Long term complications of airway stents

DM Seminar

22/02/2019

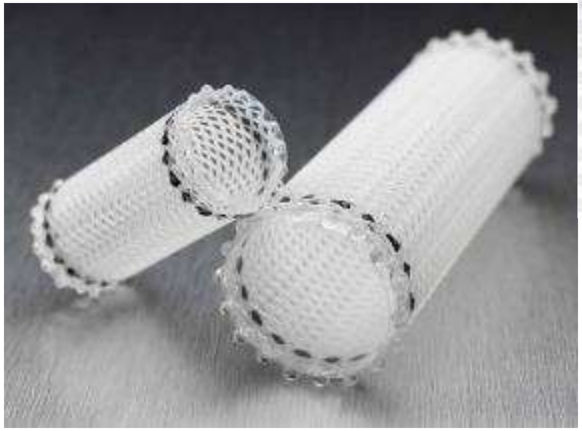
Long term complications of airway stents

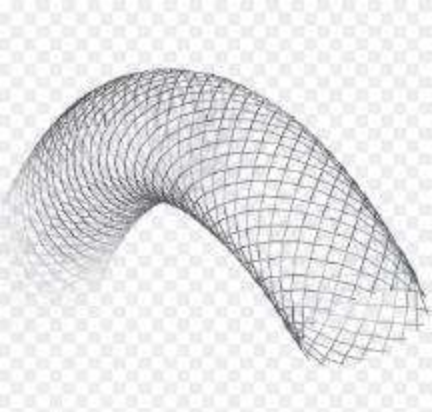
- Infection
- Granulation tissue
- Stent migration
- Tumor in-growth
- Mucus plugging
- Stent fracture
- Others: Difficulty of removing metal stents, Tracheobronchial perforation, fistula

Dynamic Y stent

Ultraflex

Polyflex





Wallstent

Aerostent

NiTi- S

Metallic Y stent

Dumon Tube stent

Complications	*Silicone stent*	*Metallic stent*
Granulation tissue in-/overgrowth	Little	**More**
Tumor in-/overgrowth	Only at ends	**Yes** in uncovered portion/stent
Migration	**Significant**	Less common, except fully covered stents
Fracture/degeneration	Very rare	**Significant** with longer follow-up
Infection	Uncommon	**More common**
Tracheobronchial Perforation	Very rare	**Possible**, more common with stiffer stents
Mucus impaction	**Common**	Uncommon

Ernst A. & Herth FJF. Principles and Practice of Interventional Pulmonology

Complications in Y- SEMS

References	No.	Type of Stent	Mean f/u	Complications
Yang et al. 2007	5	Y SEMS	16.6 wks	Nil
Yang et al. 2007	15	Y SEMS	22 wks	5 death- unrelated to stent
Han et al. 2008	35	Y SEMS (Micro-Tech)	27.5 wks	Nil
Dobbertin et al. 2009	37	Y SEMS	NA	Stent obstruction Requiring removal in 3 cases
Gompelmann et al. 2013	32/43	Covered Y SEMS	NA	Deaths- 11/32 (34 %) Tumor ingrowth- 2/18 Stent removal- 2/18 Minor complications including secretions, cough, granulation- 6/18
Wu et al. 2014	15	Y SEMS	4-136 wks	2 deaths- Infection

Incidence of complications

- 2 year Indian multicenter data of Y- SEMS (n= 38)
- Follow-up duration- 12.2 (8.7-15.7) wks

Complications	N (%)
Mortality at 3 mo	18 (47.4)
Secretions requiring bronchoscopy	12 (31.6)
Granulation tissue	8 (21.1)
Stent fracture	1 (2.6)

Madan K. et al. J Bronchol Intervent Pulmonol 2016;23:29–38

Complications in silicone Y-stents

References	No.	Mean f/u	Complications
Freitag et al. 1997	135	3 months	Granulation tissue- 5, Stent migration- 4, Ciliary dysfunction- 5, Mucus impaction- 1
Lacy et al. 1999	9	Not given	Tube block- 1, TEF- 1, Tracheal candidiasis- 1
Dumon and Dumon 2001	50	304 days	Cough- 1, Granulation tissue- 1
Dutua et al. 2004	86	> 3 years	Stent migration- 1, Severe cough- 1
Nam et al. 2009	11	1342 days	Granulation tissue- 7, Chest discomfort- 4, Mucostasis- 2, Fever- 1
Oki and Saka 2012	12	NA	Granulation tissue- 1
Oki and Saka 2013	10	836 days	Pneumonia- 2, Granulation tissue- 1, Retension of secretion- 1, Hemoptysis- 1
Oki and Saka 2015	12	NA	Retension of secretion- 1, Hemoptysis- 1
Tsukioka et al. 2015	12	NA	None

Incidence of complications

- Indian multicenter data silicone Y-stents (n= 27)
- Follow-up duration- 35.6 wks

Complications	N (%)
Stent related complications	14 (51.9)
Excess secretions and mucostasis	7 (25.9)
Granulation tissue at end of stents	4 (14.8)
Procedural complications	3 (11.1)
Tumor regrowth	2 (7)
Stent migration	1 (3.7)

Sehgal IS. et al. Lung India. 2017;34(4):311–317

References	No.	Stent used	Complications
Saad C. et al. 2003	82 patients (benign+ malignant)	SEMS- Ultraflex/ Wallstent	Infetion- 13, Granulation tissue- 12, Hemoptysis- 12, disease recurrence- 5, Migration- 4
Lemaire A. et al. 2004	54 stents in 33 patients (Benign)	SEMS	Excessive granulation tissue- 5, Restenosis of stent- 5, Migration of stent- 1, Intervention including stent dilations- 5, stent laser debridement- 3, stent removal- 3
Lemaire A. et al. 2005	172 stent in 140 patients (malignant)	SEMS	23 complications: Tumor ingrowth- 9, Excessive granulation tissue- 7, Stent migration - 5, Restenosis- 2
Gildea TR. Et al. 2006	16 stents in 12 patients(benign)	Polyflex	Stent migration- 11, Mucous plugging- 4
Ernst A. et al. 2007	58 TBM patient	Silicone stent	Partial stent obstructions- 21, Infections- 14, Stent migrations- 10
Breitenbücher A. et al 2008	62 stent in 60 patient (Malignant)	Ultraflex	Mucous plugging- 5 (8%), Stenosing granulation- 3 (5%), Tumor ingrowth- 3 (5%), Stent migration- 3 (5%)
Dooms C. et al. 2009	20 stents in 17 patients (benign)	SEMS- Alveolus, NiTi-S, Silmet	Complication rate- 75%: Stent removal- 60%, Stent migration- 65%, Stent fracture- 15%, Shriveling of stent- 10%, Granulation formation- 10%

References	No.	Stent used	Complications
Dutau H et al. 2010	17 post lung transplant	Silicone stent	Obstructive granuloma- 10, Mucus plugging- 7, migration- 7
Shah et al. 2011	212 stents in 183 patients malignant CAO	Ultraflex, Aero stents, Dumon silicone stents	Granulation tissue- 43, Stent removed- 16, Pneumonia- 14, Respiratory failure needing MV- 5
Chung et al. 2011	211 stents in 149 patients (benign+ malignant)	SEMS	Granulation tissue- 32, Stent fracture- 20, Stent migration- 16, Pneumothorax-1
Ost et al. 2012	195 stents in 172 patients	Ultraflex, Aero stent, and Dumon silicone	Pneumonia- 56, Mucus impaction- 48, Granulation tissue- 38, Stent migration- 27, Tumor overgrowth- 25, Tumor overgrowth- 25, Hemoptysis- 17, Stent strut fracture- 4, New fistula formation- 2, Death- 146/172
Lee HJ. Et al. 2017	147 stents in 134 patients (benign+ malignant)	Metallic, Silicone	Granulation tissue/Tumor obstruction- 37, Mucus impaction- 37, Stent migration- 20, Fracture- 1, distortion- 1

Infection

- Stent-associated respiratory tract infection (SARTI):
  - Clinical findings (fever, increased volume and purulence of the sputum) with or without
  - Radiological (pneumonia or lung abscess) or
  - Microbiological documentation

Agrafiotis M. et al. Respiration. 2009;78:69–74

Infection

- Impairment of ciliary function due to physical compression
- Leads to mucus aggregation and subsequent infections
- Enclosed stent in silicon or hybrid material inhibits the action of the cilia

Infection

- Systematic review of 23 articles (19 cohorts/case series and 4 case reports)
- 501 patients with airway stents
- Ninety- three (19%) out of 501 patients experienced SARTI
- Incidence of SARTI with metallic stents- 21%, polymeric- 20 % and hybrid stents- 23%

Agrafiotis M. et al. Respiration. 2009;78:69–74

Infection

- Pneumonia: Most common (47%)
- Followed by bronchial infection (24%), cavitary pneumonia/ lung abscess and intraluminal fungus ball

Organism	**%**
Staphylococcus aureus	*39%*
Pseudomonas aeruginosa	*28%*
Fungi	22%
Proteus mirabilis	6%
Streptococcus viridans	6%

Agrafiotis M. et al. Respiration. 2009;78:69–74

Infection

- Retrospective analysis of all patients who underwent airway stenting for malignant airway obstruction
- Study included 172 patients with 195 stent procedures
- Compare incidence of complications of different airway stents

Ost DE. et al. Chest 2012;141(6):1473–1481

Characteristics		Total Infection- 106 (76 patients)
Infection type	Acute bronchitis	34 (32)
	Pneumonia	72 (68)
Care site	Outpatient	48 (45)
	Admitted to hospital floor	36 (34)
	Admitted to hospital and required ICU	22 (21)
Ventilator support	No ventilatory support required during hospitalization	87 (82)
	Noninvasive positive pressure ventilation	5 (5)
	Mechanical ventilation with endotracheal tube	14 (13)
Stent removal required	Yes	12 (11)
	No	94 (89)
Death within 14 d of infection	Yes	24 (23)
	No	82 (77)

Ost DE. et al. Chest 2012;141(6):1473–1481

Table 5—*Multivariate Model for Time to Infection*

Characteristic	Hazard Ratio	95% CI	*P* Value
Dumon silicone vs Ultraflex	1.16	0.67-2.02	.59
Aero vs Ultraflex	1.98	1.03-3.81	.041

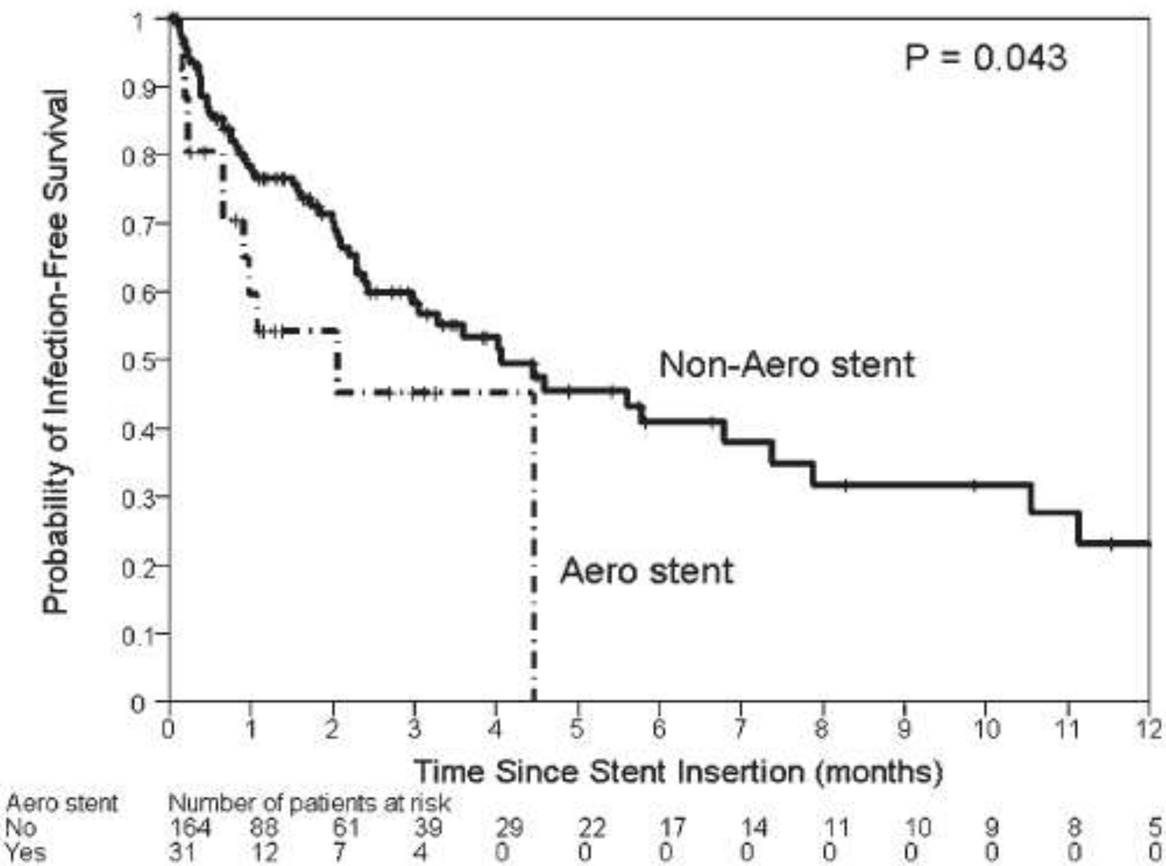


FIGURE 1. Kaplan-Meier plot of time to first respiratory infection by stent type. Aero stents (dashed line) had a significantly shorter

Aero stents- significantly shorter time to infection than other stents

Ost DE. et al. Chest 2012;141(6):1473–1481

Infection

- Retrospective cohort study
- Patients who had therapeutic bronchoscopy for malignant airways disease
- Outcomes: Lower respiratory tract infection and airway restenosis by tumor
- Twenty-three of 72 patients (32%) developed lower respiratory tract infections
- Median time to infection was 64 days

Grosu HB. et al. Chest 2013; 144(2):441–449

Characteristics		Total Infection- 23
Infection type	Acute bronchitis	5 (22)
	Pneumonia	18 (78)
Care site	Outpatient	10 (44)
	Admitted	23 (56)
Respiratory support	Yes	2 (9)
	No	21 (91)
Stent removal required	Yes	5 (22)
	No	18 (78)
Death within 14 d of infection	Yes	6 (22)
	No	17 (74)

Grosu HB. et al. Chest 2013; 144(2):441–449

Organism	No.
Pseudomonas aeruginosa	6
Actinomyces	2
a -Hemolytic strep	1
Aspergillus	1
Legionella species; not pneumophilia	1
Pseudomonas putida	1
Staphylococcus aureus , methicillin sensitive	1
Cytomegalovirus 1	1
Klebsiella pneumoniae	1
Sphingomona (*Pseudomonas) paucimobilis 1*	1
b lactamase negative *Haemophilus species*	1

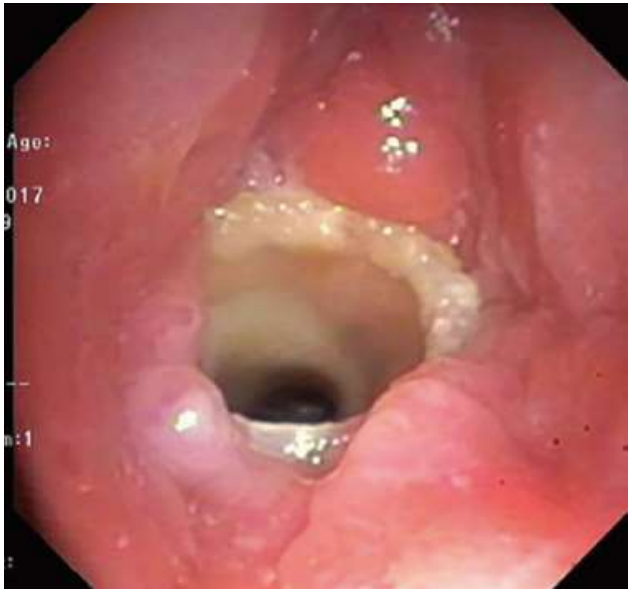
Grosu HB. et al. Chest 2013; 144(2):441–449

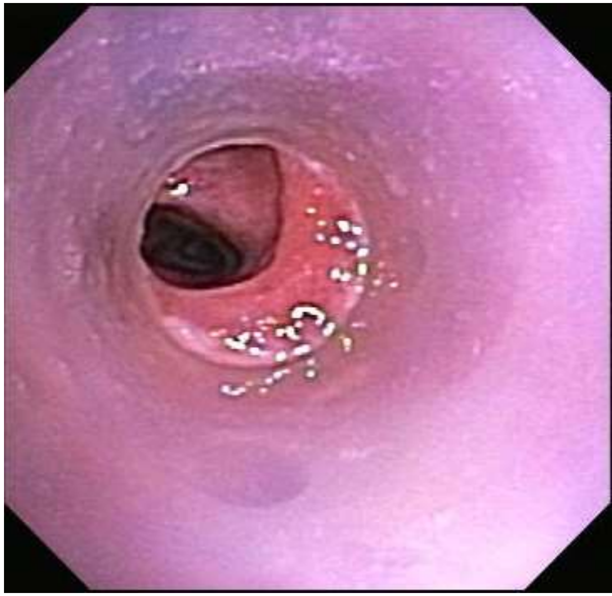
Changes in Airway Microbiology Following Placement of Airway Stents

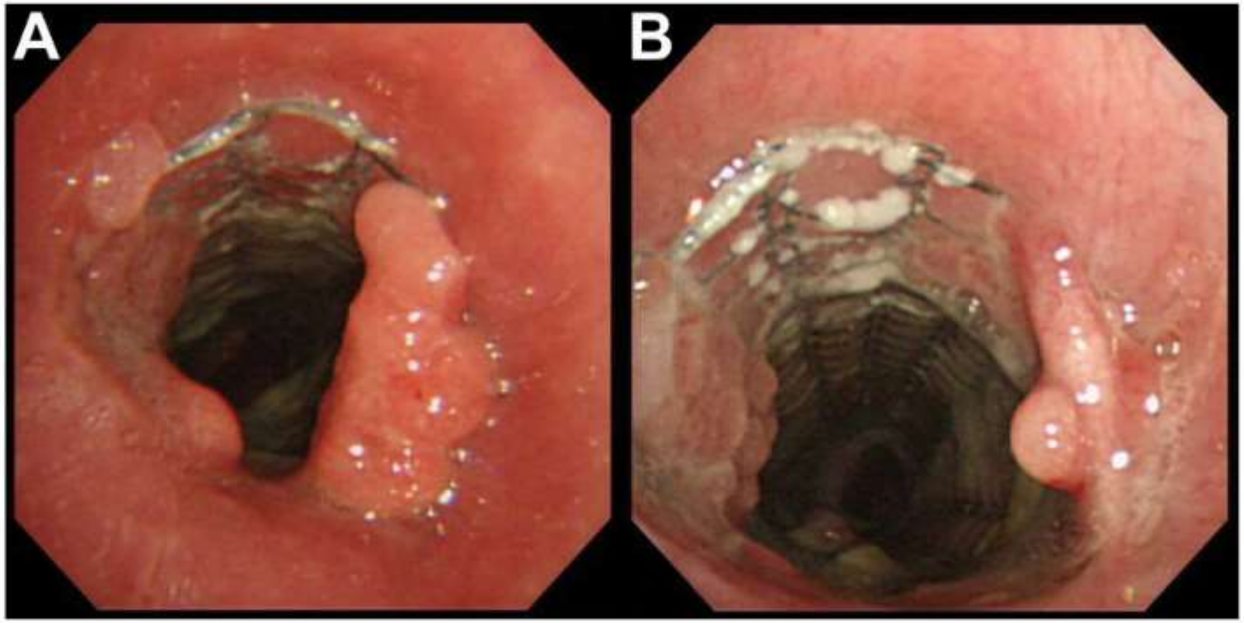
- 80% of samples: Isolated Polymicrobials with gram positive organisms predominating (61%)
- Most common Isolates with colony counts > 10^2:
  - Staphylococcus spp.- 39%
  - Streptococcus spp.- 17%
  - Micrococcus spp.- 4%
  - Corynbacteria spp.- 20%
  - Pseudomonas spp.- 14%
  - Neiserria spp.- 5%
- Associated with true lower airway infection in 18% of cases

Badamosi RA. et al. Chest 2007;(4) Suppl:p 519S

Granulation tissue







Granulation tissue

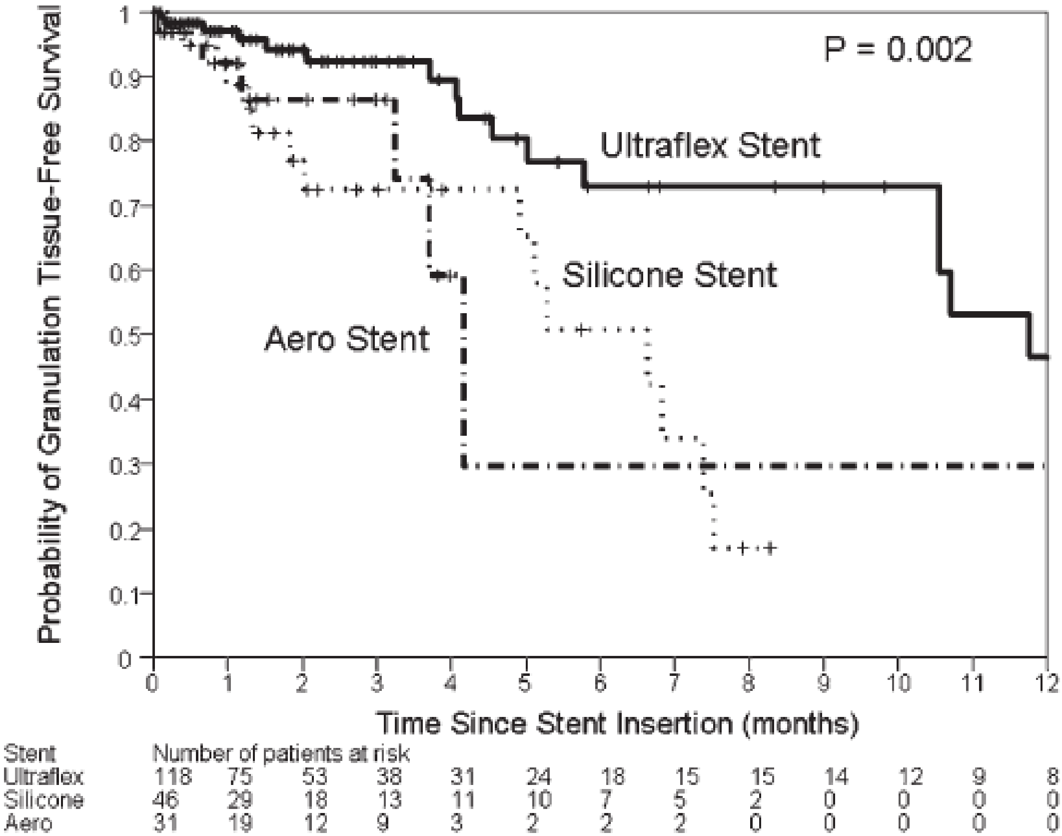
- Constant mechanical irritation resulting from stent
- Tend to occur in either proximal or distal ends of silicone and covered metallic stents
- In uncovered metallic stent, between the mesh of wire
- Development of granulation tissue associated with decreased chance of migration of stent
- Can cause obstruction of airway and stent, increase risk of infection
- Need of bronchoscopic treatment to reduce granulation tissue or even removal of stent may be warranted

Ost DE. et al. Chest 2012;141(6):1473–1481

Granulation tissue

- 212 stents in 183 patients malignant CAO
- Ultraflex, Aero stents and Dumon silicone stents
- Risk higher with silicone stents as compared to Ultraflex stents (HR 3.30, 95% CI 1.6-6.9, p= 0.002)
- Risk was higher with Aerostents (HR 2.67, 95% CI 1.03-6.95, p= 0.04)

Shah A. et al. Chest 2011;140(Supp. 4):469A



Kaplan-Meier plot of time to granulation tissue formation

Both Aero stents and silicone stents had higher incidence of granulation tissue formation than did Ultraflex stents

Table 9—*Multivariate Extended Cox Model of Time to Granulation Tissue Formation*

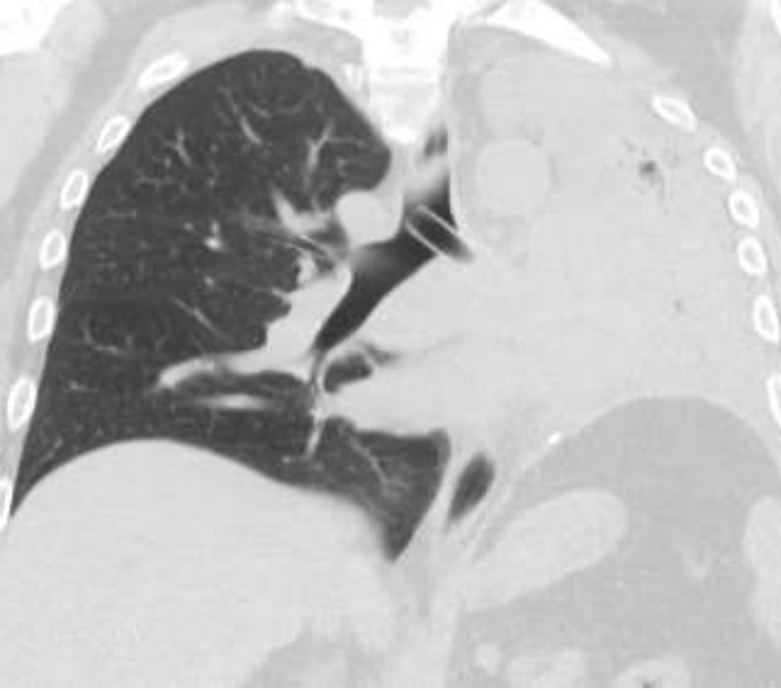
Characteristic	Hazard Ratio	95% CI	*P* Value
Dumon silicone vs Ultraflex	3.32	1.59-6.93	.001
Aero vs Ultraflex	1.60	0.61-4.21	.34
Infection: yes vs no (time varying)	5.69	2.6-12.42	<.001

Ost DE. et al. Chest 2012;141(6):1473–1481

Stent migration

- Tubular silicone stents have higher risk of migration
- Various anti-migration features:
  - External silicone studs
  - Y shape
  - Uncovered stent: Pressure on wall and granulation tissue prevents migration
  - Covered stent: Proximal and distal 5 mm are uncovered to prevent migration
  - Anti-migration fins and studs

Folch and Keyes. Ann Cardiothorac Surg 2018;7(2):273-283





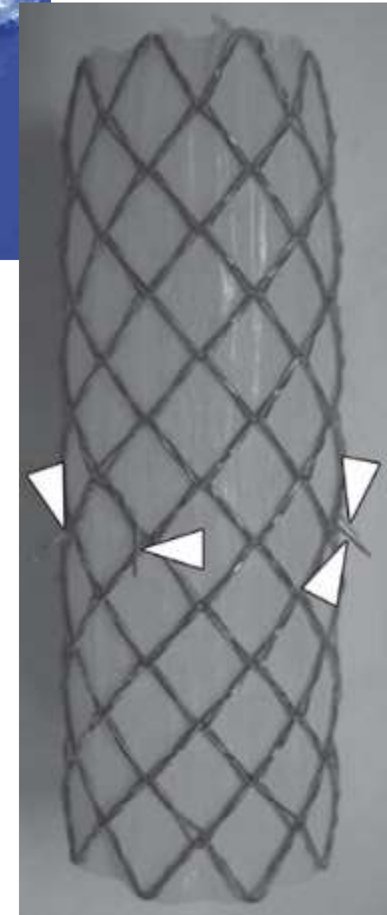


Table 7—*Multivariate Cox Proportional Hazards Model for Time to Migration by Stent Type*

Stent Type	Hazard Ratio	95% CI	*P* Value
Dumon silicone vs Ultraflex	3.52	1.41-8.82	.007
Aero vs Ultraflex	1.61	0.58-4.47	.37

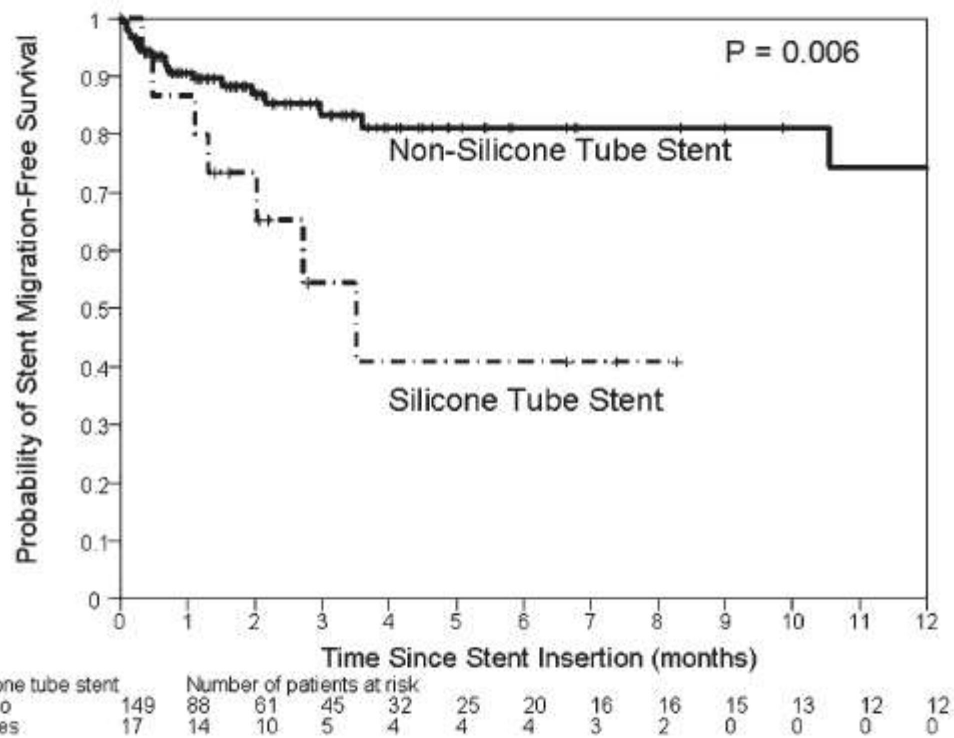


FIGURE 2. Kaplan-Meier plot of time to migration by stent type.

Silicone tube stents higher incidence of stent migration than non-silicone tube stents

Ost DE. et al. Chest 2012;141(6):1473–1481

Tumor ingrowth

- More common in metallic stents- Uncovered
- Incidence: 5–15%

Mucus plugging

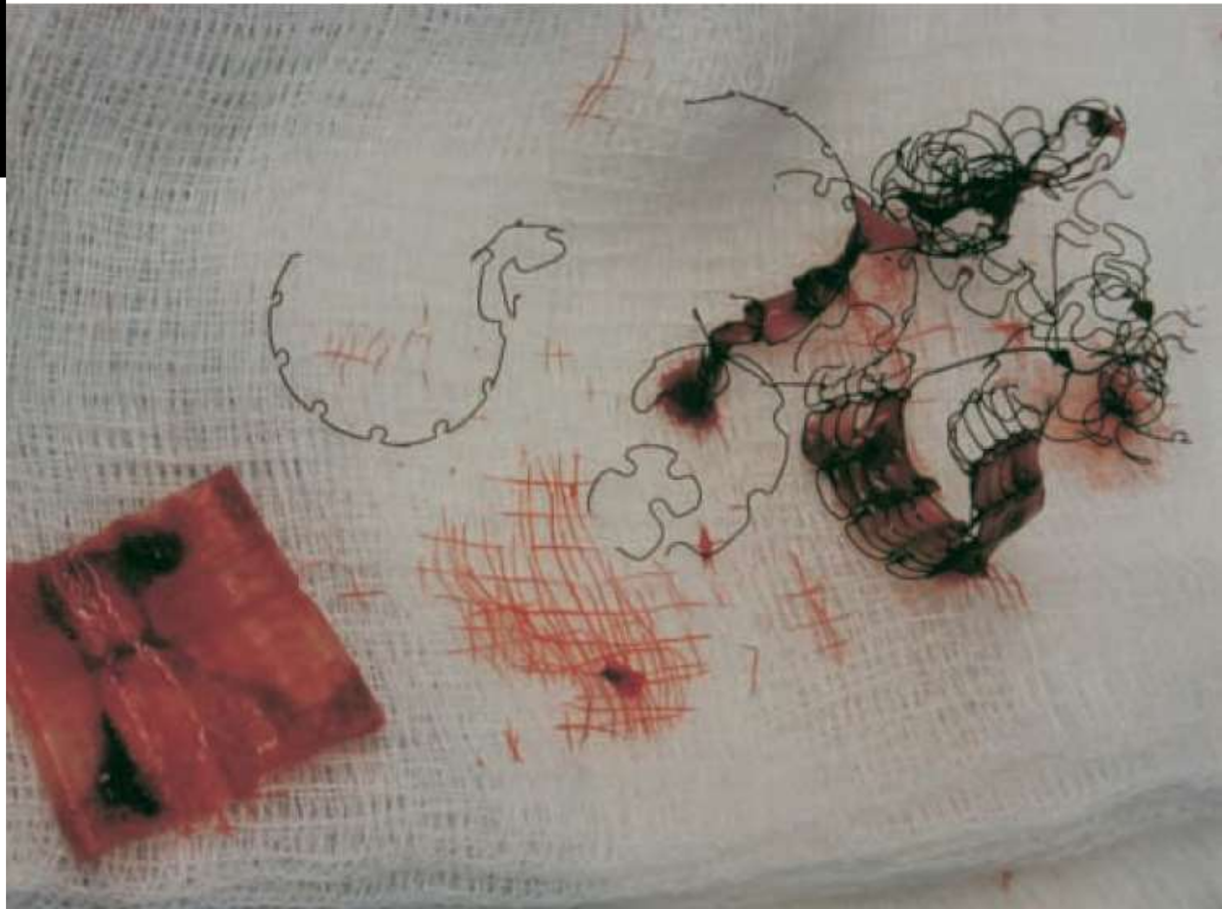
- Reported with the Dumon silicone stent in
  - 1.0–5.3% of cases with malignant disease and
  - 6.3% of cases with benign tracheal stenosis
- Rates similar to Ultraflex stent but lower than Wallstent

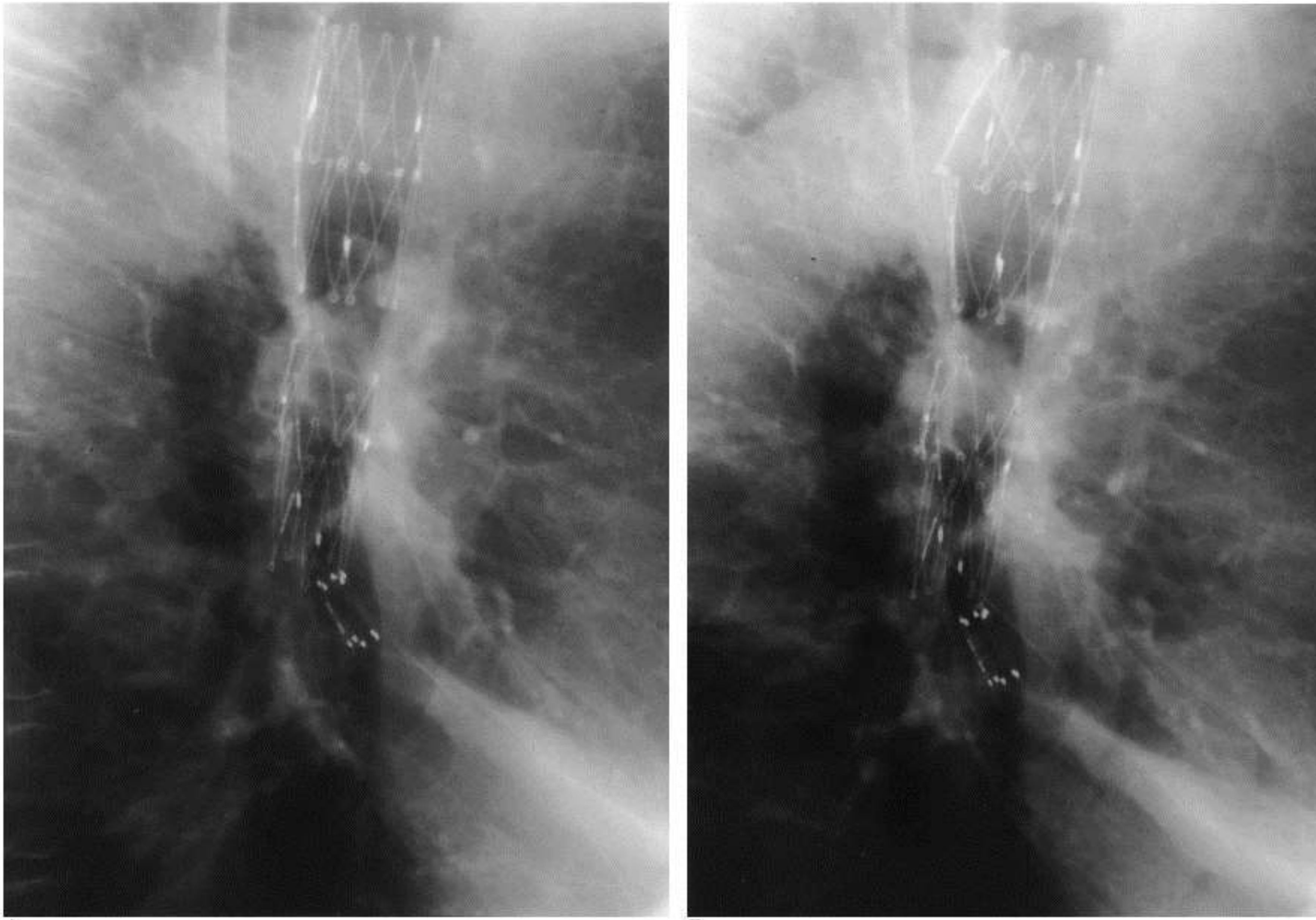
Breitenbücher A. et al. Respiration 2008;75:443–449

Stent fracture

- Uncommon complication, when they do occur it is usually with metal stents
- Commoner with more rigid metallic stent types- Gianturco stents
- Stent breakage requires urgent removal
- Increasing frequency with duration of implantation

Innabi Y. et al. EMJ Respir. 2017;5[1]:78-84





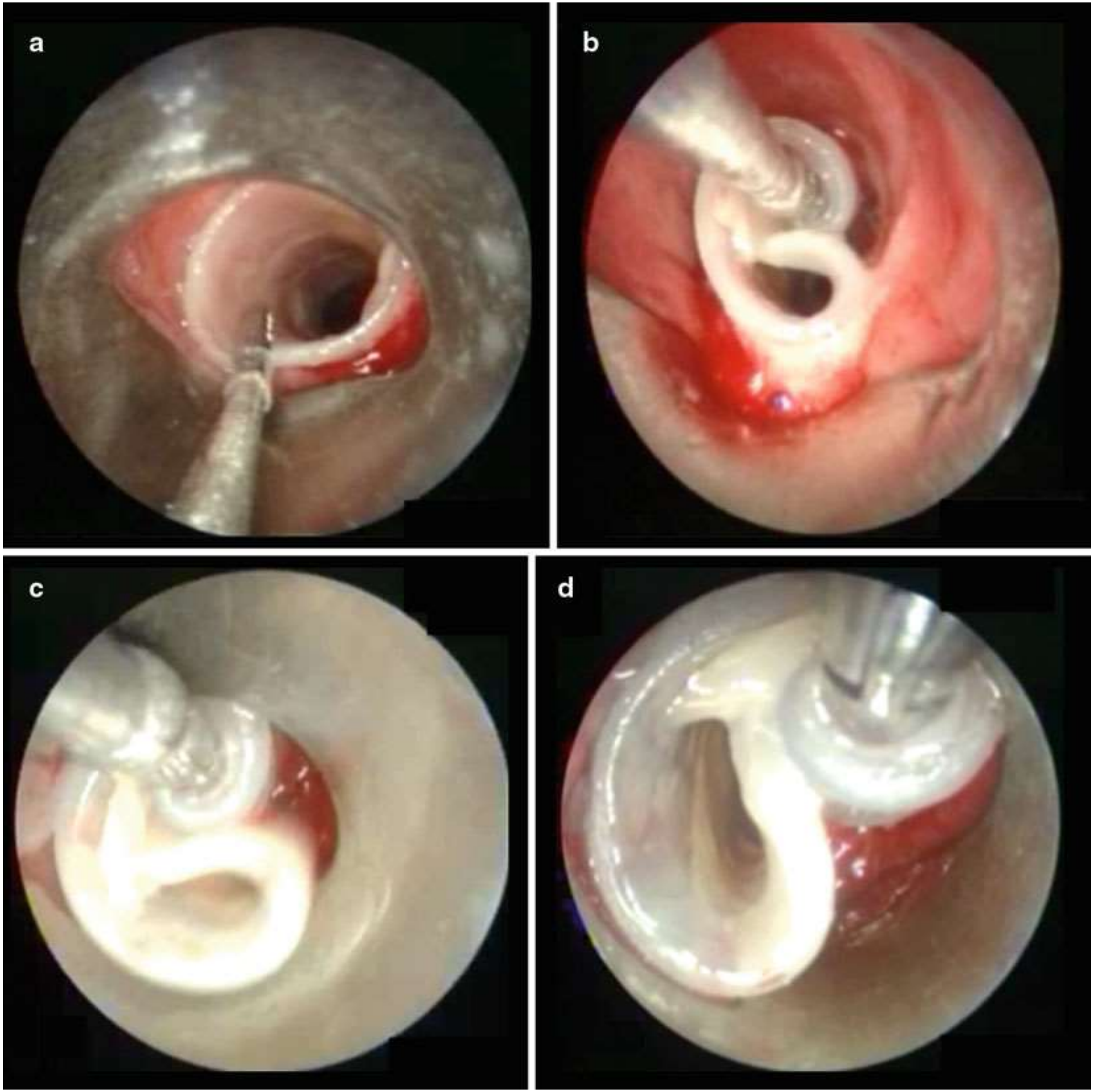
A B

(A) Lateral CRX demonstrating intact Gianturco stents in tracheal position and extending into bronchi
(B) Lateral CXR demonstrating disrupted tracheal stent (upper portion of figure), marked widening of stent, and erratic angulation of remaining fragments

Stent removal

- Complications from stents that cause airway injury or obstruction- Necessary to remove
- Removal of silicone stents: straightforward
- Involves rigid bronchoscopy and use of rigid forceps to simultaneously twist-and-pull stent into barrel of rigid bronchoscope

William Lunn. et al. Chest 2005; 127:2106–2112


a
b
c
d

Stent removal

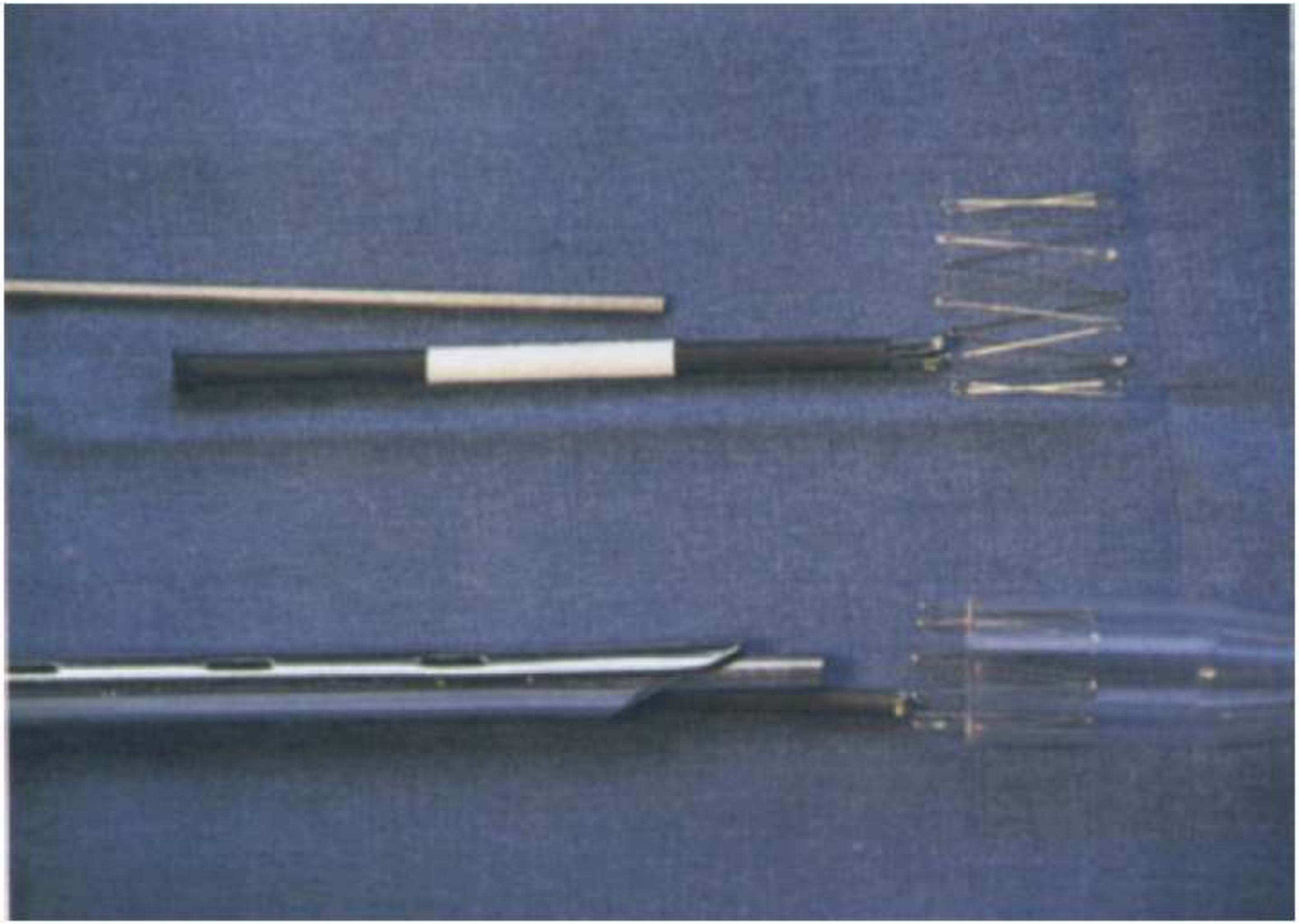
- Manufacturers recommend metallic stent removal by open surgical resection (thoracotomy)
- Removal of metallic stents in first 2 months relatively simple (prior to epithelization)
- Degree of difficulty increases with time
- Separating stent from wall with Jackson dilators or Fogarty balloon or barrel of rigid bronchoscope
- Stents removed by rigid forceps in a twist-and-turn fashion

William Lunn. et al. Chest 2005; 127:2106–2112

Stent removal

- Nashef et al. removed stents in 4 patients out of 15 patients who received **Gianturco** expanding wire stents
- Removal technique: similar to ***rolling spaghetti on a fork***, but much more difficult and at least equally messy
- Time-consuming and hindered by well-embedded barbs
- Removal may be piecemeal, requiring several fractures of stent

Nashef SA. et al. Ann Thorac Surg 1992;54:937–940



Nashef SA. et al. Ann Thorac Surg 1992;54:937–940

Table 3—*Indications for Stent Removal*

Indications	No.	% of Total
High-grade obstructing granulation tissue	14	70
With strut fracture	6	
With mucous retention	1	
Stent migration	2	13.3
With strut fracture	2	
Mucous plugging	3	10
Stent infection	1	3.3
Strut fracture with pain	1	3.3
Total	30	

William Lunn. et al. Chest 2005; 127:2106–2112

Complications

- Retained stent pieces (n= 7)
- Mucosal tear with bleeding (n= 4)
- Reobstruction requiring temporary silicone stent placement (n= 14)
- Need for postoperative mechanical ventilation (n= 6)
- Tension pneumothorax (n= 1)

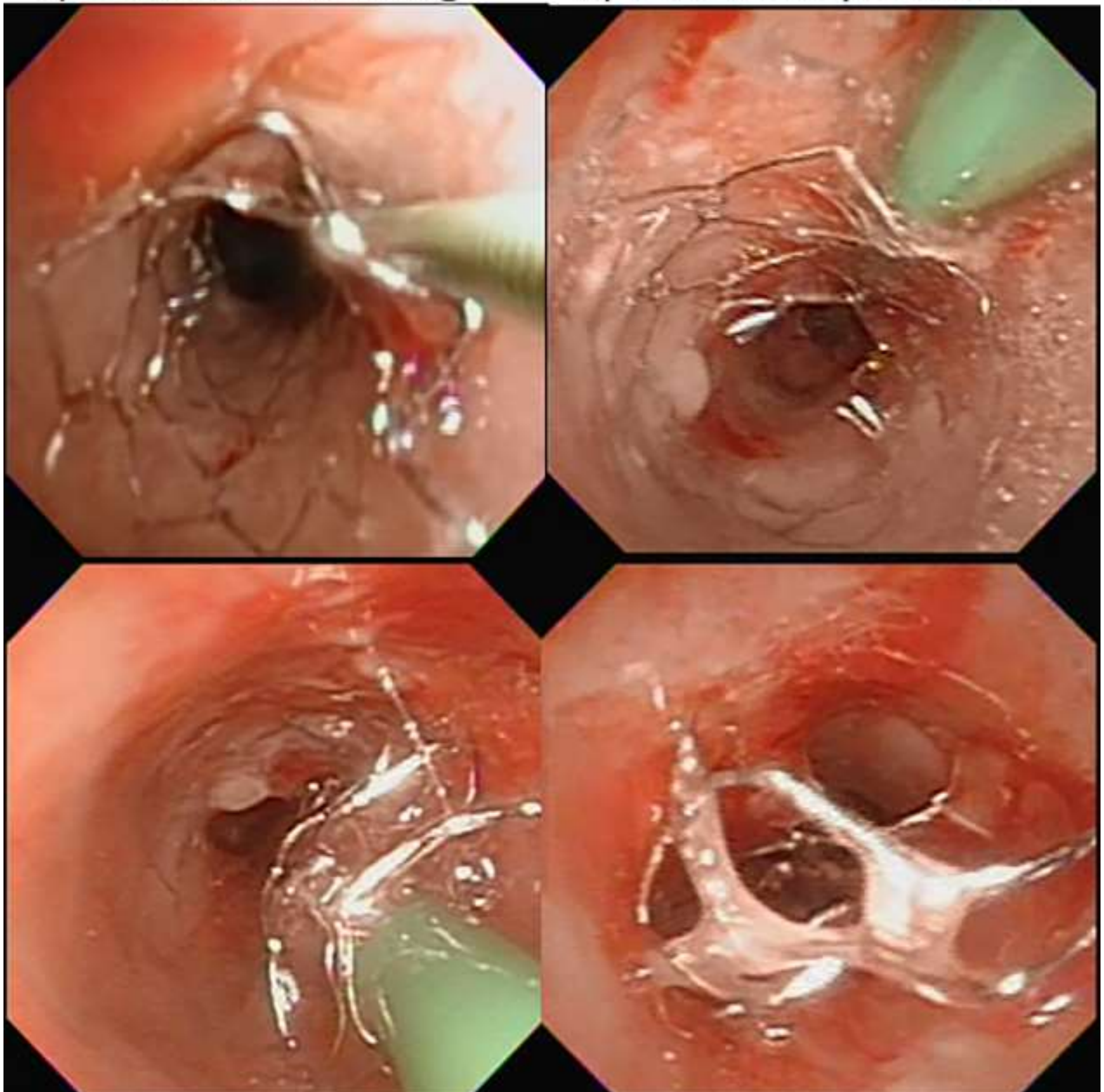
William Lunn. et al. Chest 2005; 127:2106–2112

Table 6—*Relationship of Duration of Stenting With Complications Upon Removal*

Duration of Stenting, d	Complications Experienced on Stent Removal, No.
0–30	2
31–60	1
61–90	5
91–120	9
> 120	15

William Lunn. et al. Chest 2005; 127:2106–2112

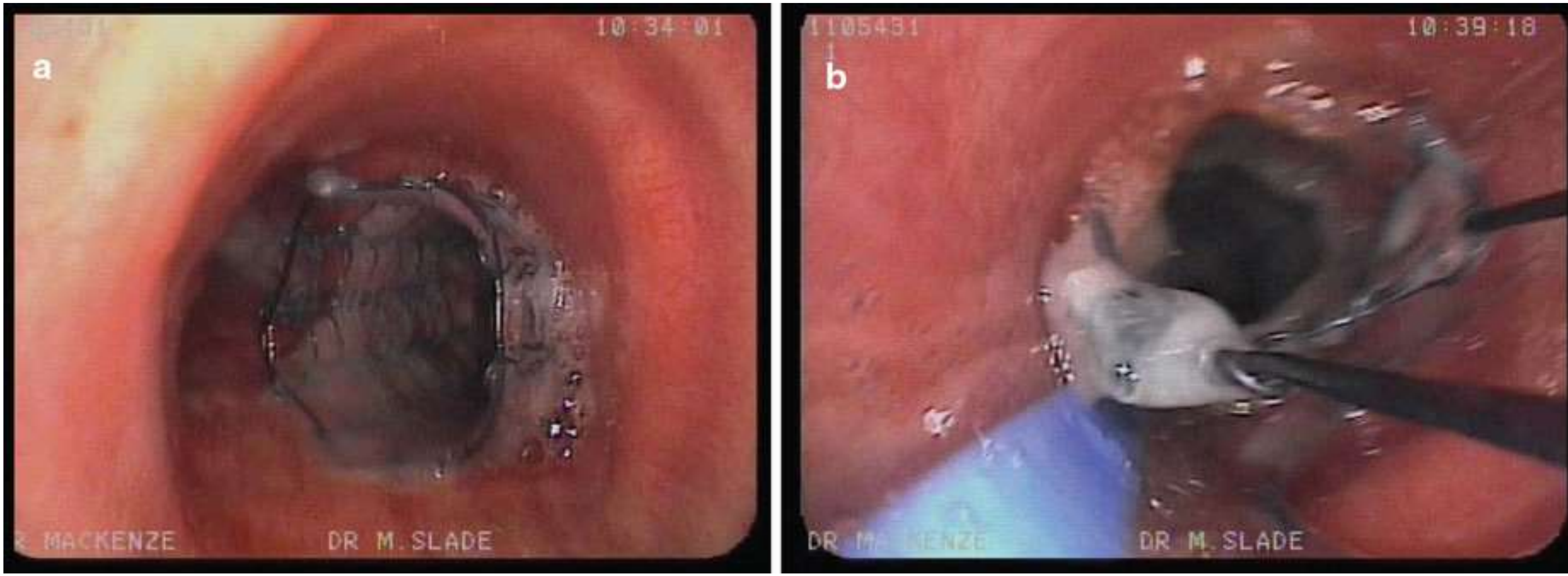
a) Guidewire inserting b) Followed by balloon



c) Inflating balloon d) A destroyed stent

Sequential steps of stent retrieval

(a) Inserting a guidewire in the gap between the stent and mucosal wall;
(b) mounting and advancing balloon catheter through the guidewire;
c) inflating the balloon to separate the stent from the mucosa;
d) the destroyed stent becoming easier for grasping by forceps during retrieval procedure



An Ultra flex-covered stent has migrated, removed by pulling it into an endotracheal tube using forceps to grab the proximal stent suture (right)

This has the effect of pulling the cylindrical stent into a more conical shape at its proximal end, facilitating removal

Complication	Treatment modality
Granulation tissue	Medical therapy Nd-YAG laser APC Photodynamic therapy Cryotherapy Brachytherapy
Mucus impaction	Suction of mucus Mechanical removal Cryo-removal
Infection	Antibiotics Rarely stent removal
Tumor ingrowth	APC Laser Brachytherapy
Migration	Repositioning if early (< 30 days) Removal (if >30 days)
Stent fracture	Removal
Tracheobronchial perforation	Stent removal if possible Repeat stenting

Take home message

- Airway stents- indicated as palliation, irrespective of underlying etiology
- Considered only after all medical or surgical options have been exhausted
- Stenting can be considered as primary treatment in some cases as bridge to other more defective treatment but may also be curative in itself
- Selection of appropriate type, size of stent help in minimizing complications
- Patient follow up for complications of stents should be done

“A stent is a foreign body and nobody is perfect”; stents require long-term management and close follow-up, and hence the optimal stent is still probably the one that can be avoided!

- H. Dutau

Role of 3D printing for custom- made stents

3D printing

- Background
- Introduction
- Steps in 3 D printing
- Clinical use

Background

- Conventional stents: Metal, silicon and hybrid
- Plethora of stents commercially available
  - Different lengths and diameters
  - Balloons or self-expanding
  - Made from polymers or metals
- But most stent: straight and round-shaped

Cheng GZ. et al. Pulm Ther (2017) 3:59–66

Background

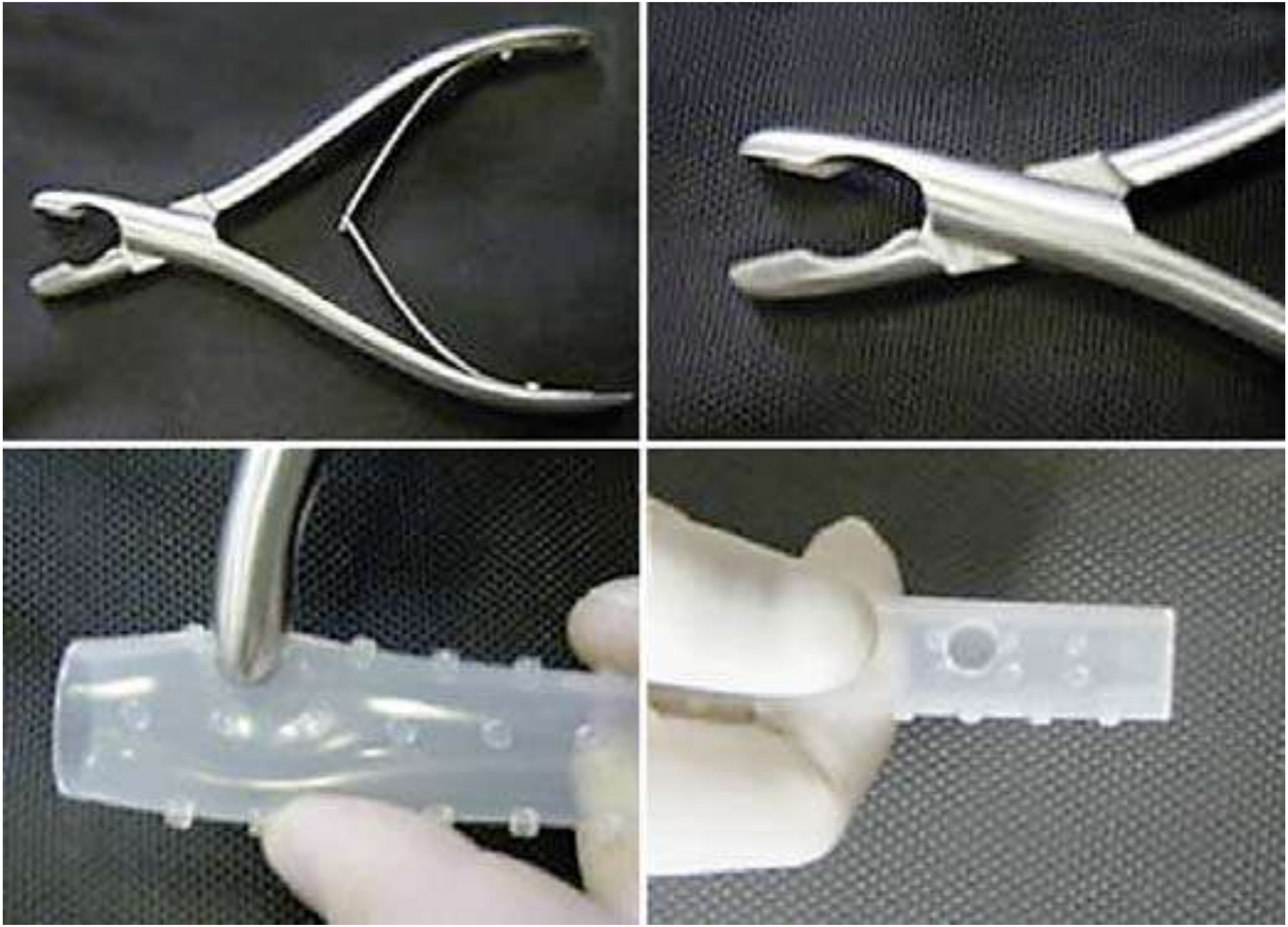
- For regular cases: reasonable compromise
- But frequently more deformed diseased airways needs to be handled
- Customization possible but requires significant time and cost

Cheng GZ. et al. Pulm Ther (2017) 3:59–66

Background

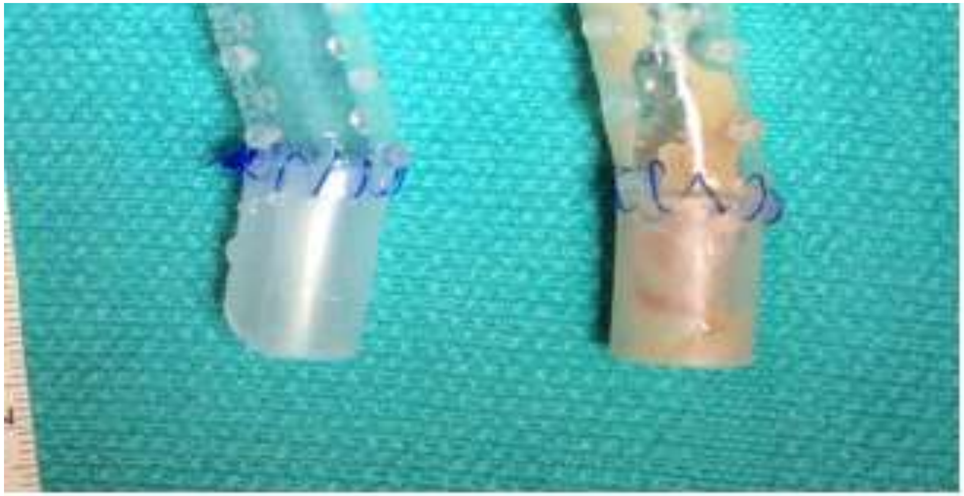
- Retrospective study
- 8-year period
- To identify patients who underwent treatment with silicone stent customized on site
- *Forty-nine* on-site customizations performed in 43 patients (5.4%)

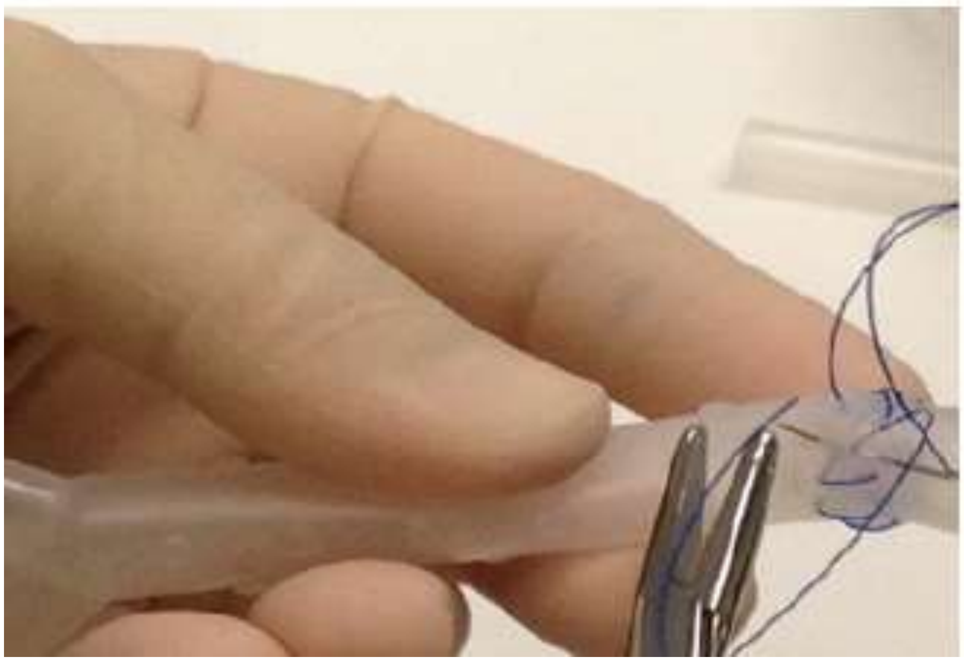
Breen DP. et al. Respiration 2009;77:447–453



A custom-cut hourglass stent

Breen DP. et al. Respiration 2009;77:447–453





Breen DP. et al. Respiration 2009;77:447–453

J-shaped stents-
tracheal and bronchial
Dumon silicone stents
cut and glued together
with silicone glue in
the operating room

Laser cutting techniques to
produce tailored metal stents
Produced after a patient-
specific prescription and sketch
from bronchoscopist.
Delivery time: Few weeks
Costs: High
Favor done by industrial
partners

Recent step of evolution:
stent manufacturers offer
modifications of their
existing products for
patient-specific prescription
2–4 weeks, hospital
receives a custom-made,
sterilized stent

Background

- Airway malformations: Stenosis, malacia, traumatic injury, or external compression
- 3 D printing- Personalized medicine
- Possible that airway stents can be personalized to tailor individual patient's airway geometry

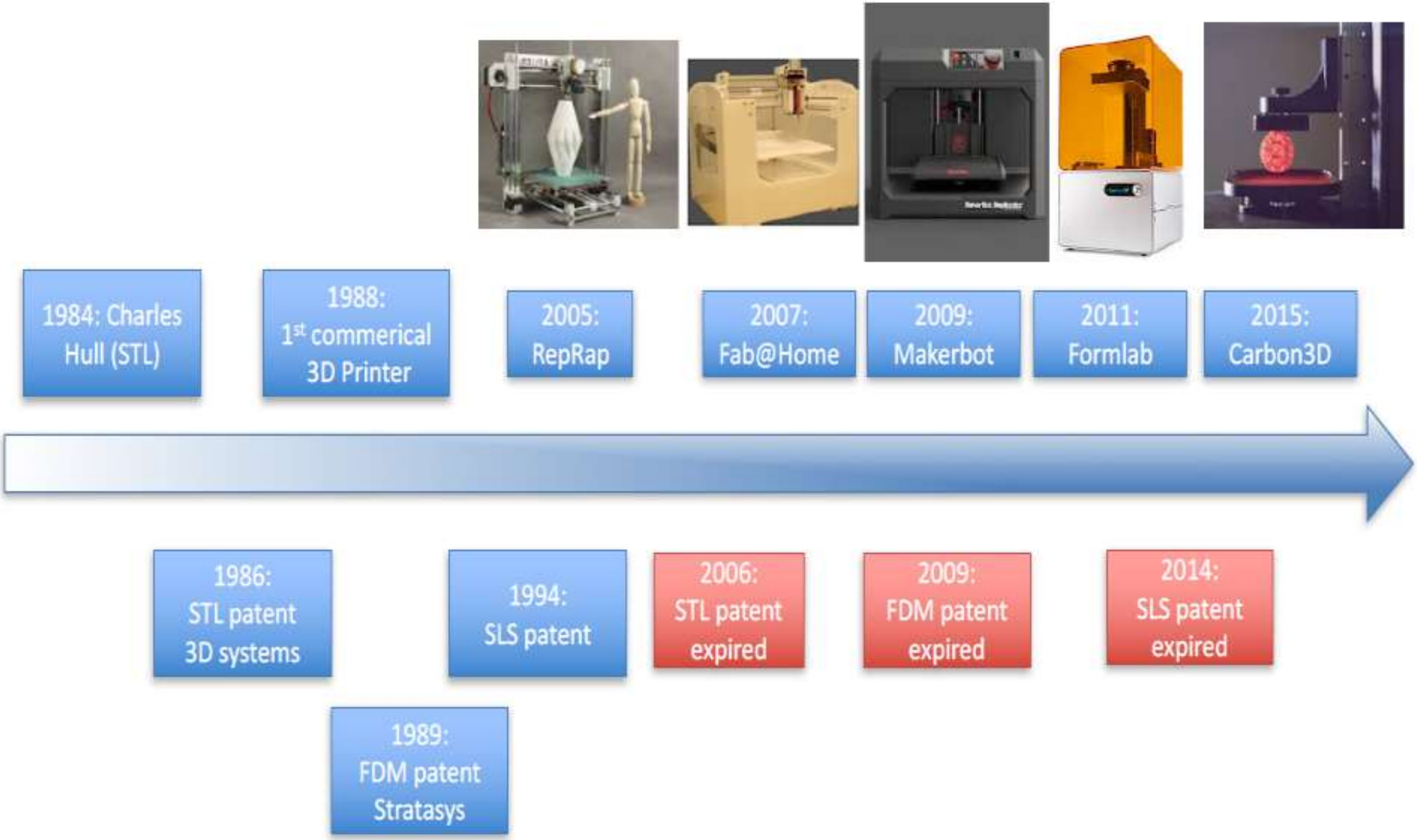
Cheng GZ. et al. Pulm Ther (2017) 3:59–66

3 D printing- Introduction

- Three-dimensional model (3D) printing is a process for making solid 3D object of virtually any shape from digital model
- Offers potential for rapid customization of medical devices
- Type of additive manufacturing

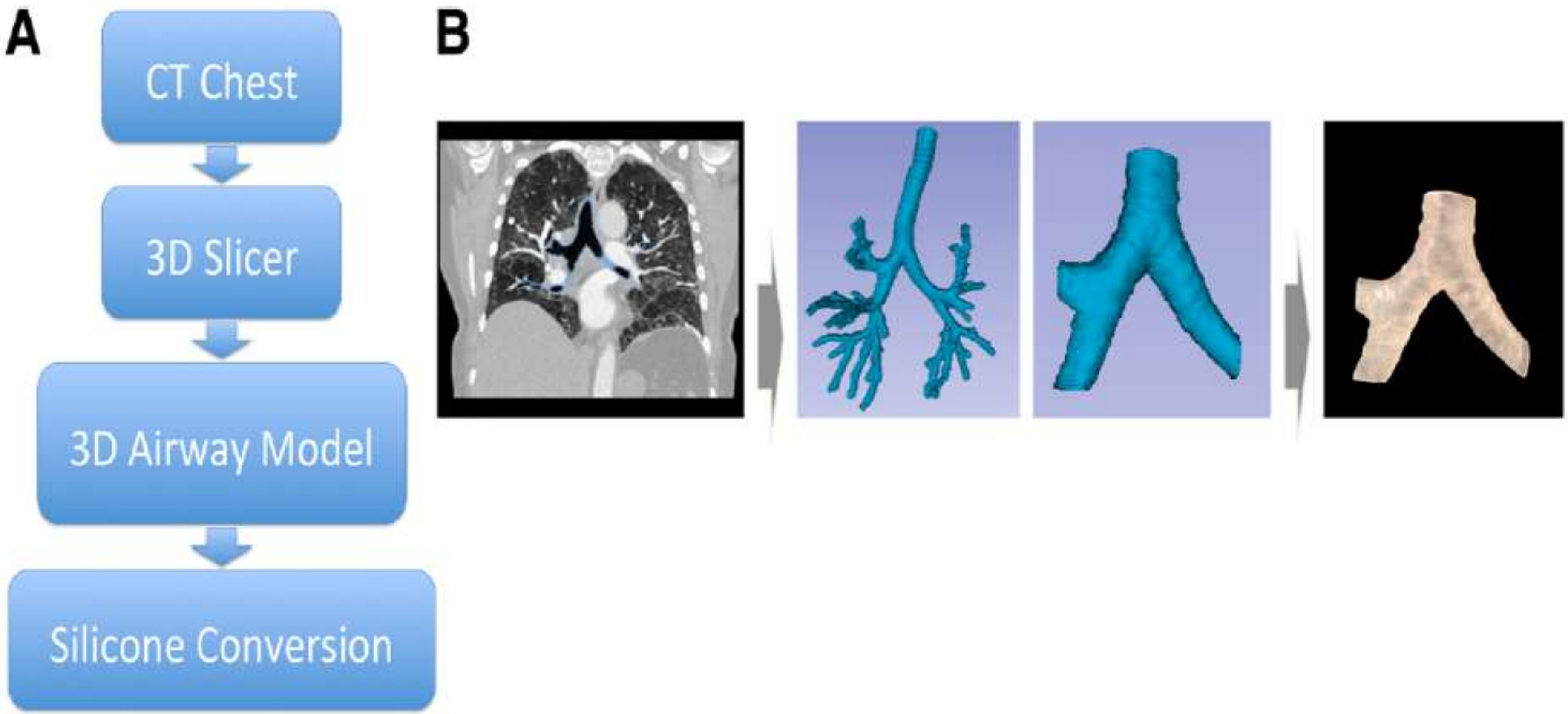
Cheng GZ. et al. Pulm Ther (2017) 3:59–66

Brief historic timeline of 3D printing development



Cheng GZ. et al. Pulm Ther (2017) 3:59–66

Steps in 3 D printing



a. Personalized stent project workflow schematic
b. 3D slicer guided stent design and rapid prototyping

Cheng GZ. et al. Pulm Ther (2017) 3:59–66

Steps in 3 D printing

- *Image acquisition*
- *CAD Designing*
  - Segmentation
  - 3D visualization
  - Tessellation
- *Generating a Construction File (stl format)*
- *3D Printing*
- *Post printing treatment*
- *Sterilization*

Chepelev L. et al. 3D Printing in Medicine. 2017;3:4

Image acquisition

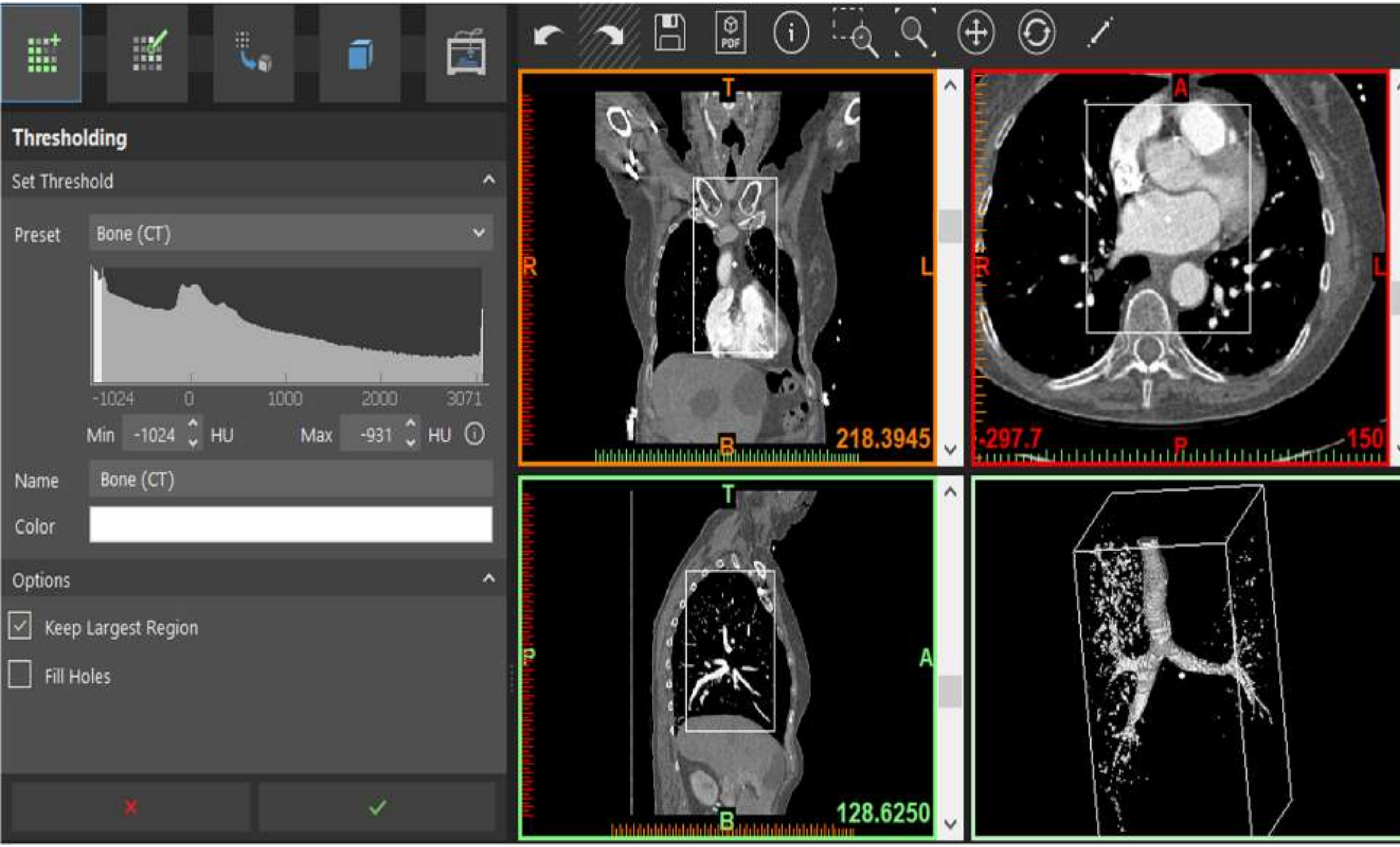
- Begins with acquisition of cross-sectional images
- CT: Most common used volumetric imaging modality
- CT has ubiquity, high signal-to-noise ratio, contrast enhancement options, and spatial resolution
- Preferable to segment images acquired with isotropic voxels, with side length on order of 1 mm

Chepelev L. et al. 3D Printing in Medicine. 2017;3:4

Segmentation

- Process of separation of relevant anatomy to be included in 3D printed model
- Selection of all voxels with corresponding density value within specified range of HU
- Results in selection of desired anatomy

Chepelev L. et al. 3D Printing in Medicine. 2017;3:14



Segmentation of the trachea

3D visualization

- Collection of methods and technologies used to visualize 3D representation of cross-sectional data volumes on 2D computer screens
- Isolating and displaying set of segmented voxels from DICOM images
- Collection of voxels representing desired anatomy needs to be transformed into printable 3D object via process referred to as tessellation
- Tessellation: Approximate shapes using set of triangles

Chepelev L. et al. 3D Printing in Medicine. 2017;3:14

Creating hollow airway models

- Trachea is hollow but represented as solid
- Hollow tool creates hollow objects based on solid objects by creating wall on outside and inside
- Wrap tool corrects and applies smoothing to model to create a watertight, printable object
- Create 3 mm-thick outside wall

Chepelev L. et al. 3D Printing in Medicine. 2017;3:14

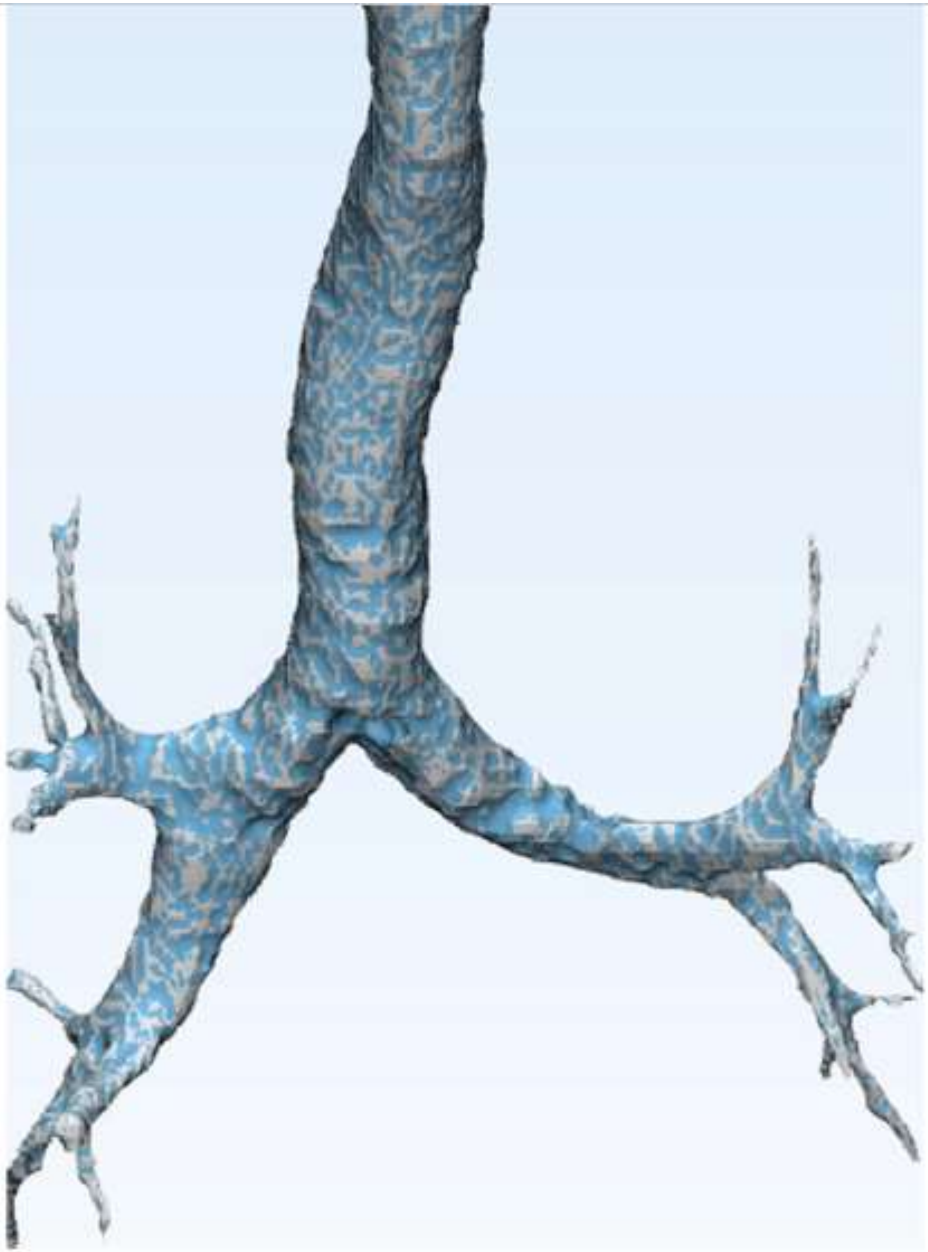
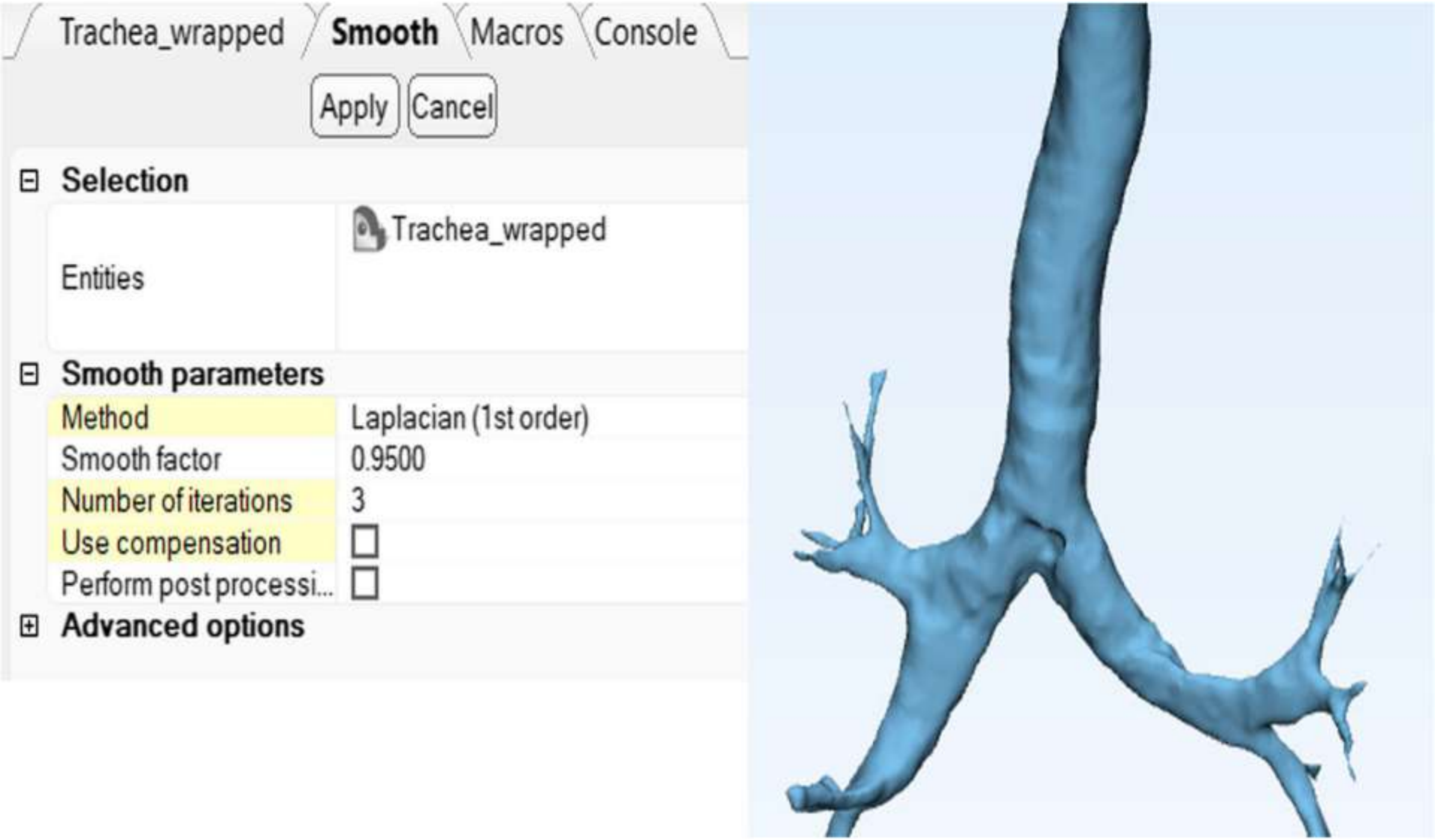
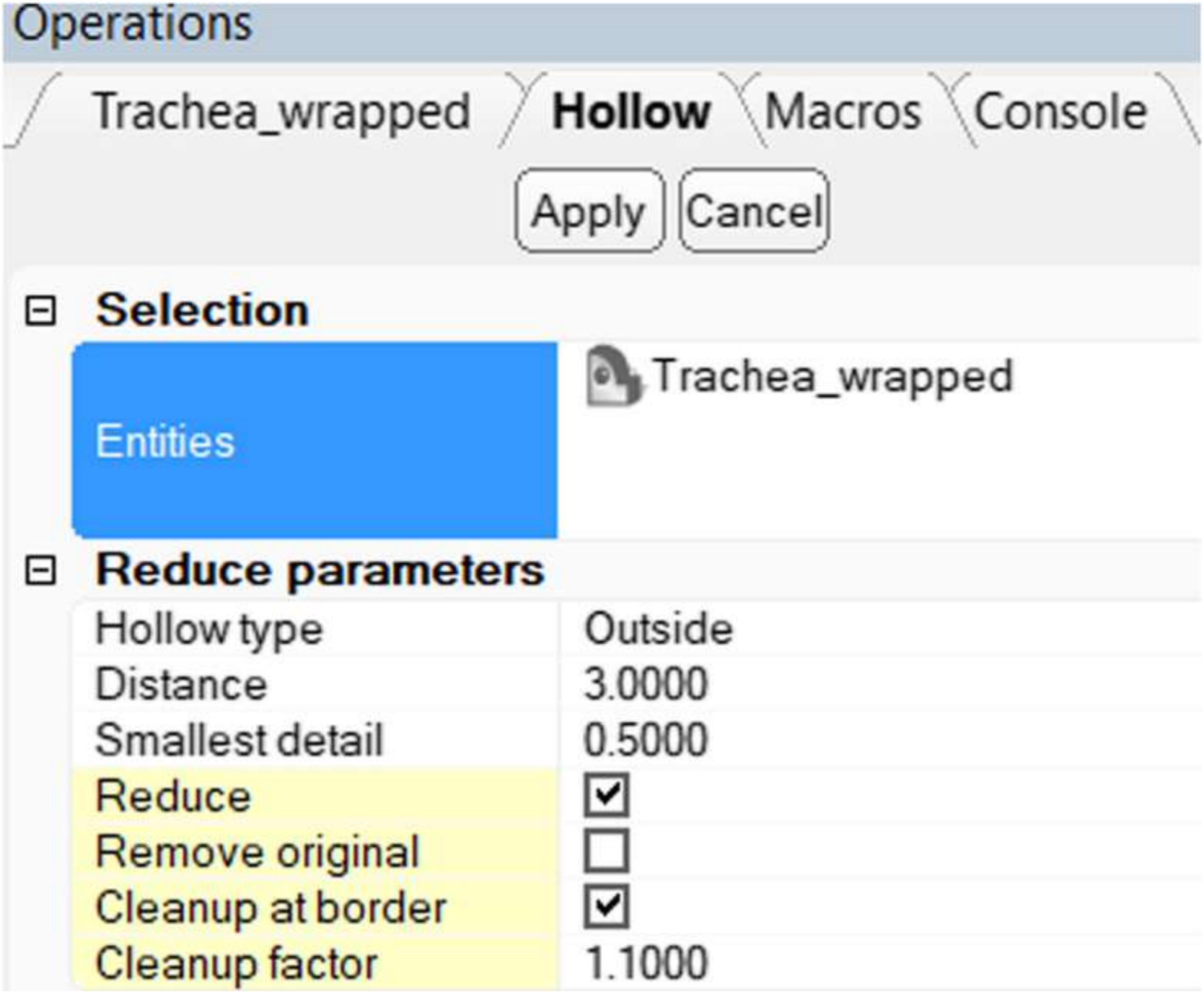


Fig. 20 The smoothed and wrapped tracheal model (blue) overlapped with the original model (grey)

Chepelev L. et al. 3D Printing in Medicine. 2017;3:14

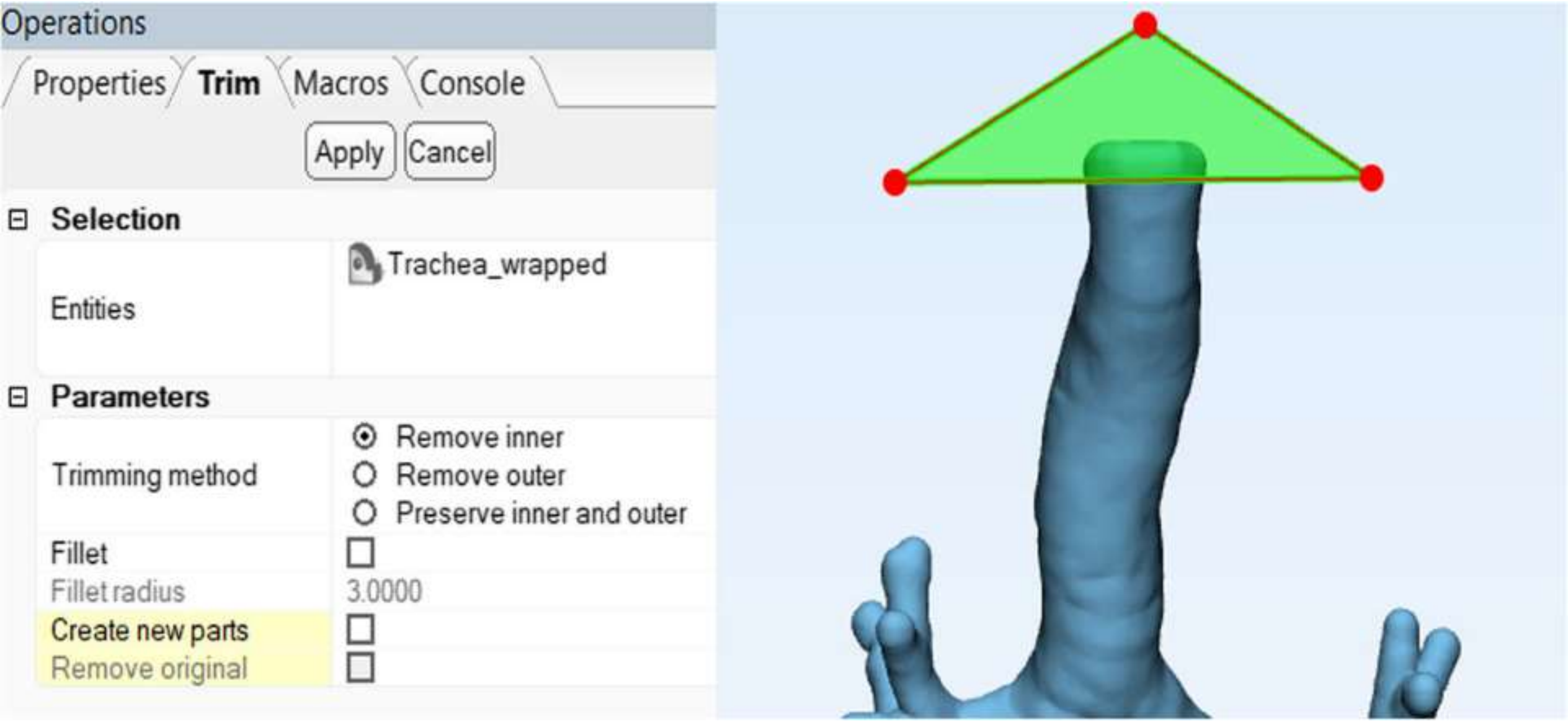


Setup of the smoothing operation *Chepelev L. et al. 3D Printing in Medicine. 2017;3:14*



Chepelev L. et al. 3D Printing in Medicine. 2017;3:14

- Hollow operation results in a hollow structure with no external opening
- In order to simulate the airway, cut off the top of this hollow structure using “Trim”



Setting up the Trim operation

Chepelev L. et al. 3D Printing in Medicine. 2017;3:14

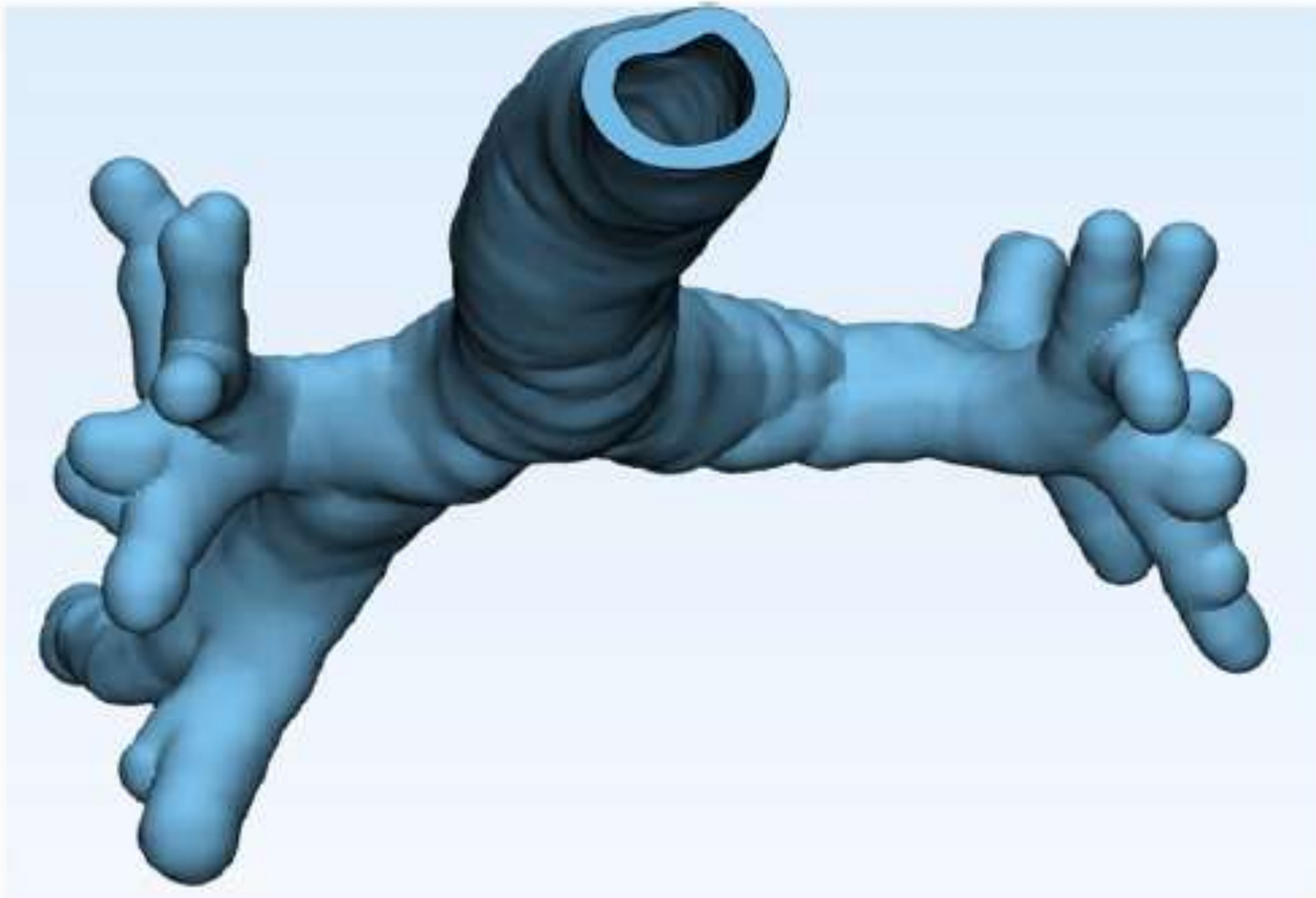
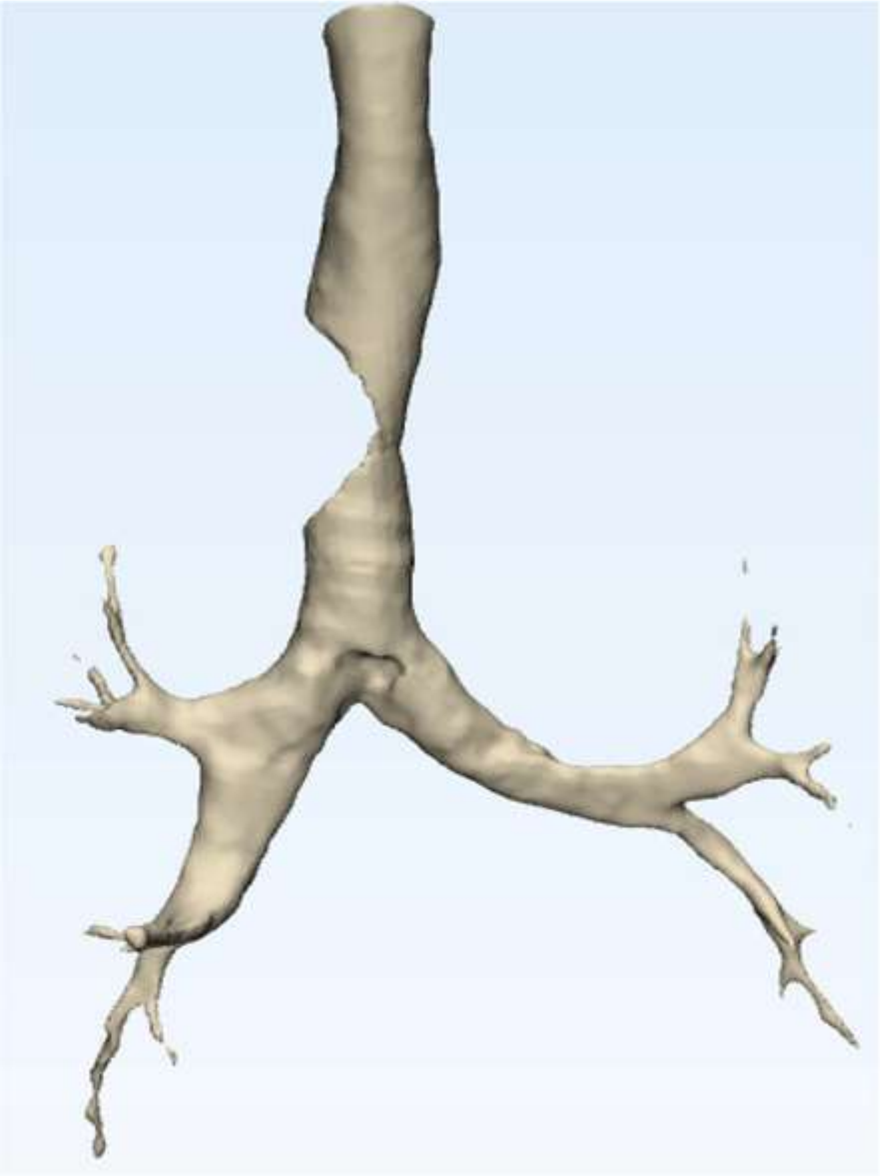


Fig. 24 Hollow model of the trachea.

Chepelev L. et al. 3D Printing in Medicine. 2017;3:14

Computer-aided design

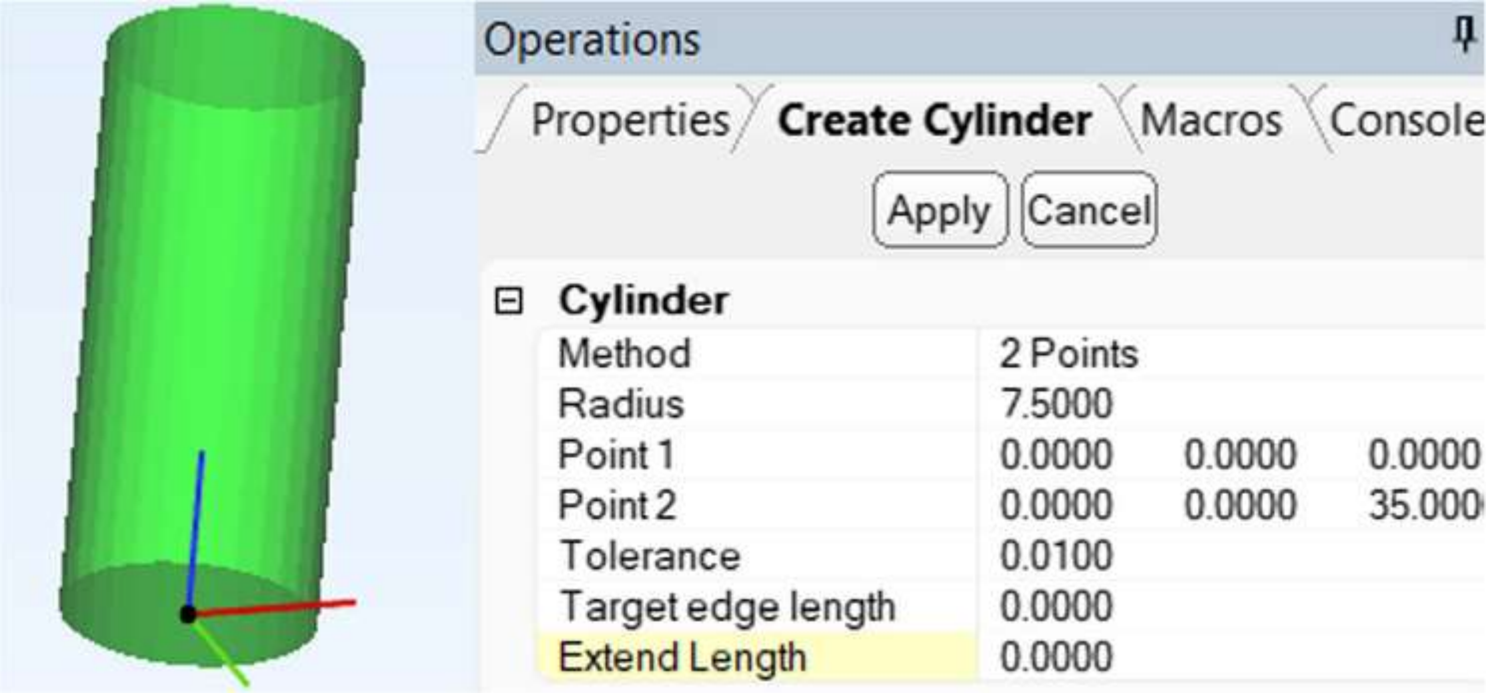
- Approach for the creation of a customized tracheal stent for simulated case
- Tracheal stenosis secondary to mass effect from an adjacent mediastinal tumor

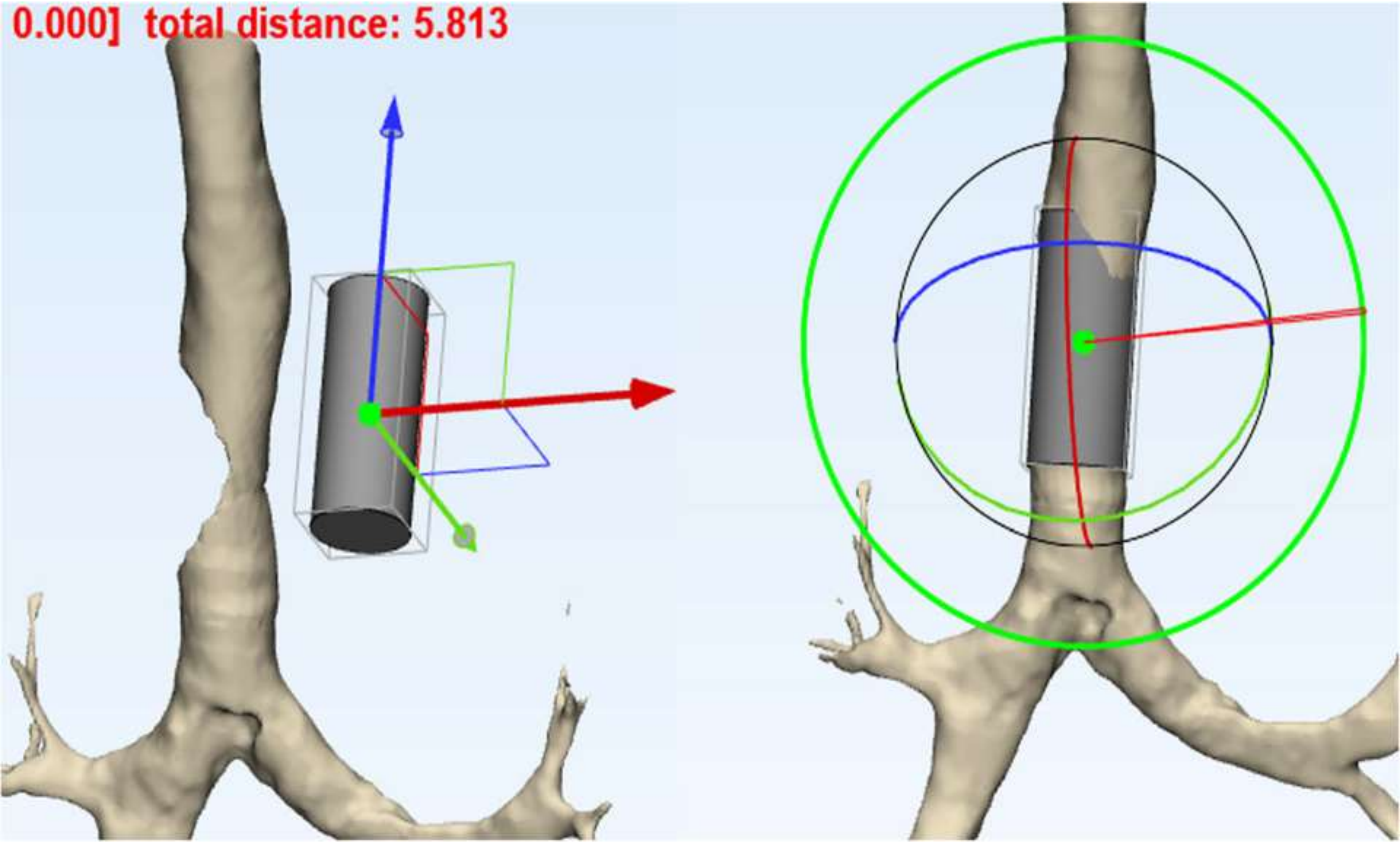


Chepelev L. et al. 3D Printing in Medicine. 2017;3:14

Computer-aided design

- Using cylinder primitive to fill in cavity left behind by tumor
- Values approximated by measuring model directly





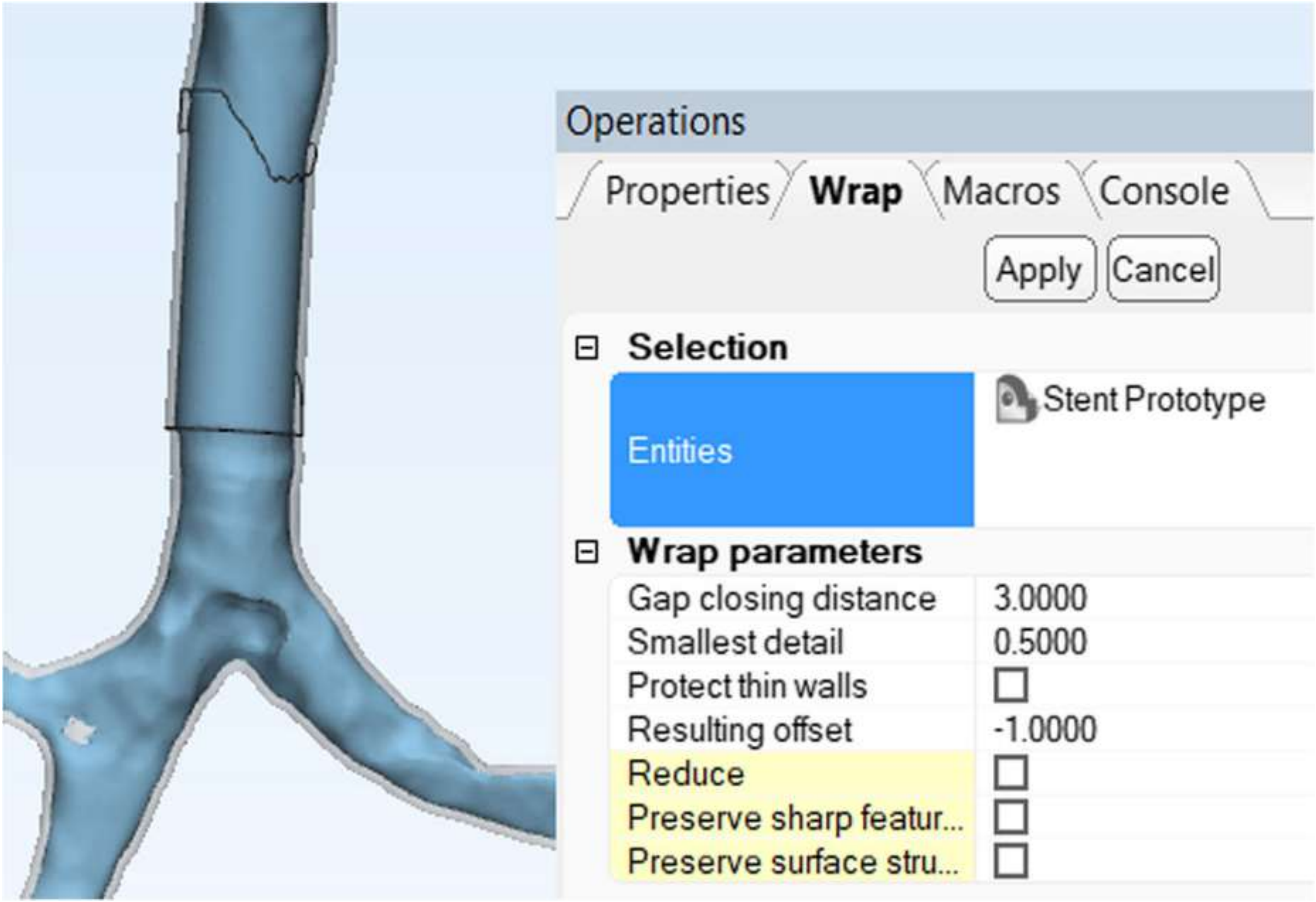
Interactive rotation and translation

Chepelev L. et al. 3D Printing in Medicine. 2017;3:14

Computer-aided design

- Resultant model, consisting of cylinder and original airway, fused into single entity, ‘Stent Prototype’
- To ensure the intended stent can be placed within trachea→ Conform to inner lumen of trachea
- Degree of scaling or offset required
- Achieved during object wrapping with an offset parameter specified as -1 mm

Chepelev L. et al. 3D Printing in Medicine. 2017;3:14

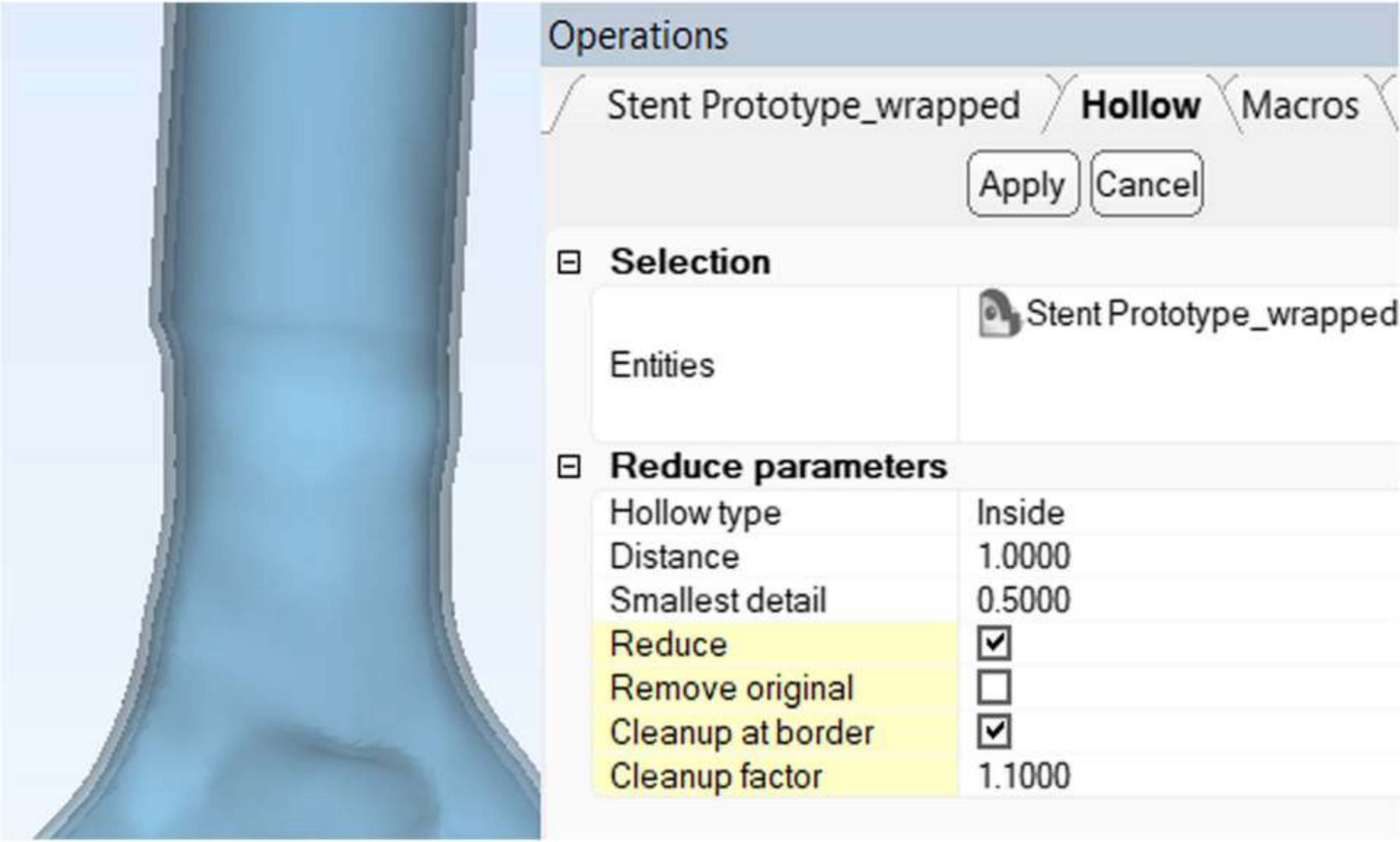


Setup and the result of the Wrap operation (blue) with a -1 mm offset in relation to the original Boolean Union result (grey, transparent)

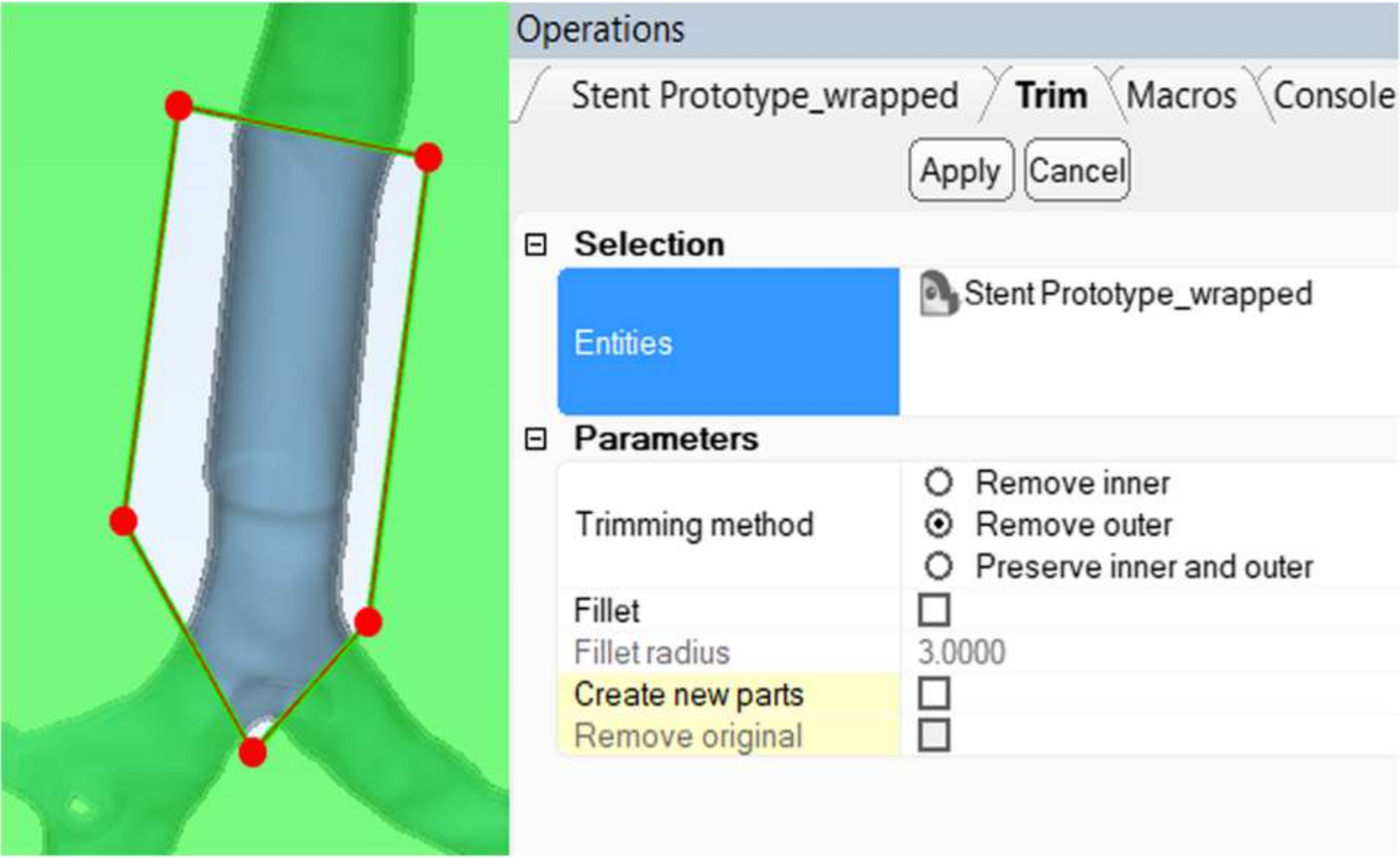
Computer-aided design

- Resultant scaled, solid model is ready to simulate a stent
- Hollow structure, opting to create 1 mm walls on inside of model
- Trim stent to desired size

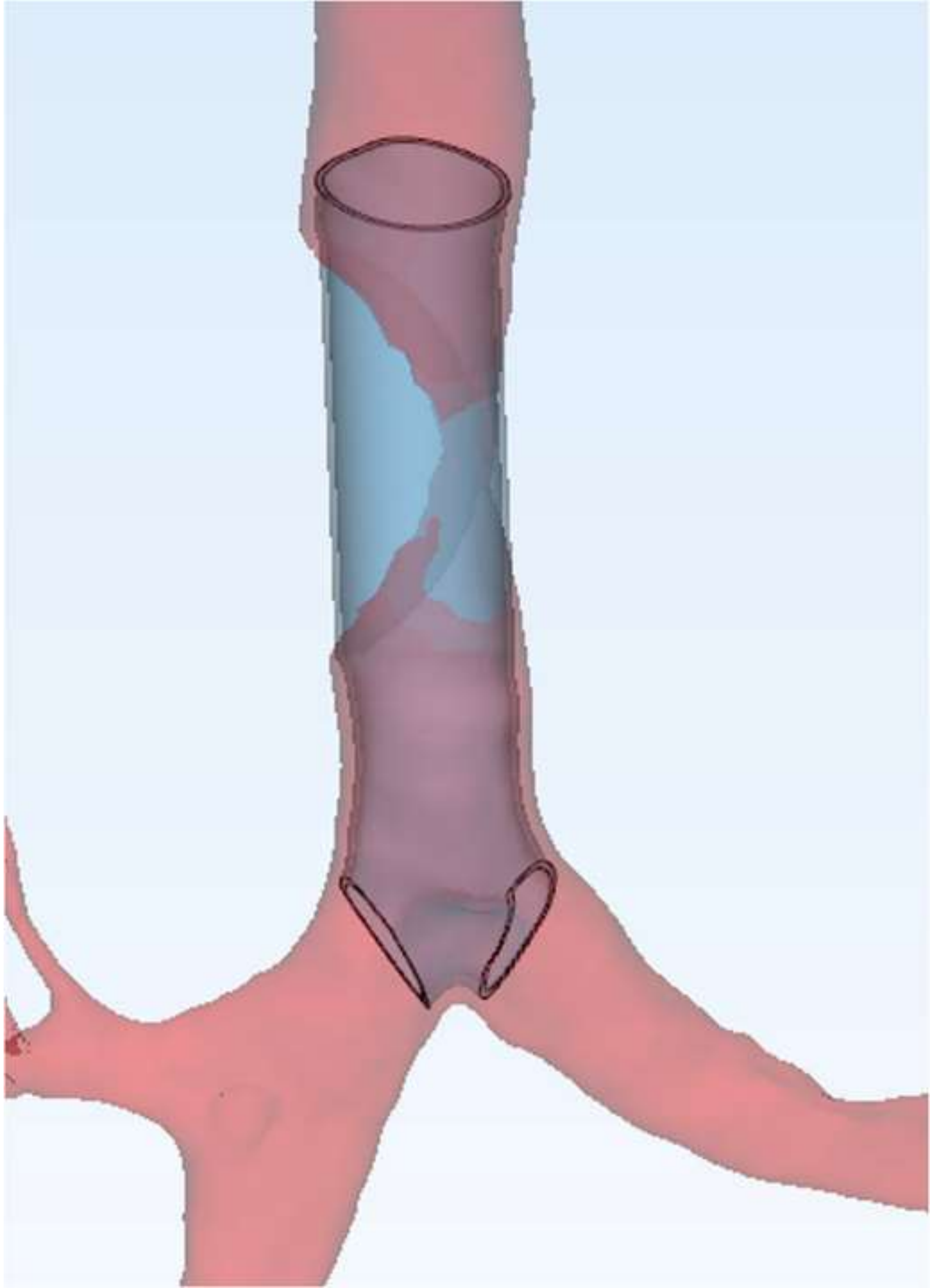
Chepelev L. et al. 3D Printing in Medicine. 2017;3:14



Setup and result of the Hollow operation



Setting up the trimming operation to create a hollow stent



Final stent (blue) inside the original airway model (red), demonstrating adherence to lumen

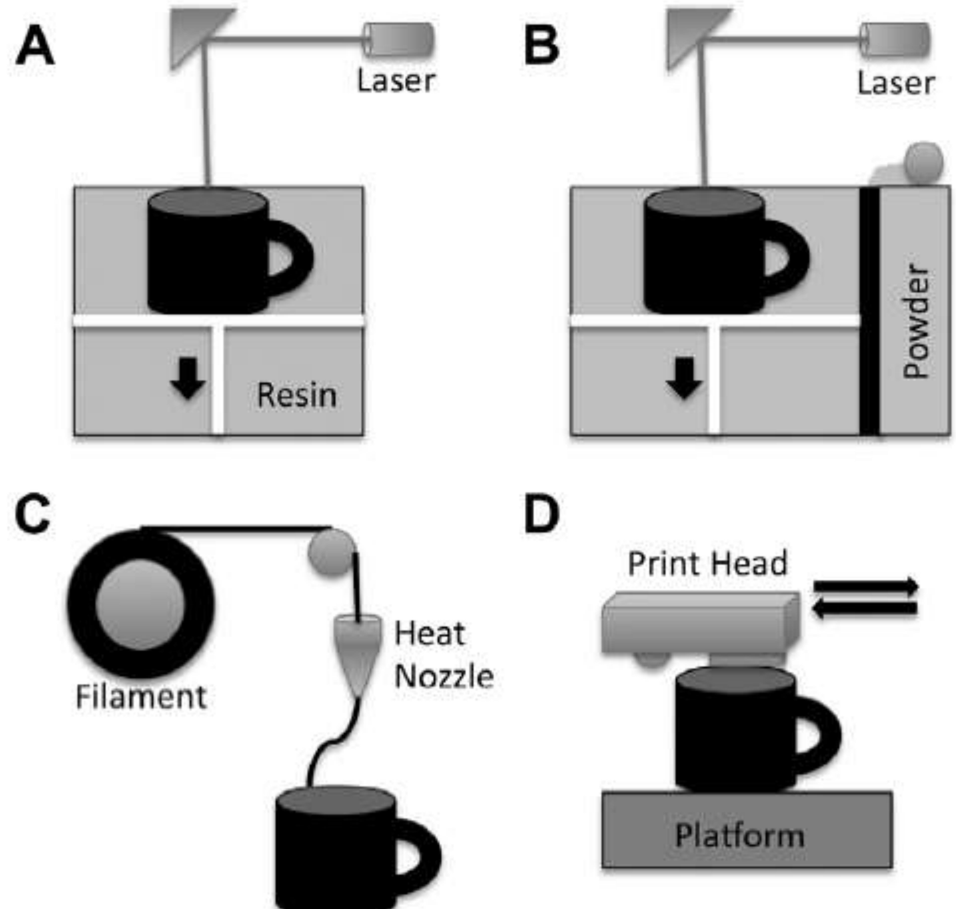
Printable 3D model

- Model further smoothed
- Non-printable parts removed or adjusted
- Vulnerable areas reinforced using range of manual manipulations and automated algorithms
- To ensure models that are robust and to minimize printing failure rates

Chepelev L. et al. 3D Printing in Medicine. 2017;3:14

3 D Printing

- Casting from 3D printed molds
- Direct 3D-printing

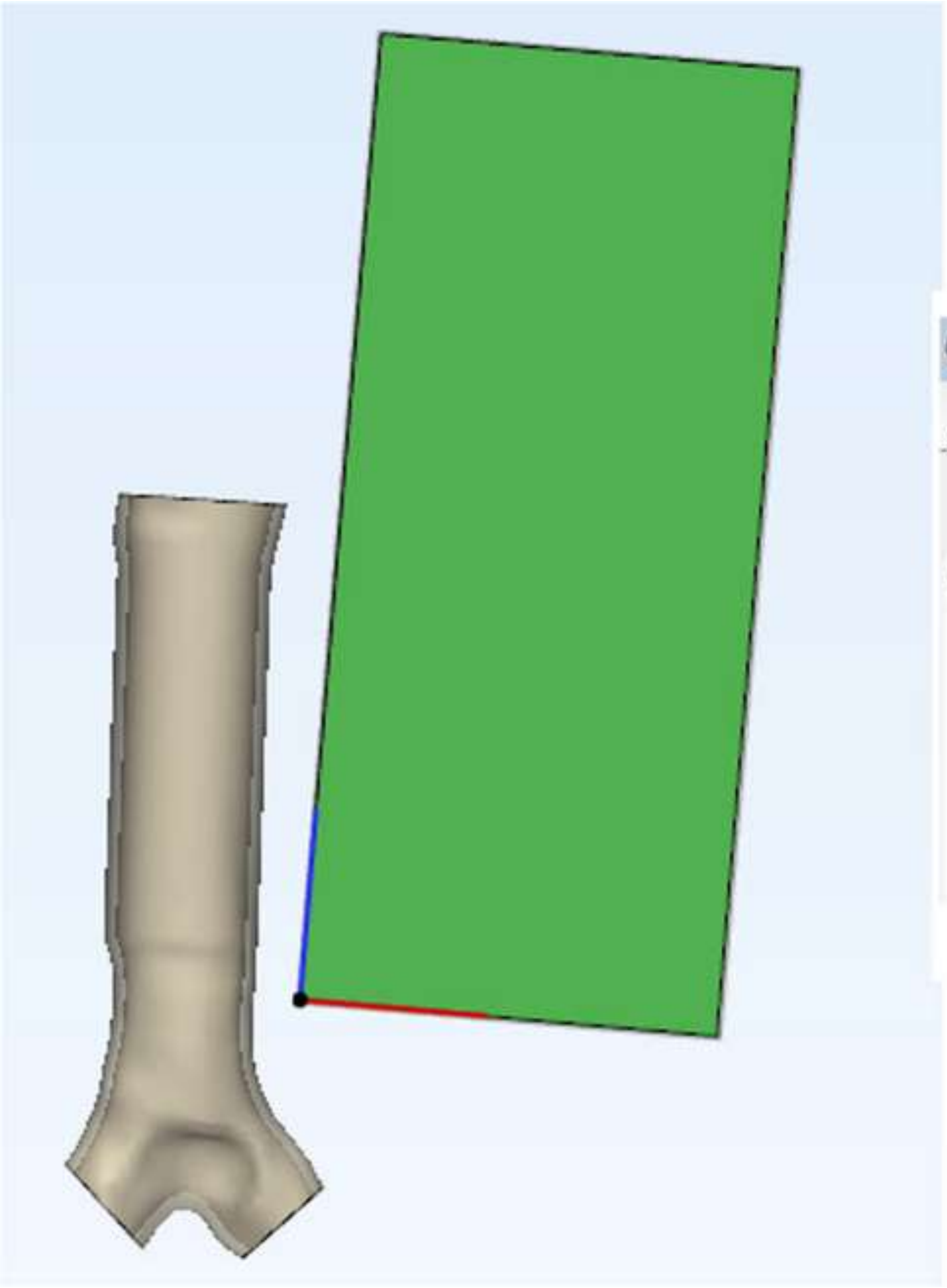


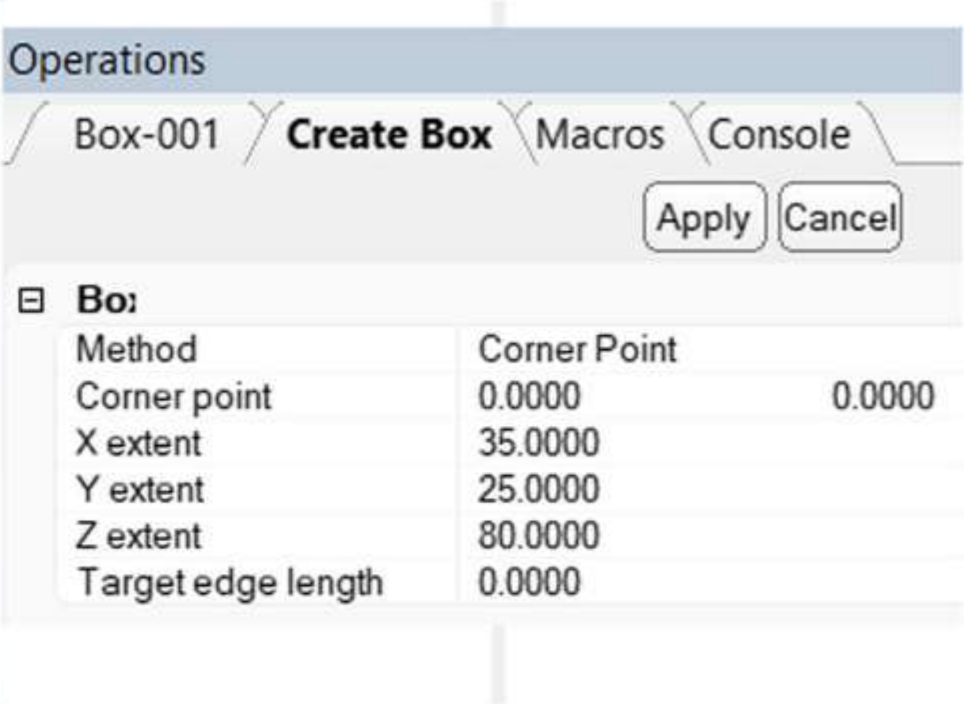
Cheng GZ. et al. Chest 2016; 149(5):1136-1142

Creating mold

- Using CAD tools
- Process will consist of design of outer and inner shell
- Molded part is retrievable and functional without destruction of mold

Chepelev L. et al. 3D Printing in Medicine. 2017;3:14



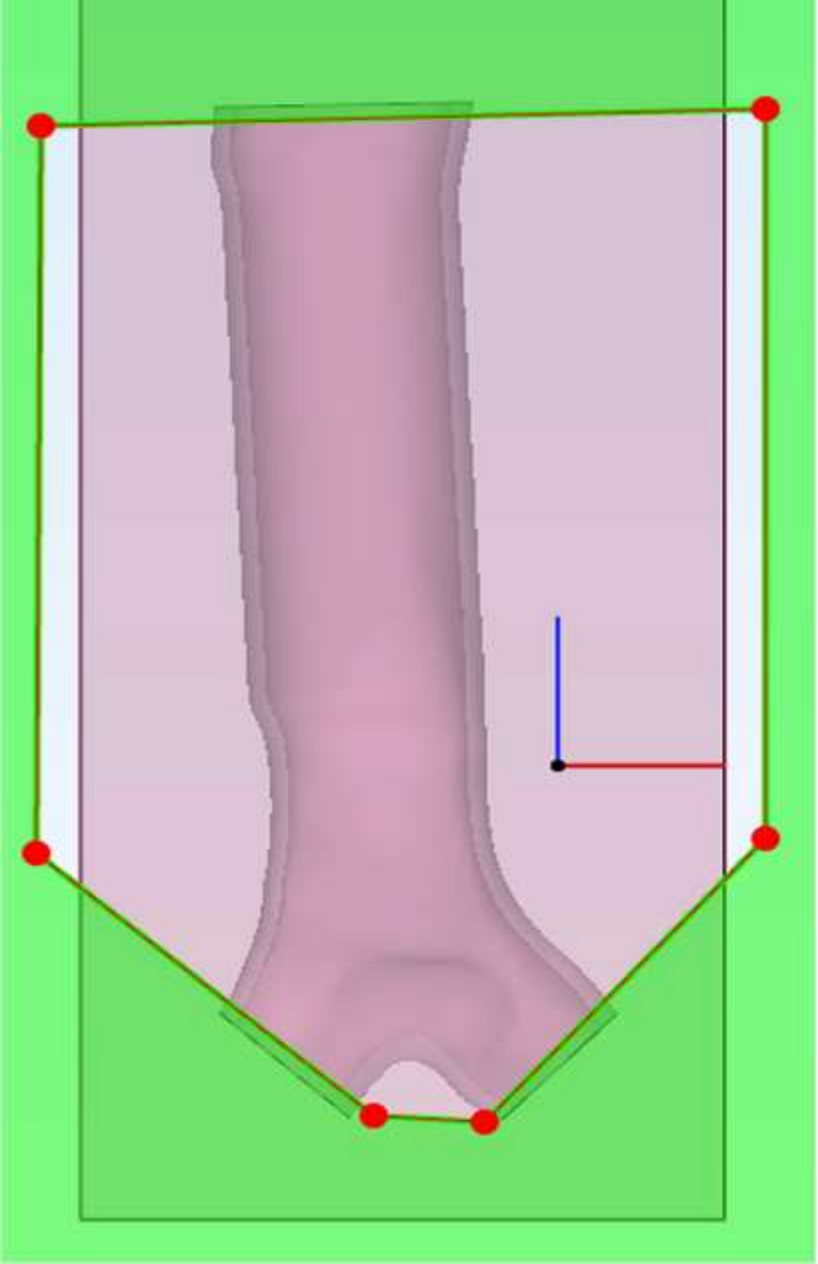


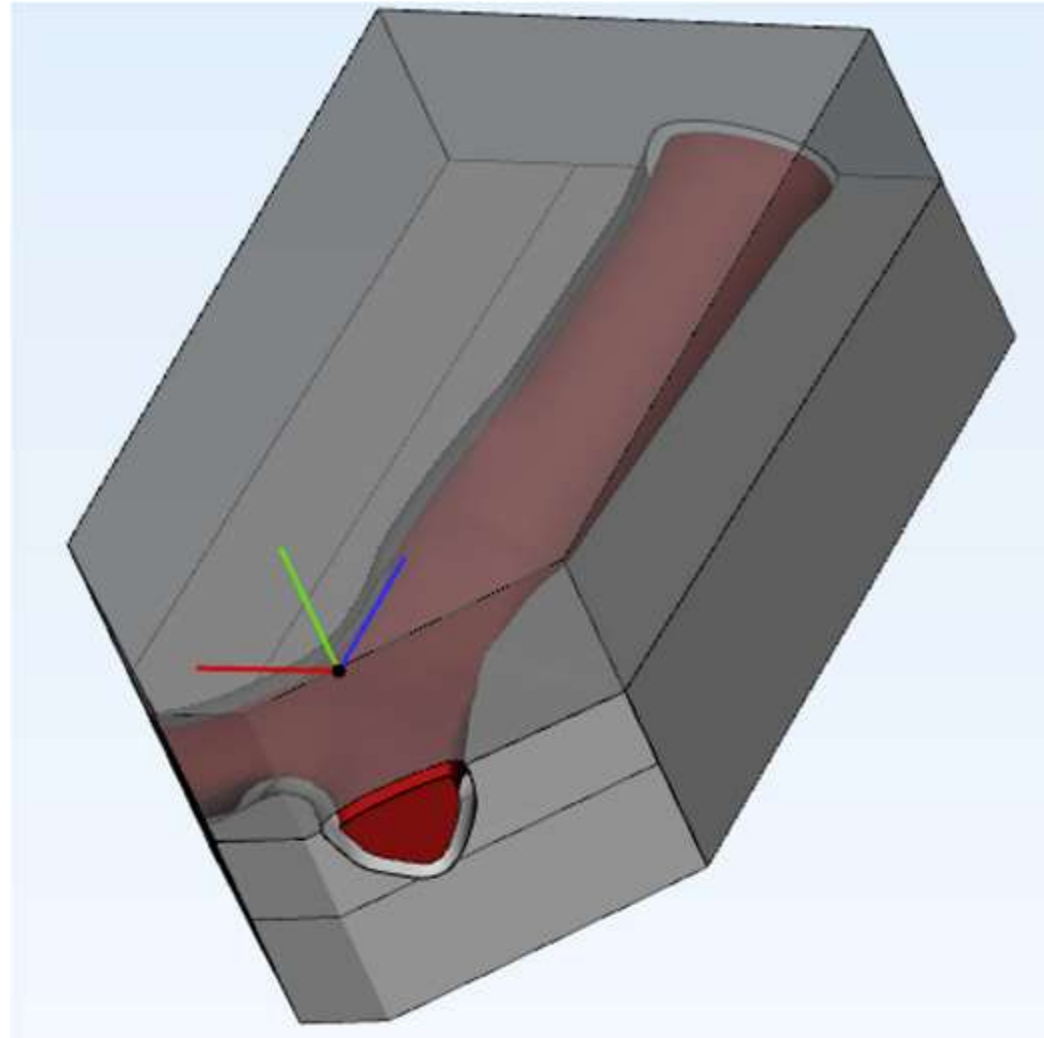
Create box primitive, ensuring complete encapsulation of the target part with primitive geometry, primitive is then moved to overlap stent model

Setup for the Create Box operation

Creating mold

- Stent model subtracted from primitive, resulting in hollow structure amenable for trimming along outer edges of stent
- Resultant trimmed product consists of two shells– inner shell that outlines internal portion of mold and outer shell that outlines external portion
- To create an openable external portion, it may be cut in two pieces using “Trim” function with ‘preserve inner and outer’ option→ result in three-part model

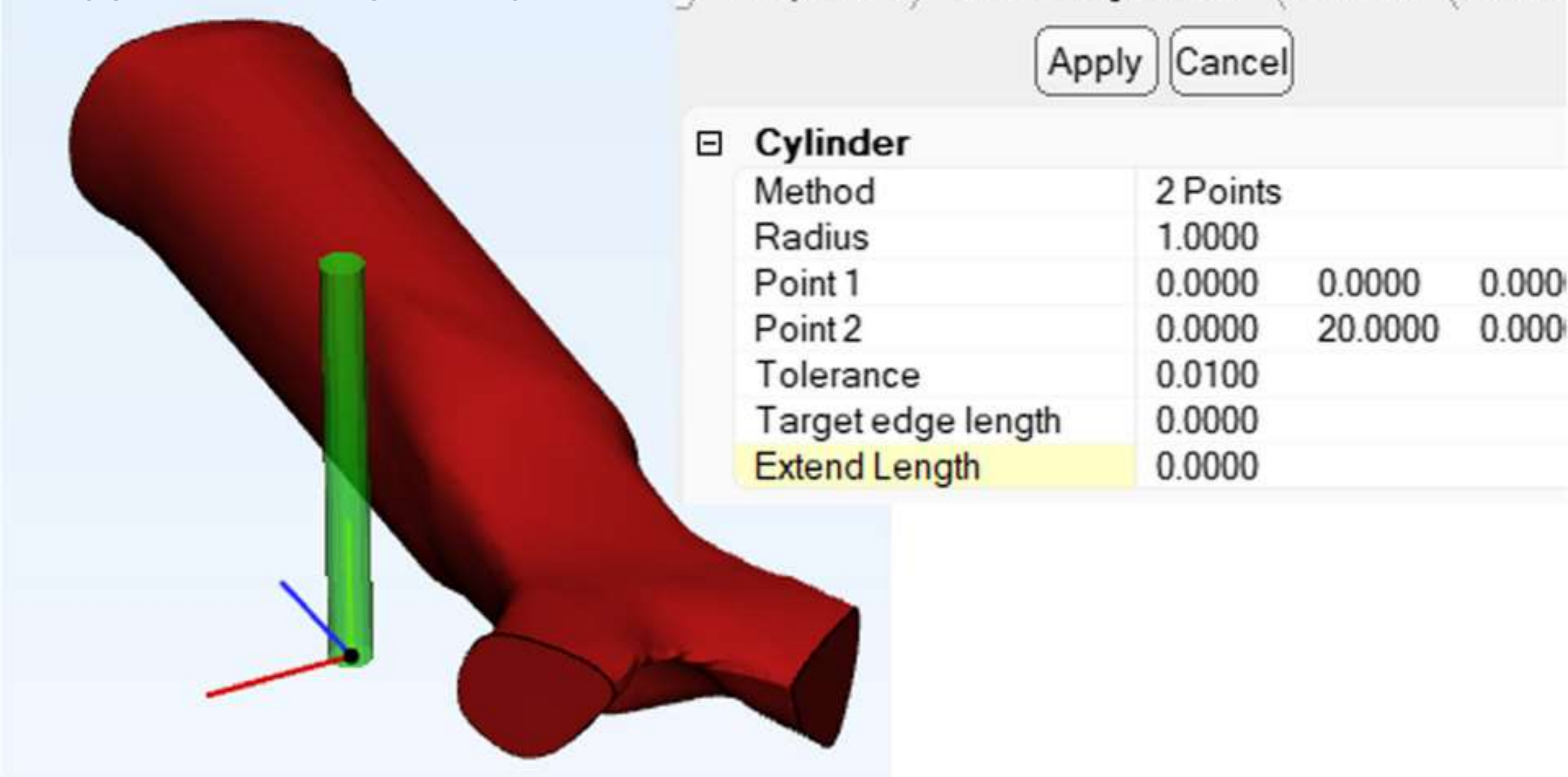




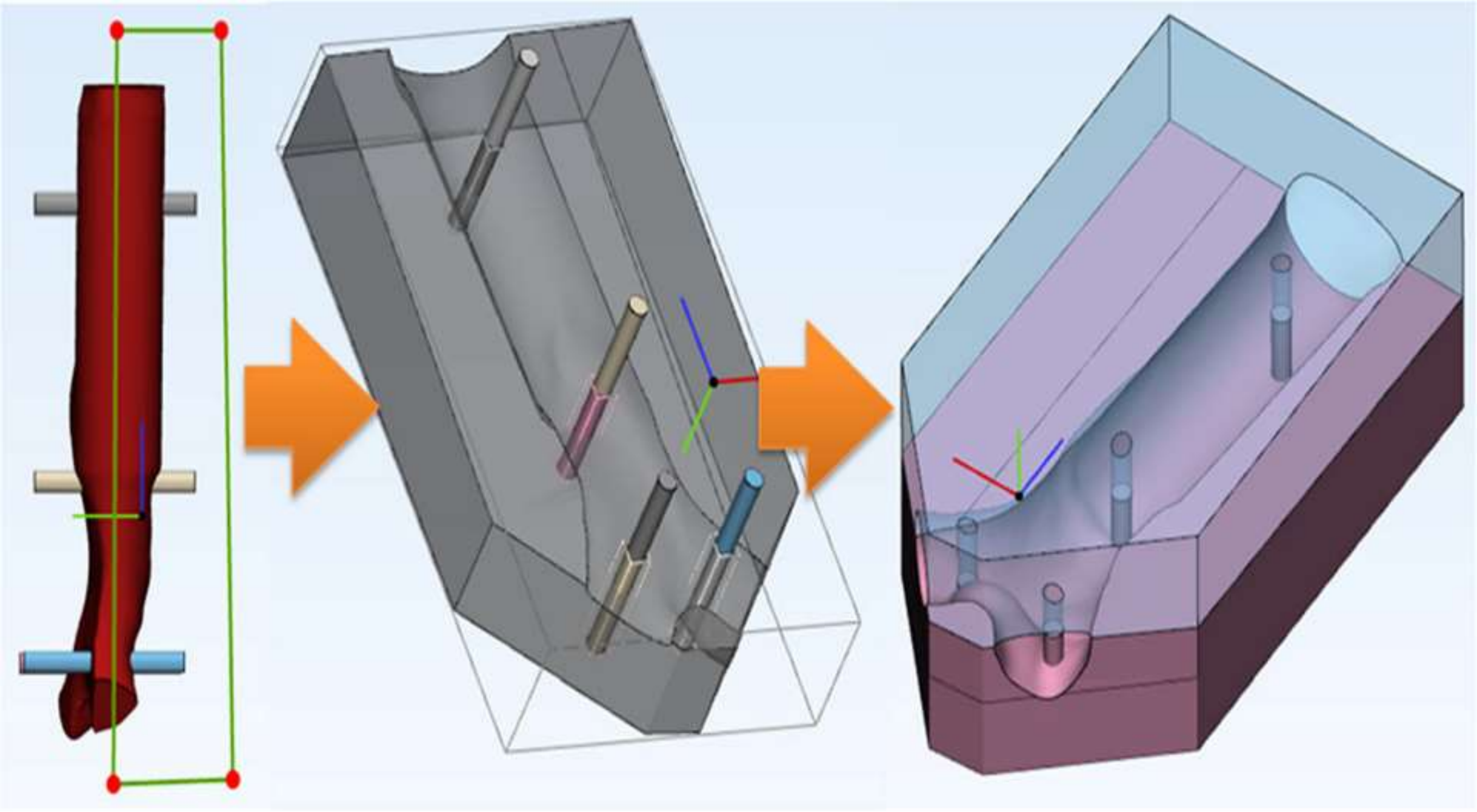
The result of separation of inner and outer portions and trimming the outer portion

Using the trimming function on the result of subtraction of the stent from the box primitive

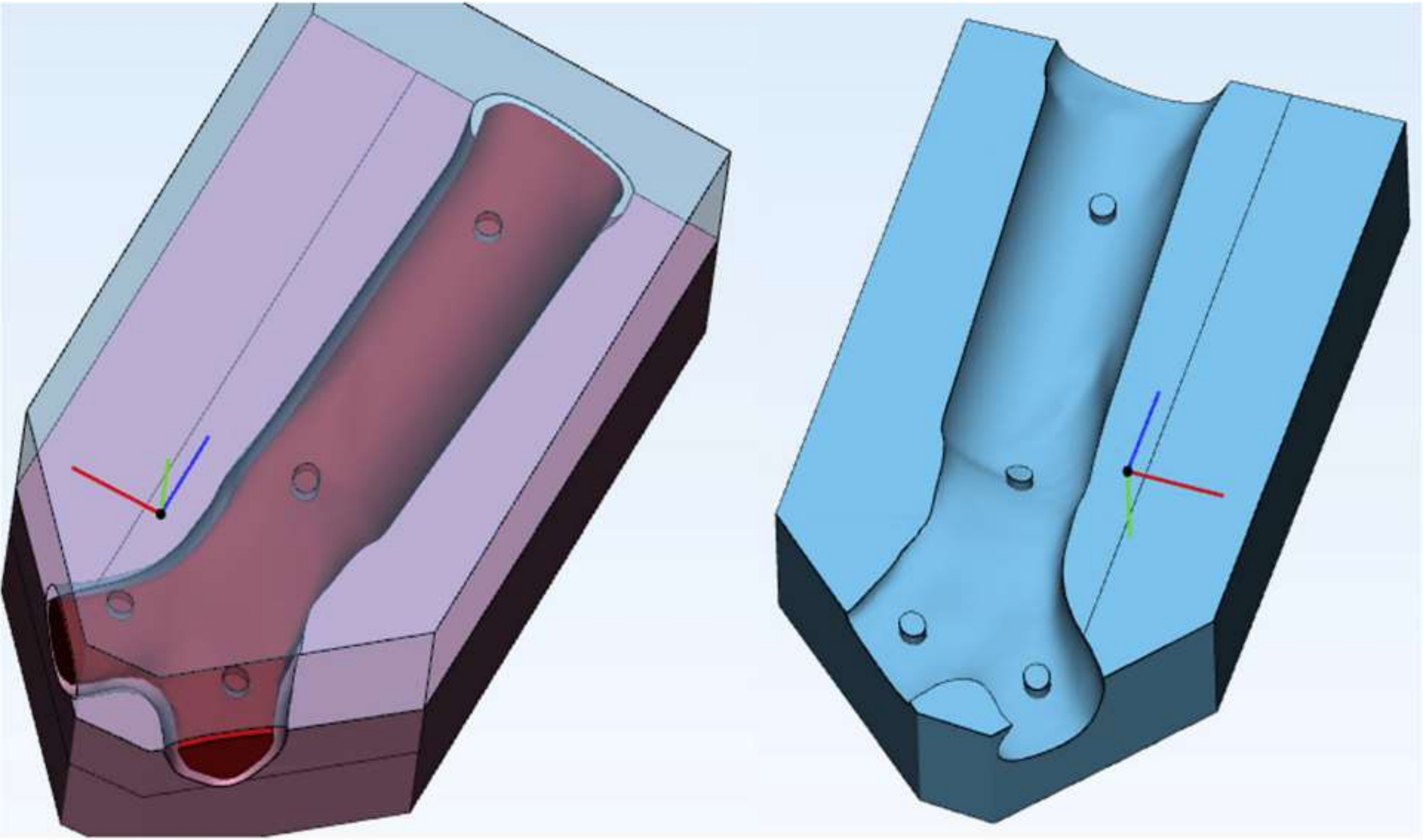
Setup for the Create Cylinder operation



To hold the inner part in place and ensure 1 mm wall thickness of stent, support cylinders created using the Create Cylinder function and aligned such that internal molding part is entirely traversed in Z axis, and the cylinders are within bounds of external portion of mold

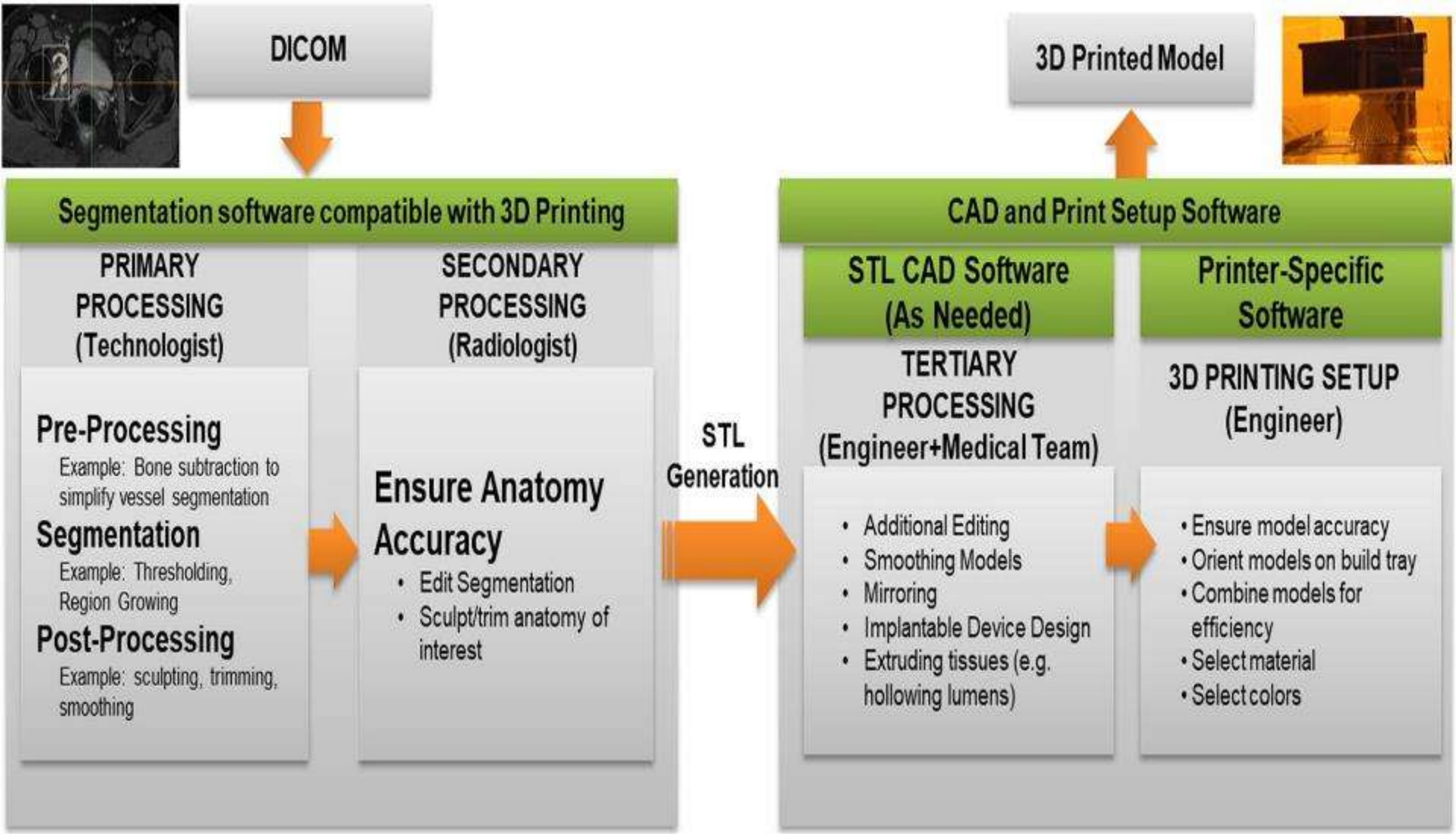


Trimming the support pins (left), using the Boolean union operation on the pins and the appropriate outer mold part (center), with the final result demonstrated (right)



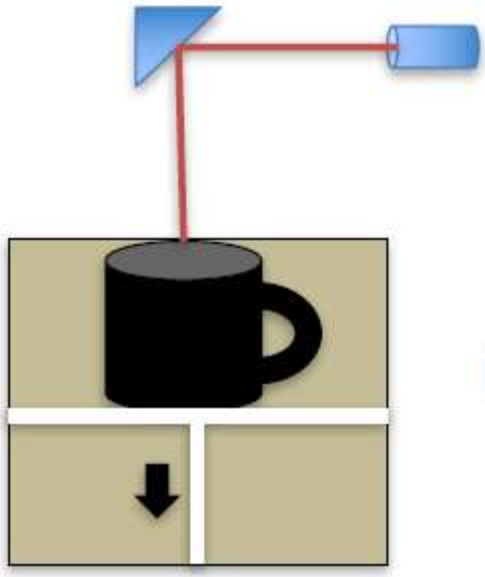
Final mold assembled (left) and with the upper part demonstrated separately
Note the support pins, which can be of variable diameter

SUMMARY

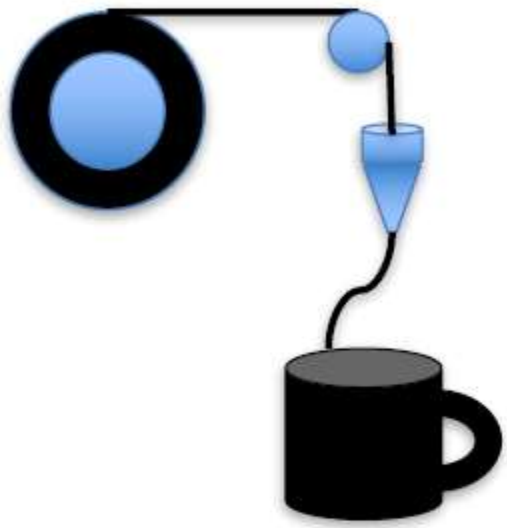


Chepelev L. et al. 3D Printing in Medicine. 2017;3:14

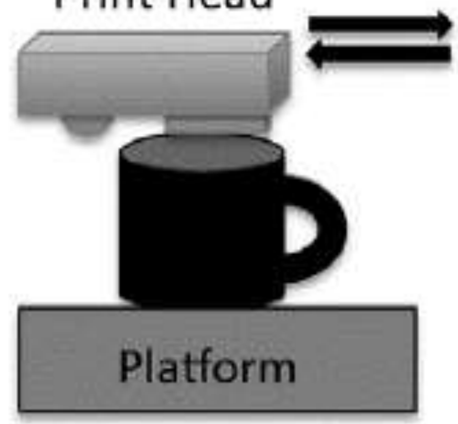
A.



B.

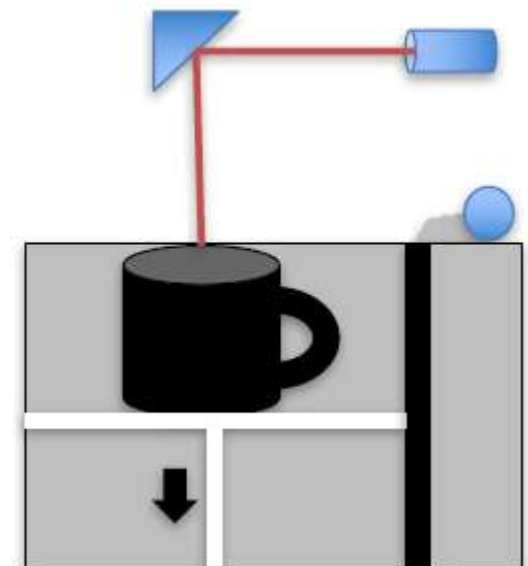


D



A. Stereolithography (SLA)

C.

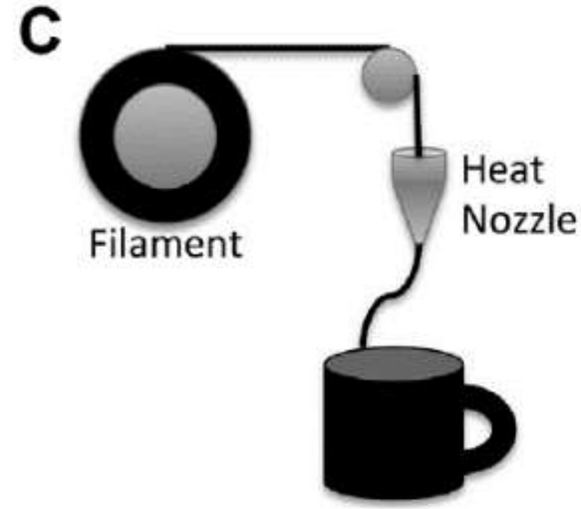


B. Fused deposition modeling (FDM)

Direct 3D-printing

C. Selective laser sintering (SLS)

Direct 3D-printing



Fused deposition modeling (FDM)

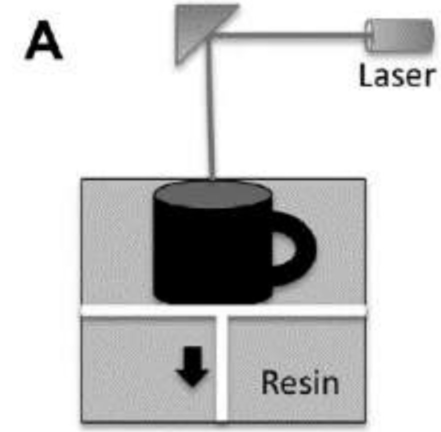
- Achieved through melting pre-formed polymer and extruding molten polymer through nozzle onto print bed
- Time-efficient and affordable
- Require structural supports during printing
- Need of subsequent manual removal of print supports (may lead to errors)
- Manual removal and cleaning prints manually: time-consuming process

Cheng GZ. et al. Chest 2016; 149(5):1136-1142

Freitag L. et al. Respiration 2017;94:442–456

Direct 3D-printing

Stereolithography (SLA) method

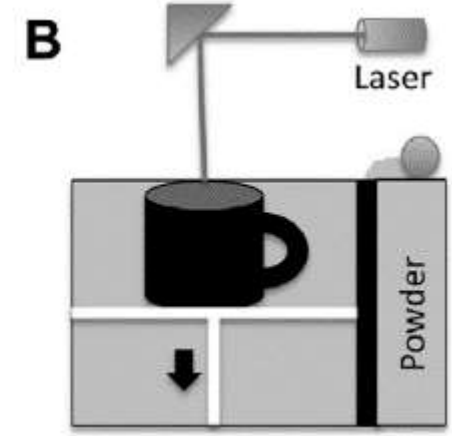


- More recent development
- Liquid monomer polymerized using an UV laser in an optical tank with printed polymer then adhering onto platform
- Platform is lifted in z-axis as each layer of print is created and resultant cured polymer left to aerate
- More advanced, detail of print greater, and resolution capability increased
- More precise and cost-effective compared to traditional casting methods
- More materials available for use in SLA
- More labor-intensive cleaning

Cheng GZ. et al. Chest 2016; 149(5):1136-1142
Freitag L. et al. Respiration 2017;94:442–456

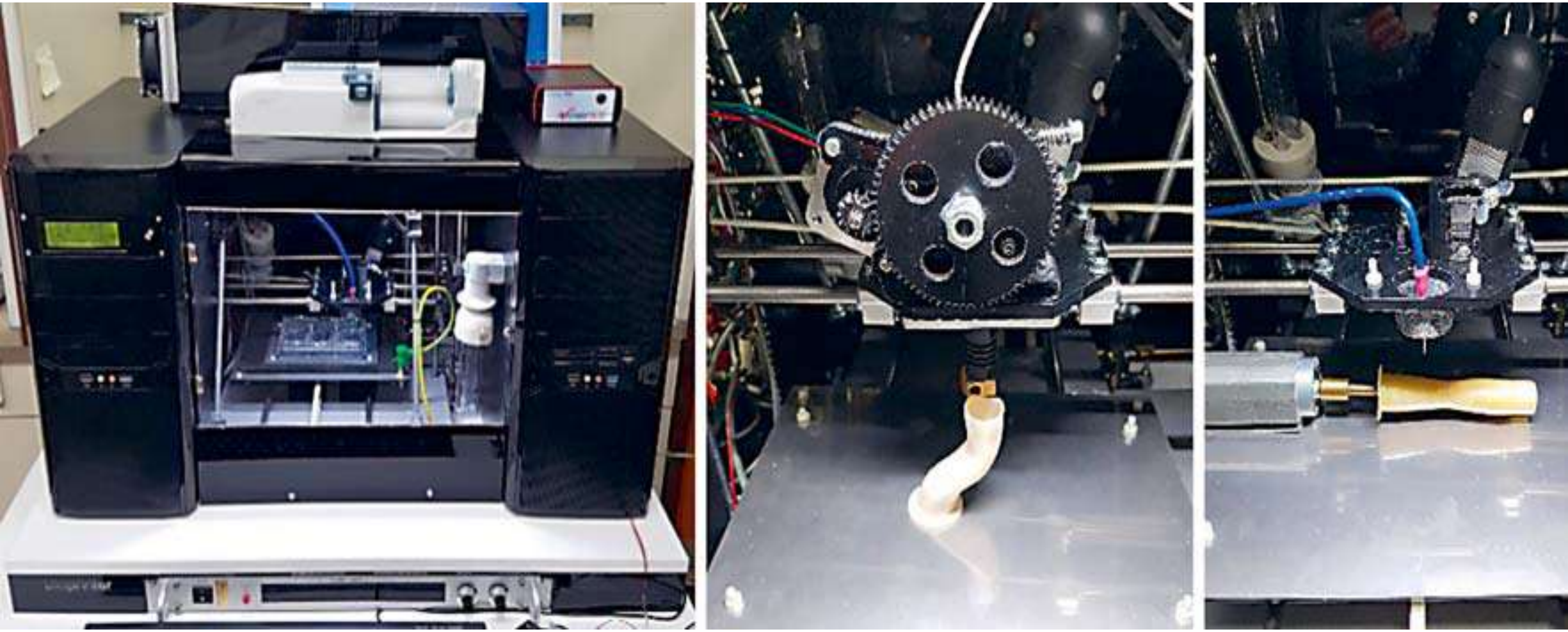
Direct 3D-printing

Selective Laser Sintering (SLS)



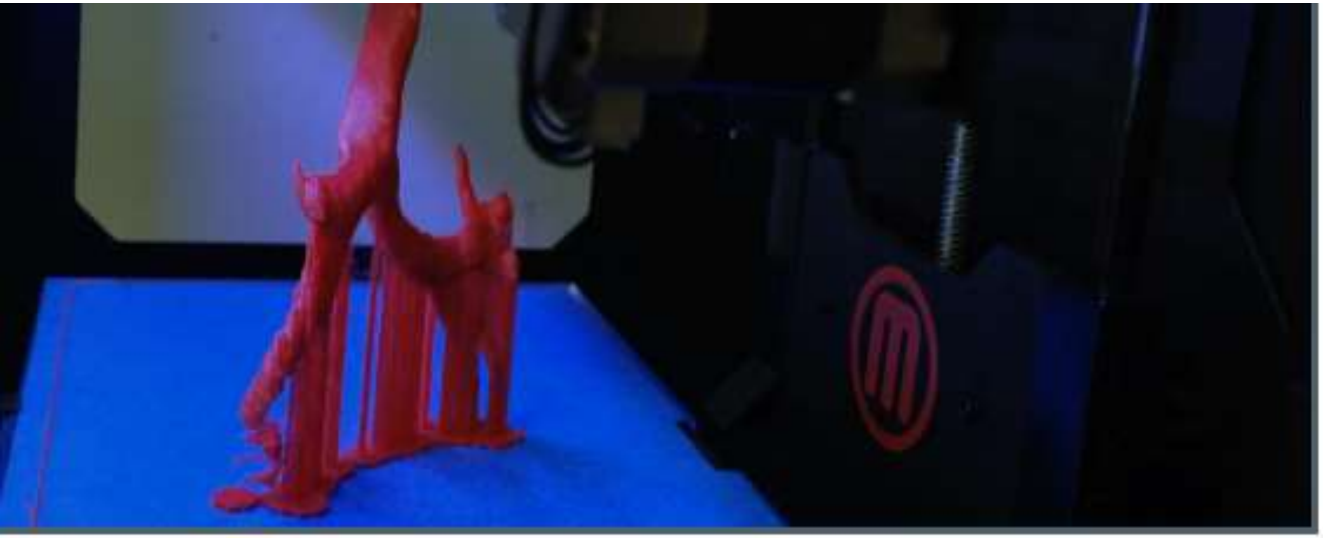
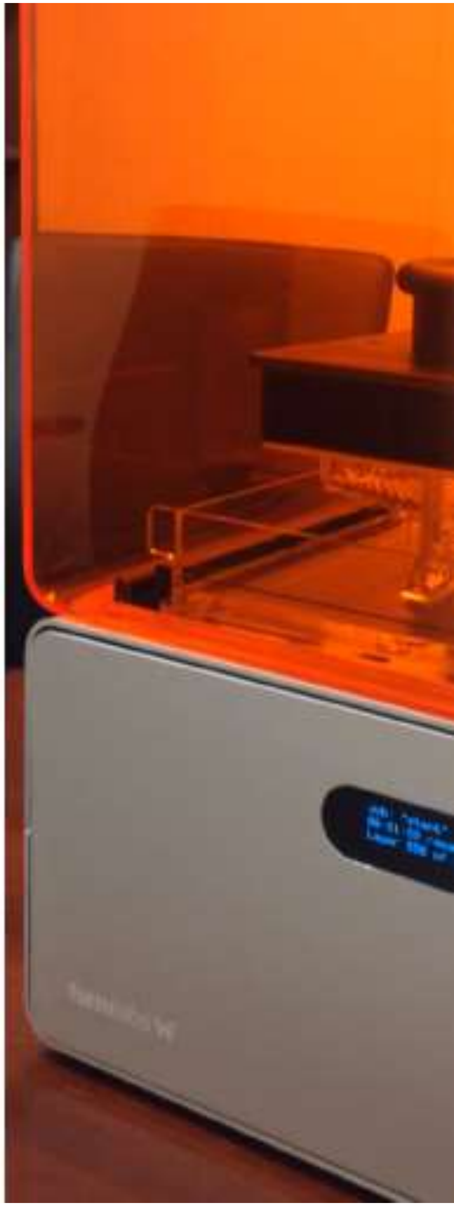
- More expensive alternative for direct 3D-printing
- Uses high-powered laser (carbon dioxide) to fuse thermoplastic powder made from plastic, metal, or ceramic
- After laser fusing cross-section, powder bed drops down one layer thickness, and new layer of thermoplastic powder is applied
- Allows variety of materials to be used and affords high accuracy and resolution but at higher cost

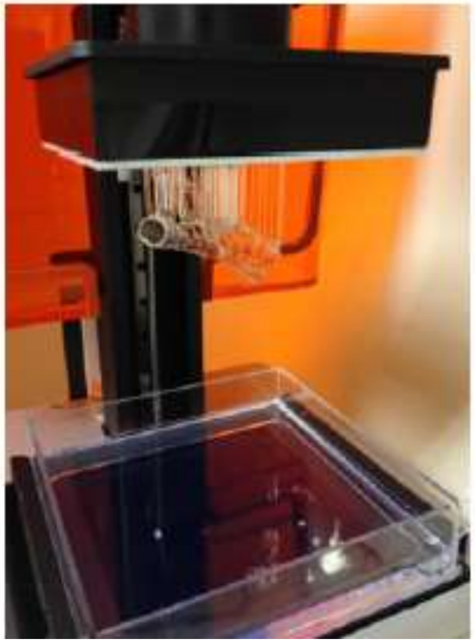
Cheng GZ. et al. Chest 2016; 149(5):1136-1142
Freitag L. et al. Respiration 2017;94:442–456



3D multimode, multimaterial printer, able to print and photocure various polymers and coverings with repellent substances or drugs and capabilities of robo spinning and electrospinning

Freitag L. et al. Respiration 2017;94:442–456

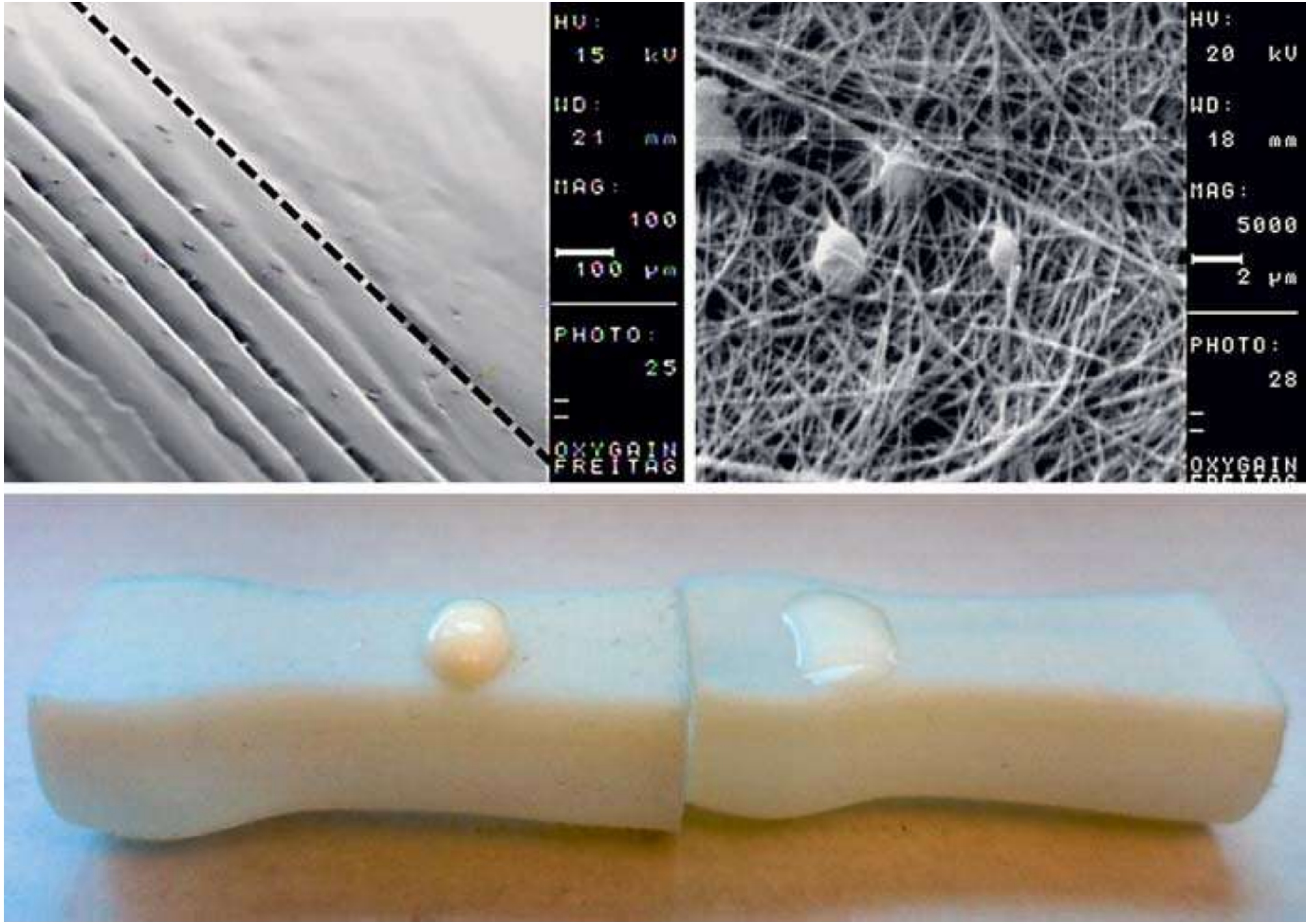






Surface treatment

- Grinding, polishing and dipping in solvents or liquid polymers
- Depends on printing material
- Semi-rigid materials as acrylonitrile or polylactic acid need more surface treatment
- Flexible, rubber like printing materials need less
- Cleaning: Remaining printing material, chemical solvents and potentially harmful stuff removed

Freitag L. et al. Respiration 2017;94:442–456



Surface treatments of 3D-printed stents

a) Electrospray coating for surface smoothing

b) Surface of a polyurethane stent treated with antibiotic containing nanofibers produced by electrospinning

c) Effect of nanocoating on wettability: left stent is nanocoated and extremely hydrophobic, right stent is untreated

Freitag L. et al. Respiration 2017;94:442–456

Sterilization

- Vapor-based sterilization techniques cannot be used since melting temperature of most polymers is too low
- Plasma or ethylene oxide processes: Ideal

Freitag L. et al. Respiration 2017;94:442–456

Stent material

- Elastic modulus strong enough to counteract tumor compression but enough flexibility to adapt to complex shape of trachea
- Shall not rupture during deployment procedure and shall not break after few thousand coughs
- Must be nontoxic and highly biocompatible
- Must be bacteria-, water- and enzyme-resistant
- Should melt at reasonable temperatures (max. 240 °C) and also be stable at body temperature
- Limit potential candidates to much smaller group

Freitag L. et al. Respiration 2017;94:442–456

Material	Print method
Polylactic acid	Fused deposition modelling (FDM)
Polycaprolactone	FDM
Methylacrylic ester acid (with photo-initiators) – FormLabsTM Dental Resin SG	Stereolithography
Medical-grade silicone	Cast and mould
CaP; hydroxyapatite and beta-tricalcium phosphate	Thermal melting
Titanium powder	Selective laser sintering
Gelatin, alginate, chitosan, fibrinogen	FDM
Collagen	Piezo Ink-jet

Jesse Xu et al. Drug Development and Industrial Pharmacy 2019;45(1):1–10

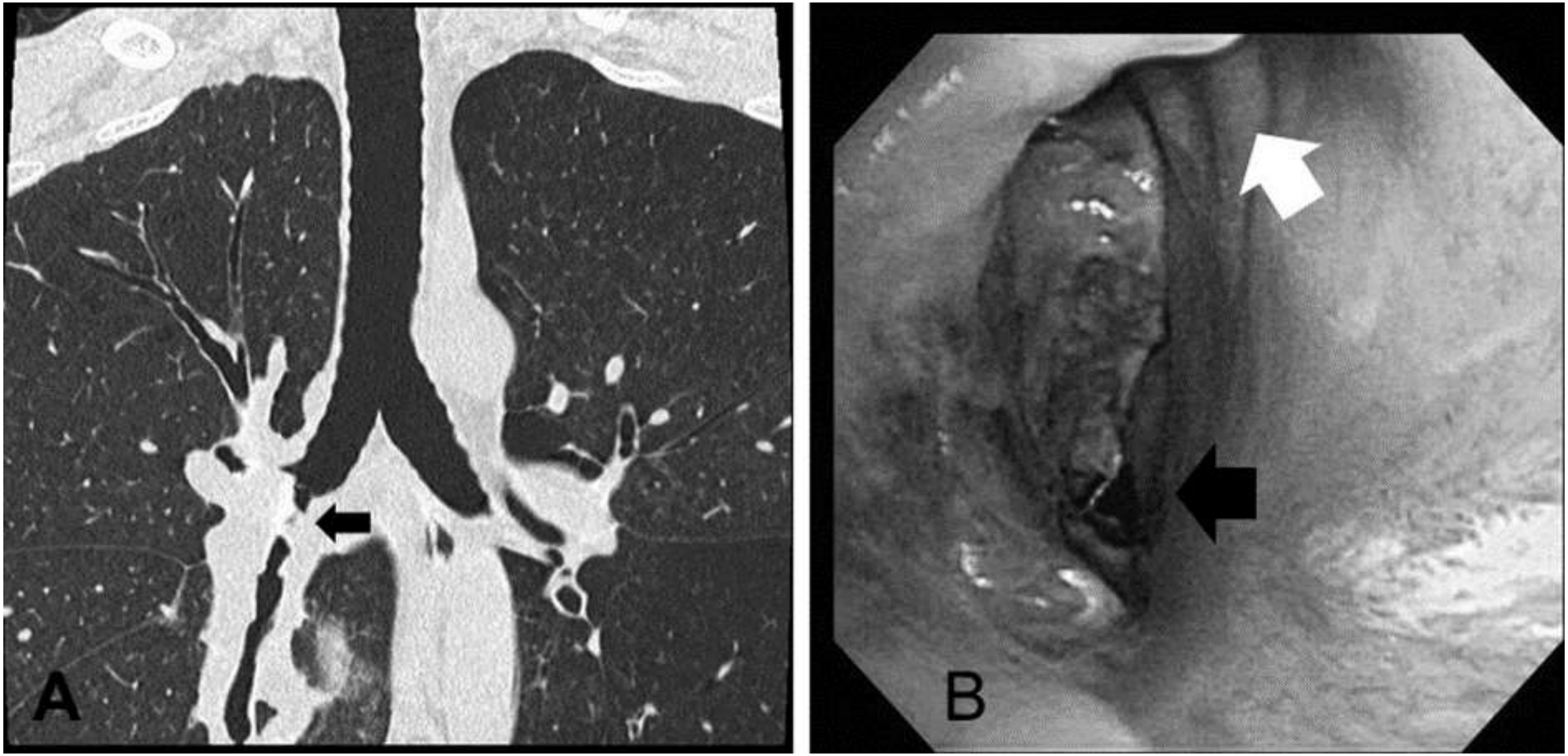
Clinical use

- Airway splints
- Airway models to plan complex surgery
- Airway stents

Airway models to plan complex surgery

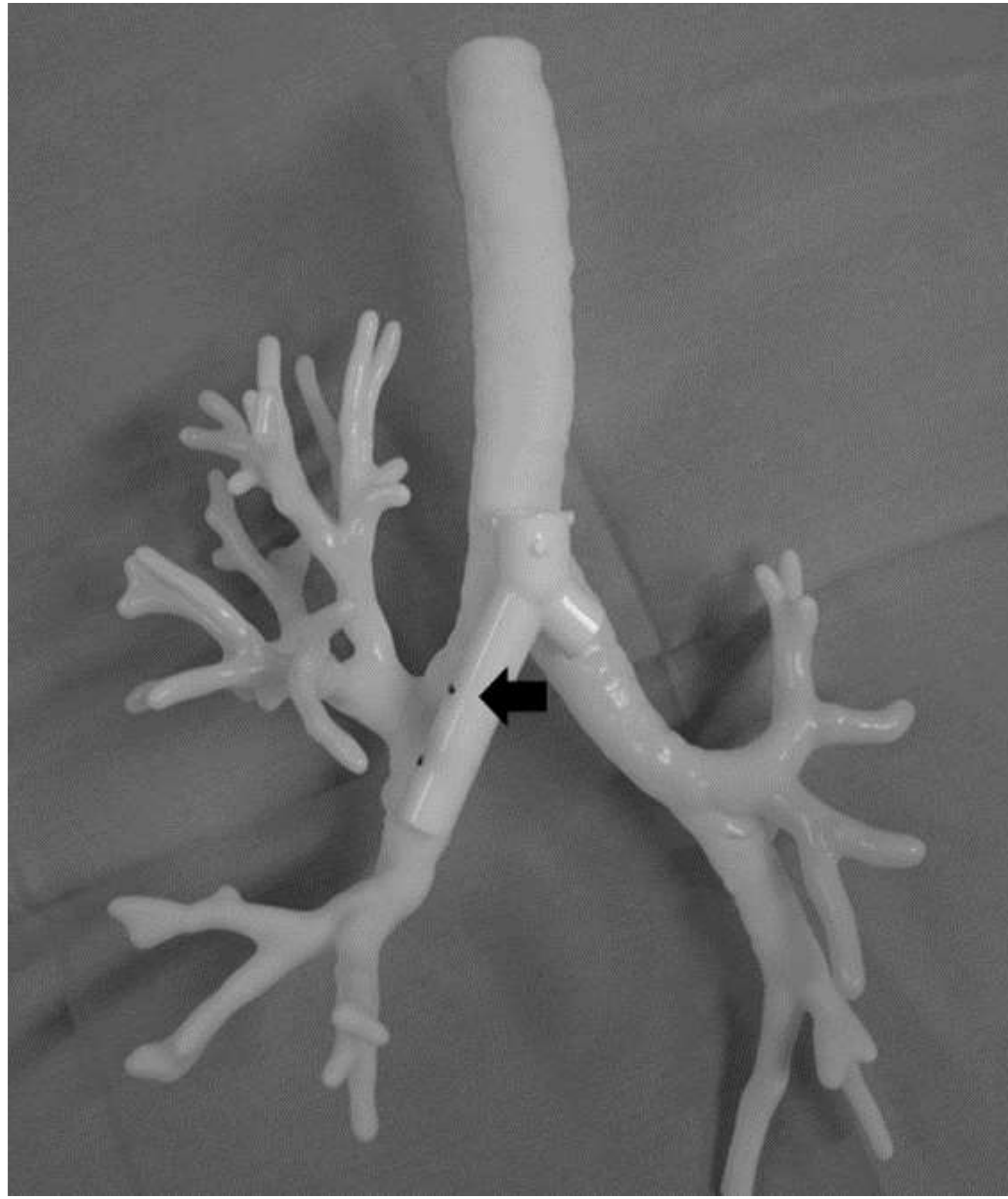
- 30-year-old man underwent right single-lung transplantation for COPD
- Bronchial anastomosis developed ischemic change, resulting in stenosis of intermediate bronchus
- Modified Y-shaped airway stent with fabricated orifice of upper lobe was inserted by rigid bronchoscopy
- Before operation, 3 D printed bronchial model of patient made for surgical simulation
- Model enabled to perform operation easily, quickly, and successfully

Miyazaki T. et al. Ann Thorac Surg 2015;99:e21–3



A) CT showing stenosis of the intermediate bronchus (black arrow)
B) Bronchoscopic findings show the stenosis and malacia at the intermediate bronchus (black arrow). The orifice of the upper lobe (white arrow) is seen

Miyazaki T. et al. Ann Thorac Surg 2015;99:e21–3



Airway silicone stent and three-dimensional (3D) printed model. The dots (black arrow) on the stent are indicated for the opening of the upper bronchus at its right arm based on the 3D printed model. The stenosis of the bronchial lumen is also correctly Replicated

Miyazaki T. et al. Ann Thorac Surg 2015;99:e21–3

1st Use of 3 D printed airway stent……

IMAGES IN PULMONARY, CRITICAL CARE, SLEEP MEDICINE AND THE SCIENCES

AJRCCM 2017;195(7):e31–e33

Treatment of Post-transplant Complex Airway Stenosis with a Three-Dimensional, Computer-assisted Customized Airway Stent

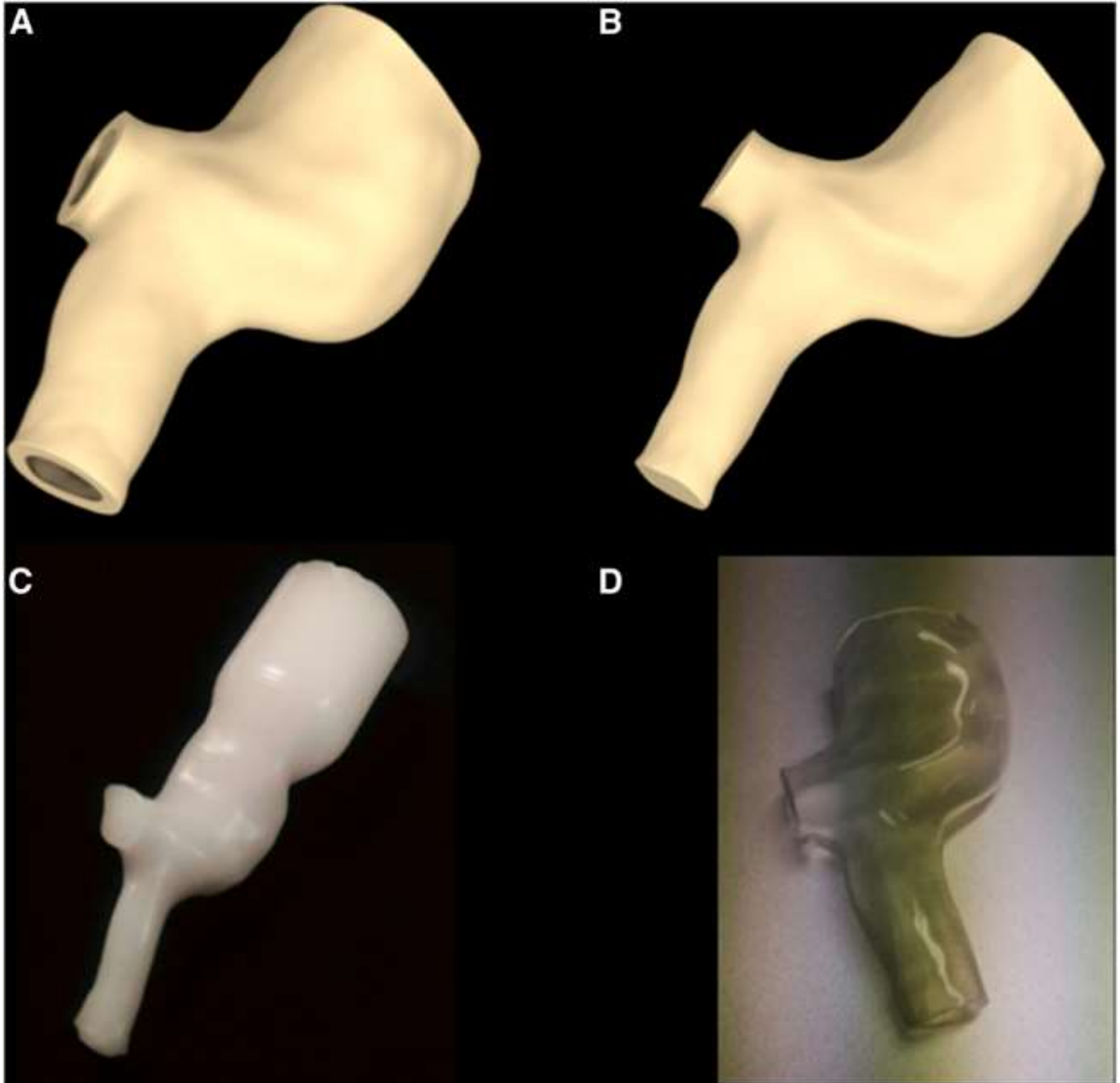
Nicolas Guibert[1], Alain Didier[1], Benjamin Moreno[2], Laurent Mhanna[1], Laurent Brouchet[3], Gavin Plat[1], Christophe Hermant[1*], and Julien Mazieres[1*]

[1]Service de Pneumologie-Allergologie, and [3]Service de Chirurgie Thoracique, Hôpital Larrey, Centre Hospitalier Universitaire de Toulouse, Université de Toulouse III (Paul Sabatier), Toulouse, France; and [2]AnatomikModeling Society, Toulouse, France

Use of 3D printed airway stent

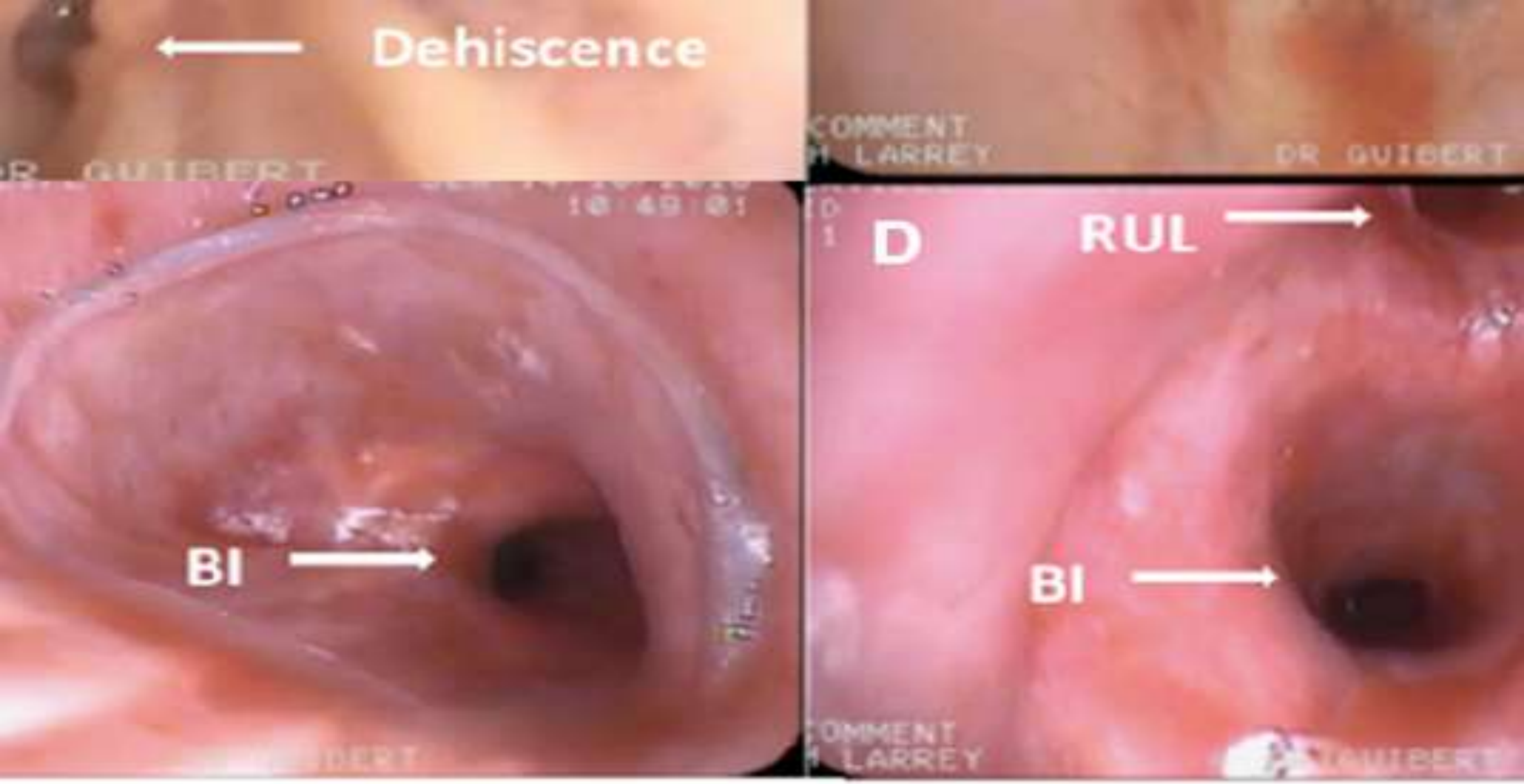
- Patient suffering from complete stenosis of bronchus intermedius (BI) with partial dehiscence of bronchial anastomosis after lung transplantation
- Complex anatomy excluded use of conventional airway stents
- Computer-assisted segmentation of airways of patient done
- Virtually relieved stenosis, closed dehiscence, and designed 3D stent and mold
- Dedicated silicone stent (PN40000) made from mold
- Under rigid bronchoscopy, BI was progressively dilated
- Stent then inserted through rigid tracheoscope

Guibert et al. AJRCCM 2017;195(7):e31–e33



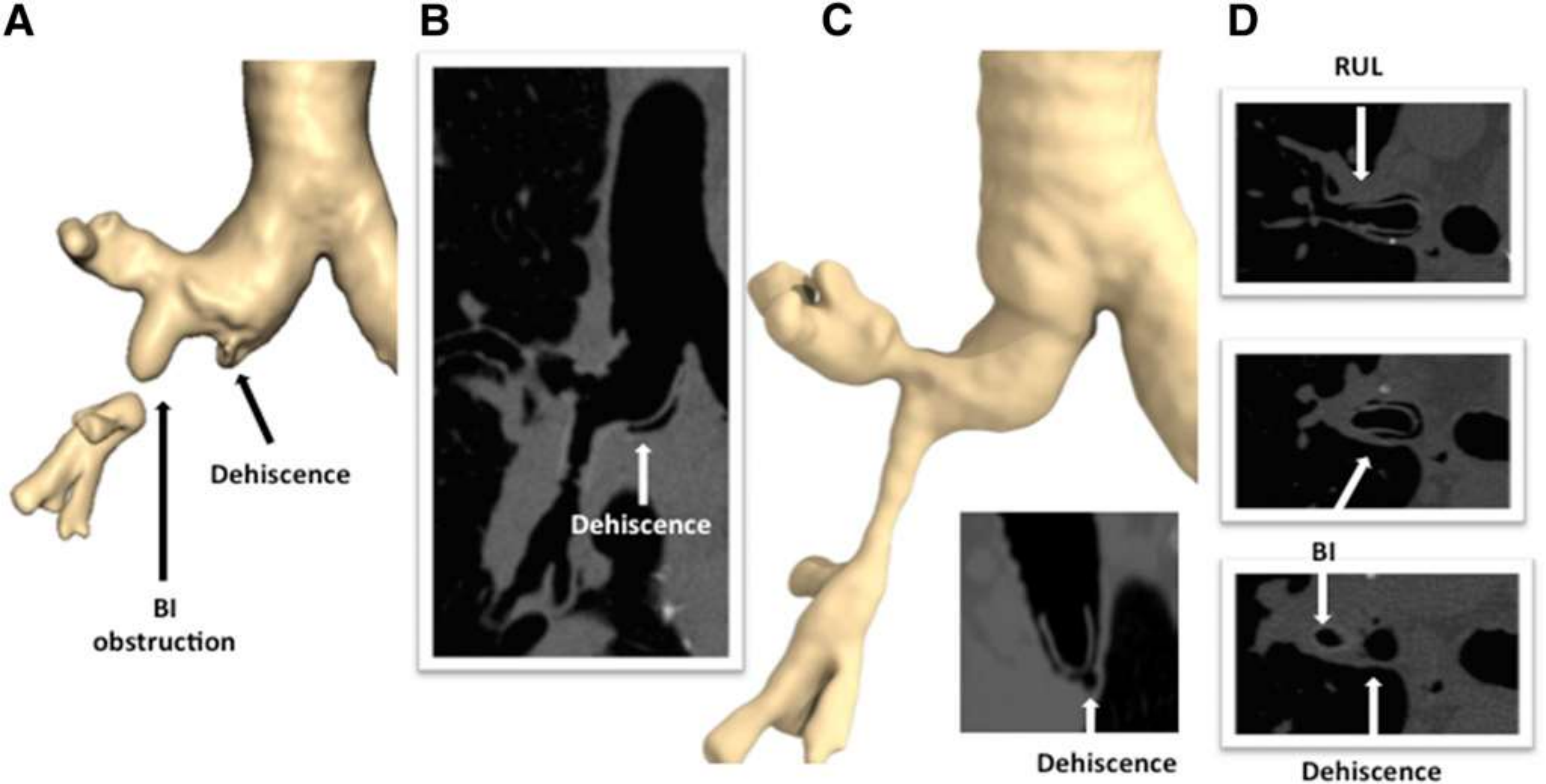
Conception and fabrication of the personalized stent. Conception of the virtual stent (A) and mold (B) based on CT scan data by CAD (C) Manufactured mold (D) 3D customized airway stent manufactured

Guibert et al. AJRCCM 2017;195(7):e31–e33



Airway stenting procedure. (A, B) Bronchoscopic view of the limited dehiscence (A) and complete bronchus intermedius (BI) obstruction (B) before balloon bronchoplasty and stenting. (C, D) Bronchoscopic view of airways after dilatation of stenosis and stenting showing great congruence of device with anatomically complex airways; (C) view of RMB from trachea, and (D) view of bronchus intermedius and RUL from RMB. 3D reconstruction of airways on basis of preoperative (top) and postoperative (bottom) CT scans

Guibert et al. AJRCCM 2017;195(7):e31–e33



Results of a computed tomography (CT) scan performed at 7 days after the intervention

(A) 3D segmentation of airways on basis of preoperative CT scan showing complete obstruction of BI and partial dehiscence

(B) Frontal CT view showing very good congruence of stent with complex airways

(C) 3D segmentation of airways on basis of postoperative CT scan (Day 7) showing ventilation of BI and exclusion of dehiscence

(D) Axial CT views showing congruence of stent at different levels of airways

Slices passing through division between right upper lobe (RUL)/main right bronchus and through BI and dehiscence

Guibert et al. AJRCCM 2017;195(7):e31–e33

Application of 3D Printing for Patient-Specific Silicone Stents: 1-Year Follow-Up on 2 Patients

Thomas R. Gildea[a] Benjamin P. Young[b] Michael S. Machuzak[a]

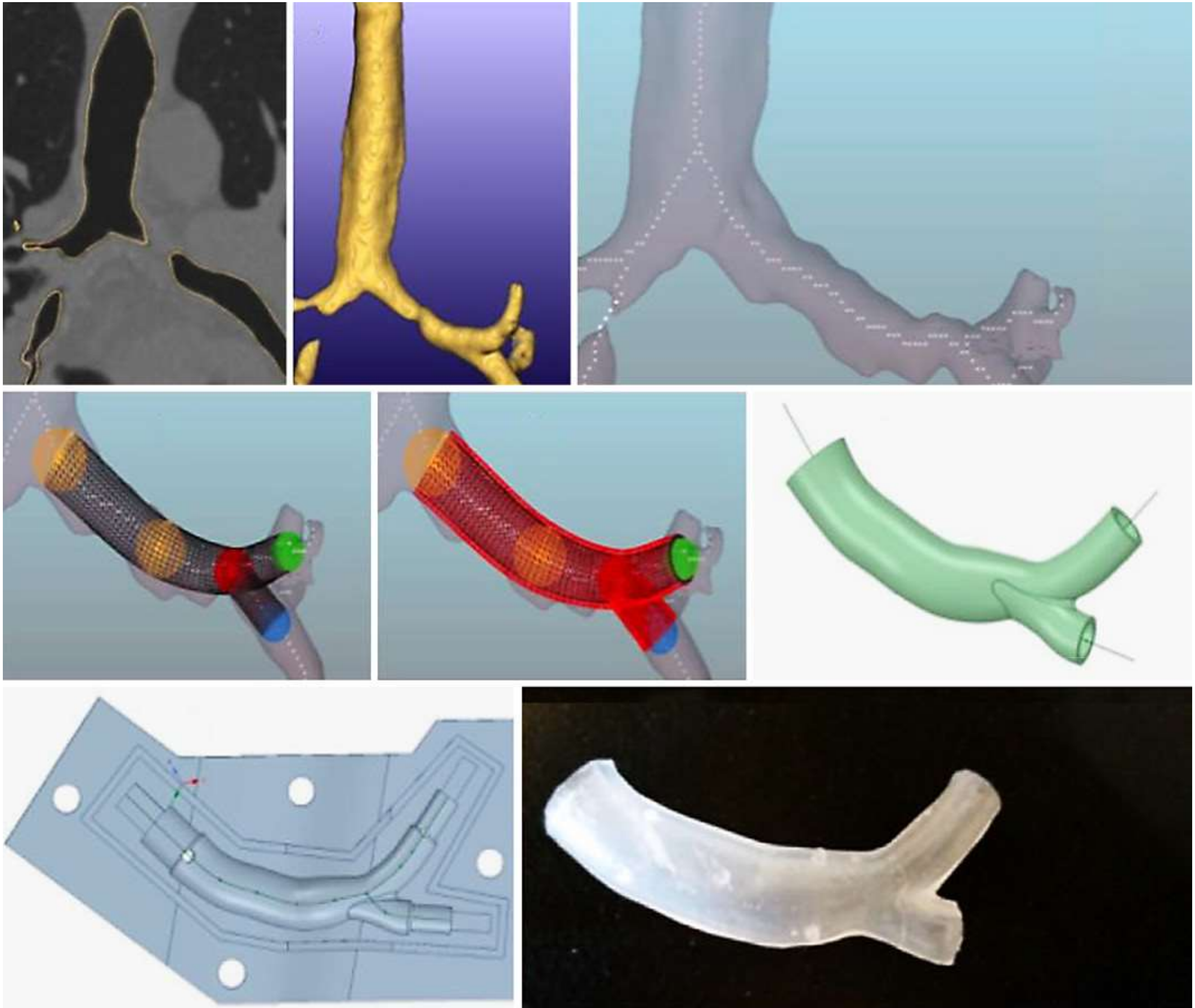
[a]Respiratory Institute, Cleveland Clinic, Cleveland, OH, USA; [b]Department of Pulmonary, Critical Care and Sleep Medicine, Case Western Reserve University, Cleveland, OH, USA

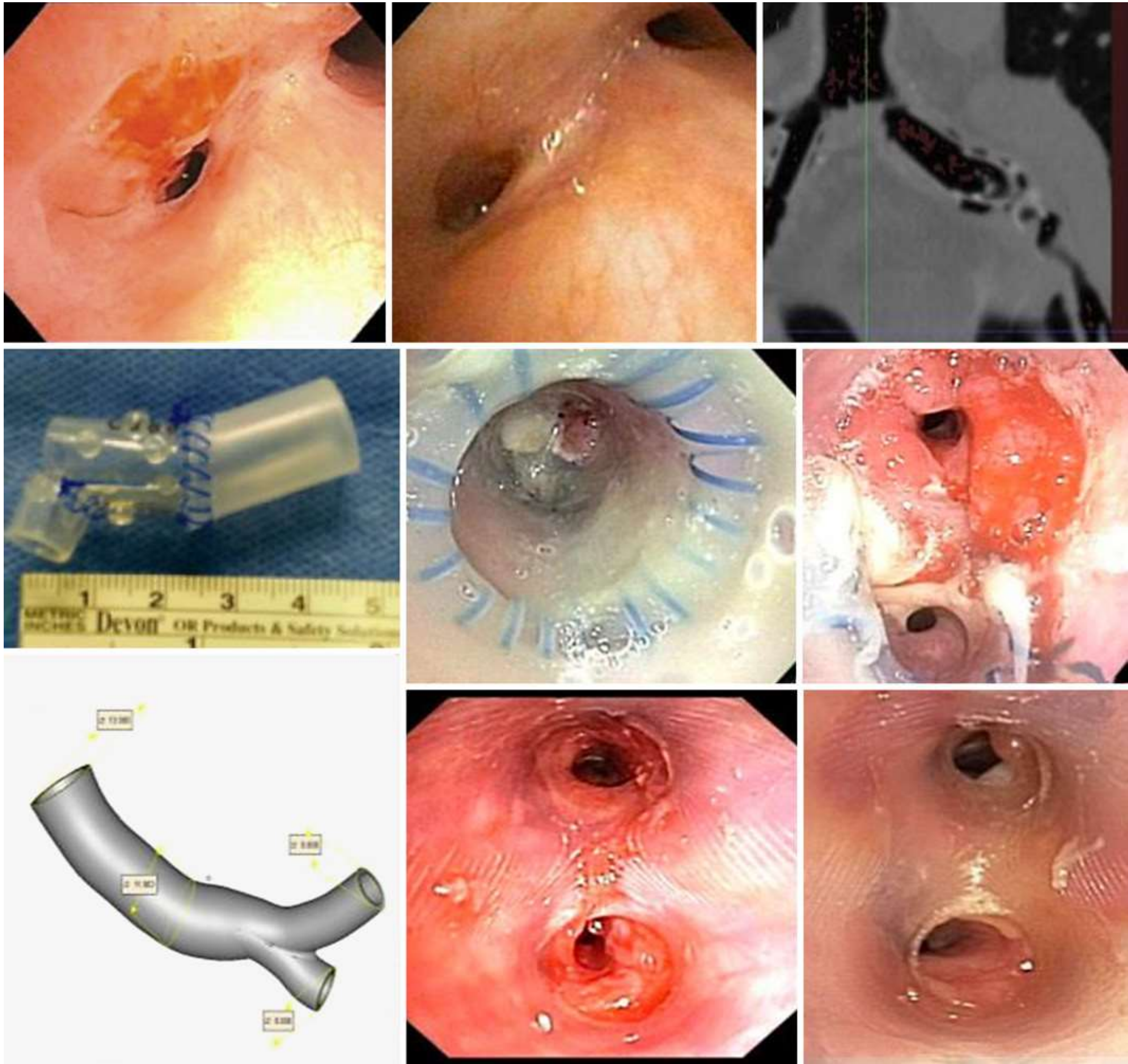
Respiration 2018;96:488–494

Use of 3D printed airway stent

- 1-year outcome of 2 patients with airway disease caused by GPA affecting left main bronchus and secondary carina
- Stents were designed, manufactured, and implanted, with outcomes monitored for > 1 year after implantation
- Both patients retained their patient-specific stents for > 1 year, with reduced frequency of procedures and procedure time after implantation

Gildea TR. et al. Respiration 2018;96:488–494

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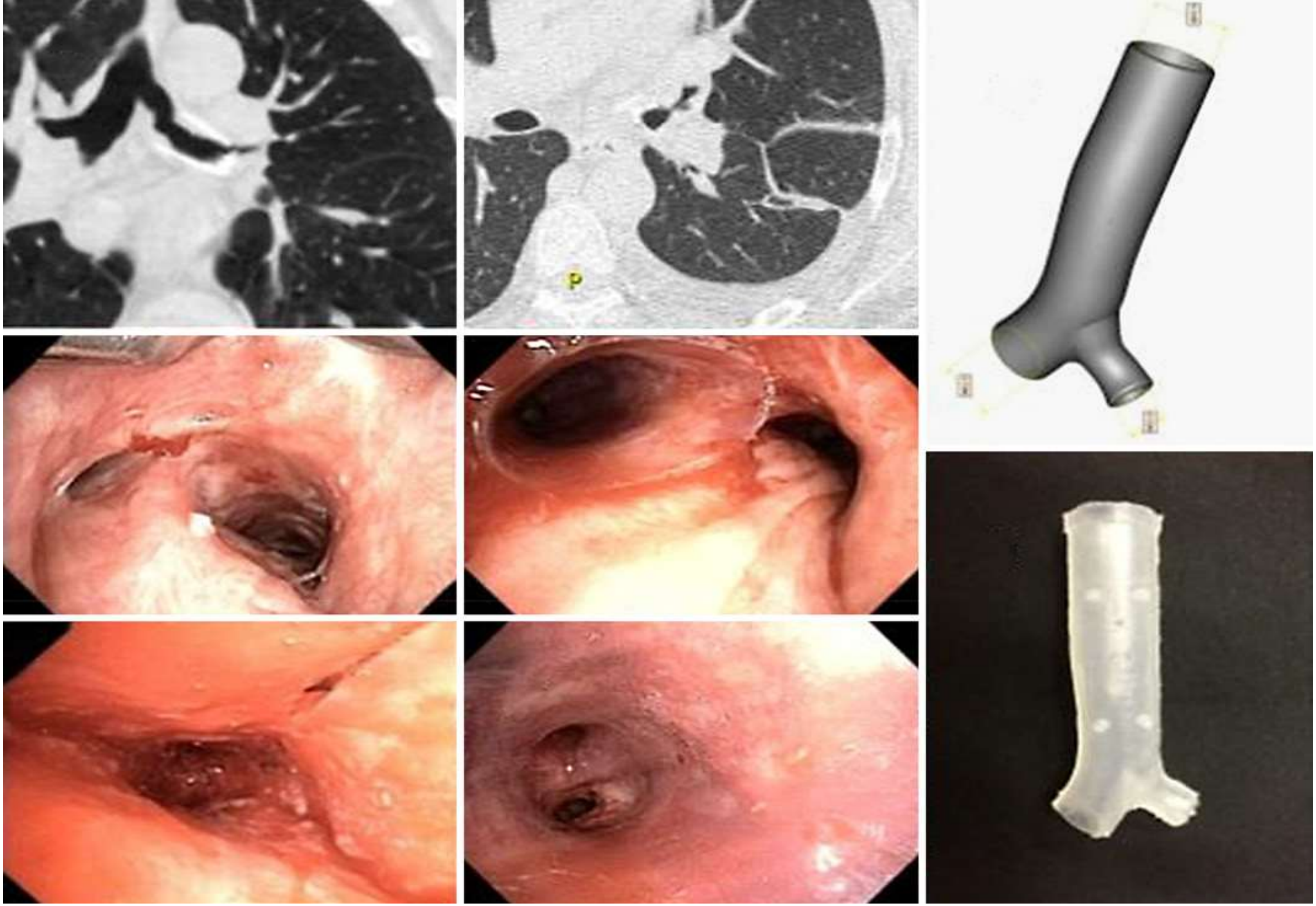
OR Products & Safety



Radiographic and airway images of Patient 2. Coronal CT chest with the original metallic stent incorporated into the left main bronchus airway wall with in-stent stenosis. Axial chest CT with stenosis in the left upper division. Main carina with recurrent stenosis after original stent extraction. Patient-specific stent in the left main bronchus. Distal left main bronchus and secondary carina. Distal left main bronchus with a patient-specific Ystent. 3D prescription stent. Patient-specific Y-stent for the left main bronchus

Patient-specific, 3-dimensionally engineered silicone Y-stents in tracheobronchomalacia: Clinical experience with a novel type of airway stent

Check for updates

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Use of 3D printed airway stent

- 69-year-old and 71-year-old male patient with tracheobronchomalacia
- Post- tracheobronchoplasty→ Temporary relief
- Condition deteriorated→ Reevaluation included dynamic bronchoscopy and dynamic computed tomography
- Stenting with conventional stents was not expected to be successful because of dimensions of central airways (largest diameter was 32 mm)

Schweiger T. et al. J Thorac Cardiovasc Surg 2018;156:2019-21

Use of 3D printed airway stent

- Patient-specific silicone Y-stent manufactured in both cases with use of 3 D print
- Stent implanted
- Alignment of stent with mucosal lining found perfect
- At follow-up 8 months and 5 months after stenting, both patient had sustained relief of symptoms
- Complications and side effects of stent placement: mucus accumulation as well as formation of granulation tissue and stent migration

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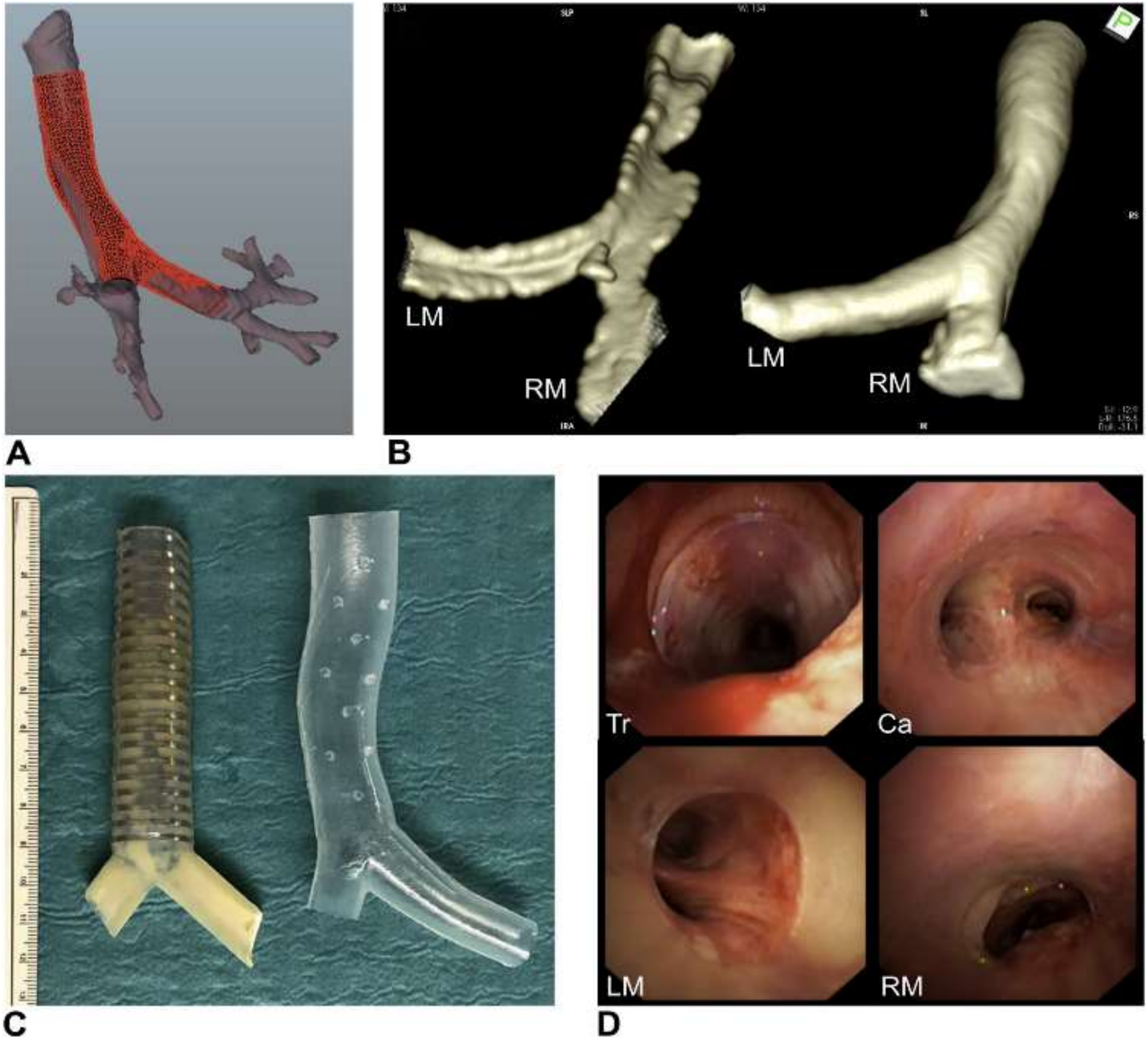

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Clinical trials

- NCT02889029:
  - Management of Complex Airway Stenoses With Dedicated Tailored Stents Wrought by 3D Computer-assisted Conception (DASCAS)
  - Recruitment not started yet
- NCT03111888:
  - Evaluating the Clinical effectiveness of 3D Printing for a patient-specific Silicone Stent Airway Implant
  - Recruitment Withdrawn

3 D printing industry

- Stratasys Limited
- 3D Systems Corporation
- Materialise NV

Take home message

- 3D-printing holds potential to solve many of airway stent issues by using personalized airway stents designed to conform to patient's anatomy and physiology
- Application of 3D printing for custom implants (including airway stents) is still in its infancy
- No published outcome comparison data between 3 D printed and standard airway stents

Take home message

- Technical limitations in 3D printing methods and lack of adequate access for clinicians and patients
- Lack of approved, 3D printable, flexible, implantable grade material suited for manufacturing endobronchial stents
- Legal hurdles and costs involved prevent industries from addressing the unmet need of truly optimized airway stent