Propagating Ultrasound Energy Through a Catheter Around Bends For Treatment of Acute Ischemic Stroke

April 14th, 2010
Societal Impact

- 3rd Leading cause of death in the United States (≈150,000)

- #1 cause of major adult disability

- Estimated $65 billion in annual direct and indirect costs in the US alone.
  - Largest cost contributors are hospital costs, at home nursing, and lost productivity.

Source: CDC/NCHS.

Different Types of Strokes (or other ischemic events)

• **13% of strokes are hemorrhagic**
  – Not the focus of this presentation
  – Bleeding in and around the brain
  – Most interventional treatments in the neurovascular system are focused around aneurysms, one cause of some hemorrhagic strokes.

• **87% of strokes are ischemic (insufficient oxygenation)**
  – Decreased blood flow to a region of the brain causing various cell death mechanisms
  – Few treatment options

• **Transient ischemic attacks (TIA)**
  – Temporary blockages resulting in no apparent neurological deficit.
  – Not a stroke

Ischemic Stroke

Time is Brain!

- Cells die almost immediately
- Cells continue to die through several different pathways long after symptom onset

Panorama of Blood Flow to the Brain
Key Concept: The Ischemic Penumbra

This is brain that can be saved!

Large vessel ischemic stroke
Collateral flow
Ischemic Penumbra

Transmission of the Longitudinal Wave

This is our region of interest...

Converts longitudinal vibration generated by the transducer to transverse motion in the Wire’s Active Zone
Amplitude Terminology

- A1 and A2 are longitudinal amplitudes
- A3 is a transverse amplitude
Anatomical Challenges in Stroke

http://www.neuropat.dote.hu/table/angio.htm
**In-vivo Recanalization with 40kHz Prototype**

Acute animal study with Ajay Wakhloo & Matt Gounis (Dec 21, 2006)
Feasibility efficacy test in porcine model

- Autologous clot injected into Ascending Pharyngeal Artery (APA)
- Completely occlude 4-5cm length of APA
- 156cm long waveguide; .004” Ø Active Section; “Free Tip”
- Achieve nearly complete re-canalization of APA in minutes
Study Goal and Approach

• Goal:
  – Transmit energy, sufficient to emulsify clot, through tortuosity representative of the neurovascular anatomy

• Approach:
  – Develop a data driven understand of how acoustic waves travel around bends
  – Experimentally identify controllable parameters in our system that have a BIG IMPACT on transmission
Bends Reflect Waves

• If bend is small enough:
  – Wave will reflect
  – Reflections from bend = Reduced Transmission

- Reflected Wave Amplitude Increases
- A2 after the bend decreases
- A3 presumably decreases
BASELINE TRANSMISSION EXPERIMENTS AT 40 KHz
Tortuosity Causes Loss from Reflections at Bends

- **Transducer**: Wave driven from transducer

- **Active Section**: No significant reflections
  - Energy transmission is independent of bend location

- **Critical Bend Diameter (CBD)**: As bend Ø decreases:
  - Reflections are significant
  - Energy transmission is attenuated by bend
  - Dependent on bend location

- **Reflections above CBD**: No reflections above CBD

- **Reflections below CBD**: Wave reflected from bend

The diagram illustrates the impact of tortuosity on wave reflections and energy transmission as the critical bend diameter (CBD) decreases.
Baseline Experiments

- Transducer/Generator response to different waveguide bend configurations:
  - Single Bend Pullbacks
  - Double Bend Pullbacks

- Observe the longitudinal wave itself:
  - Single Bend Longitudinal wave Transmission (Laser)
  - Big Impact parameter identification
Laser Vibrometer Measurements

- Non-contact measurement
- Measure transducer output
- Characterize waveguide transmission up to the active zone

Measure acoustic waves in the transducer and waveguide proximal to the active zone
Characterization Pullbacks for 40kHz System

Single Bend Continuous Pullbacks...

- **Continuous Recording:**
  - Constant displacement generator electrical response (power* A1 = 5μm)
  - A1 (transducer amplitude) with Laser
  - At 40kHz: \( \lambda \) (Wavelength) = 12.3 cm
  - \( \frac{1}{2} \lambda = 6.16 \text{ cm} \)

- **High Power Locations** separated for all bend sizes by roughly 6 cm (at 40 kHz)
  - A1 (transducer amplitude) with Laser
  - At 40kHz

- **Difference in power between high and low power locations increases as bend ø decreases**

- **Repeated for bend diameters** – 3”, 2”, 1.5”, 1”, .75”, .5”, .25”

- Periodic audible & visible (active section movement) changes at 2” bend (at 40 kHz) – estimated to be the Critical Bend Diameter (CBD)

*Power is a measure of generator response to impedance changes
Double Bend Pullbacks

- All observations from single bend pullbacks are present and further compounded with two bends.

- If a bend is present in the waveguide which is both:
  - At or below CBD
  - In a low power location

- Then the power supply does not respond to changes in impedance or load if they occur distal to the bend.

- It seems that in the anatomy for stroke, the tightest bends tend to be the most distal (good).
Now on to the wave itself…
Needed to Answer Some Primary Questions

• What does the actual wave look like before and after a bend?

• What happens to the wave in different bend configurations?

Then…

• What effect do we have on transmission by changing drive amplitude (A1) and waveguide diameter (some simple controls)?
A2 Laser Measurements

Important for laser to be at apex for best signal

Incident Laser Beams from Source

Reflected laser fringe pattern back to sensor through optics

Direction of Waveguide Vibration

Axial Cross Sectional View

In Plane or Horizontal Cross Sectional View

Amplitude Maps

A2 Before the Bend

A2 After the Bend

Bend fixed in High or Low power location
Single Bend: Transmission Experiments

**Experimental Setup**

- Active Section
- Waveguide & Catheter
- Branson 40 kHz Transducer
- 2.0” Bend

**Amplitude “Maps”**

- Distal 8 cm measurement zone
- Proximal 8 cm measurement zone
- Move laser to discrete locations on the waveguide and measure wave amplitude

**Variables**

- Bend Size
- Bend Location (fixed in high or low power)
- Waveguide Diameter
- Drive Amplitude

**Measures**

- Amplitude “Maps” were taken of the proximal wave and distal wave directly off of the waveguide with the laser vibrometer
- Generator Electrical Response to configuration

Constant waveguide diameter throughout bend and measurement zones
Proximal and Distal Amplitude Maps

High Power Location

Low Power Location

Blue Line: Amplitude Map Proximal to bend
Red Line: Amplitude Map Distal to bend

Move laser to discrete locations on the waveguide and measure wave amplitude

- Branson 40 kHz Transducer
  - A1 = 5μm
As Bend $\phi$ Decreases to or below the Critical Bend Diameter (CBD):
- A2 After the Bend generally decreases
- Low power bend locations have smaller A2 after the bend than high power locations
- The difference between A2 after the bend for high power locations and low power locations increases
Limitations of a 40 kHz Ischemic Stroke System

• 40 kHz system was sufficient to prove basic feasibility:
  – System can transmit effective acoustic energy over a longer waveguide with a thin active section for neurovascular applications

• But…
  – Cannot transmit sufficiently through clinically relevant tortuosity (i.e., carotid siphon)

The solution is to increase the frequency of the system!

http://www.neuropat.dote.hu/table/angio.htm
The theory begins with the relationship between Critical Bend Diameter (CBD) and Wavelength ($\lambda$)...
Reduce Longitudinal Wavelength ($\lambda$) to Minimize Reflections

**THEORY:**
As $\lambda$ decreases, it requires smaller diameter bends to reflect the wave (CBD decreases).

**ANALOGY:**
Tighter turning radius (CBD) in a Mini Cooper than in a Greyhound Bus (wavelength).
Choosing Optimal Longitudinal Wavelength ($\lambda$)

• We want to pick a $\lambda$ that yields:

**Target CBD = 1/8” (For Stroke)**

So that any bend above that diameter is transparent to the wave…

$y (\text{CBD}) = 0.4134x (\text{lambda})$

Assuming a linear relationship between CBD and Wavelength, we can take the ratio at 40 kHz:

$\lambda = 12.3 \text{ cm}$

$CBD = 2”$ or $5.08 \text{ cm}$

Then, solve for the wavelength at the target CBD…

$\frac{\text{CBD}}{\lambda} = \frac{5.08}{12.3} = 0.413$
Wavelength is a Function of Frequency

\[ \lambda = \frac{c}{F} \]

- **\( F = 40 \text{ kHz} \)**
  - \( \lambda = 12.30 \text{ cm} \)
  - \( c = 491600 \text{ cm/s} \)

- **\( F = 80 \text{ kHz} \)**
  - \( \lambda = 6.15 \text{ cm} \)
  - \( c = 491600 \text{ cm/s} \)

\( c = \text{speed of sound} \)
\( \lambda = \text{wavelength (longitudinal in this case)} \)
\( F = \text{Frequency (Transducer Drive Frequency)} \)

(Double Frequency)

(Half \( \lambda \))
Choosing the Right Frequency:
Tortuosity Causes Loss from Reflections at Bends

- **Transducer**
  - Wave driven from transducer
  - Active Section
  - No significant reflections
  - Energy transmission is
    - Not attenuated by bend
    - Independent of bend location

- **Critical Bend Diameter (CBD)**
  - As Bend Ø decreases:
    - Reflections are significant
    - Energy transmission is
      - Attenuated by bend
      - Dependent on bend location
CBD was marked by periodic audible & visible (active section movement) changes

- **Measures**
  - Generator Electrical Response
  - A1 (Laser)
  - Periodic audible and visible changes during pullback

- **Variables:**
  - Bend Diameter (3”, 2” 1.5”, 1”, .75”, .5”, .25”)

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**Pullbacks: Identifying Critical Bend Diameter**

[Diagram of measurement method]
High Frequency Delivers Energy Around Smaller Bends

Critical Bend Diameter as a Function of Driving Frequency

Theory reinforced with the discovery of supportive scientific research from Poland*

Added bonus: Transducer size decreases dramatically & is likely to be easier to handle.