

What's Next for Acute Ischemic Stroke

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Disclosures

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National Steering Committees: Cerenovus EXCELLENCE and ABISE II Trial, Medtronic SWIFT PRIME, VANTAGE, ENDOUSE and SWIFT DIRECT Trial, Microvention FRED Trial & CONFIDENCE Study, MUSC POSITIVE Trial, Penumbra 3D Separator Trial, COMPASS Trial, INVEST Trial, MVI neuroscience EVAQ Trial, Rapid Medical SUCCESS Trial, InspireMD C-GUARDIANS IDE Pivotal Trial

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What is not in the Guidelines ?

- Age < 18 years
- Mild Strokes: NIHSS 0-5
- Large Strokes: ASPECTS 0-6
- Time > 24 hours
- Posterior Circulation
- Distal & Medium Vessel Occlusions
- Tandem Occlusions
- Adjunctive thrombolytics

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What is the next ?

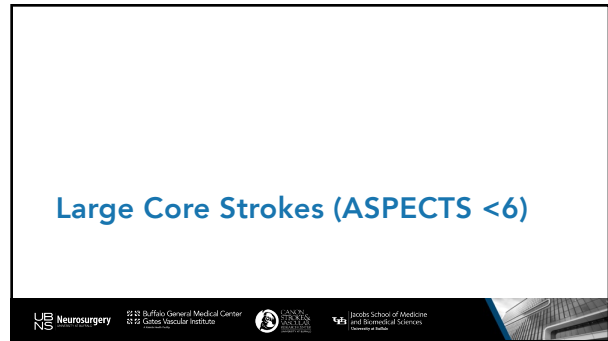
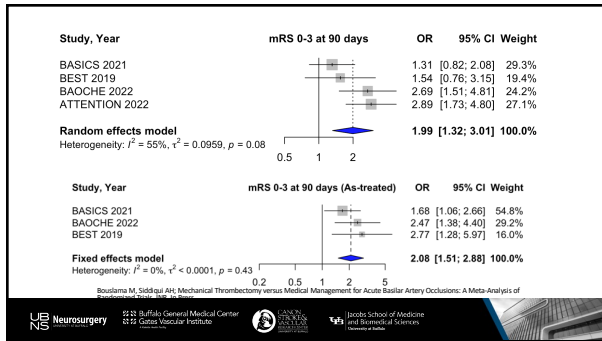
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Basilar Artery Occlusion Strokes

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<p>2019</p> <p>ORIGINAL ARTICLE</p> <p>Endovascular treatment versus standard medical treatment for vertebrobasilar artery occlusion (BEST): an open-label, randomised controlled trial</p> <p><i>Endovascular Treatment Versus Best Medical Treatment for Vertebrobasilar Artery Occlusion: The BEST Study</i> Endovascular Treatment Versus Best Medical Treatment for Vertebrobasilar Artery Occlusion: The BEST Study Endovascular Treatment Versus Best Medical Treatment for Vertebrobasilar Artery Occlusion: The BEST Study Endovascular Treatment Versus Best Medical Treatment for Vertebrobasilar Artery Occlusion: The BEST Study</p>	<p>2022</p> <p>ORIGINAL ARTICLE</p> <p>Trial of Thrombectomy 6 to 24 Hours after Stroke Due to Basilar-Artery Occlusion</p> <p><i>Trial of Thrombectomy 6 to 24 Hours after Stroke Due to Basilar-Artery Occlusion</i> Trial of Thrombectomy 6 to 24 Hours after Stroke Due to Basilar-Artery Occlusion Trial of Thrombectomy 6 to 24 Hours after Stroke Due to Basilar-Artery Occlusion Trial of Thrombectomy 6 to 24 Hours after Stroke Due to Basilar-Artery Occlusion</p>
<p>2021</p> <p>ORIGINAL ARTICLE</p> <p>Endovascular Therapy for Stroke Due to Basilar-Artery Occlusion</p> <p><i>Endovascular Therapy for Stroke Due to Basilar-Artery Occlusion</i> Endovascular Therapy for Stroke Due to Basilar-Artery Occlusion Endovascular Therapy for Stroke Due to Basilar-Artery Occlusion Endovascular Therapy for Stroke Due to Basilar-Artery Occlusion</p>	<p>2022</p> <p>ORIGINAL ARTICLE</p> <p>Trial of Endovascular Treatment of Acute Basilar-Artery Occlusion</p> <p><i>Trial of Endovascular Treatment of Acute Basilar-Artery Occlusion</i> Trial of Endovascular Treatment of Acute Basilar-Artery Occlusion Trial of Endovascular Treatment of Acute Basilar-Artery Occlusion Trial of Endovascular Treatment of Acute Basilar-Artery Occlusion</p>

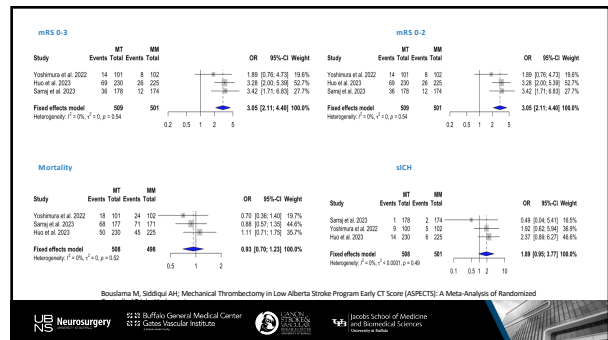
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Low ASPECTS / Large Core Thrombectomy Trials

Trial	ClinicalTrials.gov Identifier	Imaging Criteria
RESCUE JAPAN LIMIT	NCT03702413	NICT or DW ASPECTS 3-5
TESLA	NCT03805308	NICT ASPECTS 2-5
TENSION	NCT03094715	NICT or DW ASPECTS 3-5
ANGEL-ASPECT	NCT04551654	NICT ASPECTS: 3-5 or CTP [(rCBF<30%)] MRI (ADC<620) 70-100cc or both
IN EXTREMIS Large Stroke Therapy Evaluation (LASTE)	NCT03811769	NICT or DW ASPECTS 0-5 and in patients >80 years NICT or DW ASPECTS 4-5
SELECT-2	NCT03876457	NICT (ASPECTS: 3-5) or advanced perfusion imaging [(rCBF<30% on CTP or ADC<620) on MRI: ≥50cc] or both

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Considerations in Large Core Thrombectomy

Table 1 Agreement between Alberta Stroke Program Early CT Score (ASPECTS) and CT perfusion core volume categories

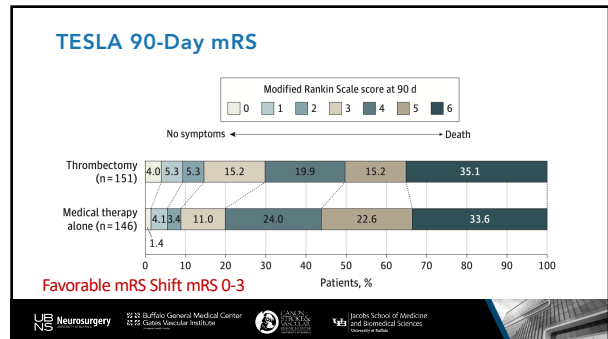
	Ischemic core <70 cc (n=1283)	Ischemic core >70cc (n=45)
ASPECTS 6-10 (n=1123)	1094 (97.4%, 96.9%)	29 (2.6%, 64.4%)
ASPECTS 0-5 (n=125)	109 (87.2%, 9.1%)	16 (12.8%, 35.6%)

McNemar Test for discordant pairs p<0.0001.

Table 3 Outcome measures

	ASPECTS 0-5 (n=125)		P Value
	Cores 70 cc (n=108)	Cores >70 cc (n=16)	
mTICI 2b/3	104 (95.4)	15 (93.8)	0.57
mTICI 3	47 (43.1)	7 (43.8)	0.96
Any PW	14 (12.8)	5 (31.3)	0.07
Hemorrhage	4 (3.7)	4 (25.0)	<0.001
FW (dL)	86.3 (43.9-147)	164.2 (127-238.2)	0.004
90-day mRS score 0-2	42 (38.9)	3 (18.8)	0.12
90-day mortality	19 (17.6)	4 (25.0)	0.5

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Mild Strokes (NIHSS <6)

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Mechanical Thrombectomy in Patients With Milder Strokes and Large Vessel Occlusions

A Multicenter Matched Analysis

Simon Nagler, MD, MSc, BSc(Ed), MD, Leah U. Krause, MD, Cameron Kloman, MD, Amir Meuser, MD, Marina Petrusen, MD, Stephen Linnman, MD, Moritz Heusinger, MD, Peter A. Pappalardo, MD, Marco A. Minnerink, MD, Stefan Teich, MD, Fabrice D. Lina, MD, Diego C. Heussen, MD, Wade S. Smith, MD, Michael H. Law, MD, and Paul G. Nugent, MD

Patient Characteristics	MT (n=77)	BMAT (n=77)	P-Value
Age, y (median [IQR])	68.5 (58-75)	68.8 (58-77)	0.887
Baseline NIHSS (median [IQR])	5.5 (3-6)	4 (4-6)	0.741
Gender (male, n (%))	42 (54.5)	45 (58.4)	0.632
Hypertension, n (%)	54 (70.1)	55 (71.4)	0.962
Dyslipidemia, n (%)	38 (49.4)	39 (50.6)	0.742
Diabetes mellitus, n (%)	12 (15.6)	13 (16.8)	0.832
Stroke, n (%)	35 (45.5)	22 (28.6)	0.005
Baseline mRS	14 (18.2)	23 (29.8)	0.062
0	65 (84.4)	58 (74.1)	
1	7 (9.1)	9 (11.7)	
2	5 (6.5)	7 (9.2)	

Outcome (n=*)	MT (n=77)	BMAT (n=77)	P-Value
OCclusion rate*			1.000
ICA-T	7 (9.1)	7 (9.1)	
Taxane	9 (11.7)	9 (11.7)	
MT	32 (41.6)	32 (41.6)	
MS	23 (29.8)	23 (29.8)	
Basilar	6 (7.8)	6 (7.8)	
ASPECTs, median (IQR)	10 (9-10)	9 (8.5-10)	0.0021
MAP, mean (median [IQR])	115 (108-126)	116 (104-146)	0.359
90-d mRS, n (%)	30 (39.0)	42 (54.5)	0.026
OR	4 (2.3)	2 (2.5)	0.415
Excellent outcome mRS, 0-1, n (%)	47 (61.0)	41 (53.2)	0.332
Good outcome mRS, 2-3, n (%)	65 (84.4)	54 (70.1)	0.023
Mortality, n (%)	3 (3.9)	4 (5.2)	0.712

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90-d mRS (n=*)	MT (n=77)	BMAT (n=77)	P-Value	OR	95% CI
0	22 (28.6)	23 (29.8)	0.32	1.34	0.78-2.35
1	29 (37.7)	19 (24.4)			
2	18 (23.2)	13 (16.9)			
3	5 (6.5)	10 (13.0)			
4	4 (5.2)	6 (7.8)			
5	0 (0)	3 (3.9)			
6	3 (3.9)	4 (5.2)			
90-d mRS (n=*)			0.01	2.29	1.29-4.08
0, 1, and 2	65 (84.4)	54 (70.1)			
3	5 (6.5)	10 (13.0)			
4	4 (5.2)	6 (7.8)			
5 and 6	3 (3.9)	7 (9.1)			

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Medical Management vs Mechanical Thrombectomy for Mild Strokes and Meta-analysis

An International Multicenter Study and Systematic Review

Simon Nagler, MD, MSc, BSc(Ed), MD, Leah U. Krause, MD, Cameron Kloman, MD, Amir Meuser, MD, Marina Petrusen, MD, Stephen Linnman, MD, Moritz Heusinger, MD, Peter A. Pappalardo, MD, Marco A. Minnerink, MD, Stefan Teich, MD, Fabrice D. Lina, MD, Diego C. Heussen, MD, Wade S. Smith, MD, Michael H. Law, MD, and Paul G. Nugent, MD

Outcome	Medical Management (n=1,183)	Mechanical Thrombectomy (n=1,132)	P-Value
Length of stay, d	11 (4)	12 (4)	.002
ICU	2 (1.4)	1 (1.4)	.38
Costs (mean±SD, \$)	13,105 (\$4,433)	944	.04
30-d mortality (%)	16.0 (17.2)	16.0 (18.2)	.992
30-d mRS	6 (37.4)	1 (17.4)	.11
Discharge mRS	2 (8.4)	1 (8.2)	.92
Neurological improvement during hospitalization*	2 (1.3)	1 (8.2)	.002
30-d follow-up	1 (0.7)	1 (8.2)	.08
90-d mortality (%)	14.0 (15.1)	15.0 (17.4)	.26
90-d mRS	10 (11.1)	7 (8.2)	.12
30-d mortality (%)	14.0 (15.1)	15.0 (17.4)	.26
90-d mRS	10 (11.1)	7 (8.2)	.12

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Ongoing Trials

IN EXTREMIS MOSTE] [LASTE

Minor Stroke Therapy Evaluation (MOSTE)

ENDOLOW

Endovascular Therapy for Low NIHSS Ischemic Strokes (ENDOLOW)

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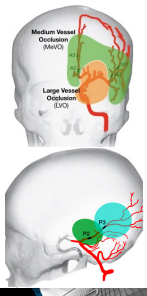
Distal & Medium Vessel Occlusion (DMVO) Strokes

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Distal & Medium Vessel Occlusion (DMVO) Strokes Prevalence

- Proximal LVOs account for 35%-40% of strokes
- Small vessel occlusions (deep and long penetrating) 20%-25%
- Hemodynamic watershed ischemia 2%-5%
- Unusual and disseminated conditions (RCS, hyperviscosity, moyamoya, etc) 1% -5%

25%- 40% are DMVOs = DMVOs ARE COMMON



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Distal & Medium Vessel Occlusion (DMVO) Strokes

DMVOs distinguish themselves from proximal LVOs by 2 key features:

- Vessel Distance and Tortuosity**
- Vessel Size** (lumen diameters between 0.75 and 2.0 mm)
For reference ICA (3.8 mm), MCA-M1 (2.7 mm), BA (3.2 mm), and VA (2.8 mm) while LS (0.5 mm)
MCA-M2 from 1.1 to 2.1 mm
MCA-M3: 1.1-1.5 mm

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Distal & Medium Vessel Occlusion (DMVO) Strokes

TWO TYPES

- Primary (de novo)
- Secondary (Clot migration of fragmentation occurring spontaneously or after IV thrombolysis of mechanical thrombectomy)
 - Embolism to a new territory (ENT) affecting fields not previously compromised by ischemia 2/2 fragmentation and loss of control of thrombus during pullback.
 - Embolism to a distal territory (EDTs) within the initial ischemic field 2/2 fragmentation and loss of control of thrombus during the initial engagement with the retrieval device.

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Clinical Course of Acute Ischemic Stroke Due to Medium Vessel Occlusion With and Without Intravenous Alteplase Treatment



50% of patients do not achieve recanalization with intravenous alteplase alone

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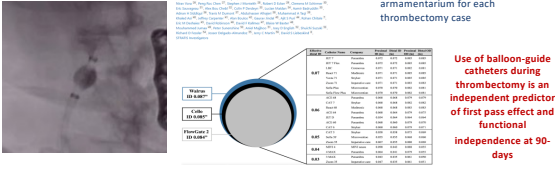
Expanding The Thrombectomy Armamentarium

Waters large bore guide catheter impact on recanalization first pass effect and outcomes: the WICKED study

Modern BGCs are more versatile and flexible than older ones

BGC use expands the armamentarium for each thrombectomy case

Use of balloon-guide catheters during thrombectomy is an independent predictor of first pass effect and functional independence at 90-days



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BGC clinical data shows powerful benefits.

Shorter Procedure Times	Better Predictor of Good Clinical Outcome	Superior Recanalization Results	Higher Rate of First-Pass Success
<p>Procedure time was 50% shorter in the BGC group than in the non-BGC group. Median 20.5 min vs 41.0 min, respectively.</p> <p>(p<0.0001) Velasco, 2016</p> <p>20.5 mins BGC Group n=102</p> <p>41.0 mins Non-BGC Group n=81</p>	<p>After adjustment for potentially associated factors (N=429; 90d mRS 0-2), BGC utilization remained independently associated with recanalization and good functional outcome.</p> <p>(p<0.0001) Kang, 2019</p> <p>60.3% BGC Group n=117</p> <p>45.1% Non-BGC Group n=106</p>	<p>The successful recanalization rate (TICI 2b-3) was significantly higher in the BGC group compared with the non-BGC group (66.8% versus 74.7%) respectively; n=955.</p> <p>(p<0.001) Baek, 2019</p> <p>86.8% BGC Group n=616</p> <p>74.7% Non-BGC Group n=439</p>	<p>The overall rate of first-pass recanalization was 63.1% (497/788) for the BGC group compared with 45.2% (208/461) for the non-BGC group.</p> <p>(p<0.01) Brinjikji, 2018</p> <p>63.1% BGC Group n=1083</p> <p>45.2% Non-BGC Group n=932</p>

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WHEN IT COMES TO ASPIRATION SIZE MATTERS

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The Evolution of Aspiration Technology

- Larger diameter systems (catheters and aspiration tubing)
- Tapered catheters (ie: 3MAX, ARC) with larger proximal diameter to increase average radius of system
- More powerful pumps

MIVI Goal: Maximize system radius (r) and length (L) while maintaining vessel access and safety

$$Q = \frac{\pi r^4 \Delta P}{8 \eta L}$$

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Novel Aspiration Tubing

Penumbra THUNDERBOLT™

- Modulated aspiration - switches between ambient pressure (iv bag) and engine pump vacuum. (-29.2 inches of mercury) 12 times per second.
- Keeps a constant column of fluid at the aspiration tip, reducing friction, increasing how much of the clot is engulfed/aspirated

SET-UP

1. Attach Suction Connector to carister
2. Plug in adapter to power port
3. Turn on Penumbra ENGINE
4. Spike a non-pressurized saline bag
5. Press PRIME

Ongoing Trial-THUNDER: Acute Ischemic Stroke Study With the Penumbra System® Including Thunderbolt™ Aspiration Tubing.

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New Category of Intracranial Access

Large Distal Platform (LDP)

The TracStar Large Distal Platform (LDP) is an .088 catheter that combines the stability of a long sheath with the flexibility of an intermediate catheter.

3x more distal flexibility than a long sheath?

3x more midshaft support than an intermediate catheter?

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Zoom(ing) Through Aspiration Thrombectomy

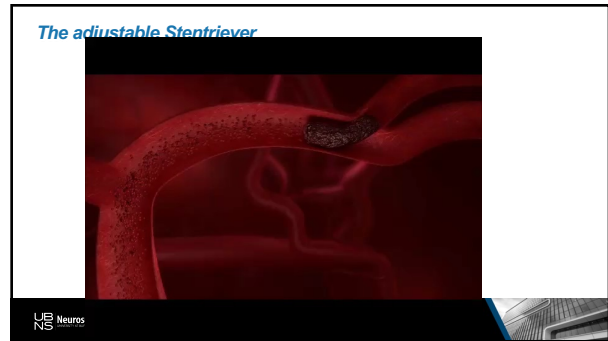
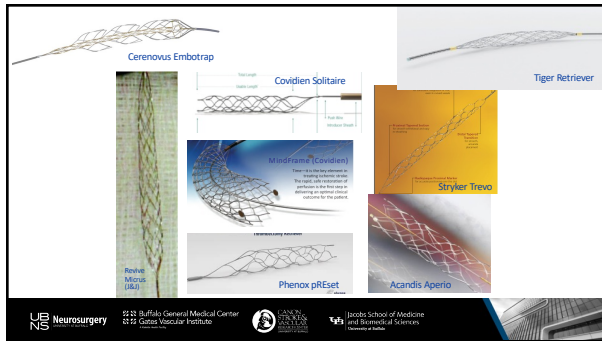
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HIPPO ADVANCED ASPIRATION SYSTEM

CHEETAH DELIVERY TOOL

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Tigertriever Technology Advantages

Total US Stroke Market by Segment

- LVO (Large Vessel Occlusion):** 750k Annual Incidence (2019)
- DMVO (Distal & Medium Vessel Occlusion):** 1.5M Annual Incidence (2019)
- SVO (Small Vessel Occlusion):** 1.7M Annual Incidence (2019)

Existing industry players can only treat LVO strokes

Only Rapid Medical can treat both LVO and DMVO stroke patients

RAPIDMEDICAL

TIGERTRIEVER
Adjustable Low-Profile

The only Stentriever with Controllable Radial Force

Radial Force (g) vs. Time

1000k US Ischemic Strokes / Year

Distal & Medium Vessel Occlusion (DMVO) Strokes

Ongoing Trials

- Endovascular therapy plus best medical treatment (BMT) versus BMT alone for Medium VeSsel Occlusion sTroke - a pragmatic, international, multicentre, randomized trial (**DISTAL**)
 - MT/ mRS shift
- EndovaScular TreAtment to imProve outcomEs for Medium Vessel Occlusions (**ESCAPE-MeVO**)
 - MT/ mRS shift
- Evaluation of Mechanical Thrombectomy in Acute Ischemic Stroke Related to a Distal Arterial Occlusion (**DISCOUNT**)
 - Stent retriever/ mRS 0-2
- Distal Ischemic Stroke Treatment With Adjustable Low-profile Stentriever (**DISTALS**)
 - Tiger retriever/Successful reperfusion (CTP or MR PWI) without sICH

Heterogeneity of Stroke Pathophysiology

- The rate of neuronal loss is **NOT ABSOLUTE**.
- Two stroke phenotypes: “fast progressors” vs “slow progressors”
- Approximately 55% LVO strokes are slow progressors
- A minority (approximately 25%) are fast progressors.²⁴
- However, the infarct growth rate is dynamic, and a continuous spectrum and intermediate progressors may also exist.
- Although reasons for and predictors of variable infarct growth rate are under investigation, it is well recognized that the robustness of collateral blood flow is a major factor, along with innate tissue resistance to ischemia.

Faster workflow and triage

Economical

Telestroke, Organization of systems of care at regional level expand EMS role in stroke triage, reduce door-to-reperfusion time

Environmental

Shift of focus to **Pre-hospital triage** supports mobile triage units, stroke ambulance

Cost and sustainability of mobile stroke units are challenges.

Vx LVO
AI-Powered LVO Detection

Vx LVO uses artificial intelligence to automatically identify suspected large vessel occlusion strokes on CT angiogram images in your network and to alert your on-call stroke team within minutes.

CT perfusion-based patient selection

- Clinical examples – two patients with same duration of stroke symptoms

Patient 1: has "penumbra" and Patient 2: has volume loss

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Automated Platforms > 90%

Baseline CTP
CBF (0.3 threshold) 1 ml Hypoperfusion (Tmax-0s) 129 ml

24 h Follow Up MRI
Infarct Volume 5 ml 100% Reperfusion

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Automated Platforms Tmax hypoperfusion

Tmax Hypoperfusion

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Automated Platforms

Automated Platforms

CBV CBF MTT [s] Tmax [s]

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OMCR | Oxford Medical Case Reports, 2019(20), 1-4
doi: 10.1093/omcr/omz042
Case Report

CASE REPORT

Reperfusion therapy of acute ischemic stroke in an all-in-one resuscitation room called a hybrid emergency room

Masahiro Kashiura^{1*}, Shunsuke Amagasa¹, Hiroyuki Tamura¹, Hidenori Sanayama², Motoshige Yamashina^{3,4}, Masashi Ikota^{3,4}, Yoshio Sakiyama², Yoshikazu Yoshino^{3,4} and Takashi Moriya¹

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Conclusions

- Thrombectomy is the gold standard for the treatment of large vessel occlusion Strokes presenting up to 24 hours from symptom onset.
- Indications keep expanding with several positive trials published in the last year (i.e large core strokes and basilar occlusions)
- Ongoing trials addressing different stroke populations will help determine who best benefits from treatment
- Selection for thrombectomy is key. Simplifying the paradigm (NCCT vs CTP) would increase the target population.

