NEW ENGLAND CENTER FOR STROKE RESEARCH

Mechanism of Flow Diverter Healing

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UMASS

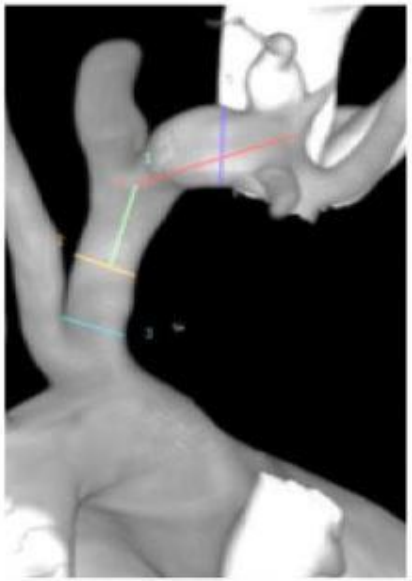
In Situ Tissue Engineering

- **The objective of this study:**
  - to demonstrate formation of the basement membrane and subsequent endothelialzation rates as a function of FD design

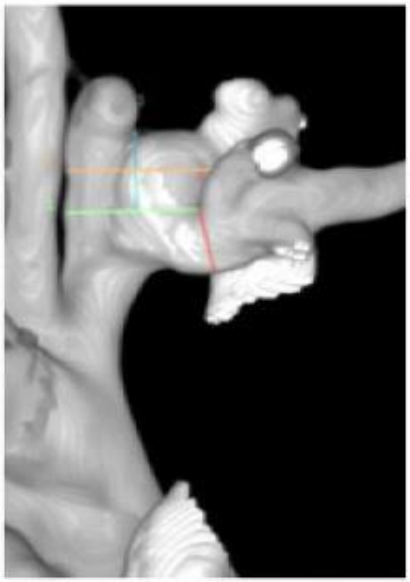
Study Design

Animal grouping	Number of 72-wire FDs	Number 48-Wire FDs	FD implant procedure	Duration
Group 1	2	2	4	**10 (± 1) days**
Group 2	2	2	4	**20 (± 2) days**
Group 3	2	2	4	**30 (± 2) days**
Group 4	2	2	4	**60 (± 2) days**
Totals	8	8	16	

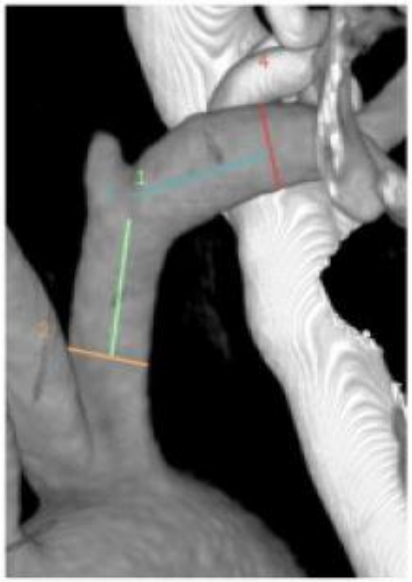
DAPT: 10mg/kg clopidogrel and 1mg/kg ASA



wide neck aneurysm along with distal fusiform vessel



complex, multilobular aneurysm

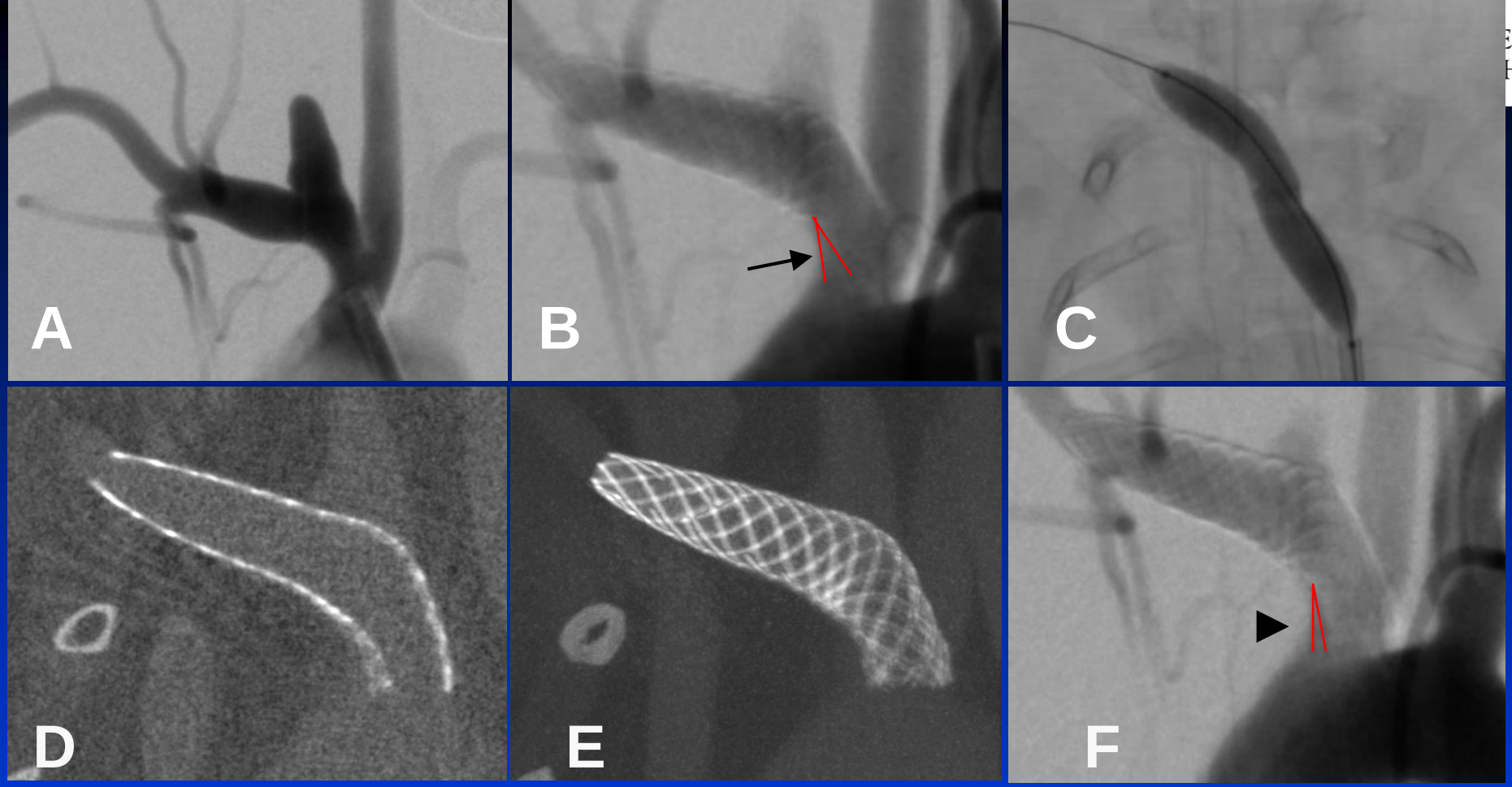


small aneurysm with wide neck and distal fusiform vessel

small neck aneurysm along with distal fusiform vessel

- **Grouping of aneurysm was based on:**
  - **aneurysm morphology**
  - **Vessel diameter proximal and distal to the aneurysm**
  - **Length of proximal segment of the vessel – landing zone!!**

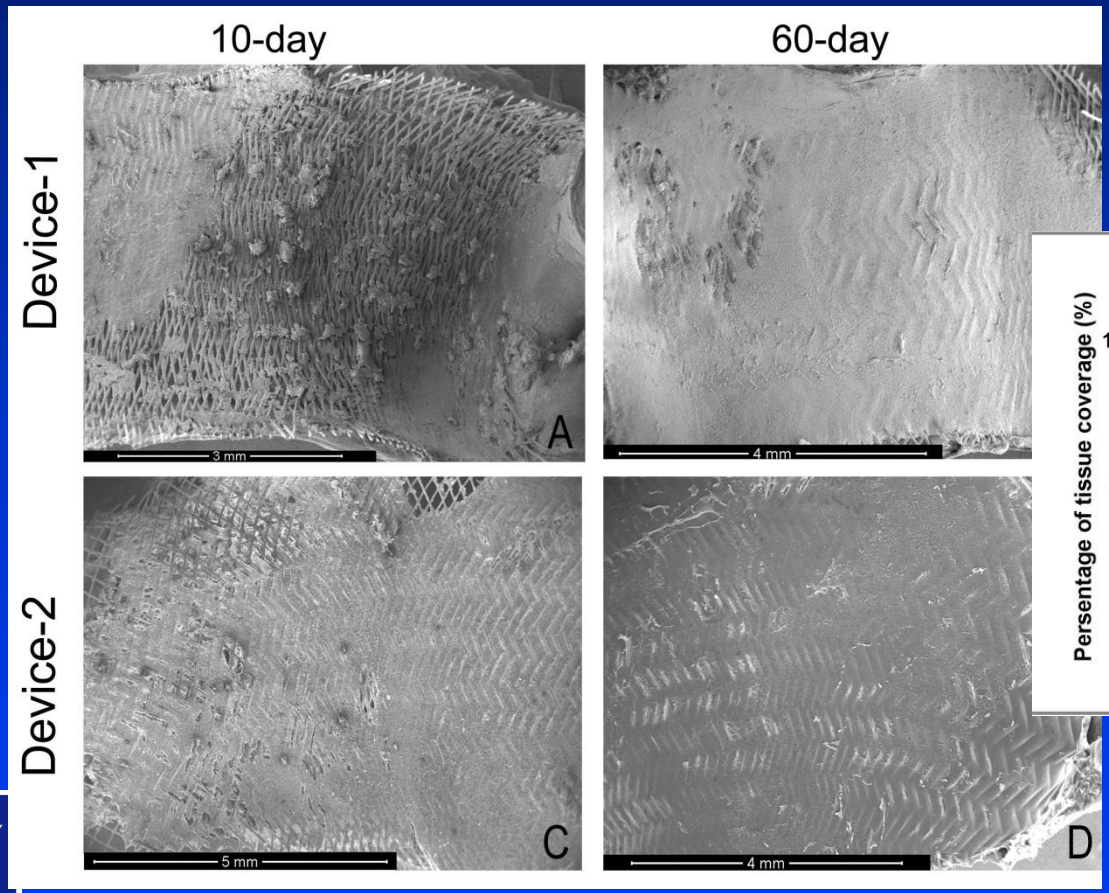
	48-wire	72-wire	p-value
aneurysm height	6.9 ±1.8	7.1 ±1.6	0.86
aneurysm width	5.5 ±2.3	5.0 ±1.9	0.64
aneurysm neck	5.3 ±1.9	4.6 ±1.4	0.47
aspect ratio	1.4 ±0.5	1.6 ±0.4	0.42
parent vessel diameter 5mm distal the aneurysm	4.6 ±1.0	4.4 ±0.6	0.64

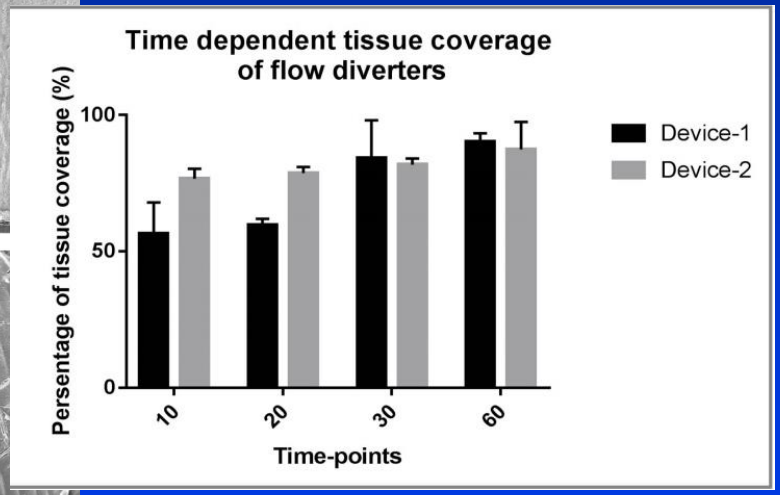


A.) Pre-procedural DSA, frontal view
B.) Post-implant angiography, FD is not apposed at the proximal site;
C.) angioplasty
D-E.) VasoCT, distal end of FD slightly compressed (deployed into a 2.5mm vessel), part bad apposition proximally
F.) after 2 attempt of angioplasty DSA showed improved apposition (arrow-head)

Basement Membrane

- Important first step, forms substrate for endothelialization





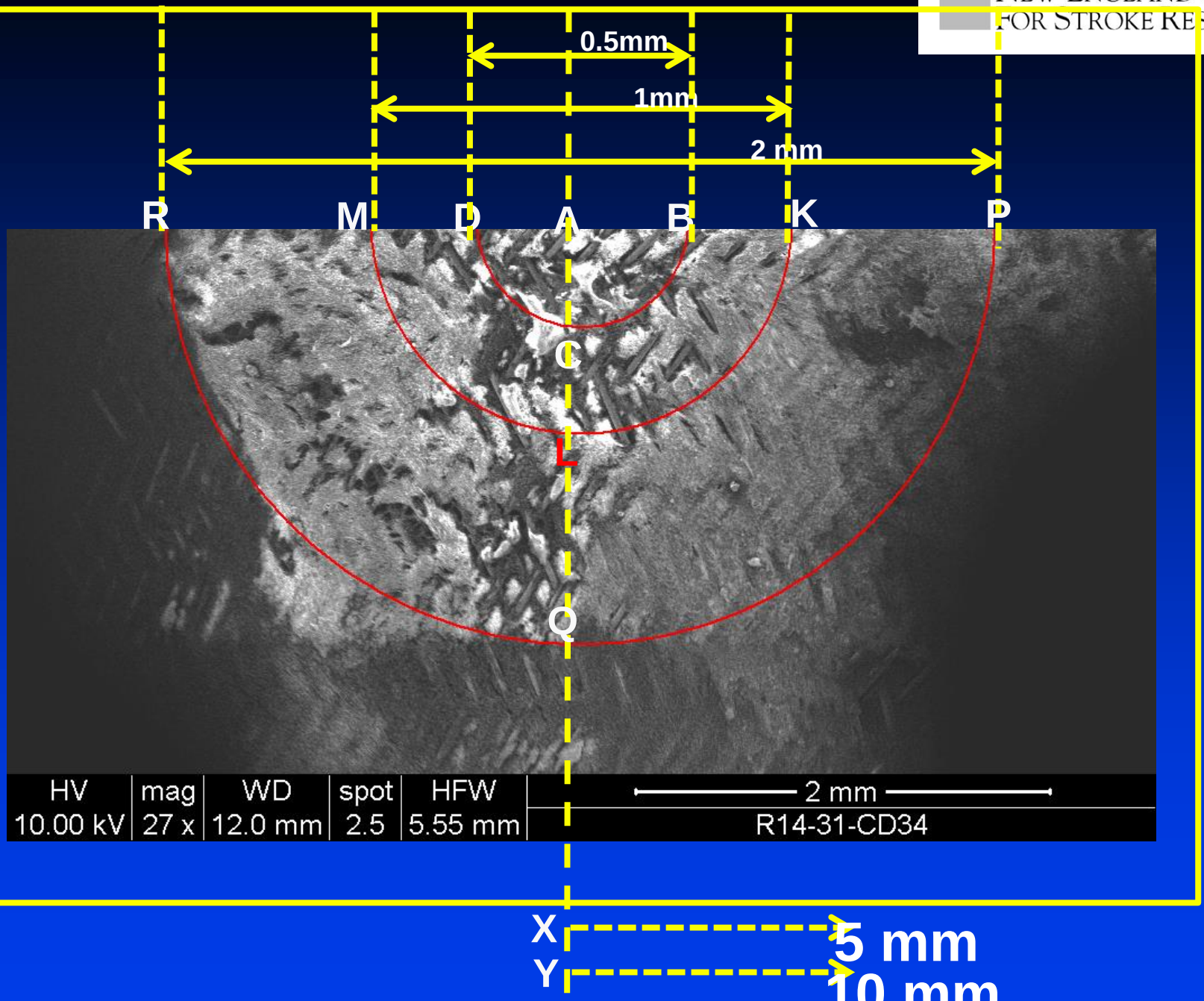
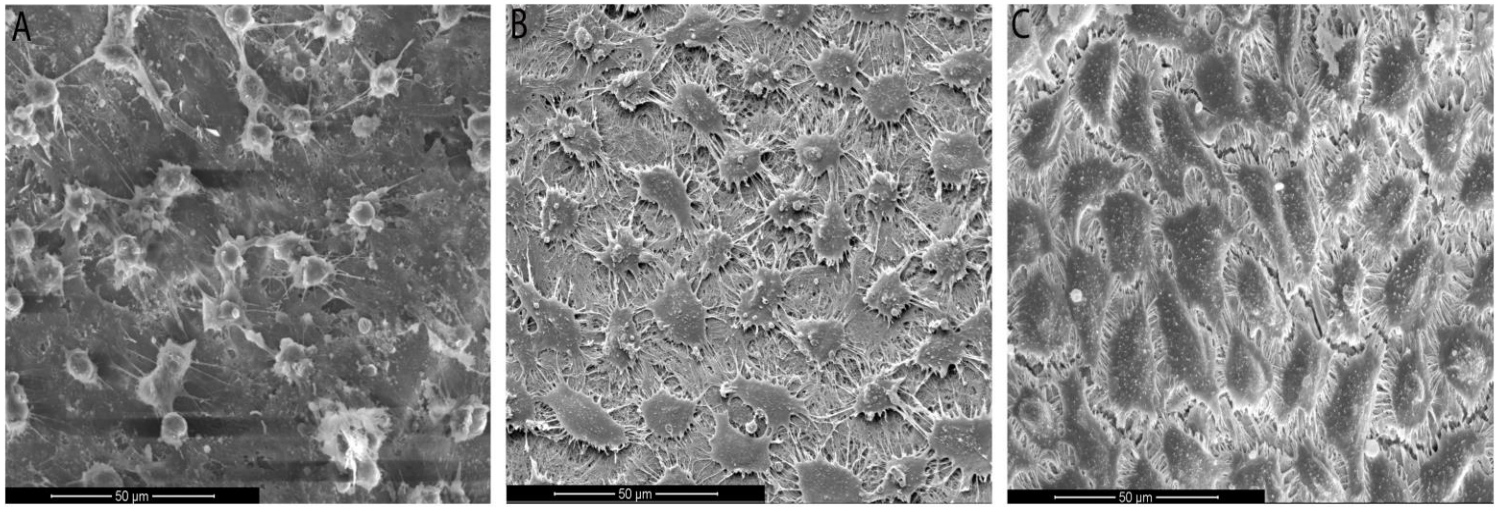
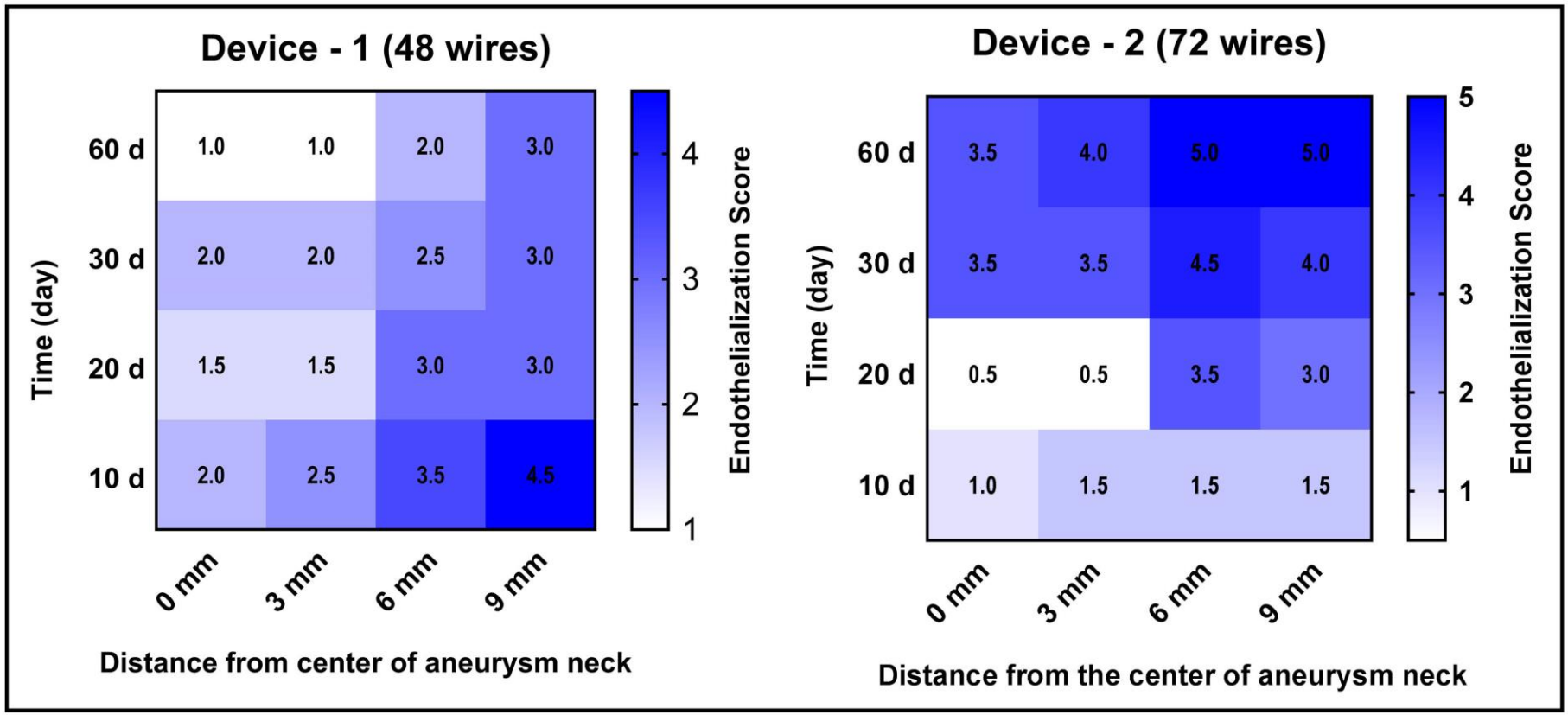

0.5mm
1mm
2 mm
R
M
D
A
B
K
P
C
L
Q
HV
10.00 kV
mag
27 x
WD
12.0 mm
spot
2.5
HFW
5.55 mm
2 mm
R14-31-CD34
X
Y
5 mm
10 mm

Table 1. Scoring system for assessing the rate of flow diverter endothelialization (S-FDE)

Score	Coverage of Struts	Description of Coverage
0	0%	No coverage
1	1-25%	Contains EPCs, inflammatory cells, red blood cells, proteins, and other components such as fibrin and collagen
2	26-50%	Contains EPCs, inflammatory cells, red blood cells, proteins, and other components such as fibrin and collagen for the beginning of the basement membrane
3	51-75%	Contains EPCs, inflammatory cells, red blood cells, proteins, and other components such as fibrin and collagen creating the basement membrane
4	76-99%	Contains EPCs and/or endothelial cells along with the components of the basement membrane
5	100%	Fully Endothelialized

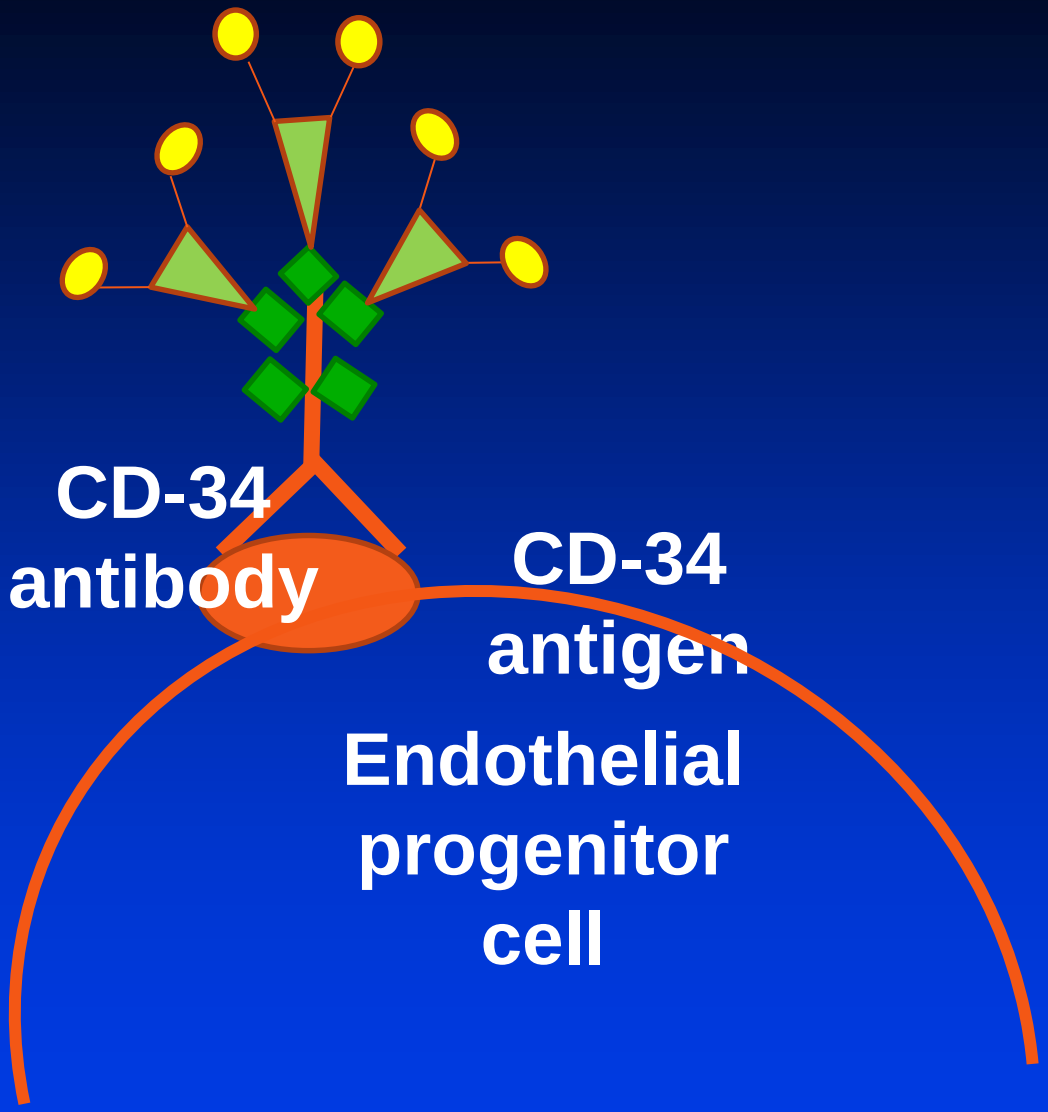


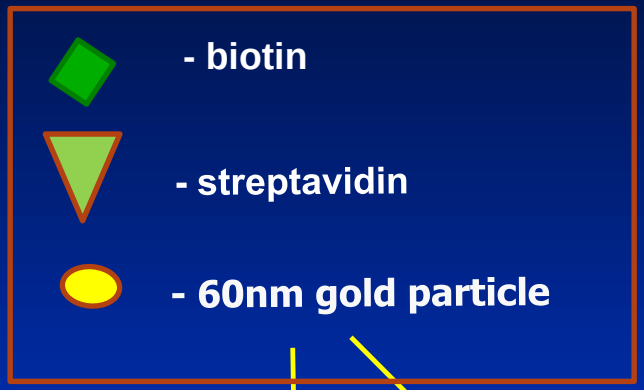
Endothelialization

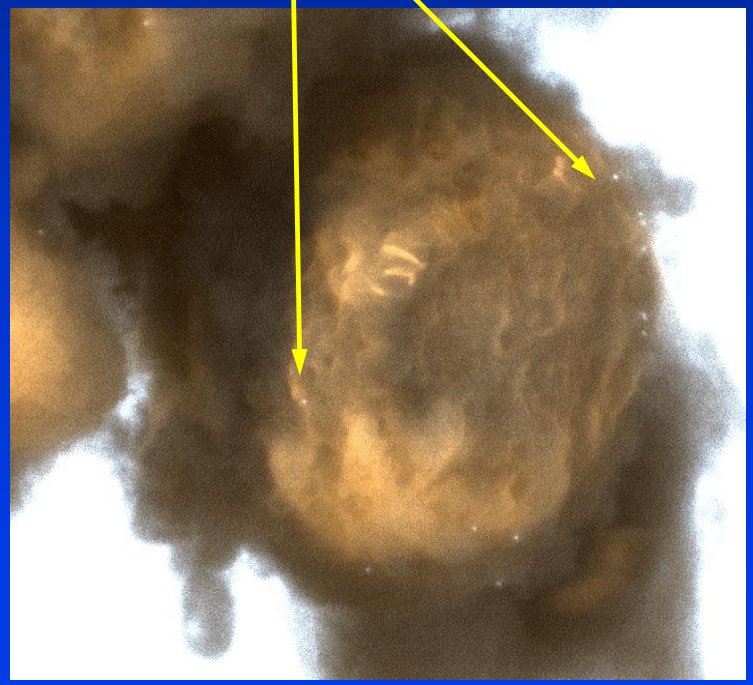


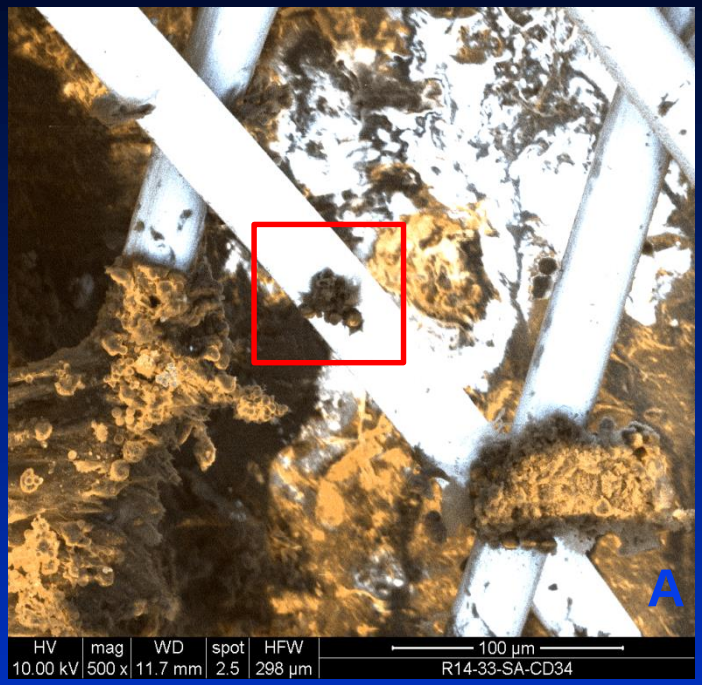
- 48-Wire (Device-1): EC scores related to location (p=0.083)
- 72-Wire (Device-2): EC scores are function of time (p=0.013)

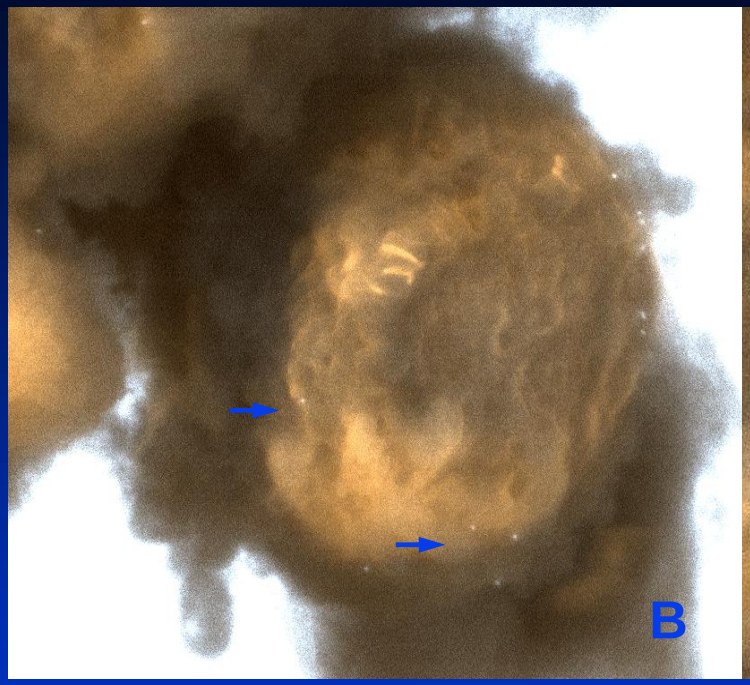
Immuno-gold labeling for SEM

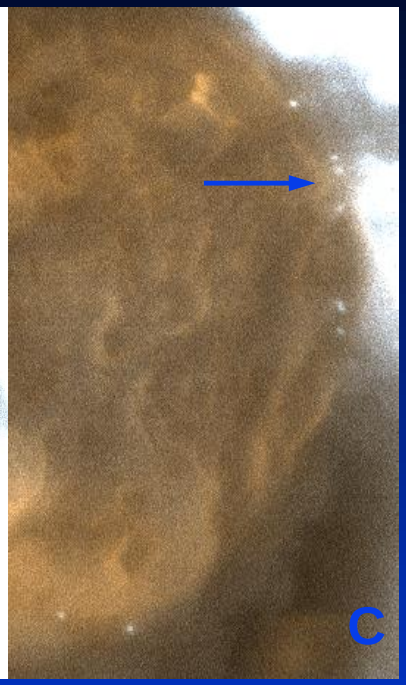












A.) 500x, image of the inner surface of the NEG implant, 10days after implantation

B.) 10,000x, the immuno-gold labeling on the surface of the cell (white arrows)

C.) manually zoom of the image B for better visualization of the gold nanoparticles

Flow Diversion: Summary

- Evidence: curative treatment of brain aneurysms
  - Treats diseased segment of the blood vessel
  - Endoluminal reconstruction is ideal
- Engineer construct and surface properties to promote rapid endothelialization
- Need to remove dependency on dual antiplatelet medication
- Need imaging tools developed specifically for technology to ensure proper deployment

NECStR

New England Center For Stroke Research

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  - Alexei Bogdanov, PhD
  - Greg Hendricks, PhD
  - Guanping Gao, PhD
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