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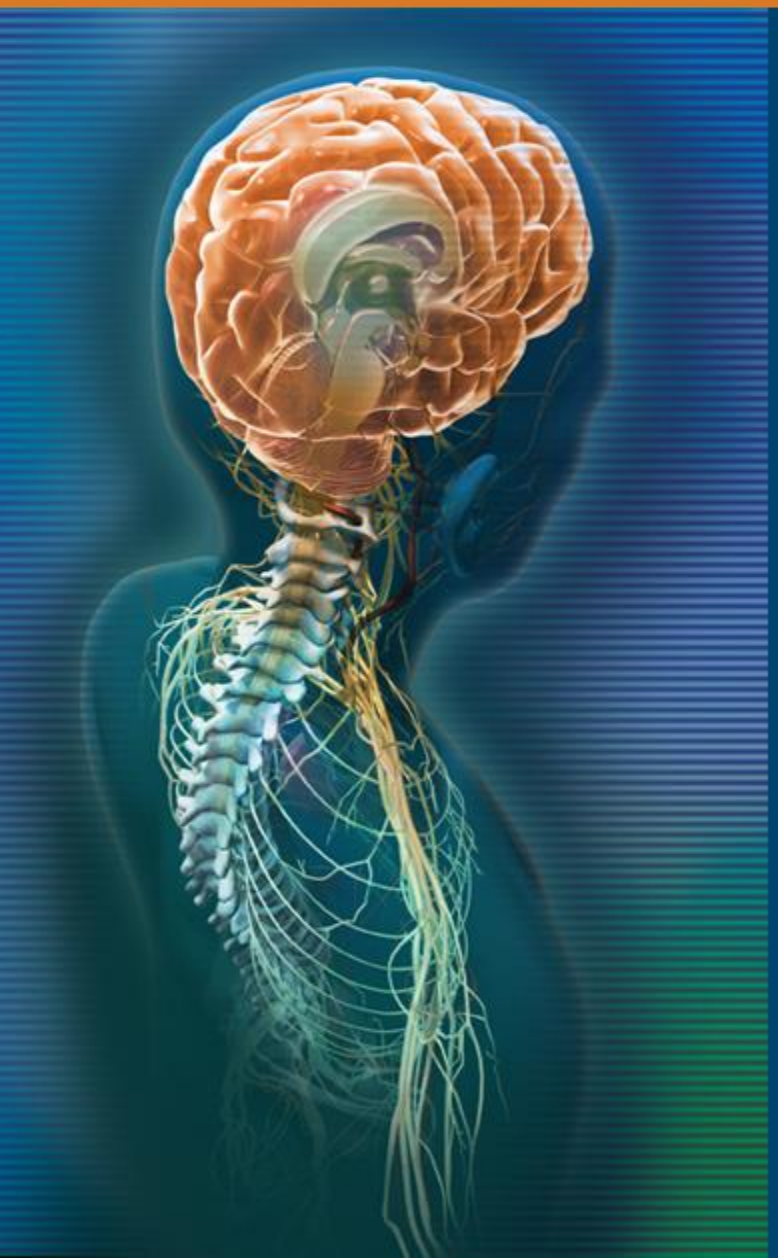

Endovascular Acute Ischemic Stroke Therapy The Evolving Landscape

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Disclosure Statement of Financial Interest

Within the past 12 months, I have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Consulting Fees/Honoraria	• Covidien • Penumbra

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CONCEPTS

The Basis of Acute Stroke Therapy

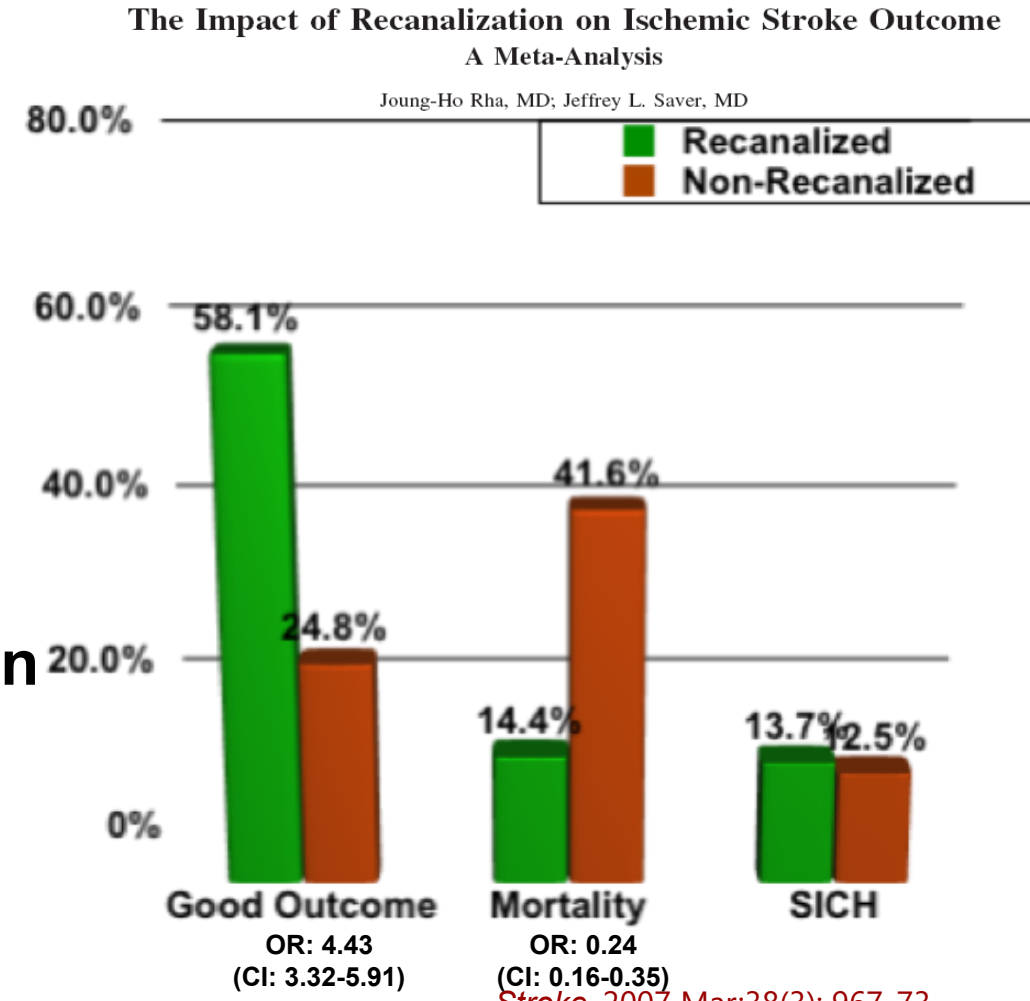
- The "recanalization hypothesis"
  - i.e. reopening of occluded vessels improves clinical outcome in acute ischemic stroke through reperfusion and salvage of threatened tissues.

- Several biologic factors weaken the relationship of recanalization to outcome in acute ischemic stroke patients:
  - time
  - collateral circulation
  - reperfusion injury…

Rha/Saver – Recan. Meta Analysis

- Review all 53 published papers (1985-2002) with data regarding vessel recanalization and functional outcome (2066 cases)
- Recanalization was assessed by catheter angiography in 46, TCD/MRA/SPECT in 7
- Clinical outcome by revascularization status was available in 33 papers for 998 patients

"Formal meta-analysis confirms a strong correlation between recanalization and outcome in acute ischemic stroke."



Stroke. 2007 Mar;38(3): 967-73

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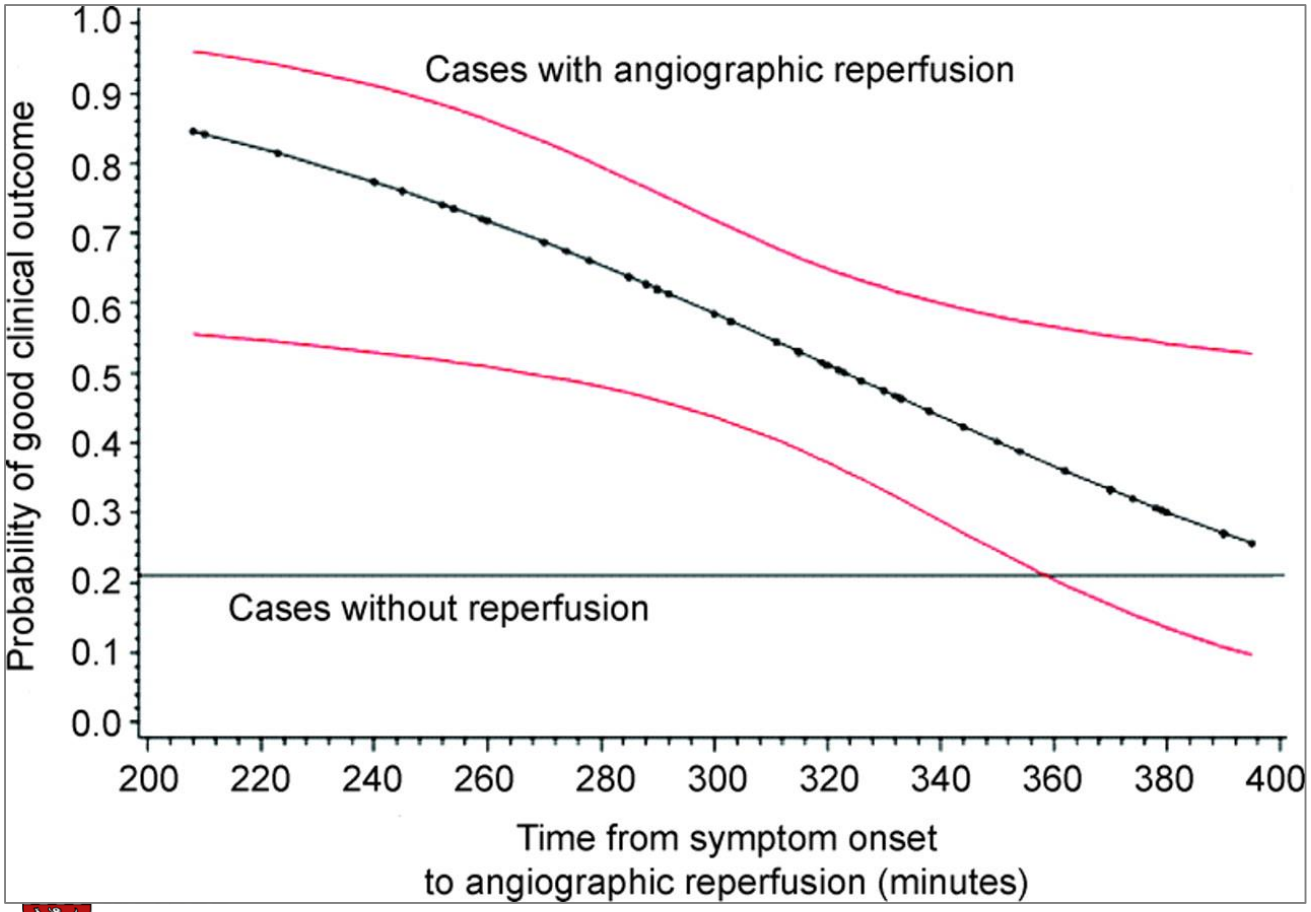
Outcome is Time Dependent

Probability of good clinical outcome over time to technically successful angiographic reperfusion



The typical LVO patient loses 1.9 million neurons/min in which stroke is untreated

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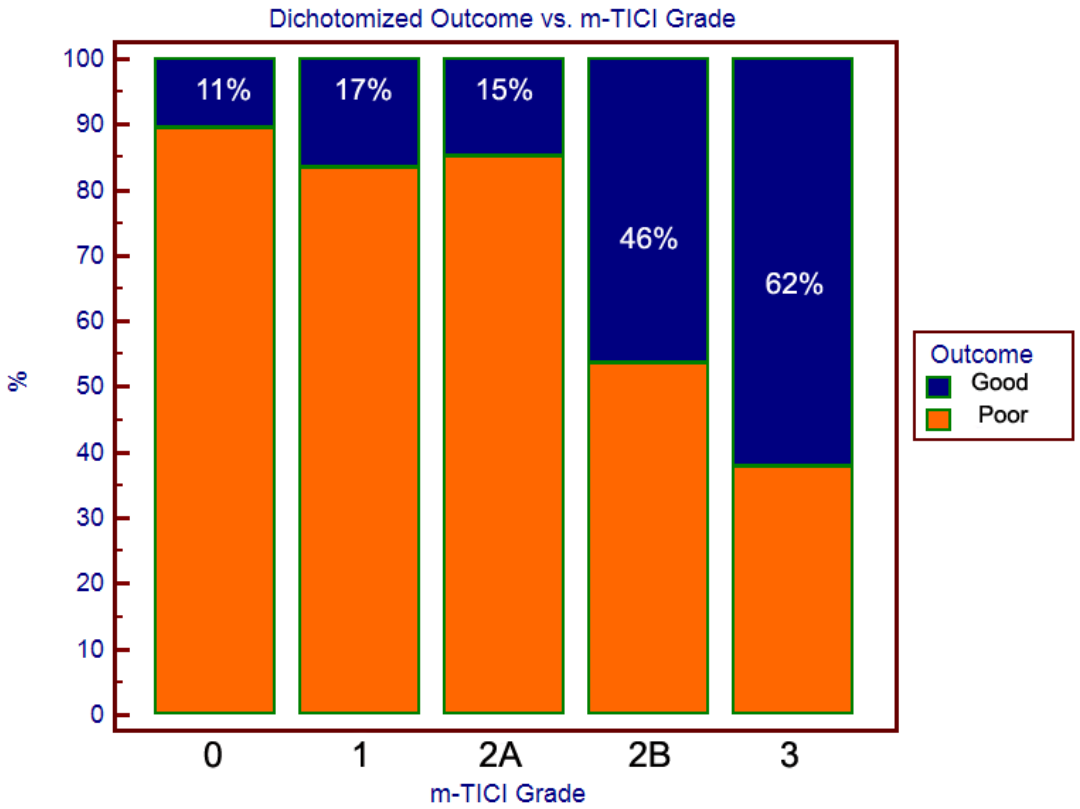
Khatri P et al. Neurology 2009
Saver J, Stroke 2006

Reperfusion Must be Robust

Recanalization and Outcome



mTICI Grades

mTICI 2a: ≤50% of target territory reperfused
mTICI 2b: >50% of target territory reperfused
mTCIC 3: Full territory reperfused

The only statistically significant difference between successive grades was **2A versus 2B** ($P<0.0001$).

(Similar results reported in DEFUSE 2, IMS III)

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Courtesy of Albert Yoo

The Basis of Endovascular Therapy

1. Establish hollow lumen from access to target
2. Work through that lumen

For stroke care:

- Establish a lumen from groin to clot face
- Dissolve clot
  - IA lytic (tPA or urokinase)
  - Microwire, balloon or catheter disruption
- Extract clot
  - Mechanical thrombectomy

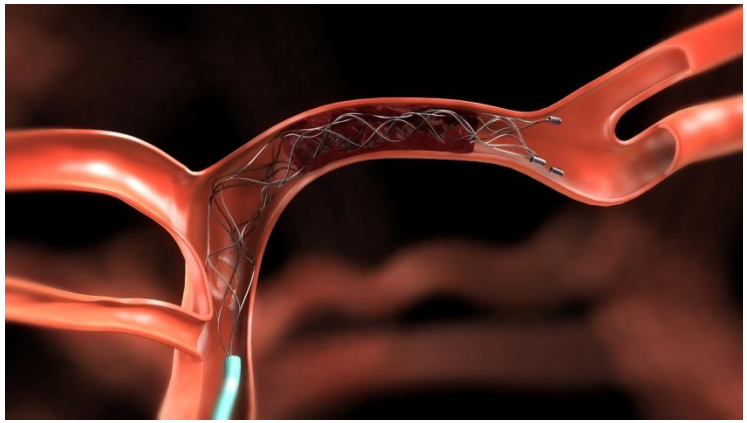
Background

- In 2015, 5 randomized controlled trials demonstrated superiority of endovascular thrombectomy to IV tPA alone for acute ischemic stroke (AIS) caused by an anterior circulation emergent large vessel occlusion (ELVO)
  - Next-generation devices
    - More effective recanal
    - Faster recanalization
  - Advanced imaging algorithms
    - Better patient selection

Background, cont.

- Stentriever thrombectomy with or without aspiration assistance was the predominant technique employed in all 5 trials

- The 2015 AHA/ASA guidelines specifically recommend endovascular therapy with a stentriever for all patients with ELVOs



Study	% stentriever
MR CLEAN	81.5
ESCAPE	86
REVASCAT	100
SWIFT PRIME	100
EXTEND IA	100

Eye-catching Numbers

"2.8 pts treated to improve mRS by a point in 1.
3.2 patients treated to produce functional outcome in 1."

EXTEND-IA

"NNT=3 for improved mRS by 1 point.
NNT=4 for independent outcome."

ESCAPE

"Increase in good outcomes from 1 in 5 to 1 in 3 after endovascular treatment"

MR CLEAN

"64 more days at home in the first 90 days after treatment"

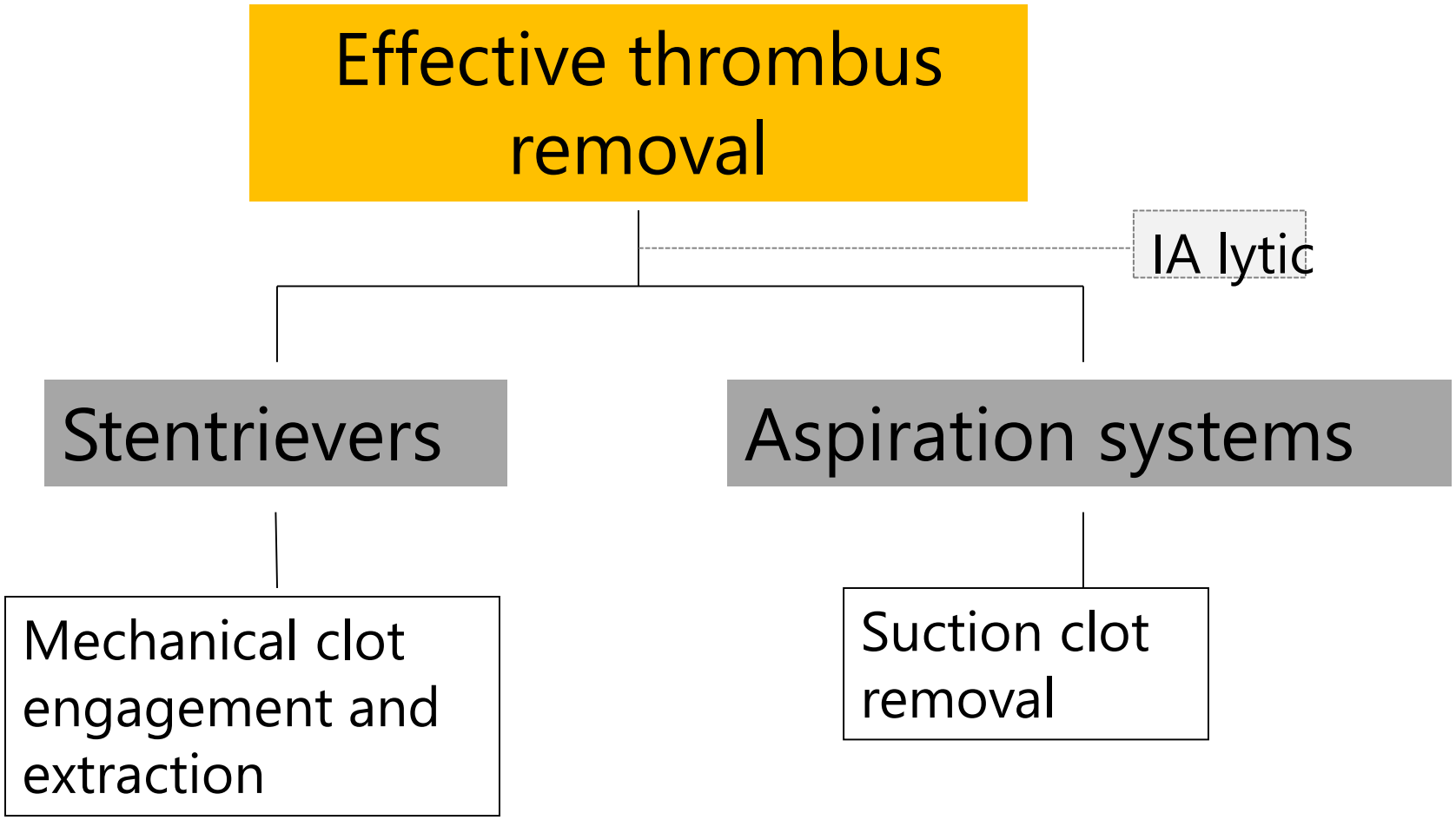
EXTEND-IA

Why Did These Trials Succeed?

1. They all used new devices
   - Significantly more efficient at recanalization to a TICI 2b/3 result.

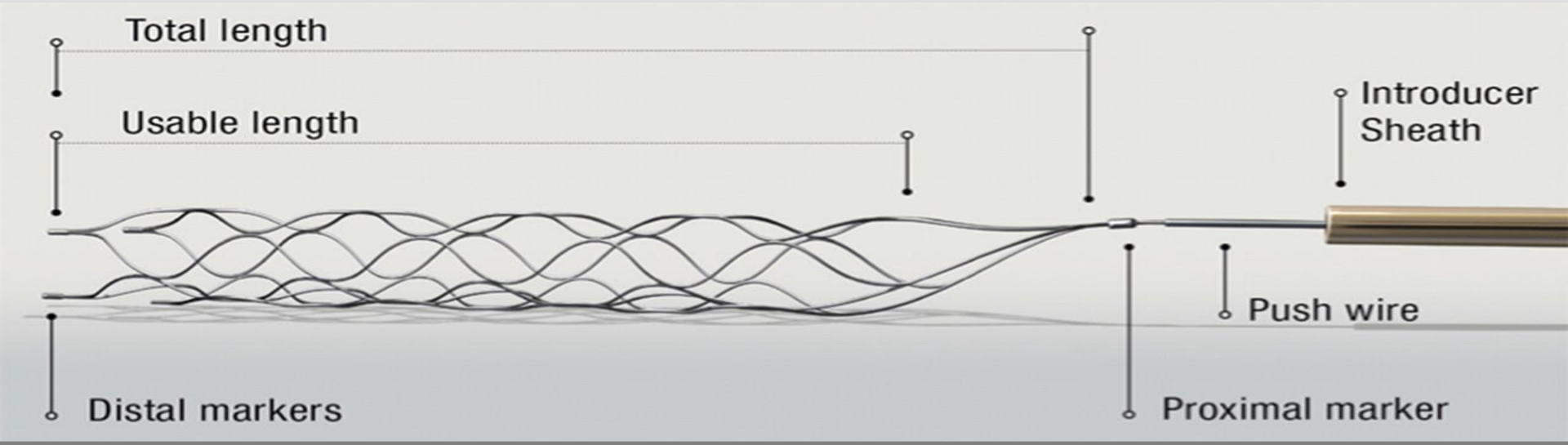
2. They used advanced imaging protocols
   - To confirm the presence of an occlusion
   - To assess parenchyma or penumbra

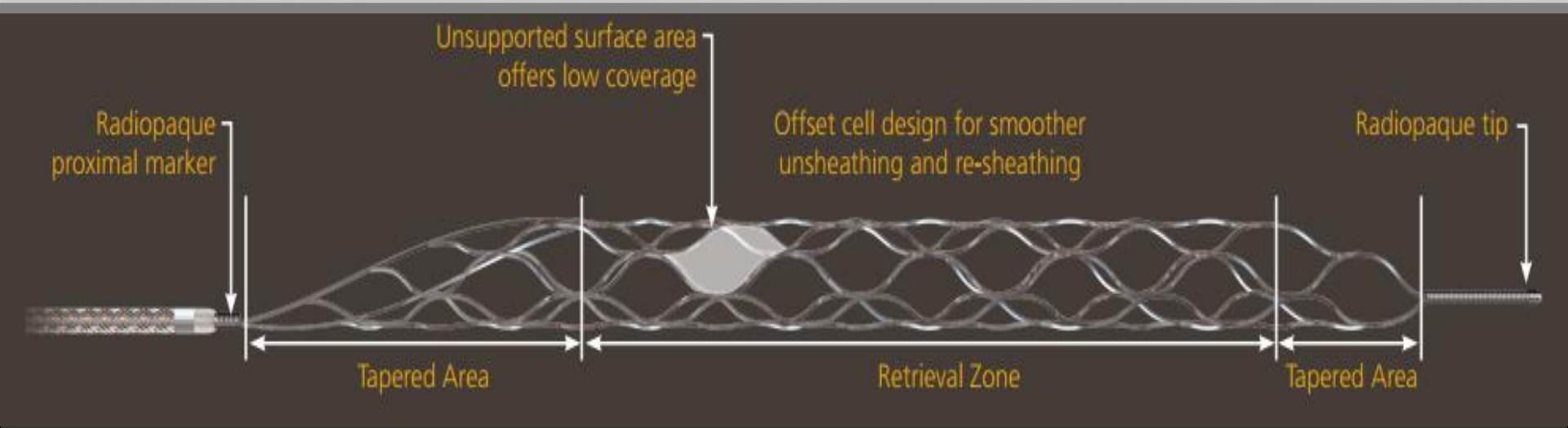
Thrombectomy Options



Both with FDA Approval 2012

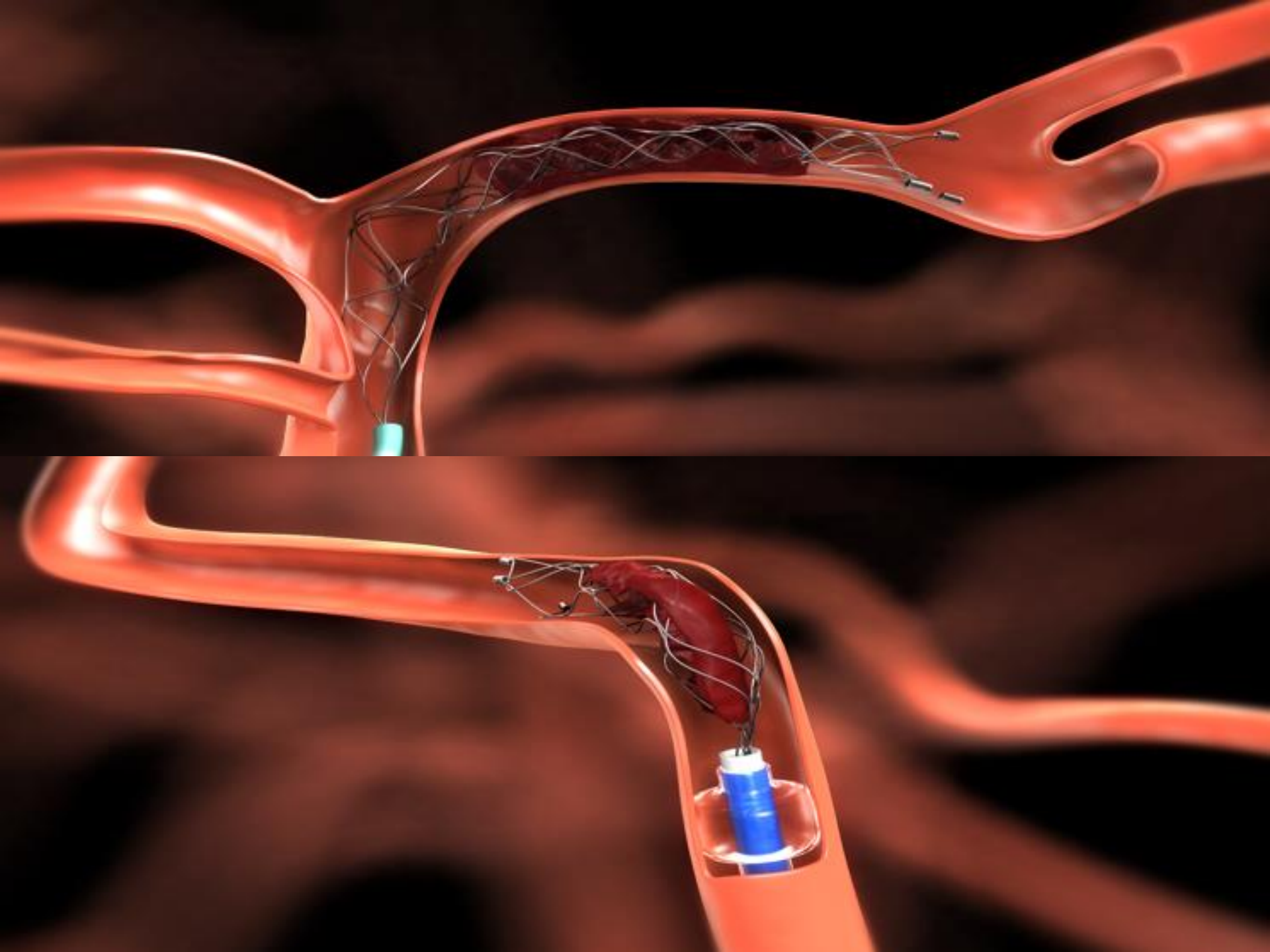
Solitaire



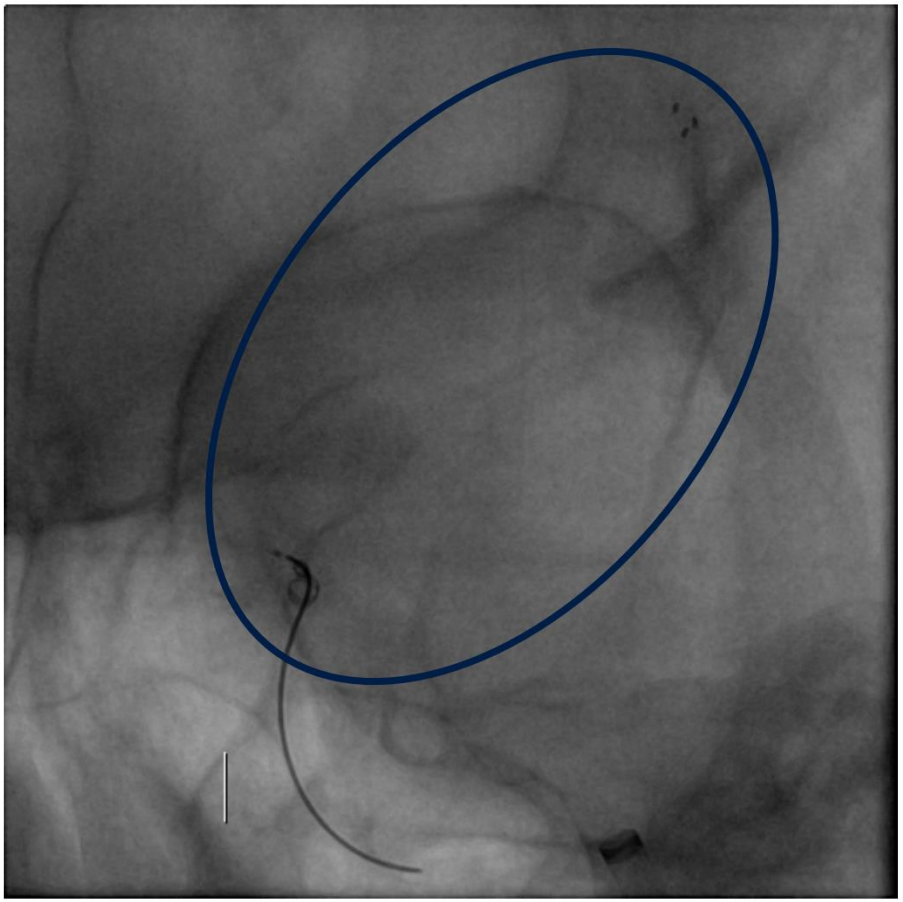


Trevo

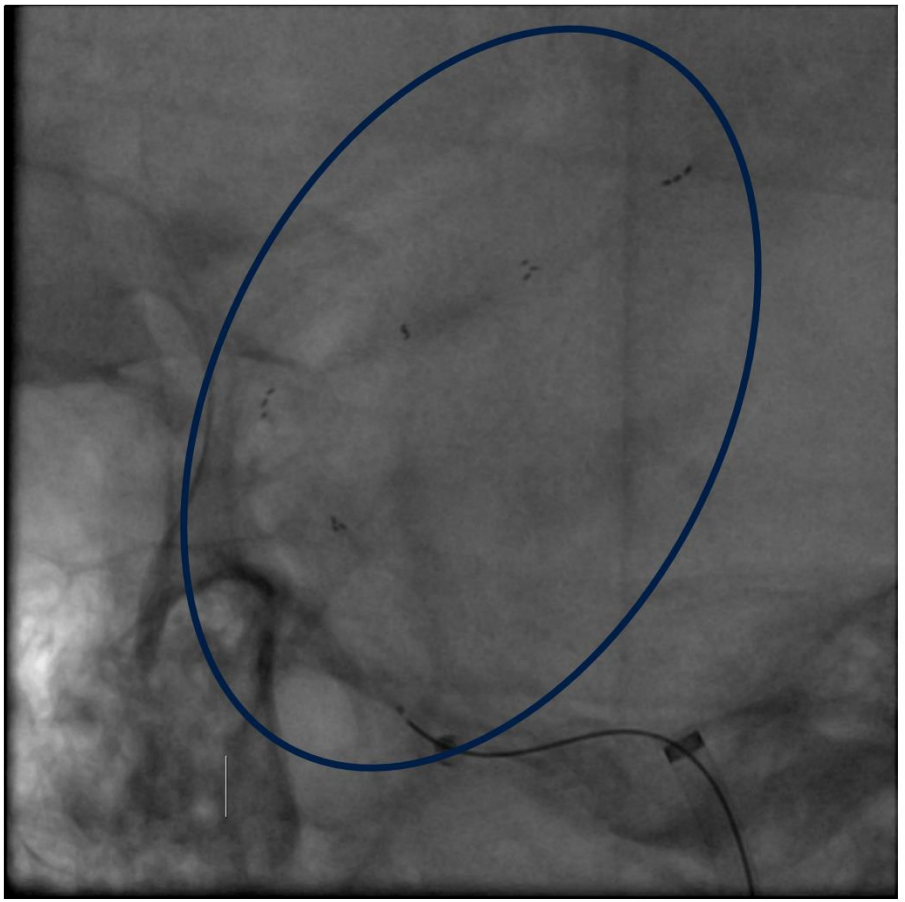
Machi P et al. J NeuroIntervent Surg 2012
Nogueira R G et al. J NeuroIntervent Surg 2012



Stentrievers: Solitaire Platinum



Solitaire™ 2 device – 4x40



Solitaire™ Platinum device – 4x40

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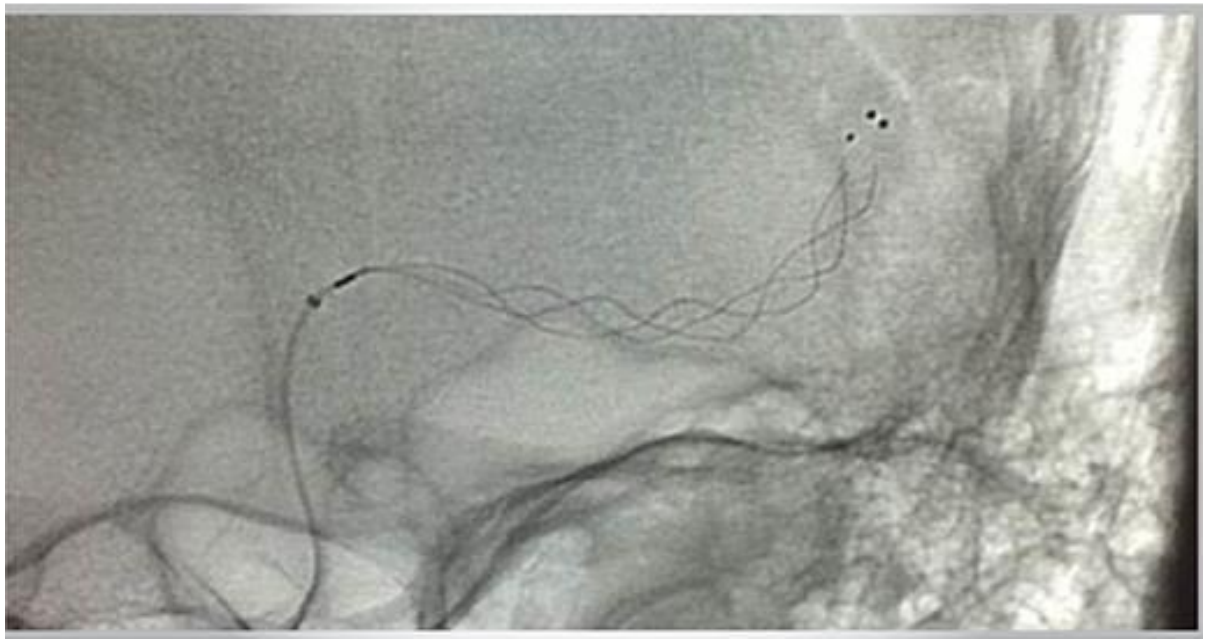
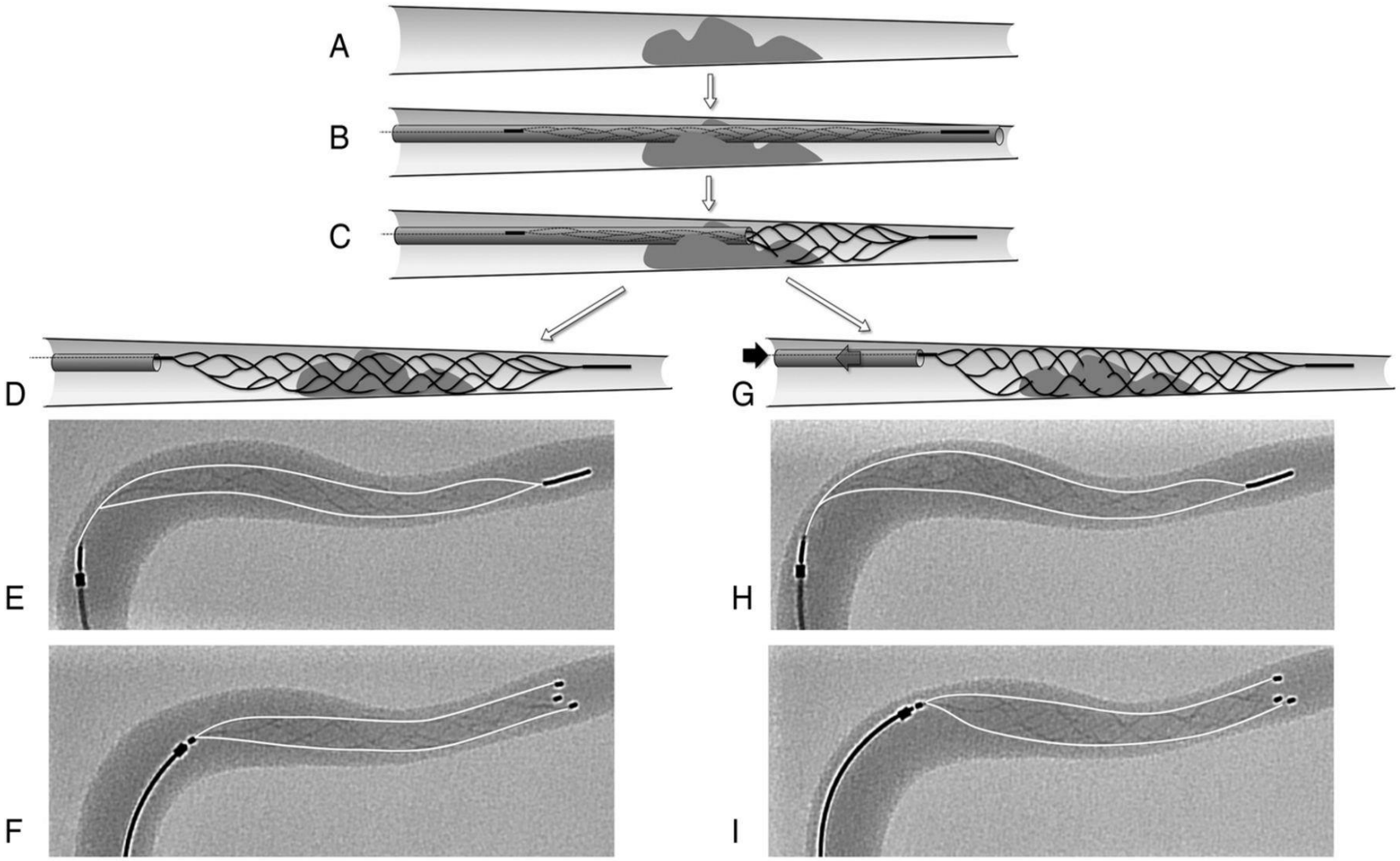
Stentrievers: Trevo Provue



Active Push Deployment



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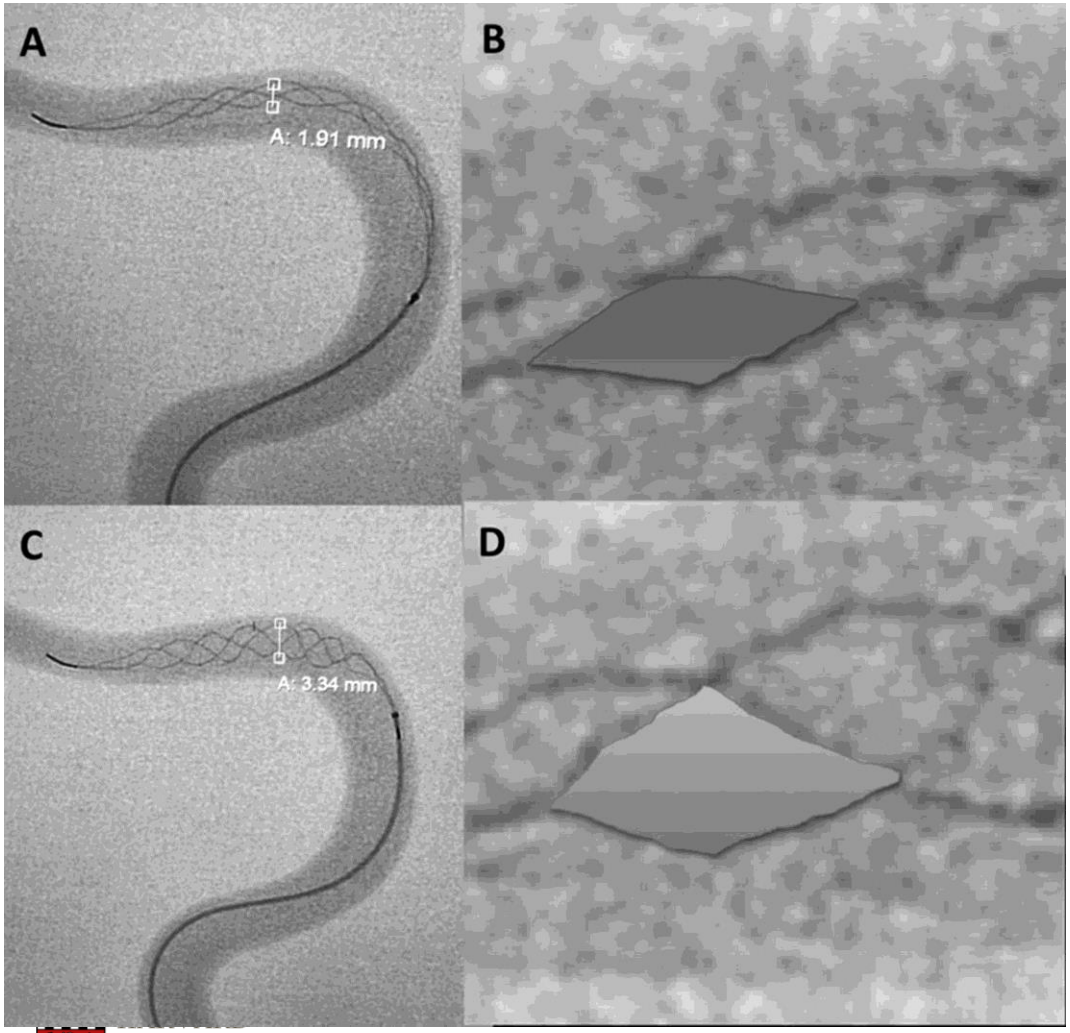
Wiesmann et al, JNIS 2016

Active Push Deployment



Push and Fluff Technique

Associated with:

↑ first pass effect

↑ TICI 3

↓ number of passes

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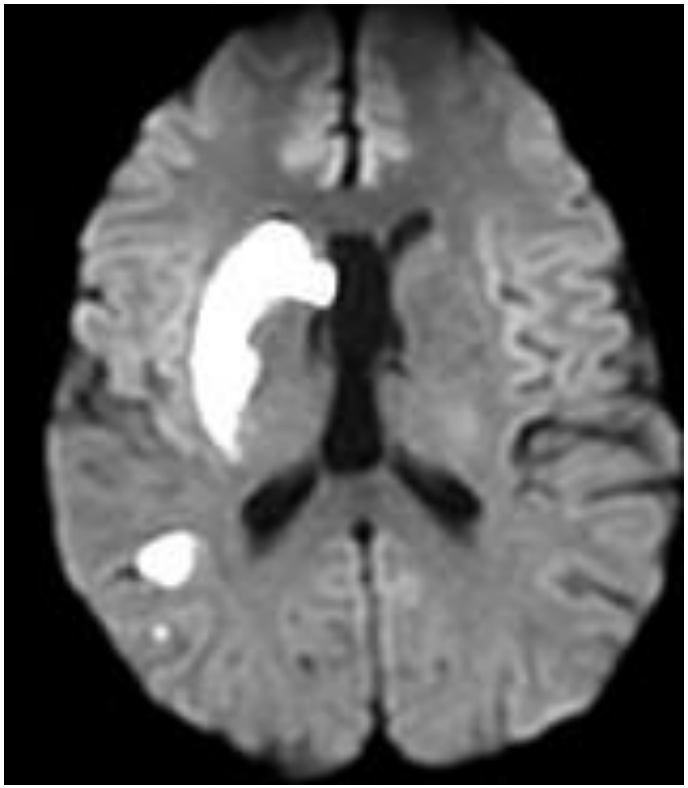
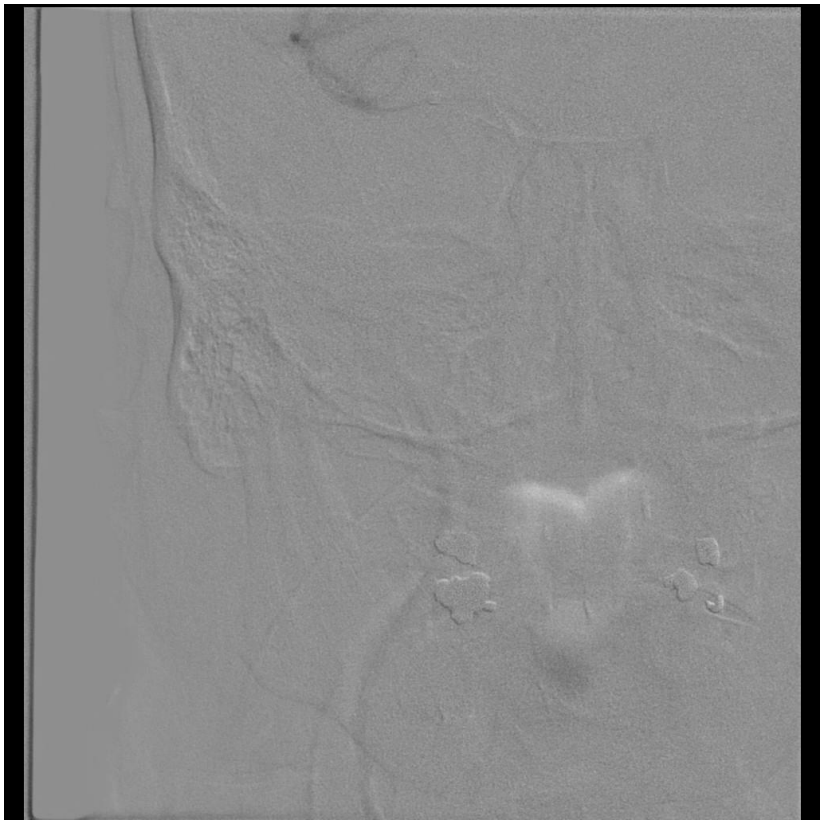
Haussen et al. Stroke. 2015

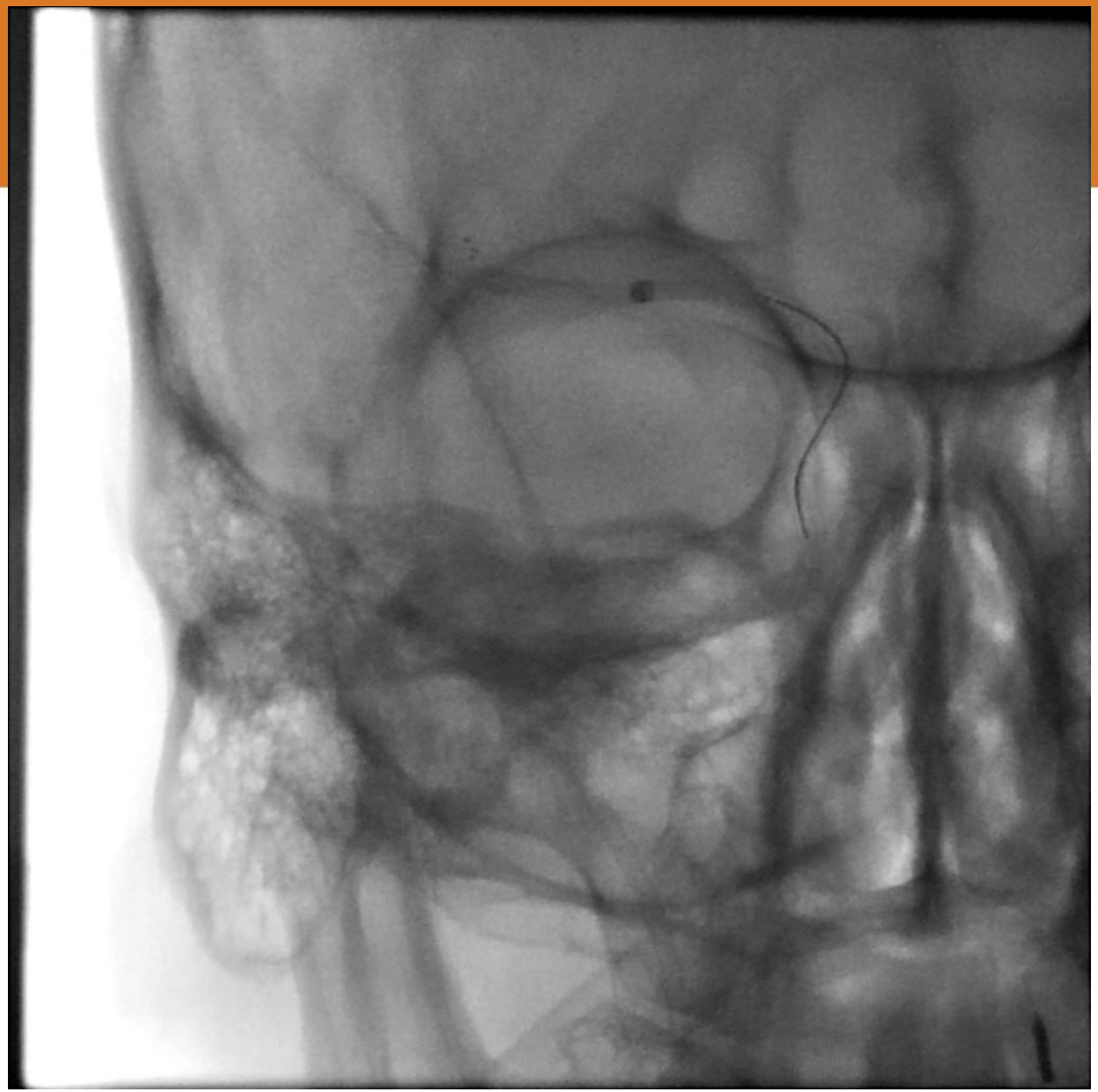
Wiesmann et al, JNIS 2016

Stroke Case: Stentriever

64M PMH gout LSW 0630h, developed dizziness, dysarthria, facial droop and left hemiparesis, NIHSS 19, received IV tPA, transferred to MGH for IAT evaluation, CTA confirmed R-MCA M1 occlusion.



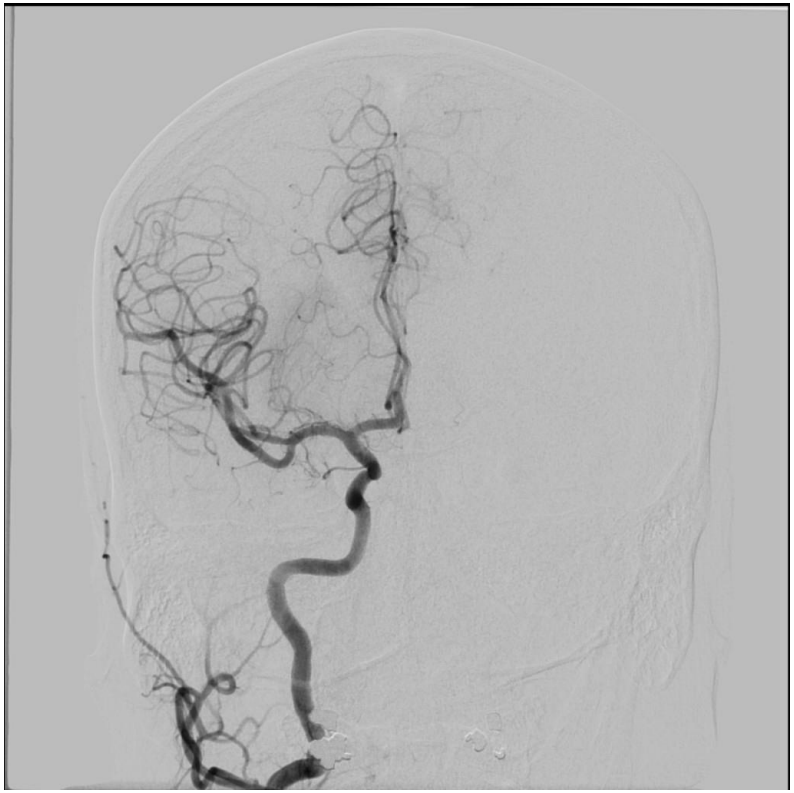


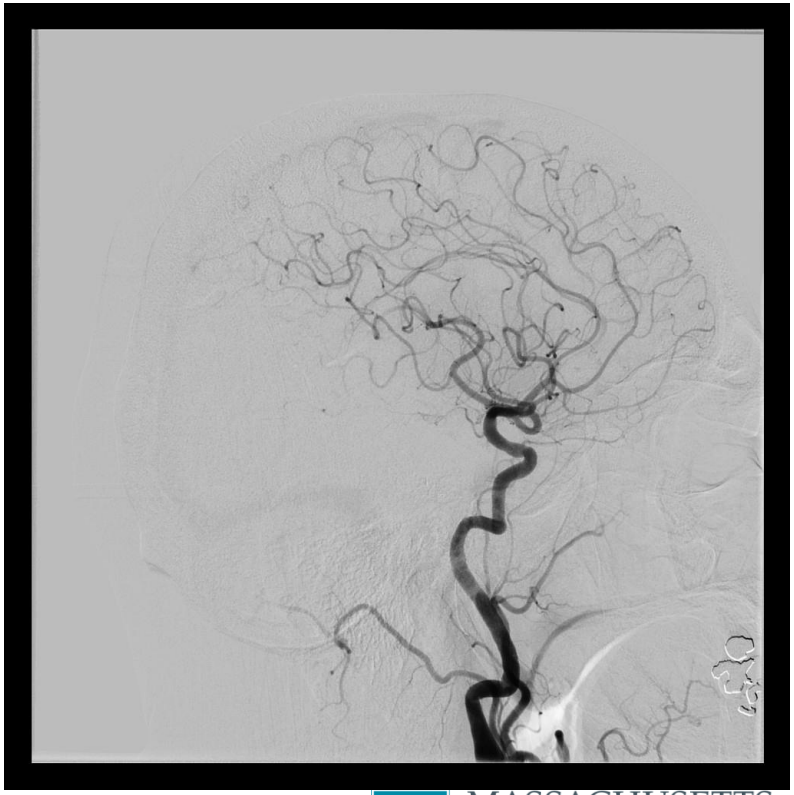


Outcome

Immediate post procedure improvement to NIHSS 5

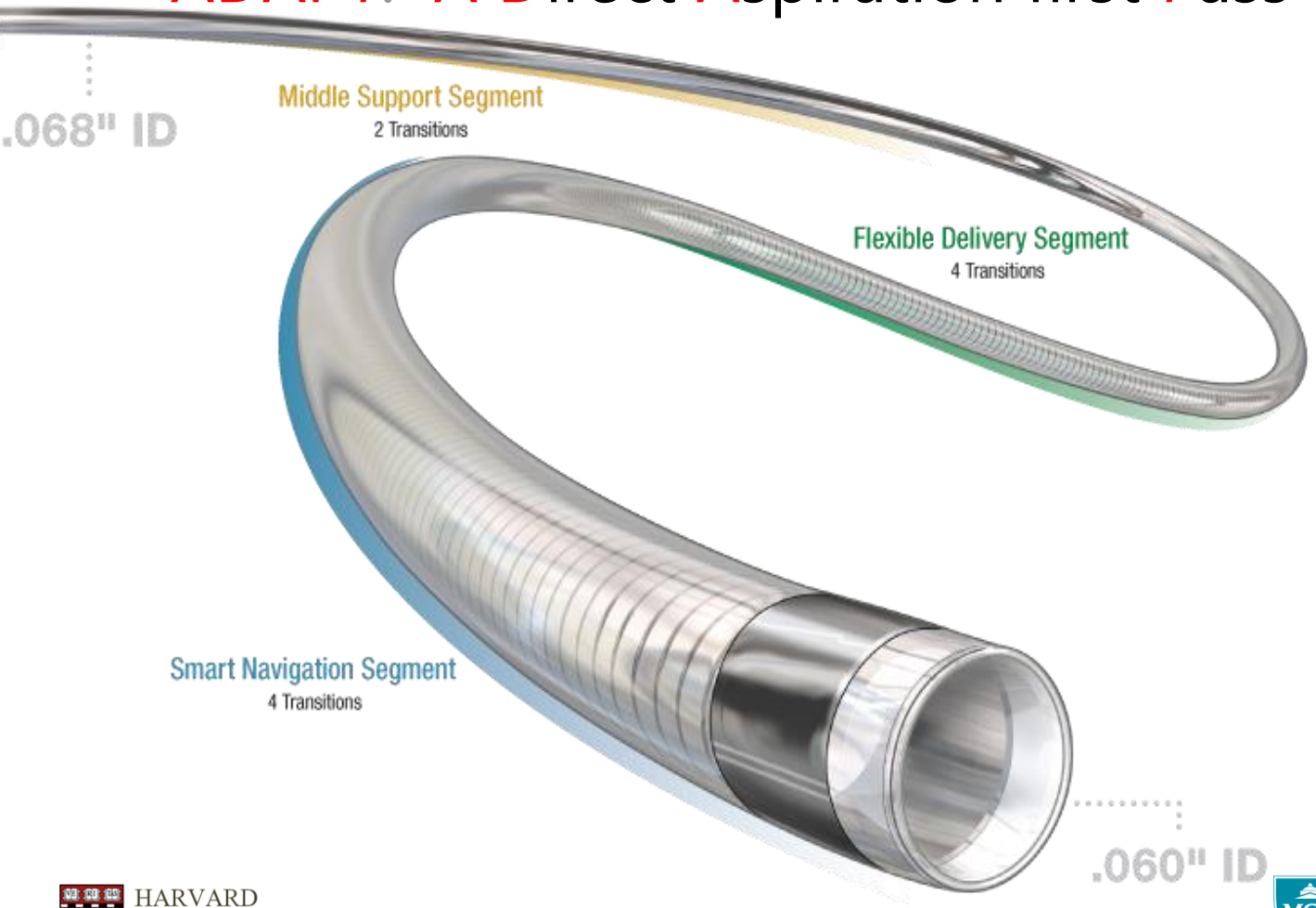
By hospital day 3, NIHSS 0





Aspiration Systems

ADAPT: A Direct Aspiration first Pass Technique



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Aspiration Systems

Penumbra
ACE 068

Medtronic
Arc

Stryker
Catalyst

Microvention
Sofia PLUS

Large bore
Flexible
Trackable
Resist collapse

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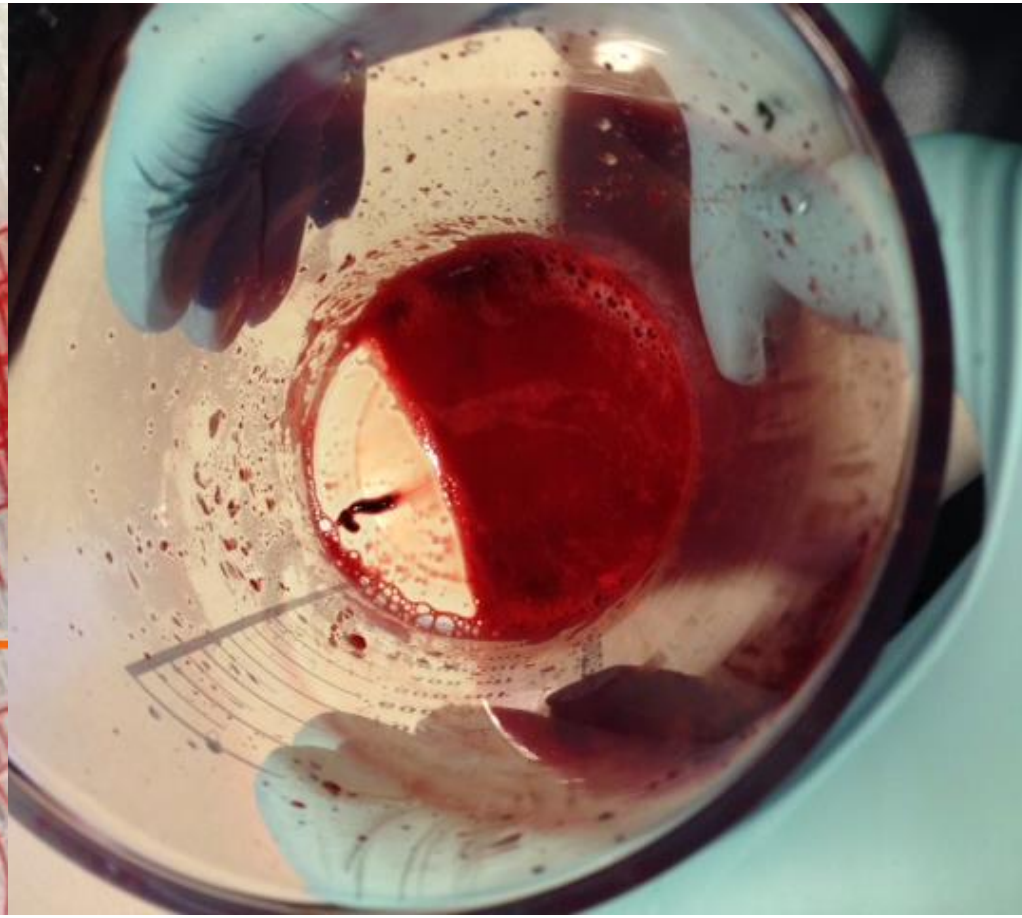
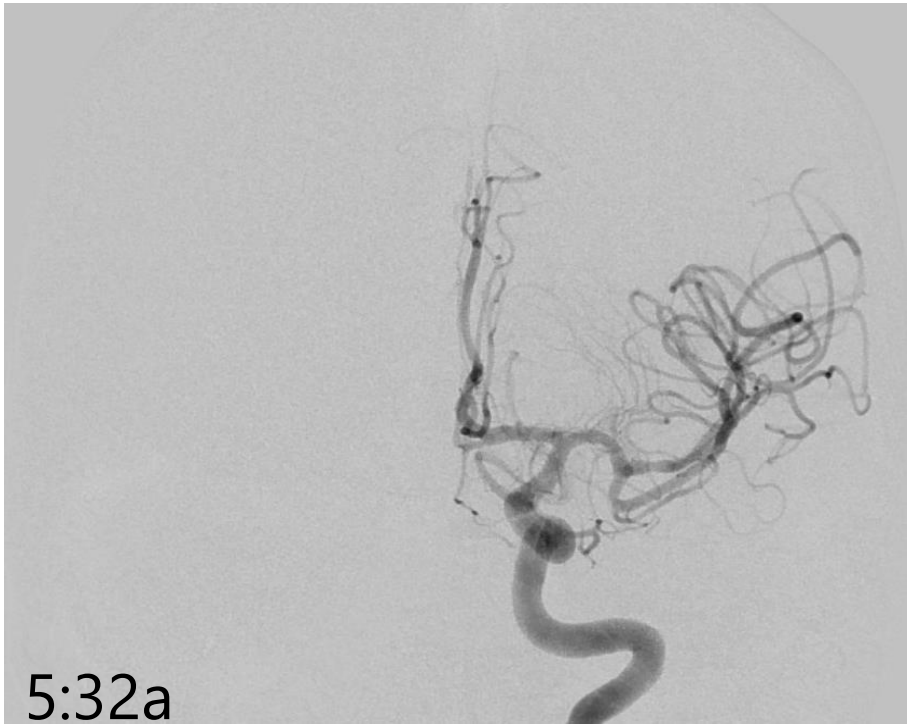
ADAPT Technique



Stroke, ADAPT Case

- 48M LSW 11:30am with NIHSS 4 L MCA syndrome (no IV tPA), followed by an acute neurological decline 3am the following day; groin puncture 5:12am
- TICI 2b recanalization s/p 1 pass ADAPT; 20 mins groin puncture to recanalization



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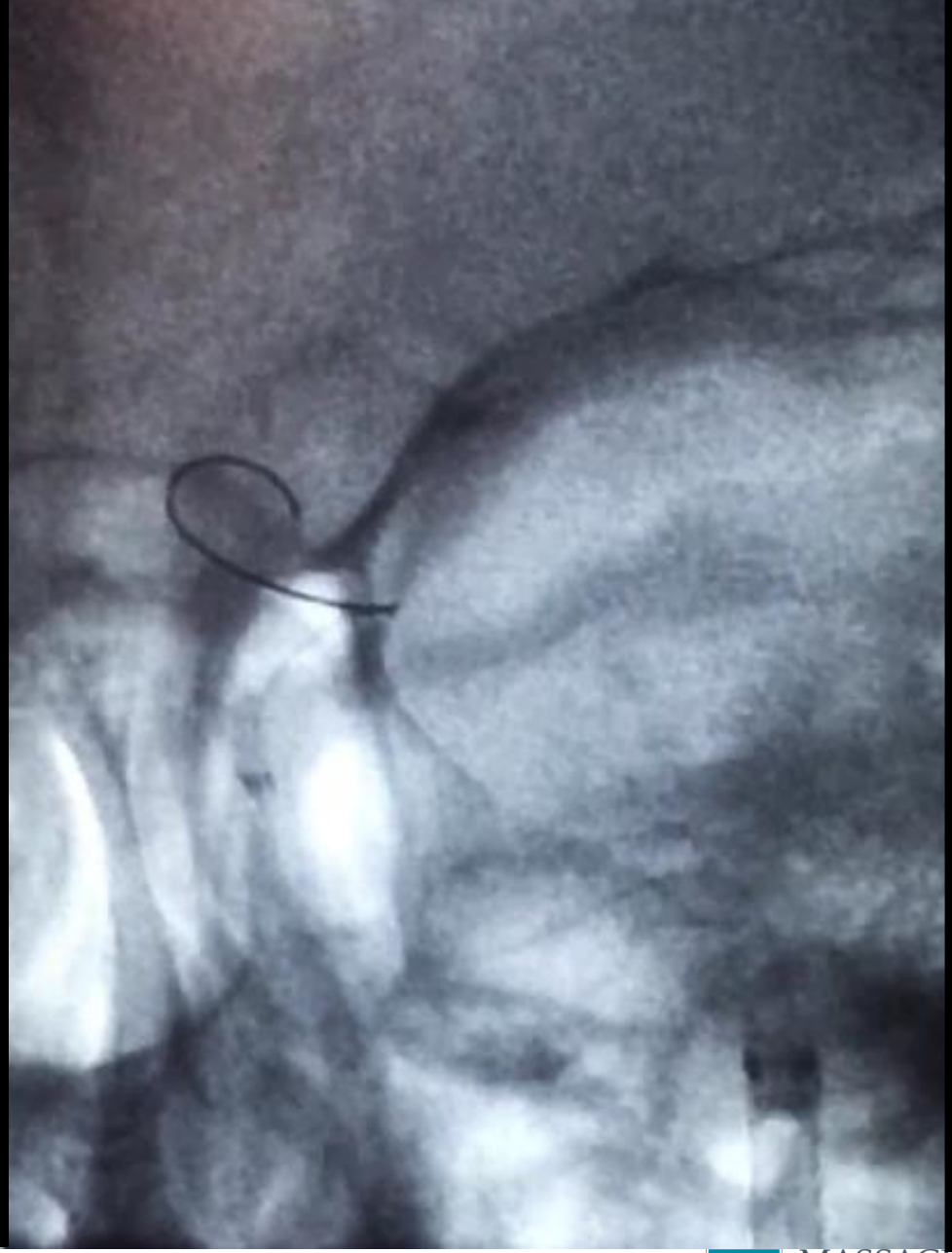

So what is important?

- Patient selection – YES
- Time – YES
- Imaging - YES
- Recanalization – YES!!!!
- Method of Recanalization - ????
- Complications - YES

Direct aspiration first-pass technique (ADAPT) versus stentriever thrombectomy in emergent large vessel intracranial occlusions

- *Methods*: To compare the angiographic and clinical outcomes of ADAPT versus stentriever thrombectomy in patients with emergent large vessel occlusions (ELVO) of the anterior intracranial circulation, the records of 129 patients from June 2012 to October 2015 were retrospectively reviewed.

Results

PATIENT DATA	ADAPT, No. (%)	Stentriever, No. (%)	*P* value
Total patients	47	70	
Age*	63.5	69.4	0.04
Male	27 (57.4)	34 (48.6)	0.45
NIHSS*	16.5	16.5	0.94
Baseline mRS >1	3 (6.4)	5 (7.1)	>0.99
Hypertension	37 (78.7)	50 (71.4)	0.40
Diabetes mellitus	12 (25.5)	20 (28.6)	0.83
Smoking (current or past)	11 (23.4)	10 (14.3)	0.23
Atrial fibrillation	16 (34.0)	35 (50)	0.13
Coronary artery disease	12 (25.5)	22 (31.4)	0.30
Previous stroke	8 (17.0)	14 (20)	0.81

*mean

- Patients were slightly younger in the ADAPT cohort
- No differences in other baseline factors

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Results, cont.

PRE-PROCEDURAL DATA	ADAPT, No. (%)	Stentriever, No. (%)	*P* value
Total patients	47	70	
Intravenous tPA	34 (72.3)	40 (57.1)	0.56
Onset to intravenous tPA (mins)*	128.9	132.1	0.78
ASPECTS*	8	8.3	0.34
Location of intracranial occlusion			
ICA	12 (25.5)	13 (18.6)	0.15
M1 MCA	33 (70.2)	43 (61.4)	
M2 MCA	2 (4.3)	14 (20)	
Left side	24 (51.1)	35 (50)	>0.99

- No differences in any pre-procedural factors

*mean

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Results, cont.

- No statistical difference in rates of TICI 2b/3 recanalization.
- 57.4% (27/47) of patients in ADAPT group had successful recanalization with aspiration alone. These patients statistically had the fasted times to recanalization and shortest procedure times compared to all groups.
- Need to use Stentriever adjunct to ADAPTdid not affect time, recanlization or procedure time relative to Stentriever alone

PROCEDURAL DATA	ADAPT, No. (%)			Stentriever (No. (%)	P value[1]	P value[2]	P value[3]
	ADAPT success	ADAPT failure/Stentriever rescue	Total				
Total patients	27	20	47	70			
Onset to groin puncture (mins)*	219.3	272.5	241.9	284.7	0.02	<0.01	0.58
ADAPT attempts*	1.3	1.3	1.3	--	--	--	--
Stentriever attempts*	--	1.2	1.2	1.9	--	--	0.27
CASPER	--	20 (100)	--	39 (55.7)	--	--	<0.01
TICI 2b/3 recanalization	22 (81.4)	17 (85)	39 (83.0)	50 (71.4)	0.19	0.44	0.26
Onset to TICI 2b/3 recanalization (mins)*	251.9	345.5	294.3	346.7	<0.01	<0.01	0.74
Procedural time (mins)*	41.8	70.4	54.0	77.1	<0.01	<0.01	0.33
Procedural complication	2 (7.4)	1 (5)	3 (6.4)	5 (7.1)	>0.99	>0.99	>0.99

*mean

[1]ADAPT versus Stentriever
[2]ADAPT success versus Stentriever
[3]ADAPT failure/Stentriever rescue versus Stentriever

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Results, cont.

OUTCOME DATA	ADAPT, No. (%)			Stentriever, No. (%)	P value[1]	P value[2]	P value[3]
	ADAPT success	ADAPT failure/Stentriever rescue	Total				
Total patients	27	20	47	70			
Any intracranial hemorrhage	6 (22.2)	11 (55)	17 (36.2)	22 (31.4)	>0.99	0.46	0.07
Symptomatic intracranial hemorrhage	1 (3.7)	5 (25)	6 (12.8)	7 (10)	0.77	0.44	0.13
Disposition							
Home	4 (14.8)	1 (5)	5 (10.6)	14 (20)	0.09	0.09	0.07
Rehabilitation	22 (81.5)	14 (70)	36 (76.6)	47 (67.1)			
7-day NIHSS*	6.4	9.3	7.6	7.3	0.81	0.55	0.24
90-day mRS*	2.2	3.3	2.7	3.0	0.83	0.23	0.53
90-day mRS 0-2	14 (51.9)	9 (45)	23 (48.9)	29 (41.4)	0.45	0.37	0.80
Death	1(3.7)	5 (25)	6 (12.8)	13 (18.6)	0.45	0.06	0.54

- No differences in 7-day NIHSS or 90-day mRS scores

*mean [1]ADAPT versus Stentriever
[2]ADAPT success versus Stentriever
[3]ADAPT failure/Stentriever rescue versus Stentriever

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Results, cont.

FACTORS PREDICTIVE of 90-day mRS 0-2	Odds ratio	Coefficient	P value
Endovascular thrombectomy technique	--	--	0.47
Age	0.95	-0.05	< 0.01
Previous stroke	0.11	-2.22	< 0.01
NIHSS	0.85	-0.16	0.01
TICI 2b/3 recanalization	23.37	3.15	< 0.01
Time to groin puncture (mins)	0.2	-0.005	0.03

- 90-day functional outcomes were not dependent upon endovascular thrombectomy technique

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Results, cont.

FACTORS PREDICTIVE of 90-day mRS 0-2	Odds ratio	Coefficient	P value
Endovascular thrombectomy technique	--	--	0.47
Age	0.95	-0.05	< 0.01
Previous stroke	0.11	-2.22	< 0.01
NIHSS	0.85	-0.16	0.01
TICI 2b/3 recanalization	23.37	3.15	< 0.01
Time to groin puncture (mins)	0.1	-0.005	0.03

- 90 day mRS was highly dependent
  - ability to achieve recanalization (OR=23.37)
  - time to groin puncture.

Conclusion

REVASCULARIZATION in the **SHORTEST TIME PERIOD** is the key to **GOOD OUTCOME**

Thank you

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