SCHOOL OF ENGINEERING
VANDERBILT UNIVERSITY

Biophotonics Center

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Bowden Lab @ Vanderbilt

Light in Dark Places, Light on Dark Faces

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Vanderbilt University

Stanford University – CS 114/214 – 23 May 2022

Outline

- About You
- About Me
- Light in Dark Places
- Light on Dark Faces
- Discussion / Q&A

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What is one thing you think:

1. Everyone else has or has done but you HAVEN'T?
2. No one else has or has done but you HAVE?

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Princeton University, BSE
Electrical Engineering
Research Interest: Optics and Photonics

Ngee Ann Polytechnic, Singapore
Lecturer

Duke University, PhD
Biomedical Engineering
Research Interest: Biophotonics

United States Senate
Arthur H Guenther
Congressional Fellow

Harvard University, Postdoc
Chemistry and Chemical Biology
Research Interest: Microfluidics, Low-cost Diagnostics

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Stanford University
Electrical Engineering / Bioengineering
Research Interest: Biophotonics
Teaching Experience: Modern Optics
(examples: Biophotonics)

Vanderbilt University
Biomedical Engineering / Electrical Engineering
Research Interest: Biophotonics and Resource-Constrained Environments
Teaching Experience: Biomedical Instrumentation, Optics for Low-Resource Settings, Mobile App Development for mHealth

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advancing state-of-the-art

DEVELOP

aiding scientific practice

DISCOVER

addressing clinical need

DEPLOY

Leverage the power of light to
Assess health
Detect disease
Monitor treatment

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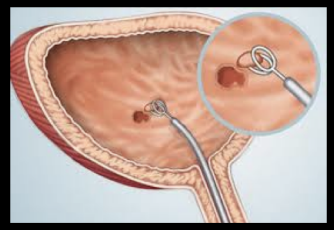
Current projects span several clinical areas



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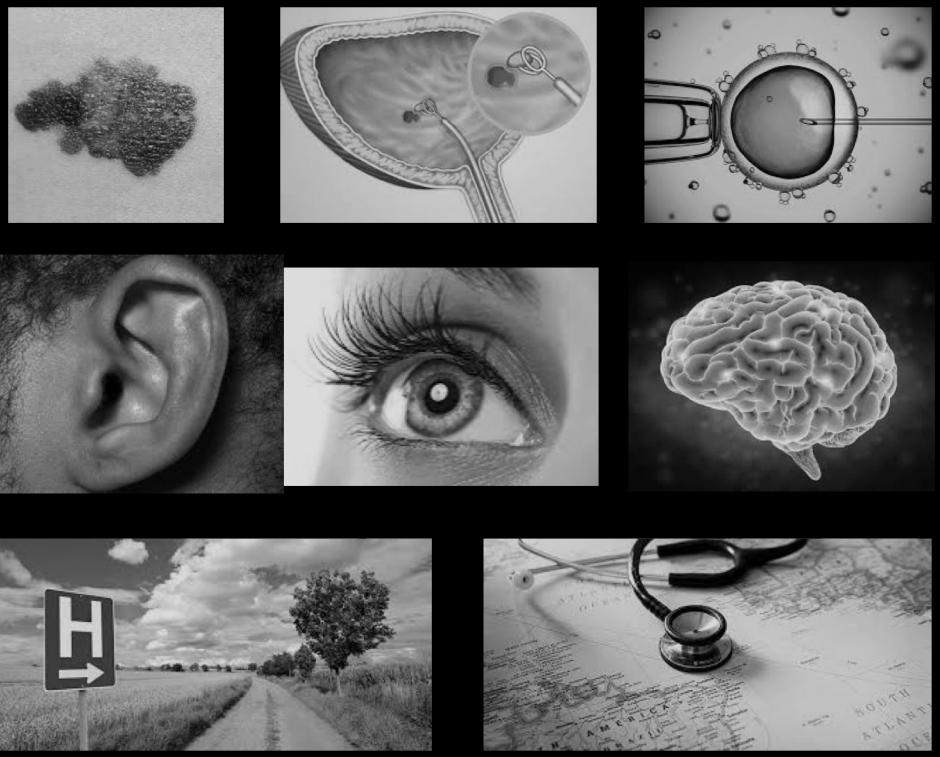
Current projects span several clinical areas



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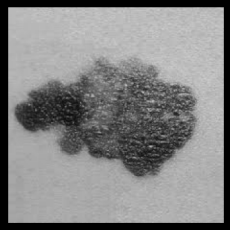
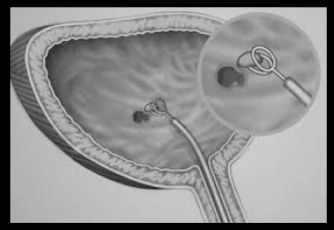
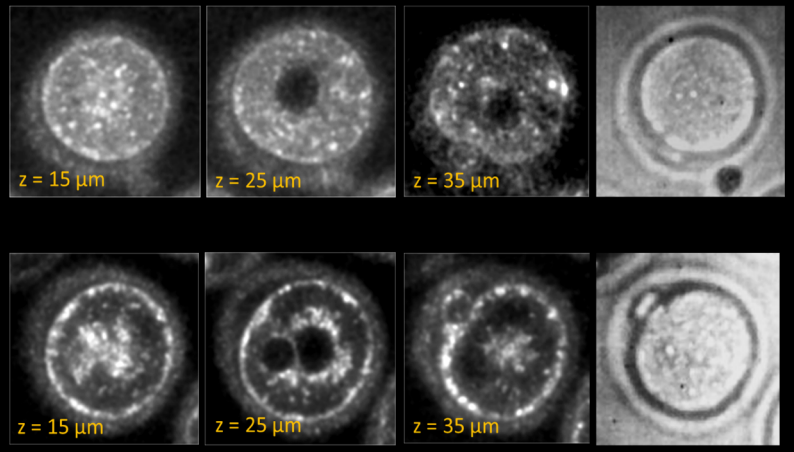
Current projects span several clinical areas

Biomarkers for IVF Embryo Viability



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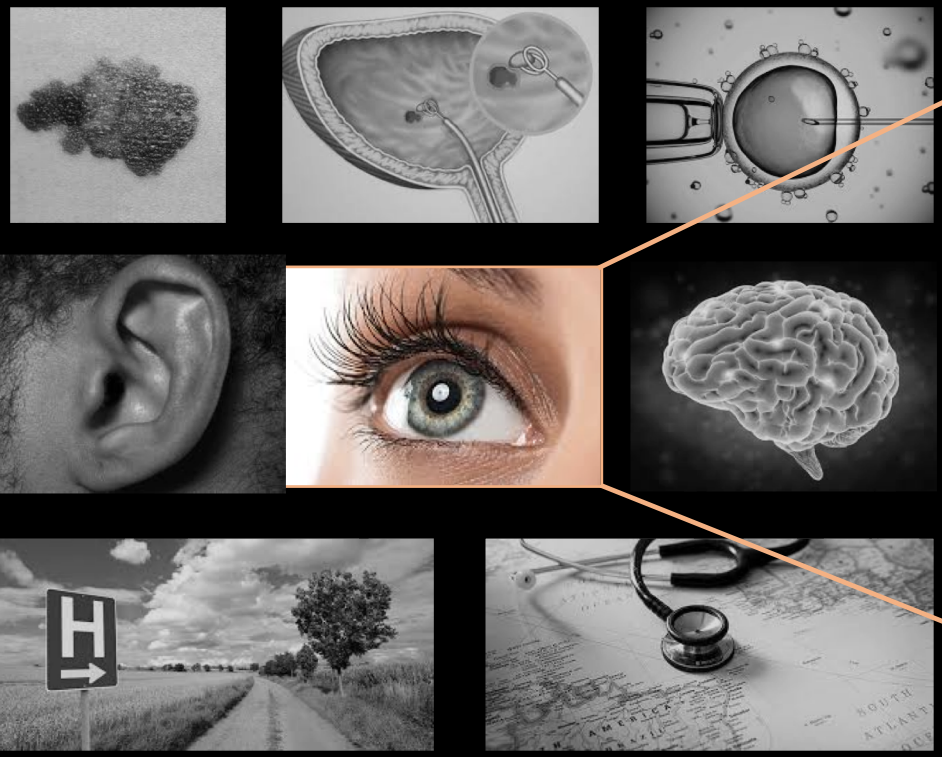
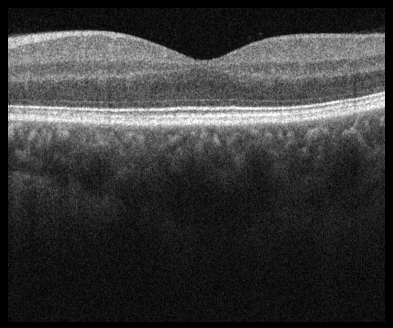
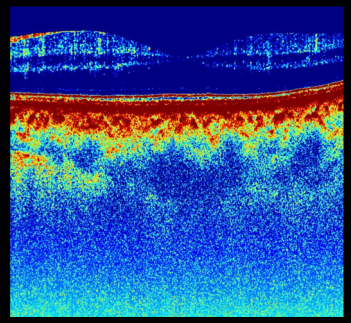
Current projects span several clinical areas



Biomarkers for glaucoma diagnosis



OCT intensity



Attenuation coefficient

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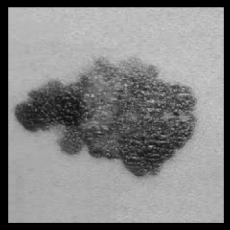
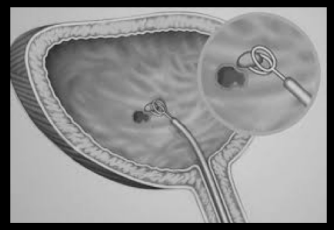
Current projects span several clinical areas

At-home neuromonitoring with fNIRS

Real-time facial landmark detection

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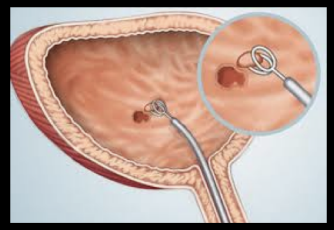
Light in Dark Places



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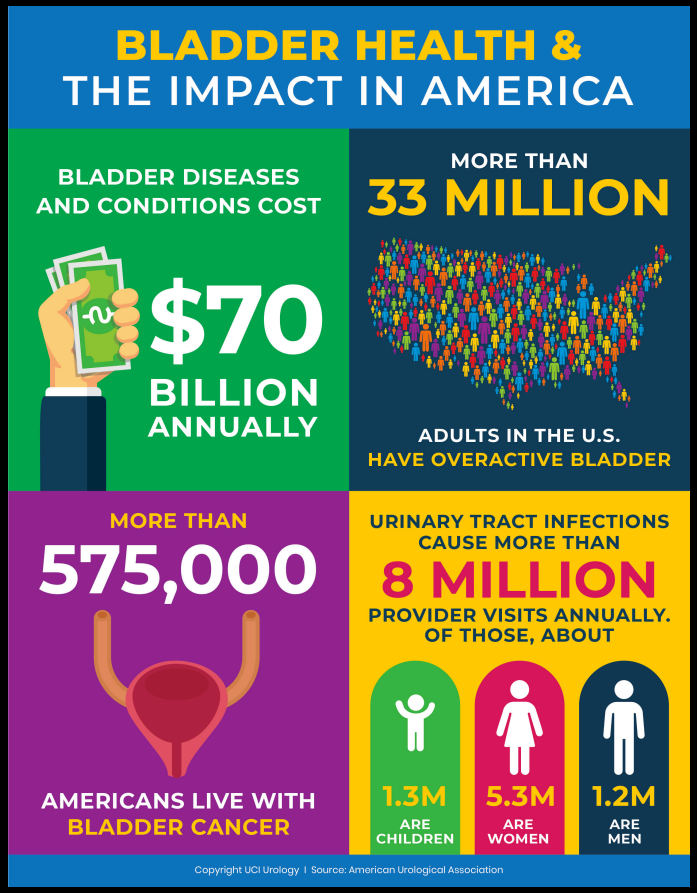

When we treat disease,
we treat people

Timothy

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Timothy, 67 years old

Military veteran
Smoker
Recurrent bladder cancer

Bladder cancer

4th most common cancer in men

74,000 new U.S. cases annually[1]

Most costly cancer / patient lifetime

50-90% recurrence rate[2]

Current clinical practice
has limited ability to detect
and treat cancer
with few, cost-effective procedures

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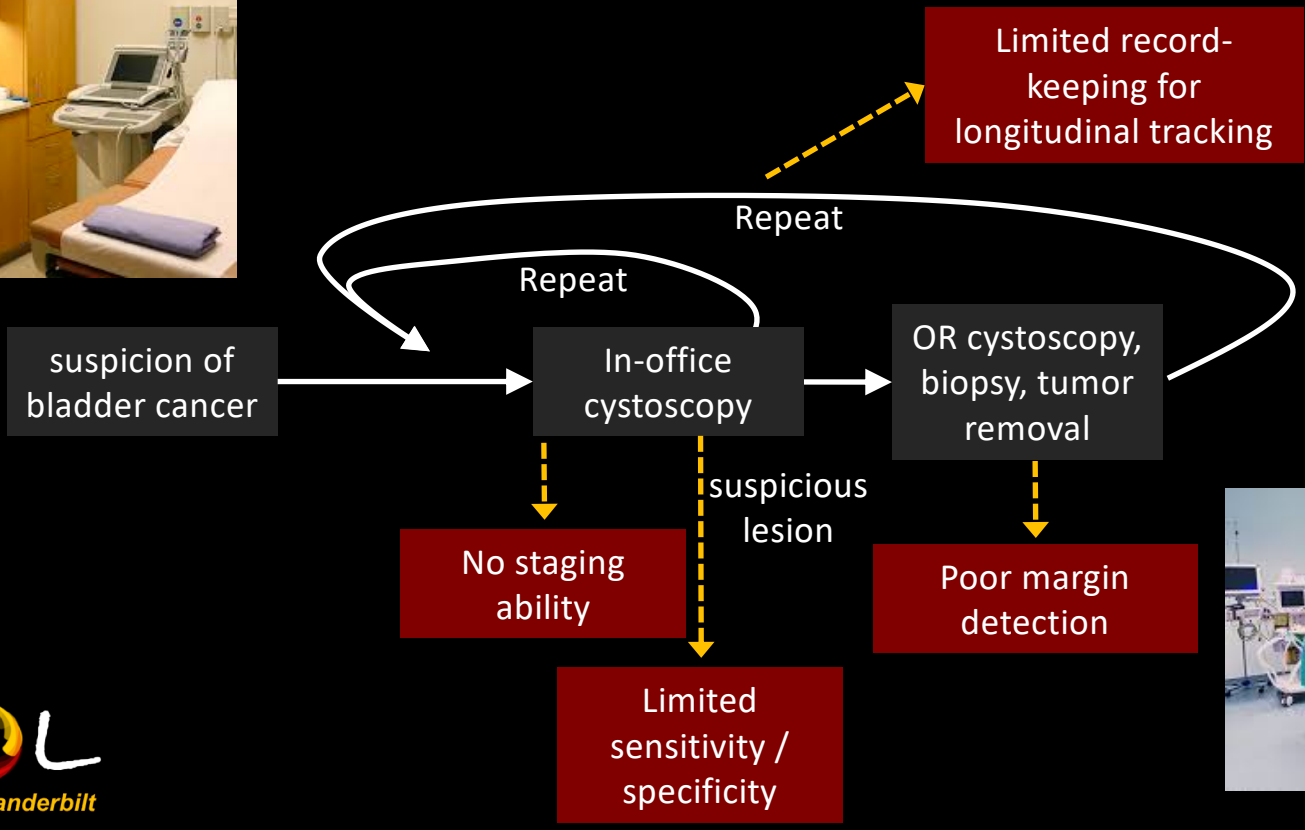
[1]Siegel, Rebecca, et al. CA: a cancer journal for clinicians 64.1 (2014): 9-29.
[2]National Comprehensive Cancer Network
Image adapted from: Fairview Health Services http://www.fairview.org/healthlibrary/

Bladder cancer detection and treatment: State of the art and limitations



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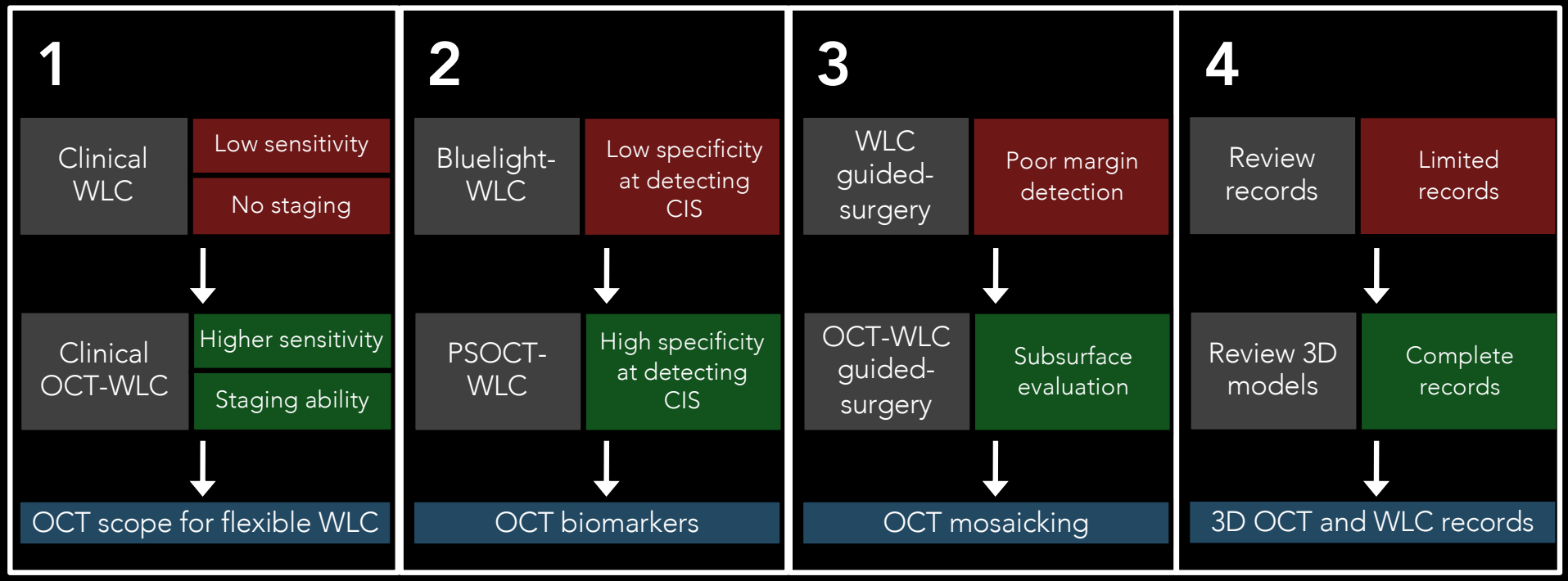

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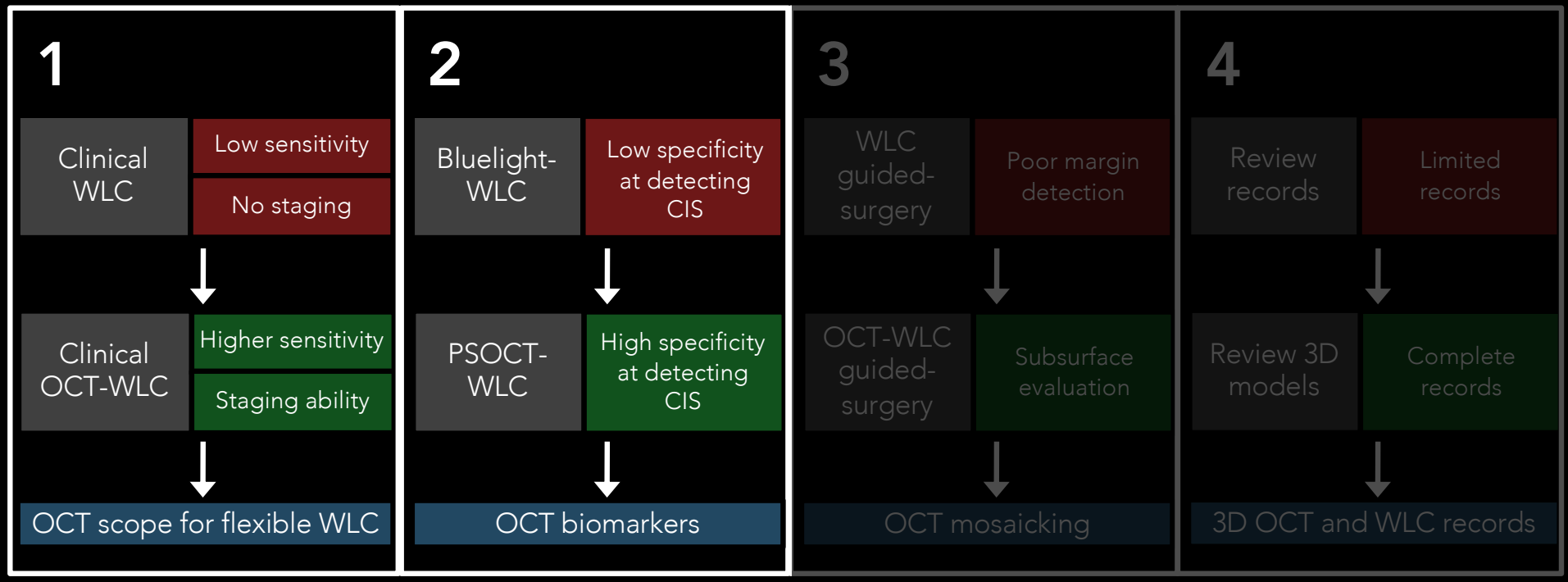
New optical tools



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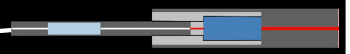
New optical tools

Optical coherence tomography (OCT)
High-resolution, non-invasive imaging

1 2



Clinical WLC	Low sensitivity	
	No staging	
↓		
Clinical OCT-WLC	Higher sensitivity	
	Staging ability	
↓		
OCT scope for flexible WLC		

2

Bluelight-WLC	Low specificity at detecting CIS
↓	
PSOCT-WLC	High specificity at detecting CIS
↓	
OCT biomarkers	

3

WLC guided-surgery	Poor margin detection
↓	
OCT-WLC guided-surgery	Subsurface evaluation
↓	
OCT mosaicking	

4

Review records	Limited records
↓	
Review 3D models	Complete records
↓	
3D OCT and WLC records	

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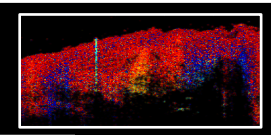
New optical tools

Polarization sensitive OCT (PS-OCT);
Label-free, enhanced contrast



1	2	3	4
Clinical WLC	Bluelight-WLC	WLC guided-surgery	Review records
Low sensitivity	Low specificity at detecting CIS	Poor margin detection	Limited records
No staging			
↓	↓	↓	↓
Clinical OCT-WLC	PSOCT-WLC	OCT-WLC guided-surgery	Review 3D models
Higher sensitivity	High specificity at detecting CIS	Subsurface evaluation	Complete records
Staging ability			
↓	↓	↓	↓
OCT scope for flexible WLC	OCT biomarkers	OCT mosaicking	3D OCT and WLC records

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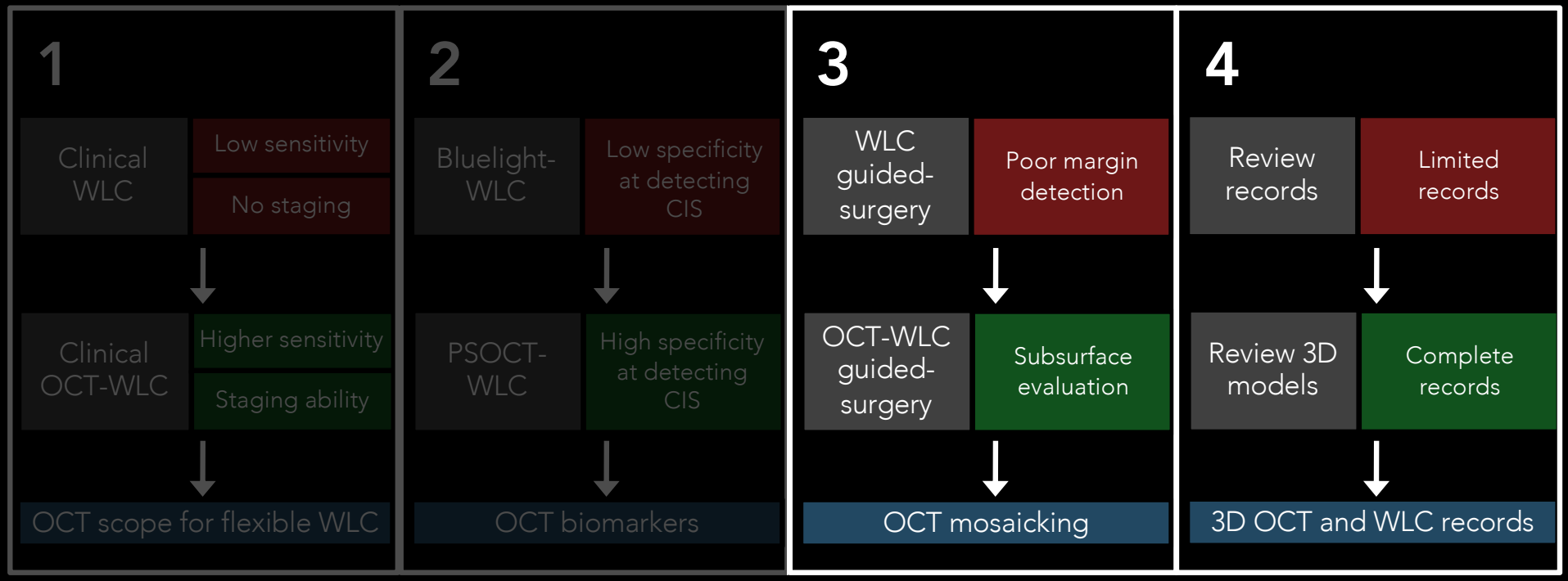
New image reconstruction methods



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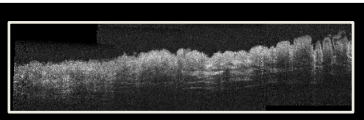
New image reconstruction methods

Mosaicking

1	2	3 	4
Clinical WLC	Bluelight-WLC	WLC guided-surgery	Review records
Low sensitivity	Low specificity at detecting CIS	Poor margin detection	Limited records
No staging			
↓	↓	↓	↓
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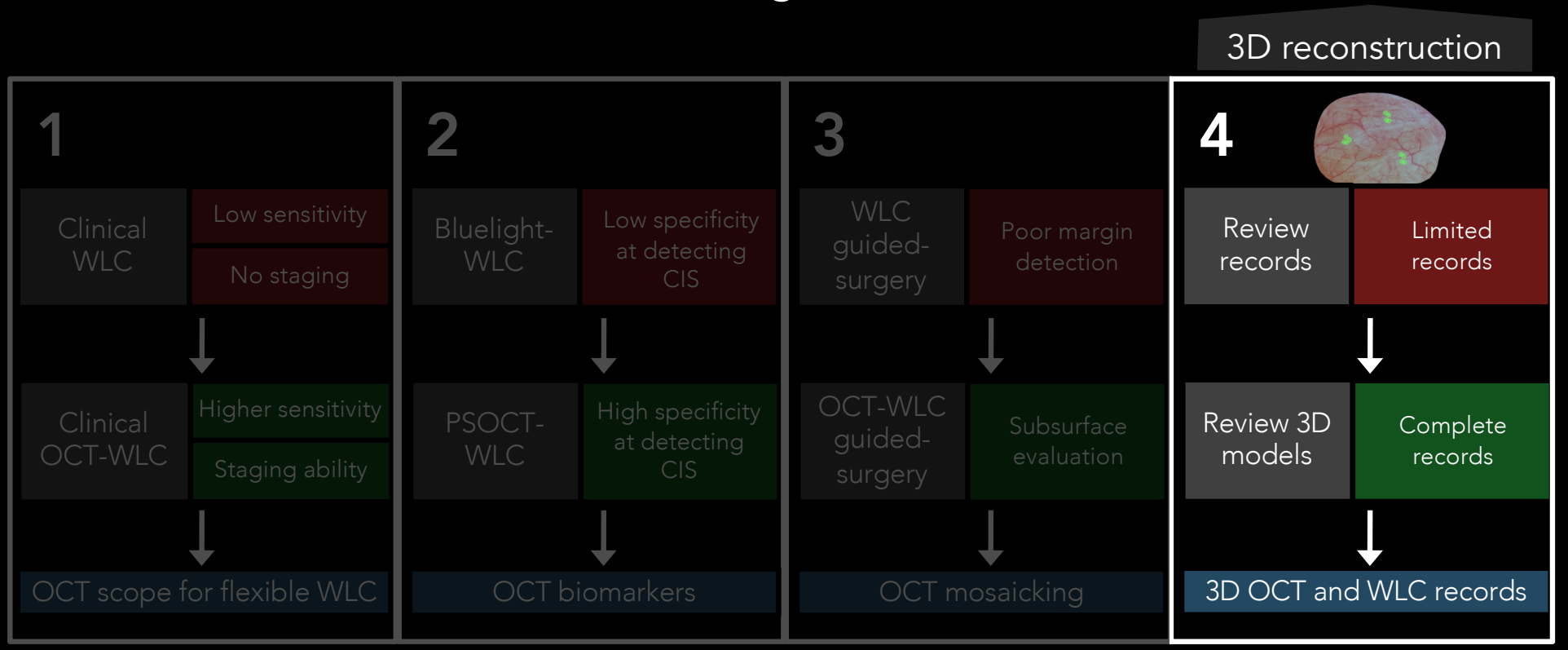
New image reconstruction methods



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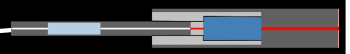
New optical tools

Optical coherence tomography (OCT)
High-resolution, non-invasive technique

1 2



Clinical WLC	Low sensitivity
	No staging
Clinical OCT-WLC	Higher sensitivity
	Staging ability
OCT scope for flexible WLC	

2

Bluelight-WLC	Low specificity at detecting CIS
PSOCT-WLC	High specificity at detecting CIS
OCT biomarkers	

3

WLC guided-surgery	Poor margin detection
OCT-WLC guided-surgery	Subsurface evaluation
OCT mosaicking	

4

Review records	Limited records
Review 3D models	Complete records
3D OCT and WLC records	

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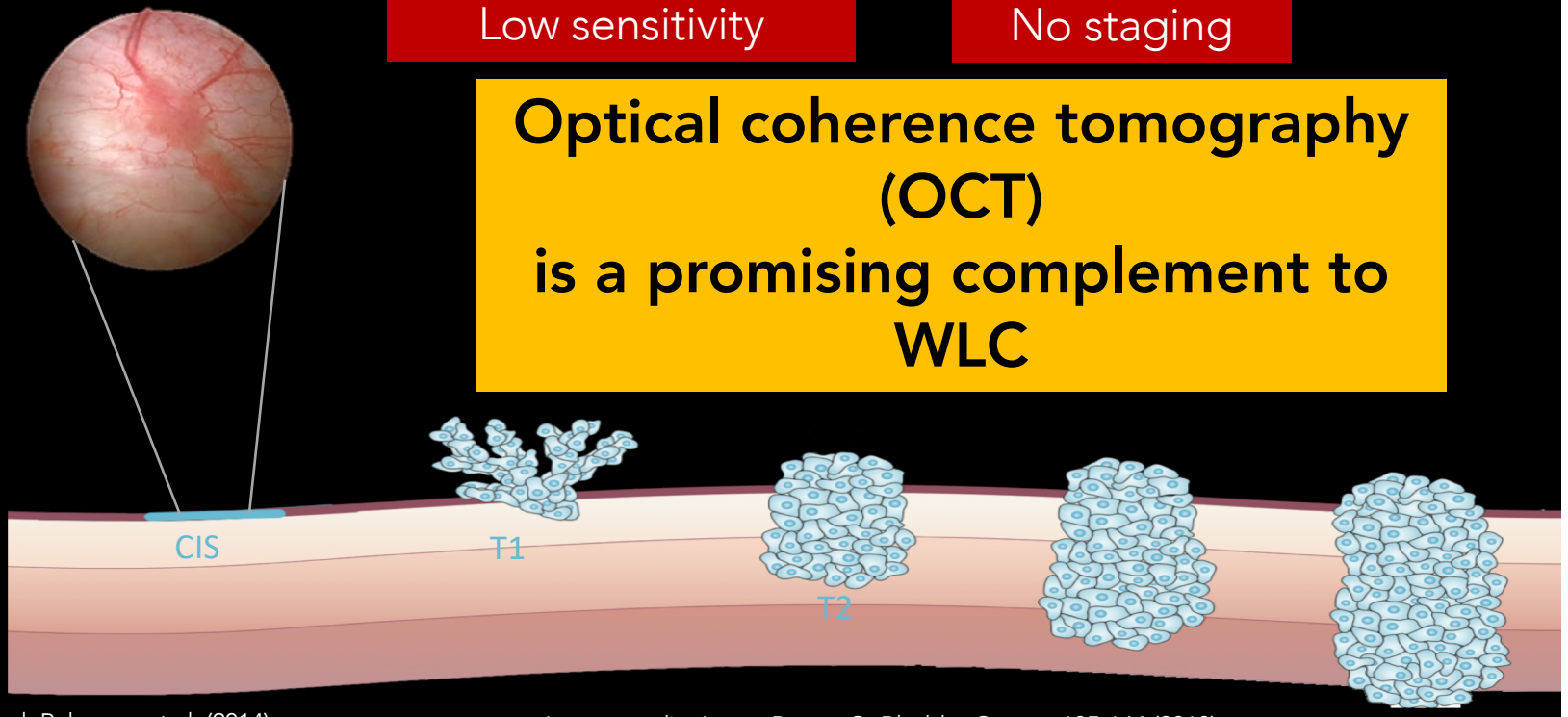
Limitations of White Light Cystoscopy (WLC)

Low sensitivity

No staging

Optical coherence tomography (OCT) is a promising complement to WLC



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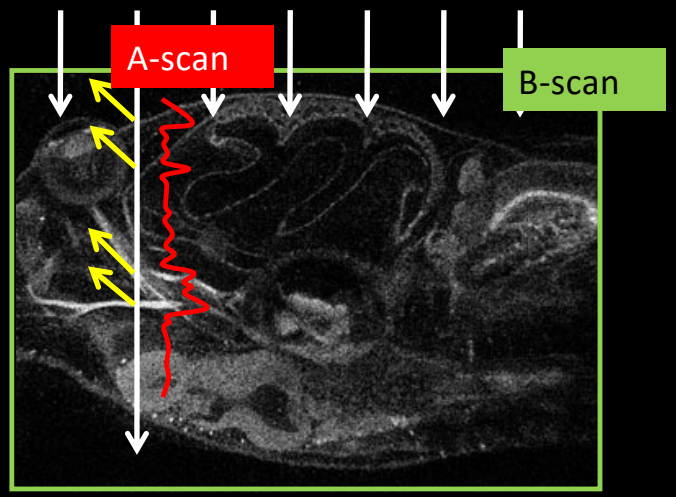
[1]Siegel, Rebecca, et al. (2014)
[2]National Comprehensive Cancer Network

Image credit: Jeong Byong C. *Bladder Cancer*, 135-144 (2018)
Image credit: Knowles, Margaret A., et. al. *Nat. Rev. Cancer*, 15, 25–41 (2015)

OCT: How it works

- Source of signal
  - Optical back scattering
- How it works
  - Time of flight
  - Interferometry
- Typical light sources:
  - Near-infrared (830nm, 1060nm, and 1310nm)
  - Broad bandwidth (~100nm) → high resolution (<10um)



Cross-sectional image of a frog tadpole
(http://www.thorlabs.com/OCT/)

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OCT images can distinguish tumor stages

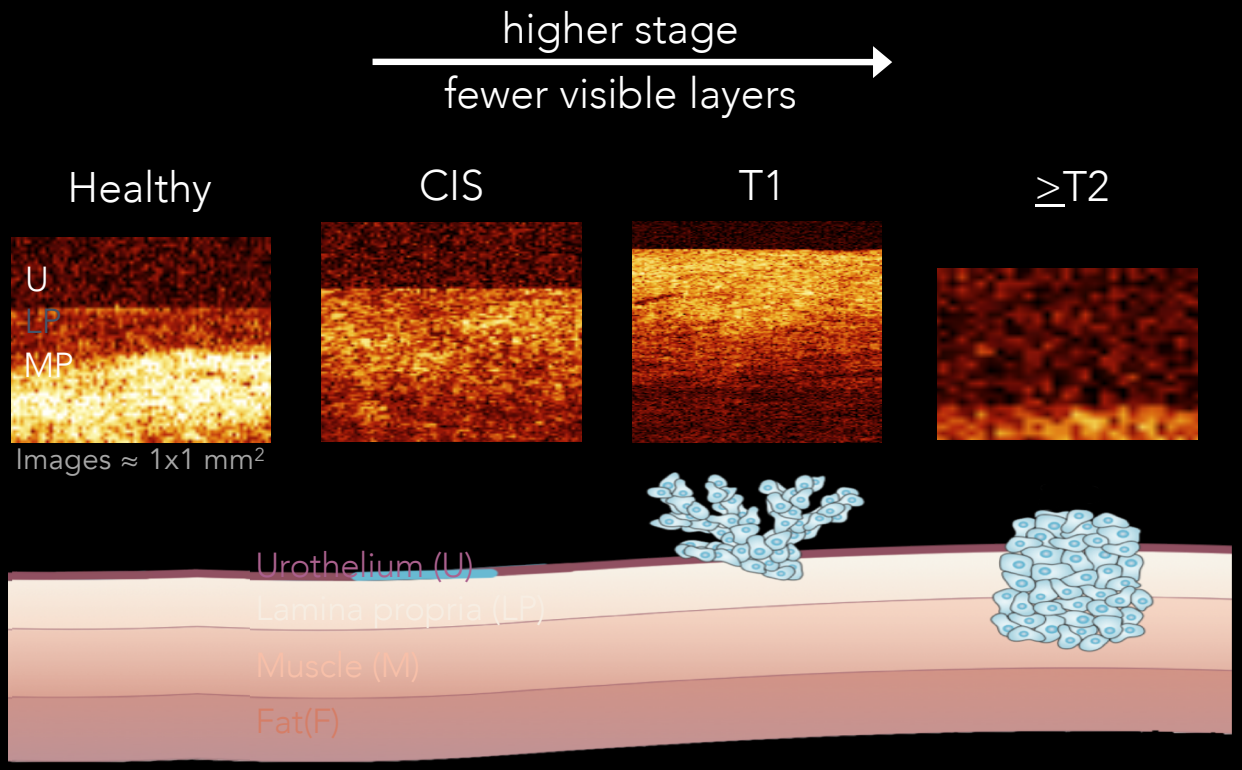

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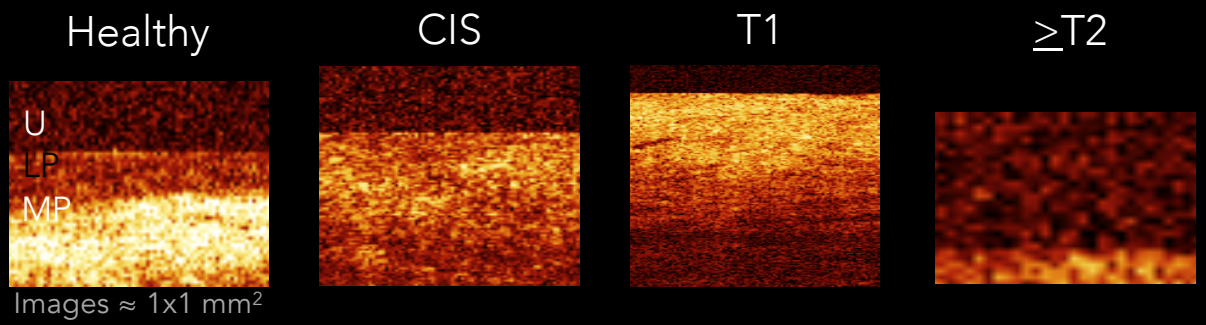
Image credit: Schmidbauer, J. et al. *Eur. Urol.* 56, 914–9 (2009).
Image credit: Knowles, Margaret A., et. al. *Nat. Rev. Cancer*, 15, 25–41 (2015)

OCT images can distinguish tumor stages

higher stage

fewer visible layers



Several studies in humans report 90-100% sensitivity[1-3]

1. Manyak, M.J., et al. J. Endourology 19.5 (2005): 570-574.
2. Lingley-Papadopoulos, C.A., et al. J. of Biomed. Optics 13.2 (2008): 024003-024003.
3. Lerner, S.P., et al. Urology 72.1 (2008): 133-137.

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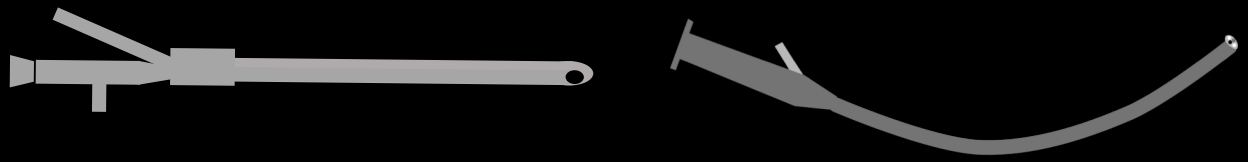
Image credit: Schmidbauer, J. et al. *Eur. Urol.* 56, 914–9 (2009).

Existing OCT endoscopes are too large and too slow to integrate with clinical cystoscopies

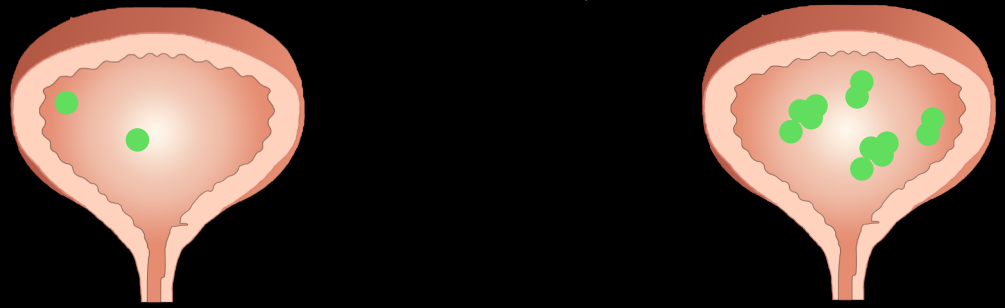
OCT endoscope miniaturization permits use in clinical settings

rigid cystoscope → flexible cystoscope



OCT acquisition speed-up permits viewing larger tissue volume

slow acquisition → fast acquisition



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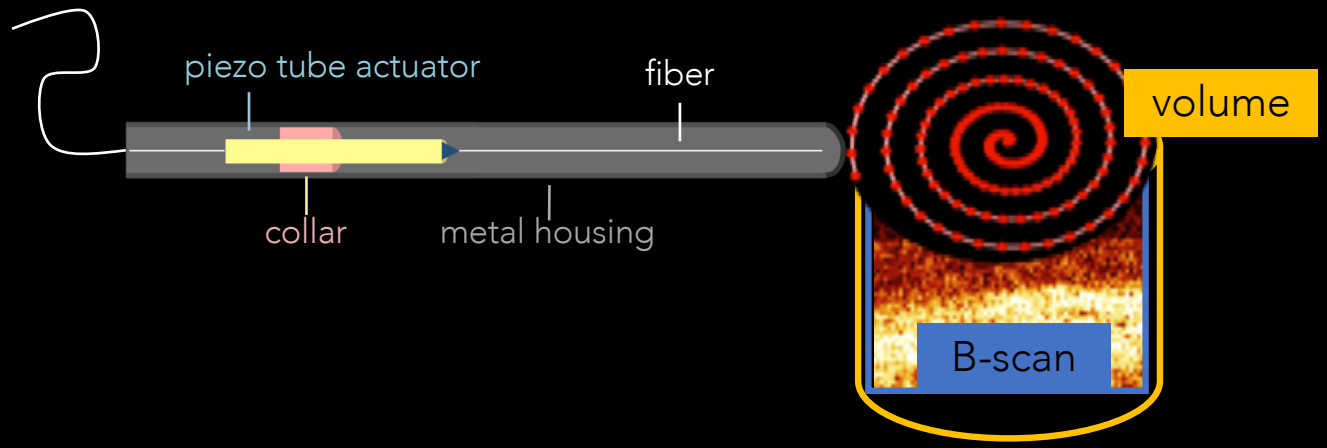
Eric Seibel, UW

Scanning fiber endoscopy (SFE)
Lens assembly for OCT imaging



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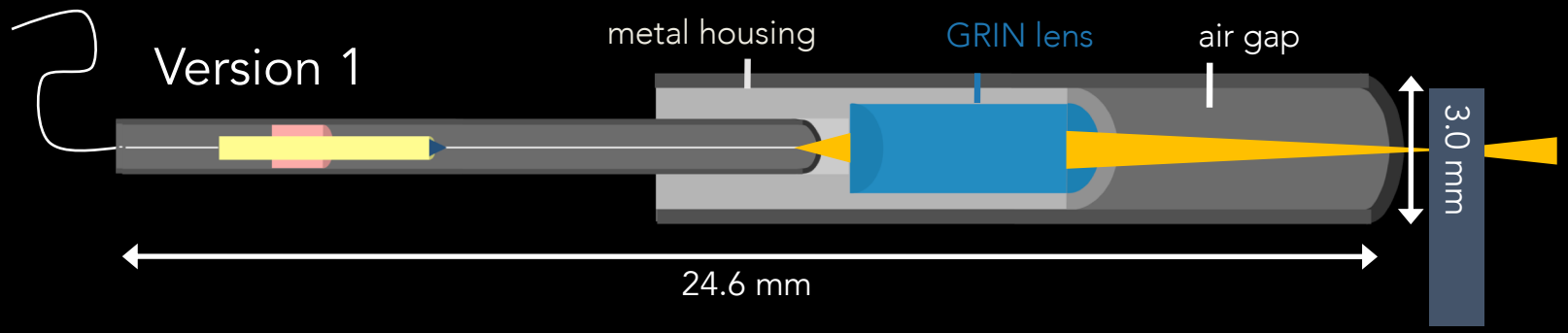
Scanning fiber endoscopy (SFE)

Lens assembly for OCT imaging



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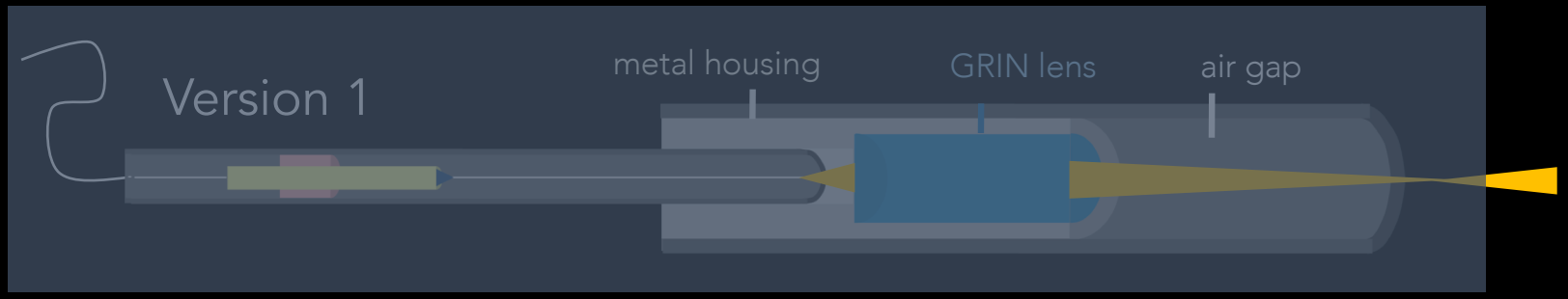
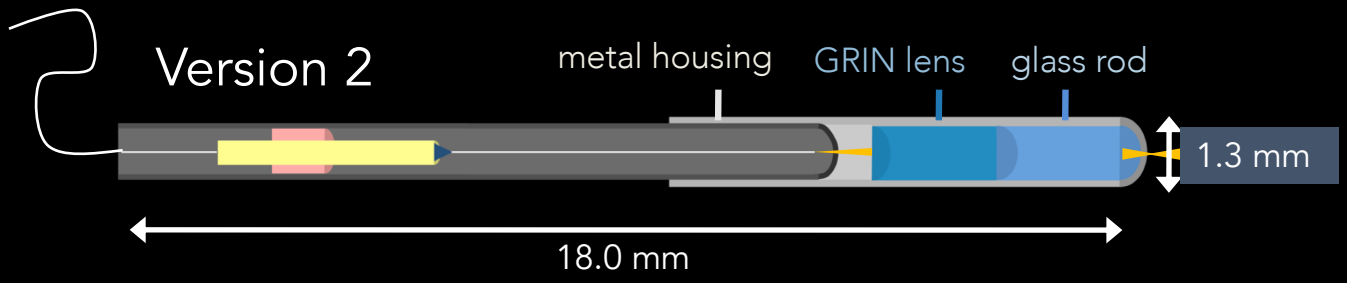
Lurie, K. L., et. al, *Opt. Letters*, **40** (13), 3165-3168 2015.

Scanning fiber endoscopy (SFE)

Lens assembly for OCT imaging





Smallest, fastest, forward-viewing OCT probe for 3D volumetric imaging

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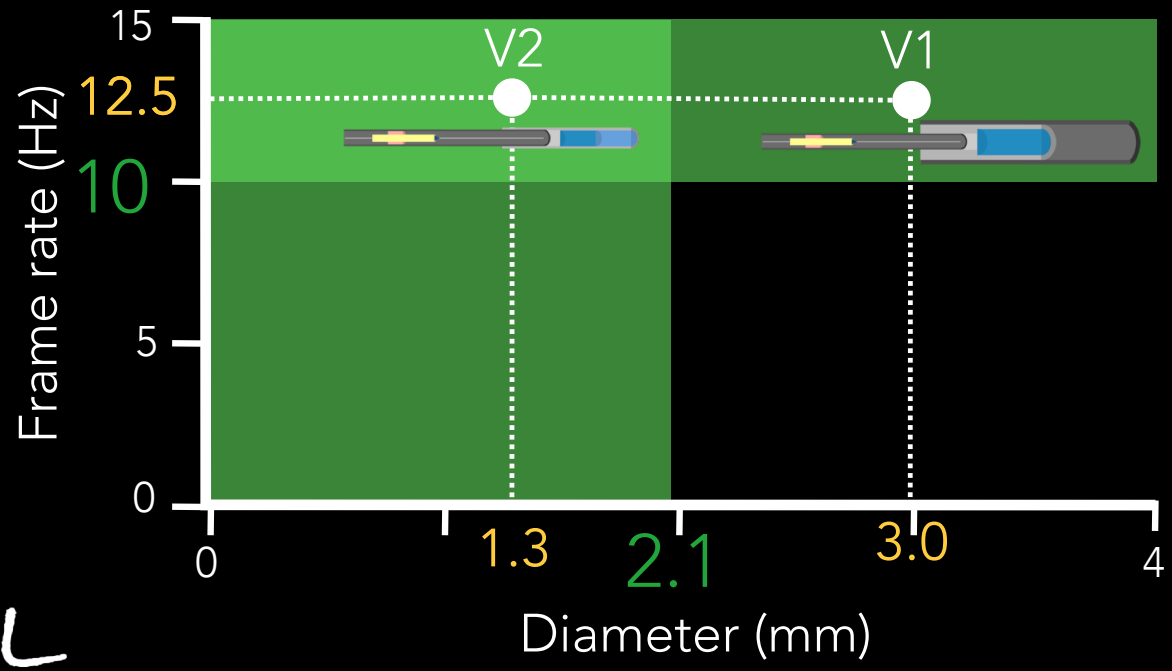
OCT scope integration with flexible WLC

Achieving design requirements



Current plans for V3 will push our new design off the chart

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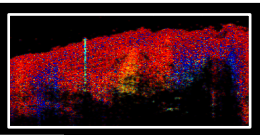
New optical tools

Polarization sensitive OCT (PS-OCT)
Label-free, enhanced contrast



1		2		3		4	
Clinical WLC	Low sensitivity	Bluelight-WLC	Low specificity at detecting CIS	WLC guided-surgery	Poor margin detection	Review records	Limited records
	No staging						
↓		↓		↓		↓	
Clinical OCT-WLC	Higher sensitivity	PSOCT-WLC	High specificity at detecting CIS	OCT-WLC guided-surgery	Subsurface evaluation	Review 3D models	Complete records
	Staging ability						
↓		↓		↓		↓	
OCT scope for flexible WLC		OCT biomarkers		OCT mosaicking		3D OCT and WLC records	

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CIS is responsible for 75% of BC recurrence

CIS

Carcinoma in situ (CIS) is a flat tumor with high risk of recurrence and progression

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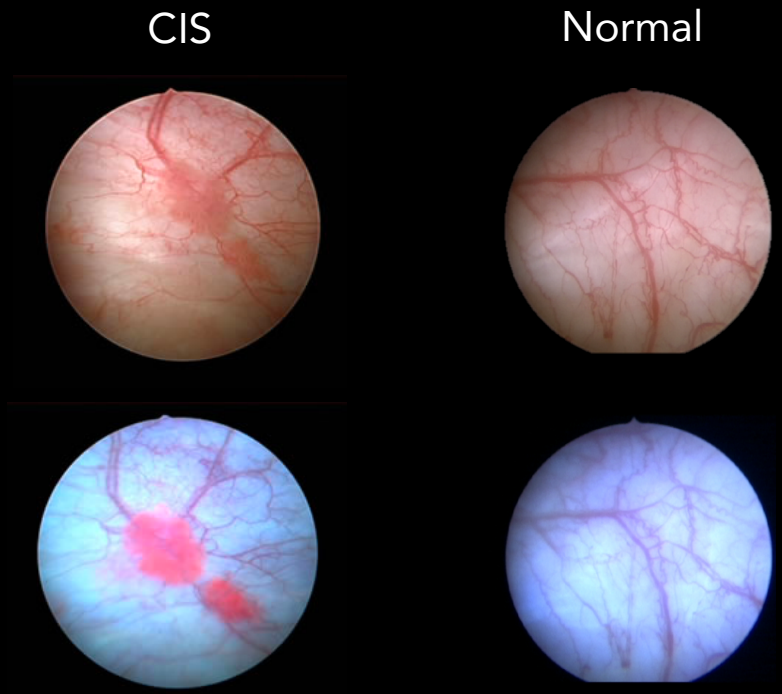
Blue light cystoscopy increases sensitivity at detecting CIS



Cancerous regions light up as a bright pink patch under blue light

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Image credit: Jeong Byong C. *Bladder Cancer*, 135-144 (2018)
Image credit: Gennifer T. Smith, et al. *Biomed. Opt. Express* **7,** 648-662 (2016);

...but it lacks specificity

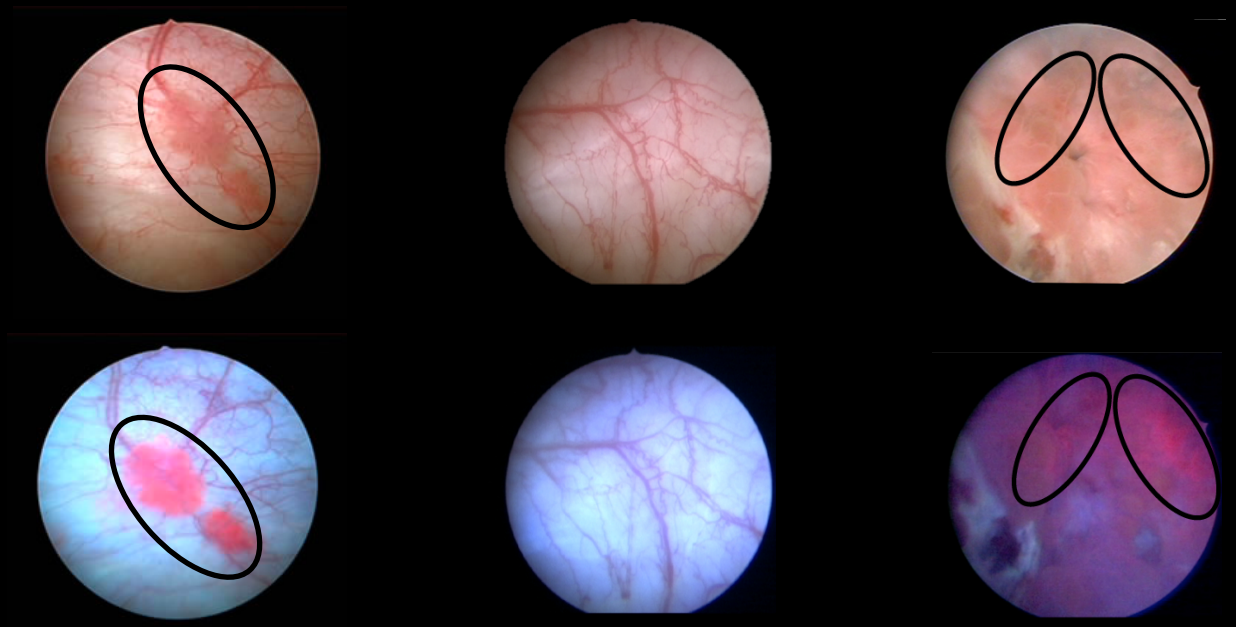

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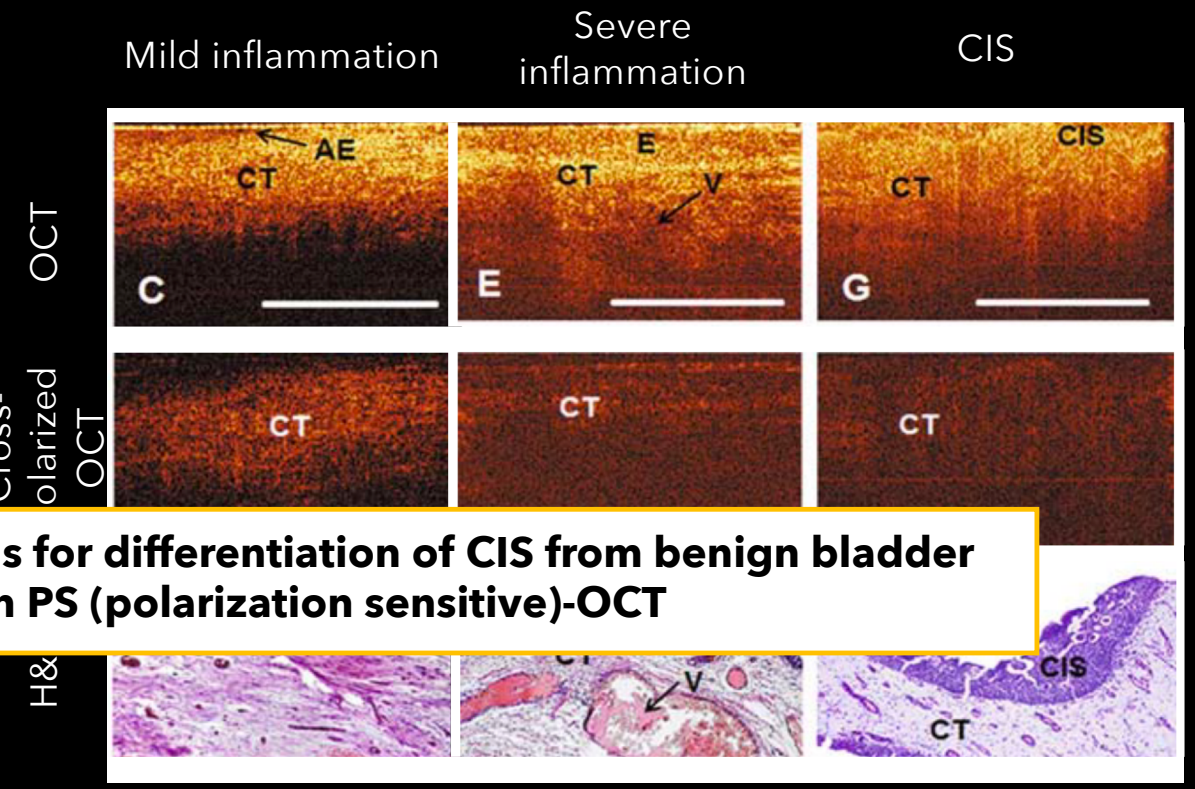
Image credit: Jeong Byong C. *Bladder Cancer*, 135-144 (2018)
Image credit: Gennifer T. Smith, et al. *Biomed. Opt. Express* **7,** 648-662 (2016);

Polarized light improves differentiation of tumor against inflammation

- Polarized light: additional contrast
- Lamina propria layer of the bladder is rich in **collagen**[1]
- Cross-polarization OCT has been shown effective for **inflammation vs. CIS**[2] – qualitative, only depolarizing ef



Goal: Quantitative analysis for differentiation of CIS from benign bladder tissues with PS (polarization sensitive)-OCT

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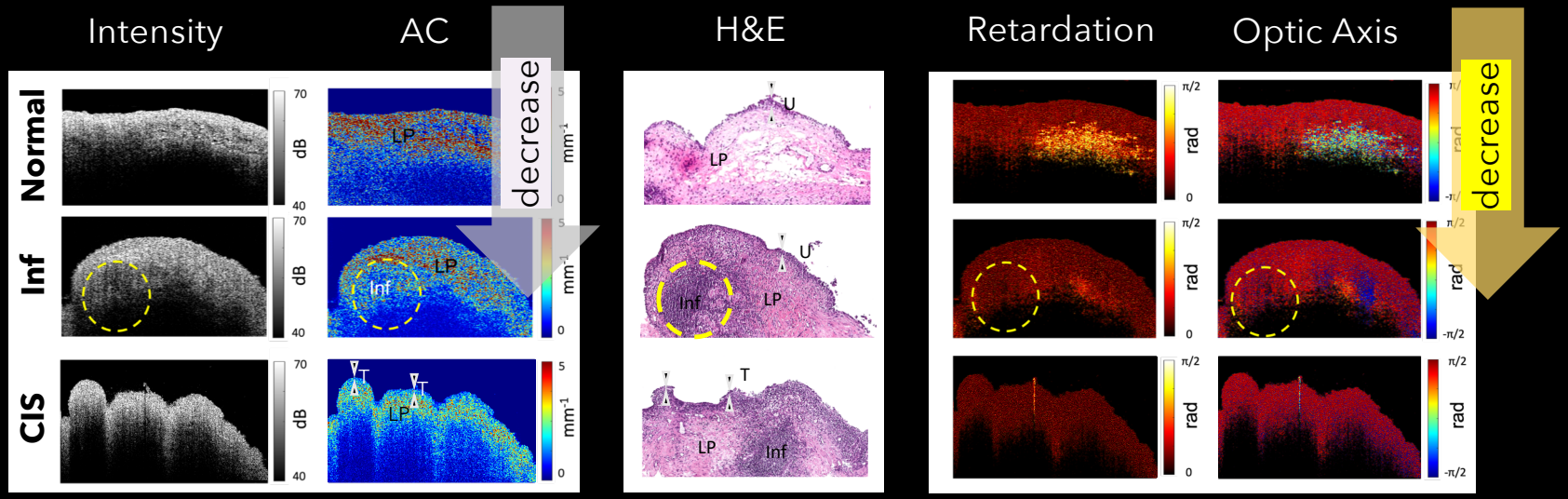
1. Ewalt, D. H. *et al. J Urol* (1992).
2. Kiseleva, E. B. *et al. Sovrem. Tehnol. v Med* (2017).

Matched PS-OCT – histology image pairs



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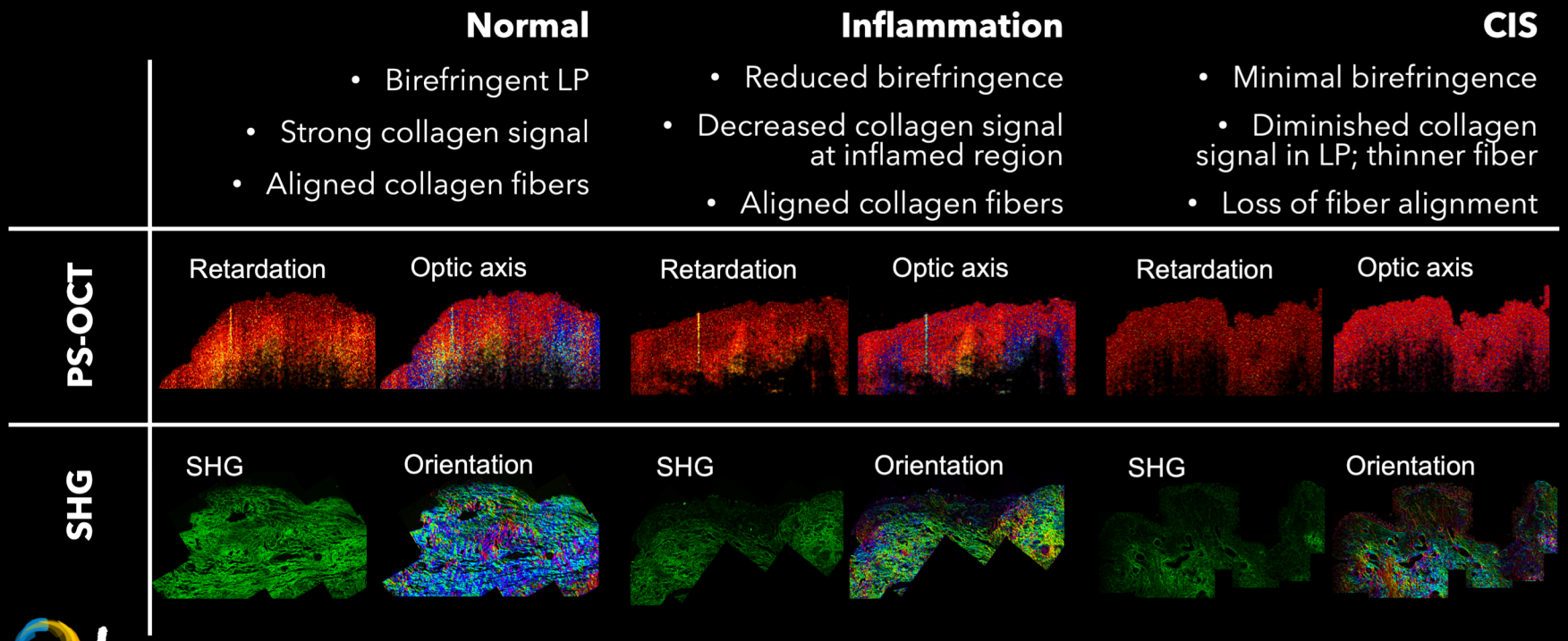
Alteration in collagen causes decrease in measured birefringence



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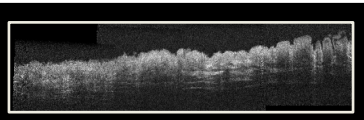
New image reconstruction methods

Mosaicking

1	2	3 	4
Clinical WLC	Bluelight-WLC	WLC guided-surgery	Review records
Low sensitivity	Low specificity at detecting CIS	Poor margin detection	Limited records
No staging			
↓	↓	↓	↓
Clinical OCT-WLC	PSOCT-WLC	OCT-WLC guided-surgery	Review 3D models
Higher sensitivity	High specificity at detecting CIS	Subsurface evaluation	Complete records
Staging ability			
↓	↓	↓	↓
OCT scope for flexible WLC	OCT biomarkers	OCT mosaicking	3D OCT and WLC records

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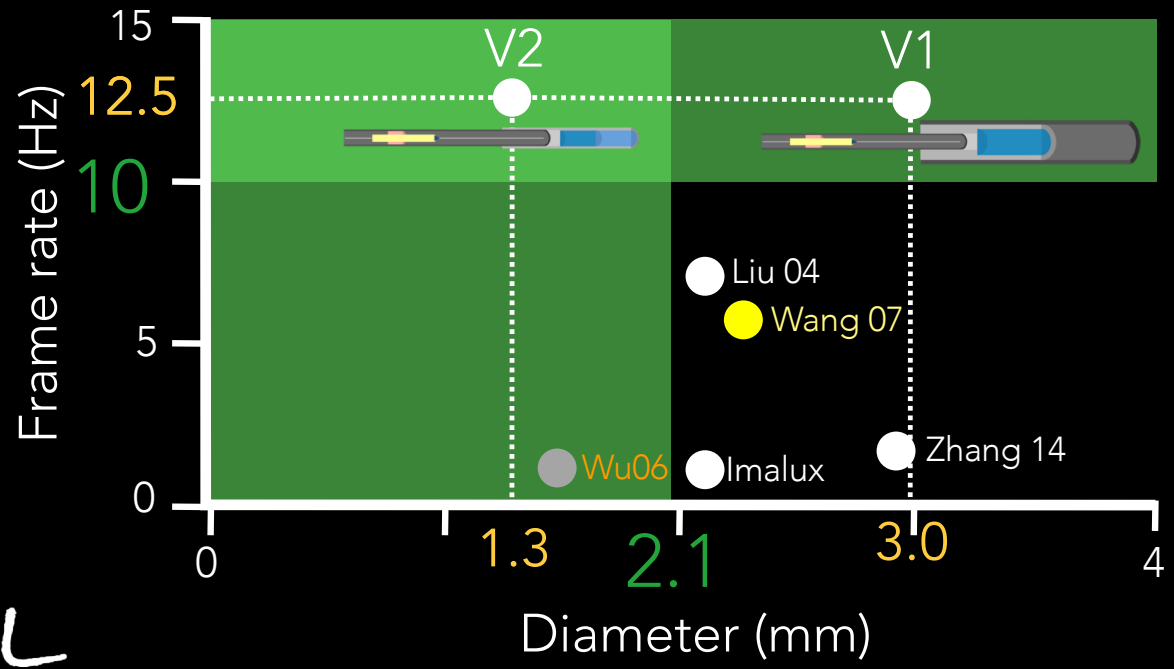
OCT scope integration with flexible WLC

Tradeoffs

Smaller parts, but smaller field of view

Higher resonance frequency, but sparse volume sampling



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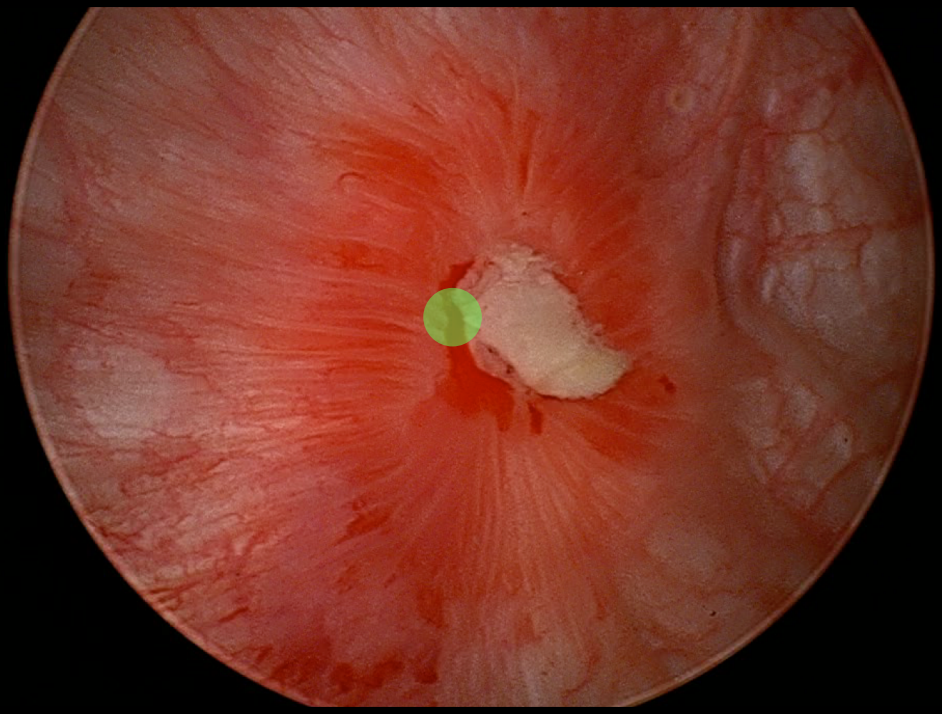
Challenge with OCT for subsurface evaluation: OCT's small field of view



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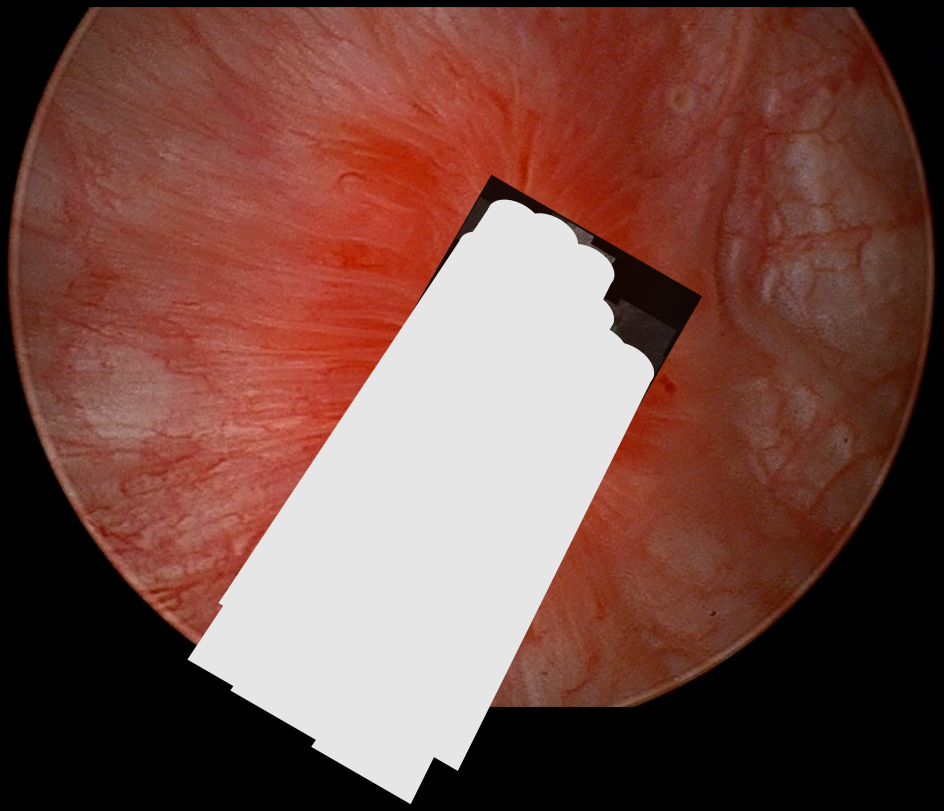
Mosaicking:
overcoming OCT's small field of view



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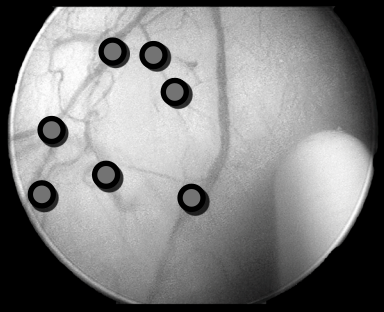
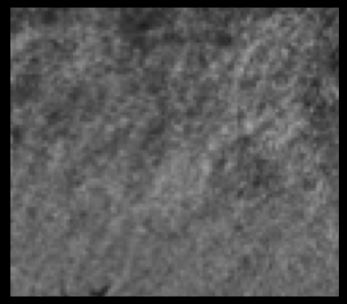
Standard mosaicking approaches cannot be directly applied to bladder OCT data

Limited features
(distinct regions)

WL image



En face
OCT image



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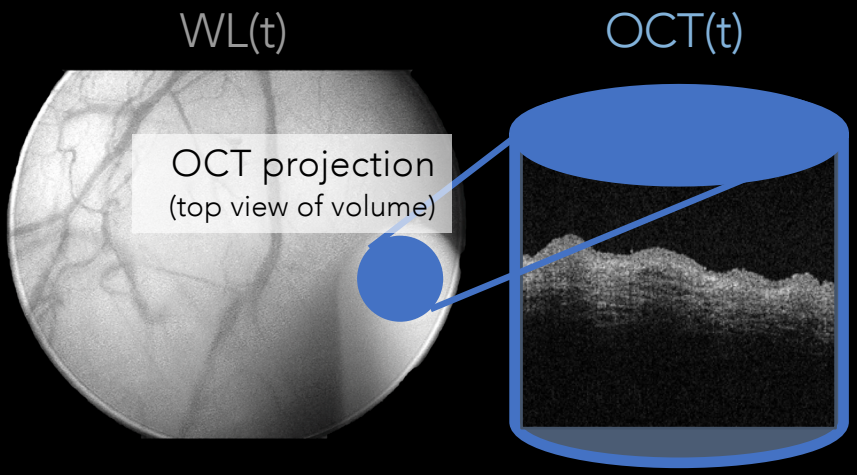
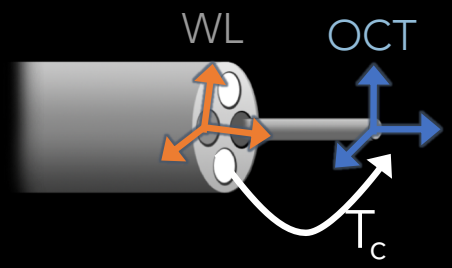
OCT-WLC system

Acquired data





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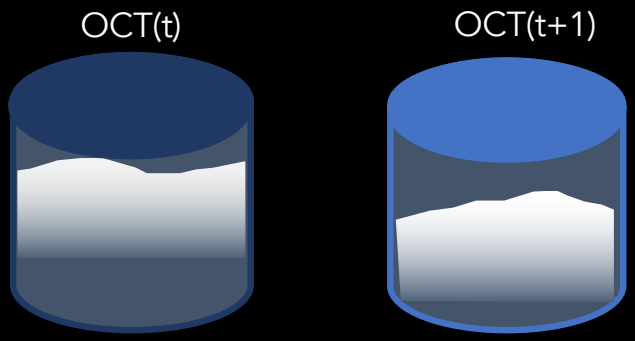

Utilize WL data to initialize alignment

Extract surface to refine alignment

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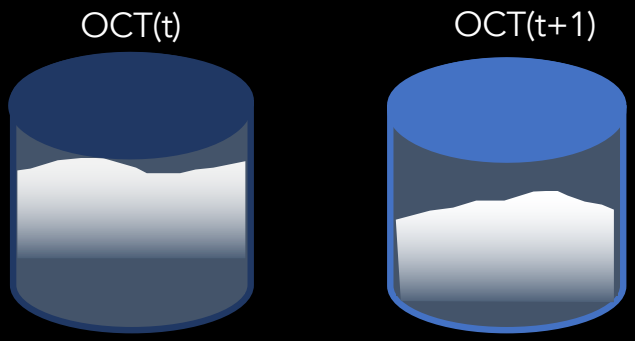

Utilize WL data to initialize alignment

Extract surface to refine alignment

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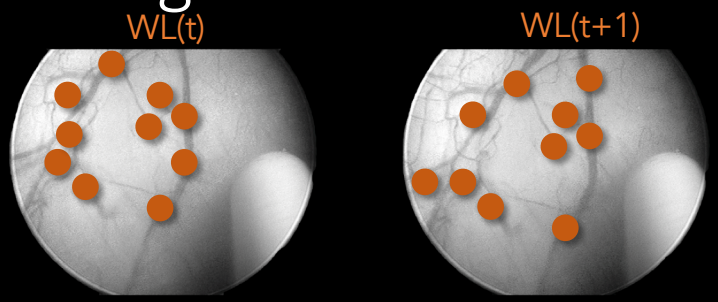
Align white light images

Detect features



Utilize WL data to initialize alignment

Extract surface to refine alignment

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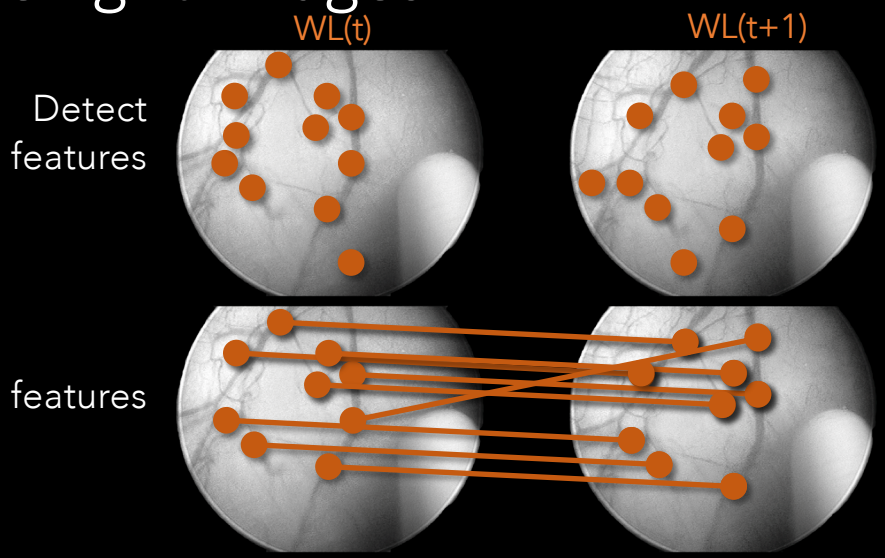
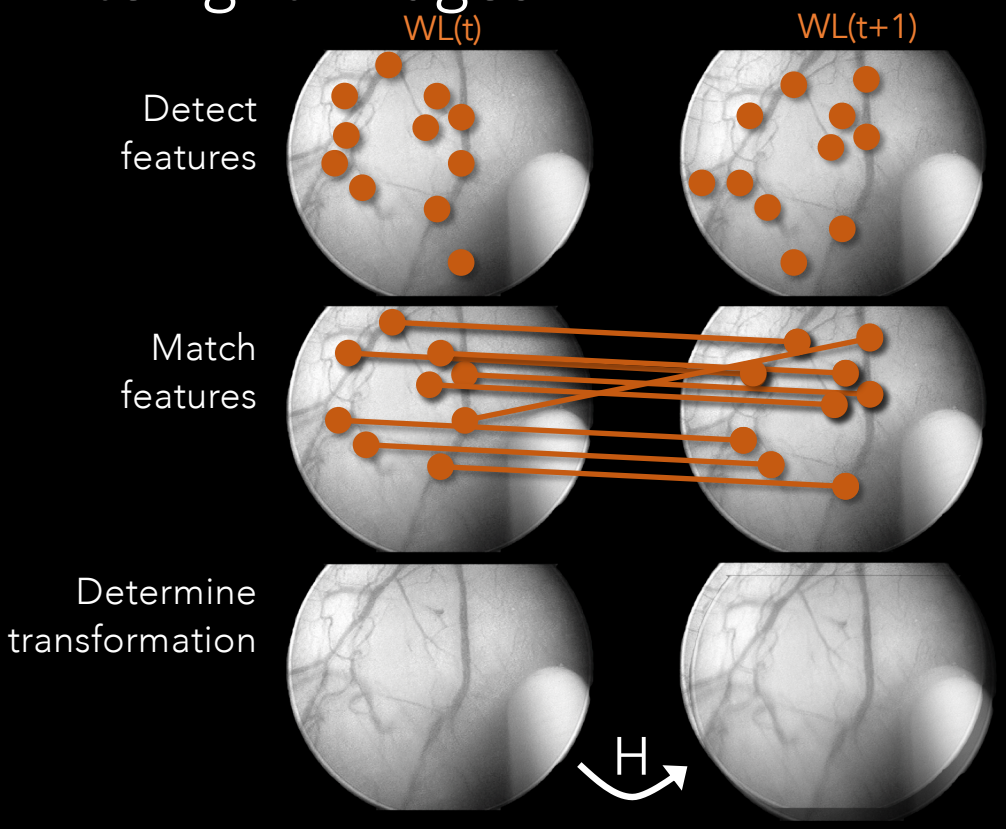
Align white light images



Utilize WL data to initialize alignment

Extract surface to refine alignment

Align white light images



Utilize WL data to initialize alignment

Extract surface to refine alignment

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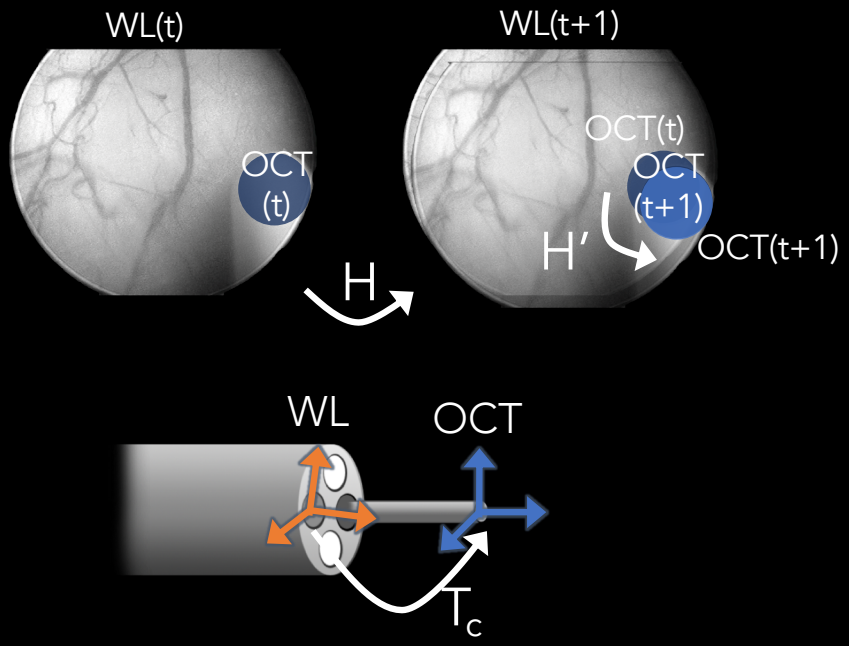
Initialize alignment of OCT volumes

using white light transformation and relationship between coordinate systems



Utilize WL data to initialize alignment

Extract surface to refine alignment

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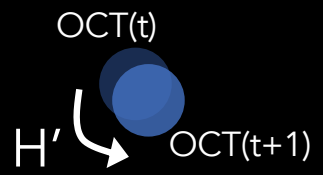
Initial alignment only aligns OCT projections (2D)

Need 3D information to align volumes in 3D



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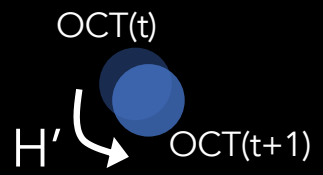
Utilize WL data to initialize alignment

Extract surface to refine alignment

Initial alignment only aligns OCT projections (2D)

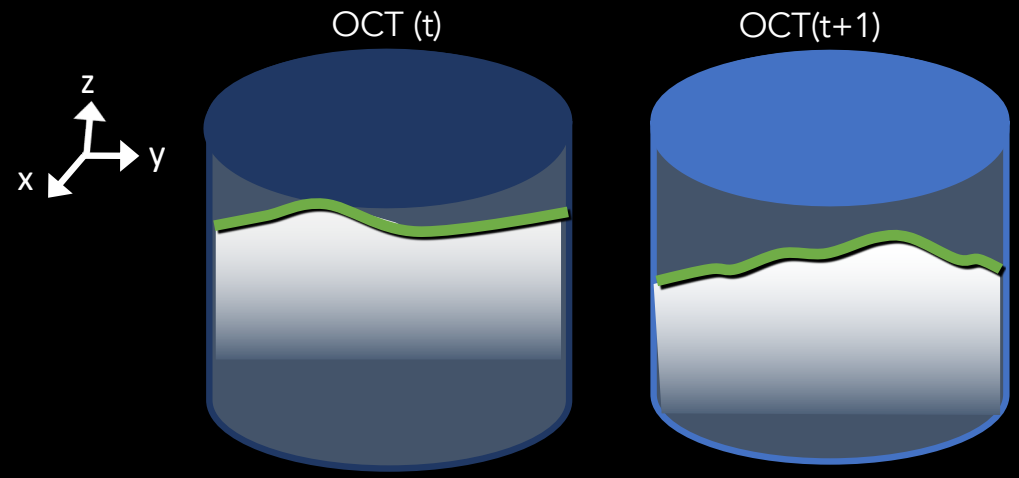
Need 3D information to align volumes in 3D



Utilize WL data to initialize alignment

Extract surface to refine alignment

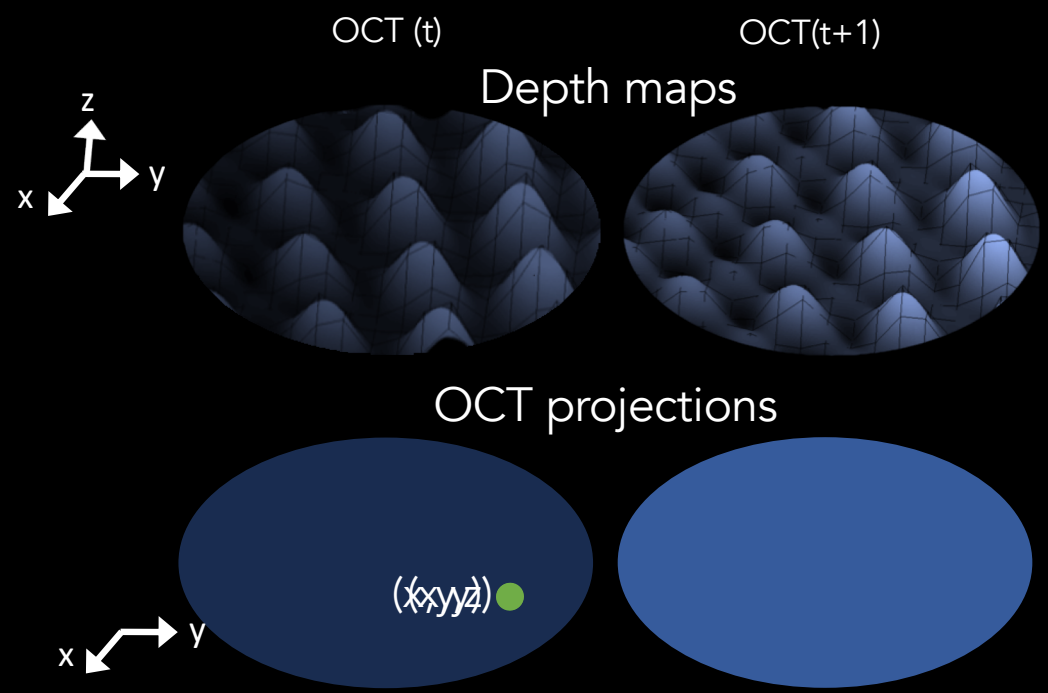
3D information comes from tissue surface



Utilize WL data to initialize alignment

Extract surface to refine alignment

3D transformation is initialized using surface depths



Utilize WL data to initialize alignment

Extract surface to refine alignment

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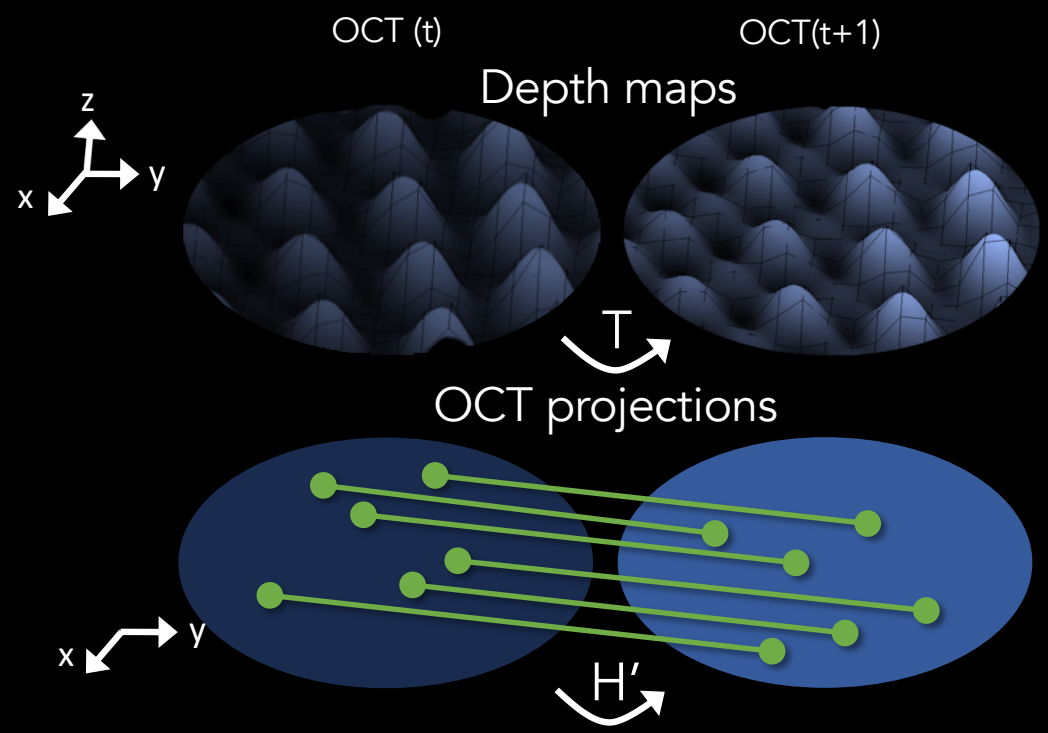
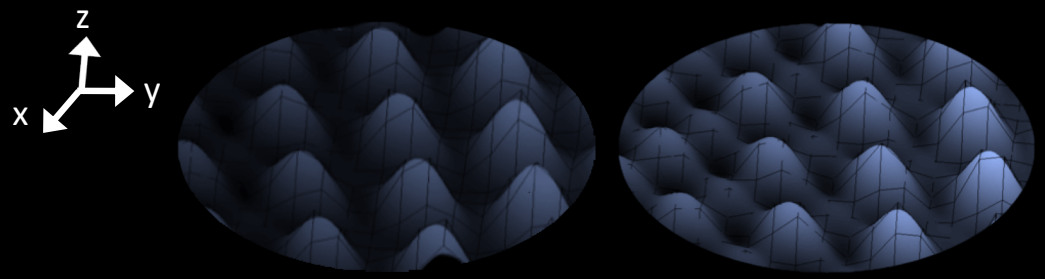
3D transformation is initialized using surface depths



Utilize WL data to initialize alignment

Extract surface to refine alignment

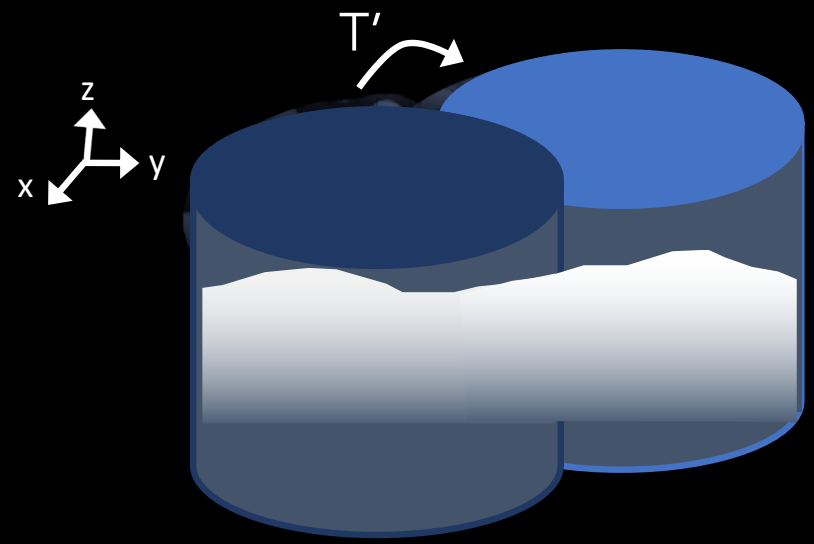
3D transformation is initialized using surface depths



Utilize WL data to initialize alignment

Extract surface to refine alignment

Surfaces are aligned to achieve final volume alignment



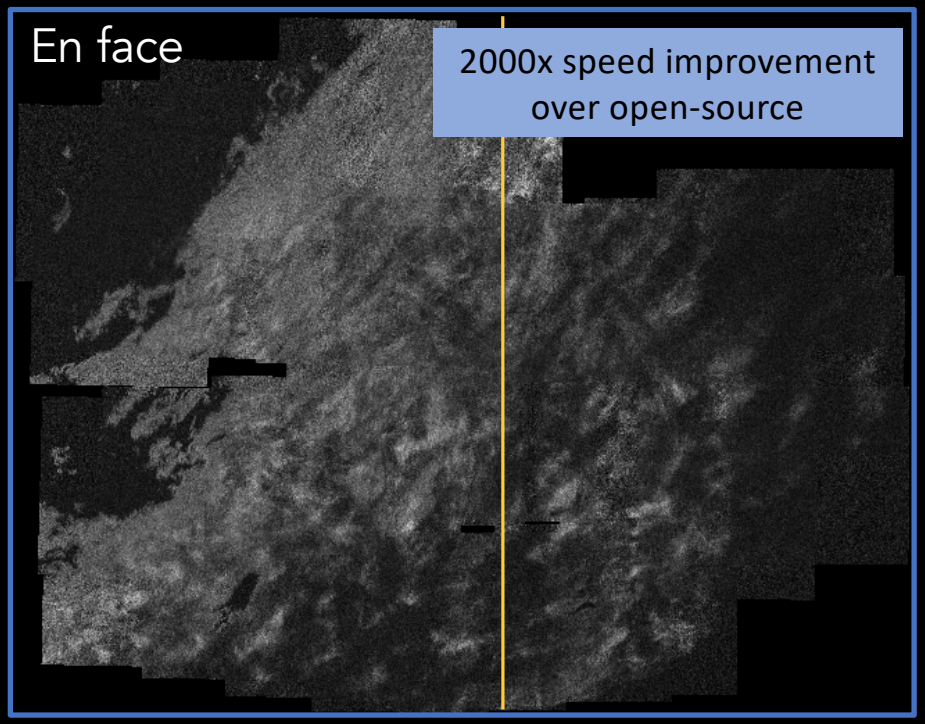
Utilize WL data to initialize alignment

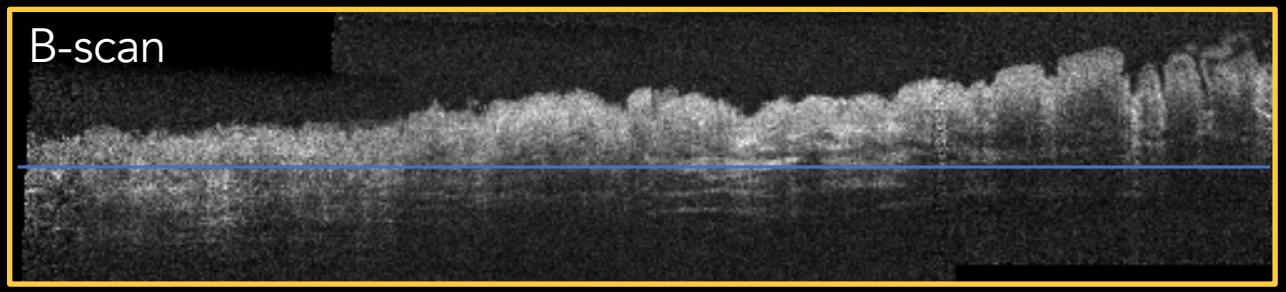
Extract surface to refine alignment

Bladder mosaic

Mosaicked volumes
33

Total volume (cm^3)
1.3 x 1.0 x 0.4





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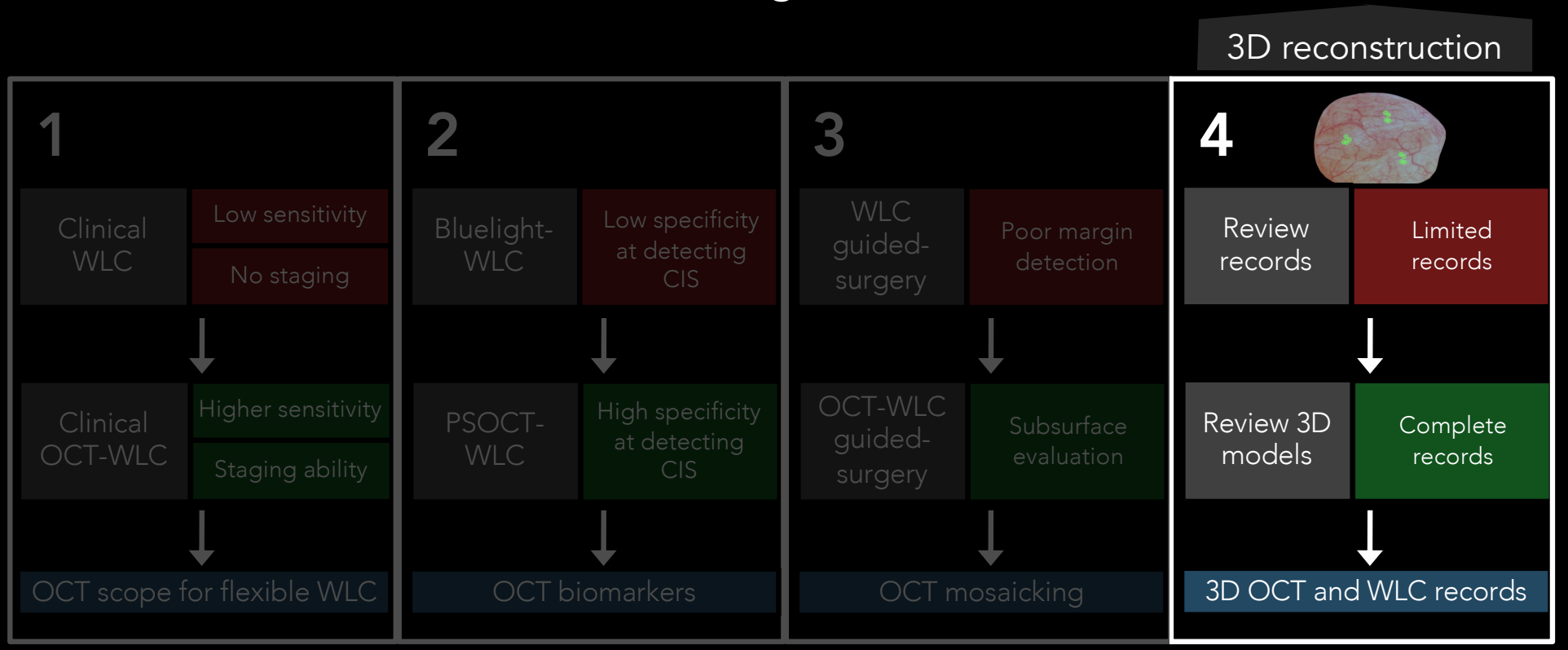
Lurie et al, IEEE TBME (2014)

New image reconstruction methods



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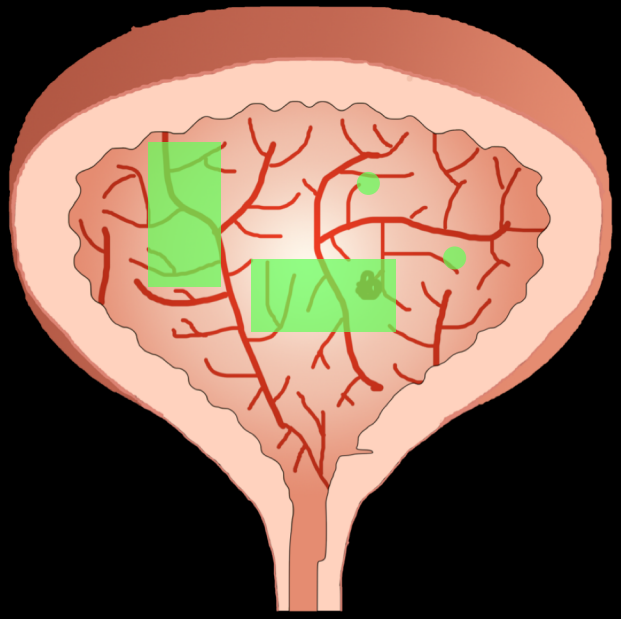
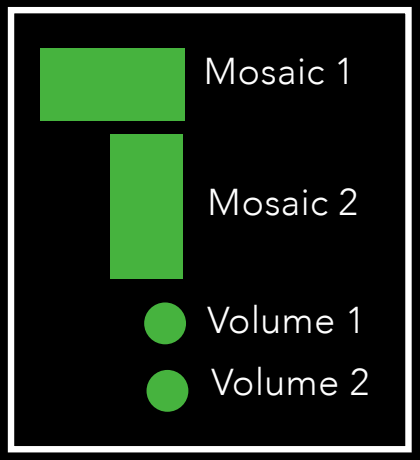
Limitation of mosaics

Detailed record of small region, but no global location

Collected data



Saved record



Bladder location of OCT data can be used to relocalize tumors

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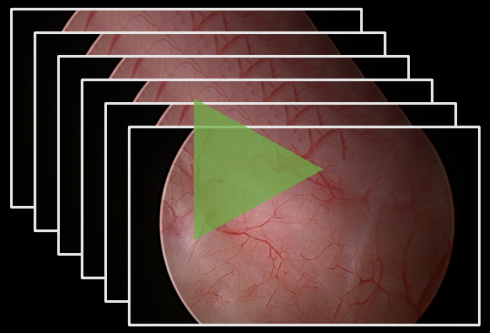
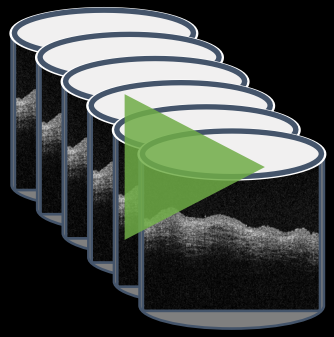
Cystoscopy data collection

Acquired data





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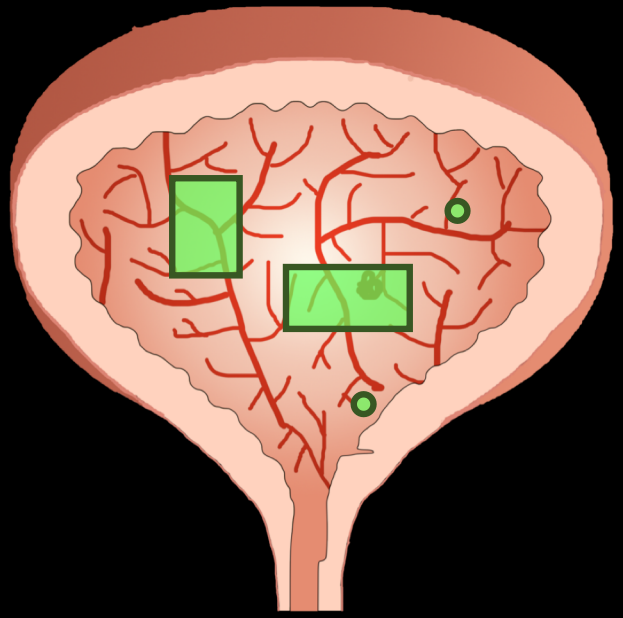
1. Reconstruct 3D model from WLC
2. Register OCT to model



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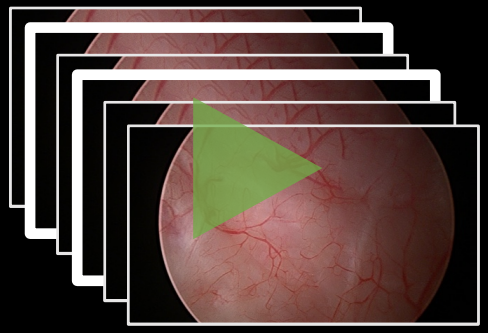
Feature detection between pairs of images

Hampered by lighting artifacts and low contrast

WLC image stream



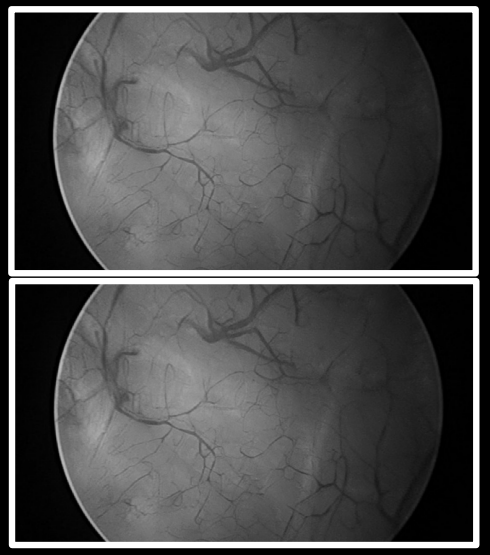


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Image preprocessing aids robust feature detection

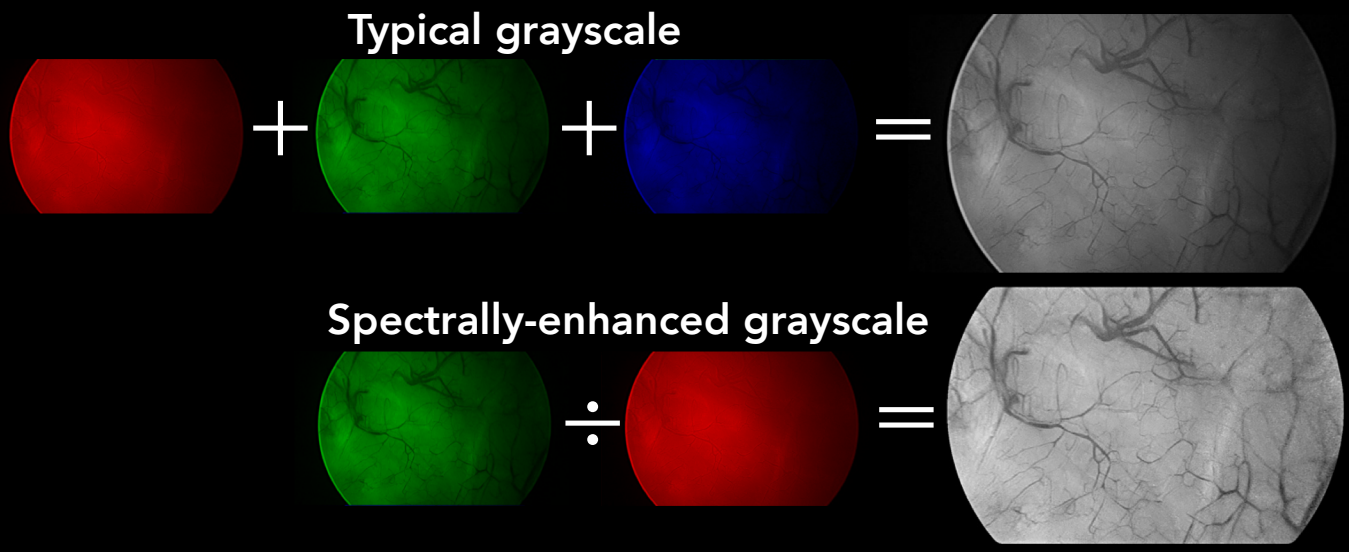

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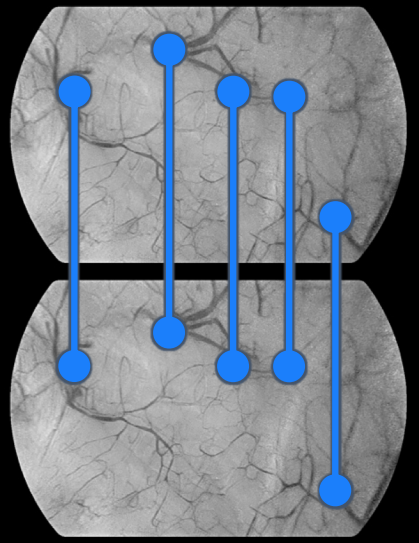
Image preprocessing aids robust feature detection



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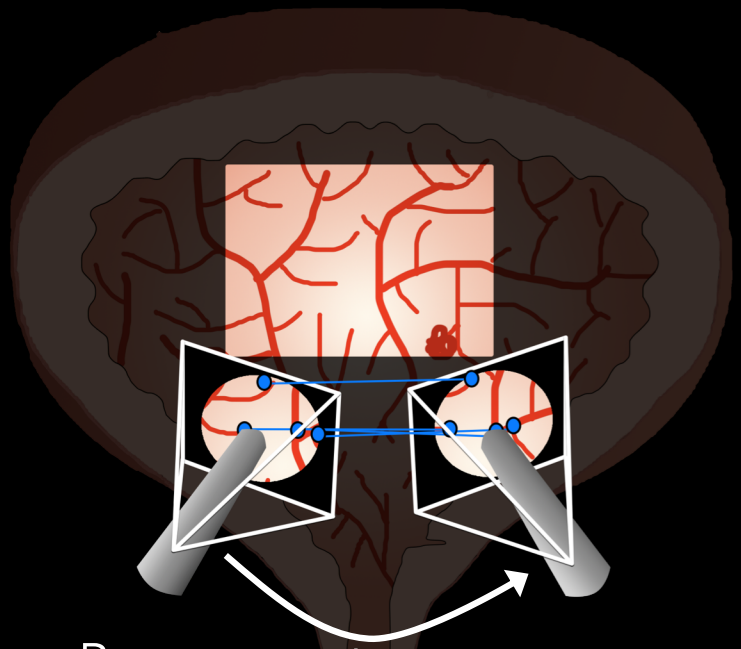
Structure from motion



Recover cystoscope pose
(position and orientation)

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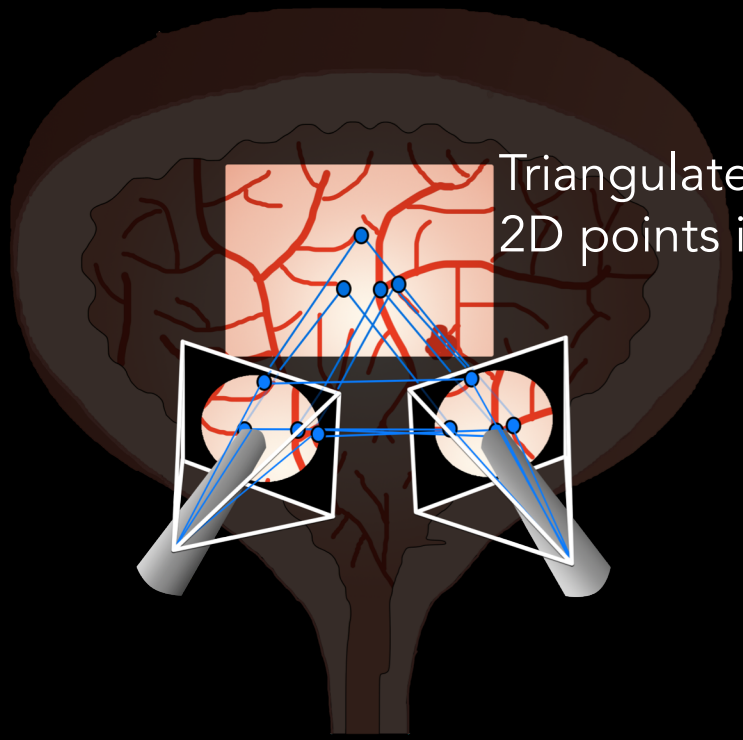
Structure from motion



Triangulate
2D points into 3D

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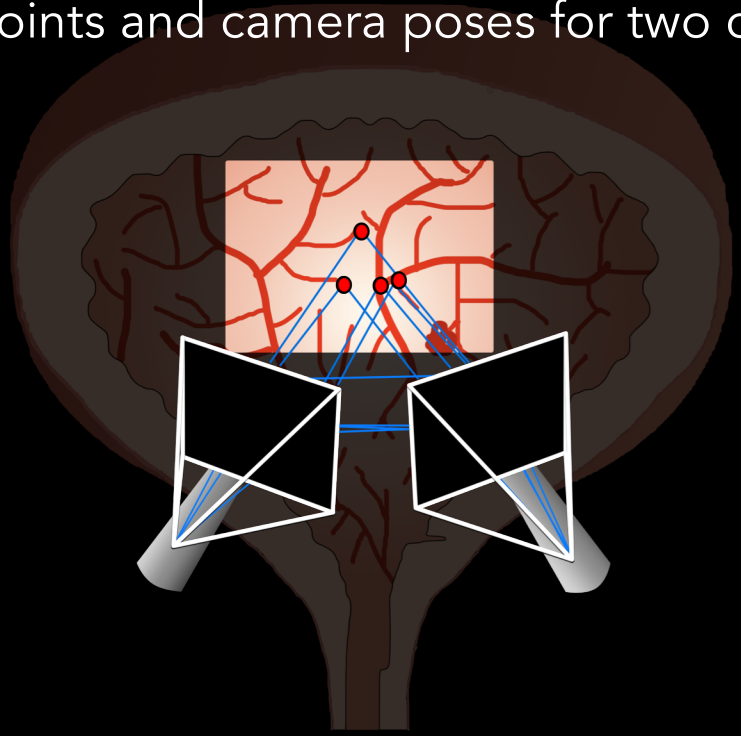
Structure from motion

Recover 3D points and camera poses for two cameras



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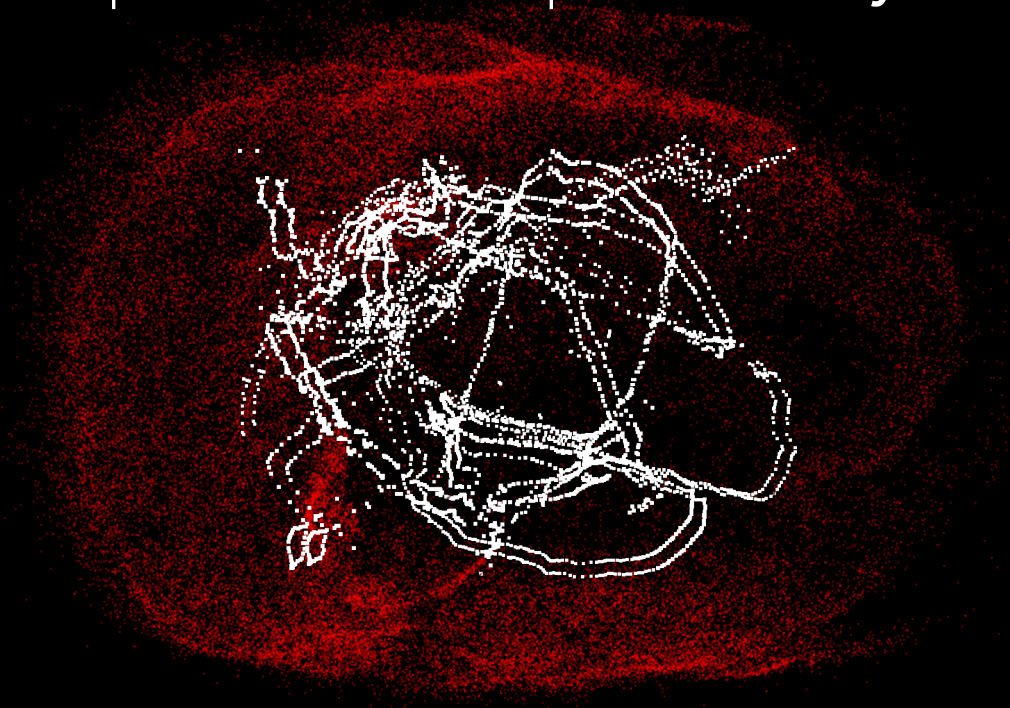
Structure from motion

Recover 3D points and camera poses for ***many*** cameras



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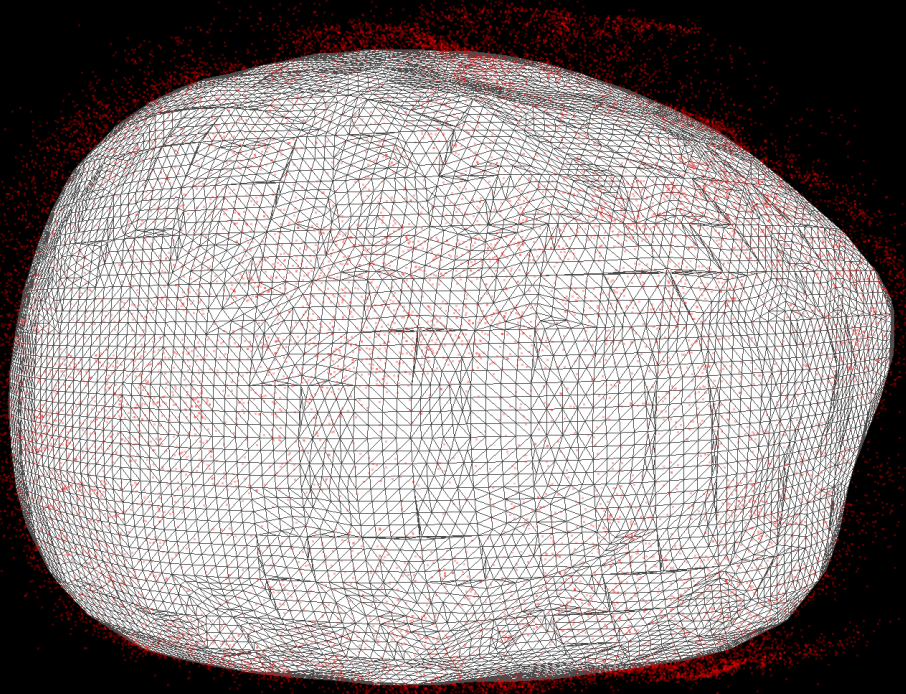
Convert point cloud to bladder shape



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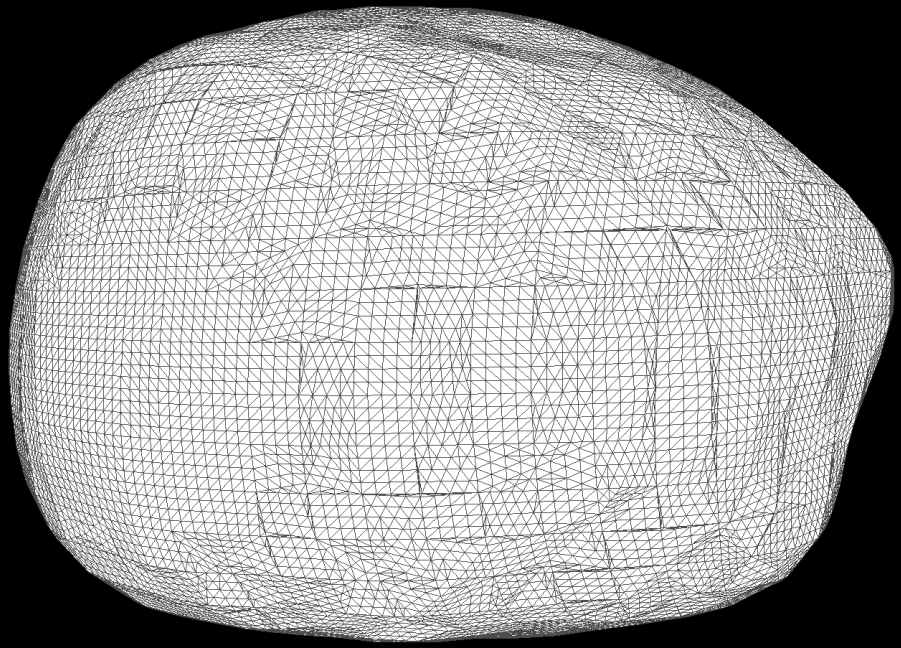
Convert point cloud to bladder shape



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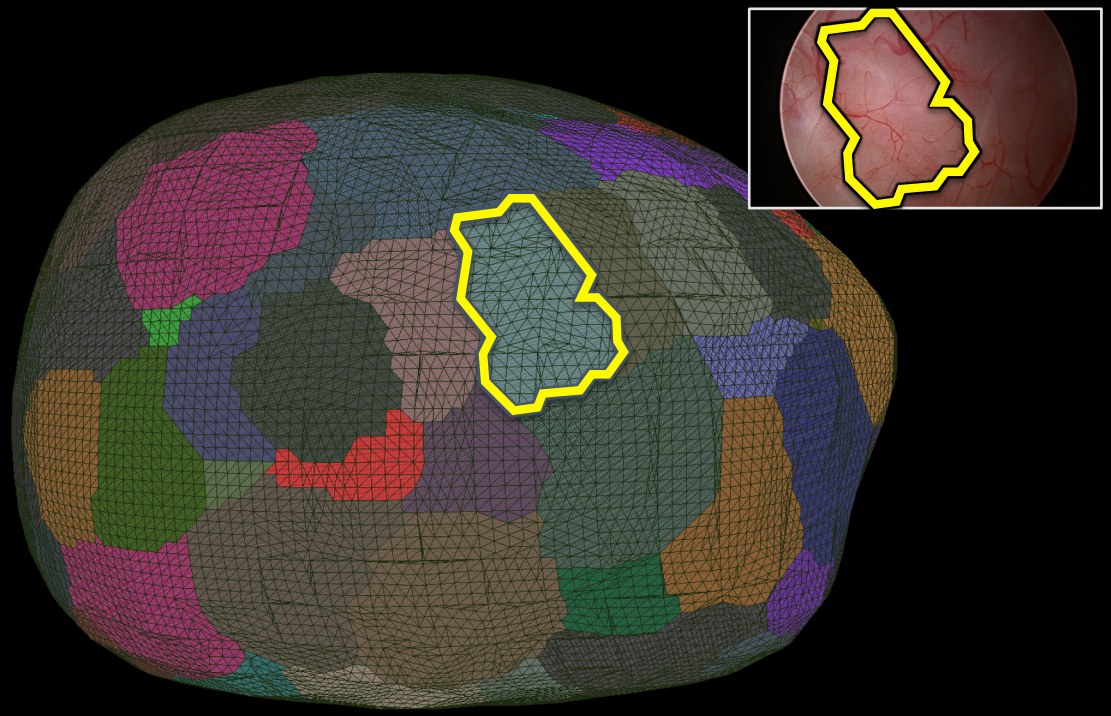
Add bladder appearance

Select images



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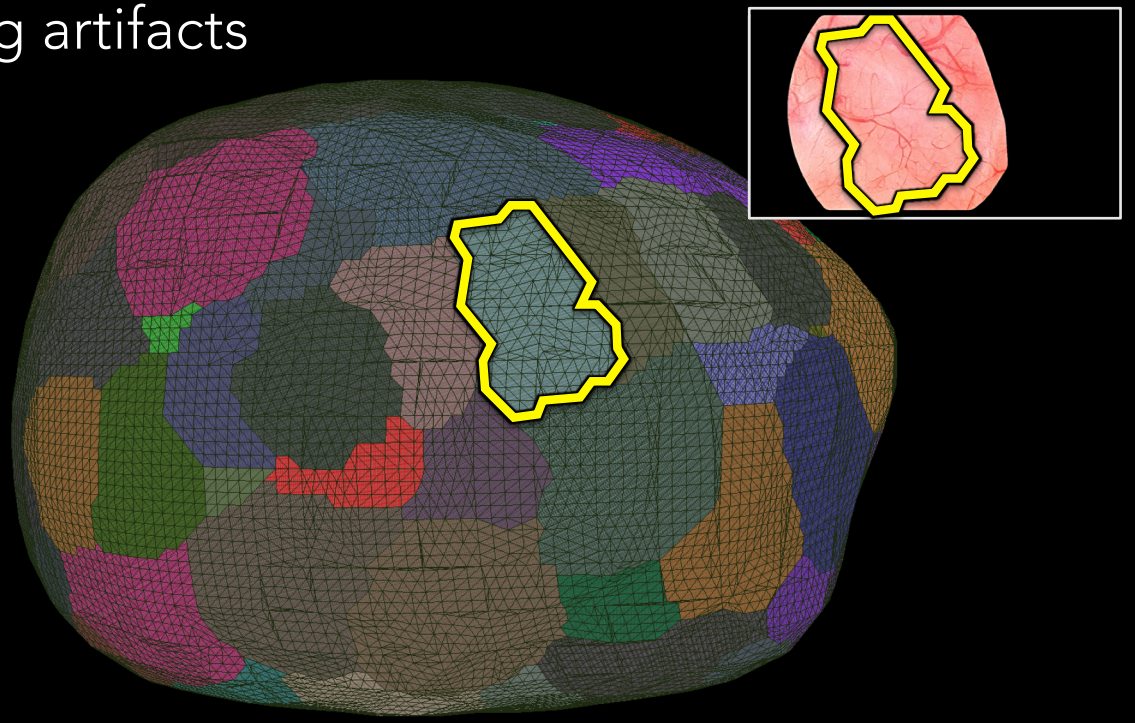
Add bladder appearance

Remove lighting artifacts



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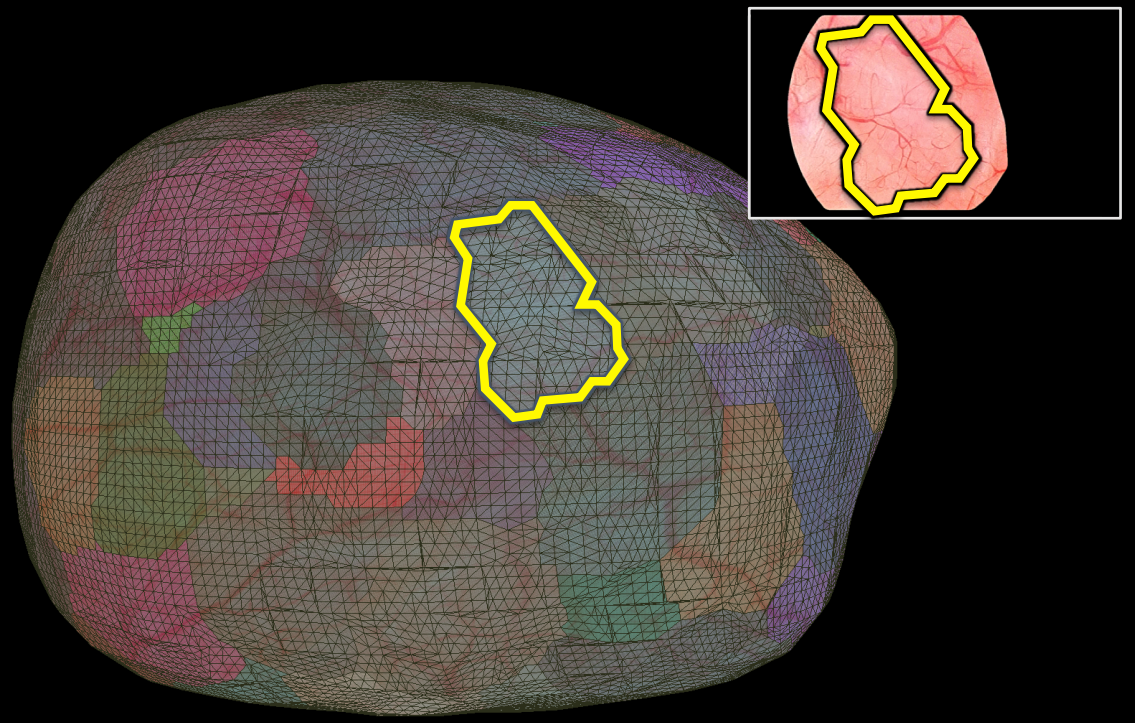
Add bladder appearance

Overlay images



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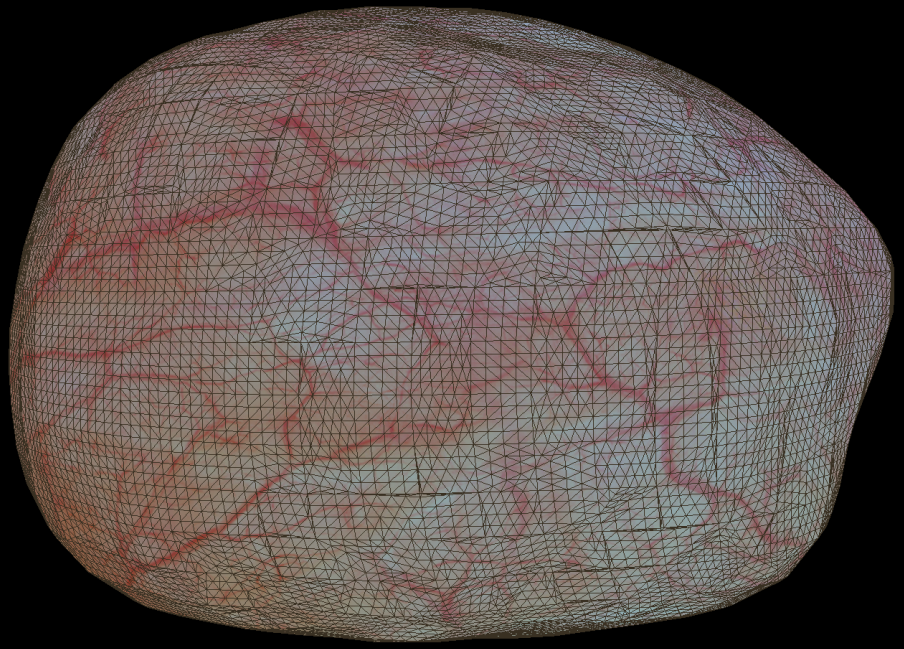
Final 3D bladder model

captures shape and appearance of bladder



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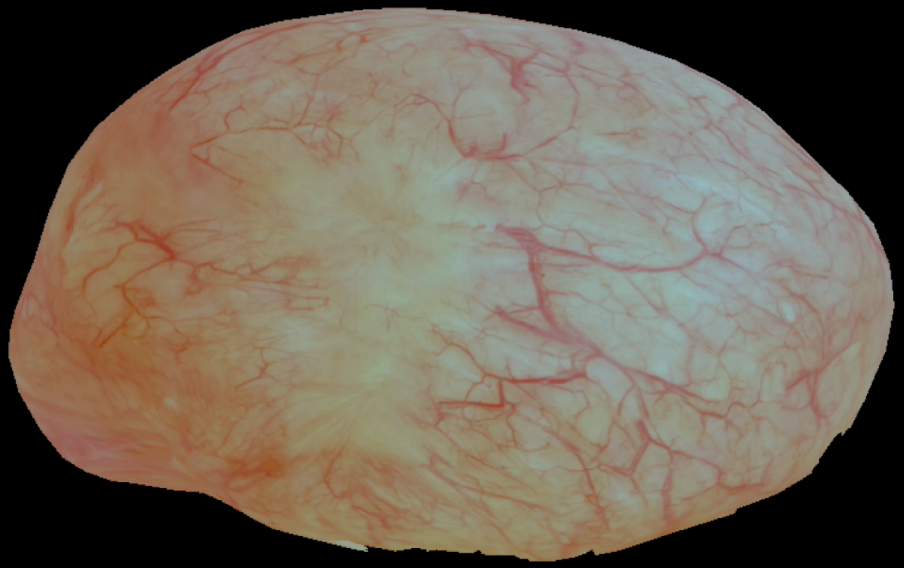
Virtual cystoscopy



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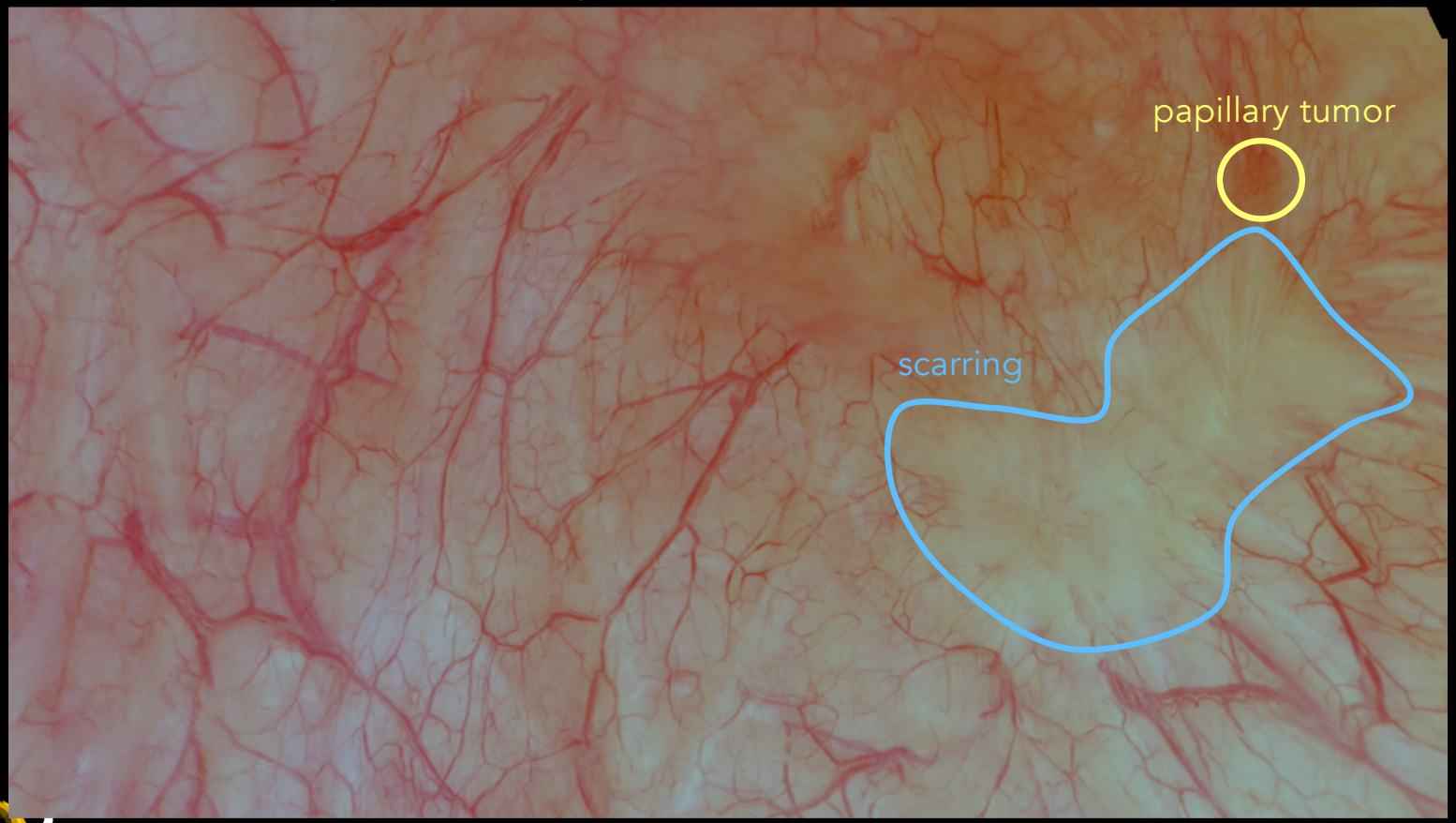
Virtual cystoscopy



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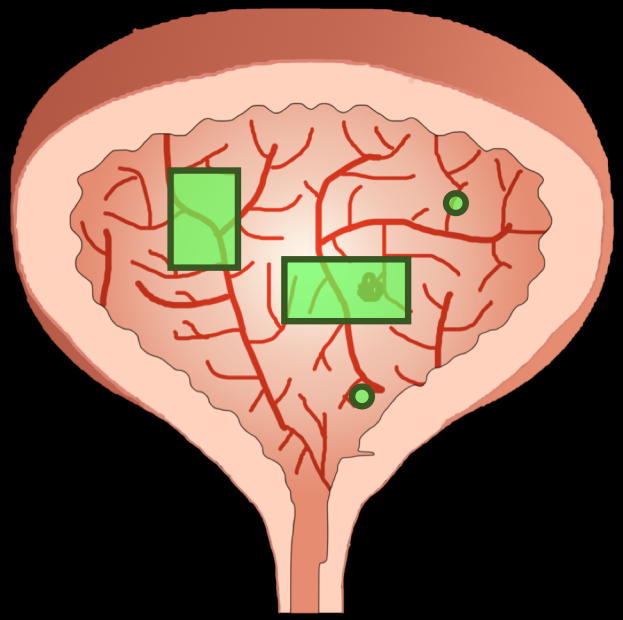
1. Reconstruct 3D model from WLC
2. Register OCT to model



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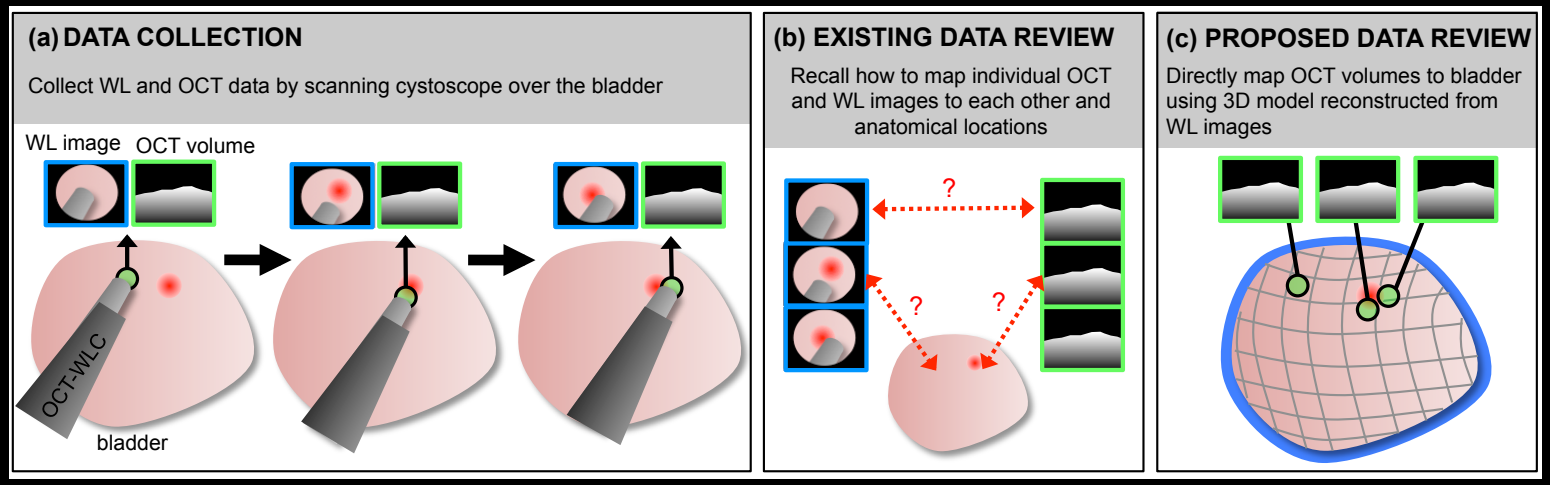

3D bladder model

PS-OCT volume stream

PS-OCT volumes registered to 3D model

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Enable early, comprehensive, accurate detection of bladder cancer

Related Lab publications

Three-dimensional, distendable bladder phantom for optical coherence tomography and white light cystoscopy Lurie et. al, JBO 19(3), 2014.

Multimodal 3D cancer-mimicking optical phantom Smith et. al, Biomed Opt. Exp, 7(2), 2015.

Automated mosaicing of feature-poor optical coherence tomography volumes with a freehand dual-modality probe Lurie et. al, IEEE Trans. in Biomed. Eng. 61(7), 2014.

Rapid scanning catherscope for expanded forward-view volumetric imaging with optical coherence tomography Lurie et. al, Optics Lett 40(13), 2015.

Automated, Depth-resolved Estimation of the Attenuation Coefficient From Optical Coherence Tomography Data Smith et al, IEEE TMI 34(12), (2015).

3D reconstruction and co-registration of cystoscopic video sequences for longitudinal Studies Lurie et. al, BOE 8(4), 2017.

Registration of optical coherence tomography data to 3D bladder models Lurie et. al, BOE 7(12), 2016.

A review of methods and applications of attenuation coefficient measurements with optical coherence tomography Chang and Bowden, JBO 24(0), 2019.

Automatically determining the confocal parameters from OCT B-scans for quantification of the attenuation coefficients Dwork et al, IEEE TMI 38(1), 2019.

Cost-efficient video synthesis and evaluation for development of virtual 3D endoscopy Zhou et al, IEEE JTEHM 9(12), (2021).

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Light on Dark Faces

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Personal experiences in Academia

- On being Black …
  - At Photonics West
  - At the Faculty Club
- On being “young”…
- On being a woman …
- On being …

Systemic racism: “…living in a system not designed with you in mind”

-- Bishop T D Jakes

The Best Algorithms Struggle to Recognize Black Faces Equally

US government tests find even top-performing facial recognition systems misidentify blacks at rates five to 10 times higher than they do whites.

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Personal experiences in Academia

Pulse Oximeters are Important for Keeping all Patients Safe

On December 17, 2020, Sjoding *et al*. published a retrospective analysis of pulse oximetry (SpO2) data from two patient cohorts indicating that in some patients, occult hypoxemia was not detected when compared to paired oxyhemoglobin saturation measured by laboratory co-oximetry (SaO_2).[1] Occult hypoxemia was defined as an SaO_2 of < 90% when the paired SpO_2 measurements were 92% or greater. The authors compared sub-groups from the cohorts self-identifying as Black and White, and found that the incidence of occult hypoxemia was three times greater in Black patients (11.7%) compared with White patients (3.6%). As the authors noted, these findings, if correct, have important patient safety implications since patient triage based upon pulse oximeter measurements could fail to lead to appropriate escalation of care. As a retrospective, uncontrolled study without objective measurements of skin tone, the analysis

FDA warns pulse oximeters less accurate for people with darker skin

An article in NEJM reports that pulse oximeters missed occult hypoxemia in more

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An unequal burden...

- the unequal burden of **service** we have to help our universities have diverse committees

- the unequal burden of **extra activities** we take on -- going to professional conferences like NSBE/ARL to be around people who actually support us, talking to students of color on campus to serve as informal mentors and support, etc. -- all which take additional time directly from our research and also require funding that our universities usually don't give us

- the unfair **scrutiny** we get from entitled students who question our qualifications because of what they see (sometimes leading to lower teaching evaluations and seriously disrespectful comments that take a mental and emotional toll)

- the unequal **anxiety** we face when we go into a room full of people who don't look like us, not sure if we will be heard or acknowledged (even though everyone can see us), or if our picture will be used without permission on the cover of some university propaganda

- the unequal **rates of success** with grant proposals because our name tips reviewers (with unconscious bias) off that we may not be white.

- the unequal **fear** we face in working late at night on campus because of who might stop us or think we're suspicious

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An unequal burden...

- the unequal burden of **service** we have to help our universities have diverse committees

- the unequal burden of **extra activities** we take on -- going to professional conferences like ARL to be around people who actually support us, talking to students of color on campus to serve as informal mentors and support, etc. -- all which take additional time directly from our research and also require funding that our universities usually don't give us

- the unfair **scrutiny** we ge f what they see (sometimes leading to low take a mental and emotional toll)

- the unequal **anxiety** we ot sure if we will be heard or acknowledged (e out permission on the cover of some university p

... none of which are acknowledged in the tenure or promotion process or in any way, nor do they often bear compensation of any kind.

- the unequal **rates of success** with grant proposals because our name tips reviewers (with unconscious bias) off that we may not be white.

- the unequal **fear** we face in working late at night on campus because of who might stop us or think we're suspicious

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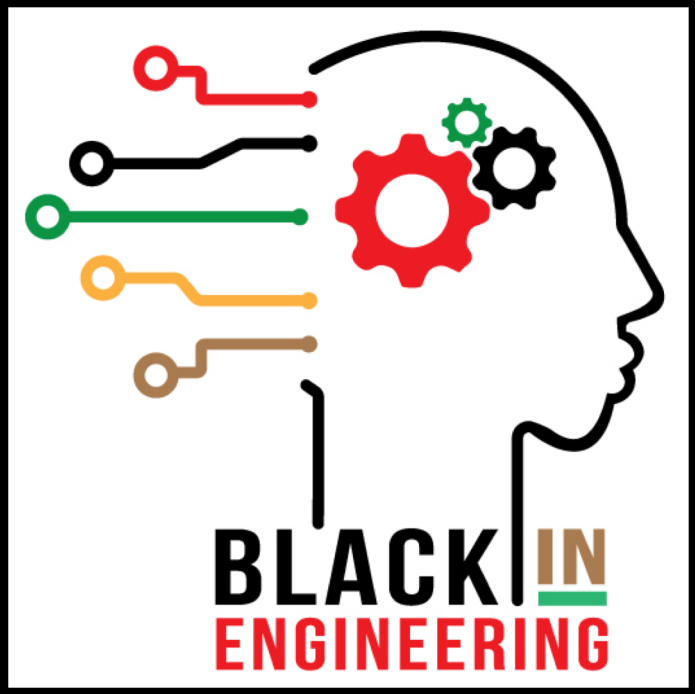
Black in Engineering Call to Action: On Becoming An Anti-Racist University



5 Principles

1. Attitude
2. Clarity
3. Institutional Accountability
4. Personal Accountability
5. Commitment and Resources

5 Constituencies

1. System-wide
2. Faculty
3. Staff
4. Graduate Students
5. Undergraduate Students

https://blackinengineering.org/action-item-list

Bowden and Buie, "Anti-Black racism in academia and what you can do about it," Nat Rev. Mat (2021)

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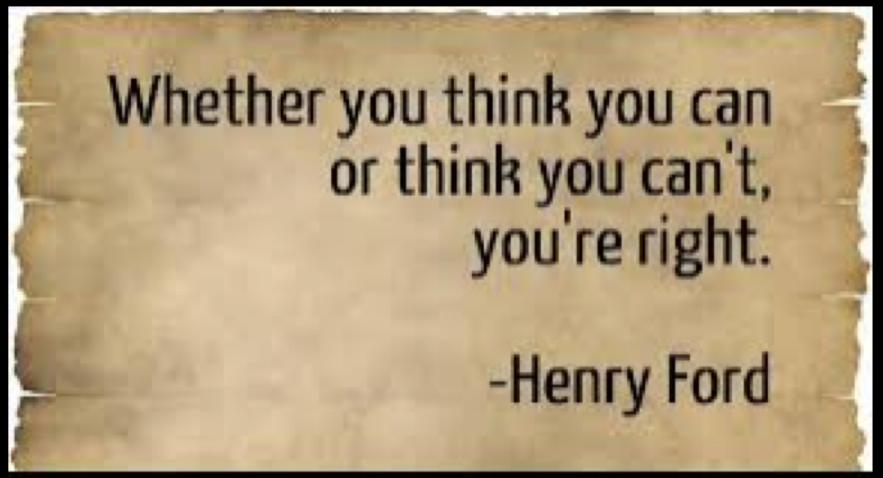
1. Attitude

- If you don’t approach this problem with the idea that you and your institution have work to do, you will find that nothing needs to be done.
- Whatever our history, the future is ours to affect. The system is *us*.
- Refusal to acknowledge this responsibility makes you complicit in perpetuating systemic racism.



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Call To Action: Recommendations on How To Become An Anti-Racist Institution

System-wide

Faculty

Staff

Graduate students

Undergraduate students

Education - training - recruitment - retention - policing - disaggregation - tokenism - community-building - funding - fundraising - accountability - promotion - mental health - admissions - networking ...

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How to Become An Anti-Racist Individual

Honestly acknowledge and repair my university's and society's racial histories

What aspects of my society or design of my university's policies and structures do I routinely overlook as contributing to racism?

In what ways do I benefit from systems where the "rich get richer" or that perpetuate intellectual impoverty?

How does my scholarship or area of interest overlook the impacts on or contributions of Black individuals?

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How to Become An Anti-Racist Individual

Examine my biases and begin to unlearn them

Acknowledge that a student's success should not be dependent on their identity, high school, or their knowledge of "the hidden curriculum"

What knowledge or expectations do I assume students have to succeed in my classroom or profession?

What process can I undertake to reveal and unlearn my personal biases?

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How to Become An Anti-Racist Individual

Acknowledge, applaud, and reward the efforts of Black staff, faculty, and students in building and improving the institution.

What Black staff, faculty or student can I acknowledge, applaud or reward this week?

Administrators: commit resources and people to actionable goals in recruiting, retaining, and supporting Black faculty, staff, and students.

What committees or people have I failed to adequately resource to take immediate action to achieve our goals?

Welcome Black members of the university as full participants, rather than treat them as tokens.

In what way have I failed to include Black members of the university as a vital partner in our institution's aspirations for greatness?

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Thank you!