Editorial

Three-dimensional printing of external airway splints for tracheomalacia

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Three-dimensional (3D) printing technology has been used to create personalized medical devices. There is growing interest in the use of 3D-printed biomaterials to create four-dimensional (4D) structure, such that the 3D-printed devices are engineered to adapt and change with tissue growth based on biomechanical and degradation properties over a specified time period (1). Huang *et al*. demonstrate the use of a 3D-printed personalized external airway splint for the treatment of severe tracheomalacia, building on work largely pioneered by Green's group from the University of Michigan (2).

Tracheomalacia is characterized by dynamic airway collapse with anterior vascular compression, posterior membranous tracheal intrusion, or both. It is an underestimated disease that is commonly misdiagnosed. Excessive airway collapse leads to ineffective ventilation and poor clearance of secretions, resulting in a wide spectrum of respiratory symptoms that can progress to bronchiectasis, and in the most severe cases, blue spells and apparent life-threatening events (ALTEs). Currently, there is little consensus on the evaluation, diagnosis, and treatment of severe tracheomalacia, including grading of symptom severity, criteria for radiographic or endoscopic evaluation, medical treatment, and surgical approach (3-5). According to the 2012 Cochrane review, there is no evidence to support any one therapy over another for the treatment of tracheomalacia (6).

Surgical options for the treatment of tracheomalacia include pexy procedures (aortopexy, anterior and/or posterior tracheopexy), internal tracheal stents, and external stabilization (3-5). Aortopexy is the most commonly used technique and addresses anterior vascular compression by indirectly elevating the anterior wall of the trachea. In a recent meta-analysis, aortopexy was effective in clinically improving more than 80% of children, however 8% showed no improvement, 4% had worsening of their symptoms, and 6% died (7). Anterior and/or posterior tracheopexy, as first reported by our group, directly address anterior malformed tracheal cartilage and posterior membranous tracheal intrusion that may limit the effectiveness of aortopexy in some cases. Tracheopexy is done under direct bronchoscopic guidance. Anterior tracheopexy elevates the anterior wall of the trachea by fixing the trachea to the sternum, whereas posterior tracheopexy fixes the posterior tracheal membrane to the anterior longitudinal spinal ligament. Initial evaluation of this technique has shown promising short-term results (3,4).

Internal tracheal stents placed by endoscopy have been described, but have largely fallen out of favor due to complications including stent migration or fracture, erosion into nearby structures, formation of granulation tissue, difficult removal, and the need for additional dilations or stents, especially with patient growth. When compared to aortopexy, tracheal stents were associated with higher failure rates and more severe stent-related morbidity and mortality (8). Internal stents are thus only used in limited situations.

External stabilization or splinting techniques have evolved with a variety of autologous and prosthetic materials to support the malacic trachea. Implantation of

prosthetic material has raised concerns in terms of long-term effects and complications including infection and erosion into nearby structures. Bioresorbable external airway splints composed of polycaprolactone (PCL) have recently been described in animal models and patient case reports (1,2,9,10). PCL is a biocompatible polyester that maintains support for 2–3 years prior to resorption. The external airway splints are customized based on computed tomography imaging of the patient's airway and made with the use of a laser-based 3D printer to anatomic specifications. The splints are designed to provide adequate rigidity and radial support to maintain airway patency and prevent external compression, but also allow internal expansion to accommodate airway growth. In 2013, Zopf *et al*. from the University of Michigan published the index case of a 3D-printed, customized, bioresorbable airway splint for a three-month-old infant with severe tracheobronchomalacia affecting the left mainstem bronchus under emergency use exemption from the Food and Drug Administration (9). This patient had been treated with tracheostomy and mechanical ventilation, transposition of the right pulmonary artery, and failed aortopexy. Sutures were placed through the wall of the left mainstem bronchus through interstices of the external splint to expand the airway. Ventilator support was weaned off by 21 days, and at one year follow up, imaging and endoscopy demonstrated a patent left mainstem bronchus.

Zopf *et al*. went on to demonstrate the effectiveness of their 3D-printed bioresorbable external airway splint in extending survival in a porcine model of severe tracheomalacia (10). A surgical model of tracheomalacia was created in two-month-old Yorkshire pigs by extraluminal resection of a tracheal ring, subperichondrial dissociation of internal tracheal mucosa, and division of the overlying tracheal rings. Tracheal collapse was observed after model creation. In all experimental animals after splint placement, there was resolution of symptoms and significantly longer survival than the control animals. Mortality in the experimental group was related to infection secondary to intraluminal mucosal needle holes, which were taken into account in subsequent modifications to the animal model for future studies.

After demonstrating a survival benefit in a preclinical porcine model of tracheomalacia, Morrison *et al*. described successful implantation of 3D-printed bioresorbable external airway splints in three infants with severe tracheobronchomalacia (1). Infants were 3-16 months old, all with tracheostomies on mechanical ventilation, with primarily severe left mainstem bronchomalacia. One patient had bilateral mainstem bronchomalacia, and the splint was customized as such. Postoperatively, follow up ranged from 11 to 38 months, with only one patient having long-term follow up at 38 months after splint bioresorption. All patients had significant improvements in their respiratory symptoms with no occurrence of an ALTE. One patient weaned off the ventilator but remains tracheostomy dependent due to proximal cervical tracheomalacia at his tracheostoma. The patient with bilateral bronchomalacia weaned off ventilator support while awake at latest follow up. The third patient remains ventilator dependent due to left segmental bronchomalacia distal to the airway splint. On comparison of airway diameter, splinted airways showed improved patency and comparable growth to the normal contralateral airway when available, demonstrating 4D structure responsive to airway growth.

Huang *et al*. report the first use of a 3D-printed bioresorbable external airway splint in an adult patient with secondary tracheomalacia from endobronchial tuberculosis (2). An artificial pleural patch was placed around the scaffold to prevent erosion into nearby structures. The patient was extubated 48 hours later and remains symptom-free with patent airway on imaging three months after surgery. There has been no adverse reaction or complication thus far.

3D printing of external airway splints for tracheobronchomalacia has been shown to be feasible, effective, and safe in preliminary studies (1,2,9). 3D printing has allowed for the precise design of customized medical devices and design modifications to adapt to a patient's specific anatomy in the era of personalized medicine. Time from initial evaluation of patient candidacy to production of the device typically requires 7 days. Early studies show promising short-term results, but as with all novel surgical techniques, further studies are needed to validate this technique and follow long-term outcomes and complications such as erosion or effects on the airway after splint bioresorption. Further work needs to be done to optimize safe design and manufacturing processes within regulatory mandates and clinical trials (11,12). Nevertheless, the current results show promise in an innovative technique with the potential to improve clinical outcomes in tracheobronchomalacia.

Given the complexity of this patient population, we favor a standardized approach to the evaluation of tracheomalacia and individualized patient care in multidisciplinary centers specializing in airway disorders. Standardized endoscopic

evaluation of tracheomalacia anatomy and severity can allow for more effective comparison of surgical techniques and discussion of longitudinal airway assessment and its correlation with clinical symptomatology. Surgical treatment must be tailored to the type of tracheobronchomalacia in each patient, taking into account associated conditions such as tracheoesophageal fistula or vascular anomalies. Further experience with 3D-printed bioresorbable external airway splints is necessary to determine criteria for patient selection and whether this technique is best used alone or in combination with aortopexy or tracheopexy.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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