NEW ENGLAND CENTER FOR STROKE RESEARCH

From Bench to Brain:

Recent Advnaces in Devices Used in Neuro-Interventions

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Associate Professor, Department of Radiology
Director, New England Center for Stroke Research
2016 AAPM Annual Meeting – Washington DC

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Disclosures

- Research Grants (last 12 months):
  - NINDS, NIBIB, NIA, NCI
  - Philips Healthcare
  - BRACCO
  - Fraunhofer Institute
  - Stryker Neurovascular
  - Codman Neurovascular
  - Medtronic Neurovascular
  - InNeuroCo Inc
  - Blockade Medical
  - CereVasc LLC
  - Cook Medical
  - Medtronic
  - Microvention
  - Neuronal Protection Systems LLC
  - Neuravi
  - Spineology Inc
  - Silk Road
  - Wyss Institute
- Consulting (fee-per-hour, last 12 months):
  - Stryker Neurovascular
  - Harris Beach, Expert Witness
  - Codman Neurovascular
- Investment (Stocks)
  - Boston Scientific Inc
  - InNeuroCo Inc

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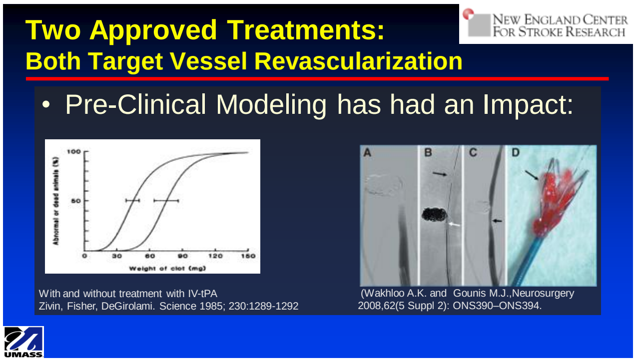
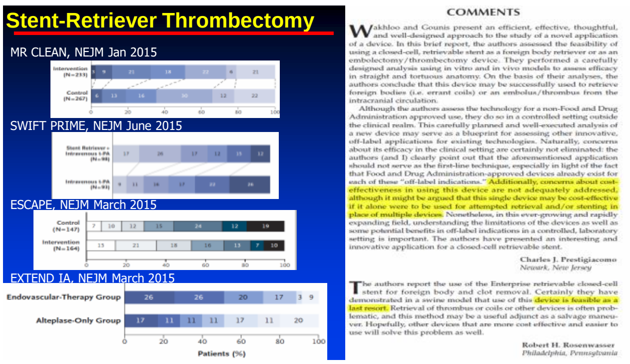
Challenges in Neuro IR





COMMENTS

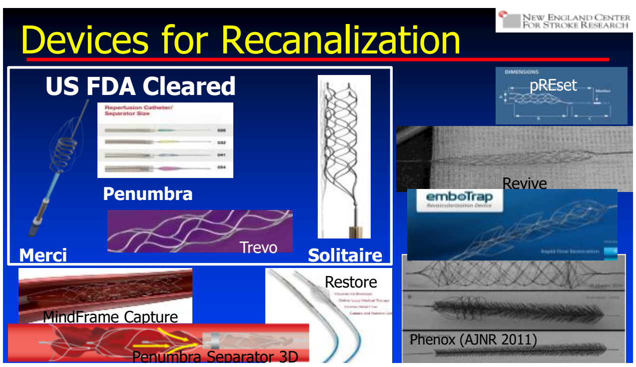
Wakhloo and Gounis present an efficient, effective, thoughtful, and well-designed approach to the study of a novel application of a device. In this brief report, the authors assessed the feasibility of using a closed-cell, retrievable stent as a foreign body retriever or as an embolectomy/thrombectomy 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



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New Generation of Cerebrovascular Devices

- ✓ Challenge in device development for cerebrovascular applications has historically been **MINIATURIZATION**
- ✓ New generation of manufacturing technology has enabled braiding wires as small as 25µm or laser cutting features as small as 5µm.
- ✓ Materials science developments are enabling a host of potential polymers and metals for endovascular implants
- ✓ Challenge – HOW CAN WE SEE THEM!

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Stents and Stent-retrievers

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Laser Cut Hypotubes

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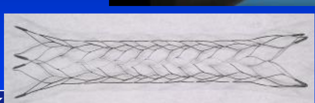

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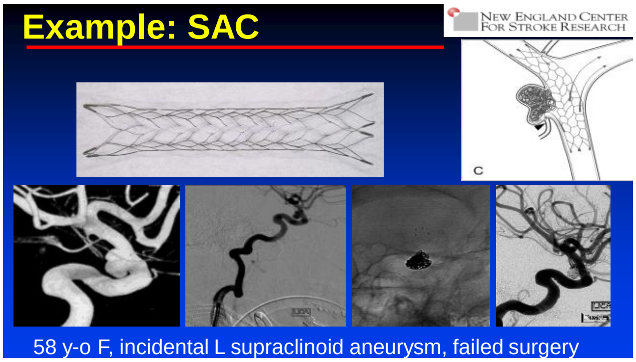
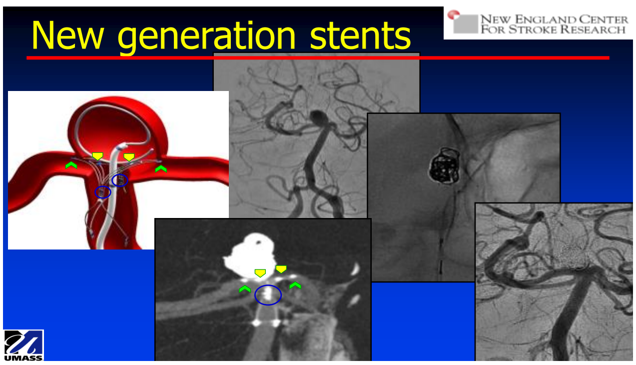
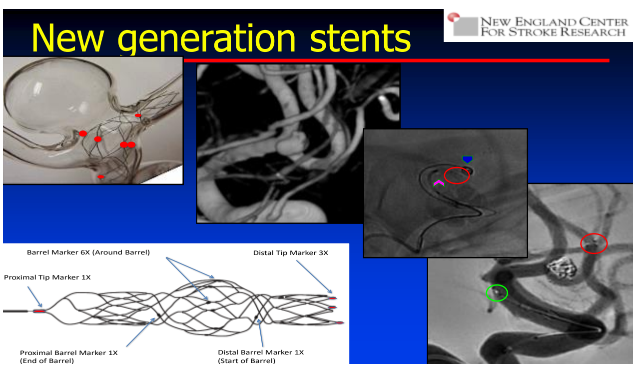
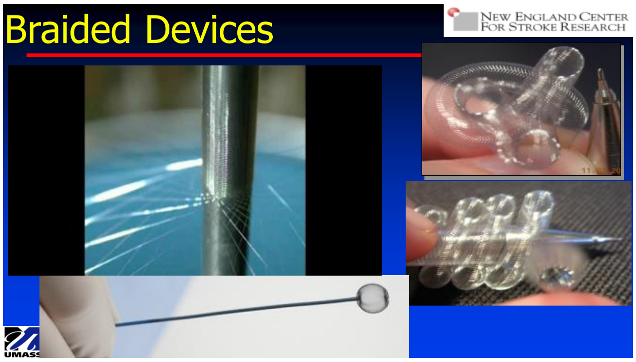
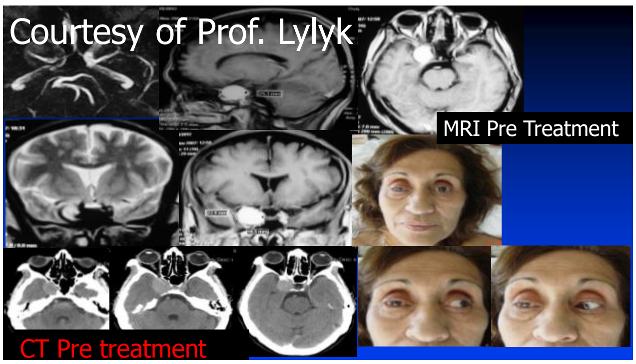
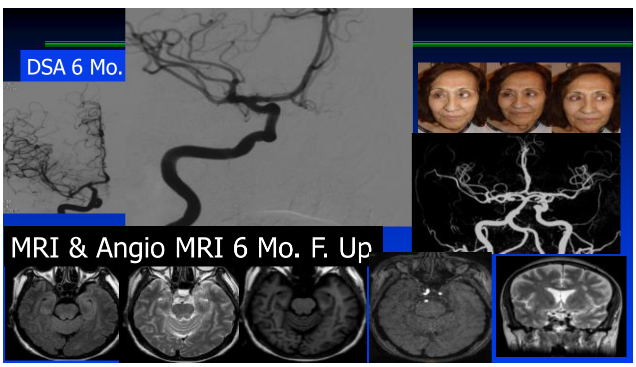

Example: SAC
New England Center
For Stroke Research
58 y-o F, incidental L supraclinoid aneurysm, failed surgery

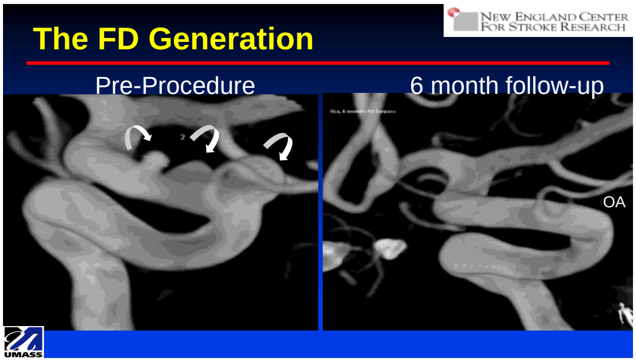

New generation stents
New England Center
For Stroke Research
UMASS

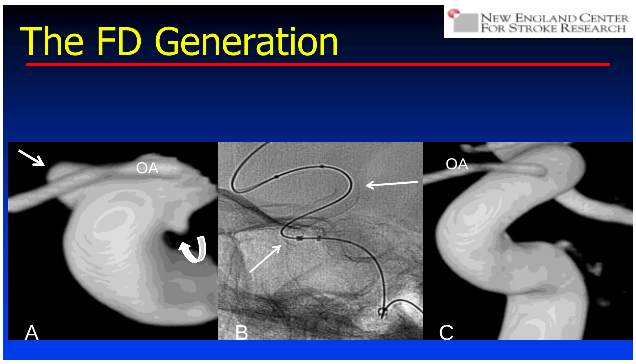

New generation stents
New England Center
For Stroke Research
Barrel Marker 6X (Around Barrel)
Distal Tip Marker 3X
Proximal Tip Marker 1X
Proximal Barrel Marker 1X
(End of Barrel)
Distal Barrel Marker 1X
(Start of Barrel)

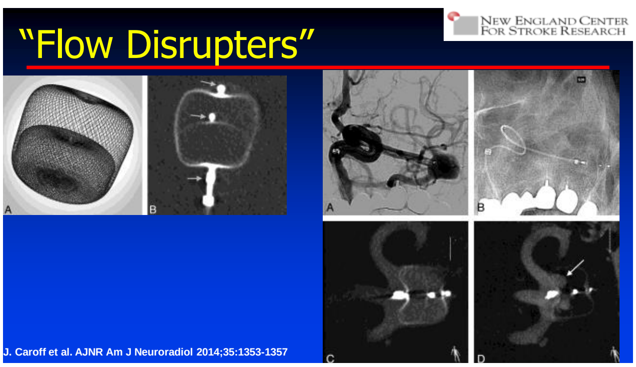

Braided Devices
New England Center
For Stroke Research


Courtesy of Prof. Lylyk
MRI Pre Treatment
CT Pre treatment


DSA 6 Mo.
MRI & Angio MRI 6 Mo. F. Up


New England Center For Stroke Research
The FD Generation
Pre-Procedure
6 month follow-up
OA
UMASS


New England Center For Stroke Research
The FD Generation
OA
OA
A
B
C


New England Center For Stroke Research
"Flow Disrupters"
A
B
A
B
C
D
J. Caroff et al. AJNR Am J Neuroradiol 2014;35:1353-1357

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Application-Specific Requirements

- FAST reconstruction – minutes
  - Typically ~2 min
  - Information is acted on (peri-procedural)
- Full-brain coverage preferred
- ~50 µm spatial resolution
- Contrast resolution: device, vessel (iodine) and brain

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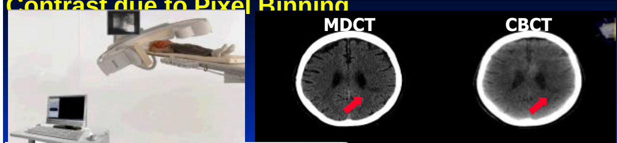
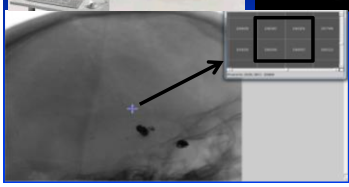
XperCT (DynaCT): CT-like Soft Tissue Contrast due to Pixel Binning





2×2 pixel binning:
- ✓ Reduce noise by averaging signals ⟶ soft tissue contrast
- ✓ Reduce data to be transferred through imaging pipeline
- ✓ Reduce reconstruction time
- ⁻ Reduce spatial resolution

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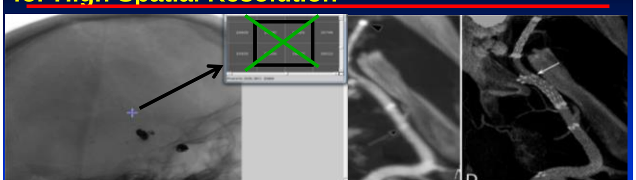
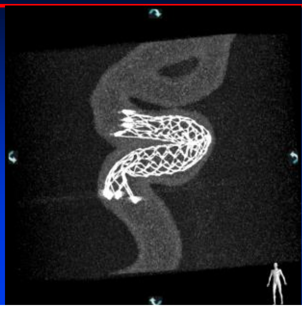
VasoCT: Non-Binned Reconstruction for High Spatial Resolution

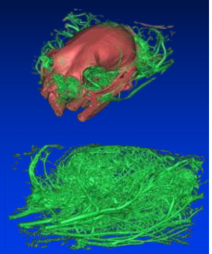


Non-binning performed to:
- ✓ Enhance spatial resolution ⟶ fine detail
- ✓ Reduced detector format to control data and reconstruction time
- ⁻ Lower signal-to-noise

Patel et al, AJNR 32, 2011

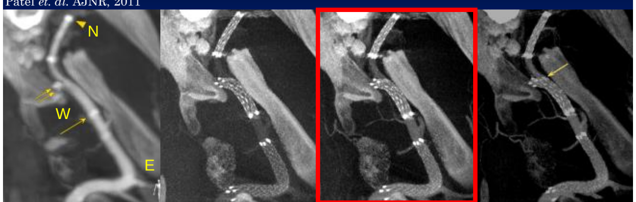
Bench/Animal - VasoCT





Contrast Injection Optimization

Patel *et. al.* AJNR, 2011



Conventional CBCT | HiRes @ 10% | HiRes @ 20% | HiRes @ 30%

IsoVue 370 (20%) – If using IsoVue 250 or Omnipaque 240 ~30%; 3ml/s for 75ml with 5s delay

Phase II: Clinical Evaluation

- IRB Approved
- 57 CBCT examinations (55 patients)
- 52 Included, 5 Excluded
- 54% GA, 46% CS
- 44 post coil
- Blinded Review (3 experienced interventional neuroradiologists from various institutions)

Patel *et. al.* AJNR, 2011

Summary of Clinical Results

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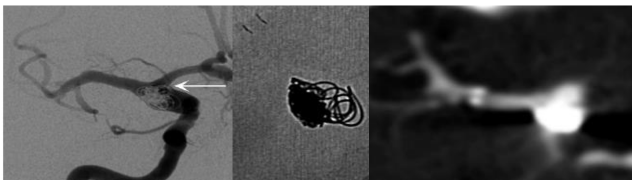
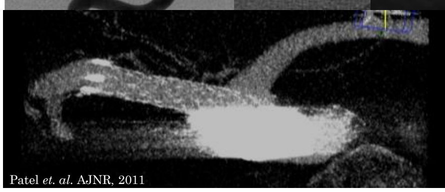
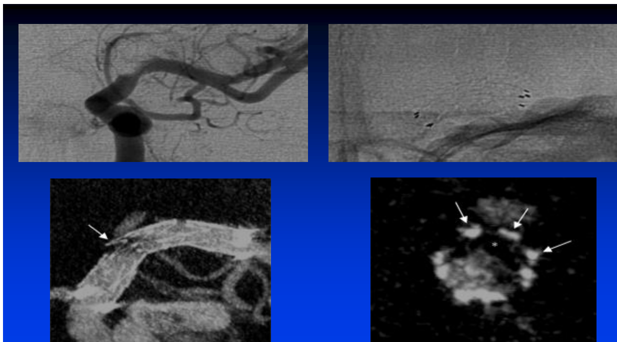
- Strengths
  - Reliably adequate visualization (> 95%)
  - In most cases, excellent visualization (> 60%)
  - 29% with notable findings
- Limitations
  - **Stent-coil relationship in 25%**
  - Low ICC for vessel quality
- Work in Progress
  - Intravenous contrast administration
  - Photon starvation

UMASS | Bench → Preclinical Model → Clinical Evaluation

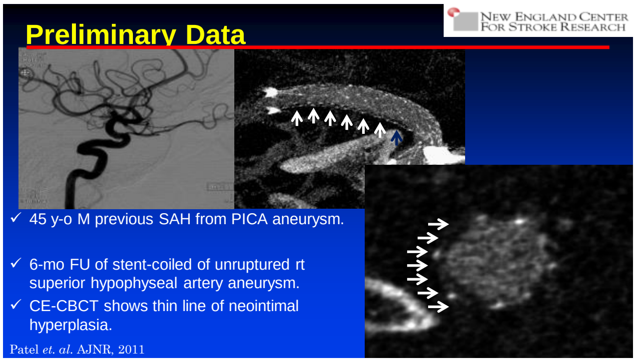



Patel *et. al.* AJNR, 2011

- 60 y-o f, R ICA aneurysm
- post-SAC embolization
- A1 Protected?



Patel *et. al.* AJNR, 2011



Preliminary Data
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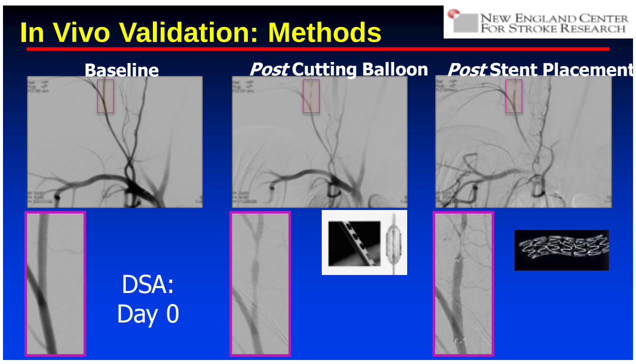
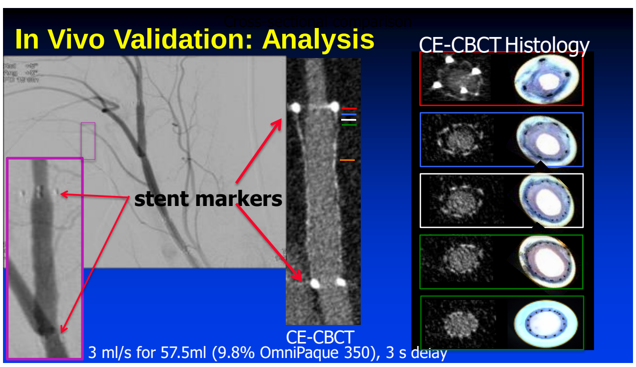
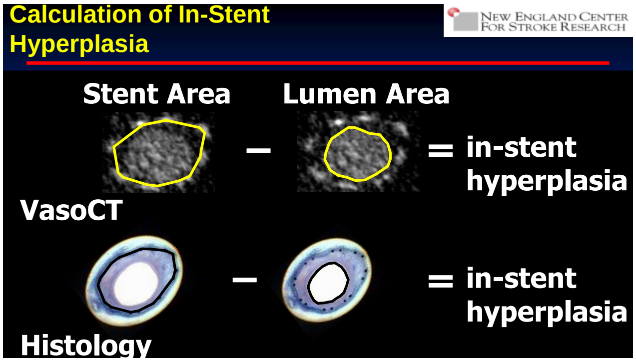
✓ 45 y-o M previous SAH from PICA aneurysm.
✓ 6-mo FU of stent-coiled of unruptured rt superior hypophyseal artery aneurysm.
✓ CE-CBCT shows thin line of neointimal hyperplasia.
Patel et. al. AJNR, 2011

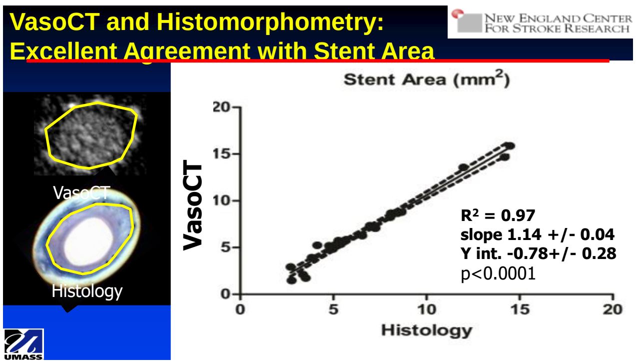


In Vivo Validation: Methods
New England Center For Stroke Research
Baseline
Post Cutting Balloon
Post Stent Placement
DSA:
Day 0



In Vivo Validation: Analysis
CE-CBCT Histology
stent markers
CE-CBCT
3 ml/s for 57.5ml (9.8% OmniPaque 350), 3 s delay


Calculation of In-Stent Hyperplasia
New England Center For Stroke Research
Stent Area
Lumen Area
– = in-stent hyperplasia
VasoCT
– = in-stent hyperplasia
Histology


VasoCT and Histomorphometry: Excellent Agreement with Stent Area
New England Center For Stroke Research
VasoCT
Histology
Stent Area (mm²)
VasoCT
Histology
0
5
10
15
20
R² = 0.97
slope 1.14 +/- 0.04
Y int. -0.78+/- 0.28
p<0.0001
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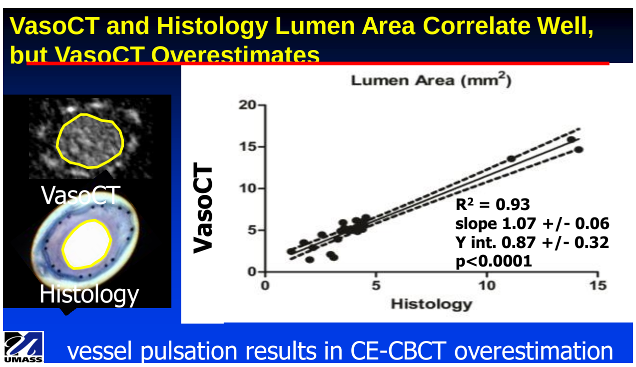
VasoCT and Histology Lumen Area Correlate Well, but VasoCT Overestimates
VasoCT
Histology
Lumen Area (mm²)
VasoCT
Histology
0
5
10
15
20
R² = 0.93
slope 1.07 +/- 0.06
Y int. 0.87 +/- 0.32
p<0.0001
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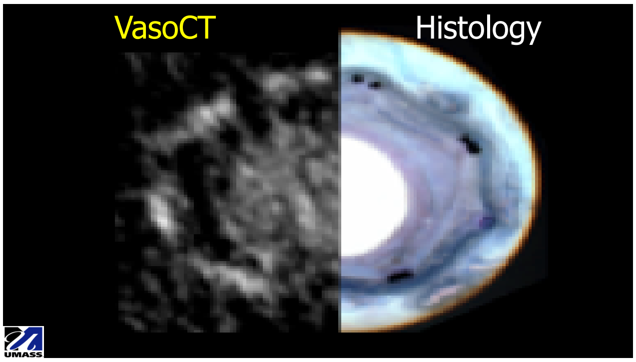
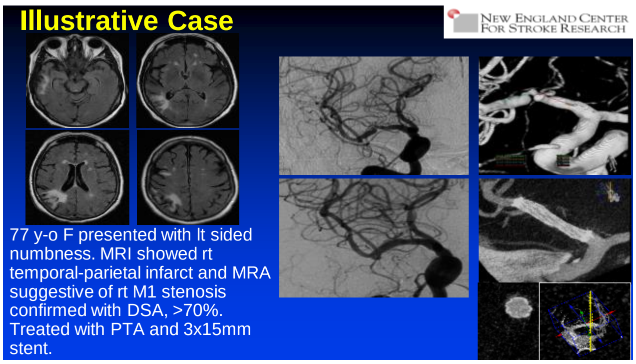
vessel pulsation results in CE-CBCT overestimation


VasoCT
Histology
UMASS


Illustrative Case
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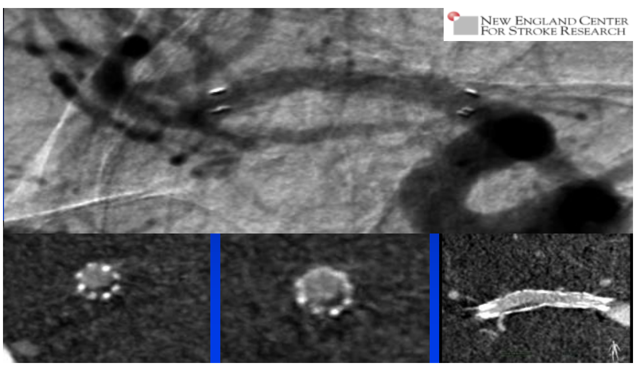
77 y-o F presented with lt sided numbness. MRI showed rt temporal-parietal infarct and MRA suggestive of rt M1 stenosis confirmed with DSA, >70%. Treated with PTA and 3x15mm stent.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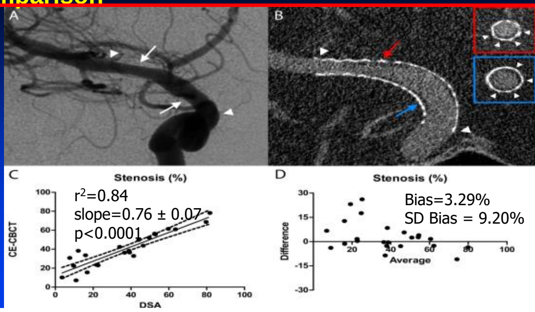
VasoCT-DSA Clinical Comparison

New England Center For Stroke Research



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Summary

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- ✓ IA-VasoCT validated against gold-standard histomorphometry in an animal model
  - ✓ In Vivo imaging modality with nearly histological precision
  - ✓ Lower limit of neointimal hyperplasia is 0.79 mm^2
- ✓ Clinical evaluation demonstrates practical workflow, and agreement with gold-standard DSA
  - ✓ IV VasoCT requires further evaluation
  - ✓ DSA must be in proper projection

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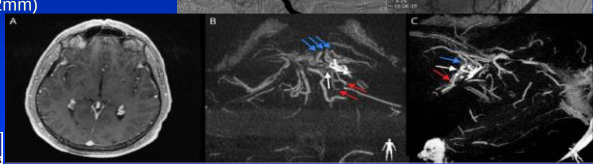
Other Applications: Micro-bAVMs

New England Center For Stroke Research

- 42 y-o M, ruptured bAVM Lt Superior Colliculus, 3mm.
- Post-embolization (nBCA) control angiogram shows complete obliteration
- 6,12 and 36 mo FU show continuous re-growth (~2mm)



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Other Applications: Micro-bAVMs

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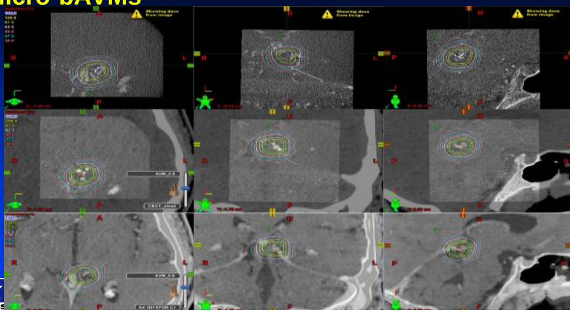

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Other Applications: Micro-bAVMs

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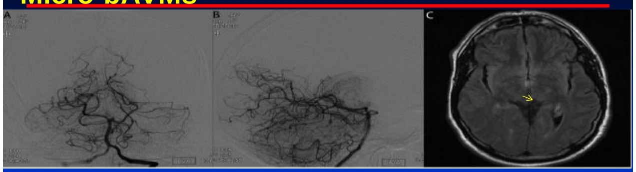

- 10-mo post-treatment DSA and MRI
- Complete cure of AVM with stereotactic radiosurgery
- No off-target side-effects

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Van der Bom et al. JNIS 2013

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Future Applications

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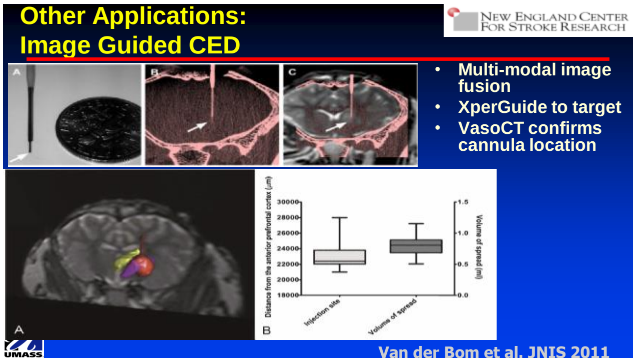
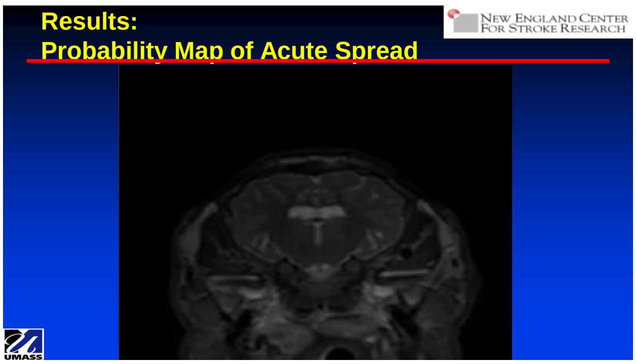

Other Applications:
Image Guided CED
New England Center For Stroke Research
Multi-modal image fusion
XperGuide to target
VasoCT confirms cannula location
Injection site
Volume of spread
Van der Bom et al. JNIS 2011
UMASS


Results:
Probability Map of Acute Spread
New England Center For Stroke Research
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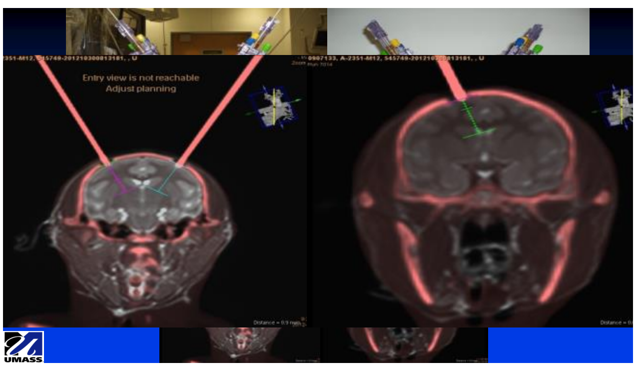
Entry view is not reachable
Adjust planning
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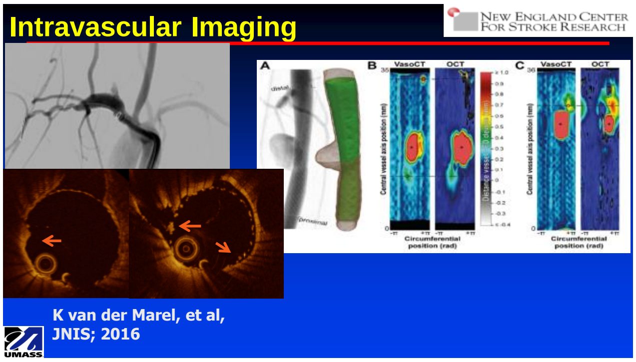
Intravascular Imaging
New England Center for Stroke Research
A
B
C
VasoCT
OCT
Circumferential position (rad)
K van der Marel, et al,
JNIS; 2016
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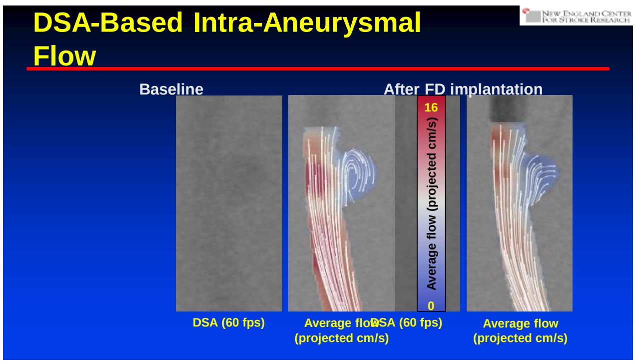
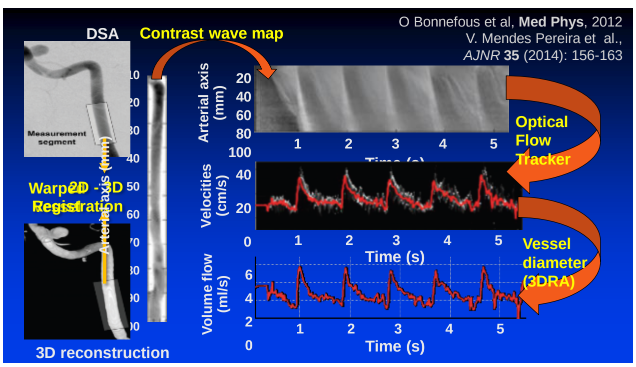
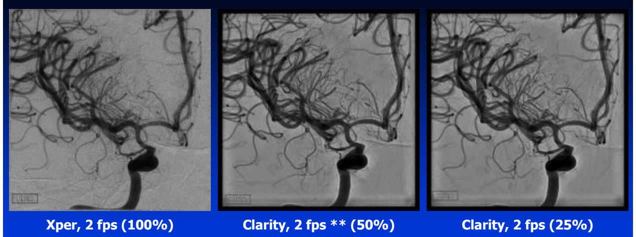

DSA-Based Intra-Aneurysmal Flow
New England Center for Stroke Research
Baseline
After FD implantation
16
Average flow (projected cm/s)
0
DSA (60 fps)
Average flow (projected cm/s)
DSA (60 fps)
Average flow (projected cm/s)


O Bonnefous et al, Med Phys, 2012
V. Mendes Pereira et al.,
AJNR 35 (2014): 156-163
DSA
Contrast wave map
Measurement segment
Warped 2D - 3D Registration
3D reconstruction
Arterial axis (mm)
Velocities (cm/s)
Volume flow (ml/s)
Time (s)
Optical Flow Tracker
Vessel diameter (3DRA)

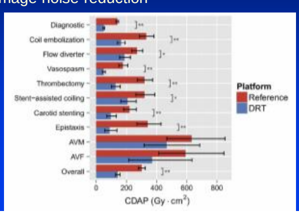
Dose Reduction

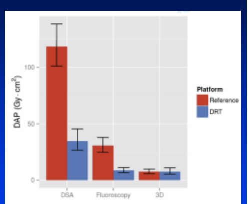


7/17/2014; 43 y/o M; diffusive SAH (supratentorial, R paramesial); diagnostic angiogram to assess source of bleeding

Clarity – 53% Dose Reduction

- Image Processing Chain
  - Real-time motion correction
  - Image contrast-dependent temporal averaging
  - Image noise reduction





- 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
  - Italo Linfante, MD - Baptist
  - Guilherme Dabus, MD - Baptist
  - Don Ingber, MD,PhD – Harvard
  - Netanel Korin, PhD-Technion
  - Johannes Boltze, MD, PhD

NECStR

- Ajay Wakhloo, MD, PhD
- Ajit Puri, MD
- Juyu Chueh, PhD
- Miklos Marosfoi, MD
- Frédéric Clarençon, MD, PhD
- Martijn van der Bom, PhD
- Kajo van der Marel, PhD
- Anna Kühn, MD, PhD
- Ivan Lylyk, MD
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- Erin Langan, BS
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- Chris Brooks, PA
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