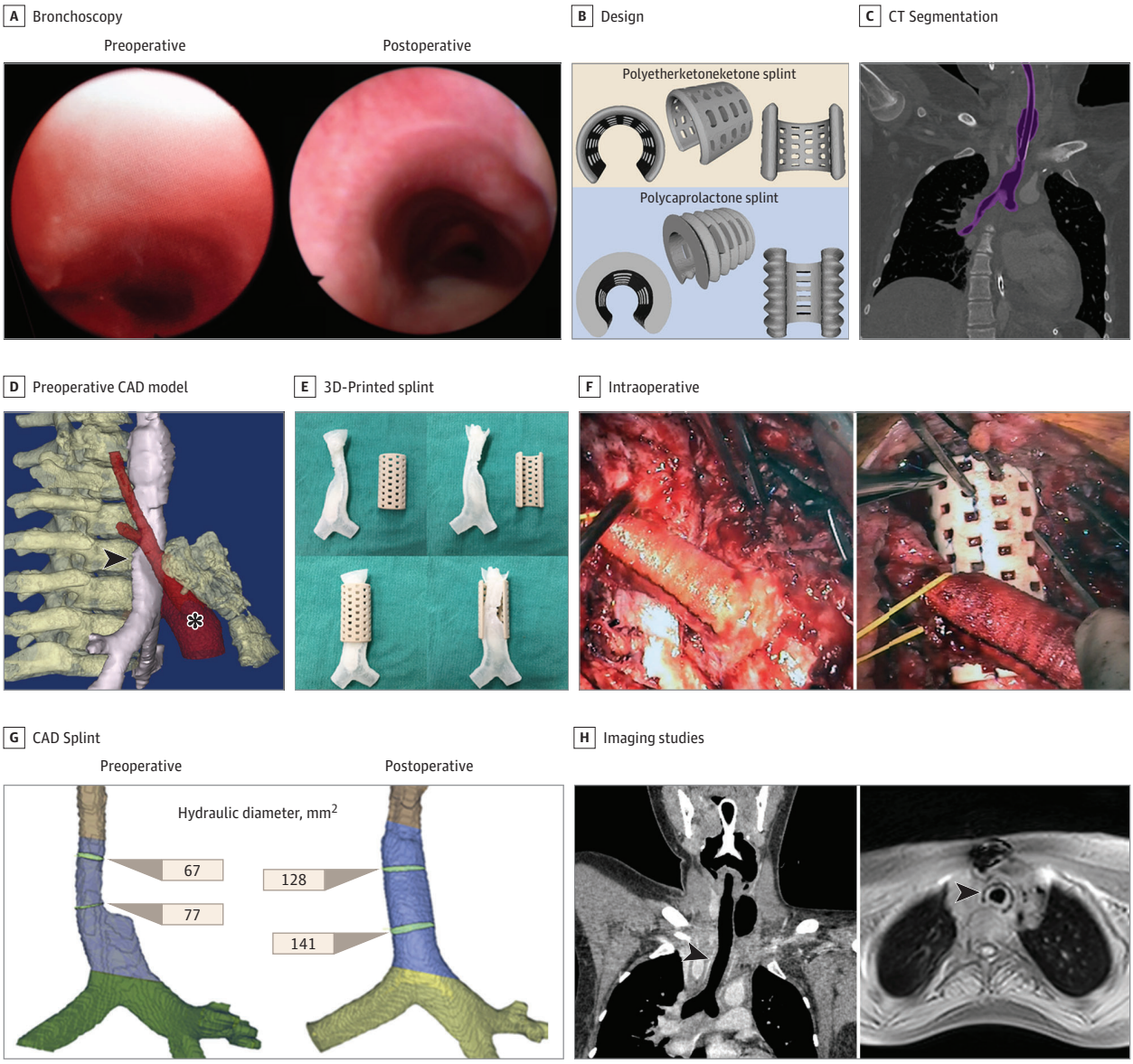
Letters

RESEARCH LETTER

Treatment of Severe Acquired Tracheomalacia With a Patient-Specific, 3D-Printed, Permanent Tracheal Splint

Tracheobronchomalacia (TBM) is a disease of excessive collapse of the primary airways resulting from intrinsic weakness or extrinsic compression. While infantile TBM typically regresses in severity over time, adult-phenotype TBM is more often persistent and progressive.[1] Severe TBM carries substantial morbidity and mortality, and interventions such as surgical excision, stenting, and tracheotomy have all been associated with life-threatening complications.[2,3]

Figure. Assessment, Design, Manufacture, and Use of a 3D-Printed Polyetherketoneketone Tracheal Splint for Treating Focal Tracheomalacia



A, Flexible bronchoscopic view of the affected trachea preoperatively and immediately postoperatively. B, Comparison of design characteristics of biopermanent polyetherketoneketone and bioresorbable polycaprolactone tracheal splints. C, Segmentation of the computed tomography (CT) scan using thresholding function to generate patient computer-aided design (CAD) model. D, Preoperative CAD model showing relationship of the spine, airway, vasculature (asterisk), and manubrium (arrowhead indicates area of malacia). E, 3D-printed, patient-specific, polyetherketoneketone tracheal splint. F, The innominate artery graft compressing the trachea (left); 3D-printed, patient-specific splint implanted onto the patient's trachea (right). G, CAD model of patient's trachea before and after implantation demonstrating significant increase in hydraulic diameter of the affected segment. H, Patient CT (left) and magnetic resonance imaging (right) 1 year after device implantation. Black arrowhead denotes location of the 3D-printed polyetherketoneketone splint.

Table. Comparison of Device Design Characteristics and Biomaterial Properties of 3D-Printed Tracheal Splints

Device Type	Bellow Height, %	Opening Wedge Angle	Wall Thickness, mm	Suture Hole Size, mm	Suture Hole Spacing	Edges of Device
Upper Boundaries of Splint Design Characteristics						
Bioresorbable	40	90°	3.0	1 × 3	Linear	Straight
Biopermanent	0	120°	1.5	2 × 2	Staggered	Rounded
Splint Biomaterial Properties						
Material	**Biocompatible**	**Time to Resorption**	**Young's Modulus of Elasticity, MPa**	**Tensile Strength, MPa**		**Surgically Modifiable**
Polycaprolactone	Yes	2-3 y	350	10		Yes
Polyetherketoneketone	Yes	Never	3000	70		No

Our group has previously had success treating infantile TBM using a bioresorbable, 3D-printed external splint.[4,5] This device generally has limitations in its application to acquired disease because of its temporary design. However, we describe a patient-specific, 3D-printed external tracheal splint for treatment of TBM, with modifications to device design and biomaterial selection yielding a biopermanent option for patients with adult-phenotype TBM.

Methods | The patient was a young woman with severe autism, thoracic scoliosis, and acquired tracheomalacia due to compression between a high-riding innominate artery and the thoracic spine within a narrowed thoracic inlet. Her disease progressed such that she experienced repeated cardiopulmonary arrests despite pharmacologic paralysis, mechanical ventilation, and continuous sedation for over 40 days. Previous attempts at treatment included manubriectomy, aortopexy, and innominate artery reimplantation. Endoscopic examination demonstrated continued severe, focal, compressive tracheomalacia (**Figure**, A [left]). Discontinuation of care was recommended by her physicians.

We hypothesized that an external splint would be effective in treating her acquired TBM. Such a device must provide long-term stiffness to maintain airway patency while avoiding fatigue failure due to repetitive-motion forces. Design modifications compared with previously used polycaprolactone (PCL) splints are summarized in the **Table** and included removing the bellowed topography to diffuse contact forces, thinning the wall structure to lighten the device, and increasing the open angle of the splint to facilitate placement (Figure, B).

Clearance for use of the device was obtained from the University of Michigan institutional review board and the US Food and Drug Administration. Using the patient's computed tomography (CT) scan imported into computer-aided design software (Mimics, version 16.0; Materialise), a model of the patient's respiratory, skeletal, and vascular anatomy was generated (Figure, C and D). Splint geometric design parameters were determined from measurements of the affected tracheal segment and used to generate the device design (MATLAB, Mathworks). The splint stereolithography model was digitally fit over the airway for design validation. The device was 3D printed using polyetherketoneketone (PEKK) (OXPEKK; Oxford Performance Materials) (Figure, E). PEKK was chosen for its material properties, superior to those of PCL for a nonresorbable implant, and for its suitability to manufacture the device via 3D printing (Table).

Implantation was performed via a midline sternotomy approach by placing the splint around the affected trachea and suspending the trachea within the splint using polypropylene sutures (Figure, F, top and bottom). Repeat endoscopy and CT imaging of the airways was performed 1 and 12 months postoperatively. Magnetic resonance imaging were performed 12 months postoperatively to assess device position.

Results | Endoscopic examination immediately after splint placement showed restoration of tracheal patency (Figure, A [right]). The patient was extubated 3 weeks after surgery and discharged by 1 month. Follow-up CT imaging demonstrated complete patency of the affected trachea (Figure, A [right]). Computed tomography analysis of the affected region from before to 1 month after splint placement demonstrated an absolute increase in tracheal hydraulic diameter of 3.1 mm (95% CI, 2.35-3.85 mm) (Figure, G). Magnetic resonance and CT imaging demonstrated that the device remained properly positioned 1 year after surgery (Figure, H). The patient remains asymptomatic, has had no additional hospitalizations, and there have been no apparent complications.

Discussion | We demonstrate successful treatment of life-threatening acquired tracheomalacia with a 3D-printed biopermanent tracheal splint in a patient for whom all prior therapeutic approaches had failed. This first-in-human use of a novel device demonstrates promising results in arresting severity and alleviating morbidity of adult-phenotype TBM.

Robert J. Morrison, MD
Shayan Sengupta, BS
Colleen L. Flanangan, MSE
Richard G. Ohye, MD
Scott J. Hollister, PhD
Glenn E. Green, MD

Author Affiliations: Department of Otolaryngology–Head & Neck Surgery, University of Michigan, Ann Arbor (Morrison); University of Michigan Medical School, University of Michigan, Ann Arbor (Sengupta); Department of Biomedical Engineering, University of Michigan, Ann Arbor (Flanangan, Hollister); Department of Cardiac Surgery, University of Michigan, Ann Arbor (Ohye); Division of Pediatric Otolaryngology, Department of Otolaryngology–Head & Neck Surgery, University of Michigan, Ann Arbor (Green).

Corresponding Author: Glenn E. Green, MD, Division of Pediatric Otolaryngology, Department of Otolaryngology–Head & Neck Surgery, University of Michigan, 1540 E Hospital Dr, SPC 5-702, Ann Arbor, MI (gegreen@med.umich.edu).

Published Online: January 26, 2017. doi:10.1001/jamaoto.2016.3932

Author Contributions: Dr Green had full access to all of the data in the study and takes responsibility for the integrity of the data and accuracy of data analysis.
Concept and design: Morrison, Flanagan, Hollister, Green.
Acquisition, analysis, or interpretation of data: Morrison, Sengupta, Ohye, Hollister, Green.
Drafting of the manuscript: Morrison, Sengupta, Ohye.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Sengupta.
Obtained funding: Hollister, Green.
Administrative, technical, or material support: Flanagan, Green.
Supervision: Morrison, Ohye, Green.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Drs Hollister and Green are listed as coinventors on a US patent for the study device. The device was provided free of charge by Oxford Performance Materials. No other disclosures are reported.

Funding/Support: This work was funded in part by National Institutes of Health (NIH) grant R21 HD076370-01 (Drs Hollister and Green) and by the National Center for Advancing Translational Sciences of the NIH under award No. 2UL1TR000433. Dr Morrison is supported by NIH grant T32 DC005356-12.

Role of the Funder/Sponsor: The funders/sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Additional Contributions: We thank the patient's guardian for granting permission to publish this information. We also thank the Michigan Institute for Clinical & Health Research IND/IDE Investigator Assistance Program (MIAP) group for their help in obtaining regulatory approval.

1. Murgu SD, Colt HG. Tracheobronchomalacia and excessive dynamic airway collapse. *Respirology*. 2006;11(4):388-406.

2. Kugler C, Stanzel F. Tracheomalacia. *Thorac Surg Clin*. 2014;24(1):51-58.

3. Valerie EP, Durrant AC, Forte V, Wales P, Chait P, Kim PC. A decade of using intraluminal tracheal/bronchial stents in the management of tracheomalacia and/or bronchomalacia: is it better than aortopexy? *J Pediatr Surg*. 2005;40(6):904-907.

4. Zopf DA, Hollister SJ, Nelson ME, Ohye RG, Green GE. Bioresorbable airway splint created with a three-dimensional printer. *N Engl J Med*. 2013;368(21):2043-2045.

5. Morrison RJ, Hollister SJ, Niedner MF, et al. Mitigation of tracheobronchomalacia with 3D-printed personalized medical devices in pediatric patients. *Sci Transl Med*. 2015;7(285):285ra64.