APPLICATIONS OF CMOS SPAD ARRAYS IN CLINICAL IMAGING AND SPECTROSCOPY

Michael G. Tanner[1,2]

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A. Kufcsák[1], K. Ehrlich[1], E. Pedretti[1], E. McShane[1], H. Chandrasekharan[1], T. Craven[2], K. Dhaliwal[2], R. R. Thomson[1,2], R. H. Henderson[3]

(plus many other contributors)

1. Institute of Photonics and Quantum Sciences, Heriot-Watt University, Edinburgh, UK
   Global Research Institute in Health and Care Technologies, Heriot-Watt University, Edinburgh, UK
2. Translational Healthcare Technologies, Centre for Inflammation Research, IRR, University of Edinburgh, Edinburgh, UK
3. Institute for Integrated Micro and Nano Systems, University of Edinburgh, UK

Translational Healthcare Technologies

THE UNIVERSITY of EDINBURGH

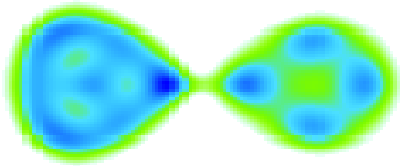
Engineering and Physical Sciences Research Council

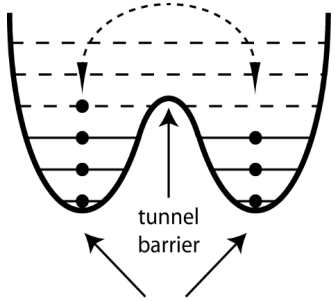
Science and Technology Facilities Council

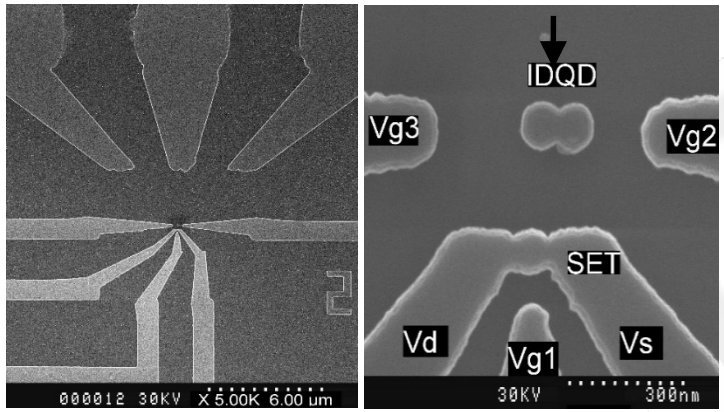
Medical Research Council

My background: Semiconductor devices and quantum

- Novel silicon quantum dot devices for quantum information processing
- Isolated Double Quantum Dots (IDQDs)







SEM images of an example of the finished oxidised device structure. Lighter areas are the oxidised active silicon regions and the darker surrounds are the underlying SiO_2 substrate.

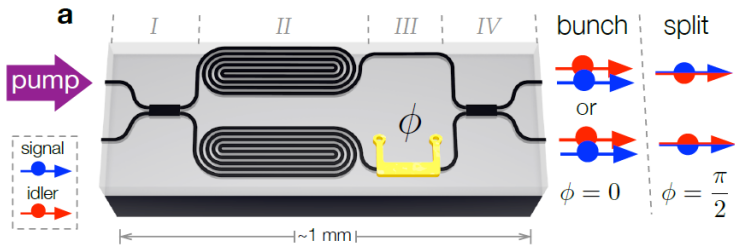
Science & Technology Facilities Council

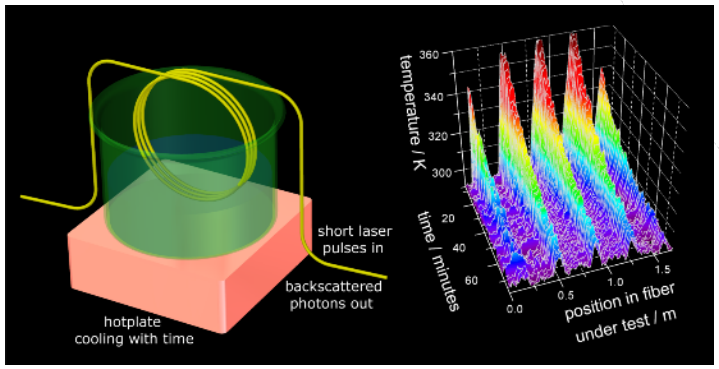
Cryogenic Instrumentation for Quantum Electronics

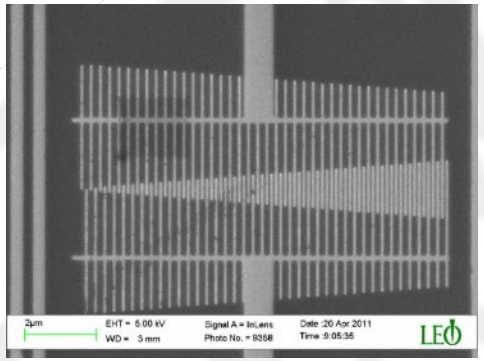
My background: Single photon counting

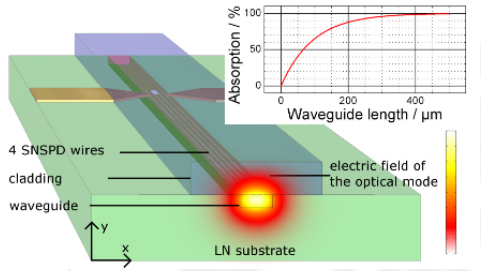
Quantum optics and fibre sensing, developing advanced sensing technologies including:

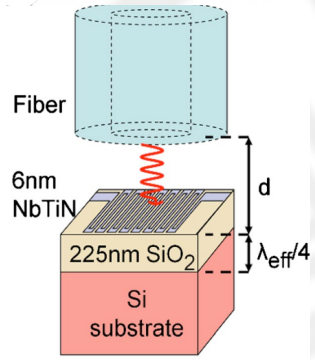
- Single photon detectors – SNSPDs
  - With Robert Hadfield (University of Glasgow)
  - Applied to: Quantum computing, Optical fibre sensing











Bridging between optics and medical research

PROTEUS
EPSRC Interdisciplinary Research Collaboration

- 2014 on: I developed a multi-disciplinary photonic fingerprinting laboratory
  - at the QMRI, University of Edinburgh
  - Combining photonics with chemistry and biology for healthcare technology
  - Translating emerging optics lab technologies to application
- Exploitation of the photonic fingerprint for imaging and sensing
  - *Miniature fibre optic probes*
  - *Time resolved spectroscopy*
  - *Endoscopic fibre imaging – both time resolved and spectral*

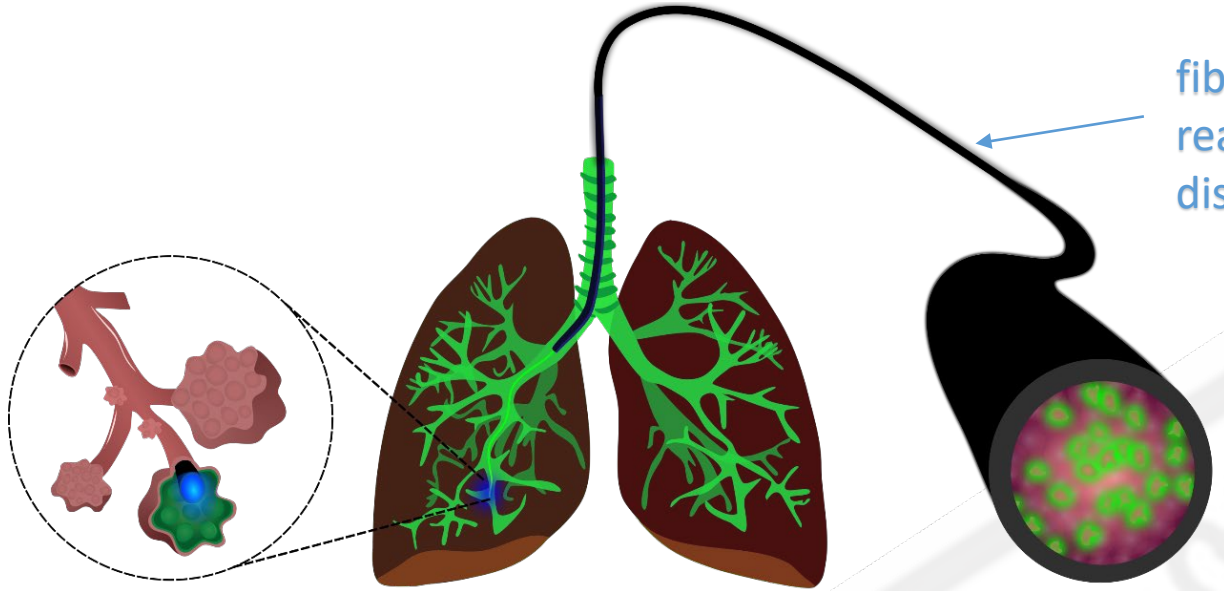
UNIVERSITY OF BATH

HERIOT WATT UNIVERSITY

THE UNIVERSITY of EDINBURGH

Health Care Challenge: Lung diseases

- Can we apply photonic technologies to lung diseases?



PROTEUS
EPSRC Interdisciplinary Research Collaboration

UKRI Engineering and Physical Sciences Research Council

Translational Healthcare Technologies

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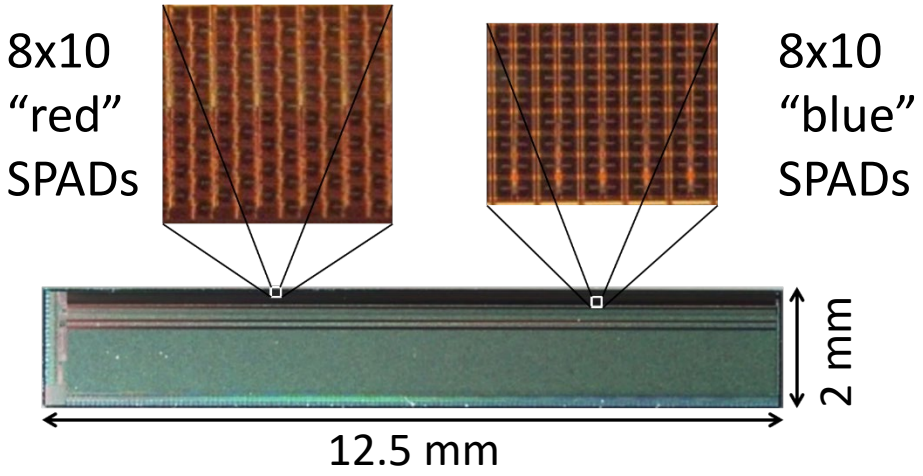
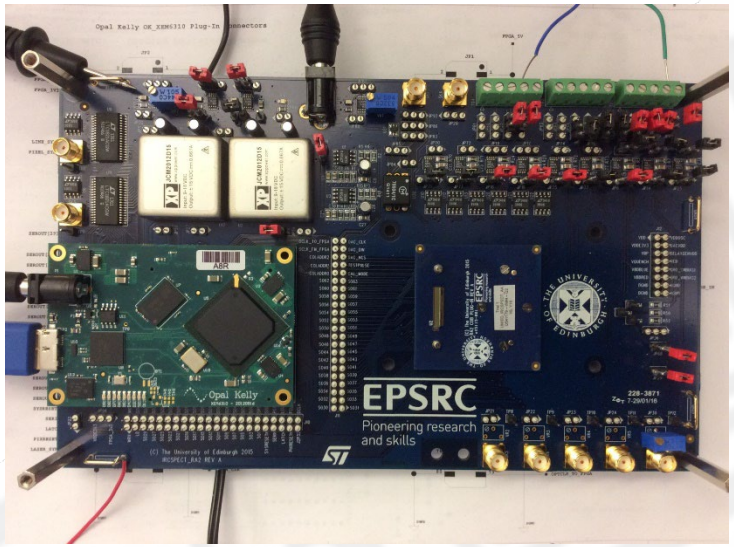
- The aim: improve point of care diagnosis and monitoring of lung disease
- The technology: miniaturised fibre optic probes for real time imaging and sensing with advance detection modalities

CMOS Single Photon Sensors - Arrays

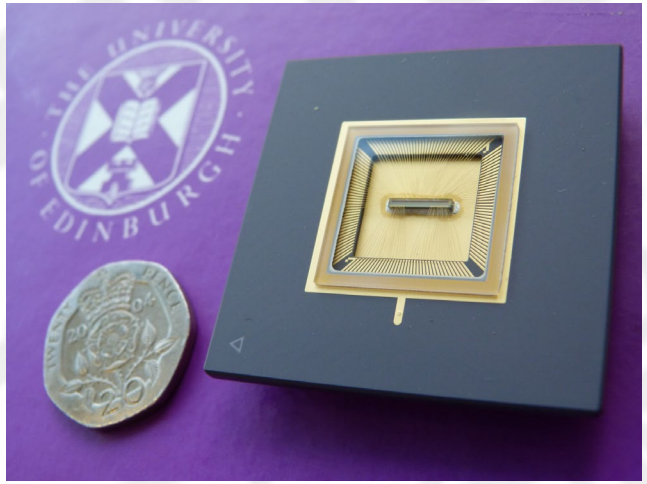
Proteus Ra-II: 512 pixel SPAD line sensor





- **Exploiting CMOS integrated single photon detector arrays for clinical application**
- **Multiplexed detectors enabling:**
  - **fast FLIM through optical fibre for clinic**
  - **time resolved spectroscopy**
  - **diffuse photon timing**

- **In house line sensor chip (Ra-II):**
  - 512 pixels (16 SPADs per pixel), ~ 10% to 50% efficiency
  - Jitter ~ 150 ps (digital timing resolution 50 ps)
  - Fast counting rates: SPC mode: 65 giga events/s, **TCSPC mode: 194 million events/s**, Histogramming mode: 16.5 giga events/s

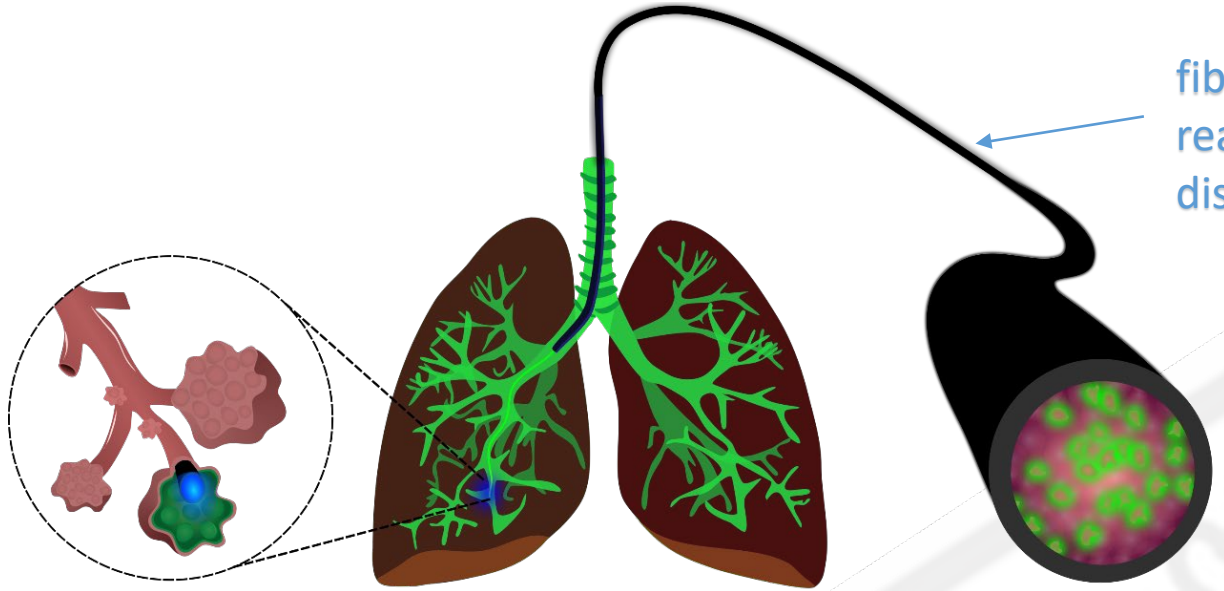


R. Henderson et al, IMNS, U. of E.

A. Erdogan *et al.*, Opt. Express, 23(5), *2015*

Health Care Challenge: Lung diseases

- Can we apply our optical technologies to lung diseases?



Translational Healthcare Technologies

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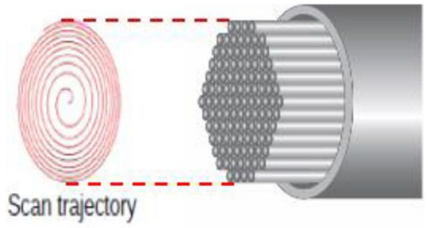
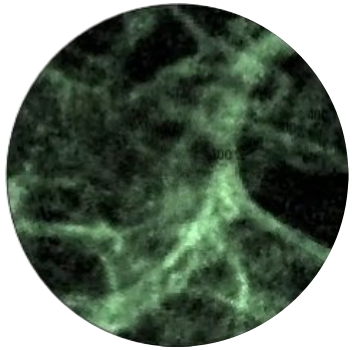
Time resolved single photon counting:

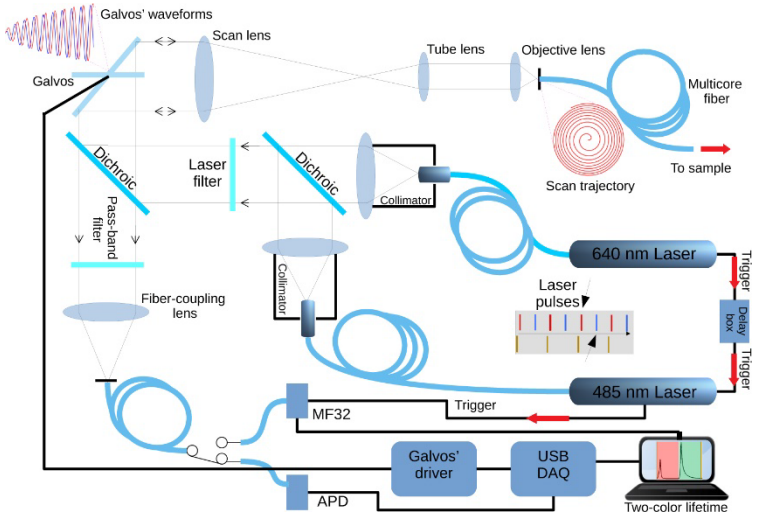
Enhancing information

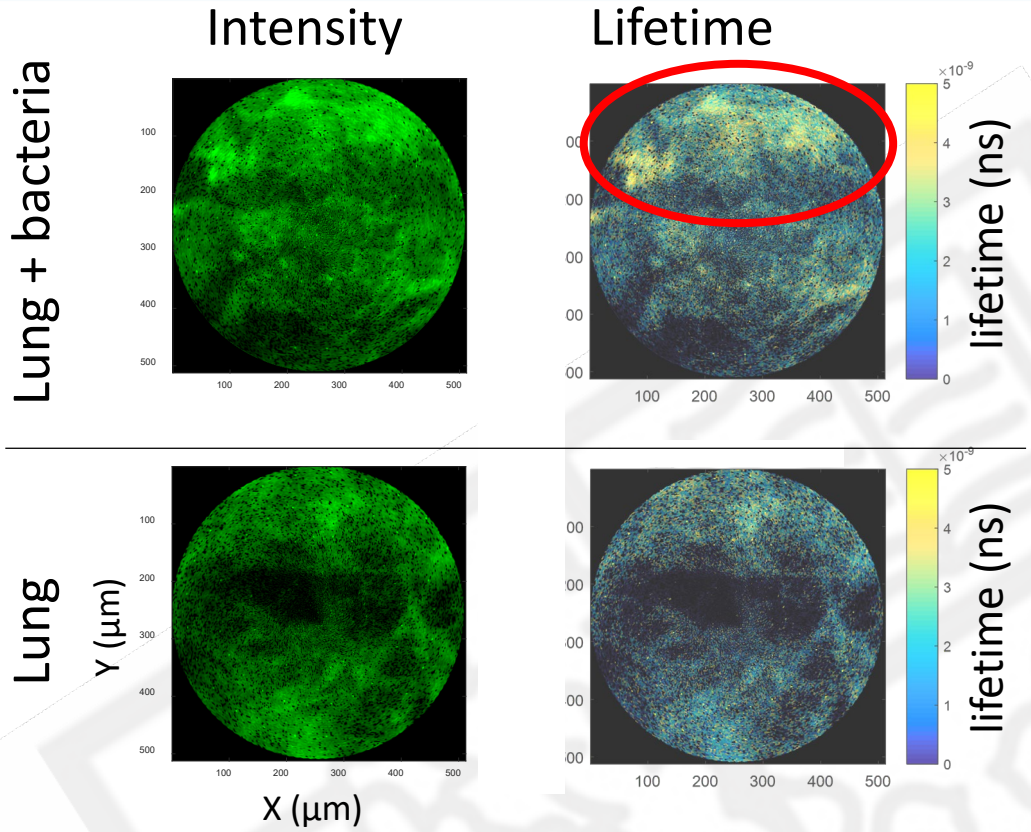
- Time resolved techniques to observe excitation dynamics
- Observing otherwise hidden features

Time resolved endoscopic imaging (FLIM)

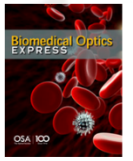








High-speed dual color fluorescence lifetime endomicroscopy for highly-multiplexed pulmonary diagnostic applications and detection of labeled bacteria

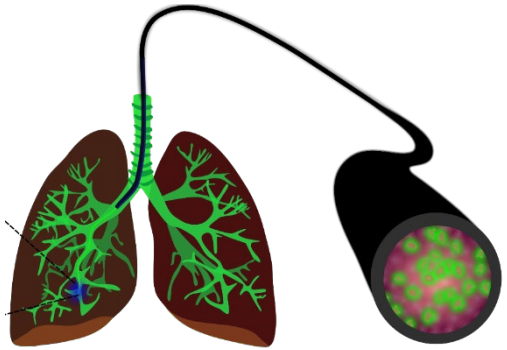


Ettore Pedretti, Michael G. Tanner, Tushar R. Choudhary, Nikola Krstajić, Alicia Megia-Fernandez, Robert K. Henderson, Mark Bradley, Robert R. Thomson, John M. Girkin, Kevin Dhaliwal, and Paul A. Dalgarno

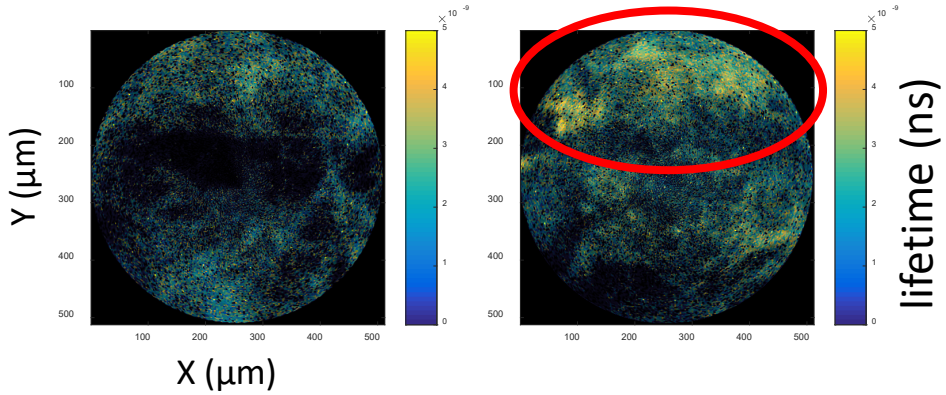
Biomedical Optics Express Vol. 10, Issue 1, pp. 181-195 (2019)

Time resolved endoscopy (FLIM)

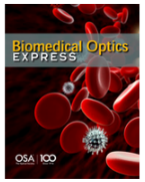
Ex-vivo tissue



lung + labelled bacteria



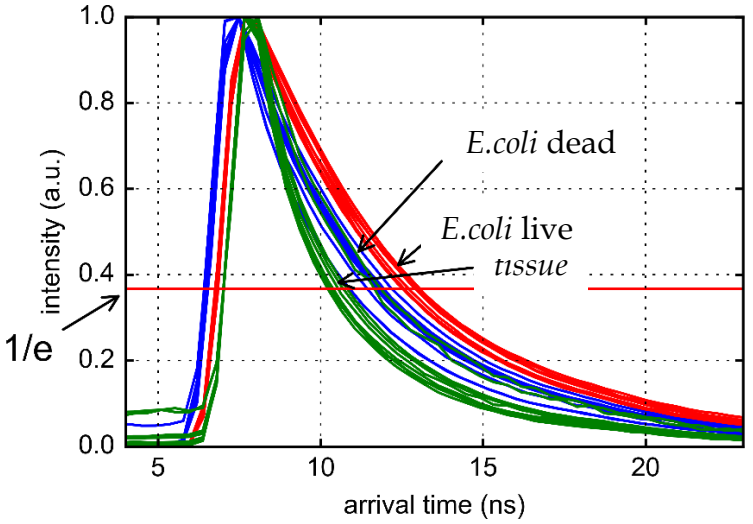
High-speed dual color fluorescence lifetime endomicroscopy for highly-multiplexed pulmonary diagnostic applications and detection of labeled bacteria



Pedretti, Tanner, Choudhary, …. Dalgarno

Biomedical Optics Express Vol. 10, Issue 1, pp. 181-195 (2019)

In human lungs (EVLP model)

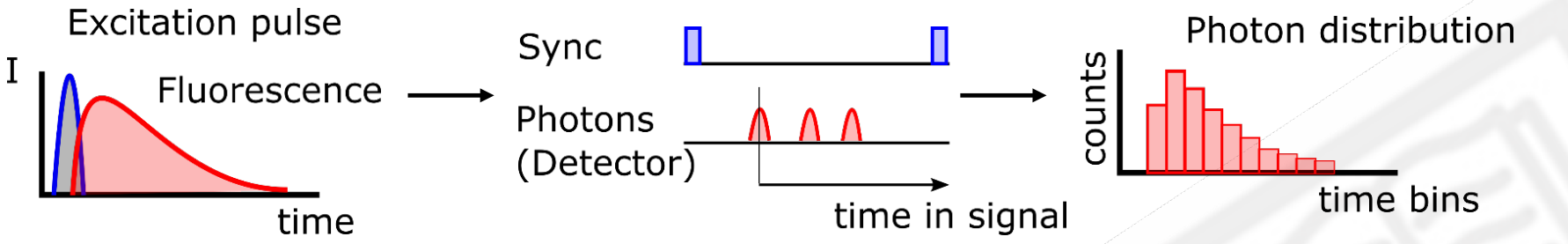


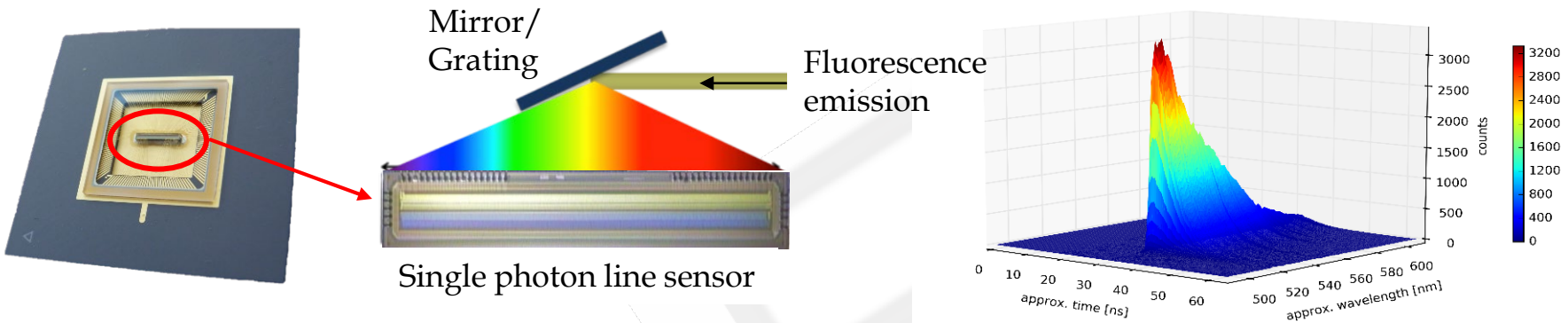
Biophotonics Congress: Biomedical Optics 2020 (Translational, Microscopy, OCT, OTS, BRAIN)
OSA Technical Digest (Optica Publishing Group, 2020), paper TTu2B.3 • https://doi.org/10.1364/TRANSLATIONAL.2020.TTu2B.3

Time-resolved single photon spectroscopy for optical fibre-based sensing of bacterial infections in the distal lung

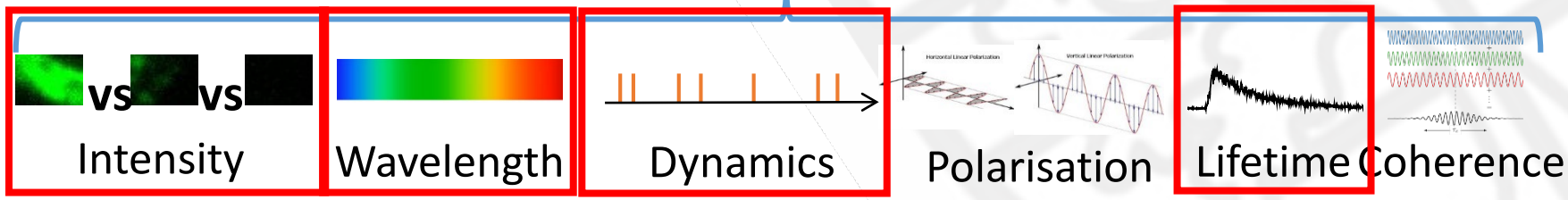
Ehrlich, Duncan, Choudhary, …. Tanner,
Biomedical Optics 2020, OSA (2020), TTu2B.3.
doi.org/10.1364/TRANSLATIONAL.2020.TTu2B.3

Time-correlated photon counting spectroscopy

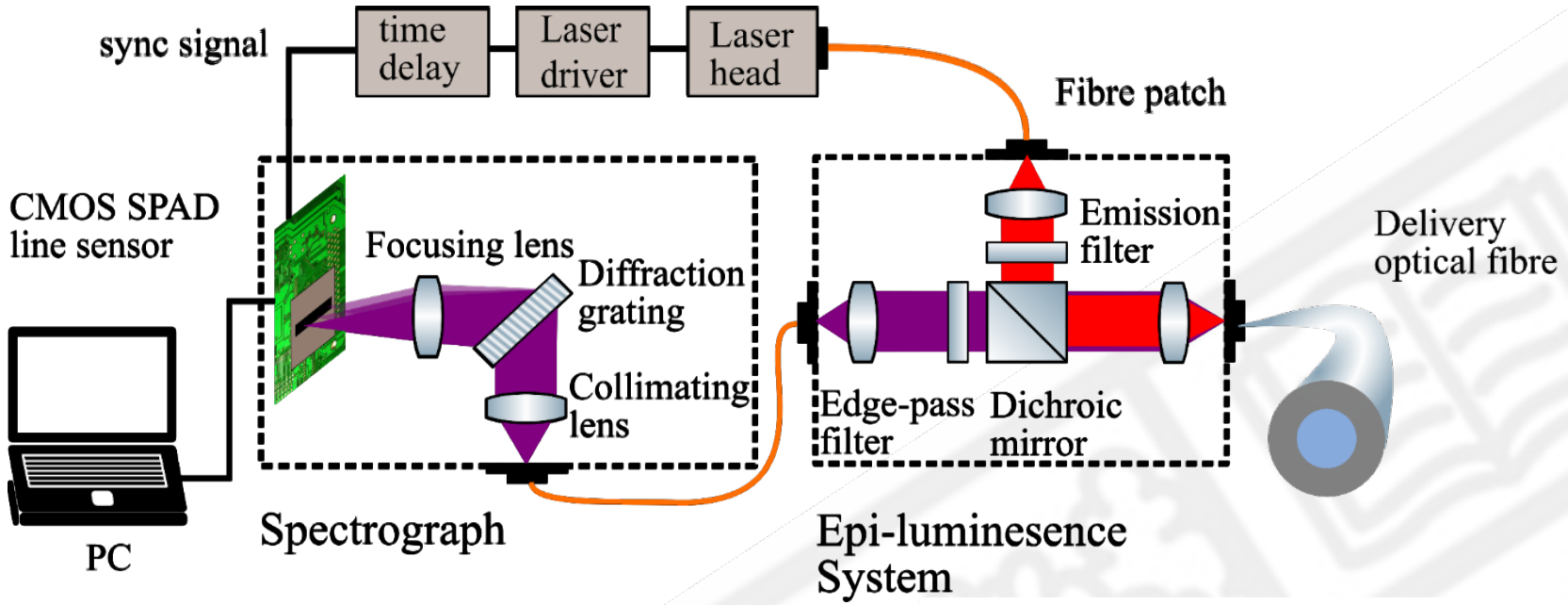


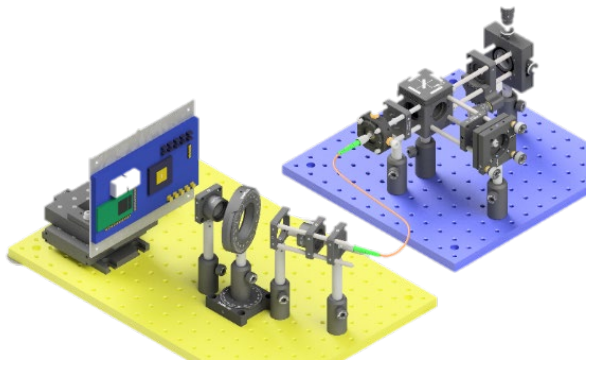


The Photonic Fingerprint



Time-resolved spectroscopy





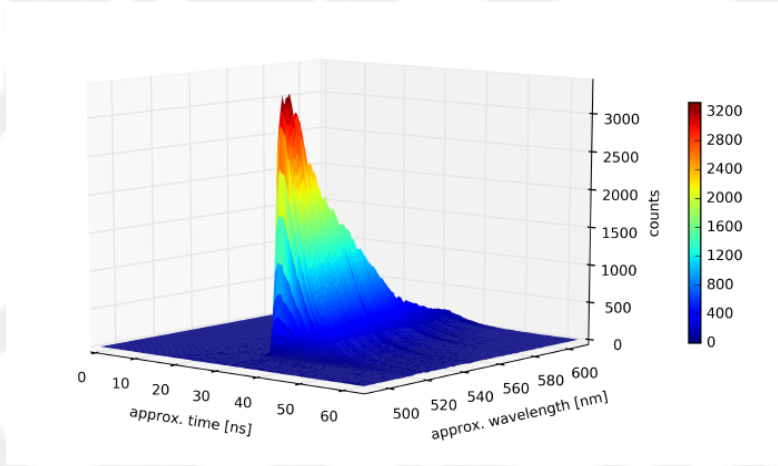
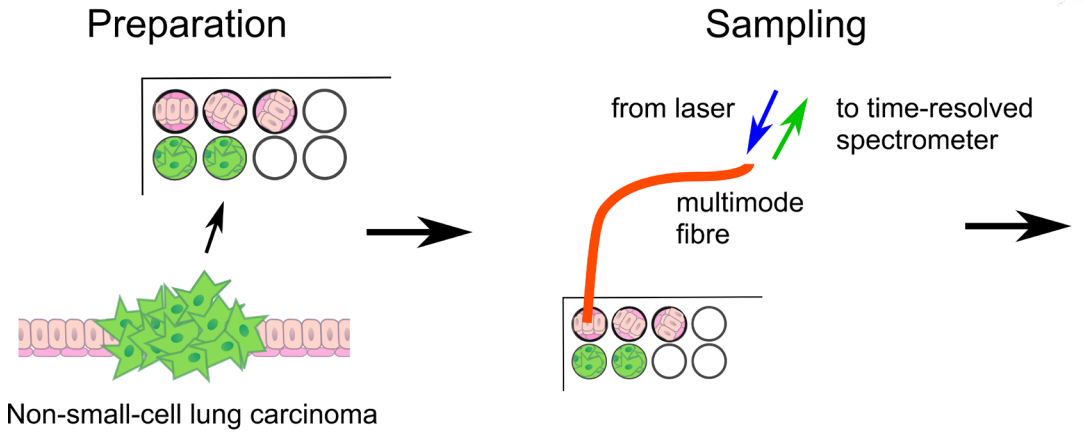


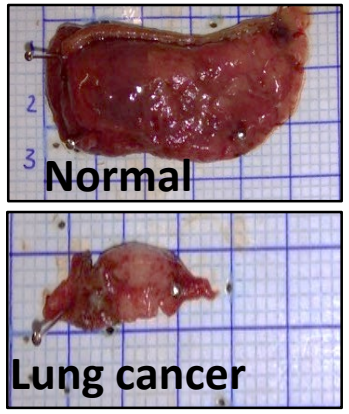
figure: K. Ehrlich, Proc. SPIE 10058, 2017

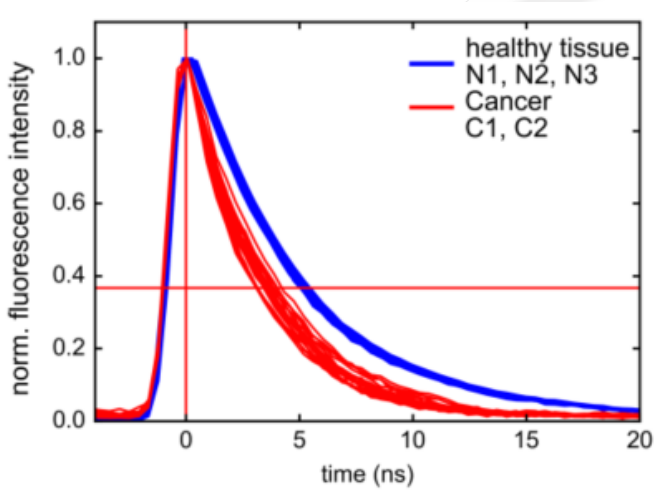
Time resolved spectroscopy for tissue health

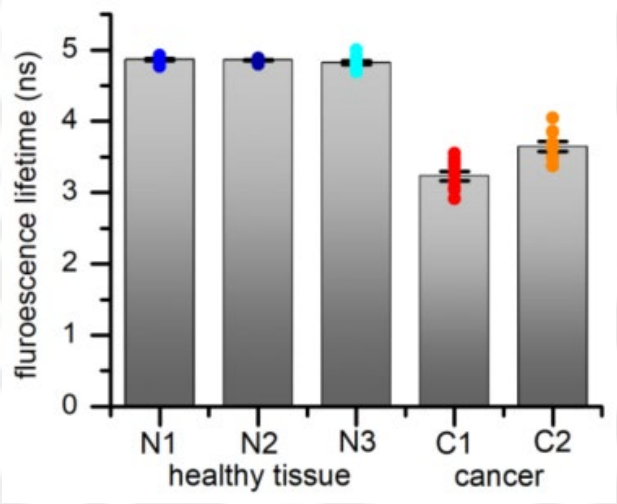
Tumour discrimination



Cancerous tissue
– direct from human biopsy







Time resolved spectroscopy for tissue health

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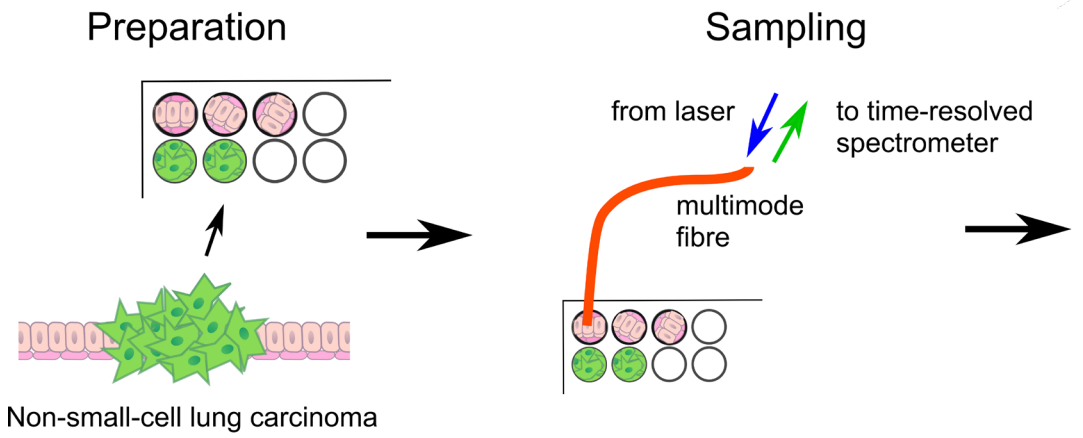
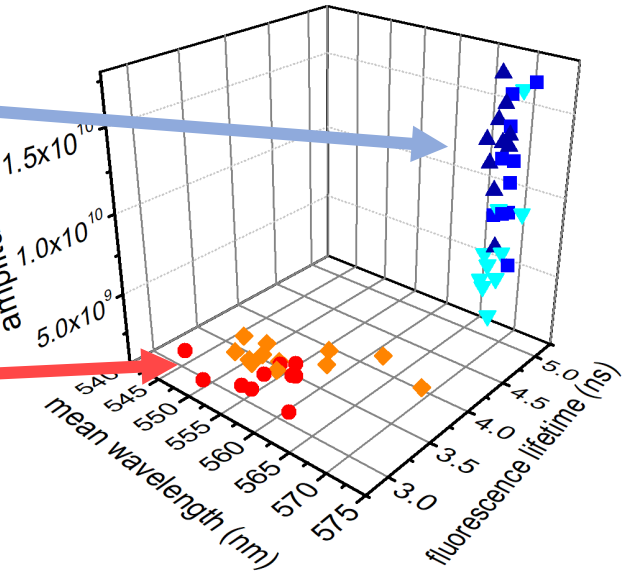


Combining signal amplitude, wavelength, and lifetime (time resolved): improved detection selectivity for cancerous tissue

normal tissue

tumours



View Item Admin

Biomedical fibre optic time-correlated single-photon counting spectroscopy with CMOS SPAD line arrays

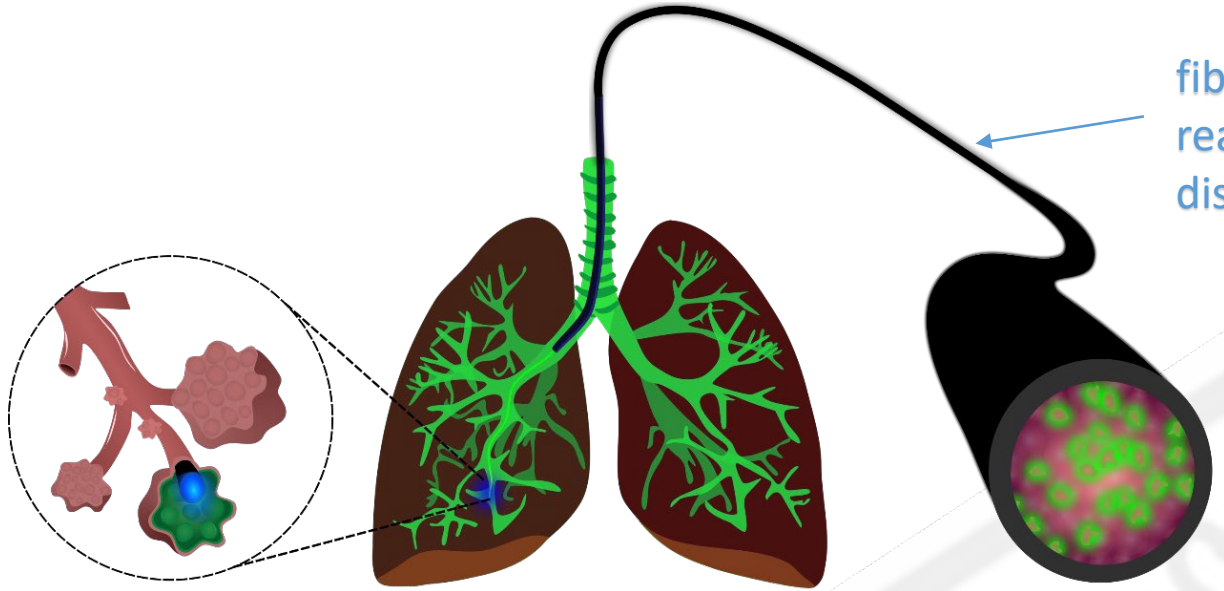
Credit: K Ehrlich, HW PhD 2019

Supervisors: M Tanner, R Thomson

http://hdl.handle.net/10399/4388

Health Care Challenge: Lung diseases

- Can we apply our optical technologies to lung diseases?



Translational Healthcare Technologies

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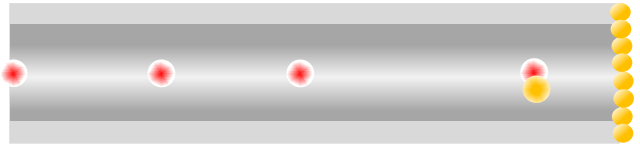
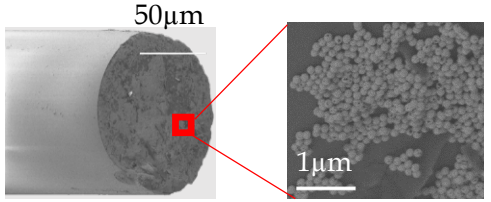
Time resolved single photon counting:

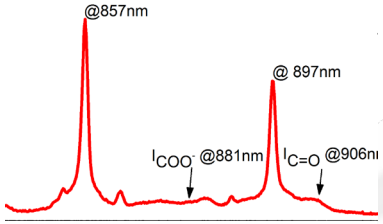
Removing unwanted signals

- Fibre optic spectroscopy with low signal / background
- Using time resolved techniques to separate the signal from the background

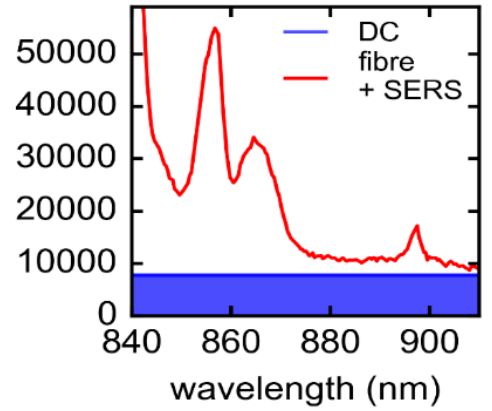
Single fibre photon counting Raman





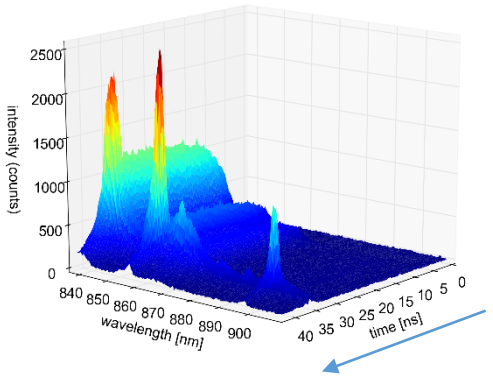


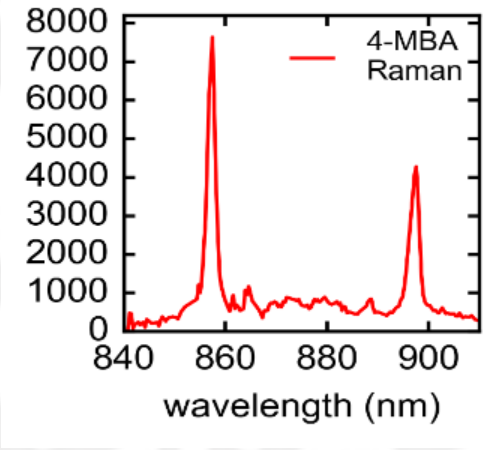
wavelength (nm)



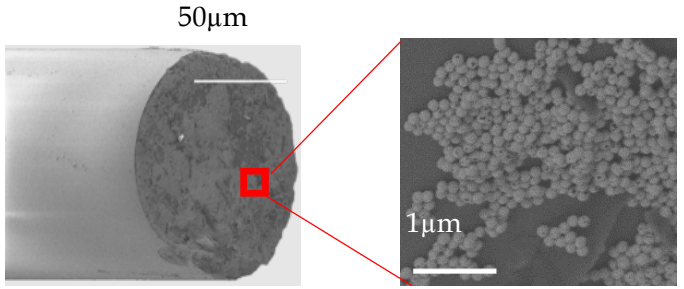
SERS

time (ns)

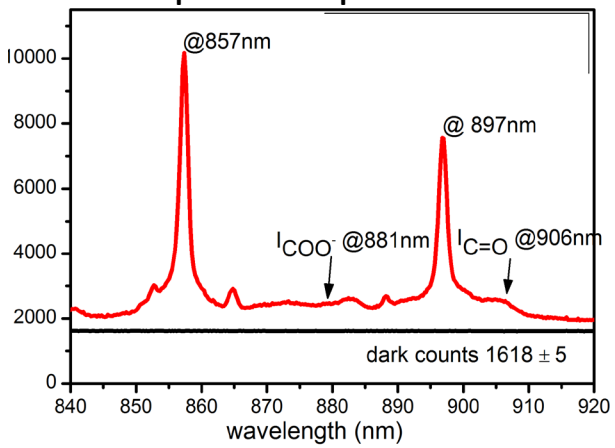


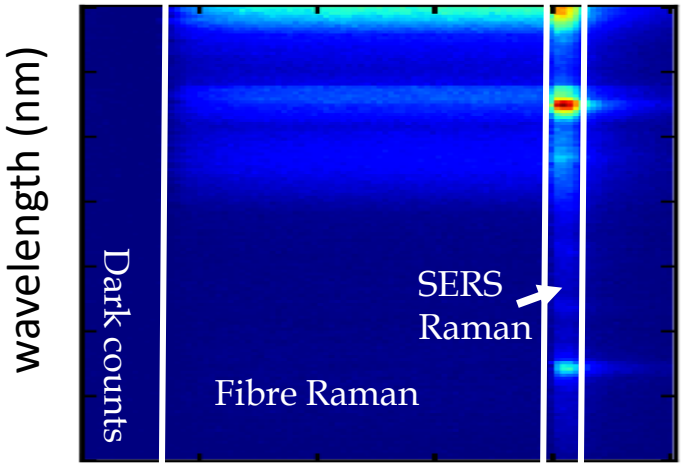


Single fibre photon counting Raman

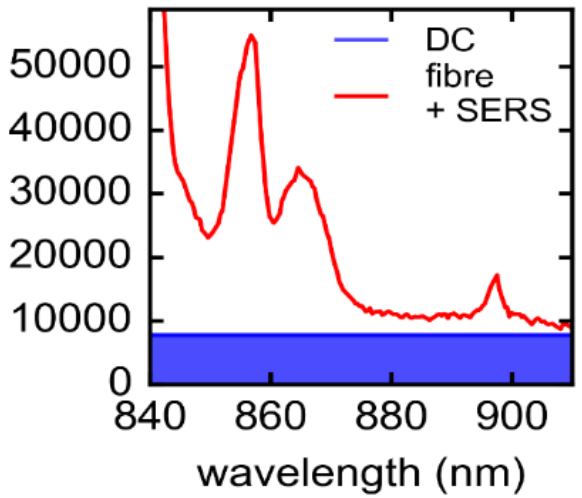


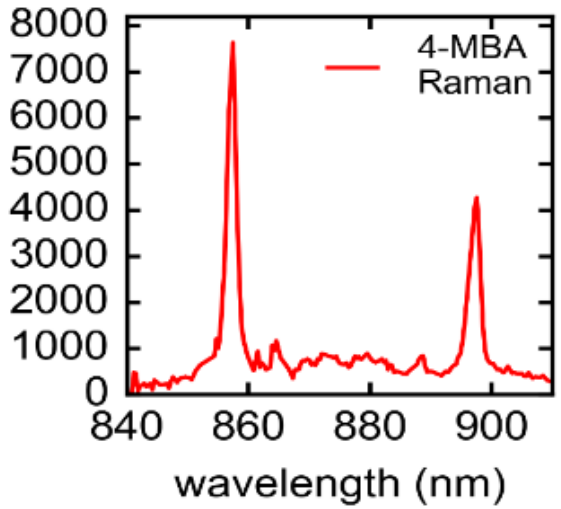
Expected spectrum





Dominated by fibre background





pH sensing through a single optical fibre using SERS and CMOS SPAD line arrays

K. Ehrlich,[1,2,*] A. Kufcsák,[3] S. McAughtrie,[2,4] H. Fleming,[4] N. Krstajic,[2,3] C. J. Campbell,[4] R. K. Henderson,[3] K. Dhaliwal,[2] R. R. Thomson,[1,2] and M. G. Tanner[1,2,5]

Opt. Express **25**, 30976-30986 (2017)

Distributed temperature sensing

Research Article Vol. 32, No. 4 / 12 Feb 2024 / Optics Express 6481
Optics EXPRESS

Photon counting fibre optic distributed temperature sensing with a CMOS SPAD array

Caitlin S. Tye,[1,*] Katjana Ehrlich,[1,2] Andrew D. M. Green,[1] R. K. Henderson,[3] and Michael G. Tanner[1]

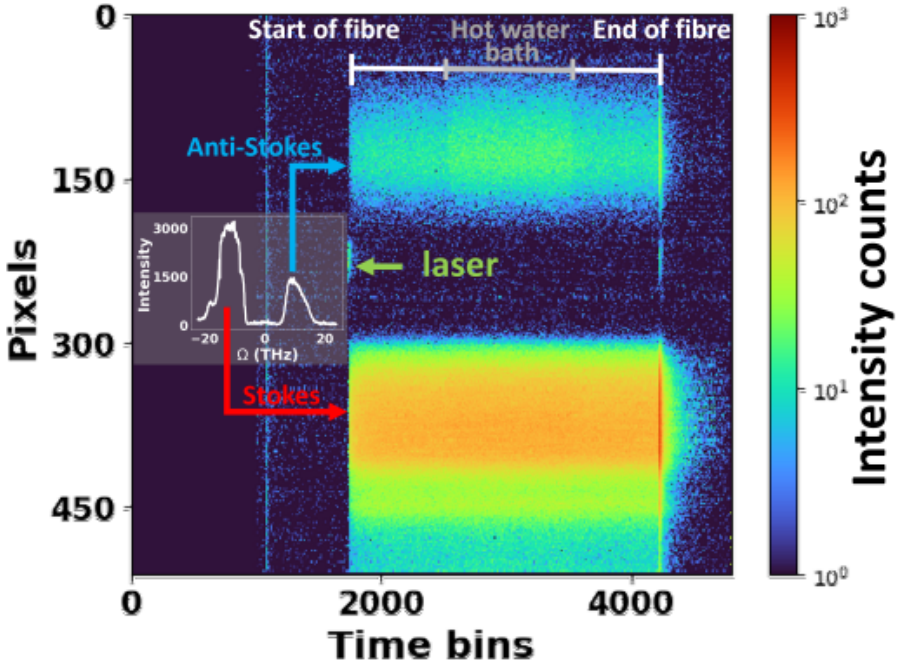
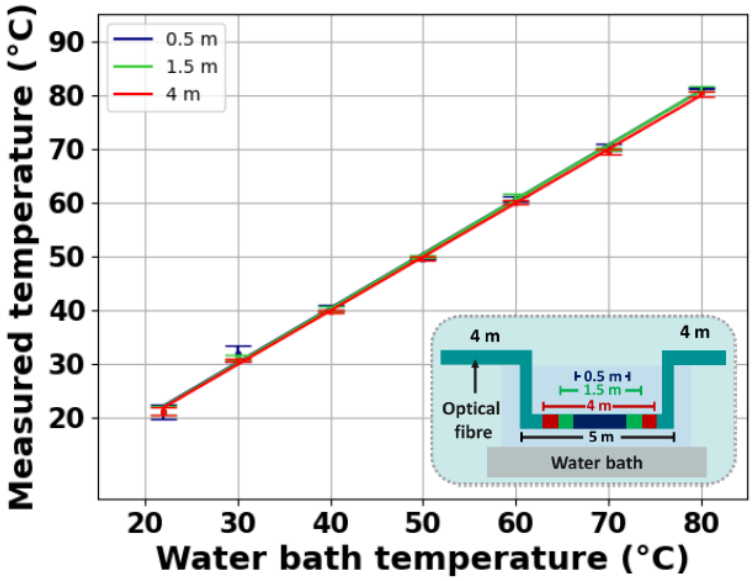


Fig. 2. Concept of spectral and time-resolved fibre Raman measurement. Intensity of photon counts is separated spectrally to detector pixels to resolve the Stokes and anti-Stokes bands. Time bins provide position information along the optical fibre under test. Inset shows an example of the measured spectrum plotted as frequency detuning from the pump wavelength.



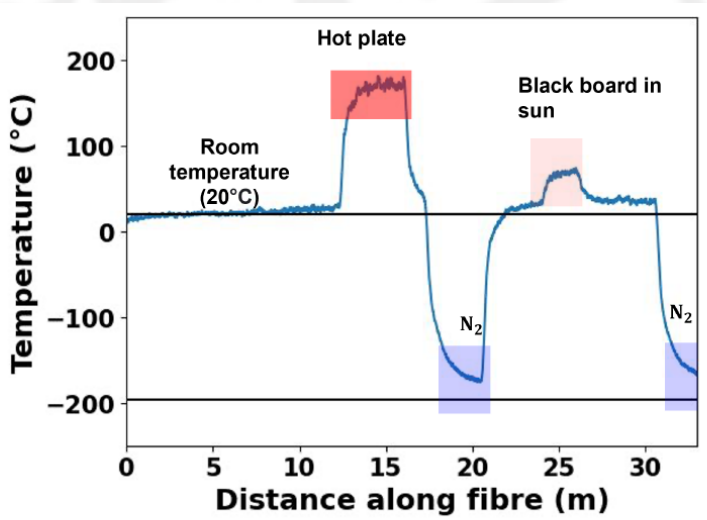
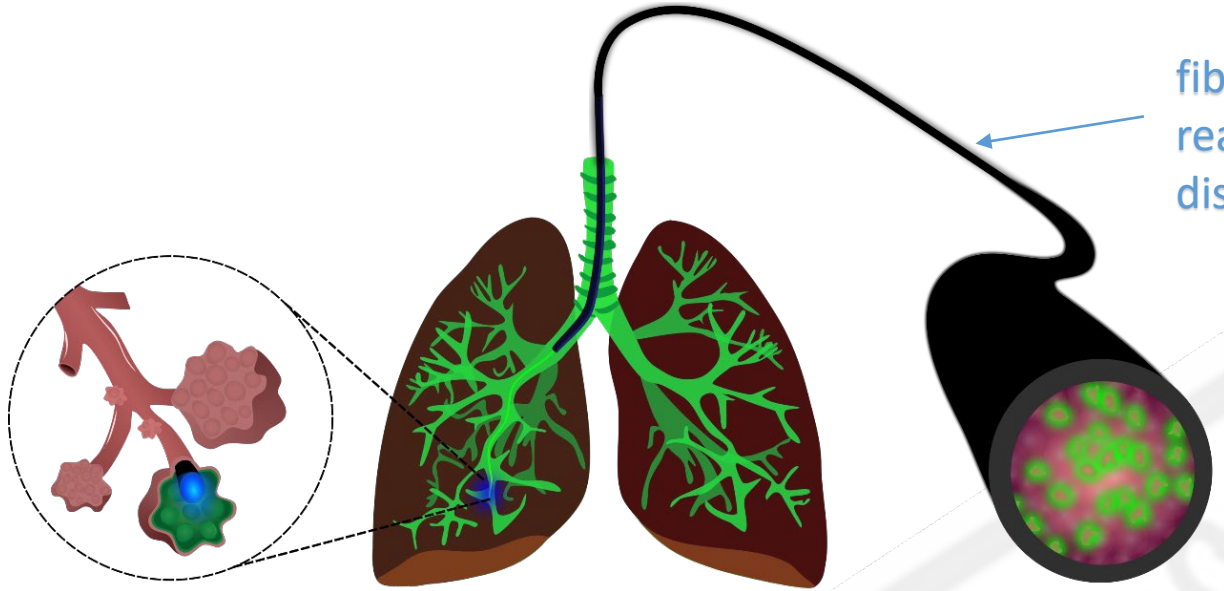


Fig. 6. Temperature measurements using a 35.0 m fibre in different environmental conditions. Data points are presented at 0.5 cm intervals.

Health Care Challenge: Lung diseases

- Can we apply our optical technologies to lung diseases?



Translational Healthcare Technologies

THE UNIVERSITY of EDINBURGH

UNIVERSITY OF BATH

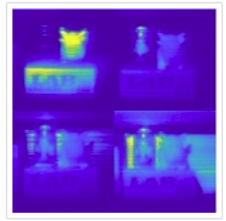
Time resolved single photon counting:

Removing unwanted signals

- Fibre optic spectroscopy with low signal / background
- Using time resolved techniques to separate the signal from the background

Time resolved imaging - “Light in Flight”

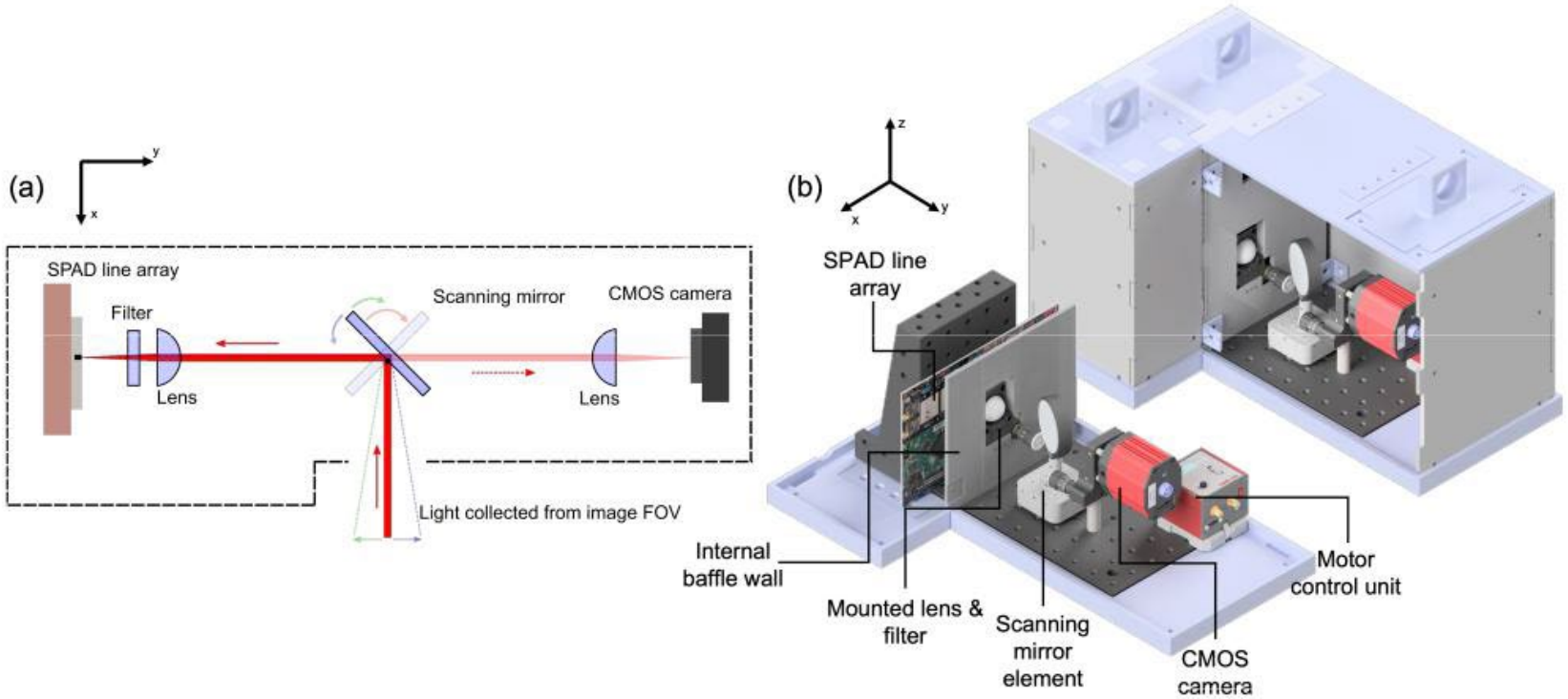
Optics Express Vol. 30, Issue 15, pp. 27926-27937 (2022) • https://doi.org/10.1364/OE.461334



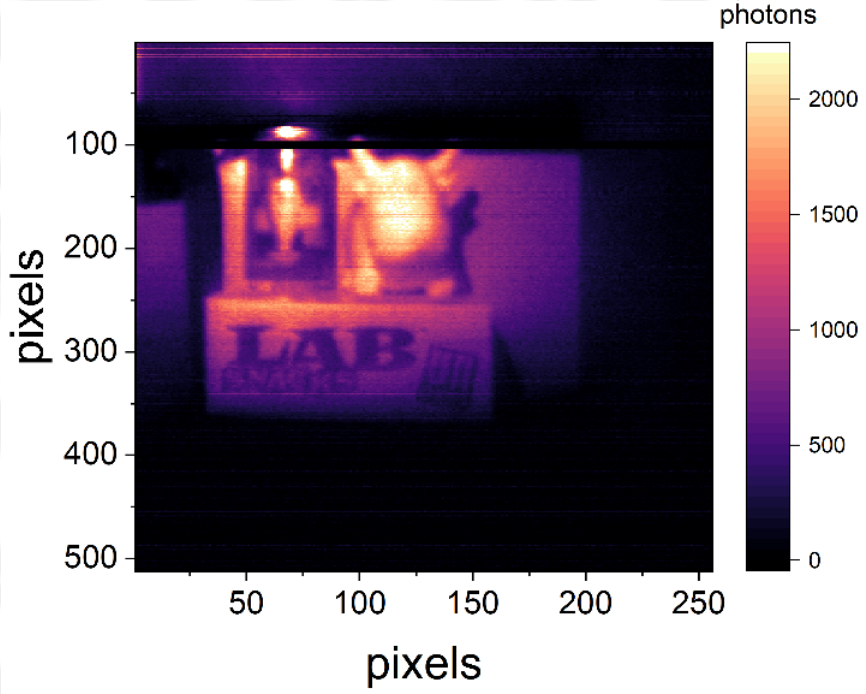
High resolution TCSPC imaging of diffuse light with a one-dimensional SPAD array scanning system

E. P. McShane, H. K. Chandrasekharan, A. Kufcsák, N. Finlayson, A. T. Erdogan, R. K. Henderson, K. Dhaliwal, R. R. Thomson, and M. G. Tanner

Author Information ▾ Find other works by these authors ▾



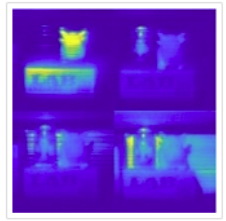
30 cm FOV at 60 cm distance



McShane, E …& Tanner, M. G. (2022). *Optics Express*, *30*(15), 27926.

Time resolved imaging - “Light in Flight”

Optics Express Vol. 30, Issue 15, pp. 27926-27937 (2022) • https://doi.org/10.1364/OE.461334



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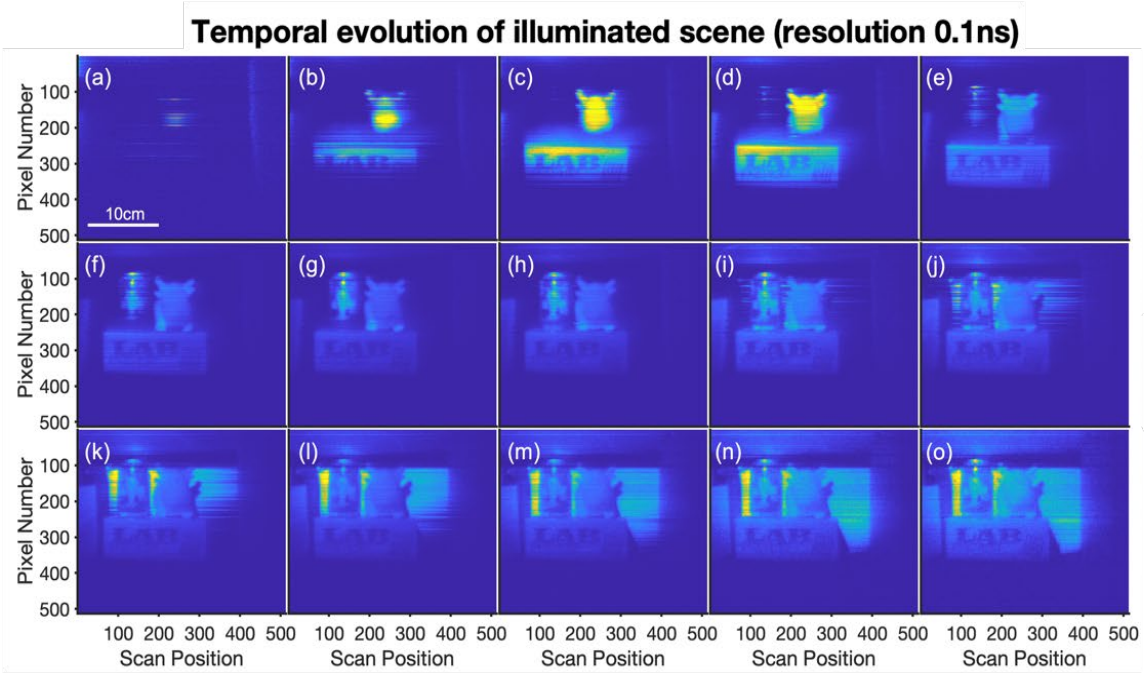
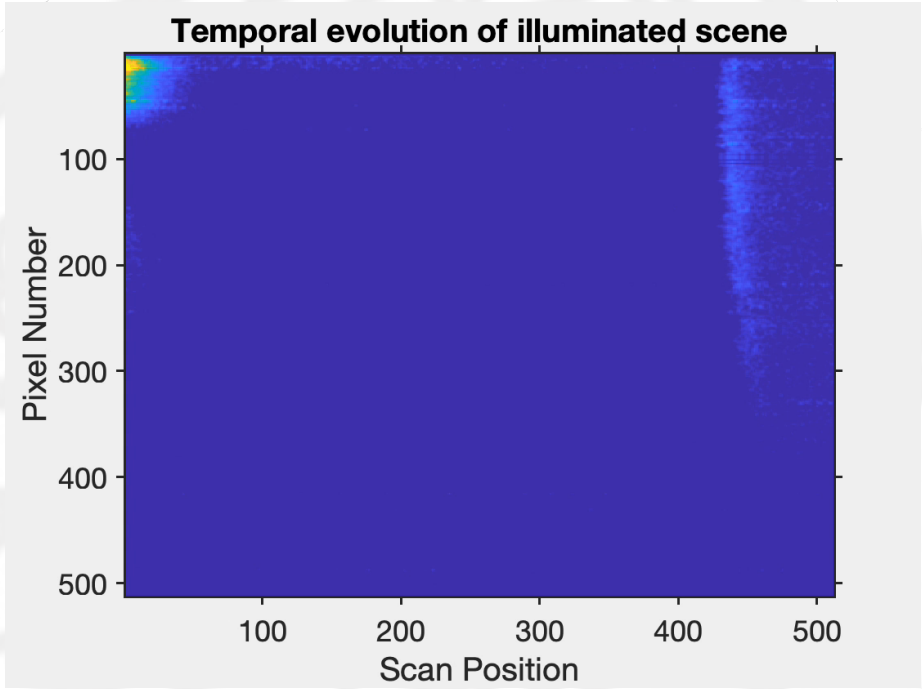
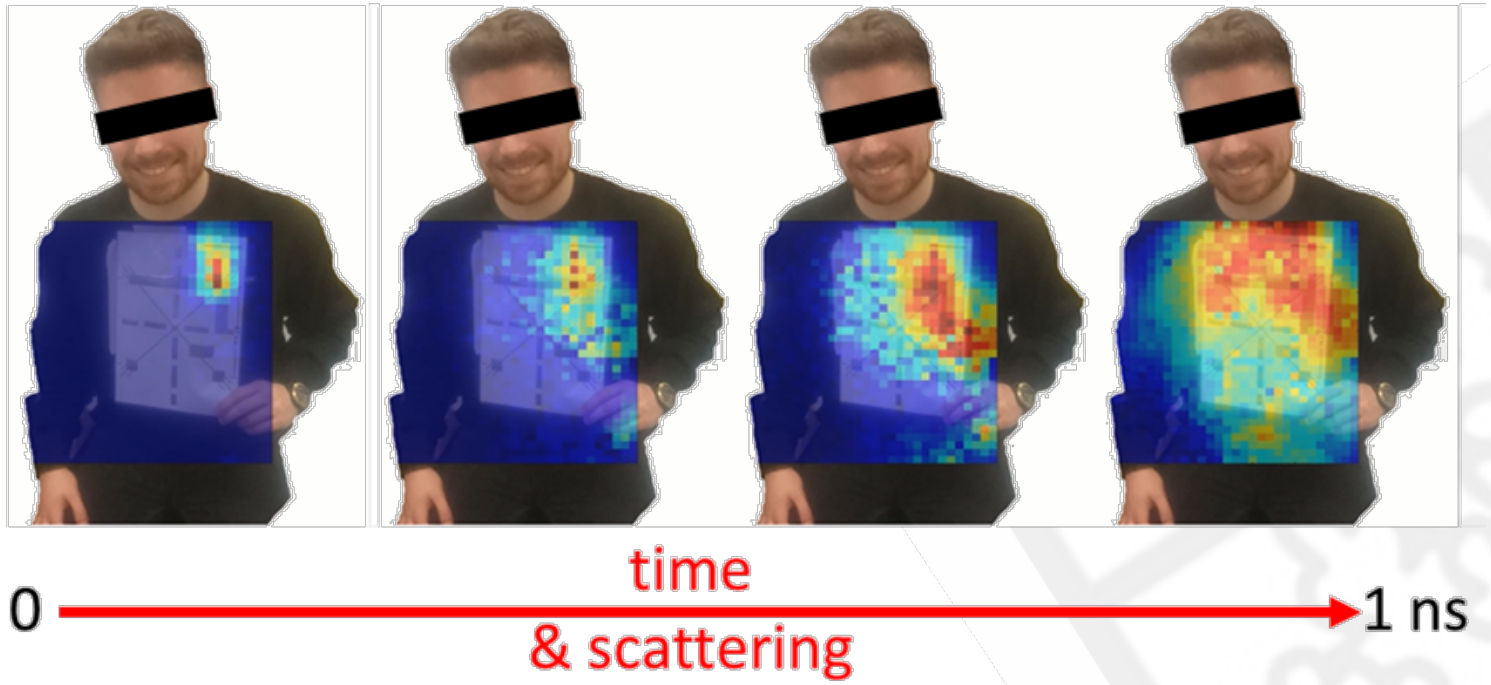




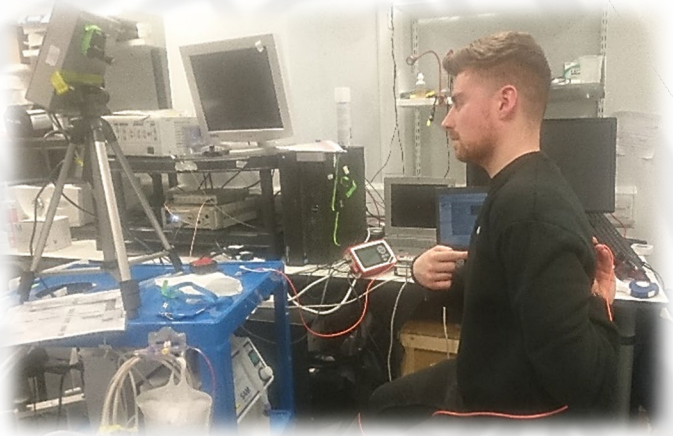
McShane, E …& Tanner, M. G. (2022). *Optics Express*, *30*(15), 27926.

Time resolved imaging – Diffuse light transit

- Small amounts of light can transit through thick human tissue



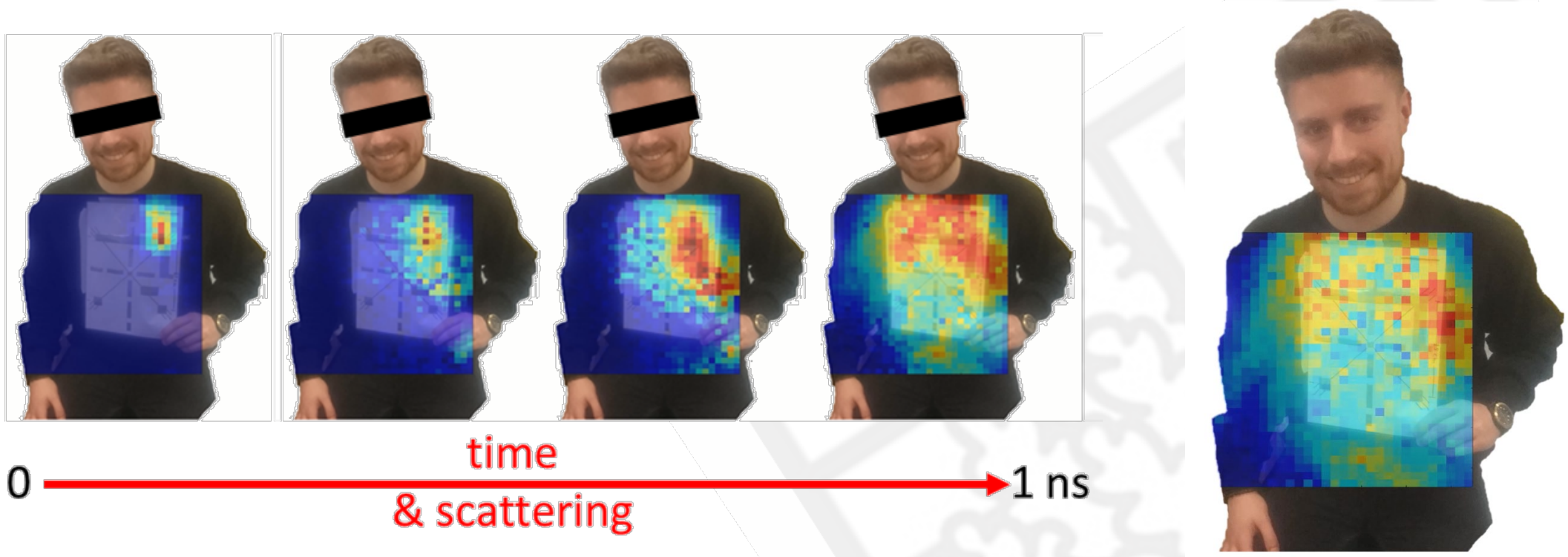
early lab trials



- As time progresses light spreads out due to scattering in the tissue
  - We can think about that in reverse and locate the source with the early light

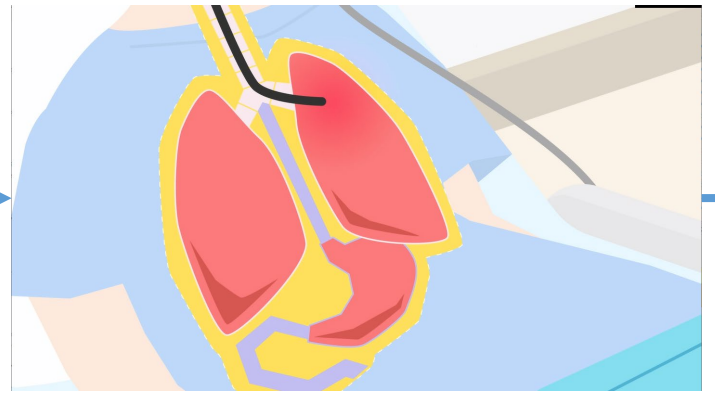
Time resolved imaging – Diffuse light transit

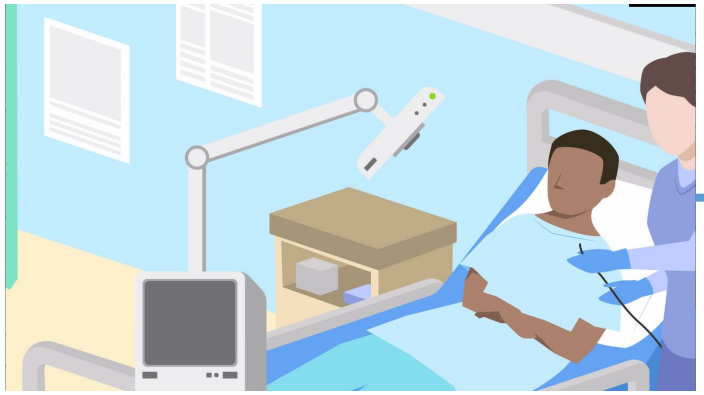
- Small amounts of light can transit through thick human tissue

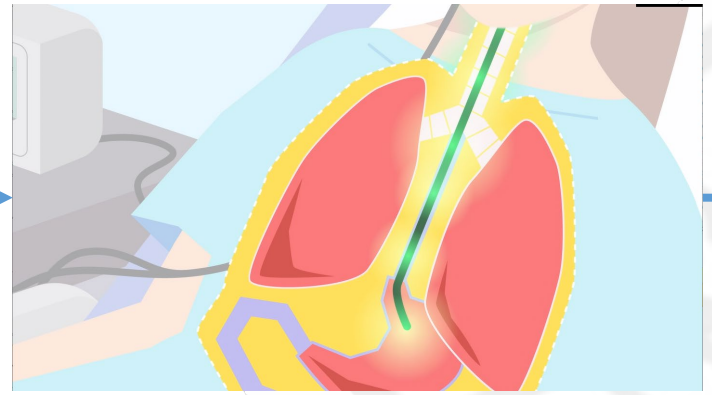


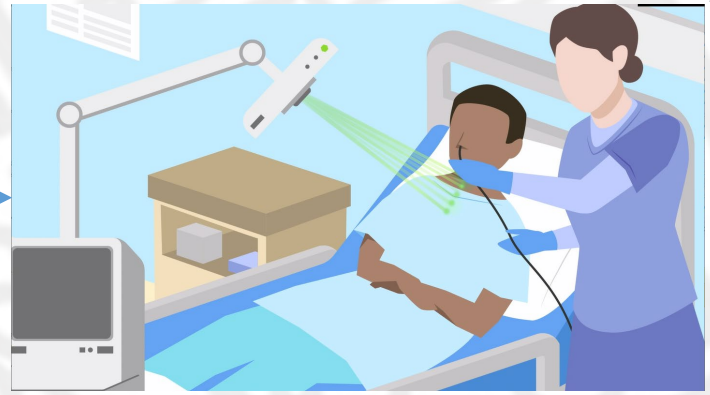
- As time progresses light spreads out due to scattering in the tissue
  - We can think about that in reverse and locate the source with the early light

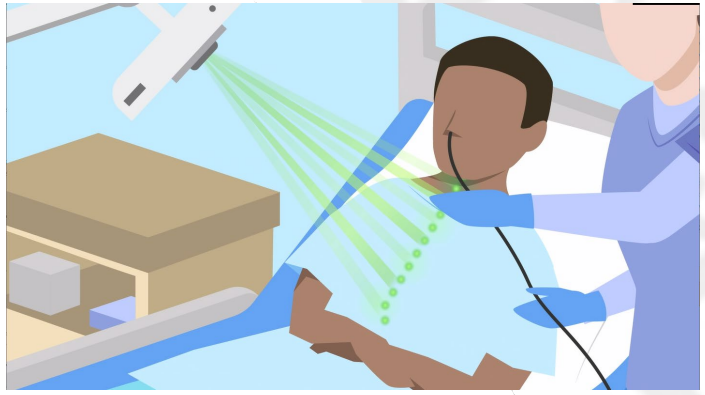
Optical medical device location – NG Tubes









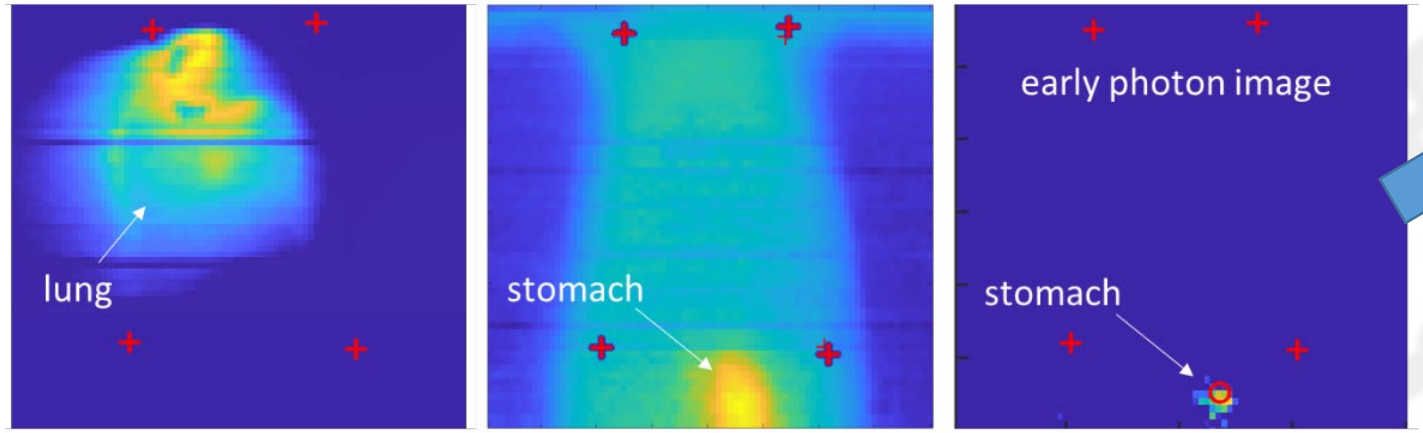


Extracts from promotional video

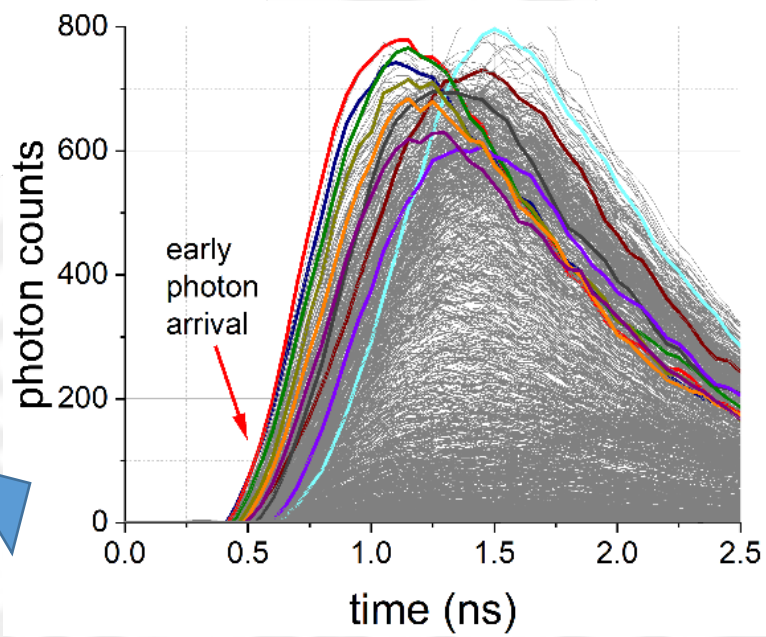
Tactile optically guided feeding tube placement

Optical medical device location - Porcine

- Mounted / portable / ready for clinic??!!
  - Not quite….



High resolution transmitted photon imaging of catheter placement. Left: placement in the lung. Middle: placement in the stomach. Right: early photon image more precisely locates the catheter tip in the stomach, below the diaphragm.



Time resolved photon counts of transmission from the tip of a catheter in the lung of a porcine cadaver at ~10 cm depth.

Technology advancement

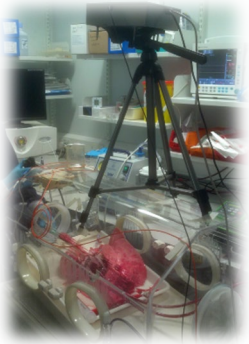
Past:

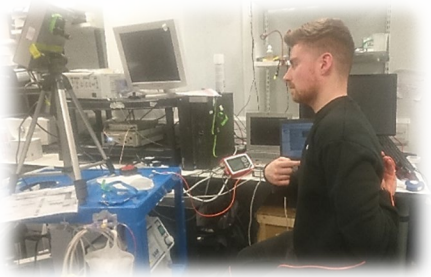
Engineering and Physical Sciences Research Council

Science and Technology Facilities Council

Concept and development
Sep 2018 - Mar 2022
International IP filed

OptoLoc Lab beta: TRL 1 → 4



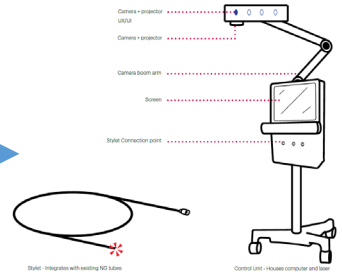


OptoLoc Lab 1.0: TRL 4 → 5/6

Development included animal/cadaver testing of *OptoLoc Lab* versions

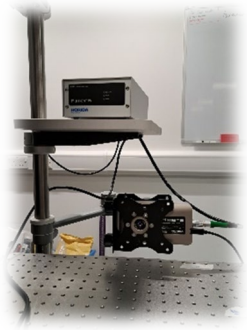
Ongoing:

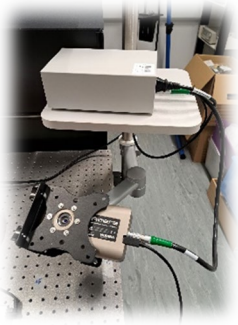
New Prototype/MVP



Dec 2022 Clinical translation
MRC-DPFS: Technical
SE HGSP: Commercial

OptoLoc Clinic 1.0: TRL 4/5/6 → 6
(demonstration in relevant environment)



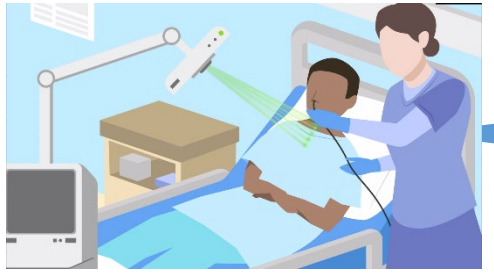


Medical Research Council

Scottish Enterprise

Cadaver testing
Q2/3 2024

OptoLoc Clinic 1.0: TRL 6 → 7
(demonstration in operational environment)



Q4 2024 – In man investigation

Scottish Enterprise and MRC funding continues

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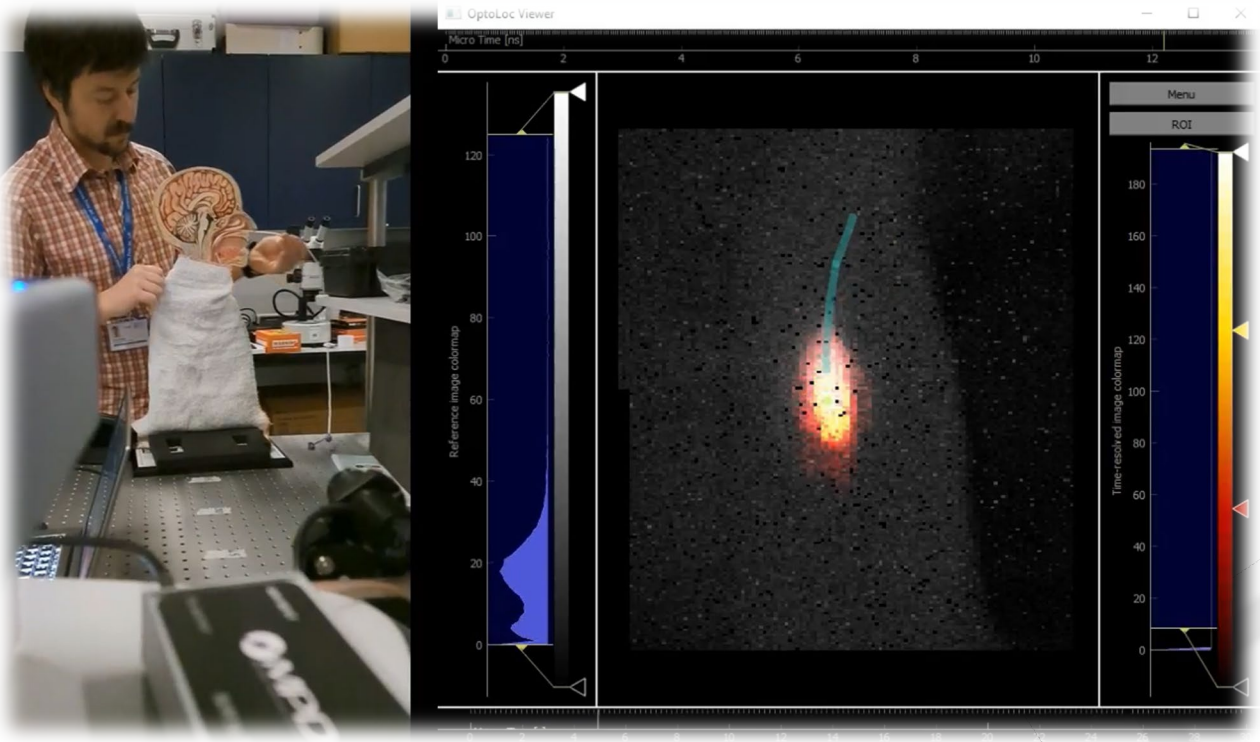
Device tracking – software and systems



- External view and NG location showed simultaneously
- Software to record path
- Future iterations will project location directly back onto torso

OptoLoc – NGTube location with photon counting

OptoLoc

Medical need

Food and Drugs in Critically Ill patients are required urgently

Placement of Tube in Lung (2% cases) can be fatal, > 3,000 Deaths/Year in the US alone,

X-ray and pH paper are resource intensive and subject to failure

Scope

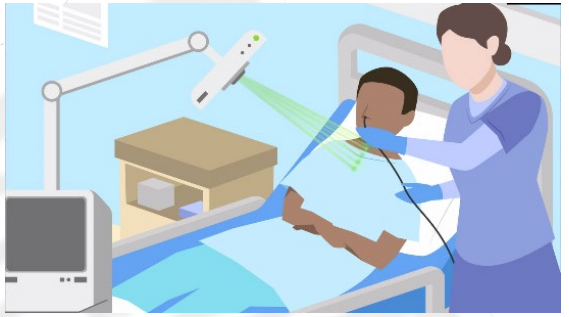
Clinical testing (Royal Infirmary of Edinburgh) Q4-2024 / Q1-2025, SpinOut supported by Scottish Enterprise, Q1-2025

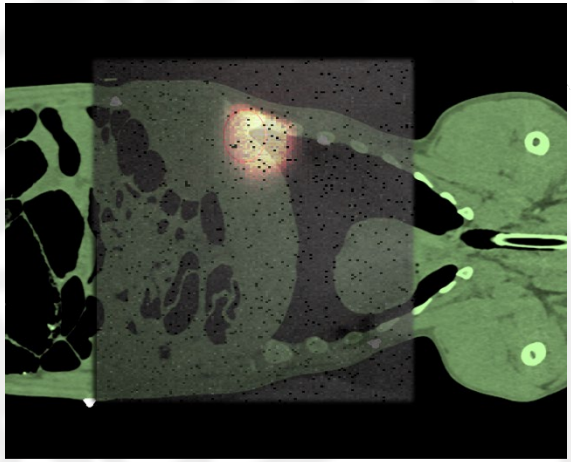
Technology

Exploiting quantum technology – single photon counting imaging. Translating from the research lab to application, observing light transit through thick tissue. Overcoming optical scattering with time resolved photon counting imaging to locate a light source – optical fibre integrated with feeding tube.

Benefits

- Faster, safer, feeding tube placement – reducing adverse events and time/cost to healthcare provider
- Removes need for X-ray confirmation
- Technology platform extends to other use cases





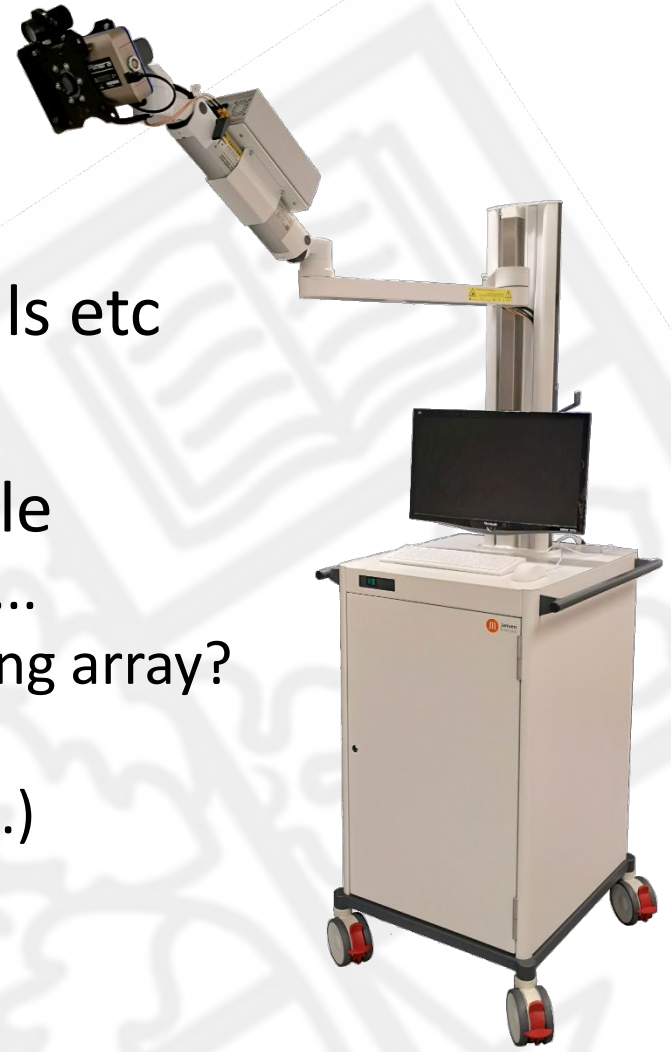
M G Tanner, M.Tanner@hw.ac.uk

MRC funded: MRC-MR/W029979/1

Scottish Enterprise supporting commercialisation

Moving to clinic, and commercial translation

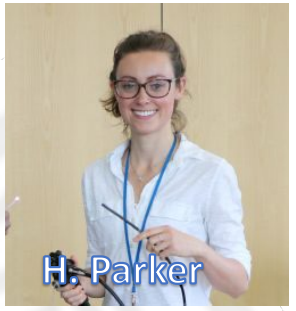
- Removing backgrounds
  - Scattered light AND room light
  - Requires some form of time resolved system
- Working through regulatory admin, pre-clinical trials etc



- To translate this – it needs to be commercially viable
  - We need to reduce the bill of materials for the system…..
  - Maybe a large area simple detector – rather than imaging array?
  - Or are any of the mass produced arrays viable?
  - (We don't need high specs, but some key functionality…)

?

Team:



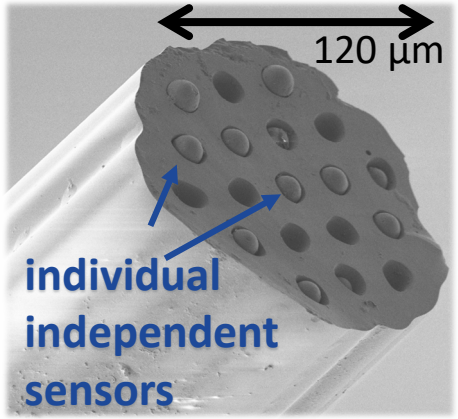
- Work included many collaborators
- Other core PIs: Prof R Henderson, Prof R Thomson, Prof K Dhaliwal, Dr T Craven
- PhD and PostDoc positions available…..

Papers: linked from tanner-lab.org

Photonics for medical probes and imaging

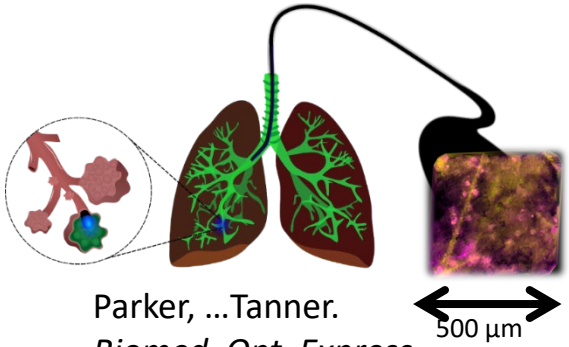
Michael G Tanner: M.Tanner@hw.ac.uk

Human hair sized fibre sensors



Choudhary, T. R., Tanner, M. et al. (2019). *Scientific Reports*, *9*(1), 7713.

Fibre-based spectral endomicroscopy

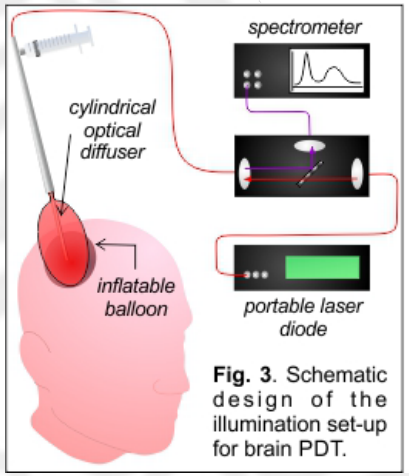


Parker, …Tanner. *Biomed. Opt. Express*, (2019) 10, 1856

Single photon counting imaging for clinic

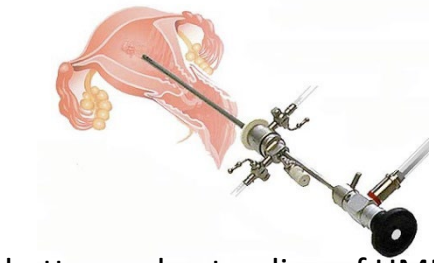
McShane, …Tanner. (2022) *Opt. Express,* 30, 27926.

Sources and spectroscopy for novel photodynamic therapy



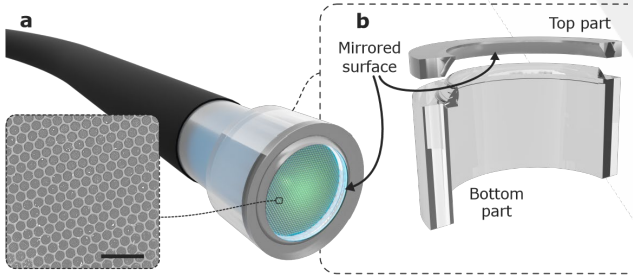
EPSRC funded: EP/W015706/1

NIR fibre spectroscopy for women's health



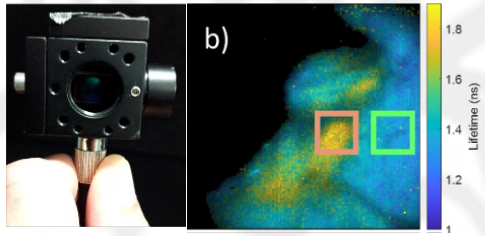
better understanding of HMB

SPIM endomicroscopy



APL Photonics 8, 016103 (2023)

Miniature widefield FLIM



Matheson et al, 2023, Optics Express

Further fibre probes, photon counting, imaging and spectroscopy for healthcare: https://tanner-lab.org

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Photons, fibres, medical applications, science

tanner-lab.org

photonic instrumentation

Translational Healthcare Technologies

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