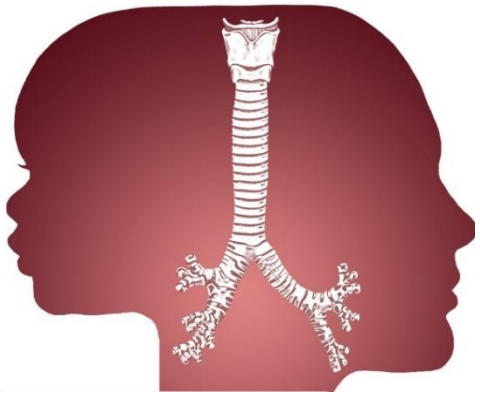
BIO-ENGINEERING
Collaboration and Possible Options in the Future



Centre hospitalier universitaire vaudois

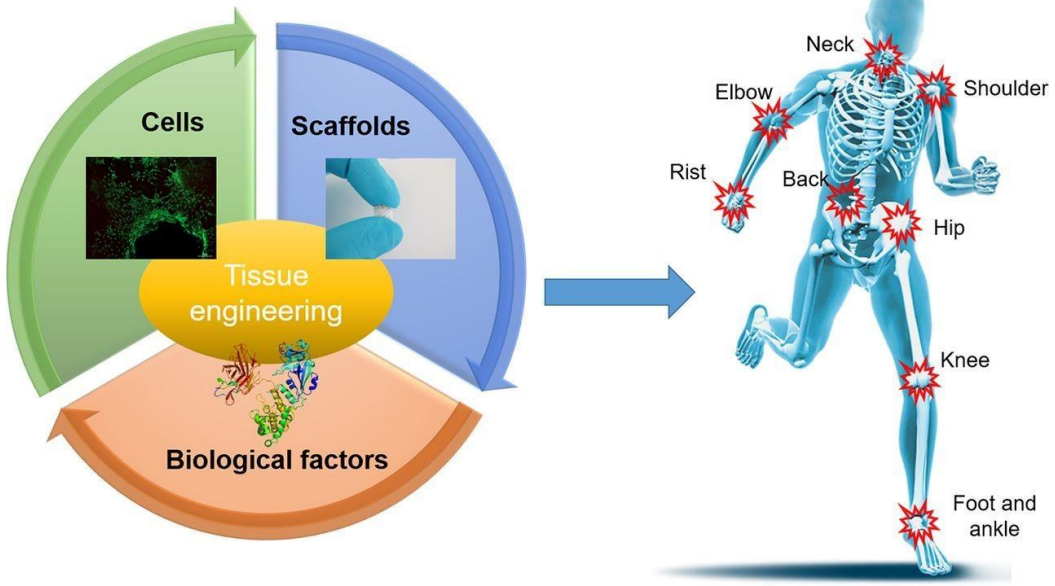
UNIVERSITE DE LAUSANNE

Kishore SANDU

Chirurgie des voies aériennes
Médecine Hautement Spécialisée
Service d'oto-rhino-laryngologie et de chirurgie cervico-faciale
Centre Hospitalier Universitaire Vaudois CHUV
Lausanne | Suisse

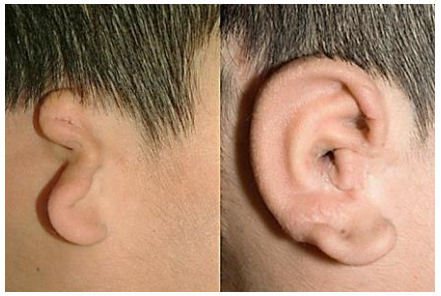
GOALS OF BIO / TISSUE ENGINEERING ….

to assemble functional constructs that restore, maintain, or improve damaged tissues or whole organs



Two of the most successful examples:
INTEGRA (skin repair post burns)
Osteopore (osseus integration)

VACANTI EAR, 1988



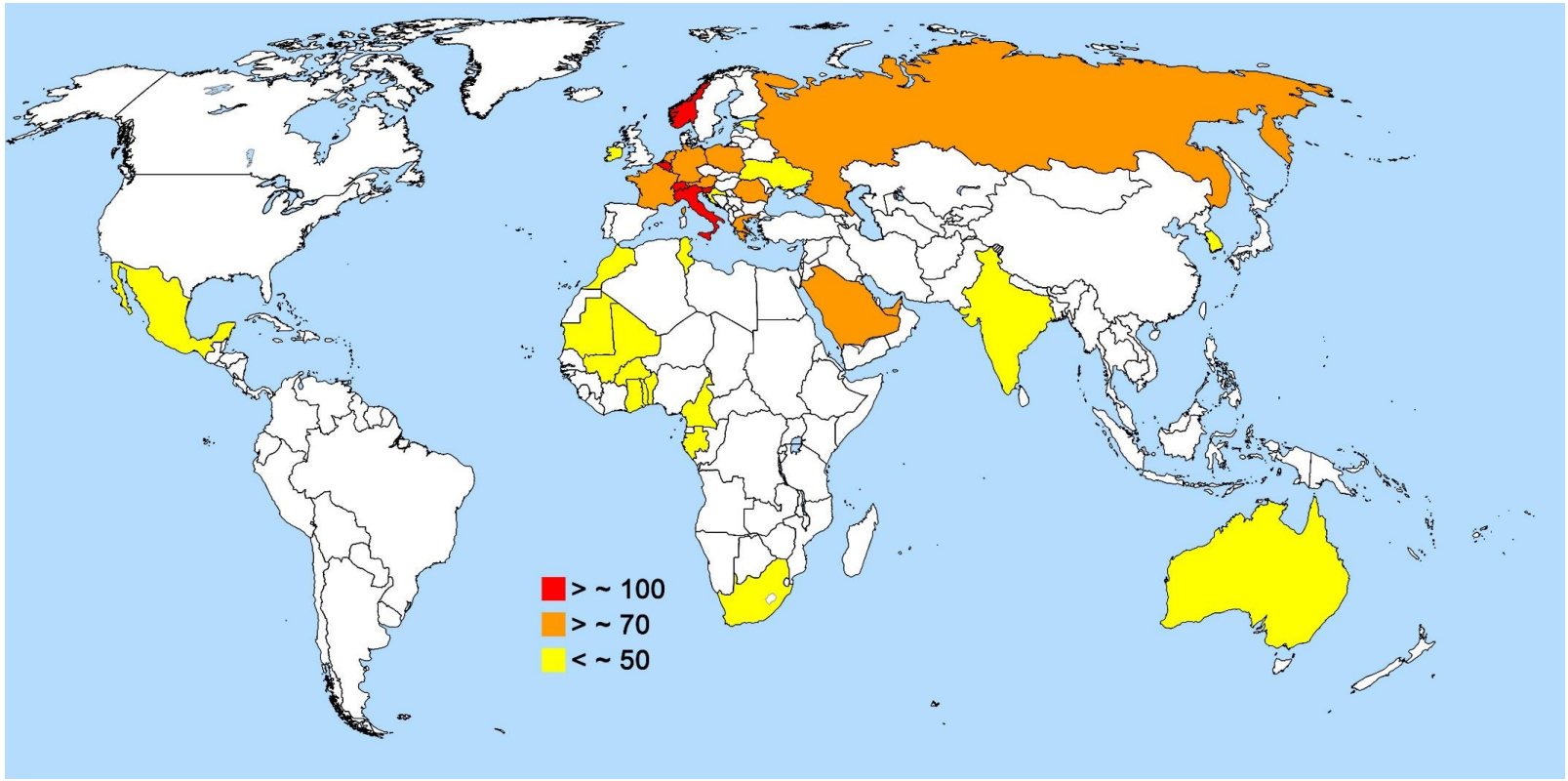
Joseph Vacanti, a surgeon, &
Robert Langer, an engineer
Massachusetts Institute of Technology

AIRWAY UNIT

- Unique in Switzerland and Europe
- *Médecine Hautement Spécialisée (Quaternary care clinic)*

  - Complex airway stenosis

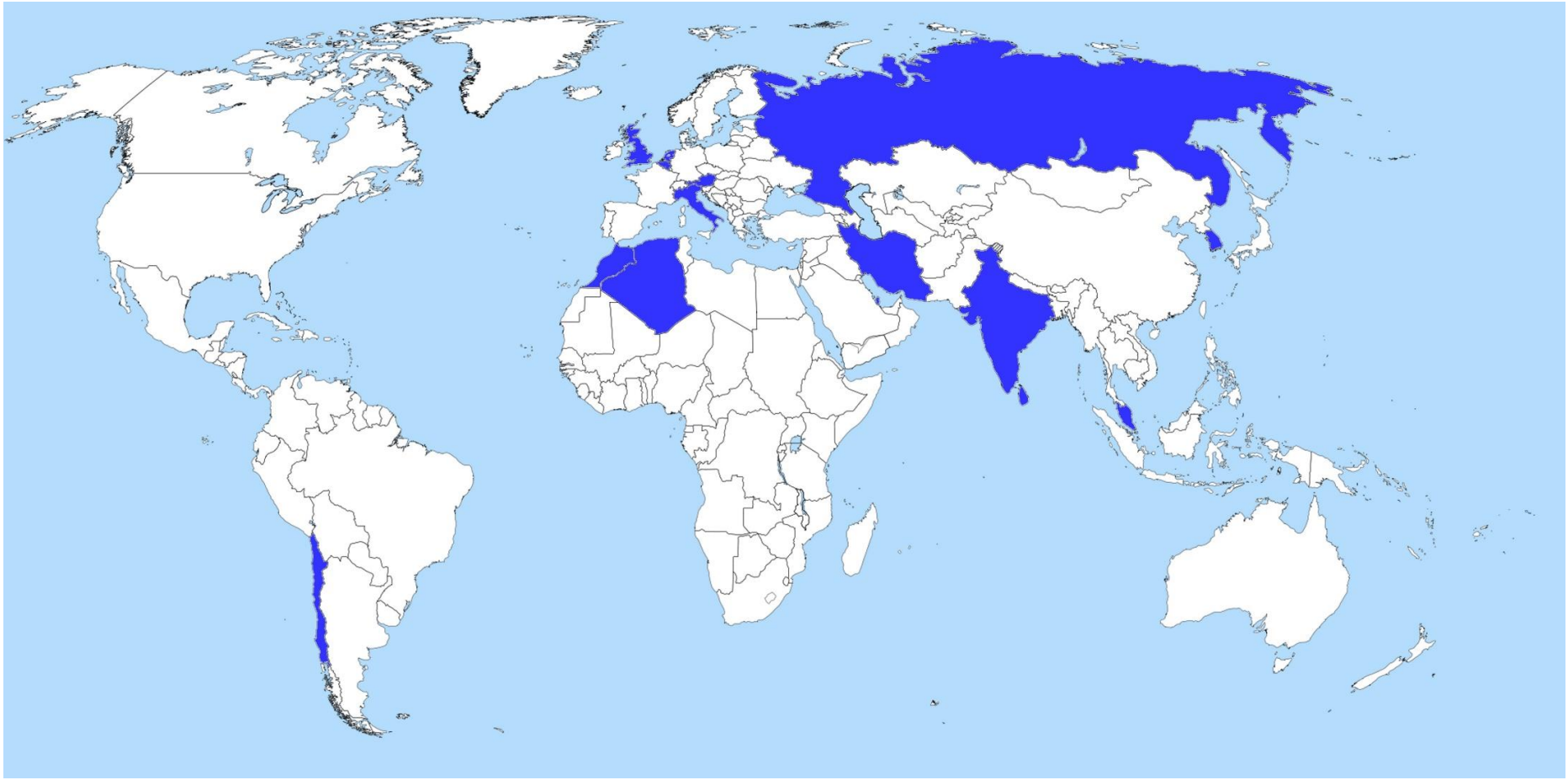
  - *Patient referral pattern*



~ 91% foreign institutions
9% Suisse (other Univ. hospitals-6%, Lausanne-3%)

Source: CHUV, Mai 2024

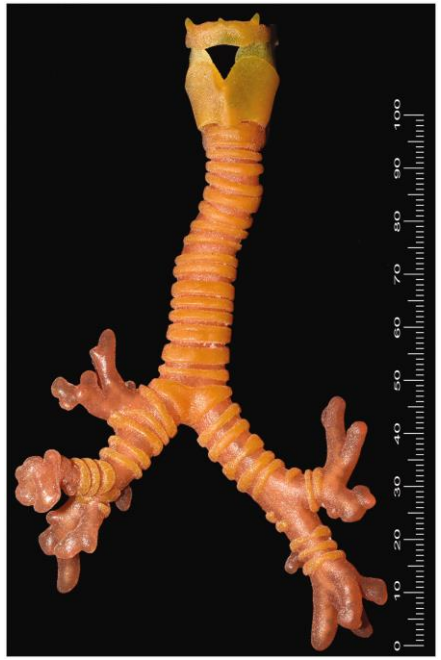
OUTREACH OPÉRATIONS DONE OUTSIDE SUISSE (N=16 PAYS)



……necessity drives innovation

IT ALL STARTS
WITH A GREAT IDEA
AND TEAMWORK

GARRETT CAMP



Des projets ambitieux qui peuvent sauver des vies et/ou les transformer……

1. **TRANSPLANTATION TRACHÉALE**

2. **VOIES RESPIRATOIRES FLASQUES (TRACHÉOMALACIE)**

[Tracheomalacia: Sarah's Story | Johns Hopkins Medicine]

LIFE CHANGING PROJECTS ….

1. FLOPPY AIRWAY (TRACHEOMALACIA)

COLLAPSING AIRWAY

2. TRACHEAL TRANSPLANTATION

WIND-PIPE CONDUITS

3. ARTIFICIAL INTELLEGENCE

WINDOW TO THE FUTURE MEDECINE

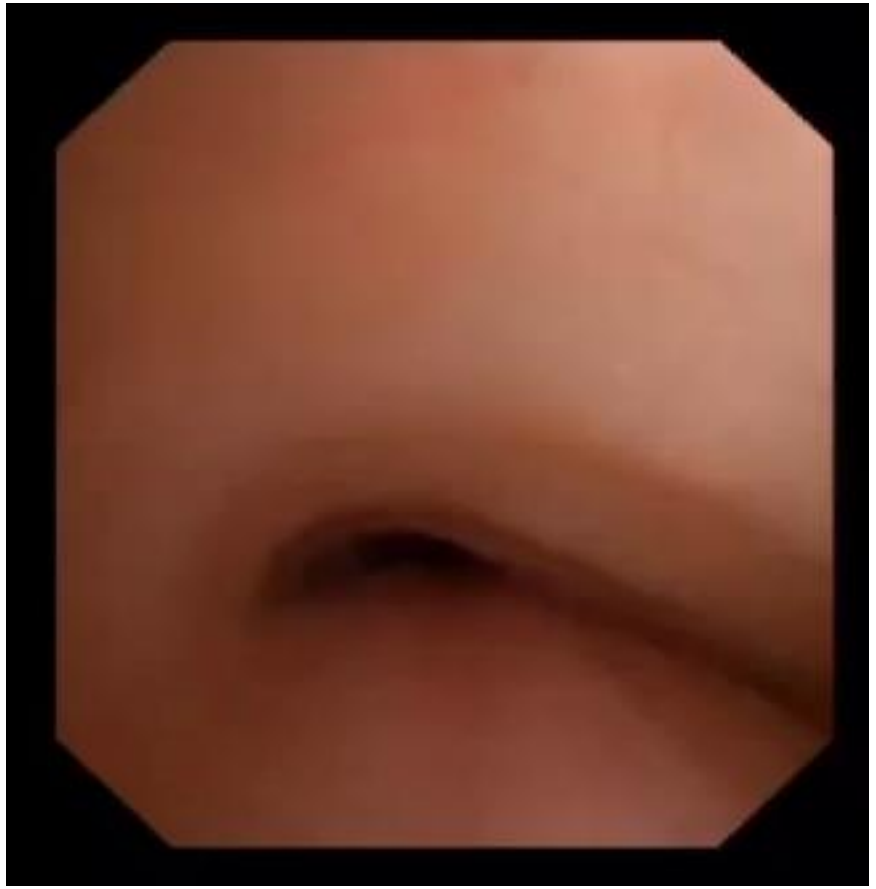
CASE 1

Severe TM associated with EA & TEF

DY 13 m boy

several dying spells at home, multiple hospitalisations

EA TEF (operated) + severe TM (tracheal dyskinesia)

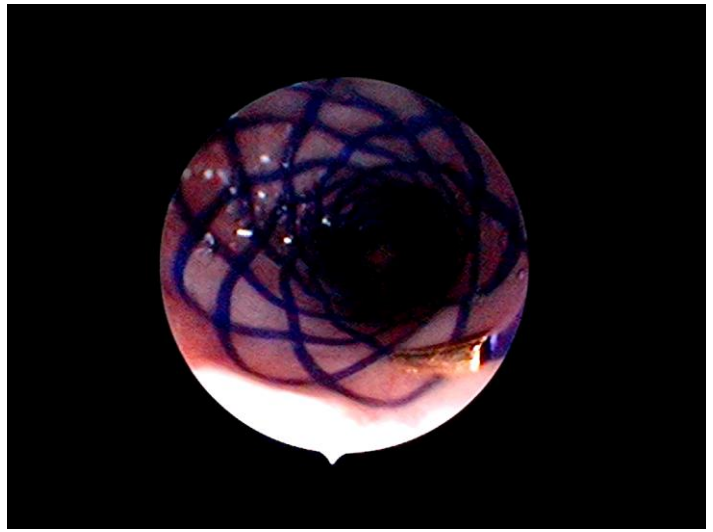


Endoscopy

CASE 2

How about Endoluminal Tracheal Stents???

Severe morbid TM



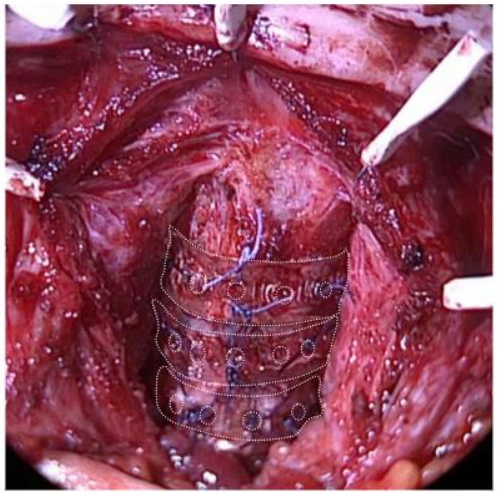
Endoluminal
Biodegradable stent

Endoluminal
Fluency metallic stent

.....What next ???

CASE 3 (CHUV)

External bioresorbable airway rigidification to treat refractory localized tracheomalacia.
Gorostidi F, Reinhard A, Monnier P, Sandu K. Laryngoscope. 2016



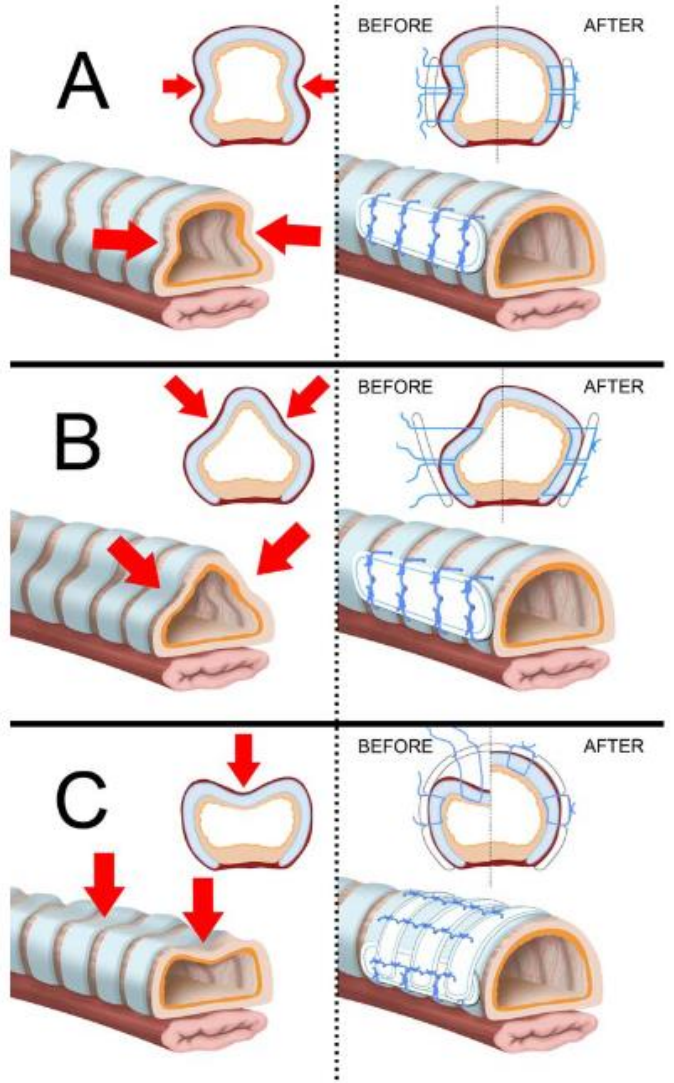
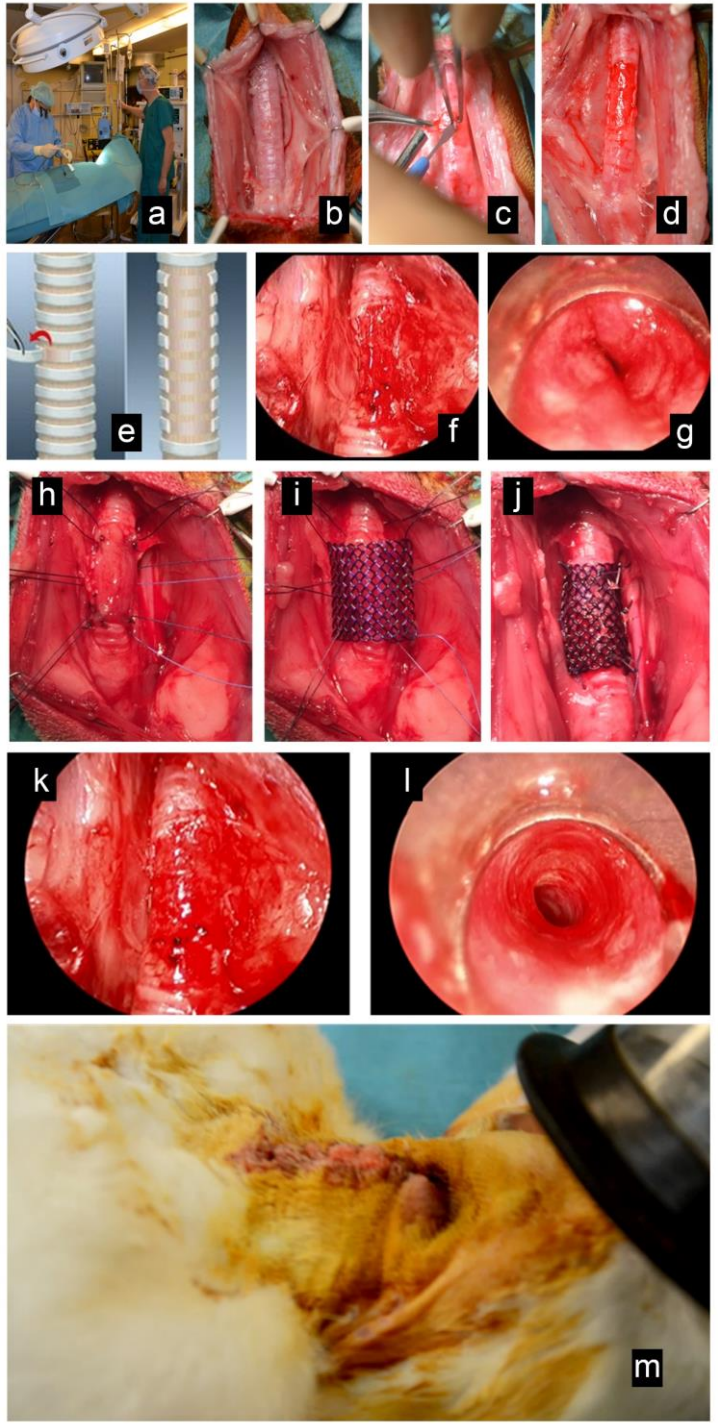
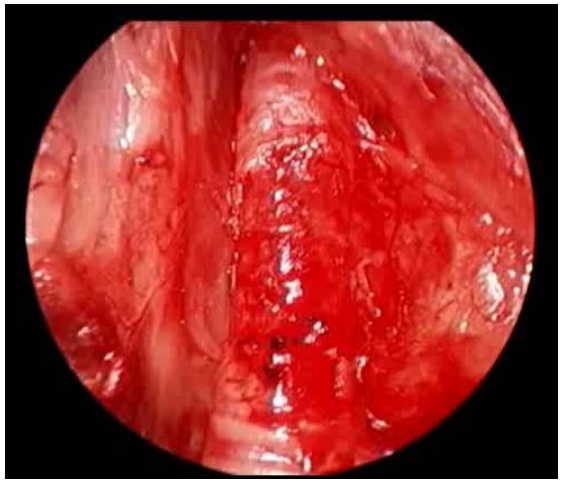
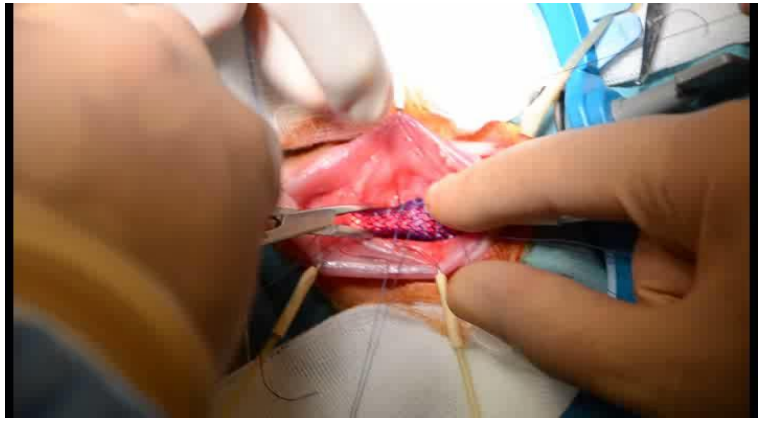


Fig. 1. (A, left) Transverse collapse; (B, left) paramedian collapse; and (C, left) anteroposterior collapse, and correspondent appropriate position for extraluminal resorbable plate fixation (A, B, C; right).

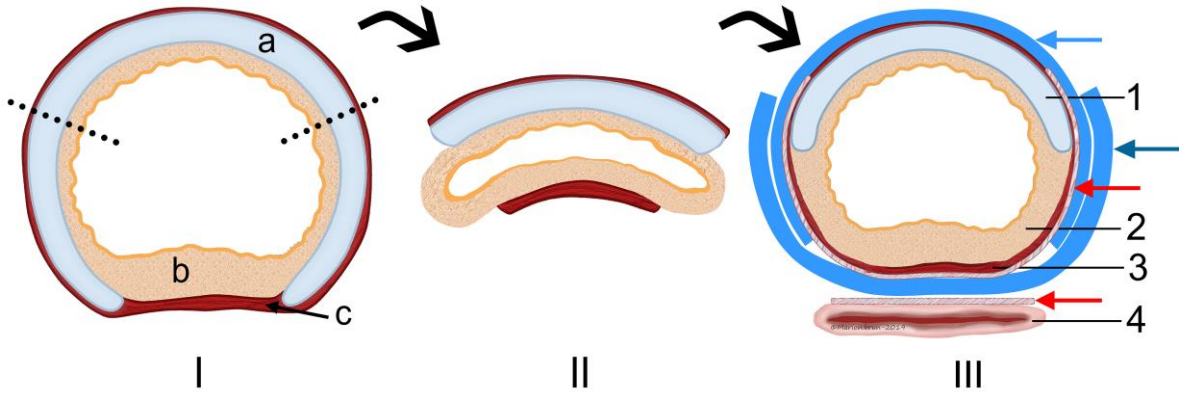






[Extraluminal biodegradable splint to treat upper airway **anterior** malacia: A preclinical proof of principle.]
Gorostidi F, Courbon C, Burki M, Reinhard A, Sandu K. Laryngoscope. 2018

DEVELOPMENT OF *TRUE TRACHEOMALACIA* ANIMAL MODEL
&
FNS SINERGIA



…….more physiological and what is seen in clinics

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Dominique PIOLETTI
Laboratoire de biomecanique en orthopedie

Nikolaos STERGIOPULOS
Laboratoire d'hemodynamique et de technologie cardiovasculaire

Kishore SANDU
Service d'oto-rhino-laryngologie


F Gorostidi


C Courbon

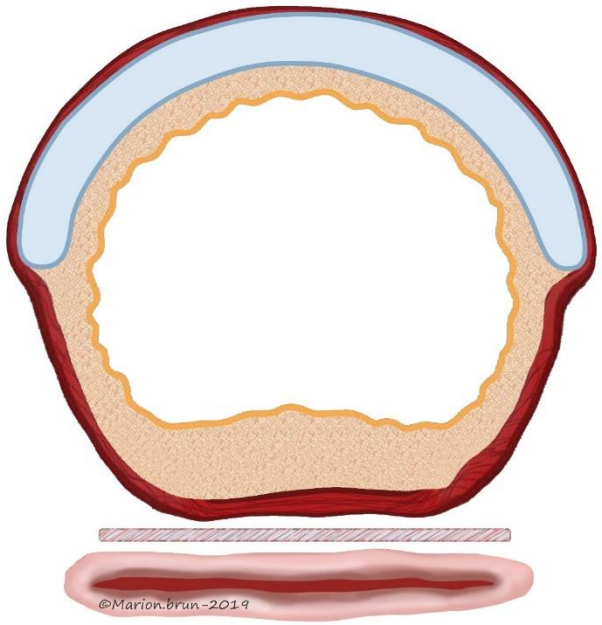

A Bergadano

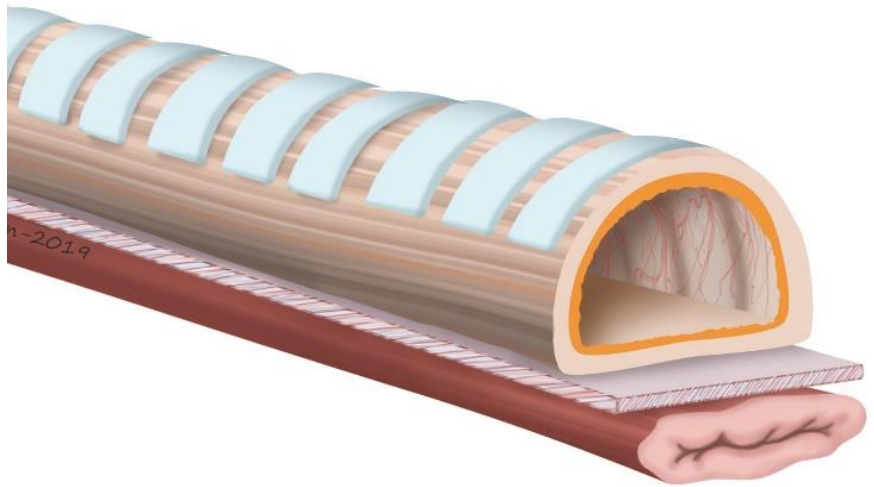

Ece Uslu

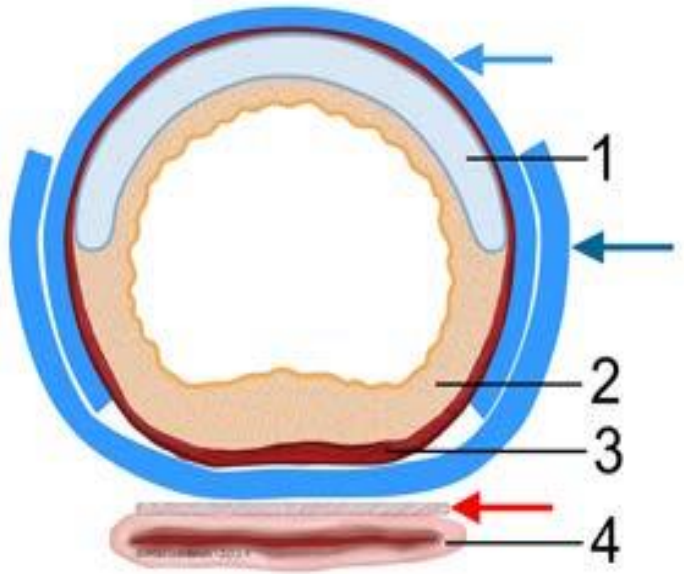
CREATION OF AN EX VIVO MODEL OF LONG POSTERIOR TO ANTERIOR TM

hydrogel-based extra-luminal splint

no pexy sutures







canton de vaud

Direction générale de l'agriculture, de la viticulture et des affaires vétérinaires

DGAV - Affaires vétérinaires
Protection des animaux

Chemin des Boveresses 155
Case postale 68
CH - 1066 Epalinges

Laure Seriot
Chemin des Boveresses 155
1066 Epalinges

Epalinges, le 12.01.2022

Expérience sur animaux - Autorisation / Décision du vétérinaire cantonal

Art. 18 al. 1, art. 24 à 26 et art. 28 Loi sur la protection des animaux du 16 décembre 2005 (LPA, RS 455) ;
Art. 139 à 147 et art. 212 Ordonnance sur la protection des animaux du 23 avril 2008 (OPAn, RS 455.1) ;
Art. 30 et 31 Ordonnance de l'OSAV concernant la détention des animaux d'expérience, la production d'animaux génétiquement modifiés et lesméthodes utilisées dans l'expérimentation animale du 12 avril 2010 (Ordonnance sur l'expérimentation animale, RS 455.163)

Numéro Cantonal	**VD3683b**
Numéro National	**33552**
Directeur- trice de l'expérimentation animale	Laure Seriot
Institut	CHUV_N Chemin des Boveresses 155 1066 Epalinges
Directeur- trice de l'expérience	Kishore Sandu
Titre de l'expérience	Development of a rabbit long tracheomalacia model and its treatment using an extra-luminal Hydrogel stent
Type de demande	Supplementary application
Autorisation Précédente	33552 / VD3683a

Wet adhesive hydrogels to correct malacic trachea (tracheomalacia) *A proof of concept*.

Uslu E, Rana VK, Anagnostopoulos S, Karami P, Bergadano A, Courbon C, Gorostidi F, Sandu K, Stergiopulos N, Pioletti DP. iScience. 2023

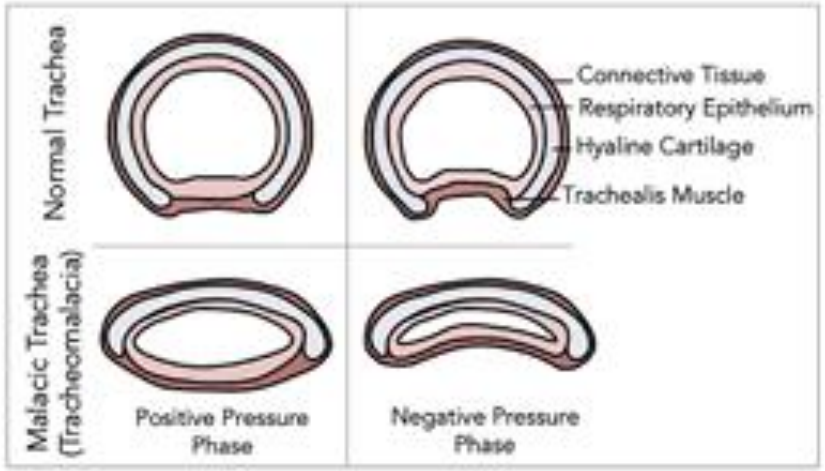


Figure 1. Representation of a normal and a malacic trachea during the positive and negative pressure phases of the respiratory cycle

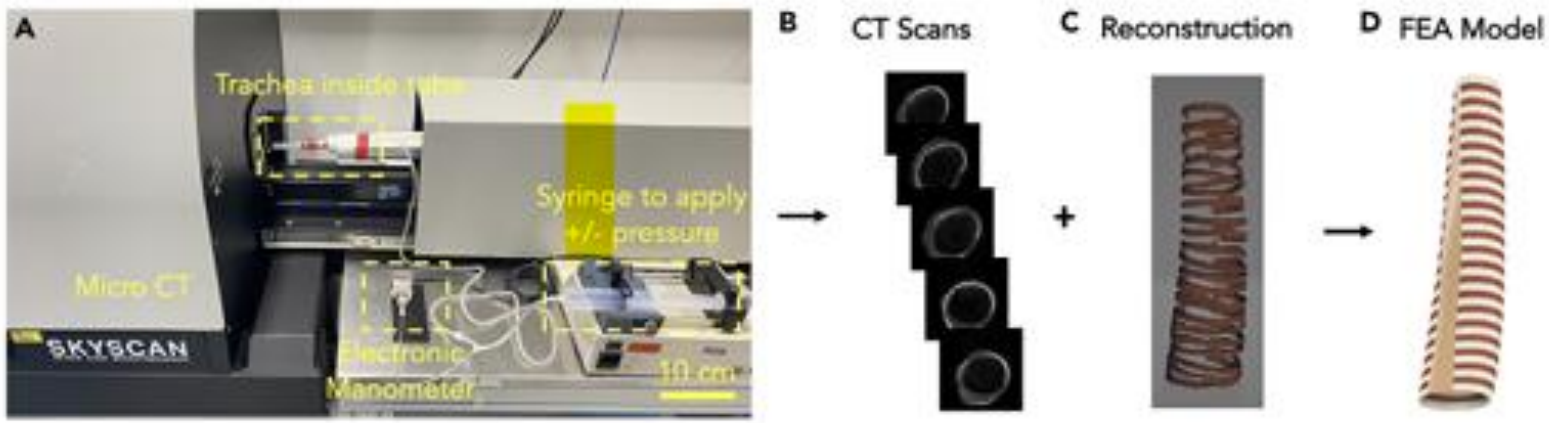


Figure 2. Experimental set-up and steps to obtain a simple trachea geometry for numerical model

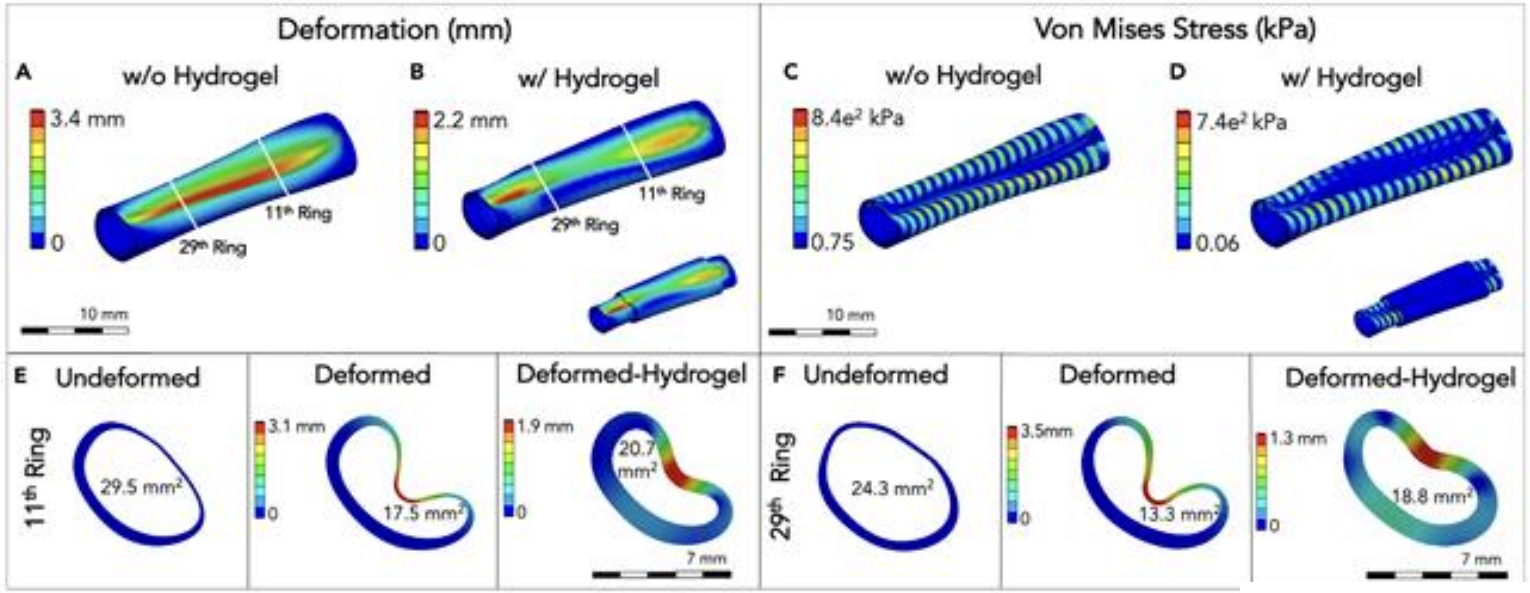


Figure 3. Indicative results of the total deformation and the stress distribution of a trachea at −15 mmHg

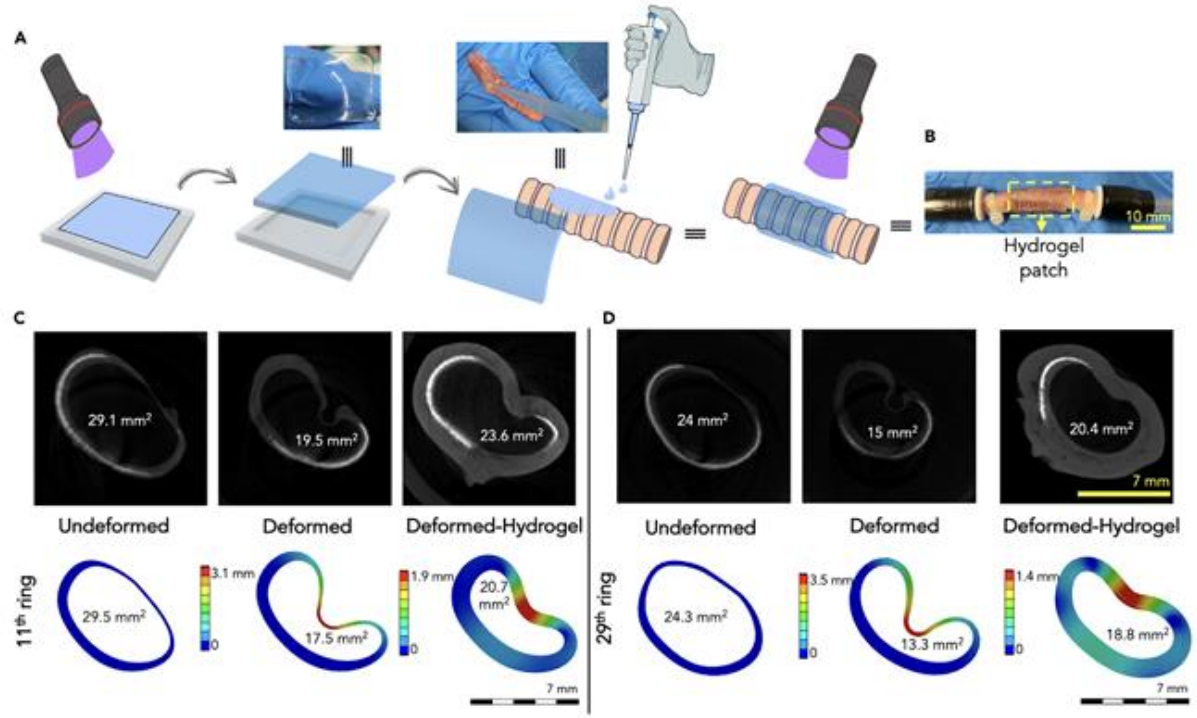


Figure 5. The potential of the adhesive hydrogel to prevent collapse in mild malacic conditions

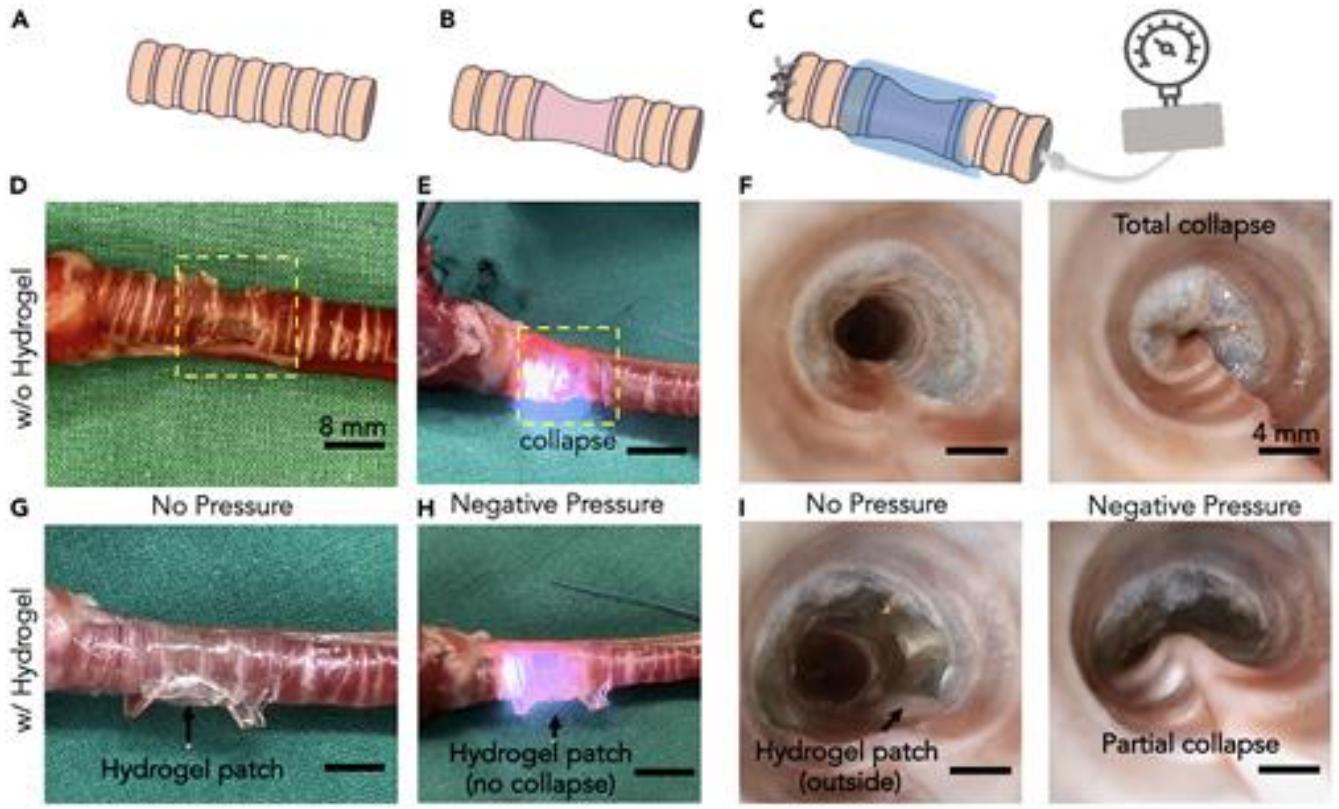
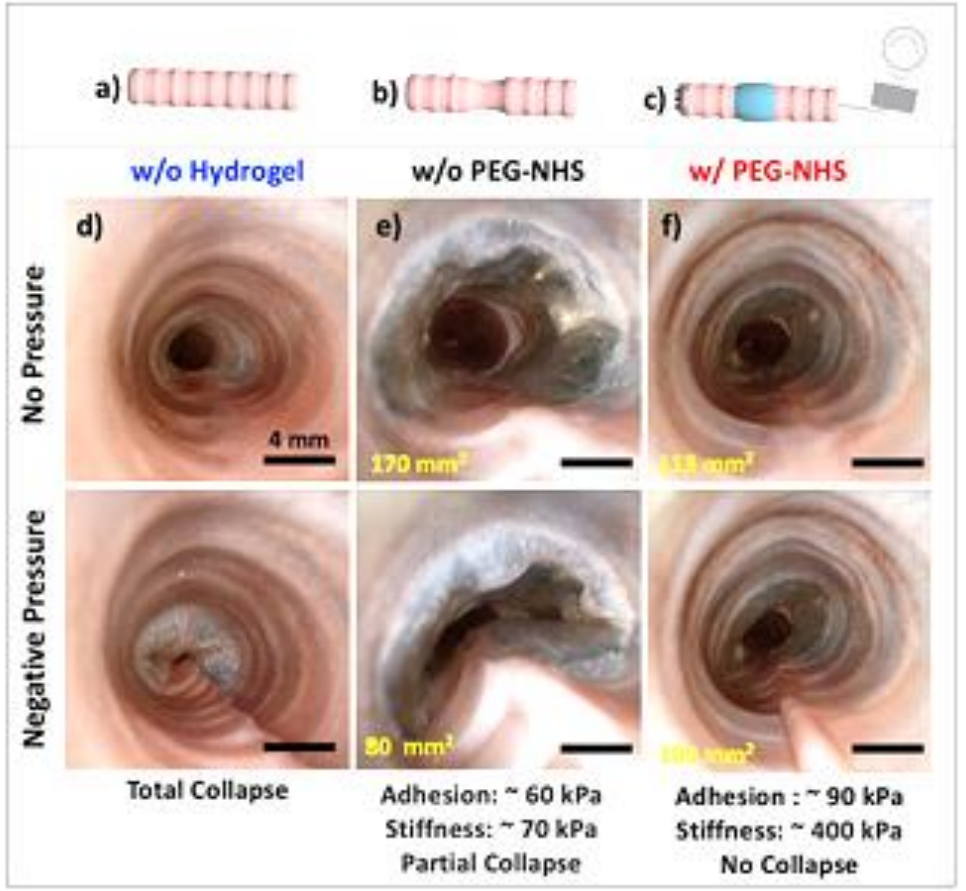


Figure 6. Procedure and results of ex vivo experiments



Tissue glue with growth factors

Enhancing Robustness of Adhesive Hydrogels through PEG-NHS Incorporation Ece Uslu,Vijay Kumar Rana, Yan heng Guo, Theofanis Stampoultzis, Francois Gorostidi, Kishore Sandu, and Dominique P. Pioletti . Interfaces2023

LIFE CHANGING PROJECTS TO MY HEART….

1. FLOPPY AIRWAY (TRACHEOMALACIA)

   COLLAPSING AIRWAY

2. TRACHEAL TRANSPLANTATION

   WIND-PIPE CONDUITS

3. ARTIFICIAL INTELLEGENCE

   WINDOW TO THE FUTURE MEDECINE

TRACHEAL REPLACEMENT

- ≠ tracheal transplantation
- special issues in children
  - > tracheal growth
  - > small diameter airway
  - > ethics :
    - currently no satisfactory tracheal substitute in adults

! STILL LONG WAY TO GO !

PREREQUISITES FOR SUCCESSFULL OUTCOME

1. Non-immunogenic, biomechanical stable tracheal scaffold

2. Outer and inner revascularization of scaffold

3. Full inner mucosal lining

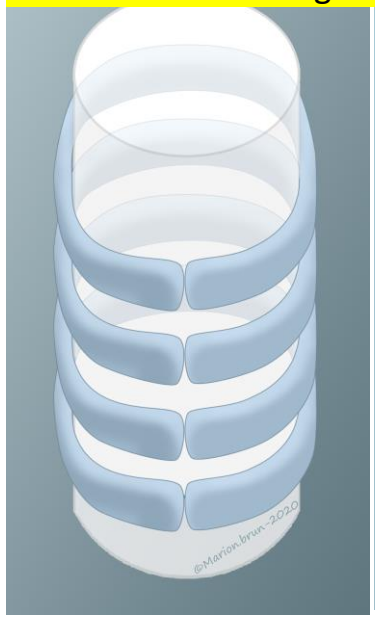
TRACHEAL REPLACEMENT

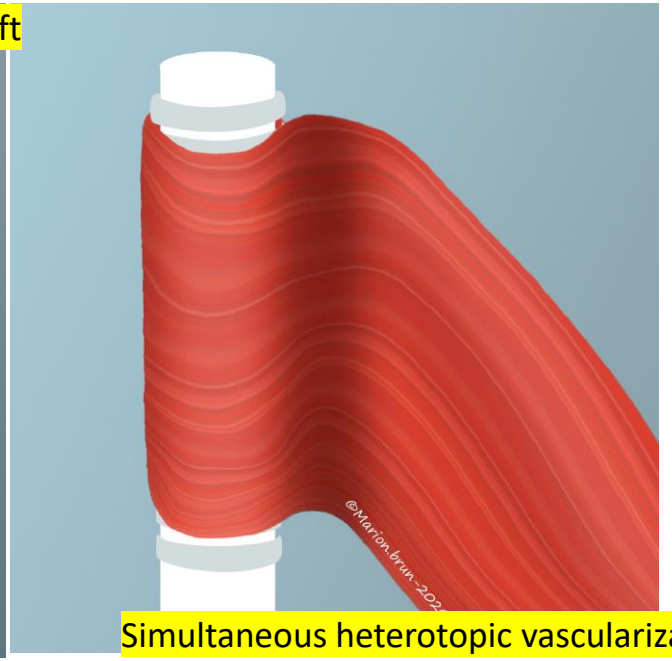
1. Tracheal scaffold
   - tracheal homograft
   - bioengineered scaffold
2. Immunogenicity suppression
   - detergent-enzymatic decellularization
3. Mucosal grafting
   - tracheonoid development
4. Revascularization
   - rabbit trachea homograft in receiver rabbit

TWIN TRACHEA PROJECT

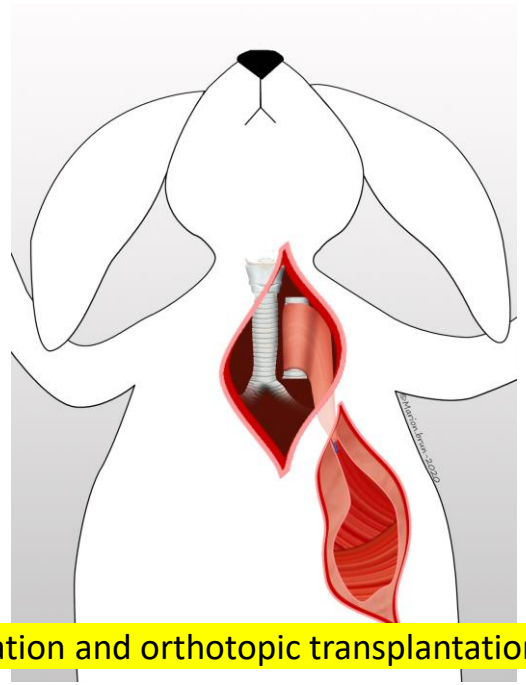
Development of a rabbit model fitted with juxtaposed *twin homo*-tracheal conduit

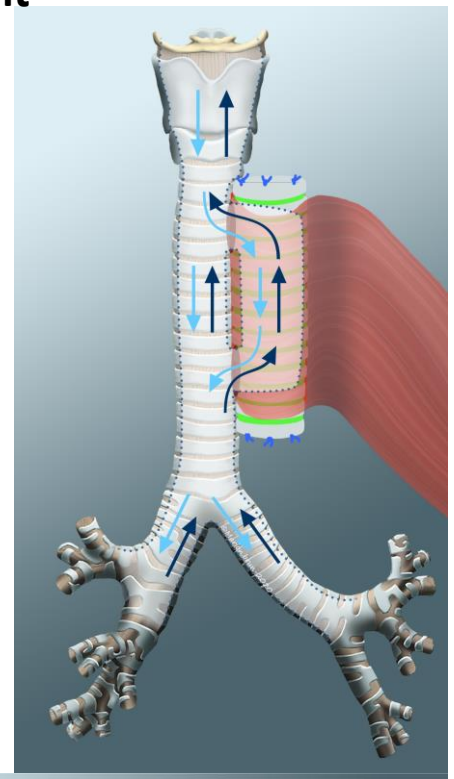
decellularised homograft

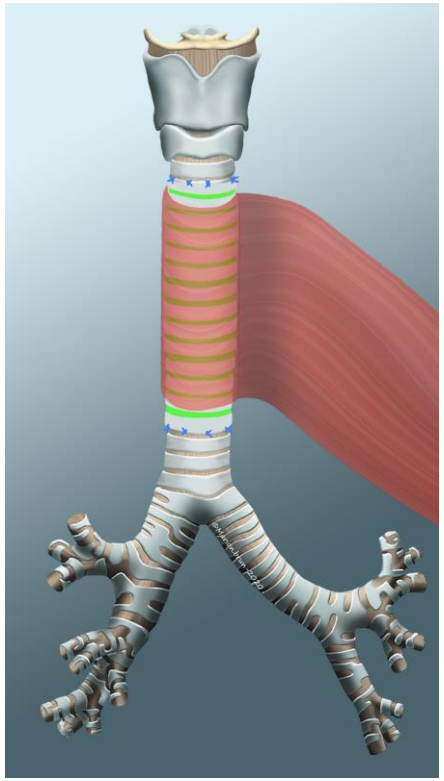




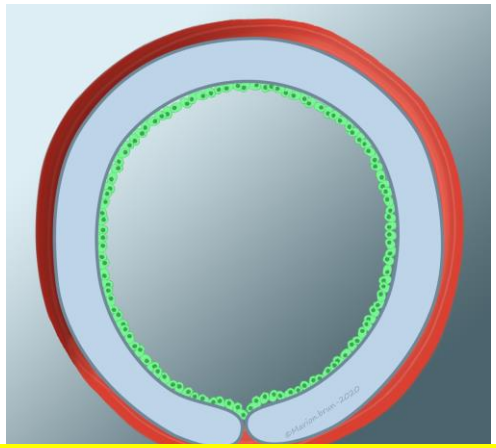
Simultaneous heterotopic vascularization and orthotopic transplantation





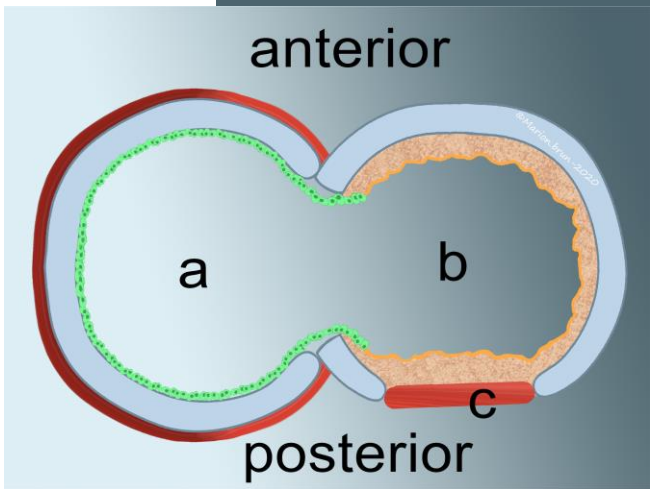


final tracheal conduit transplantation



- Matthias Lutolf, Laboratory of Stem Cell Bioengineering, EPFL
- Bio Engineering & Technology platform AGORA
  Cancer Research Center, Lausanne

rabbit large scale, genetically labeled, airway epithelial organoïds



LIFE CHANGING PROJECTS TO MY HEART….

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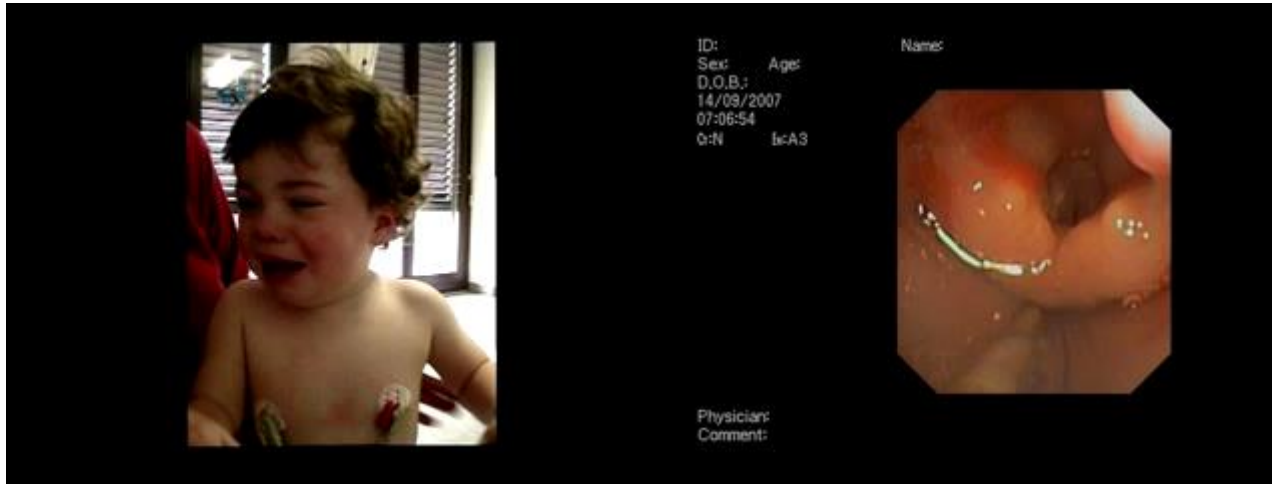
   WINDOW TO THE FUTURE MEDECINE

Artificial Intelligence & Audio-Visual analysis of abnormal respiratory sounds (stridor)



Audio-visual analysis of abnormal respiratory sounds (stridor) using Artificial Intelligence

www.nature.com/scientificreports

scientific reports

Check for updates

OPEN

Breathing sounds analysis system for early detection of airway problems in patients with a tracheostomy tube

Hyunbum Kim[1,3], Daeyeon Koh[2,3], Yohan Jung[2], Hyunjun Han[2], Jongbaeg Kim[2]✉ & Younghoon Joo[1]✉

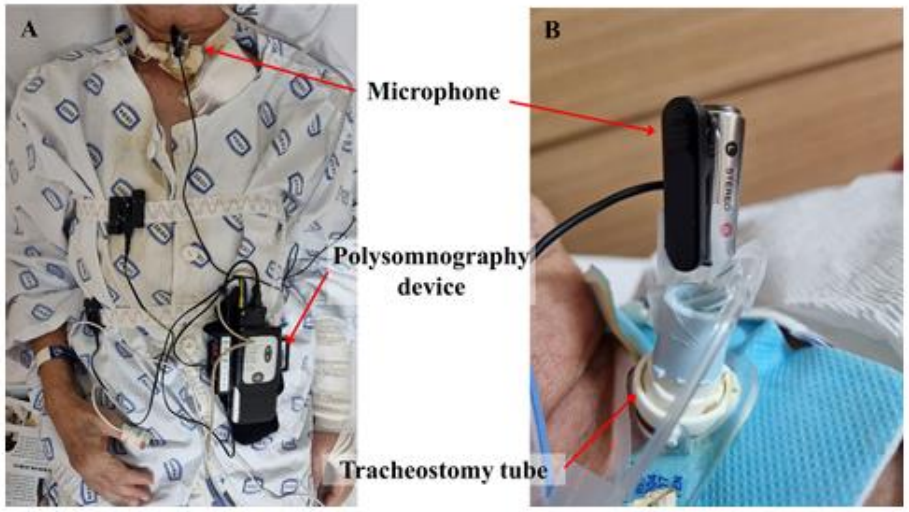


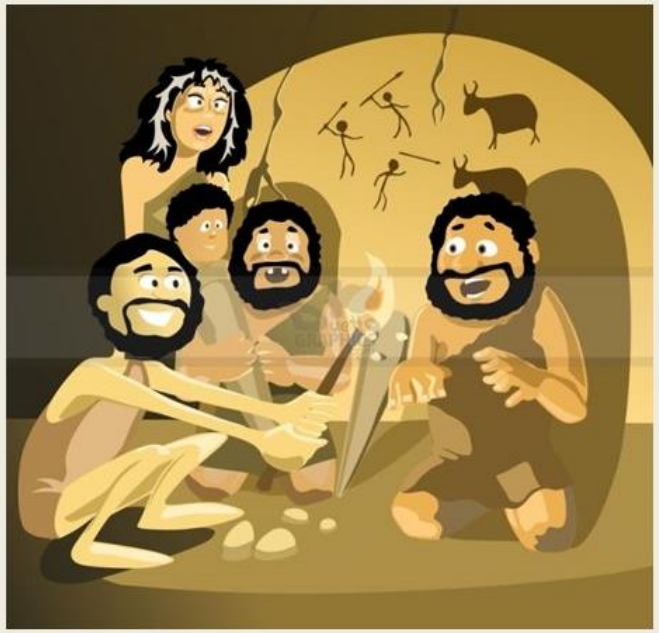
Figure 1. A photograph of the devices installed on the patient with a tracheostomy. A condenser microphone with a voice recorder and parts of a polysomnogram were set on the patient. A nasal prong connected with a polysomnogram was located at the entrance of the tracheostomy tube. A condenser microphone was located at a distance of 2–3 cm from the outer opening of the tracheostomy tube. Pulse oximetry, thoracic and abdominal bands were also set on the patient.

Clinical translation

- Early & precise detection of a critical airway / % of obstruction
- Telemedicine

There is a strange saying that says "Necessity is the mother of invention" and what it means is if you can't get something you need you will probably invent it.

Early Man is a great example of this saying because he had nothing!



…..future lies in *medical-engineer* collaborations