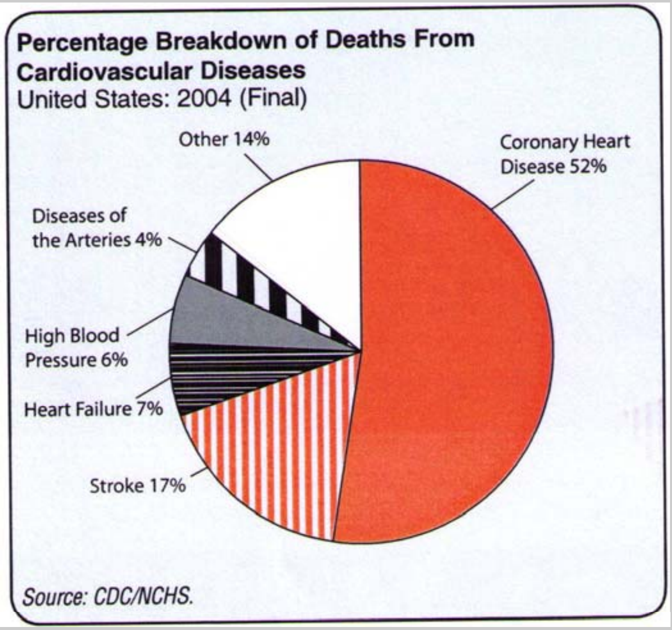
Propagating Ultrasound Energy Through a Catheter Around Bends

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.



Second largest contributor to deaths caused by cardiovascular diseases.

American Heart Association. Heart Disease and Stroke Statistics – 2008 Update. Dallas, Texas: American Heart Association; 2008. ©2008, American Heart Association

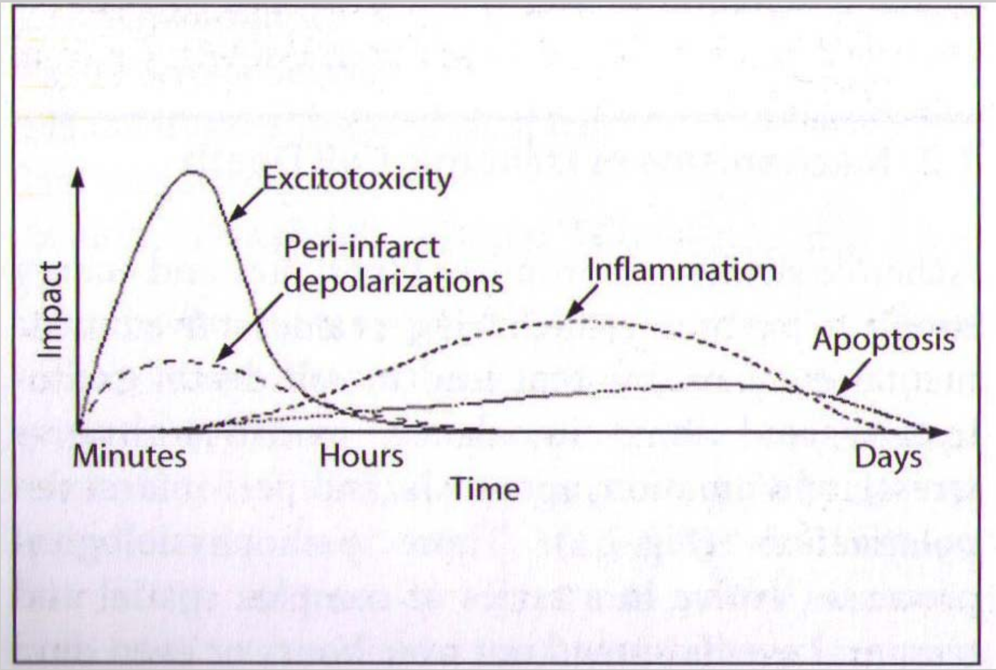
Different Types of Strokes (or other ischemic events)

- **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

American Heart Association. Heart Disease and Stroke Statistics – 2008 Update. Dallas, Texas: American Heart Association; 2008. ©2008, American Heart Association

Ischemic Stroke

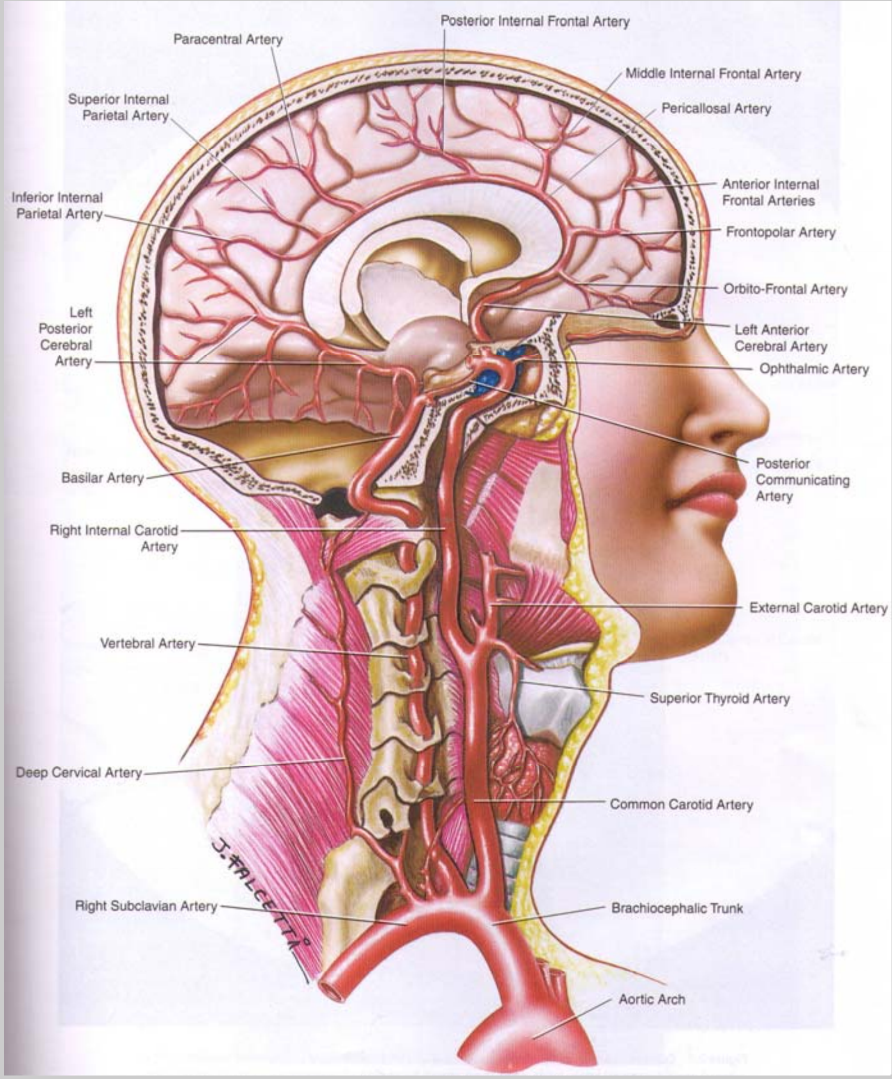
Time is Brain!

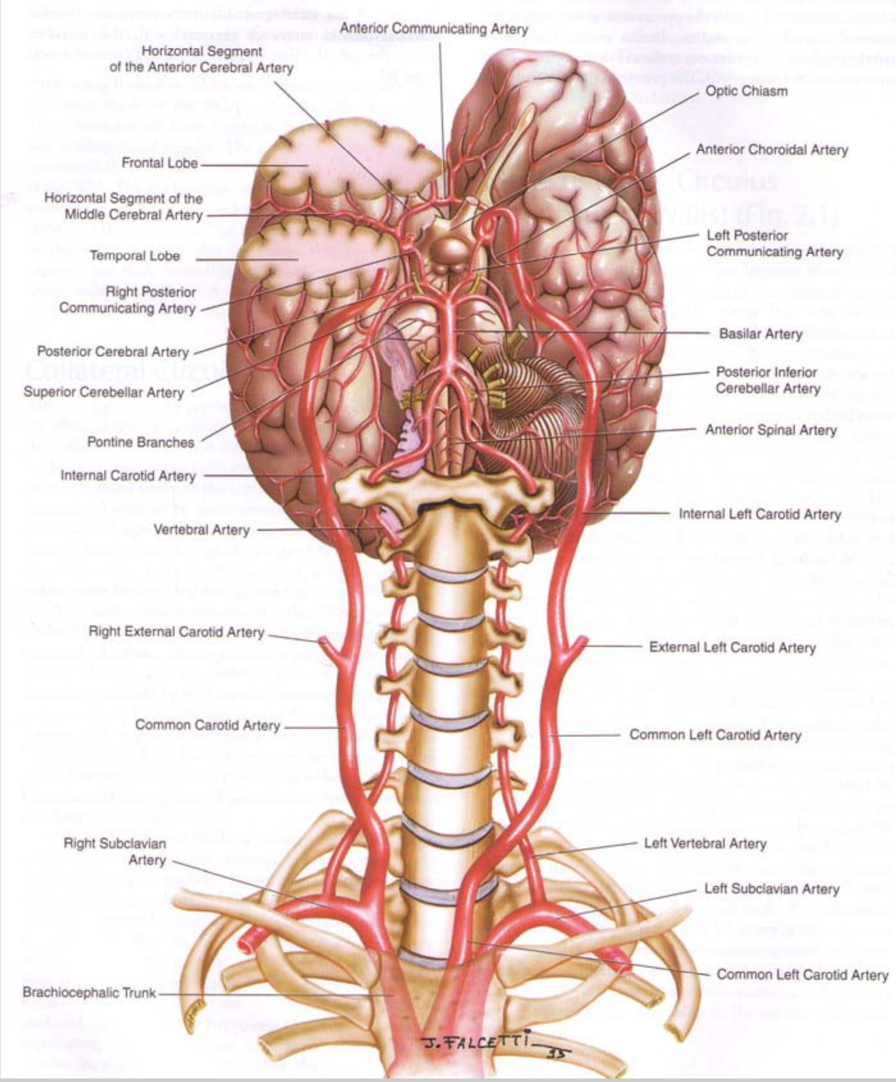


- Cells die almost immediately
- Cells continue to die through several different pathways long after symptom onset

Gonzalez, R.G., Hirsch, J.A., Koroshetz, W.J., Lev, M.H., Schaefer, P., Acute Ischemic Stroke Imaging and Intervention. ©2006 Springer-Verlag Berlin Heidelberg, Germany

Panorama of Blood Flow to the Brain





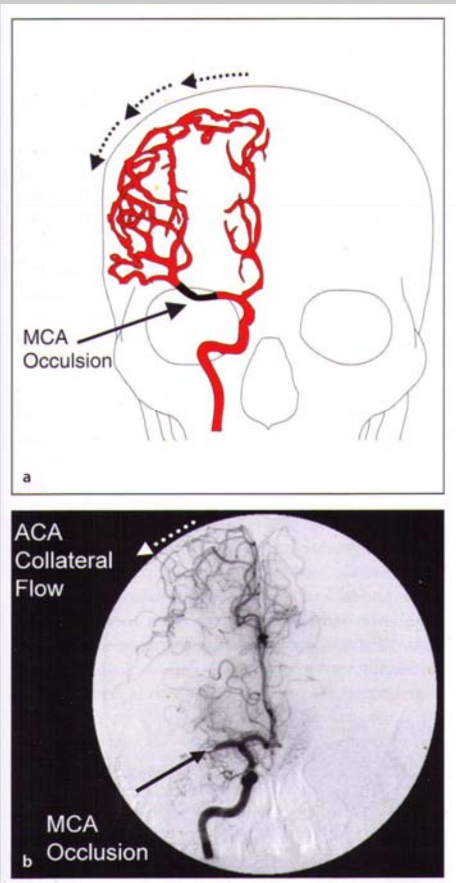
Uflacker, Renan, Atlas of Vascular Anatomy an Angiographic Approach. ©2007 Lippincott Williams & Wilkins, Philadelphia, PA

Key Concept: The Ischemic Penumbra

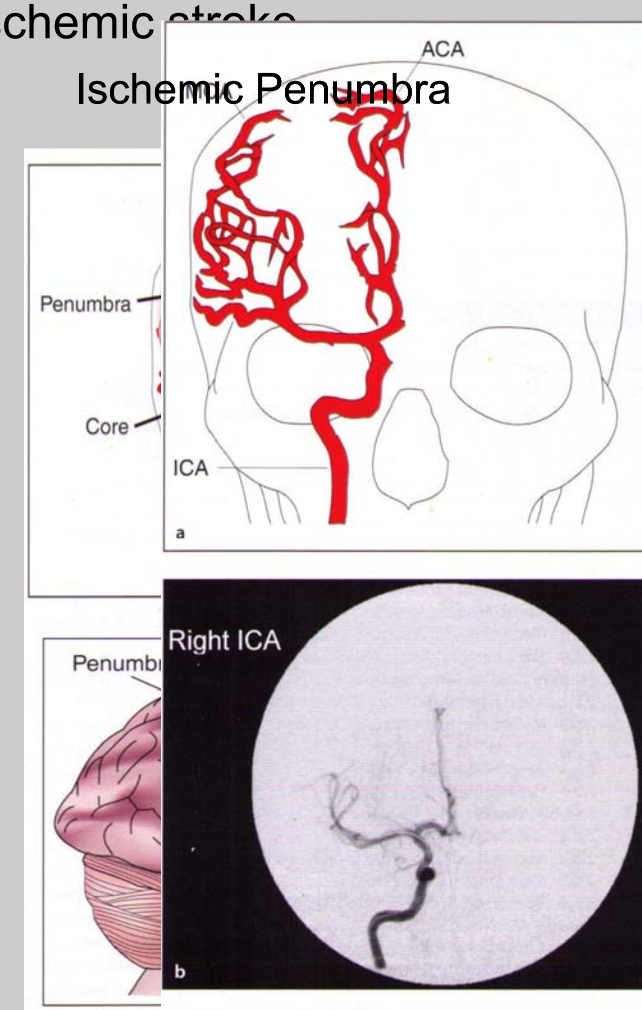
This is brain that can be saved!

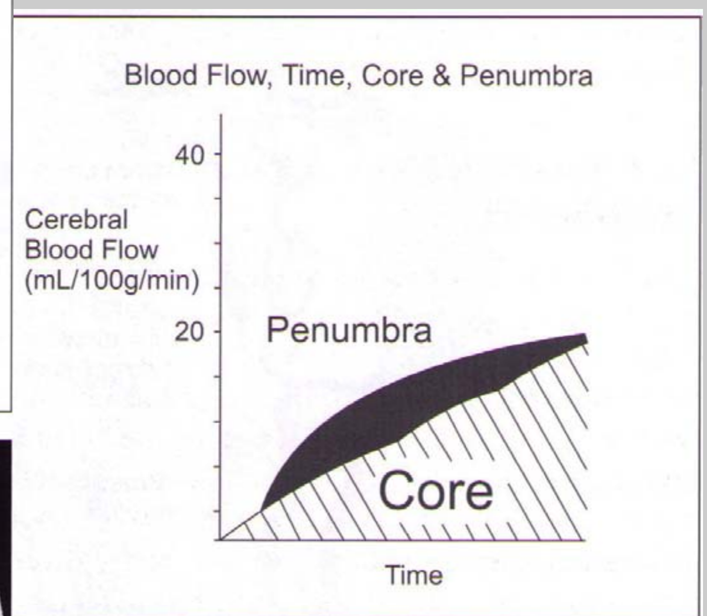
Large vessel ischemic stroke

Collateral flow



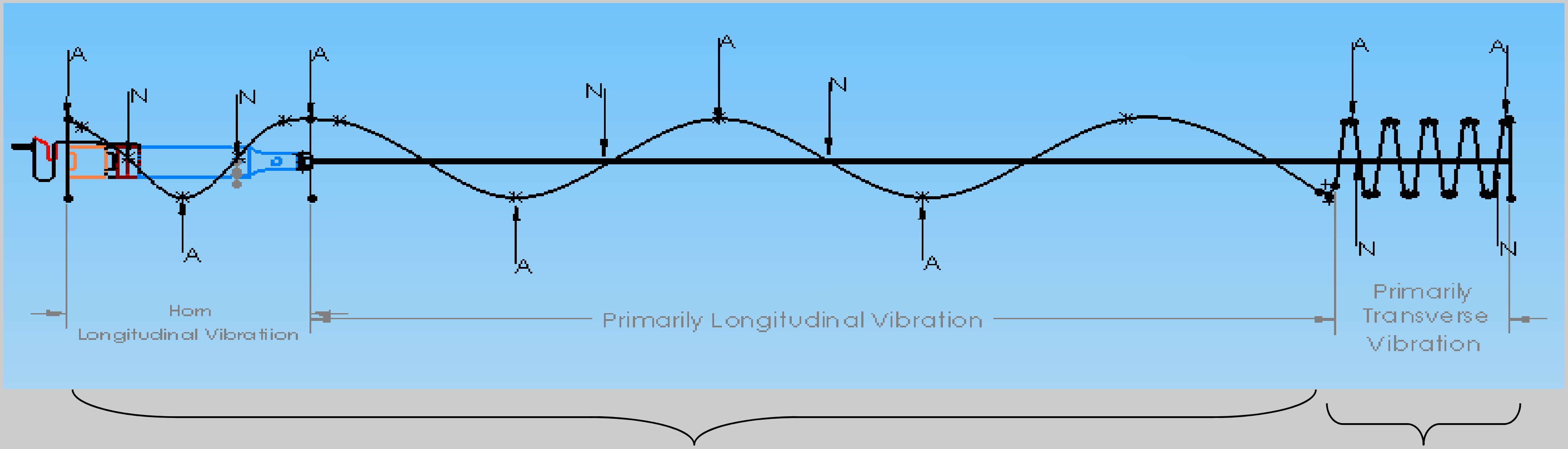
Ischemic Penumbra



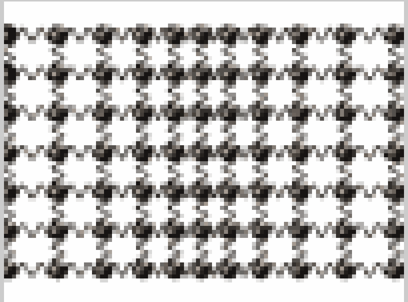


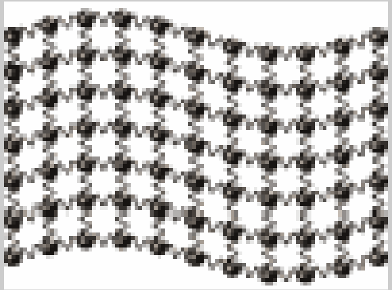
Gonzalez, R.G., Hirsch, J.A., Koroshetz, W.J., Lev, M.H., Schaefer, P., Acute Ischemic Stroke Imaging and Intervention. ©2006 Springer-Verlag Berlin Heidelberg, Germany

Transmission of the Longitudinal Wave



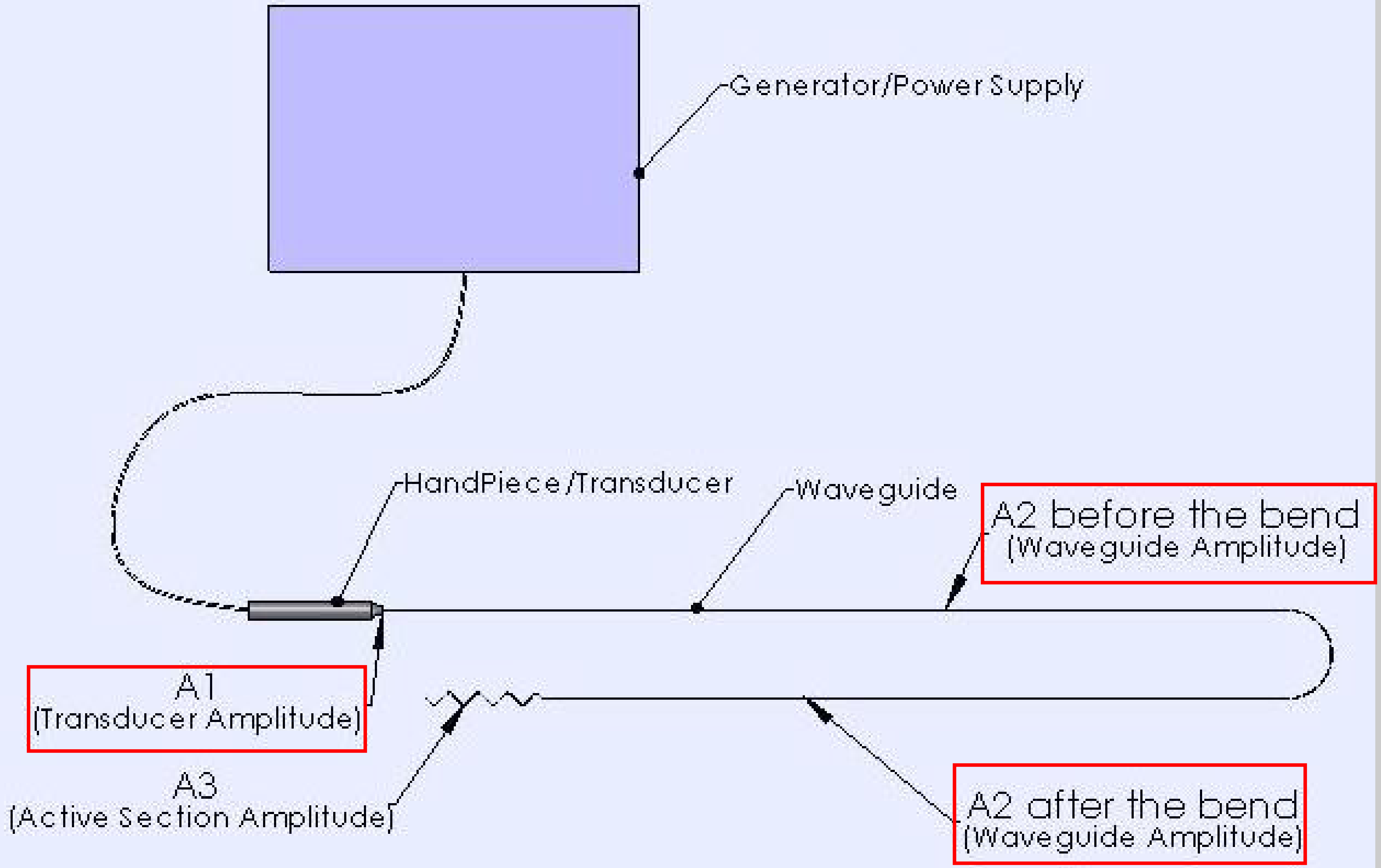
This is our region of interest…





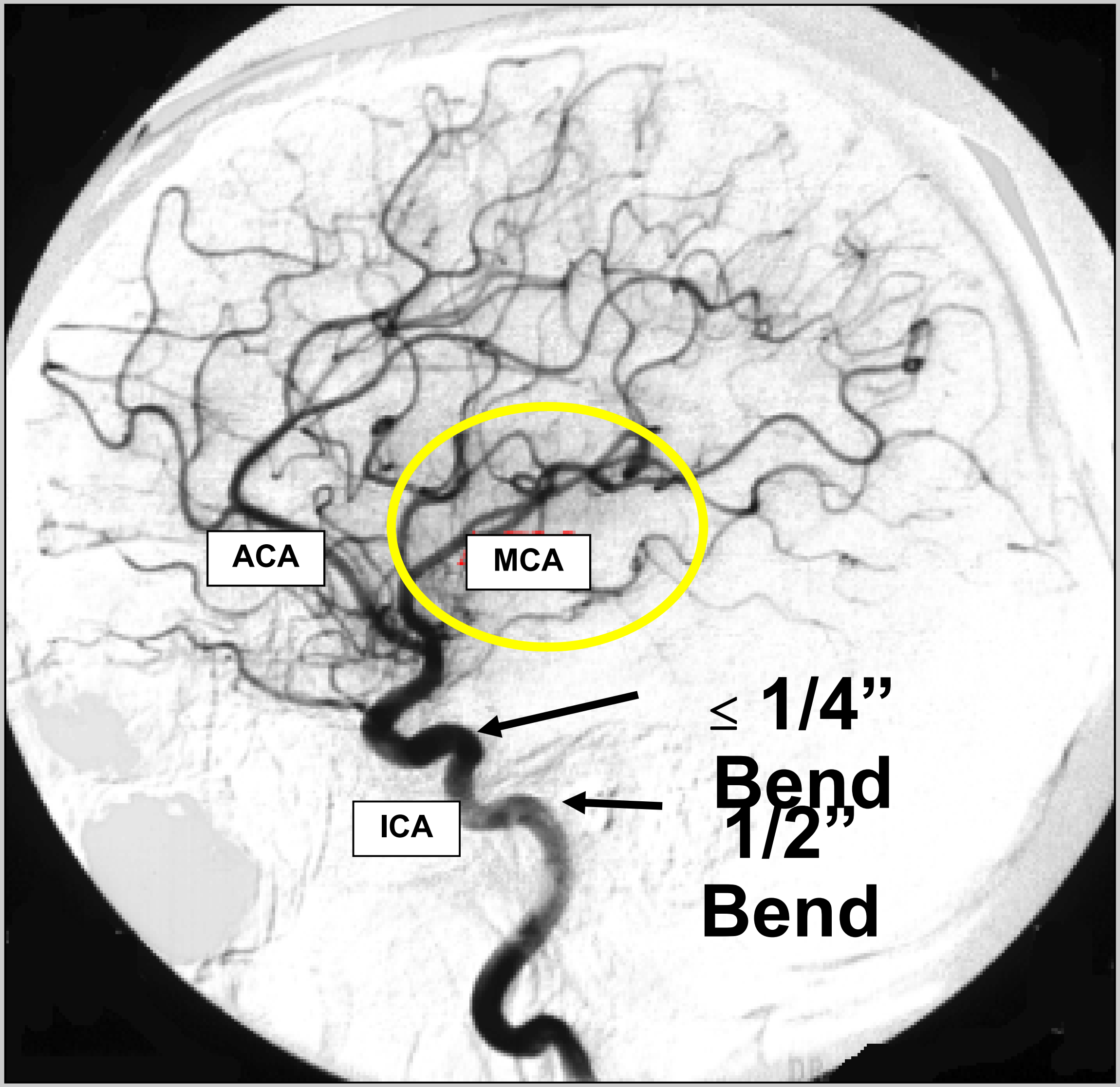
Converts longitudinal vibration generated by the transducer to transverse motion in the Wire's Active Zone

Amplitude Terminology



- A1 and A2 are longitudinal amplitudes
- A3 is a transverse amplitude

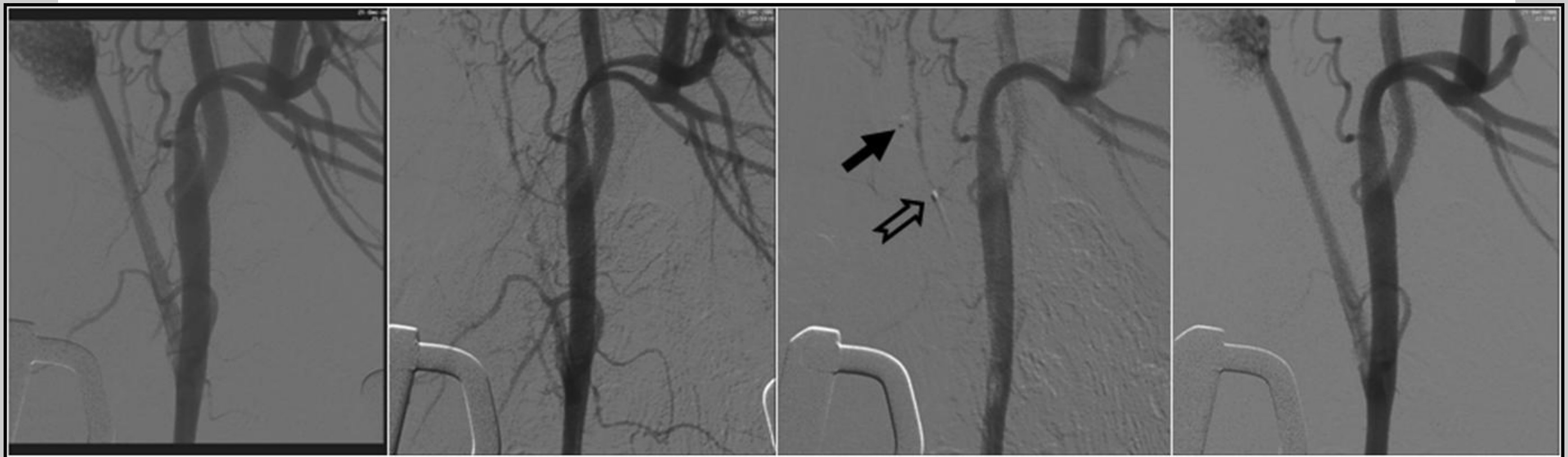
Anatomical Challenges in Stroke



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



Ascending Pharyngeal Artery (APA) Pre-Test

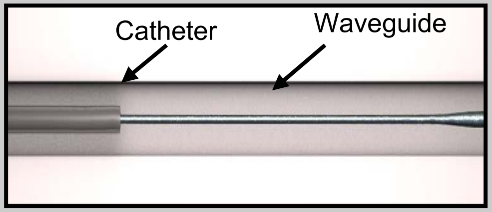
TIMI 0 Flow After Injection of Autologous Clot in the APA

Activation of the OMT Wire; Tip of Active Section (Arrow) and Microcatheter (Open Arrow)

TIMI 3 Flow Restored After Activation of the OMT Wire for <3 Minutes

- **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**

“Free Tip”

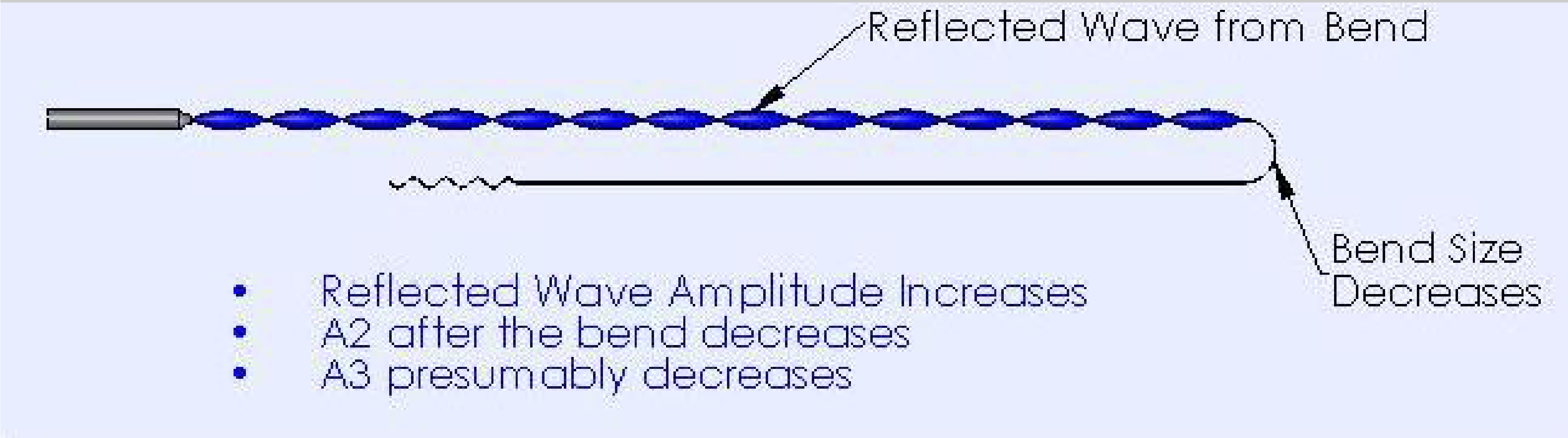


Study Goal and Approach

- 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

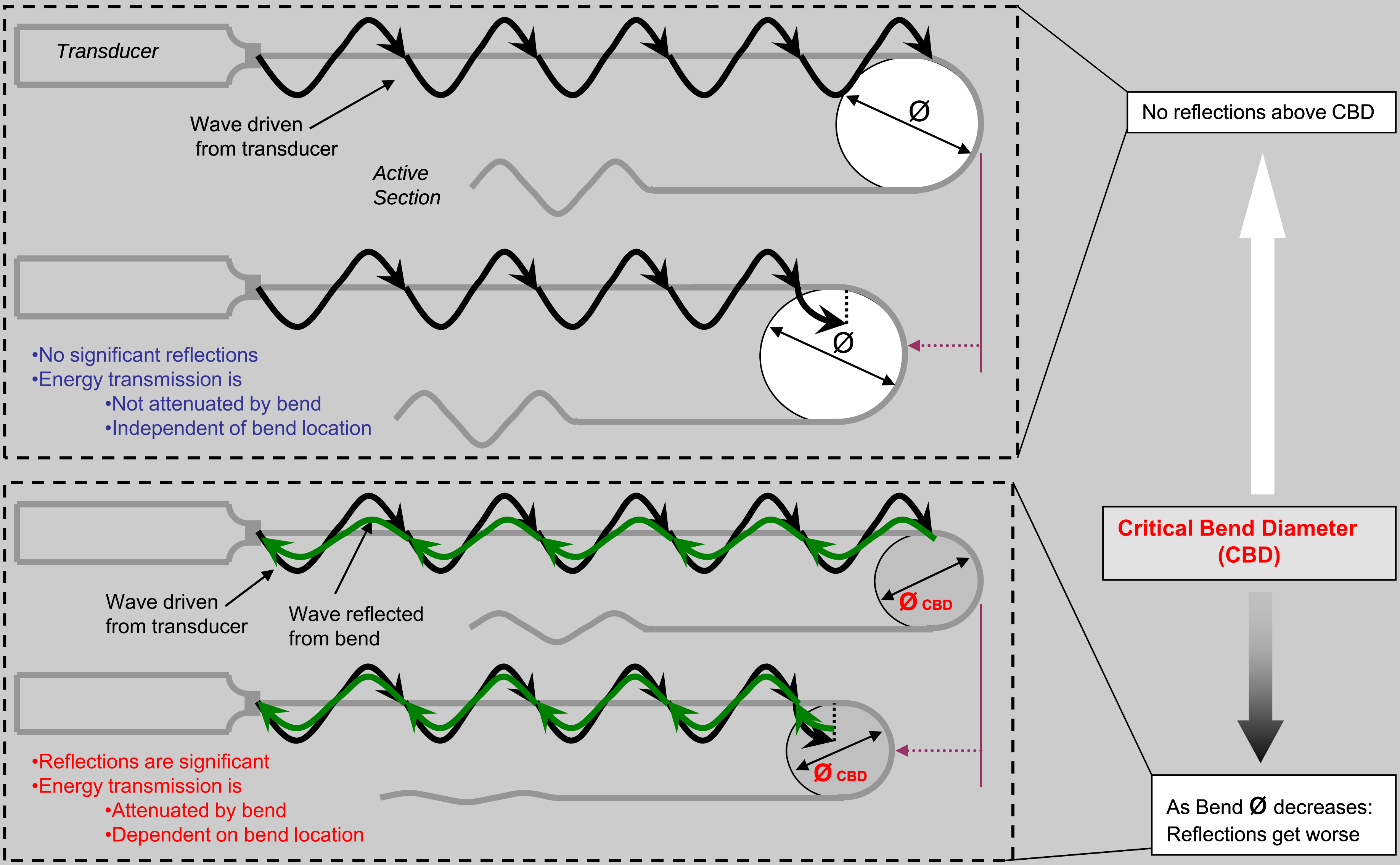
Bends Reflect Waves

- If bend is small enough:
  - Wave will reflect
  - **Reflections from bend = Reduced Transmission**



Baseline Transmission Experiments at 40 kHz

Tortuosity Causes Loss from Reflections at Bends

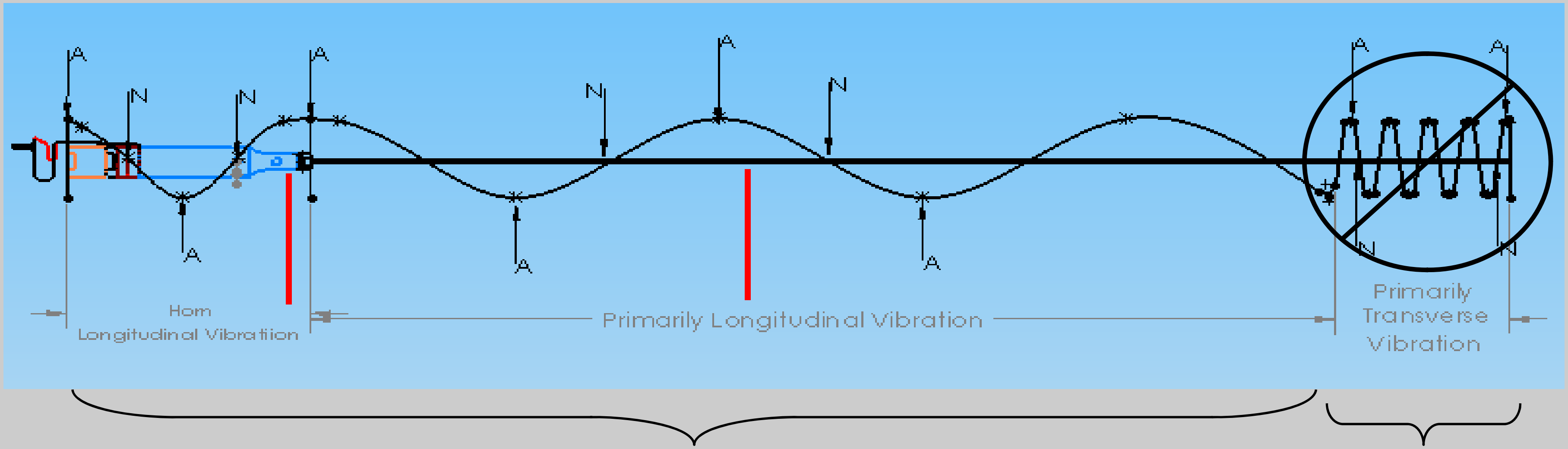


Baseline Experiments

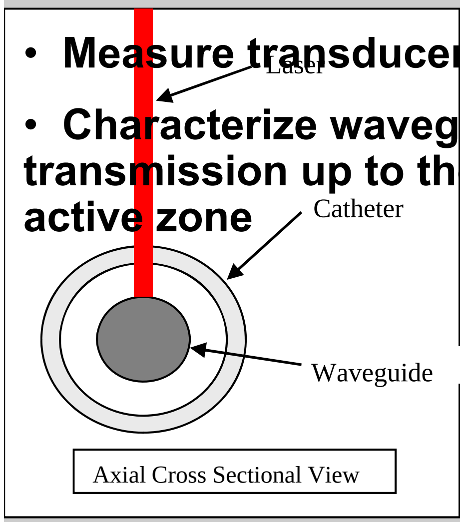
- Transducer/Generator response to different waveguide bend configurations:
  - Single Bend Pullbacks
  - Double Bend Pullbacks

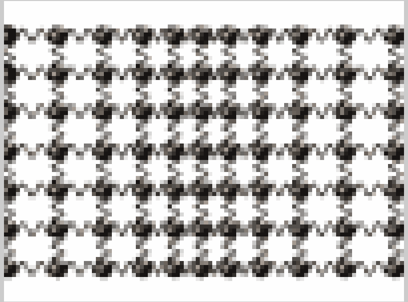
- Observe the longitudinal wave itself:
  - Single Bend Longitudinal wave Transmission (Laser)
  - Big Impact parameter identification

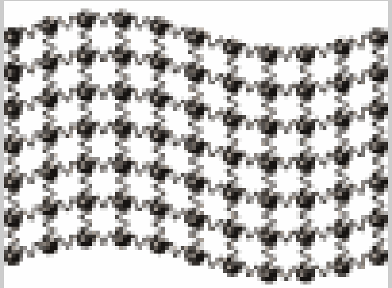
Laser Vibrometer Measurements



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



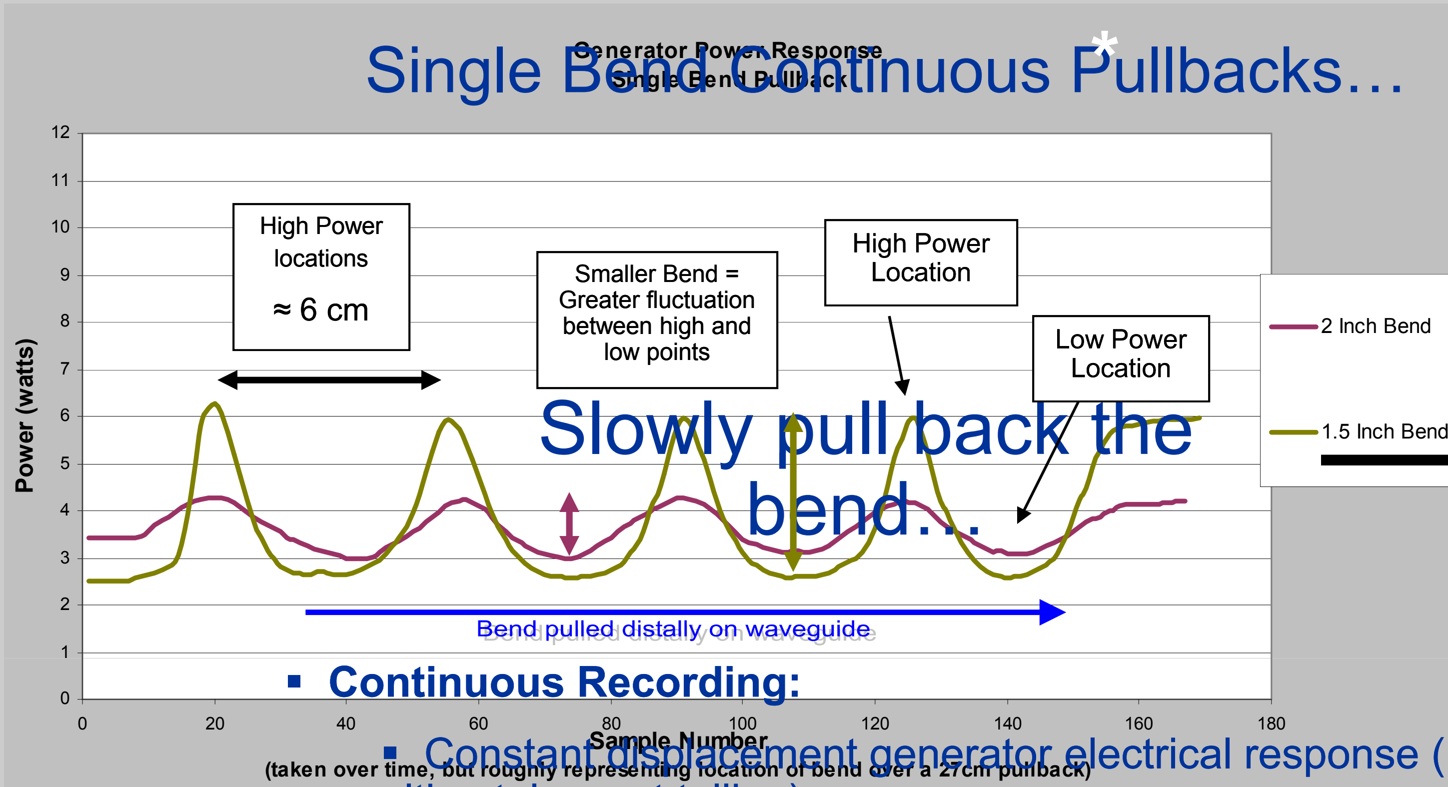




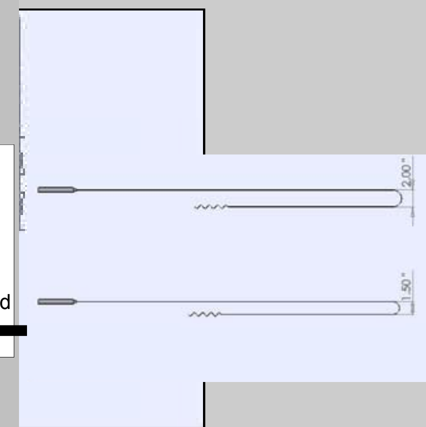
Measure acoustic waves in the transducer and waveguide proximal to the active zone

Characterization Pullbacks for 40kHz System

Single Bend Continuous Pullbacks…*



Slowly pull back the bend…



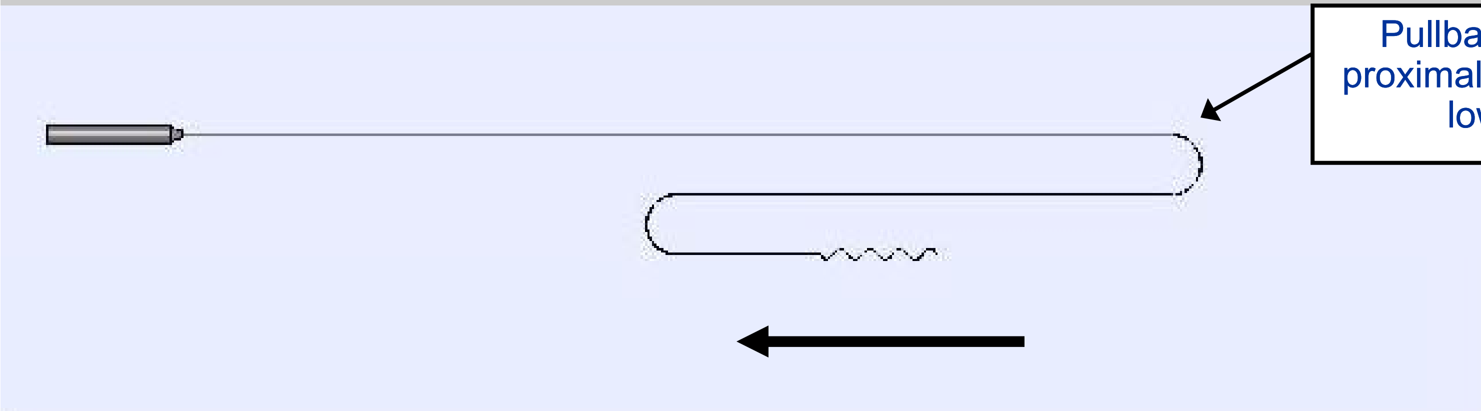
- Branson Transducer
- A1 = 5µm

- **Continuous Recording:**
  - Constant displacement generator electrical response (power ultimately most telling)
  - A1 (transducer amplitude) with Laser
- ***Repeated*** *for bend diameters – 3”, 2”, 1.5”, 1”, .75”, .5”, .25”*

- High Power Locations separated for all bend sizes by roughly **6 cm (at 40 kHz)**
  - At 40khz λ(Wavelength)=12.3 cm **½ λ = 6.16 cm**
- ***Difference in power between high and low power locations increases as bend ø decreases***
- 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



Pullback executed with the proximal bend fixed in a high or low power location

- 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…

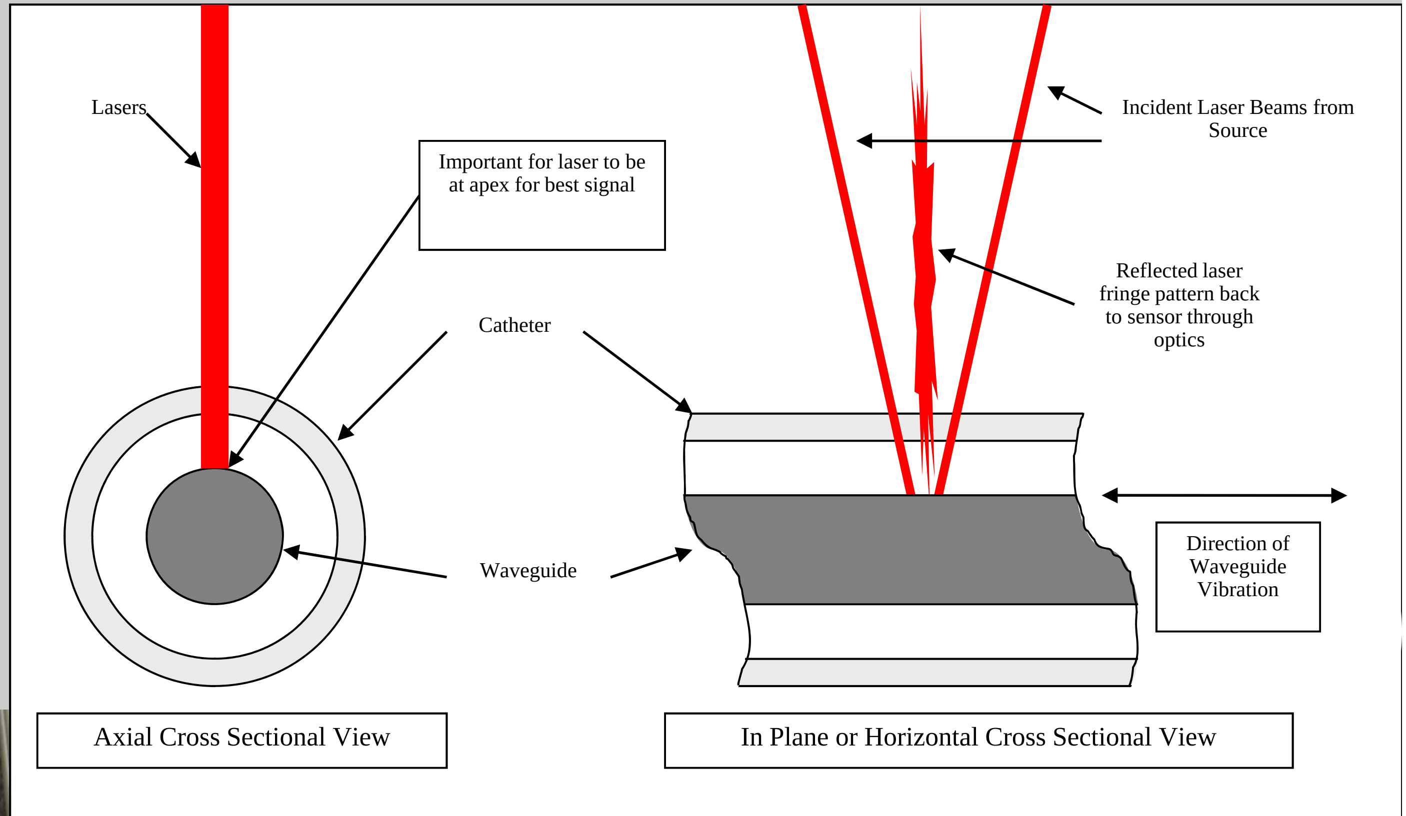
Needed to Answer Some Primary Questions

- What does the actual wave look like before and after a bend?
- What happens to the wave in different bend configurations?

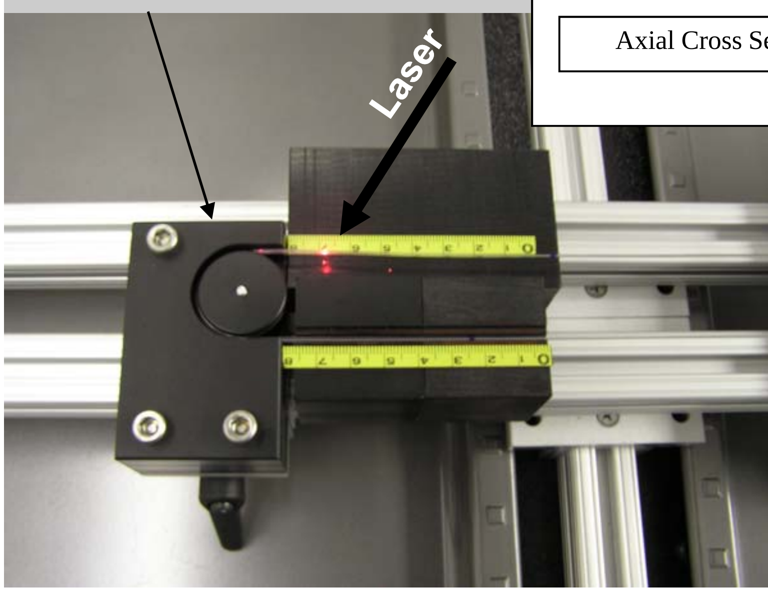
Then…

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

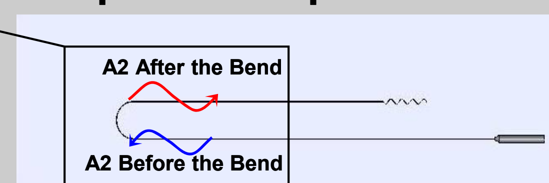
A2 Laser Measurements



Bend fixed in High or Low power location

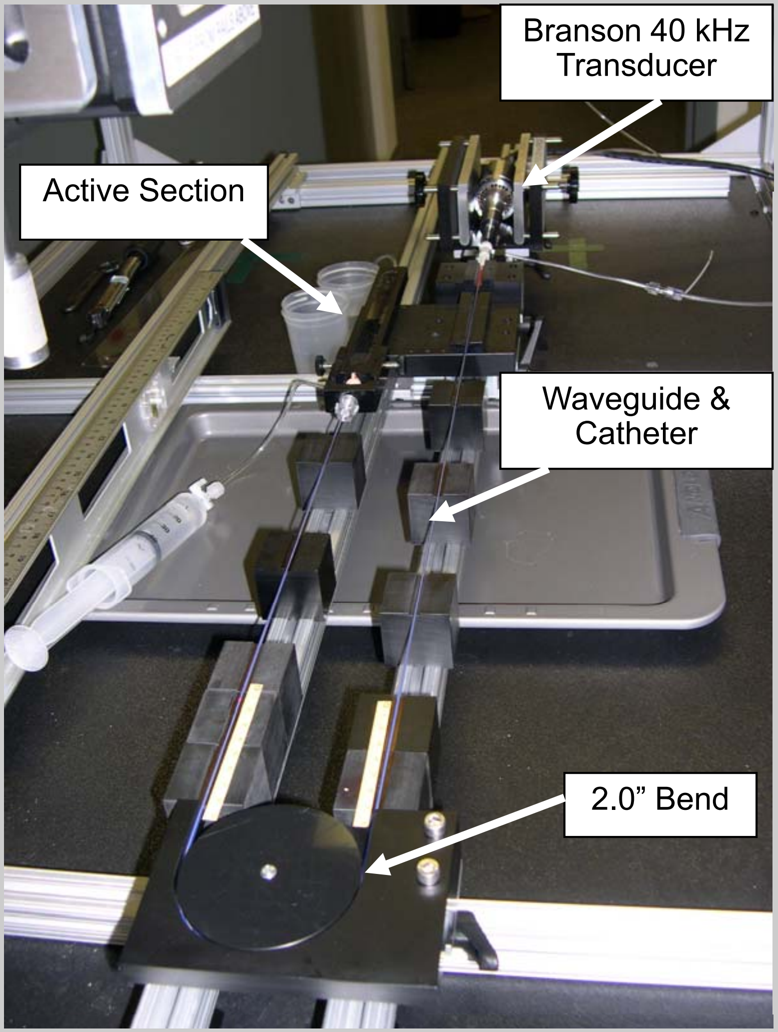


Amplitude Maps



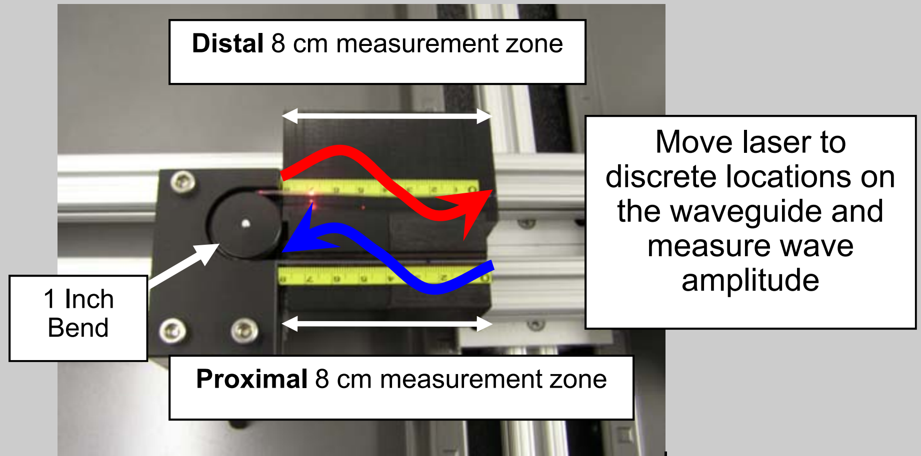
Single Bend: Transmission Experiments

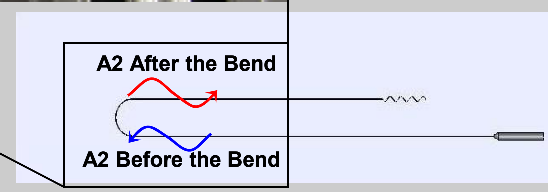
Experimental Setup



Constant waveguide diameter throughout bend and measurement zones

Amplitude “Maps”





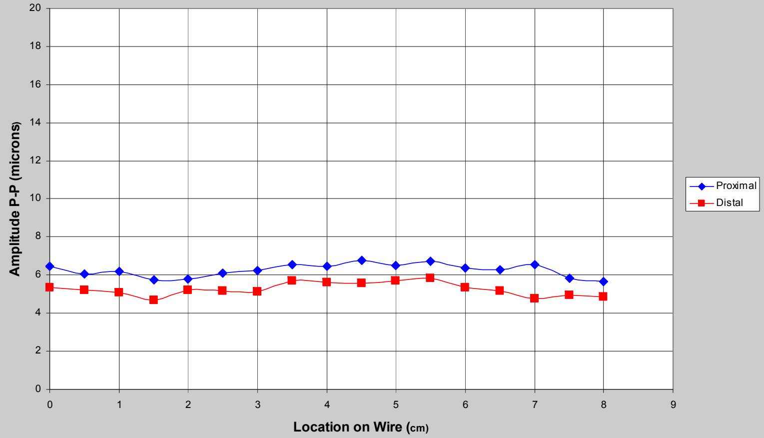
- Variables
  - Bend Size
  - Bend Location (fixed in high or low power)
  - Waveguide Diameter
  - Drive Amplitude
- Measures
  - Amplitude “Maps” were taken of the proximal wave and distal wave directly off of the waveguide with the laser vibrometer
  - Generator Electrical Response to configuration

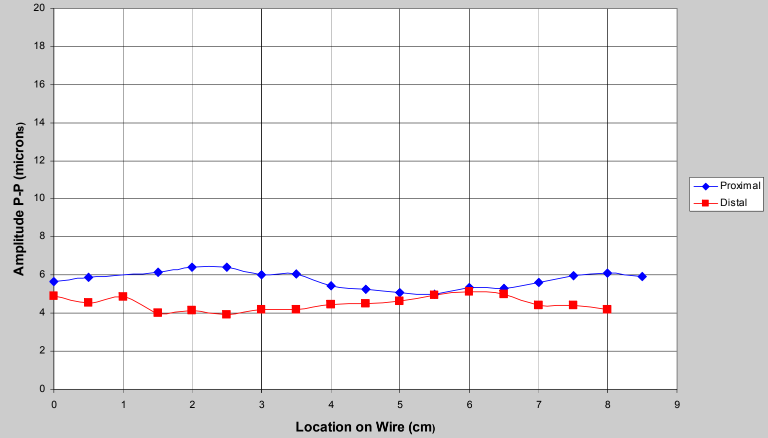
Proximal and Distal Amplitude Maps

High Power Location

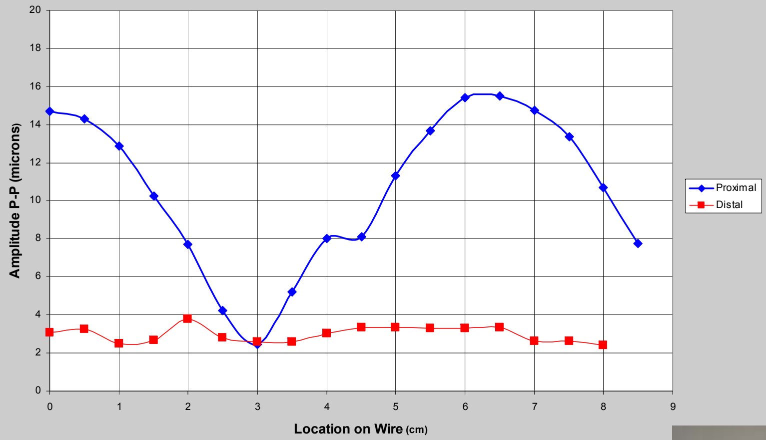
Low Power Location

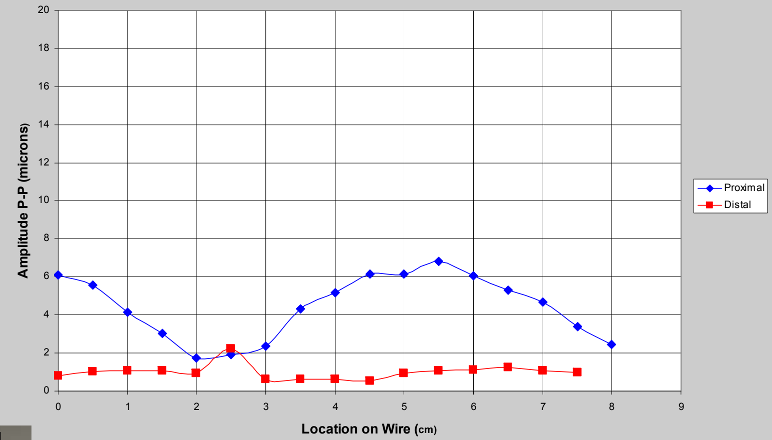
2 Inch Bend





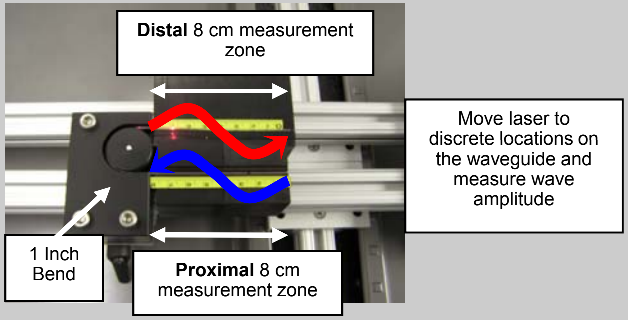
1 Inch Bend





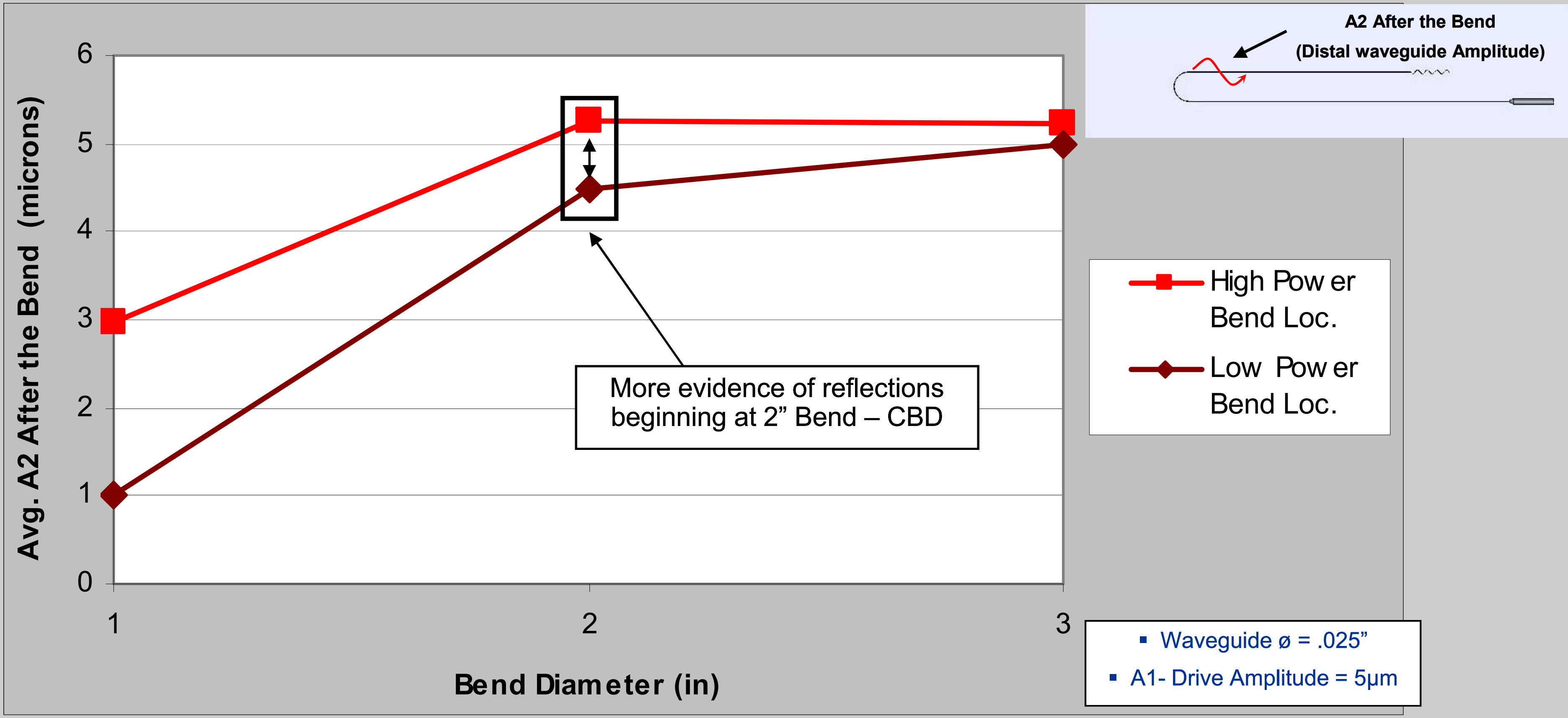
Blue Line: Amplitude Map **Proximal** to bend

Red Line: Amplitude Map **Distal** to bend



- Branson 40 k Hz Transducer
  - A1 = 5μm

A2 After the Bend

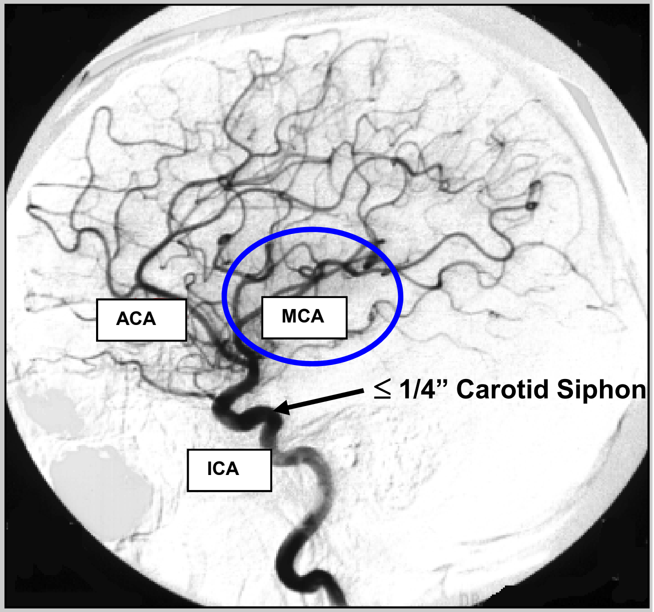


- **As Bend ø Decreases to or below the Critical Bend Diameter (CBD):**
  - **A2 After the Bend generally decreases**
  - **Low power bend locations have smaller A2 after the bend than high power locations**
  - **The difference between A2 after the bend for high power locations and low power locations 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)



http://www.neuropat.dote.hu/table/angio.htm

The solution is to increase the frequency of the system!

HIGHER DRIVE FREQUENCY

The theory begins with the relationship between Critical Bend Diameter (CBD) and Wavelength (λ)…

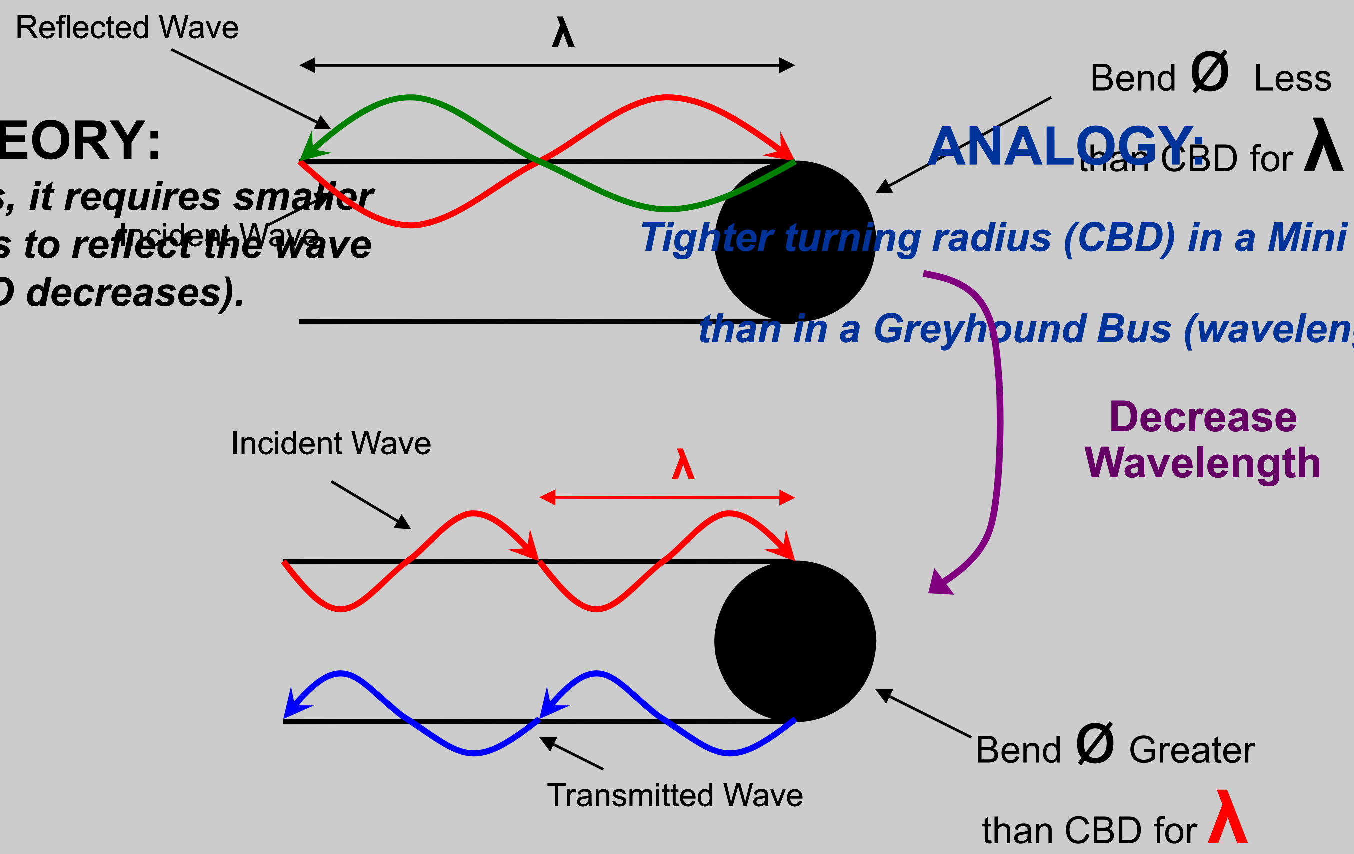
Reduce Longitudinal Wavelength (λ) to Minimize Reflections

THEORY:

As λ decreases, it requires smaller diameter bends to reflect the wave (CBD decreases).

ANALOGY:

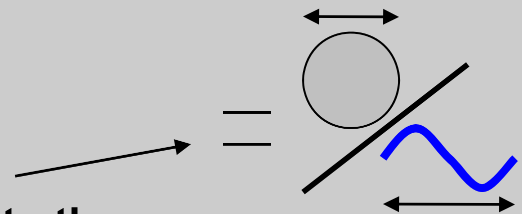
Tighter turning radius (CBD) in a Mini Cooper than in a Greyhound Bus (wavelength).



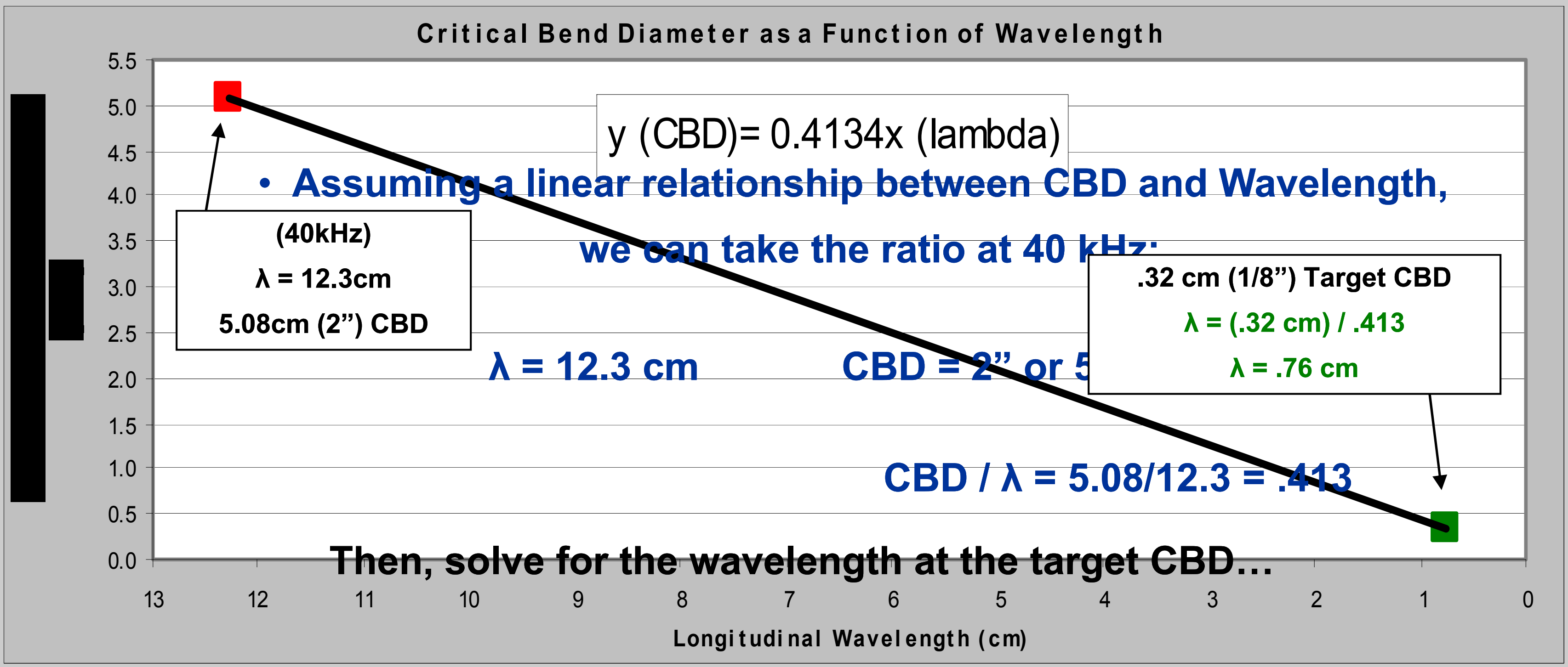
Choosing Optimal Longitudinal Wavelength (λ)

- **We want to pick a λ that yields:**

Target CBD = 1/8" (For Stroke)



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

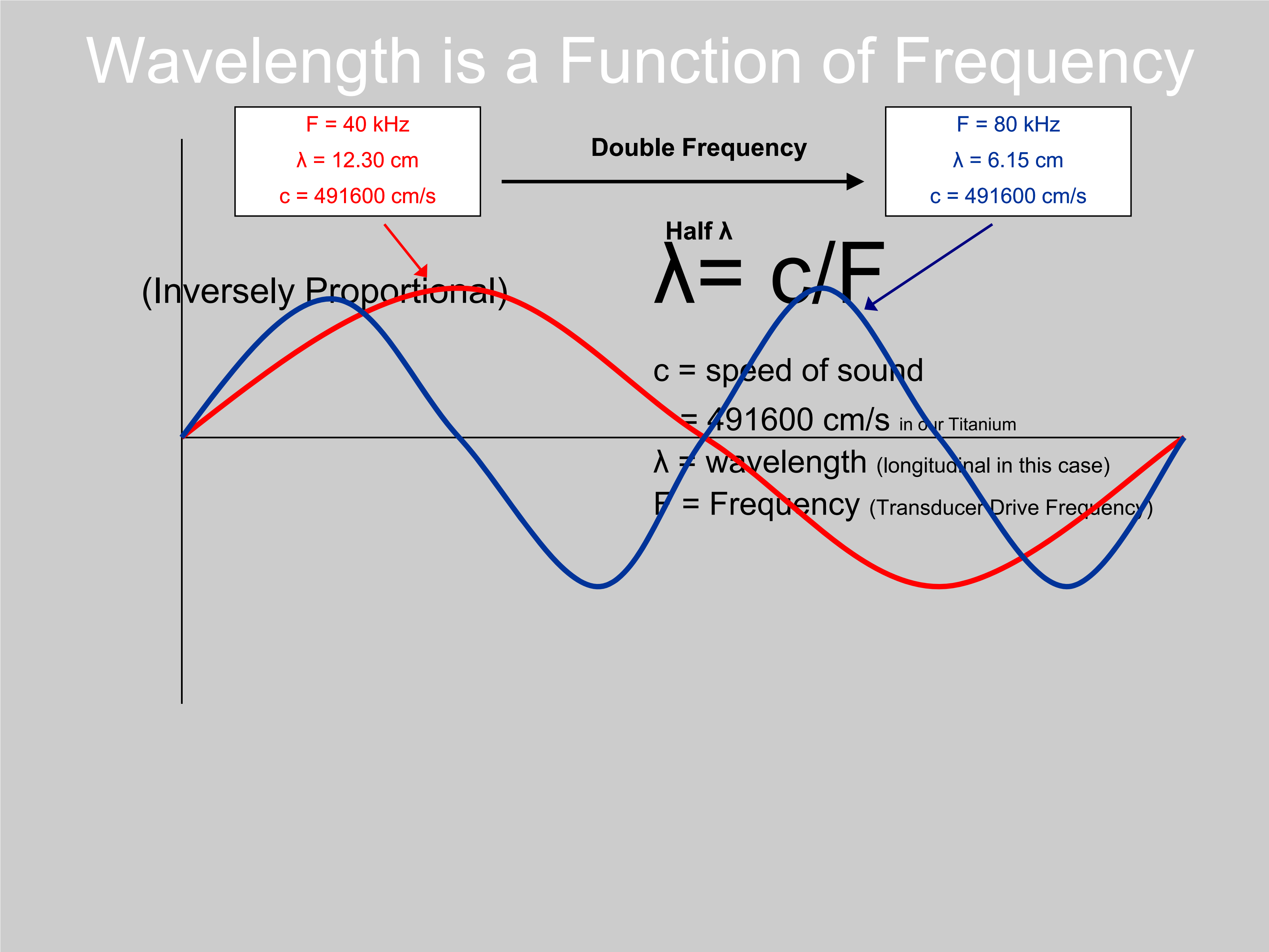


- **Assuming a linear relationship between CBD and Wavelength, we can take the ratio at 40 kHz:**

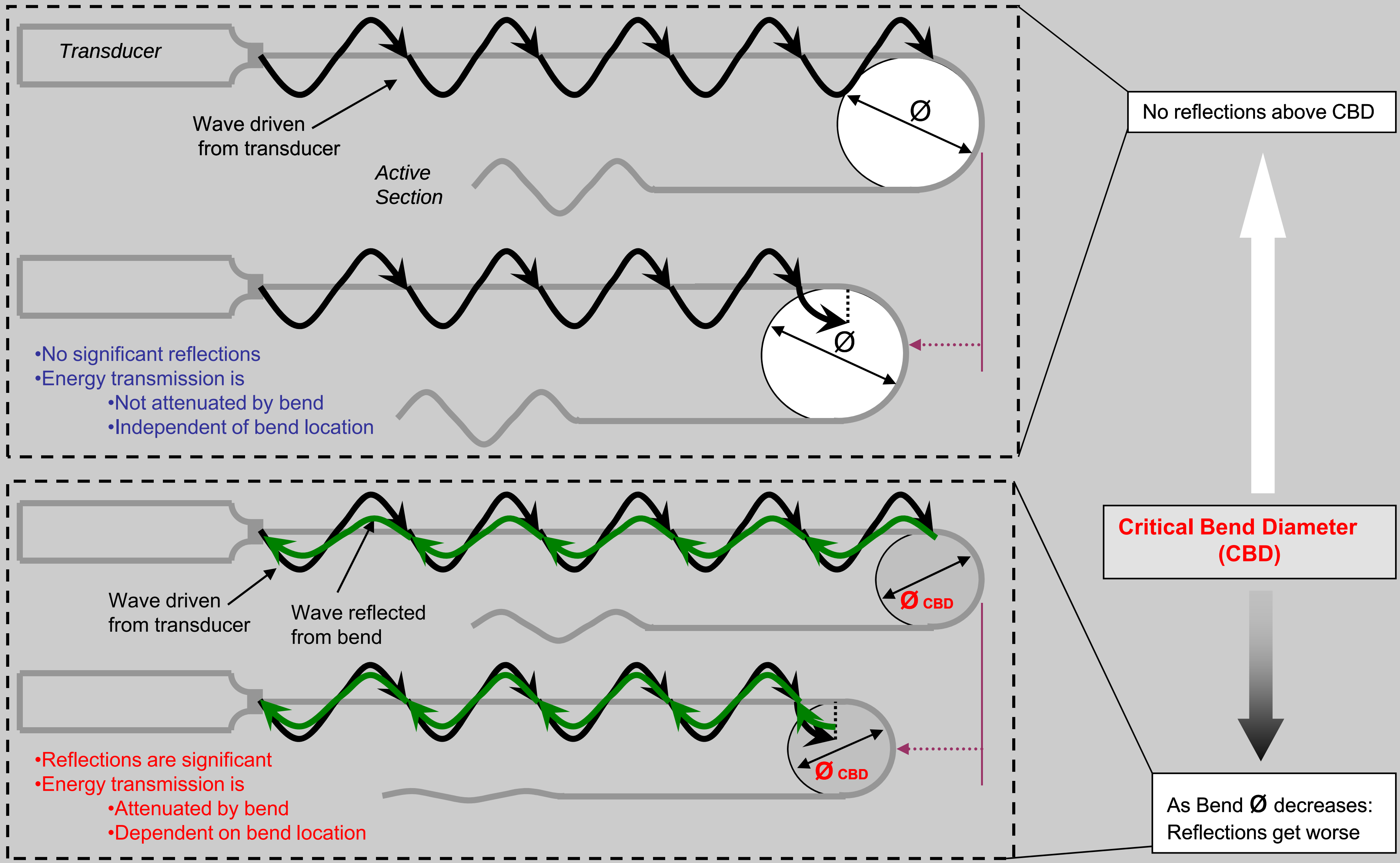
λ = 12.3 cm **CBD = 2" or 5**

CBD / λ = 5.08/12.3 = .413

Then, solve for the wavelength at the target CBD…

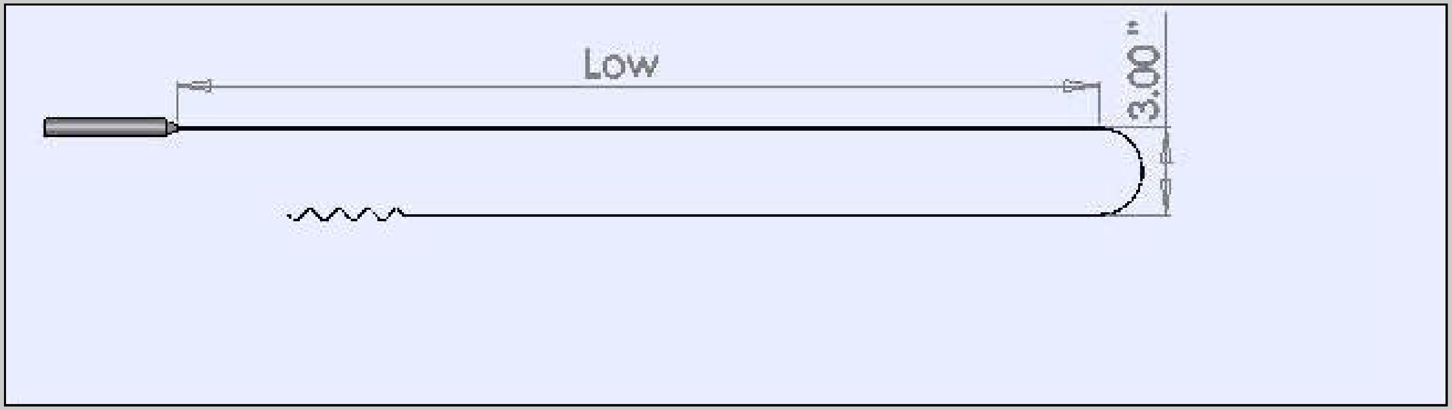

Wavelength is a Function of Frequency
F = 40 kHz
λ = 12.30 cm
c = 491600 cm/s
Double Frequency
F = 80 kHz
λ = 6.15 cm
c = 491600 cm/s
Half λ
(Inversely Proportional)
λ= c/F
c = speed of sound
= 491600 cm/s in our Titanium
λ = wavelength (longitudinal in this case)
F = Frequency (Transducer Drive Frequency)

Choosing the Right Frequency: Tortuosity Causes Loss from Reflections at Bends



High Frequency Transducer Continuous Pullbacks

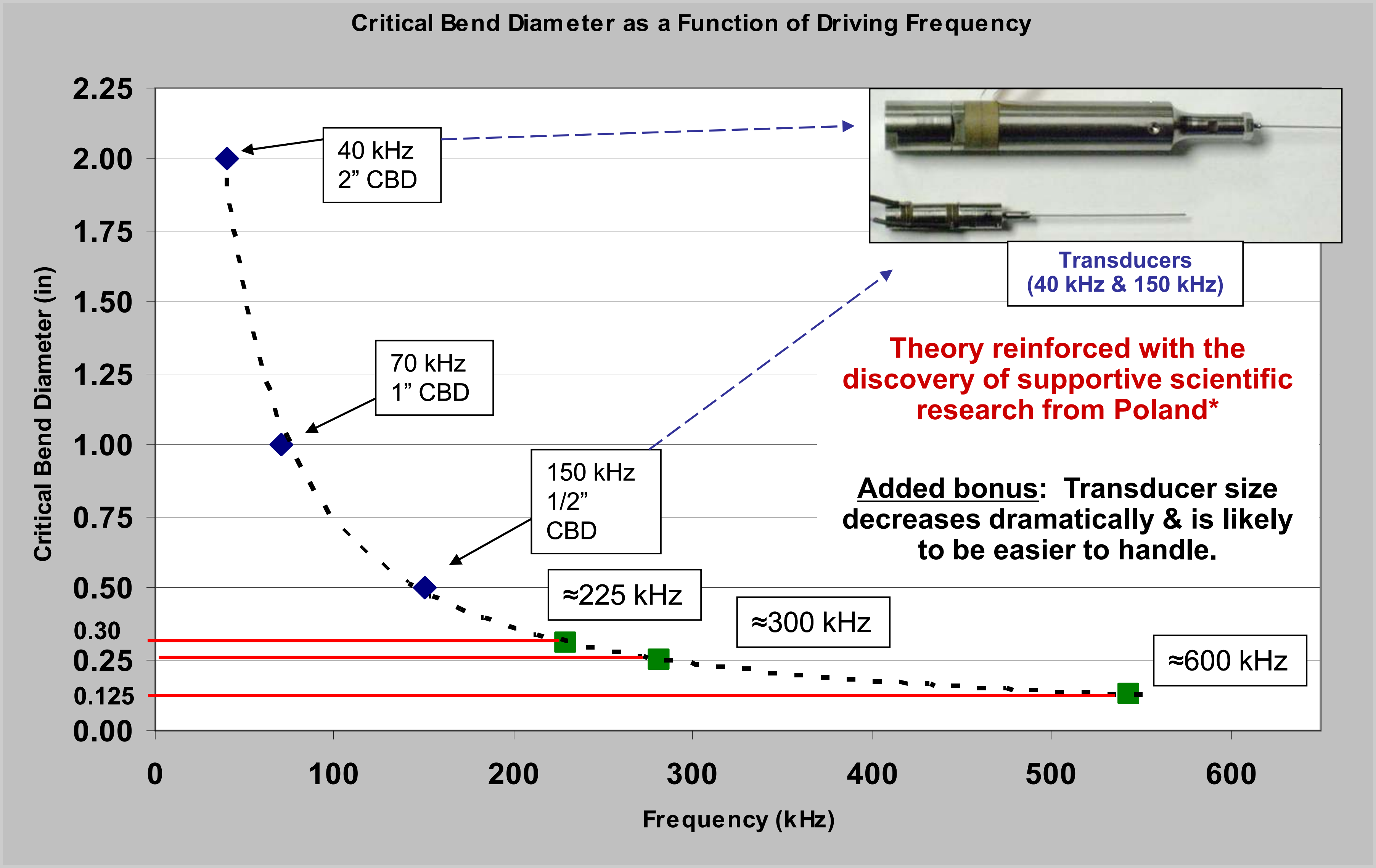
Pullbacks: Identifying Critical Bend Diameter



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”)

High Frequency Delivers Energy Around Smaller Bends



* Leszek Filipczynski, *Propagation of Ultrasonic Waves in Spirals.* Warsaw, Poland, 1962.