NEW ENGLAND CENTER FOR STROKE RESEARCH

# Stent-Retriever Thrombectomy: From Bench to Brain, and Back

Matthew Gounis, PhD
Associate Professor, Department of Radiology
Director, New England Center for Stroke Research

*SIMI 2016 – 25th Anniversary; Buenos Aires*

UMASS

# Disclosures

- Research Grants

(last 12 months):

  - NINDS, NIBIB, NIA, NCI
  - Philips Healthcare
  - Fraunhofer Institute
  - Stryker Neurovascular
  - Codman Neurovascular
  - eV3 Neurovascular / Covidien
  - InNeuroCo Inc
  - Blockade Medical
  - CereVasc LLC
  - Cook Medical
  - Neuronal Protection Systems
  - Spineology Inc
  - Silk Road
  - Wyss Institute
  - Microvention
  - Gentuity

- Consulting

(fee-per-hour, last 12 months):

  - Stryker Neurovascular

- Investment (Stocks)
  - Boston Scientific Inc
  - InNeuroCo Inc

NEW ENGLAND CENTER FOR STROKE RESEARCH

UMASS

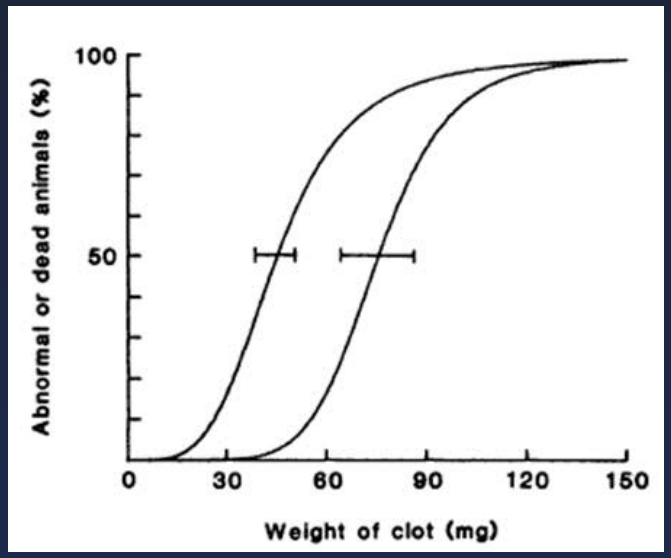
# Acute Ischemic Stroke: Pre-Clinical Investigations for Devices – Does it Translate to Humans?


UMASS

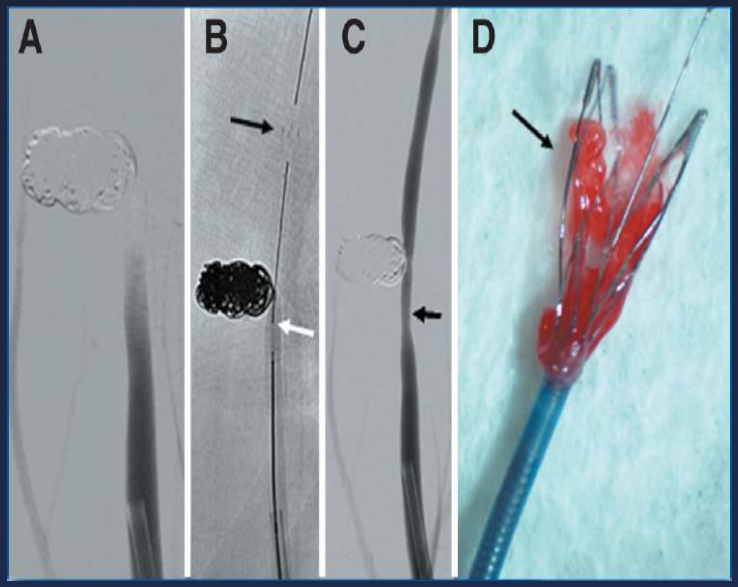
# Two Approved Treatments:
## Both Target Vessel Revascularization

NEW ENGLAND CENTER FOR STROKE RESEARCH

- Pre-Clinical Modeling has had an Impact:




With and without treatment with IV-tPA
Zivin, Fisher, DeGirolami. Science 1985; 230:1289-1292

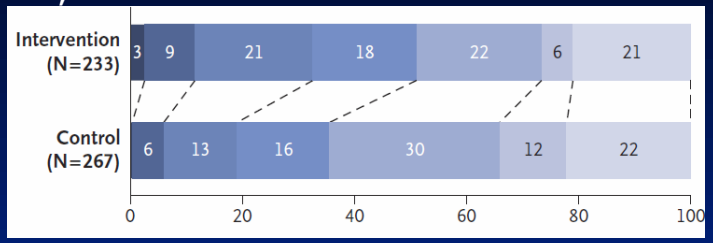



(Wakhloo A.K. and Gounis M.J.,Neurosurgery 2008,62(5 Suppl 2): ONS390–ONS394.

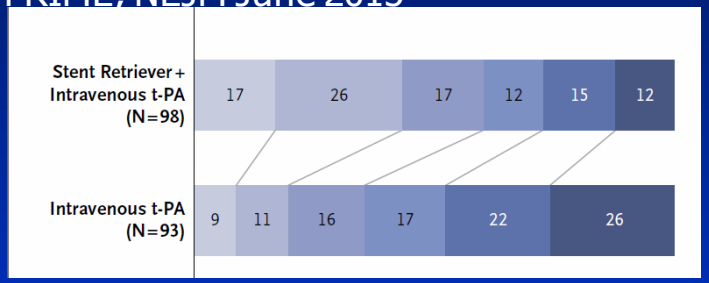
UMASS

# Stent-Retriever Thrombectomy

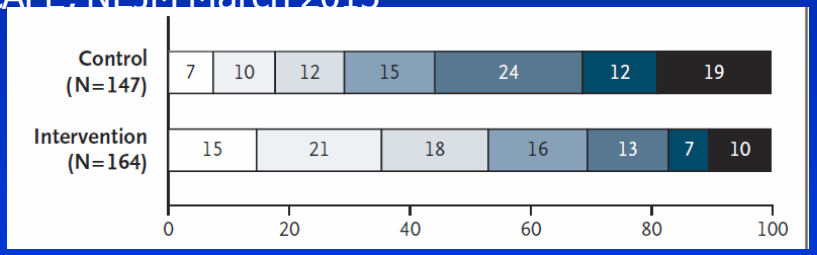
MR CLEAN, NEJM Jan 2015



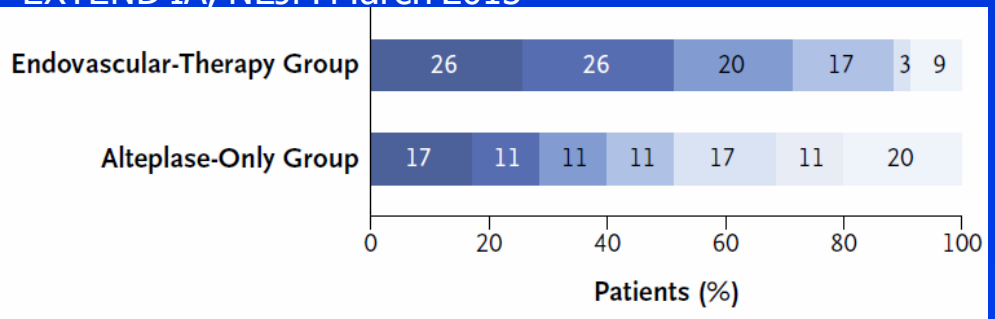

SWIFT PRIME, NEJM June 2015




ESCAPE, NEJM March 2015




EXTEND IA, NEJM March 2015




## COMMENTS

Wakhloo and Gounis present an efficient, effective, thoughtful, and well-designed approach to the study of a novel application of a device. In this brief report, the authors assessed the feasibility of using a closed-cell, retrievable stent as a foreign body retriever or as an embolectomy/thrombectomy device. They performed a carefully designed analysis using in vitro and in vivo models to assess efficacy in straight and tortuous anatomy. On the basis of their analyses, the authors conclude that this device may be successfully used to retrieve foreign bodies (i.e. errant coils) or an embolus/thrombus from the intracranial circulation.

Although the authors assess the technology for a non-Food and Drug Administration approved use, they do so in a controlled setting outside the clinical realm. This carefully planned and well-executed analysis of a new device may serve as a blueprint for assessing other innovative, off-label applications for existing technologies. Naturally, concerns about its efficacy in the clinical setting are certainly not eliminated: the authors (and I) clearly point out that the aforementioned application should not serve as the first-line technique, especially in light of the fact that Food and Drug Administration-approved devices already exist for each of these "off-label indications." Additionally, concerns about cost-effectiveness in using this device are not adequately addressed, although it might be argued that this single device may be cost-effective if it alone were to be used for attempted retrieval and/or stenting in place of multiple devices. Nonetheless, in this ever-growing and rapidly expanding field, understanding the limitations of the devices as well as some potential benefits in off-label indications in a controlled, laboratory setting is important. The authors have presented an interesting and innovative application for a closed-cell retrievable stent.

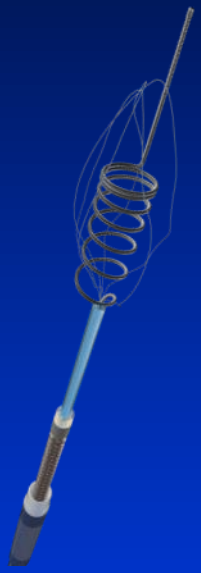
**Charles J. Prestigiacomo**
*Newark, New Jersey*

The authors report the use of the Enterprise retrievable closed-cell stent for foreign body and clot removal. Certainly they have demonstrated in a swine model that use of this device is feasible as a last resort. Retrieval of thrombus or coils or other devices is often problematic, and this method may be a useful adjunct as a salvage maneuver. Hopefully, other devices that are more cost effective and easier to use will solve this problem as well.

**Robert H. Rosenwasser**
*Philadelphia, Pennsylvania*

# Devices for Recanalization

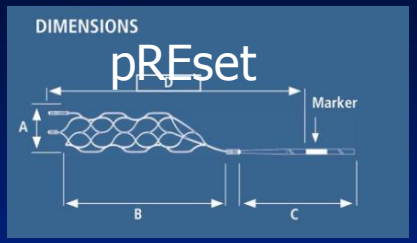
## US FDA Cleared

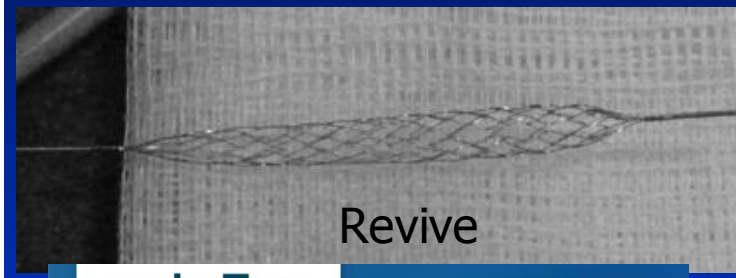



**Penumbra**

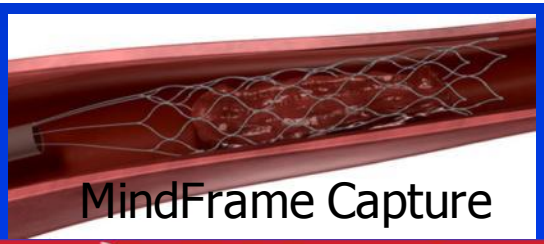

**Merci**

**Solitaire**

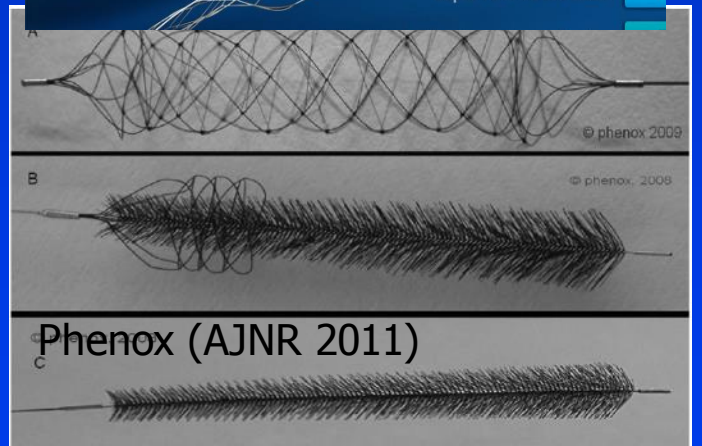




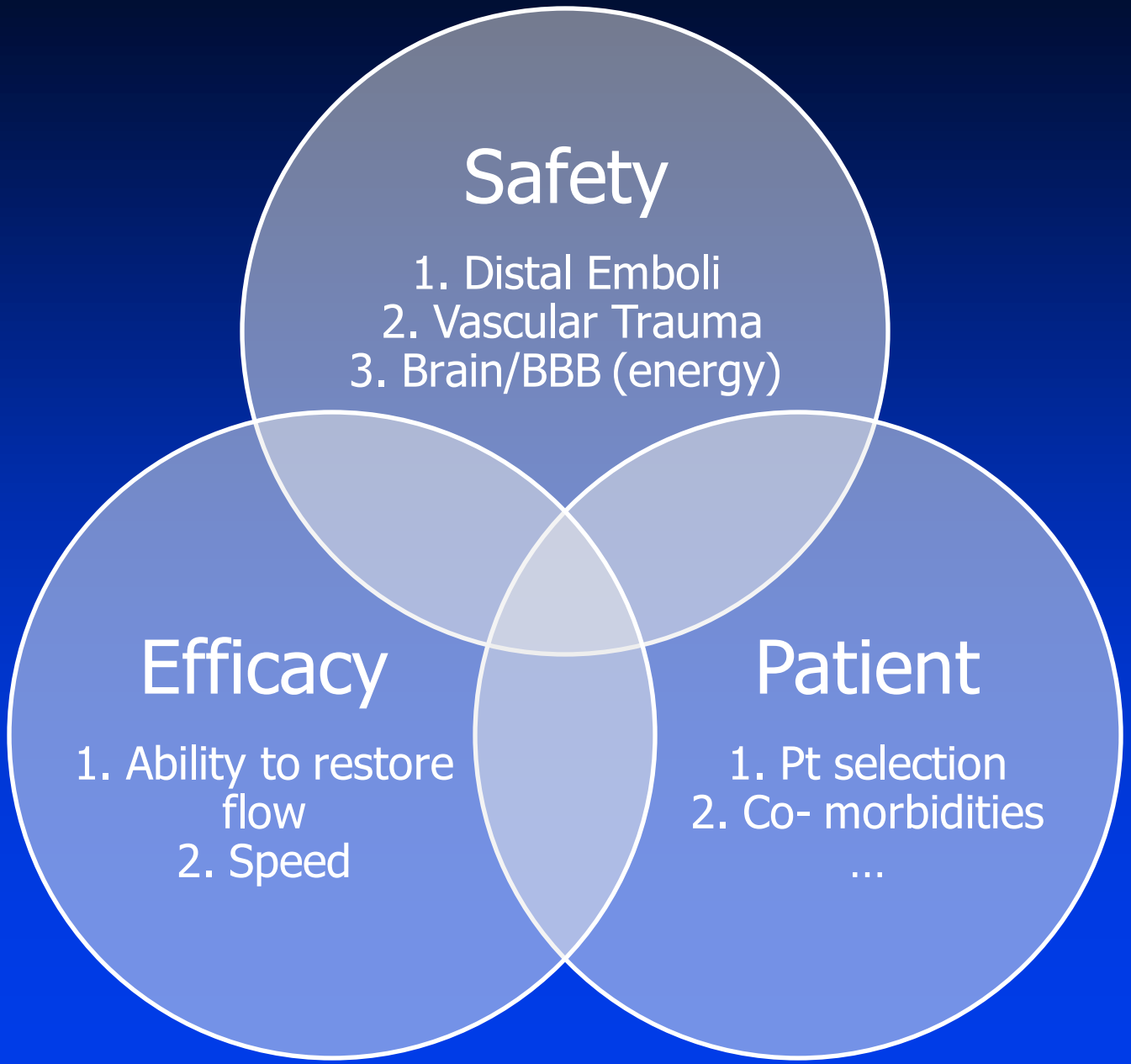





Phenox (AJNR 2011)

# Considerations



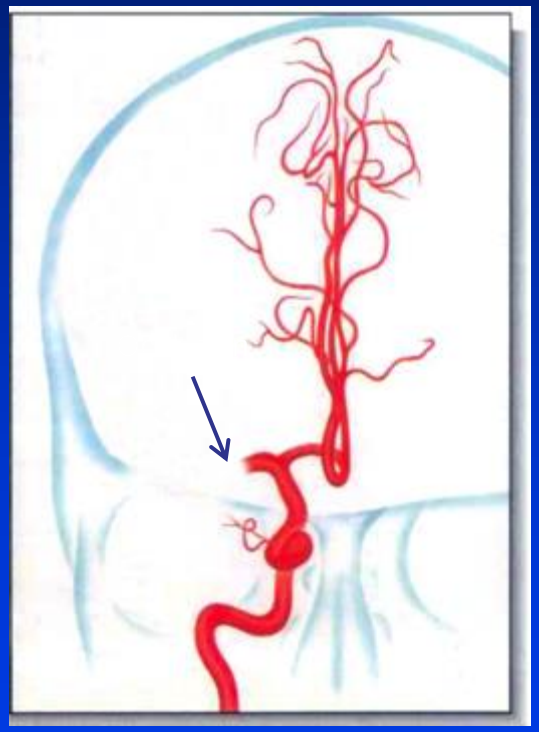
# Distal Emboli

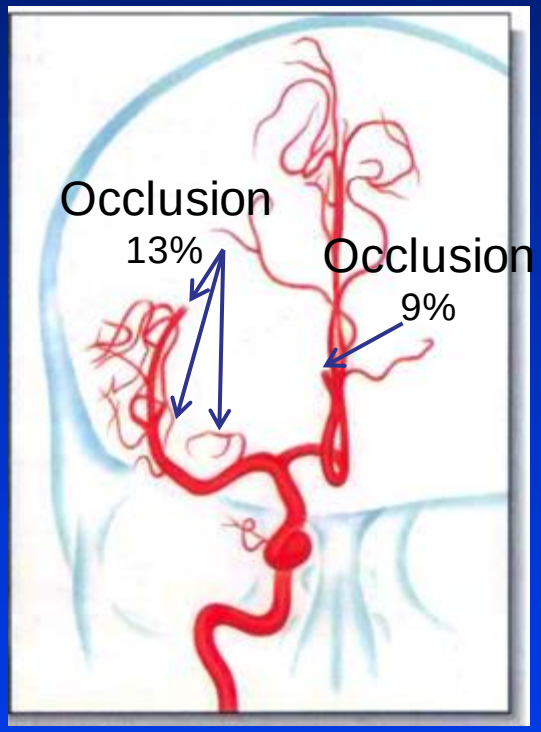


**Thrombectomy <8hrs**

**Partial Recovery or Deterioration**

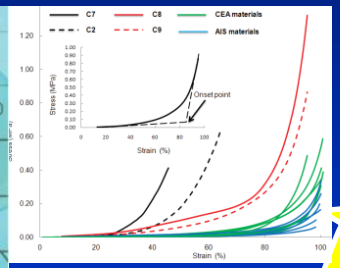
Normal → Occlusive clot → Fragmentation*





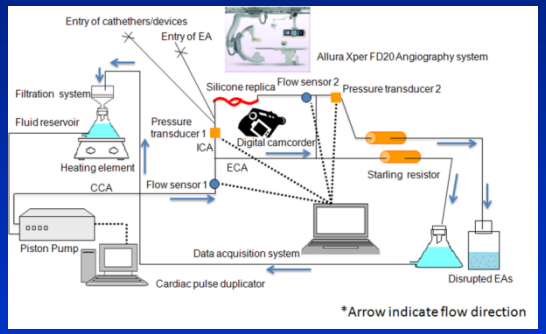

* Bonafe: ESMINT 2012

# In Vitro Assessment of Safety and Efficacy

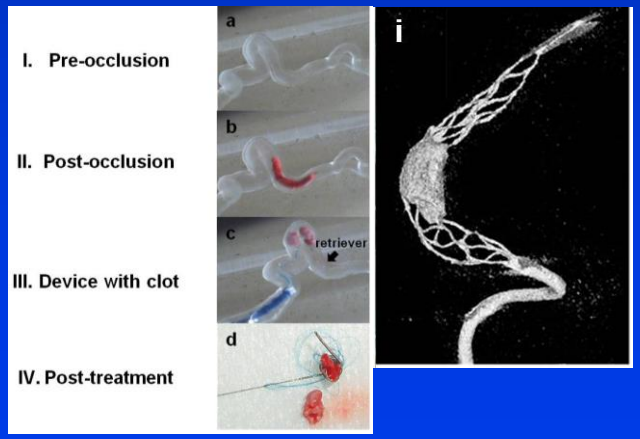



Clot Model

Circulation Loop




Imaging/ Medical Device

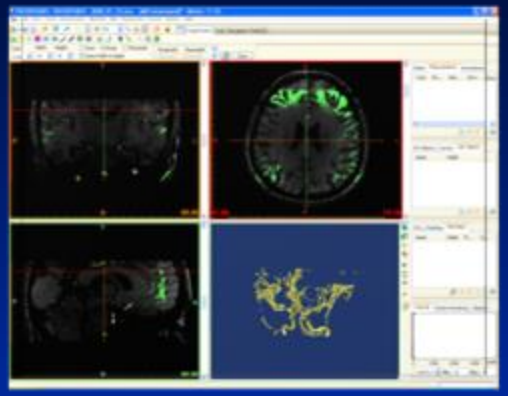



Bench-top Treatment Optimization

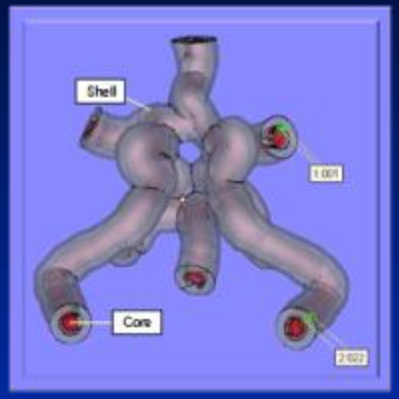
Vascular Model

# Population Based Vascular Replica





MRA Dataset




Computer Core-Shell Model

Fused Deposit Manufacturing

Physical Core-Shell Model

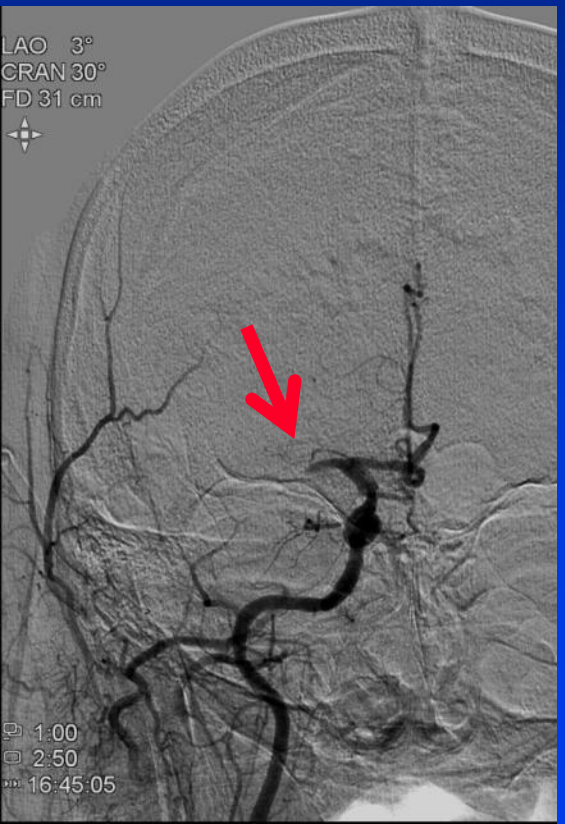
Silicone Replica

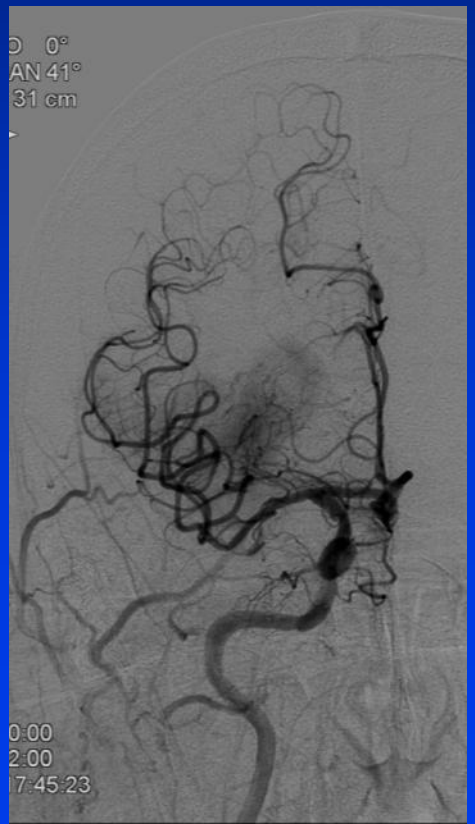
J Chueh, AK Wakhloo, and MJ Gounis. AJNR 2009

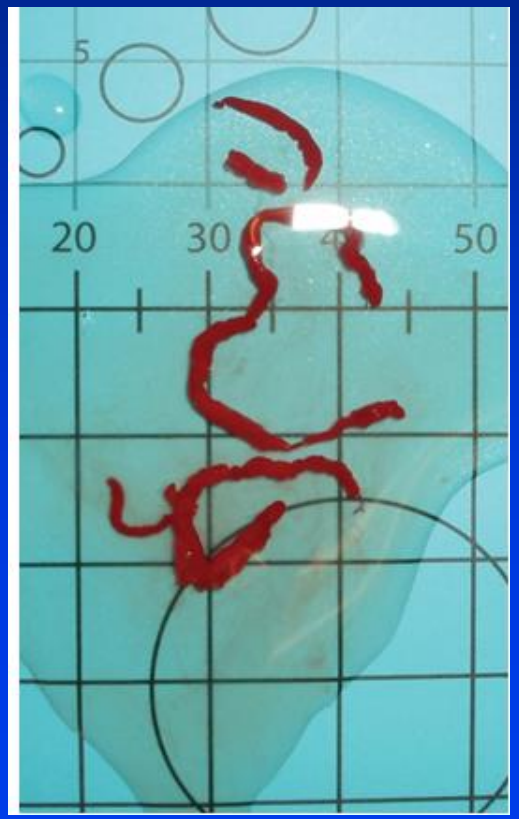
# Mechanical Analysis of Clot Modeling

NEW ENGLAND CENTER FOR STROKE RESEARCH

- 64 y-o M, Acute Ischemic Stroke
  - Entered ED >4.5hrs after symptom onset
  - CBV-MTT Mismatch
- Thrombus retrieved from R MCA with Penumbra Aspiration Device



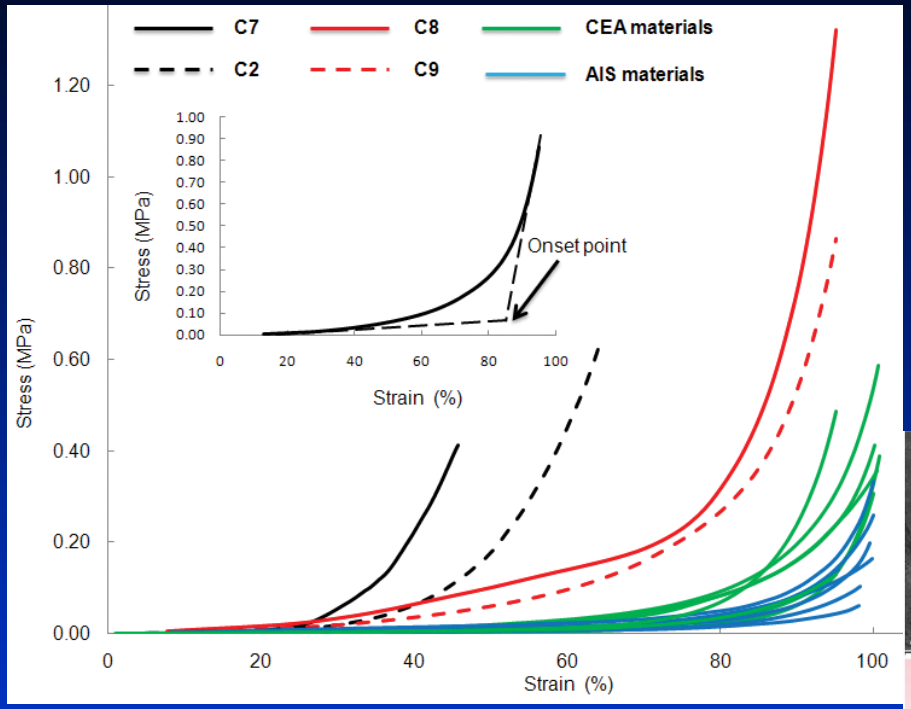



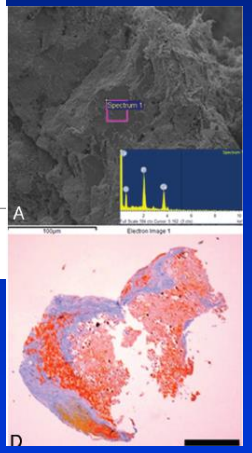

UMASS

# Mechanical Analysis of Clot





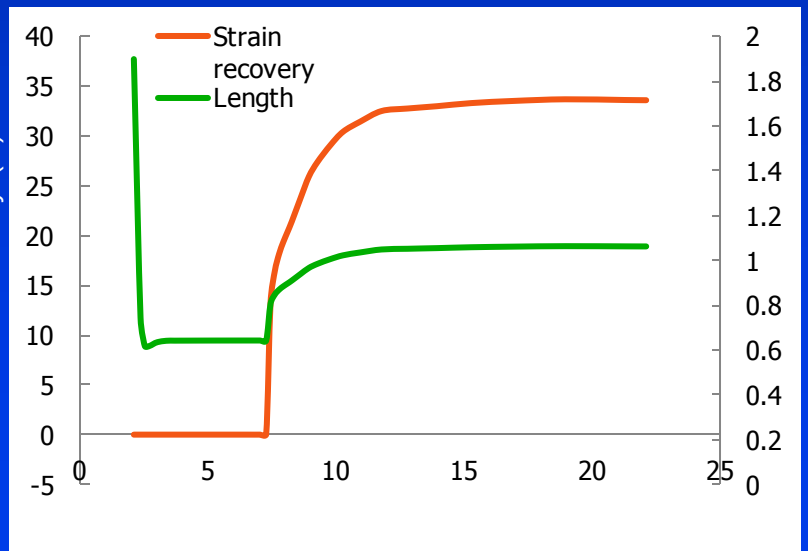

- Clot modeling – Need to know bulk mechanical properties

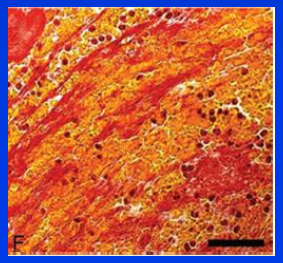


– Stress-Strain: DMA compression test



– Stress relaxation: Propensity for fragmentation

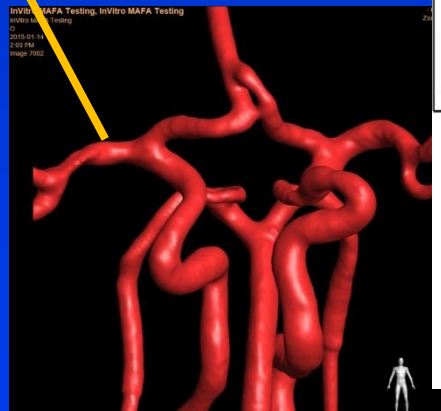


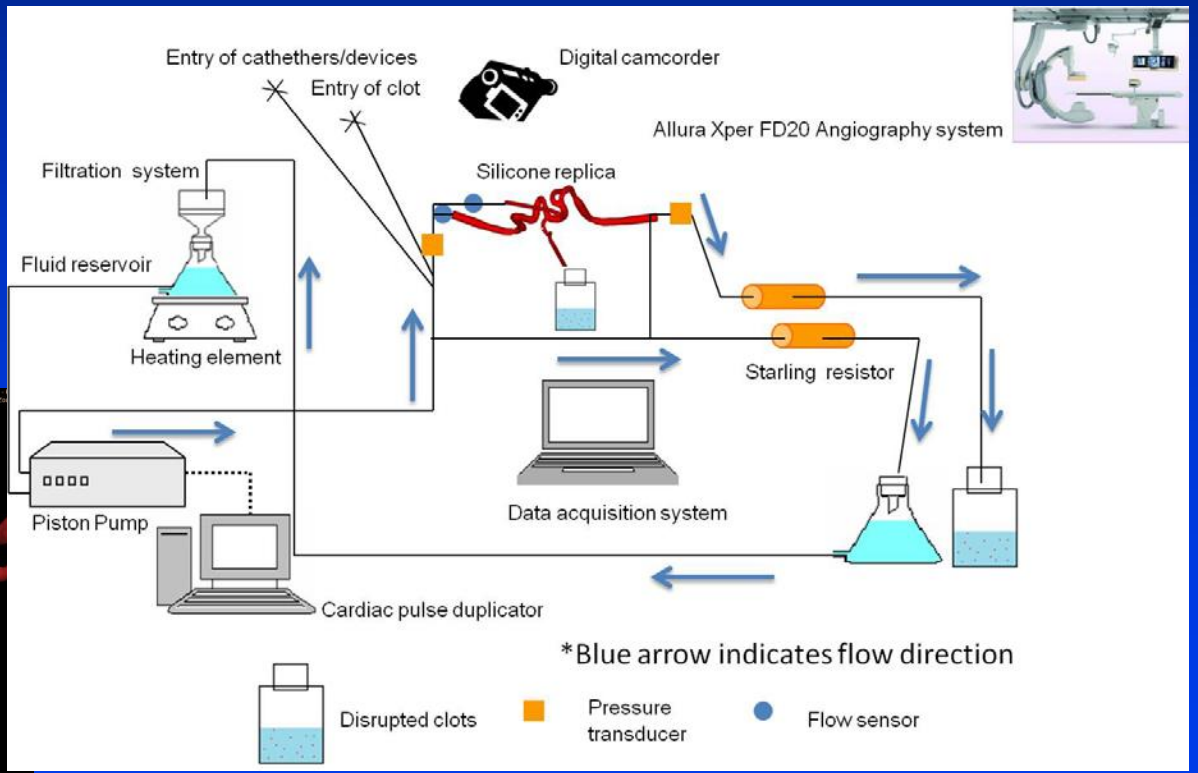



Chueh, Silva, Hendricks, Wakhloo, Gounis. AJNR 2011 32:1237

# "Model System"

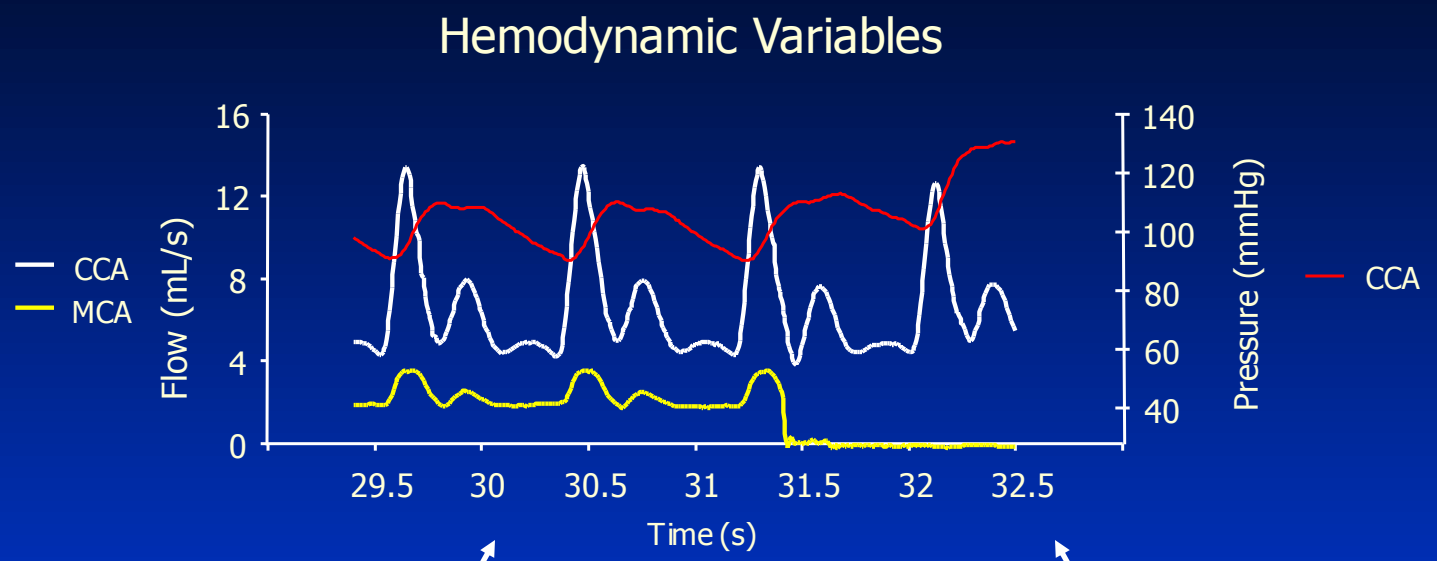
- Efficacy
  - Measures time and amount of flow restoration to thrombosed MCA in model
- Safety
  - Blood analog fluid is captured for particle/fragmentation analysis

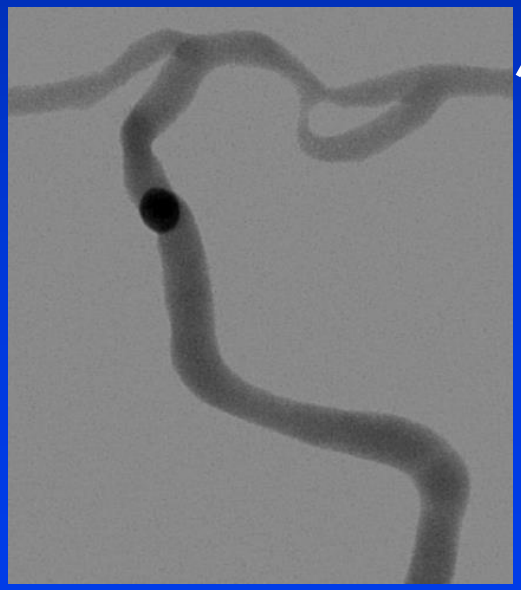


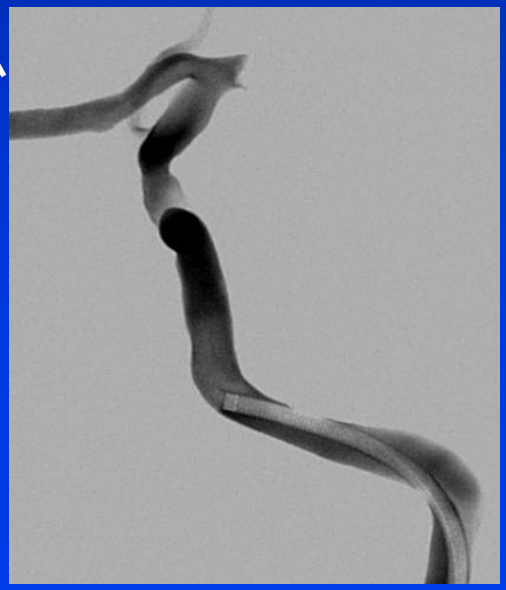



UMASS

# Vascular Occlusion

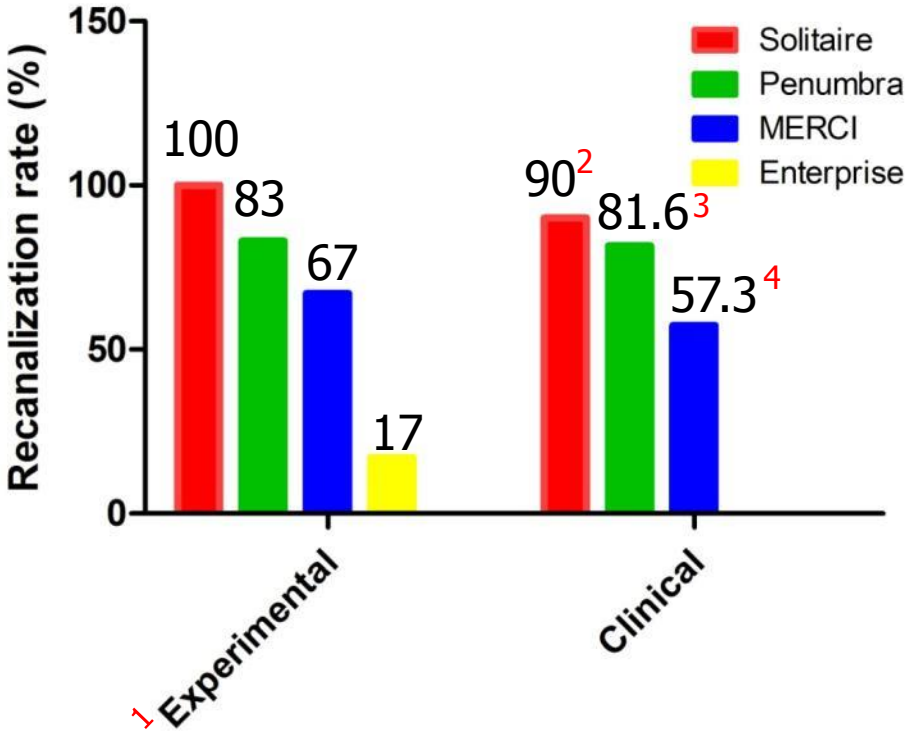


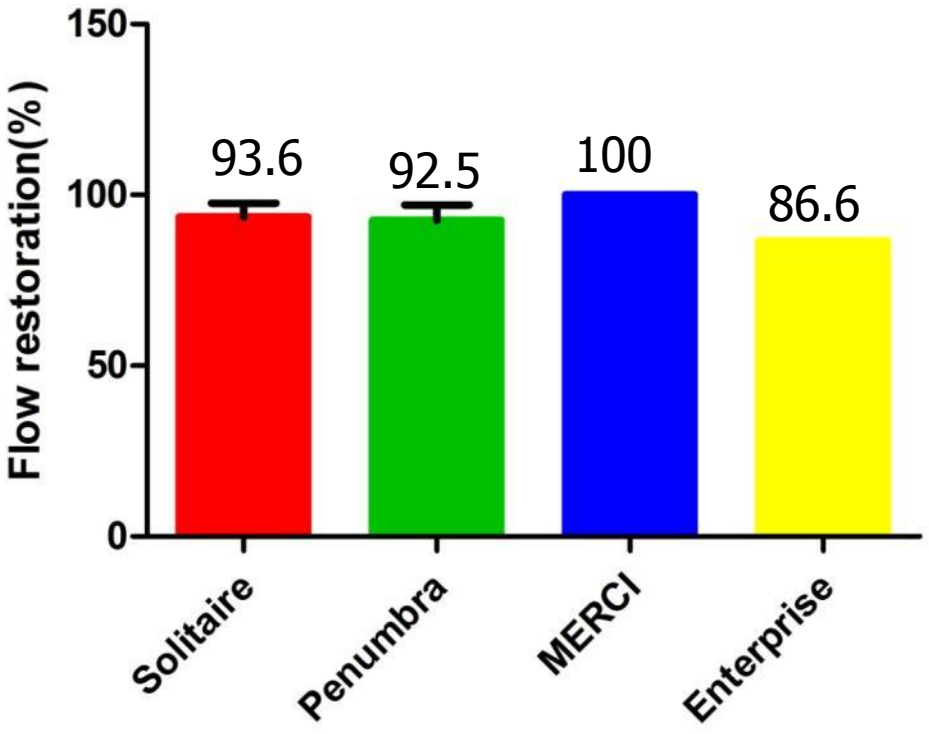





# Efficacy Metrics







1. *Chueh, Wakhloo, Gounis. AJNR 2012*
2. *Castaño C, Dorado L, Guerrero C, et al., Stroke 2010,41(8):1836*
3. *Penumbra Pivotal Stroke Trial Investigators. Stroke. 2009;40:2761–2768.*
4. *Smith WS, Sung G, Saver J, et al., for the MERCI Trial Investigators. Stroke 2008, 39: 1205*


UMASS

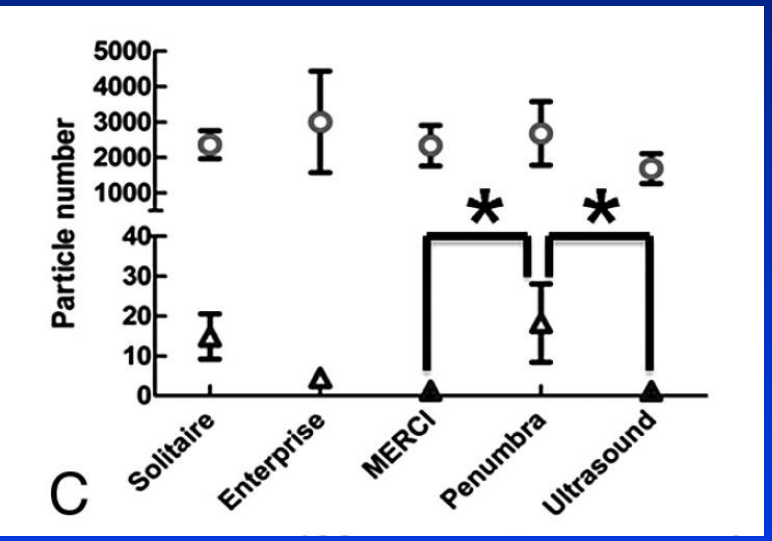
# Distal Emboli: A Modifiable Risk

# Translation?

NEW ENGLAND CENTER FOR STROKE RESEARCH

Experimental

Clinical




=

**Table 2. Neurological and Functional Outcomes From Open versus Closed Vessels**

| Outcome | Percent With Outcome | | | |
|---|---|---|---|---|
| | Overall (N=125) | TIMI 2–3 (N=102) | TIMI 0–1 (N=23) | *P** |
| Discharge NIHSS 0–1 or improved by ≥10 | 27 | 32 | 5 | 0.0127 |
| Good clinical outcome at 30 days† | 30 | 35 | 9 | 0.0199 |
| mRS ≤2 at 90 days | 25 | 29 | 9 | 0.0596 |
| Death at 90 days | 33 | 29 | 48 | 0.1384 |

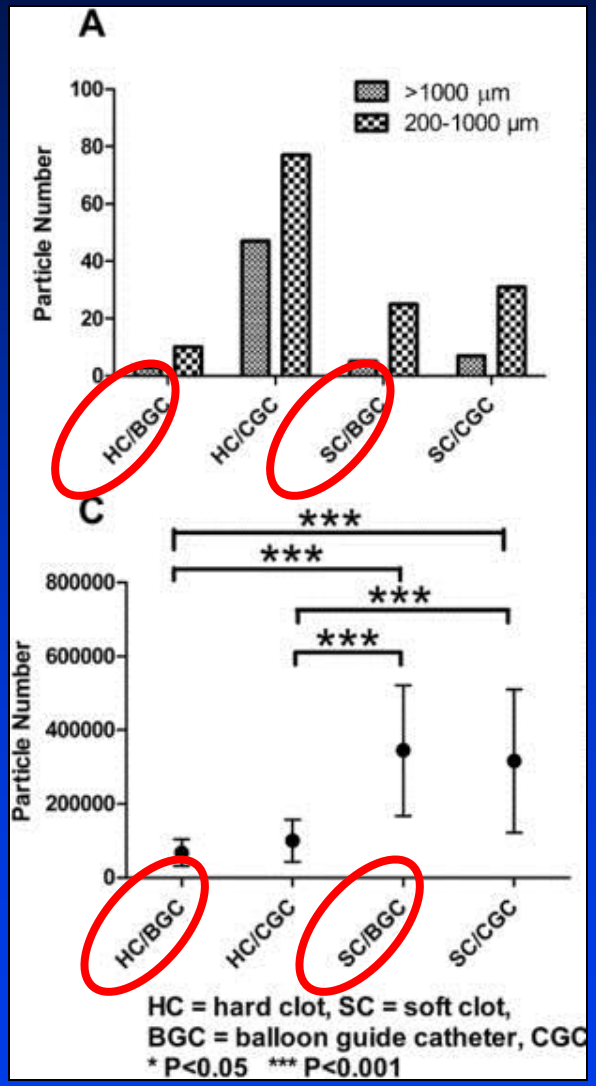
Chueh J.Y. et al. *AJNR*. 2012; 33: 1998

Stroke 2009;40:2761

# Translation?

NEW ENGLAND CENTER FOR STROKE RESEARCH

## Experimental




=

## Clinical

**Table 3. Independent Predictors of Clinical Outcome With Solitaire Treatment for Acute Ischemic Stroke**

| Variable | Nparm | DF | $\chi^2$ | *P* Value>$\chi^2$ |
|---|---|---|---|---|
| Age, y | 2 | 1 | 94.54 | <0.001* |
| Hypertension | 2 | 1 | 3.93 | 0.0476 |
| Atrial fibrillation | 2 | 1 | 16.8 | <0.0001* |
| Initial NIHSS score | 2 | 2 | 9.47 | 0.0088* |
| Site | 8 | 5 | 9.85 | 0.08 |
| IV tPA | 2 | 1 | 128.46 | <0.0001* |
| TOG | 2 | 1 | 0.58 | 0.45 |
| TIMI success | 2 | 2 | 2.75 | 0.25 |
| BGC | 2 | 1 | 66.66 | <0.0001* |
| General anesthesia | 2 | 2 | 5.56 | 0.026 |
| Procedure time | 2 | 2 | 5.56 | 0.06 |

BGC indicates balloon guide catheter; DF, degrees of freedom; IV tPA, intravenous tissue plasminogen activator; NIHSS, National Institutes of Health Stroke Scale; Nparm, number of parameters; TIMI, thrombolysis in myocardial infarction; and TOG, time of onset to groin puncture.

*Statistically significant.

Chueh J.Y. et al. *Stroke*. 2013; 44: 1396-1401

Nguyen T et al. Stroke 2014;45:141-5

# Flow Restoration Procedure

- **Group 1:**

Thrombectomy through an 8Fr balloon guide catheter (BGC) positioned at the cervical ICA

- **Group 2:**

Thromboaspiration via a 5Fr intracranial guide catheter (Solumbra) in the origin of the MCA

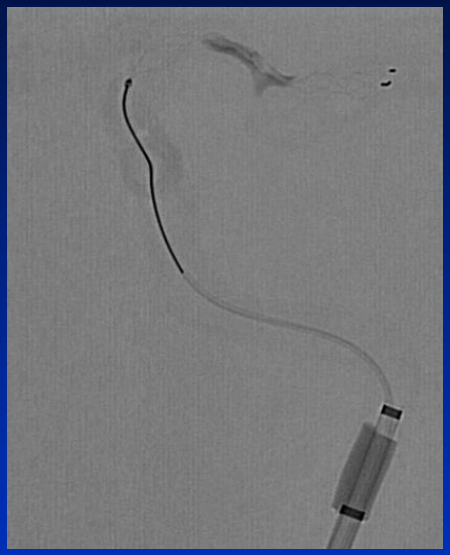
- **Group 3:**

Thrombectomy through a 6Fr guide catheter (CGC) with the tip placed at the origin of the cervical ICA

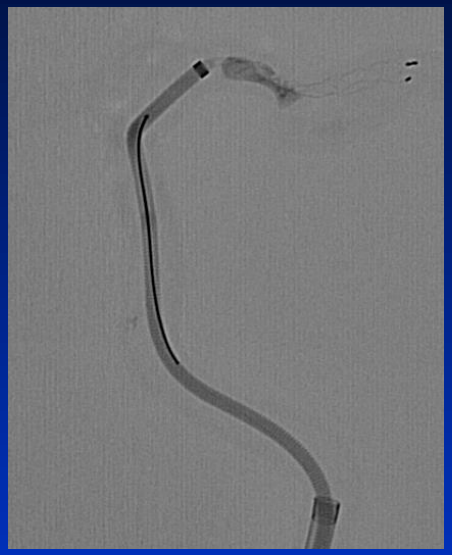
- **Group 4:**

A Direct Aspiration first Pass Technique (ADAPT). Aspiration through a 5MAX

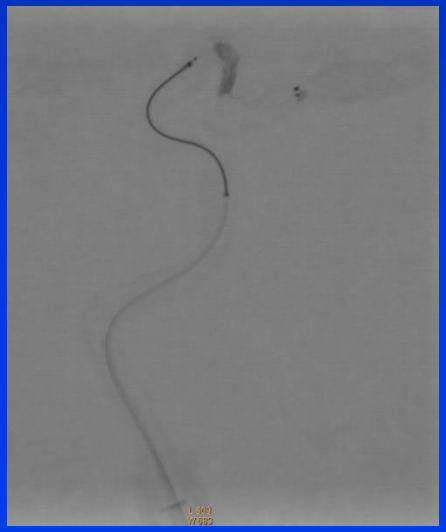
**Group 1: BGC**



**Group 2: Solumbra**



**Group 3: CGC**

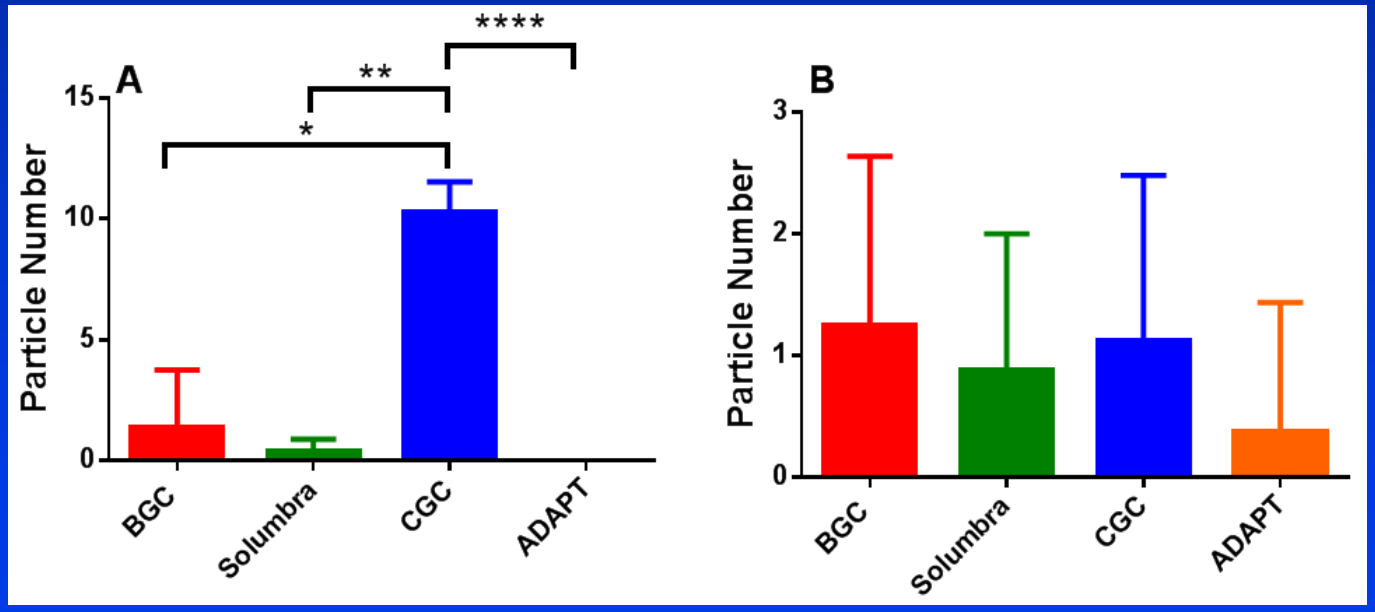


**Group 4: ADAPT**

# Emboli >1000 µm

- Using CGC during mechanical thrombectomy significantly increased the risk of hard emboli formation.
- There was no statistical difference in the creation or large particle emboli in the soft clot group between all four different access techniques.

Hard Clot



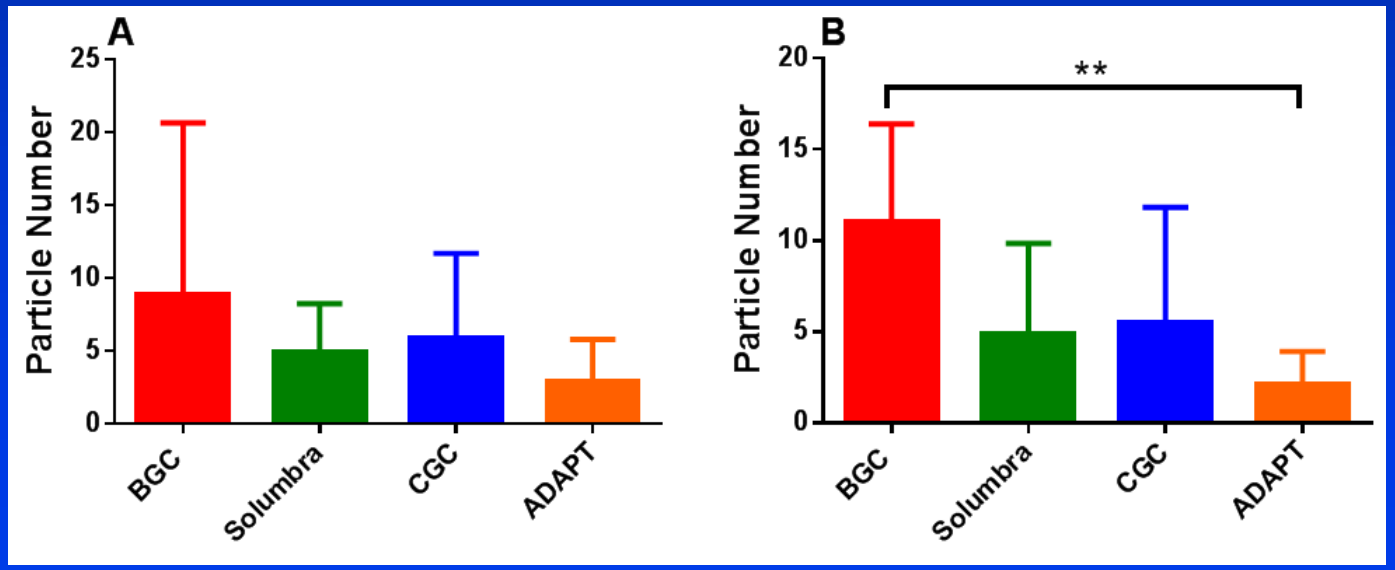

Soft Clot

# Emboli with size between 200-1000 µm

NEW ENGLAND CENTER FOR STROKE RESEARCH

- Average number of emboli (regardless of clot type):
  - ADAPT<Solumbra<CGC<BGC
  - Significant difference was seen between the BGC and the ADAPT techniques in the soft clot group

Hard Clot

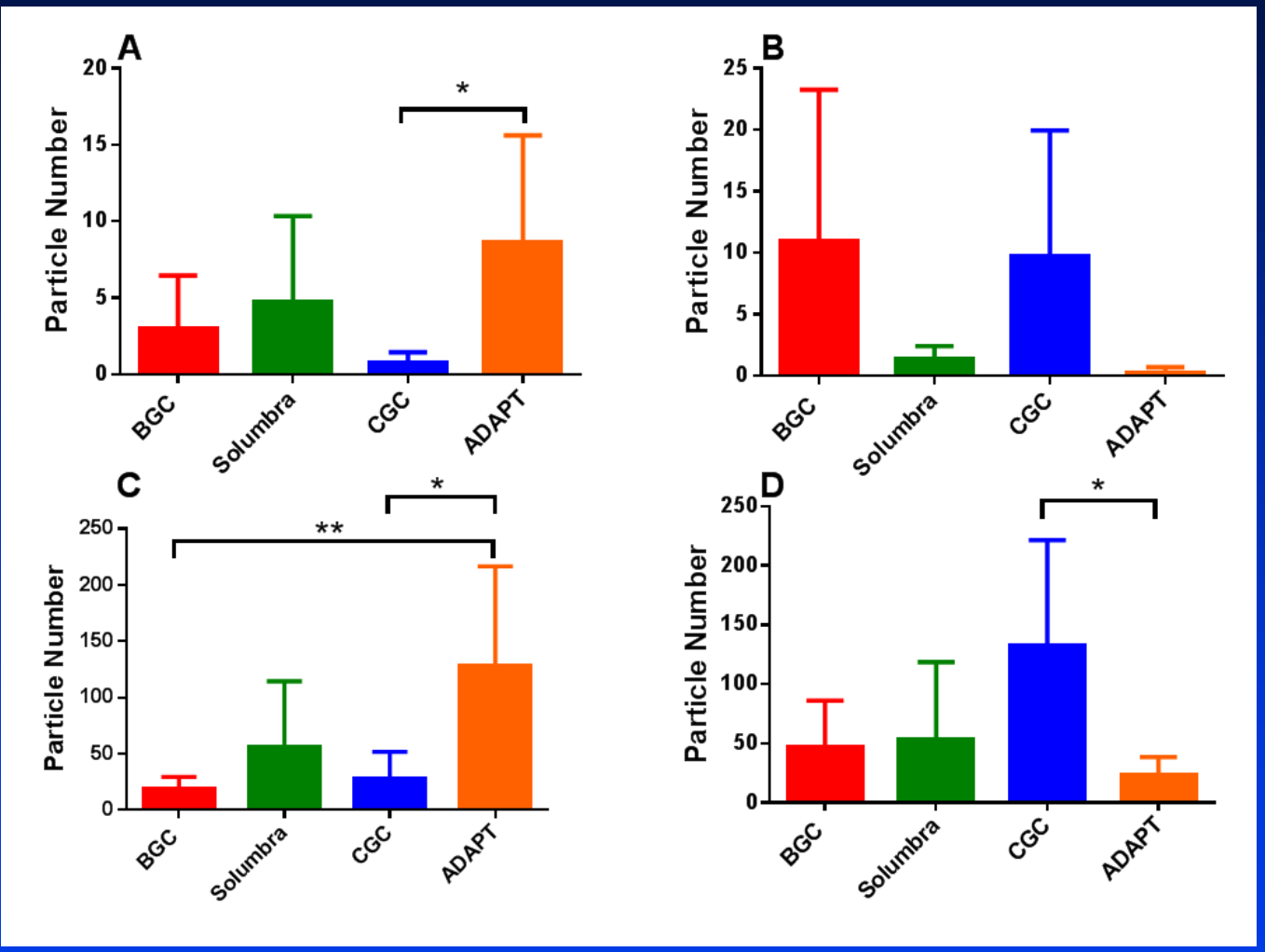



Soft Clot

UMASS

# Emboli with size between 50-200 µm






- **Figure A and B**

---Size range: 100-200µm

- **Figure C and D**

--- Size range: 50-100µm

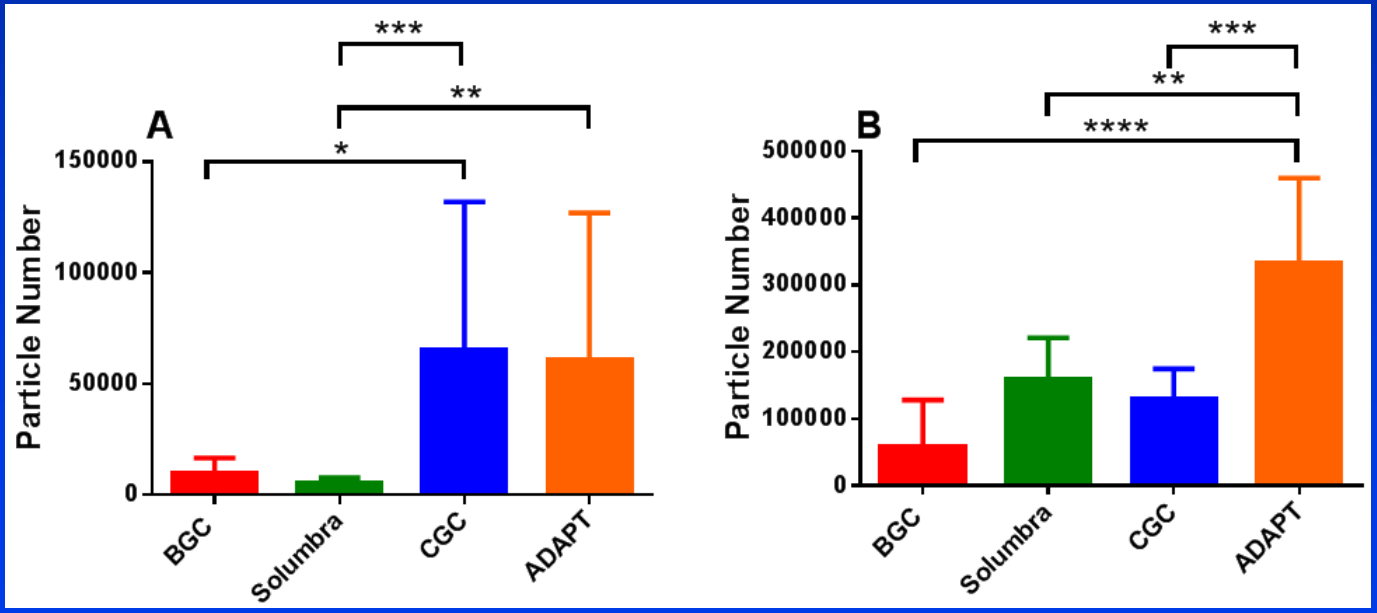
UMASS

# Emboli <50 µm



- The majority of the emboli (>90%) generated during the thrombectomy procedure had a size <50µm (mean size: 12.3µm).
- There was a significant increase in the number of particles generated during thrombectomy using the soft clot model

Hard Clot

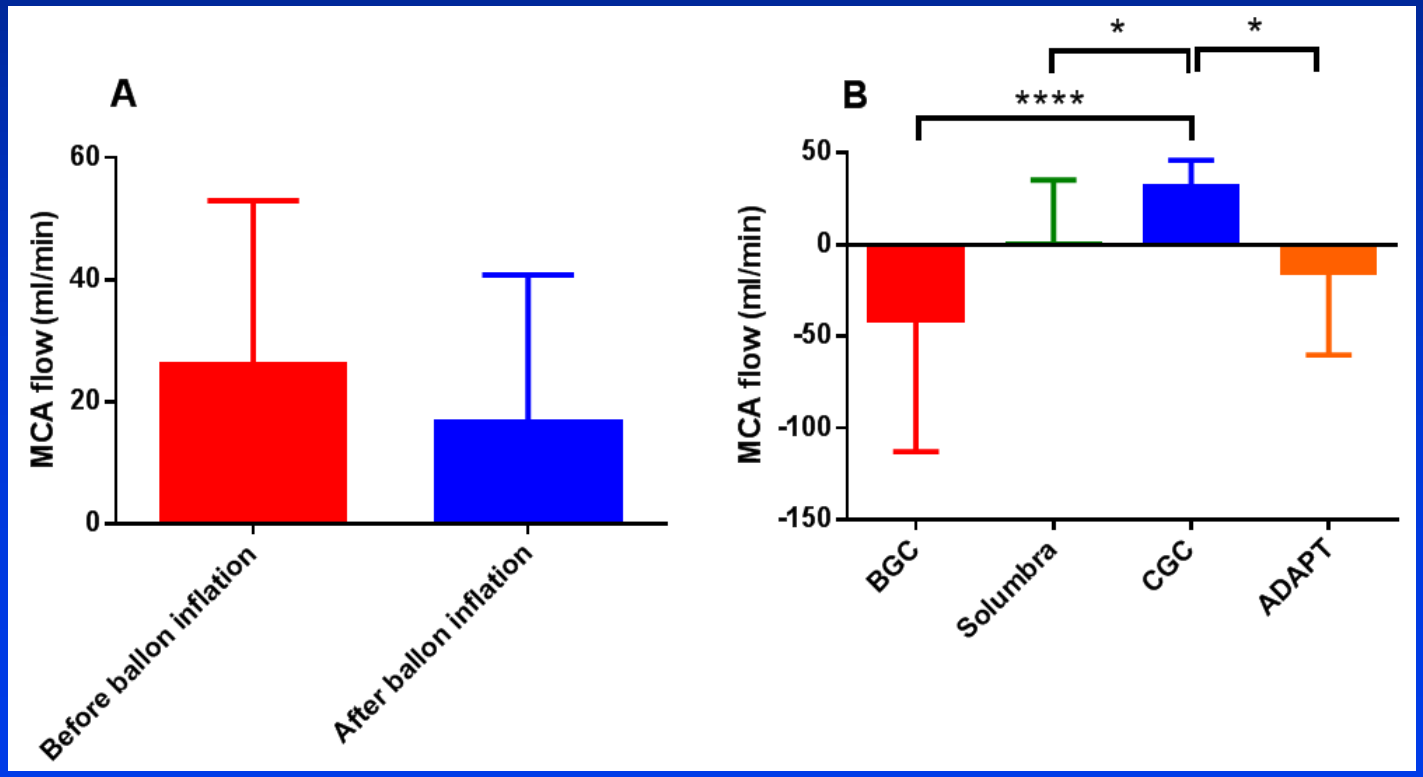



Soft Clot

# MCA Flow during Aspiration



- PComA and ACA present, temporary ICA occlusion provided by the BGC during mechanical thrombectomy didn't significantly change the restored MCA flow
- Temporary occlusion with the BGC and direct aspiration through the 5MAX resulted in flow reversal in the MCA (Figure B).

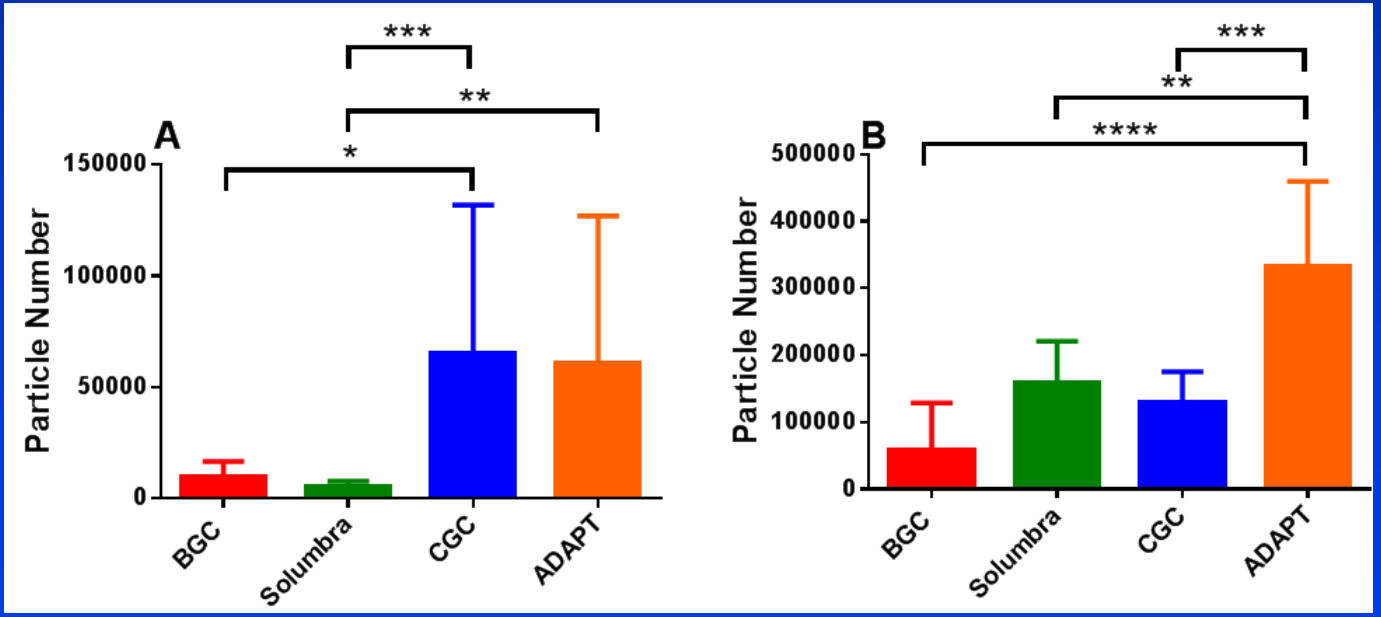


# Total Number of Distal Emboli

NEW ENGLAND CENTER FOR STROKE RESEARCH

- Hard clot model: **Solumbra or BGC were most effective in reducing the rate of forming clot fragments** compared to the CGC or the ADAPT technique.
- Soft clot model: Thrombectomy with the **BGC technique** reduced total embolic particle creation by at least **2-fold compared** to the other techniques.

Hard Clot




Soft Clot

UMASS

# Conclusion

NEW ENGLAND CENTER FOR STROKE RESEARCH

- Use of the BGC technique during a SR thrombectomy was associated with statistically lower rates of soft distal emboli across a broad range of embolic particle sizes.
- The Solumbra technique was shown to be numerically, although not statistically, superior in several hard clot subgroups.
- When encountering hard clot, use of the Solumbra or ADAPT techniques in addition to the BGC may provide an additional reduction in distal emboli and may be considered for comprehensive distal emboli reduction.

JY Chueh et al. Stroke. 2013; JY Chueh et al. JNIS 2016

UMASS

# ARTS

NEW ENGLAND CENTER FOR STROKE RESEARCH


UMASS

Stroke
JOURNAL OF THE AMERICAN HEART ASSOCIATION
American Stroke Association℠
A Division of American Heart Association

# Balloon guide catheter improves revascularization and clinical outcomes with the Solitaire device: analysis of the North American Solitaire Acute Stroke Registry

Nguyen TN, Malisch T, Castonguay AC, Gupta R, Sun CH, Martin CO, Holloway WE, Mueller-Kronast N, English JD, Linfante I, Dabus G, Marden FA, Bozorgchami H, Xavier A, Rai AT, Froehler MT, Badruddin A, Taqi M, Abraham MG, Janardhan V, Shaltoni H, Novakovic R, Yoo AJ, Abou-Chebl A, Chen PR, Britz GW, Kaushal R, Nanda A, Issa MA, Masoud H, Nogueira RG, Norbash AM, Zaidat OO.

Stroke. 2014 Jan;45:141-5

# NASA Balloon Guide Catheter

Nguyen T et al, Stroke

| | Balloon Guide Catheter(N=149 | No Balloon Guide Catheter(N=189) | P Value |
|---|---|---|---|
| Emboli in new territory | 8 (5) | 10 (5.2) | 0.9 |
| **Recanalization TICI3** | **80 (53.7)** | **61 (32.5)** | <0.0001 |
| Recanalization TICI2b-3 | 113 (76) | 133 (71) | 0.3 |
| Procedural factors | | | |
| **Procedure time (SD)** | **120 (28.5)** | **161 (35.6)** | 0.02 |
| Time onset to groin or first angio (SD) | 348 (230.7) | 375 (252.7) | 0.3 |
| General anesthesia | 97 (84.4) | 99 (60) | <0.001 |
| Number of passes (mean, SD)<br>(Median, IQR) | 1.8 (1.2)<br>1 (1-2) | 1.9 (1)<br>2 (1-3) | 0.3 |
| IA tPA | 40 (26.9) | 60 (31.8) | 0.3 |
| Simultaneous Penumbra & Solitaire | 18 (12.1) | 34 (18.1) | 0.1 |
| **Rescue therapy** | **29 (20)** | **54 (28.6)** | 0.05 |
| Clinical Outcome | | | |
| **Discharge NIHSS**<br>Mean (SD)<br>Median (IQR) | <br>**12 (14.5)**<br>**6 (1-18)** | <br>**17.5 (16)**<br>**11 (4-42)** | 0.002 |
| **Good clinical outcome (3 months)** | **65 (51.6)** | **62 (35.8)** | 0.02 |

Radiology

# Comparison of a Balloon Guide Catheter and a Non–Balloon Guide Catheter for Mechanical Thrombectomy[1]

- 183 consecutive patients with MCA/ ICA T occlusion in Germany.

- stent retriever with a balloon guide catheter (n = 102) at one center vs non–balloon guide catheter (n = 81) at the other center.

Aglaé Velasco et al Radiology 2016

# Results



- Recanalization with BGC in 89.2% of thrombectomies (91 of 102) versus 67.9% (55 of 81) NBGC (P = .0004).
- 1-pass thrombectomy rate with BGC was higher (63.7% [65 of 102] vs 35.8% NBGC [29 of 81] respectively; P = .001).

Aglaé Velasco et al Radiology 2016

# Results

NEW ENGLAND CENTER FOR STROKE RESEARCH

- Procedure duration was significantly shorter with BGC than NBGC group(median, 20.5 minutes vs 41.0 minutes, respectively; P <.0001)

- Median number of passes in the BGC group was one (range 1–6 ) versus two passes (range, 1–7) in the NBGC group (P = .0002).

Aglaé Velasco et al Radiology 2016

UMASS

# Clot-Device Interaction

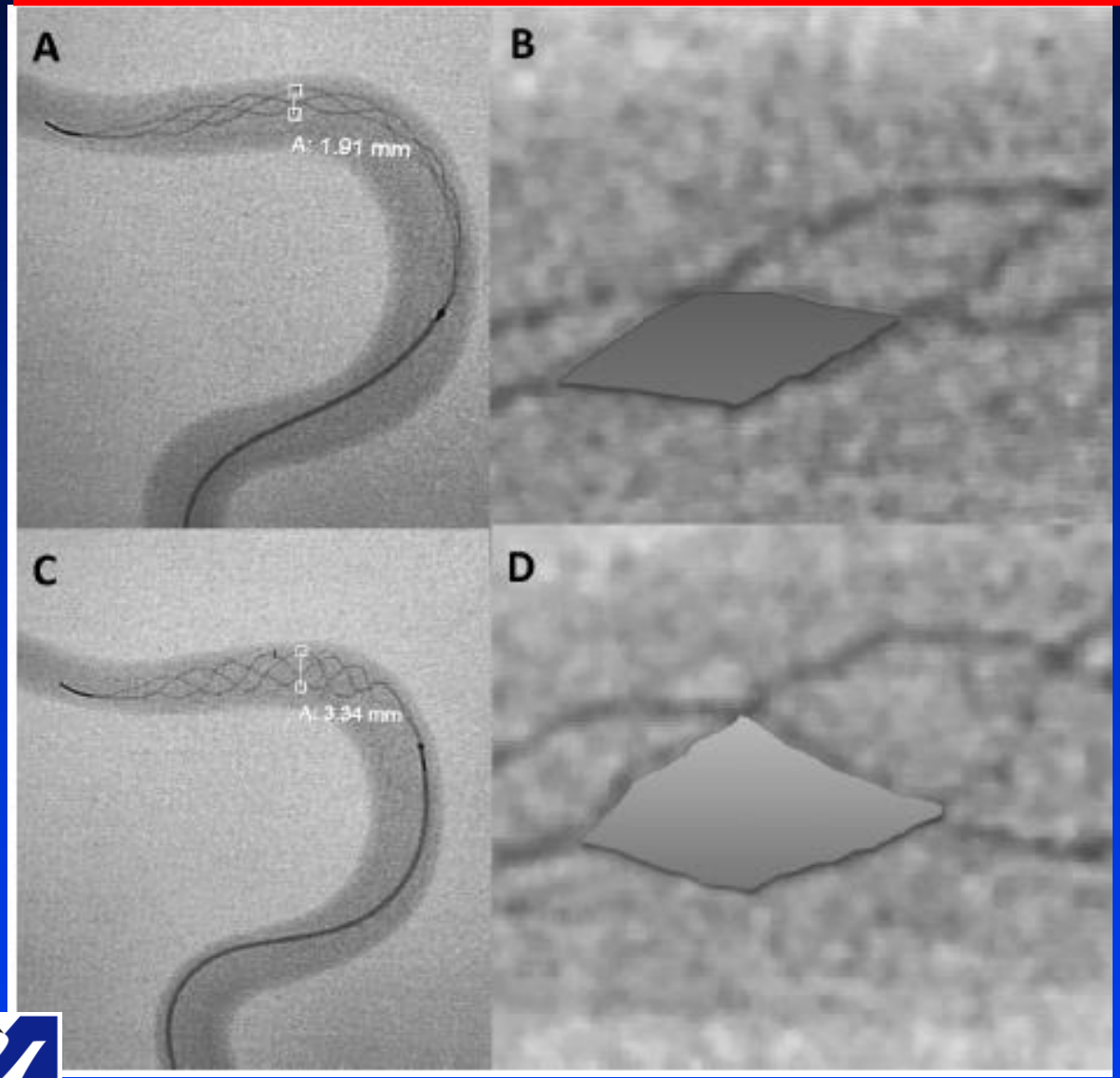
# SR Deployment Technique

## Optimizating Clot Retrieval in Acute Stroke
### The Push and Fluff Technique for Closed-Cell Stentrievers

Diogo C. Haussen, MD; Leticia C. Rebello, MD; Raul G. Nogueira, MD

Stroke. 2015;46:2838-2842.

# Haussan et al. Stroke. 2015;46:2838-2842.




- Max. TREVO diameter-1.9 mm, with SUT.
- PFT-max. diameter of 3.3 mm (75% larger) with 25% device foreshortening versus SUT.

- Mean cell size area was 2.4 $mm^2$ for the SUT compared with 3.7 $mm^2$ in the PFT (51% larger)

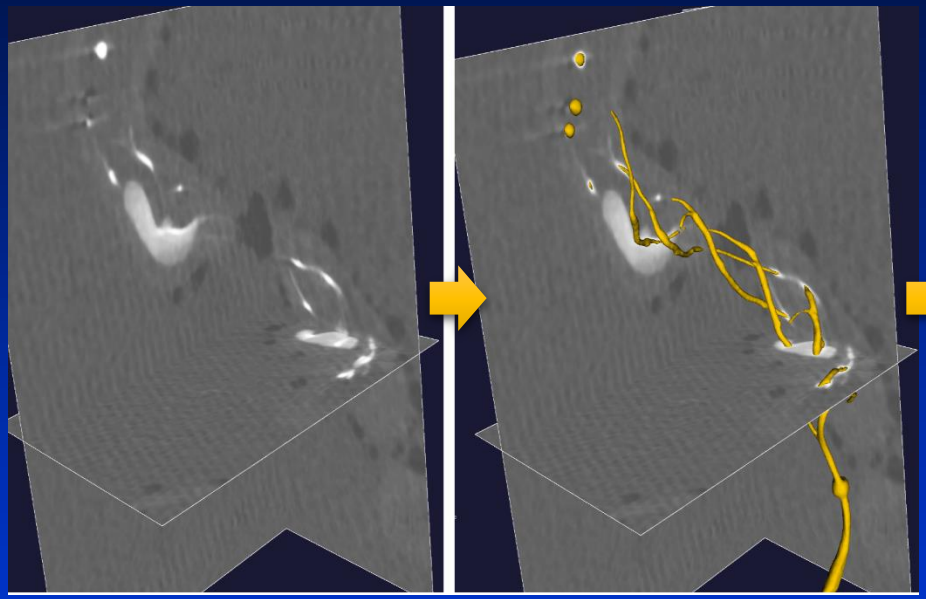
# Results

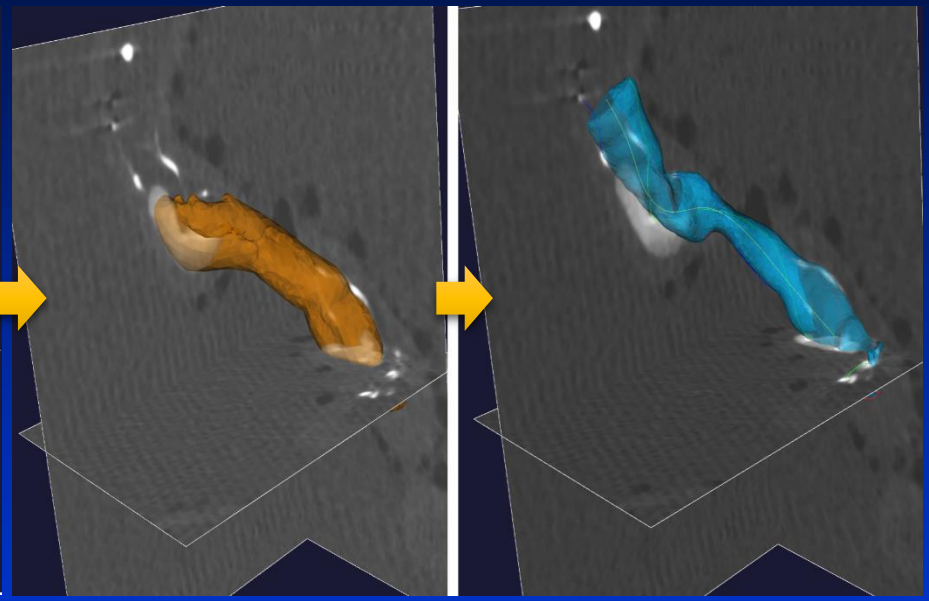
- PFT -higher rate of first pass reperfusion (54% versus 36%; P=0.03) and a lower number of passes (1.3±0.8 versus 1.8±1.0; P<0.01).
- mTICI-3 reperfusion was achieved more frequently in the PFT group (58% versus 40%; P=0.03).
- PFT was independently associated with a lower number of Trevo passes (P=0.01) and higher rates of first-pass reperfusion (P=0.01) and complete (mTICI-3) reperfusion

# Hypothesis

- Altering technique change clot-device interaction (cheese-grating)
- With NiTi devices, there is temporal increase in clot-device interaction

# Clot Integration Factor





High-resolution reconstruction of cone-beam CT image

Extraction of visible marker wires

Segmentation of the contrast-enriched clot

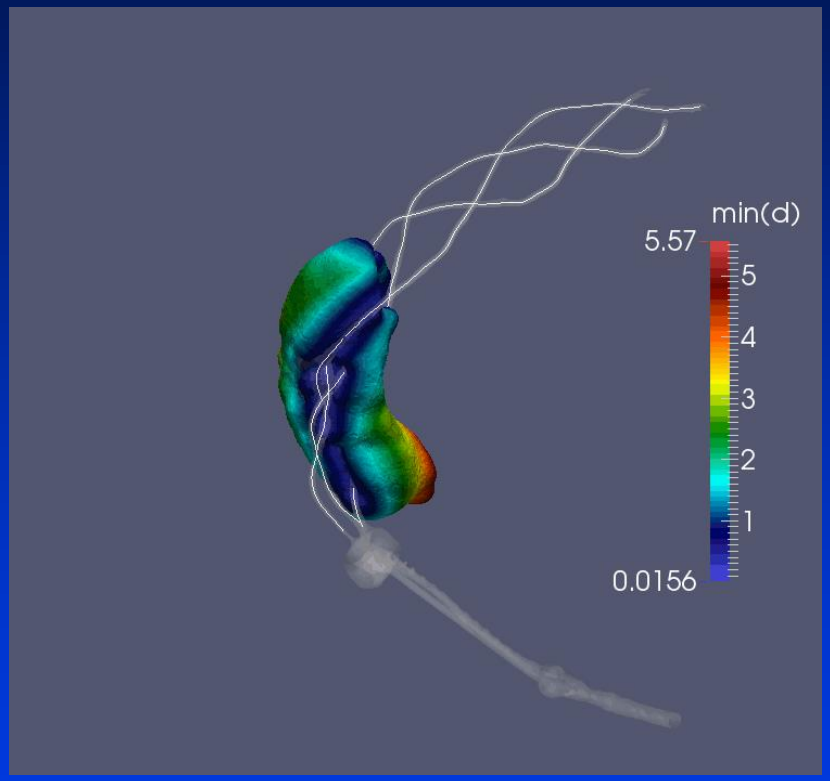
Determination of the inner volume of the stent-retriever

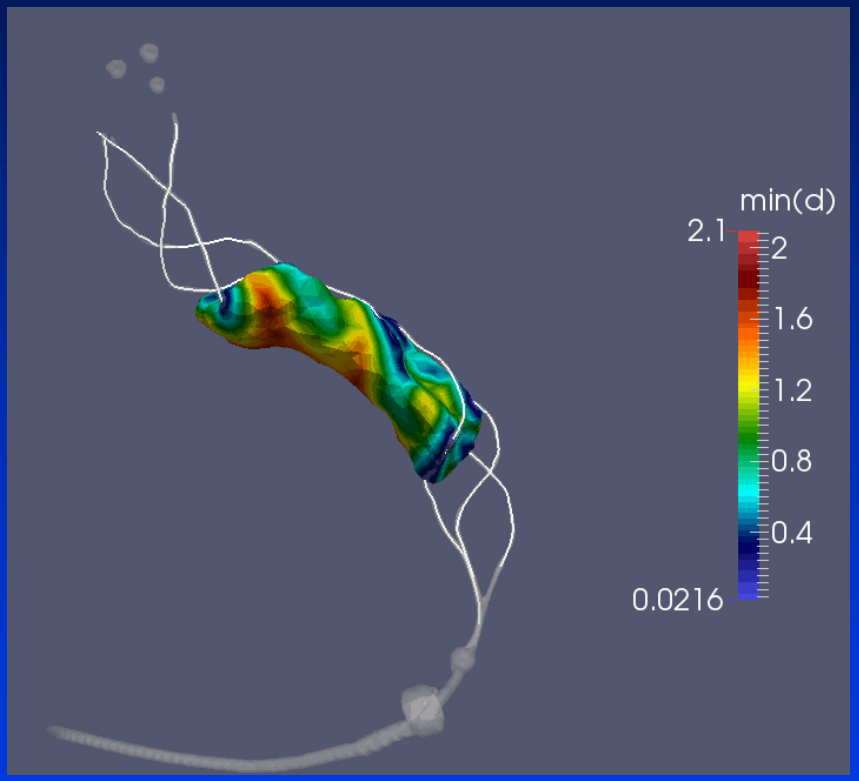
$$\text{Clot Integration Factor} = \frac{\text{Volume of Clot–Device Intersection}}{\text{Volume of Clot}}$$

Kajo van der Marel, et al. JNIS 2016

UMASS

# Clot Integration Factor



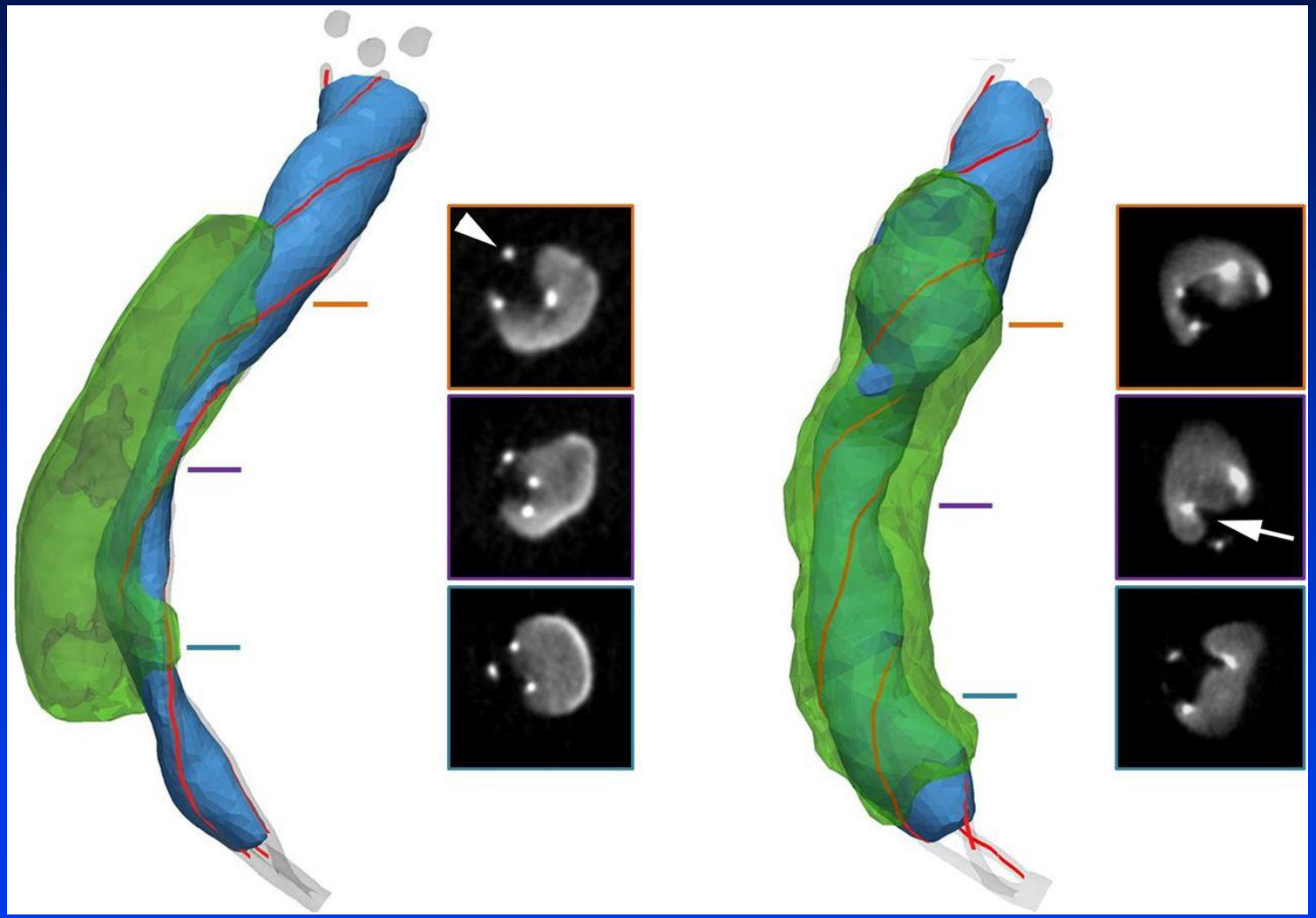

Unsheathing

Unsheath-Push

**Kajo van der Marel, et al. JNIS 2016**

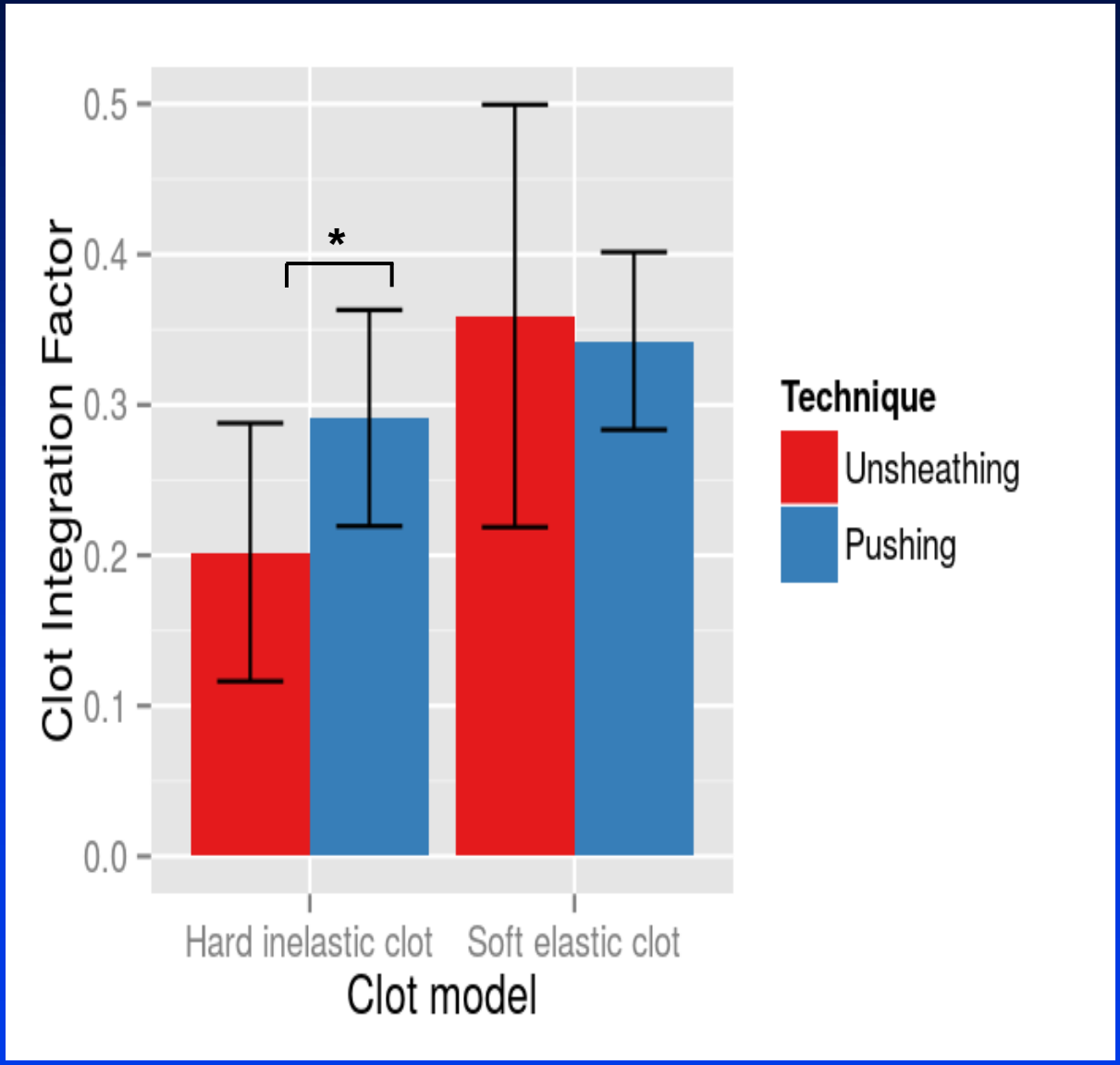
UMASS

# Clot Integration Factor

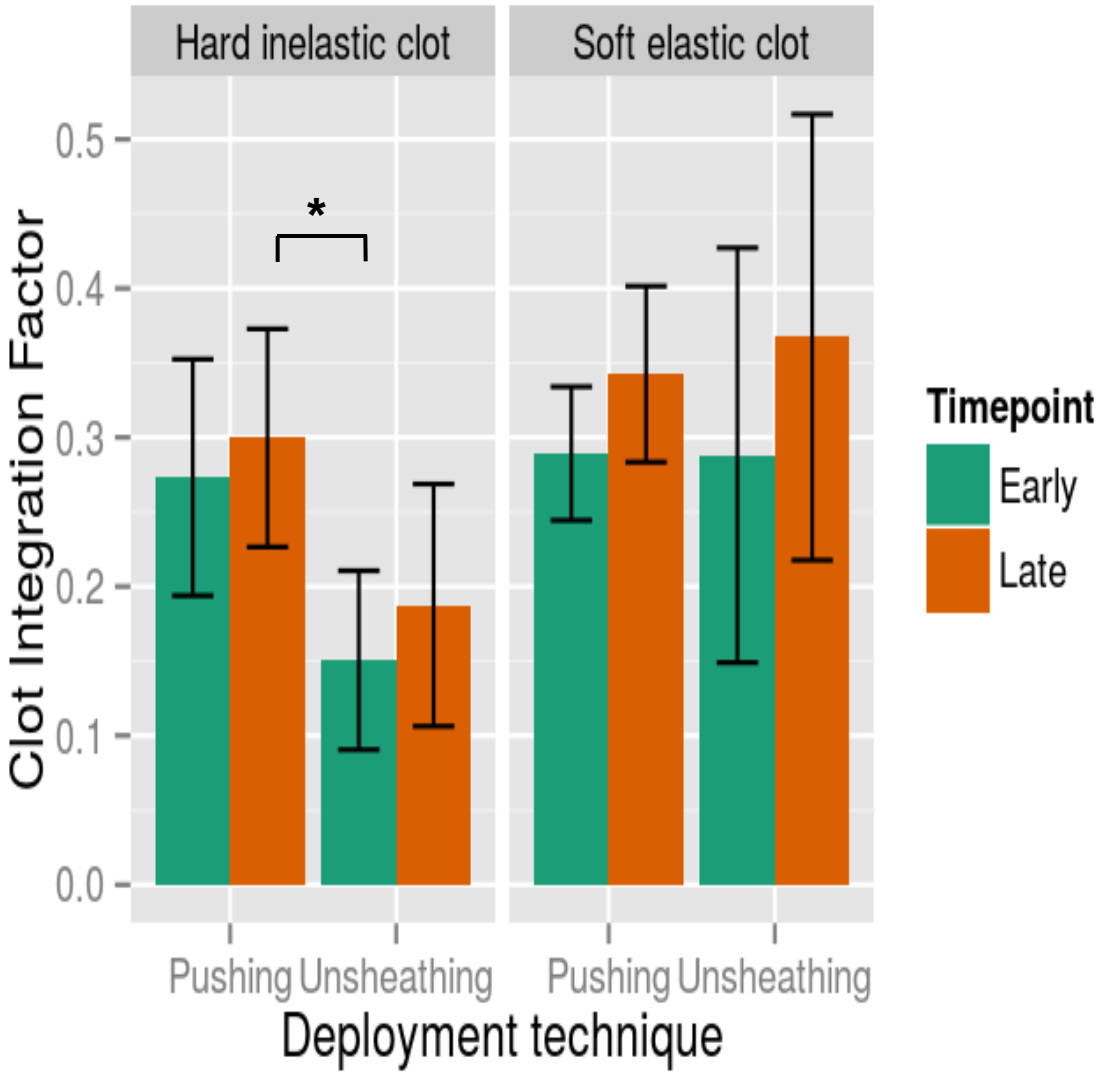


Kajo van der Marel, et al. JNIS 2016

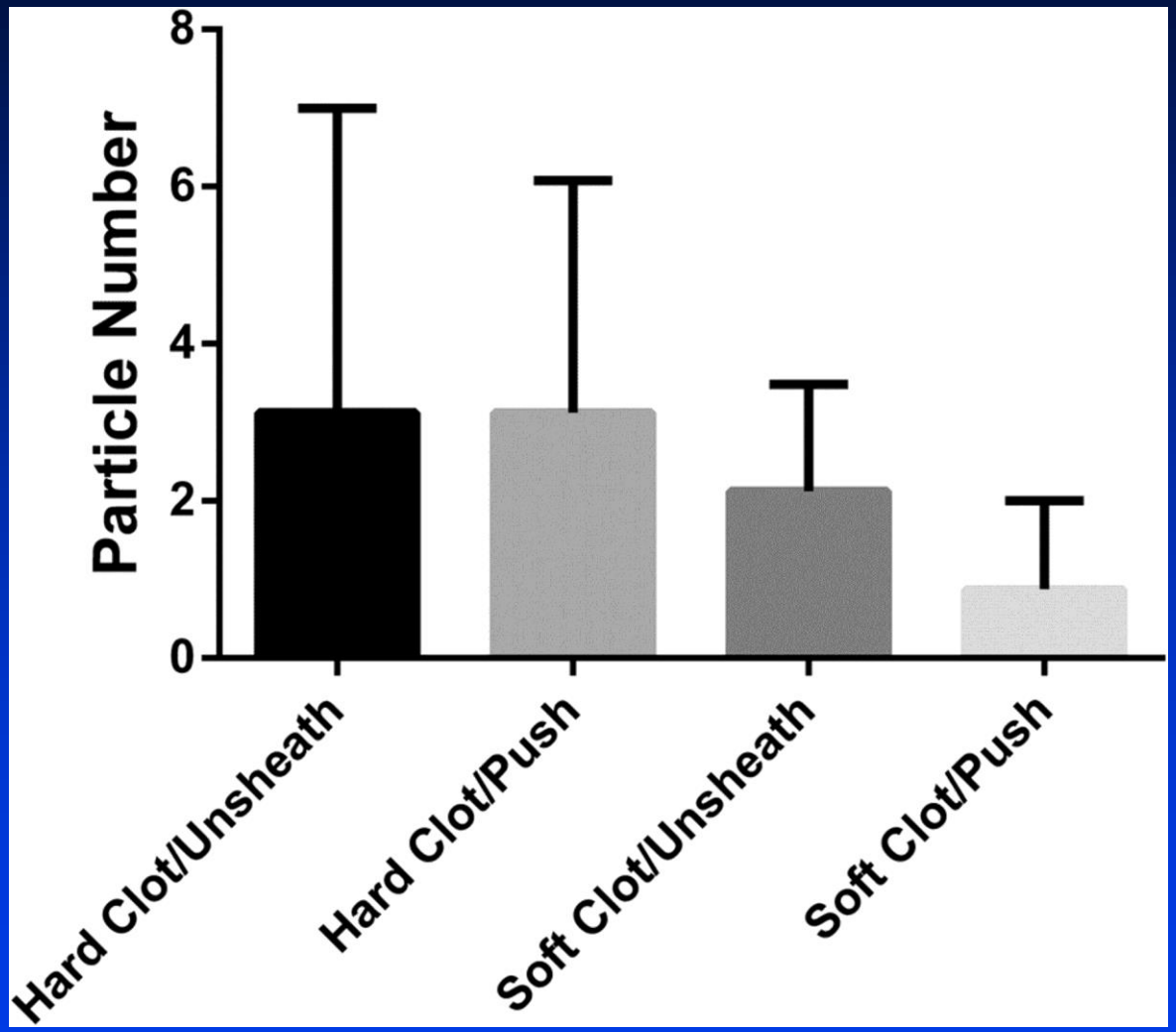
# Pushing increases CIF in Hard Clot



# CIF Increases with Time in all Clot



# No Change in Clot Fragmentation




Kajo van der Marel, et al. JNIS 2016

# Summary

## CIF: pushing vs. unsheathing

- Hard clot: higher CIF with pushing technique

## CIF: Time

- Hard clot & pushing technique significantly increased CIF over time between the post-deployment (early) and the final (late) time points.

# Summary

- Regardless of delivery technique, CIF increased over time for both hard inelastic clot and soft elastic clot models

- Device development has evolved rapidly (Avg life for a medical device is ~18 months).
- We need better models to address:
  - Combined therapies
  - Subtle differences between technologies
  - What technology to use for what underlying disease
- Unlikely that one model will address all questions. Select a model appropriate to the question asked.
- Multicenter preclinical trials – the way of the future

UMASS

- UMass Collaborations
  - Marc Fisher, MD
  - Neil Aronin, MD
  - Alexei Bogdanov, PhD
  - Greg Hendricks, PhD
  - Guanping Gao, PhD
  - Miguel Esteves, PhD
  - Linda Ding, PhD
  - Srinivasan Vedantham, PhD
  - John Weaver, MD
- Collaborations
  - Alex Norbash, MD – BU
  - Thanh Nguyen, MD - BU
  - Italo Linfante, MD - Baptist
  - Guilherme Dabus, MD - Baptist
  - Don Ingber, PhD – Harvard
  - Nati Korin, PhD - Technion
  - Johannes Boltze, MD, PhD – Frauhofer Institute
  - Raul Nogueira, MD - Emory

# NECStR

- Ajay Wakhloo, MD, PhD
- Ajit Puri, MD
- Juyu Chueh, PhD
- Miklos Marosfoi, MD
- David Rex, MD, PhD
- Martijn van der Bom, PhD
- Kajo van der Marel, PhD
- Anna Kühn, MD, PhD
- Frédéric Clarençon, MD, PhD
- Ivan Lylyk, MD
- Mary Howk, MS, CRC
- Thomas Flood, MD, PhD
- Erin Langan, BS
- Olivia Brooks
- Olena Fartushna, MD
- Chris Brooks, PA
- Mary Perras, NP
- Shaokuan Zheng, PhD