# Implantable Pressure Sensors

25th Chemnitzer Seminar, 14 June 2016

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Institute of Biomedical Engineering

Funding: Wellcome Trust and Department of Health

Imperial College London

# Project No 1: Permanently Implantable Cardiovacular SAW pressure sensors

## Team:

| | |
|---|---|
| Principal Investigator: | Prof. Chris McLeod |
| Co investigator: | Dr Reza Bahmanyar |
| Clinical Co Investigator: | Prof. Sir Magdi Yacoub |
| Interventionist: | Dr. Iqbal Malik |
| Research Associate: | Dr Longfang Zou |

## Current State:

- 12 years since conception.
- The implant system is successfully tested in porcine model.
- Chronic animal studies under way.
- Optimisation is currently being done for first in man (phase 1 clinical studies) planned to start in 2018.

# Project No 2: Intraocular Wireless Pressure Sensor for Glaucoma Patients

**Team:**

Principal Investigator: Dr Reza Bahmanyar
Co investigator: Prof. Chris McLeod
Clinical Co Investigator: Prof. Francesca Cordeiro

**Current State:**

- 3 years young!
- Proof of concept is done.
- Prototypes fabricated and tested.
- Patent filing discussions started.
- Preparing the case for funding to complete the implant system and perform animal studies.

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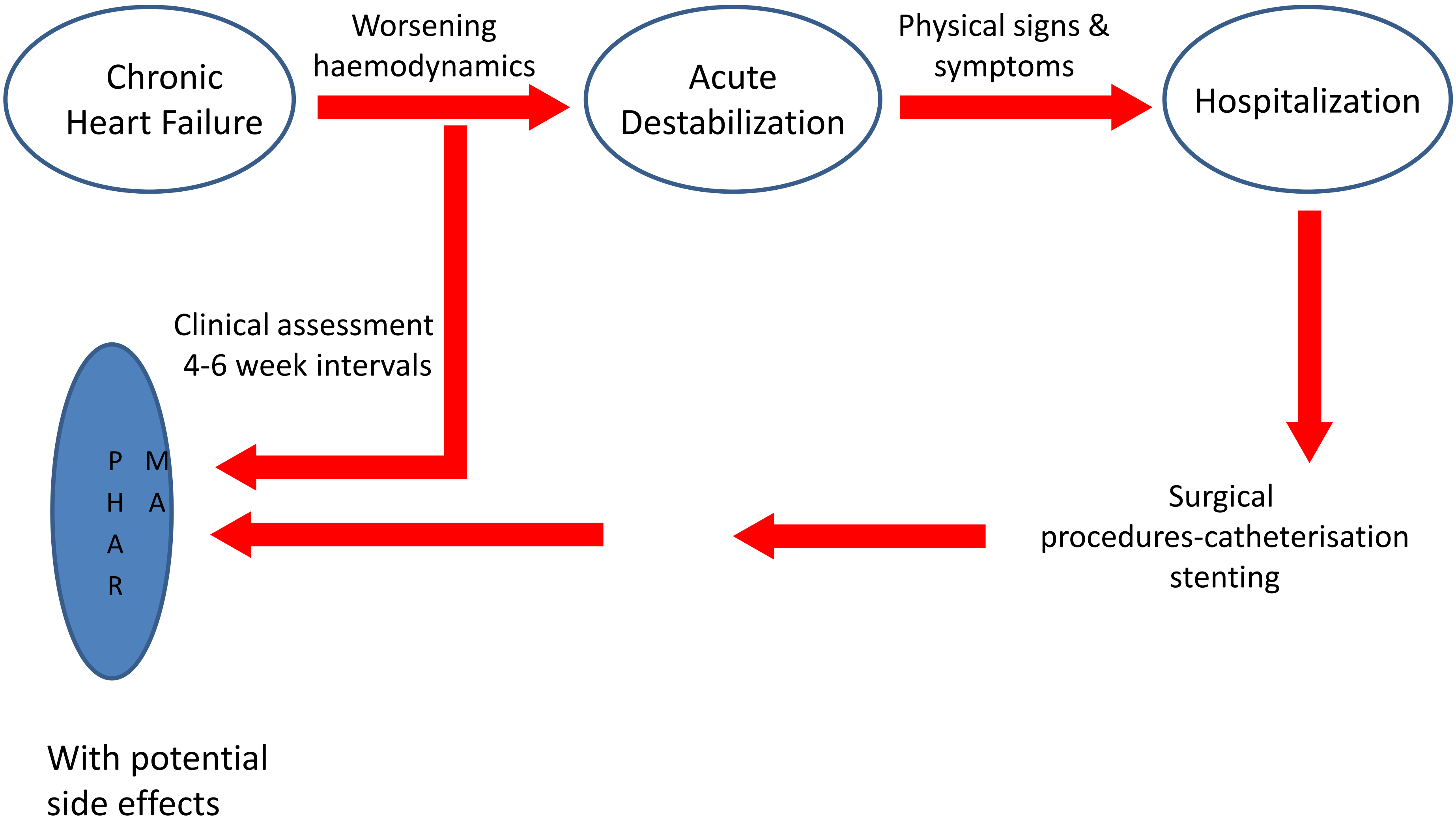
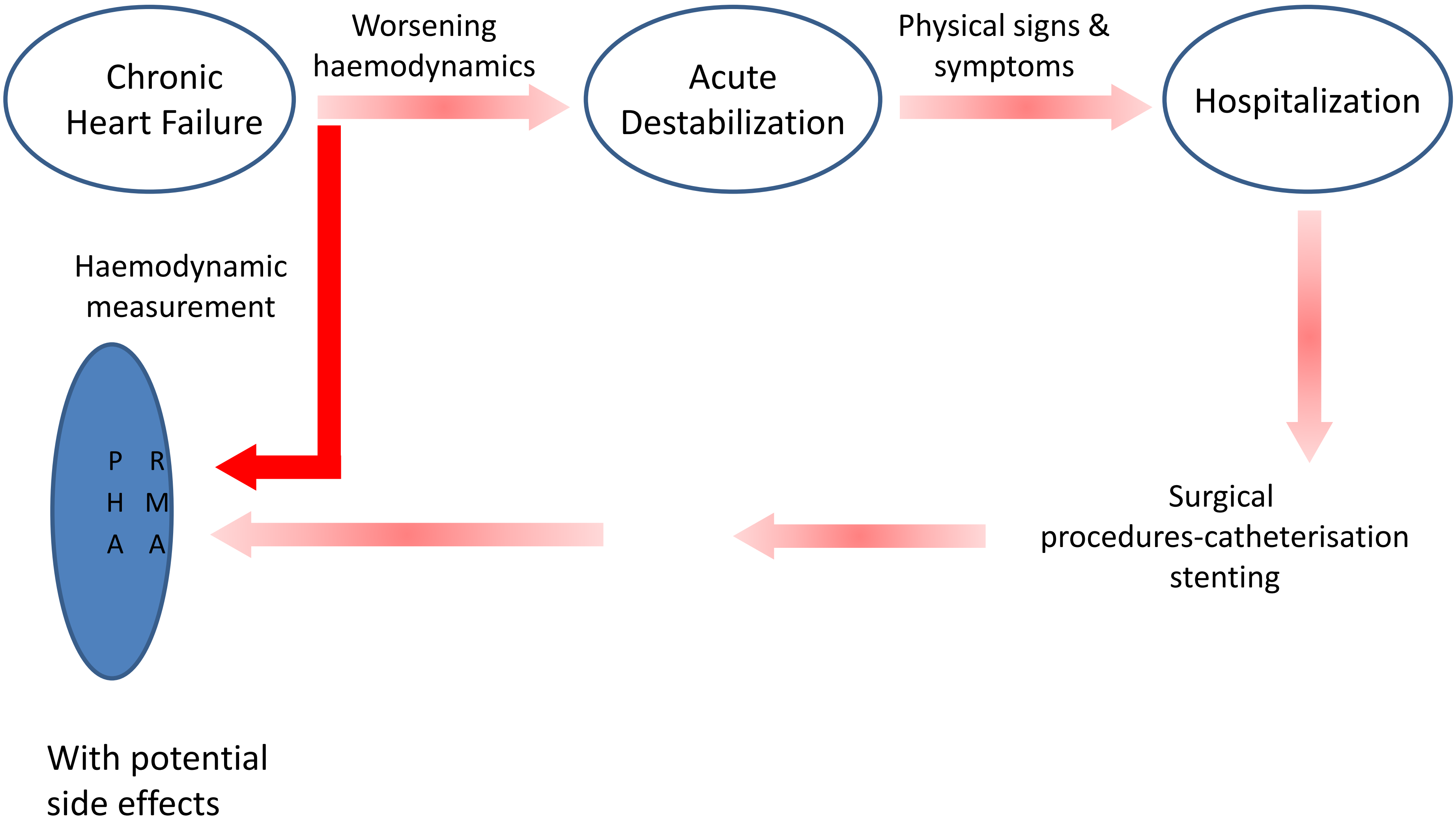
# The Cardiovascular Sensor

# Progression and Treatment of Heart Failure (1)

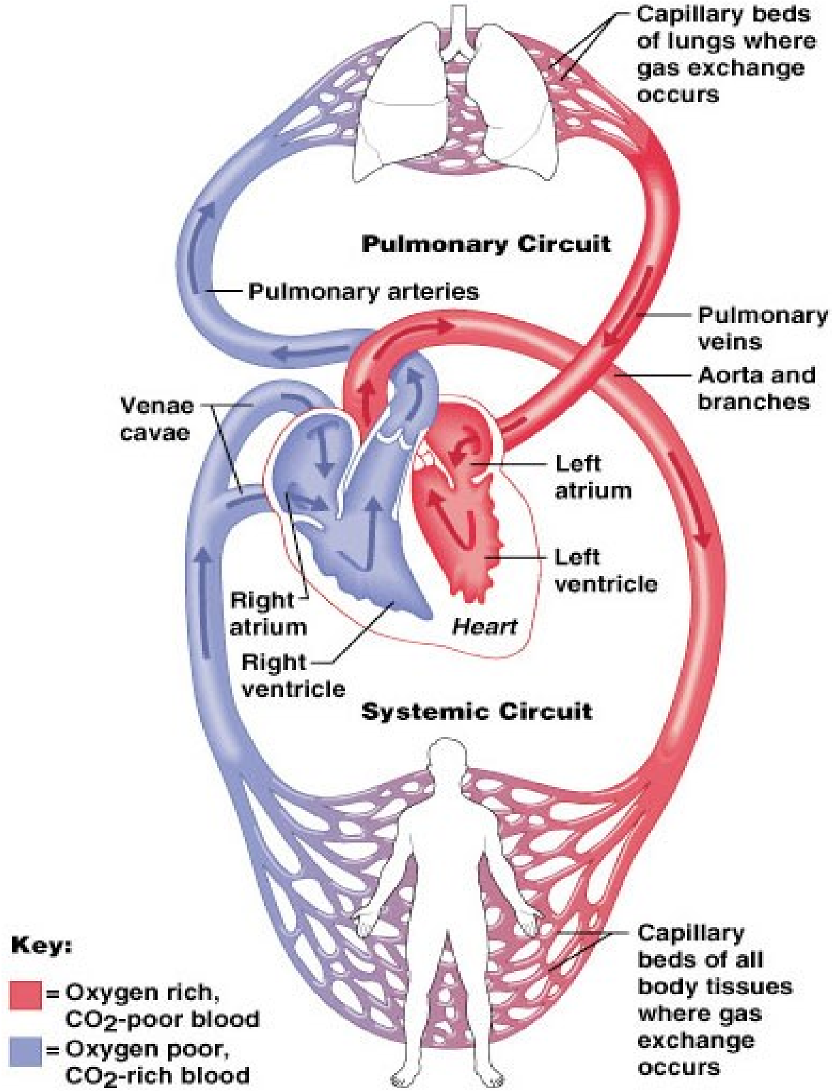


# Progression and Treatment of Heart Failure (2)



# Pathway of Blood Through the Heart and Lungs

**<u>Heart failure (CHF)</u>**
<u>Left</u> side fails => pulmonary congestion and suffocation
<u>Right</u> side fails => peripheral congestion and edema




**<u>Safety</u>**
Clotting in PA => embolism in lung section
Clotting on left side could cause a heart attack or a stroke

Systemic arterial pressure can be measured non-invasively.

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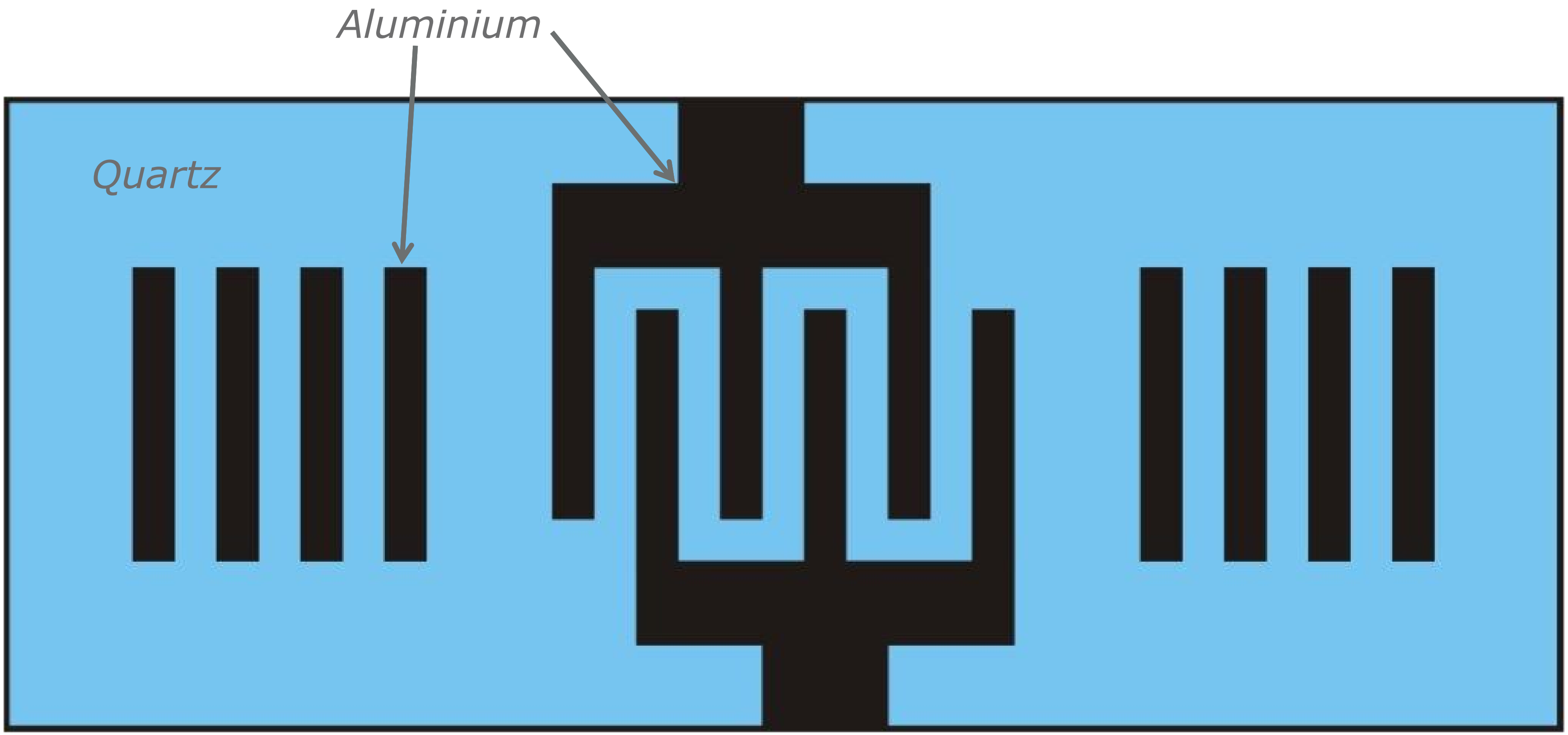
# Cardiovascular SAW Pressure Sensor

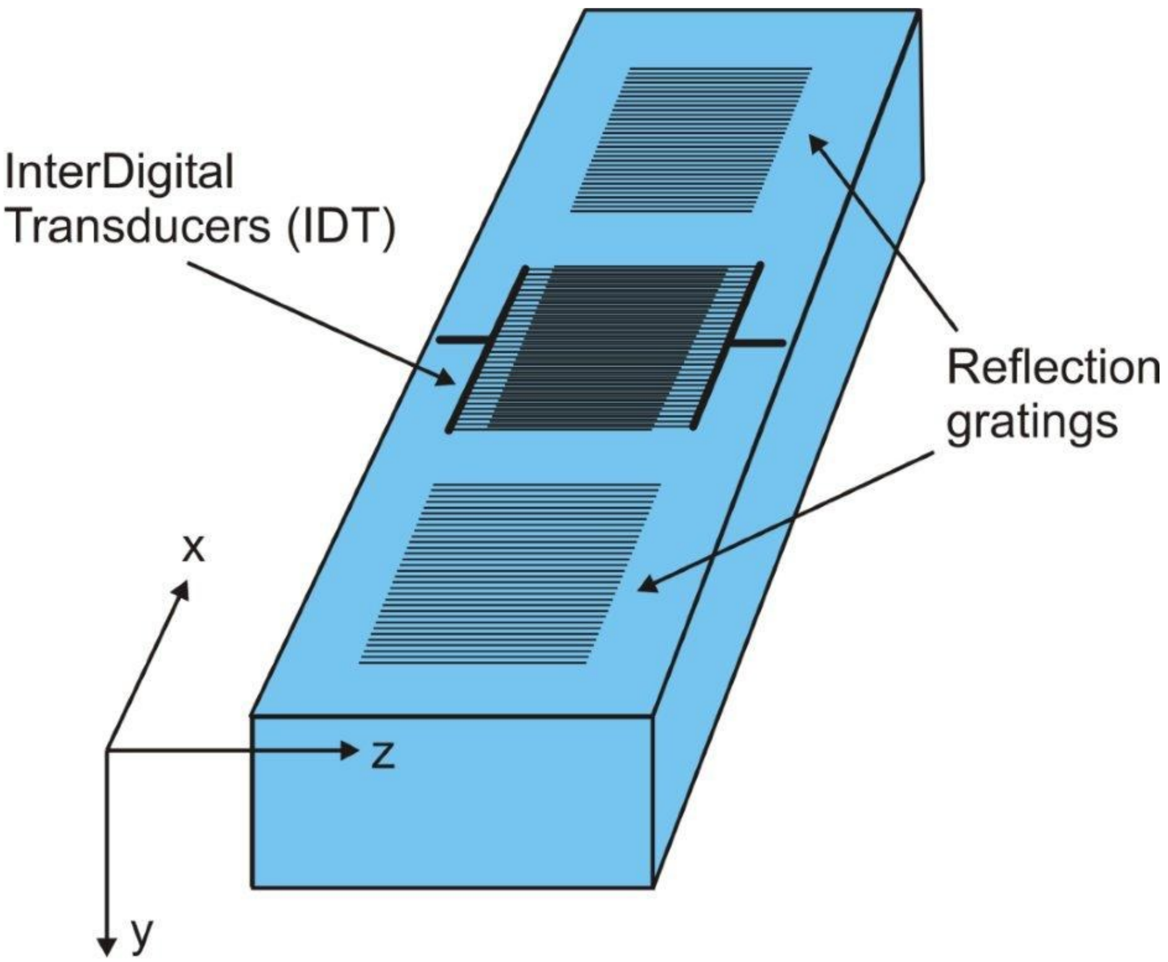
Aim: To measure blood pressure inside right atrium (RA) or pulmonary artery(PA) wirelessly using Surface Acoustic Wave (SAW) transponders.

- Develop an Implantable pressure sensor using SAW Resonators.
- Deliver and implant the sensor (inside right atrium or pulmonary artery).
- Read the sensor pressure wirelessly (measure its resonant frequency accurately).

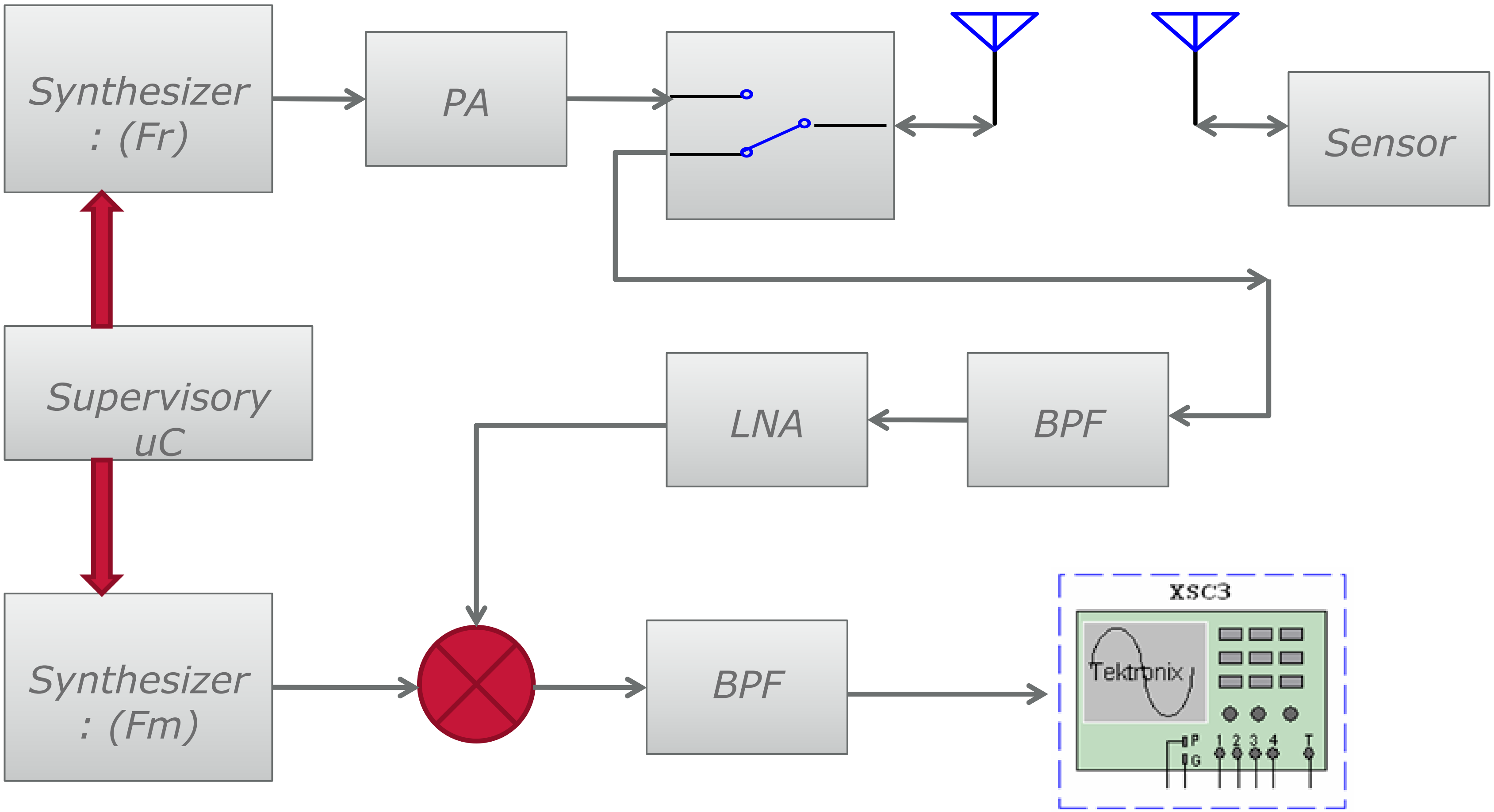
# SAW Resonators



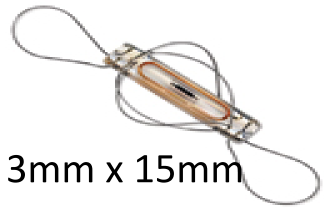
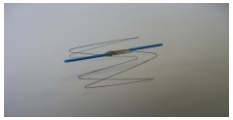
# Pressure Sensors



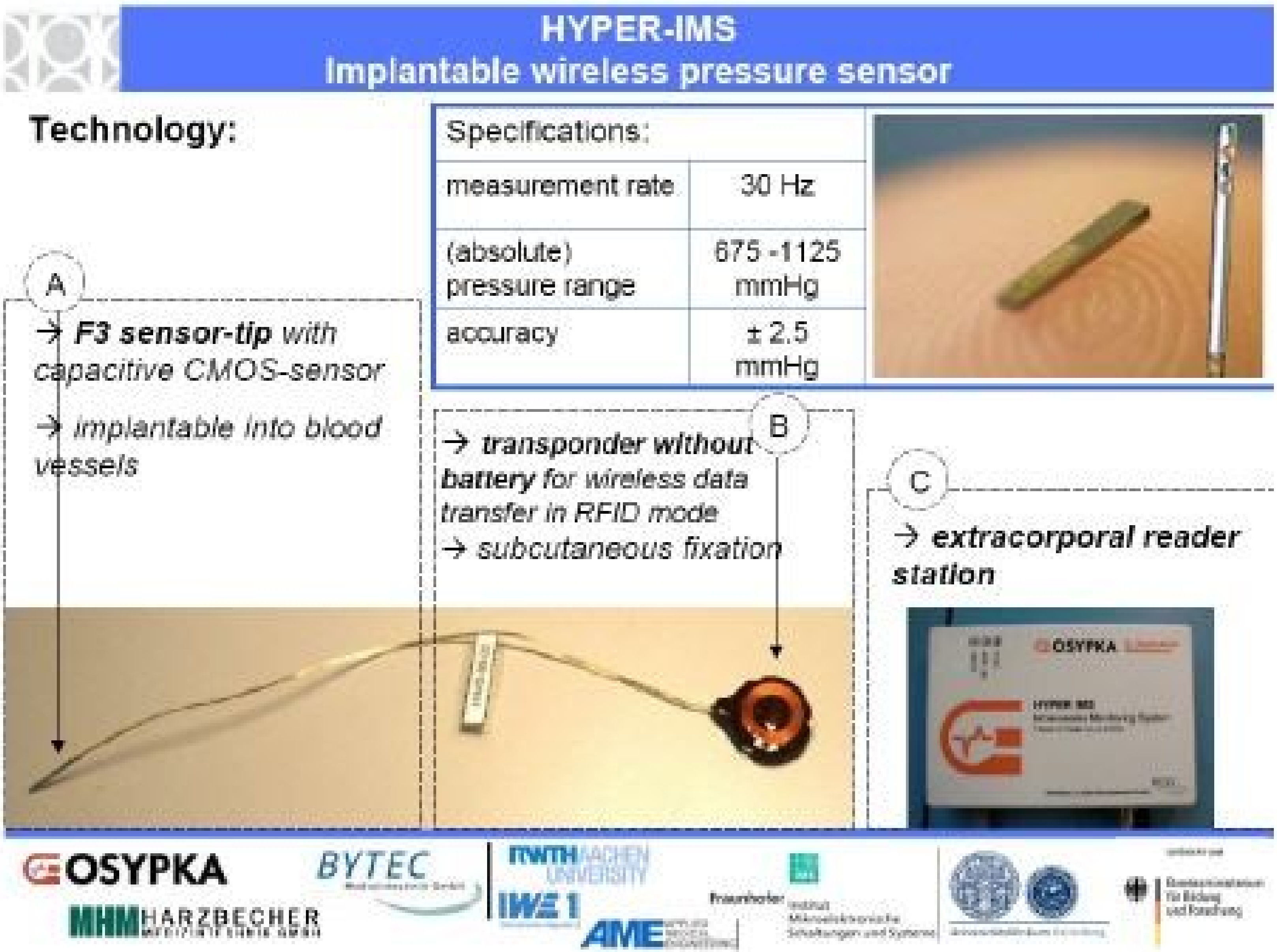
# SAW Interrogating System



# Sensors in development (see also Chronicle & Heartpod)

| | **Description** | **Size** | **State of development** |
|---|---|---|---|
| St Jude Medical<br>cardiomems | Low-frequency MEMS pressure sensor (35-45 MHz) | <br>3mm x 15mm | Clinical trials, PA for Heart Failure. CHAMPION trial |
| Boston Scientific<br>Remon | Acoustic Pressure sensor – 5s / 30s or continuous with implanted battery |  | Taken over by Boston Scientific; no trials yet in public; mothballed 2013. |
| Imperial College London | High Frequency 868 MHz SAW pressure sensor | <br>3mm x 7mm | Early animal testing – PAP, LAP and LVP. |
| ISSYS<br>INTEGRATED SENSING SYSTEMS | Magnetically coupled MEMS sensor |  | Under development for Intra-Cranial Pressure, Left Atrial Pressure |
| endotronix<br>Wireless health monitoring | MEMS pressure sensor | | Early animal testing- PAP |

# IMF-Fraunhofer Osypka. (Note internal lead)



# CardioMems' CHAMPION trial

## Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial

*William T Abraham, Philip B Adamson, Robert C Bourge, Mark F Aaron, Maria Rosa Costanzo, Lynne W Stevenson, Warren Strickland, Suresh Neelagaru, Nirav Raval, Steven Krueger, Stanislav Weiner, David Shavelle, Bradley Jeffries, Jay S Yadav, for the CHAMPION Trial Study Group**

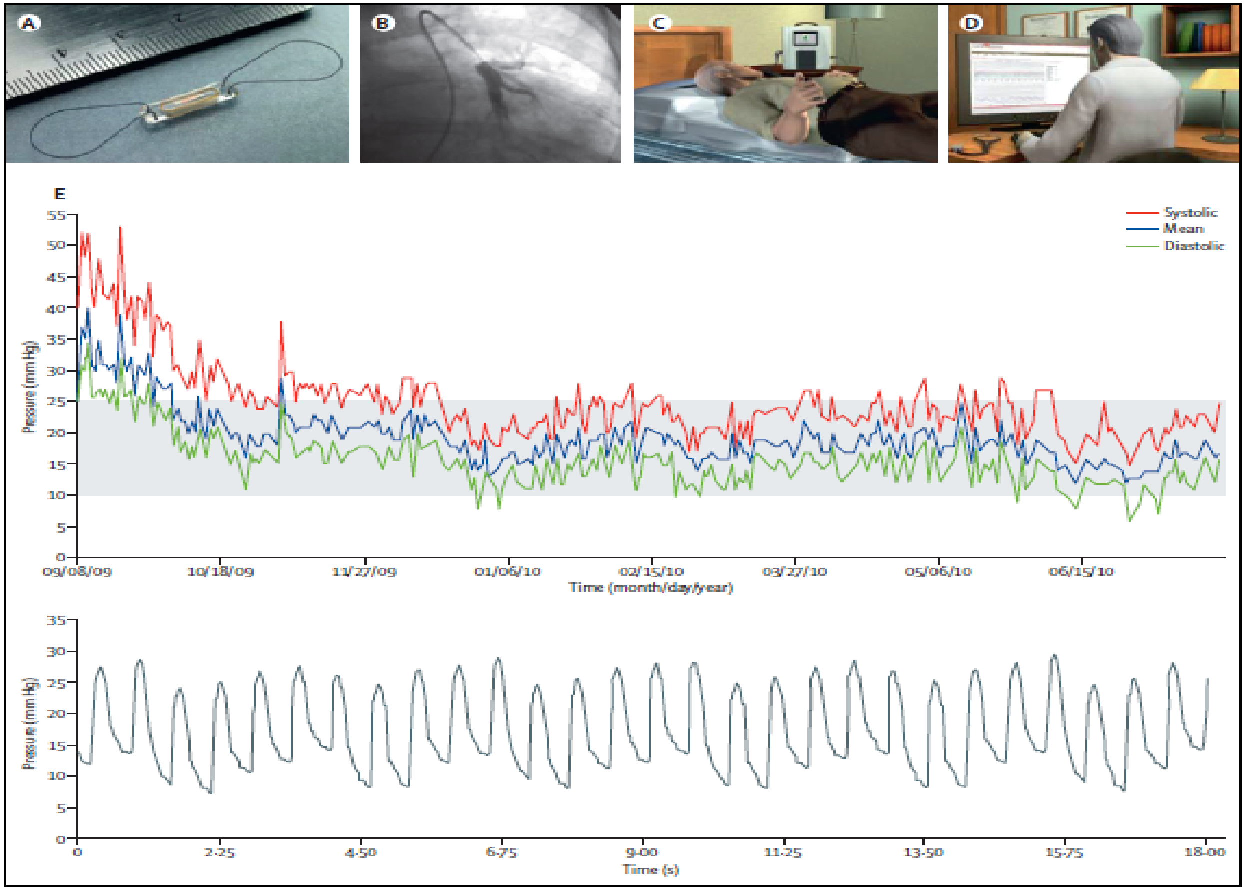



**Figure 1: Implantable haemodynamic monitoring system**
(A) CardioMEMS sensor or transmitter. (B) Transcatheter is implanted into a distal branch of the descending pulmonary artery. (C) Patient is instructed to take daily pressure readings from home using the home electronics. (D) Information transmitted from the monitoring system to the database is immediately available to the investigators for review. (E) Transmitted information consists of pressure trend information and individual pulmonary artery pressure waveforms.

*Lancet* 2011; 377: 658–66
Published Online
February 10, 2011
DOI:10.1016/S0140-6736(11)60101-3

# CardioMems device and trial

CHAMPION trial reported Eur Soc Cardiology HF Congress 2010 and Lancet article (Vol 377, Feb 19th 2011, pp 658-666)

**Relative risk reduction (%)**

| | PA-pressure sensor-guided therapy (n=270) | Standard management (n=280) |
|---|---|---|
| **HF re-hospitalization** | **31** | **44** |
| **Re-hospitalization (annualized rate)** | **45** | **73** |

FDA approved and CE marked.

**Compare with:**

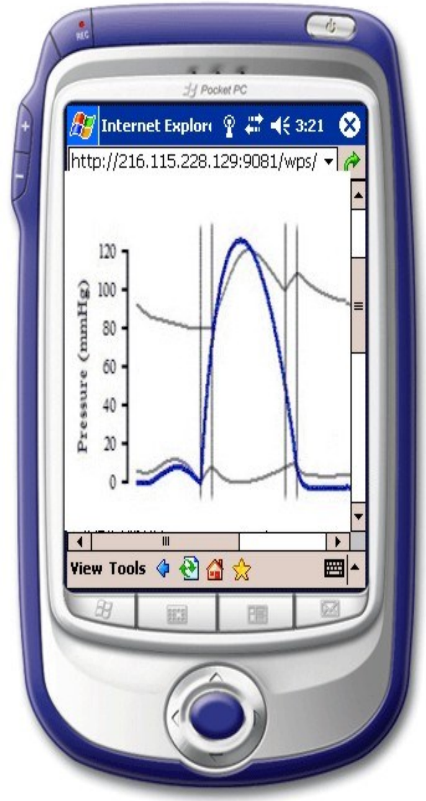
- Tele-HF trial, reported 2010 *New England J Med.* No effect from patient reporting using Telemedicine
- TIM-HF trial, reported 2010 Am Heart Assoc. No effect from patient reporting using Telemedicine

**Potential improvements:**

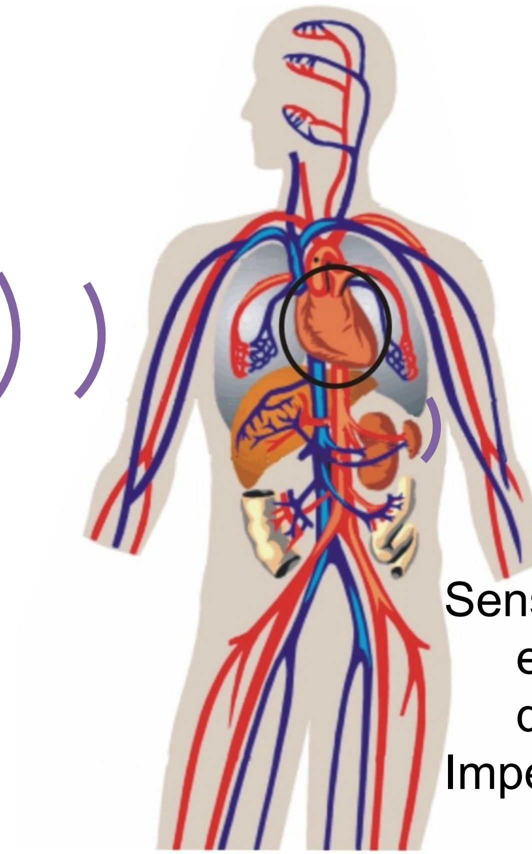
- More frequent measurement to capture spiking, response to physical activity
- Alarm
- Verification of data
- Procedure-free usage

# SAW Technology approach

mHealth connectivity to NHS computer server; service design. University of Oxford




Data -> Information



Sensor and endovascular delivery. Imperial College

Wireless communication & signal generation. Imperial College

# Features of SAW sensors relevant to implantation

- Wireless, range in air c.3 metres, but only cms in tissue
- High Q, (10000 at 400MHz, 4000 at 1 GHz) =>Network of sensors
- Zero power and no limit on lifetime.
- Independently sensitive to temperature and pressure.
- Easily scalable pressure range – set by membrane thickness.
- Temperature sensitivity- from insensitive to $\pm 0.1^{o}C$ over part of $25^{o}C$ to $45^{o}C$ range
- Inert materials, quartz platinum/gold and nitinol. Aluminium can be encapsulated.
- Excellent long-term stability – design target 10 years minimum $\pm$1mmHg/yr for pressure.
- Small size – temperature 1mm x 1mm,

  pressure 3mm x 7mm

# Physical design of the sensor

- Width constraint 3mm for endovascular access and deployment
- Low-profile form to avoid disturbing flow ~1mm
- Longitudinal (dipole) aerial compatible with deployment site
- Pressure ranges 0-50 mmHg (~7kPa) or 0-250mmHg (~33kPa)
- At 434 MHz, $\lambda_t$ = 9cm; at 868 MHz, $\lambda_t$ = 4.5cm ($\lambda_t$ = tissue wavelength)
- At 434 MHz, $\lambda_{saw}$ = 7.2µm; at 868 MHz, $\lambda_{saw}$ = 3.6µm
- Q α 1/f
- Local reference pressure
- SAW surface cannot be mass loaded

===➔ 3mm x 3mm diaphragm, bonded to quartz carrier, forming cavity
SAW resonator on inside surface of the cavity
Sensor diaphragm thinned to < 50µm.
868 MHz
Additional, pressure-insensitive (REF) SAW resonator

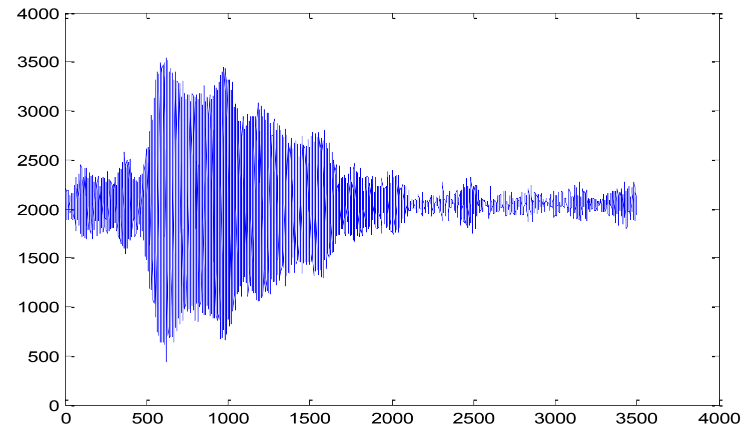
# Reader design

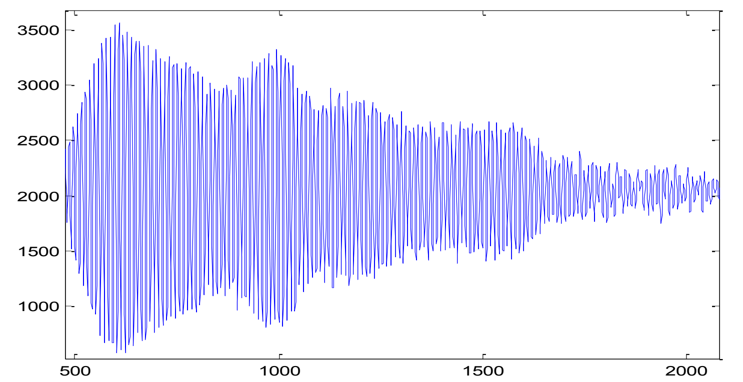
- 33dBm excitation pulse, shaped.
- Better than -80dBm sensitivity
- Fully programmable sampling
- On-board freq estimation <1kHz
- On-board storage for (RF samples) measured freq
- On-board atmospheric pressure measurement
- On-board movement and posture detection
- Industry-standard USB and wireless BLE links
- Battery powered for >1 week exchange interval
- Integral or cabled external aerial
- mHealth system compatible using smartphone etc

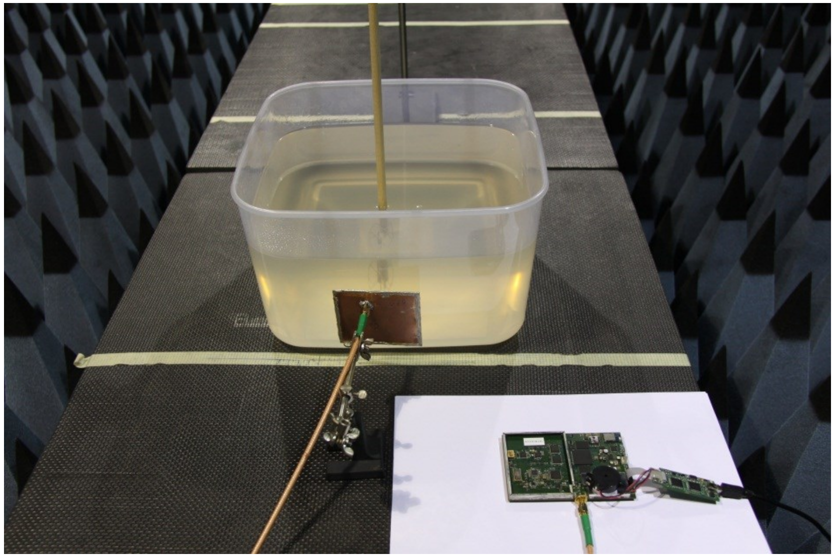
=➔ 11cms x 7cms x 1.4cm board.

# Results

- Sensor 4cms deep in tissue phantom
- 30dBm excitation pulse
- 12-bit ADC range
- 1200-1300 usable sample points
- Frequency resolved to c.3 kHz
- Increase S/N by averaging
- Real-time processing
- Independent measurement of REF

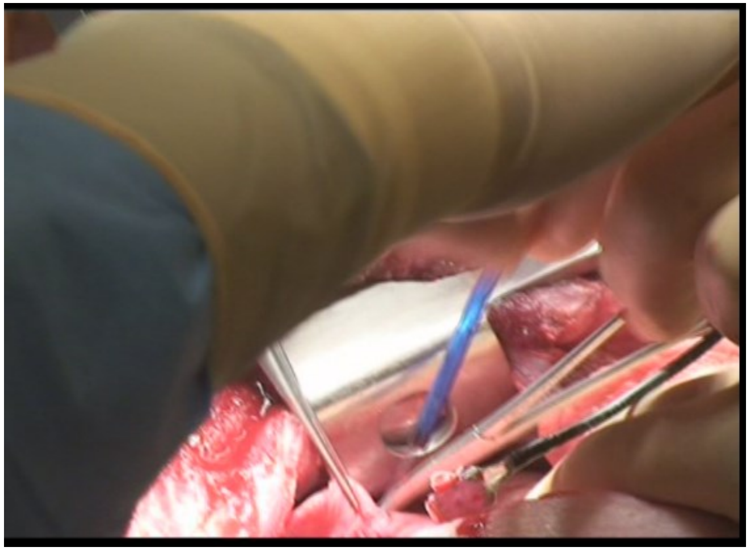


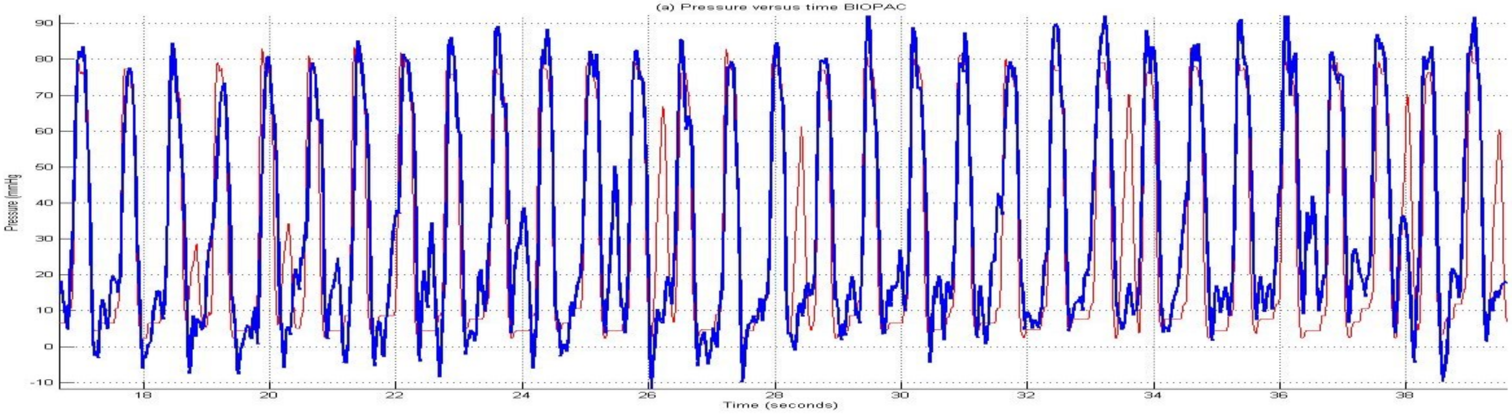



# In-vivo experiments

*Placement of wired device into the left ventricle of the heart. Simultaneous measurements with SAW device and conventional catheter.*

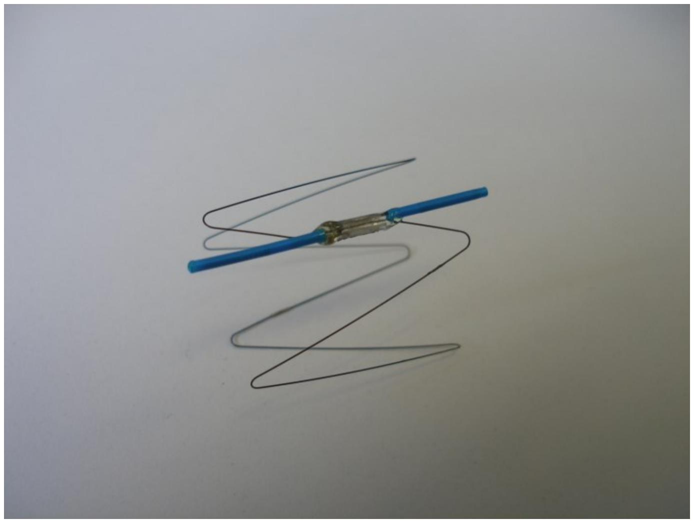




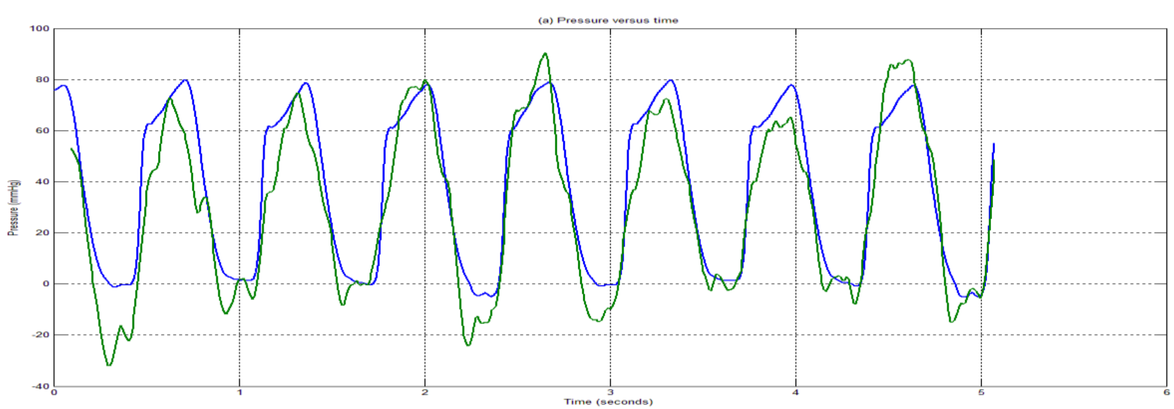

*SAW sensor (blue) compared to catheter tip pressure (red)*

*Copyright Imperial College London 2010*

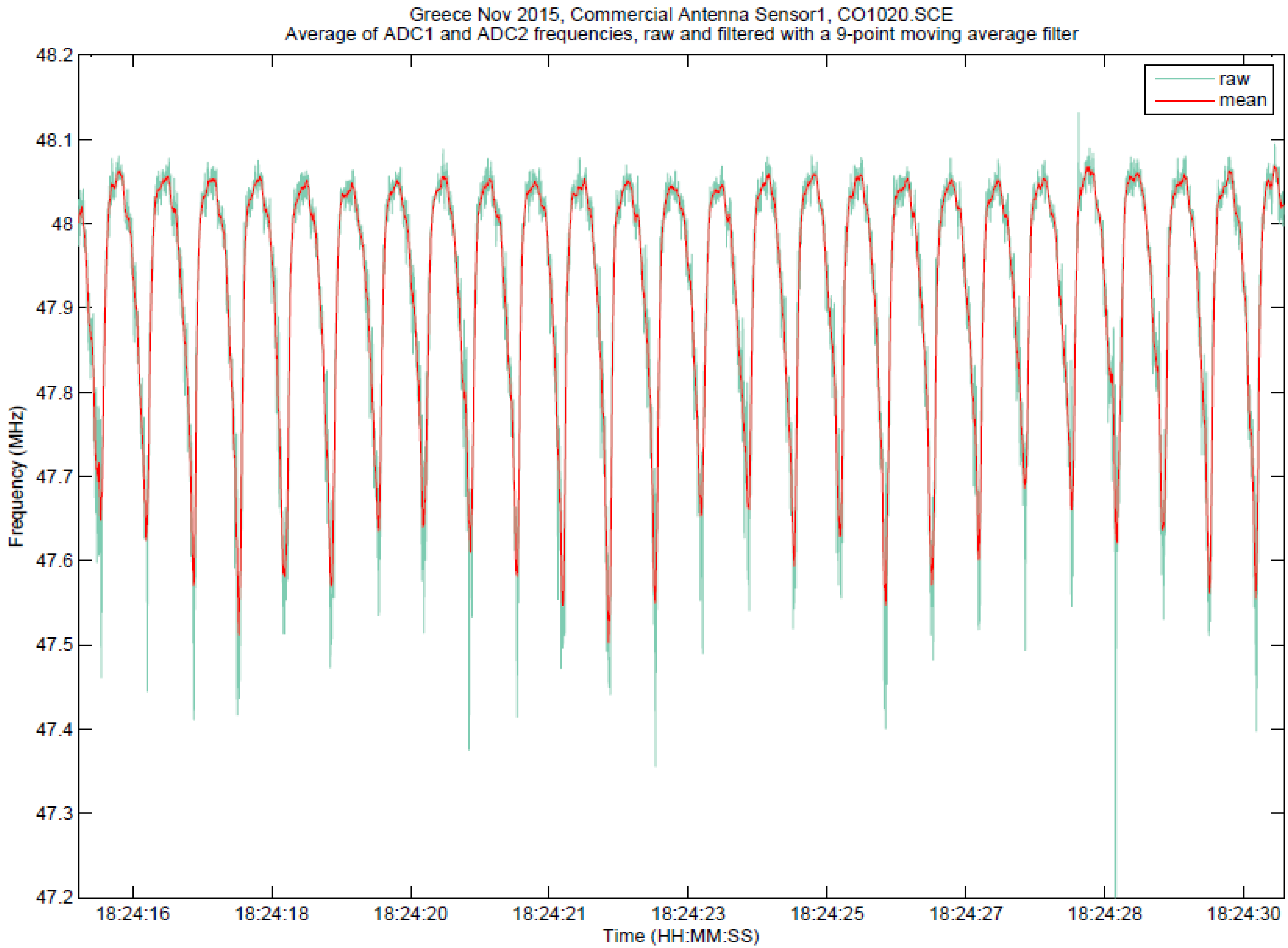
# Implanted sensor, complete with aerial and retaining stent. March 2011 version



Acutely implanted sensor in LV; simultaneous Catheter measurement



# Wireless Measurement in Pig Pulmonary Artery



# Competent Authority, MHRA(UK) or FDA(US)

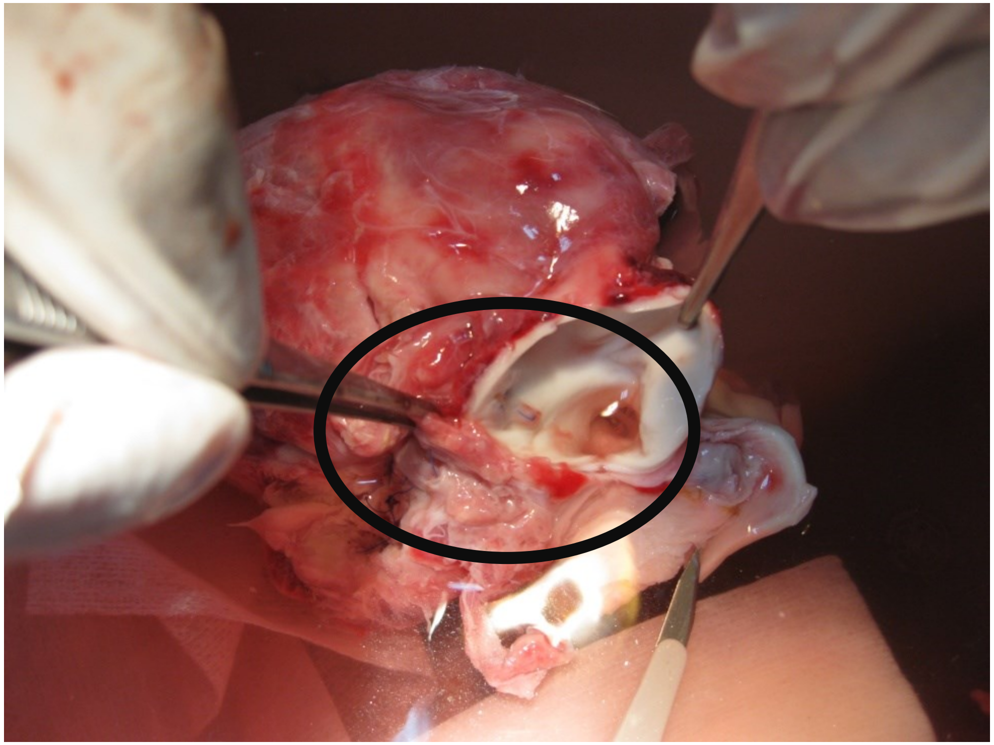
- "An assessment of toxicological risks is necessary for the assurance of biological safety. (Other biological risks, such as microbial contamination, are excluded from this type of assessment.) It is evident from Annex VIII of the Medical Devices Directive that a biological safety evaluation needs to be carried out before any clinical investigation is commenced. "
- "The main safety aim is that the device will not compromise the clinical condition or safety of the patient or user or other persons, <<provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient...>>.

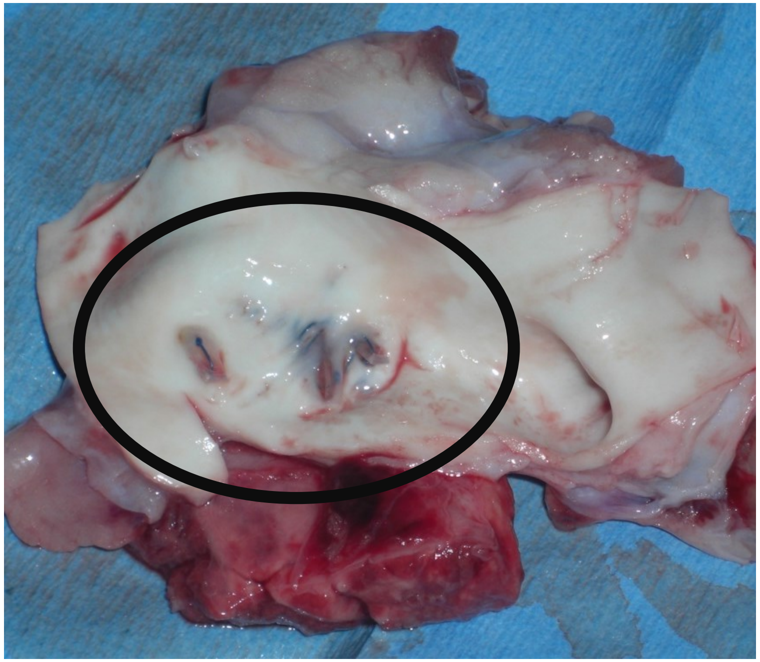
*"GUIDANCE ON THE BIOLOGICAL SAFETY ASSESSMENT"*
*MHRA bulletin n. 5, February 2011*

# Phased clinical trials

- Phase 1 – Safety. First do in animals all that can be done. Small number (10-20) patients; leads to CE mark.
- Phase 2 – Efficacy. Show that it works without adverse incidents. Choose trial endpoints and power of study.
- Phase 3 – Show patient benefit.

# PA tissue exposed for analysis

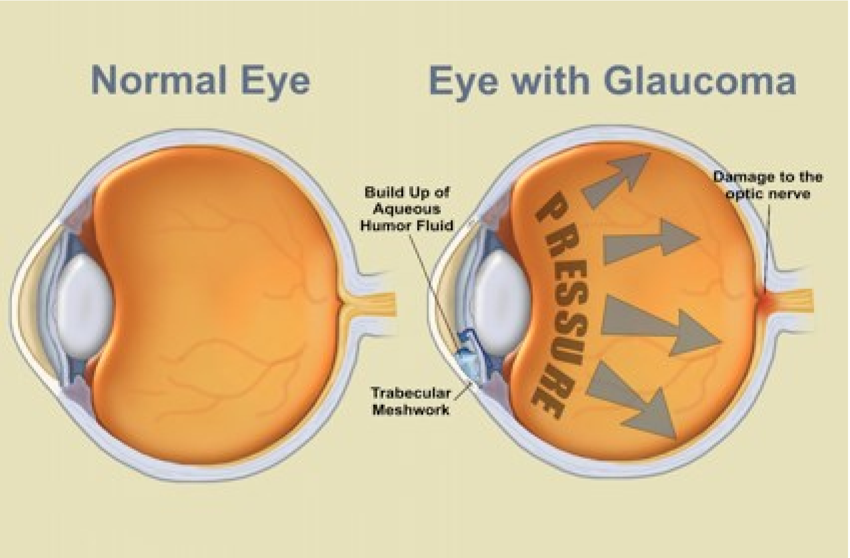




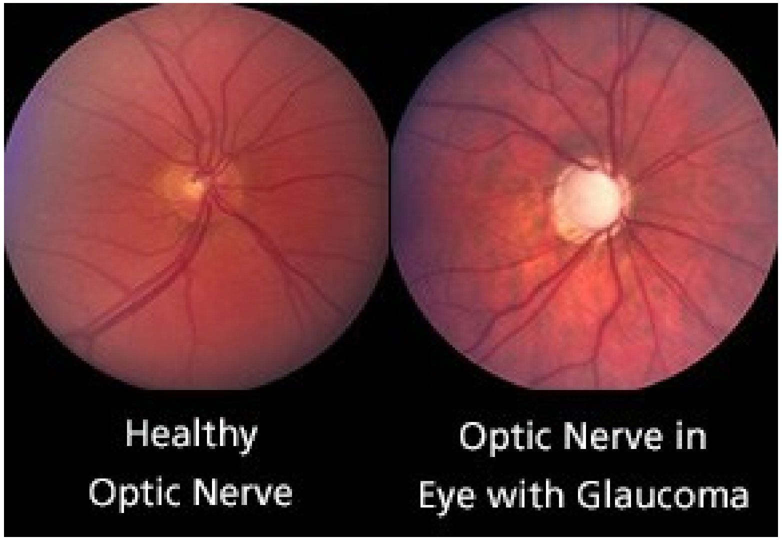
# The Glaucoma Sensor

# Glaucoma and IOP

- Glaucoma is a medical Condition of Sustained Raised Intraocular Pressure (IOP)
- IOP results in gradual and accumulative damage to the optic nerve tissue, in the posterior segment of the eye.
- Retinal Ganglion Cell Death and Enlarged Optic Disc Cupping
- Visual Field Loss, Blindness

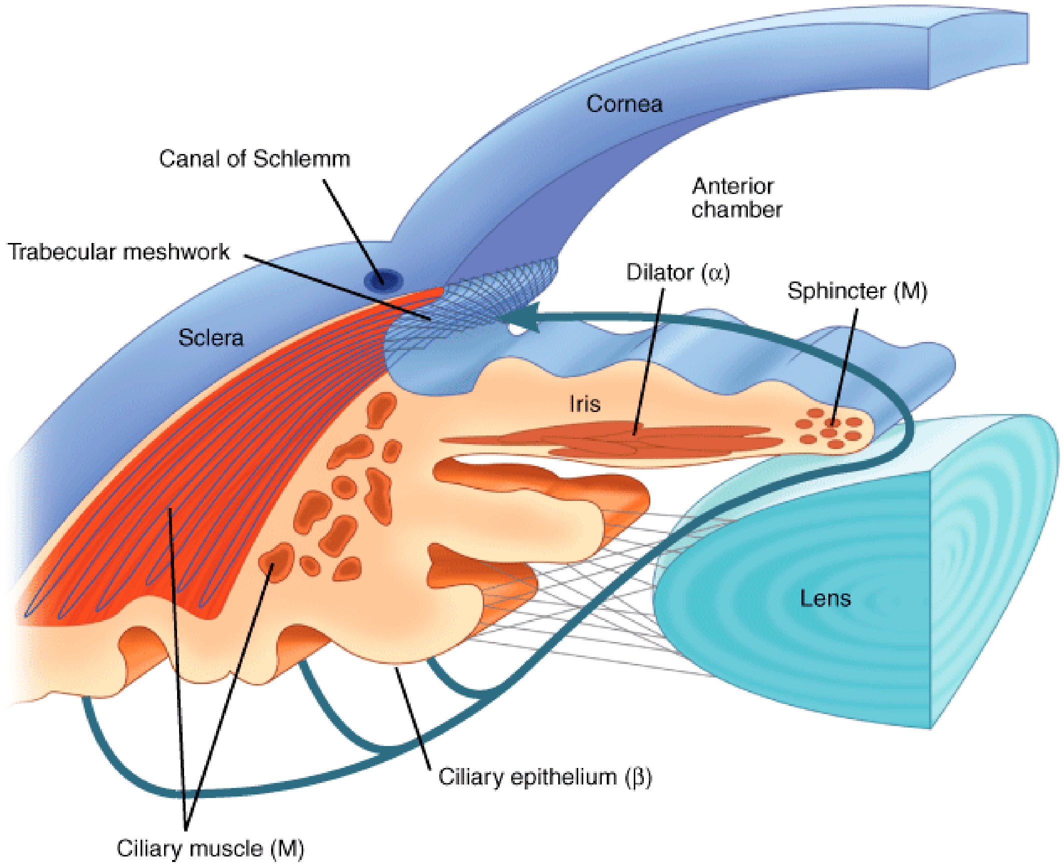






# Ciliary Body and Intraocular Fluid

- Ciliary Body secretes aqueous fluid in the eye
- Intraocular aqueous fluid flows into the Anterior Chamber
- Aqueous fluid supplies nutrients
- Trabecular Meshwork drains the fluid out of the eye
- Normal Intraocular Pressure – 12-21mmHg




Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 11th Edition*: http://www.accessmedicine.com

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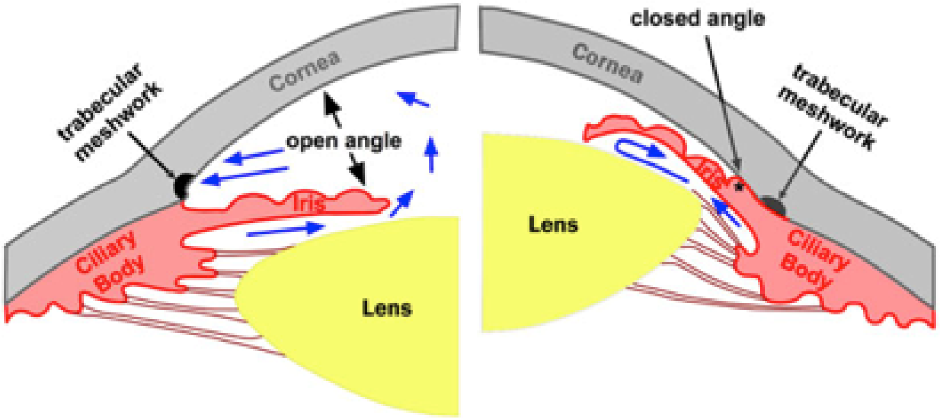
# Types of Glaucoma

- Open Angle Glaucoma (Left) – Commonest
  - Trabecular Meshwork Dysfunction
- Closed Angle Glaucoma – can be acute or chronic
  - Increased pressure pushing the iris/lens complex forwards, blocking the trabecular meshwork – vicious cycle



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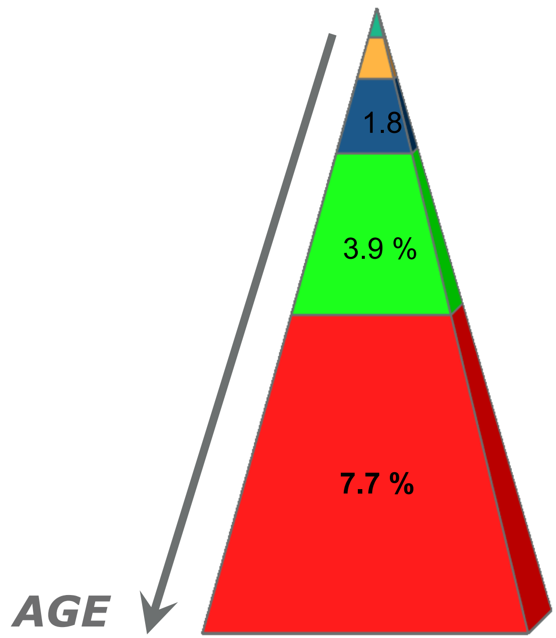
# Glaucoma – Clinical Need

- Leading cause of irreversible blindness - 15% of world blindness
- Strongly age-related
- Significant cause of disability – UK lifetime costs > age 65 £41,652
- Late diagnosis - lack of screening test



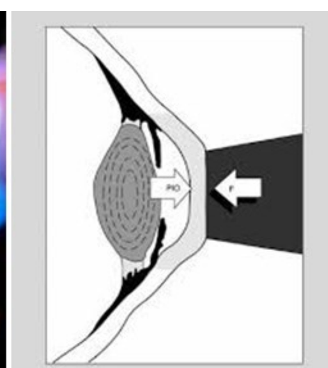
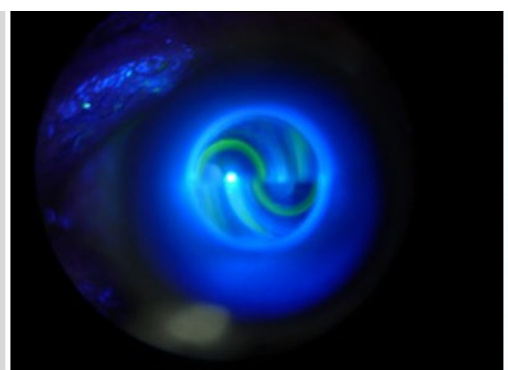

| *Age* | *%* |
|---|---|
| *40-49* | *0.7* |
| *50-59* | *1.0* |
| *60-69* | *1.8* |
| *70-79* | *3.9* |
| *>80* | *7.7* |

# IOP

- IOP major modifiable risk factor
- All treatment aimed at lowering IOP
- Gold standard for IOP measurement is Goldmann Applanation
- 1mmHg reduction reduces progression by 10%
- 1mmHg elevation increases risk of progression

  from baseline 10% - 12%

  at follow-up 12% – 19%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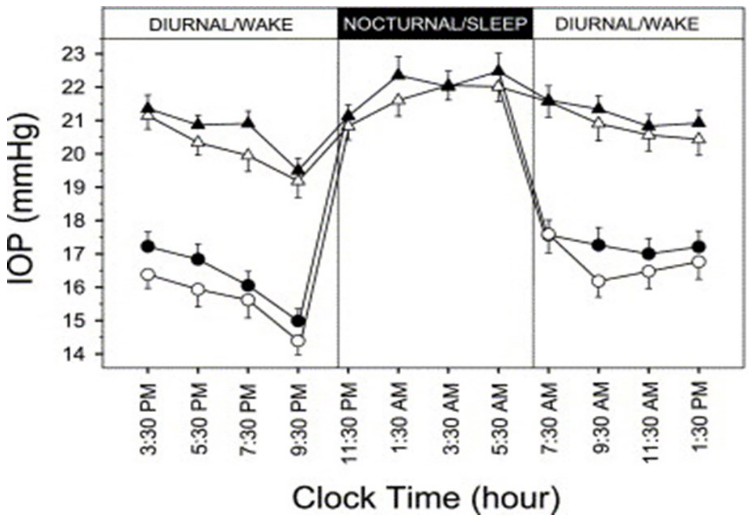
# Problems with Current IOP Measurements

- Snap shot IOP
- Physiological and positional variation
- Indirect measure for continuous monitoring: Not reliable



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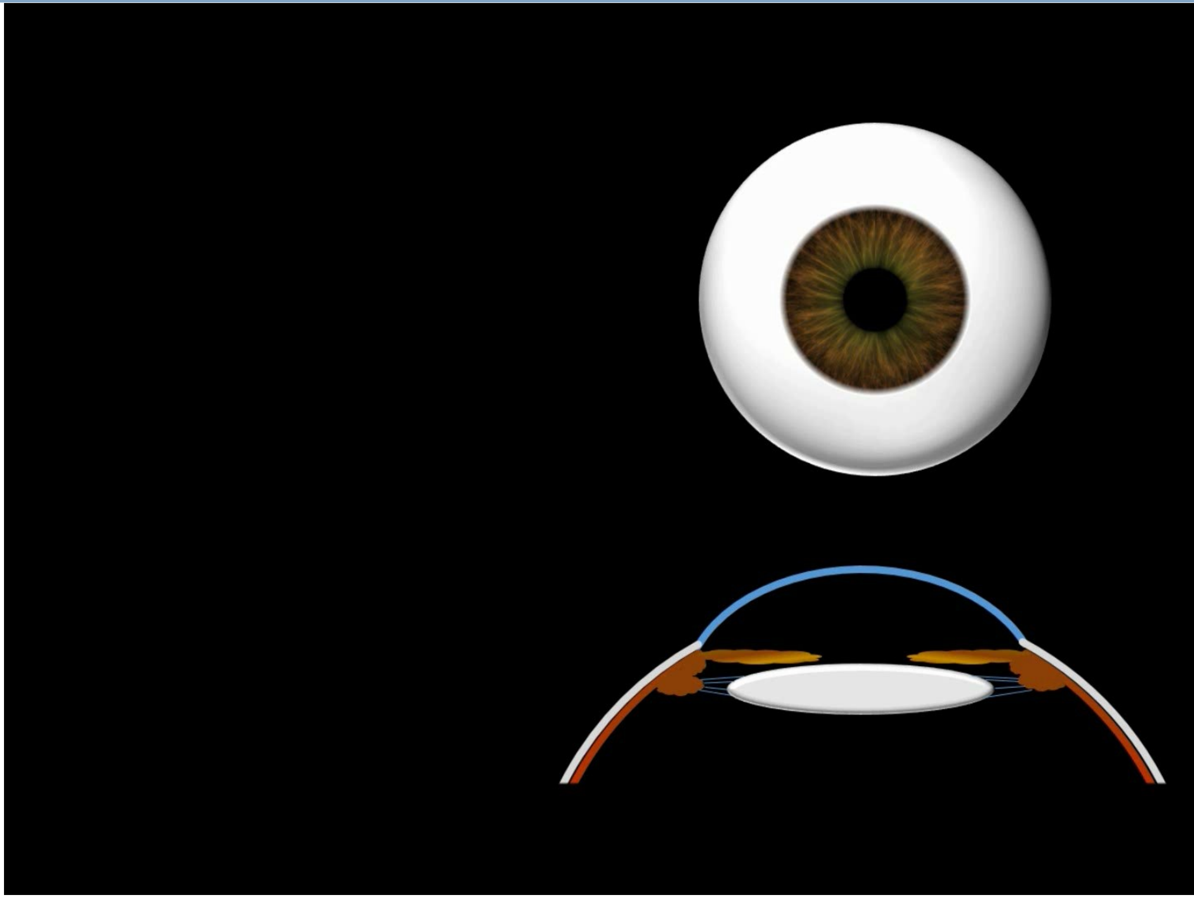
# Proposed IOP Measuring Implant

- A small battery-less and wireless sensor
- Can be delivered through a 22-gauge needle into the eye in a clinical outpatient setting
- Can be interrogated wirelessly by an RF reader.
- Can be paired to telehealth system via a wireless link.



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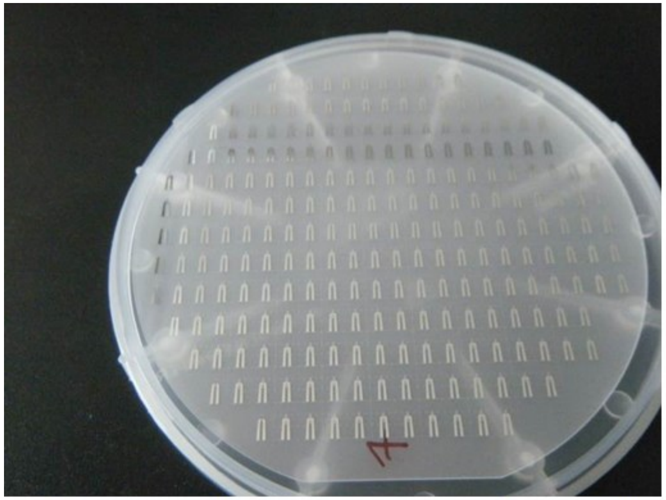
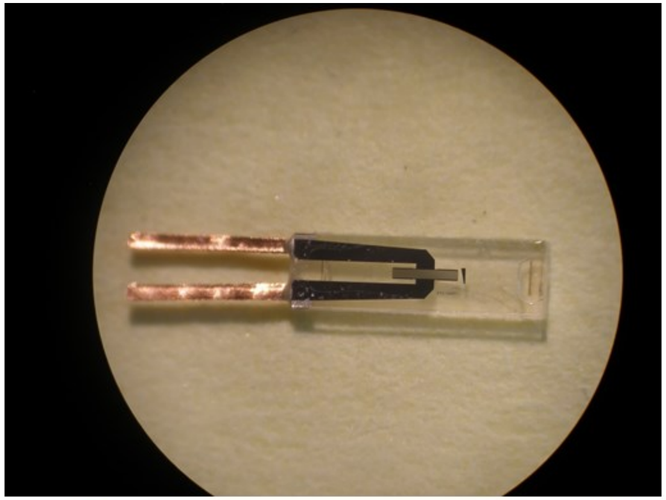
# Cardiovascular Sensor is too big for the eye!

- Due to size constraints, sensors should operate at GHz frequencies.
- Conventional pressure sensors based on SAW technology are large for the eye.
- Not efficient in GHz frequencies.



Resonators on quartz wafer



Pressure sensor assembly

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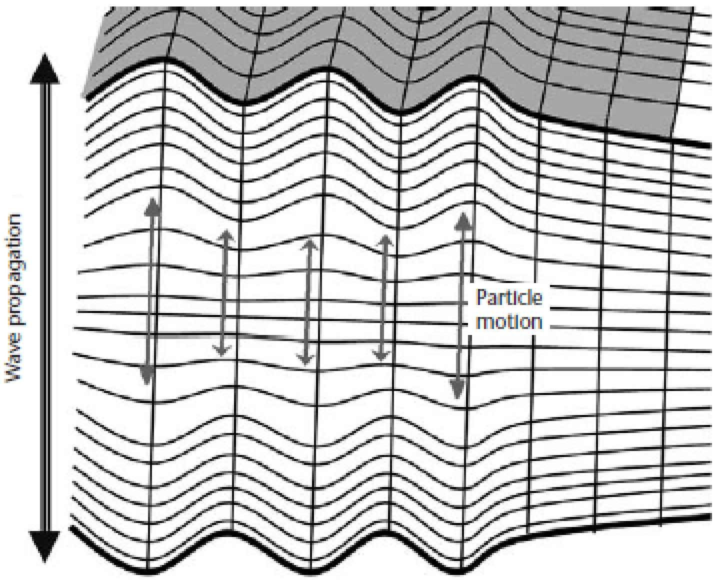
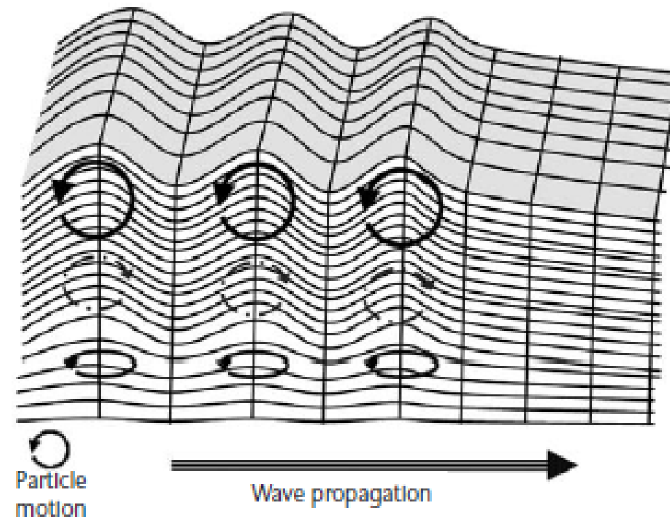
# Film Bulk Acoustic Wave Resonators (FBARs)

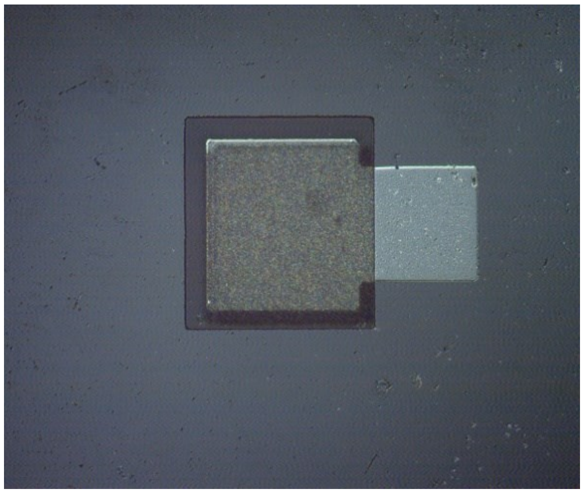


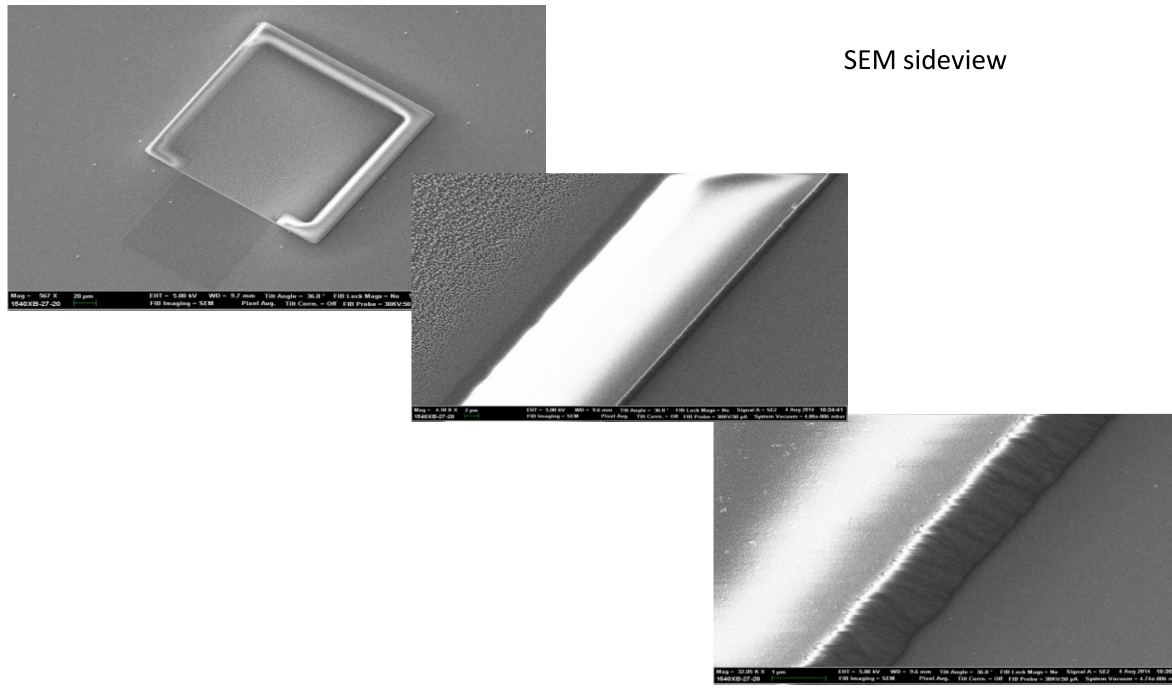

*Bulk Wave (longitudinal)*



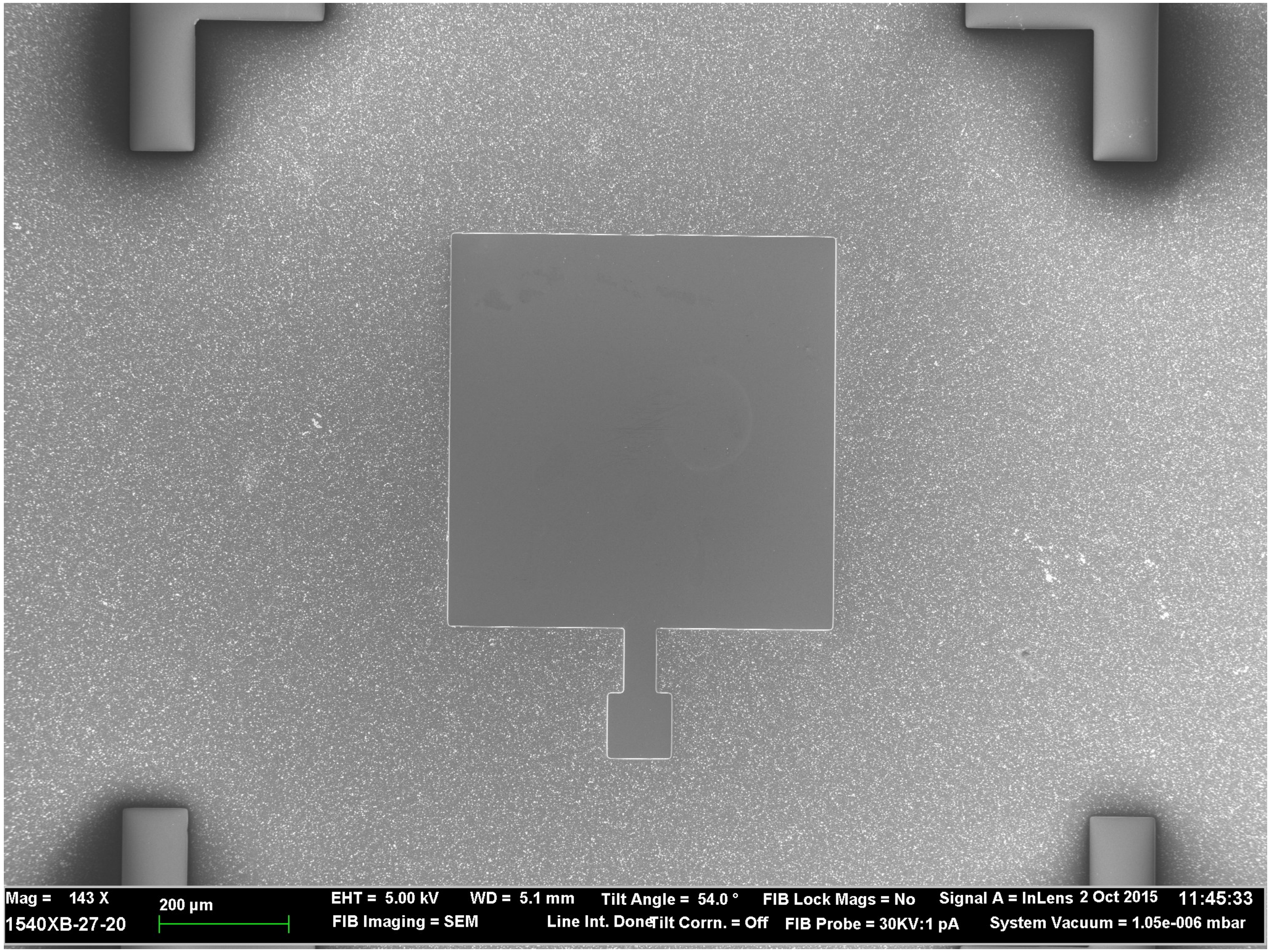

*Rayleigh Wave*

# FBAR Fabrication (at LCN)





SEM sideview


Mag = 143 X
1540XB-27-20
200 µm
EHT = 5.00 kV
WD = 5.1 mm
Tilt Angle = 54.0 °
FIB Lock Mags = No
Signal A = InLens
2 Oct 2015
11:45:33
FIB Imaging = SEM
Line Int. Done
Tilt Corrn. = Off
FIB Probe = 30KV:1 pA
System Vacuum = 1.05e-006 mbar

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# Moral of the Story

Measuring physical (e.g. pressure) and biochemical (e.g. glucose concentration) quantities inside the human body can assist in managing relevant medical conditions and assessing the efficiency of treatments. This requires biocompatible miniature implants of high longevity that can be interrogated wirelessly. Producing such devices is challenging and demands creative use of existing, and developing novel technologies to achieve:

- Miniaturisation without compromising the functionality.
- Increasing the longevity without compromising safety and biocompatibility.
- No cross-interference with other wireless systems.

# Thanks for you attention

# Questions?