## The Next Disruptive Technologies: New Ways to Treat Old Diseases



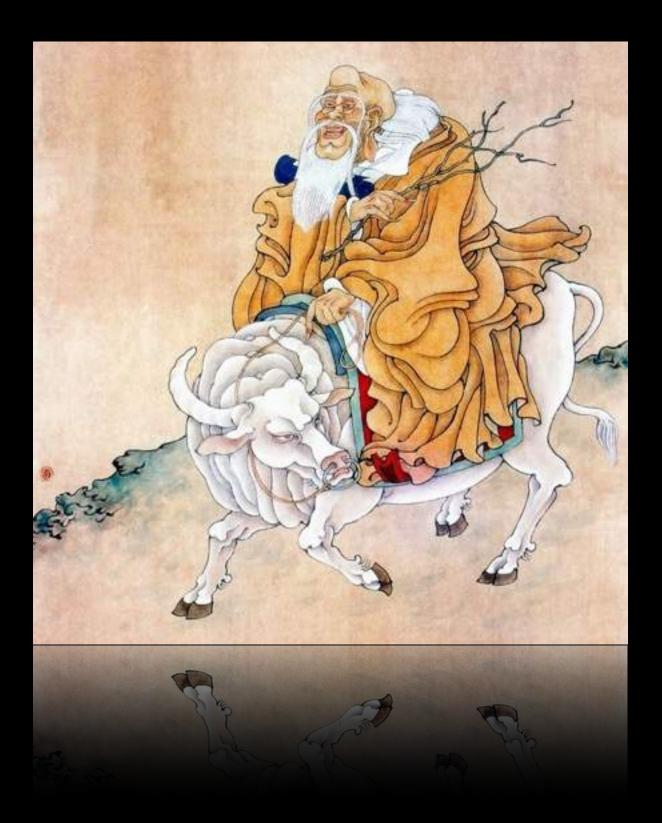
### Martin Elliott 37<sup>th</sup> Gresham Professor of Physic

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.





@ProfMJElliott

## Lao Tzu, 6th Century BC Chinese Poet



my specialty not cancer or genetics

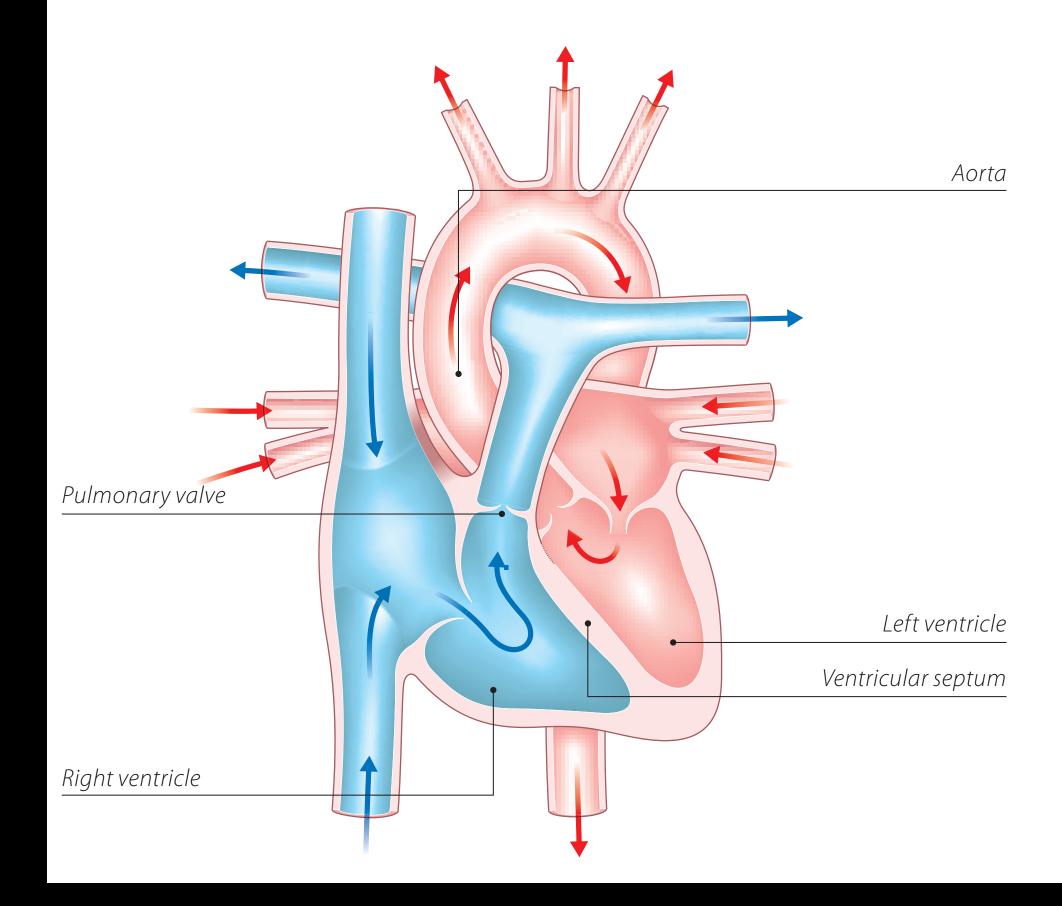
# Susie Thoms Edward Green Jeff Jacobs





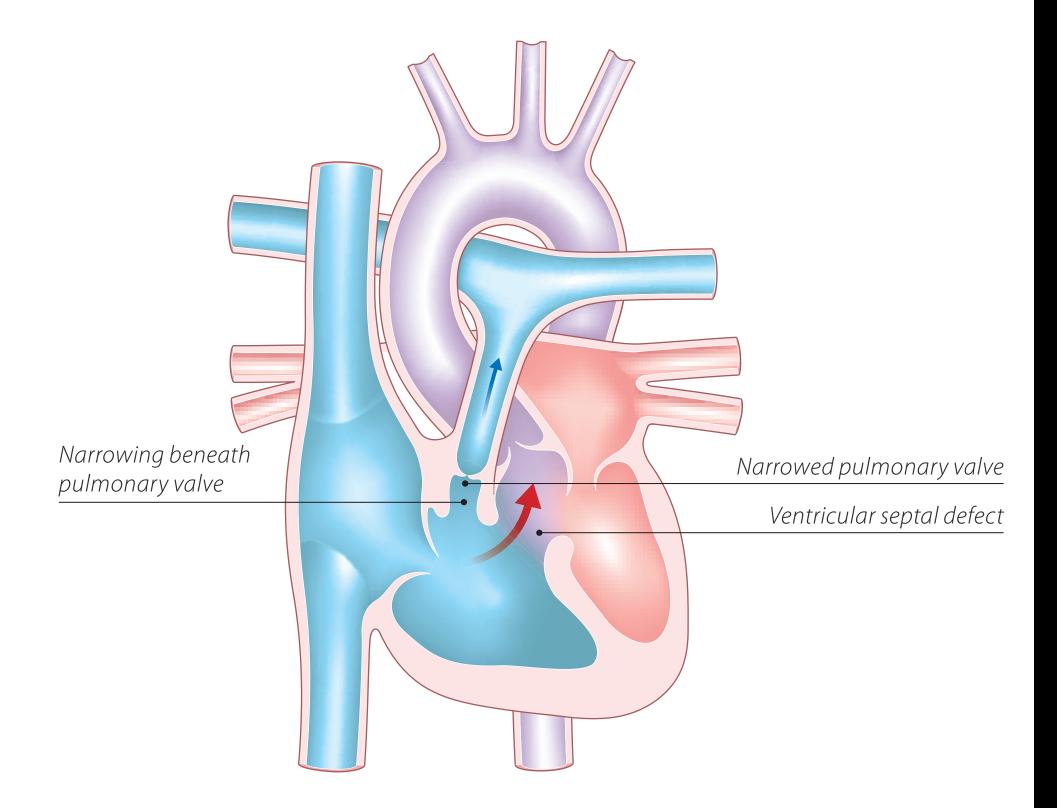
### What is Tetralogy of Fallot?

### The normal heart



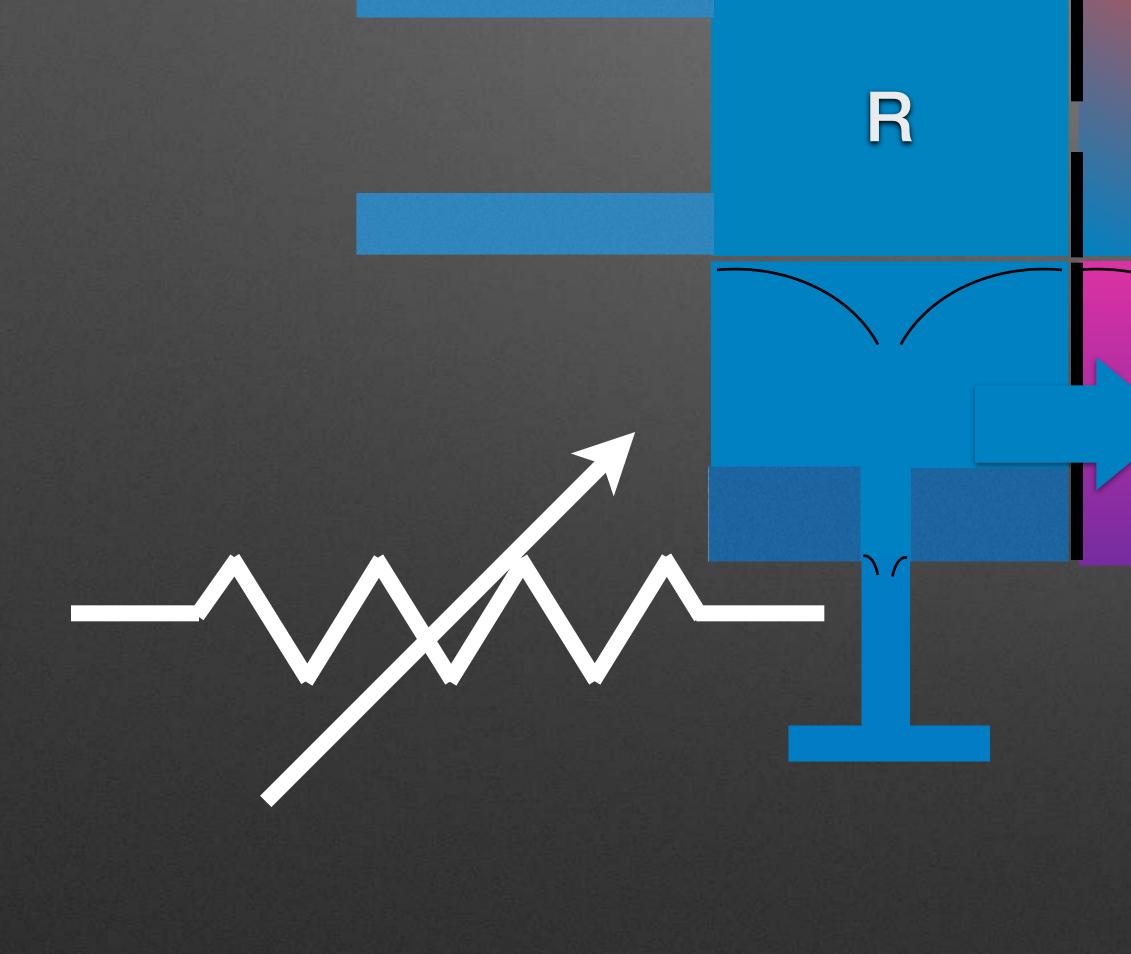


### **Tetralogy of Fallot**





### Tetralogy of Fallot

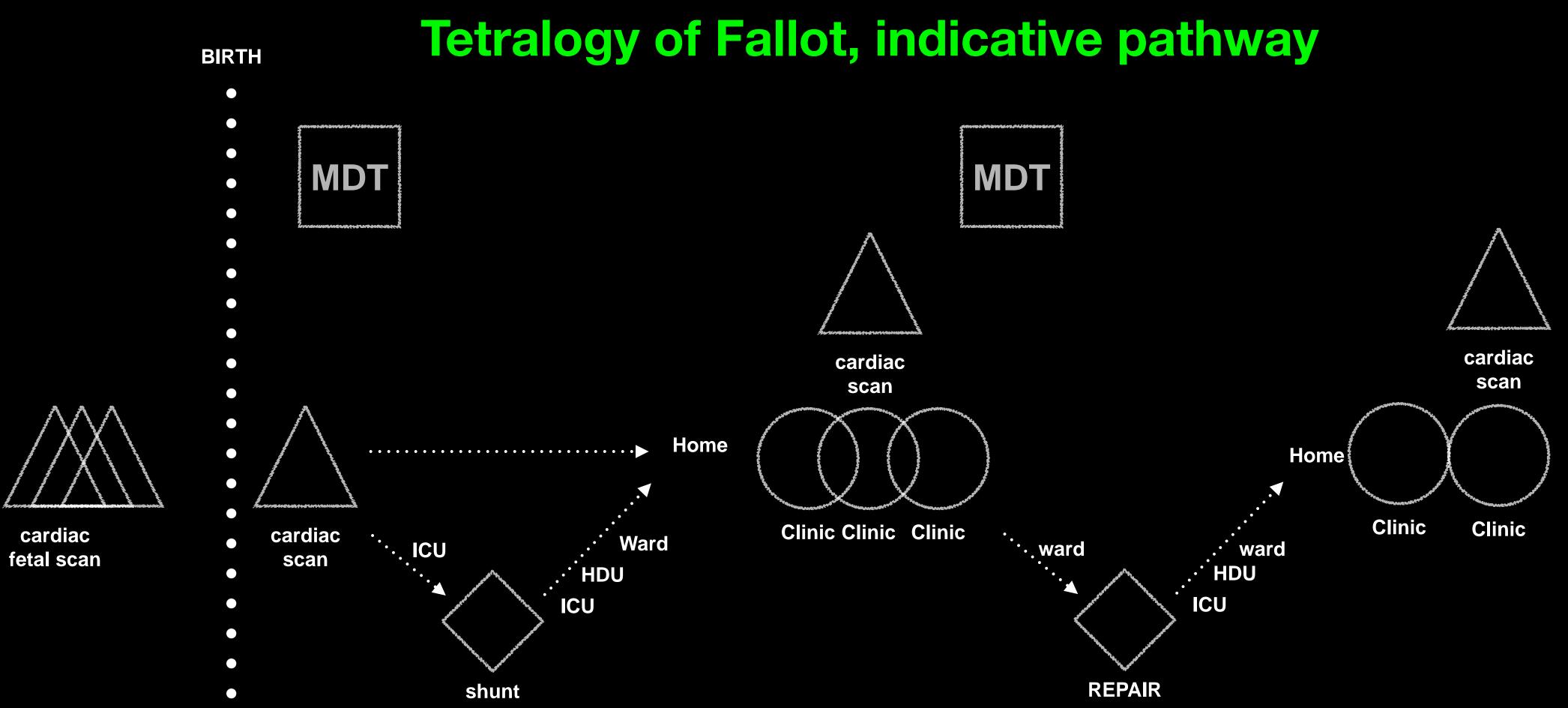




@ProfMJElliott







good local local specialist or local or regional centre regional unit

generic

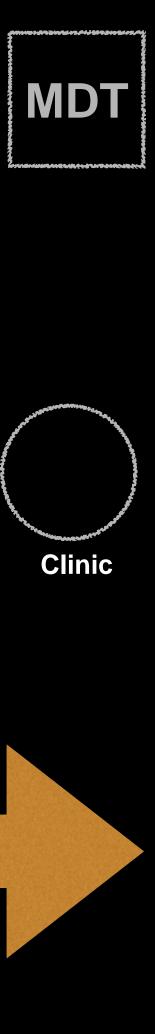
fetal scan



### pathway of care







# The Purpose of Prenatal Diagnosis

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



# psychologically, socially, medically, financially



# termination of pregnancy

# 

99%

total



@ProfMJElliott

### abortion statistics, **DH June 2014**

# 

### cardiac 11%



martin.elliott@gosh.nhs.uk

-070-



# improving fetal ultrasound





@ProfMJElliott

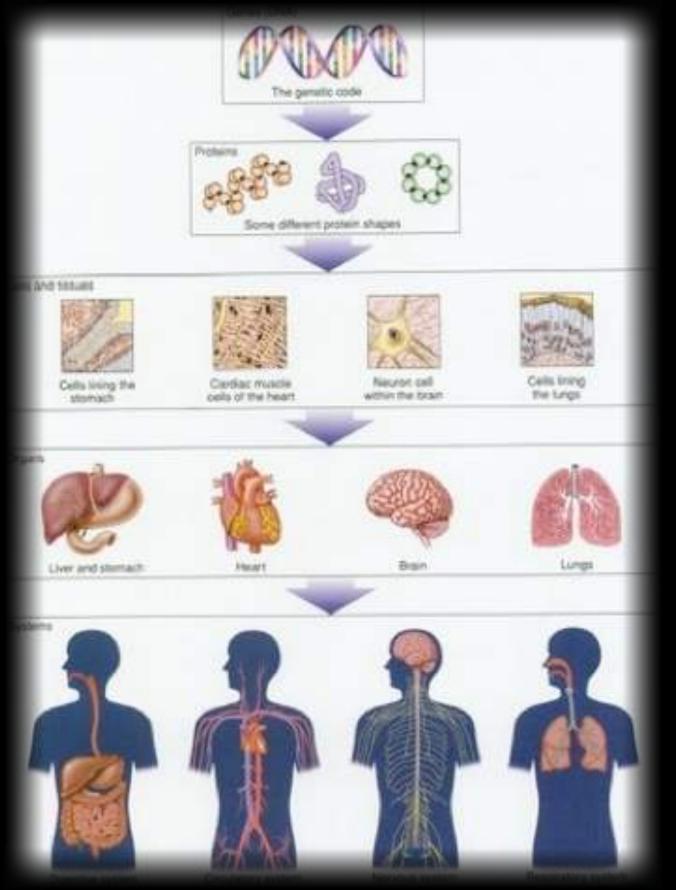






## **Diagnosis by genetics?**

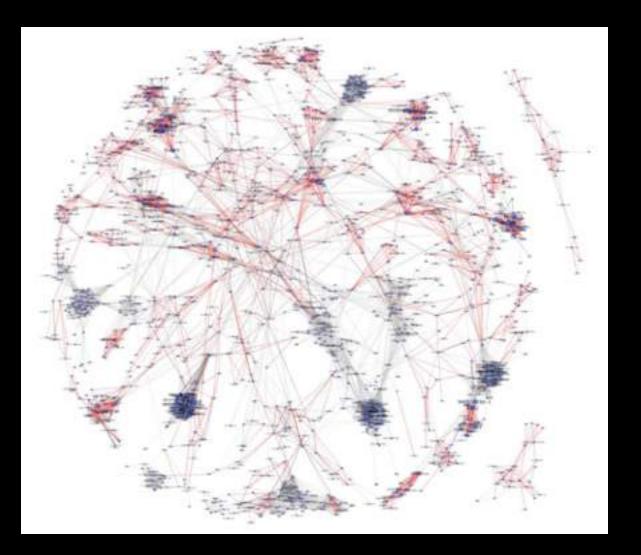
### genotype



### phenotype



@ProfMJElliott

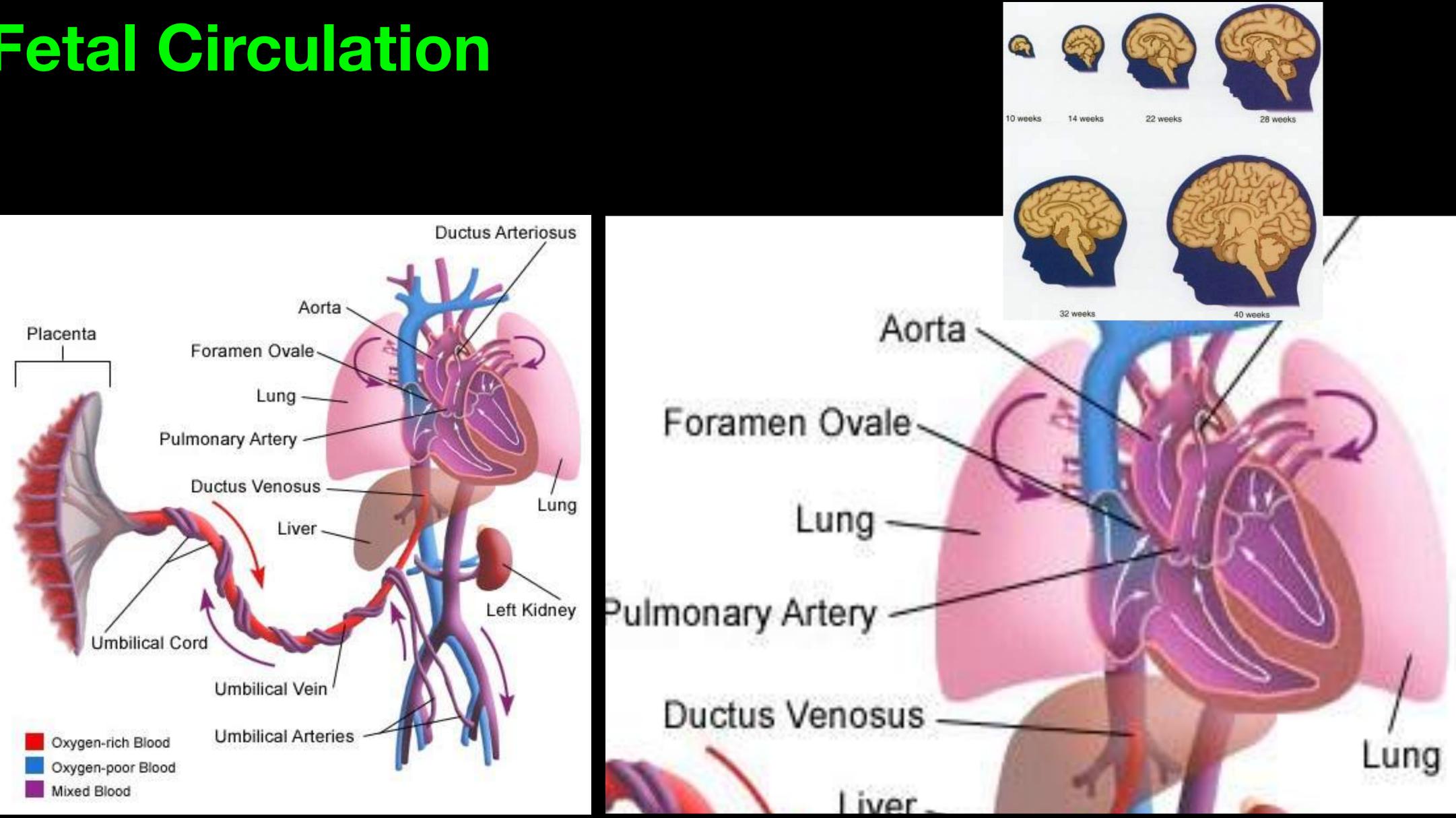




## what to do with so much information?



## **Fetal Circulation**





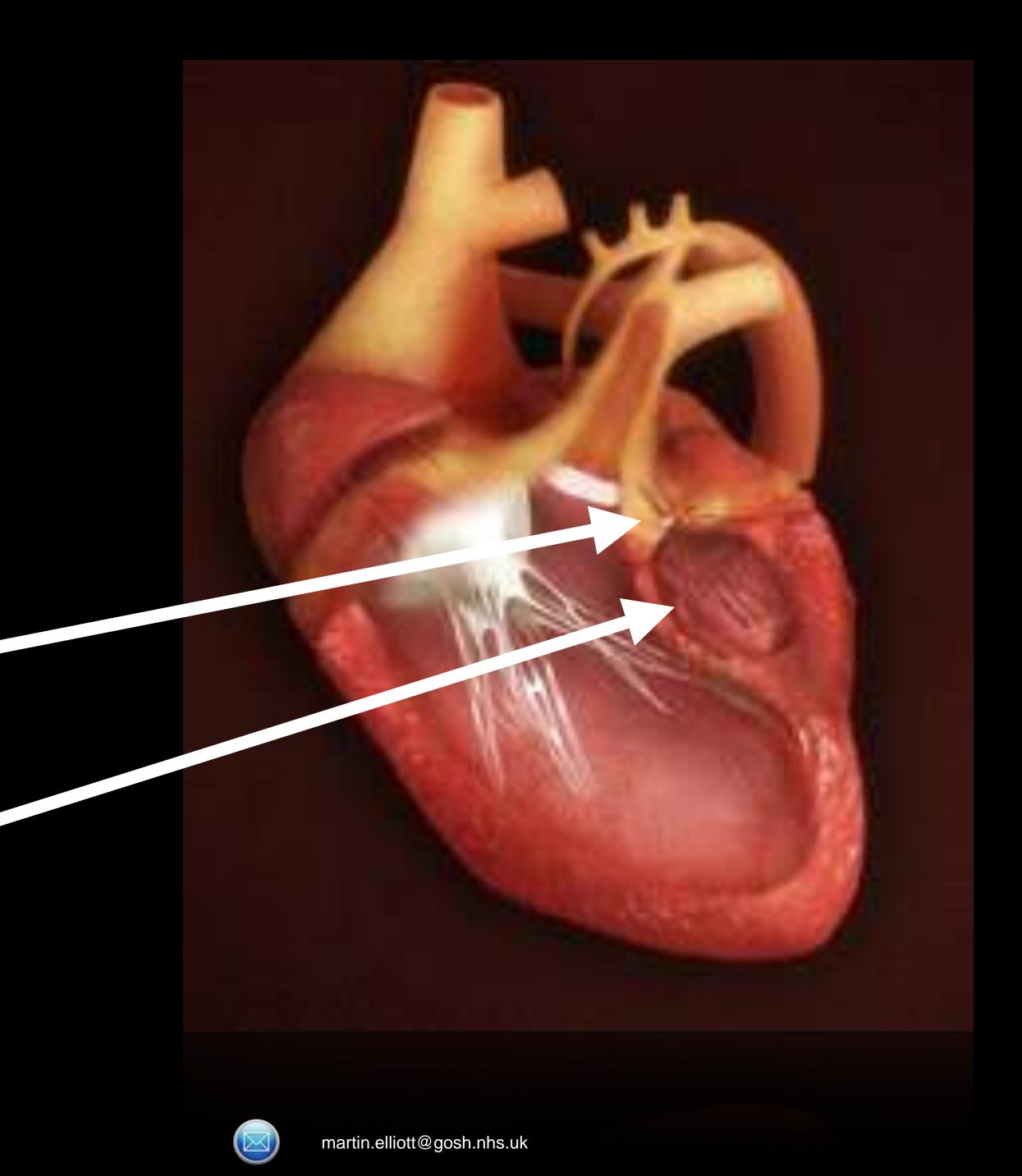


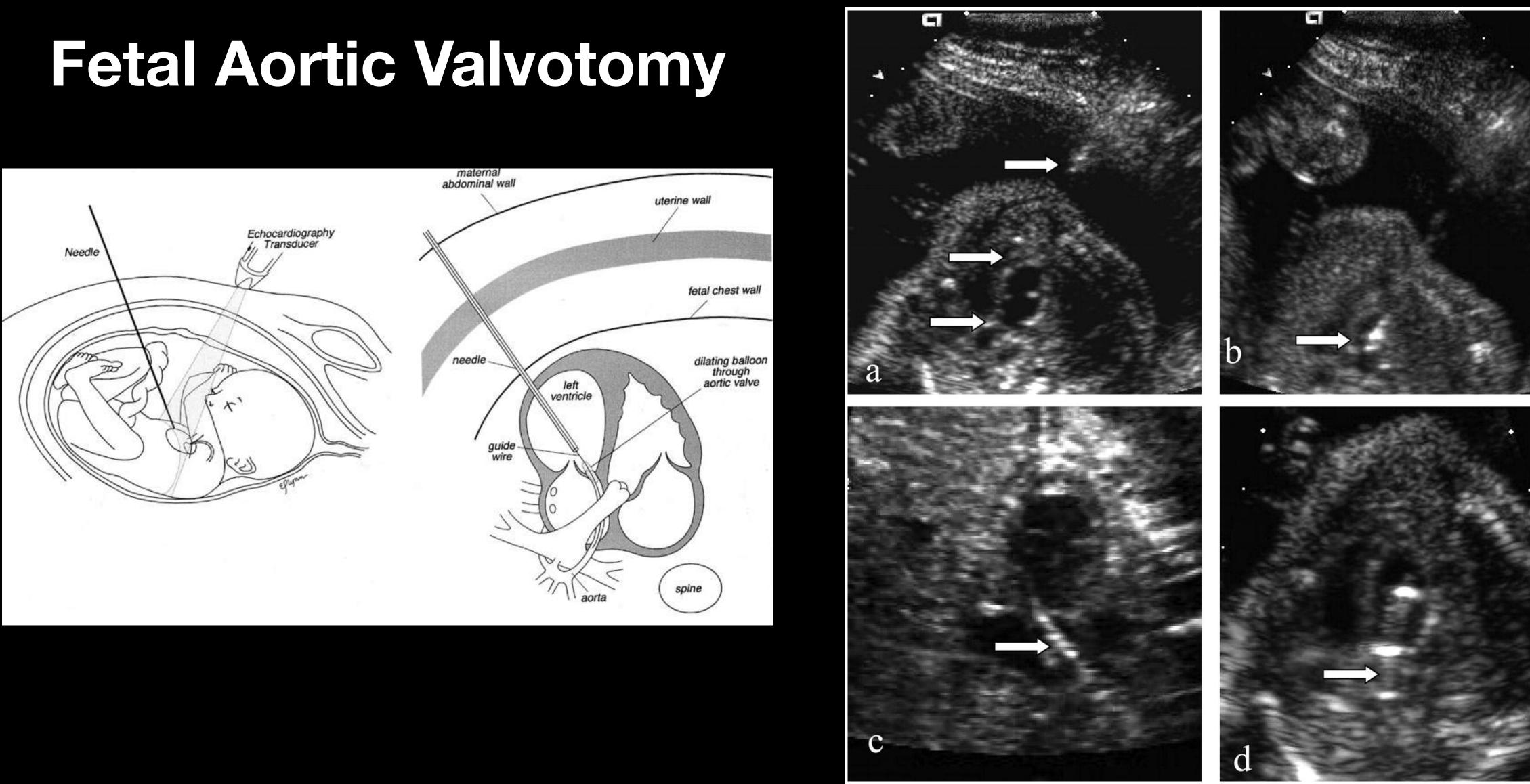
### Hypoplastic Left Heart Syndrome

### tiny aortic valve

### tiny left ventricle







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

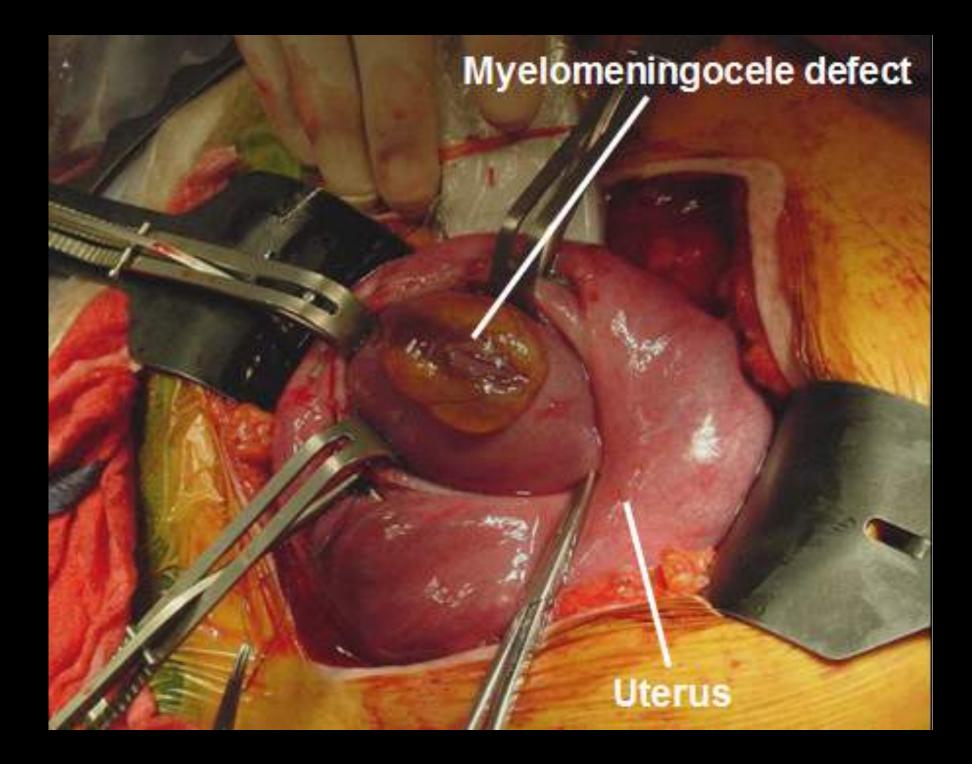








### Spina Bifida

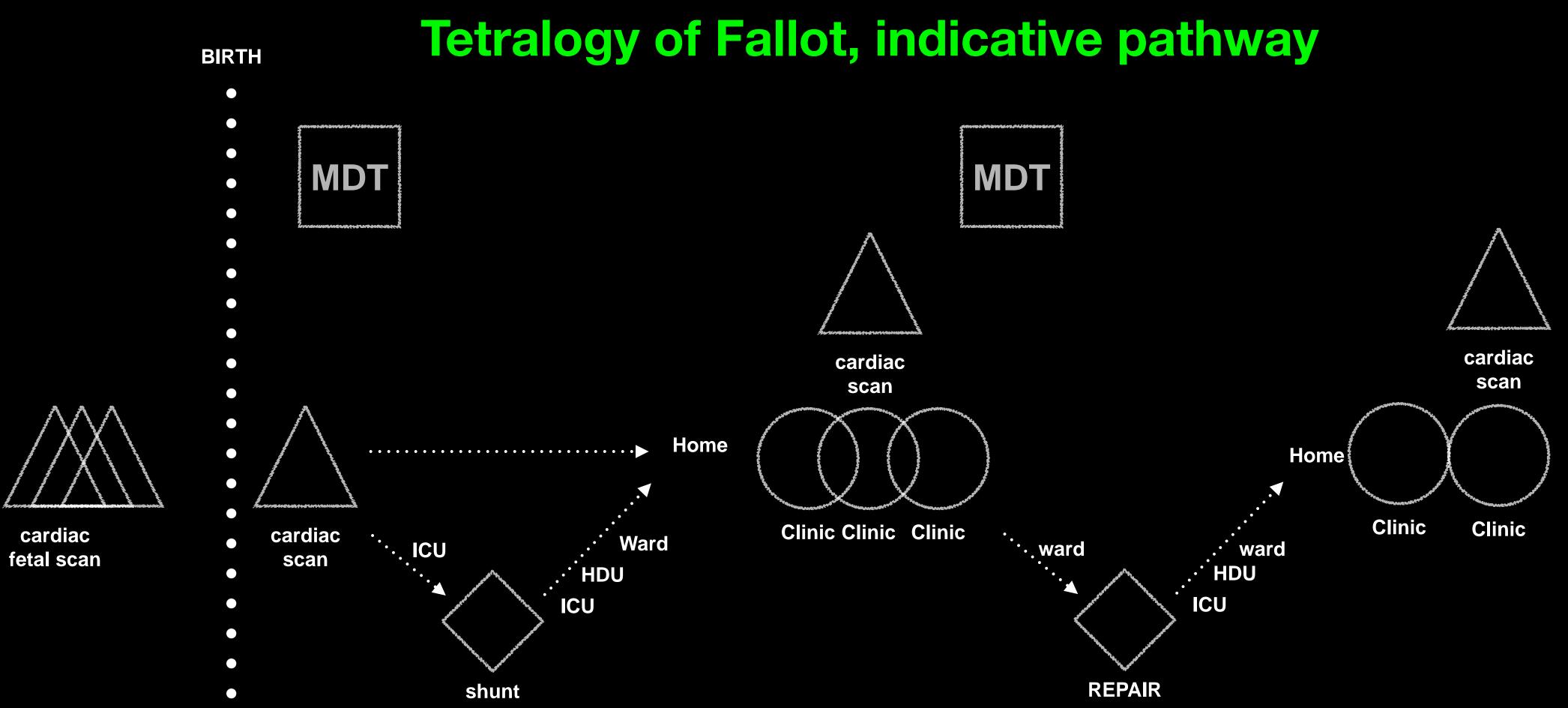




@ProfMJElliott







good local local specialist or local or regional centre regional unit

generic

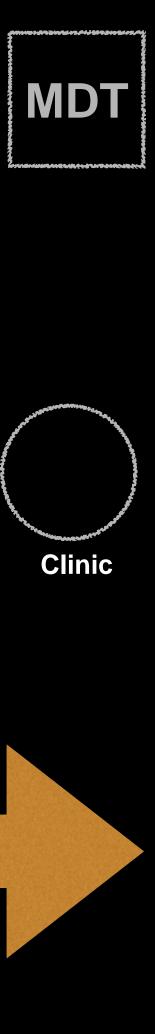
fetal scan



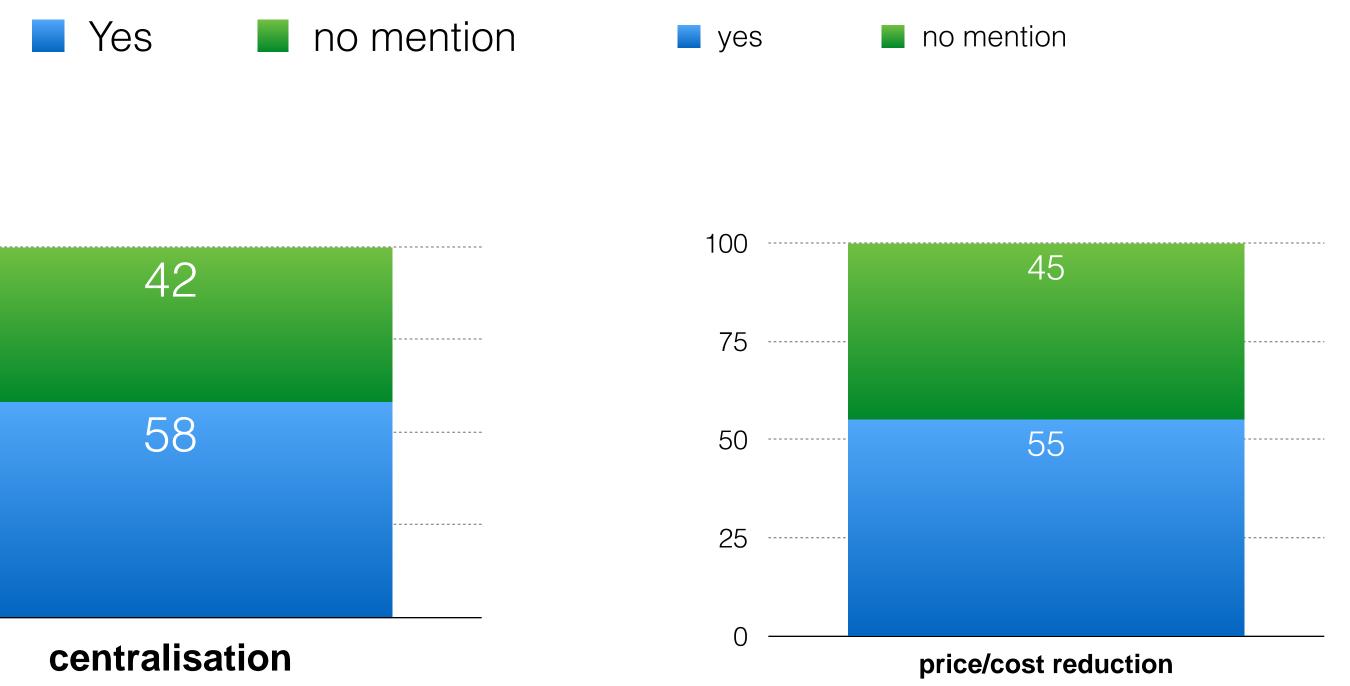
### pathway of care

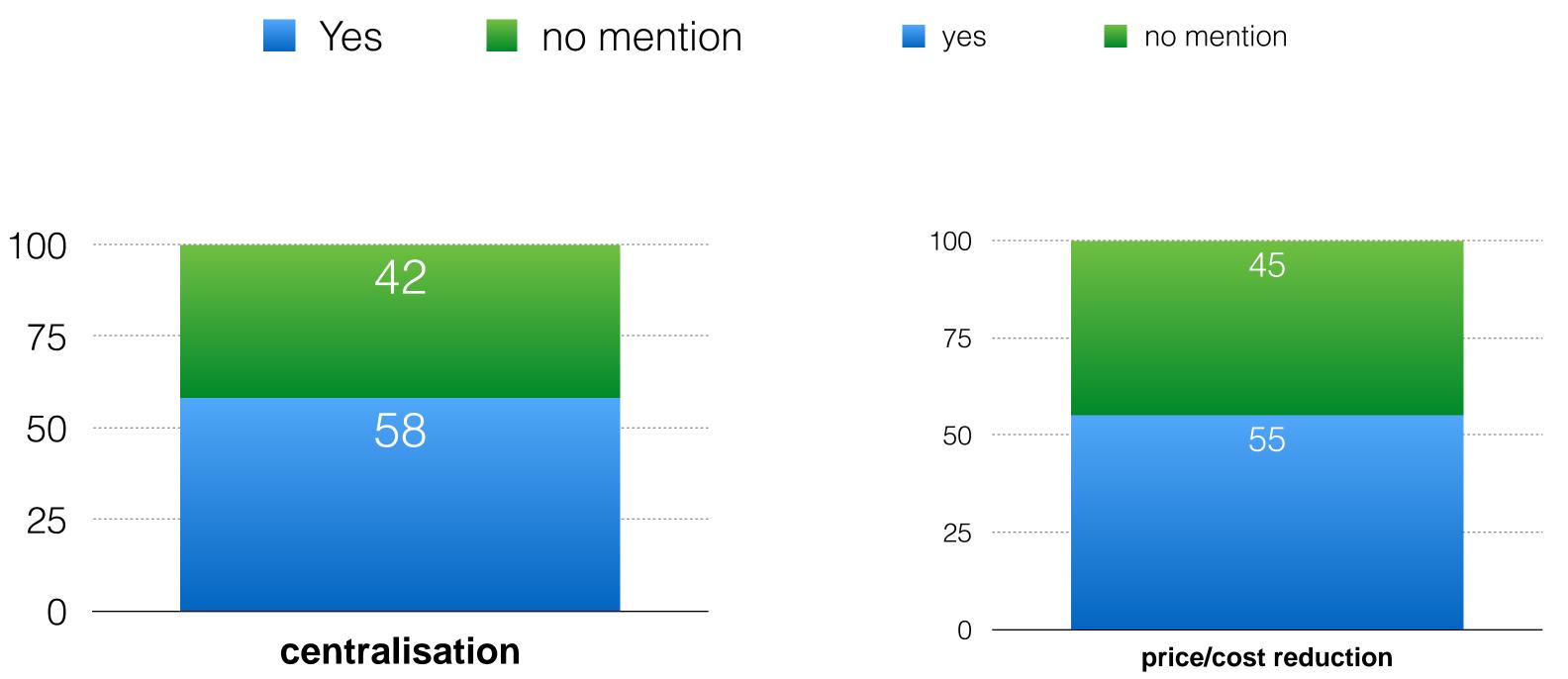






### What is coming next in the field of Resourcing and Organisation?











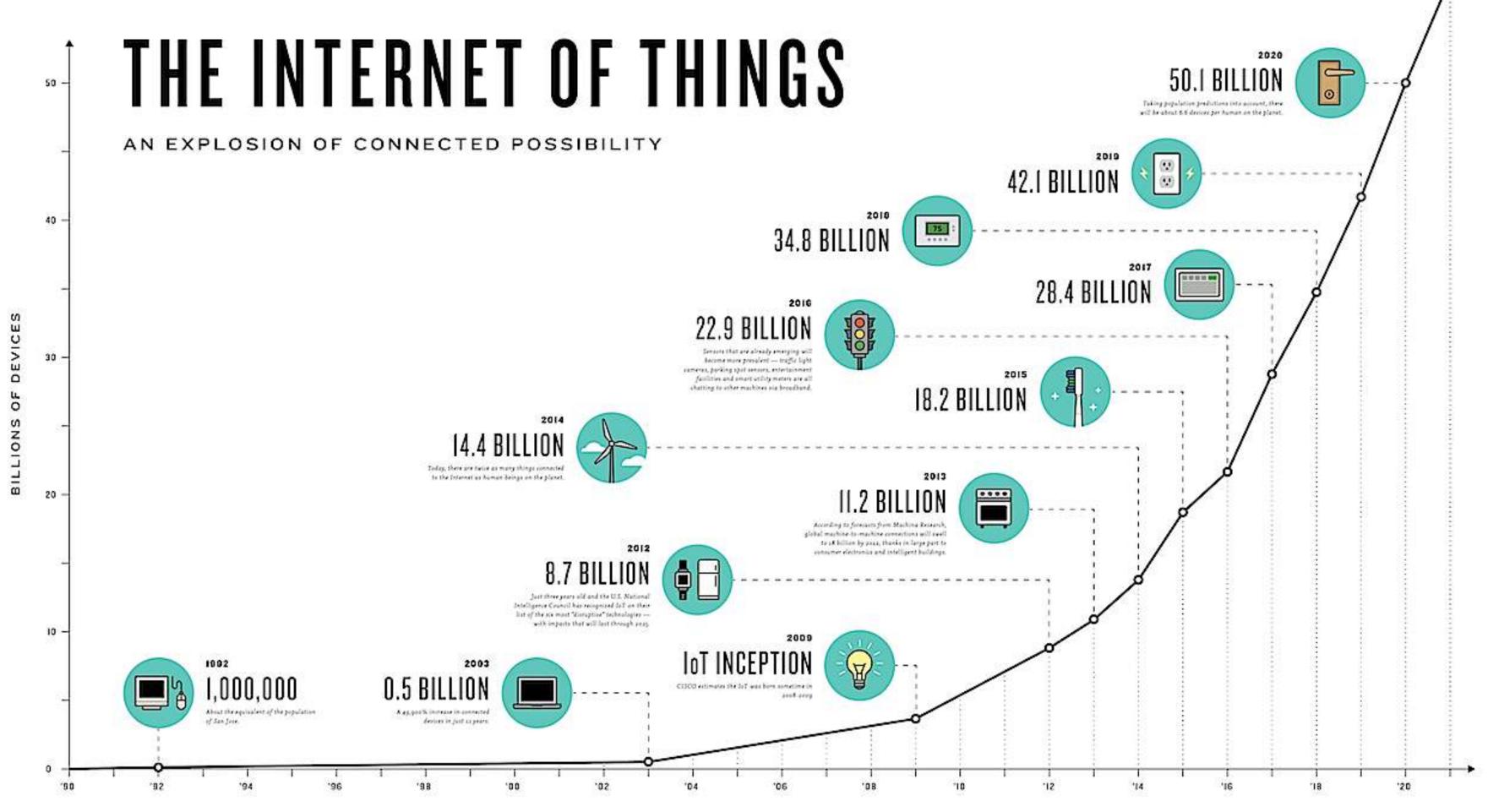
martin.elliott@gosh.nhs.uk

Profession 1

.0

 $\boxtimes$ 





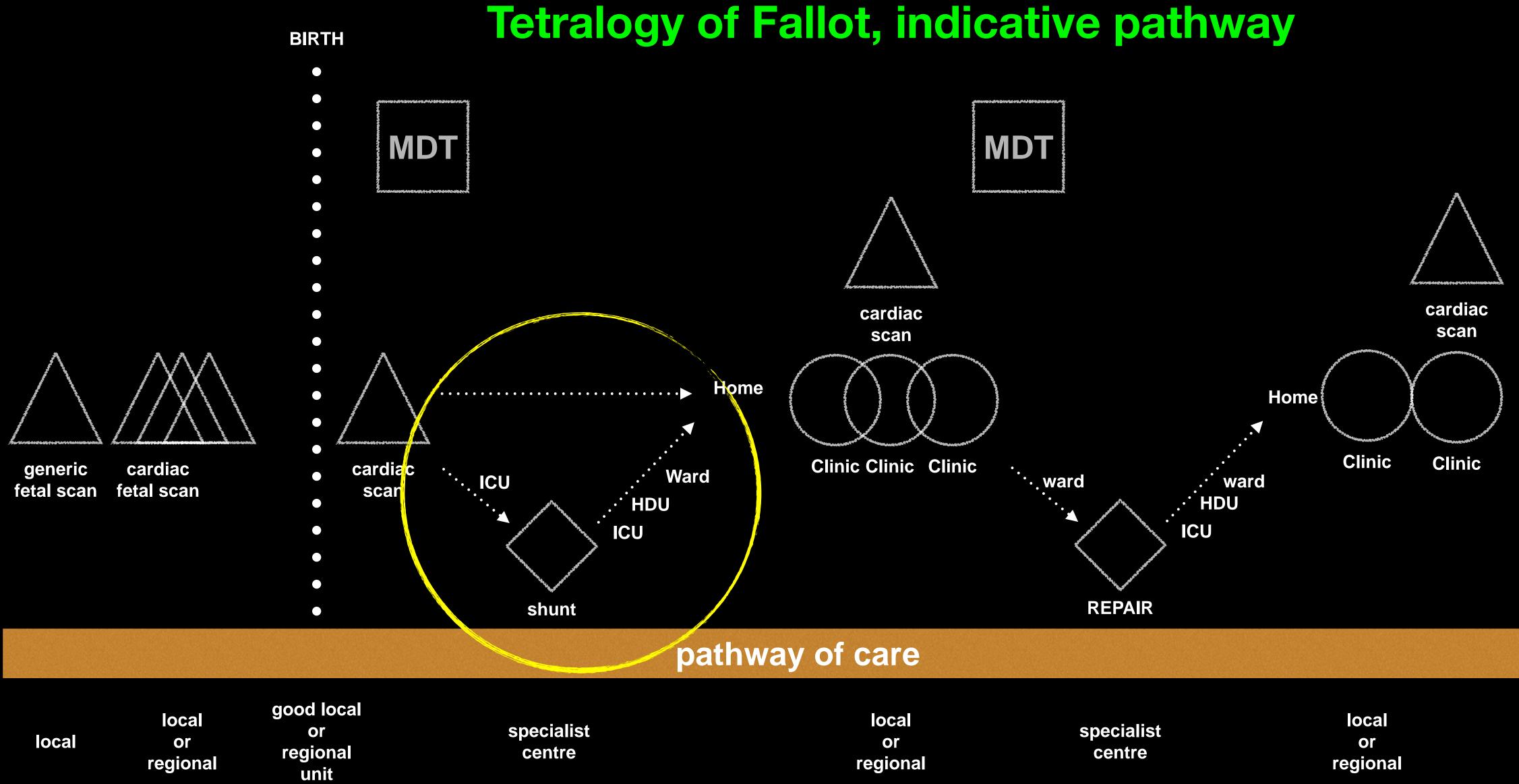
YEAR



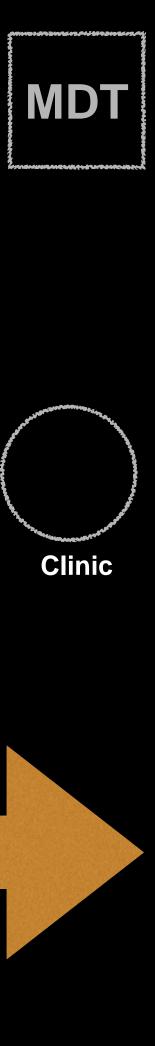


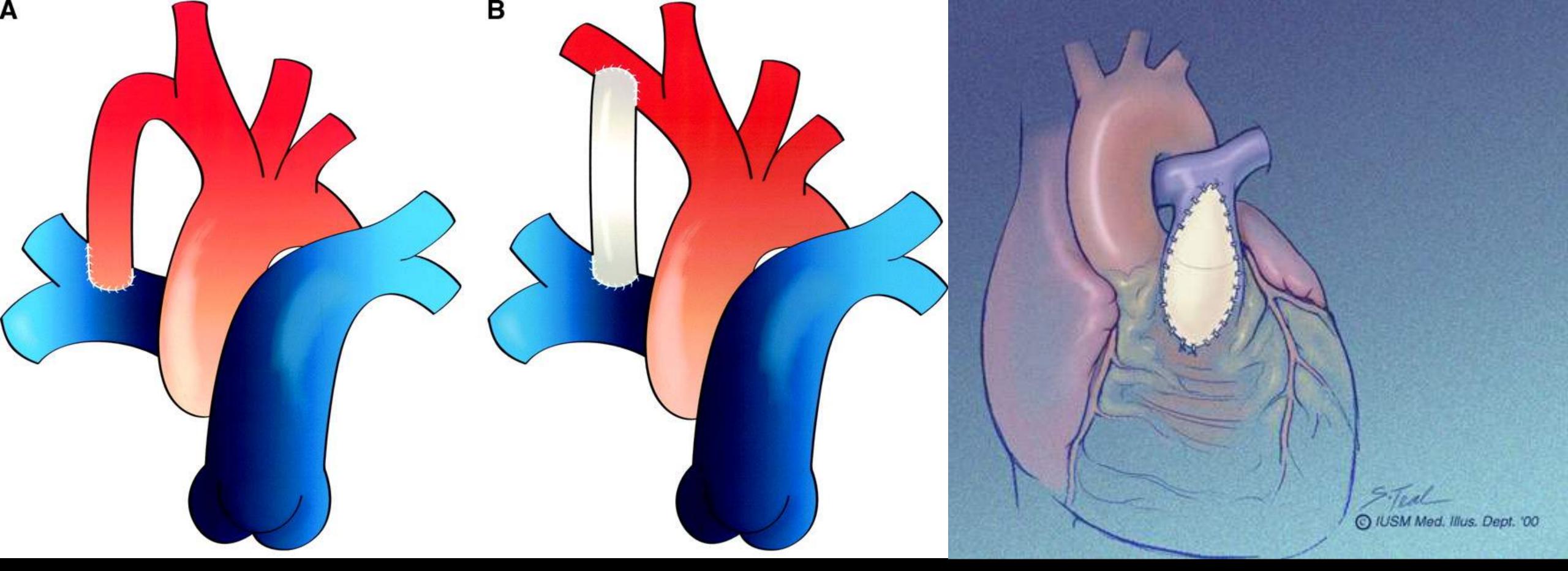












### Blalock-Taussig

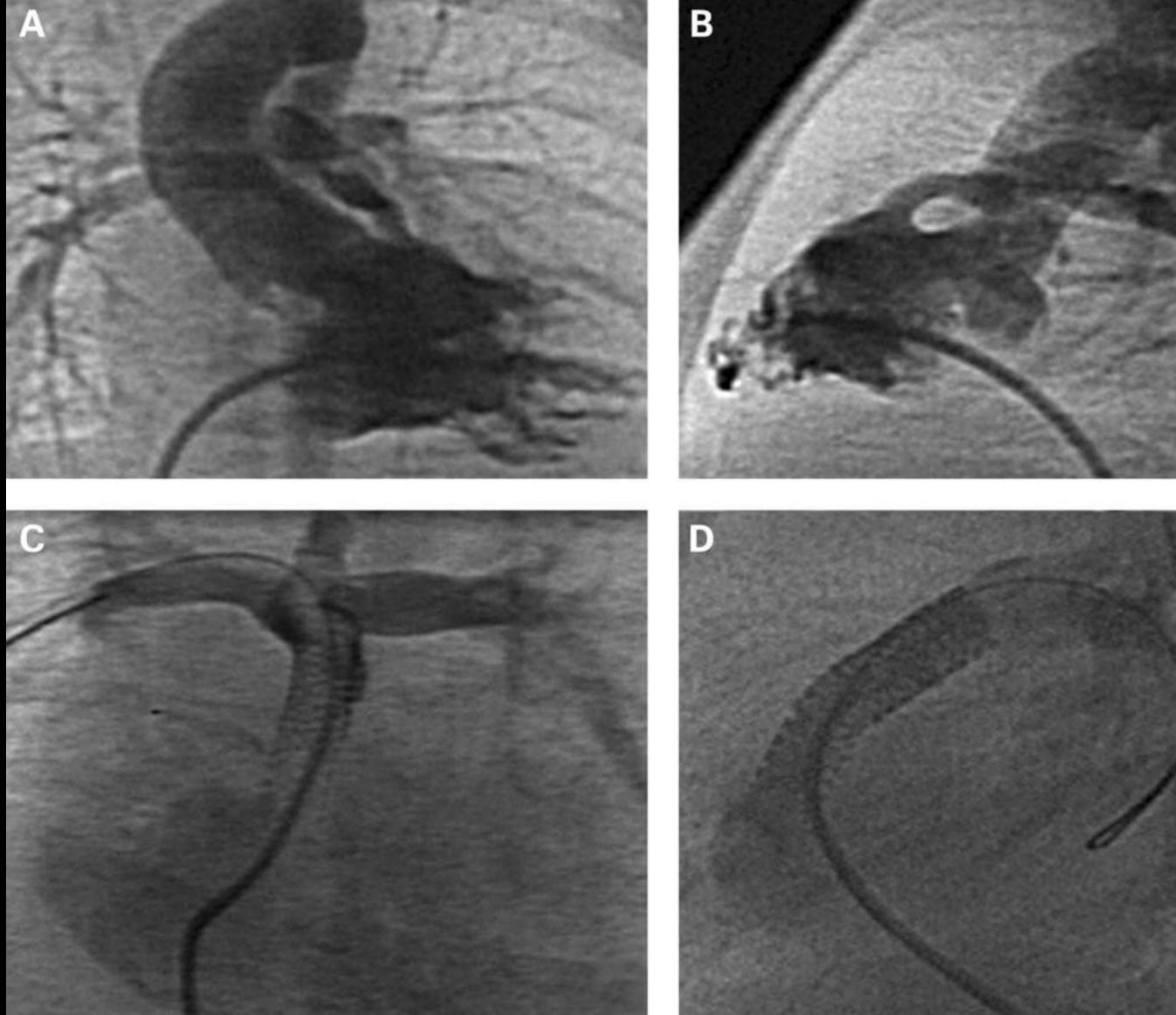
### Modified B-T

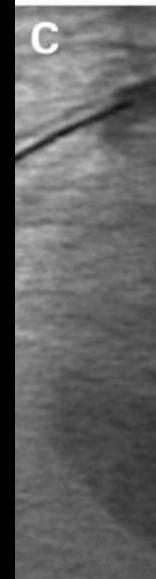


### RV outflow tract patch



## **Trans-Venous Catheter Inserted Stent**

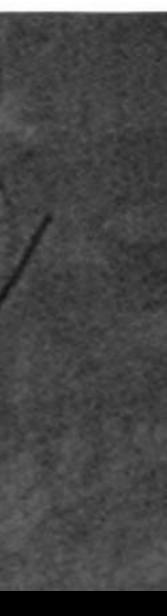




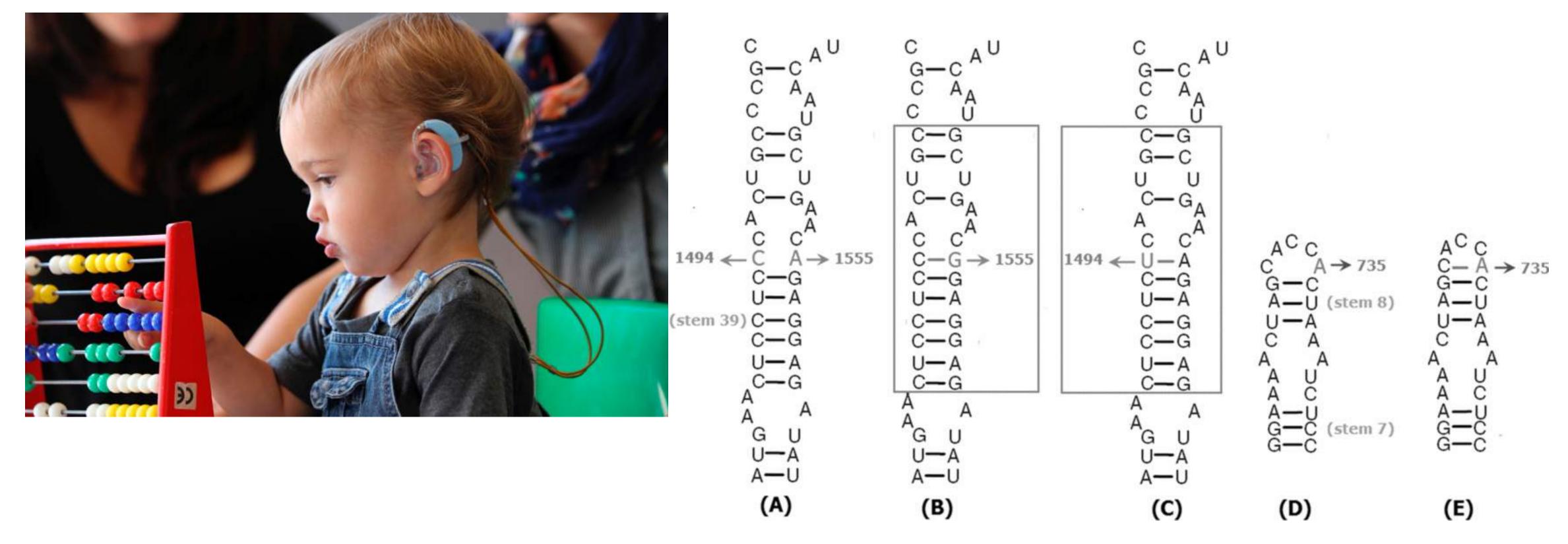












### Figure 3 Secondary structure of parts of the mitochondrial 12S rRNA showing the localizations and effects of the m.1555A>G, m.1494C>T and m.735A>G mutations

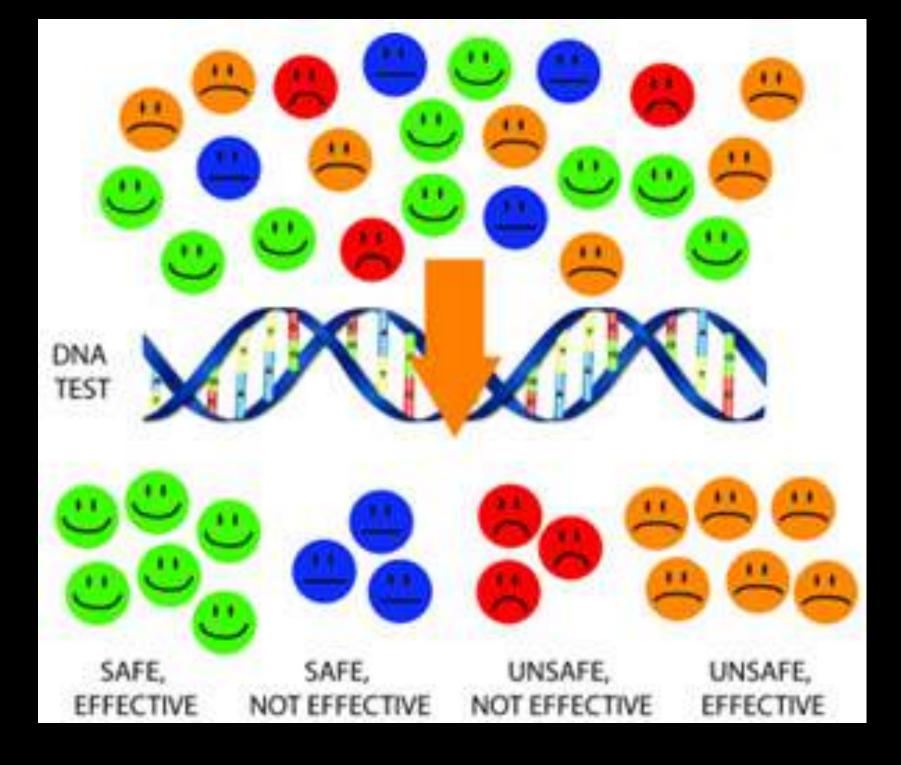
### Bioscience Reports (2010) 30, 405-411 - Emna Mkaouar-Rebai, Nourhene Fendri-Kriaa and others.

www.bioscirep.org

The era of personalised medicine....

the right treatment for the right patient at the right time

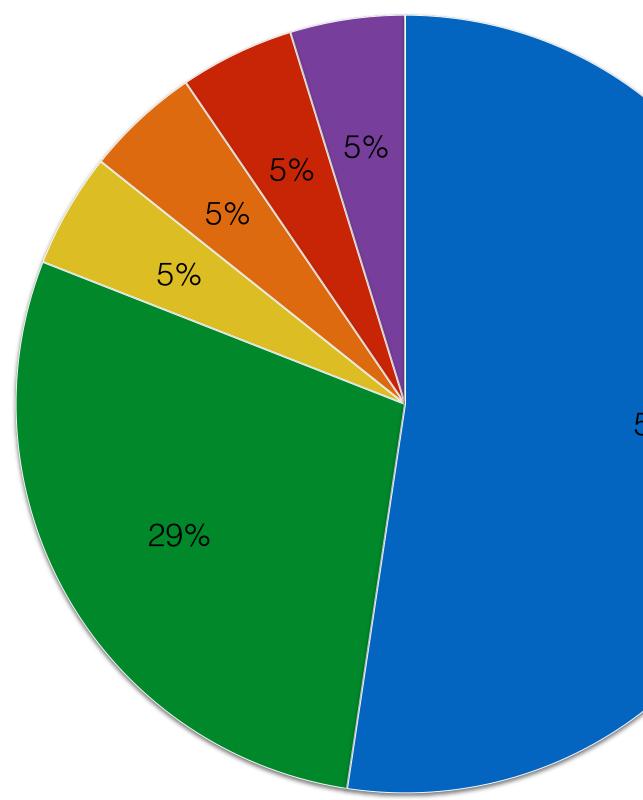




### Our plan: Determine genetic risk for ALL children at GOSH (and store the genome data)



## What does 'Personalised Medicine' mean to you?





52%

lindividualised
Precision
Fundamental
Surveillance
Nothing
Private



# "I've always practiced personalised medicine; I know my patients, and they know me"





# 1 medical article every 26 secs

## **3.4 MILLION Articles**

are archived in PMC.

Content provided in part by:

1668

Full Participation Journals

305

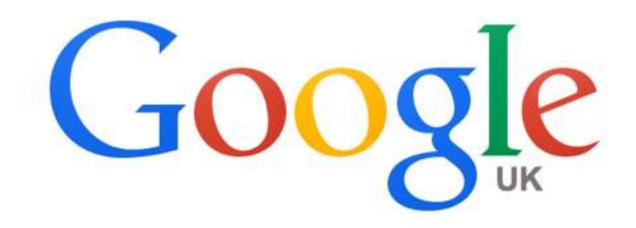
NIH Portfolio Journals

3150

Selective Deposit Journals



# can't read 5000 per day!



**Google Search** 

I'm Feeling Lucky



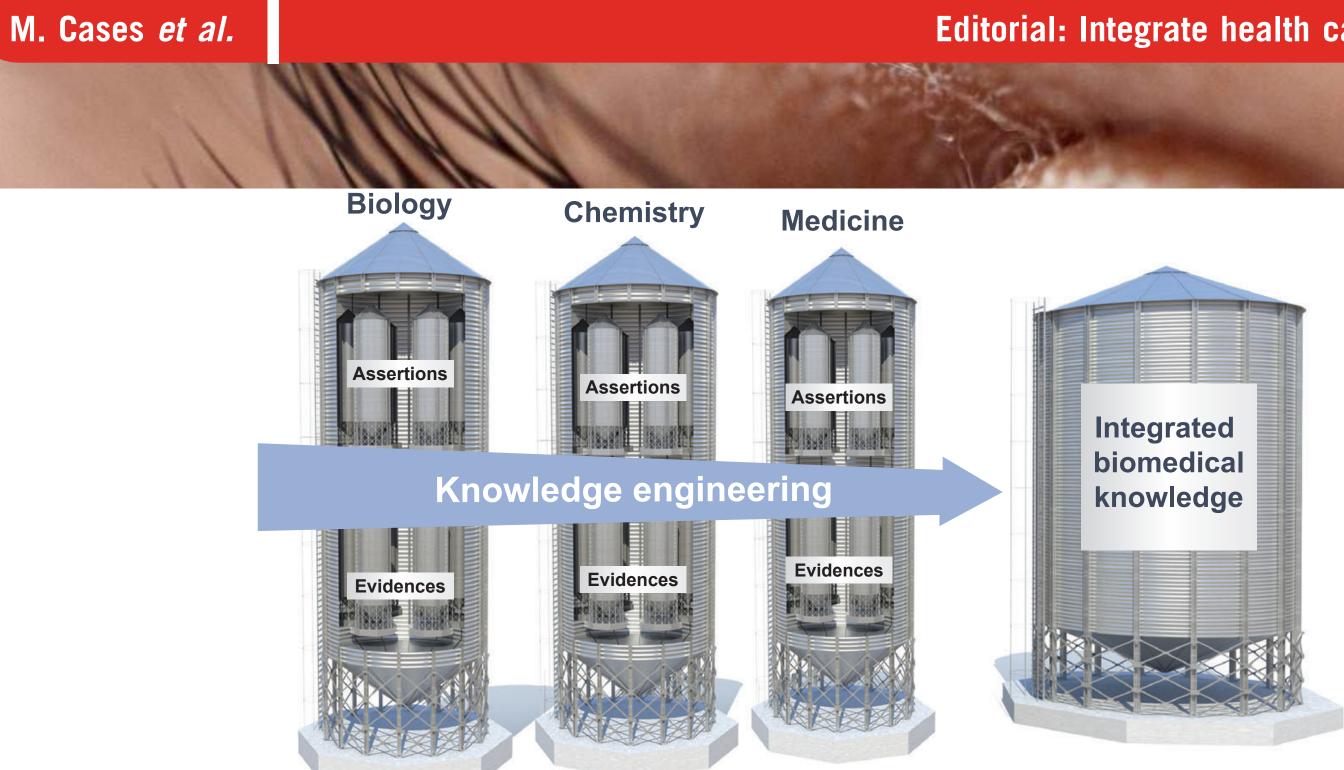
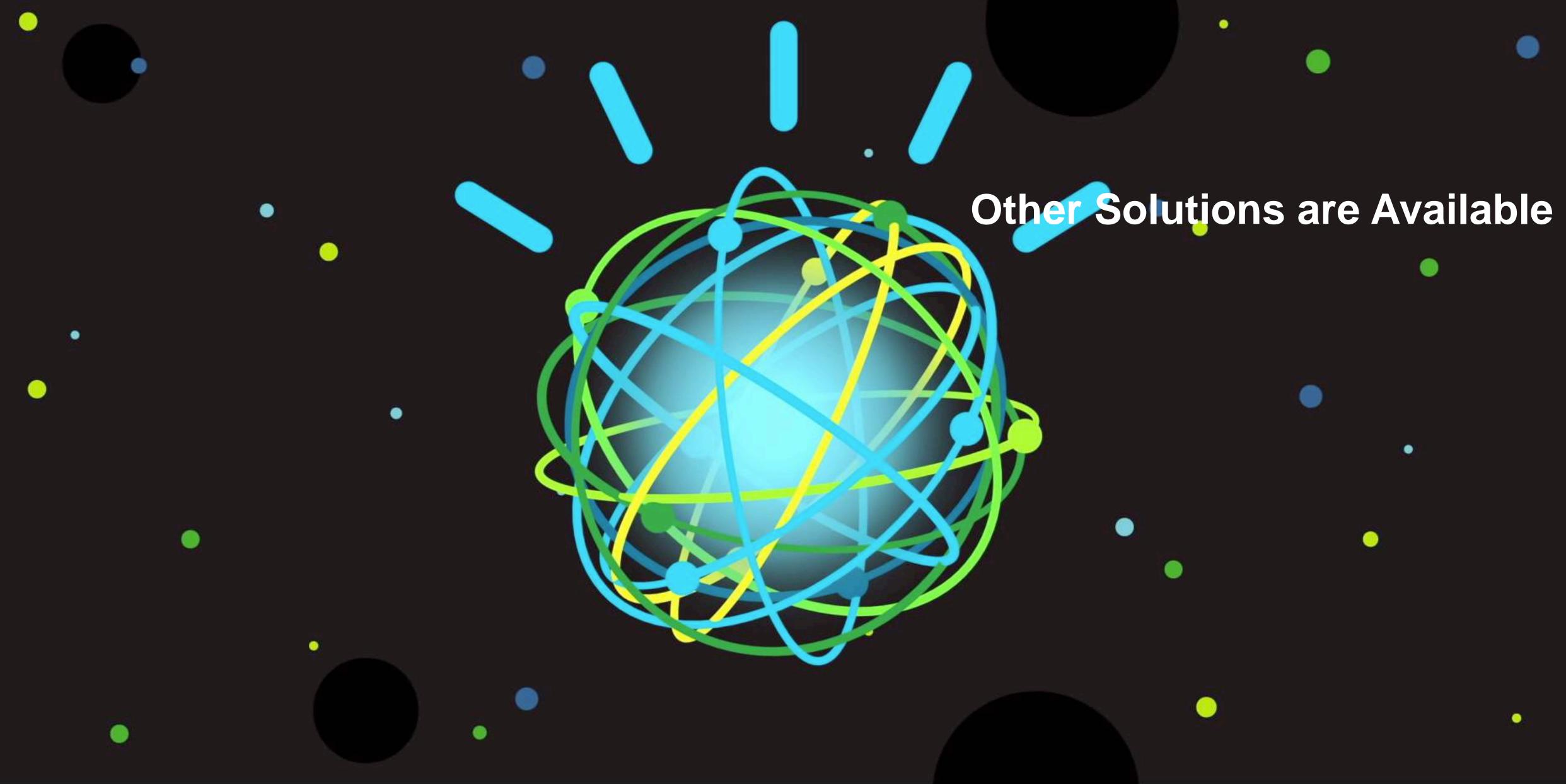


Fig. 1 Interdiscipline and intradiscipline knowledge 'silos' to be overcome. The 'intradiscipline silos' are the partitions between the different evidences and between the assertions developed from the evidences and from earlier assertions.

### **Editorial: Integrate health care and research**

Journal of Internal Medicine, 2013, 274; 321–328

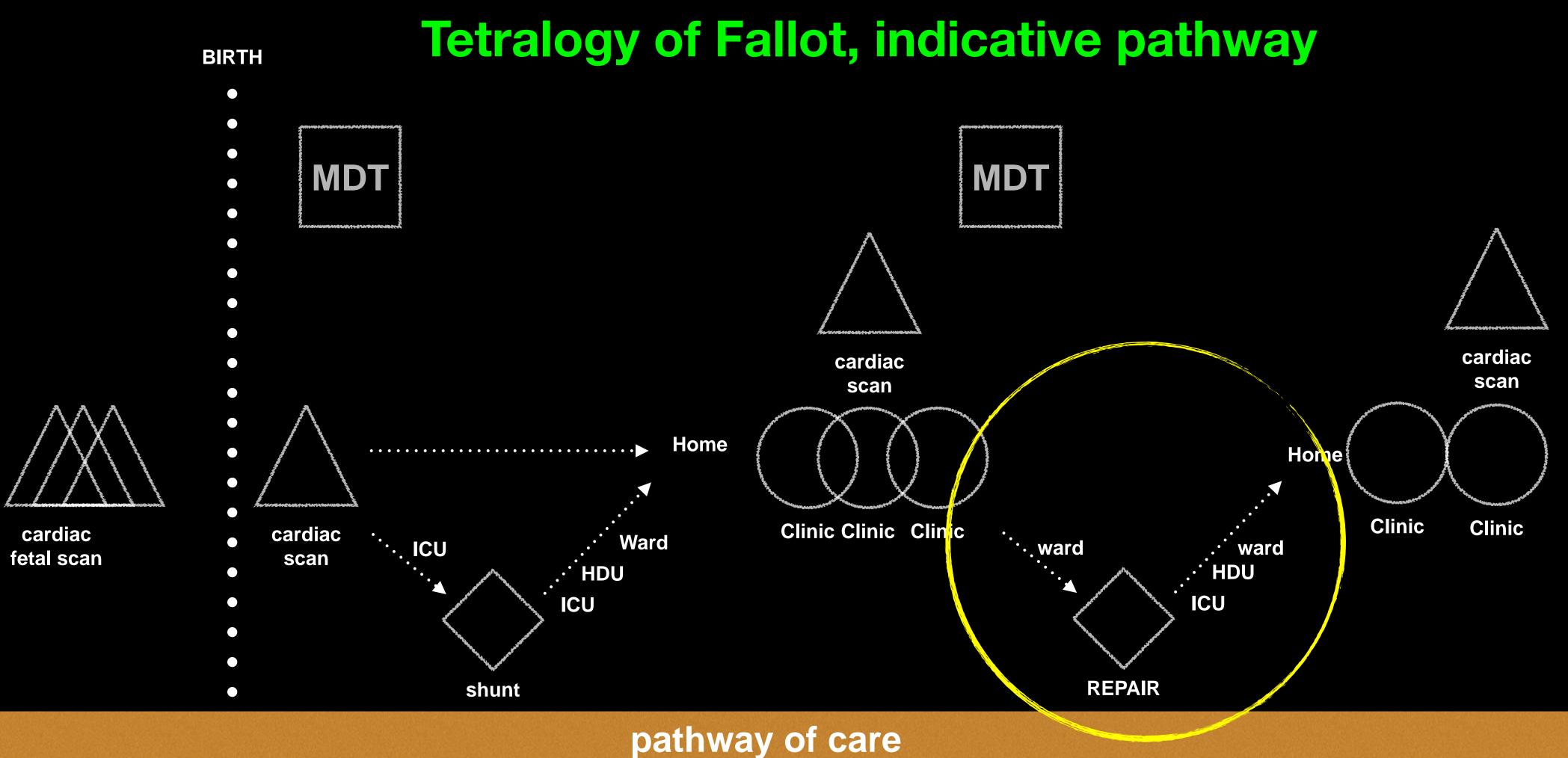




THINKACADEMY

# better care, lower cost, more knowledge





localgood locallocalorlocalorregionalregionalunitunit	specialist centre
---	----------------------

generic

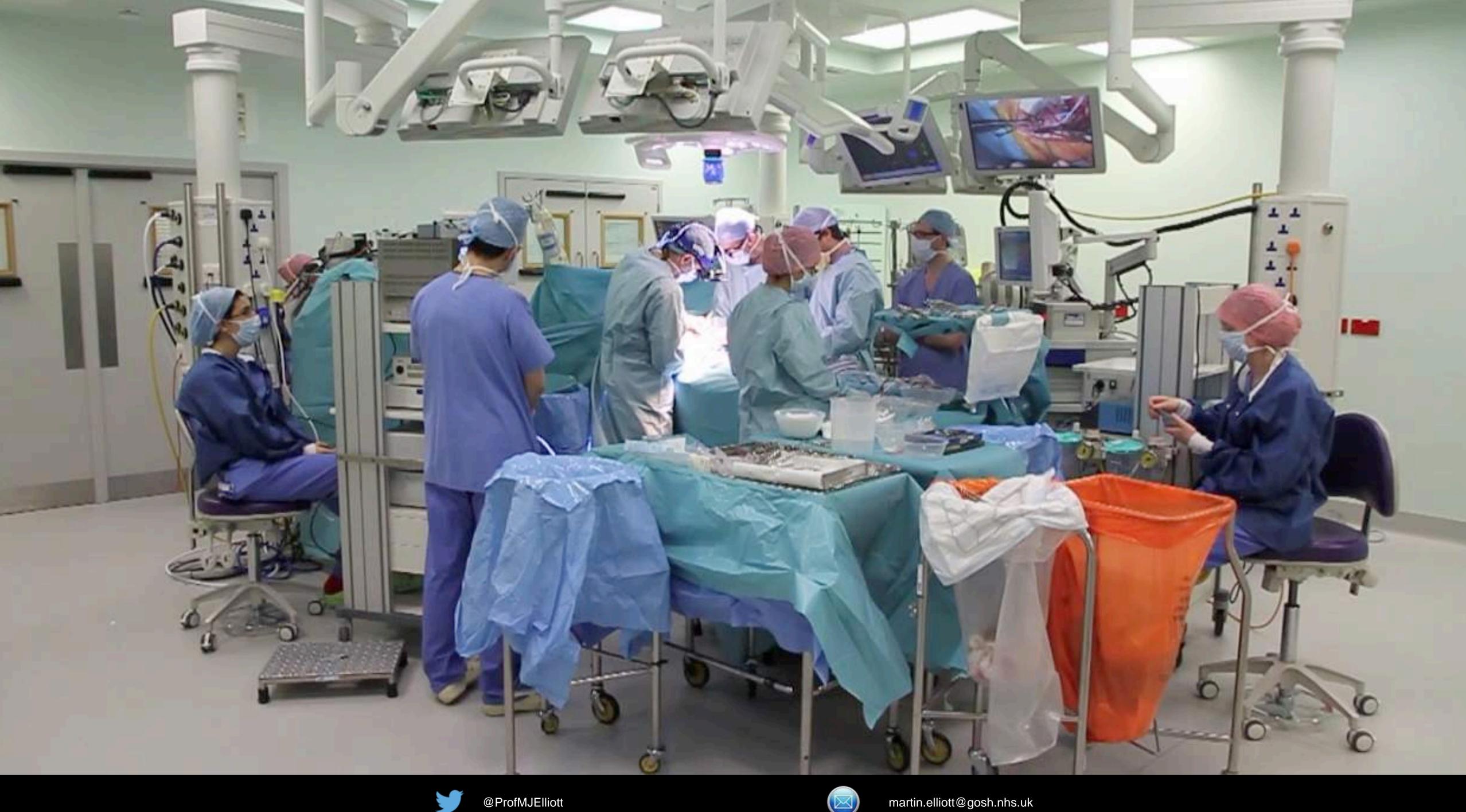
fetal scan

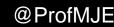






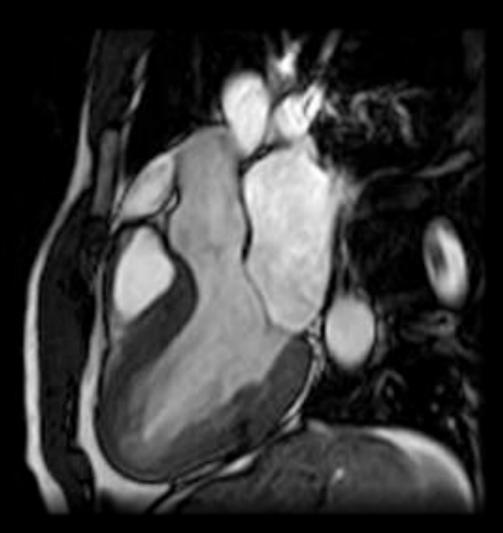










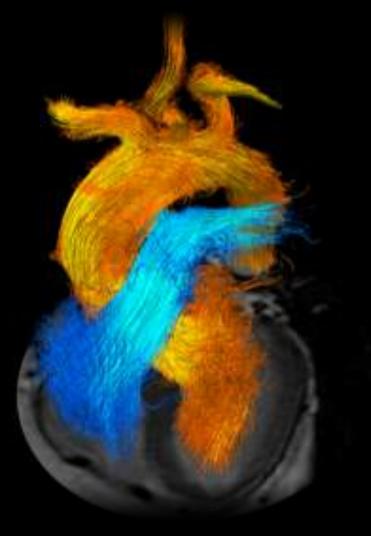








## flow







@ProfMJElliott



Courtesy: C Roobottom, Plymouth





## 3D image of the atrium



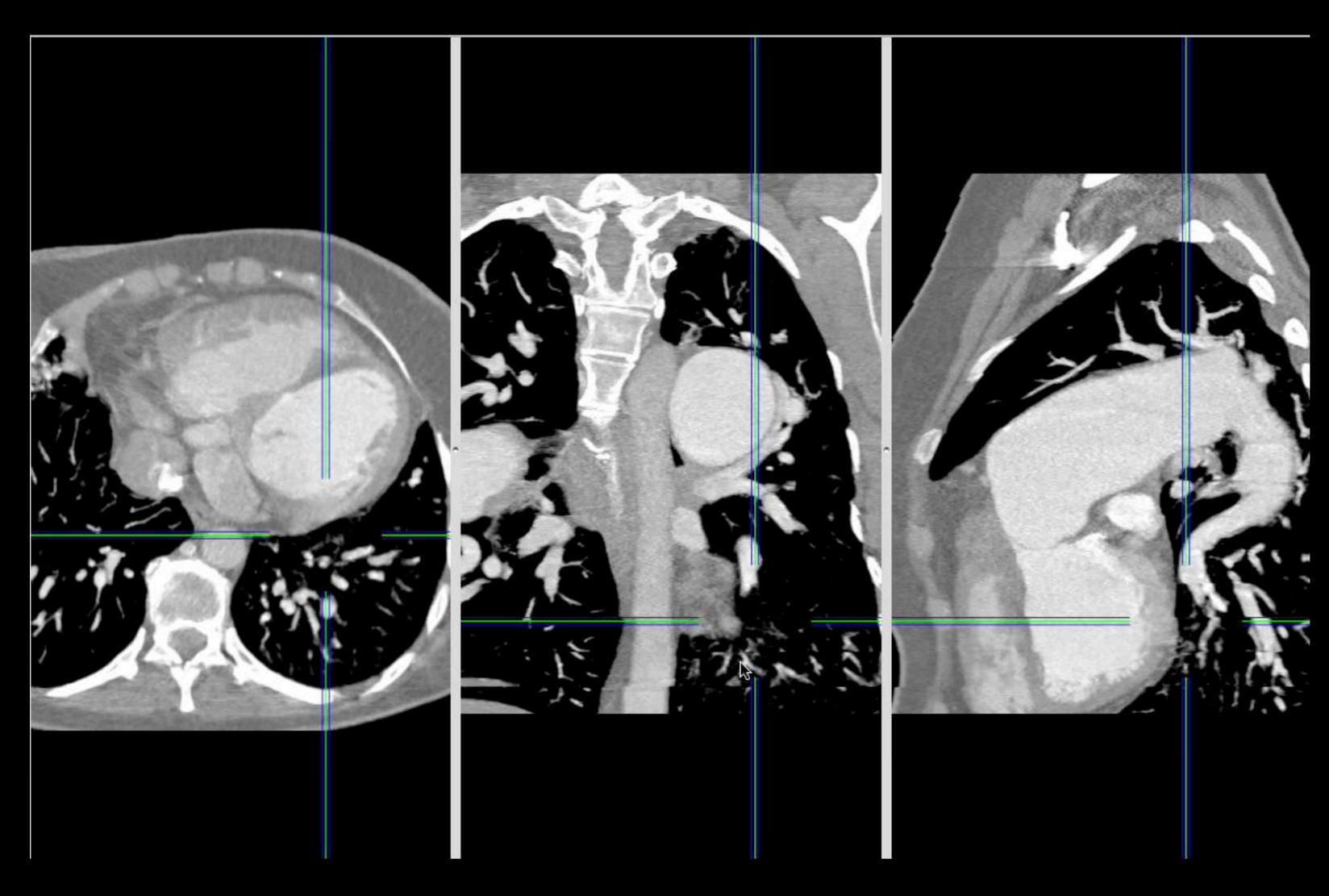
@ProfMJElliott







# Vessels/ airways





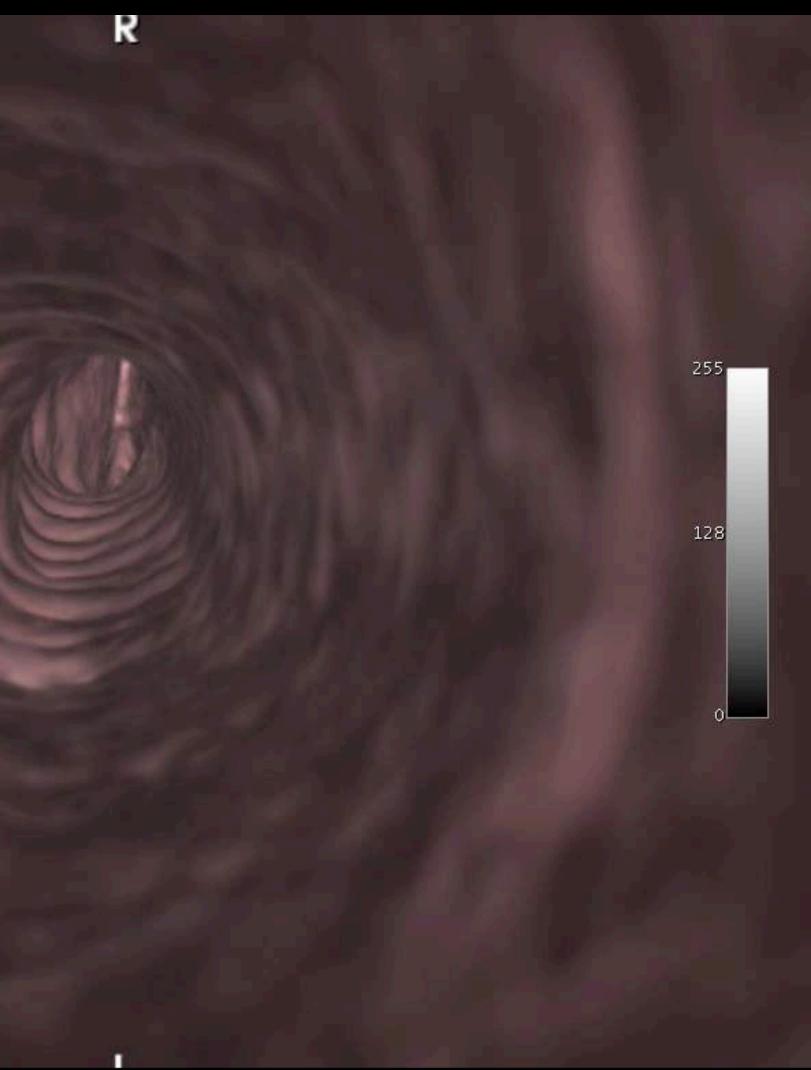


# Vessels/Airways



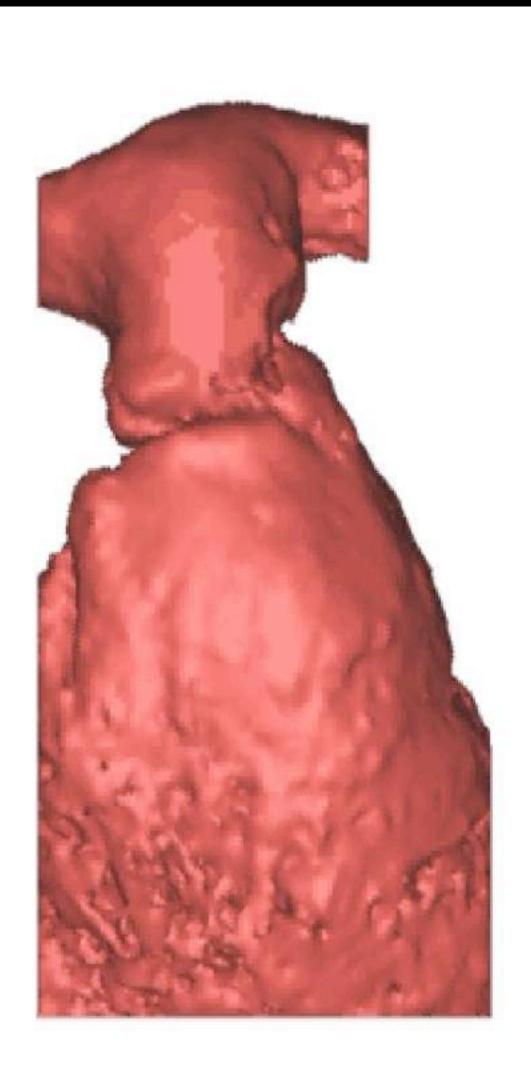


@ProfMJElliott

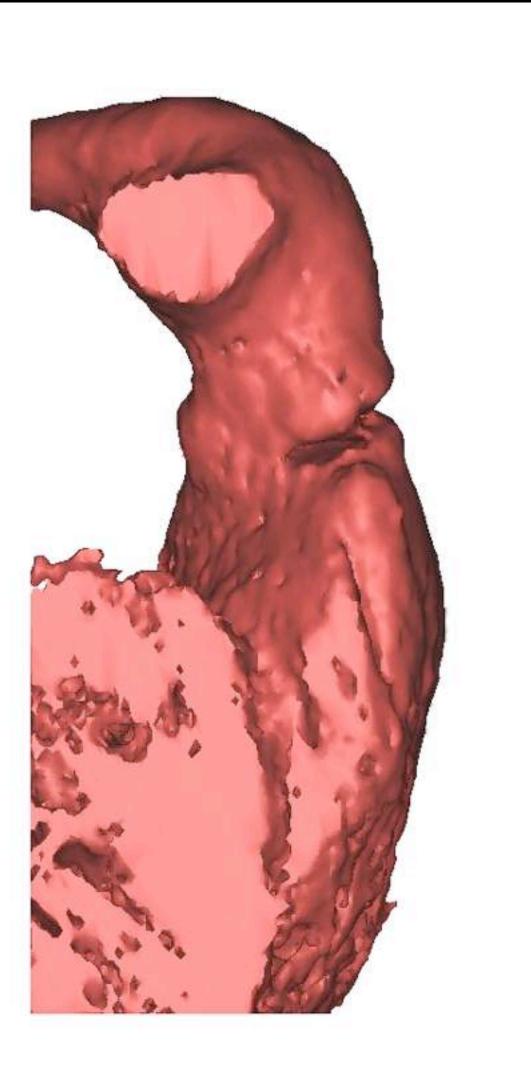




# 3D data for device planning

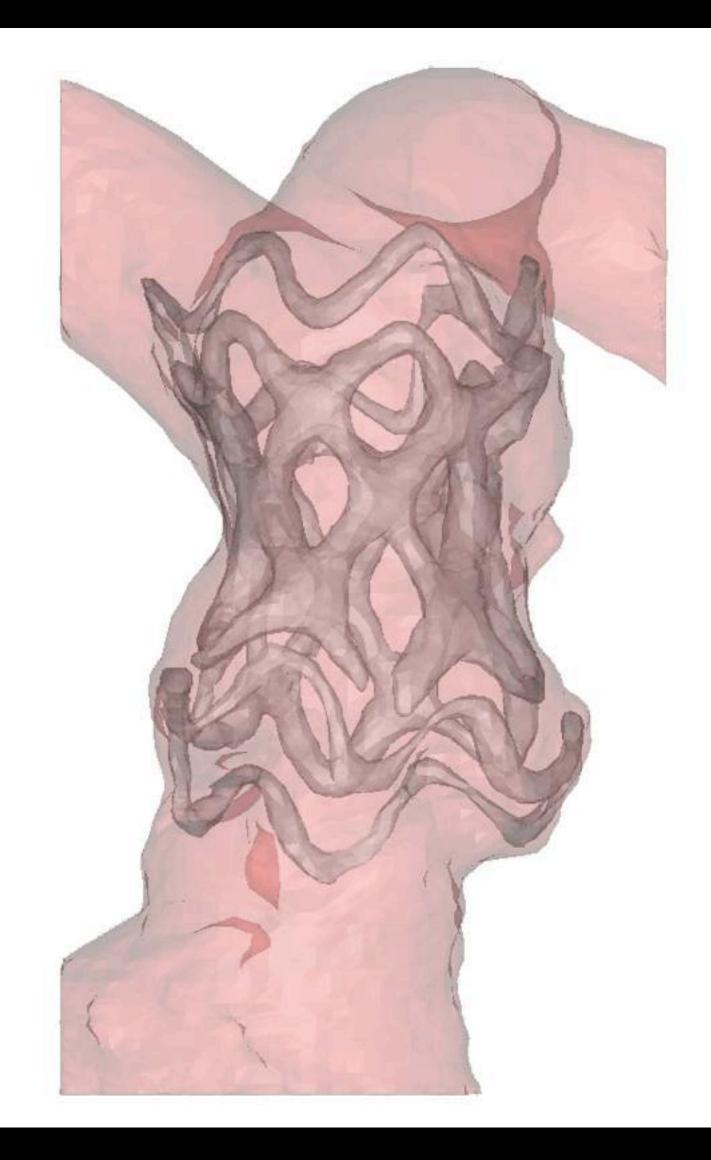








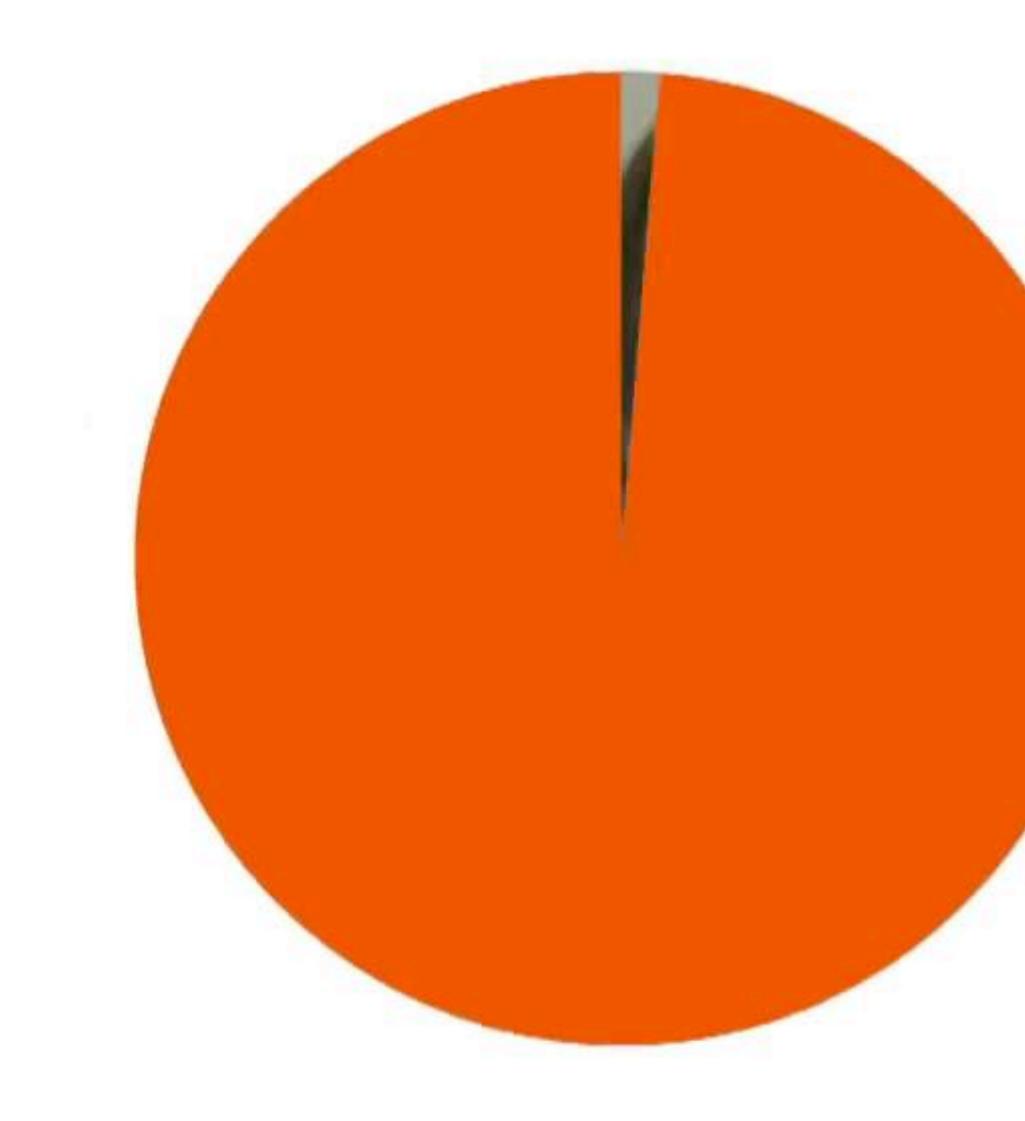
# How will a device function?











# USA TODAY TECH

# scale understanding confidence



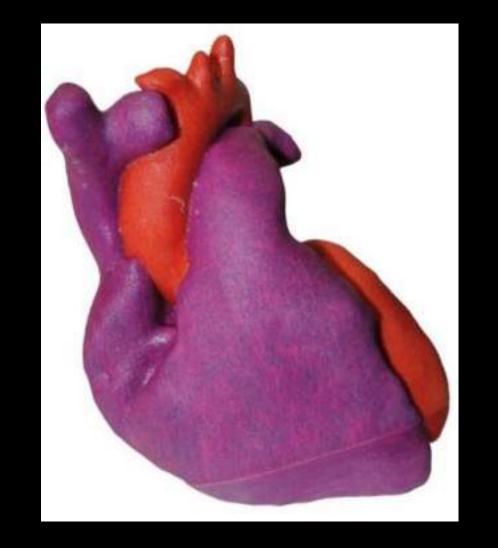






# we use these every day











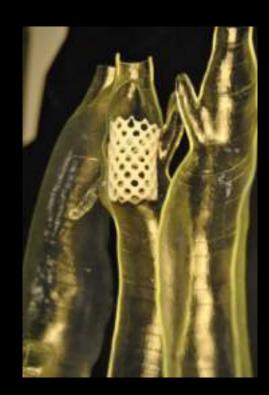
@ProfMJElliott









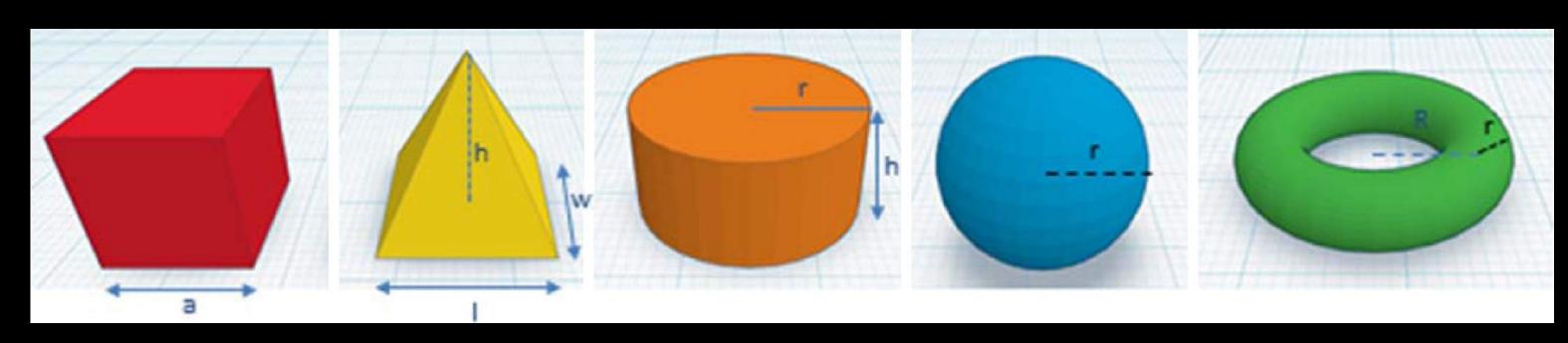




#### Effect of geometry on drug release from 3D printed tablets

Alvaro Goyanes<sup>a</sup>, Pamela Robles Martinez<sup>a</sup>, Asma Buanz<sup>a</sup>, Abdul W. Basit<sup>a,b</sup>, Simon Gaisford<sup>a,b,\*</sup>

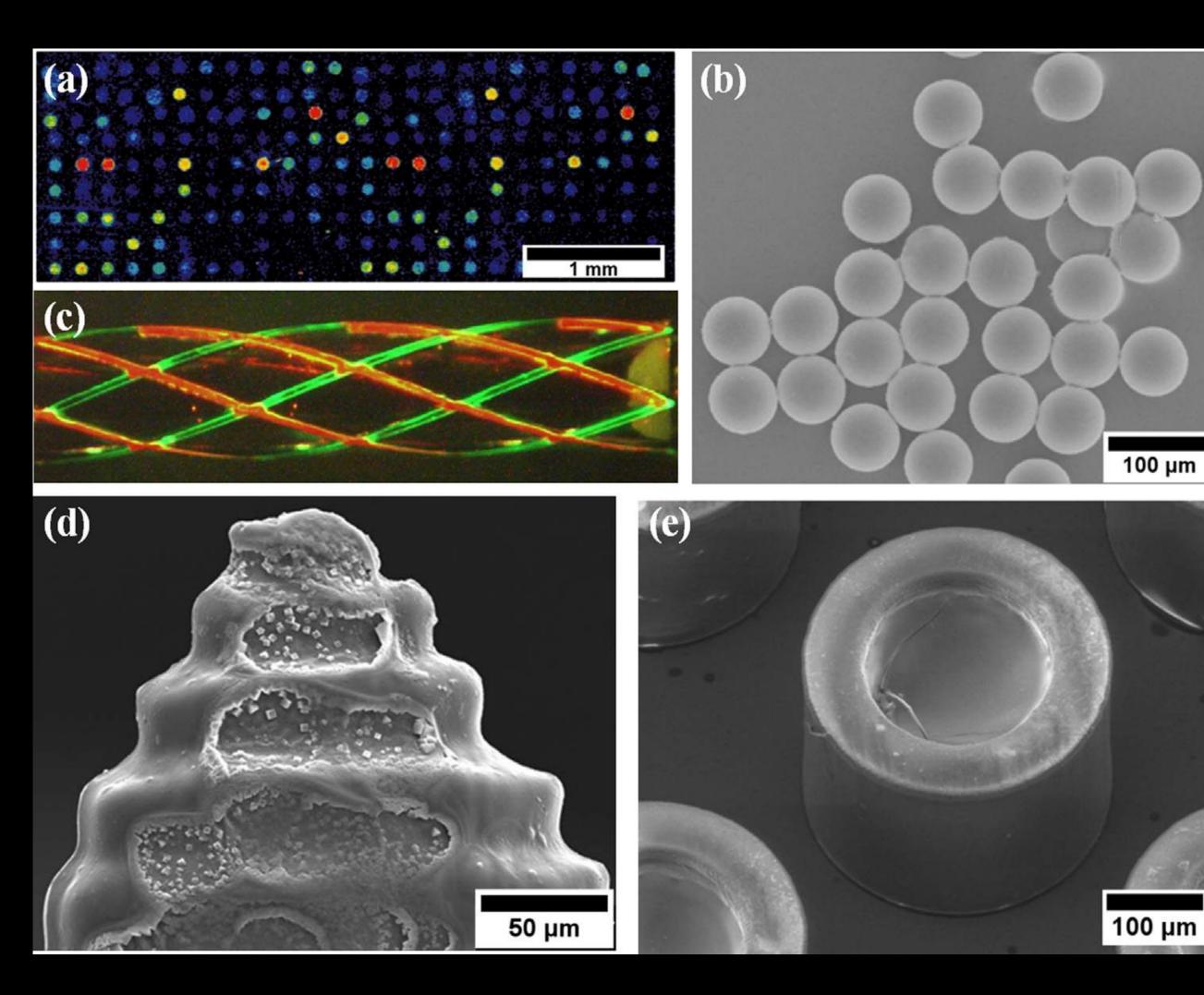
#### http://dx.doi.org/10.1016/j.ijpharm.2015.04.069











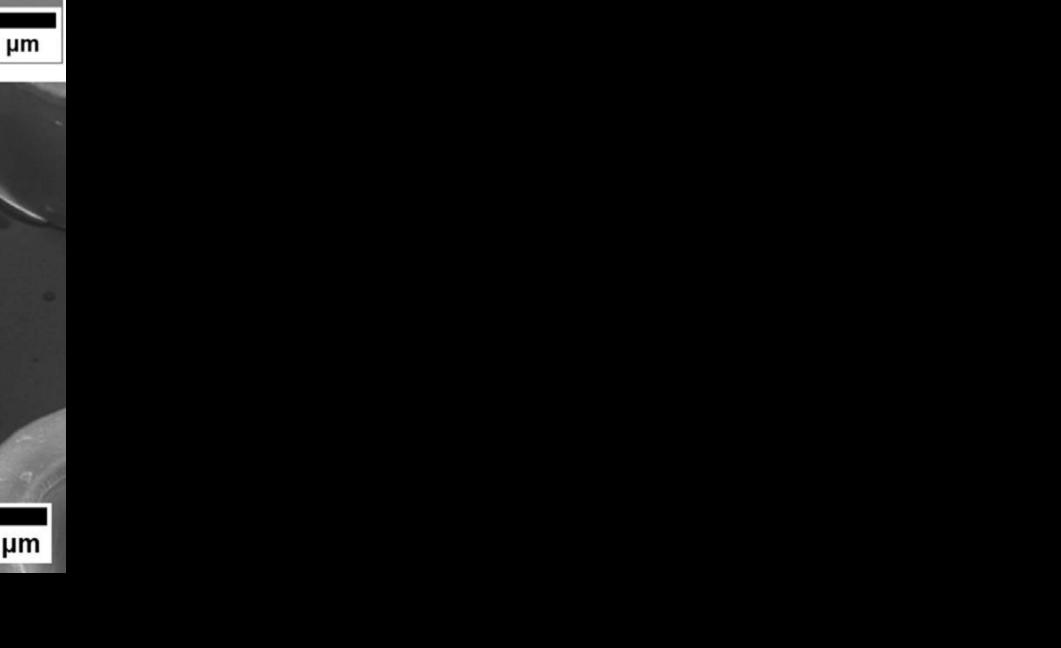


Personalised medicine

Inkjet printing for pharmaceutics – A review of research and manufacturing

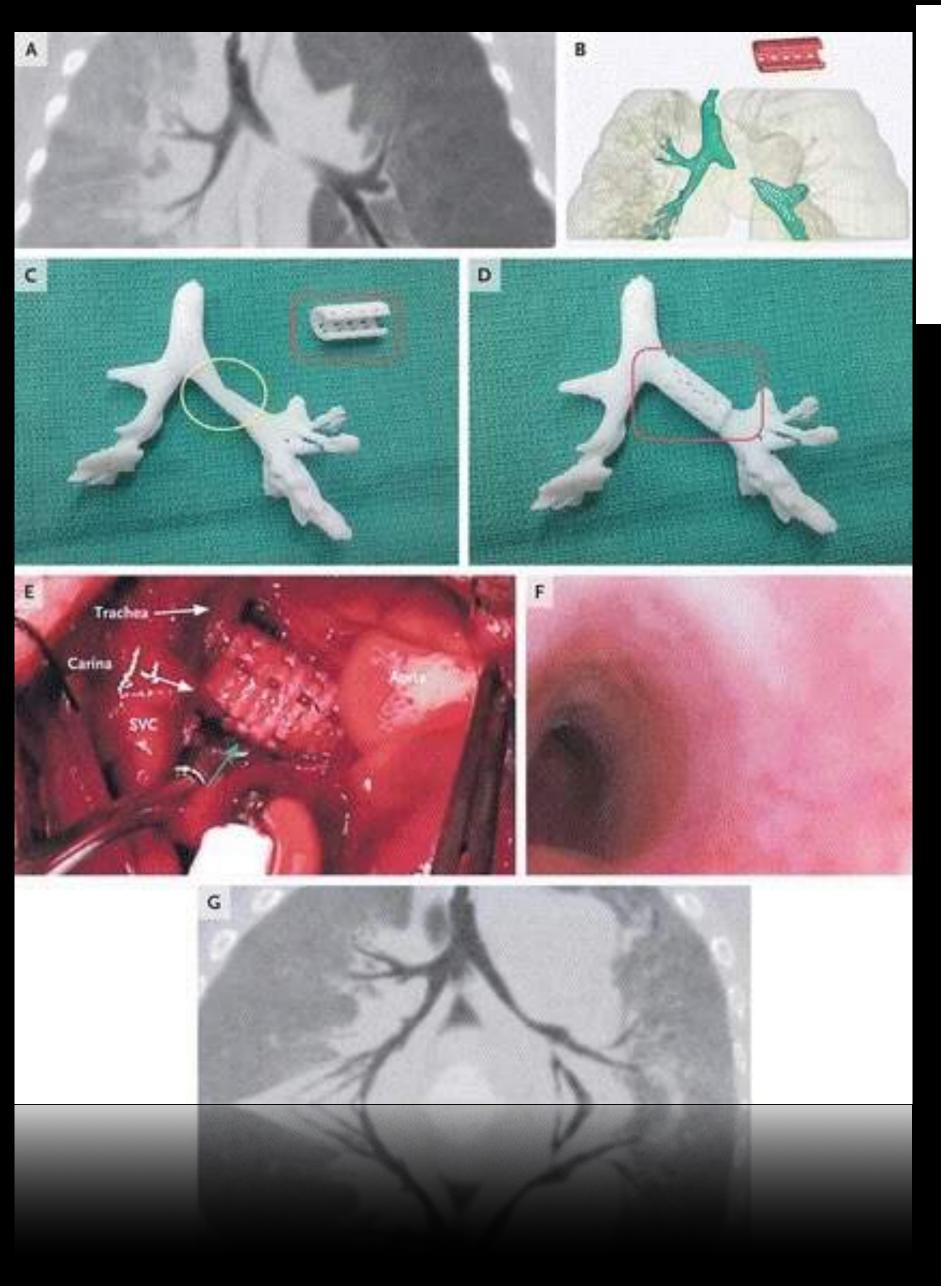
Ronan Daly<sup>a,\*</sup>, Tomás S. Harrington<sup>b</sup>, Graham D. Martin<sup>a</sup>, Ian M. Hutchings<sup>a</sup>

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









# Bioresorbable Airway Splint Created with a Three-Dimensional Printer

N Engl J Med 2013; 368:2043-2045 | May 23, 2013 | DOI: 10.1056/NEJMc1206319







# no surgery please





#### **Transcatheter Versus Surgical Closure** of Perimembranous Ventricular **Septal Defects in Children**

A Randomized Controlled Trial

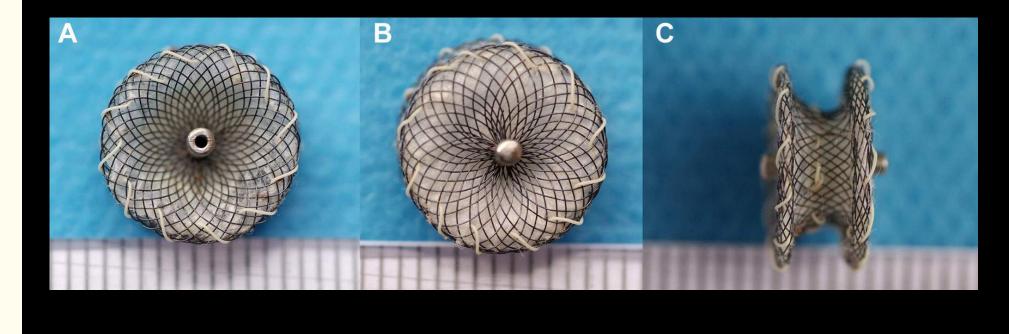
http://dx.doi.org/10.1016/j.jacc.2014.01.008

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



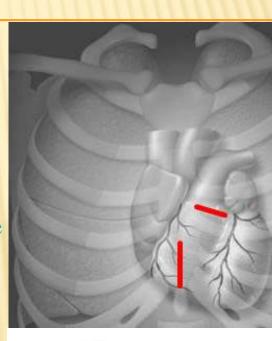






#### **THE PROCEDURE**

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



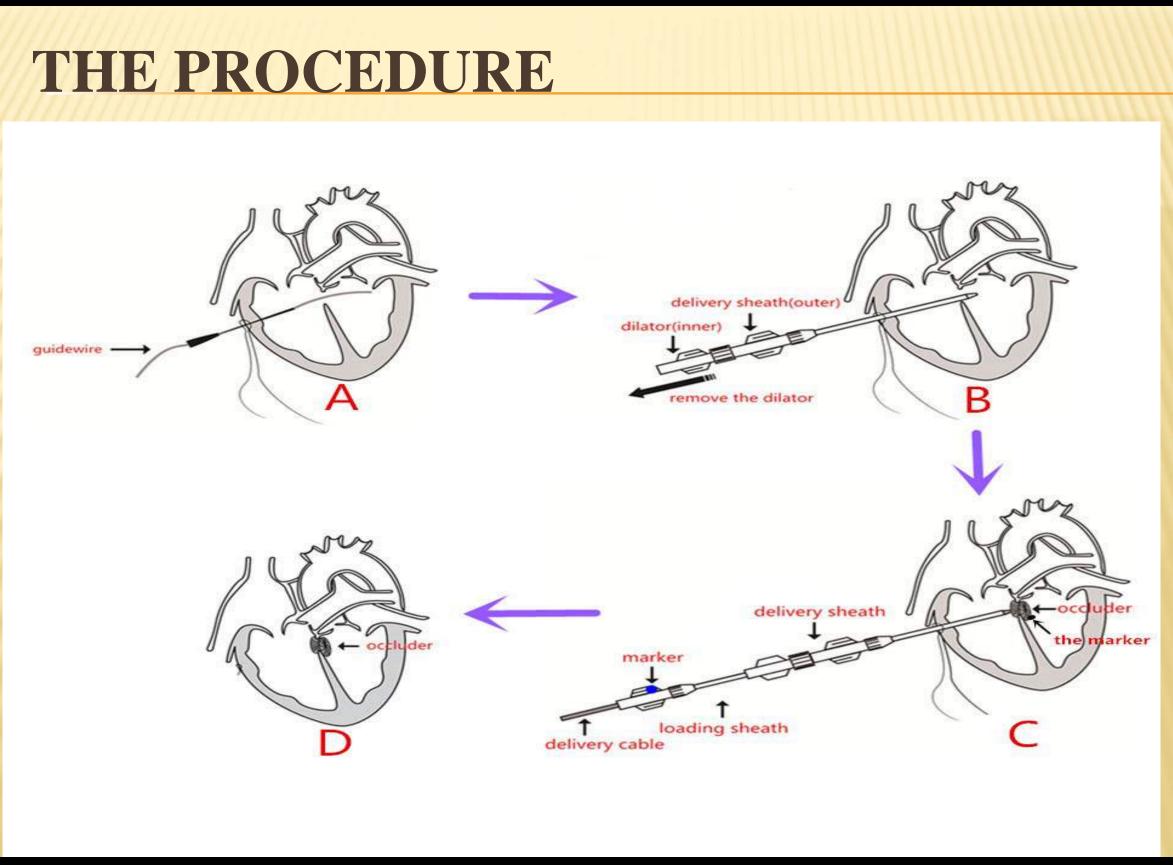
胄岛][童胜脏巾]



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

Heart Center, Qingdao Women and Children's Hospital Qingdao University P. R. China The second second

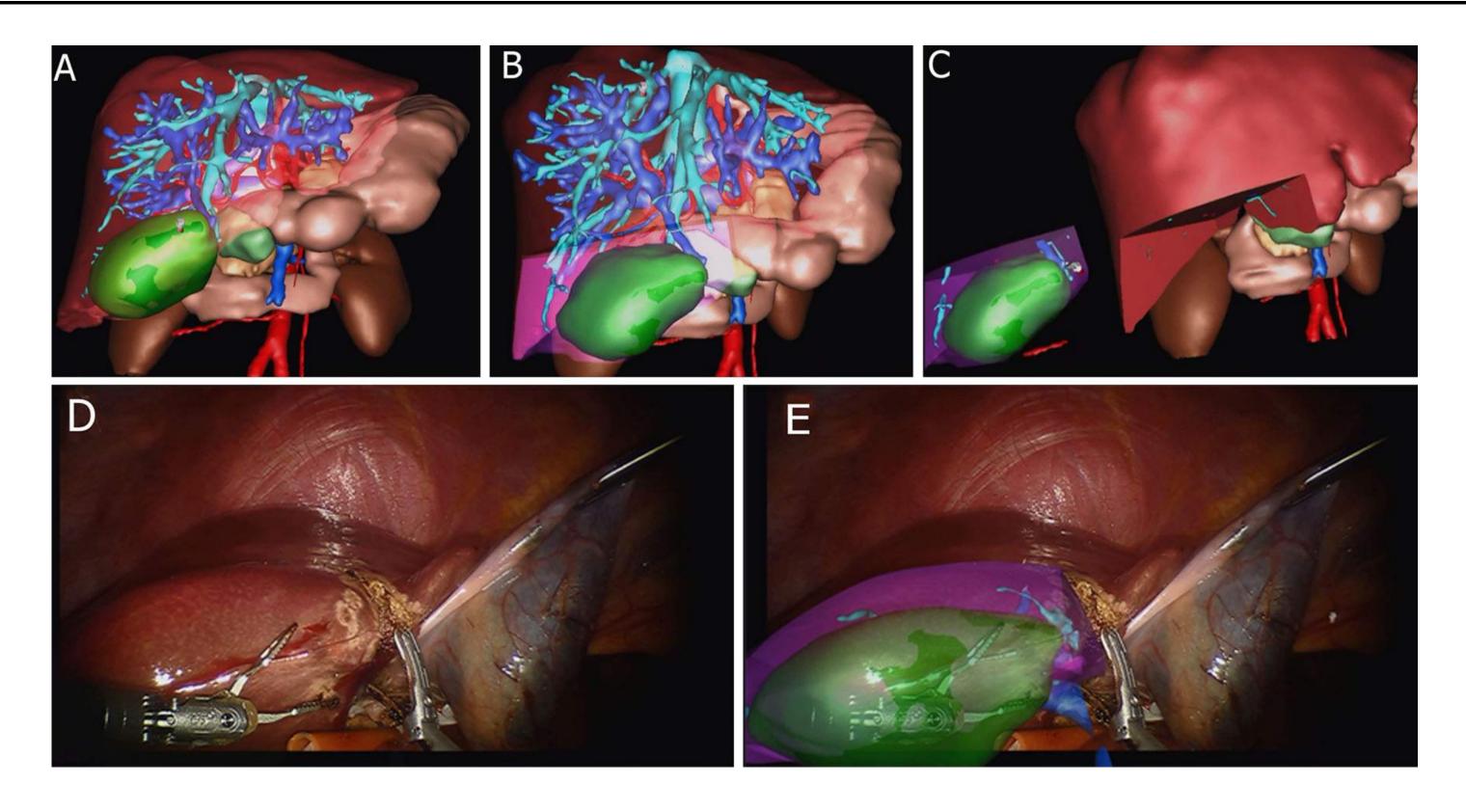




## many less long term complications no radiation







# **Augmented Reality**

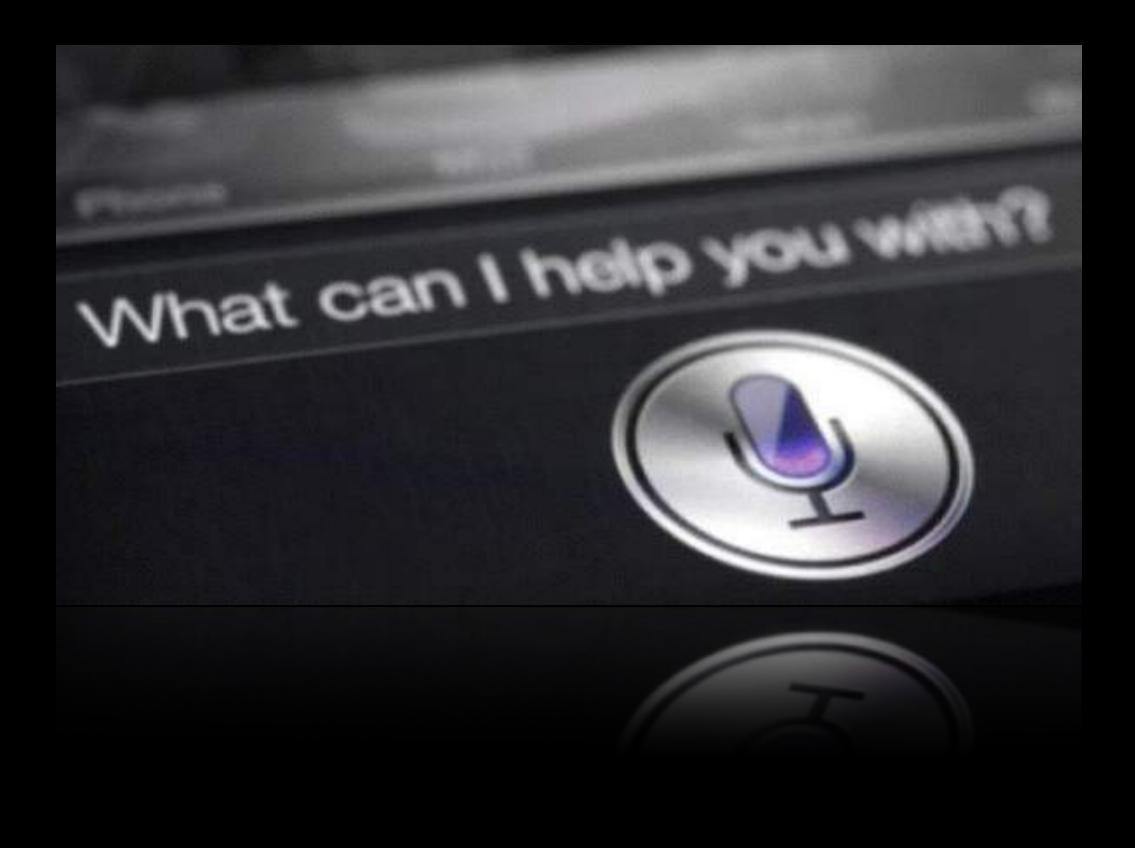
#### **VR-Render Software**



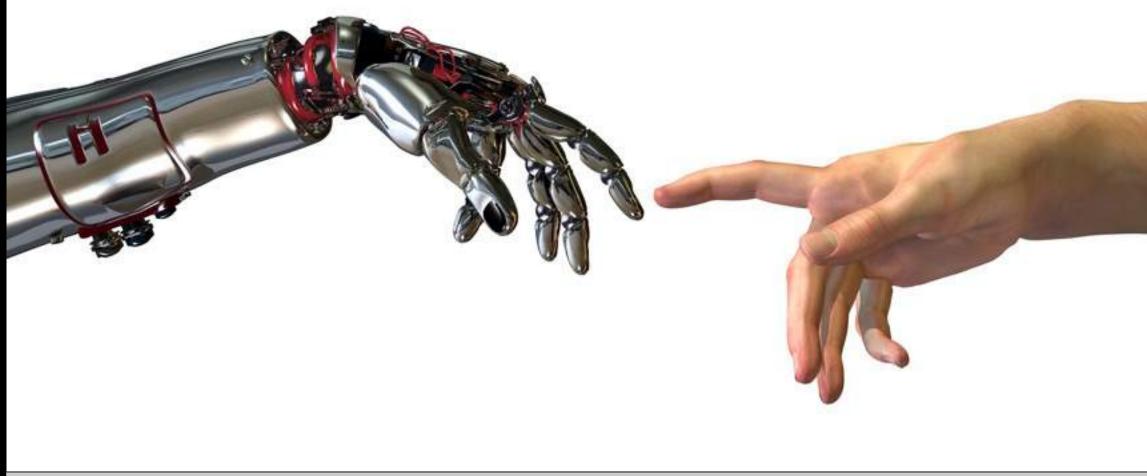
618













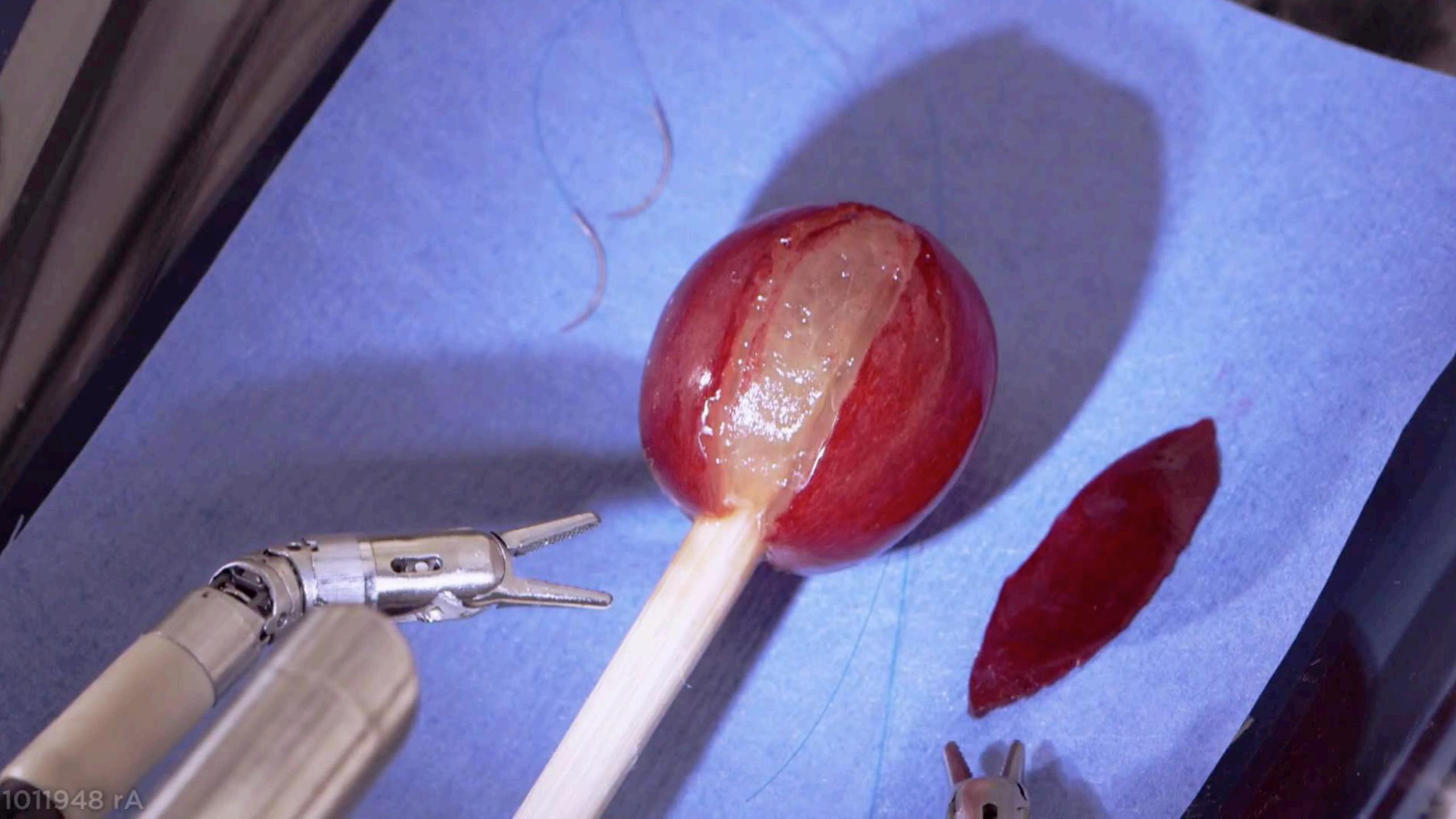












# Think About It

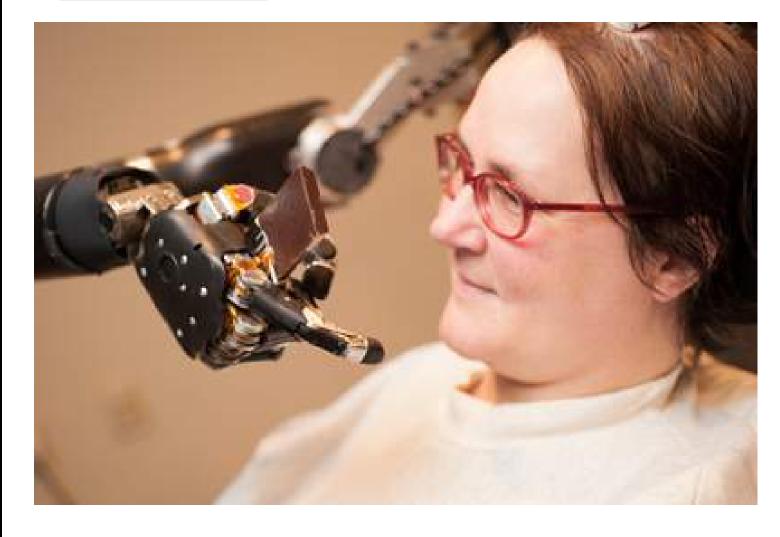






#### This Woman Flew an F-35 Simulator with Her Mind

by BRENDAN MCGARRY on MARCH 2, 2015

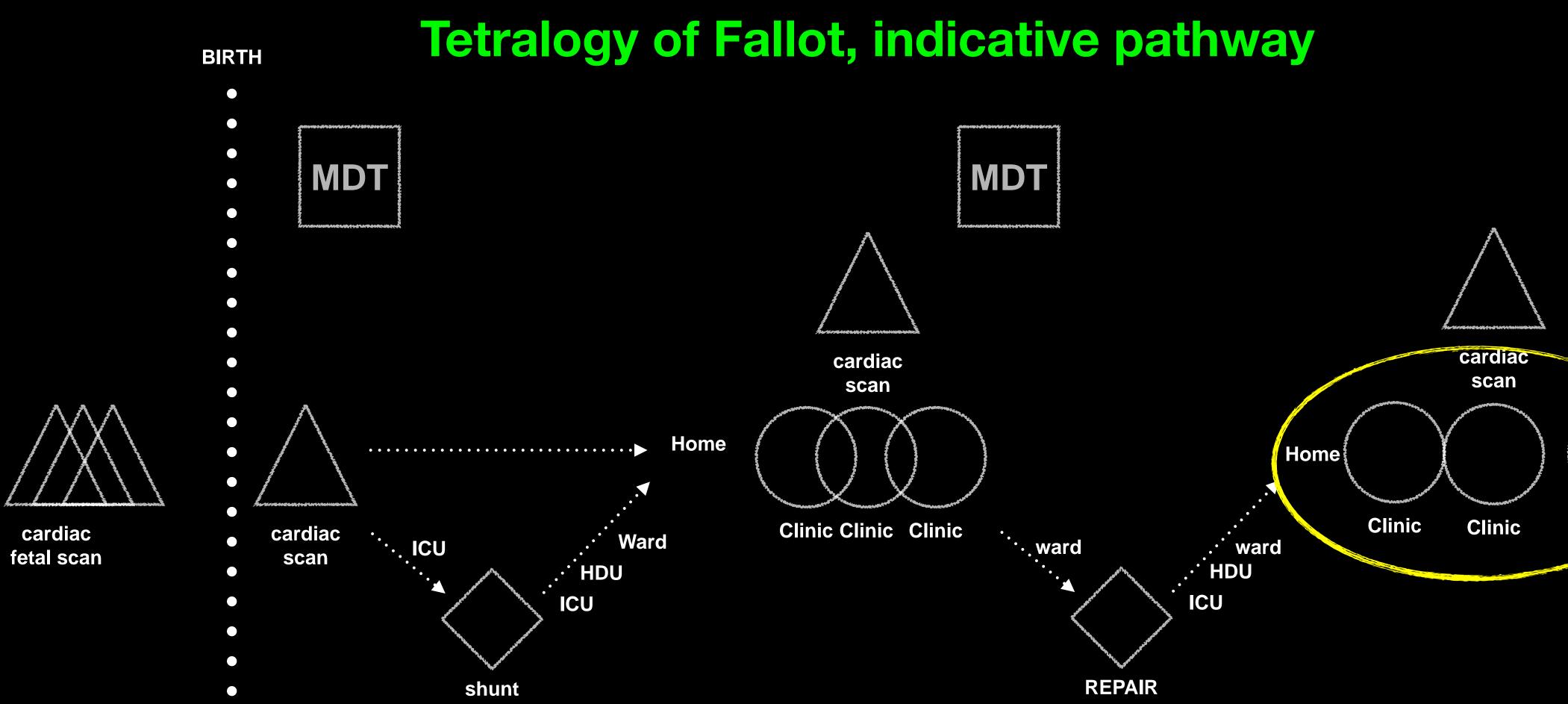


http://defensetech.org/2015/03/02/this-woman-flew-an-f-35-simulator-with-her-mind/









localgood locallocalorlocalorregionalregionalunitunit	specialist centre
---	----------------------

generic

fetal scan



#### pathway of care











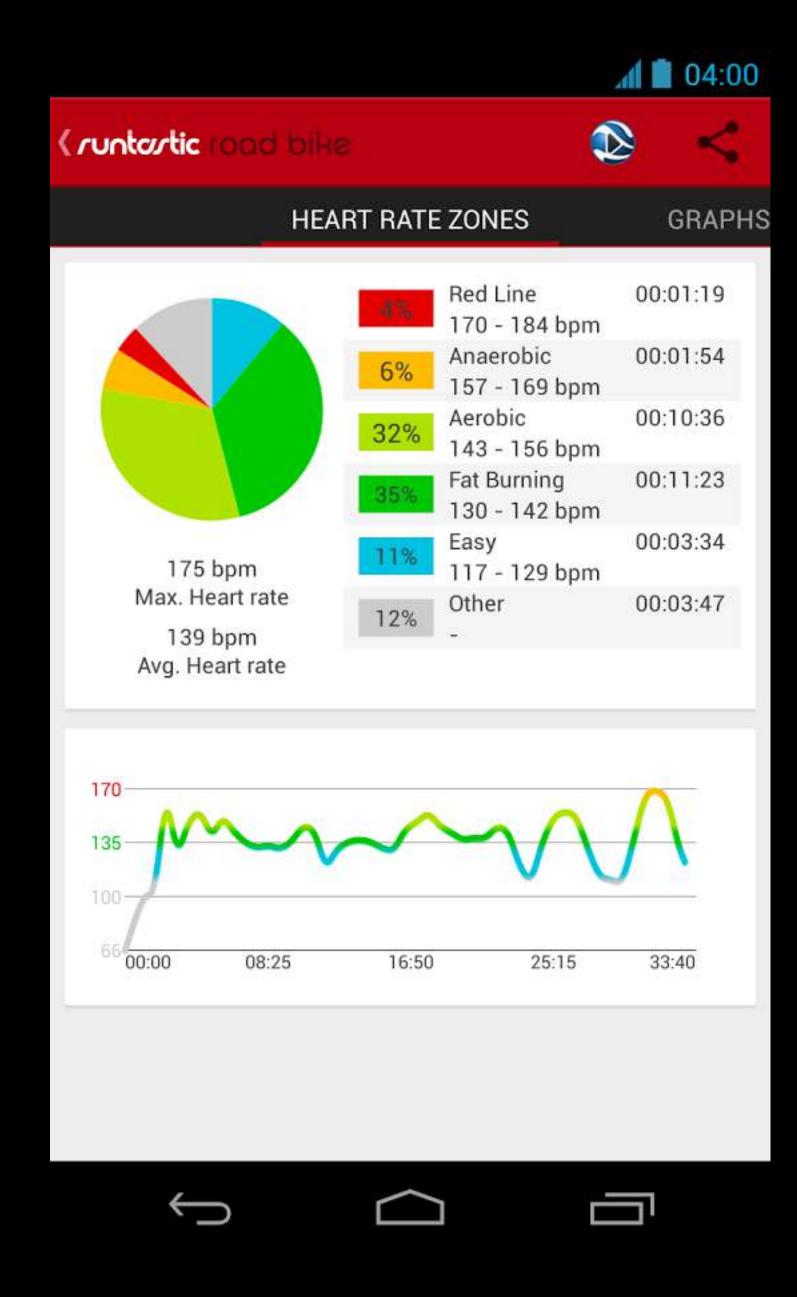




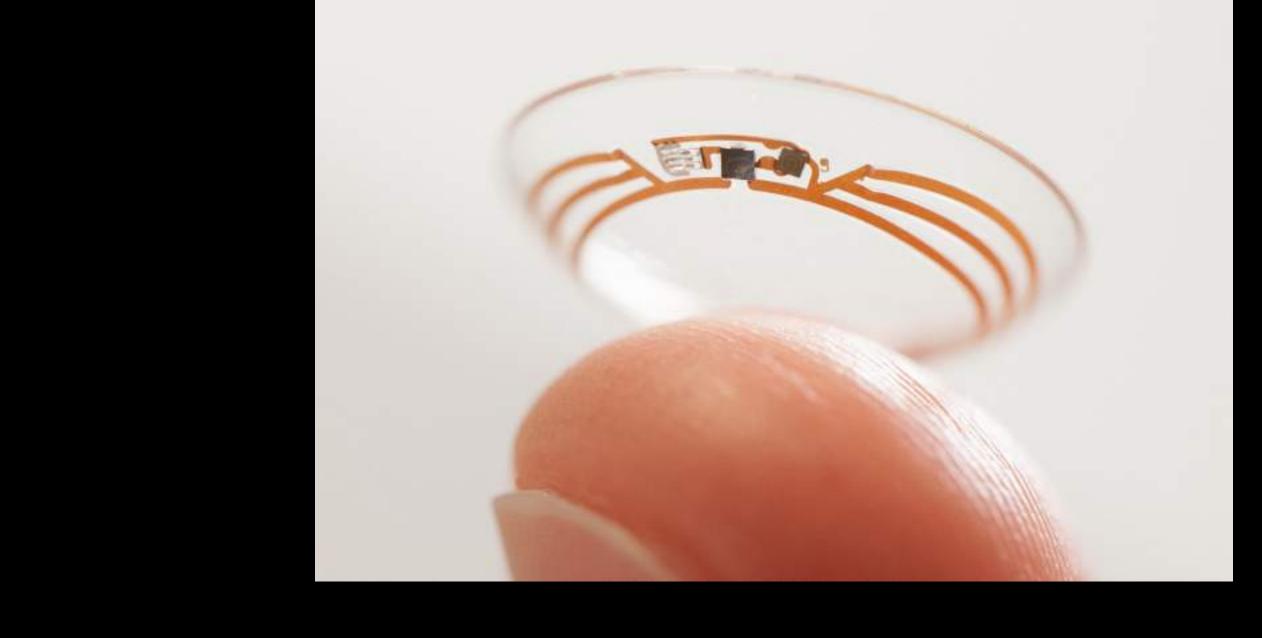


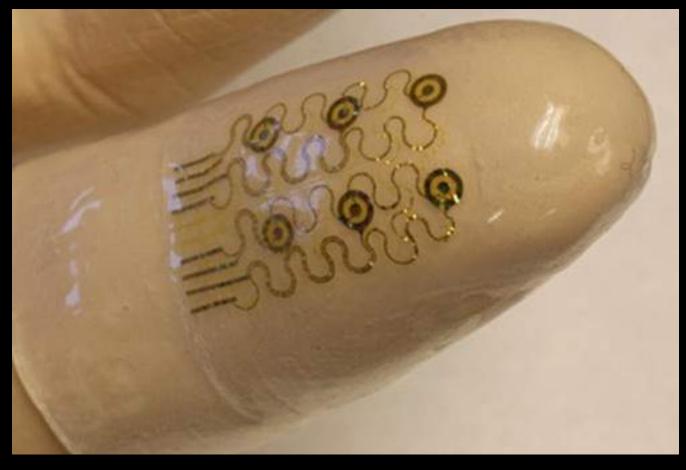








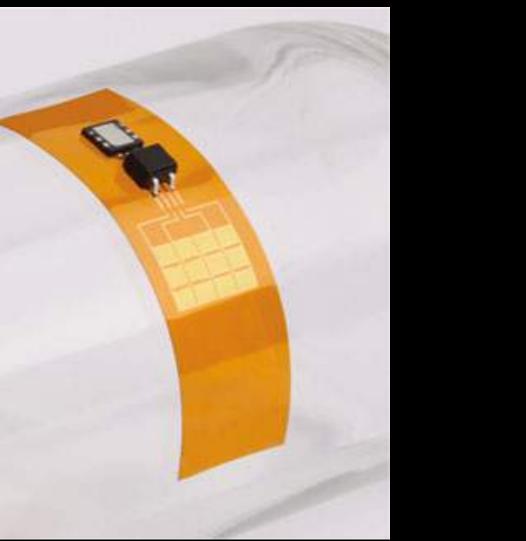


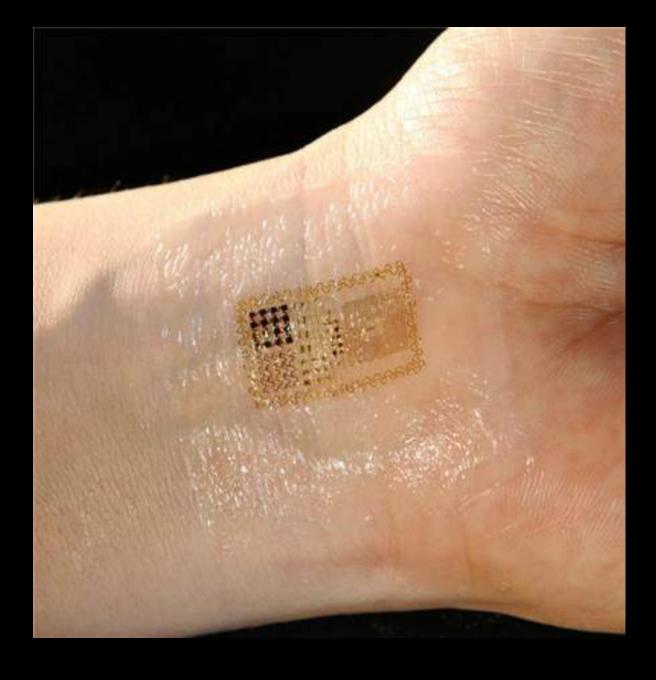




C Dagdeviren et al, Proc. Nat. Acad. Sci. USA, 2013, DOI: 10.1073/pnas.1317233111













#### + GPS

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

# HealthPatch® MD



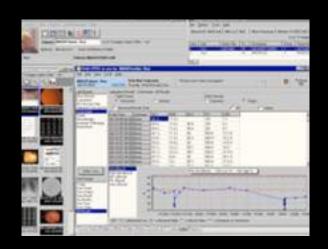






# \$10,000,000





## EPR-sourced data

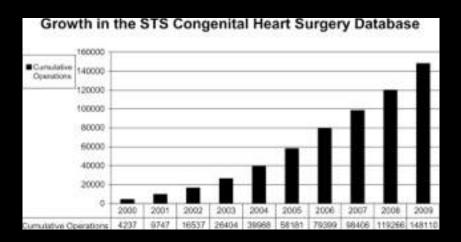
#### machine-sourced data





# big data in medicine





#### registry data

#### patient-sourced data





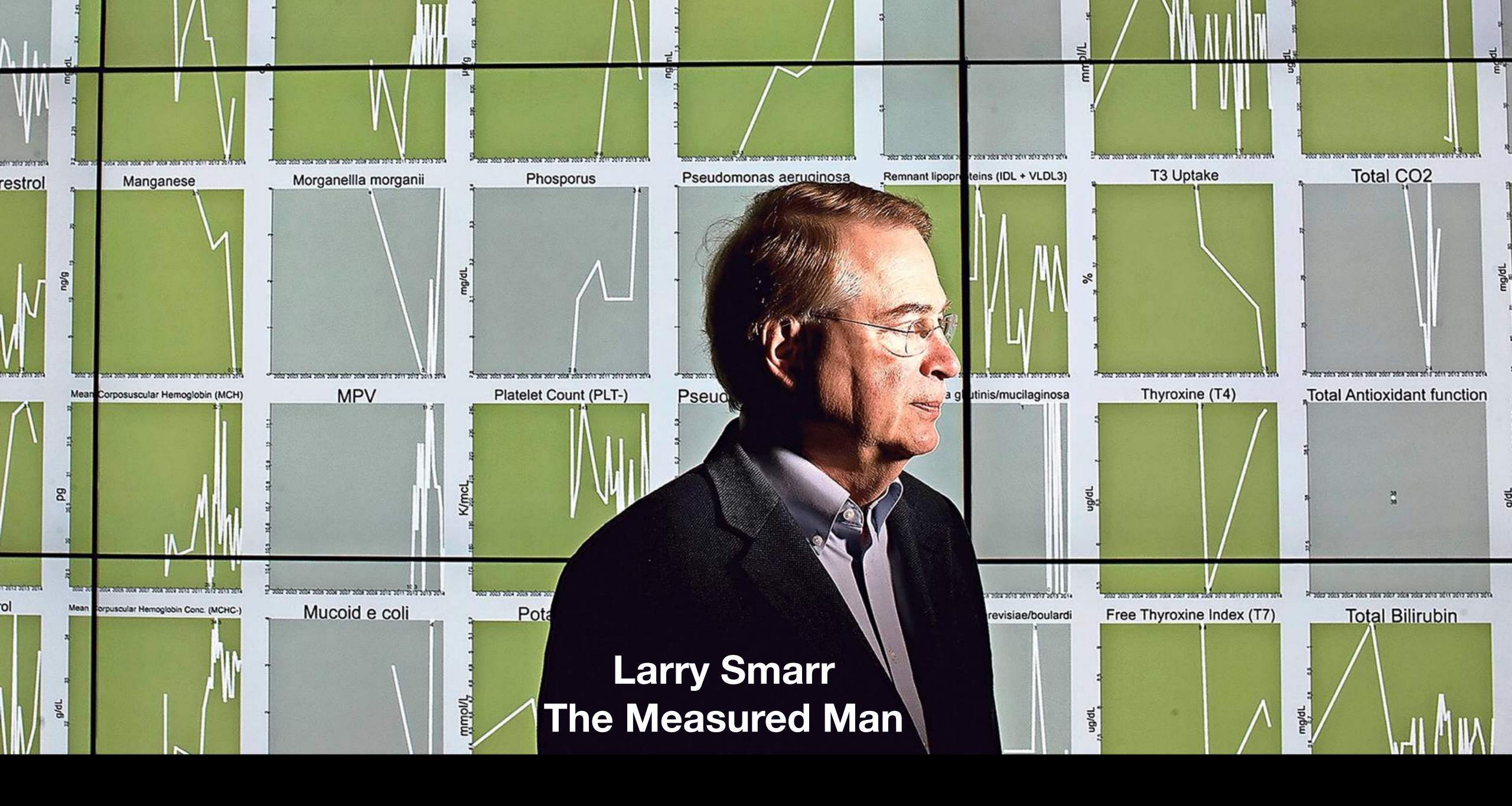
#### the measure















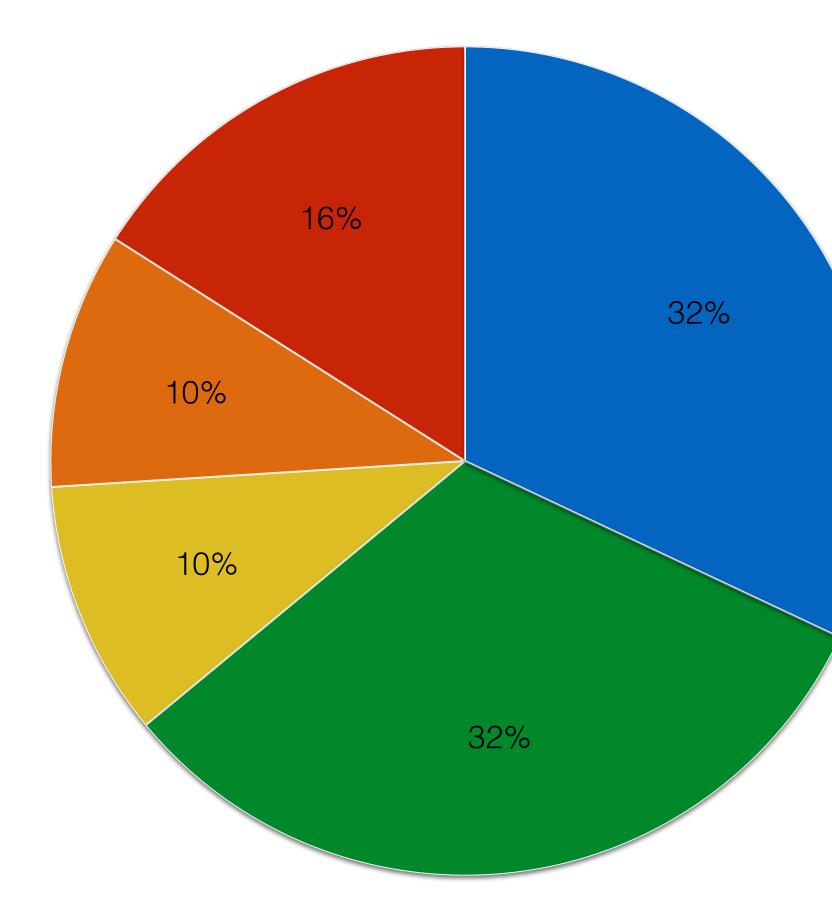
# I know where you are I know what you are doing I know how you are



@ProfMJElliott



#### What is coming next in the field of Data?





Economic Efficency

- Improve Public Health
- Improve Quality
- Data Managers are needed
- Other

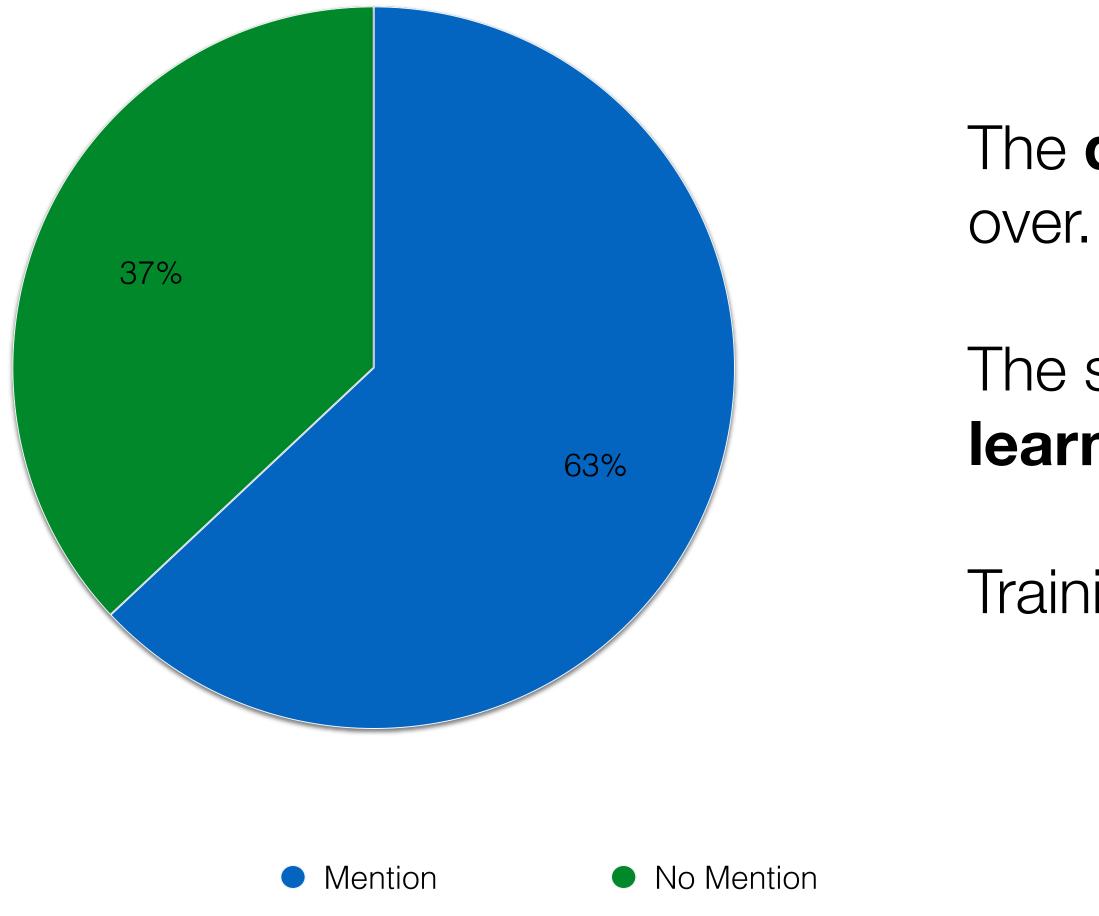
*'More public reporting More IT professionals will have jobs (costing more money) Large scale data analysis is absolutely possible--ask the NSA'* 







#### Simulation



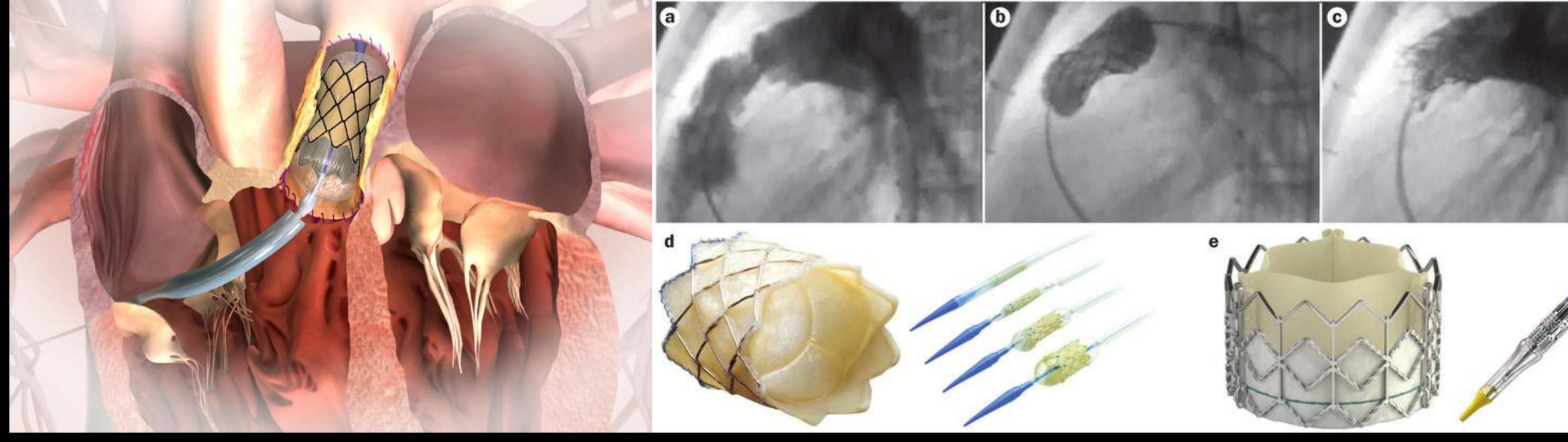


#### The days of trial and error in learning may be

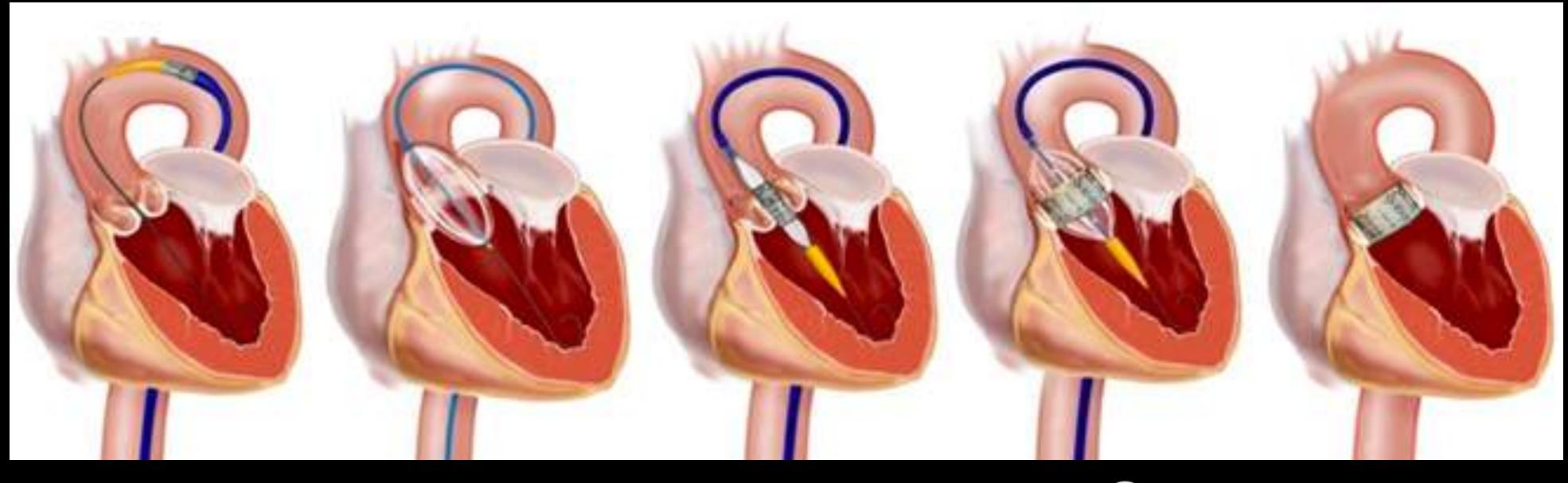
# The system and patients will not tolerate a learning curve.

Training in simulators ... will be necessary.





## **Trans-Catheter Insertion of Heart Valves**





# >100,000



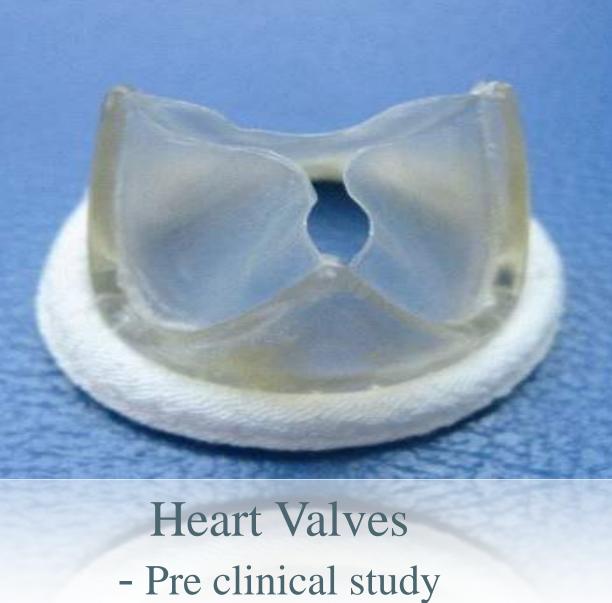


#### Lacriminal Duct - Transplanted into Human

# Heart Valves

**Nasal Reconstruction** - Pre clinical study

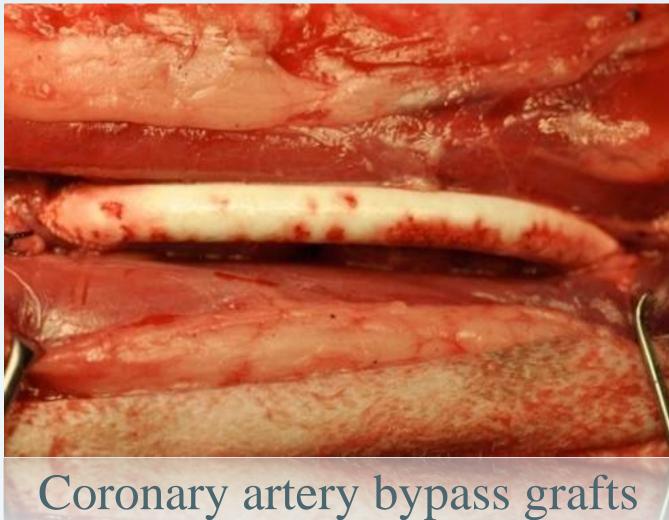




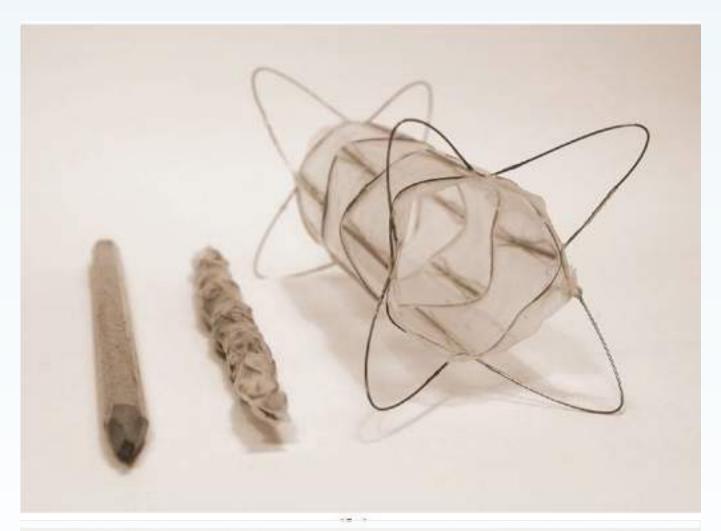
# 

# **POSS PCU** Current Applications





- Pre clinical trials



Stents - Pre clinical study

## THE CULTURE OF ORGANS

by ALEXIS CARREL

CHARLES A. LINDBERGH

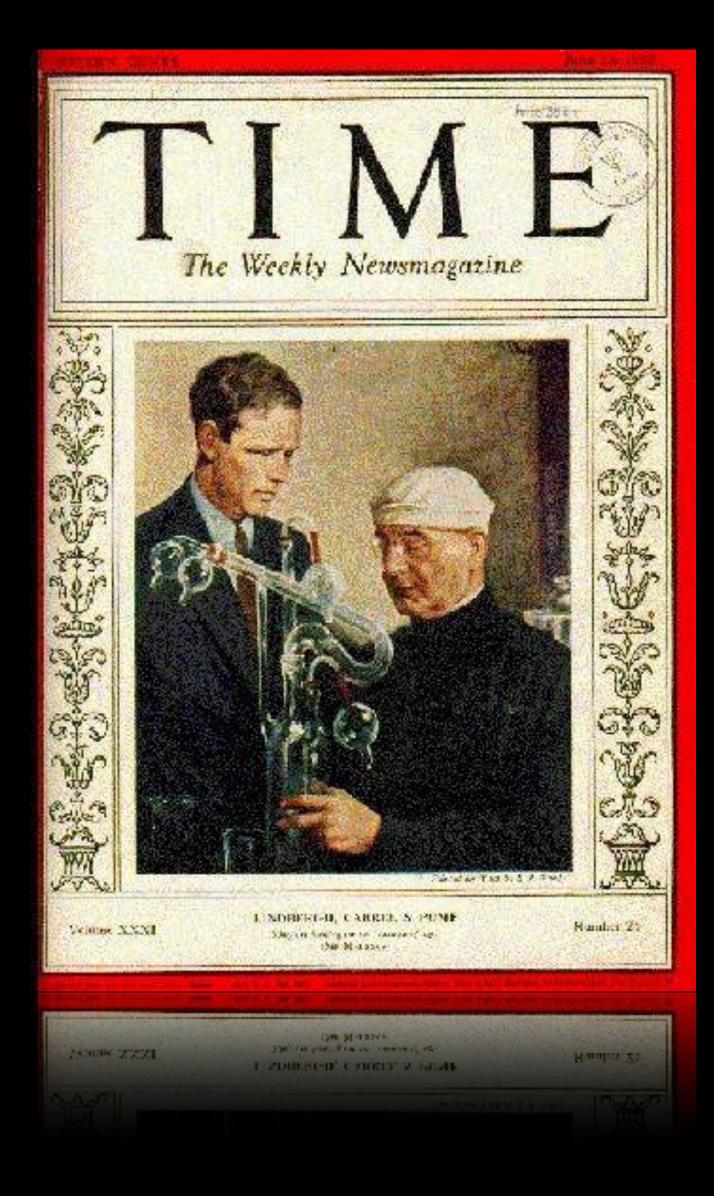
With a 111 manuscriptions.

#### 0

#### PAUL B. HOEBER, INC.

MEDICAL BOOK DEPARTMENT OF HARPER & KROTHERS MEMARNING MEMARNING





1938



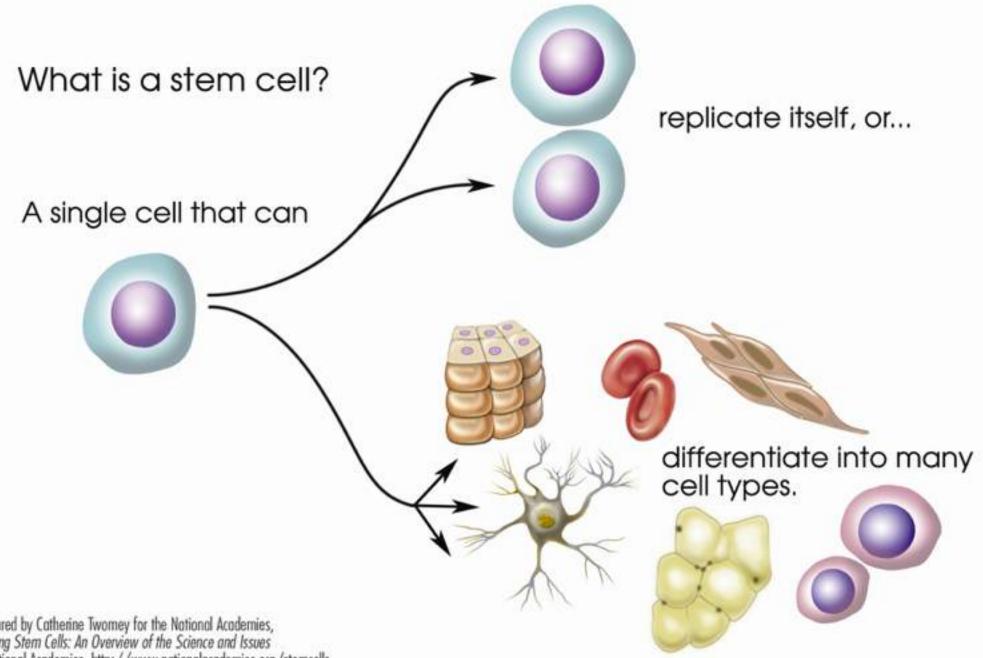
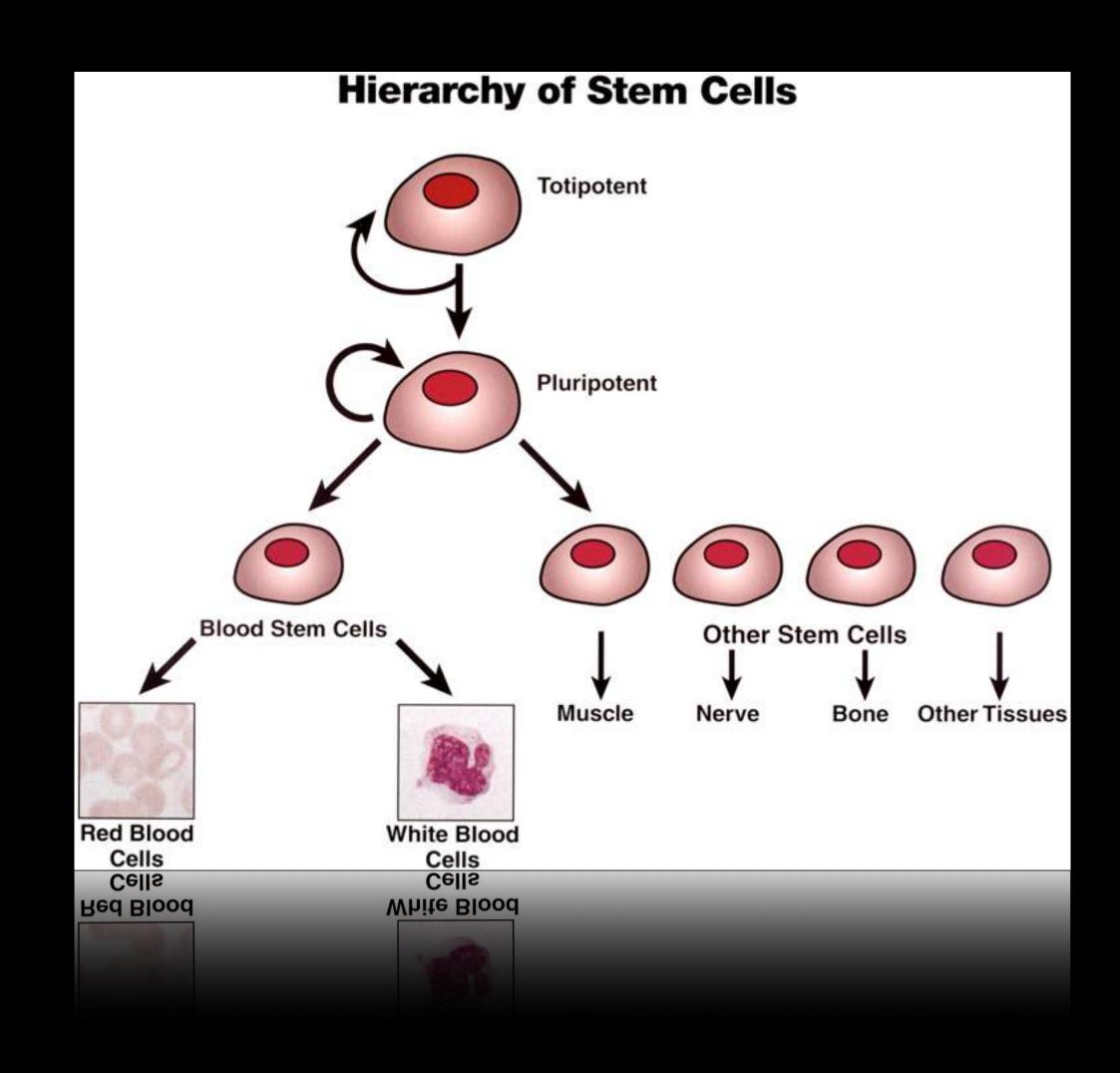


Image prepared by Catherine Twomey for the National Academies, Understanding Stem Cells: An Overview of the Science and Issues from the National Academies, http://www.nationalacademies.org/stemcells. Academic noncommercial use is permitted.

Image prepared by Catherine Iwomey tor 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.









#### Ciaran, and his amazing mother, Colleen

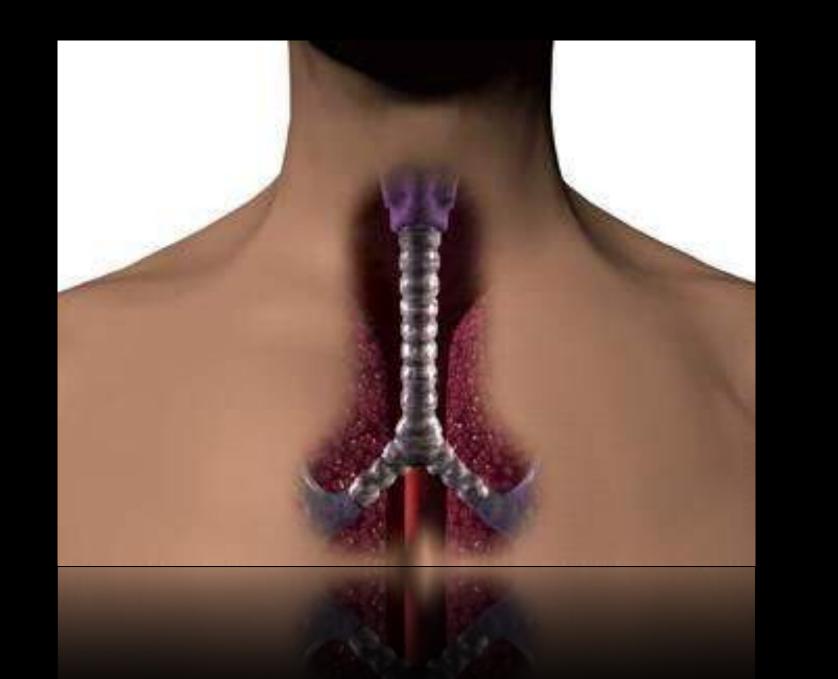
# always in the first 10

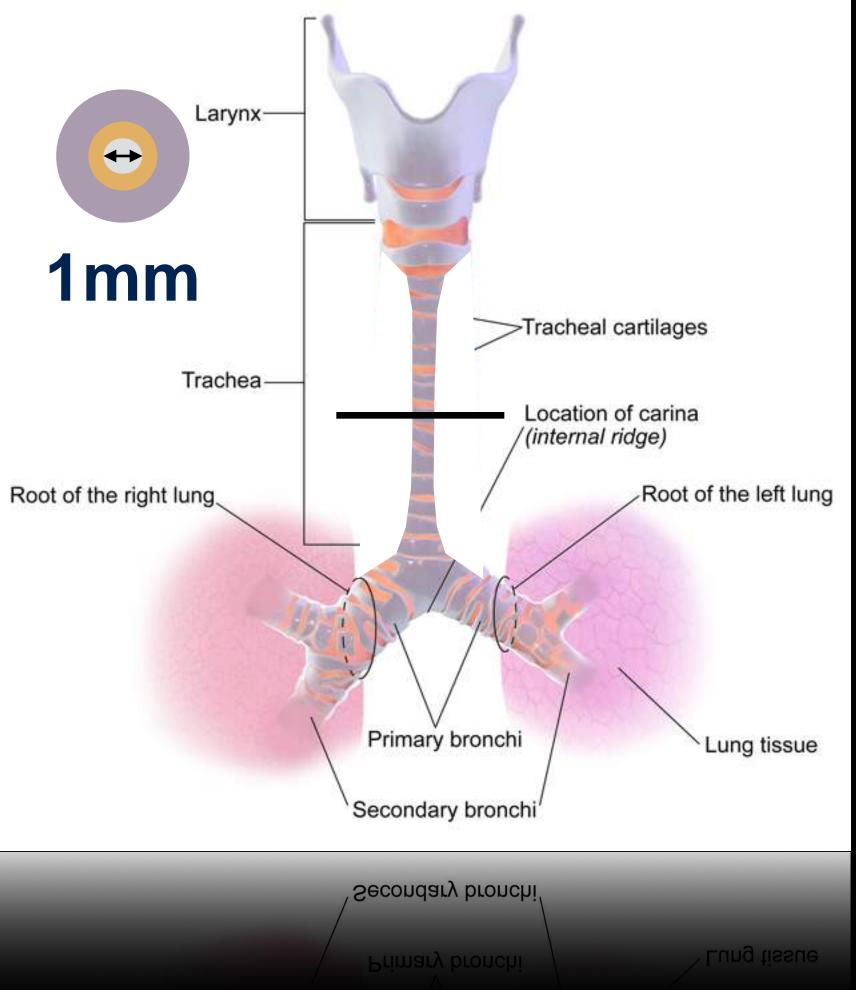






#### The Trachea

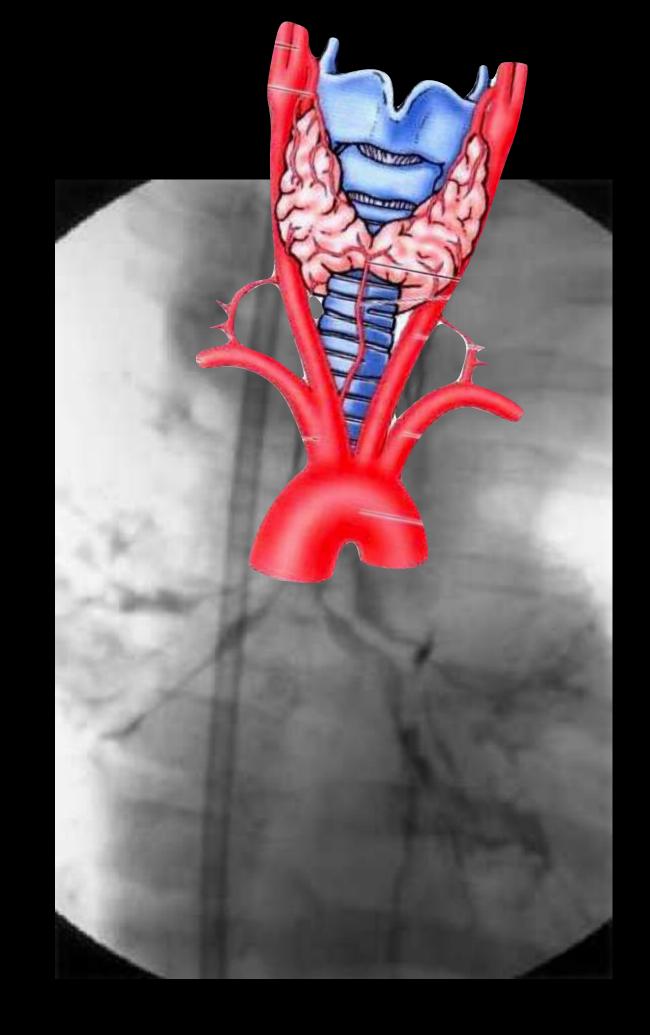




## long segment congenital tracheal stenosis









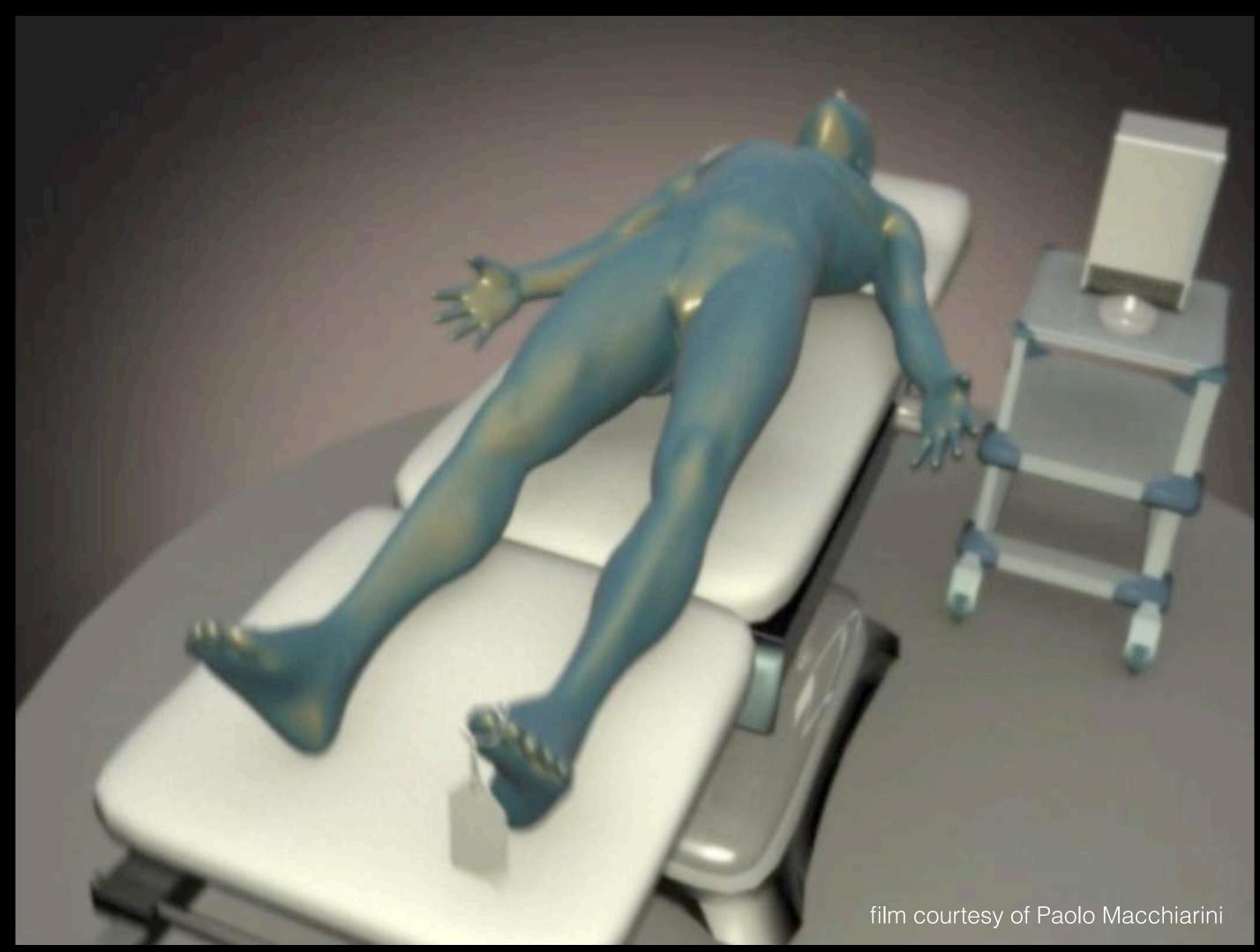
# age 3 years



## in the first 2



### **Stem-call Supported Tracheal Transplant**



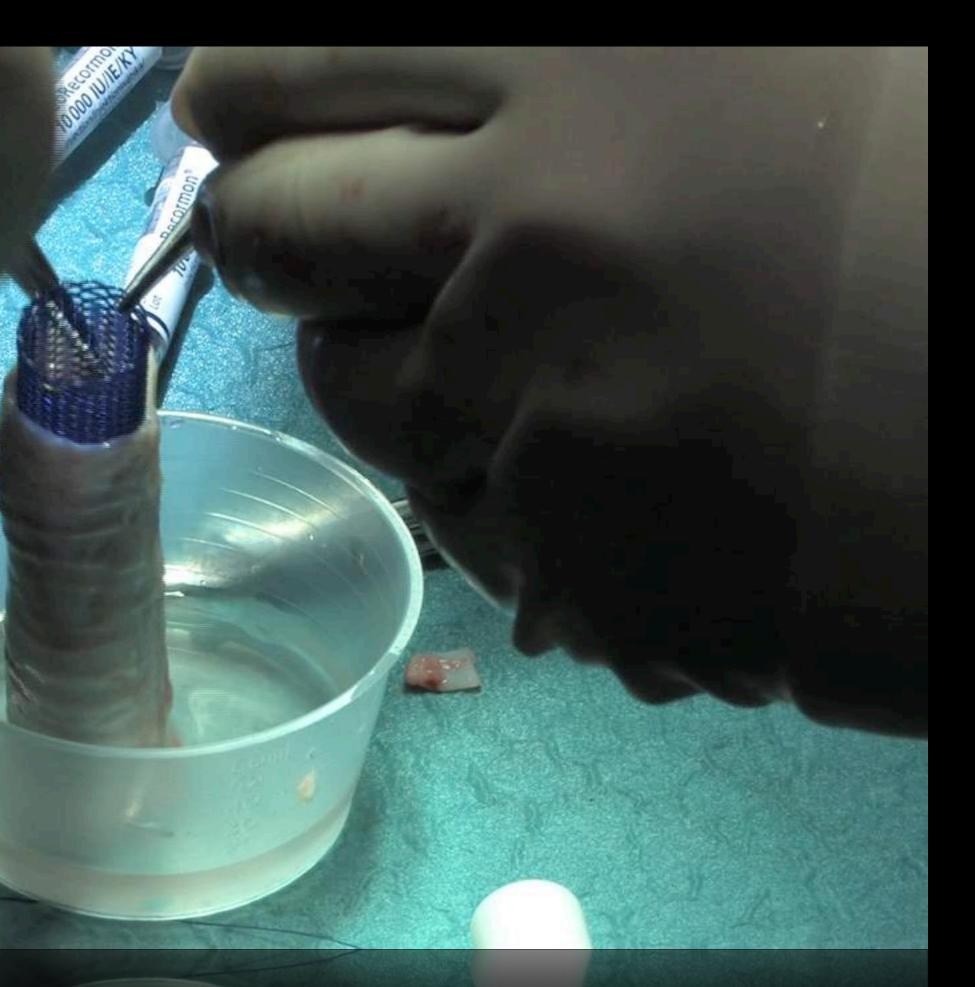




### 1st in a child

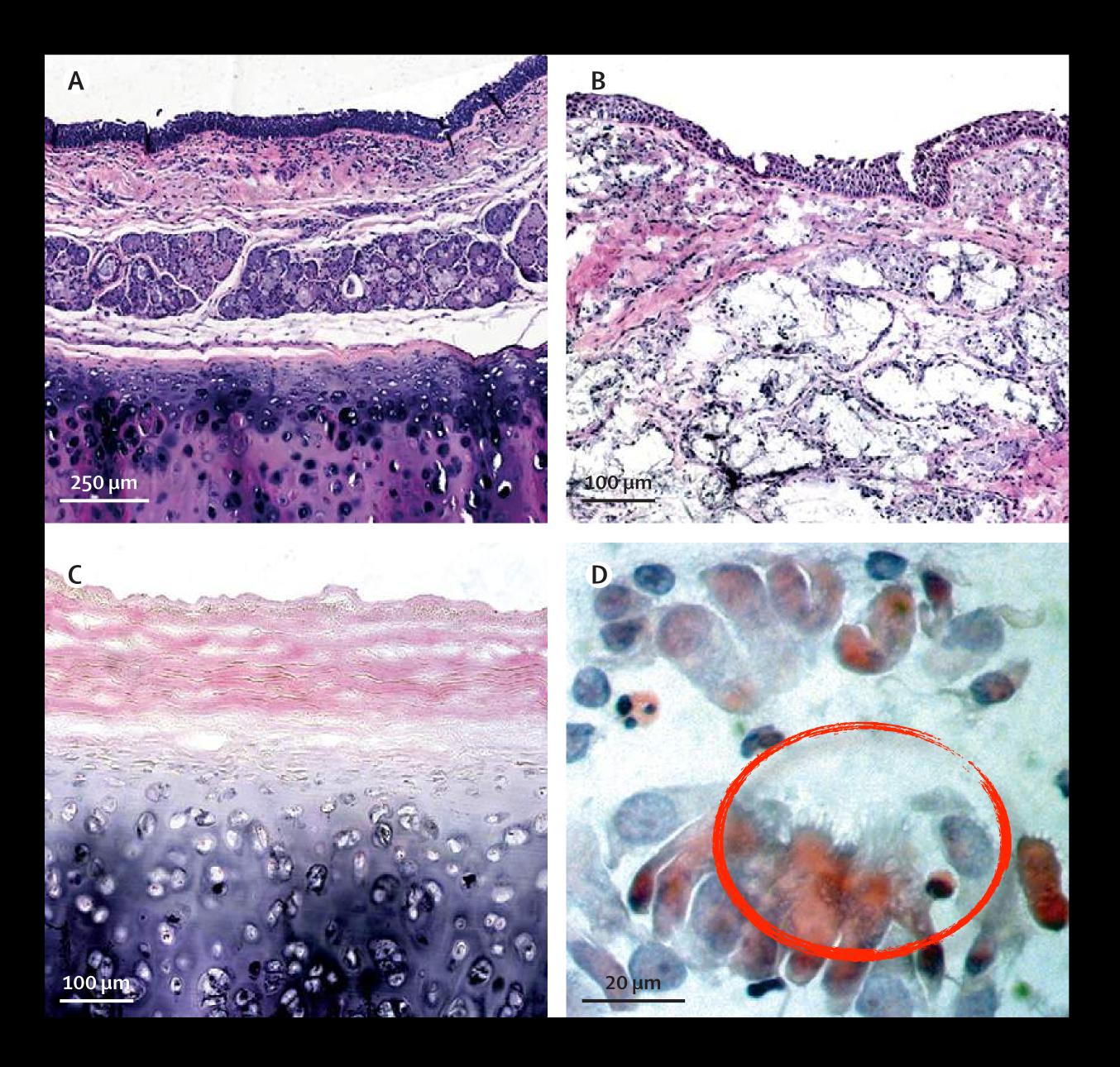


1st stem cell transplant



### In 1st 10 absorbable stents







### cilia



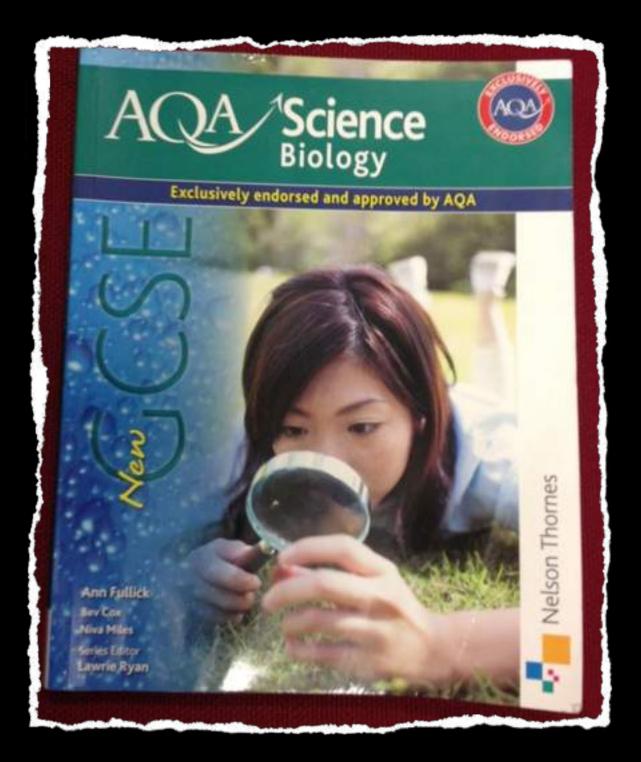






## Irish Child of Courage 2012





## **GCSE Textbook** 2012



#### problems when stem cells

unv embryonic stem cells come from aborted embryos. Others come from yonv empryos in fertility treatment. This raises ethical issues. There are spate emoty who feel this is wrong. They question people, include the potential human being as a source of cells, even to cure others.

some people feel that as the embryo cannot give permission, using it is a some people and polyton of its human rights. As well as this, progress with stem cells is slow. pere is some concern that embryonic stem cells might cause cancer if they used to treat sick people. This has certainly been seen in mice. Making cells is slow, difficult, expensive and hard to control.

e What is the biggest ethical concern with the use of embryonic stem cells?

#### the future of stem cell research

scientists have found embryonic stem cells in the umbilical cord blood of amborn babies. These may help to overcome some of the ethical concerns.

scientists are also finding ways of growing the adult stem cells found in bone marrow and some other tissues. So far they can only develop into a inted range of cell types. However, this is another possible way of avoiding me controversial use of embryonic tissue. Adult stem cells have been used successfully to treat some forms of heart disease and to grow some new organs such as tracheas (windpipes).

The area of stem cell research known as therapeutic cloning could be very useful. However, it is proving very difficult. It involves using cells from an adult to produce a cloned early embryo of themselves. This would provide a source diperfectly matched embryonic stem cells. In theory these could they be used to grow new organs for the original donor. The new organs would not be rejected by the body because they have been made from the body's own cells.

Most people remain excited by the possibilities of embryonic stem cell use in thating many diseases. At the moment, after years of relatively slow progress. hopes are high again that stem cells will change the future of medicine. We don't know how many of these hopes will be fulfilled; only time will tell.



Figure 2 For years, funding for stem cell research in the US was blocked by the government. In 2009 President Obama changed that ruling so US research could move forward. However, the battle



Figure 3 In 2010 Ciaran Finn-Lynch was the first child to be given a life-saving new windpipe grown using his own stem cells

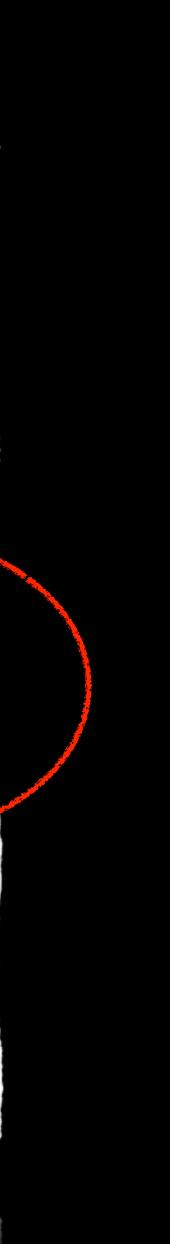
#### Key points

#### Embryonic stem cells (from human embryos) and adult stem cells (from adult bone marrow) can be made to differentiate into many different types of cell.

Stem cells have the potential to treat previously incurable conditions. We may be able to grow nerve cells or whole new organs for people who need them.

Summary questions

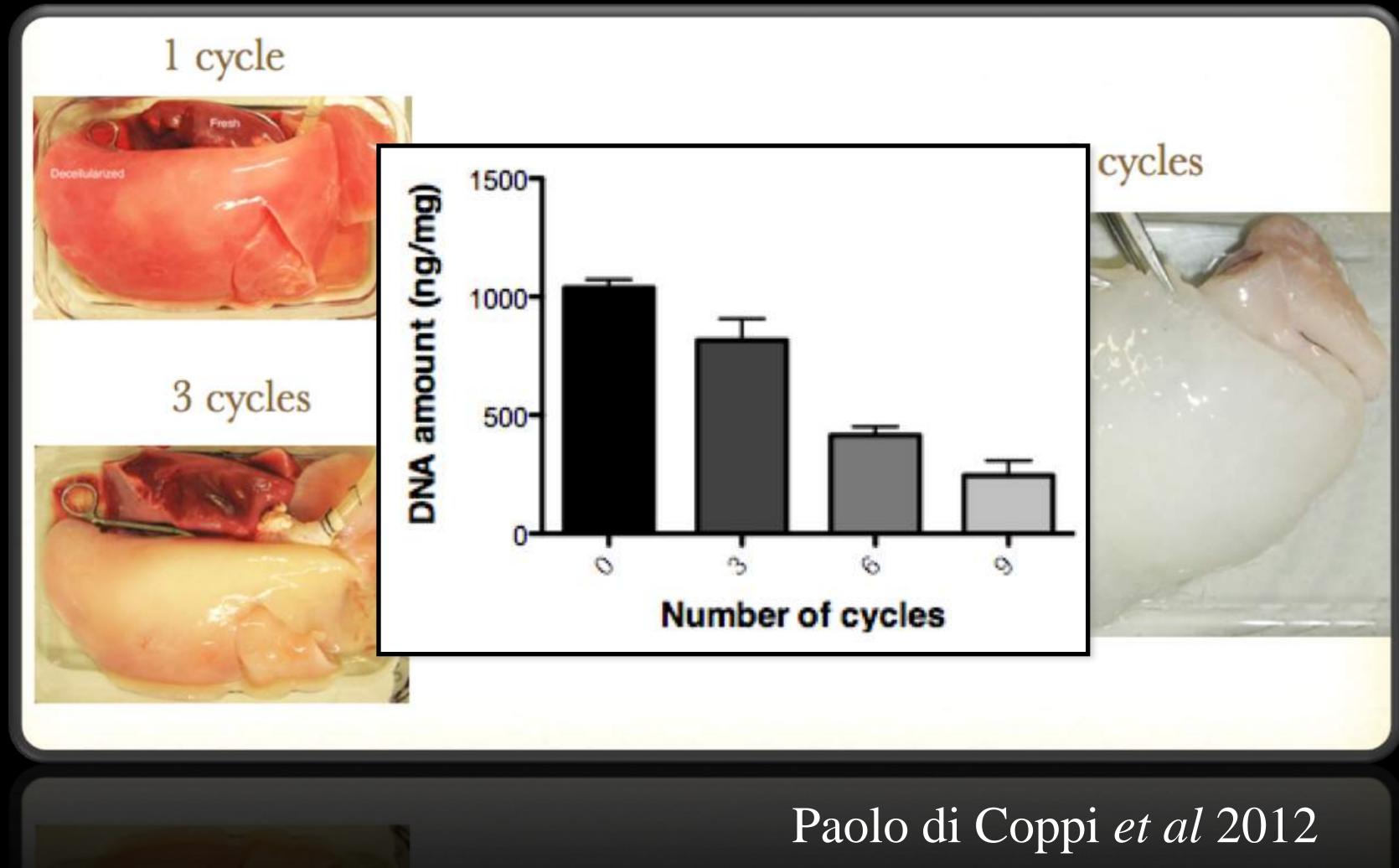
- 1 Copy and complete using the words below:
- bone marrow differentiate embryos hollow inner stem cells Unspecialised cells known as can (divide and change) into many different types of cell when they are needed. Human stem . The embryo forms a cells are found in \_\_\_\_\_ and in adult \_\_\_\_ ball of cells and the \_\_\_\_\_ cells of this ball are the stem cells.
- 2 a What are the advantages of using stem cells to treat diseases?
- b What are the difficulties with stem cell research? C How are scientists hoping to overcome the ethical objections to using animal scientists hoping to overcome the ethical objections to using
- embryonic stem cells in their research?







## Decellularised sheep lung



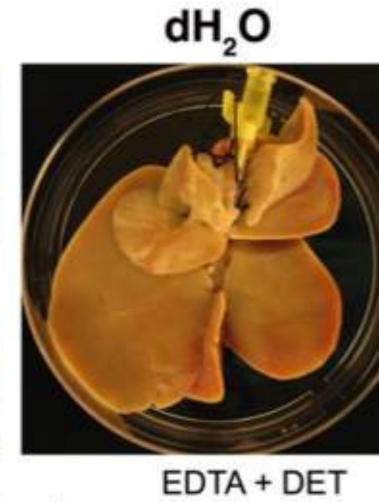




### Fresh

### Liver





1000

Fresh DET 1 cycle 1 cycle -----



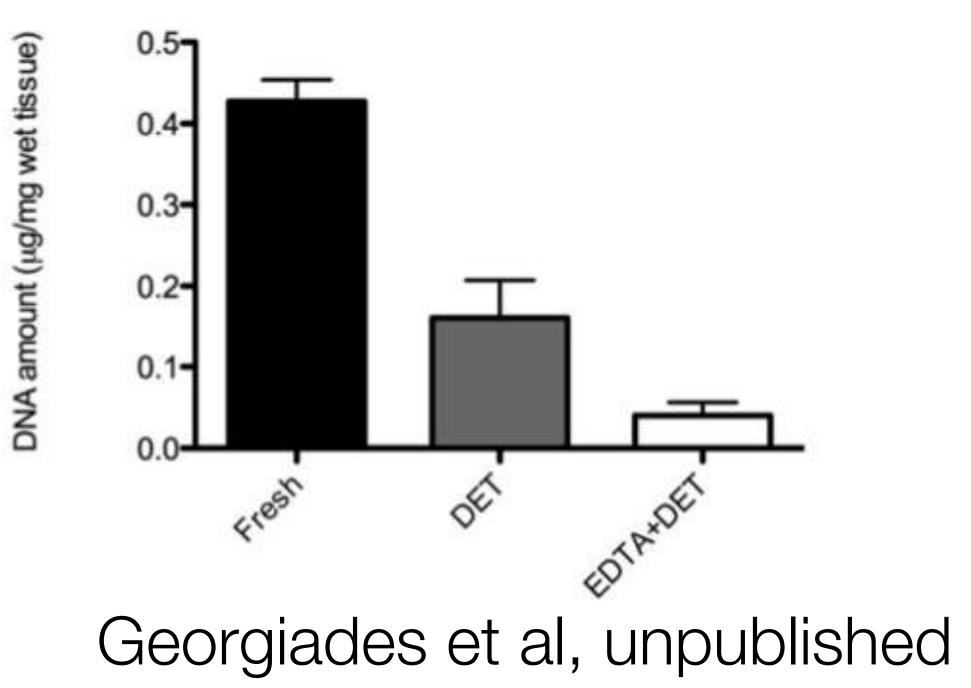
@ProfMJElliott

4% SDC

### 1M NaCI/DNAse















@ProfMJElliott

## Oesophagus

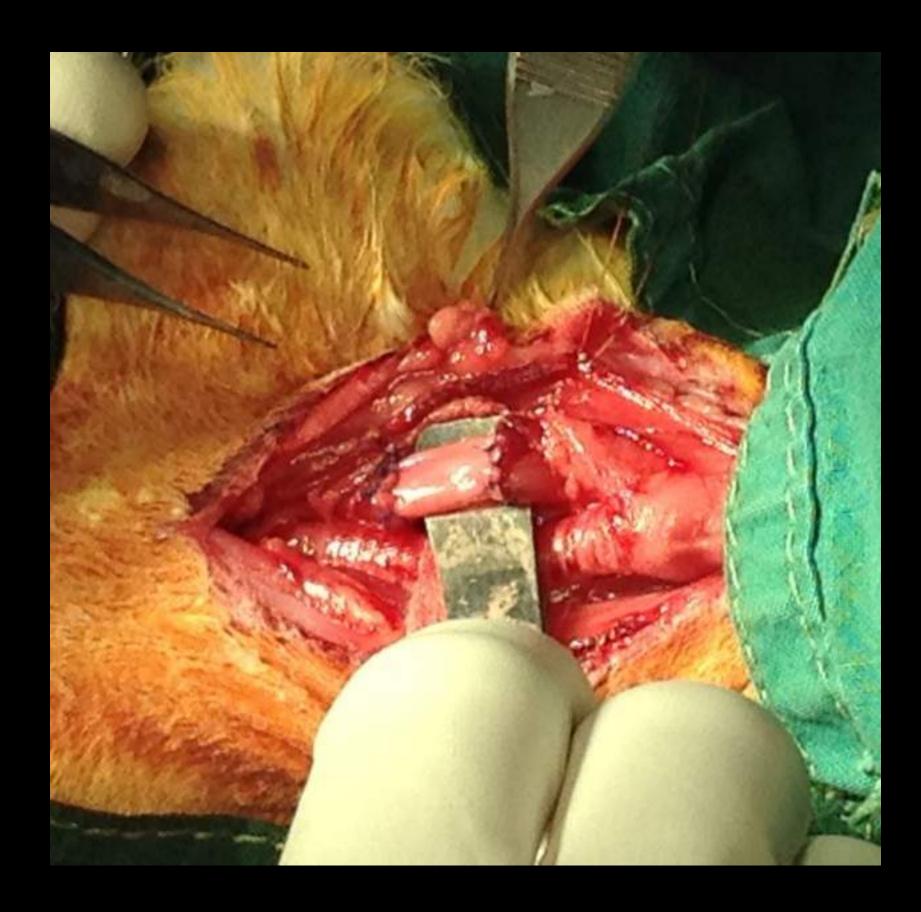








## **Orthotopic Implantation- Rabbit**





@ProfMJElliott





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

### Rabbit Muscle

### Remove Rabbit Cells

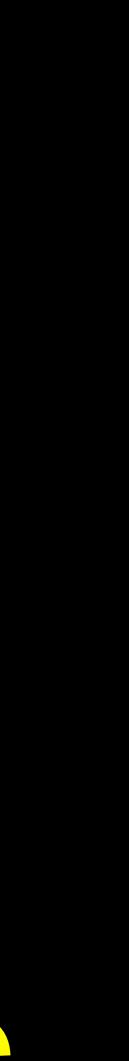


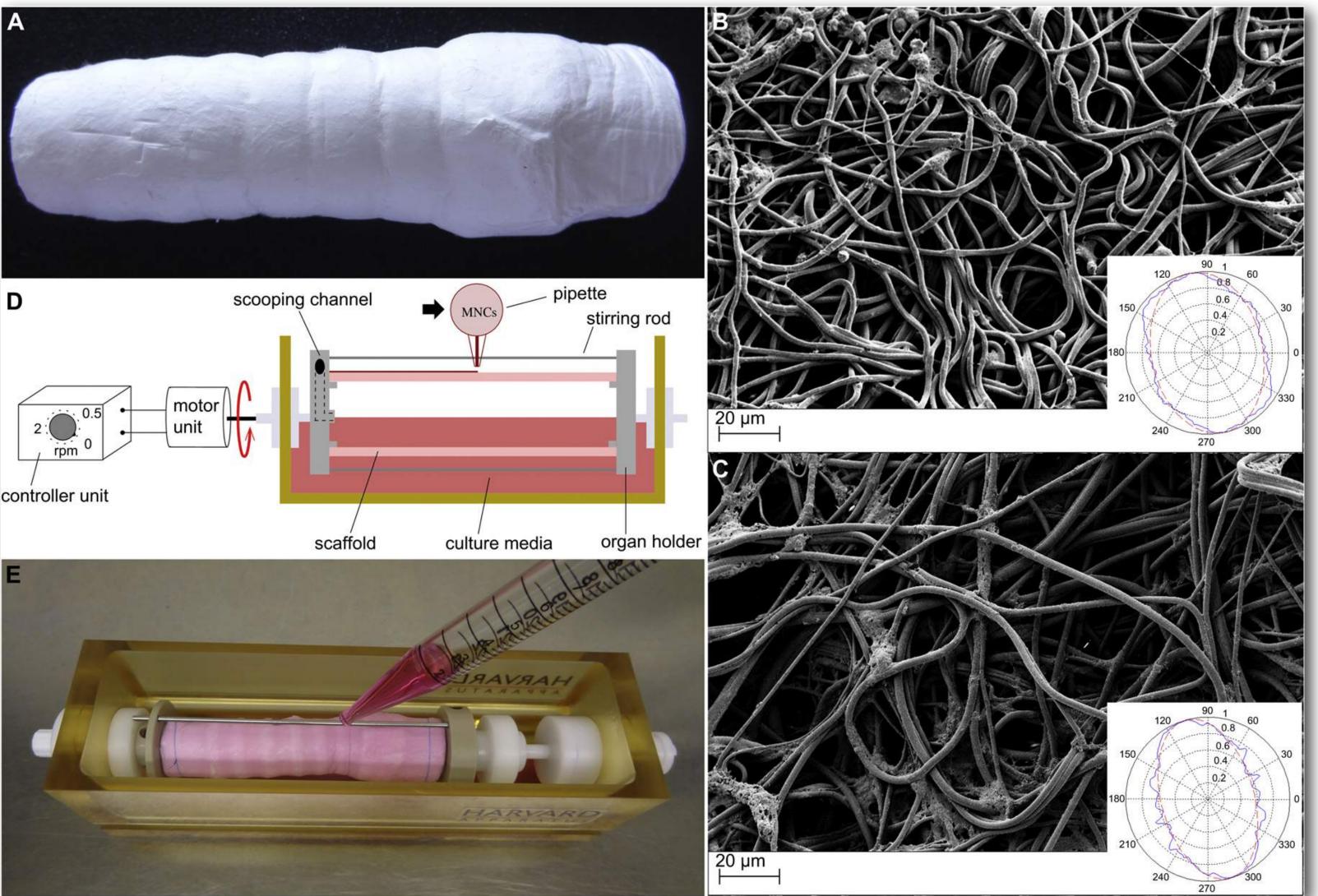
### Populate with Rat Cells

### Transplant to Rat









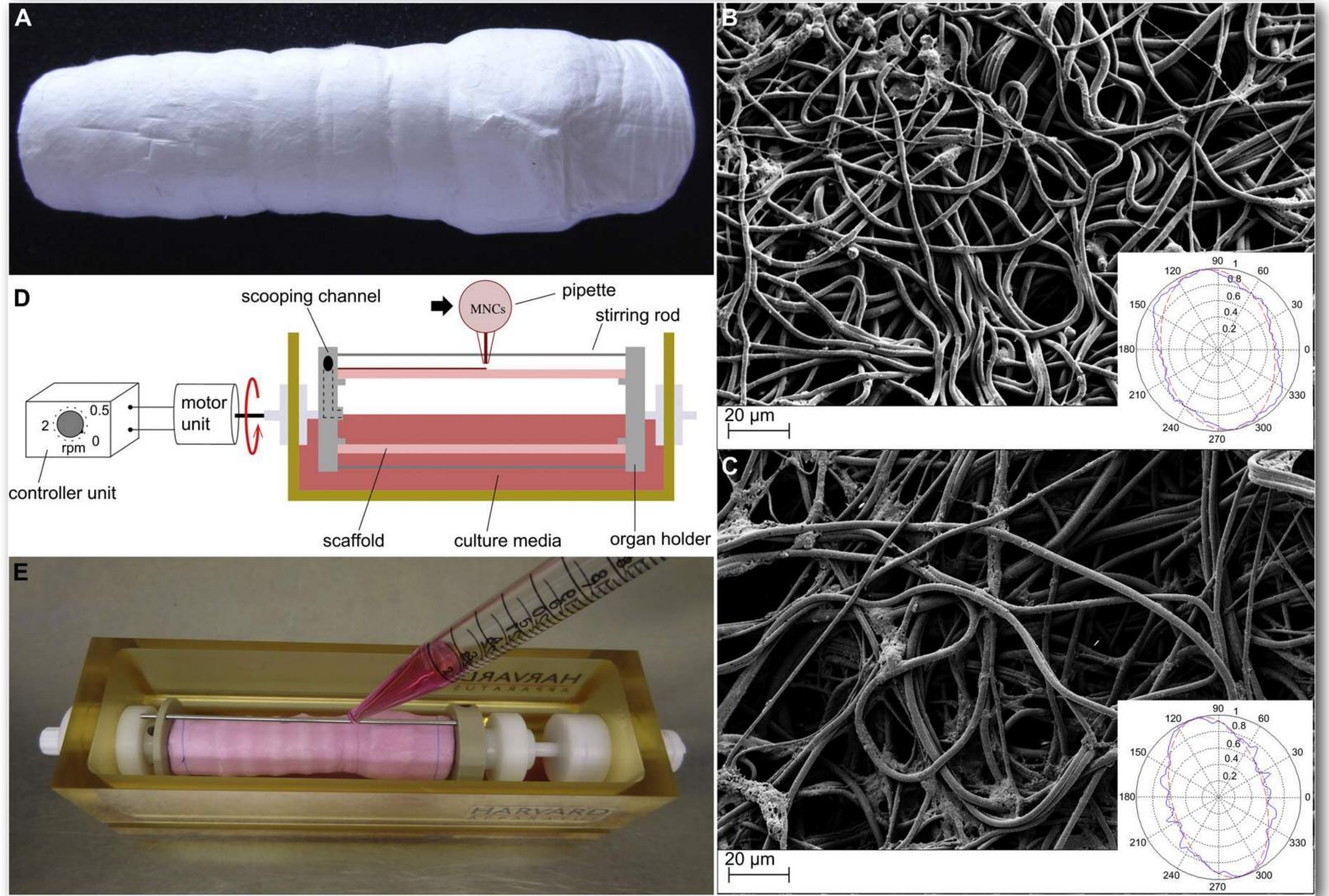


Fig. 4. Picture of a synthetic tracheal scaffold made of PET/PU-based nanofibers (A). SEM images of a synthetic scaffold showing the fiber network made of PET/PU. Insets report the computed fiber alignment pattern. Magnification 1,500×; scale bar representing 20 µm (internal B; external C). Schematic 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).



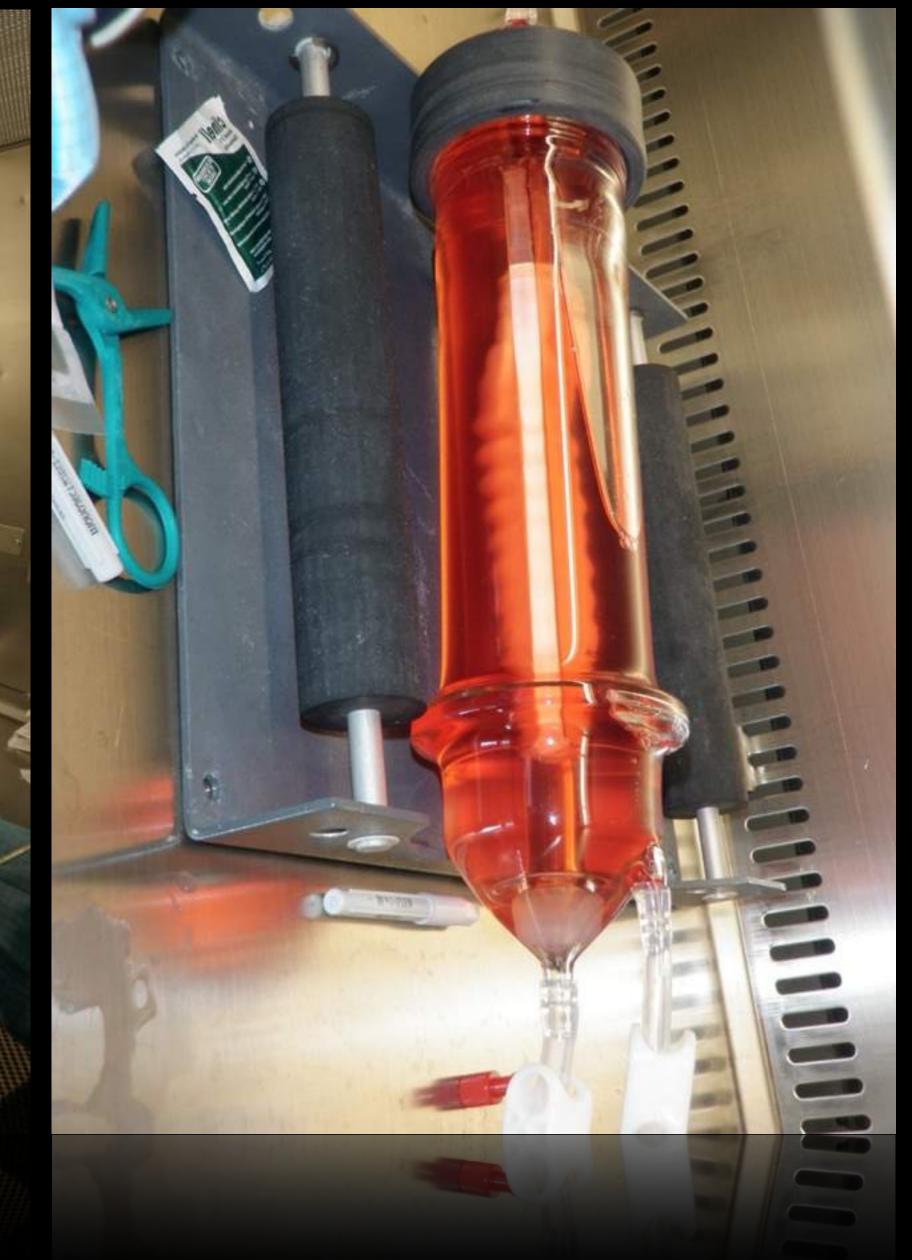


P. Jungebluth et al. / Biom

als 34 (2013) 4057–4067







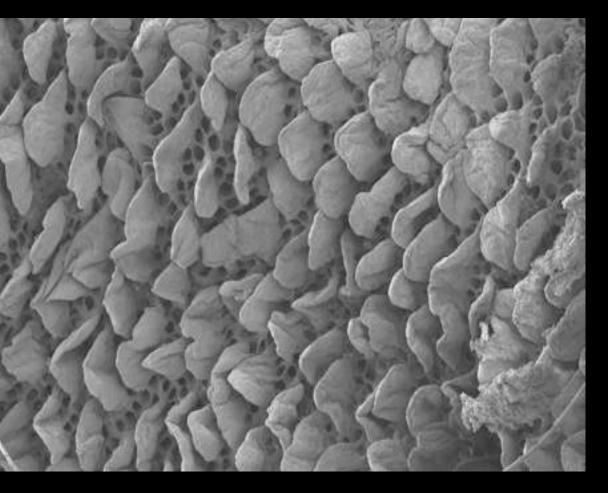


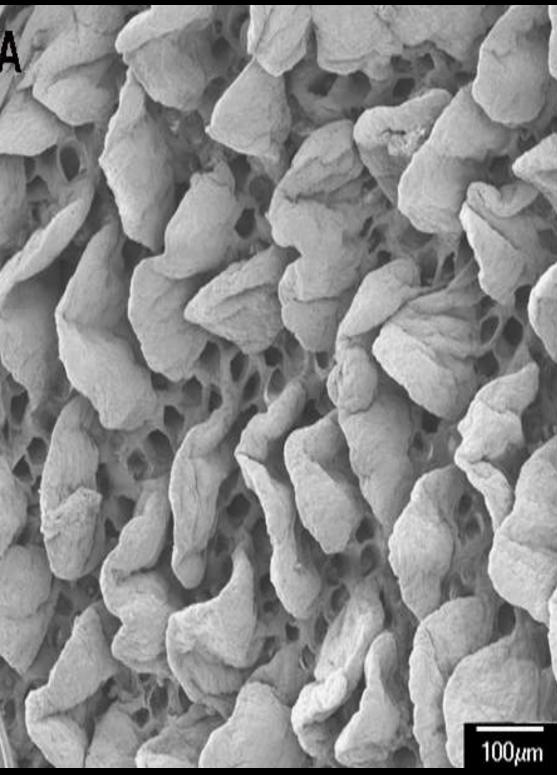
#### A rat decellularized small bowel scaffold that preserves villus-crypt architecture for intestinal regeneration

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

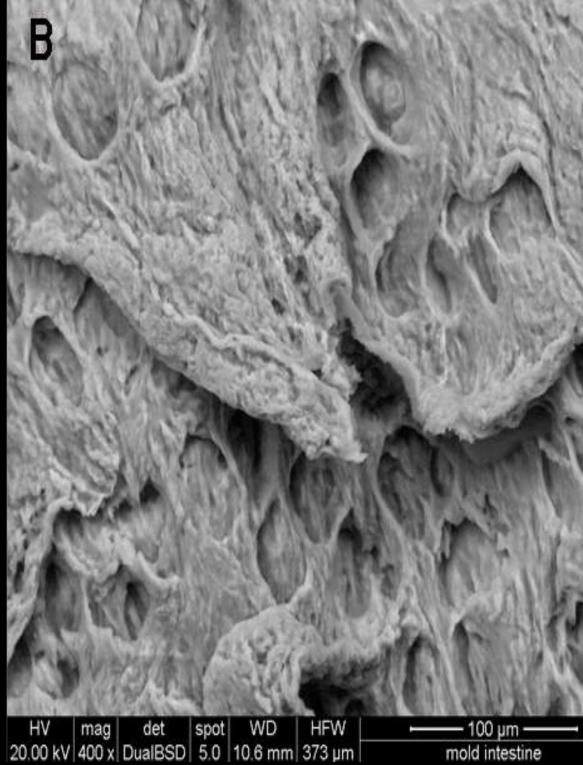






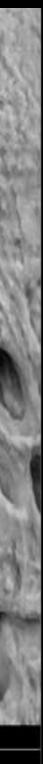






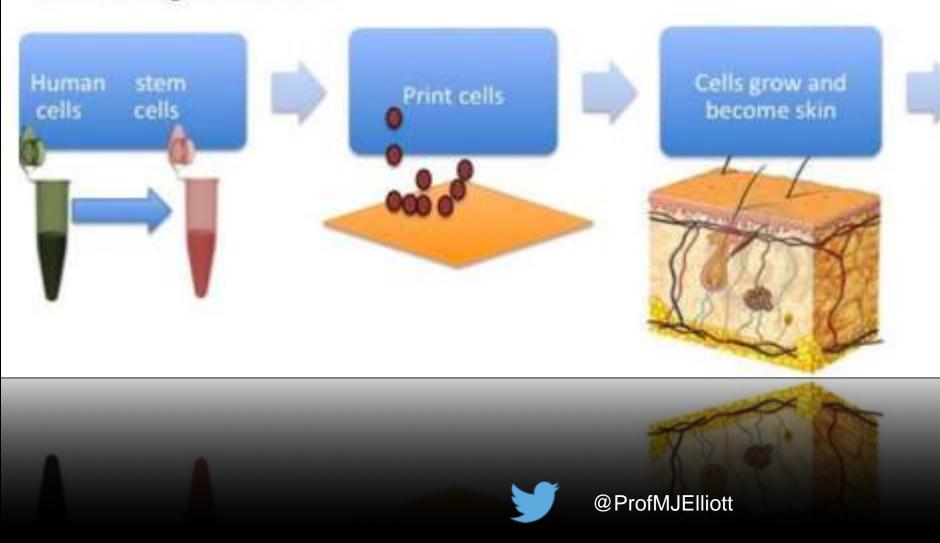








#### SkinPrinting human skin



# Wake Forest regenerative medicine team

# Ink jet printing of stem cells direct to damaged skin

### **Commercialised Process**

martin.elliott@gosh.nhs.uk



.

Transplantation

SkinPrint

# **3D Printing Organs?**

### Professor A. Atala, Wake Forest



@ProfMJElliott





### too much technology?





# technological Titans ethical Liliputians

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

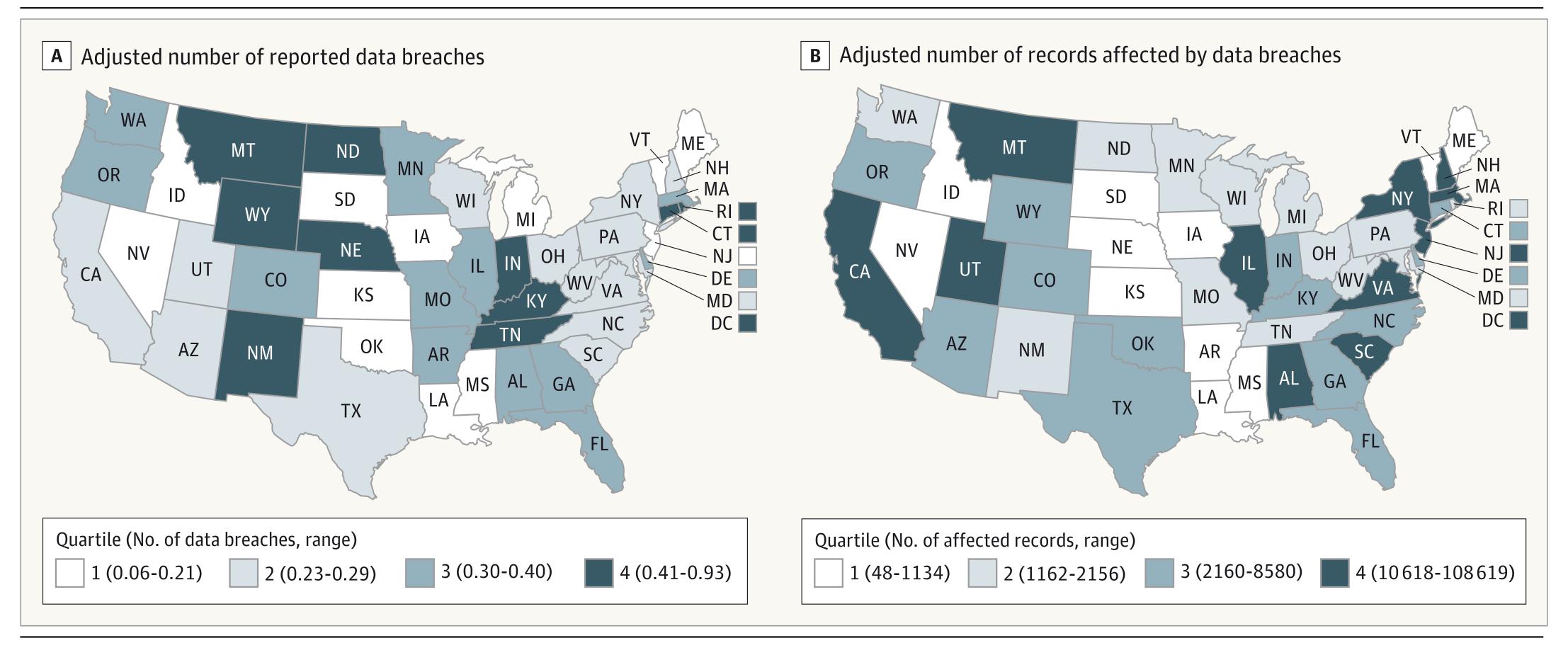


@ProfMJElliott



# 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



## 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.





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,

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.



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.



### IT'S INSANELY EASY TO HACK HOSPITAL EQUIPMENT



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

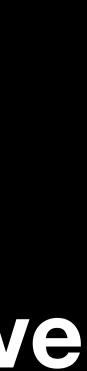
Computerworld | Oct 22, 2014 6:43 AM PT

When the FDA <u>released</u> 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**







## 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





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