ESC Heart & Brain Workshop

Innovation: The Future of Stroke Treatment
North American and Personal Perspective

Supported by Bayer, Bristol-Myers Squibb and Pfizer Alliance, Boehringer Ingelheim, Daiichi Sankyo Europe GmbH and Medtronic in the form of educational grants. The scientific programme has not been influenced in any way by its sponsors.
Stroke: Next Horizon in Medicine
The Game Has Changed

Major Opportunity; Major Challenges

INNOVATION is Key

L.N. Hopkins, MD
SUNY Distinguished Professor Neurosurgery and Radiology
Founder: Gates Vascular and Jacobs Institute

Elad Levy, MD
Adnan Siddiqui, MD, PhD
Ken Snyder, MD, PhD
Jason Davies MD, PhD

University at Buffalo Neurosurgery
Disclosure Statement of Financial Interest

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

Affiliation/Financial Relationship

- Grant/Research Support
- Consulting Fees/Honoraria
- Major Stock Shareholder/Equity
- Royalty Income
- Ownership/Founder
- Intellectual Property Rights
- Other Financial Benefit

Company

- Toshiba, Medtronic, Microvention
- None
- Claret, Boston Scientific, Medina, Ostial, Apama, Ocular, Silk Road, TSP
- None
- None
- None
- None
16 Million Strokes per Year
World wide

Patient Outcomes
• 1/3 recover
• 1/3 die
• 1/3 destroyed
Until 2015

*All we had was tPA*

- FDA-approved stroke treatments (up to 2016)
  - 1) IV tPA
    - Time constraints
    - 22 exclusion criteria
    - Ok for small distal vessels, not LVO
  - ~60% dead or disabled at 60 days

*Smith et al: Stroke 36:1432-38, June 2005*
Can Stroke be Reversed?

Y E S !!
Nothing in Medicine Matches the Staggering Change...  
*From Severe Stroke One Minute to Normal the Next*
A Rando Treatmen
O.A. Berkhemer, P.S.S. Fr
W.J. Schonew
J. Staals, J.
P.A. Brouwen
E.J. van Dij
B.A.A.M. 
P.C. Vroemen, O. Es
A.V. Tielenk, H.M. den
E.W. Steyerberg, H.Z. Fl
L.F.M. Beenen, R. van de

The NEW

2015 Game Changer

MR CLEAN

REVASCAT

MR CLEAN

REVASCAT

THRAICE

THERAPY

SWIFT PRIME

EXTEND-IA
What’s the Catch?

Time IS Brain
We are approaching coronary reperfusion rates, BUT...

The clinical results (MRS) are not so good

Trends in complete reperfusion rates in coronary and cerebral reperfusion trials

Saver JL, Stroke 2013;44:270-277
Time is Brain

Meaning What??

In each minute we lose:
- **1.9 million** neurons,
- **14 billion** synapses (connections)
- **12 km** (7.5 miles) of nerve fibers

New Data from 2015:
If we can reopen a blocked brain artery ...
Within 2 hours:
- **Recovery rate is 90% !!**

After 6 hours:
- **Recovery rate is 20-30% !!!!**
Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

CT perfusion-based patient selection

Is the Brain Viable??

Patient 1: has “penumbra” and likely to benefit from intervention

Patient 2: has volume loss (arrow) and no “penumbra”
## Co-primary endpoints

<table>
<thead>
<tr>
<th></th>
<th>Trevo</th>
<th>MM</th>
<th>Treatment benefit (95% CI)</th>
<th>Bayesian probability of superiority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 90 weighted mRS</td>
<td>5.5 ± 3.8</td>
<td>3.4 ± 3.1</td>
<td>2.1 (1.20, 3.12)</td>
<td>&gt;0.9999*</td>
</tr>
<tr>
<td>Day 90 mRS (0-2)</td>
<td><strong>48.6%</strong></td>
<td><strong>13.1%</strong></td>
<td>35.5% (23.9%, 47.0%)</td>
<td>&gt;0.9999*</td>
</tr>
</tbody>
</table>

**NNT for 90-day functional independence = 2.8**

*Similar to p<0.0001*
Amazing Parallels

Brain is much more sensitive to ischemia
Acute Ischemic Stroke Care Delivery

Best Model = Myocardial Infarction (stemi)

• “Time is Brain” >>> “Time is muscle”

• Rapid Revascularization is the goal

• How can we achieve Revascularization in < 2 hours??
  • Treatment location close to onset !!!
  • STEMI model- mandated door to revascularization times
Stroke Demographics

*Patients close to a Comprehensive Stroke Center are in luck \* OTHERS ARE NOT*

- >50% population in towns with < 30,000

- Most “Stroke Centers” are NOT Comprehensive
  - *Transfer times are long*

- Comprehensive Stroke Centers (CHS)
  - rare in cities with < 150,000
Why NOT Train Many More Neurointerventionalists?

Not enough work in small towns

*Where they need to be*

“Short transfer times” are a myth
16 Million Acute Ischemic strokes worldwide
30-40% amenable to clot removal
??? 24/7/365 Comprehensive Stroke Centers

TIME IS BRAIN...2 Hours!!!

Many more physicians needed...
Where will they come from??

New stroke Interventionists
In existing hospitals
How we do Stroke training
It’s All About Technology

Access
Getting to the clot
Safely removing it
Innovation: Devices
Evolution of stroke devices

- Microcatheters
- Wires
- 2016 clot retrievers
- ????????????????
And Practice...

Mentice Endovascular Simulation -
Any Interested MD with catheter skills can learn to do this

And create a Multidisciplinary Stroke Team

Population Health Demands a Solution

If we don’t do it... someone else will
Another possibility…

What Do Cardiologists Do All Day?

Fix narrowed and blocked arteries

... on Awake Patients

... on a Moving Target!!
Infrastructure for the provision of emergent endovascular care exists

Cardiac centers in most cities
Cardiac centers have the necessary tools

Acute stroke intervention techniques
- clot removal, angioplasty etc
- Similar for other interventionists

Training is absolutely necessary but...
- Better technology will shorten learning
- Training programs can be developed
For rural areas and smaller cities:

*a New Paradigm*

Retrieve the clot immediately and then ship to a major neuro center

If necessary

i.e. Get the artery open... First!!
The Public Health Urgency Created by the Success of Mechanical Thrombectomy Studies in Stroke

Authors

L. Nelson Hopkins MD\textsuperscript{1-4} and David R. Holmes Jr MD\textsuperscript{5}
INNOVATION IN STROKE CARE

Collisions ... Collaboration ... Innovation
Impact of Cardiovascular Disease and Stroke

- 1 in 3 adults (81.1 million in US) live with 1 or more types of cardiovascular disease.
- Leading causes of death and disability in the world
- Hundreds of billions of $$ economic loss every year.

Neuro, Cardiac, Peripheral

- Same Diseases
- Same Arteries
  - Vascular highway
- Similar Tools

Why are we not together?
Innovation

Building a Better Future for Stroke

Systems of Care

Technology

A North American Perspective
Stroke is a Complex Public Health Issue
Time Really IS Brain!!

Huge Public Health Challenges

Challenges

• Patient & Physician awareness
• Inertia
• Cataclysmic specialty shift
• Reimbursement
• Man Power
• Systems of care
• Technology

• SPEED to treatment goals:
  • Onset – revascularization < 2 hours
  • Home to ER door ~ 1 hour
  • ER Door – CT scan-- needle ~ 30 minutes
  • Needle to Revascularization ~ 30 min
Innovation in Systems of Care

New Infrastructure
Why a Vascular Center in Buffalo?

U.S. Stroke Belt
Why Buffalo?

Source: US Census Bureau Postcensal Population Estimates (ICD9 430-438.9)
Why a Vascular Center?

Number One Crippler and Killer
Heart    Head    Legs

Vascular Disease Specialists Work in Silos

Cardiology   Neurosurgery   Vascular Surgery   Radiology   Engineers   Physicists   Cell Biologists
Why a Vascular Center?

Goal #1: Break Down the Silos

Cardiology  
Vascular Surgery  
Radiology  
Physicists  
Cell Biologists
Goal #2:
Change the Treatment Paradigm

Future Vascular Care Delivery?
Goal #3: 
Build an Innovation Center

COLLISIONS. COLLABORATION. INNOVATION.

Independent Center for Innovation in Medicine
How the building was conceived …

**Multidisciplinary Collaboration**

Yazdani Studios & Jacobs Family

**FAILURE ANALYSIS ADVISORY COUNCIL (FAAC)**

**JACKSON HOLE, WYOMING**

Cardiology, Radiology, Vascular Surgery, NS, Vascular Med

**FINDING** Synergies for Better Patient Care
Clinical & Architectural Vision…
Vascular Center of the Future (25 Yrs)

Connectivity
Collaboration
Flexibility

Patients as Partners
- Wellness
- Research

University as partner
Hospital as partner
Industry as Partners
- Innovation
- Clinical Research
- Education

Independent Jacobs Institute

“Collisions”
Yazdani “Sandwich” Design Fits Vision

Meat = Jacobs Institute
Gates Vascular Institute

- Toshiba Stroke and Vascular Research Center
- Jacobs Institute i2R
- Cath Labs
- Vasc OR’s
- Hotel
- Emergency

Gates Vascular Institute
$300M
1 Acre Floorplate
Fourth Floor - 15 Cath Labs on One 1-Acre Floor Plate

Cath Labs

Control

Core

Collaboration Area

Patient Access
Innovation in Med Tech
The Usual Innovation Pathway
First Steps: Idea Evaluation & Raise $$$
Friends, Family, Angels, VC

i2R Shortcut
I2R Shortcut
First “Valley of Death”
IDEA TO PROOF OF CONCEPT

• 1-2 years
• 1-2 Million
• High energy
• Grit
• **90+% Failure Rate**
Jacobs Institute i2R Concept

i2R “Idea to Reality” Center = Idea to Proof of Concept
Improving the Process ...Avoiding the 1st Valley of Death

- i2R = Nascent idea to commercially ready product
- No up front cost for the Inventor...
  - JI equity or royalties if successful in the marketplace (5-10 years)
  - Failure... NO COST to the inventor
  - Success... JI gets minor equity stake (5-8%)
- Assistance with placement in an Accelerator

Innovation Funded by
Philanthropy in an Independent Not for Profit Environment
In the heart of a major clinical and research complex
Focus = Vascular Disease
Make a Prototype
Testing ... 3D patient specific vascular models
Mentice Endovascular Simulation
Toshiba Stroke and Vascular Research
Vivarium
Animal Models
Visitors get Excited

- Want to be part of it
- Companies donate equipment
- Trainees become ambassadors
OCCUPORTUNITY

Never a Better Opportunity for Buffalo

You’ll always miss 100% of the shots you don’t take.
an actual drawing, handed to a flight attendant on a Quantas flight by an 8 yr old girl

dear Captain
My name is Nicola I'm 8 years old, this is my first flight but I'm not scared. I like to watch the clouds go by. My mum says the crew is nice. I think your plane is good. thanks for a nice flight don't fuck up the landing

Luv Nicola
xx xx
Innovation
The Future of Medicine...and Neurosurgery

Come Innovate With Us