

The Next Disruptive Technologies:

New Ways to Treat Old Diseases



M a r t i n E l l i o t t

37th Gresham Professor of Physic

Professor of Cardiothoracic Surgery at UCL

Consultant Paediatric Cardiothoracic Surgeon

&

co-Medical Director

The Great Ormond Street Hospital for Children

*Those who have knowledge, don't predict.
Those who predict, don't have knowledge.*



Lao Tzu, *6th Century BC Chinese Poet*



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my specialty
not cancer or genetics

Susie Thoms
Edward Green
Jeff Jacobs



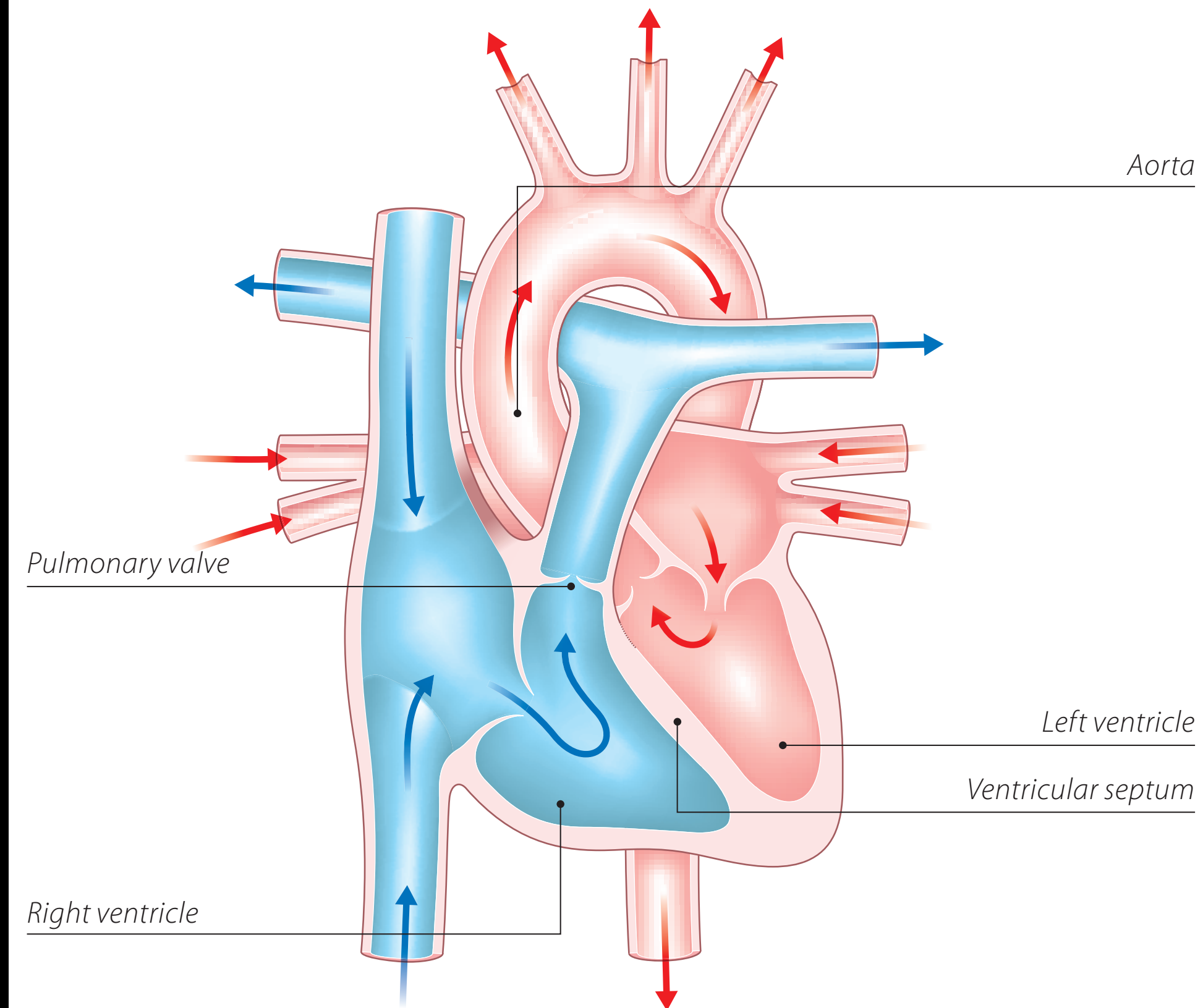
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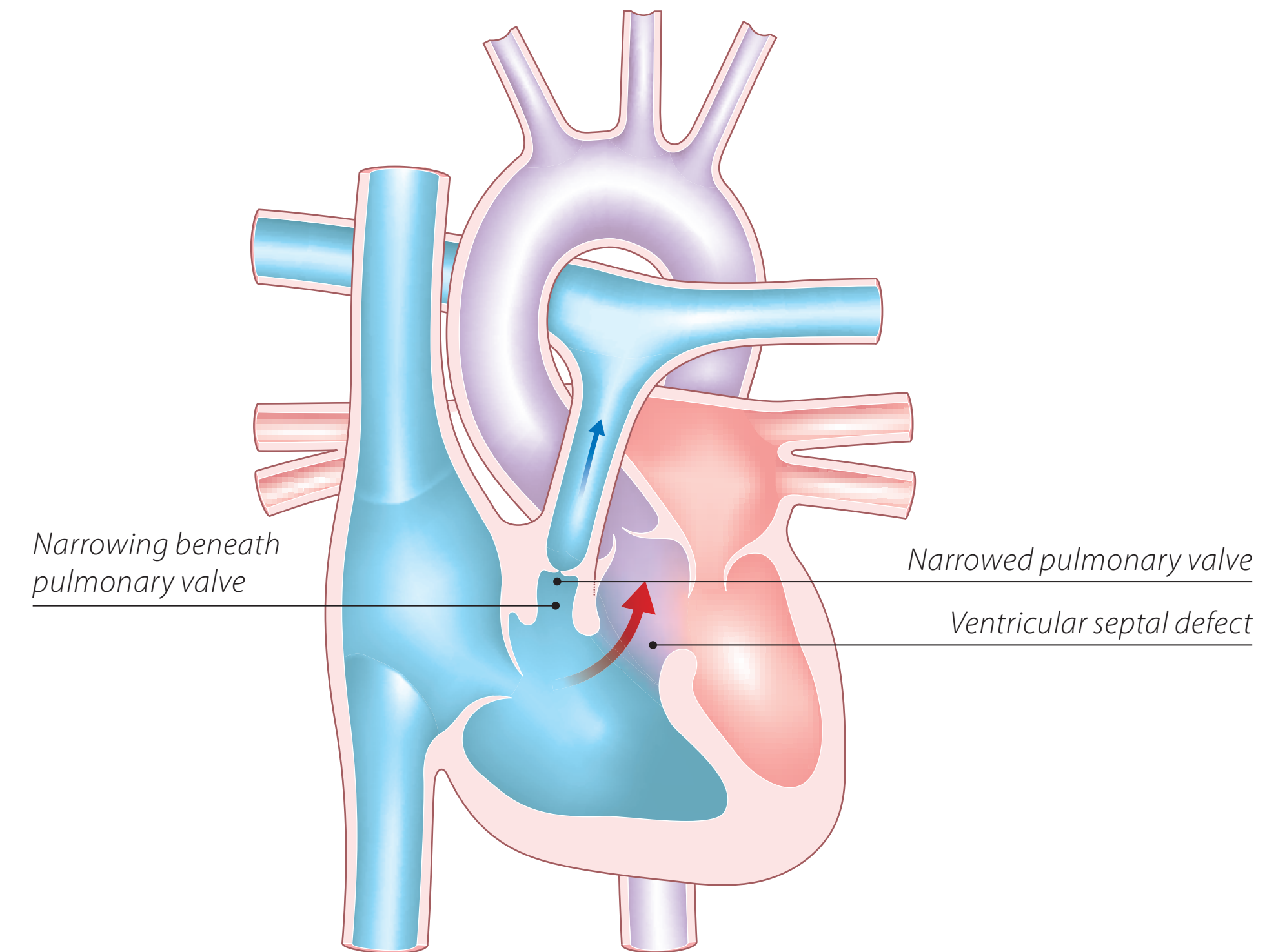
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What is Tetralogy of Fallot?

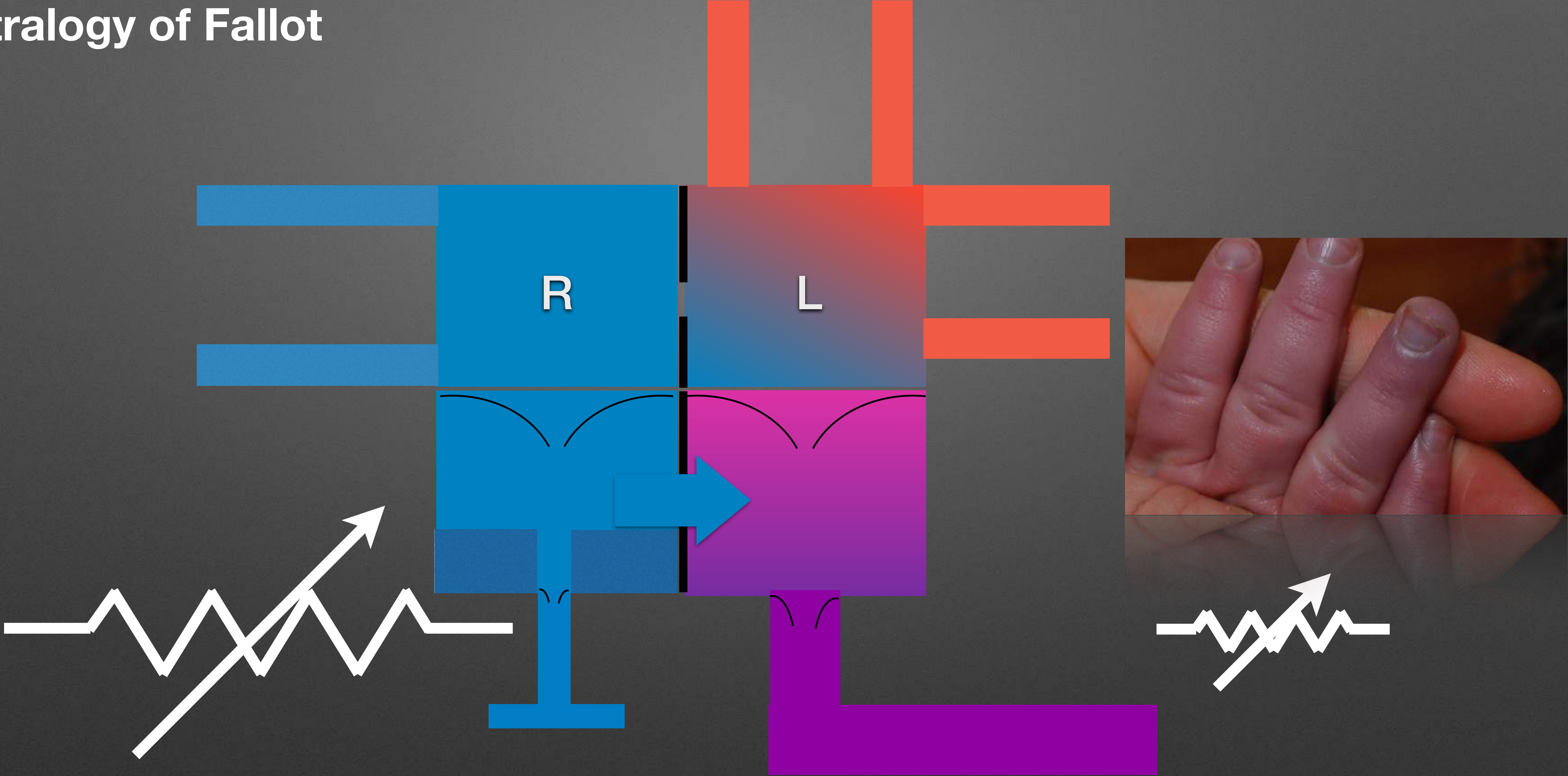
The normal heart



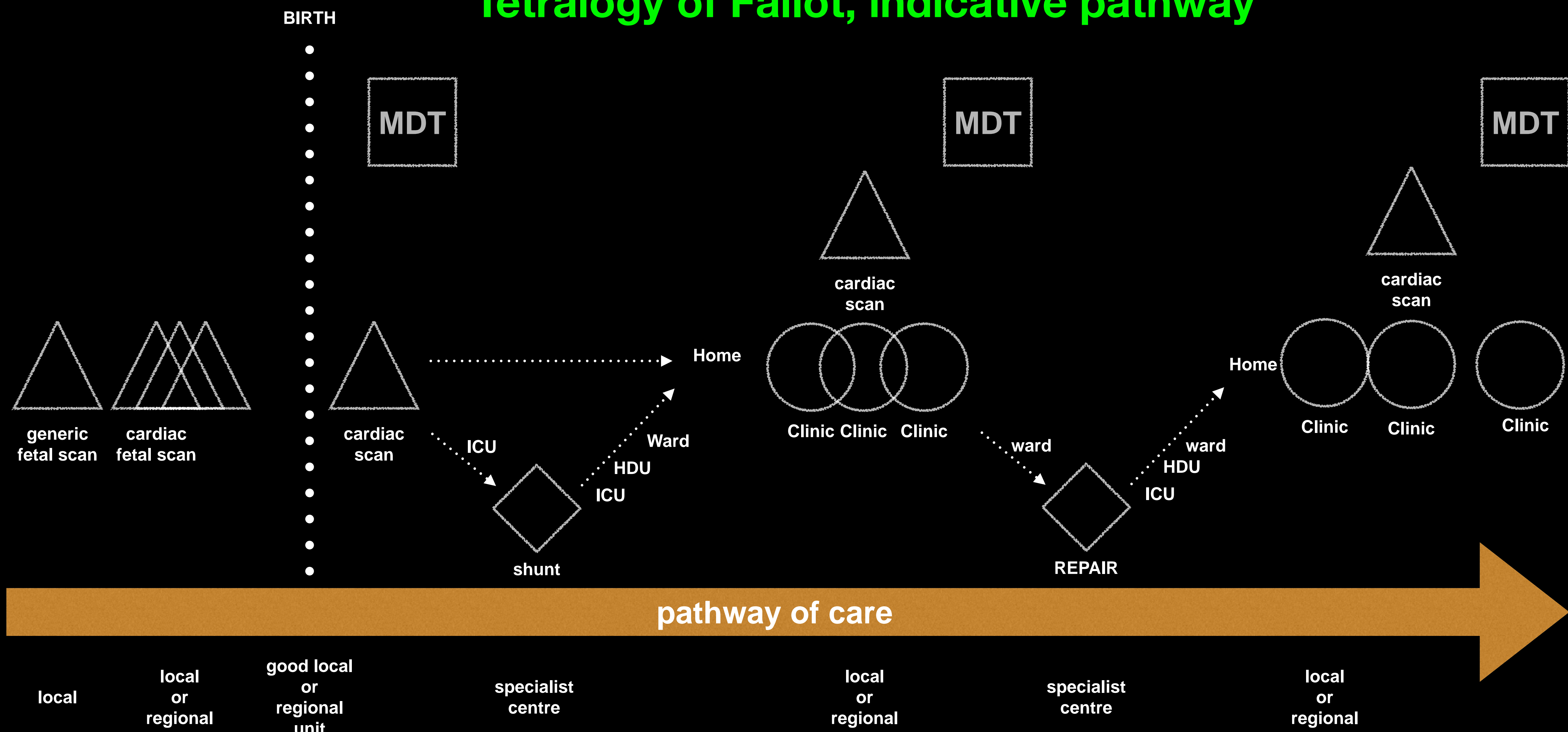
Tetralogy of Fallot



Tetralogy of Fallot



Tetralogy of Fallot, indicative pathway



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The Purpose of Prenatal Diagnosis

- to give the parents **a chance to prepare;** psychologically, socially, medically, financially
- to facilitate **timely treatment,** medical or surgical
- to **give them choice** re termination



termination of pregnancy

185,331

total

99%

abortion statistics,
DH June 2014

1%

307

cardiac

11%



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improving fetal ultrasound



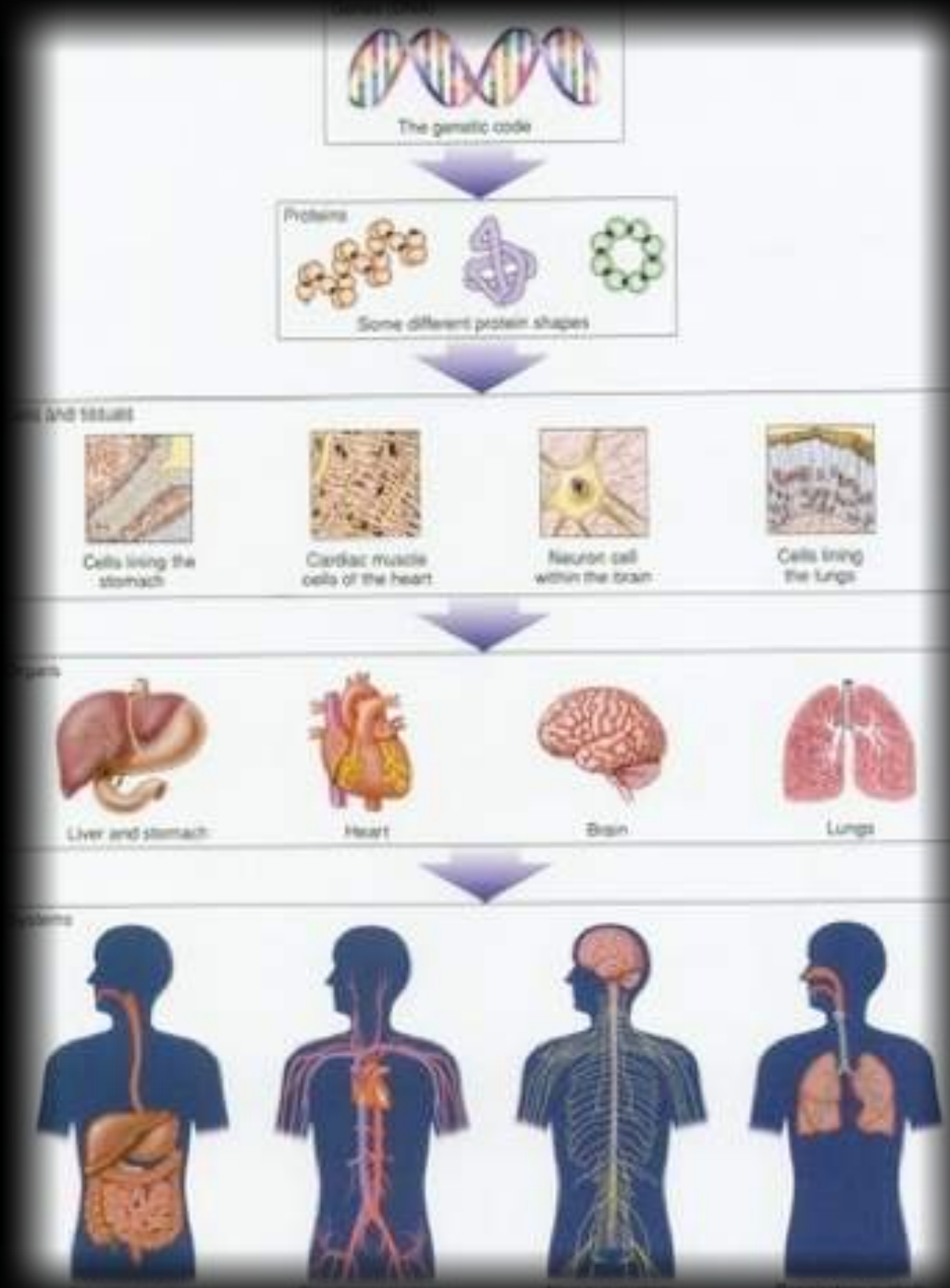
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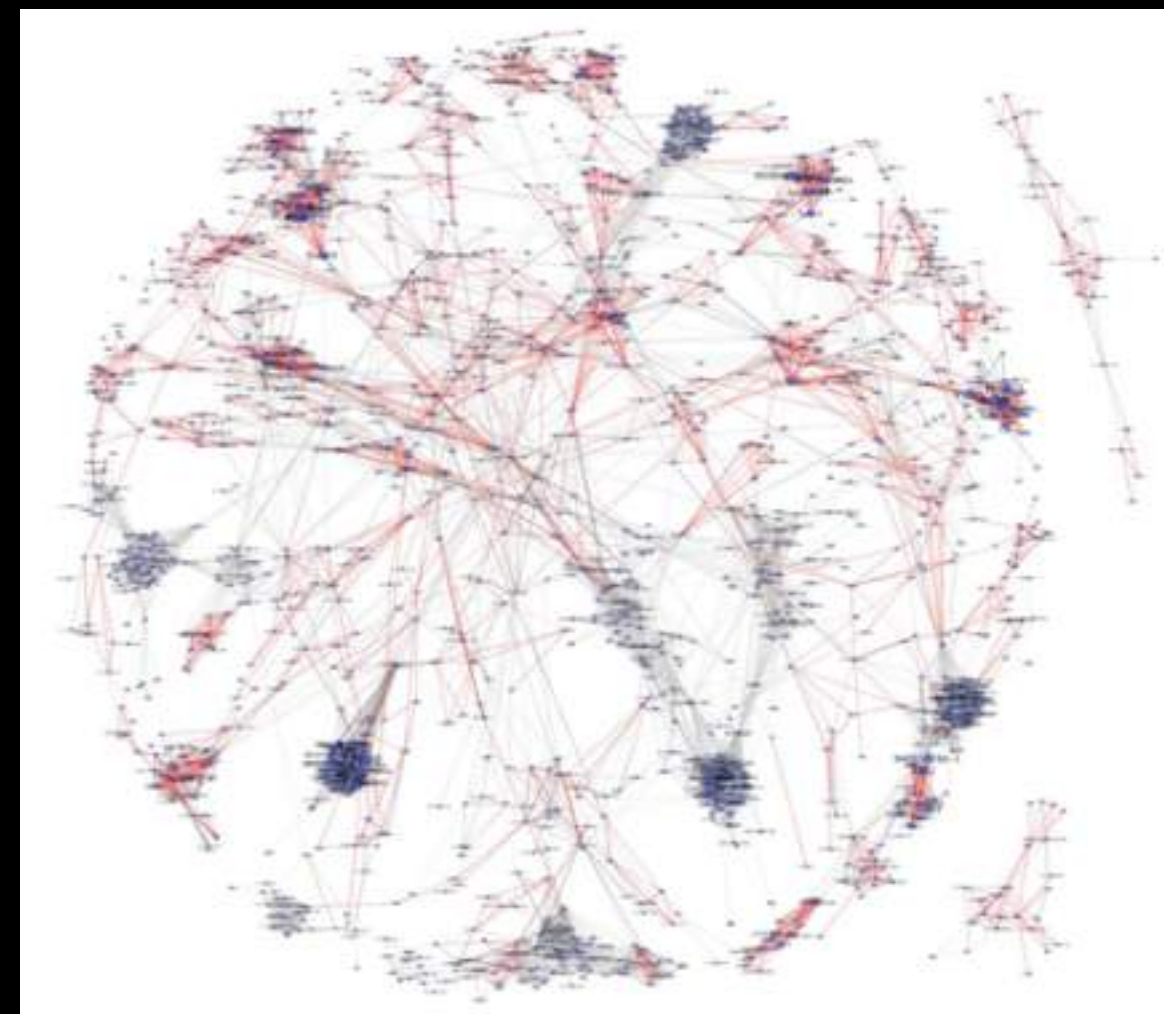
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Diagnosis by genetics?

genotype



phenotype



what to do with
so much
information?

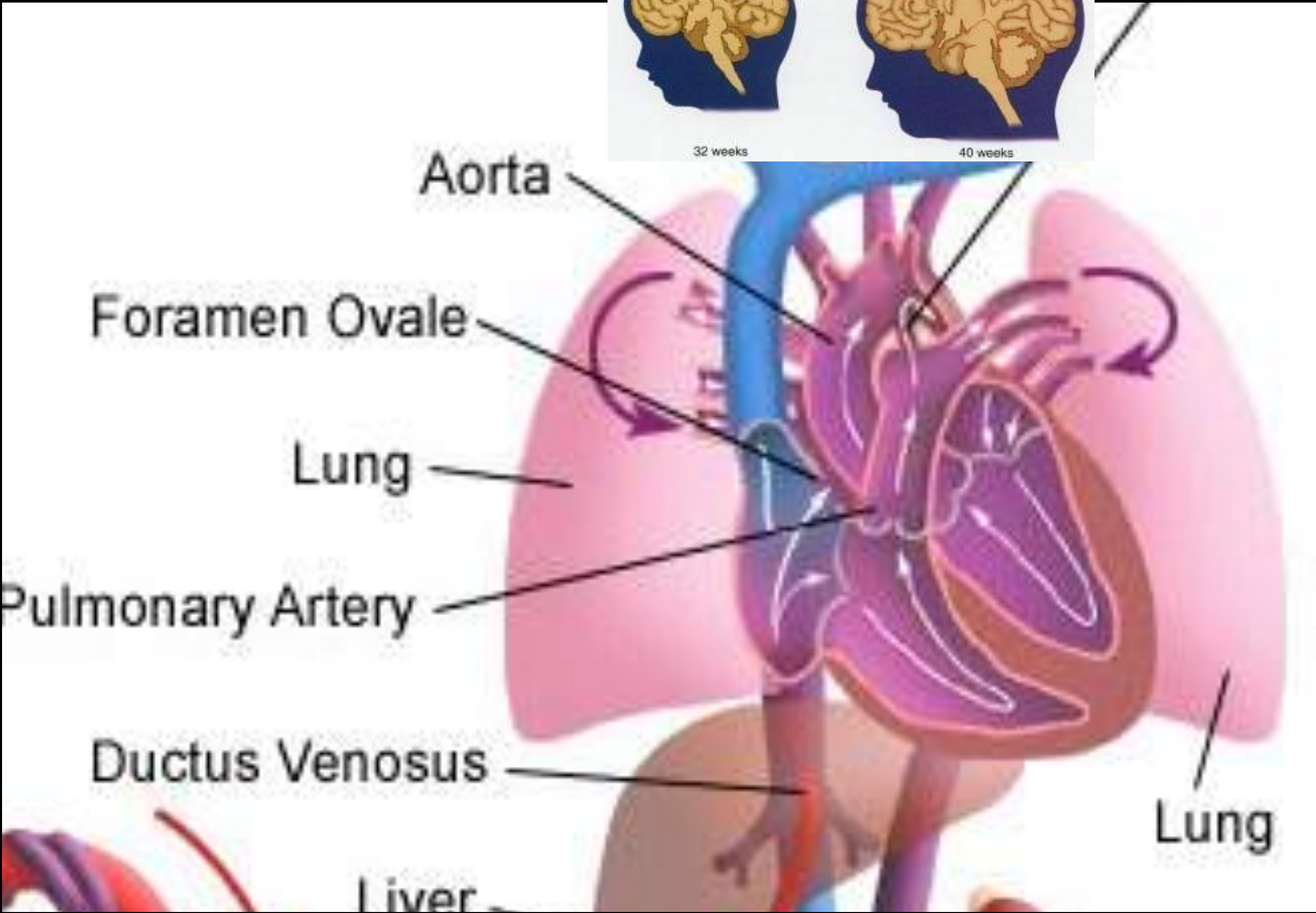
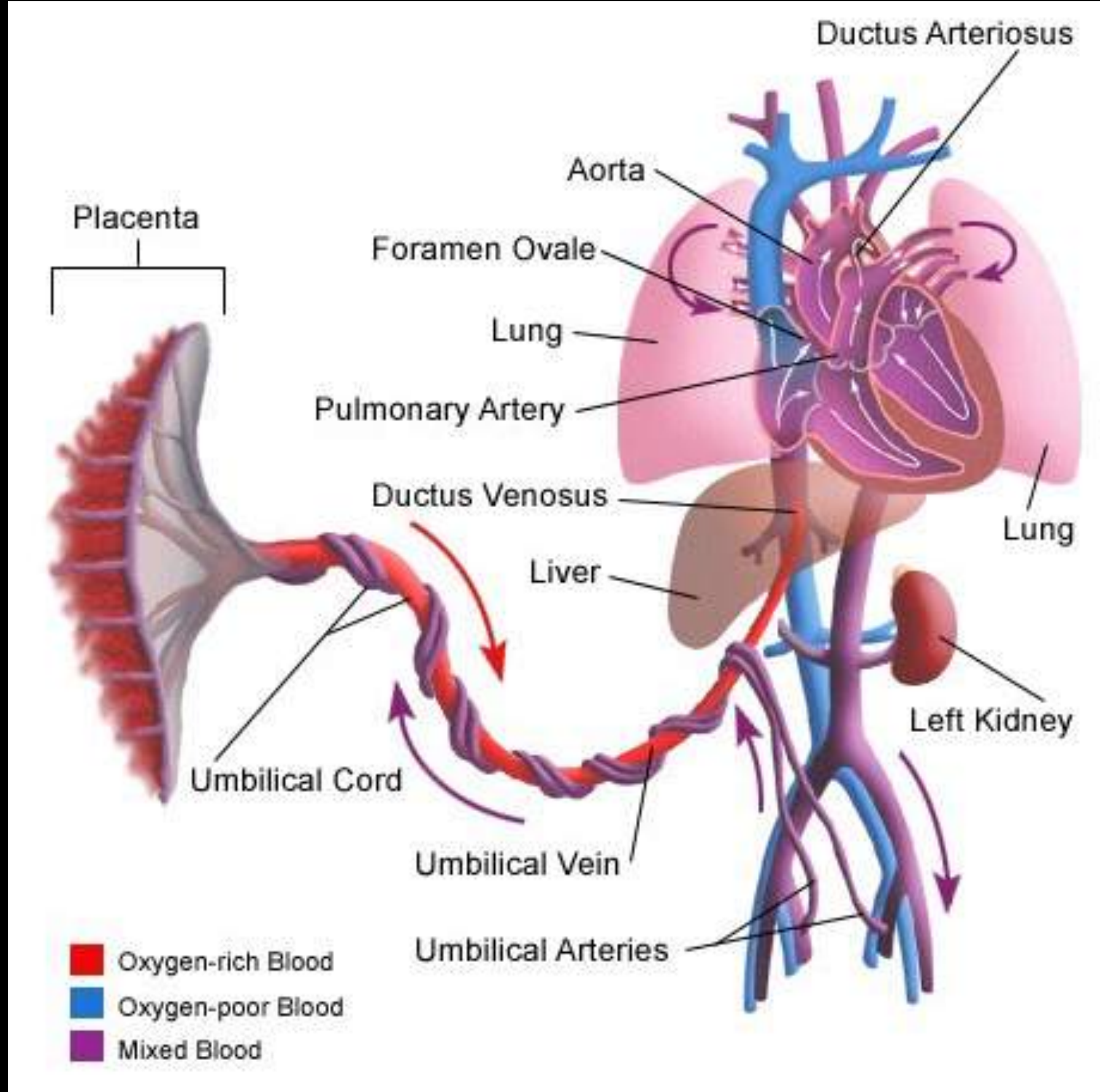
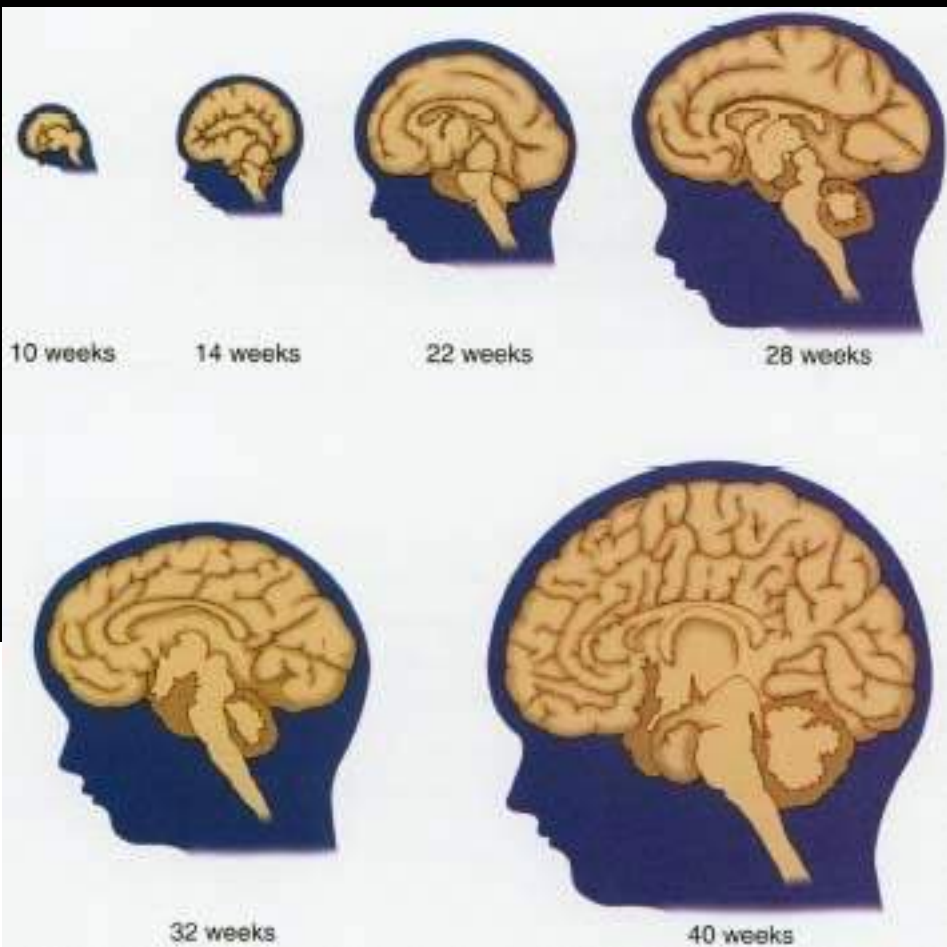


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Fetal Circulation



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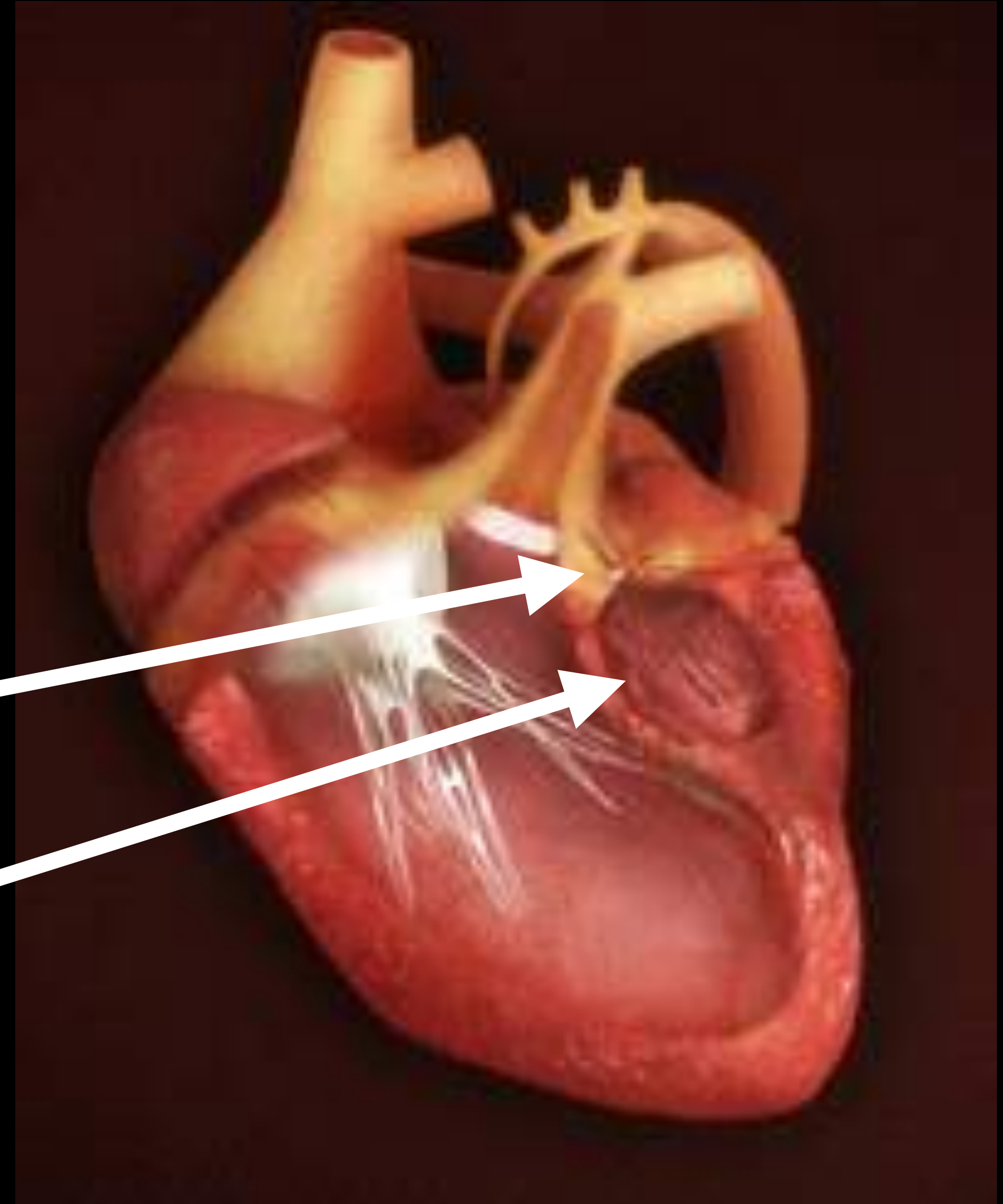


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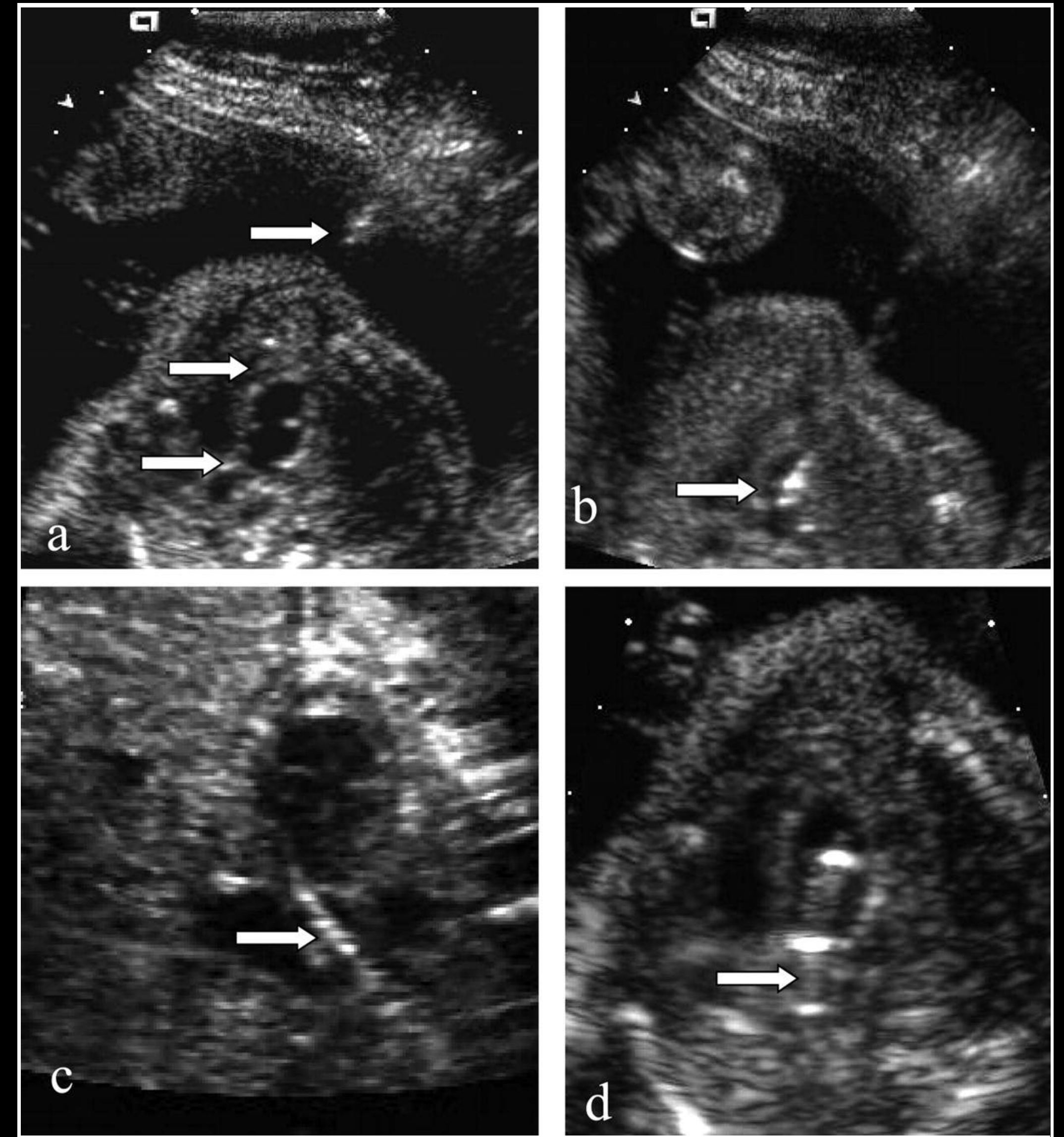
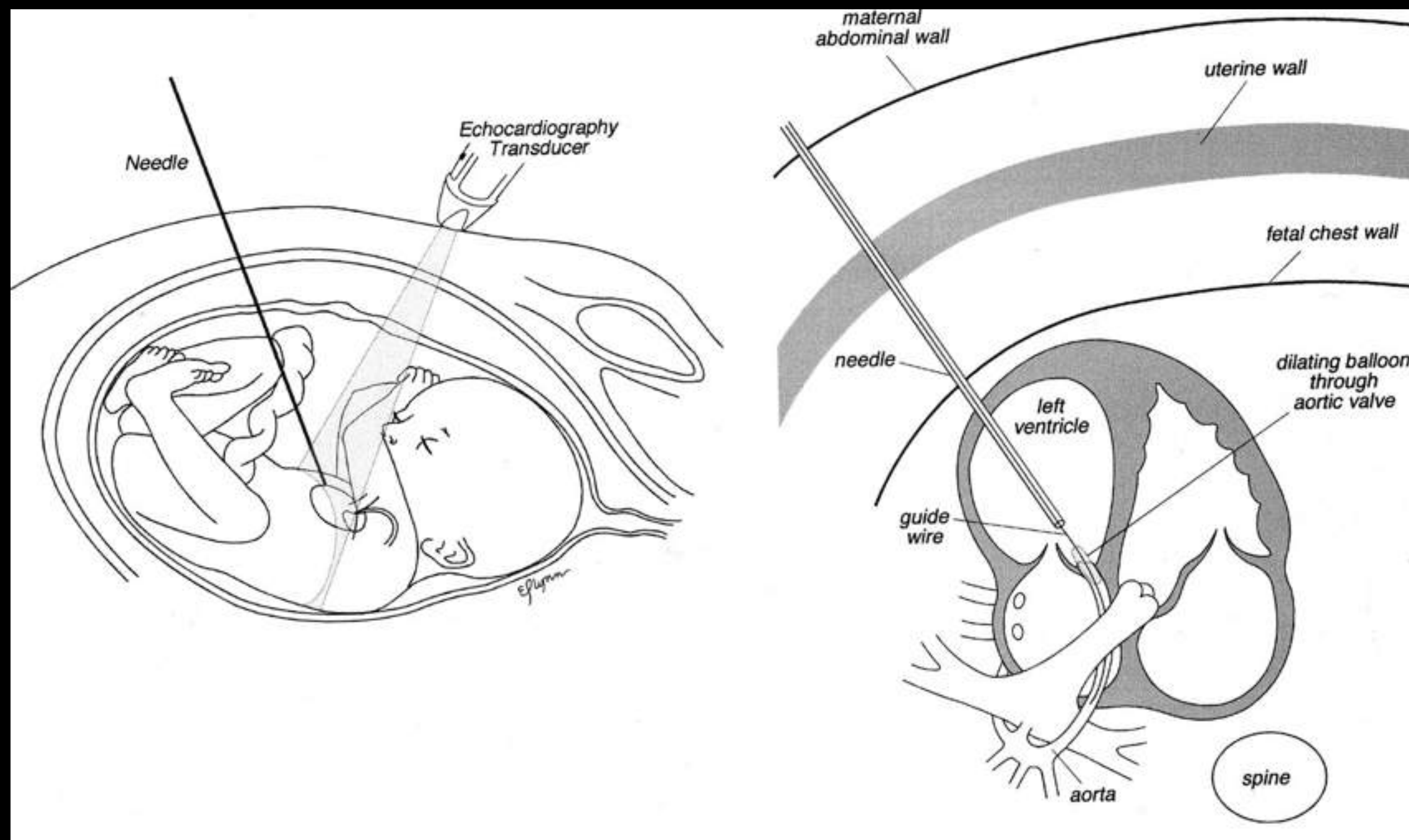
Hypoplastic Left Heart Syndrome

tiny aortic valve

tiny left ventricle



Fetal Aortic Valvotomy



Freud LR, McElhinney DB, Marshall AC, et al. Fetal Aortic Valvoplasty for Evolving Hypoplastic Left Heart Syndrome. Post natal outcomes in the first 100 patients. Circulation 2014;**130**:638-45

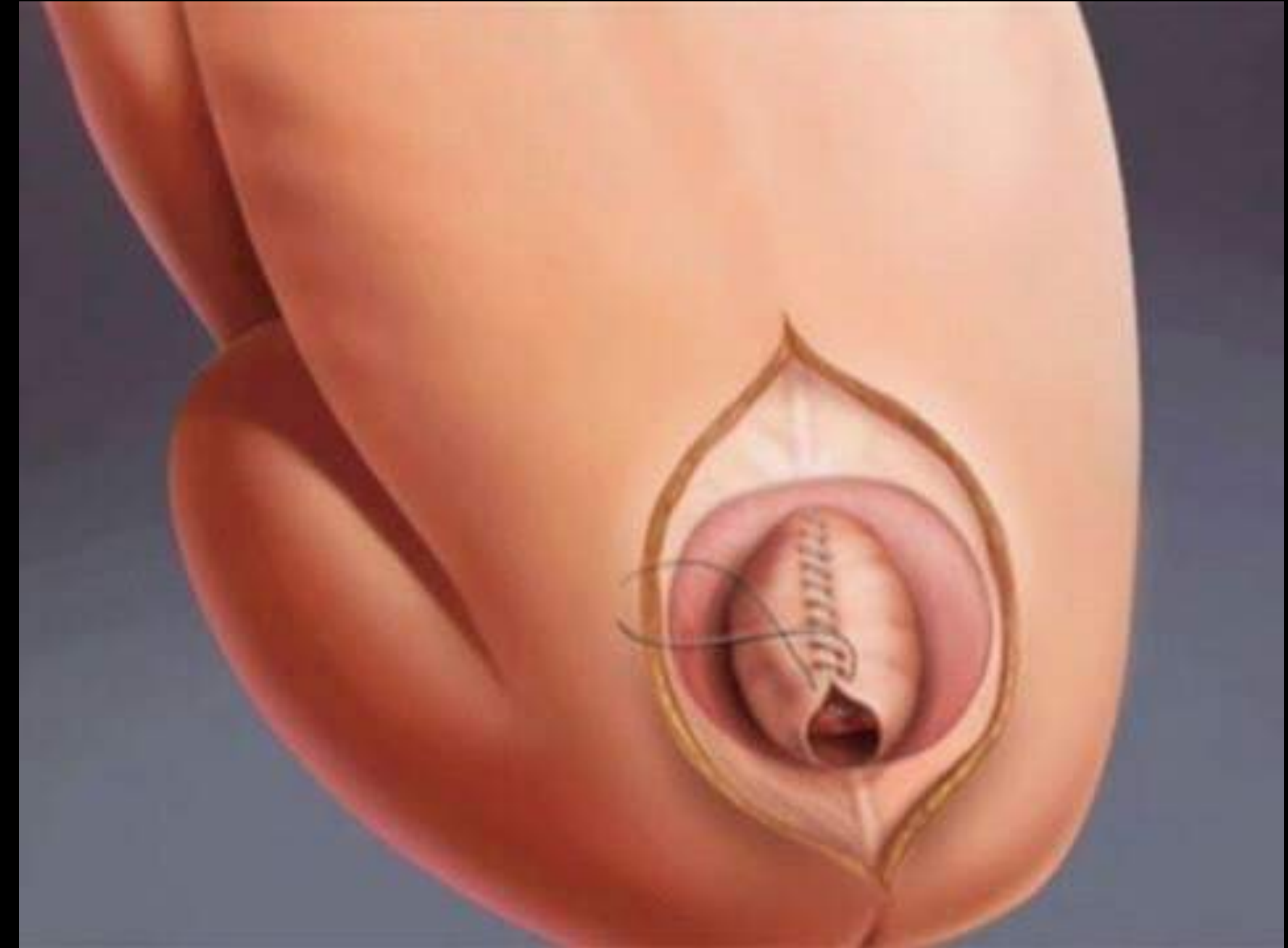
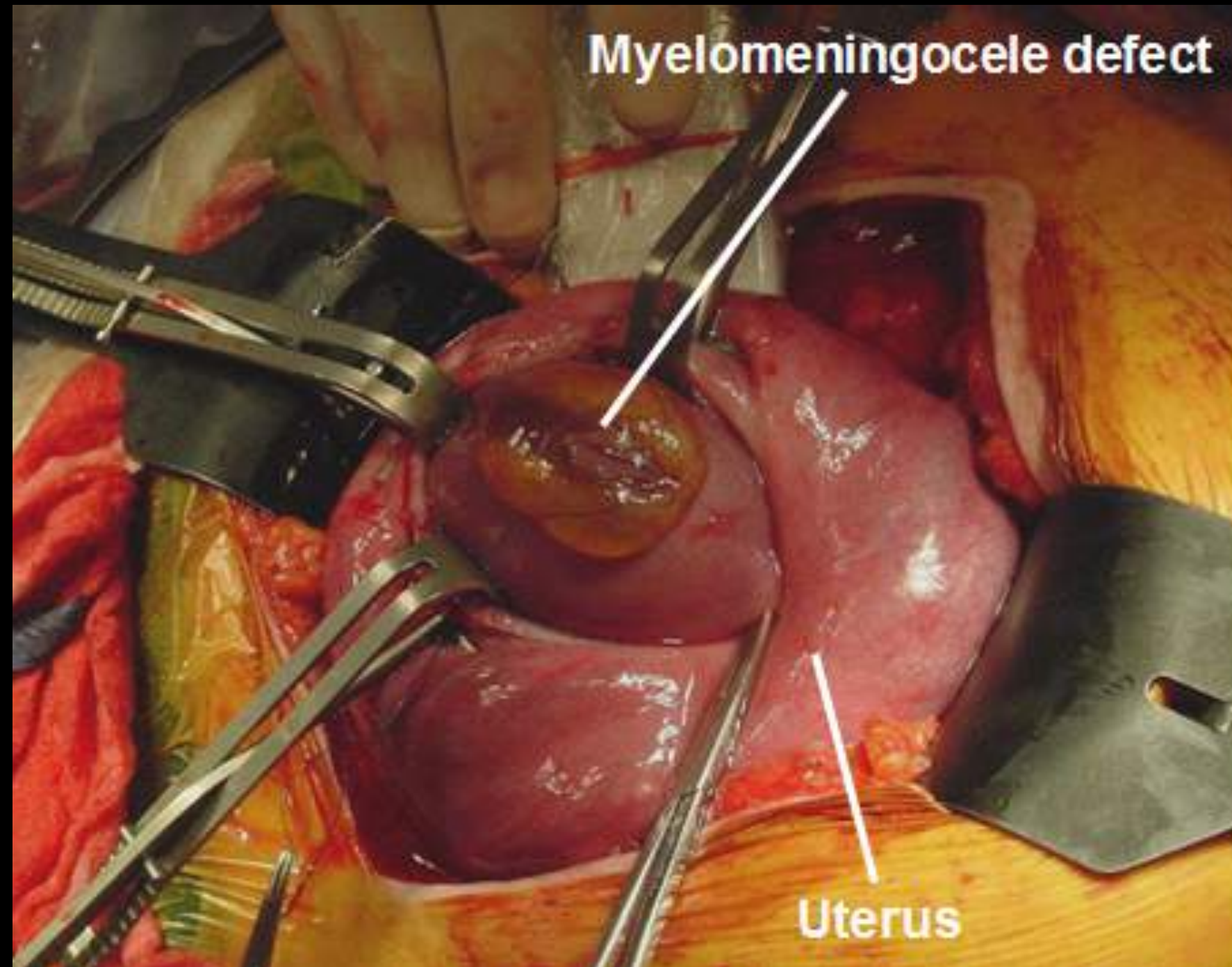


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Spina Bifida



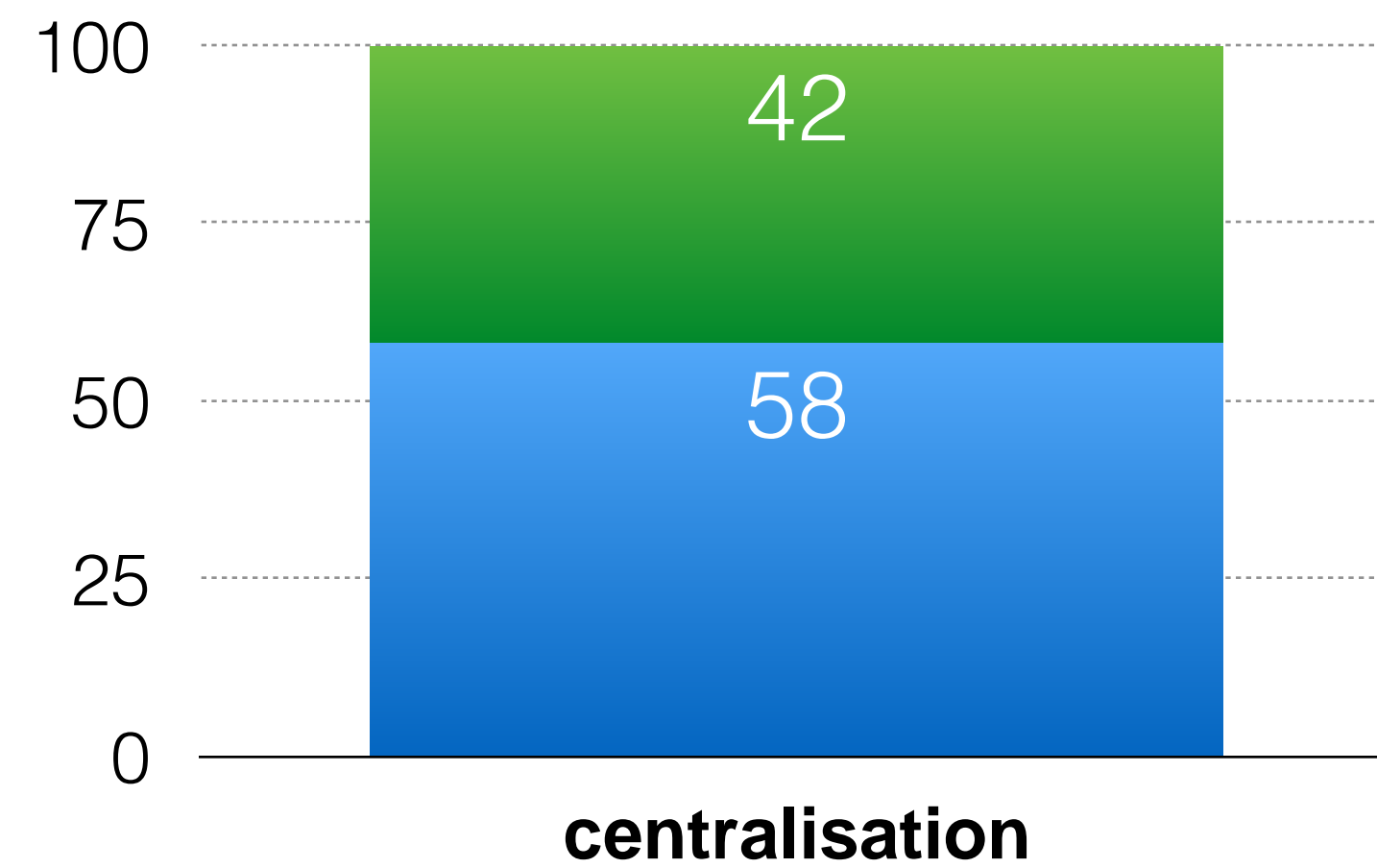
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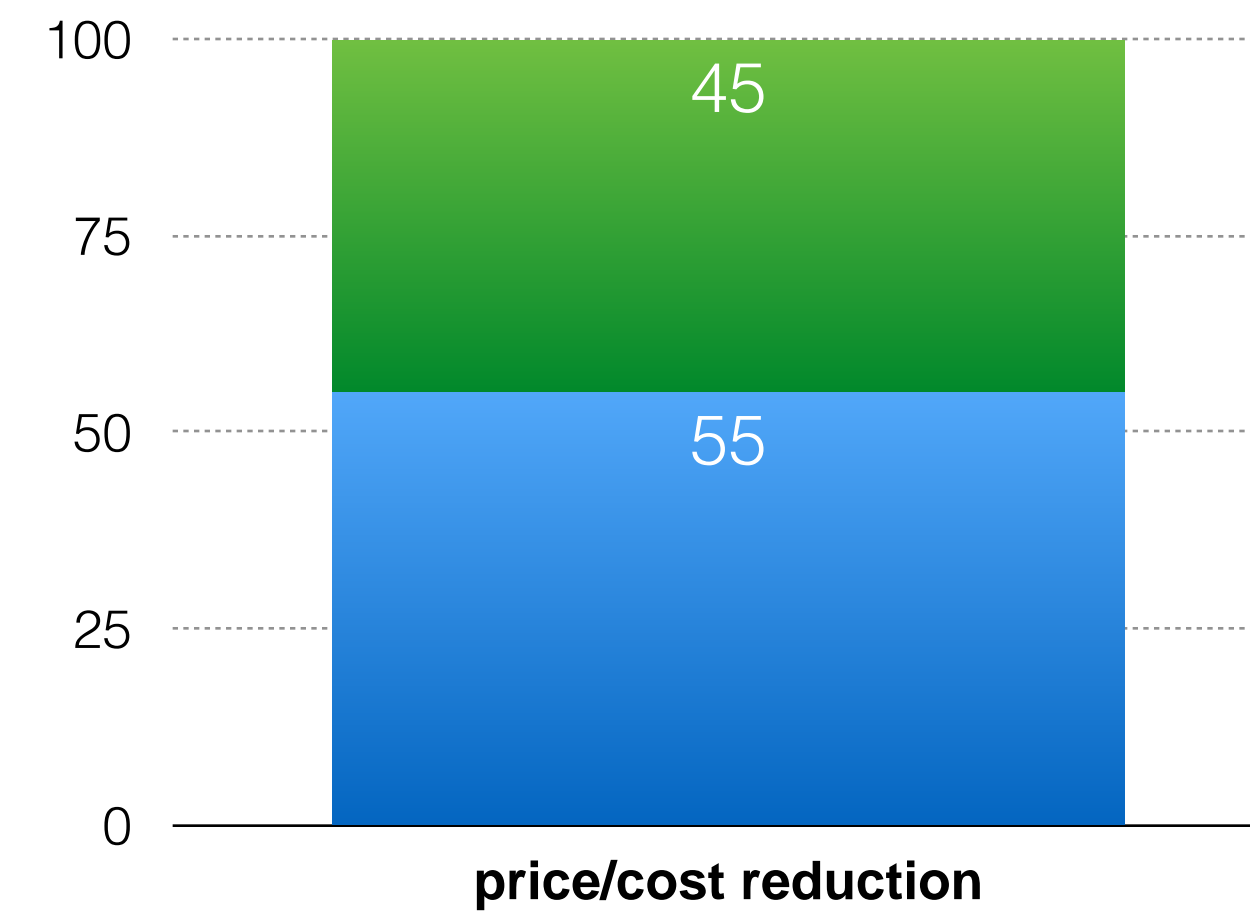
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What is coming next in the field of Resourcing and Organisation?

■ Yes ■ no mention



■ yes ■ no mention



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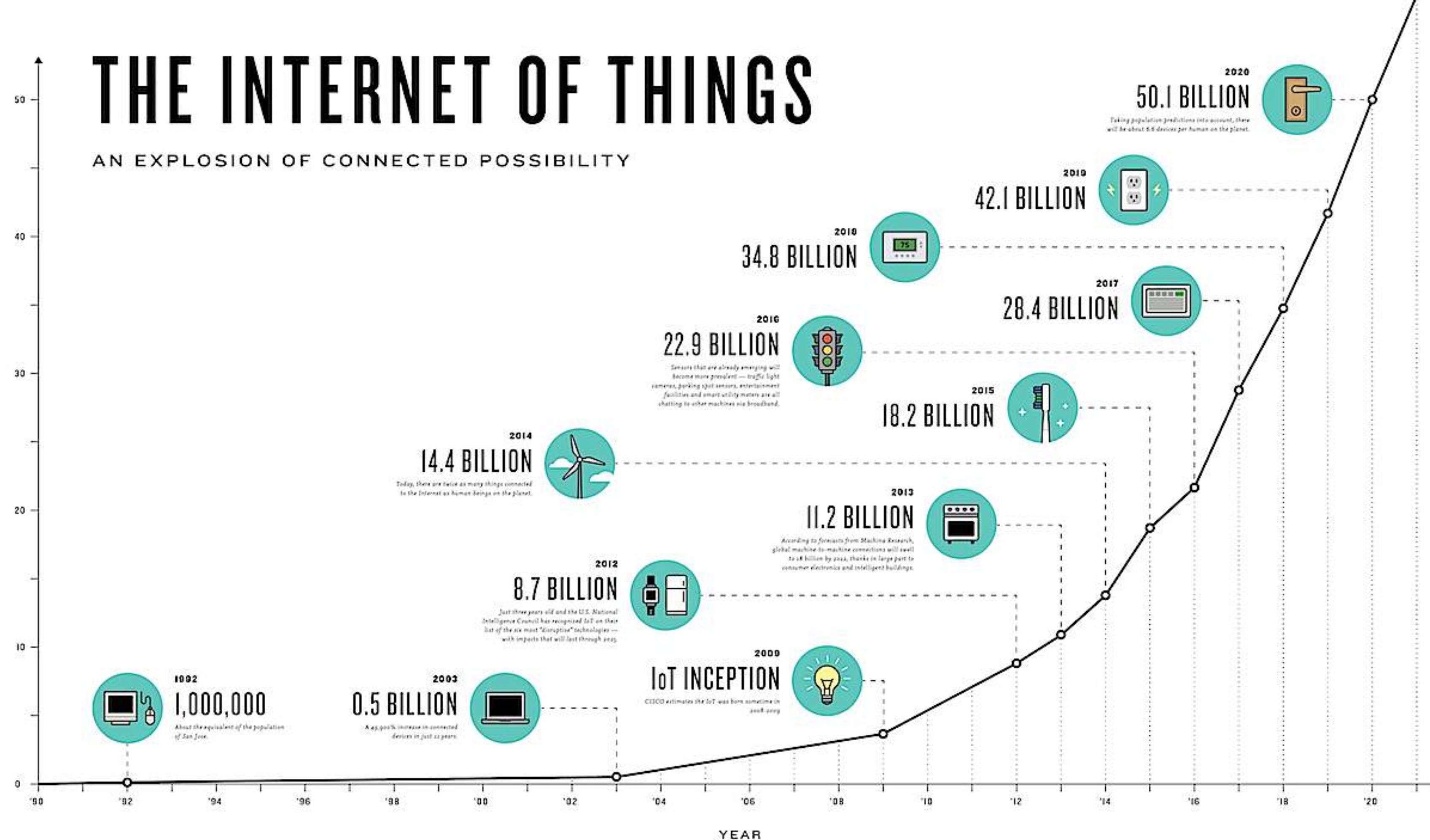


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THE INTERNET OF THINGS

AN EXPLOSION OF CONNECTED POSSIBILITY

BILLIONS OF DEVICES

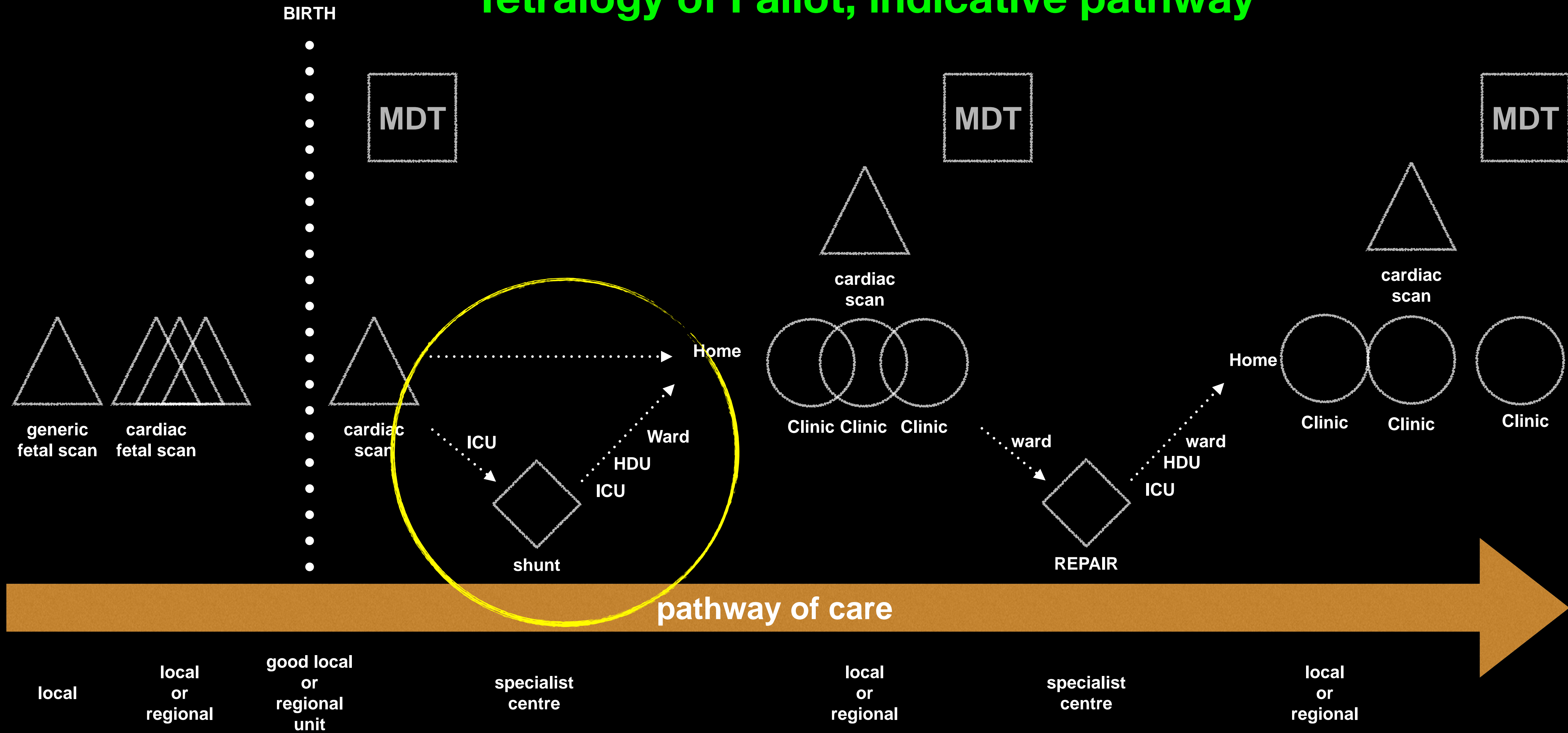


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Tetralogy of Fallot, indicative pathway

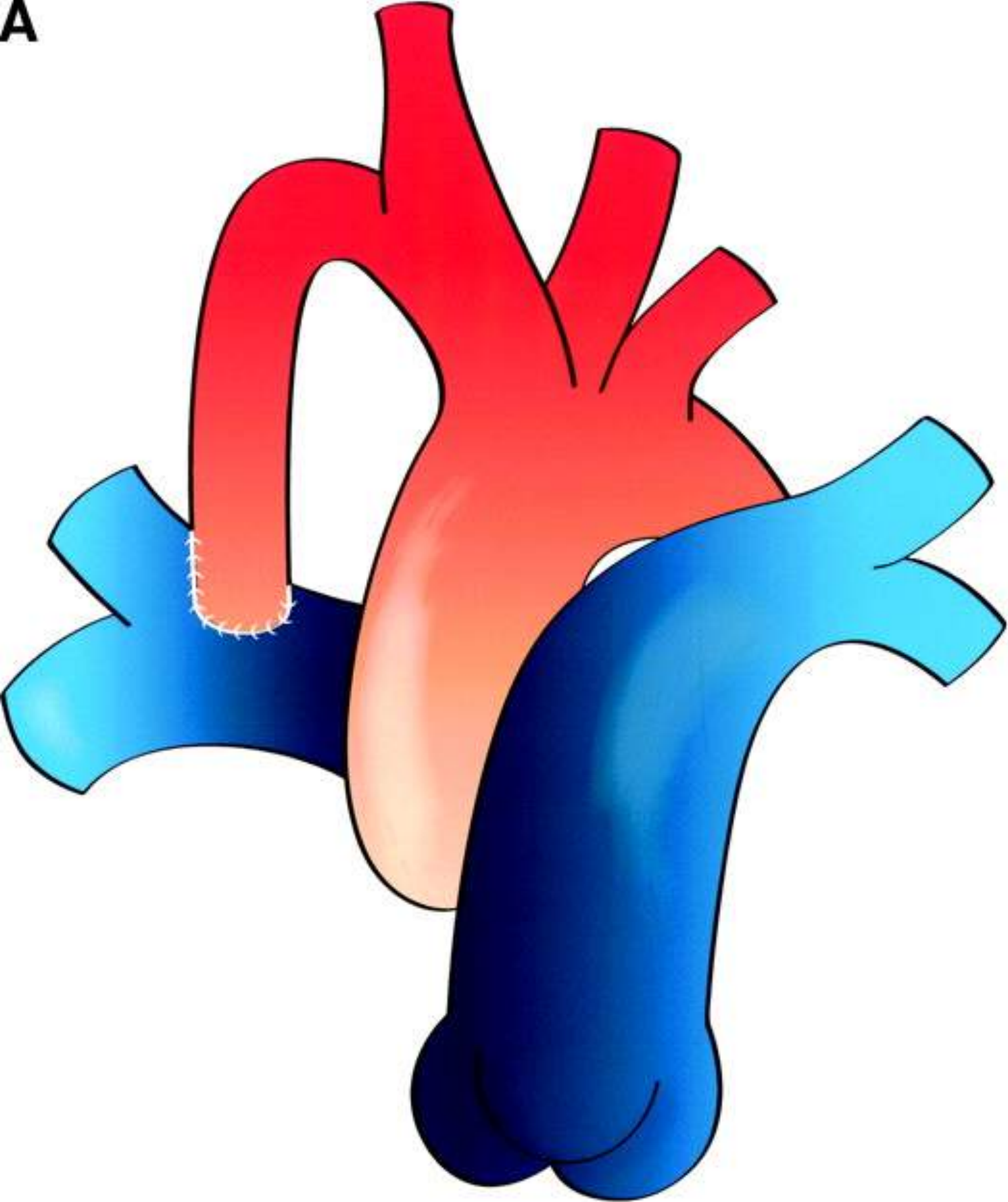


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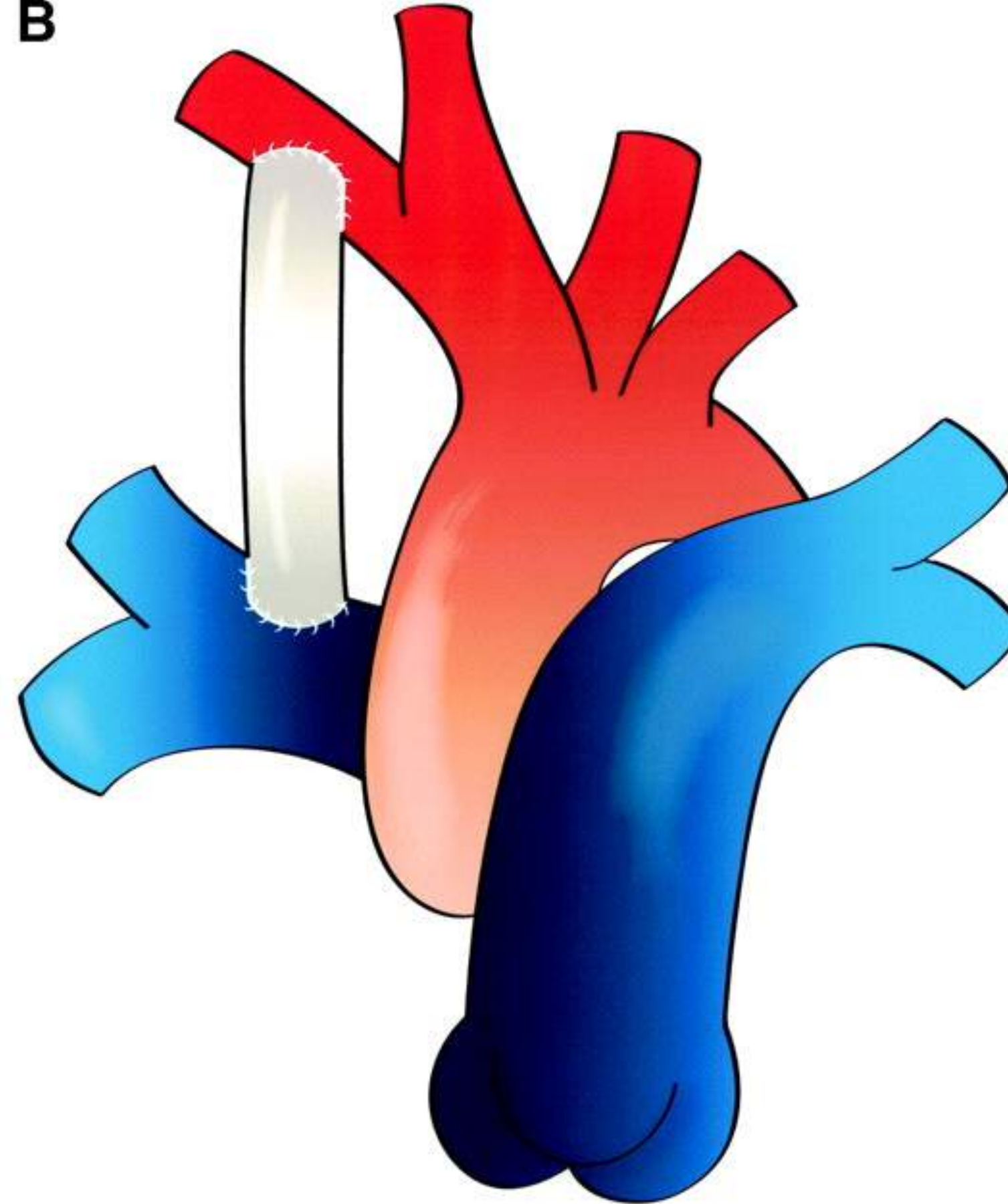
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A

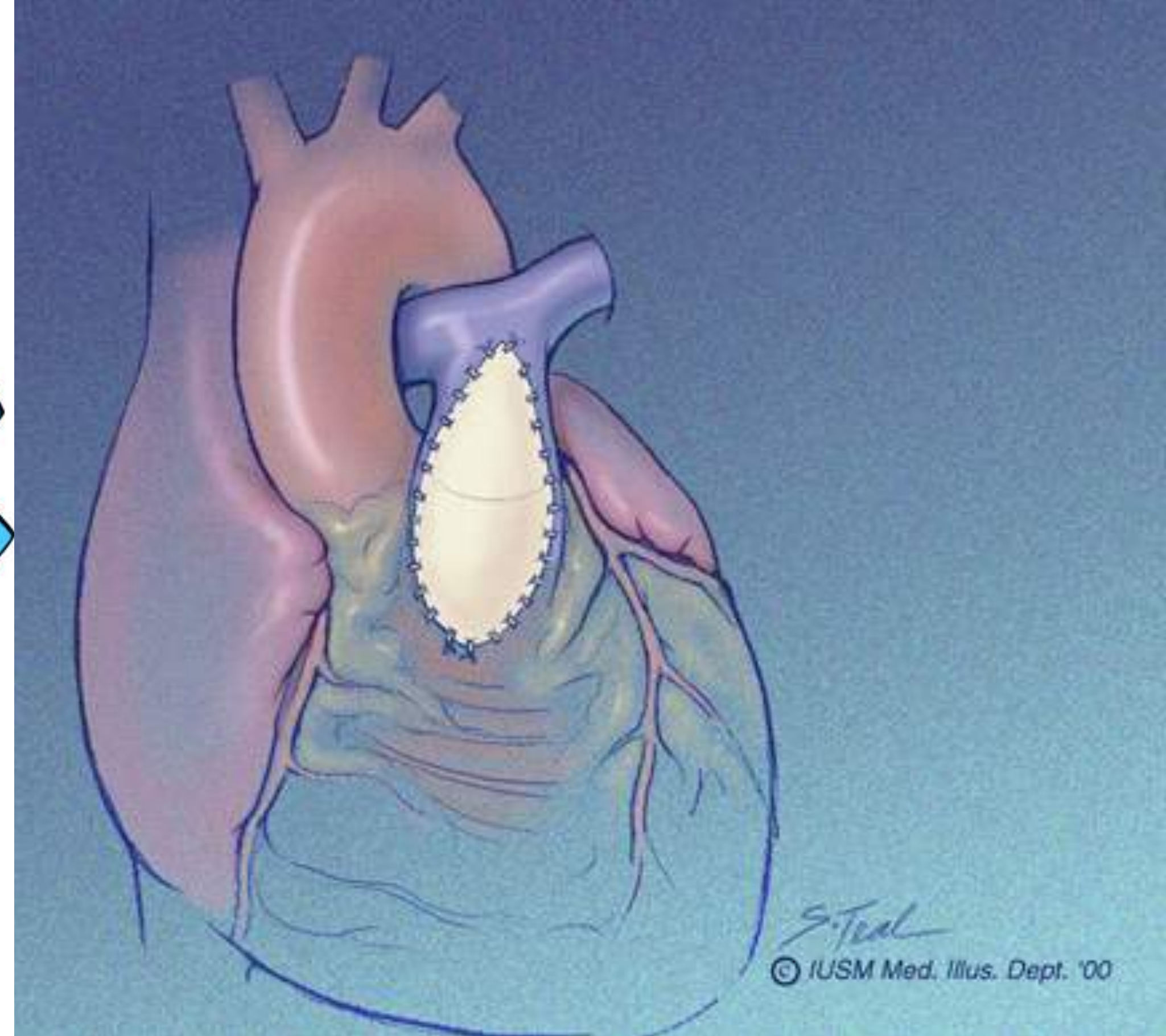


Blalock-Taussig

B



Modified B-T



RV outflow tract patch



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Trans-Venous Catheter Inserted Stent

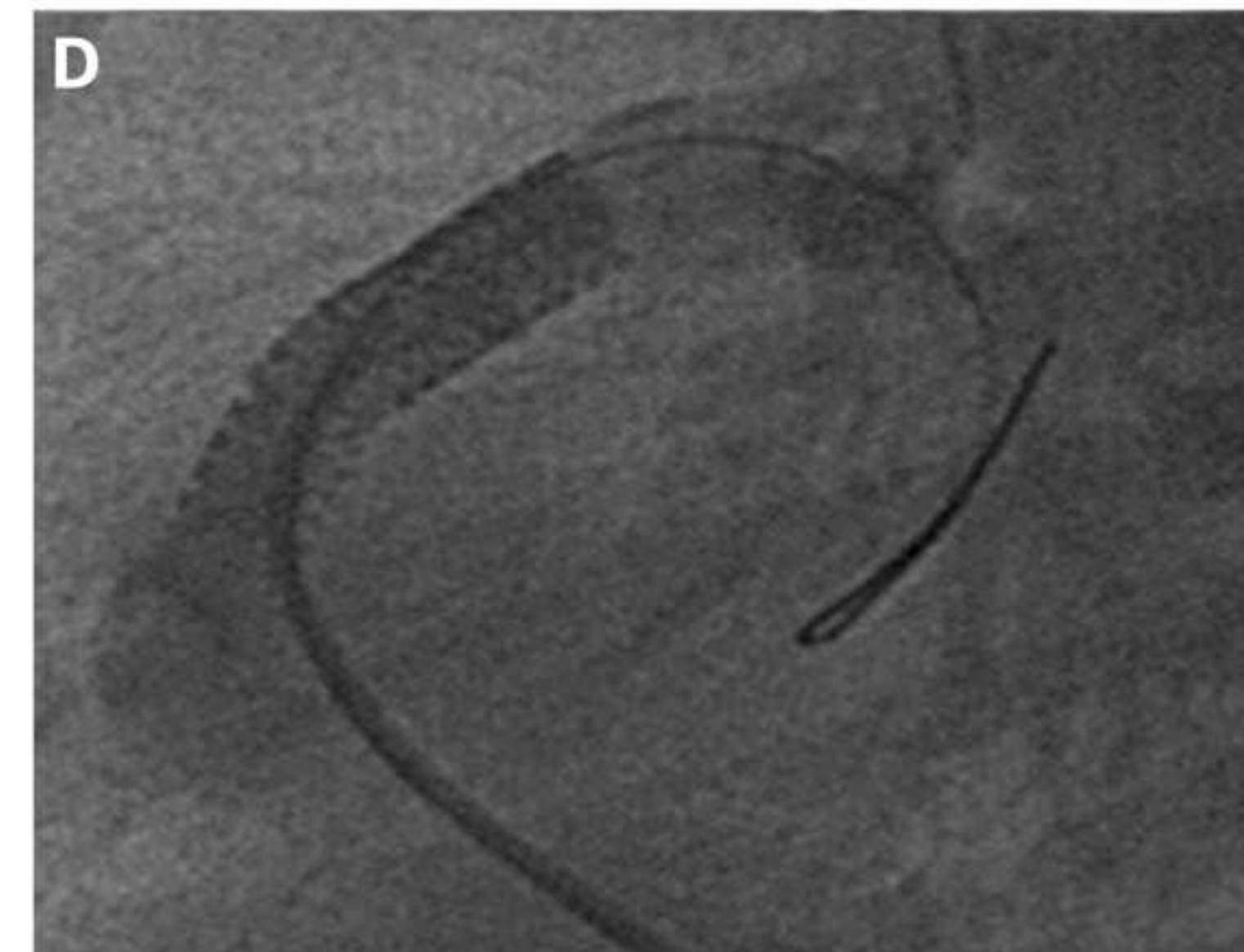
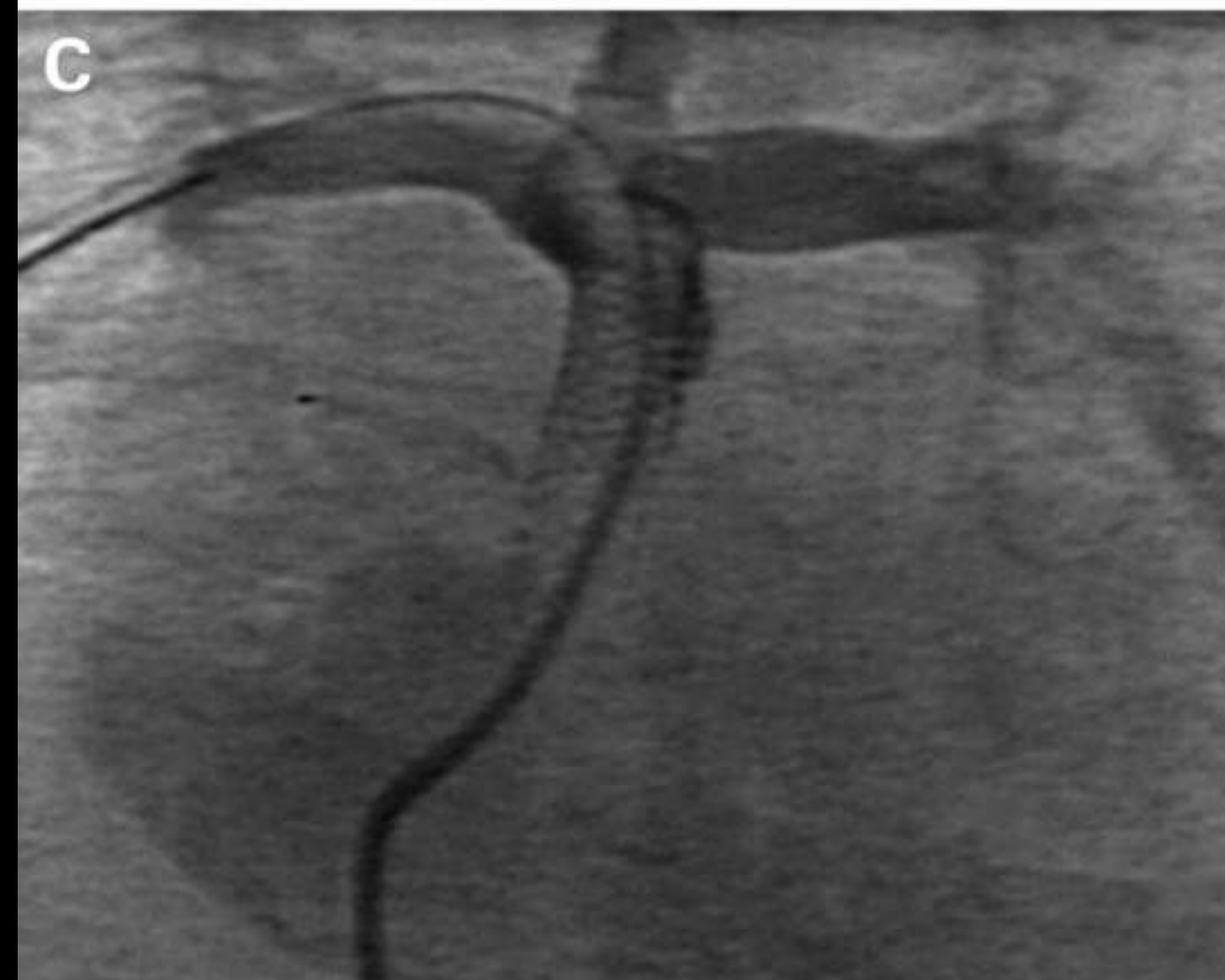
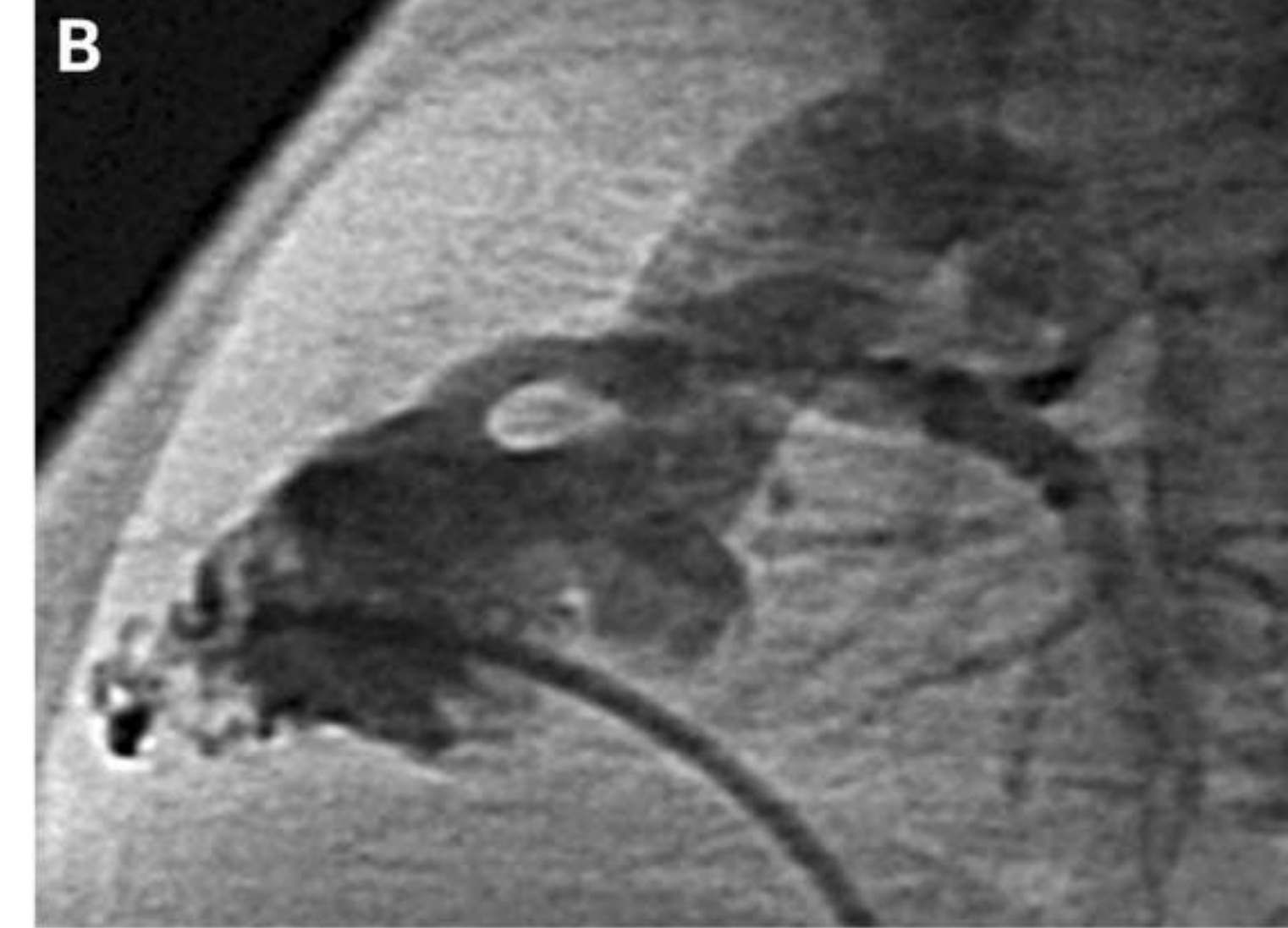
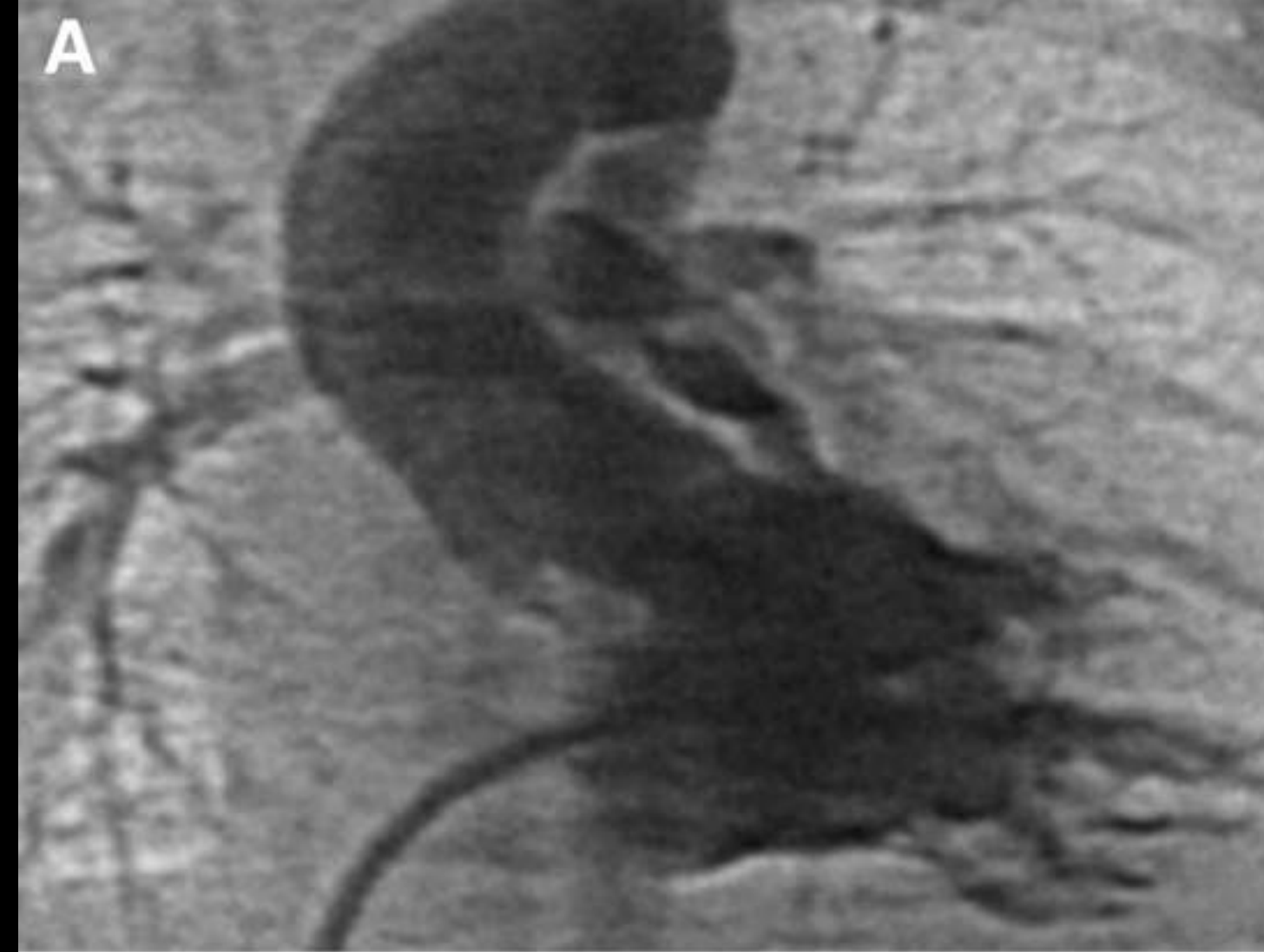
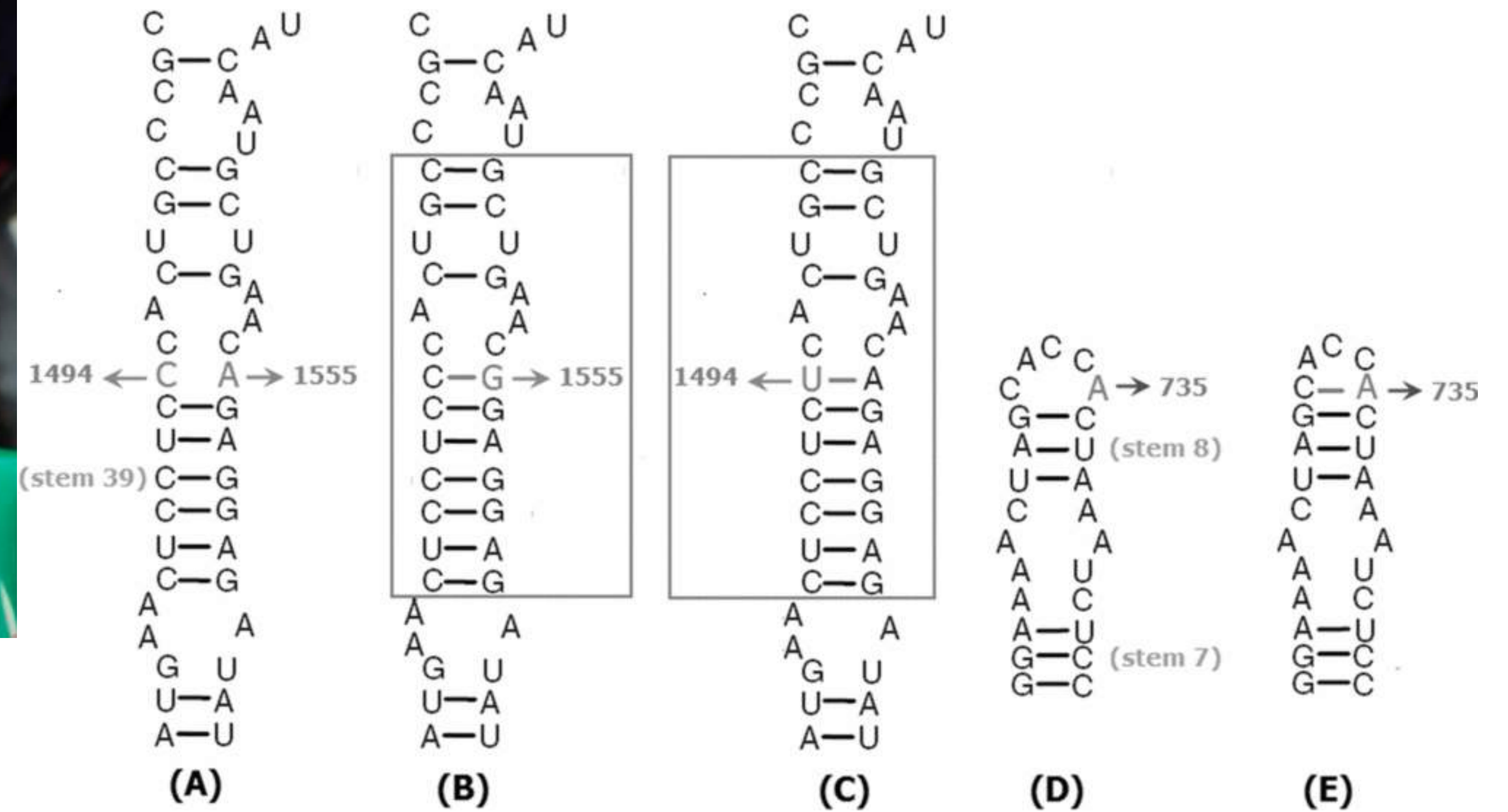
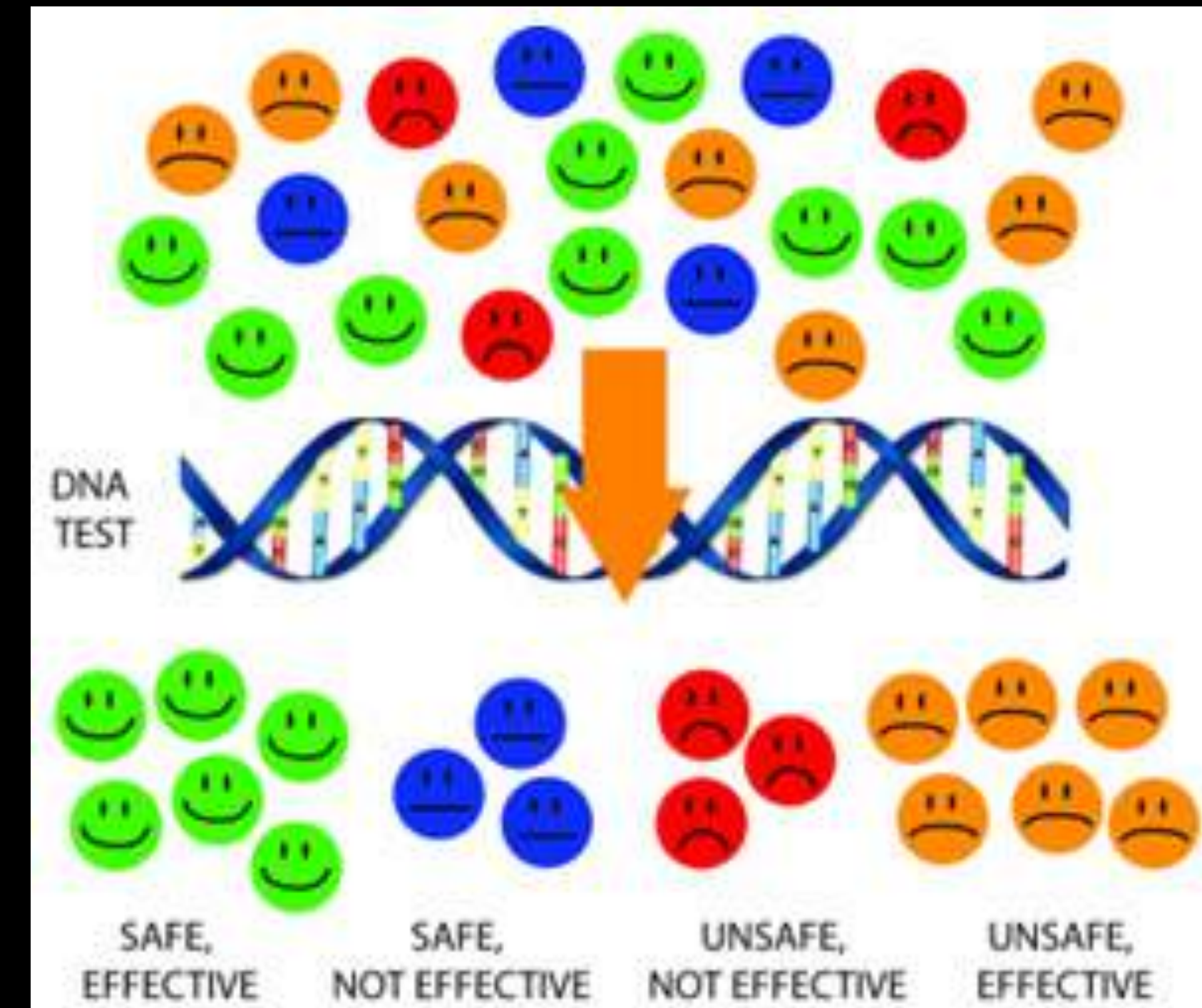


Figure 3 Secondary structure of parts of the mitochondrial 12S rRNA showing the localizations and effects of the m.1555A>G, m.1494C>T and m.735A>G mutations



The era of personalised medicine....

the right treatment for
the right patient at
the right time



Our plan:

Determine genetic risk for ALL
children at GOSH (and store the
genome data)

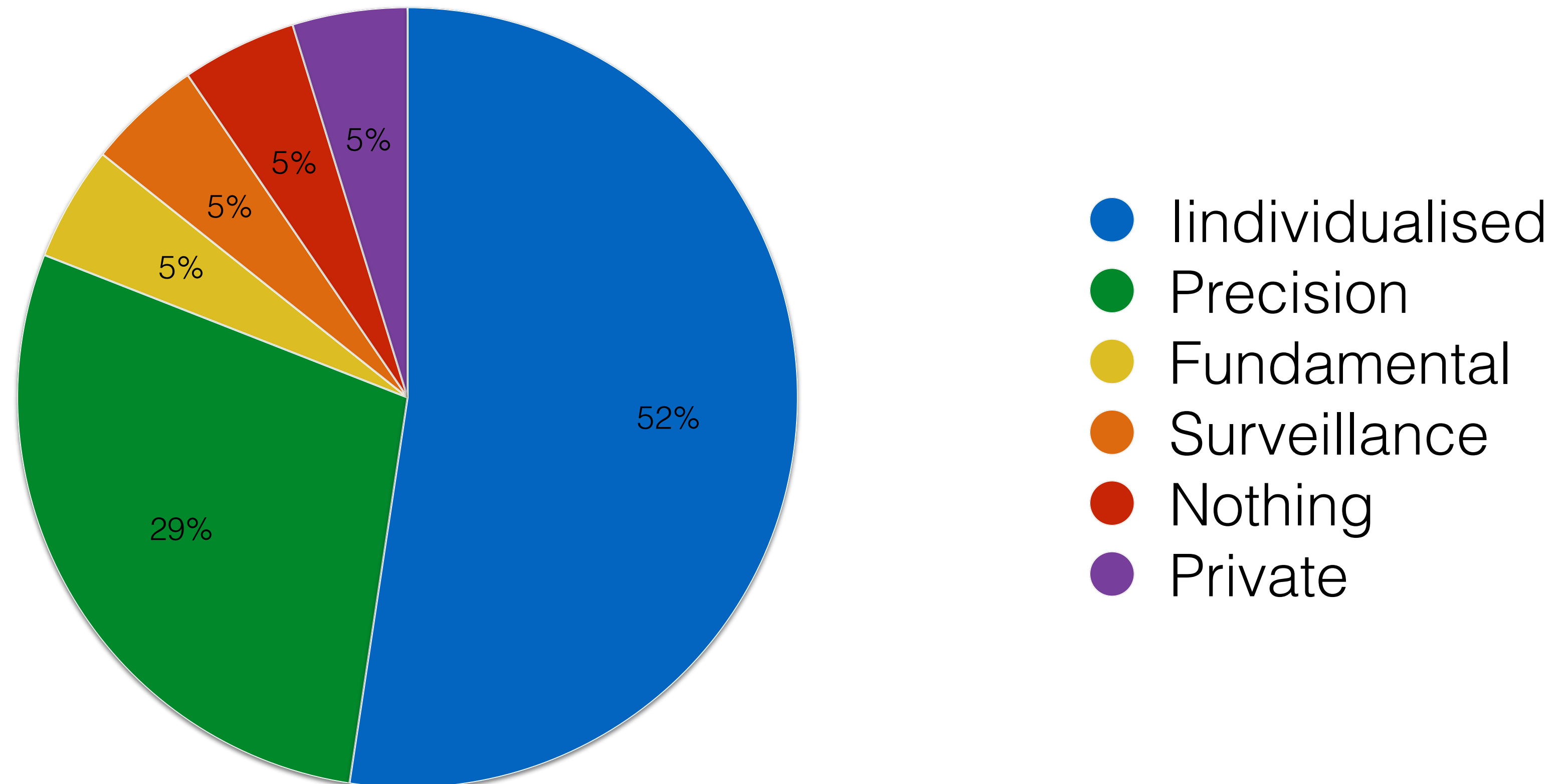


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What does 'Personalised Medicine' mean to you?



**“I’ve always practiced
personalised medicine;
I know my patients, and they know me”**



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1 medical article every 26 secs

I can't read 5000 per day!

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I'm Feeling Lucky



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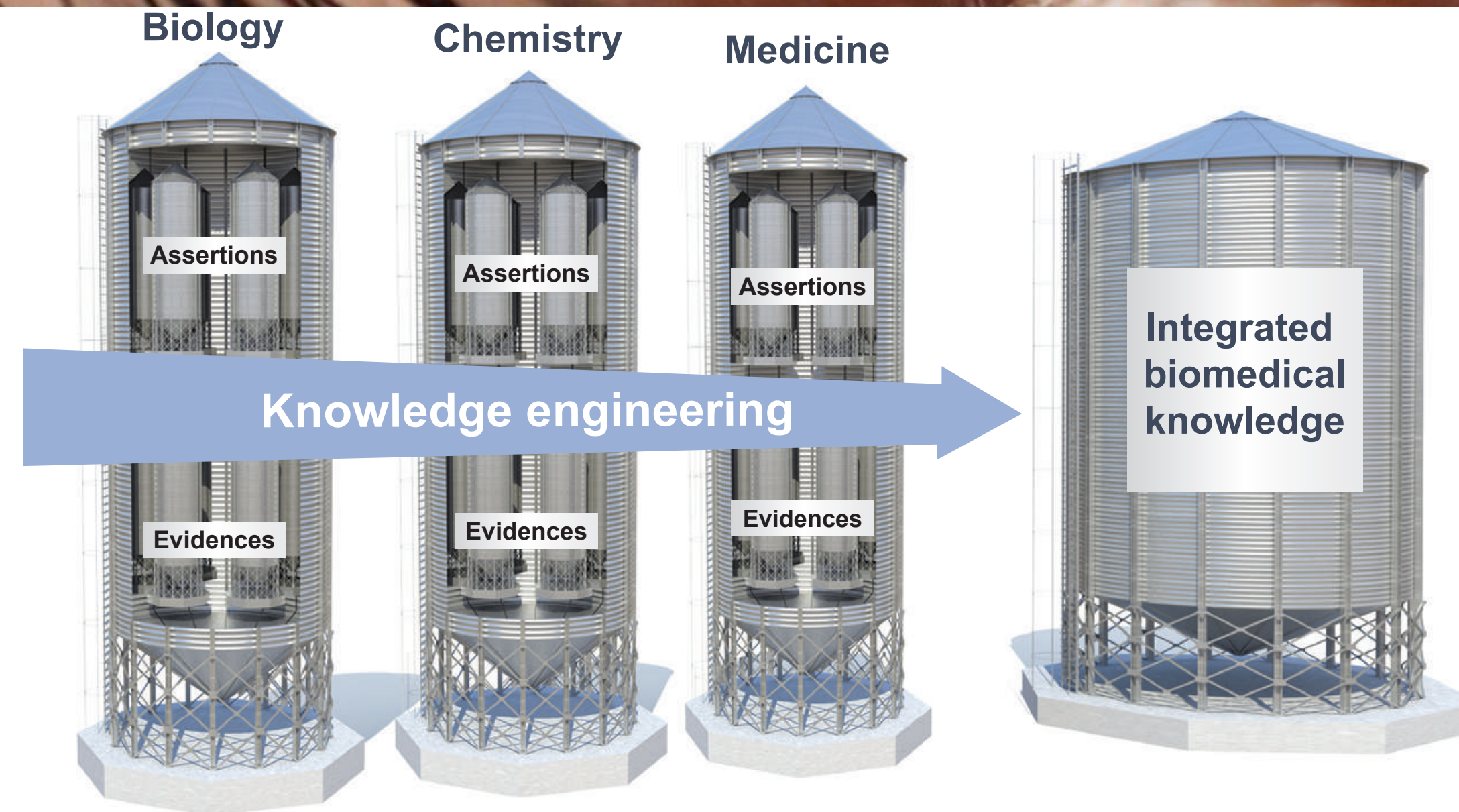


Fig. 1 Interdiscipline and intradiscipline knowledge ‘silos’ to be overcome. The ‘intradiscipline silos’ are the partitions between the different evidences and between the assertions developed from the evidences and from earlier assertions.

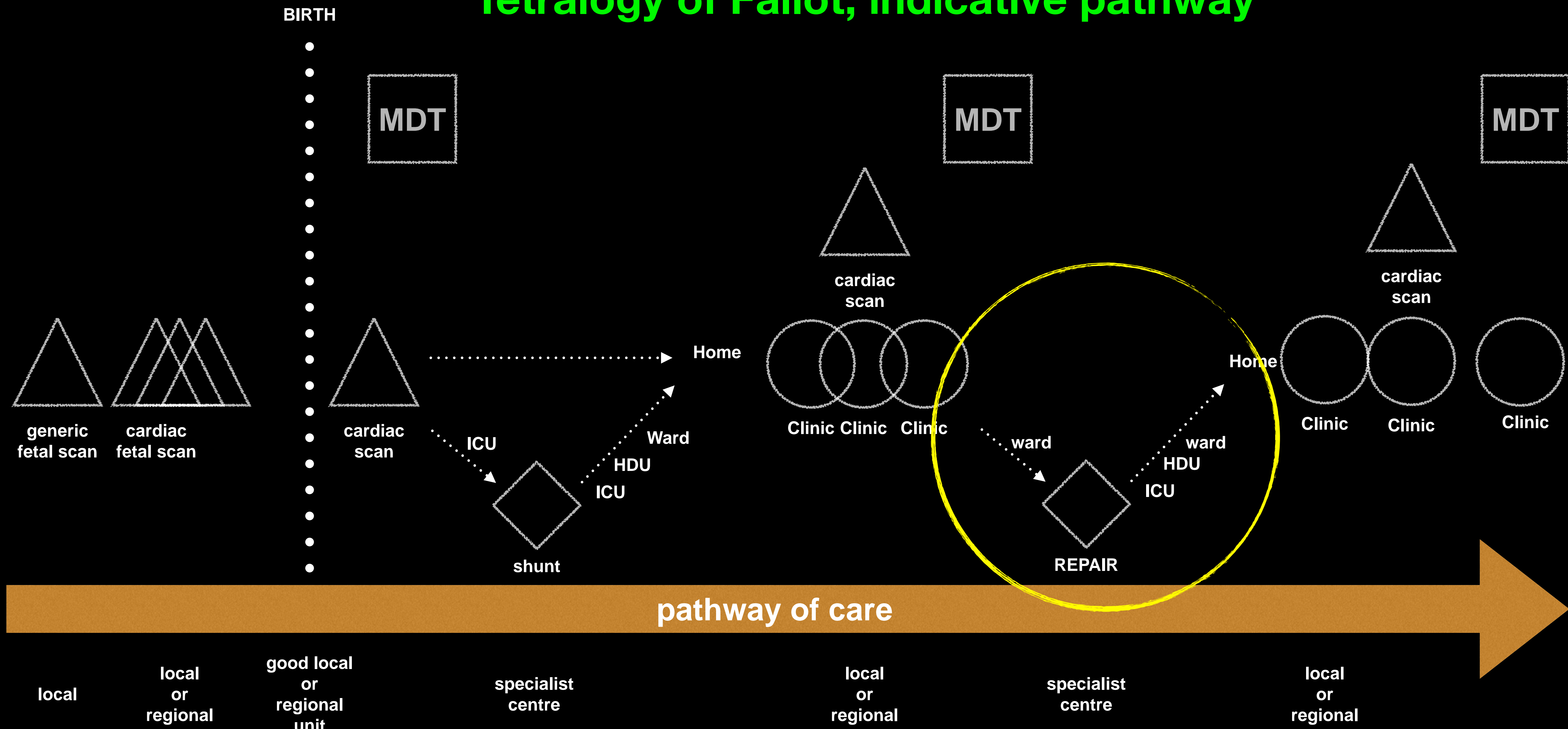


Other Solutions are Available

better care, lower cost, more knowledge



Tetralogy of Fallot, indicative pathway



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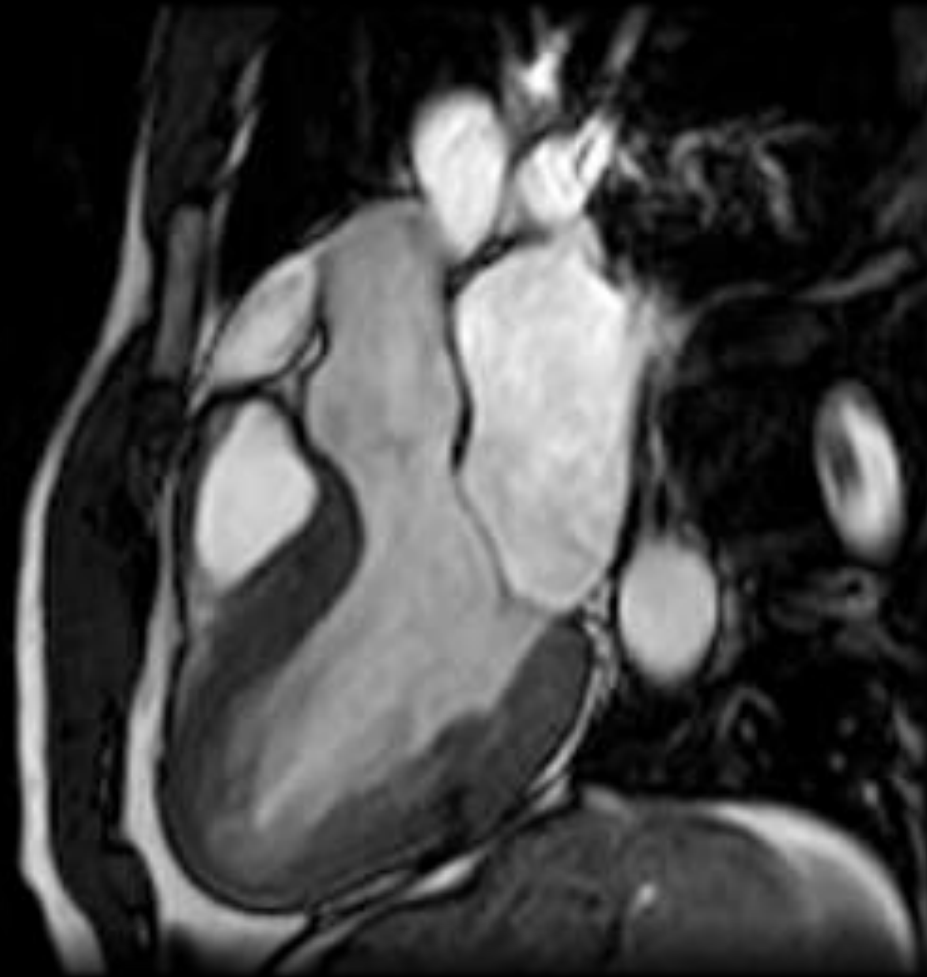


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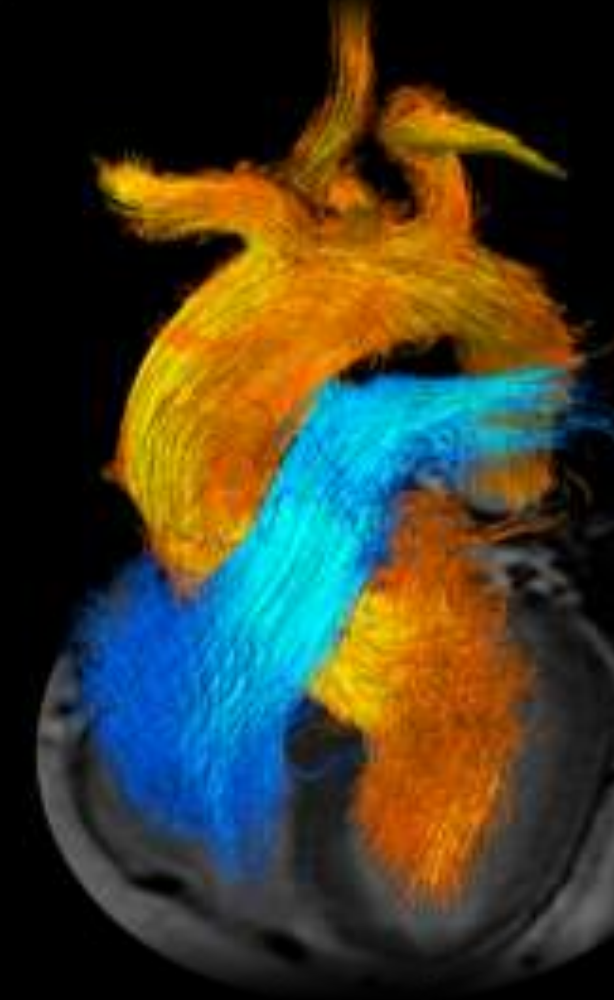
2D



3D



flow



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Courtesy: C Roobottom, Plymouth

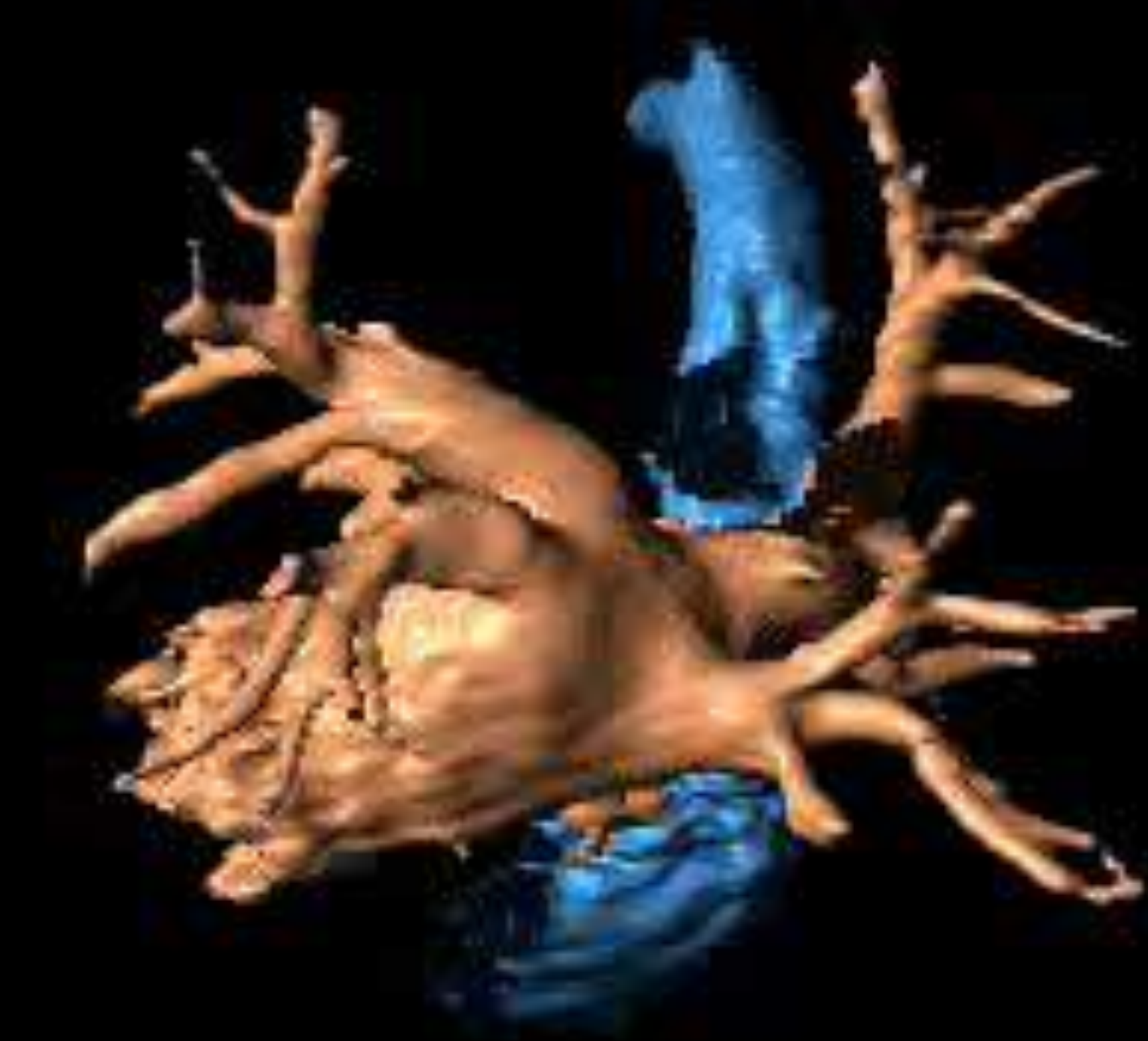


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3D image of the atrium

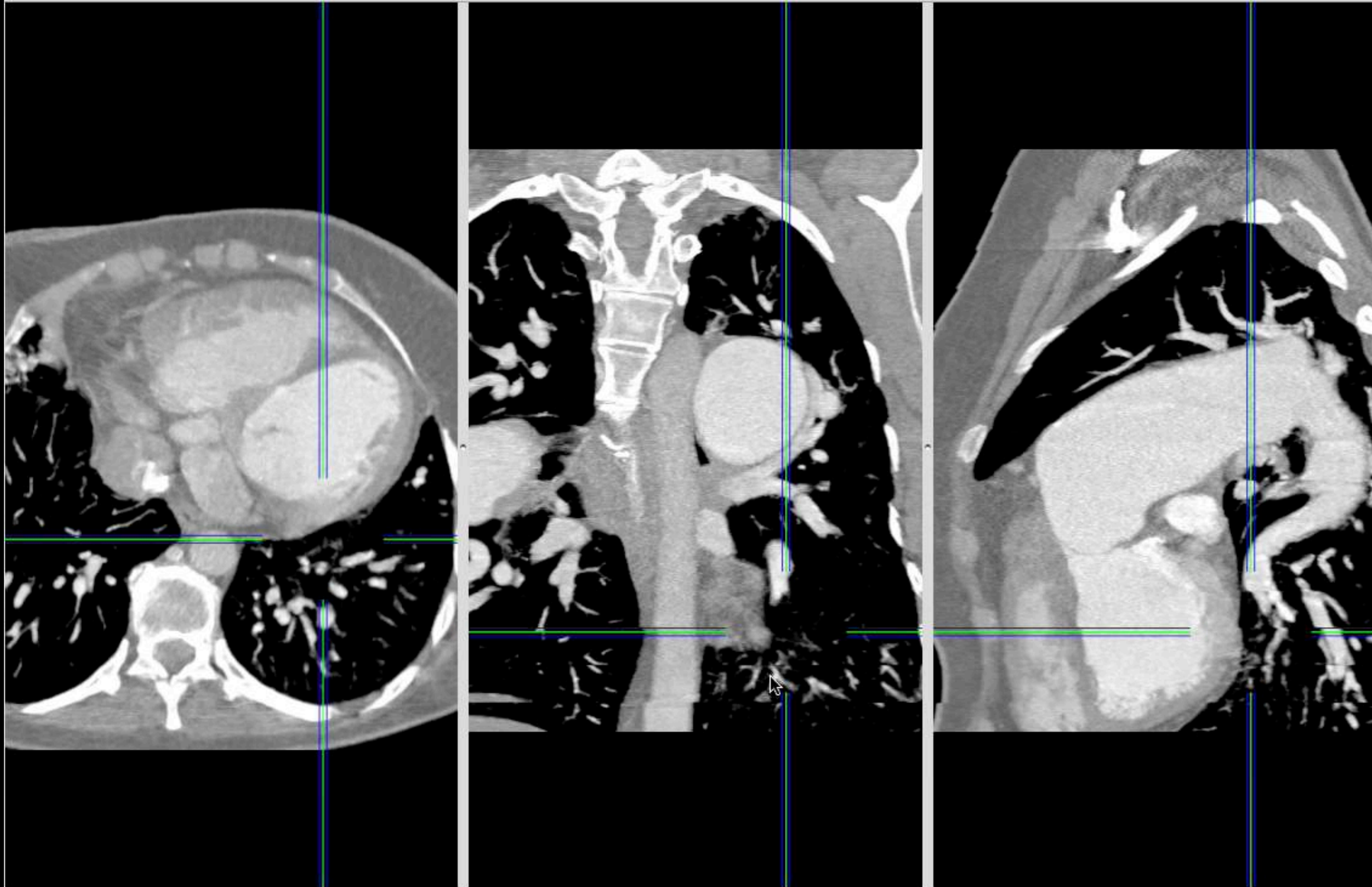


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Vessels/ airways



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Vessels/Airways

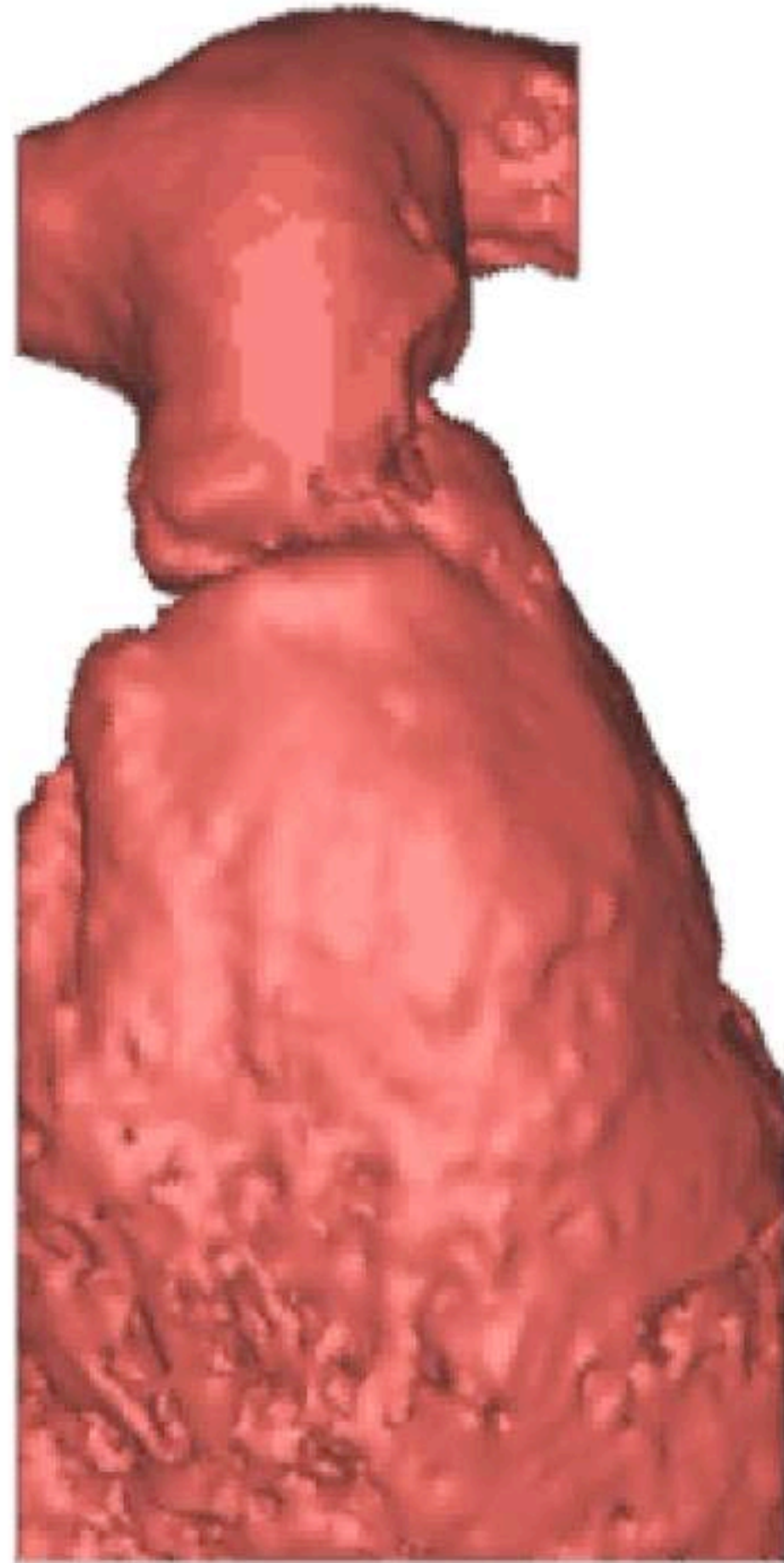


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3D data for device planning

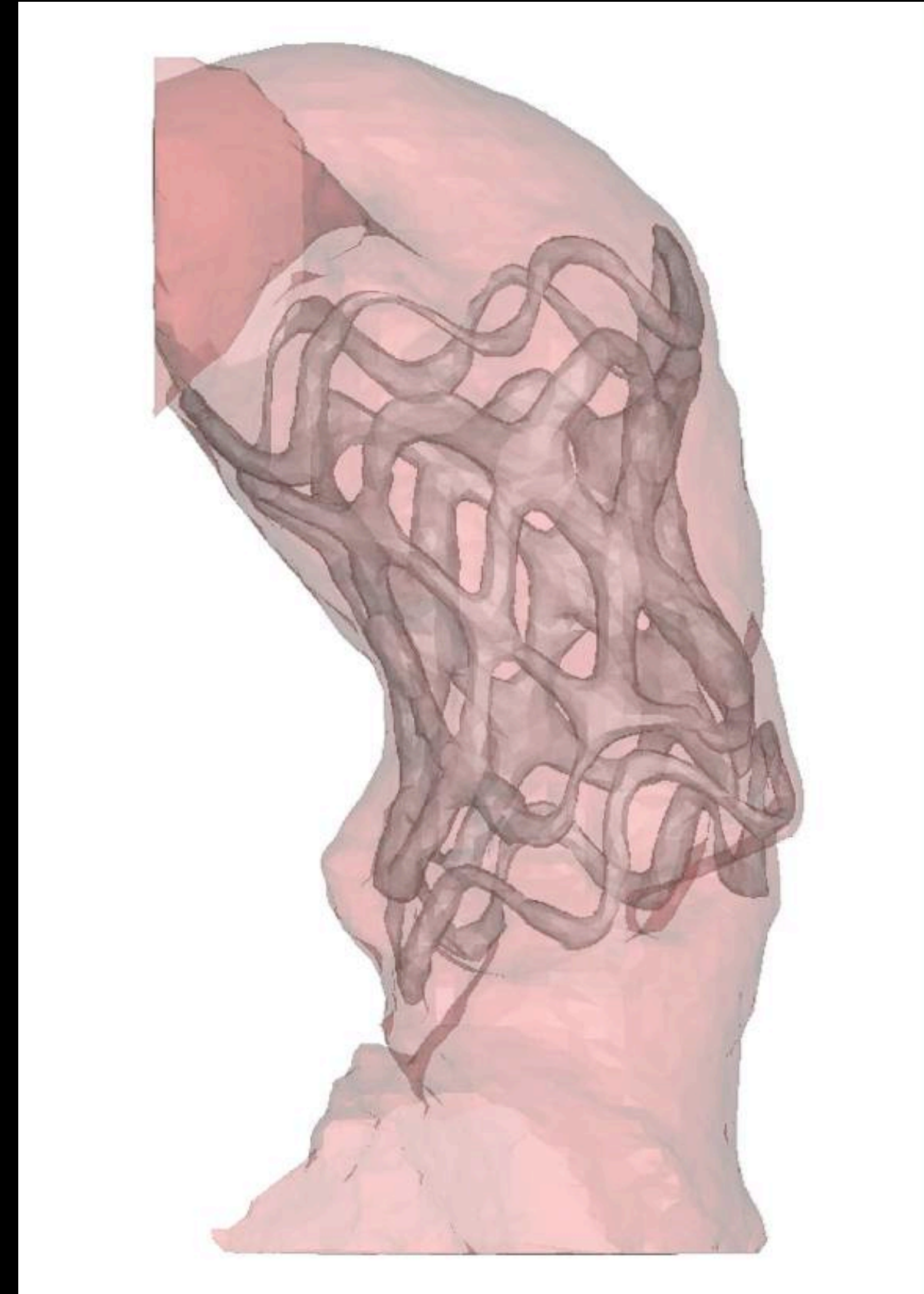
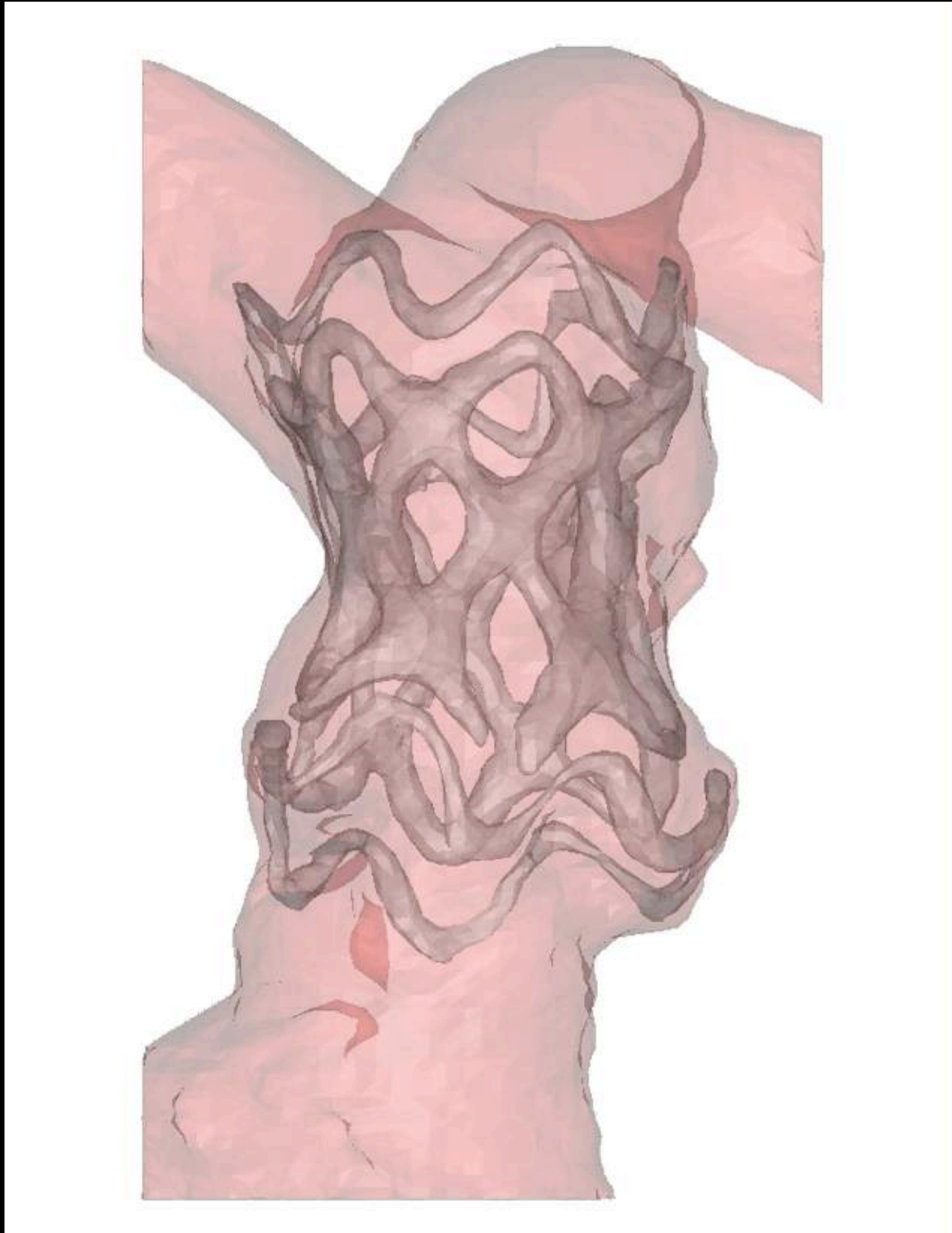


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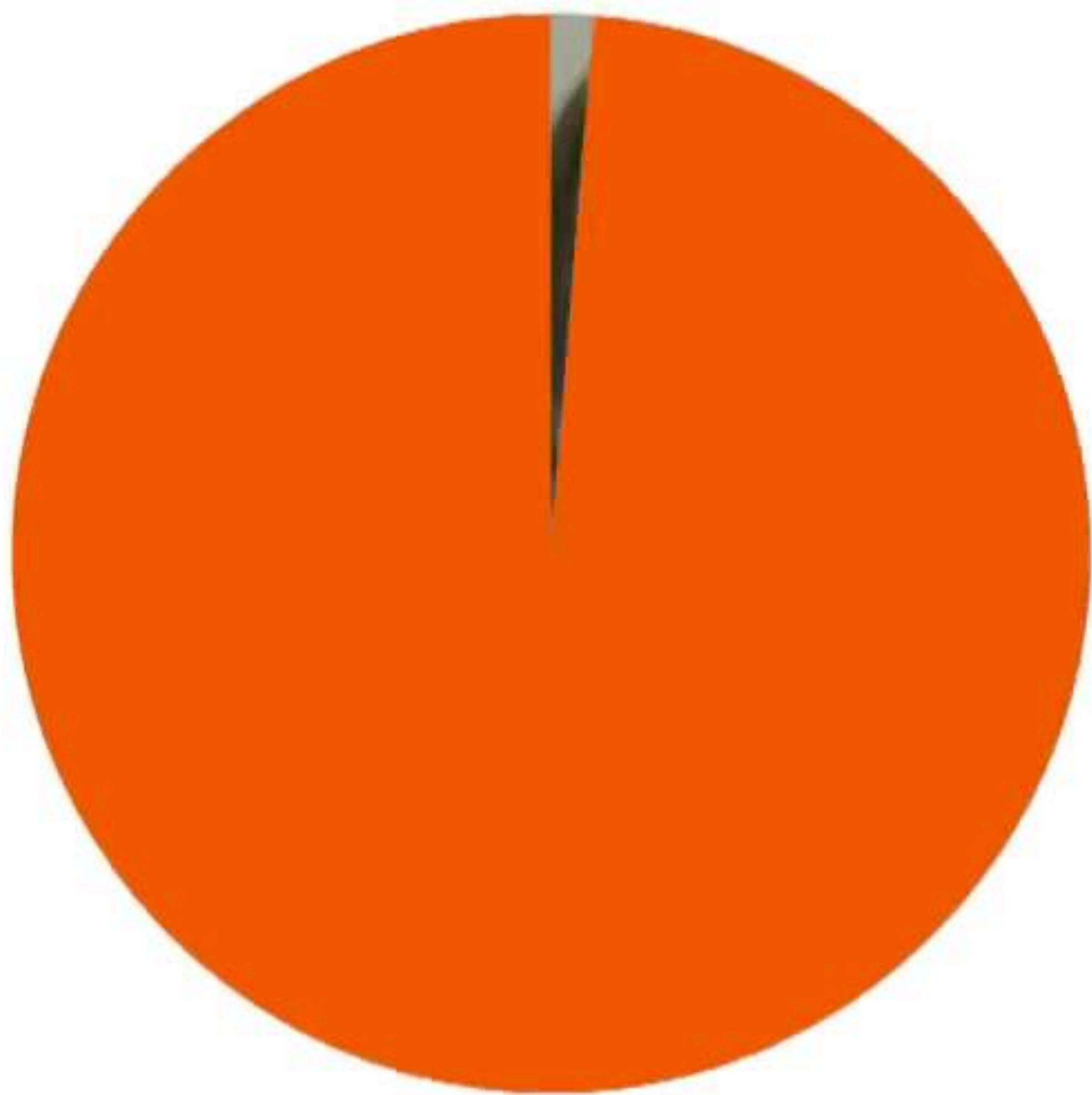
How will a device function?



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**USA
TODAY
TECH**

scale
understanding
confidence



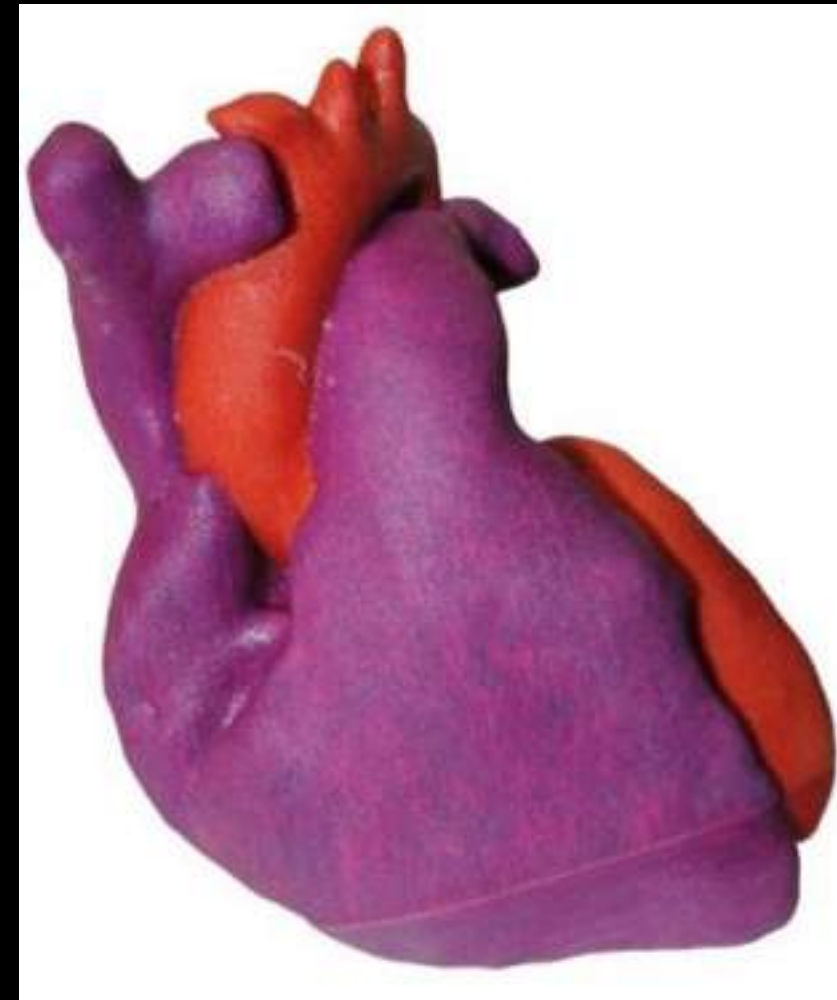
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we use these every day



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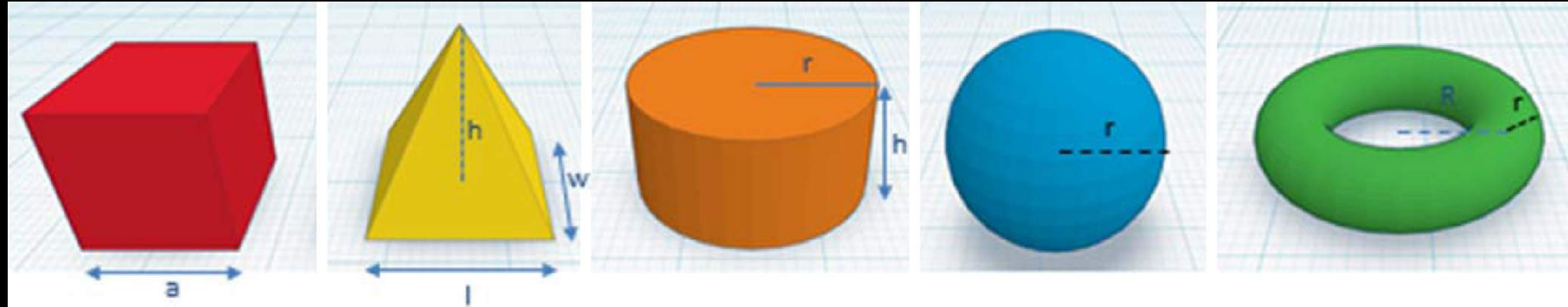


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Effect of geometry on drug release from 3D printed tablets

Alvaro Goyanes^a, Pamela Robles Martinez^a, Asma Buanz^a, Abdul W. Basit^{a,b},
Simon Gaisford^{a,b,*}

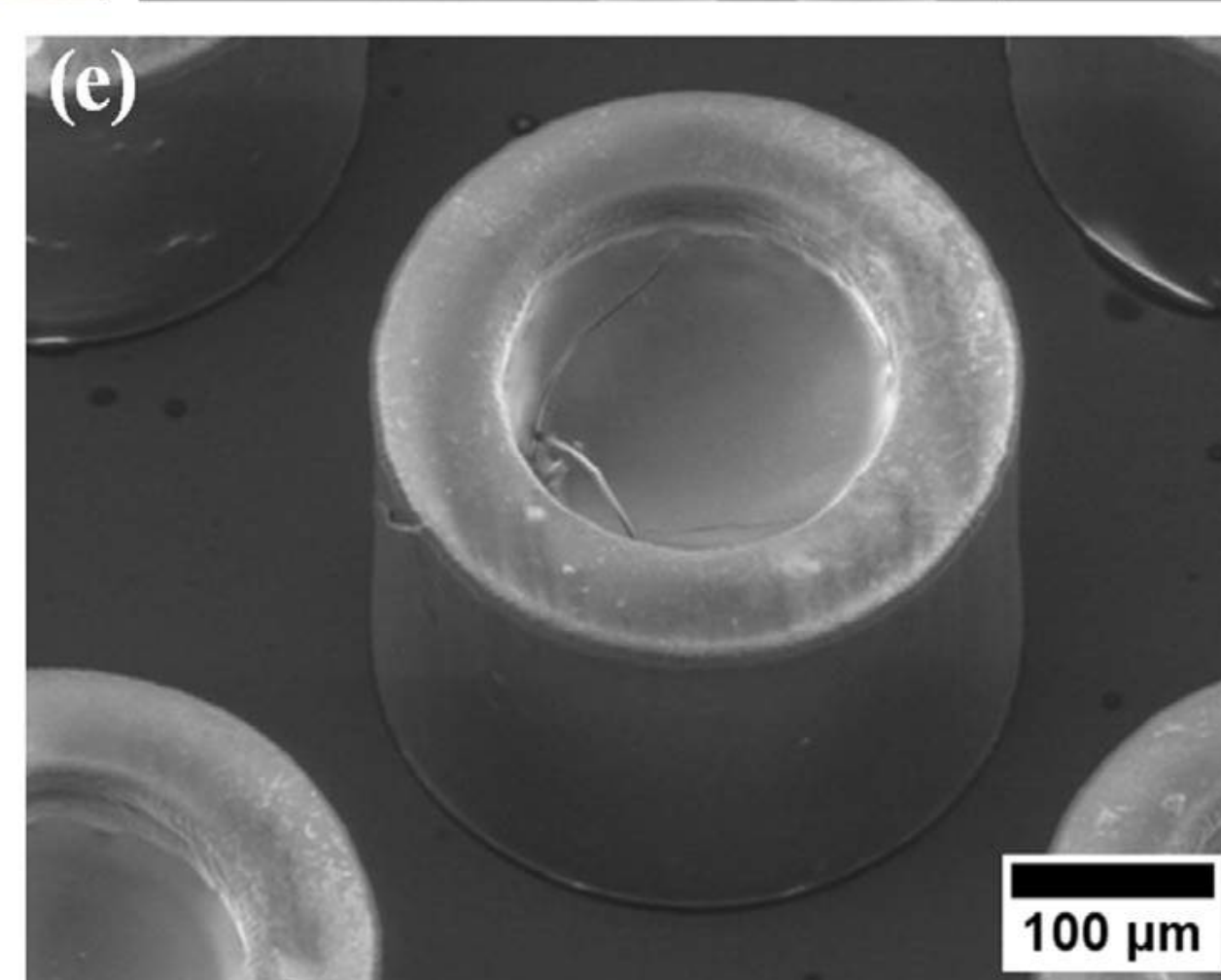
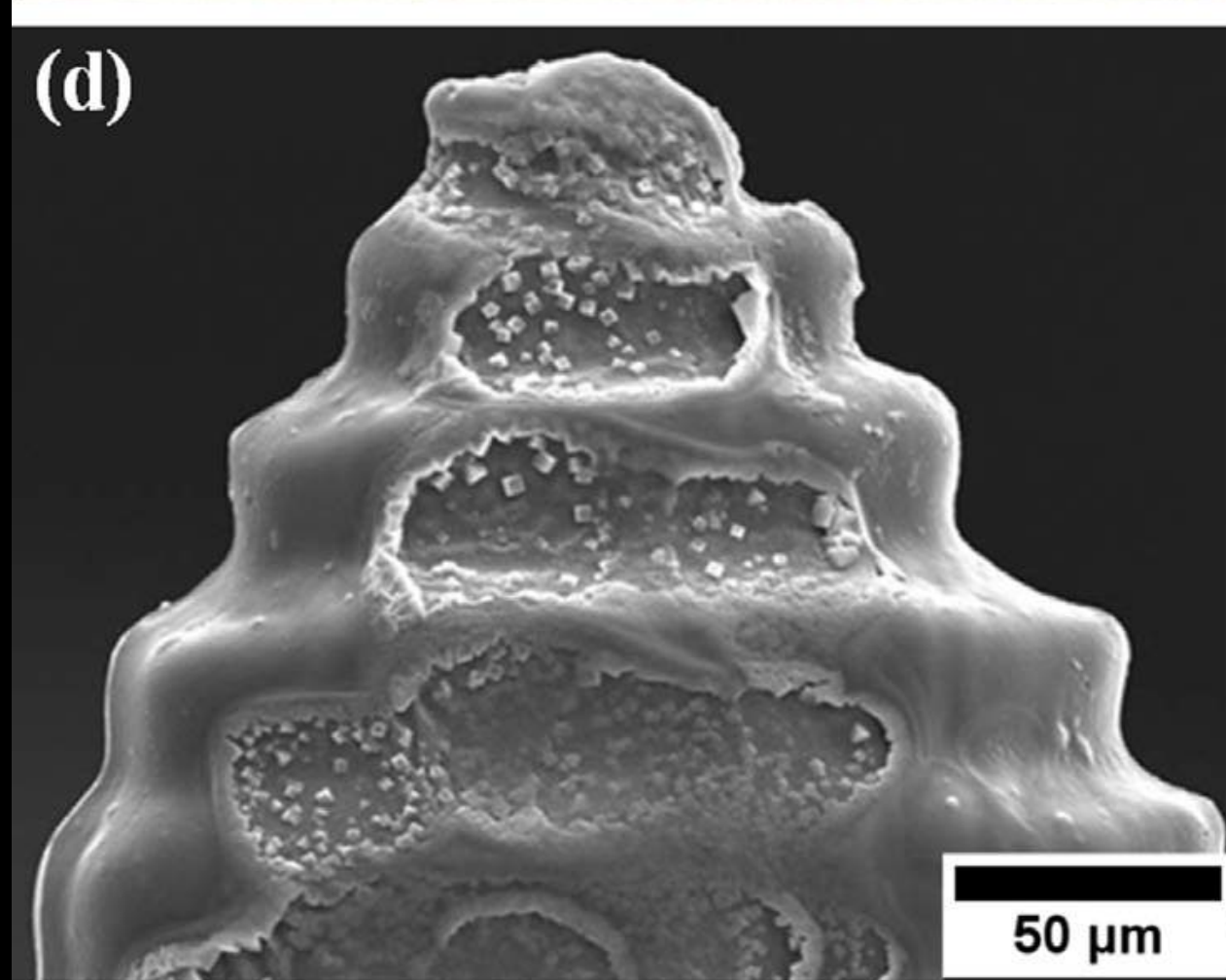
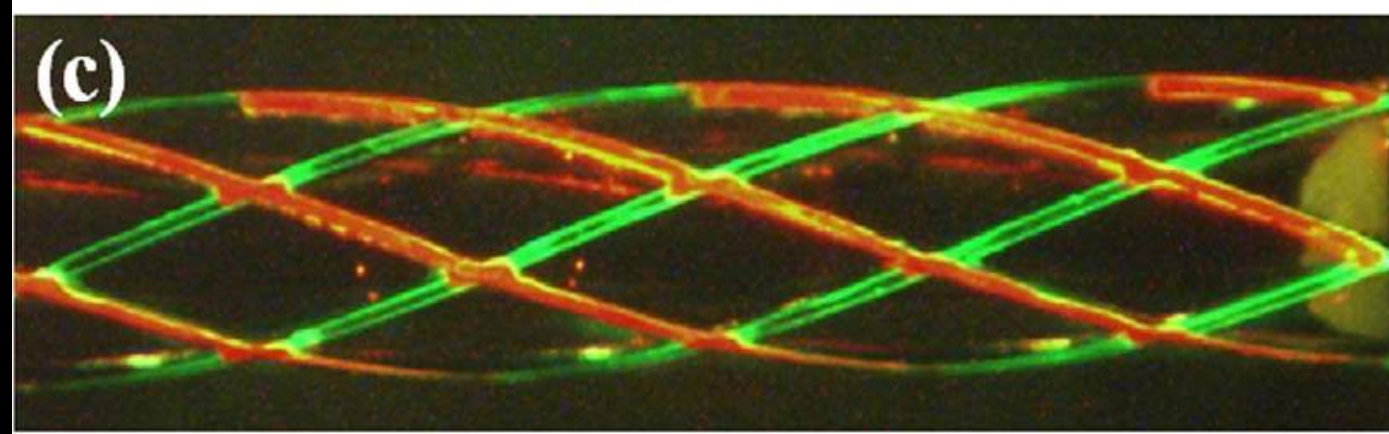
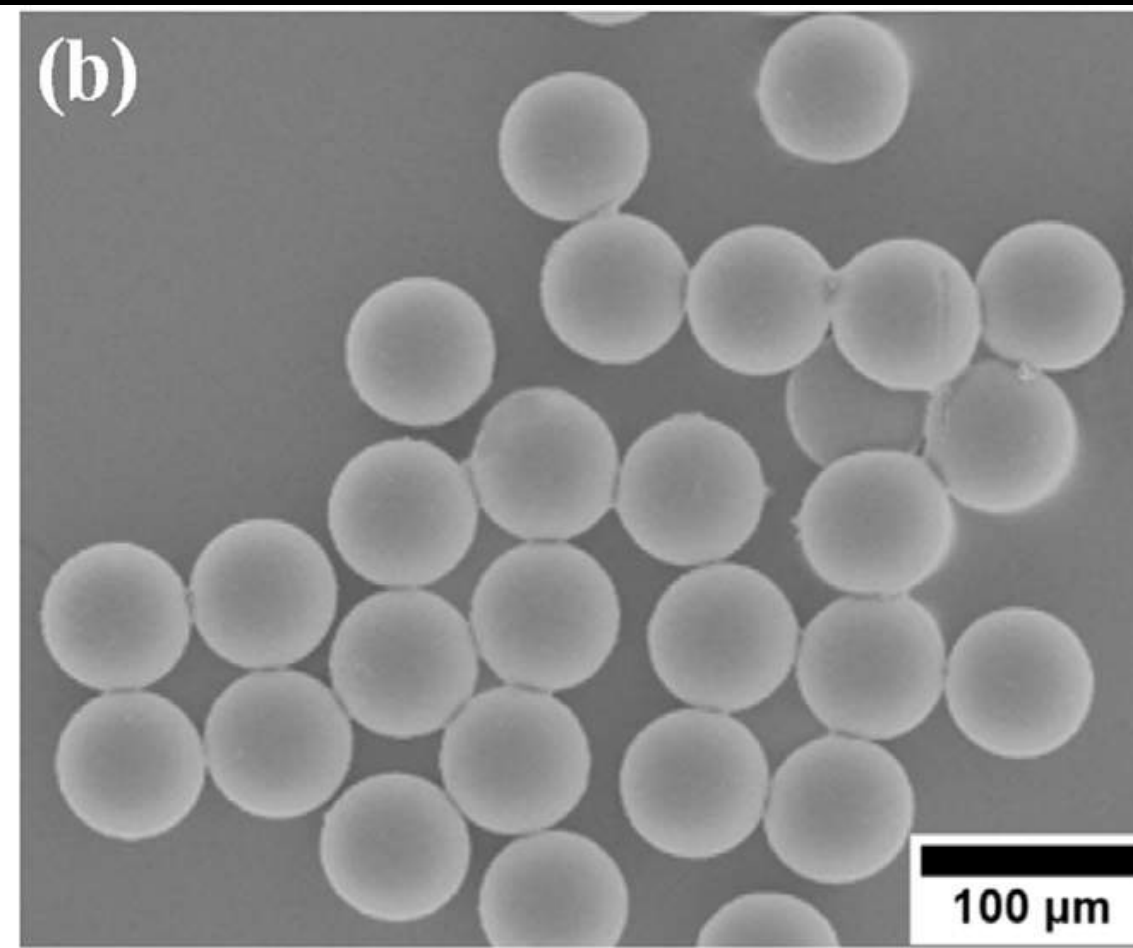
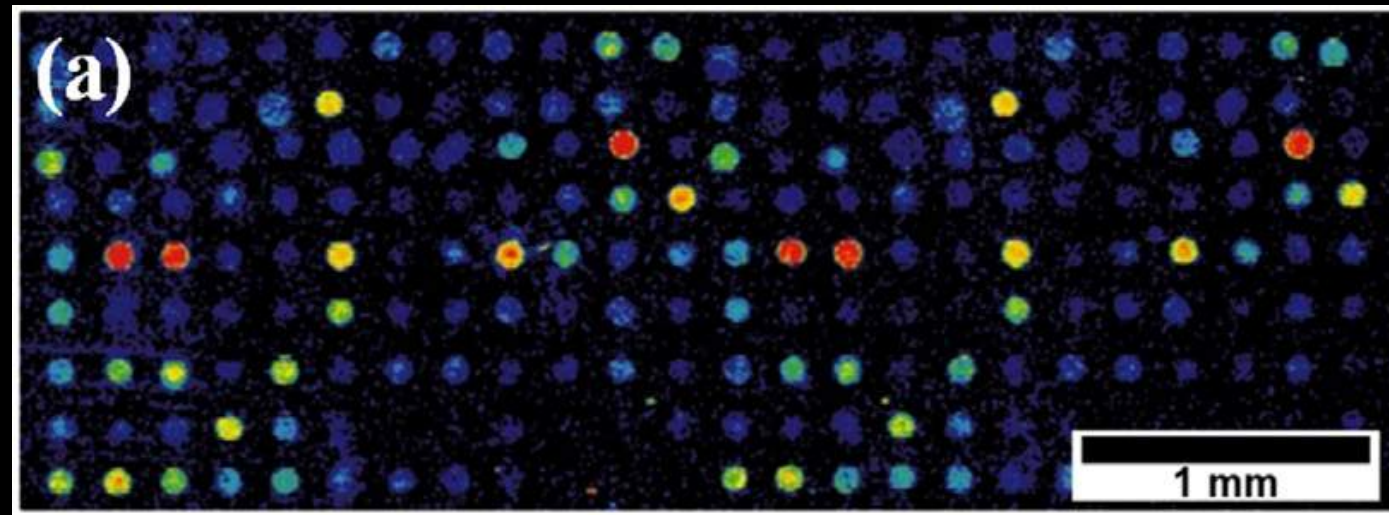
[http:// dx.doi.org/10.1016/j.ijpharm.2015.04.069](http://dx.doi.org/10.1016/j.ijpharm.2015.04.069)



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Personalised medicine

Inkjet printing for pharmaceuticals – A review of research and manufacturing

Ronan Daly^{a,*}, Tomás S. Harrington^b, Graham D. Martin^a, Ian M. Hutchings^a

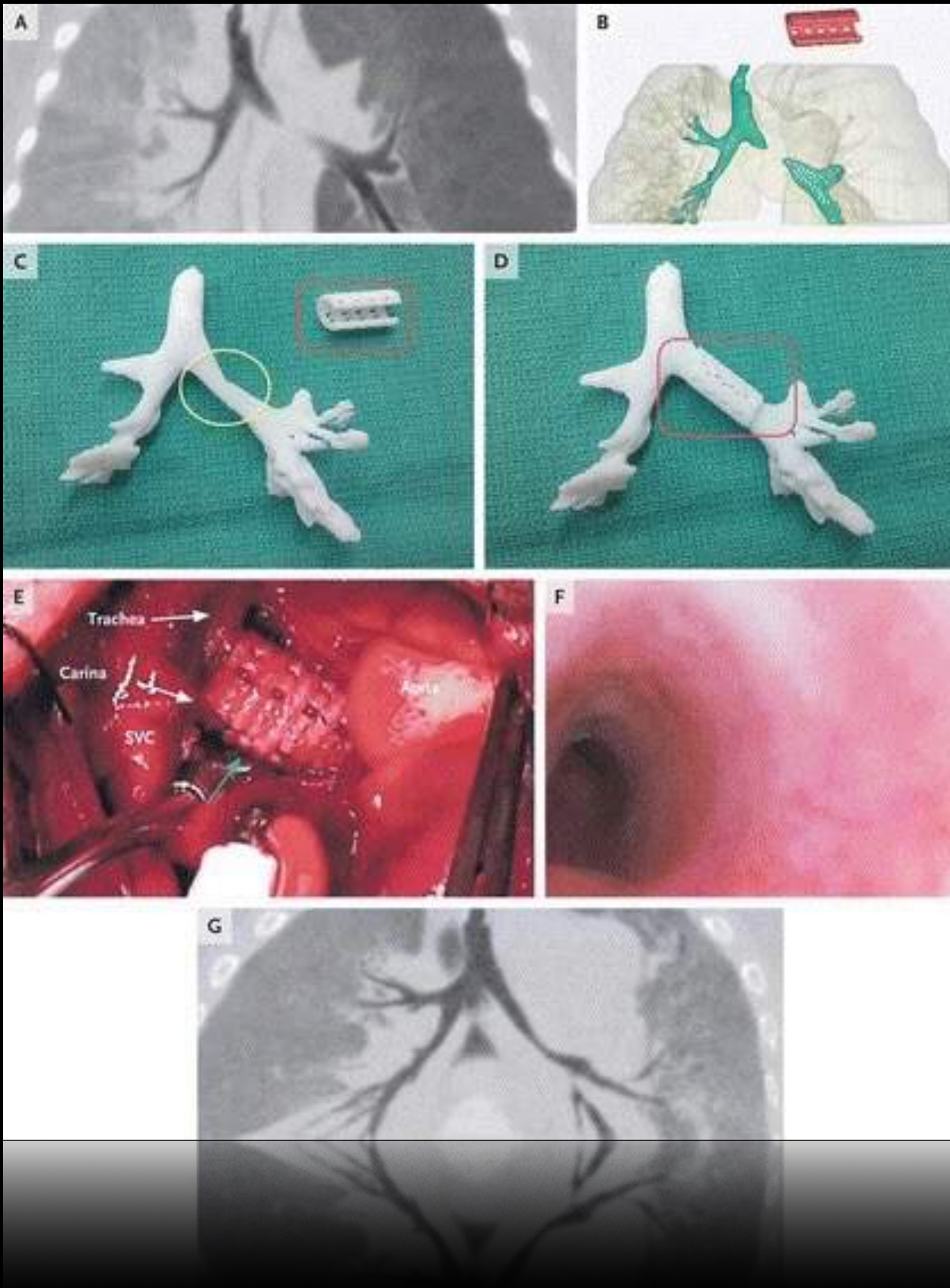
<http://dx.doi.org/10.1016/j.ijpharm.2015.03.017>



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Bioresorbable Airway Splint Created with a Three-Dimensional Printer

N Engl J Med 2013; 368:2043-2045 | [May 23, 2013](#) | DOI: 10.1056/NEJMc1206319



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no surgery please



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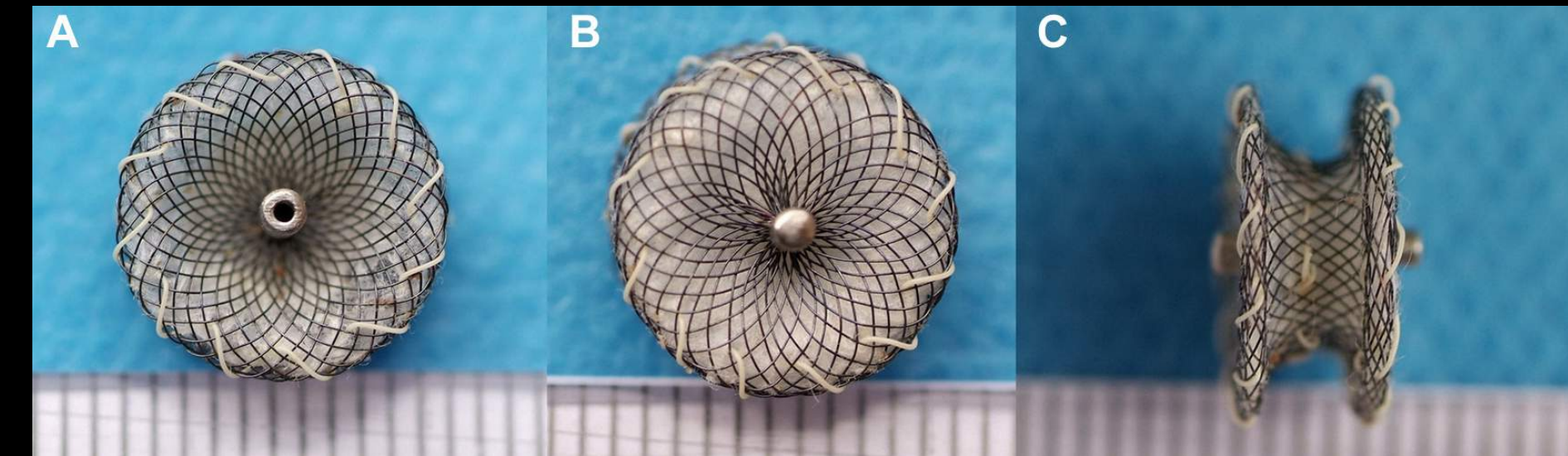
Transcatheter Versus Surgical Closure of Perimembranous Ventricular Septal Defects in Children

A Randomized Controlled Trial

<http://dx.doi.org/10.1016/j.jacc.2014.01.008>



Jian Yang, MD, PhD,* Lifang Yang, MD,* Shiqiang Yu, MD, PhD,* Jincheng Liu, MD, PhD,*
Jian Zuo, MD,* Wensheng Chen, MD, PhD,* Weixun Duan, MD,* Qijun Zheng, MD,*
Xuezeng Xu, MD,* Jun Li, MD,* Jun Zhang, MD, PhD,* Jian Xu, MD,* Lijun Sun, MD, PhD,*
Xiuling Yang, MD,* Lize Xiong, MD, PhD,* Dinghua Yi, MD, PhD,* Lei Wang, MD,†
Qingchun Liu, MD,‡ Shuping Ge, MD,*§ Jun Ren, MD, PhD*||



**less complications, less blood, shorter stay
no long term harm**



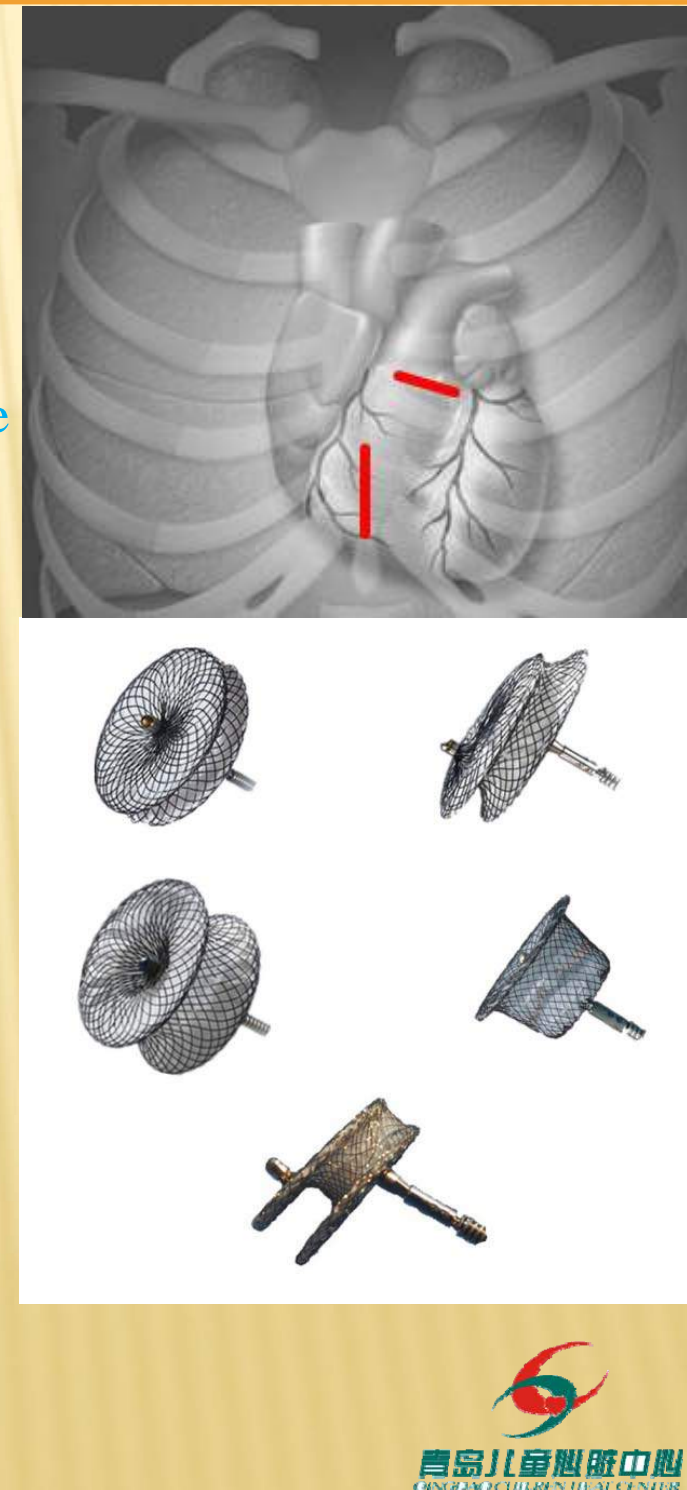
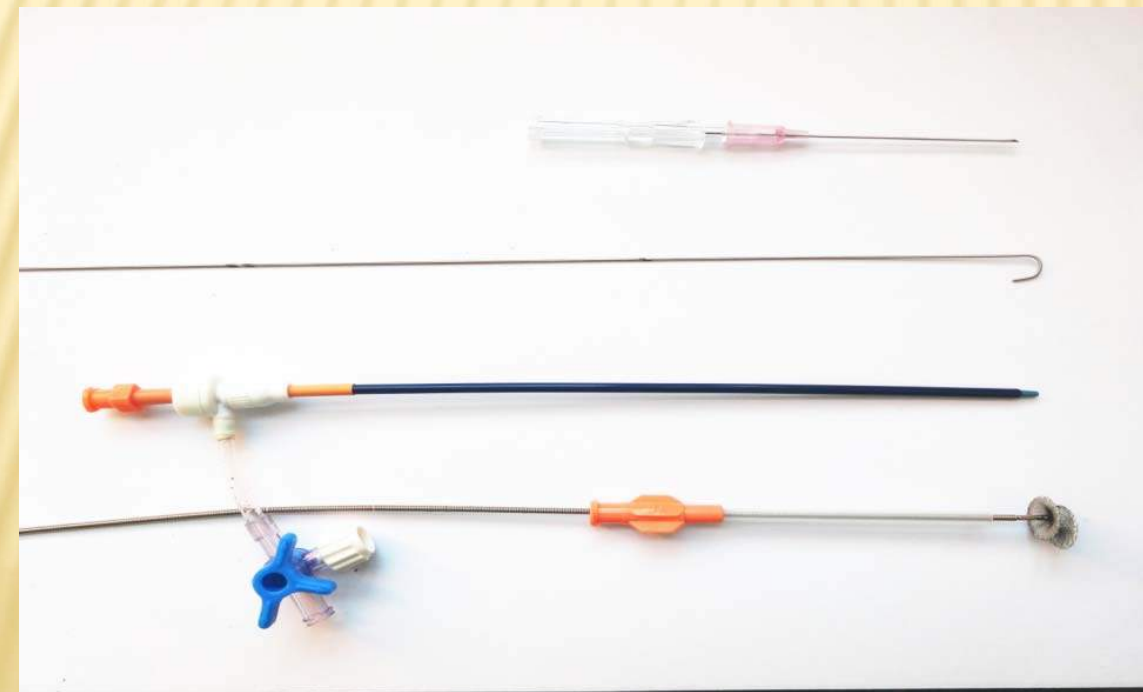
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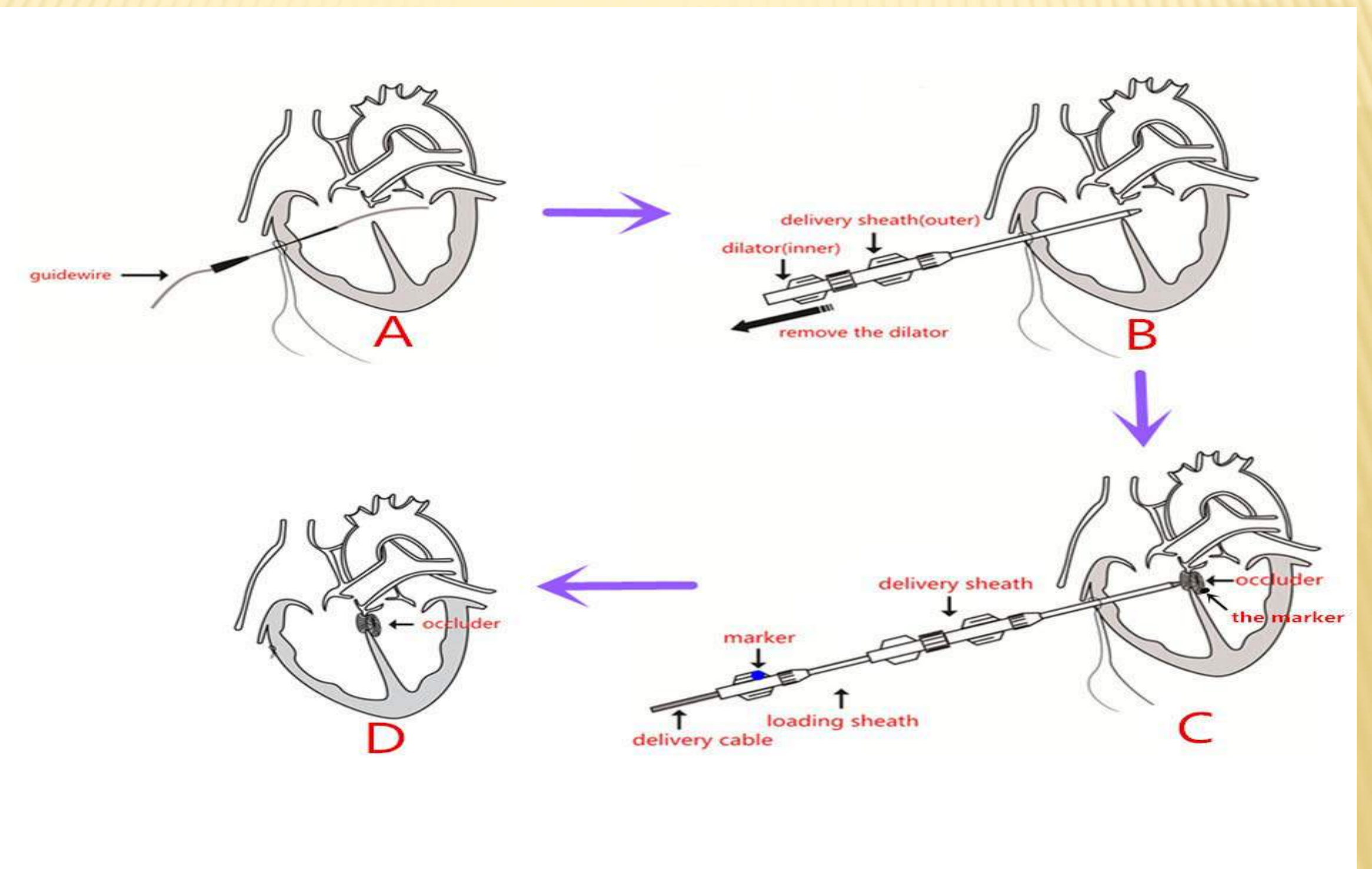
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THE PROCEDURE

- ✖ Minimally invasive transthoracic device closure of VSDs (MITDC)
- ✖ Hybrid technique surgical repair and transcatheter closure
- ✖ Device
- ✖ Delivery set



THE PROCEDURE



QS Xing, Q Wu, L Shi, YH Xing, GL Yu

Heart Center, Qingdao Women and Children's Hospital
Qingdao University

P. R. China

many less long term complications
no radiation



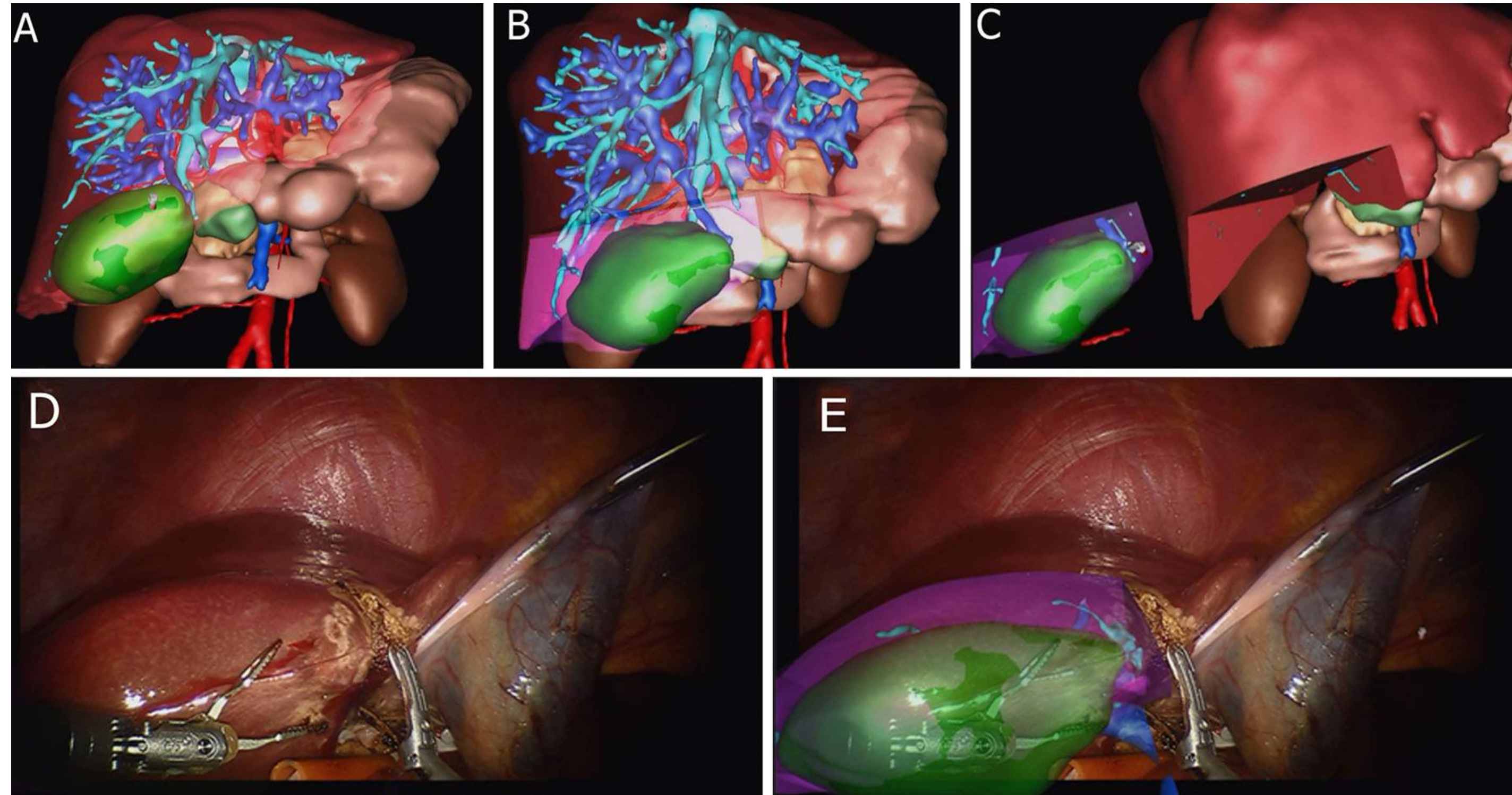
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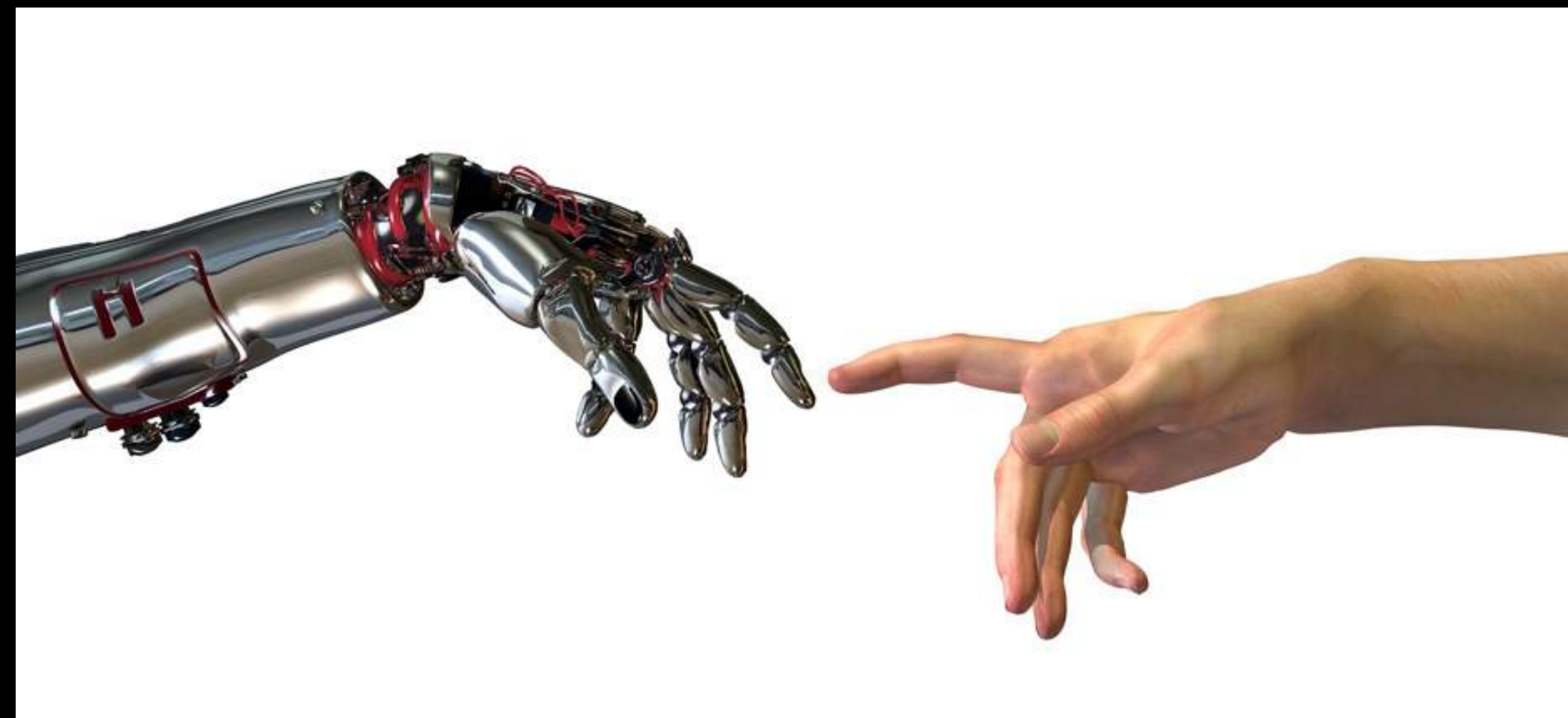
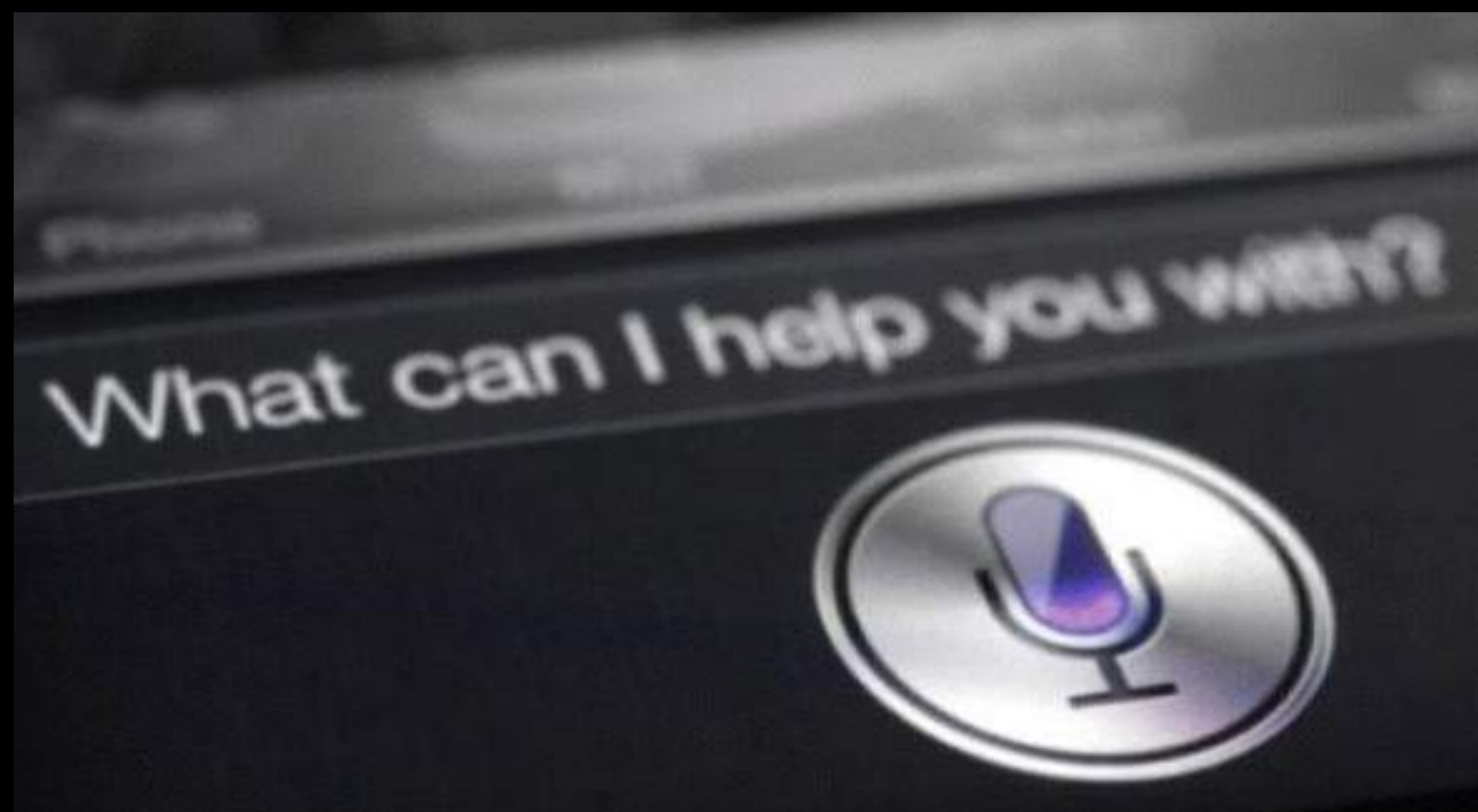


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Augmented Reality

VR-Render Software





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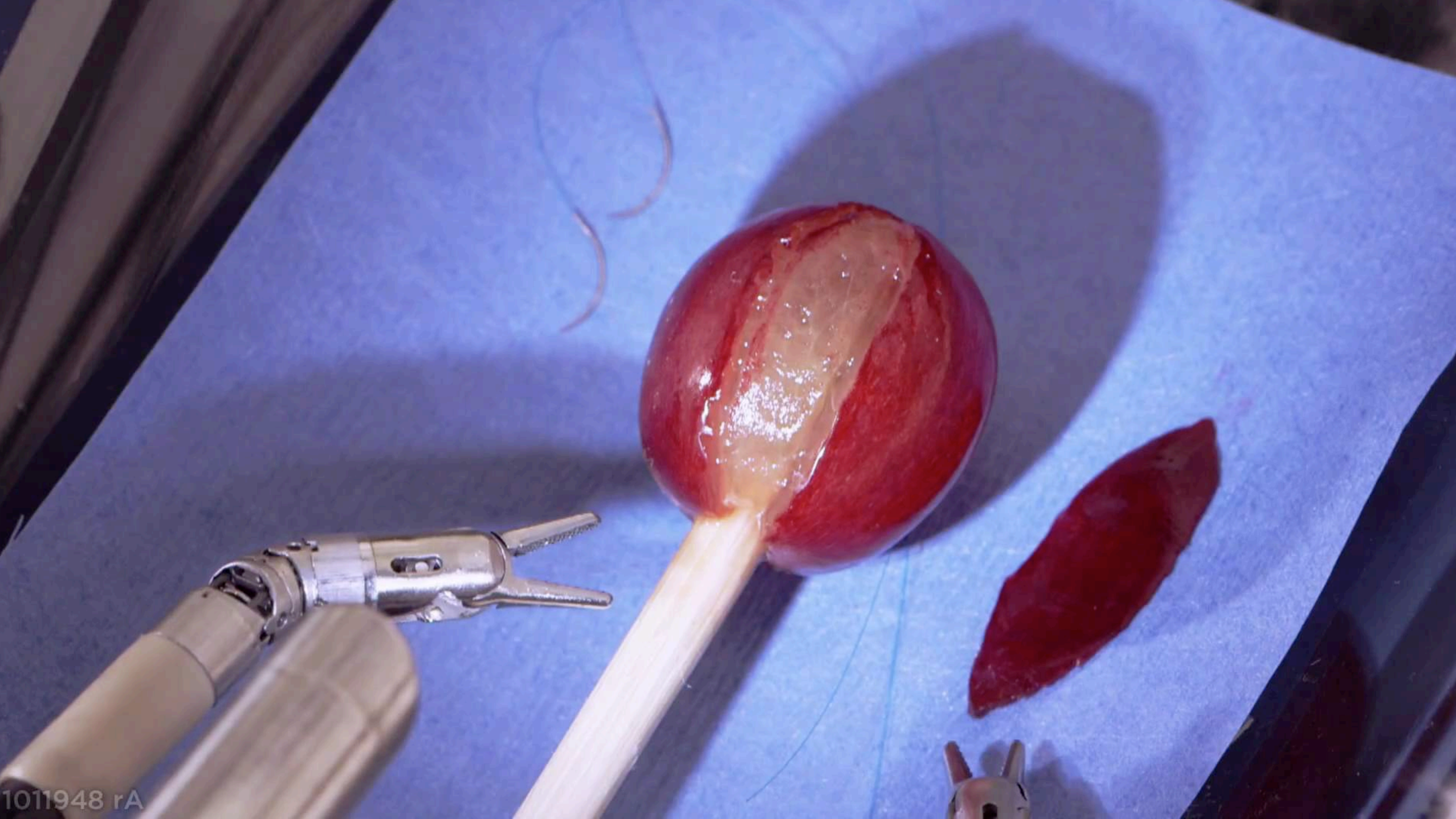
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Think About It



This Woman Flew an F-35 Simulator with Her Mind

by BRENDAN MCGARRY on MARCH 2, 2015



<http://defensetech.org/2015/03/02/this-woman-flew-an-f-35-simulator-with-her-mind/>

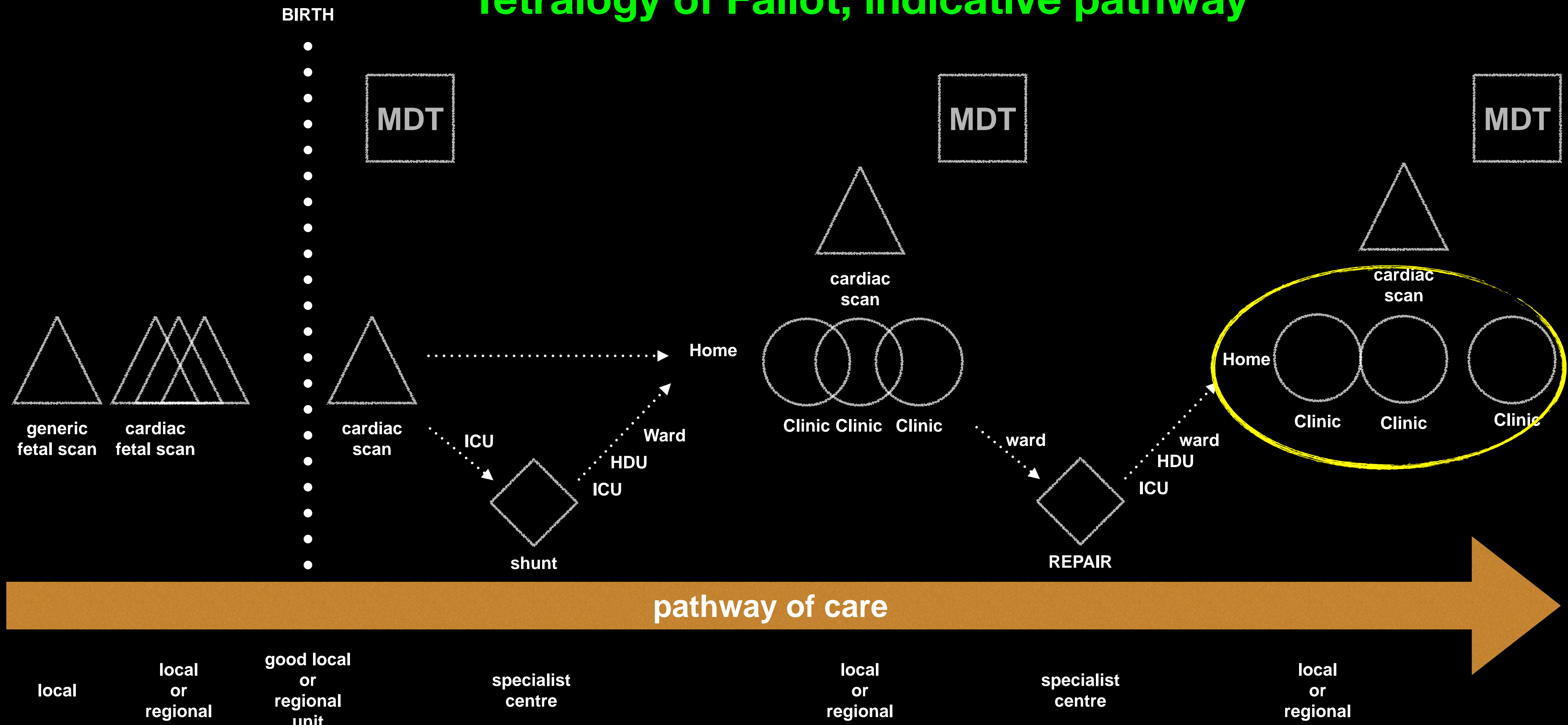


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Tetralogy of Fallot, indicative pathway



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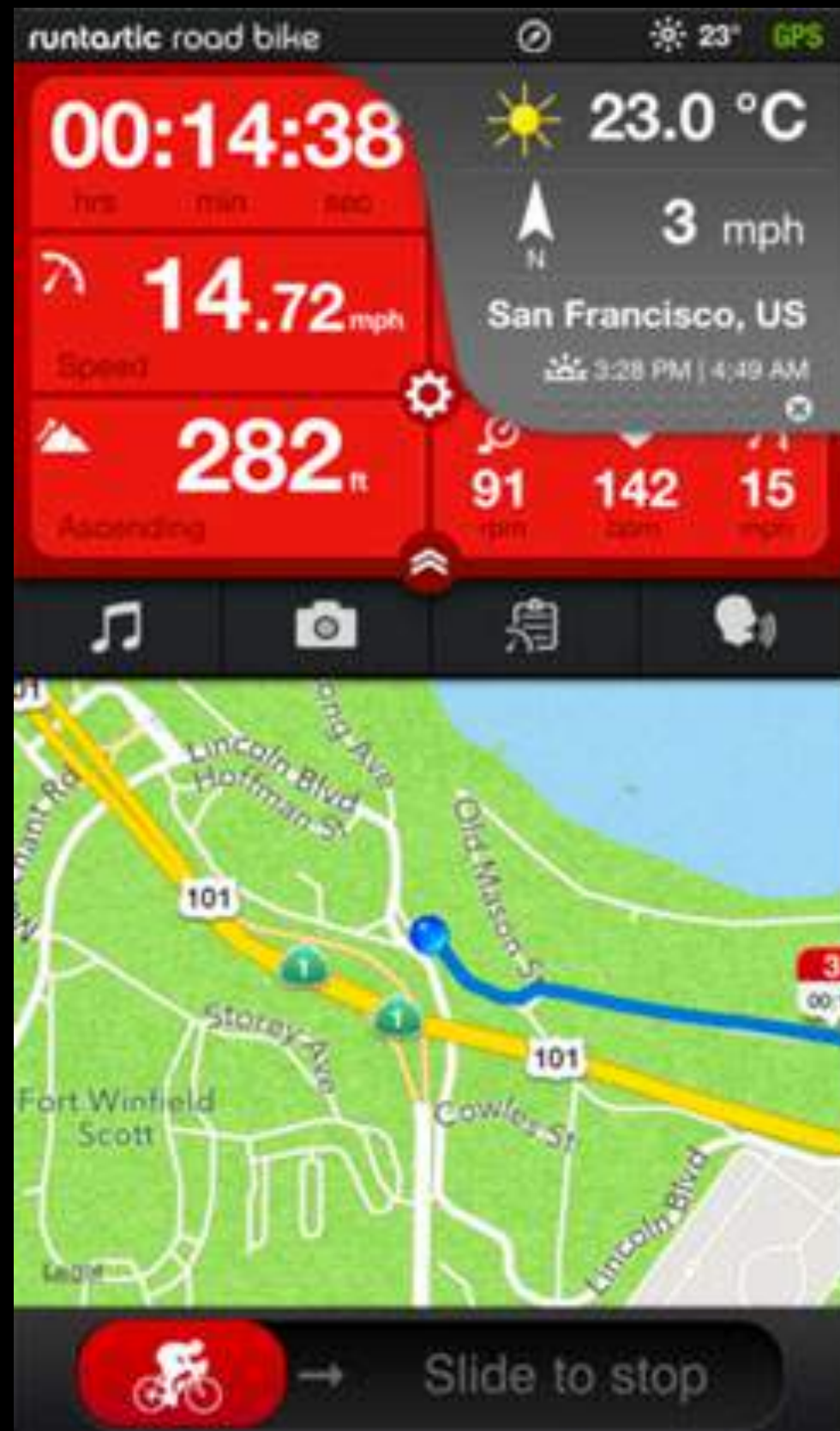
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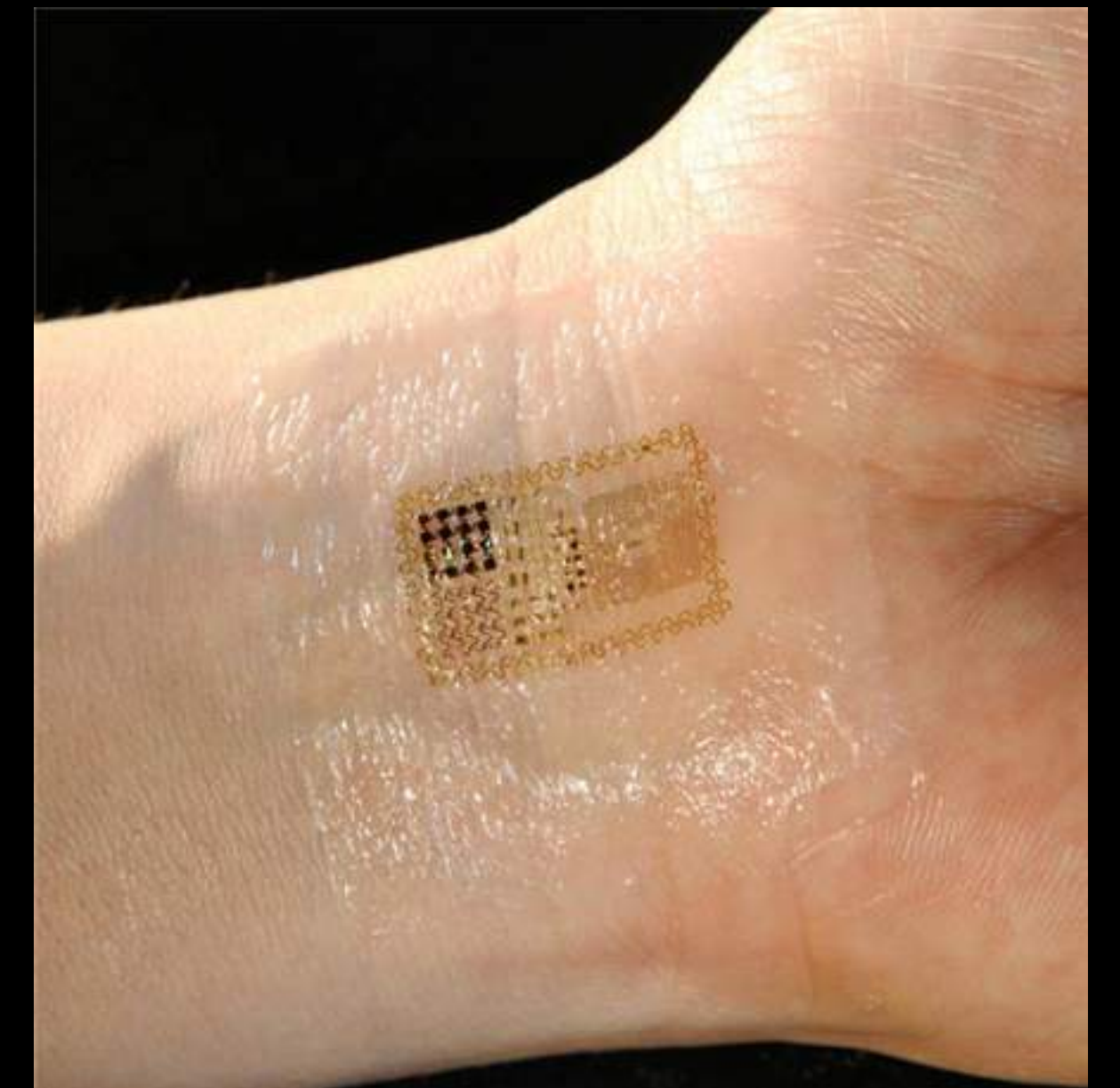
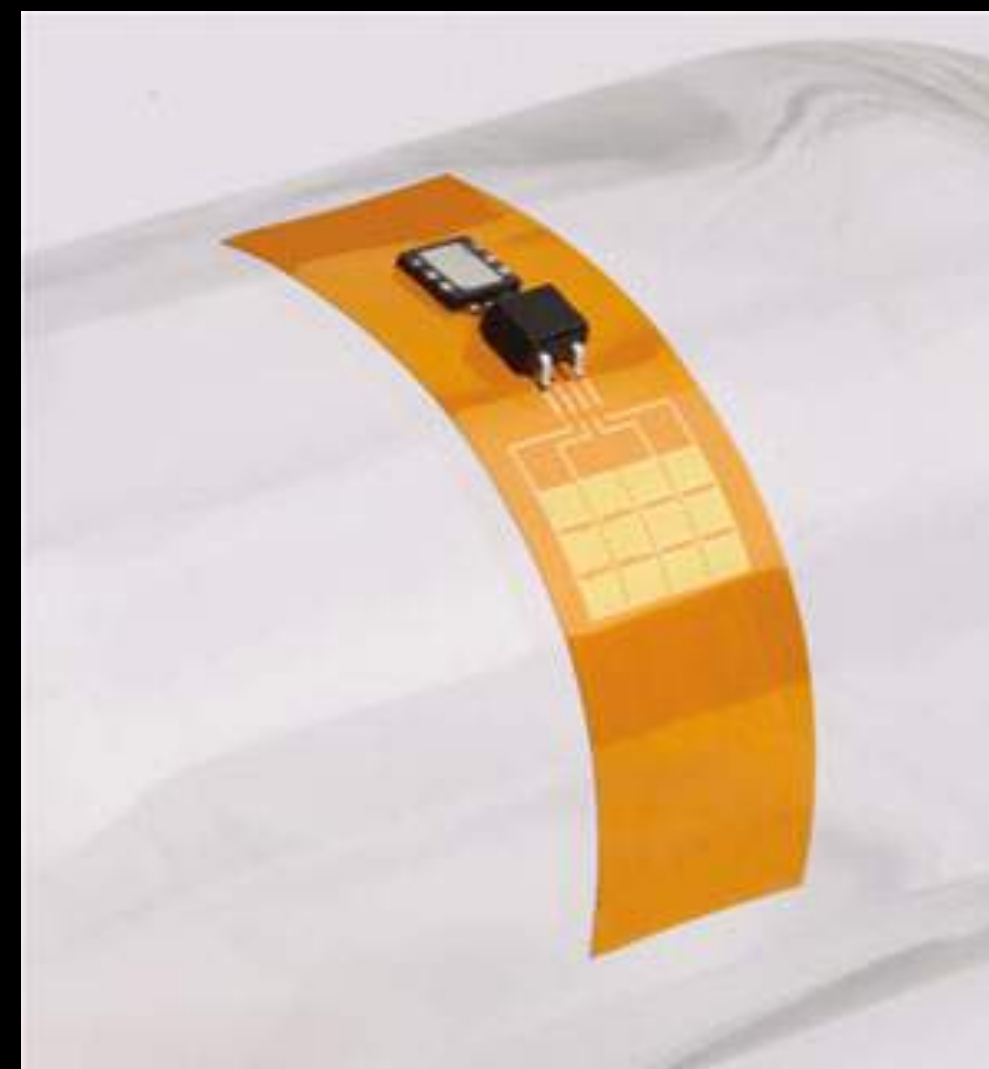
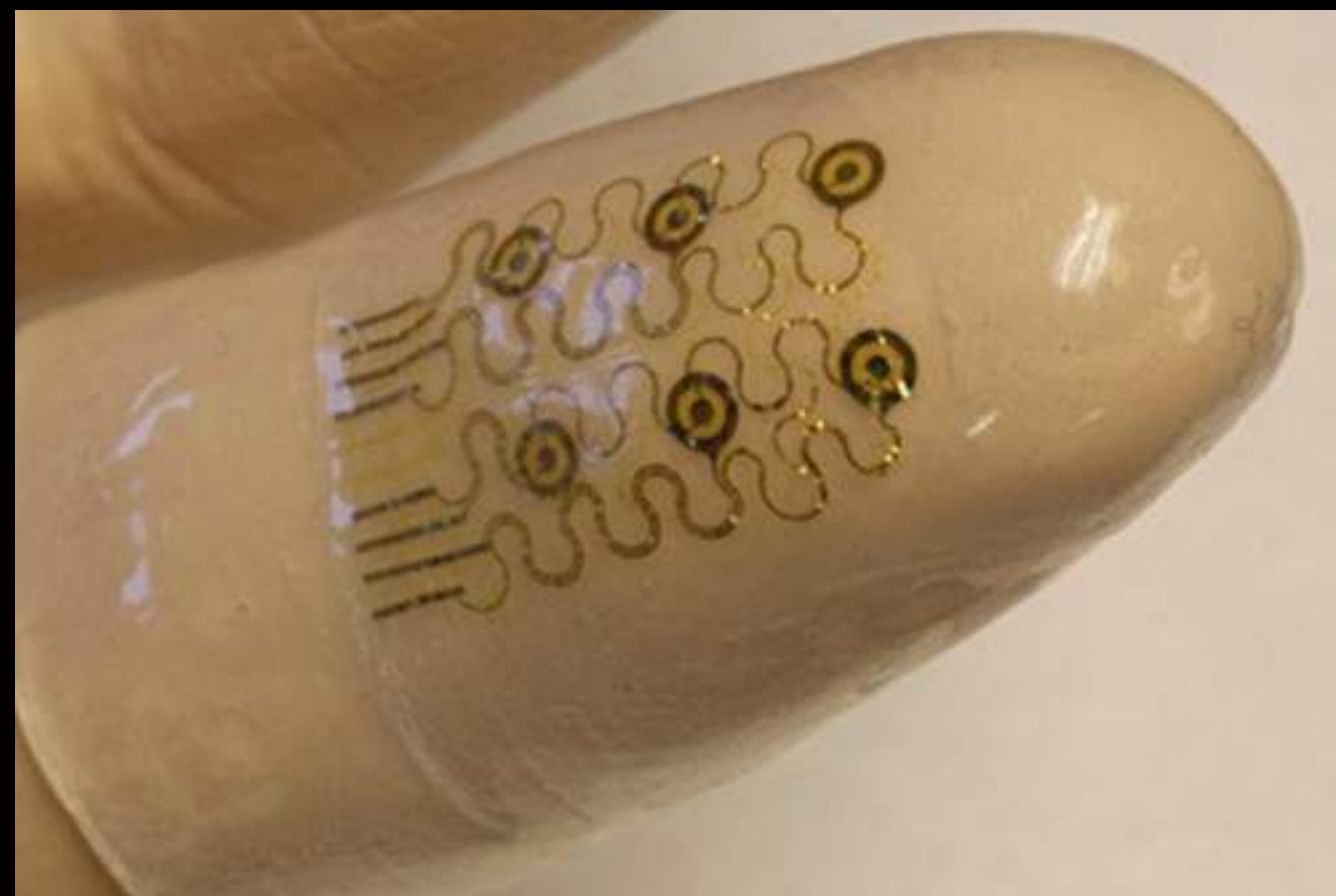
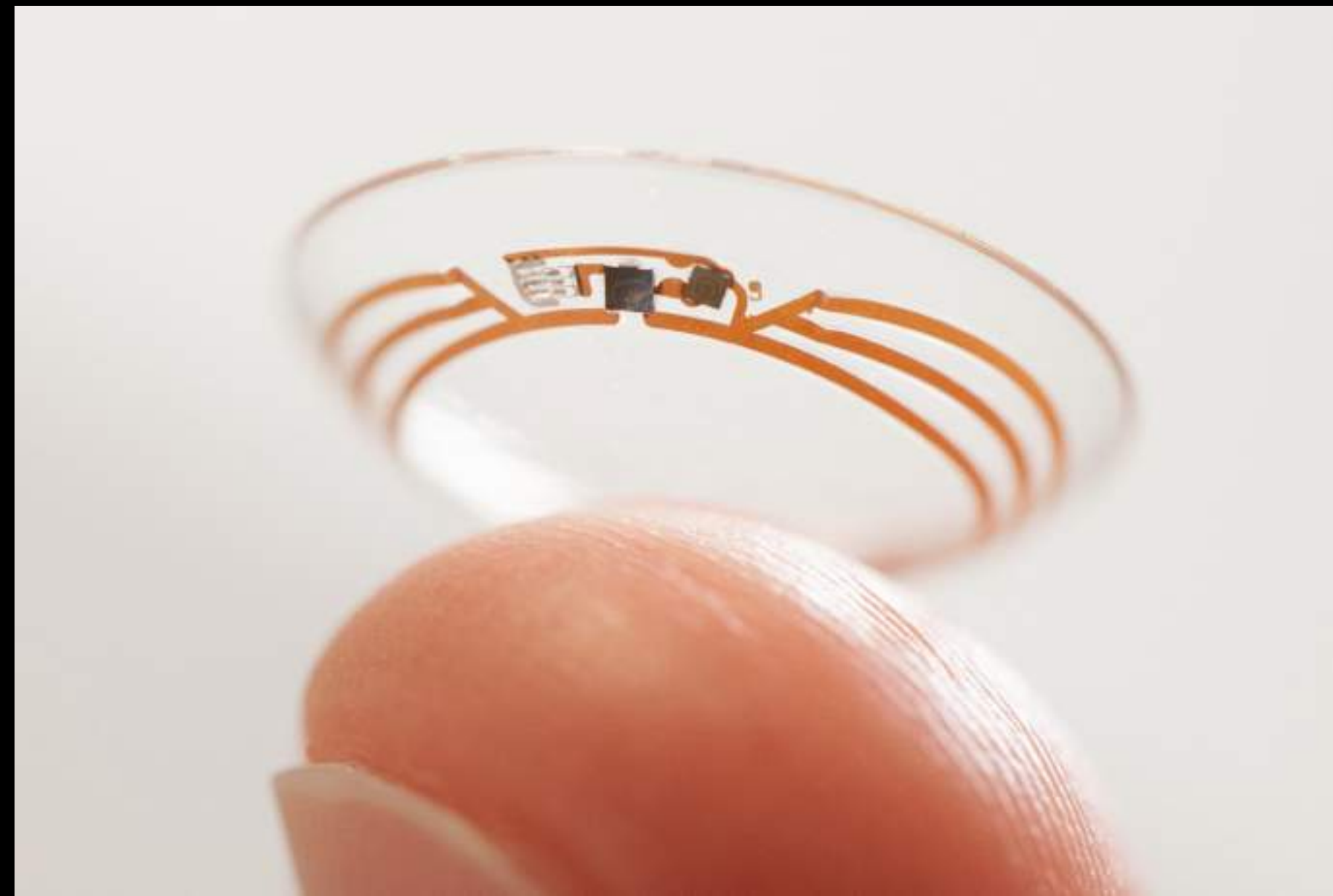
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C Dagdeviren et al, *Proc. Nat. Acad. Sci. USA*, 2013, DOI: 10.1073/pnas.1317233111



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+ GPS

Single-Lead ECG
Heart Rate
Heart Rate Variability
Respiratory Rate
Skin Temperature
Body Posture including Fall Detection/Severity
Steps



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\$10,000,000



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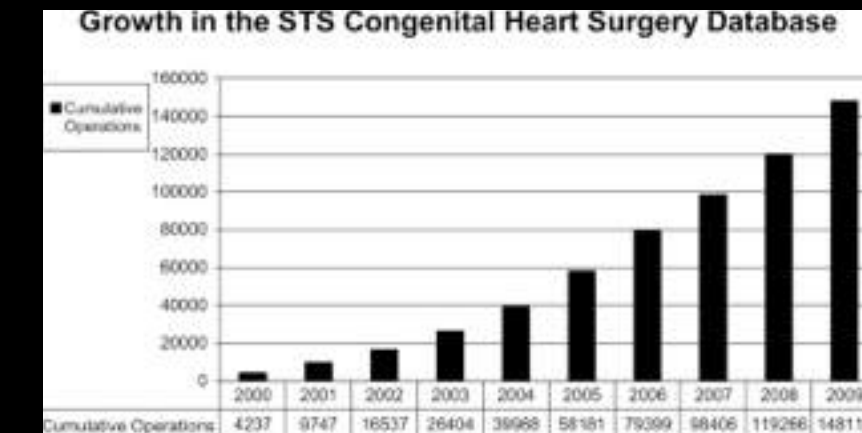
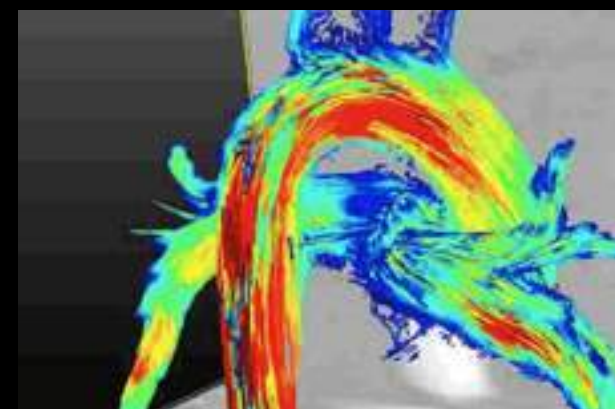
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big data in medicine



EPR-sourced data

machine-sourced data



registry data

patient-sourced data



the measure

hospital at home, less need for outpatients, more data



real outcomes

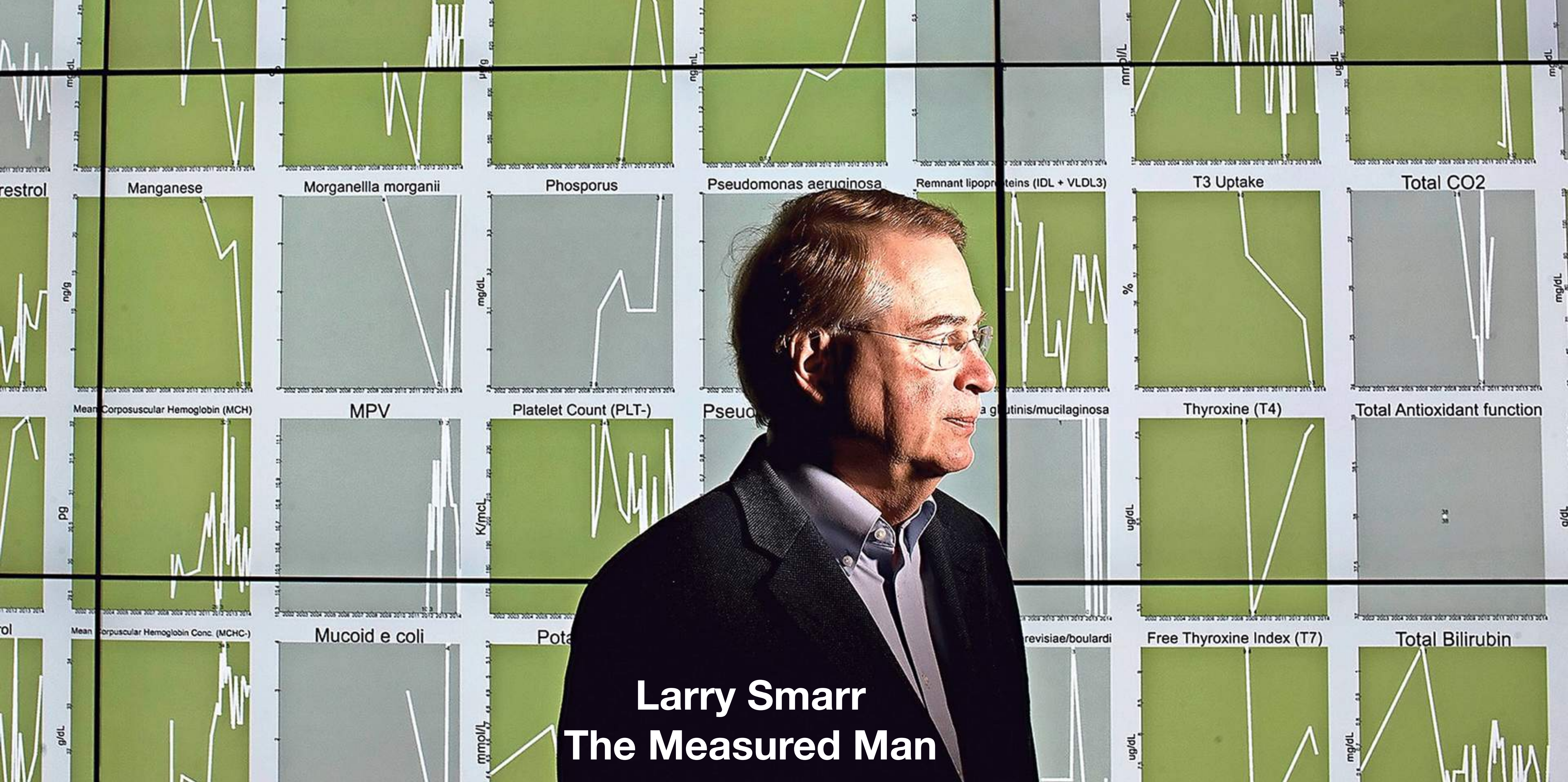
time



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Larry Smarr
The Measured Man



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I know where you are

I know what you are doing

I know how you are

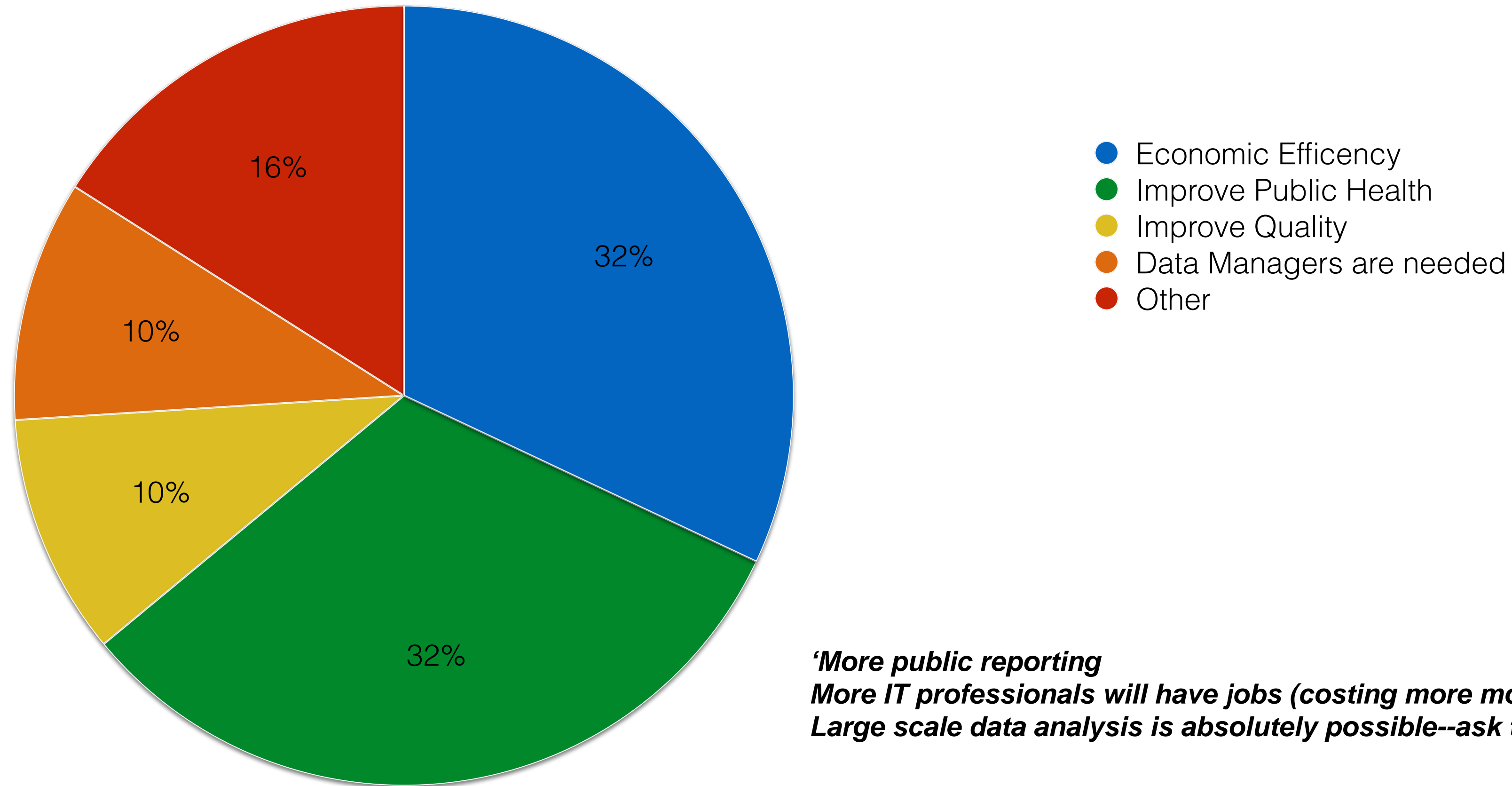


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What is coming next in the field of Data?



***'More public reporting
More IT professionals will have jobs (costing more money)
Large scale data analysis is absolutely possible--ask the NSA'***

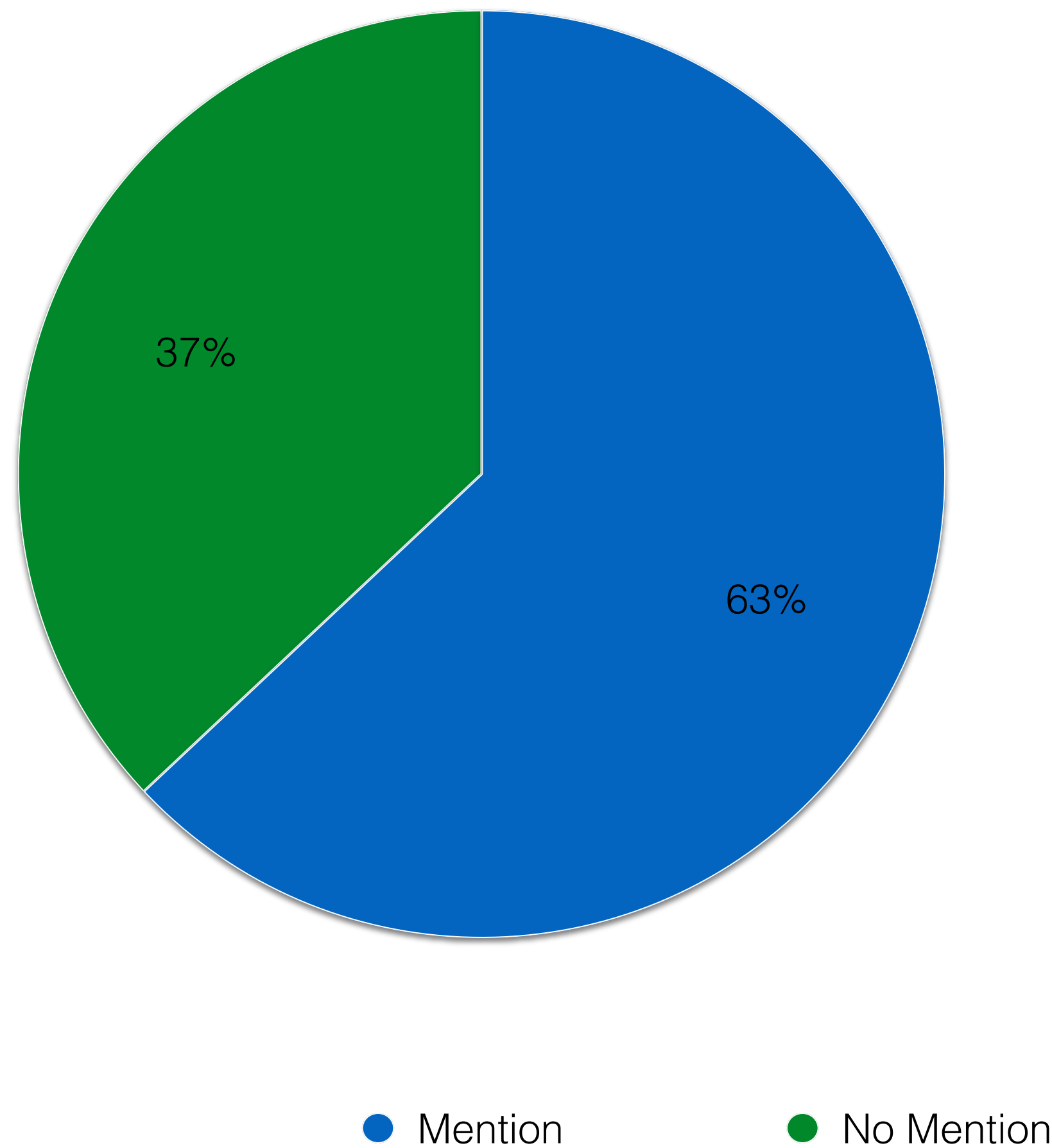


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Simulation

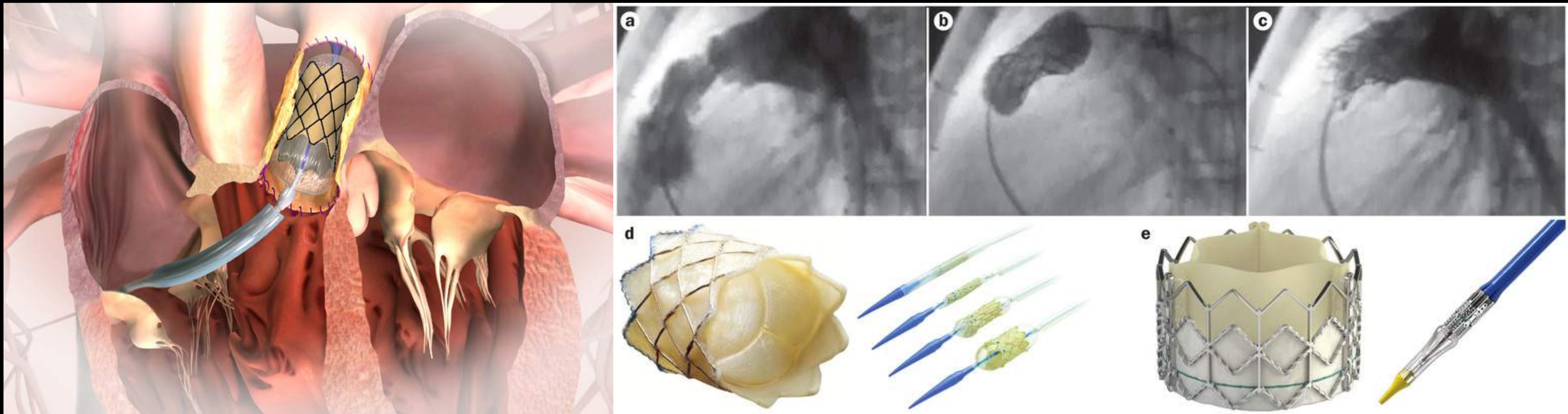


The **days of trial and error** in learning may be over.

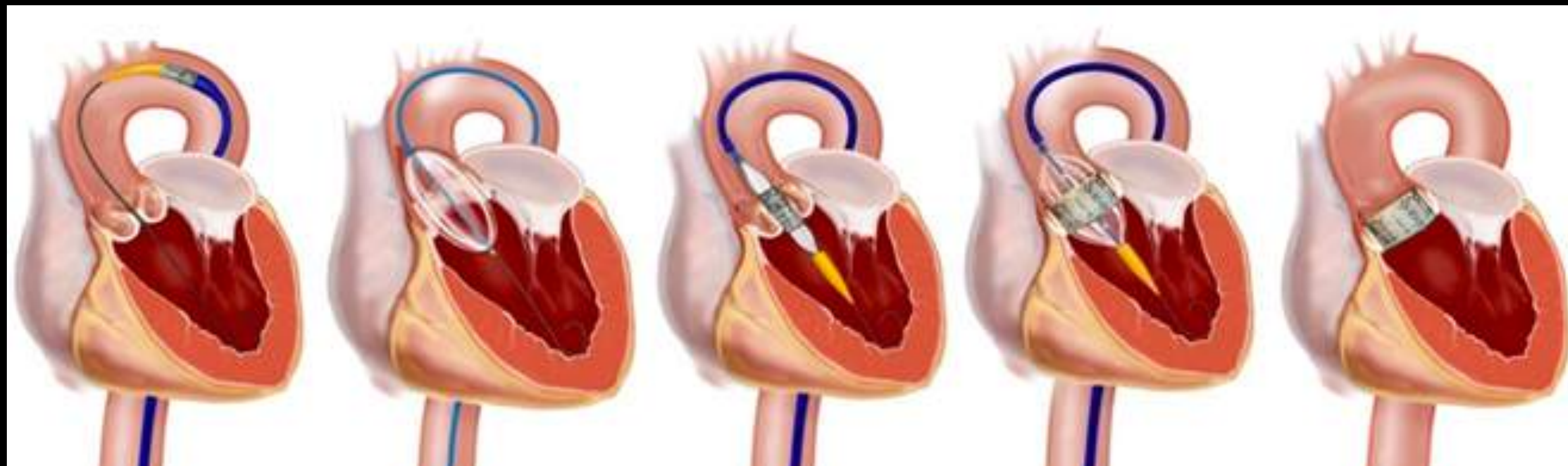
The system and patients **will not tolerate a learning curve.**

Training in simulators ... **will be necessary.**





Trans-Catheter Insertion of Heart Valves



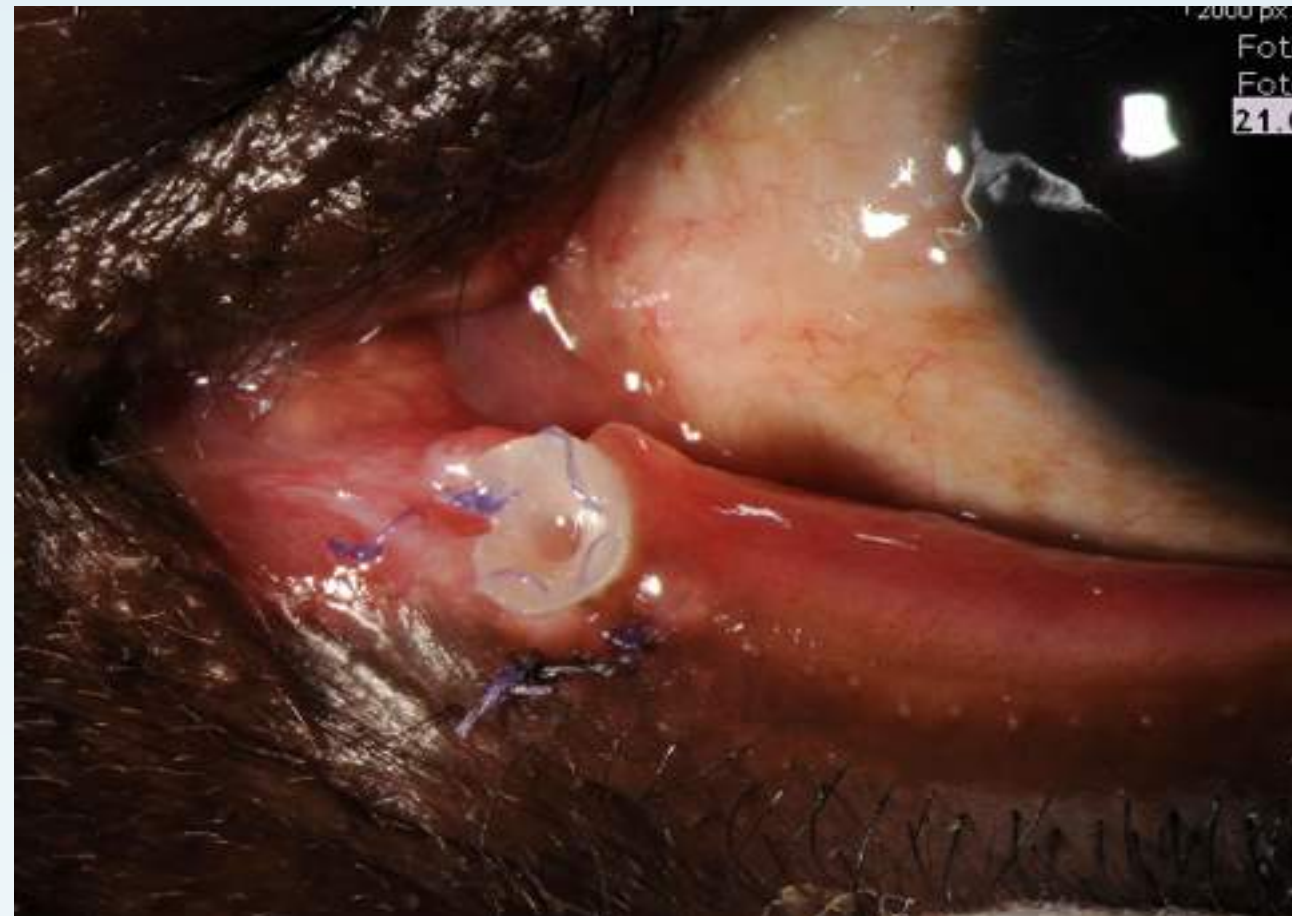
>100,000



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Lacrimal Duct
- Transplanted into Human

POSS PCU Current Applications



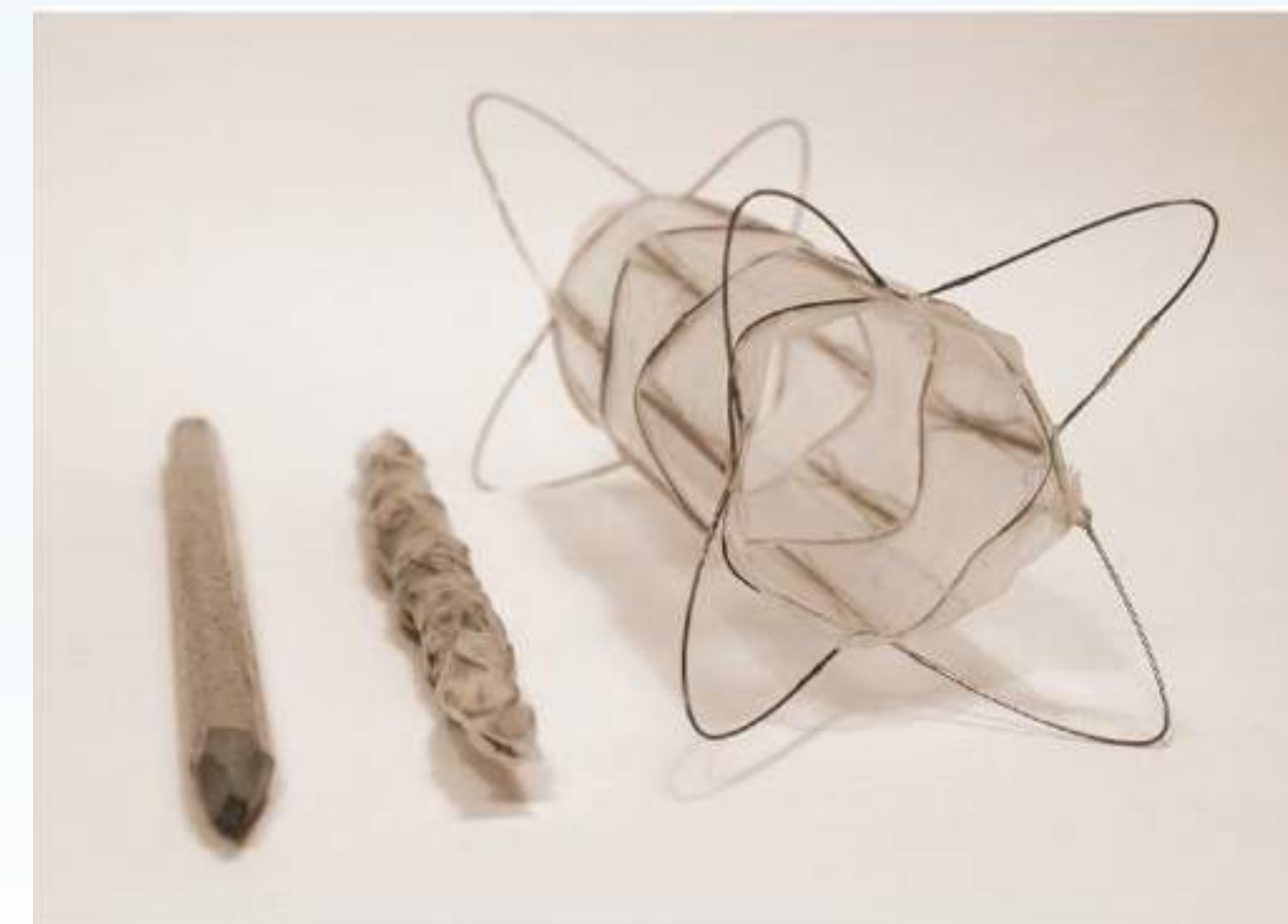
Coronary artery bypass grafts
- Pre clinical trials



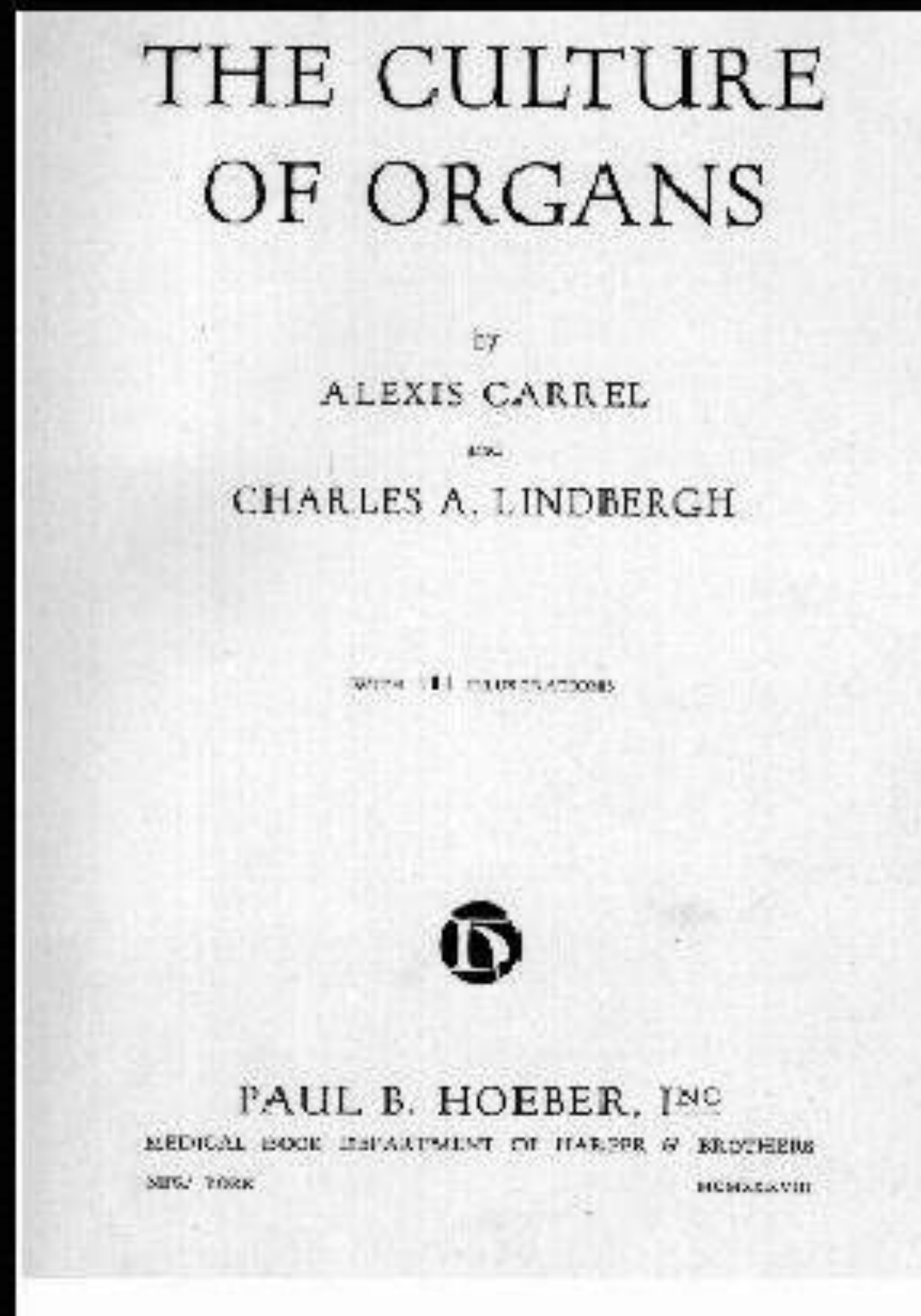
Heart Valves
- Pre clinical study



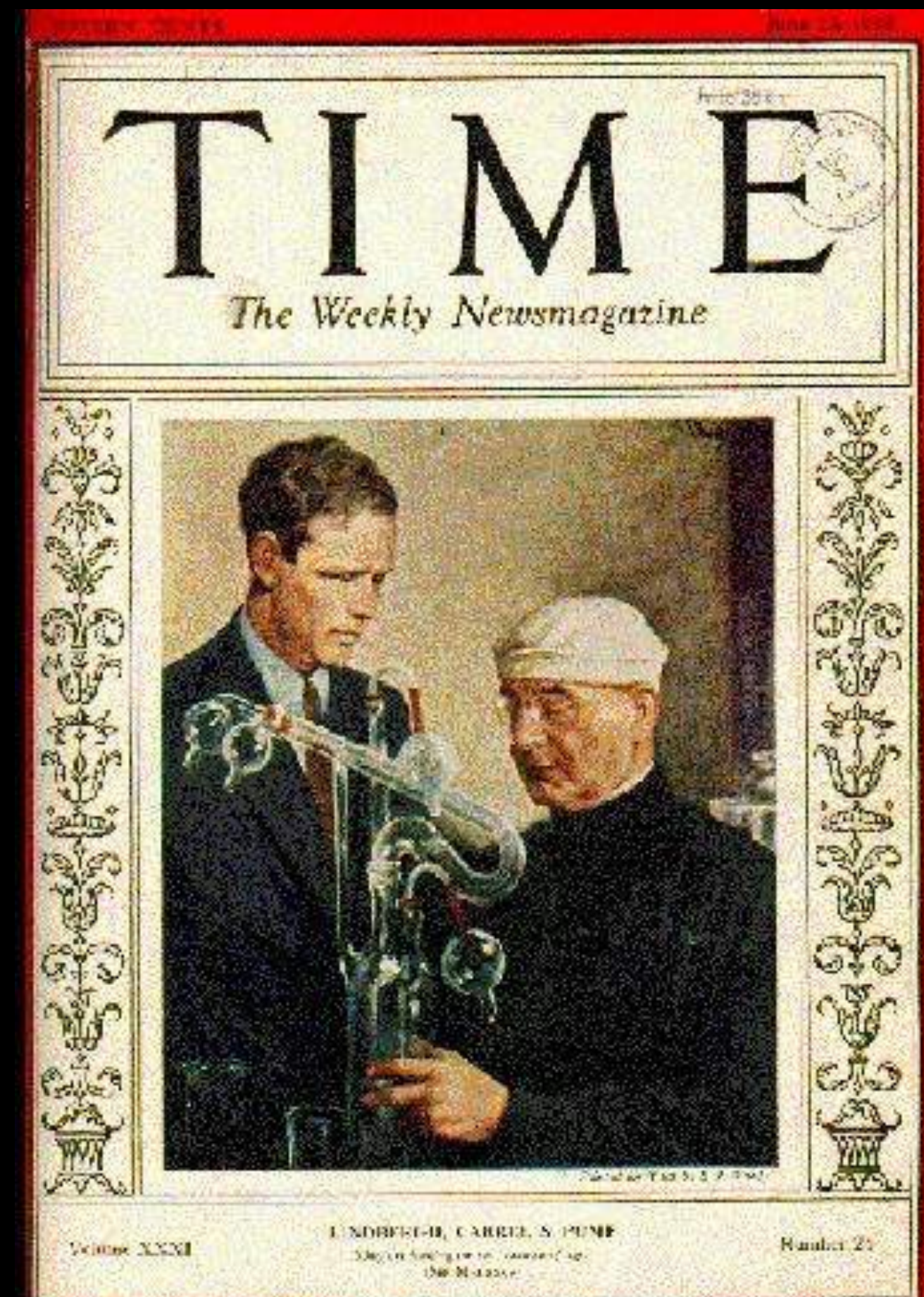
Nasal Reconstruction
- Pre clinical study



Stents
- Pre clinical study



1938



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What is a stem cell?

A single cell that can

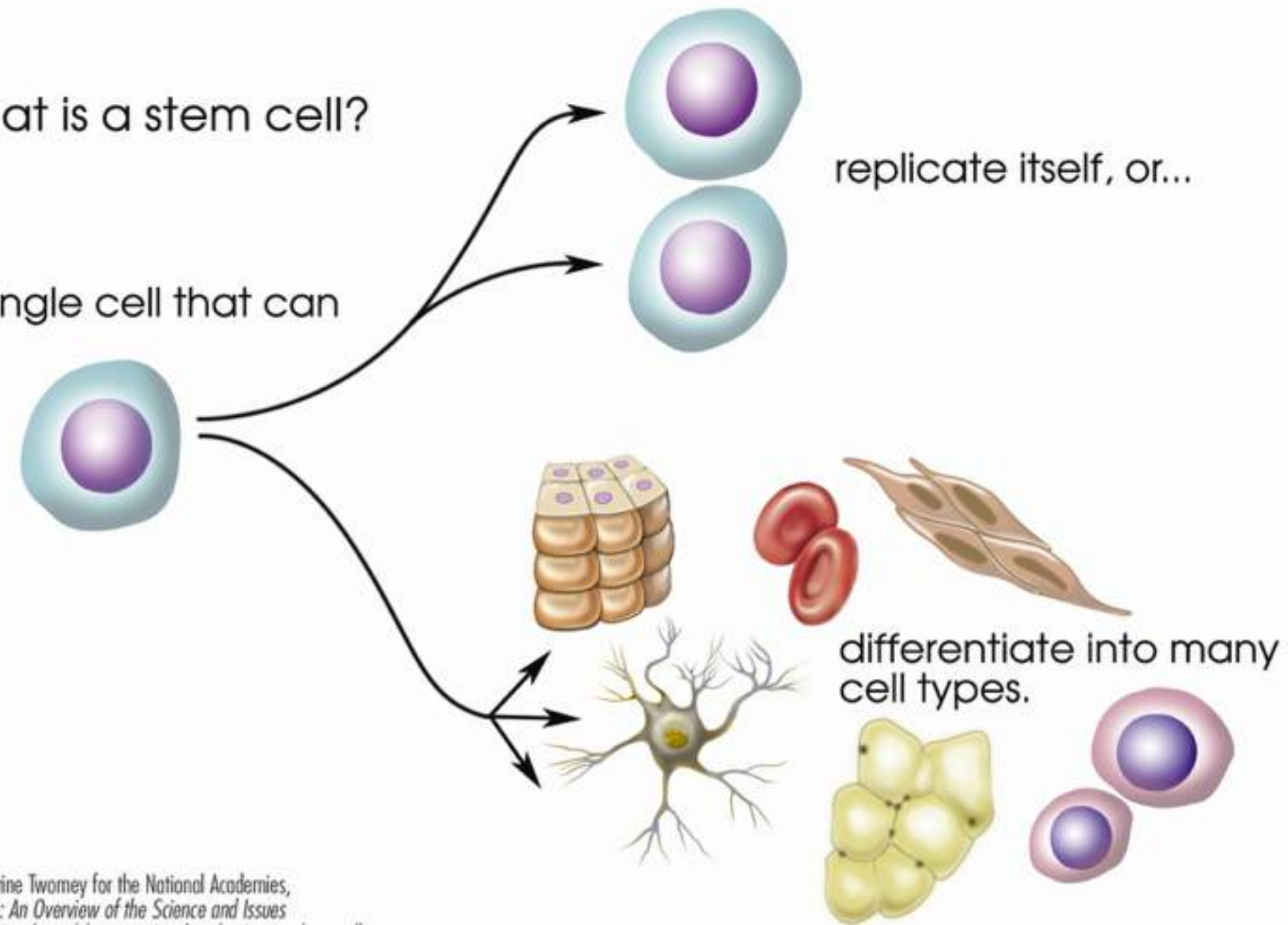
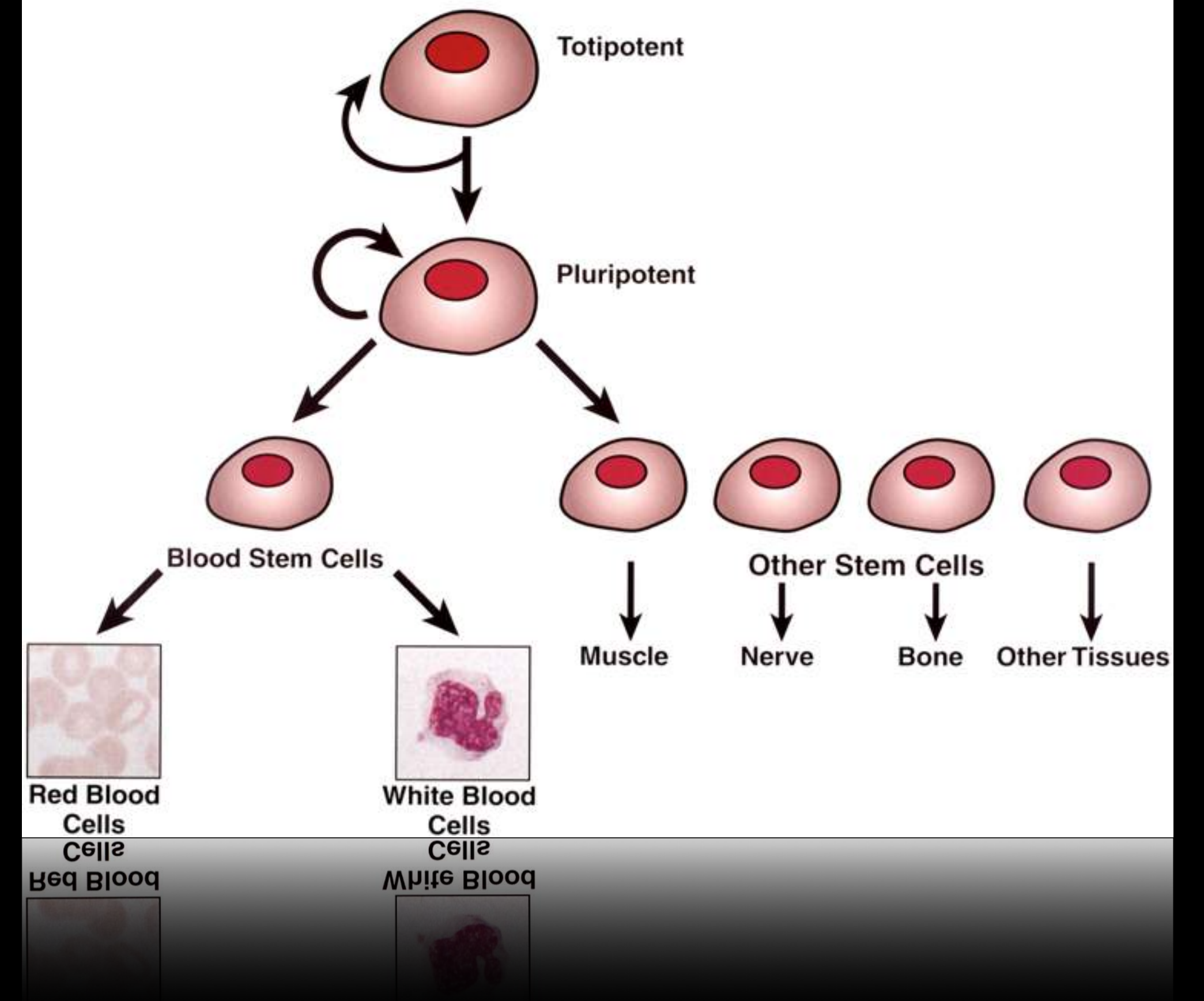


Image prepared by Catherine Twomey for the National Academies, *Understanding Stem Cells: An Overview of the Science and Issues* from the National Academies, <http://www.nationalacademies.org/stemcells>. Academic noncommercial use is permitted.

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Hierarchy of Stem Cells



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Ciaran, and his amazing mother, Colleen

always in the first 10

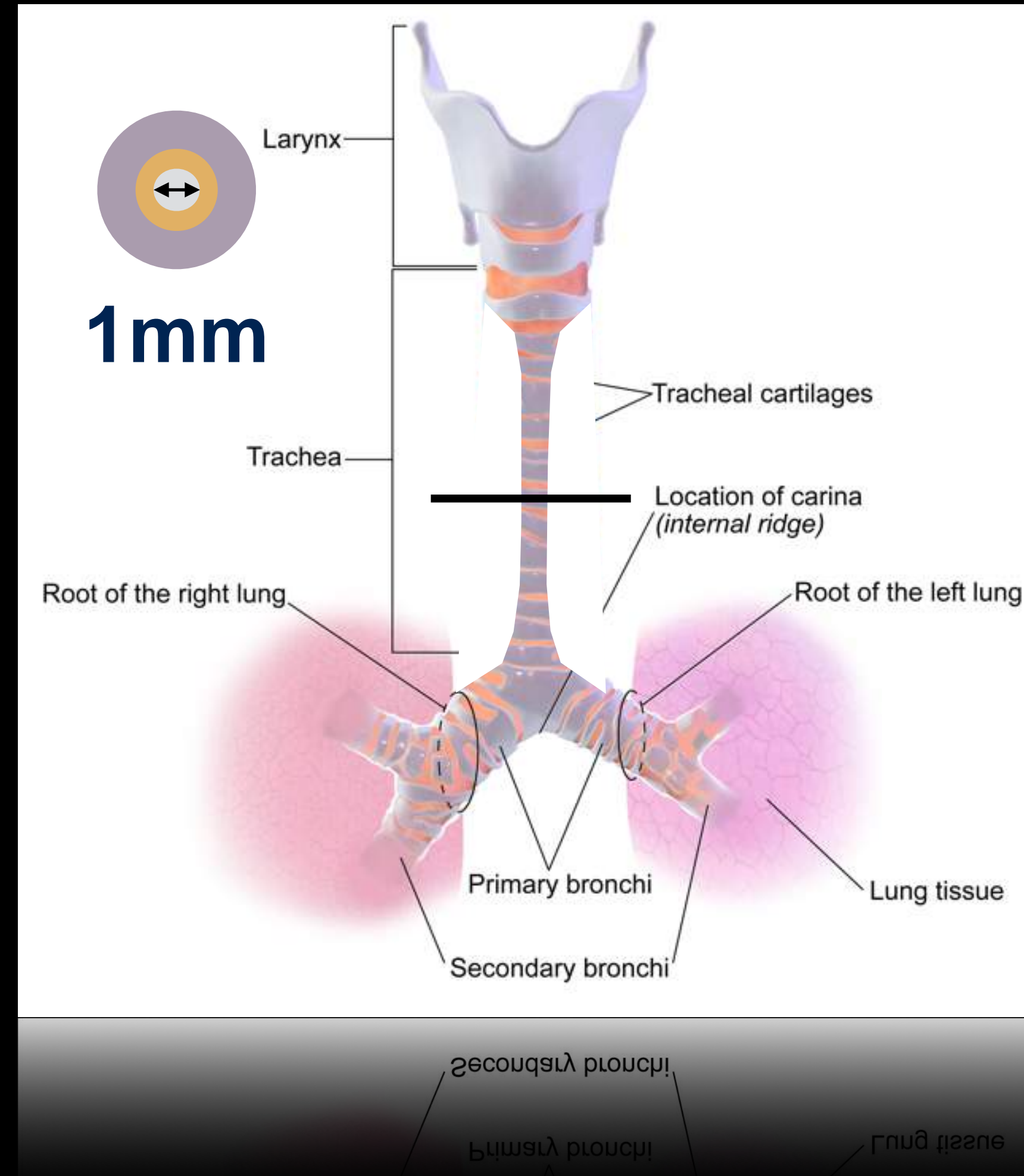


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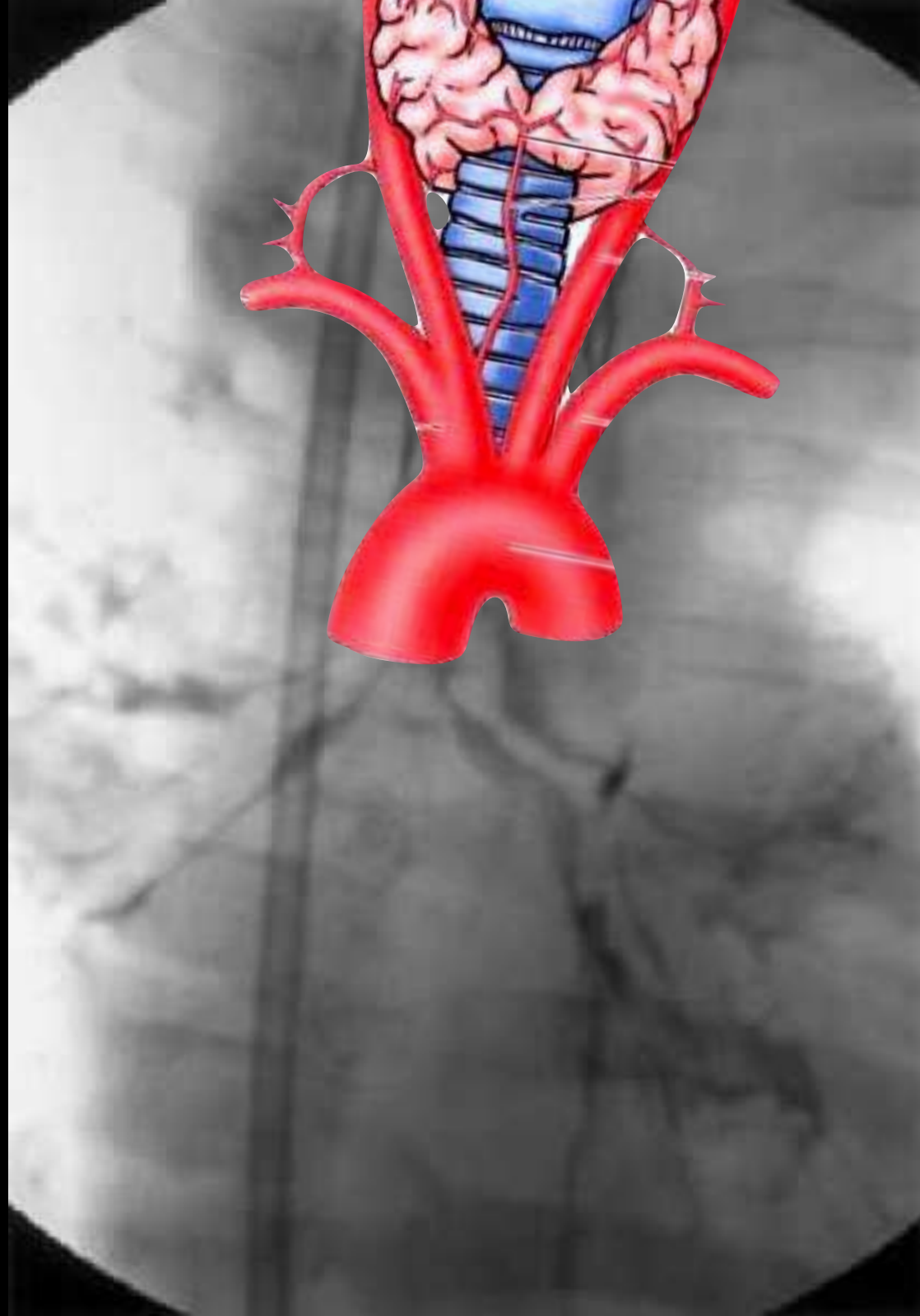
The Trachea



long segment congenital tracheal stenosis



age 3 years

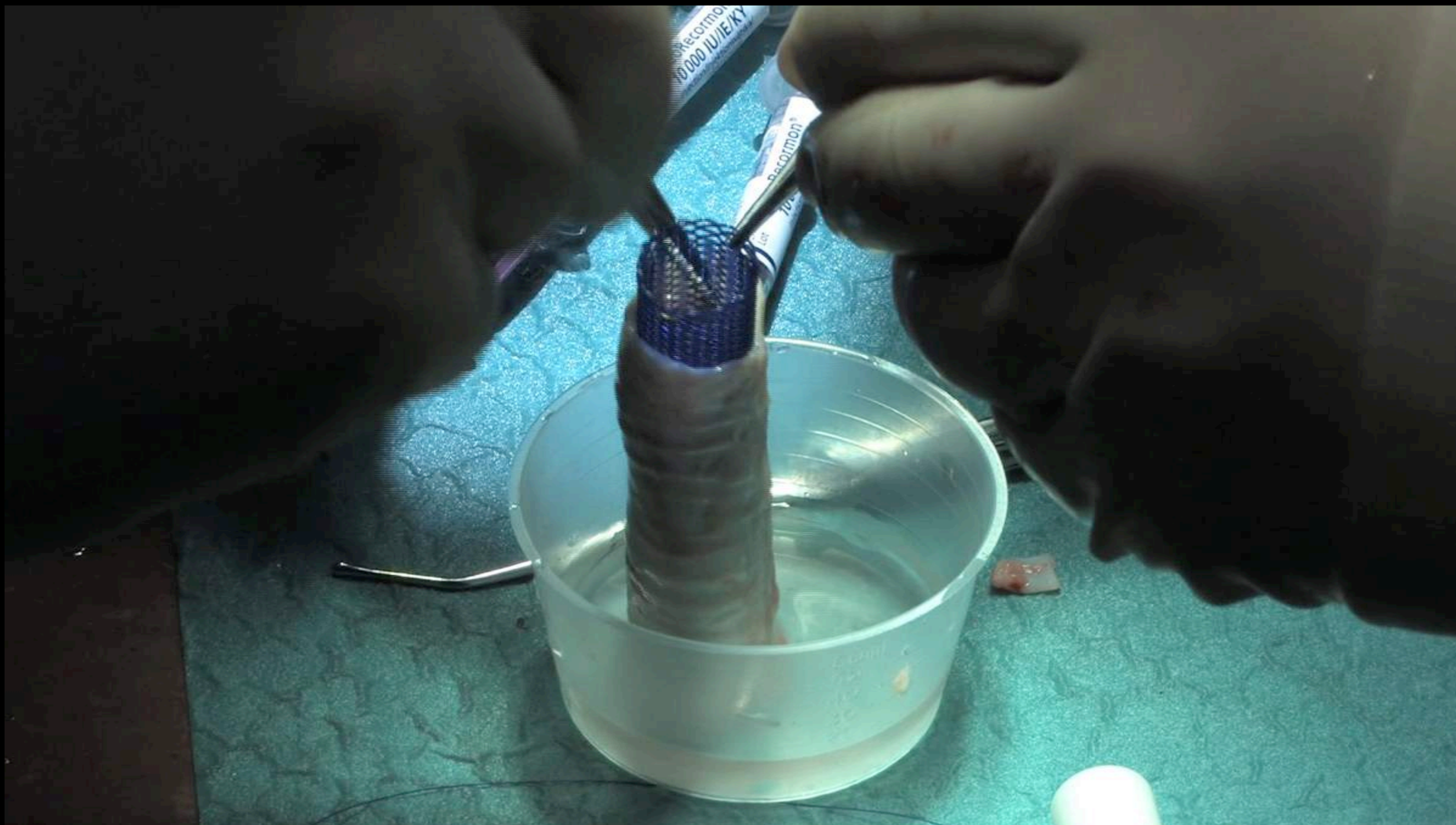


in the first 2

Stem-cell Supported Tracheal Transplant

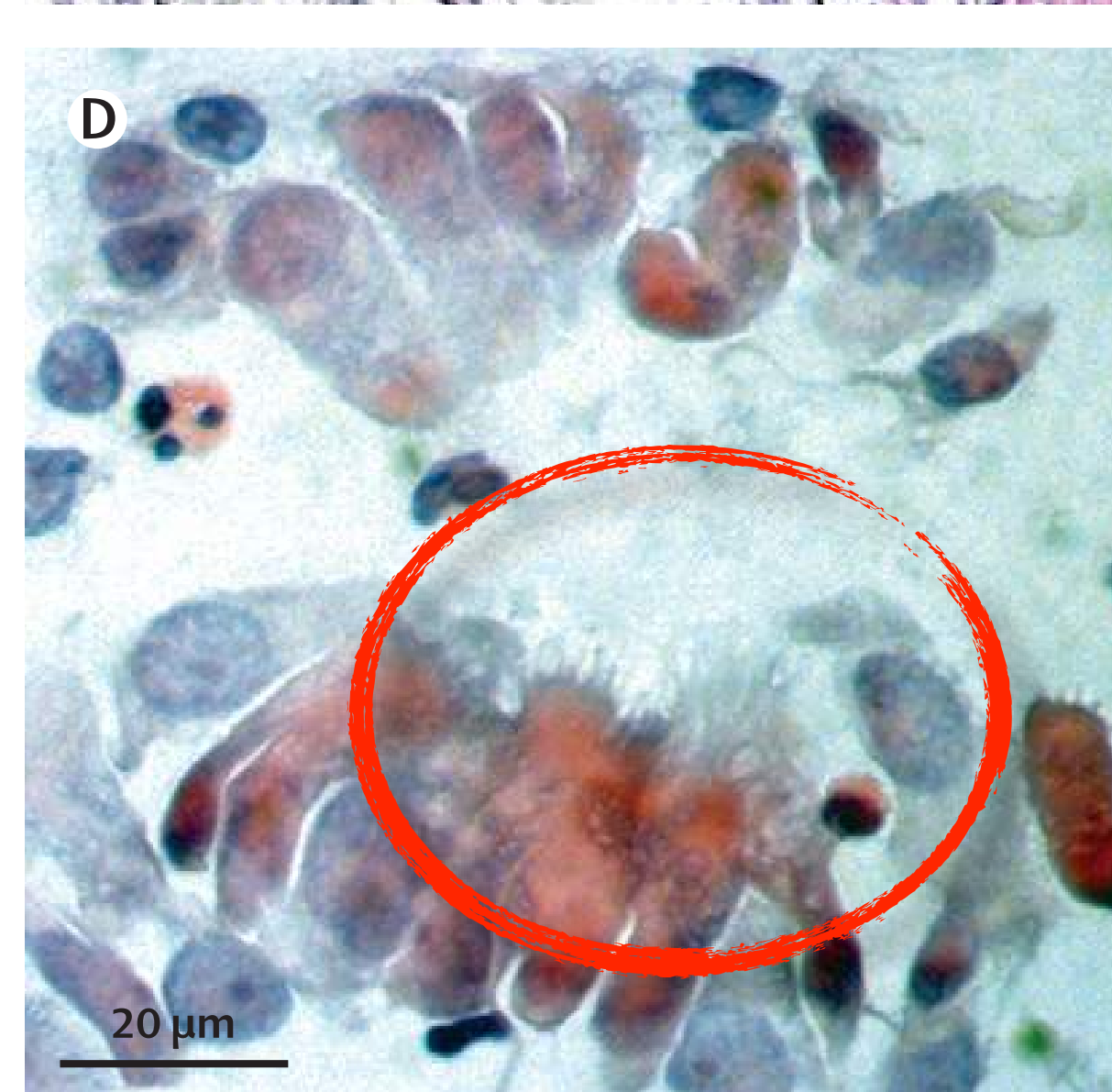
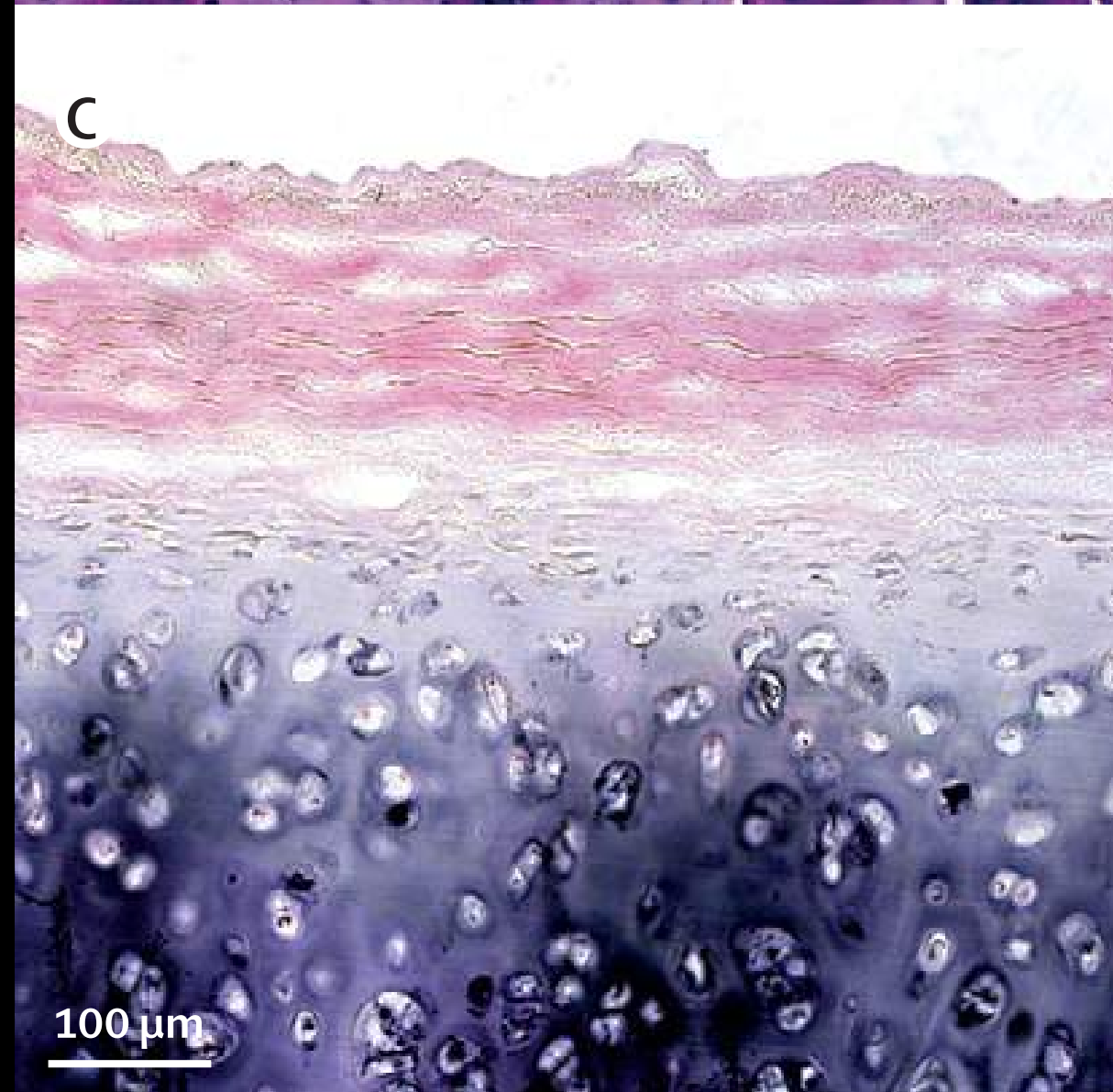
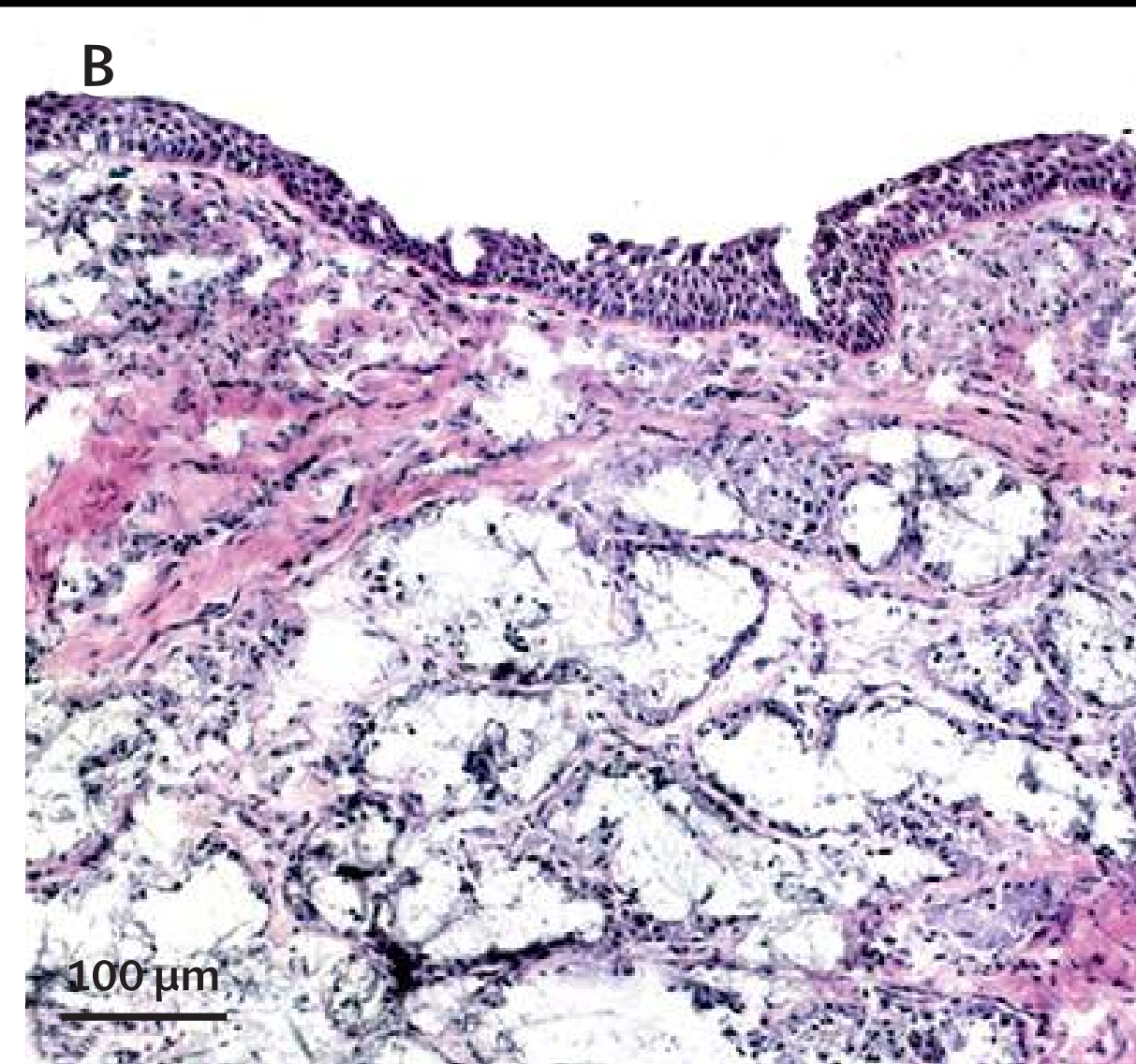
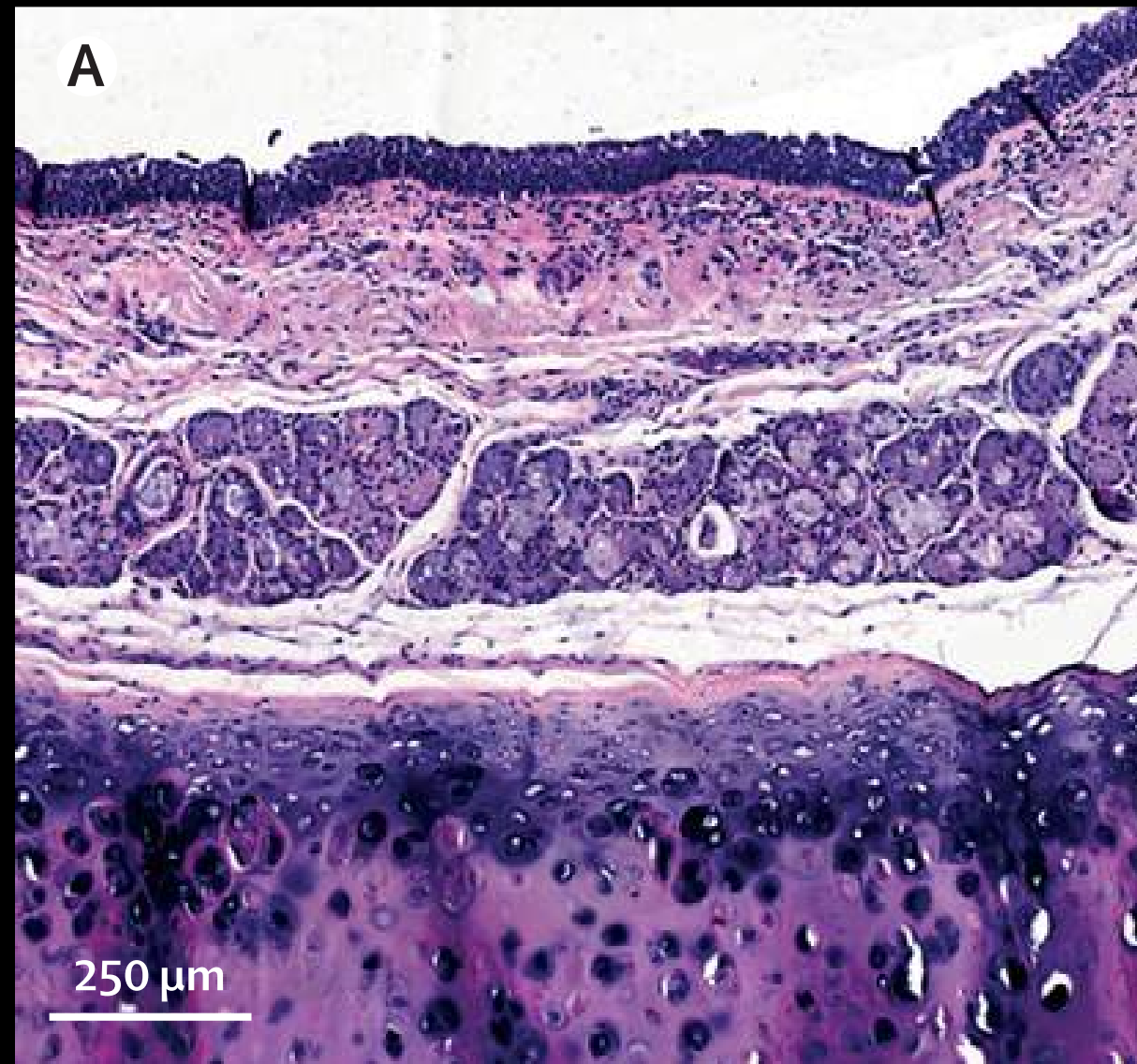


1st in a child



1st stem cell transplant

In 1st 10 absorbable stents



cilia



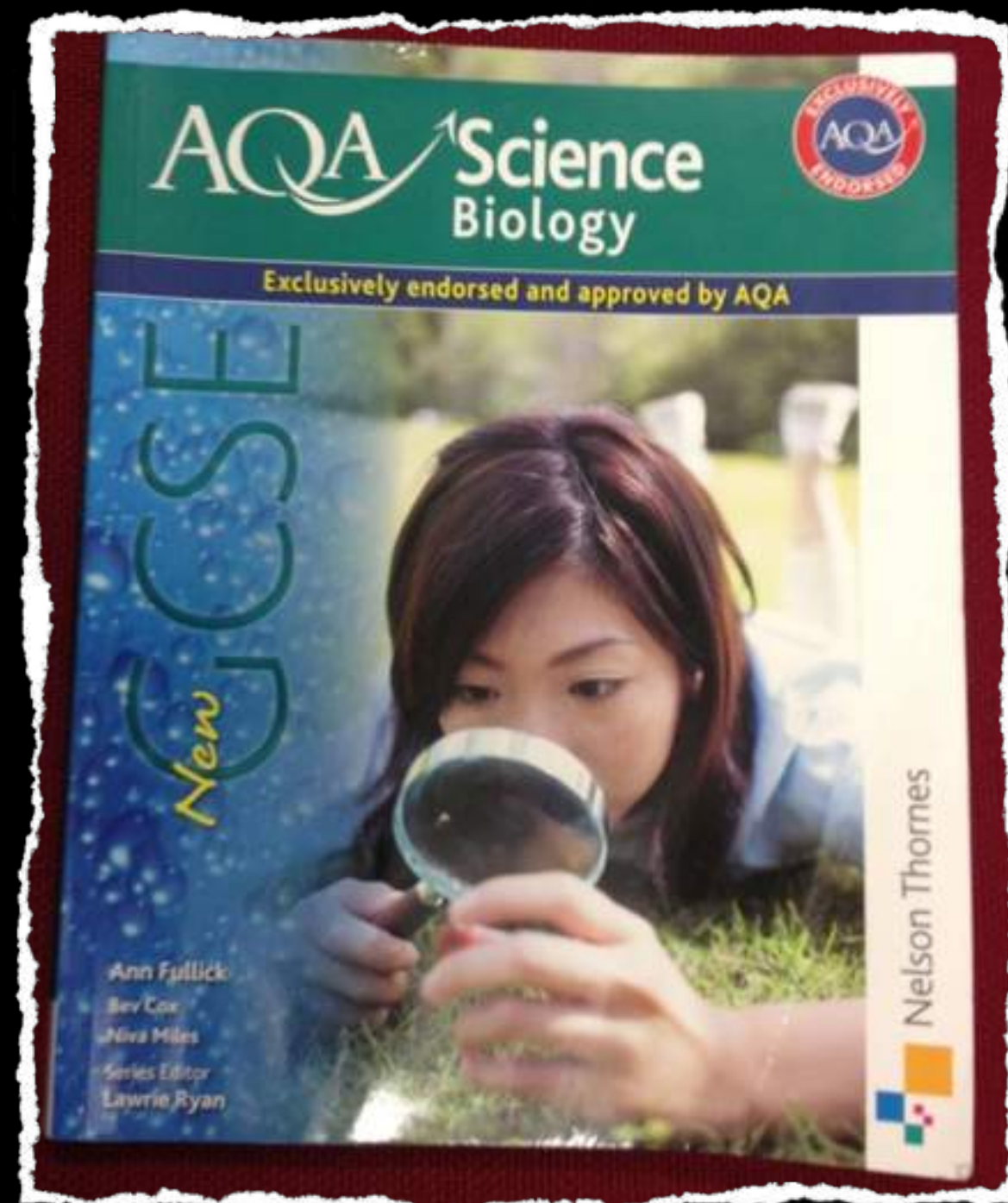
Irish Child of Courage 2012



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GCSE Textbook 2012



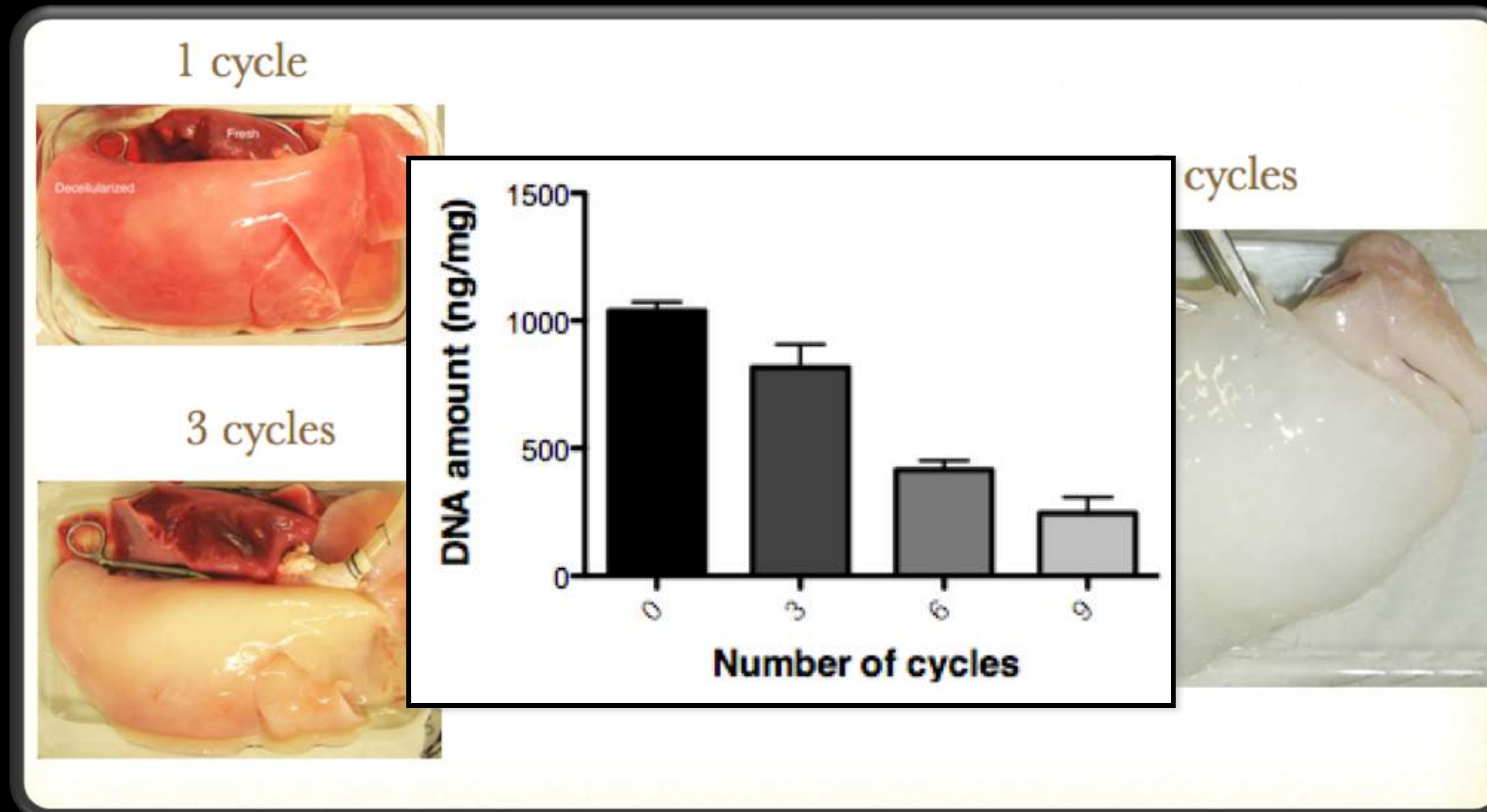


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Decellularised sheep lung



Paolo di Coppi *et al* 2012

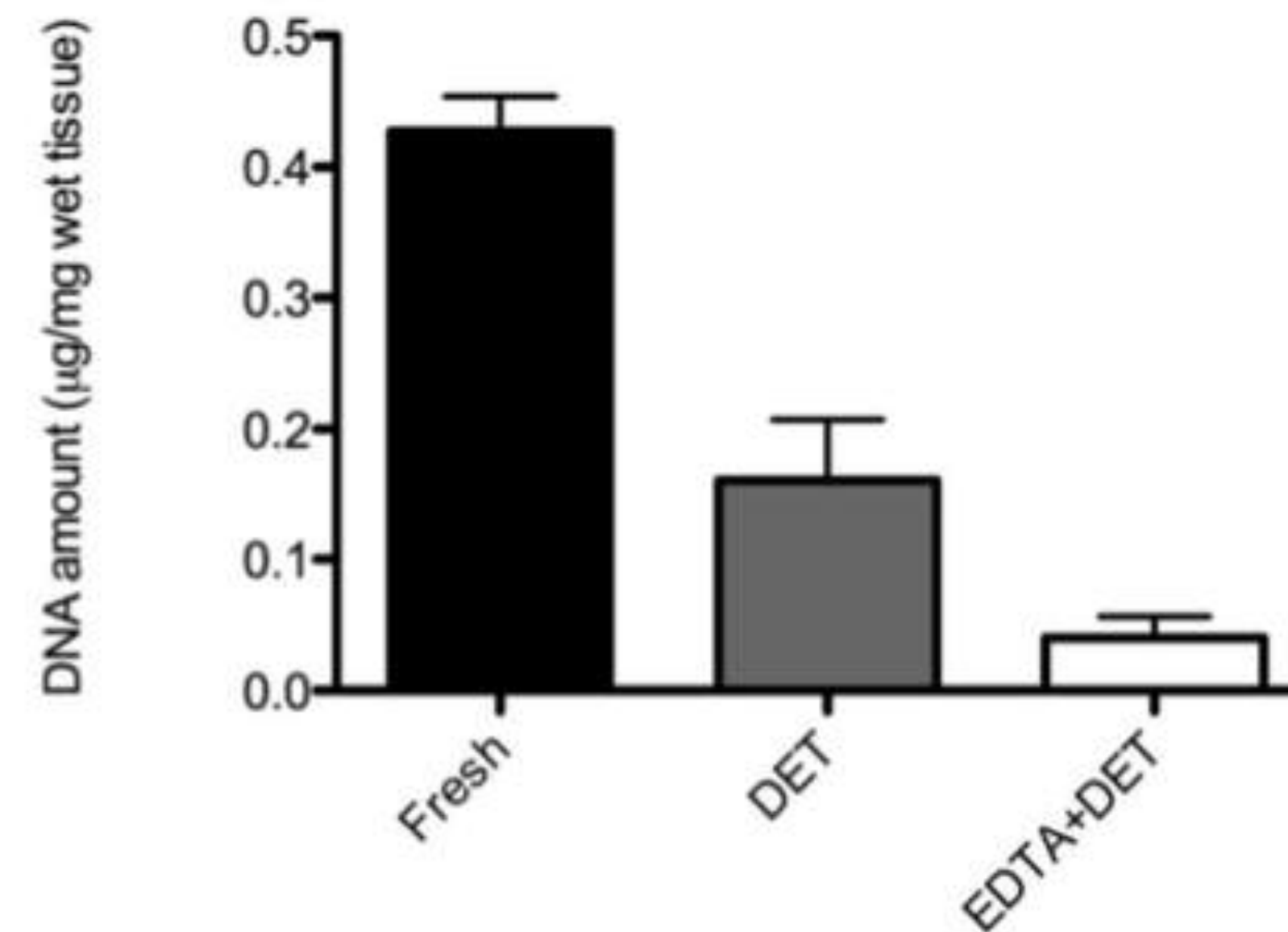
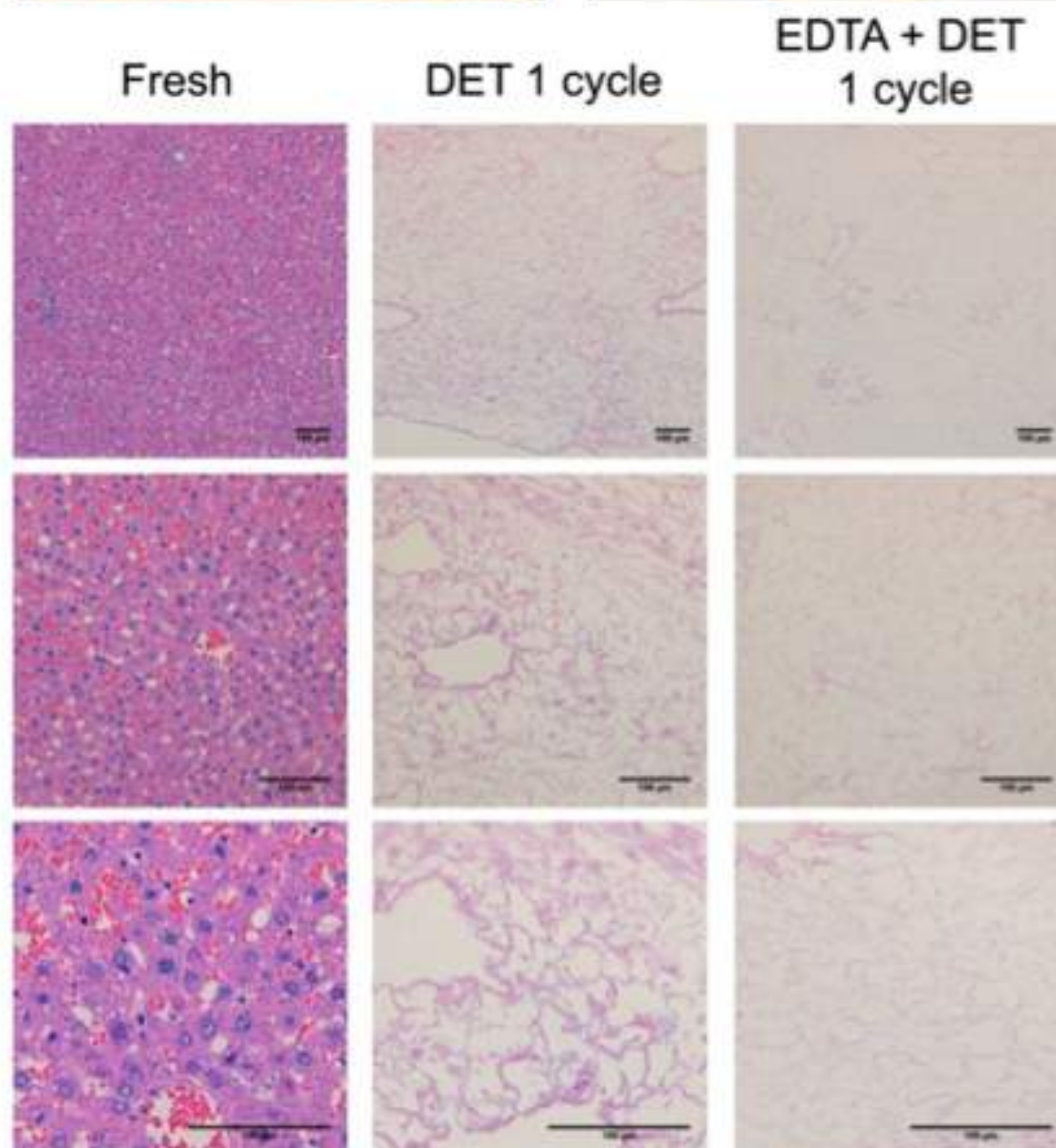
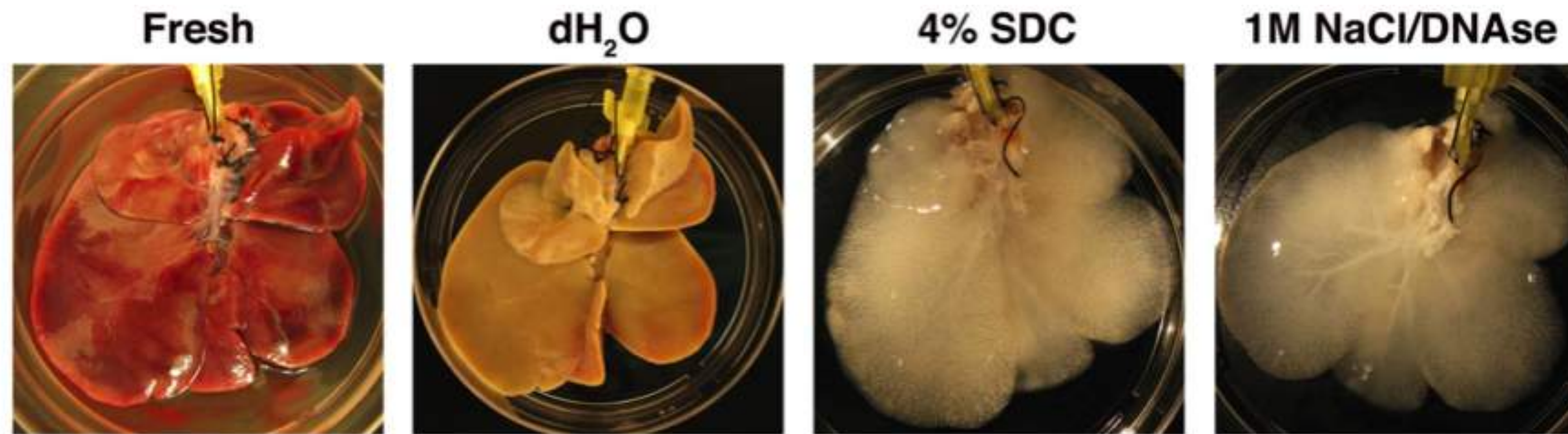


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Liver



Georgiades et al, unpublished

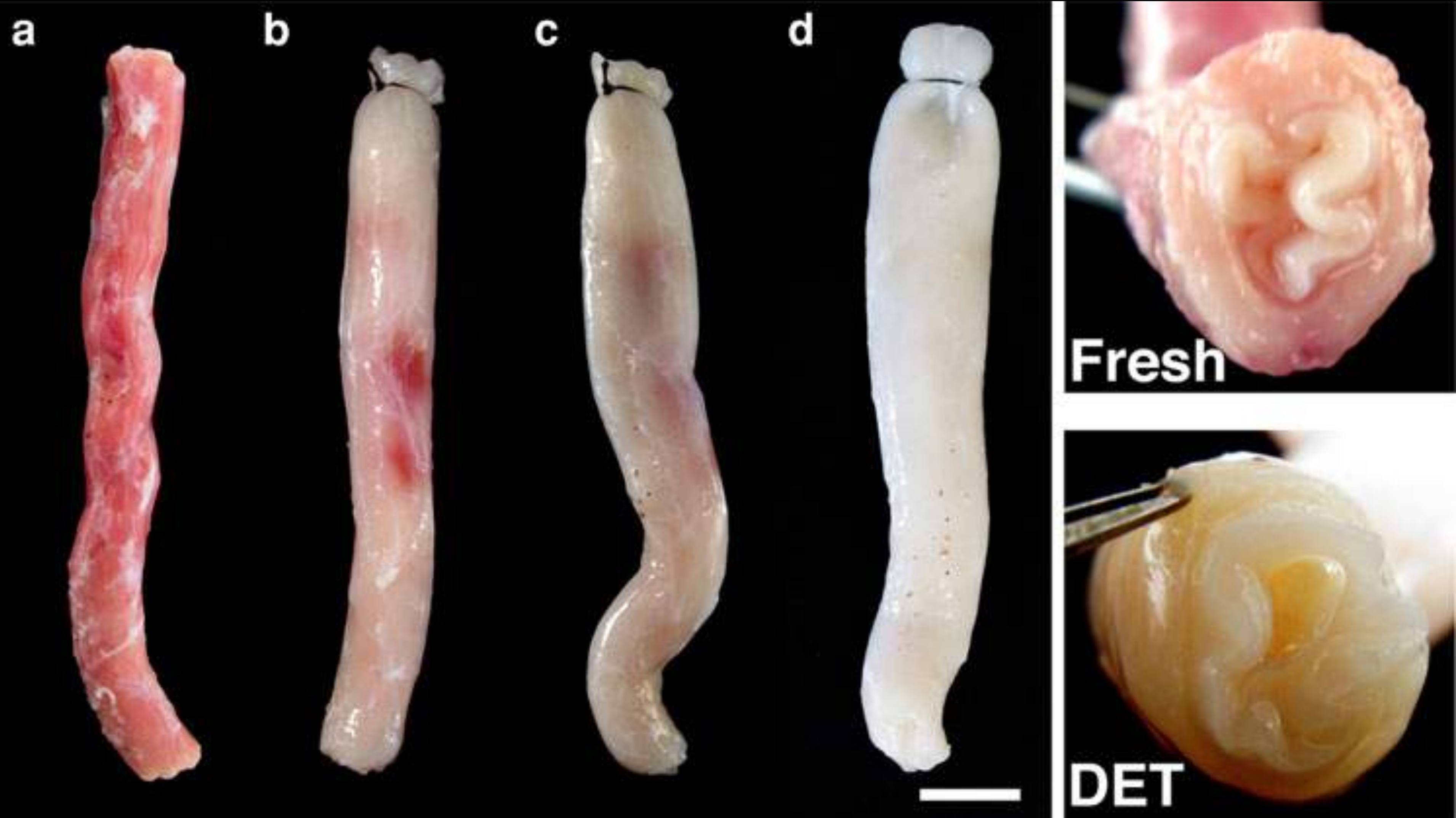


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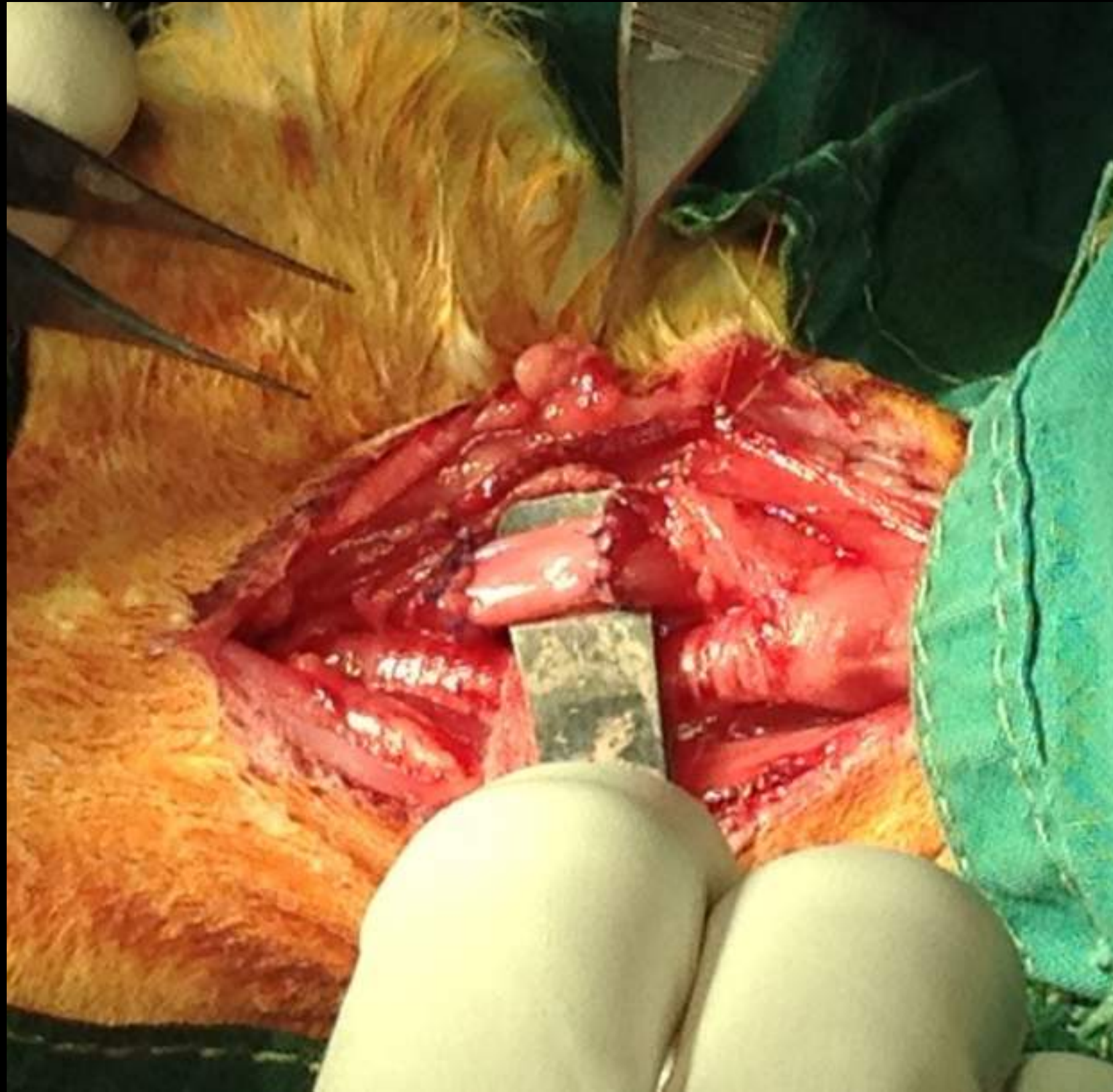


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Oesophagus



Orthotopic Implantation- Rabbit



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Could we transplant tissue from one species to another without rejection?

Rabbit Muscle

Remove Rabbit Cells

Populate with Rat Cells

Transplant to Rat

YES



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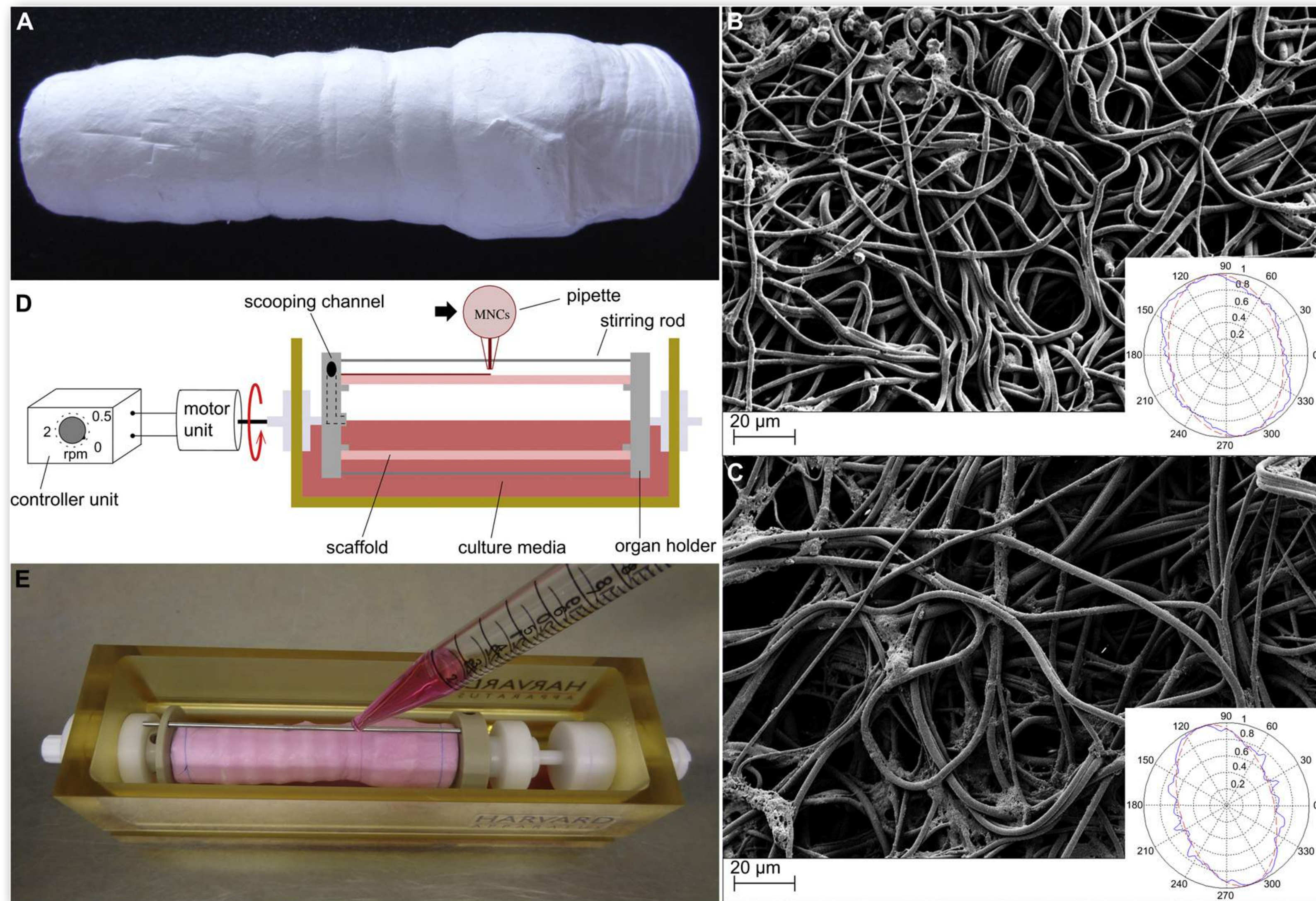


Fig. 4. Picture of a synthetic tracheal scaffold made of PET/PU-based nanofibers (A). SEM images of a synthetic scaffold showing the fiber network made of PET/PU. Insets report the computed fiber alignment pattern. Magnification 1,500 \times ; scale bar representing 20 μ m (internal B; external C). Schematic drawing of the bioreactor culturing system composed of the bioreactor, motor unit and controller unit with a synthetic tracheal scaffold mounted inside with an organ holder (D). Image of the seeding process on the tracheal scaffold inside the bioreactor prior to transplantation (E).



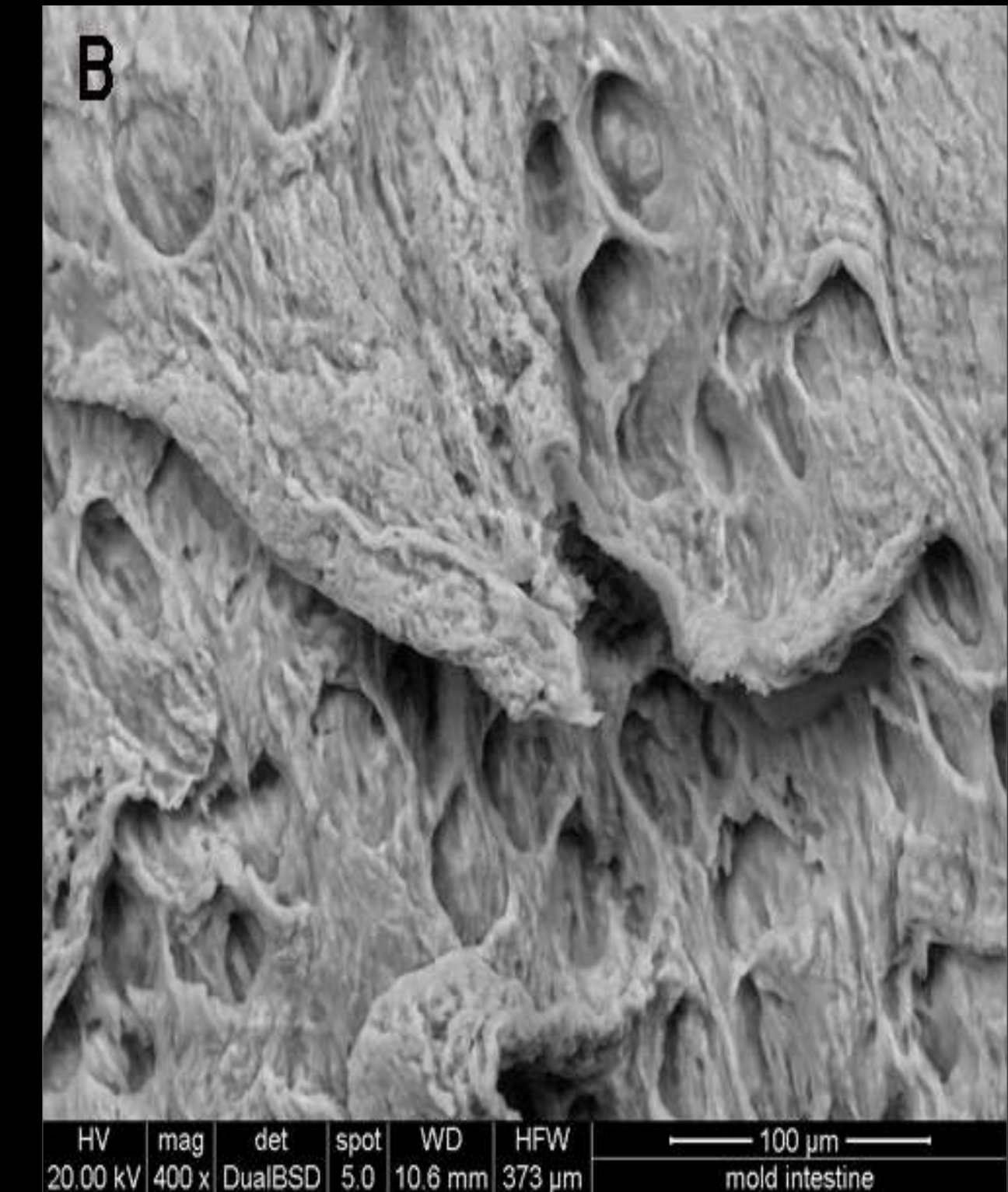
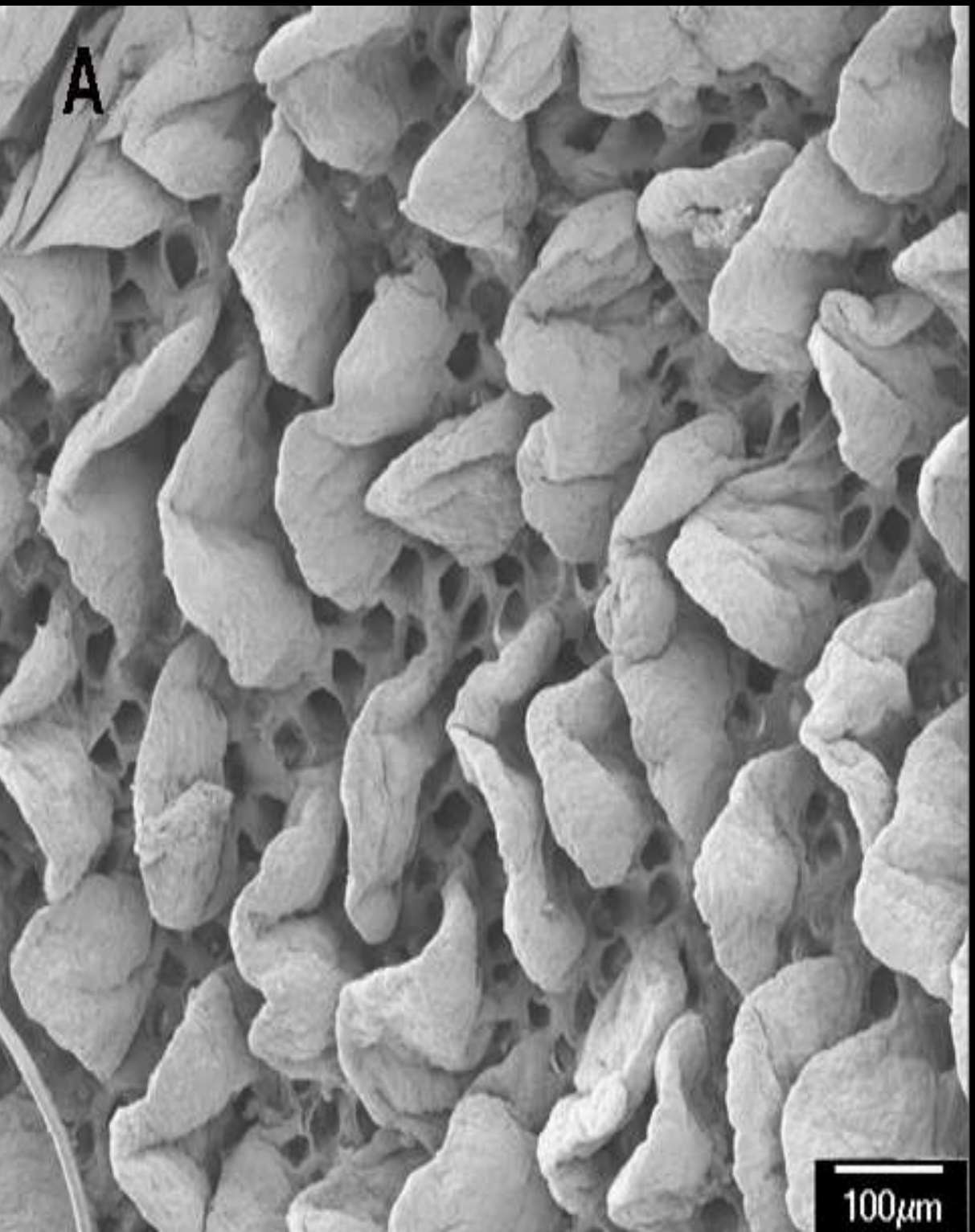
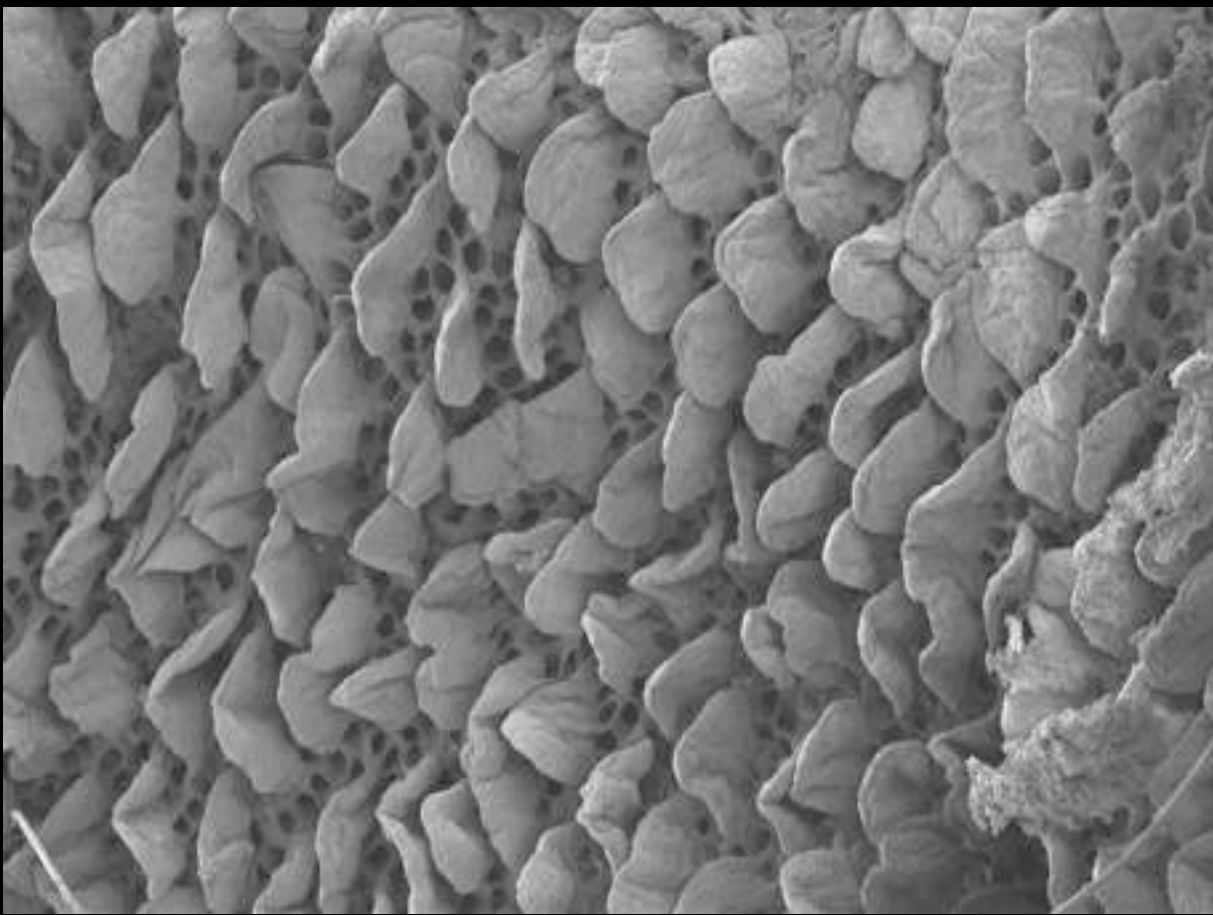
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A rat decellularized small bowel scaffold that preserves villus-crypt architecture for intestinal regeneration

Giorgia Totonelli^a, Panagiotis Maghsoudlou^a, Massimo Garriboli^a, Johannes Riegler^b, Giuseppe Orlando^c, Alan J. Burns^d, Neil J. Sebire^e, Virpi V. Smith^e, Jonathan M. Fishman^a, Marco Ghionzoli^a, Mark Turmaine^f, Martin A. Birchall^g, Anthony Atala^c, Shay Soker^c, Mark F. Lythgoe^b, Alexander Seifalian^h, Agostino Pierro^a, Simon Eaton^a, Paolo De Coppi^{a,*}



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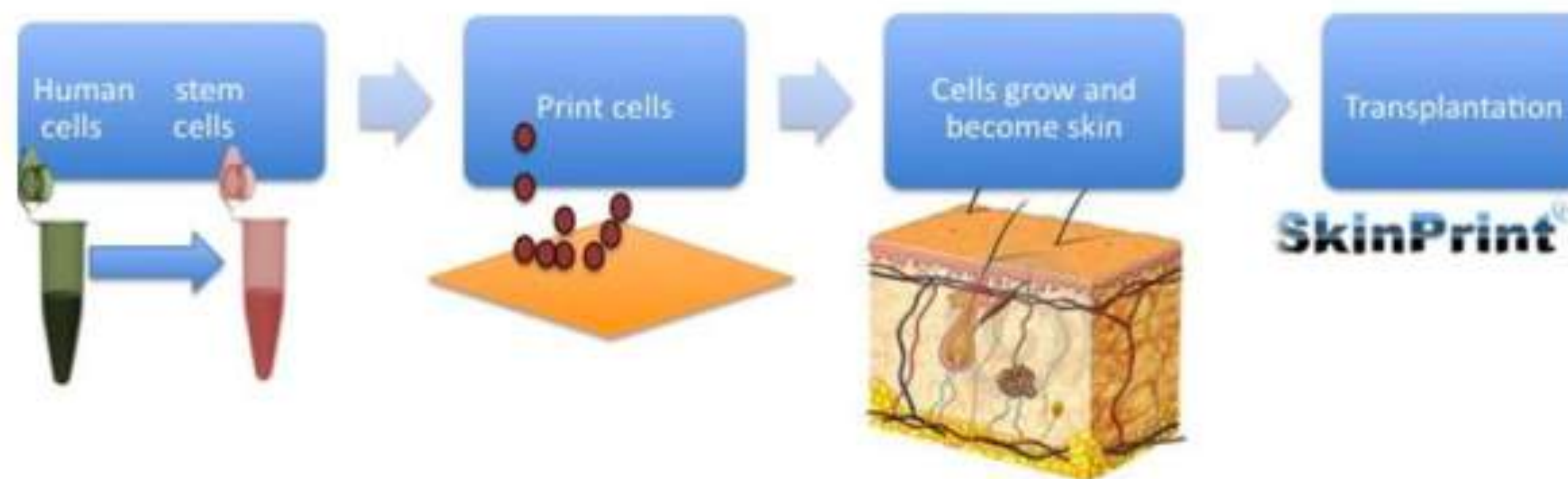
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**Wake Forest
regenerative medicine team**

**Ink jet printing of stem cells
direct to damaged skin**

SkinPrinting human skin



Commercialised Process



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3D Printing Organs?

**Professor A. Atala,
Wake Forest**



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too much technology?



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technological Titans and ethical Lilliputians

Bjørn Morten Hofmann
Too Much Technology
BMJ 2015;350:h705



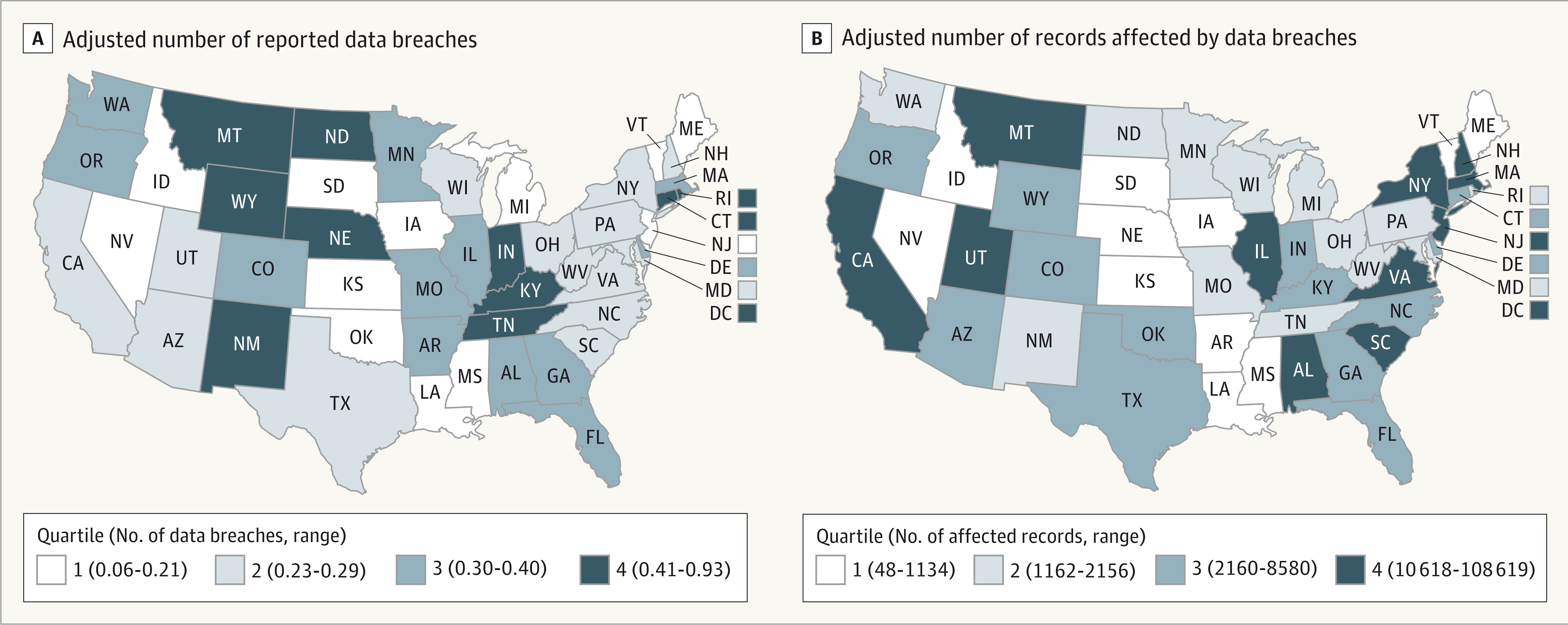
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949 breaches, 29.1 million records

Figure. Adjusted Number of Data Breaches and Affected Records Between 2010 and 2013 by State and Quartile



JAMA April 14, 2015 Volume 313, Number 14



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Hackers DO hack hospitals

Healthcare DDoS Attack: Mitigation Lessons

Boston Children's Hospital CIO Offers Insights After Disruption

By Marianne Kolbasuk McGee, September 10, 2014.



Daniel Nigrin



The main lesson from a **distributed-denial-of-service** attack on **Boston Children's Hospital** last spring is that such attacks represent a real threat in healthcare that must be mitigated, says CIO Daniel Nigrin, M.D.

Until that incident, many healthcare organizations, just like Boston Children's, didn't put disruptive DDoS attacks high on their list of threats to mitigate,

A distributed denial-of-service (DDoS) attack by 1 or 2 people or bots is an attempt to make a machine or network resource unavailable to its intended users.

Aims to temporarily or indefinitely interrupt or suspend services of a host connected to the Internet.

By 2014, the frequency of recognised DDoS attacks had reached an average rate of **28 per hour**.



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IT'S INSANELY EASY TO HACK HOSPITAL EQUIPMENT



Photo: Charles Thatcher/Getty Images

WHEN SCOTT ERVEN was given free rein to roam through all of the medical equipment used at a large chain of Midwest health care facilities, he knew

NEWS ANALYSIS

DHS investigates 24 potentially deadly cyber flaws in medical devices

DHS is investigating 24 cases of potentially deadly cybersecurity flaws in medical devices and hospital equipment.

Computerworld | Oct 22, 2014 6:43 AM PT

When the FDA released recommendations to manufacturers to strengthen the cybersecurity of medical devices earlier this month, the agency quoted Dr. Suzanne Schwartz as saying, "There is no such thing as a threat-proof medical device." Now, coinciding with the

Cyber Security Must Improve



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this is
why we must
keep trying



special thanks to

Dr Susannah Thoms

Mr Edward Green

Professor Jeff Jacobs

Professor Andrew Taylor

Professor Paolo di Coppi

Mr Parker Moss

Mr David Barron

Mr Michael Bone

Dr Sara Pasquale

Dr Michael Burch

Dr Silvia Schievano

Professor Neil Sebire

Professor Andrew Copp

Professor Martin Birchall

Professor David Goldblatt

Professor William J Gaynor

Professor Francesco Muntoni

Members of the American Society of Thoracic Surgeons

European Congenital Heart Surgeons Foundation

Catherine Mohr, Da Vinci, Inc.

Anne Berner MP (Finland)

Afshad Mistri, Apple



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Treatments Interventions Individualised
Artificial Monitoring Cellular
Engineering printed therapies
repair devices medicine diagnosis
Caner Non support
Therapy invasive Hearts
term Valve Fetal Better
Regenerative Catheter Cancer
circulatory based Mechanical VADs
assist Treatment Long Imaging
Implantable Valves techniques