Laser Sintered Resorbable PCL Splints for Treating Tracheoobronchomalacia (TBM)

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Outline

- Tracheobronchomalacia
- Tracheal Splint Clinical Goals & Design
- Laser Sintering PCL Splints
- Clinical Use and Outcomes
- Quality Control: Current & Future
Tracheobronchomalacia (TBM)
Tracheobronchomalacia (TBM) in Humans

- Compression of airway, typically by malformed vascular structures
- Complete collapse on expiration
- Currently treated by tracheostomy/ventilators 1-2 years
- Significant complications, including death
- Need for patient specific implants due to different defect geometry (length, diameter, number)
- Stents have failed in children; FDA warning metallic tracheal stents
- Implanted splints external to airway found to give better results, but produced in an ad hoc manner
Tracheal Splint Clinical Goals and Design
Clinical Design Goals: Implanted Splint External to Airway

Mechanical Requirement: **M**; Biomaterial Requirement: **B**; Surgical Requirement: **S**

- The splint should provide radial compressive mechanical support to keep the airway open and patent:  **M/B** – 0.12 MPa artery; 0.01 MPa exhalation
- The splint should provide this radial mechanical support for a period of 24-30 months to allow tracheal remodeling and development:  **M/B**
- The splint should allow transverse and bending displacement, not interfering with cervical motion: **M**
- The splint should allow growth and expansion of the tracheobronchial complex during this 24-30 month period: **M** - estimated 15N growth force
- The splint should not cause adverse tissue reaction or remodeling:  **B/M** - Biocompatible
- The splint should not interfere with the mucociliary architecture with the tracheobronchial lumen; it therefore should be placed externally:  **B/S**
- Second surgical procedure should be avoided to remove the splint; therefore, the splint should be bioresorbable:  **S/M** – resorbable in 3 years
- Surgical placement of the splint and attachment of the tracheobronchus into the splint should be straightforward:  **S**; suture holes in splint to “sling” airway
- Patient Specific to account for different malacic airway diameter/length:  **S/M**
Patient Specific Image-Based Design for Splint

- MATLAB program to automatically generate bellow design w/suture holes
- Design variables: inner diameter, open angle, spiral angle, bellow height, wall thickness, suture hole width, etc (> 3,000,000 design perturbations)
- Input parameters from CT measurements from MIMICS Digital Model
- Fit splint to patient model in MIMICS
- Perform finite element analysis: compression, bending, opening (growth)
- Complex patient specific design requires 3D printing
Laser Sintering PCL Splints
Design and Manufacture Process: Outline

CT Scan - 3D Patient Model in Mimics

Splint Design & Analysis - MATLAB/MIMICS/FEA

Receive Raw PCL

Mill PCL

Receive HA

Blend PCL & 3-5% HA

Laser Sinter Splints

Set Parameters

Mimics: 1. Generate Splint STL 2. Size Splint to Malacic Defect

Slice Splint STL Files

Store Raw PCL

Store HA

Test Splint Geometry & Mechanics

Package & Label Splint

Sterilize Splint
Scaffold/Implant Manufacturing by 3D Printing

• Modular Image-Designed Scaffolds fabricated by laser sintering

Complete Video at http://www.mottchildren.org/news/archive/201403/babys-life-saved-after-3d-printed-devices-were-implanted-u

Modular Image-Designed Scaffold

PCL Laser Sintering

Final Manufactured Scaffold
Materials and Equipment

- EOS P100 Laser Sintering System ([www.eos.info/en](http://www.eos.info/en))

- CAPA 6501 Polycaprolactone (PCL) purchased from Polysciences ([www.polysciences.com](http://www.polysciences.com)) Target Mw = 50kDa

- Hydroxyapatite (HA) Plasma Biotal ([www.plasma-biotal.com](http://www.plasma-biotal.com))

- Need to Cryogenically Mill Resorbable Polymers (PCL, PLA) Jet Pulverizer ([www.jetpulverizer.com](http://www.jetpulverizer.com)); Fraunhofer ([http://www.umsicht.fraunhofer.de/en.html](http://www.umsicht.fraunhofer.de/en.html)); Evonik ([http://north-america.evonik.com](http://north-america.evonik.com)); Target Particle Size Range: 25\(\mu\)m < x < 125 \(\mu\)m; Median 40-60 \(\mu\)m

References:
Partee et al., 2006, J Man Sci Eng, 128:531-540
Williams et al., 2005, Biomaterials, 26:4817-4827
Lohfield et al., 2012, Acta Biomaterialia; 8:3446-3456
Eosoly et al., 2010, Acta Biomaterialia; 6:2511-2517
PCL Laser Sintering Parameters

- Important PCL Laser Sintering Parameters: Bed Temperature, Laser Power, Laser Scanning Speed, Scan Spacing, Hatch Spacing, Beam Offset

- **Laser Power**: 1 - 5.4 Watts; Typically 4 Watts (UM)

- **Bed Temperature**: 38 – 56°C; Typically 50-56°C (UM)

- **Laser Scanning Speed**: 900 – 1800 mm/s; Typically 1000-1500mm/s (UM)

- **Scan Spacing**: .07 - .2mm; Typically 0.15 – 0.2mm (UM)

References (see prev slide): Eshragi/Das (2010/2012); Lohfield (2012); Eosoly (2010; 2012); Partee (2006); Williams (2005)
Clinical Use and Outcomes
Design & Implantation of Patient Specific Splints

Patient 1:
Left Bronchus;
IRB Approval, Emergency through FDA
NEJM (2013), 368:2043-2045.
31 months post-surgery

Patient 2:
Bilateral Bronchi;
IRB Approval, Emergency through FDA
8 months post-surgery

Patient 3:
Left Bronchus;
IRB Approval, Emergency through FDA
6 months post-surgery
Pre-Op and Post-OP Patency

Patient 1: Left Bronchus; Exhalation Scans

Patient 2: Bilateral Bronchi; Exhalation Scans

Patient 3: Bronchoscopy
Bronchial Growth in Patients

Hydraulic Diameter Measures Averaged along Bronchus in MIMICS

- **Patient 1**
  - 3 months at surgery
  - 16 months at surgery

- **Patient 2**
  - Right
  - Left

- **Patient 3**
  - 5 months at surgery

Diagram showing changes in hydraulic diameter over time post-operatively for three patients.
All Patients Pre- and Post-Op

Patient 1 – Pre-Op
Patient 1 – 2nd Birthday
Patient 2 – Pre-op 16 months
Patient 2 – First time sitting up
Patient 3 – Pre-Op
Patient 3 – Post-Op 2 months
Quality Control: Current & Future
Quality Control Checks for Each Build

- **Powder**: Check particle size range; Powder Visual Inspection; Humidity Solid Hygrometer Should be 10% to 35% relative humidity

- **Build**: Check for errors on build log; visual inspection for part dragging; visual inspection for sintered “islands” when unpack build; stair stepping on parts

- **Geometry**: Caliper Measures (current); Micro-CT to assess part geometry/density (implementing)

- **Mechanical Properties**: Standard cylindrical test specimens for modulus; splint specimens opening, compression, bending geometric stiffness (implementing)
Geometry Quality Control

- For topology optimized (optimized for stiffness/permeability) microstructures, compare designed vs manufactured geometry by microCT (implementing for splint)

Design/Fabrication Process

Design to Fabricated Strut/Throat Comparison

Fidelity depends on Unit Cell Size & thus Feature resolution; Dias et al, (2014), 36:448-457
Solid Test Cylinder Modulus
1. Affected by Laser scanning parameters: Bed Temp, Laser Power, Scan Speed 1200-2500 mm/s
2. Anisotropic due to layering
   \( E_x = 295.5 \pm 4.4 \text{ MPa parallel to bed} \)
   \( E_y = 292.7 \pm 9.9 \text{ MPa parallel to bed} \)
   \( E_z = 311.7 \pm 1.2 \text{ MPa laser direction} \)

Optimized Microstructures
1. Topology optimized for desired stiffness/permeability
2. Compare FE idealized to laser sintered mechanically tested
3. Correlation deviates from 1 to 1 as feature sizes get smaller (< 0.8mm)

Coelho et al, (in press) Med Eng Phys
**Mechanical Testing Quality Control - Splint**

**Compression:**
Simulate exhalation loading

**Opening:**
Simulate growth and inhalation loading

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**Design Target:**

1. Withstand arterial compression & respiration pressure
2. Allow growth

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\[ Ku = f; \Rightarrow \]

\[ f \left( \text{artery/exhalation pressure} \times \text{length} \times 1\text{mm}; \frac{N}{\text{mm}^2} \times \text{mm} \times \text{mm} \right) \]

\[ K = \frac{N}{u(\text{target}\{.1\text{comp};.2\text{open}\} \times \text{inner diameter};\text{mm})} \]

**Stiffness in compression** (.12N * length / .1 * ID) \( \approx 10 \text{N} / \text{mm} \)

**Stiffness in opening** (.12N * length / .2 * OpenAngle) \( \leq 2 \text{N} / \text{mm} \)

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**Patient 1** - Compression: 128.6 ± 11.8 N/mm; Opening: 2.77 ± 0.26 N/mm;

**Patient 2** - Compression: 72.2 ± 14.6 N/mm (11mm); Opening: 1.43 ± 0.12 N/mm;
195.8 ± 16.2 N/mm (23mm); Opening: 2.43 ± 0.15 N/mm;

**Pig Preclinical** - Compression: 28.5 ± 1.6 N/mm; Opening: 0.43 ± 0.05 N/mm; 20% growth over 8 months
Fatigue & Degradation Quality Control

- For resorbable materials, need to determine affect of sintering on fatigue & degradation

- Sintering doesn’t significantly change/degrade PCL molecular weight prior to implantation; ~40% loss of Mw by 18 months *in vivo* (spine cage in pig).

- Fatigue properties depend significantly on geometry; Have run spine cages to 5 million cycles in dry environment – need to test in solution
Conclusions

- Developed Laser Sintered, resorbable PCL patient specific splint for treating tracheobronchomalacia; Successful in 3 patients up to 31 months

- Fabricated topology optimized scaffolds with complex microstructure

- Splints with 0.4 to 2.8 N/mm opening stiffness allowed growth in patients and preclinical pig model; 28 to 195 N/mm compression stiffness protects malacic airway

- Laser parameters (scan speed, bed temp, scan power, particle size) significantly affect device geometry, mechanical properties (stiffness, strength, fatigue) & degradation (need to be tested)

- Ability to meet geometric and mechanical requirements depends on how close feature size is to minimum resolvable sintering feature -> closer to minimum feature size will mean larger deviation between design & actual properties
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