www.brn.cat

PERMANYER

BRN Rev. 2024;10(2):79-84

BRN Reviews

REVIEW ARTICLE

3D Printed tracheobronchial stents: personalized medicine in silicone

Nicolas Guibert*, Valentin Héluain, and Gavin Plat

Department of Pulmonology, Toulouse University Hospital, Toulouse, France

ABSTRACT

The large arsenal of commercially available airway stents covers most situations of malignant and non-malignant central airway stenoses. Airway stents are however associated with a high rate of complications like migration and granulation tissue reaction that are often due to a lack of congruence of the stent with the patient's airways. Patient-specific stents using 3D printing have been developed in the past decade to improve patient's tolerance and the safety profile. We herein review the existing literature regarding these customized devices, ongoing research, discuss their potential indications and the next steps towards a transition into routine.

Keywords: 3D printed. Silicone. Tracheobronchial stents.

***Correspondence to:**
Nicolas Guibert
Email: guibert.n@chu-toulouse.fr

Received: 28-05-2024
Accepted: 10-06-2024
DOI: 10.23866/BRNRev:2024-M0109
www.brnreviews.com

RATIONALE FOR THE DEVELOPMENT OF CUSTOMIZED 3D STENTS

The large arsenal of commercially available airway stents (AS, silicone or self-expandable metallic stents [SEMS]) can relieve airway patency in the vast majority of situations of central airway stenoses, particularly malignant. Some complications of AS, like migration and granulation tissue reaction, are, however, linked to a lack of congruence of the stent with the patient's anatomy[1-3]. Patient-specific AS using 3D printing have been developed in the past decade to improve patient's tolerance and the safety profile, with an increasing amount of published clinical data[4-7]. We herein review the existing literature regarding "3D stents" and discuss what might be the best indications and the next perspectives.

MANUFACTURING OF "3D PRINTED" STENTS

Apart from highly complex shapes with multiple bifurcations[6], 3D stent implantation is identical to any stenting procedure. However, designing the stent requires a learning curve. Designing the virtual stent starts with the patient's computed tomography (CT) scan but obviously needs a correction of the diseased segment(s), and that implies an anticipation of what diameter(s) can be obtained after the first steps of the procedure (dilation with a balloon or rigid tube for example). This prediction is based both on the physician's experience in the specific disease being treated and on outcomes obtained during previous procedures (AS is rarely the frontline bronchoscopic treatment of non-malignant stenoses). We suggest matching the anatomy of the patient in all non-diseased areas to avoid the expected complications of AS (granulation tissue reactions, migration); but not at the level of the stenotic portion where a tubular shape will allow for a good radial force similar to what we are used to with conventional silicone devices. Figure 1 shows the examples of two "virtual" stents.

Two solutions exist for 3D stents (https://novatech.fr/en/tracheal/bronchial-stents/novatechr-3d/novatechr-3d in Europe, https://www.visionairsolutions.com/patient-specific-stents in the United States), and both follow a similar two-step, mold-based process. The methodology for the Novatech™ device (which the authors are used to) is presented in figure 2. After computer-assisted segmentation of the airways and correction of the stenosis using the CT images (AnatomikModeling™, in close collaboration with the treating physician), a virtual stent is designed from which an injection mold ("negative") is 3D printed and used for the stent fabrication. The turnaround time for the manufacturing of the stent (from prescription to delivery) is approximately three weeks.

PREFERRED INDICATIONS FOR CUSTOMIZED 3D STENTS

If 3D stents are commercially available, very few data have been reported in the literature[8], and indications are thus not clearly established. However, based on nine years of experience of use in clinical trials and routine, we have gained confidence regarding what may be the clear, potential, or bad indications. Before going into detail on these situations, it

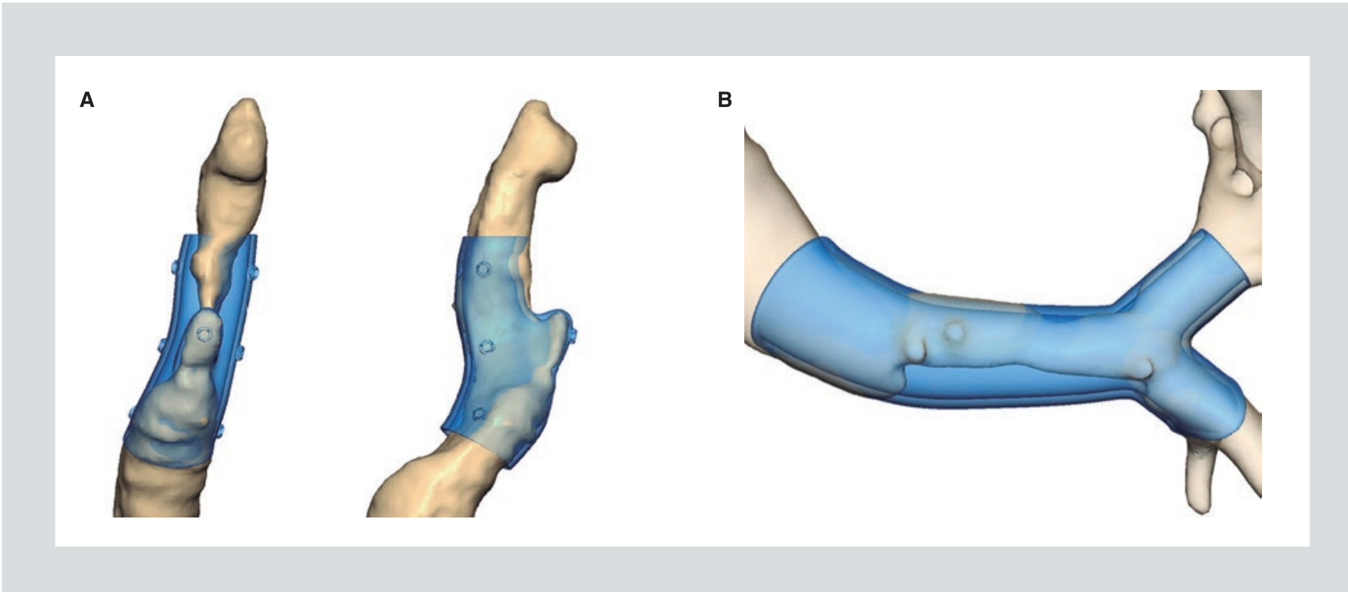

Figure 1. Examples of two virtual stents. **A**: post tracheotomy complex stenosis. The cavity created by the previous tracheotomy is used to stabilize the stent after failure of conventional stents (migrations); **B**: malacia of the left anastomosis. In both cases the virtual correction (virtual stent in blue) of the distorted airways (in beige) can be observed.

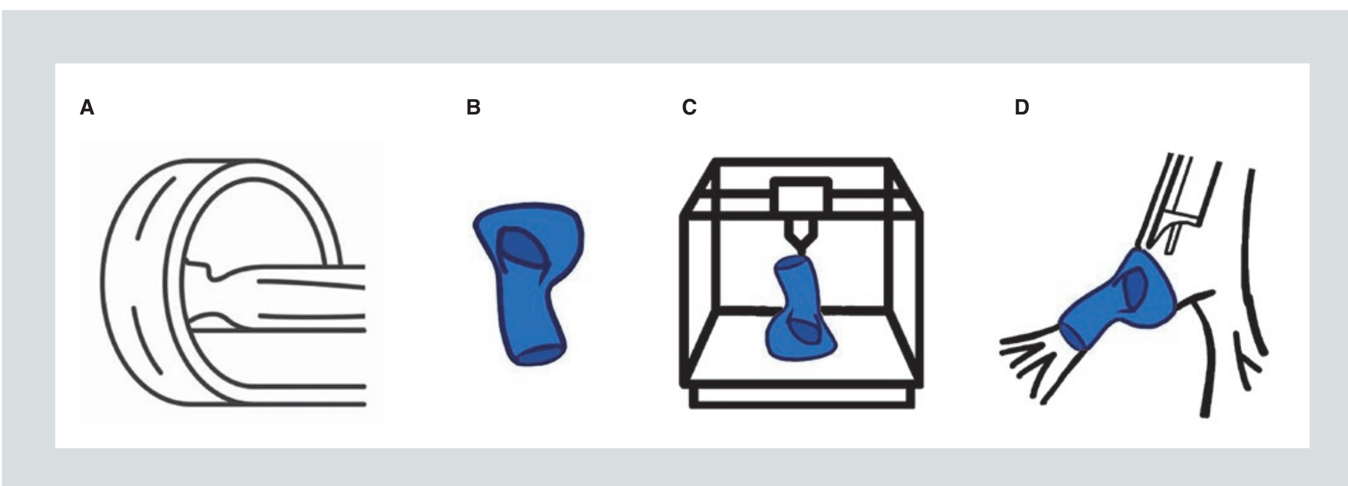

Figure 2. Manufacturing of a customized 3D stent: **A**: CT scan acquisition in forced inspiration; **B**: design of a virtual stent; **C**: 3D printing of a mold in which is injected medical-grade silicone; **D**: implantation of the stent under rigid bronchoscopy and general anesthesia.

is important to remember the prerequisite that AS is rarely the frontline solution for non-malignant airway stenoses. The subchapters that follow describe the use of 3D stent when airway stenting has been indicated (i.e. after surgery has been discussed and ruled out, and simpler bronchoscopic interventions, such as iterative dilations, have failed).

Clear indications

Obviously, given the initial rationale, these new stents benefit the most in "anatomically complex" situations. This was the main inclusion criterion in our proof-of-concept study (NCT02889029) where it was arbitrarily defined as "commercially available airway stent not suited based on a consensual decision by three interventional pulmonologists or failed (complication requiring stent removal)”. The best example is represented by all anastomotic complications. Almost any time a stenosis occurs after surgery involving the airways, the distortion, unusual angles, or discrepancy between diameters make it difficult to manage with conventional stents. Post-transplantation anastomotic complications are, in our practice, the most frequent indication for 3D stents. The need for AS is often long, if not definitive (malacia), and even when conventional devices can be placed, complications usually occur (granulation tissue reaction, mucus plugging, migration), requiring stent replacement. 3D stents probably improve tolerance, reduce the complication rate, and might decrease the number of stents per year used for patients who need AS in the long term. Anastomotic complications of other airway surgeries (sleeve lobectomy, right upper lobectomy with carinal resection, tracheal and/or carinal resections) are for the same reasons good indications[6]. Figure 3 shows an example of the use of a 3D stent for complete occlusion of the anastomosis between the carina and the *bronchus intermedius* after right sleeve lobectomy following the failure of other devices.

Potential indications

Tracheal stenoses are among the most frequent non-malignant indications for AS. The most frequent and concerning complication in this context is migration. Granulation tissue reaction is usual but rarely induces significant airway narrowing, the trachea being large. Mucus plugging is rarely symptomatic in terms of dyspnea (it can cause halitosis but rarely complete stent occlusion because stents in this indication are large and short). Whether 3D stents can decrease the risk of migration is thus the main question here. It depends on the anatomy of the patient. In case of usual tracheal anatomy (tubular), it is unlikely that a 3D stent will prevent migration, while in case of distorted anatomy, the latter can be used to design the stent and prevent migration (see figure 1A for example).

Bad indications

Diffuse tracheobronchomalacia (TBM) is usually considered a bad indication for AS, as it leads to early improvements in dyspnea and quality of life; however, stent-related complications (mucus plugging, infections in particular) due to mucus clearance issues in most patients (49 complications in 58 patients in the study by Ernst et al.[9]). AS is thus usually considered a therapeutic test, with the early improvements allowing for anticipation of the benefit of a tracheobronchoplasty. Matching the patient’s anatomy does not prevent mucus clearance alteration, making 3D stents useless in this indication. The only use we have had is in a patient with both TBM and tracheobronchomegalia, for whom airway diameters were too wide to be covered by commercially available stents. This 3D stent was still only used as a bridge to (robotic) surgery.

Perspectives

Perspectives are reglementary, technical and scientific. One main limitation of 3D stents is the manufacturing process necessitating an intermediate step of molding. 3D printing

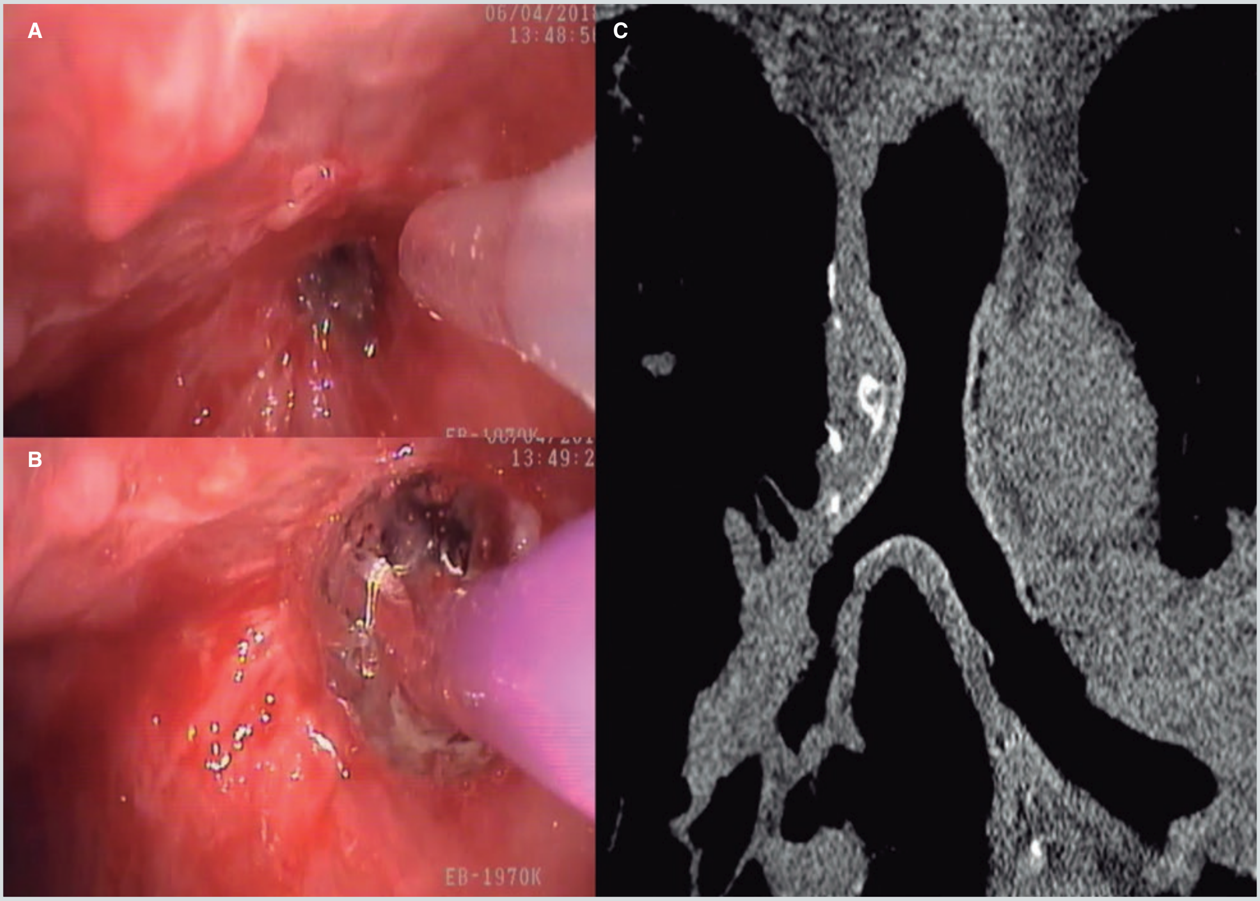

FIGURE 3. Example of a patient (from the DASCAS trial) treated with a 3D stent for an anastomotic complication after sleeve lobectomy. Commercially available stents failed: due to the difference in caliber between the right (thin stenotic *bronchus intermedius*) and left branches (normal left main bronchus), silicone Y stents could not be used (the right branch would not unfold) and bifurcated SEMS induced dramatic and stenosing granulation tissue reaction on the right side. **A**: visualization of the orifice of the *bronchus intermedius* after perforation with electrocoagulation, allowing for the passage of a dilation balloon. **B**: balloon dilation of the stenosis. **C**: CT scan one week after 3D stent implantation. Note the good congruence with the airways and the difference in caliber of the right and left branches of the stent. DASCAS: Dedicated Airway Stents for Central Airway Stenoses; SEMS: self-expandable metallic stents.

silicone is technically feasible, but silicone is not thermoplastic. Syringe extruding silicone is not very precise, making it difficult to get a good resolution as the material slumps and flow distorts during extrusion. Moreover, the device created must be biocompatible. We are thus far from being able to directly print stents from the CT scan, which will/would also raise reglementary issues (https://www.fda.gov/medical-devices/3d-printing-medical-devices/3d-printing-medical-devices-point-care-discussion-paper). There is also an increasing amount of data regarding the usefulness of biodegradable stents, in particular for anastomotic complications after transplantation[10]. Combining the two technologies would be appealing in this latter indication where the anatomy is often distorted and the need for AS usually transient. A polymer (or combination of polymers) candidate that is biodegradable, biocompatible, 3D printable and flexible is however not easy to identify.

But before these technical challenges, it will be important to better define the place of 3D stent in the treatment algorithm for the management of non-malignant stenoses. They are usually considered for "anatomically complex" stenoses, but the trigger for this definition is highly subjective and might strongly vary across physicians. We have so far only proof-of-concept published data, and the Treatment of Central Airway Stenoses Using Computer-Assisted Customized 3D Stents (TATUM) trial should give more answers regarding the efficacy in terms of symptoms and quality of life. But the most important question remains whether they can overperform standard devices in non-complex situations (when conventional stents are feasible), whenever a long-term need is expected. We can anticipate a better tolerance and decrease in complications rate, but only a randomized controlled trial comparing 3D and standard devices will be able to confirm this (or not).

In conclusion, customized "3D" stents may improve tolerance and reduce complications in "complex", non-malignant airway stenoses, but their place needs to be better determined, ideally through randomized controlled trials.

FUNDING

None.

CONFLICTS OF INTEREST

None.

ETHICAL DISCLOSURES

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

REFERENCES

1. Rosell A, Stratakos G. Therapeutic bronchoscopy for central airway diseases. Eur Respir Rev. 2020;29:190178.
2. Aravena C, Gildea TR. Advancements in airway stents: a comprehensive update. Curr Opin Pulm Med. 2024;30:75-83.
3. Guibert N, Saka H, Dutau H. Airway stenting: Technological advancements and its role in interventional pulmonology. Respirology. 2020;25:953-62.
4. Guibert N, Didier A, Moreno B, et al. Treatment of Post-transplant Complex Airway Stenosis with a Three-Dimensional, Computer-assisted Customized Airway Stent. Am J Respir Crit Care Med. 2017;195:e31-e33.
5. Guibert N, Didier A, Moreno B, et al. Treatment of complex airway stenoses using patient-specific 3D-engineered stents: a proof-of-concept study. Thorax. 2019;74:810-13.
6. Guibert N, Mazières J, Moreno B, et al. 'Double-bifurcated' stent: when 3D is not an option. Thorax. 2023;78:735-6.
7. Aravena C, Gildea TR. Patient-specific airway stent using three-dimensional printing: a review. Ann Transl Med. 2023;11:360.
8. van Beelen S, Smesseim I, Guibert N, Wijma I, Burgers S. Broadening the scope for three-dimensional printed airway stents. ERJ Open Res. 2023;9: 00673-2022.
9. Ernst A, Majid A, Feller-Kopman D, et al. Airway stabilization with silicone stents for treating adult tracheobronchomalacia: a prospective observational study. Chest. 2007;132:609-16.
10. van Pel R, Gan T, Daniels JMA, et al. Lung transplant airway complications treated with biodegradable airway stents: The Dutch multi-center experience. Clin Transplant. 2024;38:e15289.