Cancer Viewing Glasses for Fluorescence Image-Guided Cancer Surgery

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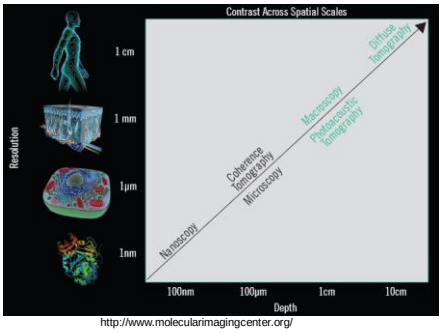
Disclosure

I do not have financial conflict of interest based on the materials presented



http://www.molecularimagingcenter.org/

Outline

Challenges in oncologic surgery

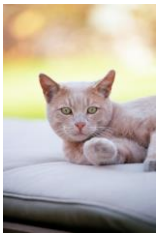
Molecular approaches to light up cancer cells

Cancer viewing goggles

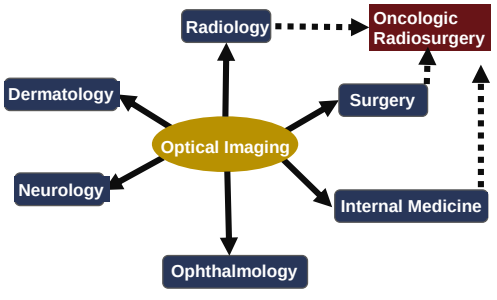
Conclusions

Optical imaging: a pesky orphan in radiology

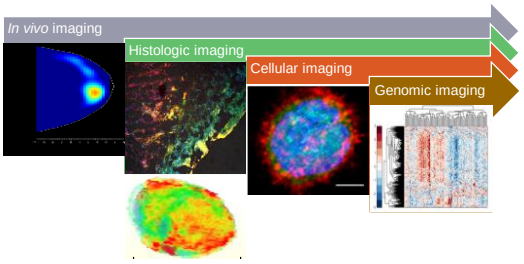
- X-ray: an empire
- MRI: a mansion
- Nuclear imaging: a home
- Ultrasound: a room
- OI: cute but homeless!



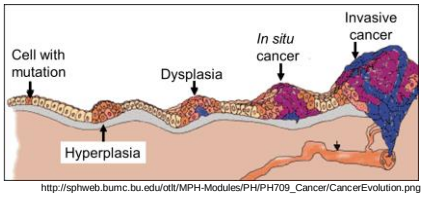
Optical imaging: an orphan no more



Multiscale imaging reveals cancer complexity



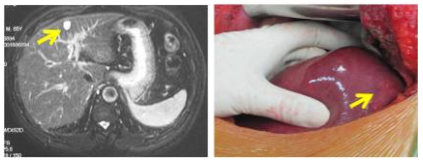
Cancer – the enemy within



http://sphweb.bumc.bu.edu/otlt/MPH-Modules/PH/PH709_Cancer/CancerEvolution.png

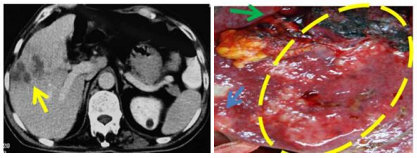
Uncontrolled cell growth and altered function

Oncologic surgery



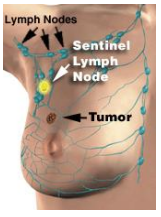
Primary treatment method for most solid tumors

Challenges in the operating room



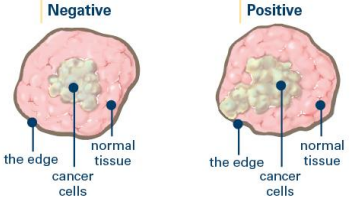
Where is the tumor?

Challenges in the operating room



Where is the sentinel lymph node; what is the status?

Challenges in the operating room



Is the surgical margin negative?

Net surgical outcome

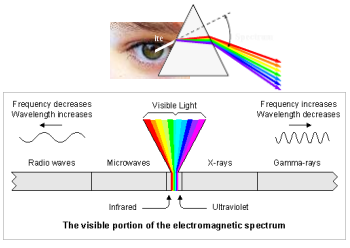
"Nurse, get on the internet, go to SURGERY.COM, scroll down and click on the 'Are you totally lost?' icon."

Subjective decision; variable outcomes

Goal

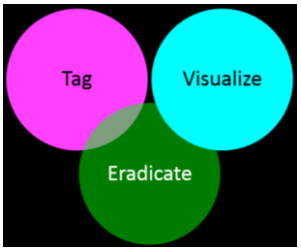
- **Eliminate guesswork**
- **Prevent local relapse**
- **Selectively kill cancer cells**

The power of light

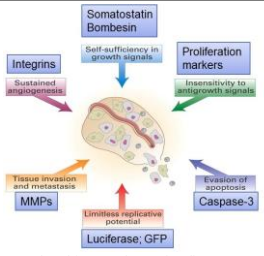


The visible portion of the electromagnetic spectrum

Strategy

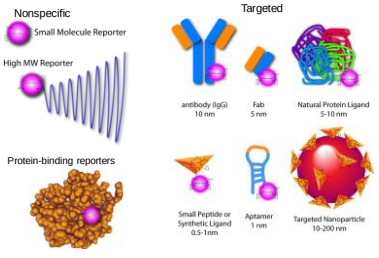


Tumor survival pathways

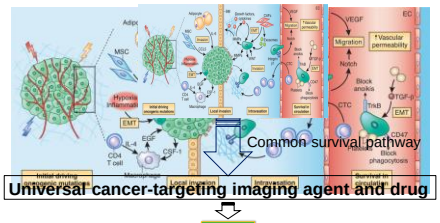


Adapted from Hanahan et al. *Cell* 2000, *100*:57

Fluorescent molecular probes



An intractable proposition

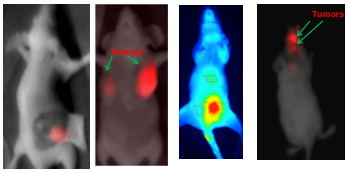


Universal cancer-targeting imaging agent and drug

LS301

L. Wan, et al. Nature Medicine 19, 1450–1464 (2013)

LS301 targets diverse tumors



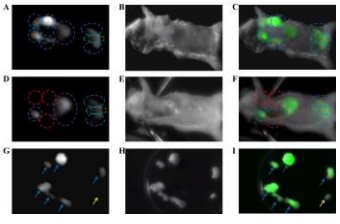
Subcut 4T1-luc mammary tumor model

4T1-luc orthotopic mammary tumor model

Orthotopic HT29 colon cancer model

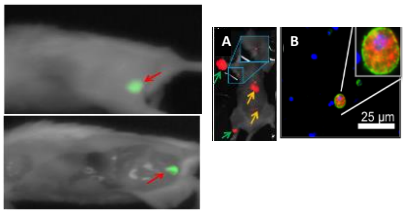
Orthotopic DBT brain cancer model

LS301 identifies spontaneous tumors

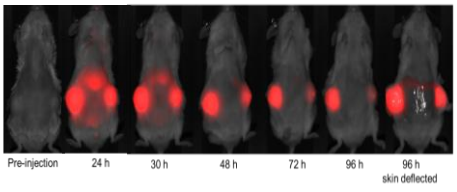


Transgenic mouse MMTV-PyMT spontaneous breast cancer model

LS301 identifies microscopic tumors

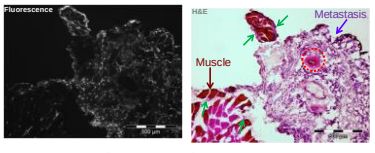


LS301 selectively binds to human cancer tissue



PDX breast cancer model

Detection of invading tumor margins



Green Arrow: Invading Cancer Frontier
Red Cycle: Blood Vessels

Optical surgical guidance systems

Non-ionizing radiation – suitable for OR

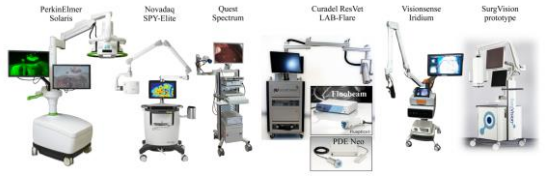
High detection sensitivity – ideal for MI

Real-time feedback – improves surgical decisions

Detection of small cancer cells – minimize relapse

Affordable – relative to other imaging methods

Fluorescence image guidance systems in clinic



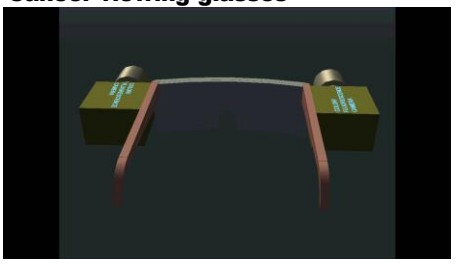

REVIEW

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

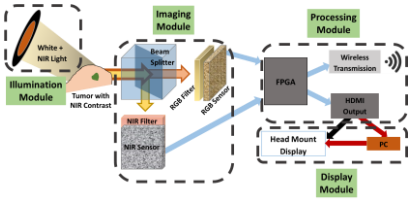
DSouza, et al. J. Biomed. Opt. 21(8), 080901 (2016)

Crowded operating room

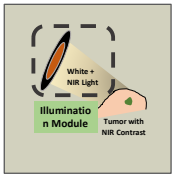
Cancer viewing glasses



Schematic



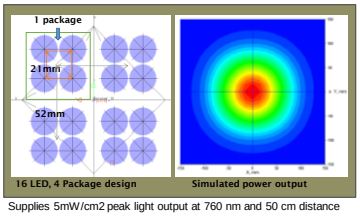
Illumination module



Goals:

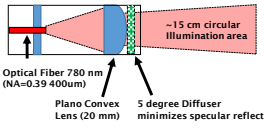
- Maximize spectral separation
- Maintain light output >5 mW/cm^2
- Maintain surgical lights

NIR light source



Supplies 5mW/cm2 peak light output at 760 nm and 50 cm distance

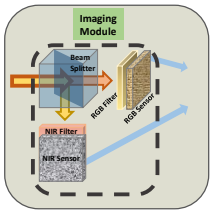
NIR light source



Generation 2: Laser light source

10 mW/cm^2, 50 cm distance

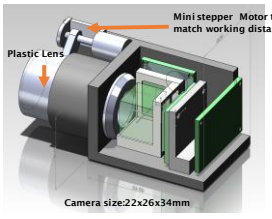
Imaging module



Goals:

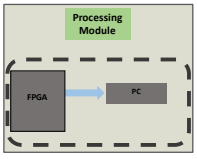
- Signal detection
- Compact form-factor
- Autofocusing

Imaging module



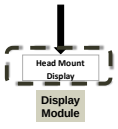
Zhu, et al. J. Biomed. Opt. 2015

Processing module



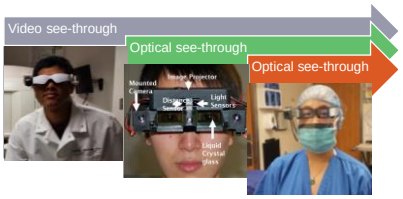
Goals:
- Real-time image processing
- Generation of color-NIR images
- User-friendly operation

Display module



Goals:
- High resolution, large field-of-view
- Compact and light-weight
- Ease of use

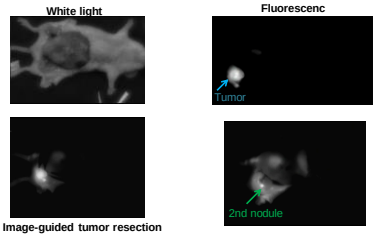
Prototypes



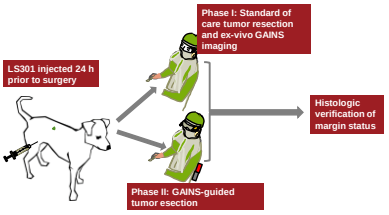
Specifications

Characteristics	GAINS System Specification
NIR sensor quantum efficiency	36% at 810 nm
Lens	F/1.75, f= 19.6mm, FOV = 15.5˚ and working distance = 850mm
NIR-Color co-registration error	<0.1 mm
Weight	30 gm (camera). 330 gm (camera + HMD)
Illumination	16 LED light, 760 nm, 5mW/cm2 at 50 cm
Spatial resolution	320 um
Frame Rate	24 fps
Detection limit	1nM LS301 and ICG, SBR>1.2, 24fps, 50 cm
Depth detection limit	5mm in tissue mimicking phantom, SBR>1.2, 24 fps, 50 cm

Detection/resection of multifocal tumors

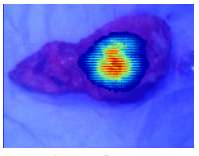


Companion dog clinical trial



CVG detects canine tumors

Intraoperative use



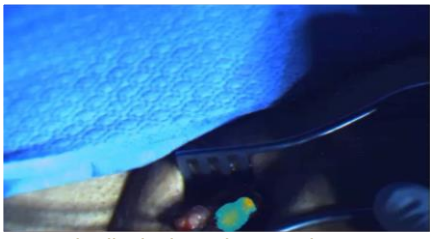
Ex vivo tumor fluorescence

LS301 specifically accumulates in canine tumors

Clinical trials

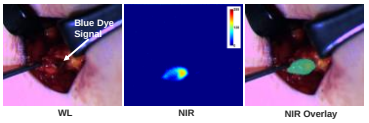
- Number of patients completed: 58
- Cancer types: breast, skin, liver
- Image guidance: sentinel lymph node, margin assessment, survey of surgical ROI
- Contrast agent: ICG

Real-time visualization



SLN visualization in a Melanoma patient

SLN visualization in a BC patient

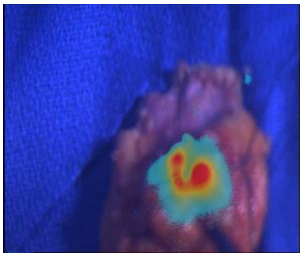


Detected Deep-Seated SLNs

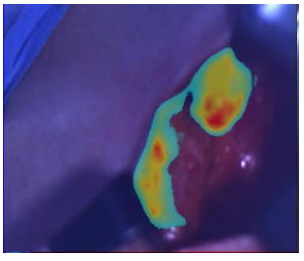
SLN detection	Radionuclide tracking	CVG tracking
Sensitivity	86.67 ± 0.27 %	100%

11 BC patients

Partial mastectomy

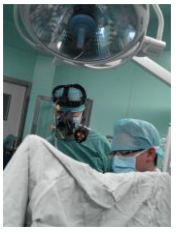


Prediction of margin positivity

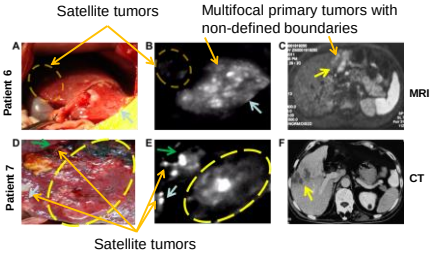


Hepatocellular carcinoma

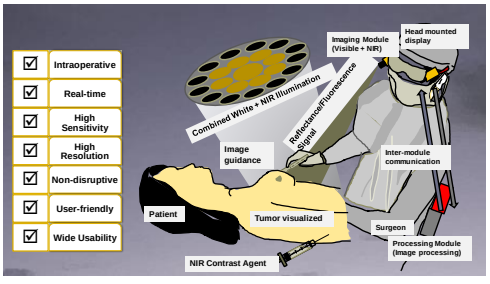
- Leads to 600,000 mortalities annually
- Does not respond well to chemotherapy and radiotherapy
- Poor surgical outcome: 80 % to 90% of cancer relapse



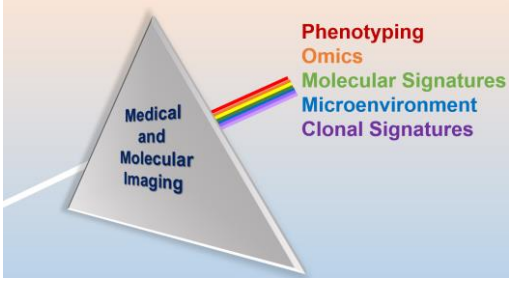
Intra-hepatic arterial ICG injection



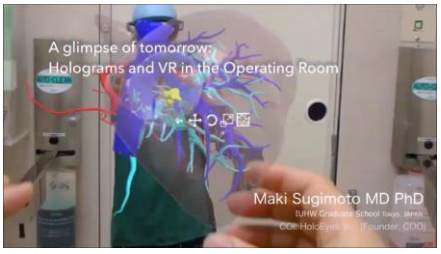
Summary



Viewing cancer complexity via imaging



Deep learning augmented reality



Courtesy of Dr. Maki Sugimoto, IUHW Graduate School, Tokyo, Japan; Full video available at: https://youtu.be/jG_nFBszt-I

Conclusions

- Developed a broad spectrum tumor-targeting NIR molecular probe
- Developed cancer vision goggles for image guided surgery
- Efforts toward multicenter clinical trials in progress

Collaborators

Washington University in St. Louis
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Sensors
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- DOD BCRP
- National Science Foundation
- Siteman Investment Program

ORL
Optical Radiology Lab