Minimally invasive imaging of microstructure and function in living subjects
Opportunities for real-time informatics

LIANG Kaicheng

Team Leader and Senior Research Scientist

Institute of Bioengineering & Bioimaging (IBB)

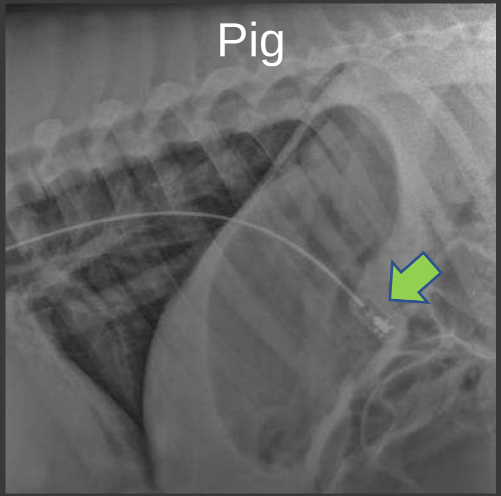
Bioinformatics Institute (BII)

NTU Lee Kong Chian School of Medicine

My background

- Biomedical engineer (autonomous robotics at Duke)

Fiber optic imaging system



Medical device design and pre-clinical validation

- Electrical engineer (photonics and optical imaging at MIT)

Clinical imaging team at VA Boston (Harvard teaching hospital)

- Clinical researcher (assisted in >200 endoscopies)

Led new cardiology AI project

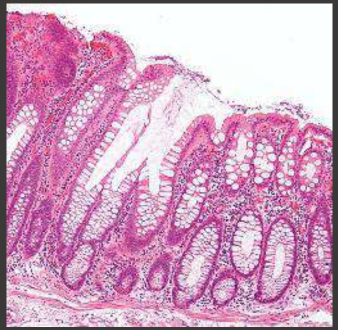
- Machine learning postdoc at BII

Surgery and biopsies require tissue microscopy

- Small samples of excised tissue are assessed, down to cell nuclei
- In surgery, must ensure malignant tissue is all removed

Biopsy/Resection

Fixing, embedding, sectioning



H&E-stained tissue (‘histology’)

Pathologist reading

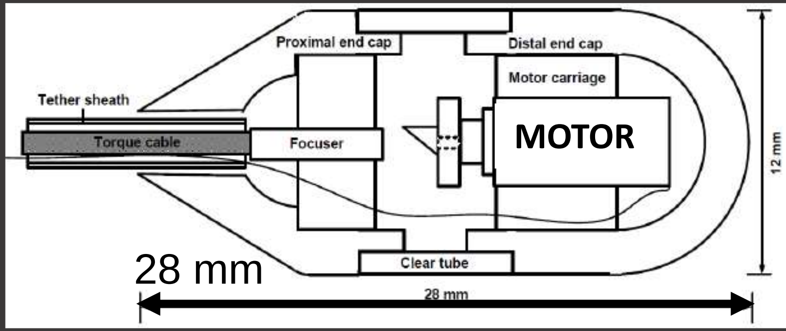
Slow! Usually 1-2 days. For some surgeries, wait 30-60 min. for frozen sections

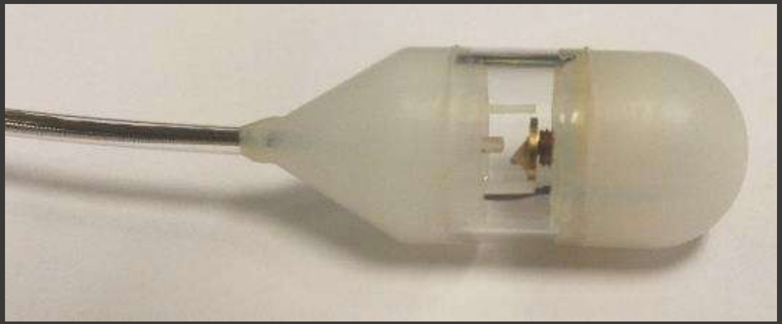
- Biopsies can miss areas of disease
- Limited amounts of tissue can be removed

Real time ‘intra-operative’ imaging of tissue ***before and right after*** excision: Thorough coverage, rapid feedback, better patient outcomes!

My specialty – Ultra-high speed OCT

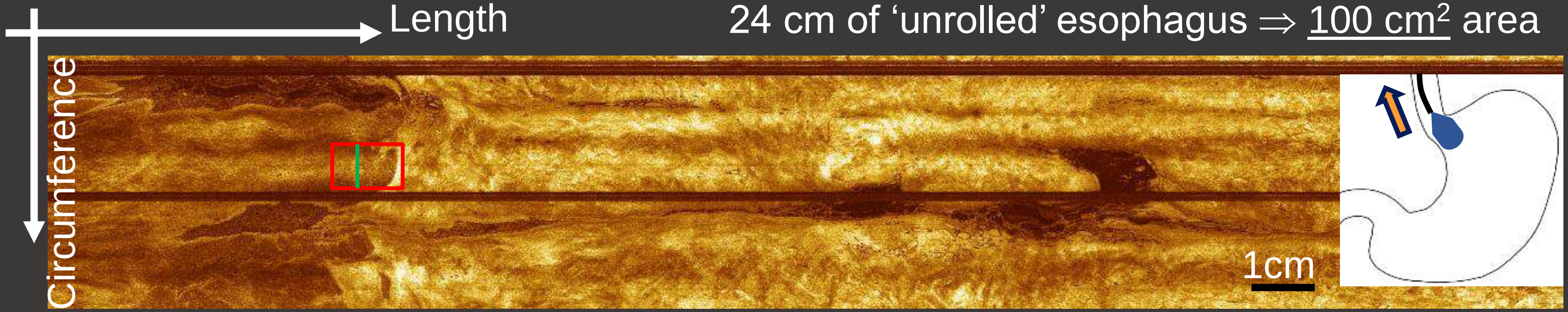
- Optical Coherence Tomography (OCT): non-invasive, ~10 µm resolution
- Real-time 3D endoscopic imaging *in vivo*. Millions of depth scans per second!
- Awake Endoscopy: unlimited 'optical biopsies' in patients *without sedation*



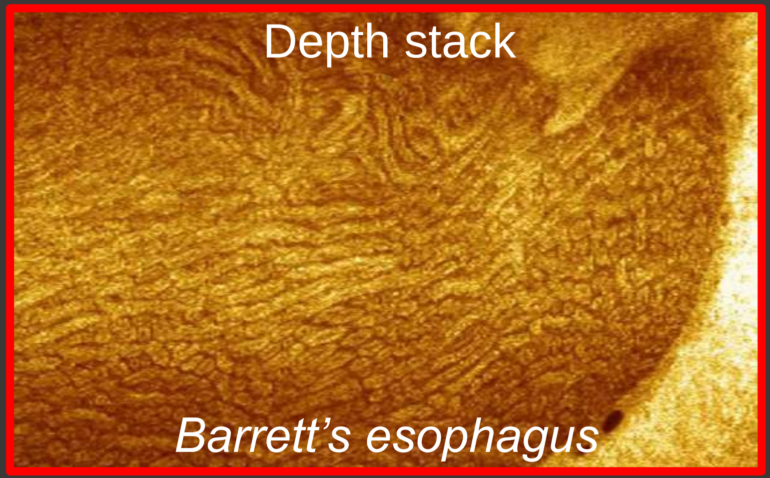


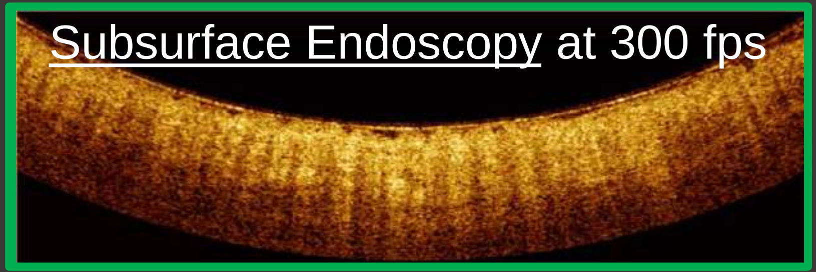
K Liang et al, *Am. J. of Gastro.* 2016,
BMJ Open Gastro. 2020
MIT Helen Carr Peake Research Prize 2017
Am. Gastro. Assoc. Certificate of Recognition

24 cm of 'unrolled' esophagus ⇒ 100 cm^2 area



20 sec imaging time



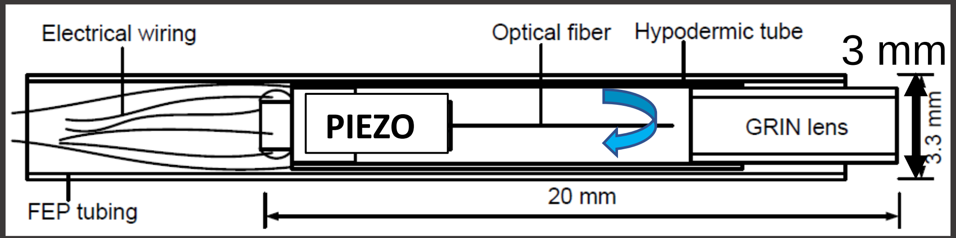


3D 'Google Maps' microscopy

Technologies – Microscanning

Competitive edge: ultracompact scanners for all-modality endoscopic microscopy

In a forward viewing fiber optic probe (w/ piezo actuator)

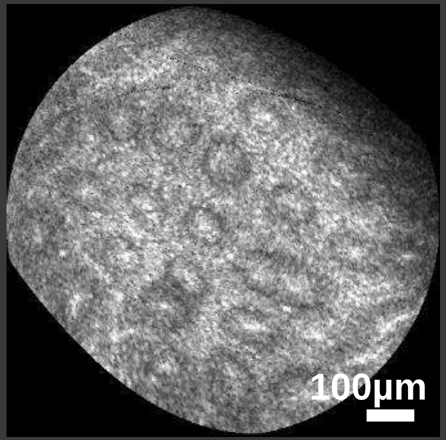


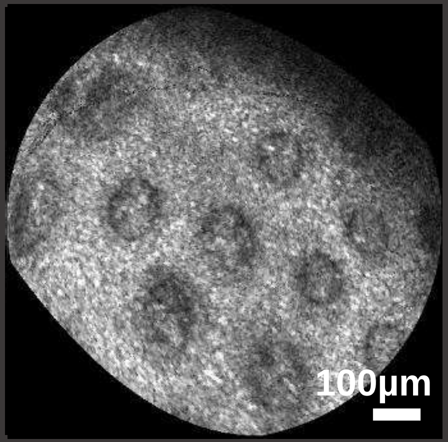
~1 mm^2 field of view
20x more than commercial instruments

3D stacks!

K Liang et al, *Optics Letters* 2017

Normal colon vs polyp in human patient

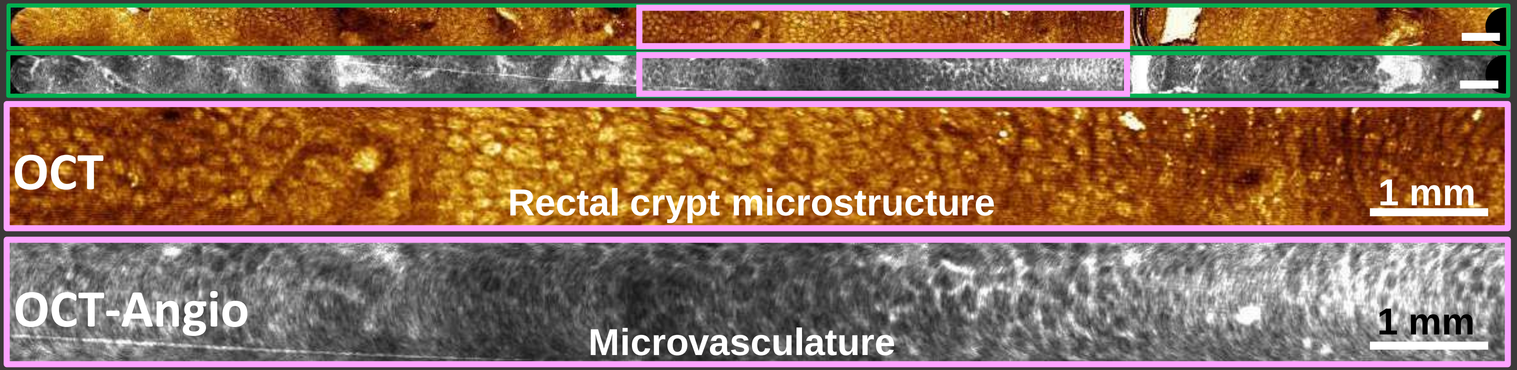




Then a tethered capsule with larger field of view (piezo + motor)

Tubular strip ⇒ 40 mm^2 field of view
800x more than commercial instruments

First-in-human study

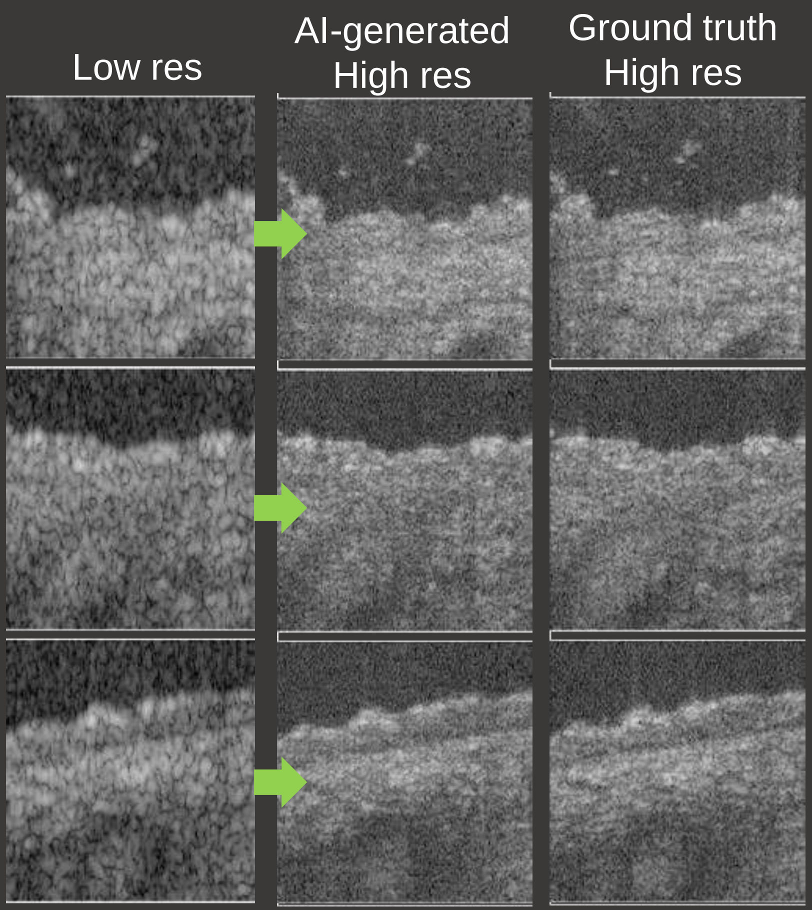


K Liang et al, *Optica* 2018, *Biomedical Optics Exp.* 2015, Two US Patent Apps

Technologies – AI for imaging

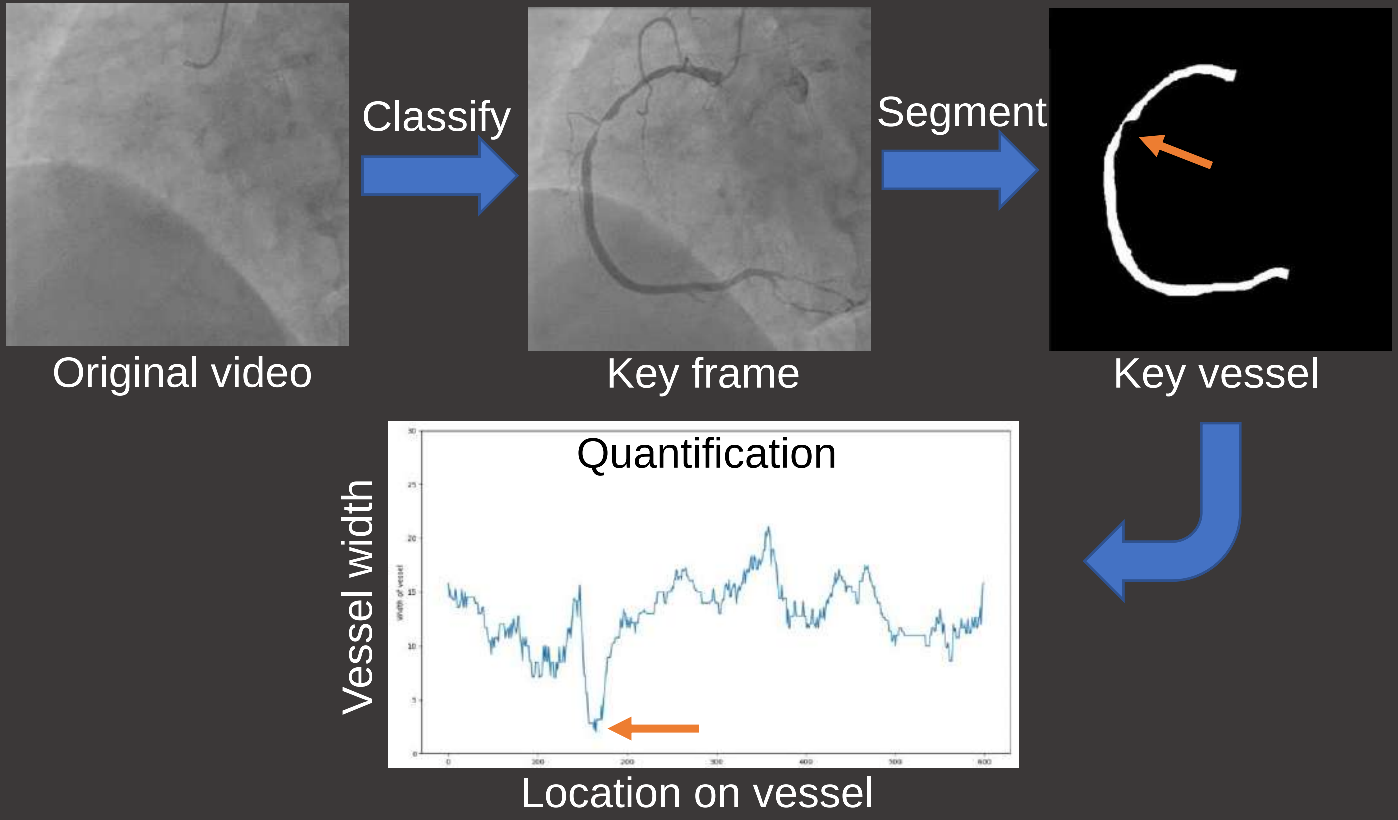
Deep learning for optics and medical imaging

Enhancing OCT resolution



K Liang et al, arXiv preprint 2020

Analyzing coronary artery imaging video sequences



What's next?

C. Zhou et al., HK Lee, K Liang
A*STAR AI Seed Grant (PI: K Liang)

Ongoing projects

Challenge: *margins of surgical resections are qualitatively assessed on the macro-scale, often requiring repeat surgeries*

Extreme miniaturization of endoscopic microscopes

- <1.5mm diameter with few-micron resolution, compatible with keyhole surgery and laparoscopy (and pre-clinical imaging!)
- Use case: identifying margins of invasive brain glioblastoma at cellular level (collaborator: Dr. Aaron Foo, NUH Neurosurgery)

Algorithms and optical tech for quantitative fluorescence at the margins

- Objective real-time assessment of uptake of clinical fluorescence dyes
- Use case: liver cancer margins with indocyanine green (collaborator: Dr. Alvin Tan, Sengkang Hospital General Surgery)

Funded by NRF Fellowship (2021-2026)

Emerging topics

Challenge: *3D cultures are known to develop microstructure, but cannot be visualized longitudinally without destructive staining*

OCT as non-destructive assay for organoid morphology and necrosis

- High speed volumetric screening of viability
- Use case: selecting organoids for orthotopic implantation (collaborator: Dr. Jamie Mong, IBB)

OCT as quality control of cultured food

- Structure and cellular organization is critical to texture and sensation in the mouth
- Use case: studying food microstructure (collaborators: Prof. Hanry Yu, IBB, Dr. Andrew Wan, SIFBI)

Thank you!

liangkc@ibb.a-star.edu.sg
liangresearch.com