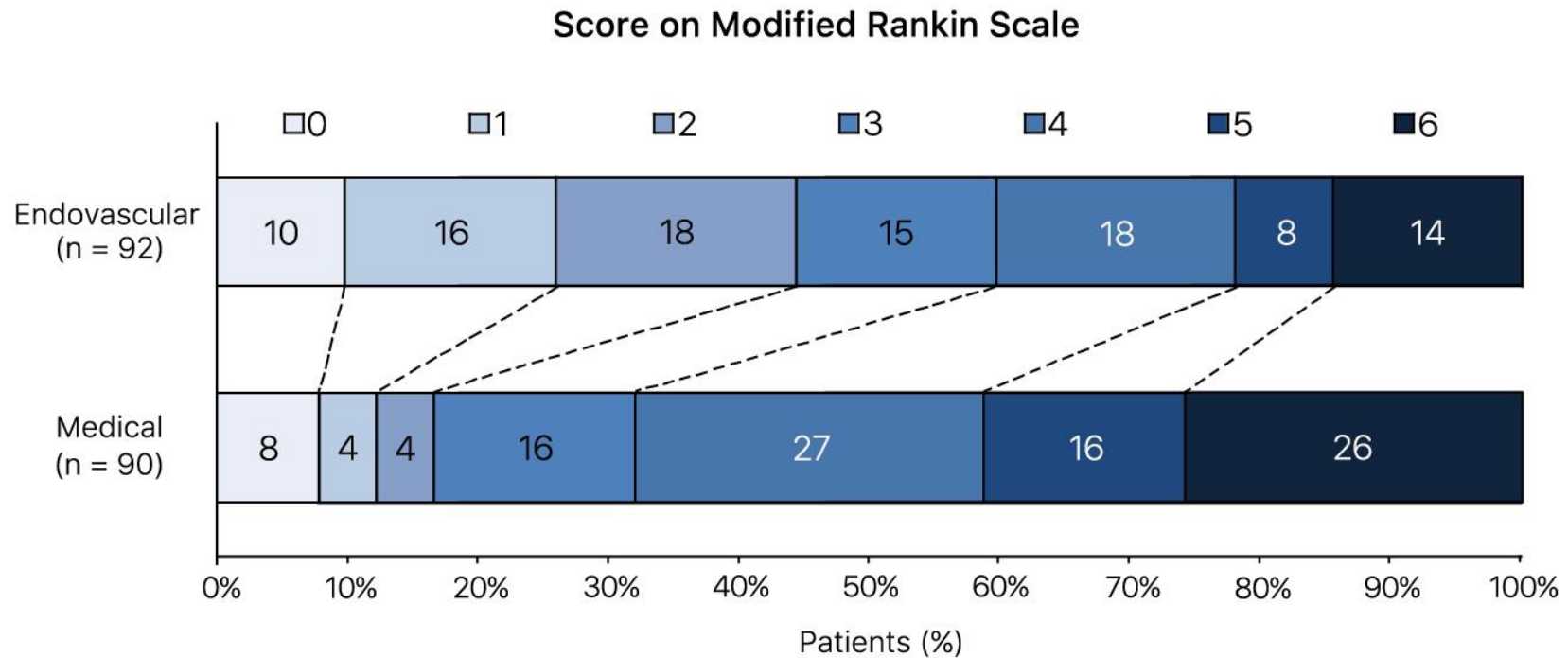
Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

G.W. Albers, M.P. Marks, S. Kemp, S. Christensen, J.P. Tsai, S. Ortega-Gutierrez, R.A. McTaggart, M.T. Torbey, M. Kim-Tenser, T. Leslie-Mazwi, A. Sarraj, S.E. Kasner, S.A. Ansari, S.D. Yeatts, S. Hamilton, M. Mlynash, J.J. Heit, G. Zaharchuk, S. Kim, J. Carrozzella, Y.Y. Palesch, A.M. Demchuk, R. Bammer, P.W. Lavori, J.P. Broderick, and M.G. Lansberg, for the DEFUSE 3 Investigators*

- 6-16 hours since LKN
- ICA or MCA occlusion
- Core < 70 ml
- Perfusion defect (Tm>6s):core ratio ≥ 1.8 using RAPID CT or MRI

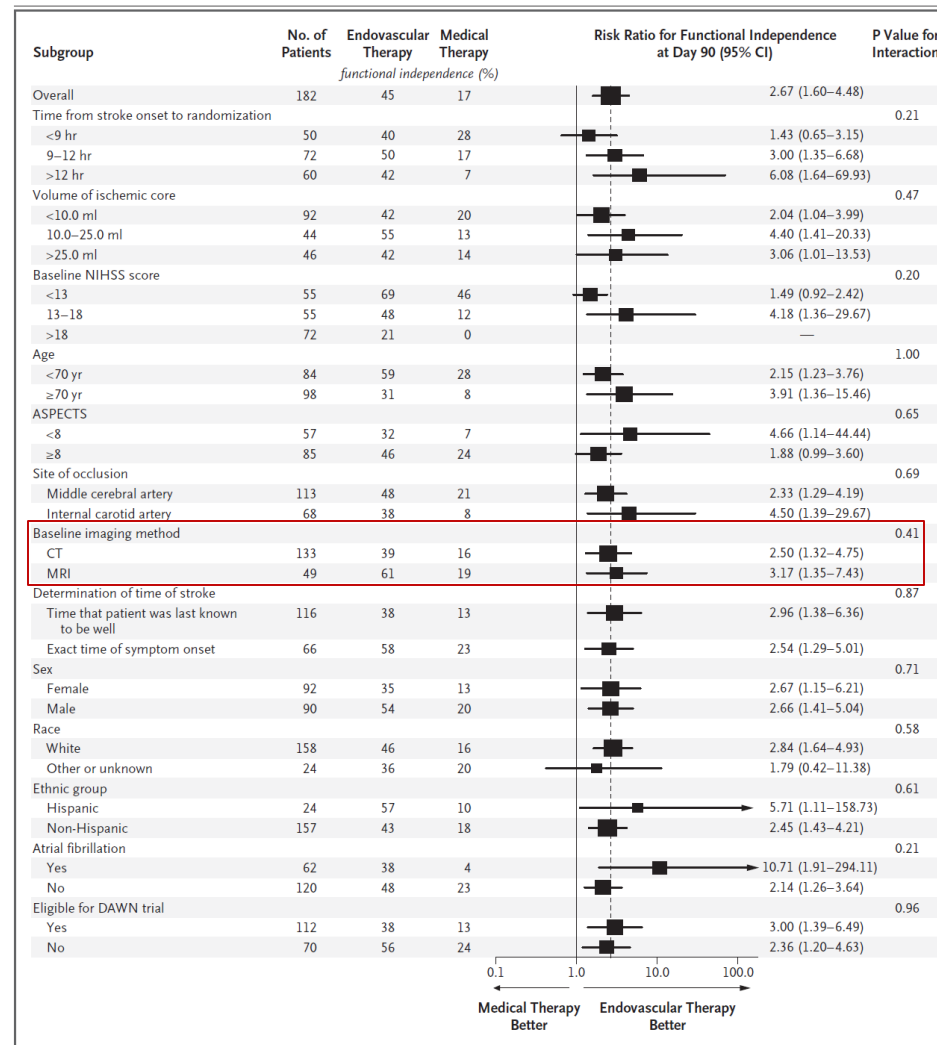


DEFUSE 3: Primary outcome



DEFUSE 3: Treatment effect similar in patients selected with CT vs. MR

Treatment effect similar in patients selected with CT vs. MR



Guidelines get the last word...

2.2. Brain Imaging	COR	LOE	New, Revised, or Unchanged
<p>1. All patients admitted to hospital with suspected acute stroke should receive brain imaging evaluation on arrival to hospital. In most cases, noncontrast CT (NCCT) will provide the necessary information to make decisions about acute management.</p>	I	B-NR	Recommendation revised from 2013 AIS Guidelines.
<p>Diagnostic testing is most cost-effective when it leads to a change in treatment that improves outcomes, not just a change in treatment. Although diffusion-weighted magnetic resonance imaging (DW-MRI) is more sensitive than CT for detecting AIS,^{66,67} routine use in all patients with AIS is not cost-effective.^{68,69} NCCT scanning of all patients with acute stroke has been shown to be cost-effective primarily because of the detection of acute ICH and the avoidance of antithrombotic treatment in these patients.⁷⁰ In many patients, the diagnosis of ischemic stroke can be made accurately on the basis of the clinical presentation and either a negative NCCT or one showing early ischemic changes, which can be detected in the majority of patients with careful attention.^{66,71,72} In some patients with negative NCCT such as those with puzzling clinical presentations or those with uncertain clinical stroke localization for early carotid endarterectomy (CEA) or stenting, demonstration of an area of restricted diffusion on DW-MRI may lead to a change in treatment that improves outcomes. There are inadequate data at this time to establish which patients will benefit from DW-MRI, and more research is needed to determine criteria for its cost-effective use.</p>			See Table XV in online Data Supplement 1 .