The importance of stent and clinical study design – when?

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Designing is Cyclic and Iterative

- Design inputs, i.e. Clinical requirements drive the design and development process
- Feedback repeats the design process
- We as users need to provide feedback
Design Inputs

• Inputs and Requirements (Design Criteria)
• Ideally, requirements lead to a design centered in a Venn diagram
• An optimized design is achievable
Design Constraints

• Design inputs have real world constraints
• Requirements and constraints often compete
• The ideal design is unachievable
Types of Requirements and Criteria

- Clinical Requirements (i.e. Safety, Patency)
- Engineering Requirements (Functionality, Specifications)
- Regulatory requirements
- Intellectual Property
- Manufacturability
- Development Cost
- Time to market
Intellectual Property Requirements

- Intellectual Property (IP) has become a requirement for medical devices to protect the product and company, especially in the United States.
- According to US Patent & Trademark Office, the total number of medical device patents granted has increased by approx. 169% from 7,443 in 2009 to 19,992 in 2014.
Regulatory Requirements

- **ISO 13485**: Medical devices – Quality management systems – Requirements for regulatory purposes
- **ISO 14971**: Medical devices – Application of risk management to medical devices
- **21 CFR 820**: FDA Quality System Regulation
- **ISO 25539-2**: Cardiovascular implants Part 2: Vascular stents
- **ISO 10993**: Biological evaluation of medical devices
- **ISO 11135**: Sterilization of health care products
- **FDA Guidance**: Non-clinical engineering tests and recommended labeling for intravascular stents and associated delivery system
Clinical Requirements

• The purpose of the venous stent is to maintain an open lumen to allow flow, and reduce congestion and hypertension
• Effectiveness determined through patency rates
• Safety through low adverse events rates
• Improvement of venous symptomatic scores, i.e. CEAP and VCSS, can also be requirements
• Quality of Life Vital – EQ5D, VeinesQol-Sym
Engineering Requirements

– Crush Resistance
– Flexibility
– Radial Strength
– Deployment
– Scaffolding (Coverage)
– Diameters & Lengths

“The ideal stent would be flexible with moderate radial force, no foreshortening, and allow for very precise and accurate placement.” - Brooke Spencer, MD, FSIR

“Some desirable features are common to all stents, not just venous devices, and include precise deployment, good visibility, and flexibility of both a low profile delivery catheter and the deployed stent. However, certain attributes are more suited for venous applications, such as larger diameters (≥14 mm) and appropriate levels of radial force and crush resistance.” - Mahmood K. Razavi, MD, FSIR

Engineering Conflicts and Optimization

- **Design Conflicts**
  - Strength vs Flexibility vs Foreshortening
  - Scaffolding/Coverage vs Flexibility
  - Crush Resistance and Radial Strength vs Deployment

- Each requirement is a “lever” that can be moved, however, it may affect and move other levers

- Optimization of a design is based on how all the levers are prioritized
Other Requirements/Constraints

• Manufacturability
  – Without efficient manufacturing process, product cost can be high
  – Without robust manufacturing process, defects and yields may jeopardize product quality

• Development Cost
  – Increases with more design features and optimization
  – Increases with design complexity

• Time to market
  – Multi-year long process from concept to product release
  – First-to-market typically establishes leadership and market share
**Stent Strength**

**Chronic Outward Force:**  
How much the stent pushes outward. Changes with diameter expansion. Often called Radial Force.

**Crush Resistance:**  
How much the stent can resist a single load.

**Radial Resistive Force:**  
How much circumferential load a stent can resist.
Radial Resistive Force

Radial Resistive Force: How much circumferential load the stent can take

16mm Stent Radial Strength

- Radial Resistive Force

Hoop Strength (N) vs. Diameter (mm)

- Hybrid
- Open Cell
- Closed Cell
- Braided
Crush Resistance

Closed Cell

Open Cell

Hybrid

Braided
Arterial Not ‘Strong’ Enough
Not ‘Strong’ Enough

Arterial stent

Expanded with Venous Stent
Flexibility
What gets good results

- Technical
- Flow
- Clotting

Stent Choice
Placement
Errors
Mistakes

Inflow!!!
CFV

APLS
Behcet’s
Anti-coagulation
Venous Stenting is Not New...

• Significant body of clinical work
  – Existing stents (off label)...Wallstent
  – Good success treating venous outflow obstruction (peer review publications)

• Current generation of stents in USA IDE trials IDE and available OUS
  – VIVO Trial – Zilver Vena (Cook Medical)- completed
  – VIRTUS Trial – VICI VENOUS STENT (VENITI, Inc.) - completed
  – Venovo (Bard) – Started recruitment
  – Abre (Medtronic) – To Come this year
  – Sinus Venous/Obliquus (Optimed) – No trial as yet
  – Wallstent (BSCI) – No trial

Safety and efficacy of current designs
Conclusions

• The stent alone is not the panacea
• Know each device and technical issues
• Be honest in feedback and know this is just the beginning – 1st generation stents
• We need long term patient outcome data to support use
• We do not have data yet to know if this is durable
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