

Translating Optical Systems into Surgery & Radiotherapy: *Academic & Industry*

Air ionization from
300 Gy/sec @ 9 MeV

Brian W. Pogue PhD

MacLean Professor of Engineering, Dartmouth

Medical Physics PhD Program



DARTMOUTH



**Dartmouth-
Hitchcock**

Financial COI Disclosures

DoseOptics LLC: President and co-Founder

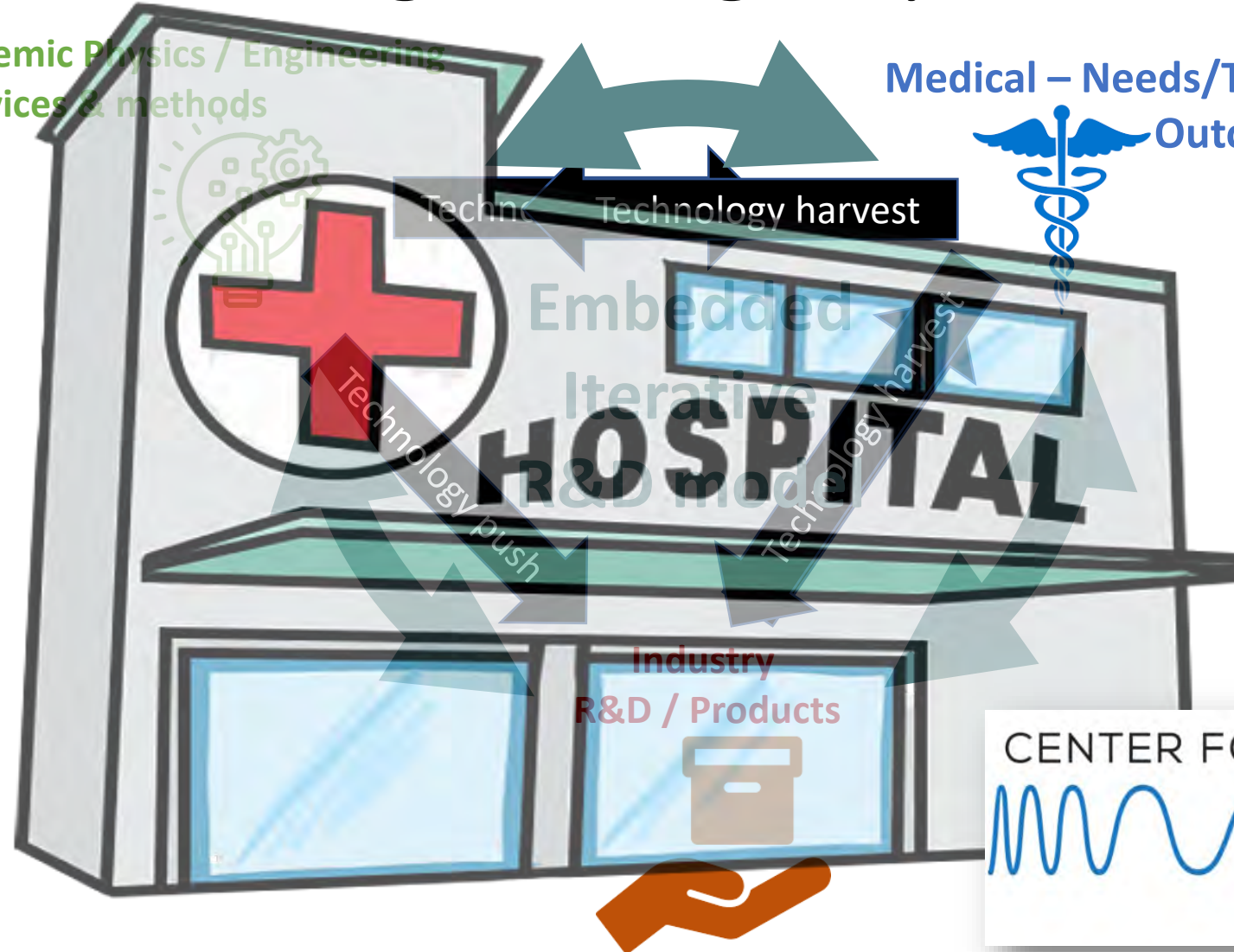
QUEL Imaging LLC: President & co-Founder

Journal of Biomedical Optics: Editor-in-Chief

Designing New Med Tech in Academic Engineering/Physics

Academic Physics / Engineering
– Devices & methods

Medical – Needs/Trials
Outcomes



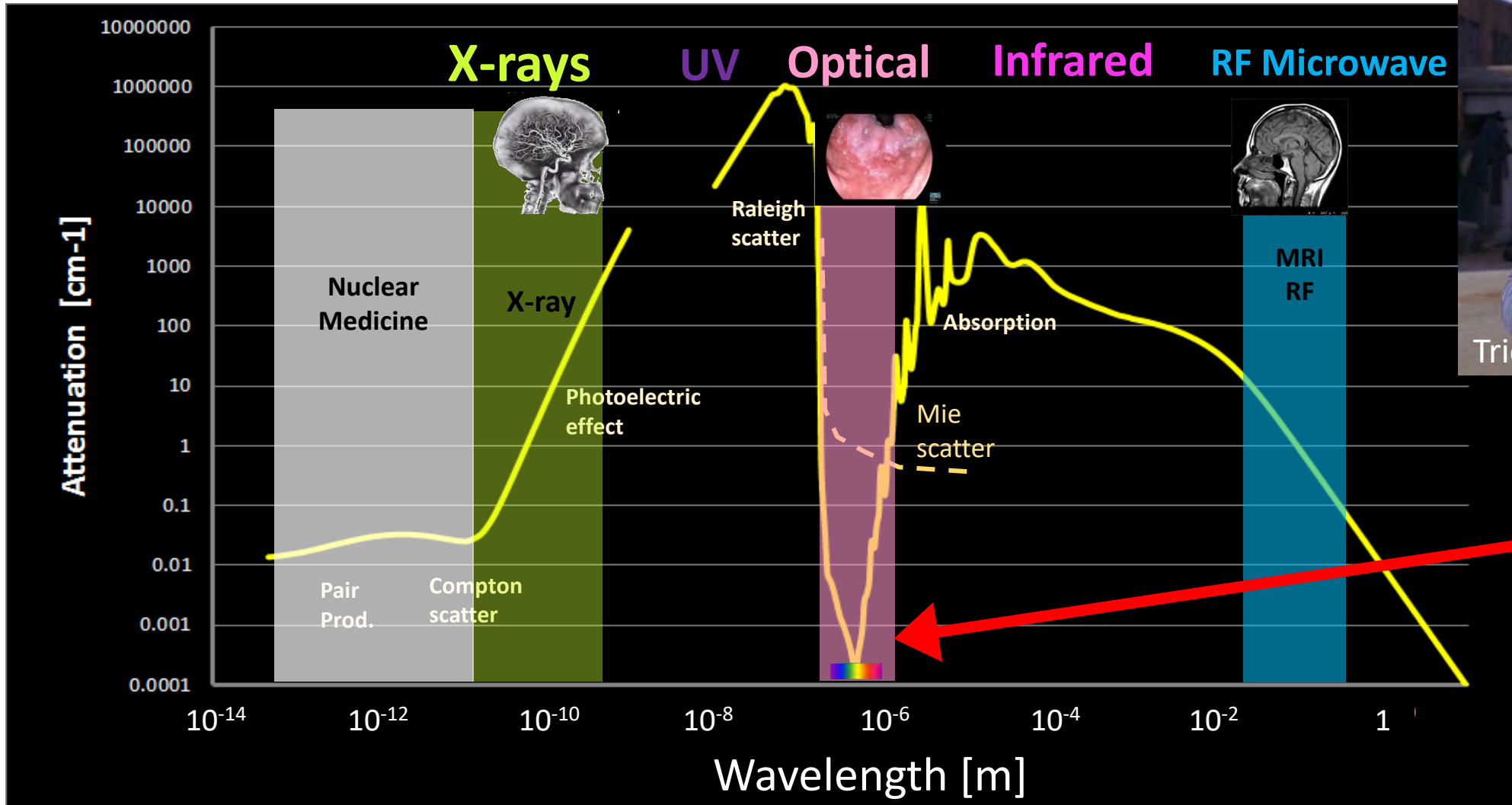
CENTER FOR **IMAGING**
MEDICINE
AT DARTMOUTH

Physical Space & Teams for Engineering/Physics Research Inside the Medical Center



Designing Optical Devices for Medicine

For Imaging the Human Body, there are 3 'Windows'

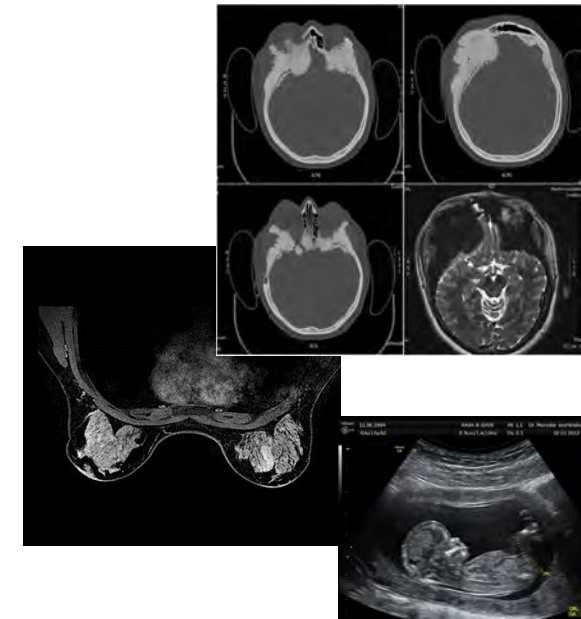
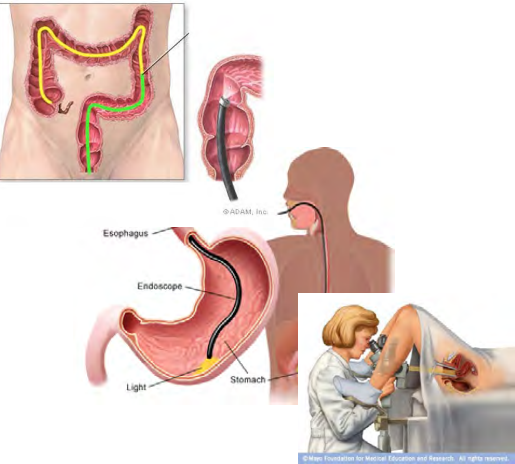
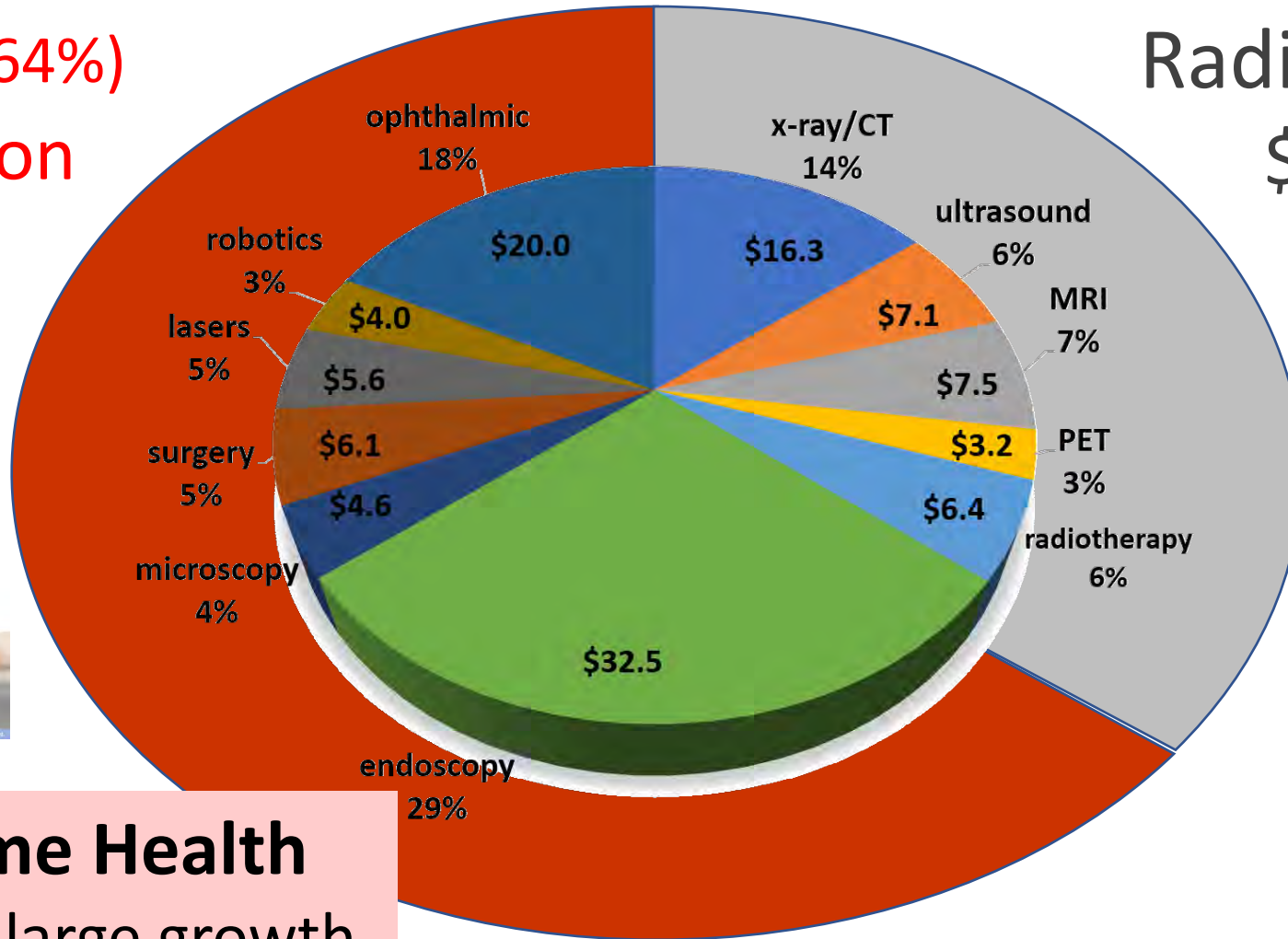


Most useful molecular information is optical!

Global Market for Medical Imaging Technologies

Optical (64%)
\$73 billion

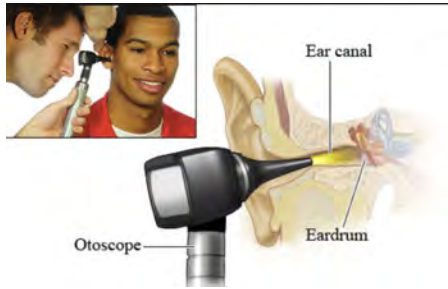
Radiological (36%)
\$40 billion



+ Mobile/Home Health
\$20-40 billion + large growth

Clinical Optical Devices – Enormous variation in Design & Economics

otoscopy \$\$



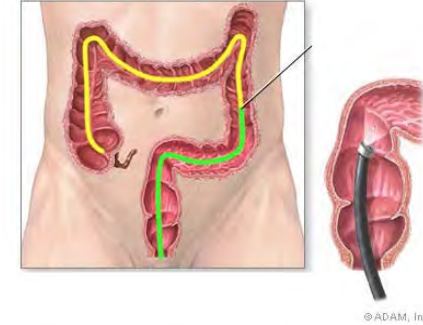
ophthalmoscopy \$\$



dermoscopy \$\$



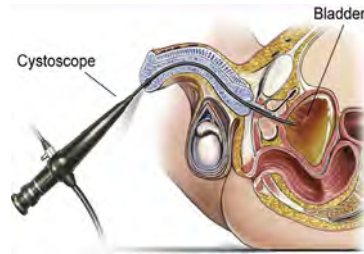
colonoscopy \$,\$\$\$



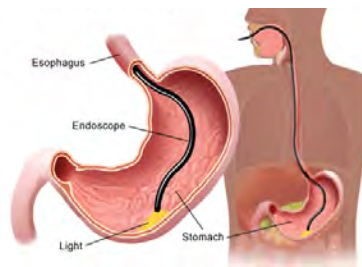
colposcopy \$\$\$



cystoscopy



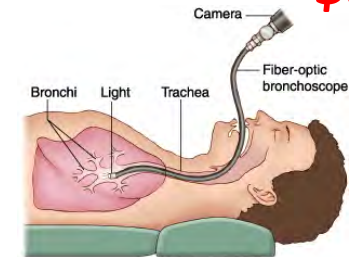
endoscopy \$,\$\$\$



nasoendoscopy



bronchoscopy \$,\$,\$,\$



laparoscopy \$,\$,\$,\$



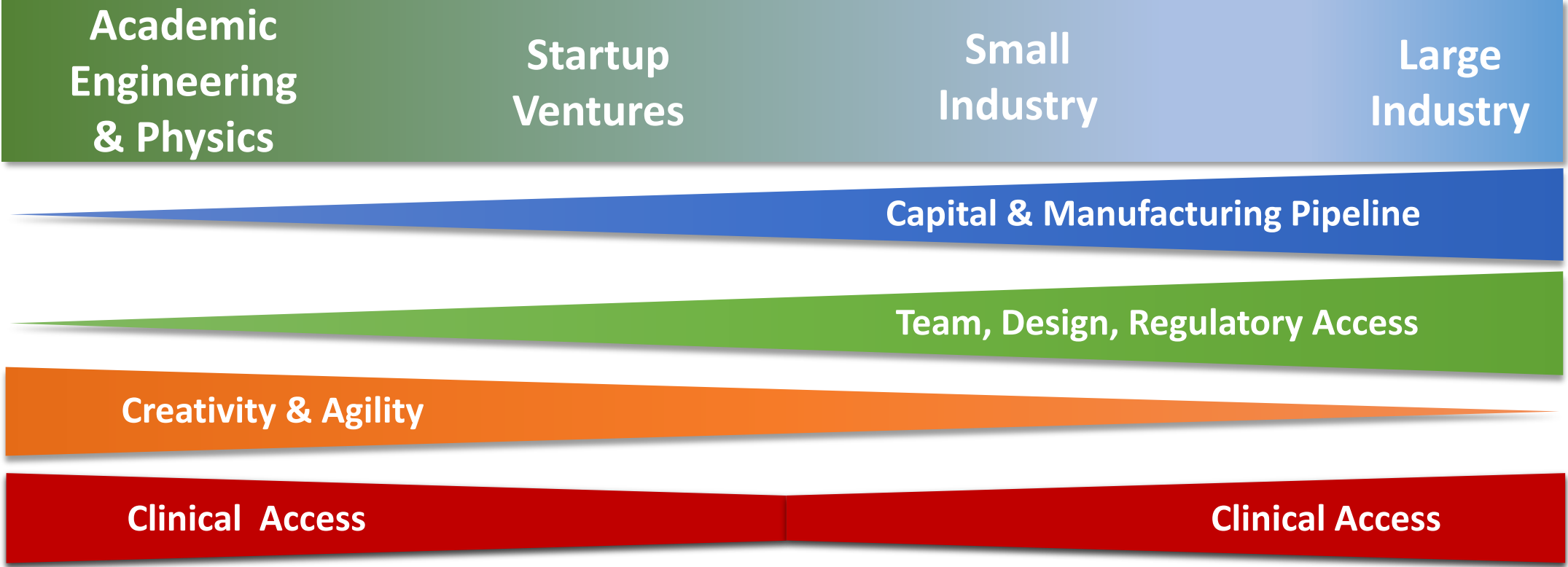
surgical microscopy \$,\$,\$,\$,\$



robotic surgery \$,\$,\$,\$,\$,\$



How do we make better use of academic research so that it impacts medicine?

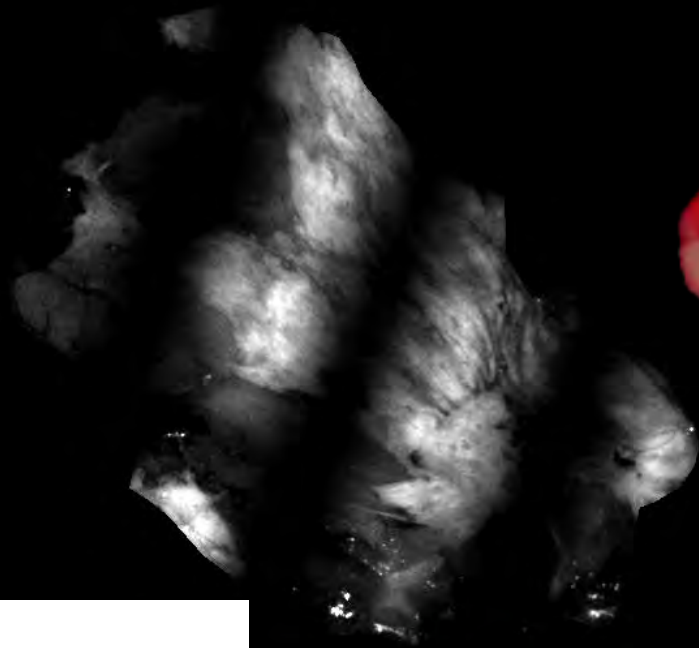


EXAMPLE 1

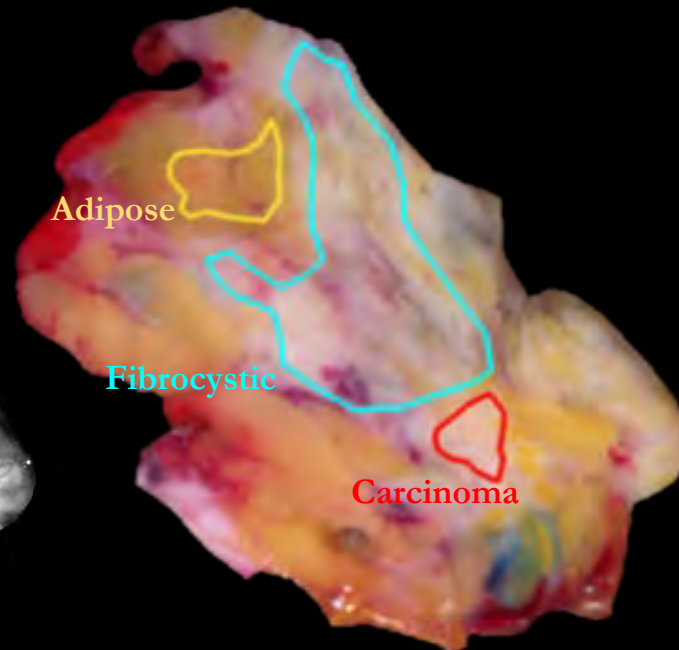
Designing a New System
for Surgical Guidance

Surgical Guidance via Structured Light Scatter Imaging

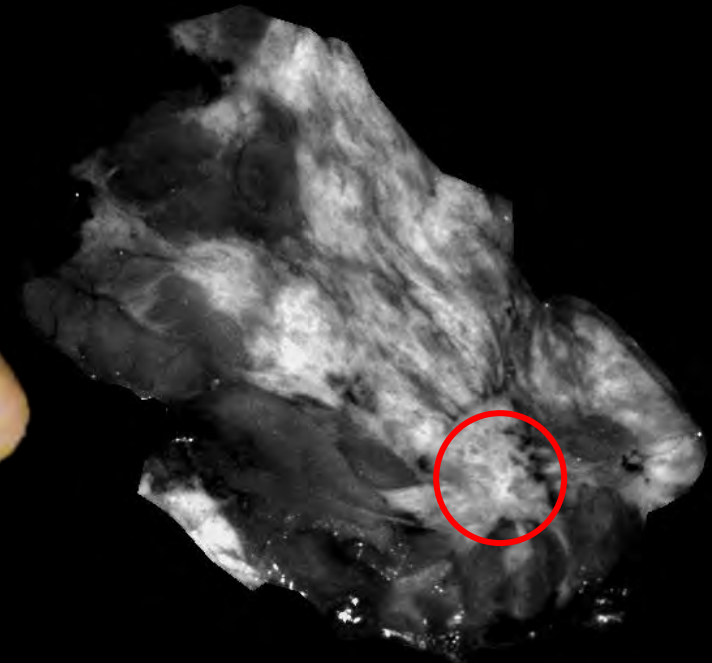
Structured light



Normal White Light



Demodulated Scatter



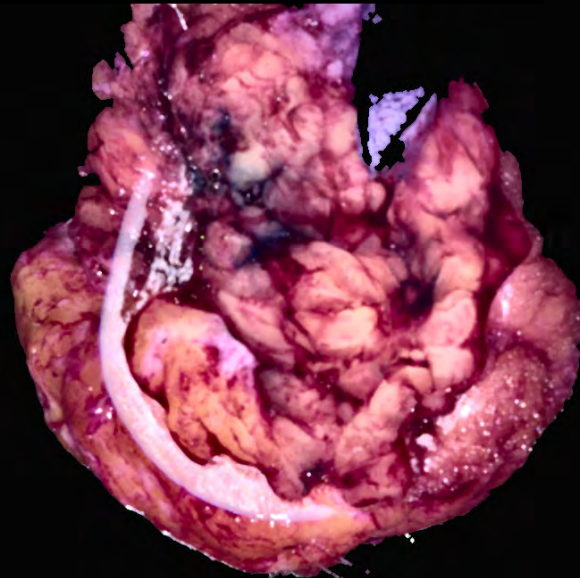
$f_x = 0.05 \text{ 1/mm}, \varphi = 0^\circ$

$f_x = 0.05 \text{ 1/mm}$

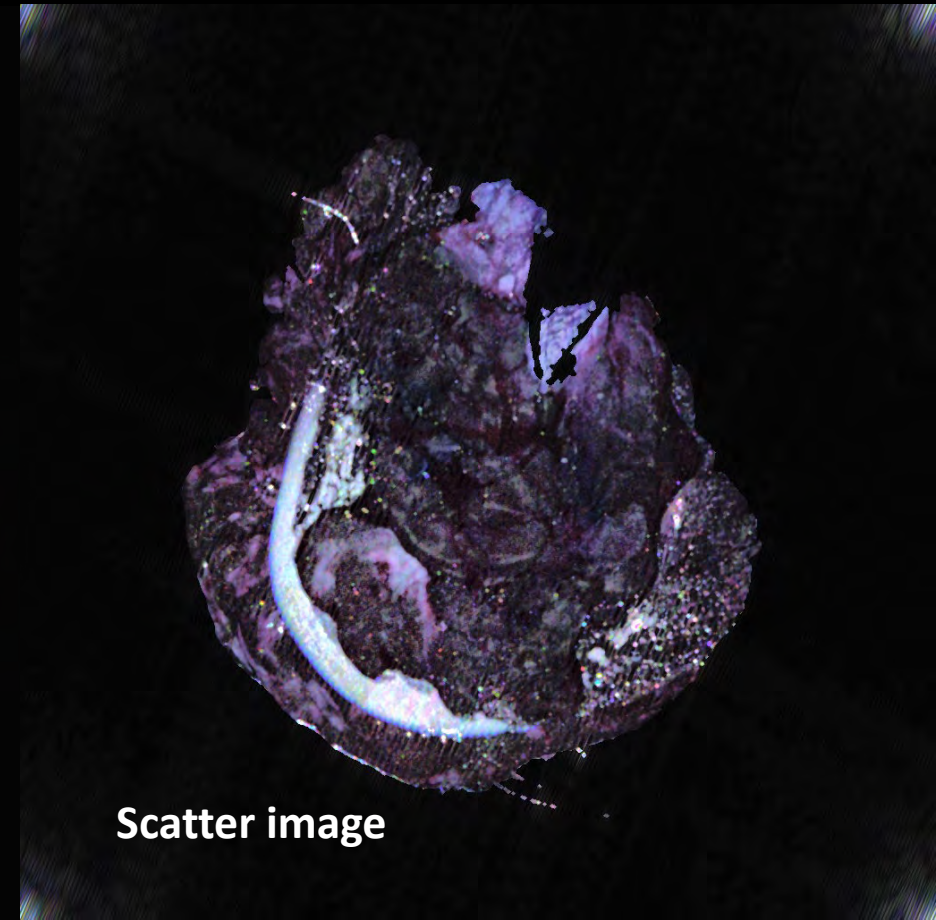
Specimen Imaging in Breast Lumpectomy: x-ray & optical scatter



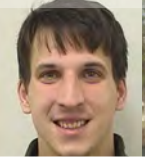
X-ray microCT



Optical image

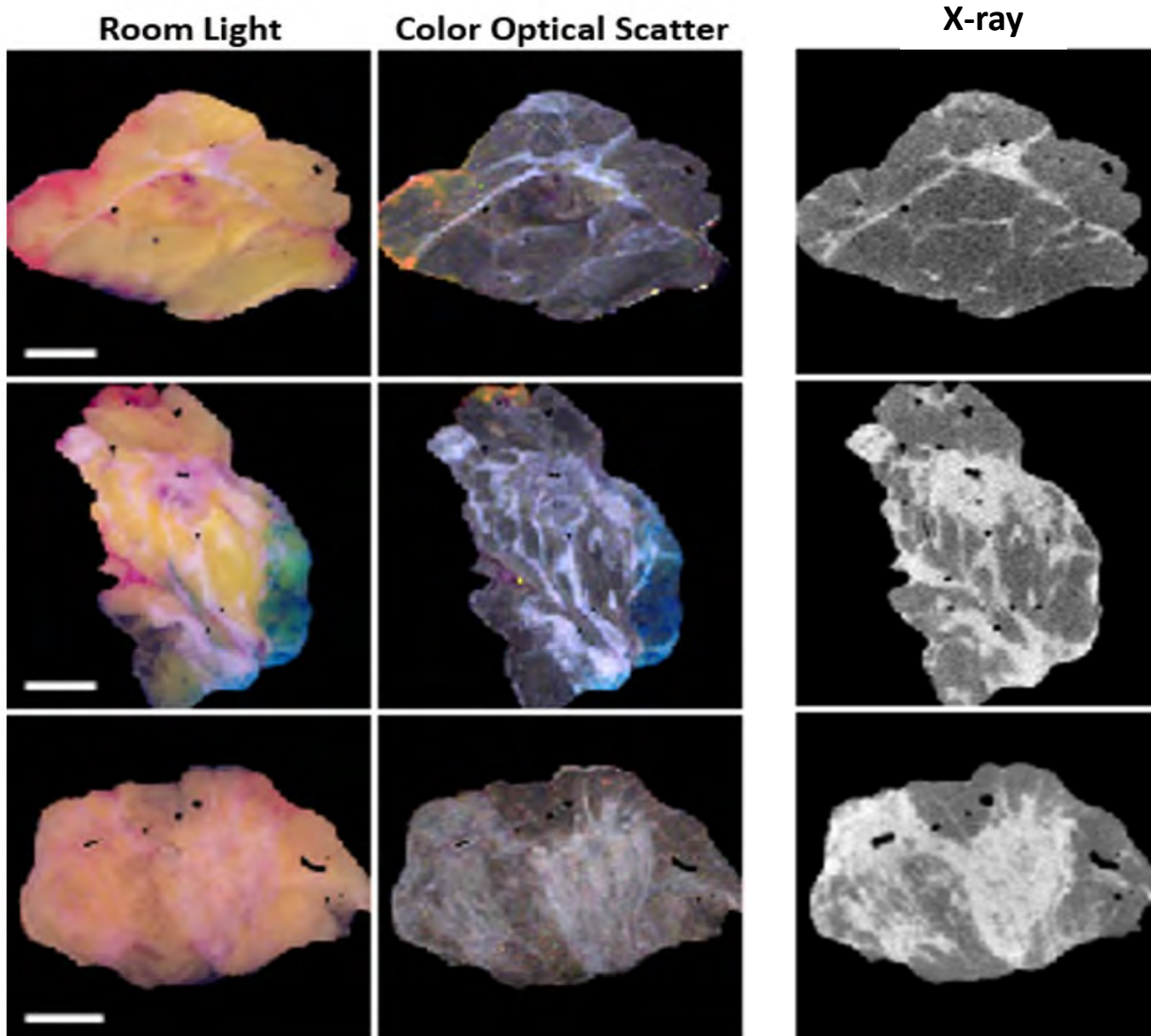


Scatter image



Streeter Maloney McClatchy Laughney

Specimen Imaging in Breast Lumpectomy



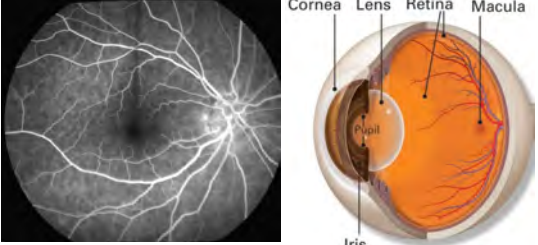
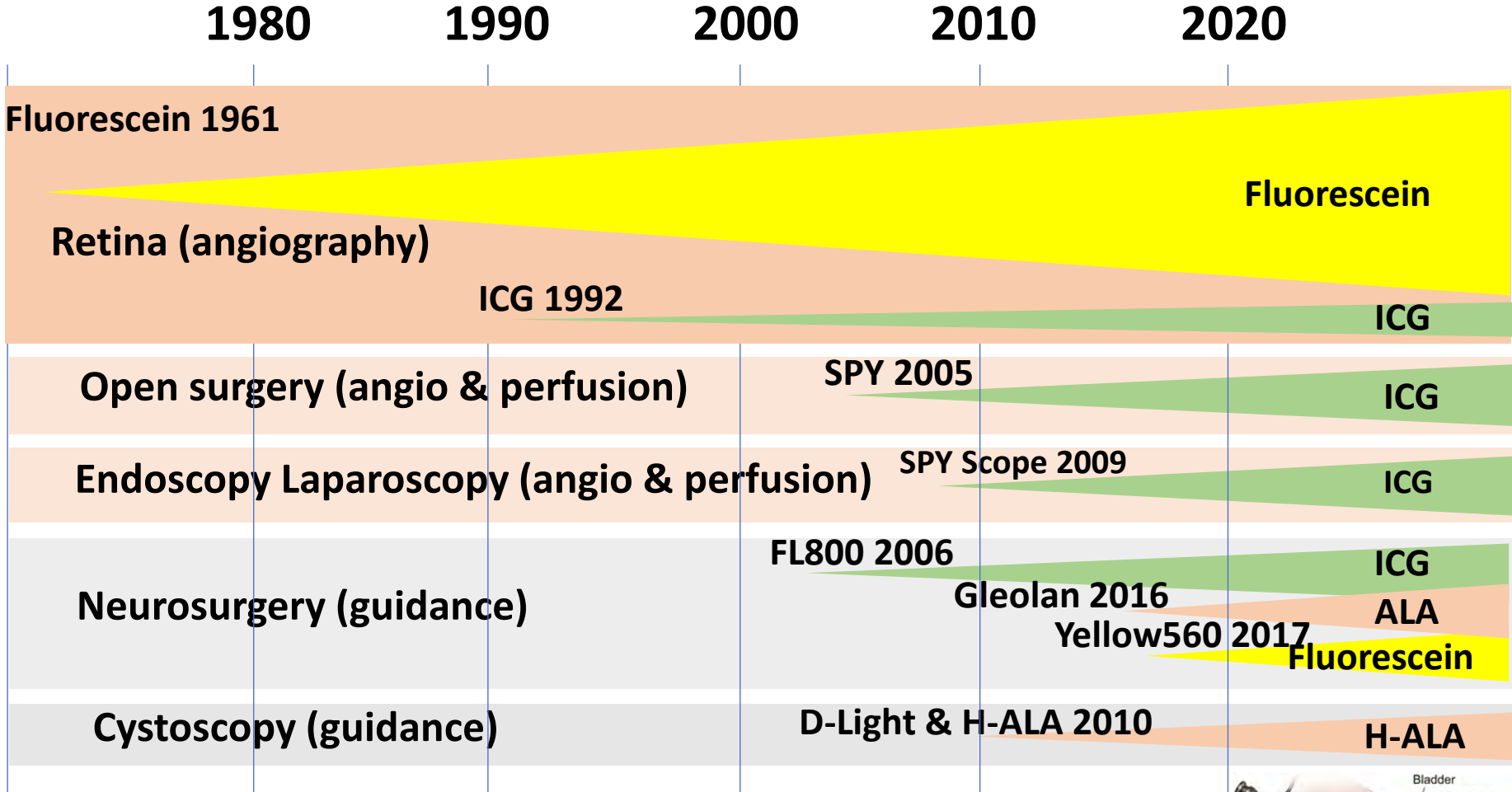
- Reveals connective tissue structures and ducts similar to x-rays
- Presentation is in real time during the surgery
- **Clinical trial ongoing**
– 55 of 100 patients completed



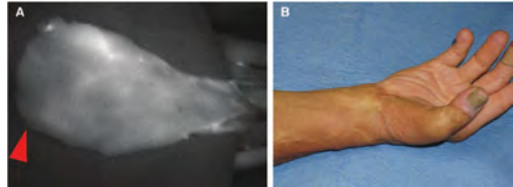
Example 2

Surgical *Molecular* Imaging

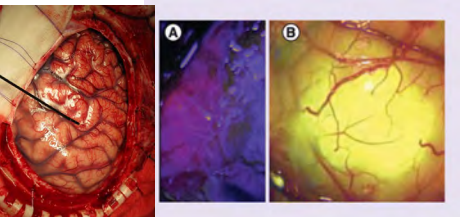
Fluorescent Surgery Market Growth



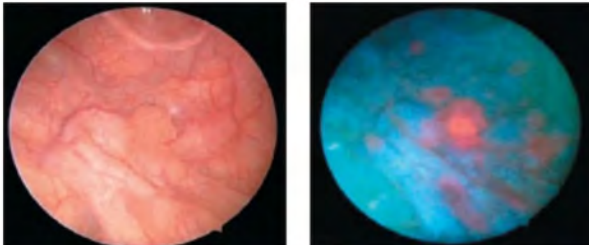
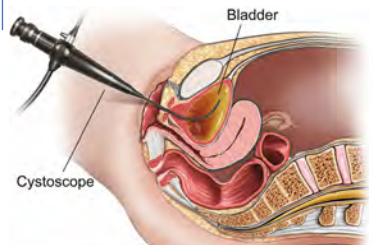
\$130M



\$35M



~\$10M

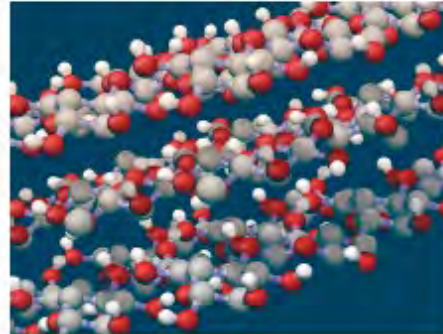


Targets for Molecular Guidance & Therapy



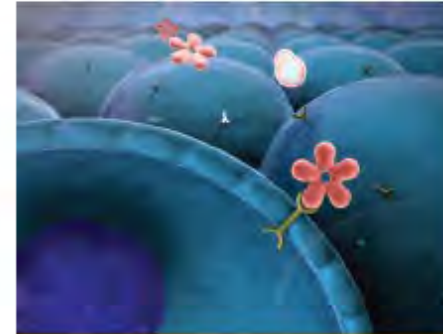
STRUCTURAL

- ▶ Epithelium
- ▶ Connective
- ▶ Nerves
- ▶ Muscle



METABOLIC

- ▶ Respiration
- ▶ Enzymes
- ▶ Carbohydrate
- ▶ Minerals



IMMUNOLOGIC

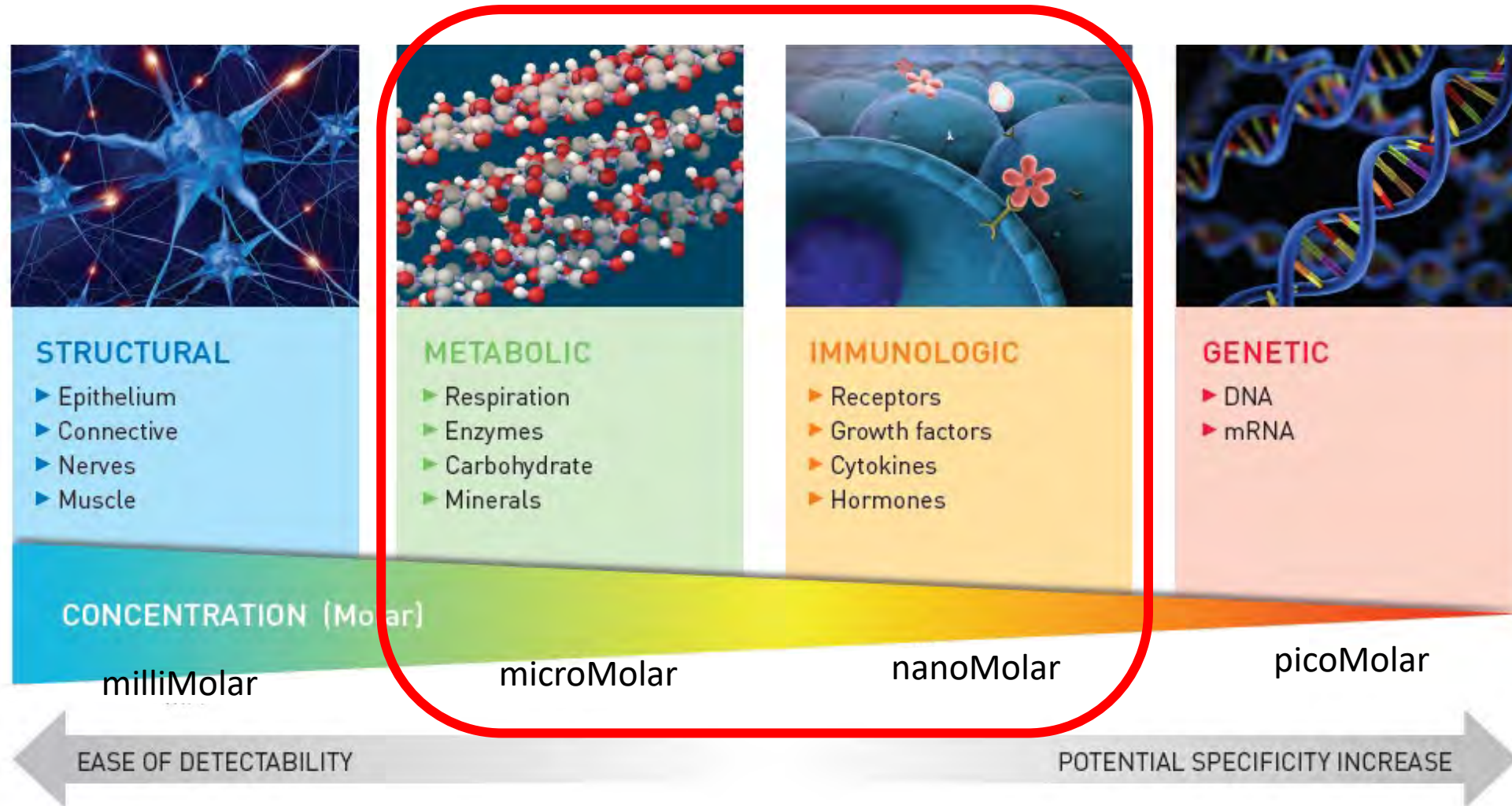
- ▶ Receptors
- ▶ Growth factors
- ▶ Cytokines
- ▶ Hormones



GENETIC

- ▶ DNA
- ▶ mRNA

Molecular reporters of cancer are largely immune cell signalling molecules!



Review of Fluorescence Surgical Systems



Dsouza et al, J. Biomed Optics 2016

Journal of Biomedical Optics 21(8), 080901 (August 2016)

REVIEW

Review of fluorescence guided surgery systems: identification of key performance capabilities beyond indocyanine green imaging

Alisha V. DSouza,^{a,*} Huiyun Lin,^{a,b} Eric R. Henderson,^c Kimberley S. Samkoe,^{a,d} and Brian W. Pogue^{a,d,*}

^aDartmouth College, Thayer School of Engineering, Hanover, New Hampshire 03755, United States

^bFujian Normal University, MOE Key Laboratory of OptoElectronic Science and Technology for Medicine, Fujian Provincial Key Laboratory for Photonics Technology, Fujian 350007, China

^cDartmouth-Hitchcock Medical Center, Department of Orthopaedics, Lebanon, New Hampshire 03756, United States

^dDartmouth College, Geisel School of Medicine, Department of Surgery, Hanover, New Hampshire 03755, United States

1. **Real-time overlay** of white/fluorescence
2. **Ambient room light** operation
3. **Ergonomics** high
4. **High sensitivity** to tracer
5. **Multi-fluorophore** ability
6. **Quantify** tracers in image

Today several systems exist for molecular guided surgery!



Medtronic



stryker



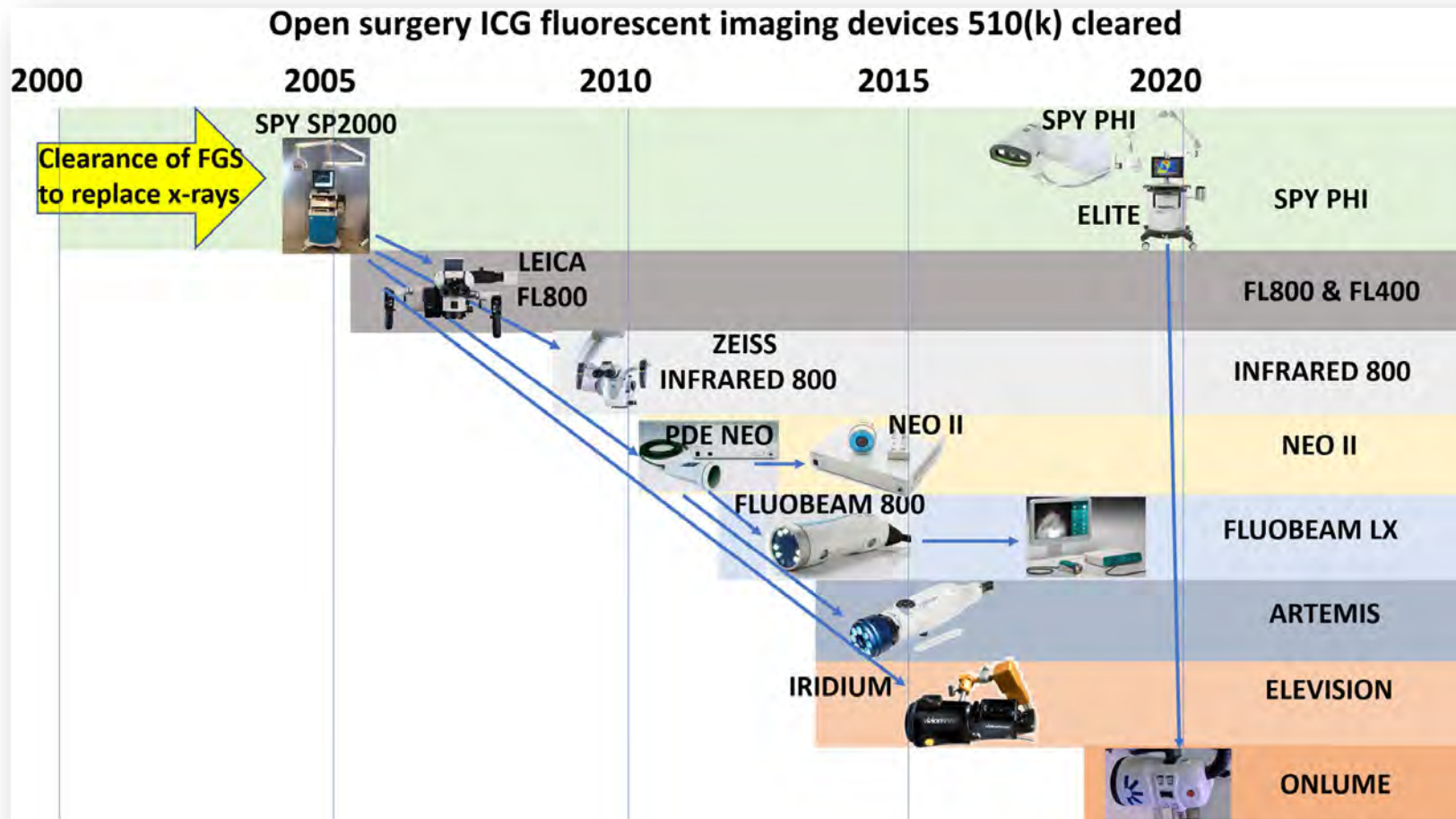
QUEST Medical, Inc.



FLUOPTICS.

**Review of successful pathways for regulatory approvals
in open-field fluorescence-guided surgery**

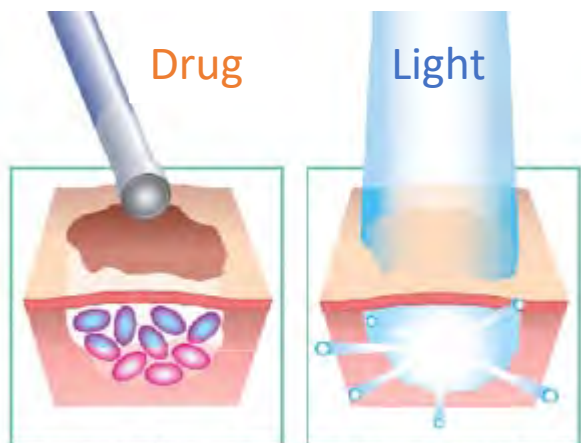
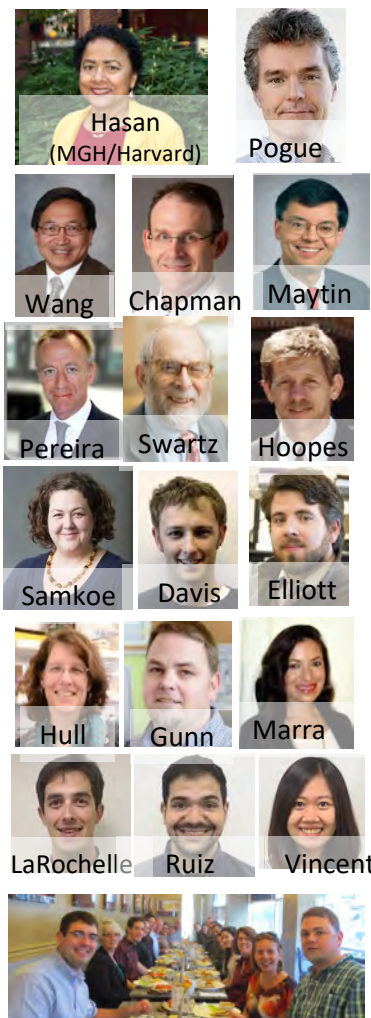
Brian W. Pogue^{a,b,*} and Eben L. Rosenthal^c



Example 3

Photodynamic Therapy

Collaborative Program – Photodynamic Therapy



Light Activated Chemotherapy

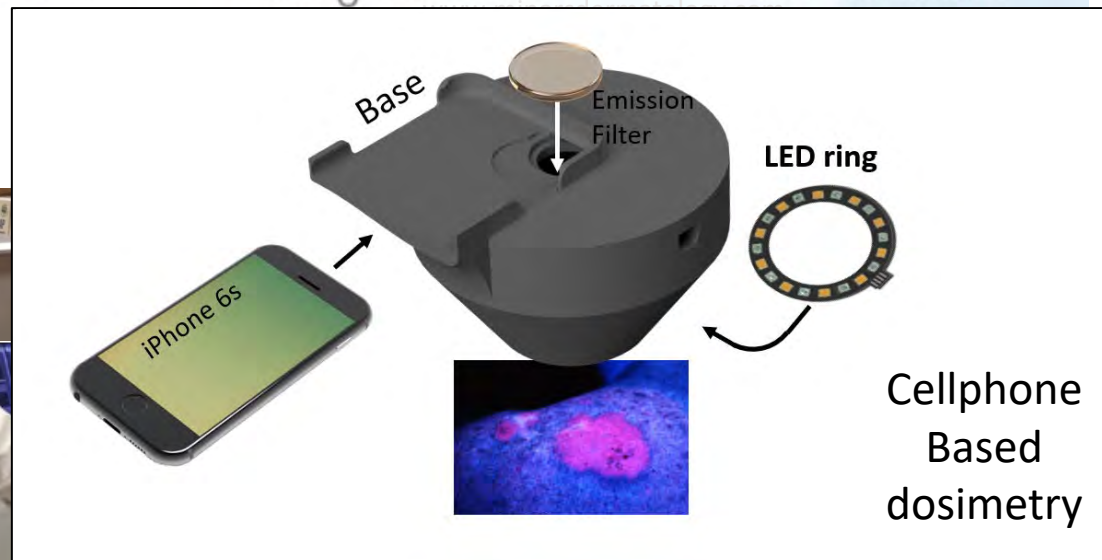
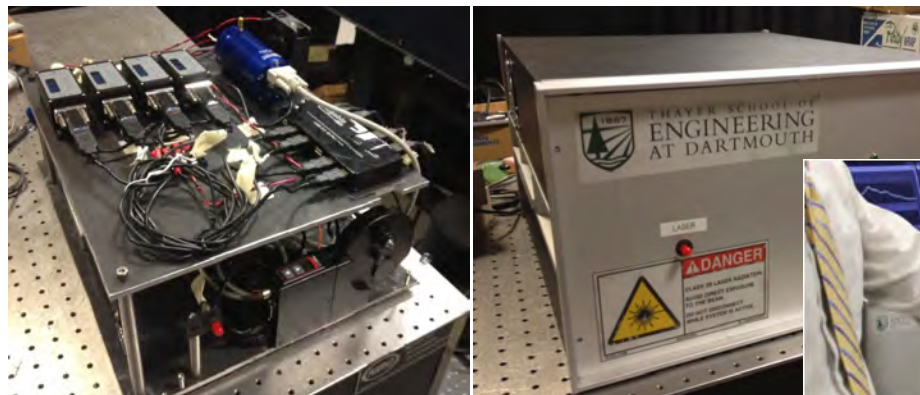


Before Treatment

During Treatment*

After Treatment

Photosensitizer dosimetry



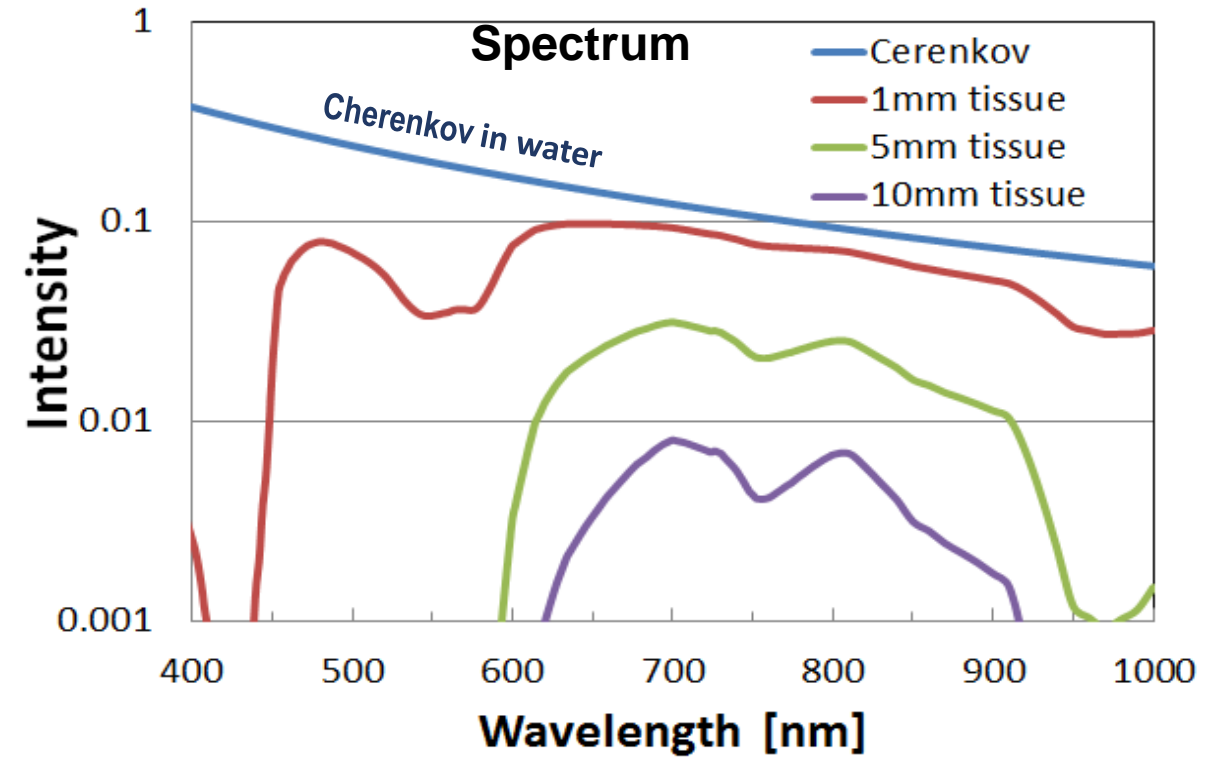
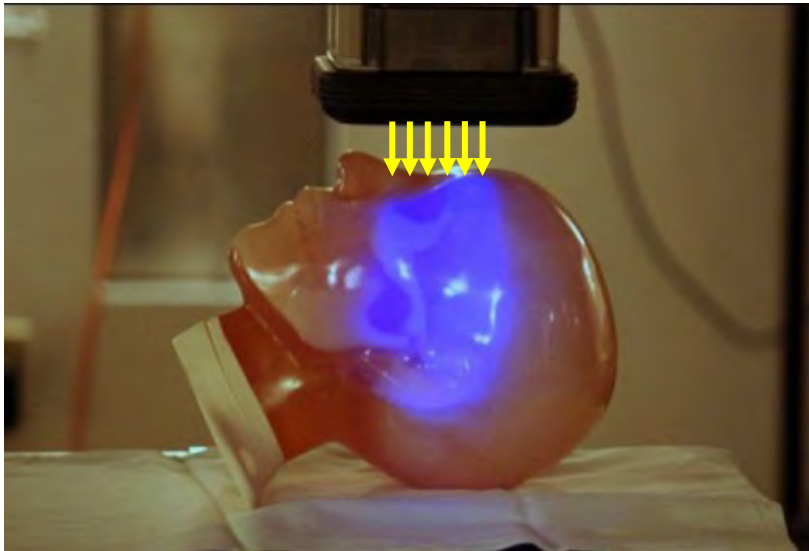
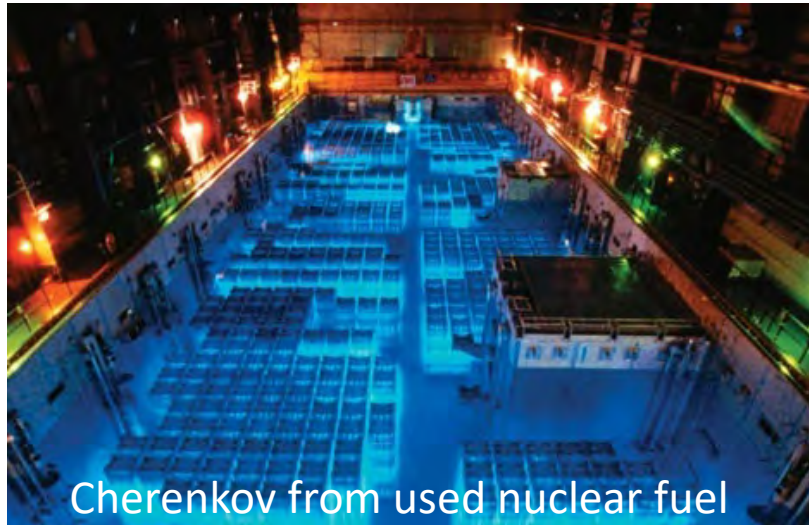
Example 4

Radiation *Dose* Imaging

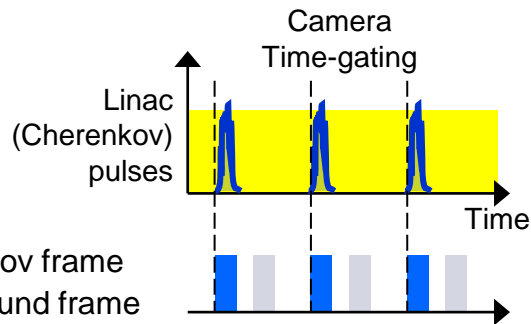
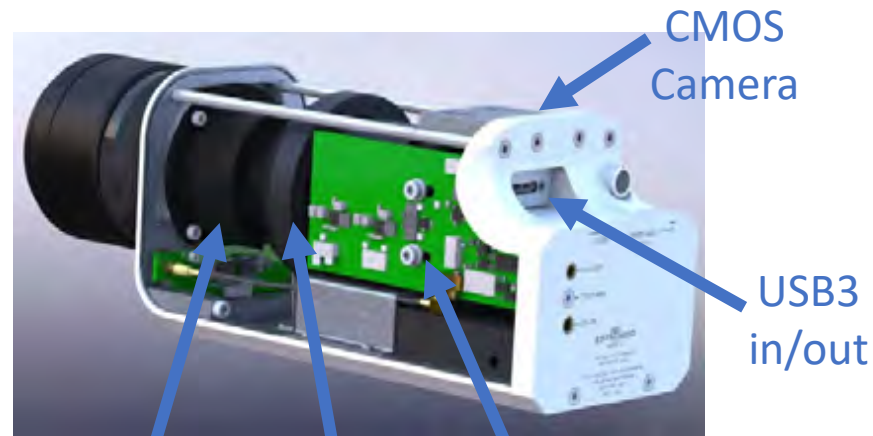
Radiation Therapy via Linear Accelerator



LINAC Radiation Dose produces pulses with Cherenkov light

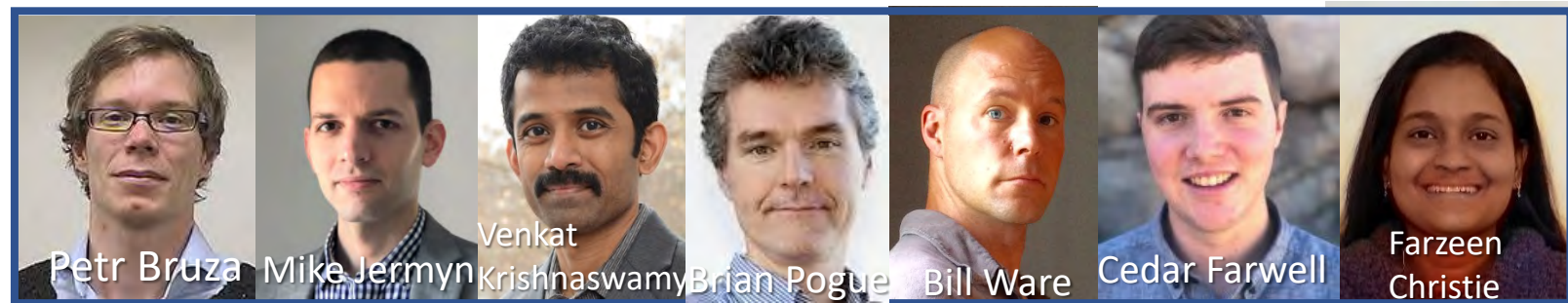


Time-gated Intensified Camera System



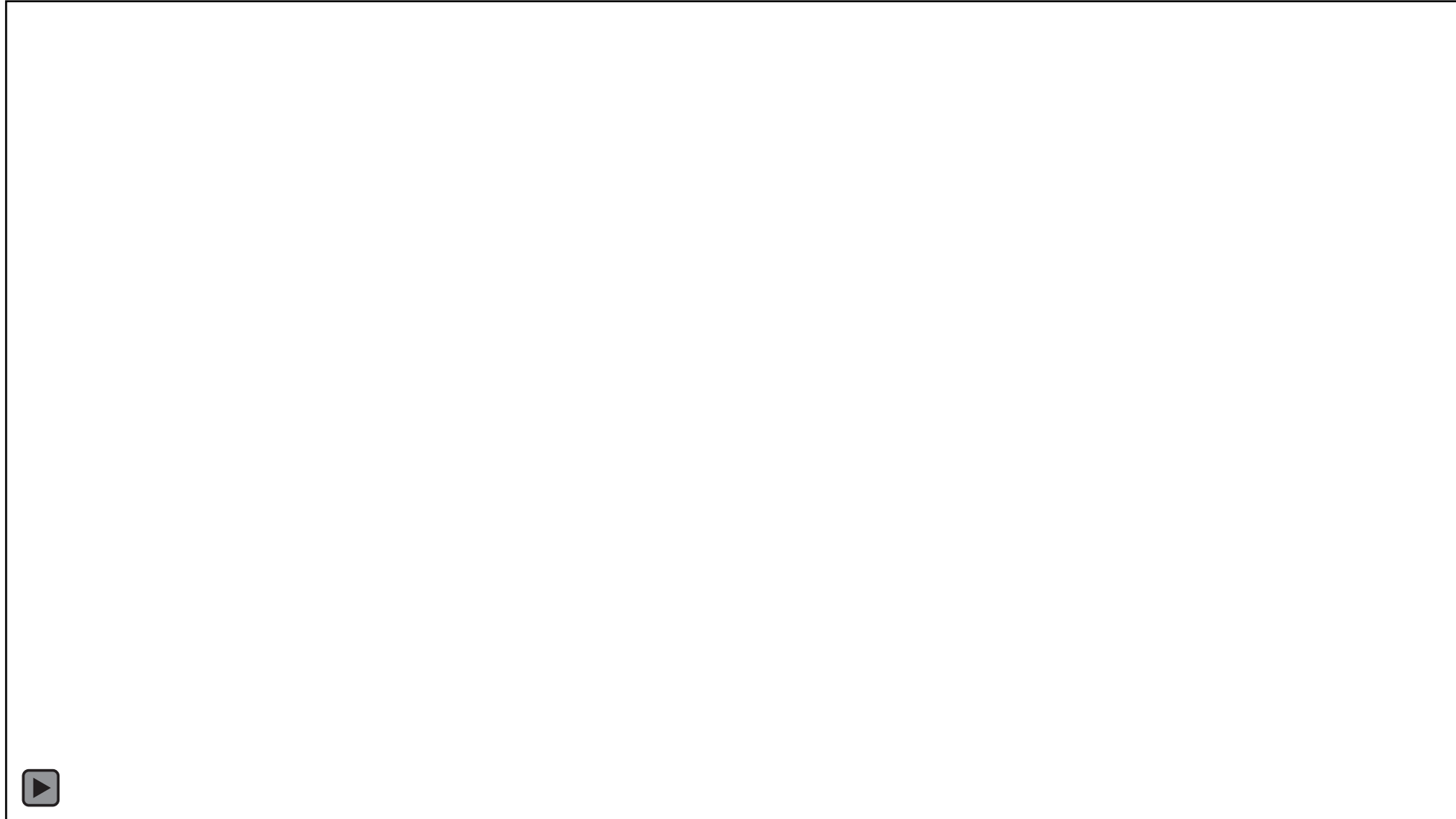
Single photon imaging with room lights on!

The DoseOptics Team



DISCLOSURE: B. Pogue is founder & president of DoseOptics.

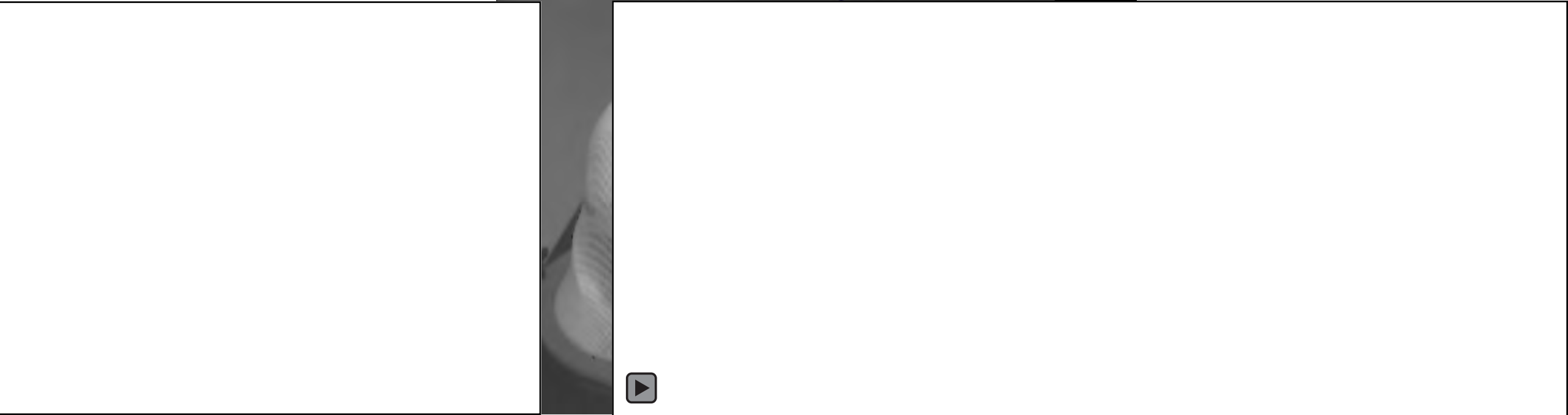
Cameras installed in all Dartmouth Linac Rooms



**Additional
User sites:**
Dartmouth
U Penn
Wash U
Emory
Harvard/MGH



Cherenkov Imaging in Radiation Therapy



Jarvis et al, IJROBP 2014
Jarvis et al, IJROBP 2021

Hachadorian et al, Nature Comm 2020
Alexander et al, Phys Med Biol 2018

Tendler et al, IJROBP 2019
(60+ papers published!)

Clinical Cherenkov imaging: 64 patient experience

International Journal of
Radiation Oncology • Biology • Physics

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Physics Contribution

Initial Clinical Experience of Cherenkov Imaging in External Beam Radiation Therapy Identifies Opportunities to Improve Treatment Delivery

Lesley A. Jarvis, MD, PhD,* Rachael L. Hachadorian, MS,[†] Michael Jermyn, PhD,[†] Petr Bruza, PhD,[†] Daniel A. Alexander, MS,[†] Irwin I. Tendler, PhD,[†] Benjamin B. Williams, PhD,*[†] David J. Gladstone, ScD,*[†] Philip E. Schaner, MD, PhD,* Bassem I. Zaki, MD,* and Brian W. Pogue, PhD[†]

*Department of Medicine, Section of Radiation Oncology, Geisel School of Medicine at Dartmouth, Hanover, New Hampshire; and [†]Thayer School of Engineering at Dartmouth, Hanover, New Hampshire

Received Jun 5, 2020. Accepted for publication Nov 5, 2020.

Purpose: The value of Cherenkov imaging as an on-patient, real-time, treatment delivery verification system was examined in a 64-patient cohort during routine radiation treatments in a single-center study.

Methods and Materials: Cherenkov cameras were mounted in treatment rooms and used to image patients during their standard radiation therapy regimen for various sites, predominantly for whole breast and total skin electron therapy. For most patients, multiple fractions were imaged, with some involving bolus or scintillators on the skin. Measures of repeatability were calculated with a mean distance to conformity (MDC) for breast irradiation images.

Results: In breast treatments, Cherenkov images identified fractions when treatment delivery resulted in dose on the contralateral breast, the arm, or the chin and found nonideal bolus positioning. In sarcoma treatments, safe positioning of the contralateral leg was monitored. For all 199 imaged breast treatment fields, the interfraction MDC was within 7 mm compared with the first day of treatment (with only 7.5% of treatments exceeding 3 mm), and all but 1 fell within 7 mm relative to the treatment plan. The value of imaging dose through clear bolus or quantifying surface dose with scintillator dots was examined. Cherenkov imaging also was able to assess field match lines in cerebral-spinal and breast irradiation with nodes. Treatment imaging of other anatomic sites confirmed the value of surface dose imaging more broadly.

Corresponding author: Lesley A. Jarvis, MD, PhD; E-mail: lesley.a.jarvis@dartmouth.org

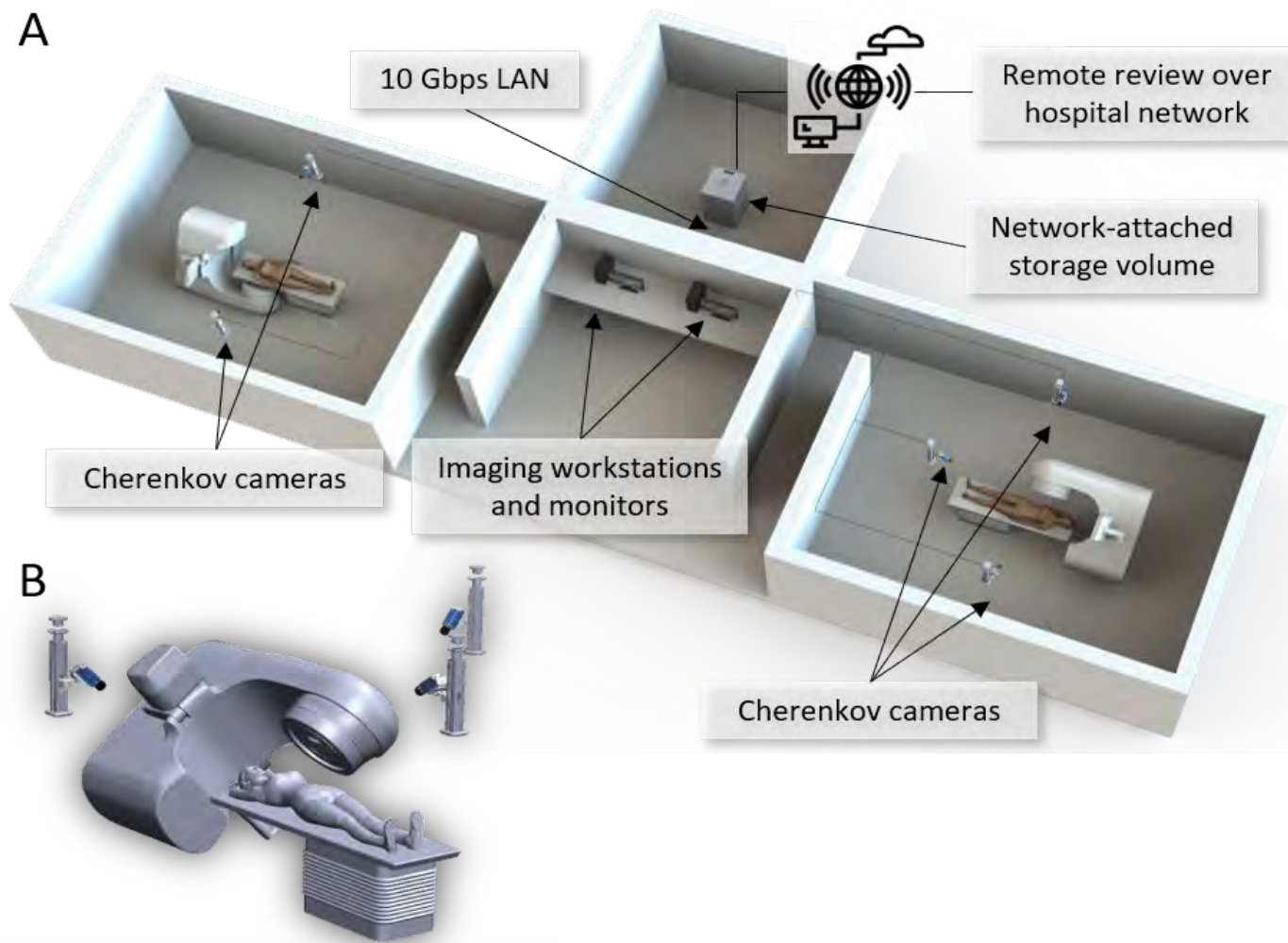
This work has been funded by grant R01 EB023909 from the National Institutes of Health, with hardware support through R44 CA232879 and with the support of the Norris Cotton Cancer Center shared resources in P01 CA023108.

Disclosures: L.A.J. and B.W.P. have a financial interest in DoseOptics, which manufactures cameras used in this study and is funded by SBIR grants; they also have a conflict of interest management plan at Dartmouth College and Dartmouth-Hitchcock Medical Center, which includes an independent review of the research integrity before publication. L.A.J. has a patent pending (application no. 62/874,124). R.L.H. has a patent pending (application no. 62/874,124). M.J. and P.B. are employees of DoseOptics.

I.I.T. has a patent issued (WO/2019/165196). M.J. has a patent (WO 2019/143972 A2) pending to Dartmouth/DoseOptics LLC. P.B. has patents pending (62/967,302; 62/873,155; PCT/US19/14242; and PCT/US19/19135). D.J.G. has a patent issued (US10,201,718 B2, 2/12/2019). B.W.P. has patents (US 10201718 B2 and US 9731150 B2) issued to DoseOptics LLC and a patent (WO 2019/143972 A2) pending to Dartmouth/DoseOptics LLC. The remaining authors reported no disclosures or conflicts of interest.

Research data are stored in an institutional repository and will be shared upon request to the corresponding author.

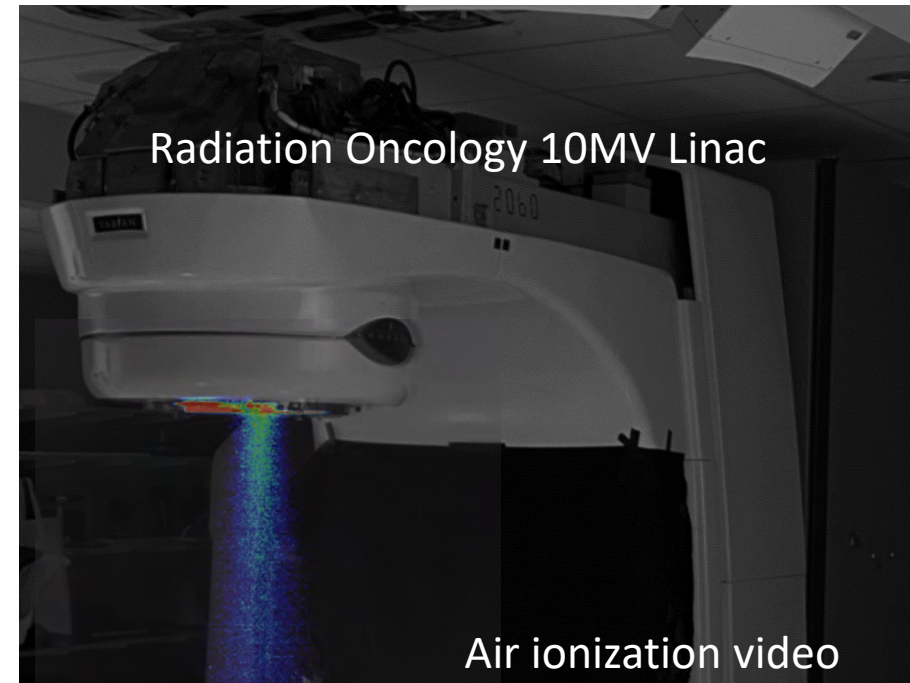
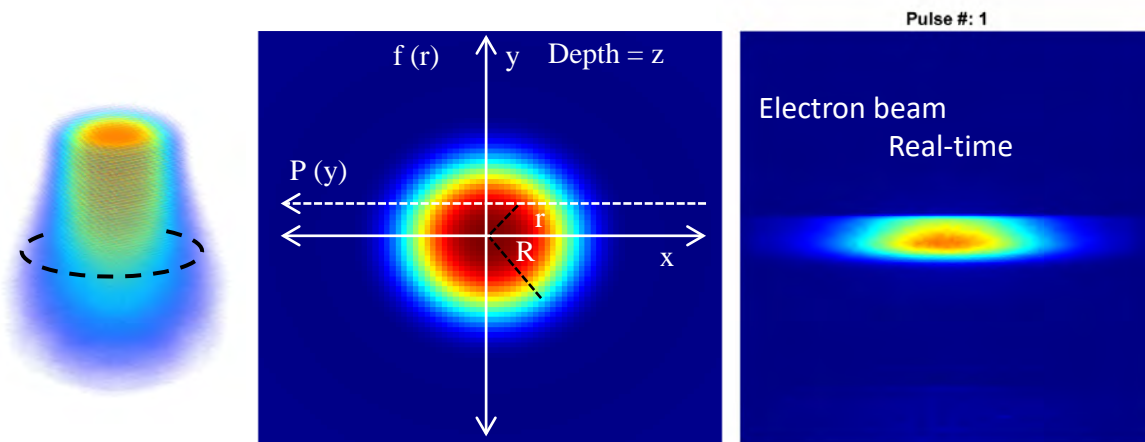
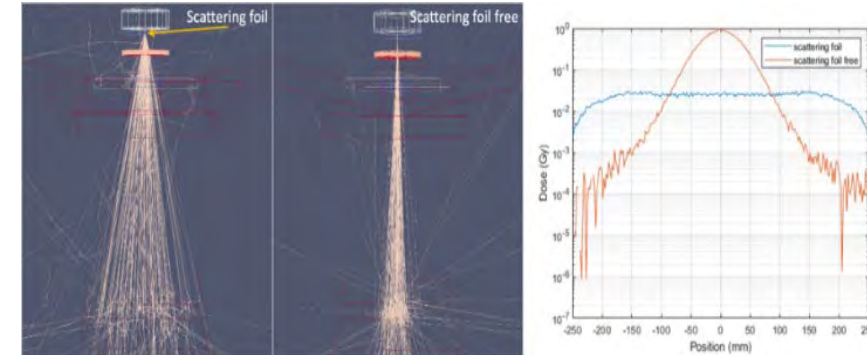
Supplementary material for this article can be found at <https://doi.org/10.1016/j.ijrobp.2020.11.013>.



Clinical Linac FLASH – Commissioning & QA

- Ultra-High Dose Rate Linac conversion (300Gy/sec)
 - Carousel port cover removed
 - Air value disabled
 - Manual position of carousel
 - Target actuator restricted
 - Energy set to 10 MV
 - Turn off servo control

Beam with & without scattering foil



Rahman et al, IJROBP 2021
Rahman et al, IJROBP (in review)
Ashraf et al, Med Phys (in review)


Assessing Value in Biomedical Research

The PQRST of Appraisal and Reward

John P. A. Ioannidis, MD, DSc^{1,2,3}; Muin J. Khoury, MD, PhD^{4,5}

Author Affiliations | Article Information

Promotions, Tenure
& grant funding are
Largely based upon these



P – Productivity = publications, grants → pubs, trials

Q – Quality = citation rate, follow quality standards

R – Reproducibility = was it repeated by others

S – Sharing = data & resources to others

T – Translation = start ups, licensing, clinical trials

Independent
Measures of
Success



BEAMSITE



Cherenkov imaging in Radiotherapy



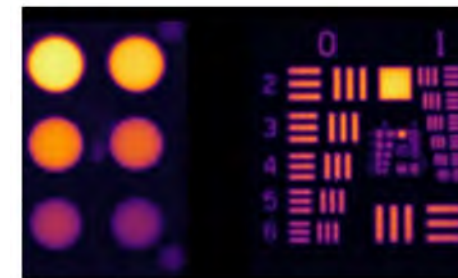
After all the simulation, planning and checking, treatment delivery is where it all comes together.

BeamSite give clinical teams the power to see what's happening during the most important time.

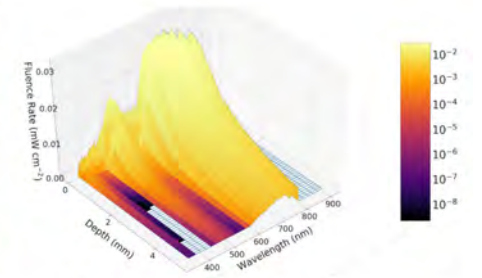
3D Printed Phantoms



Cellphone diagnostics

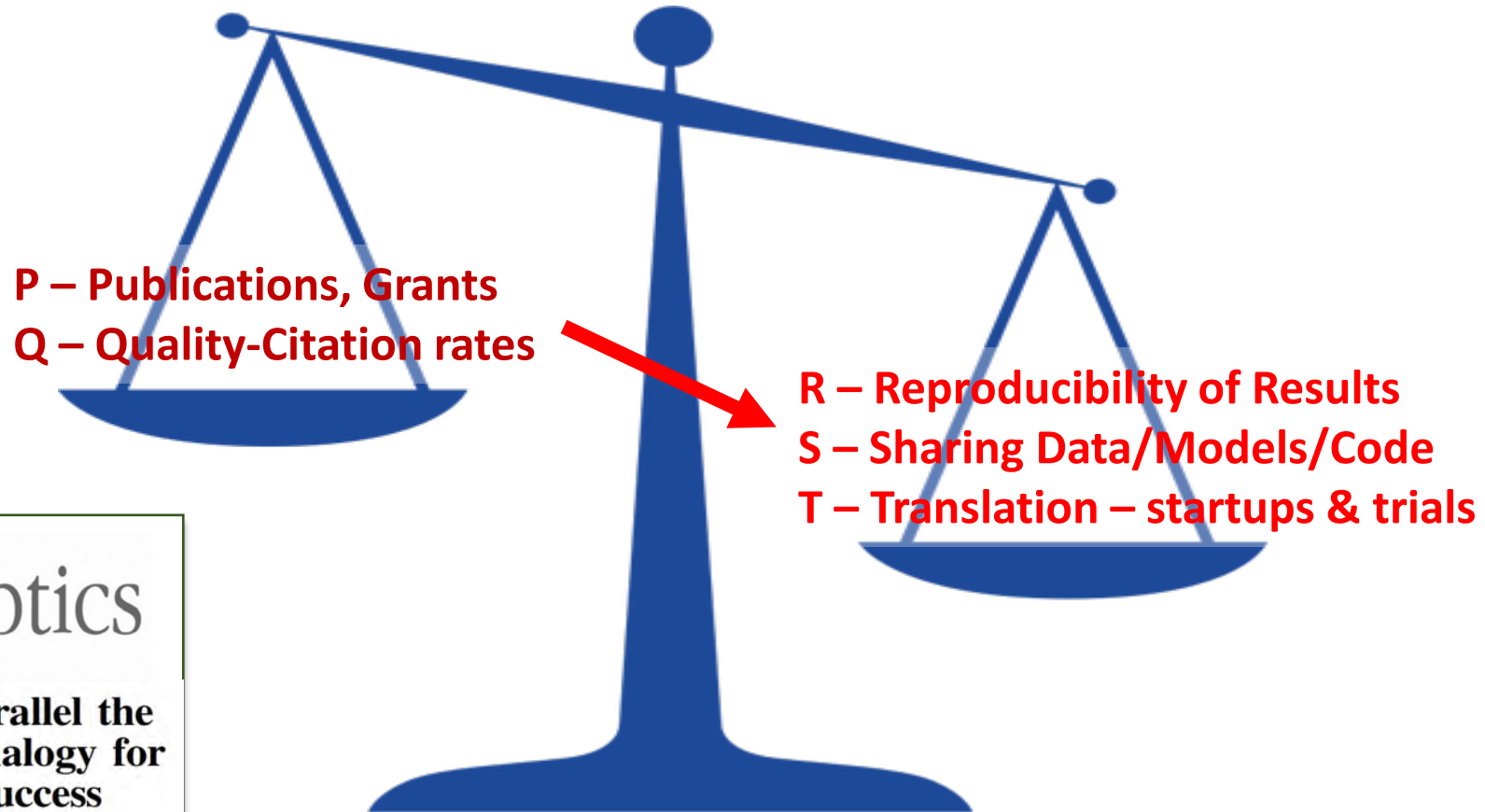


Optical Surgical Systems



Dosimetry for Optical Therapy

Rebalancing the definition of Success



Journal of
Biomedical Optics

**Grant Funding Needs Parallel the
Start-Up Venture: An Analogy for
Translational Research Success**

Brian W. Pogue



Journal of Biomedical Optics

Editor-in-Chief: Brian W. Pogue, Dartmouth College

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Thank You!

