A Methodology for Ultrasound Product Development

Applications in HIFU and High Frequency

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Outline

- Ultrasound Medical Devices – the Challenges
- Device Development Process
- Outline of a Project
- Case Study: HIFU for fat ablation
- Case Study: High Frequency for Imaging
- Case Study: Ranging Catheter
- What we've learned - 3 lessons

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Ultrasound Medical Devices – the Challenges

- Technology adoption by clinicians

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- Disposable vs. capital equipment

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- Technology adoption by clinicians
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- The “Quick’n Dirty” catch
- Reproducibility of results
- Other technologies: RF, drugs, MRI, video
- Regulatory hurdles
- The market, reimbursement, funding …

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- No time to learn new tricks
- Minimal change from current procedure
- Anything that will make it easier is OK

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The "Quick'n Dirty" Catch

Dilemma:

1. Concept requires quick and cheap proof
2. Build prototype – cheap. Undesirable features will be fixed later.
3. Having prototype, do animal tests
4. Go for FDA approval (510k or PMA)
5. Go to production – any changes will require redoing animal tests for FDA.

(Oops!)

Ultrasound Medical Device Challenges

Regulatory

Fundamental

- Bioeffects
  - Efficacy
  - Safety
- Design Control
- Process Control

Bureaucratic

- Documentation
- Design Control
- Process Control
- PMA or 510k backup

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Development Project Outline

Goal: Risk Reduction!

- Lay out the ground work
- Develop device and evaluate
- File patents
- Set up manufacturing
- … wait for business success!

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Laying out the ground work

- The IP landscape
- The biology landscape
- Modeling tools
- Prototyping available
- Measurements available
- Technology landscape

The IP Landscape

- Information search
  - Patents database
  - Literature – journal articles
  - Awareness – networking
- Legal determinations
  - Freedom to operate
  - Technology protection

The Biology Landscape

- Tissue properties
  - Acoustic
  - Thermal
  - Irreversible changes
- Ranges of variations – model and human
  - Anatomical
  - Physiologic
  - In vitro vs. in vivo
- Transferability across species
  - Animal model not available for all conditions
  - Diet matters
  - Size matters

Project outline: Biology first and last

1. Determine the effect sought
2. Understand the tissue
3. Model the interaction
4. Design and model the beam
5. Design the transducer and system (Des. Control)
6. Test on repeatable (phantom) model
7. Measure
8. Iterate from 3 until confident with the physics
9. Test in tissue
10. Iterate from 2 until confident with the biology
11. Test in humans
12. Iterate from 2 until confident with the results

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Modeling Sound in Tissue

- Experimental
  - Live and excised tissue are very different
  - Interceding tissue
    - Bone (e.g. for brain)
    - Fat
    - Muscle layers
- Modeling issues
  - Non-linearity (KZK)
  - Acoustics affects thermal affects acoustics …
  - If heat matters, boundary conditions are key
    - Beam entrance
    - Perfusion

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Case Study: HIFU for Fat Ablation

- Goal: Dissolve fat under skin
- IP status: patentable
- Biology: very complicated
  - Tissue: skin, fat, muscle
  - Success determined by heat, damage, resorption
  - Huge anatomical variability
- Physics: Heat tissue to 50C, 4 seconds, 15-25 mm deep
- Beam: F/1.2, 3 to 4 MHz, 30W max
- Transducer: water standoff for coupling and cooling
- Tests: phantom had to be developed

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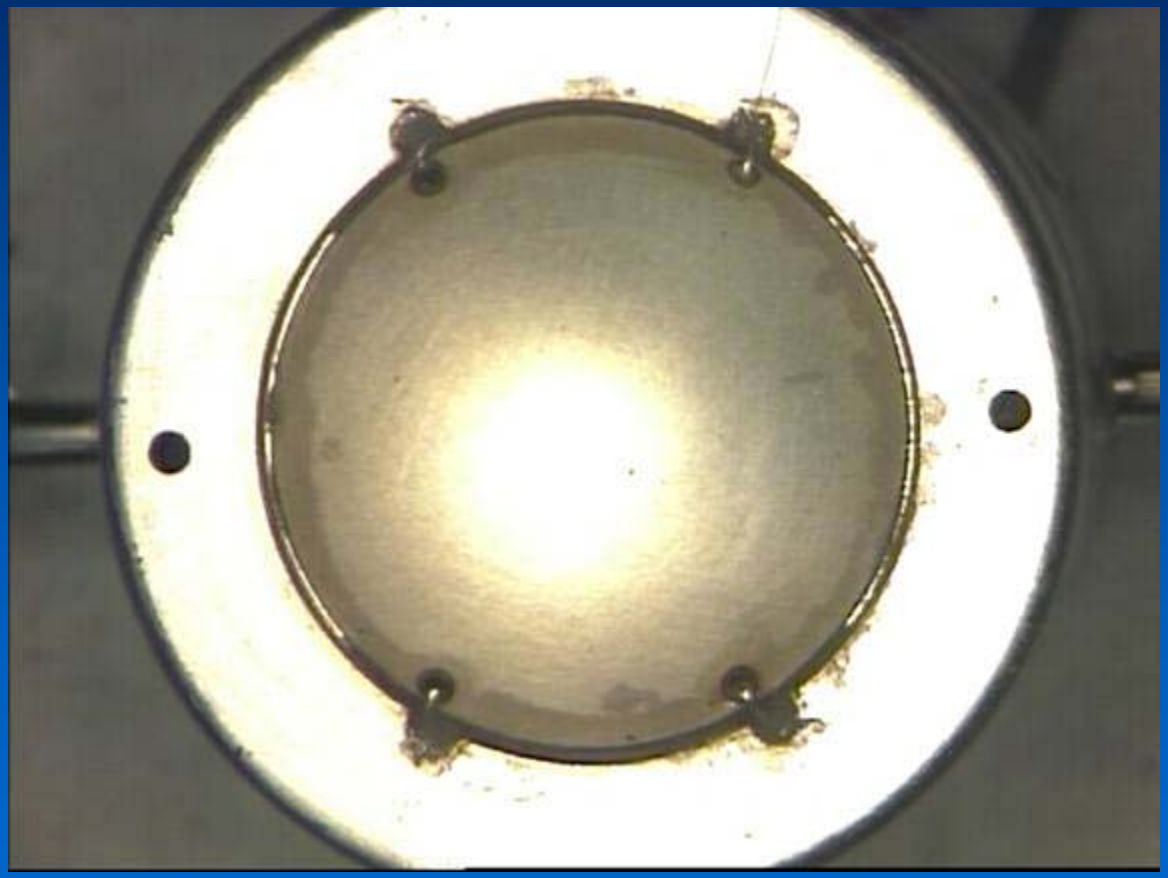
Case Study: HIFU

Transducer Modeled and Built



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Case Study: HIFU

Location Problems

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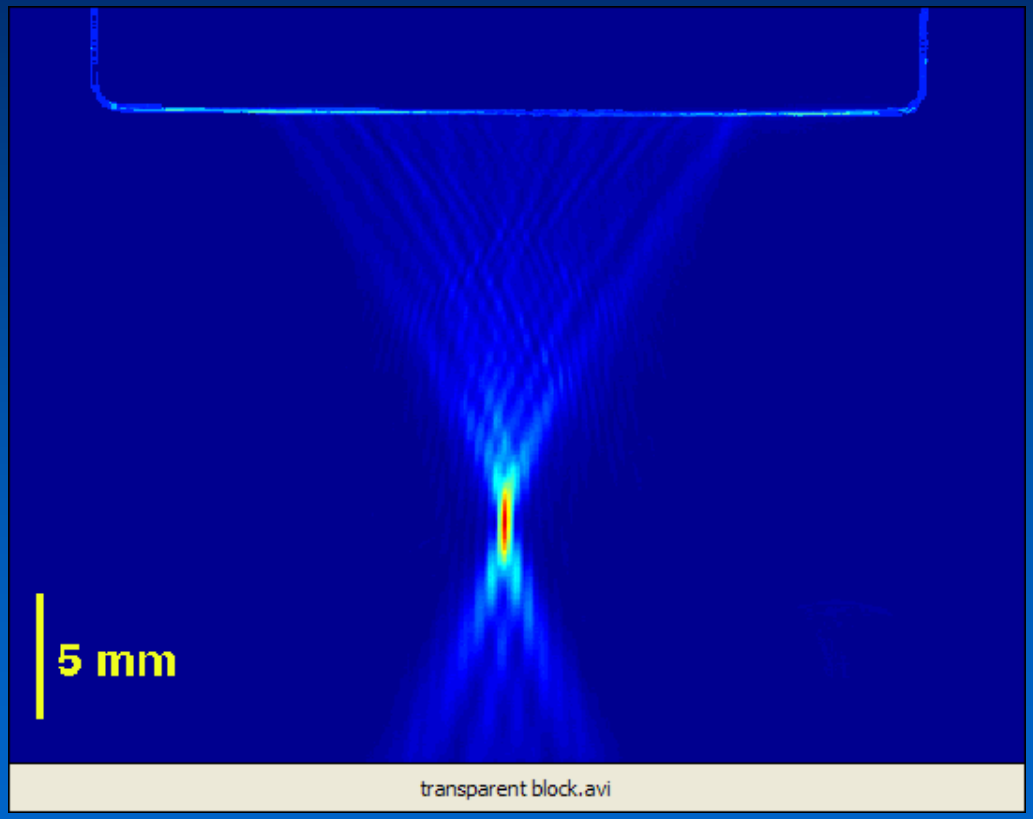
Case Study: HIFU

Tissue Modeling, Effects on Gel



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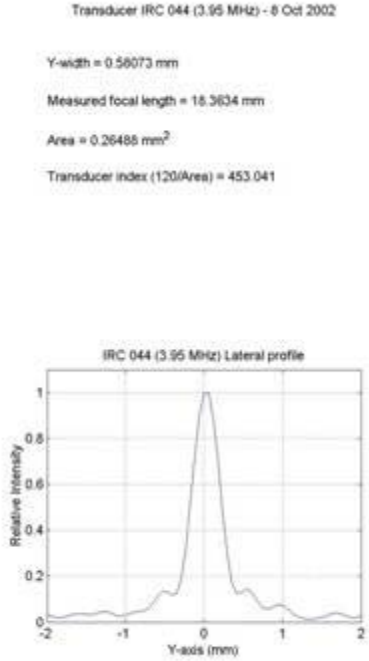
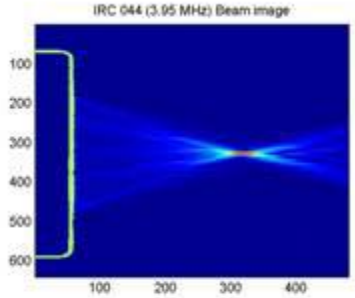
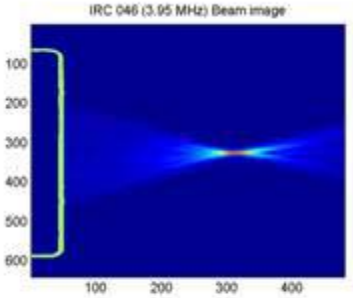
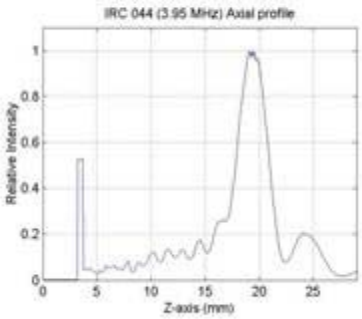
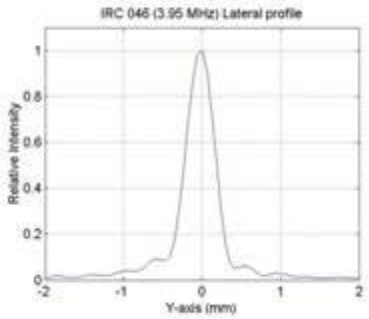
Case Study: HIFU
Uniformity Problems

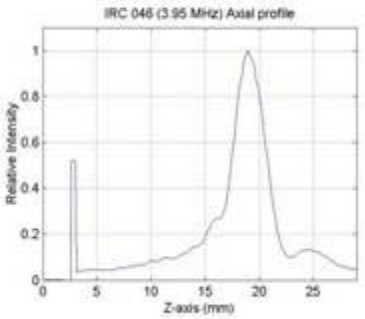












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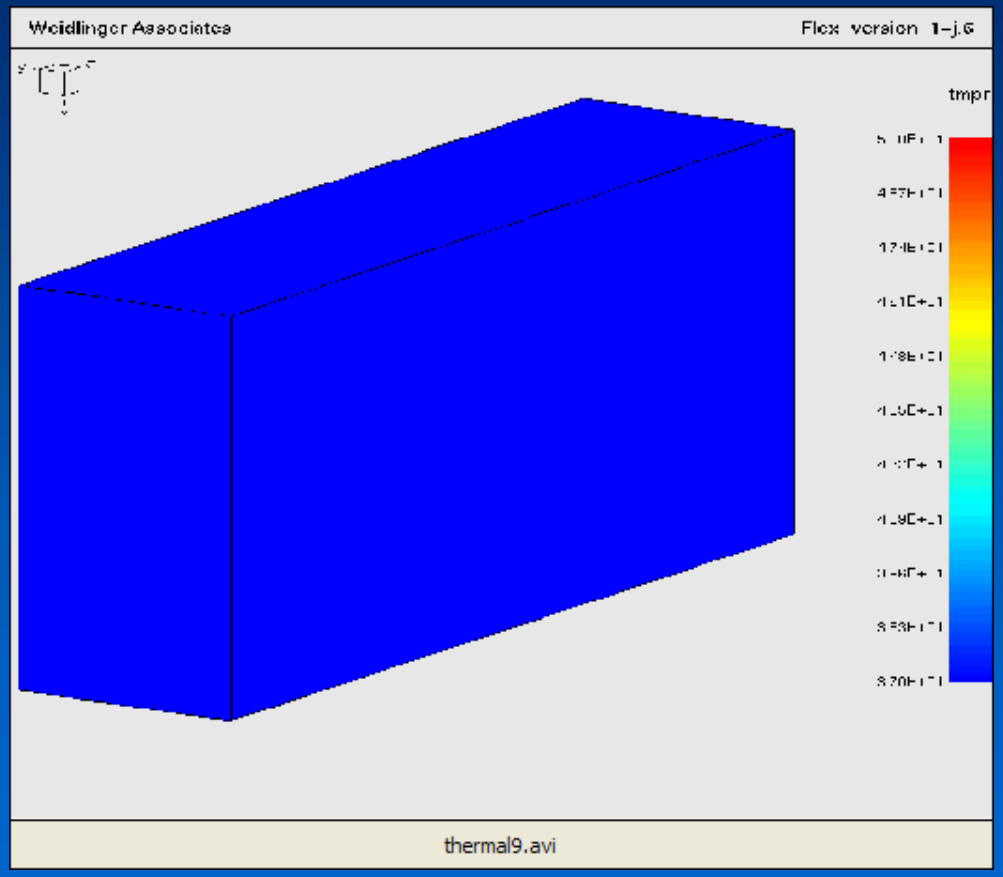
Case Study: HIFU

Problem – Beam Entrance Heating



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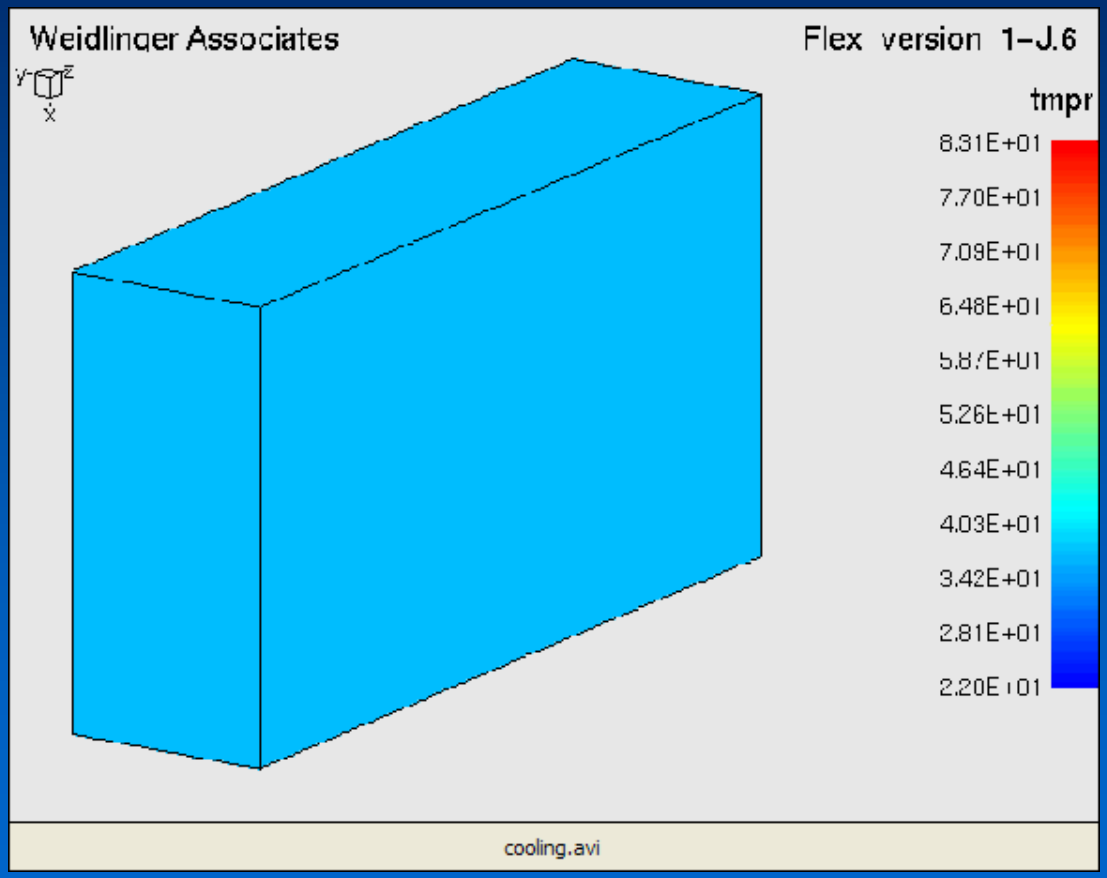
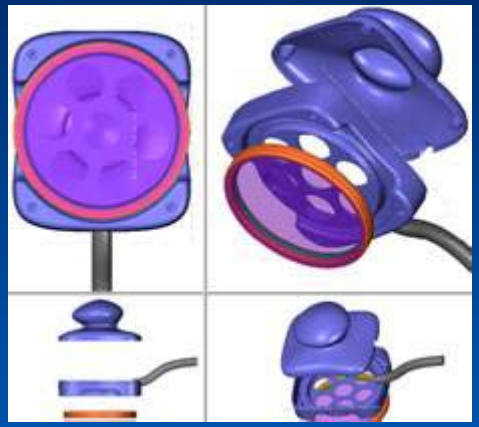
Case Study: HIFU

Surface Cooling



Case Study: HIFU

Transducers and Drivers - Prototype



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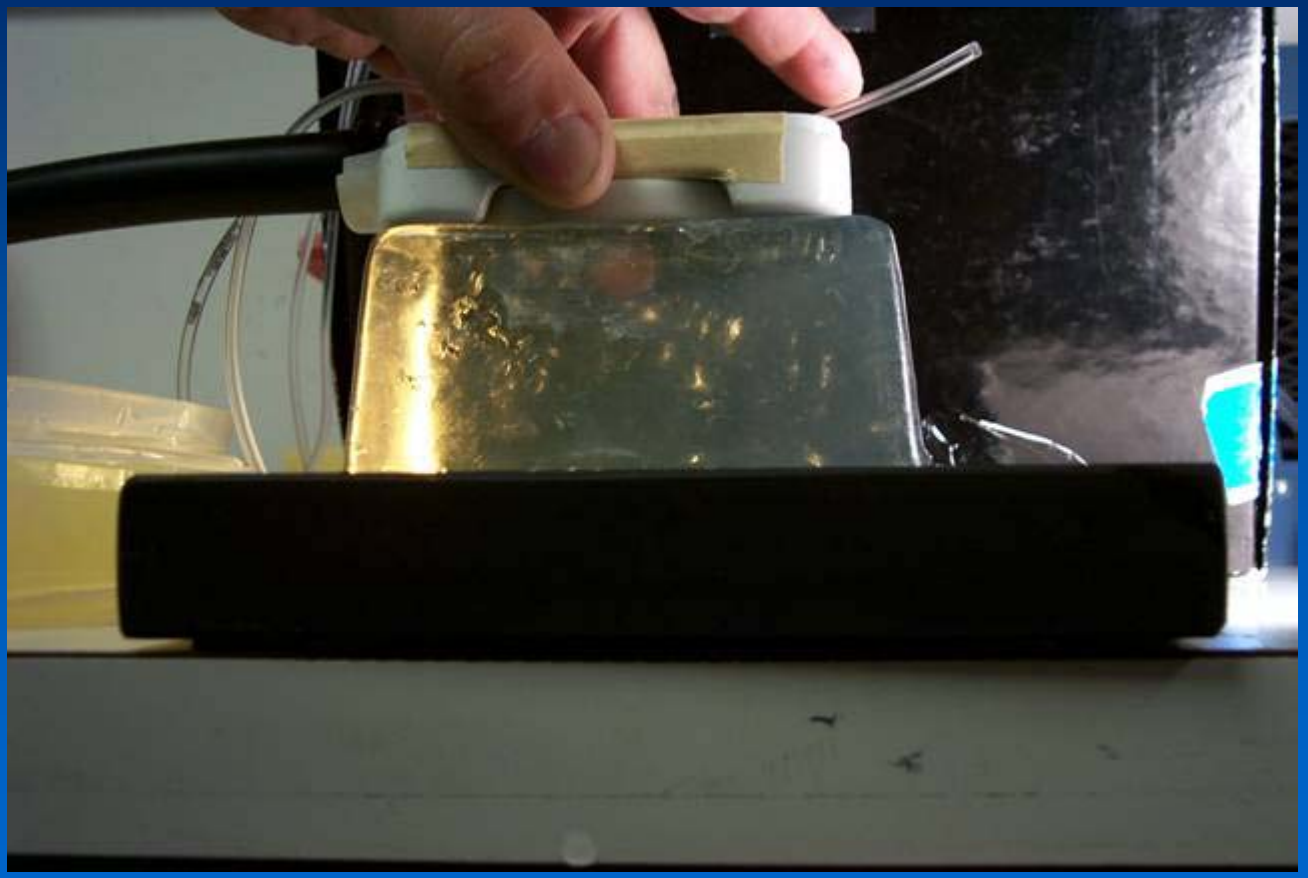
Case Study: HIFU

Gel Burns



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Case Study: HIFU

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Case Study: HIFU

Conclusions

- Tested in animal model
- Raised $27M
- Transferred for development in house
- Evolved, about to market 4 years later

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Case Study: HF transducer for imaging

- Goal: transducer for imaging at 30 um axial res.
- Tissue: eye
- Beam: F/2 25-45 MHz 3mm diameter
- Transducer: water standoff for coupling
- Tests: water echo

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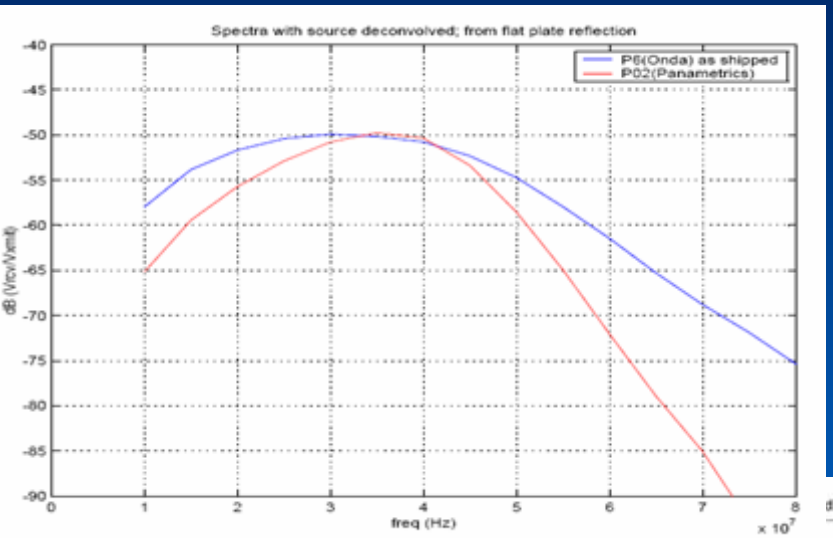
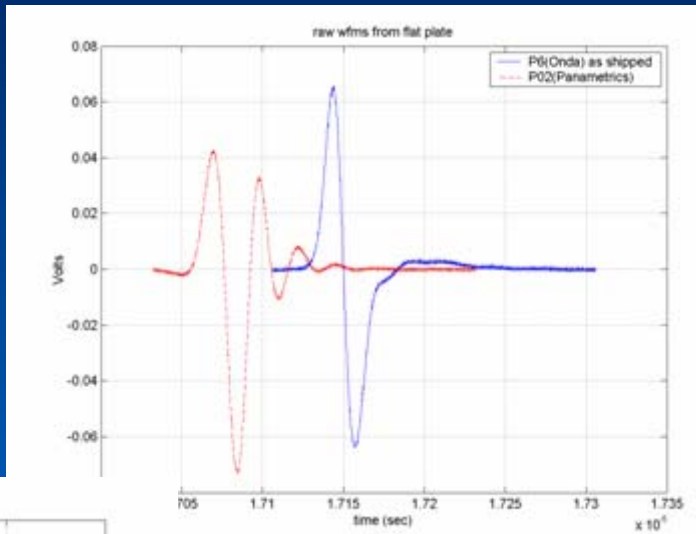
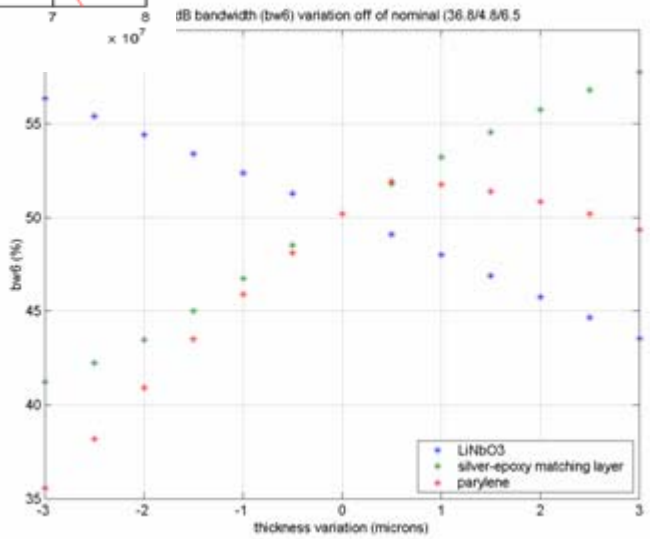
Case Study: High Frequency Imaging

Modeling the Transducer

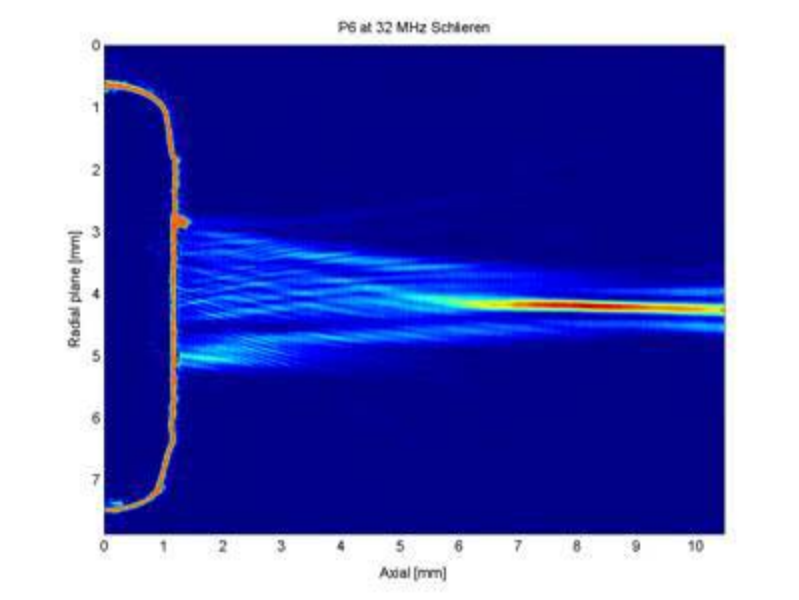


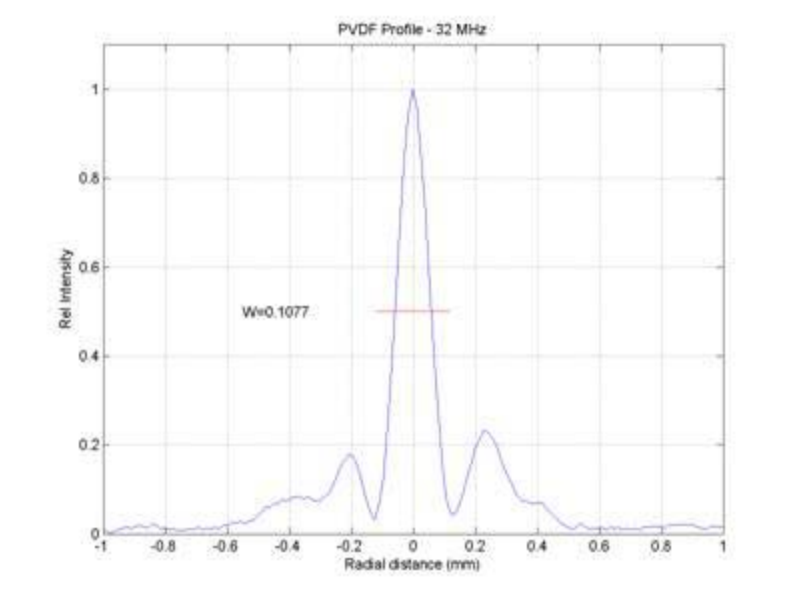




Case Study: High Frequency Imaging

Generated Beam





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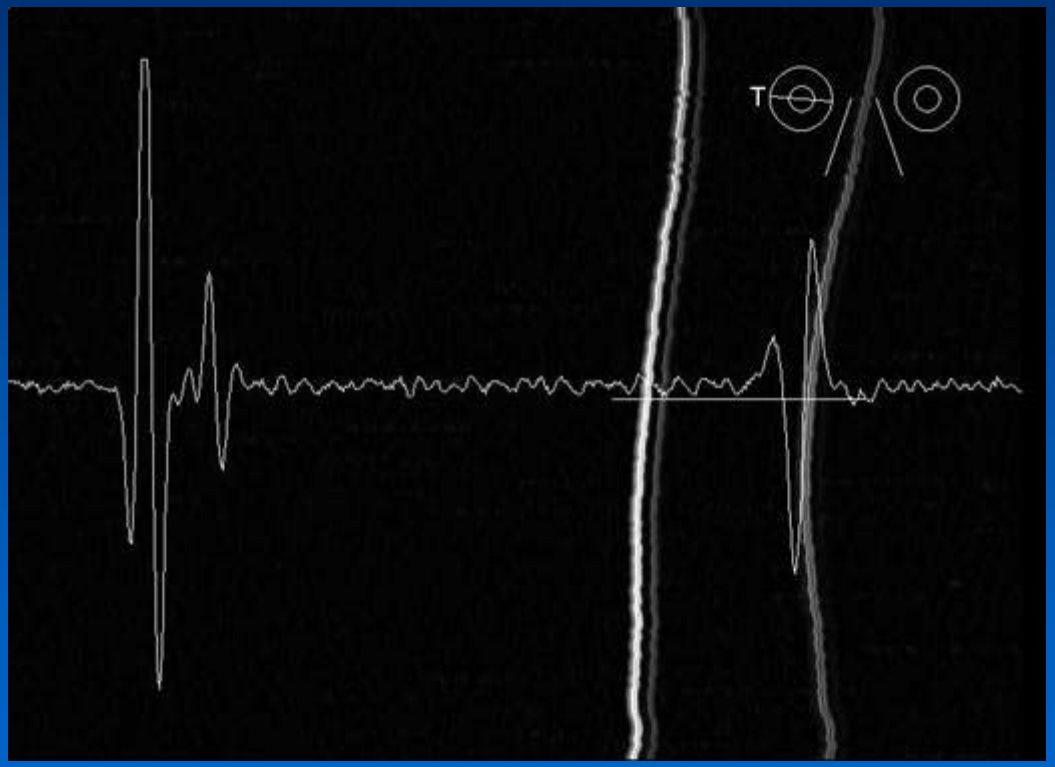
Case Study: High Frequency Imaging

Transducer and Image



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Conclusions

- Device improves over previous type
- Funds unavailable
- On hold

Case Study: Ranging Catheter

- Goal: transducer on a catheter for axial ranging, 250 um axial res.
- Tissue target: pericardium
- Beam: defocused 12-15 MHz 2.5mm diameter
- Transducer: direct contact with tissue
- Tests:
  - Water is (acoustically) good enough
  - Animals, humans

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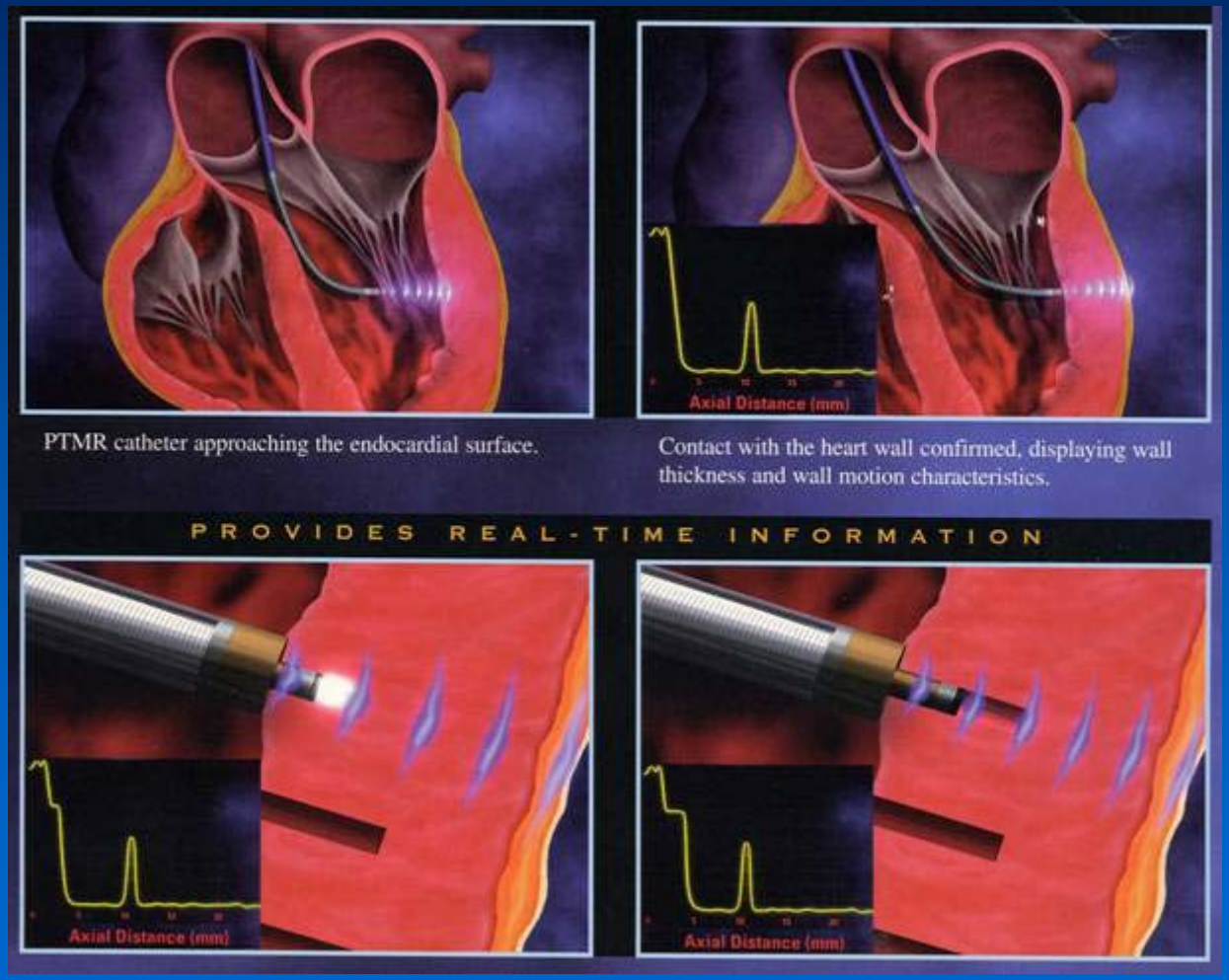
Case Study: Ranging Catheter
Application



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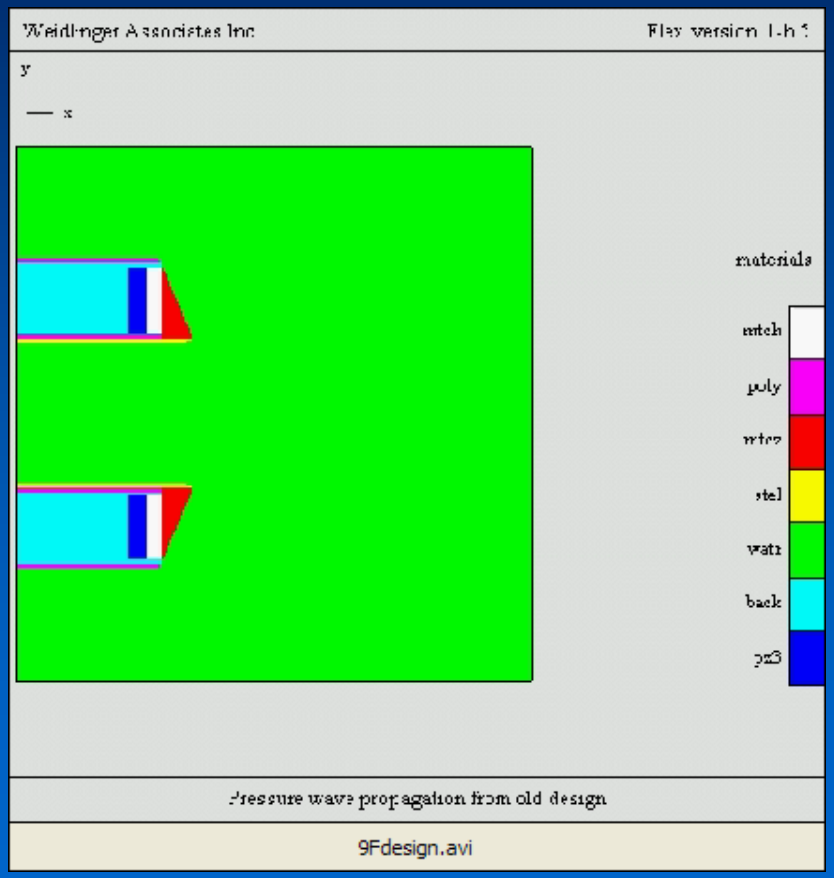

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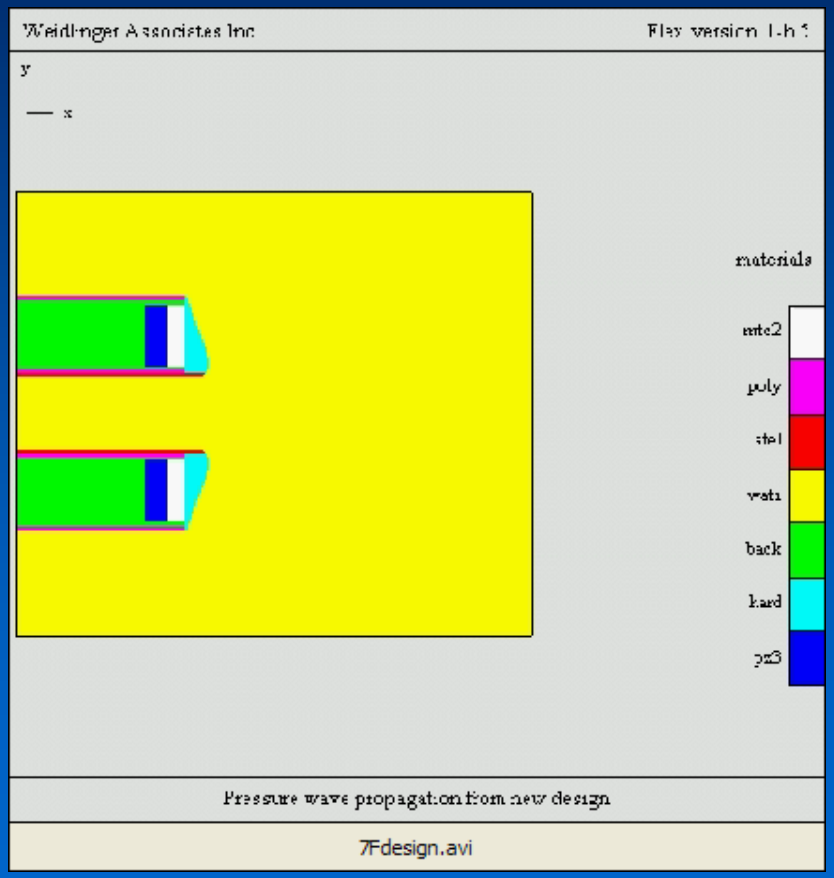

Case Study: Ranging Catheter
Application

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Case Study: Ranging Catheter

Conclusions

- “Enabling technology”
- Successfully tested in humans
- Company merged with its competitor
- TMR technology fell in disfavor
- Product cancelled

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What we've learned - 1

- Ultrasound medical device development presents multifaceted challenges that need to be addressed in an integrated, multifaceted approach

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Lesson:

Follow a disciplined product development and *integrate all the details.*

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What we've learned - 2

- A good medical device requires doing the homework, yet successful medical products are rare.

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Lesson:

Do not discount the cost of development based on speculation of future sales

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What we've learned - 3

Medical device developers expect IP as part of the engineering work *because* IP is the most precious commodity, embodied in the engineering work.

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Lesson:

IP is valuable, don't give it away.

Thank you !