

Multifunctional and targeted fluorescence OCT for tumor detection

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**Commercial interests: Patents*

Corporate Sponsored research: Heidelberg Engineering



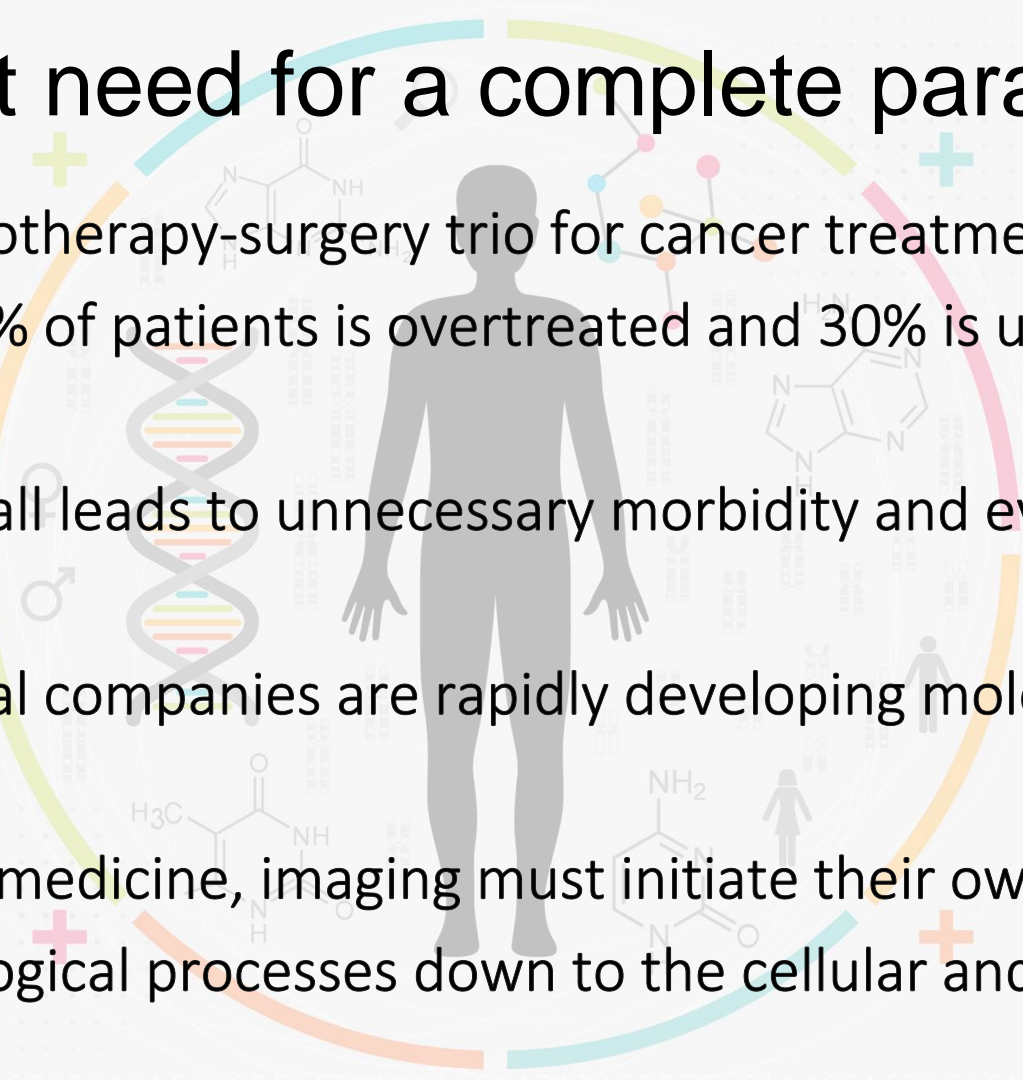
Medical Photonics - MEDPHOT

TTW Perspectief Grant – 5.4 M euro

OPTICAL METHODS FOR PERSONALIZED MEDICINE
NOVEL TECHNOLOGY INTEGRATED WITH A CLINICAL NEED

Consortium of
4 universities (VU, UvA, UU, TU Delft)
3 Hospitals (Amsterdam UMC, UMC Groningen, Leiden UMC)
12 companies

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 otherapy-surgery trio for cancer treatme
 % of patients is overtreated and 30% is u
 all leads to unnecessary morbidity and ev
 al companies are rapidly developing mol
 medicine, imaging must initiate their ow
 ological processes down to the cellular and



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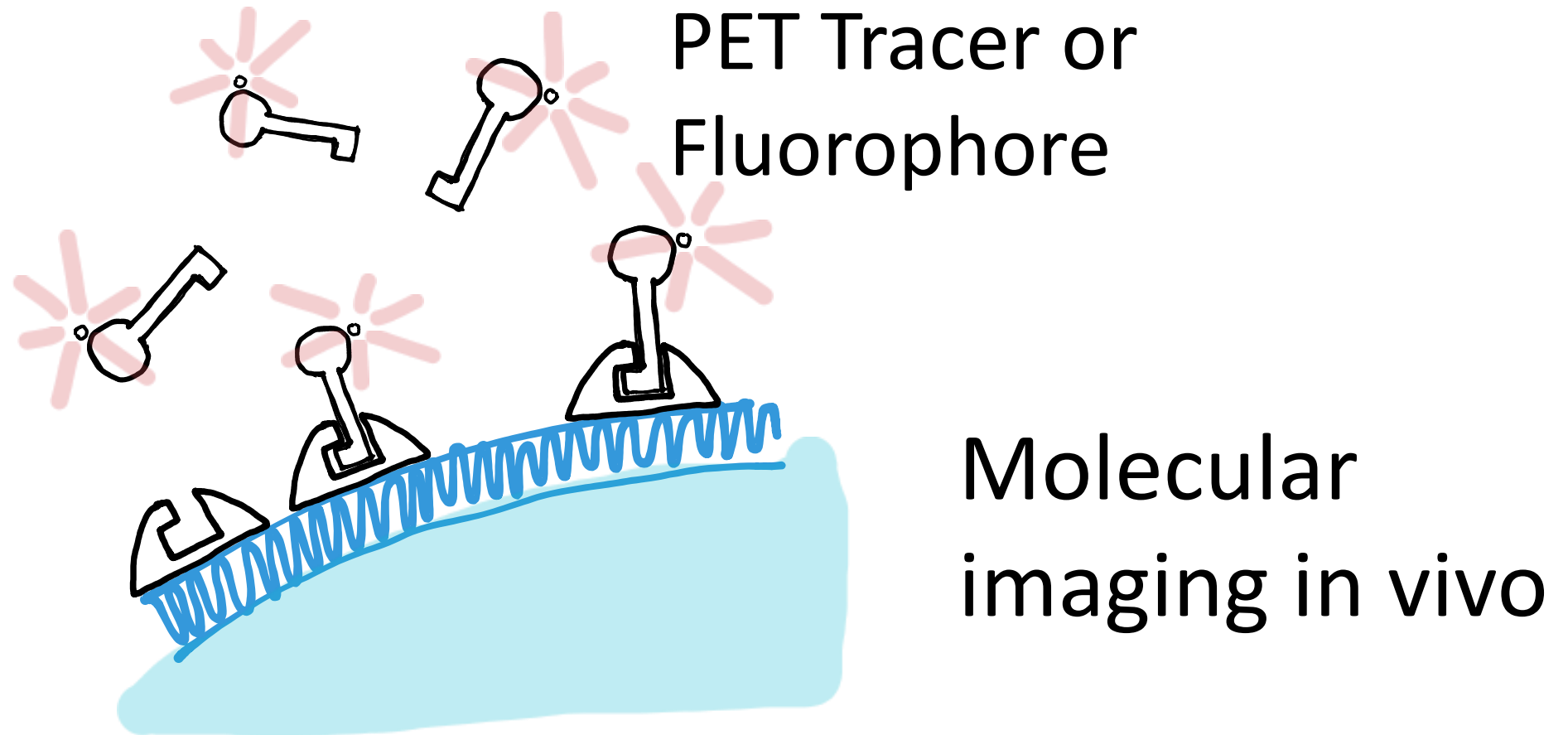
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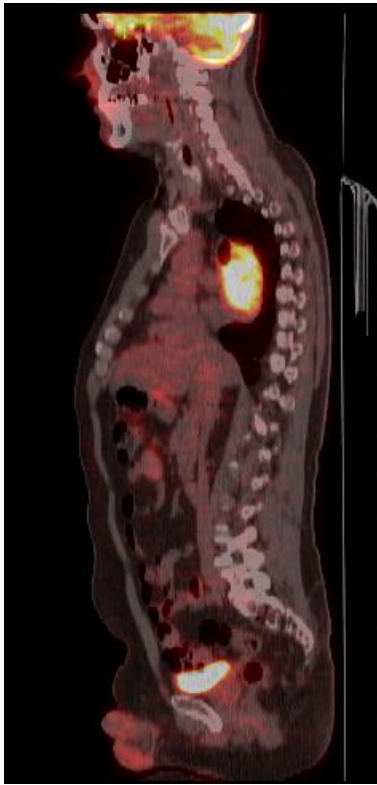
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Monoclonal antibodies (mAb) can specifically target cell surface receptors or signaling proteins

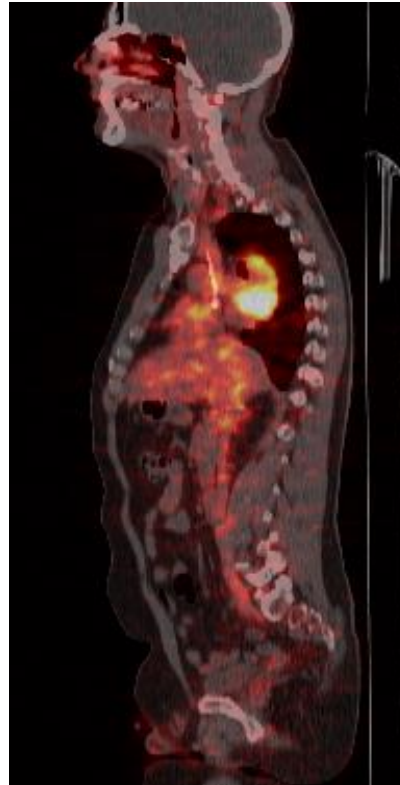


Immuno-PET can be used to verify that a monoclonal antibody targets a cancer specifically

^{18}F FDG PET-CT
Before treatment



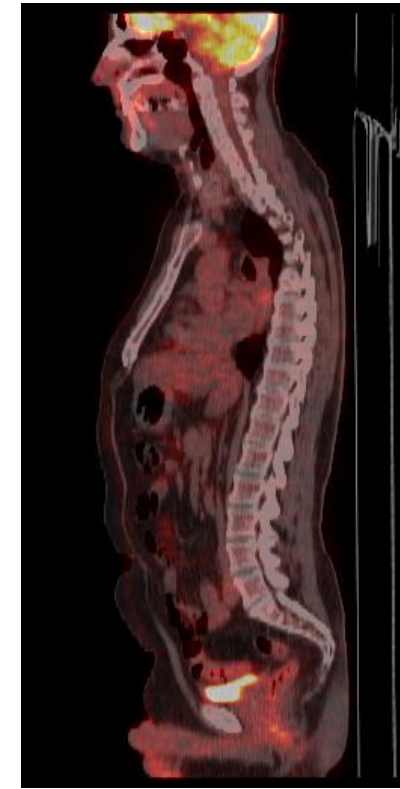
^{89}Zr -rituximab PET-CT
Before treatment



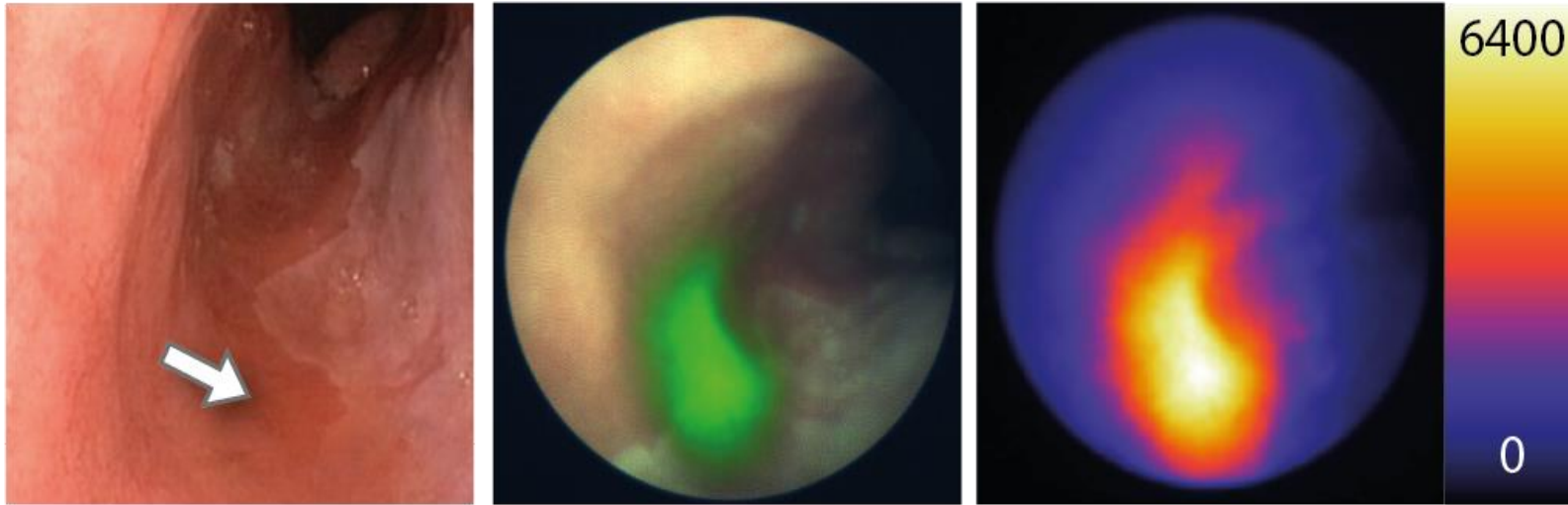
Treatment



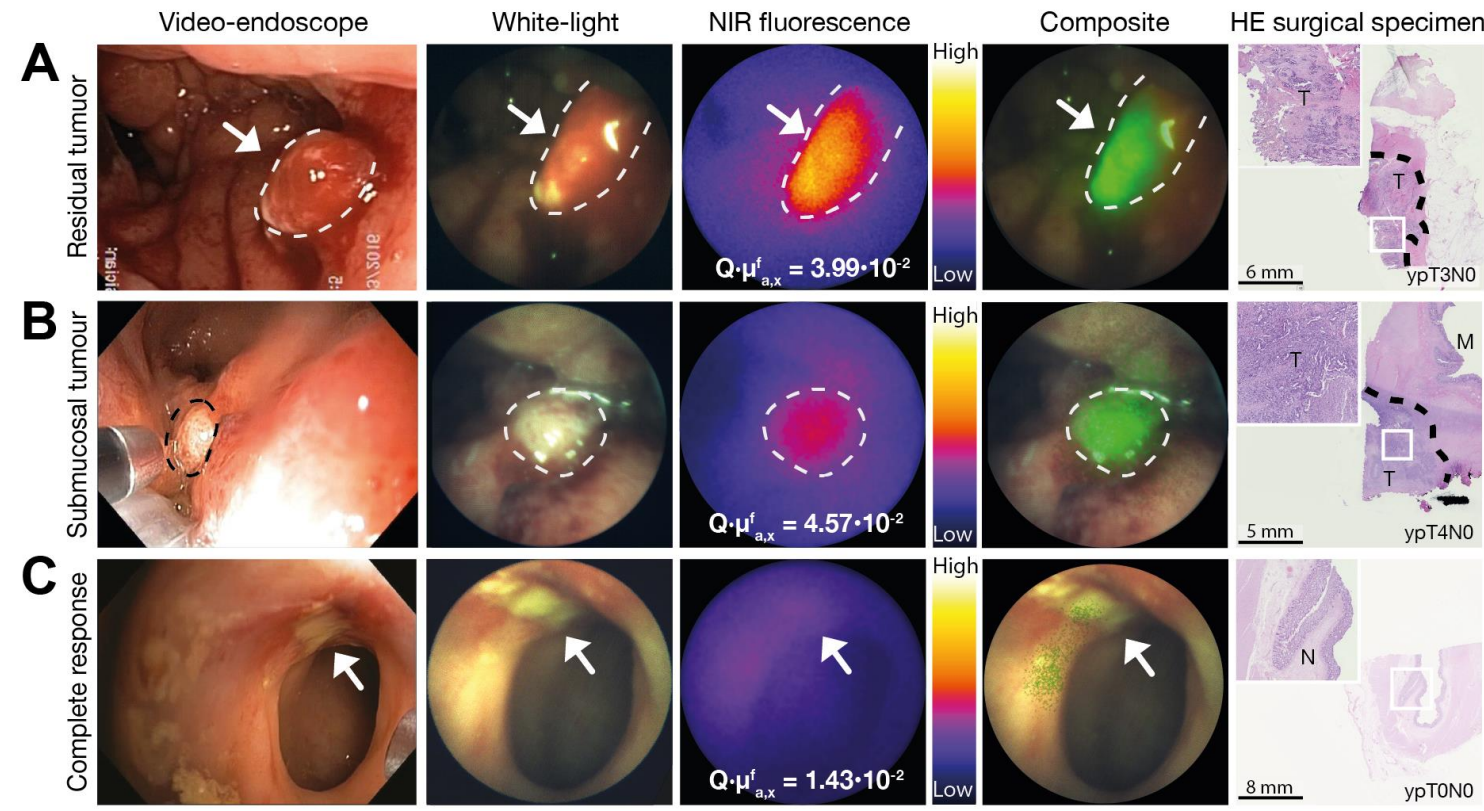
^{18}F FDG PET-CT
3 months after treatment



Slide courtesy of Prof. Guus van Dongen, VUmc

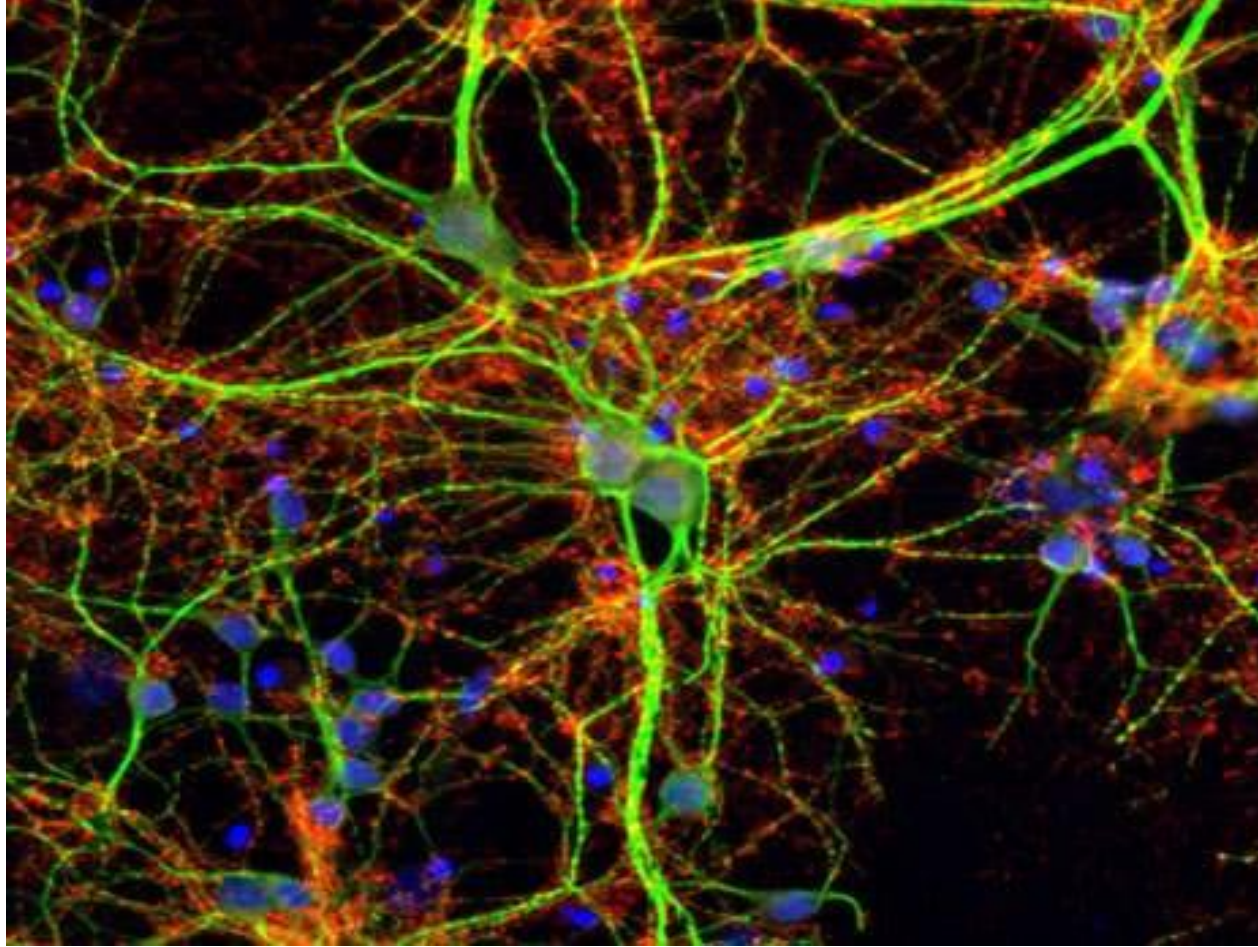


Molecular imaging of cancer



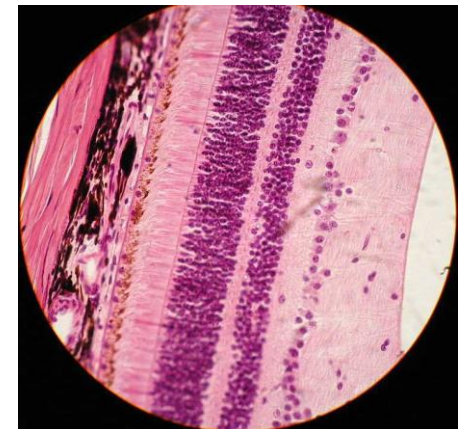
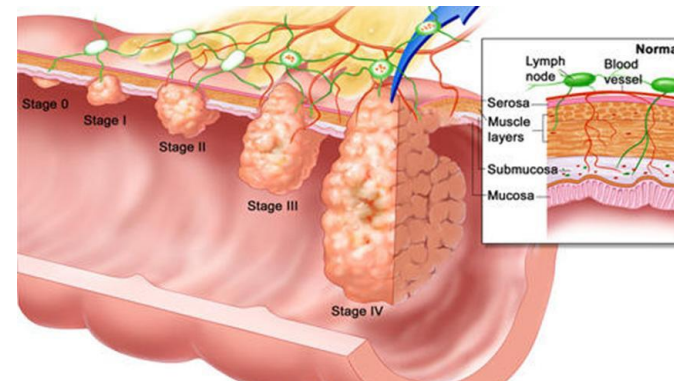
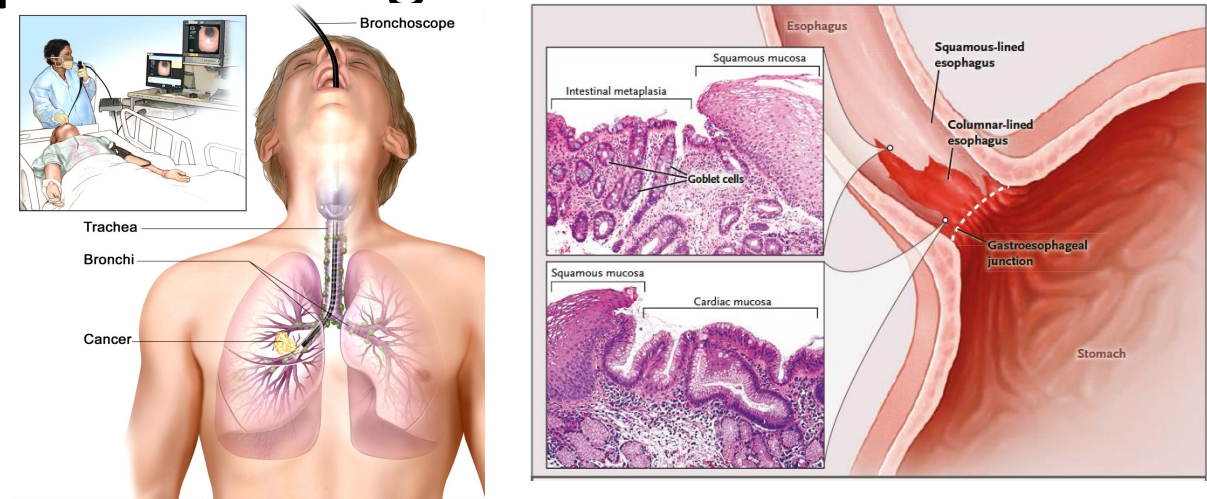
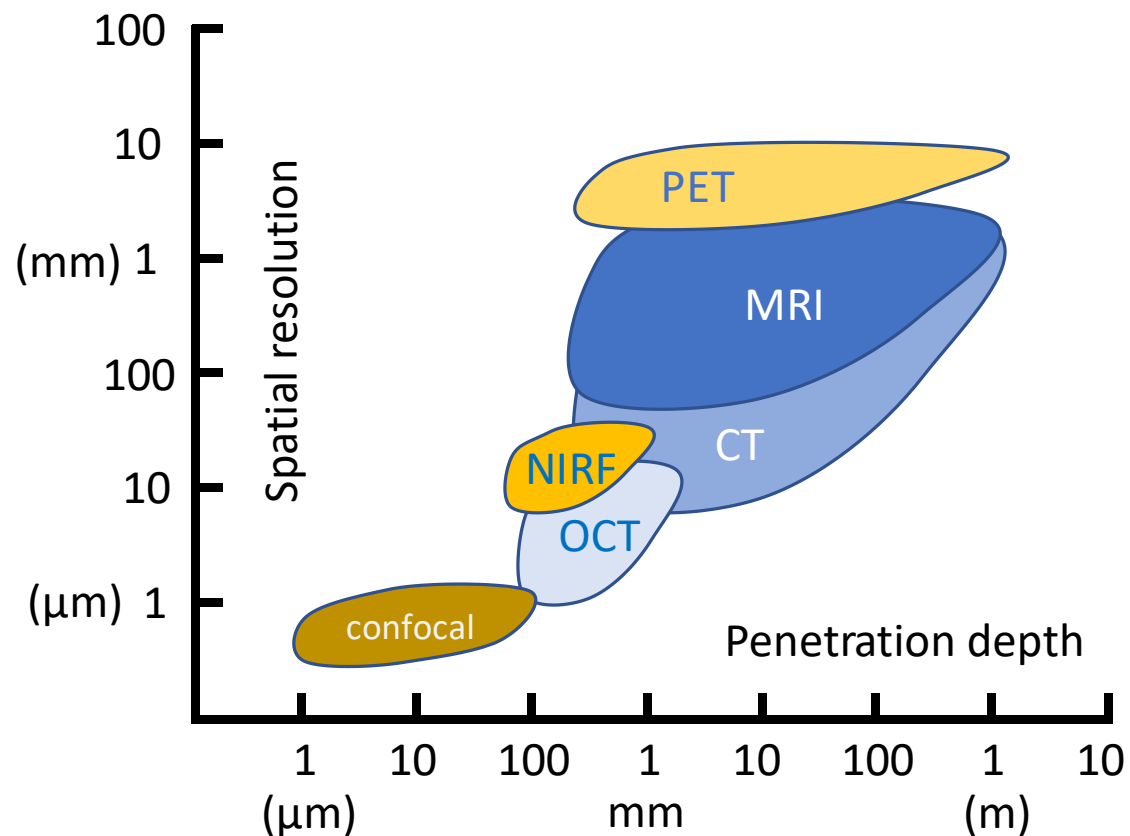
Nagengast et al, GUT, 2018
Tjalma et al, GUT, 2019

Different mAb's can be labeled with different fluorophores –
Study of interactions

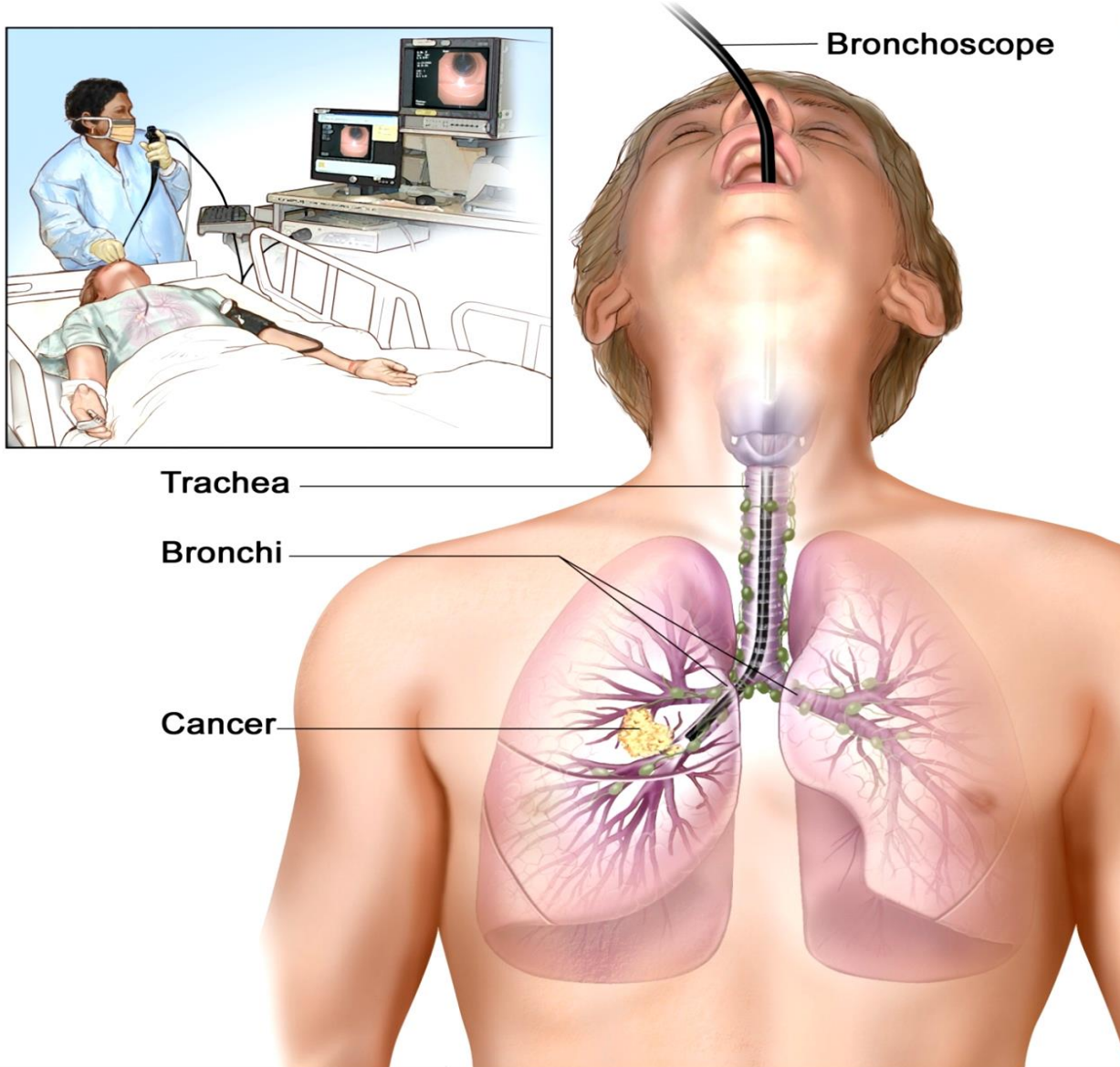


MEDPHOT's aim is to realize this in vivo in patients

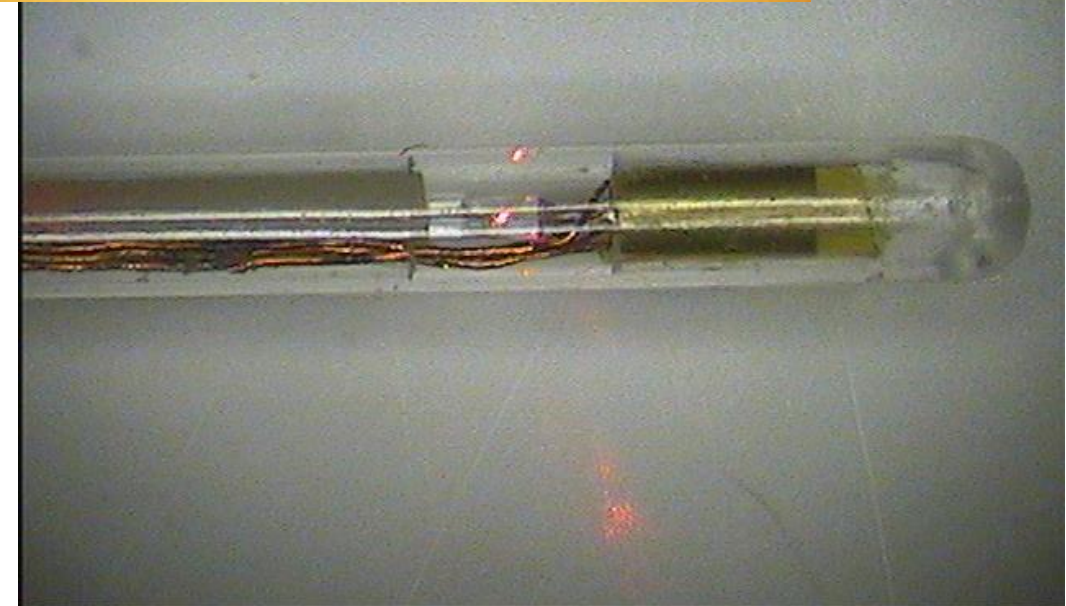
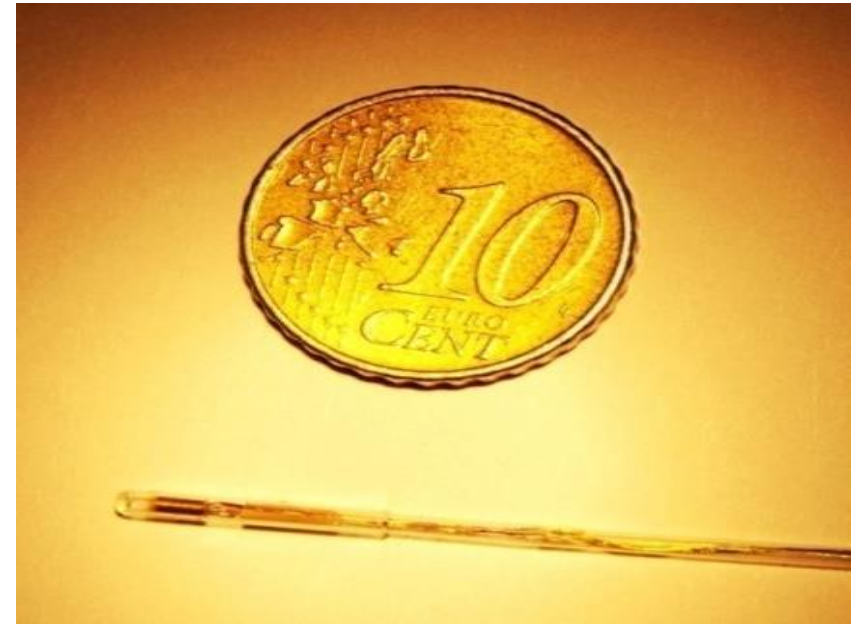
- Huidige klinische structurele en moleculaire afbeeldingstechnieken hebben een beperkte resolutie
- Optische technieken kunnen een paradigma verschuiving bewerkstelligen in resolutie en patientezorg



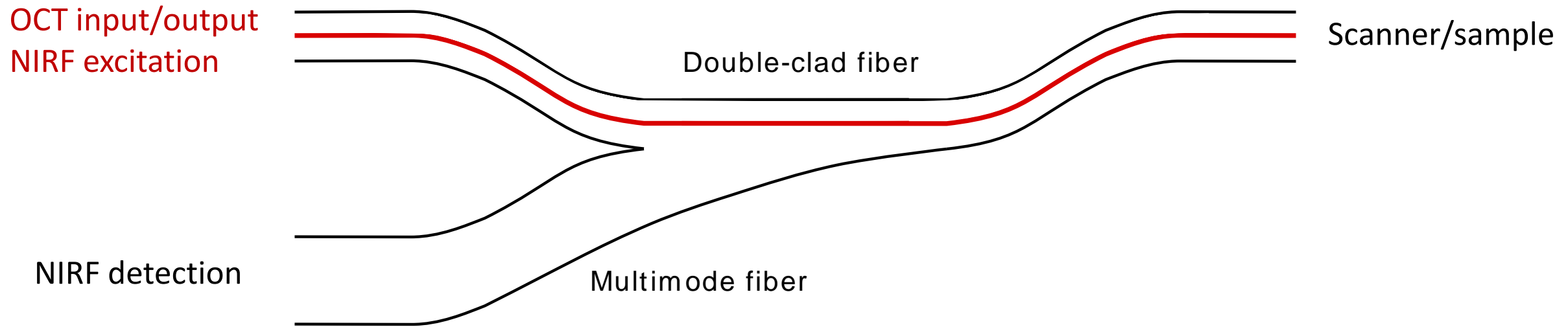
Endoscopic Optical Fourier Domain Imaging (OFDI) - Catheter

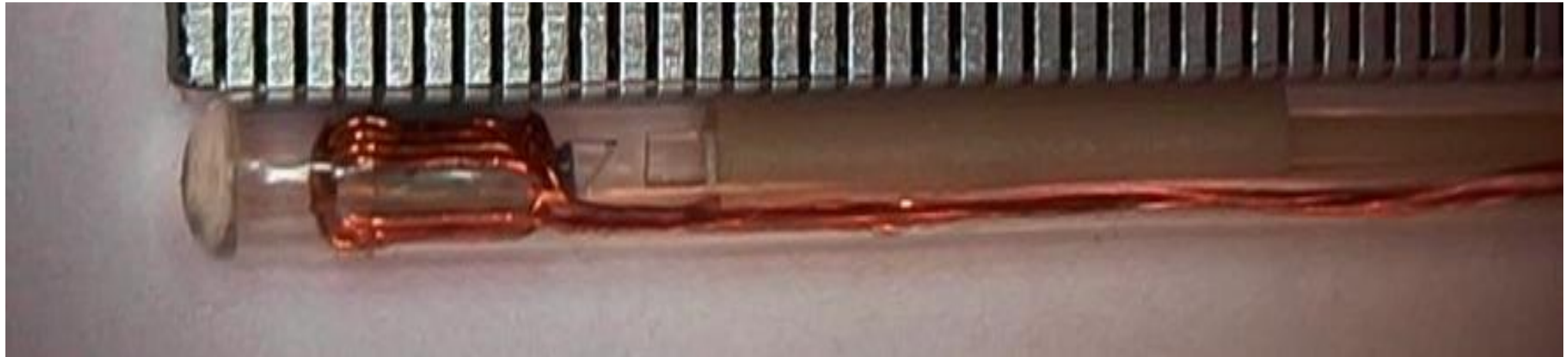
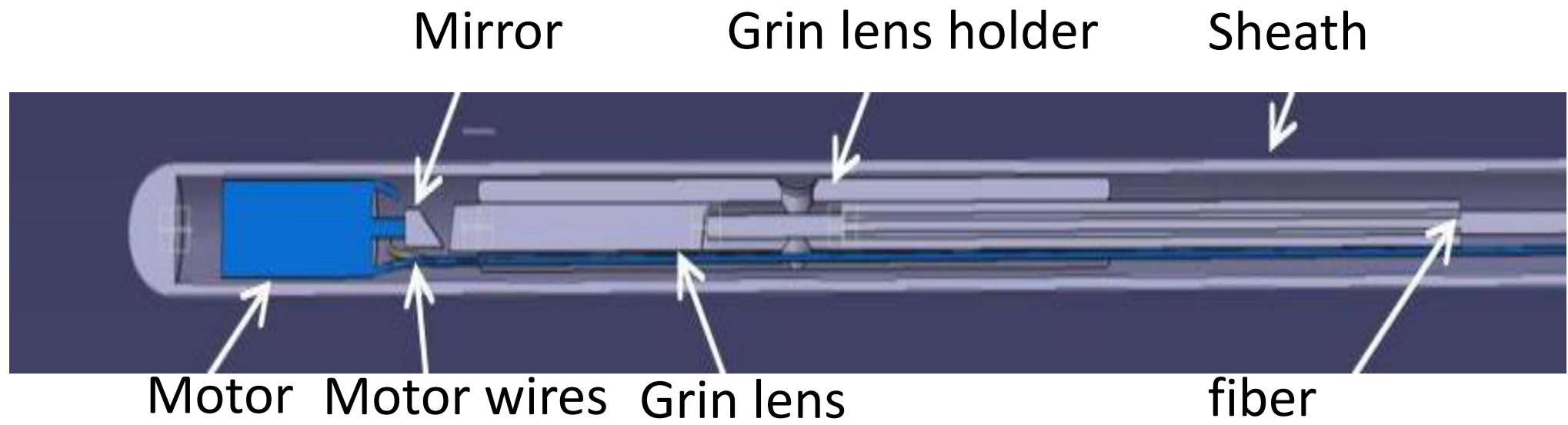


copied from <http://www.ehealthlines.com>



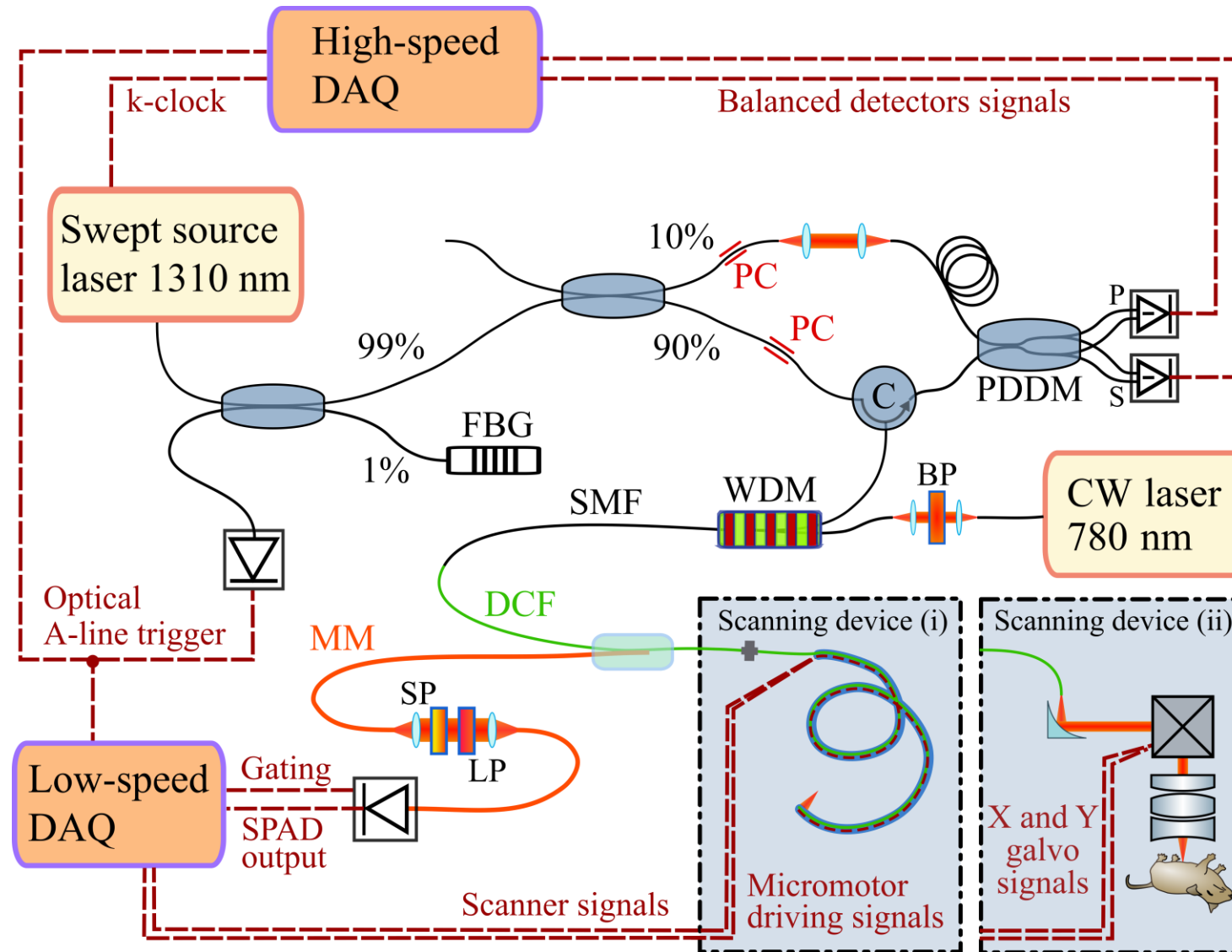
Optical fibers are ideal for making endoscope and for robustness
but OCT and NIRF have opposite requirements





1.35 mm diameter

We combined OCT and NIRF in an all-fiber setup

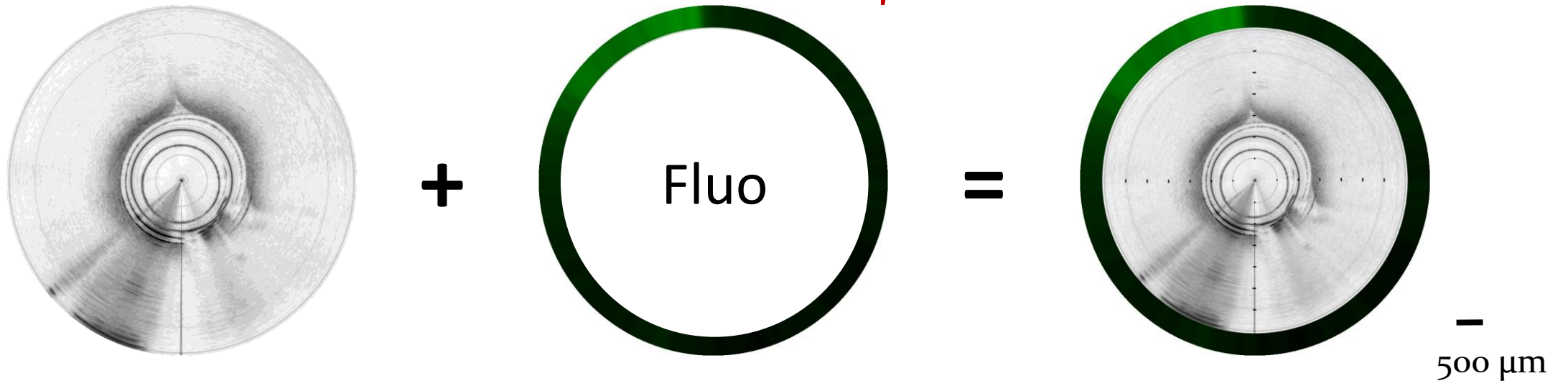
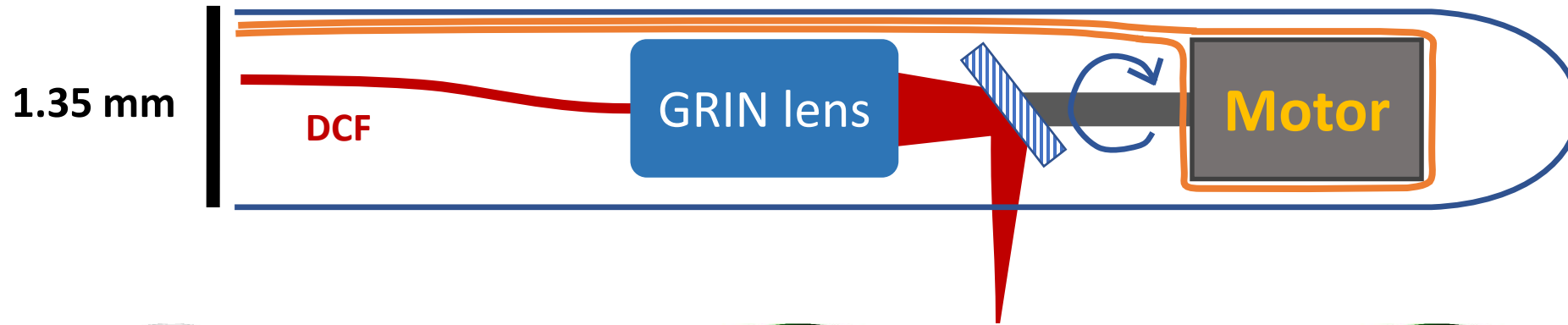


We use near infrared fluorescence (800 nm) for reduced:

scattering,
absorption,
and autofluorescence of the tissue.

The only versatile NIR fluorescent dye
considered safe for clinical use is **IRdye800**

With double clad fibers we can produce
NIRF-OCT images via an endoscope



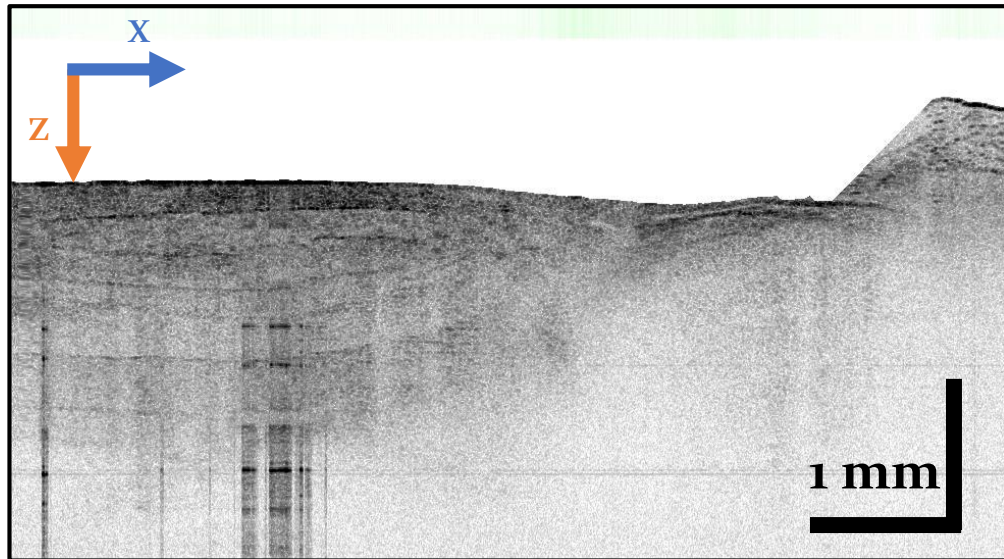
Imaging the mouse peritoneum, Human cancer cell line,
fluorescently labeled labetuzemab.

We can detect tumors with the endoscope

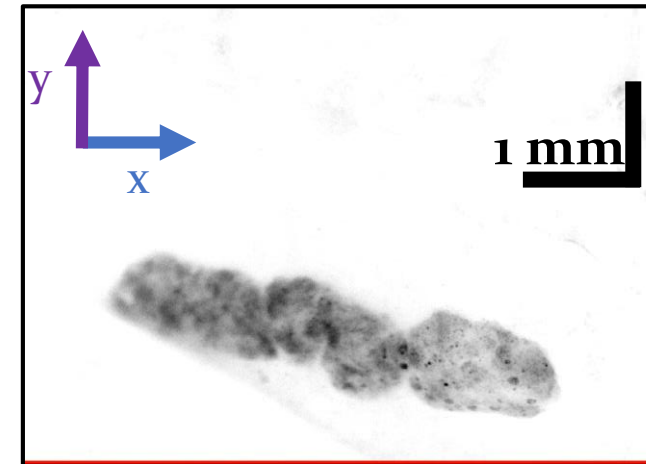
Cross sectional OCT
and NIRF



Simultaneous OCT and NIRF, High resolution structural and molecular imaging

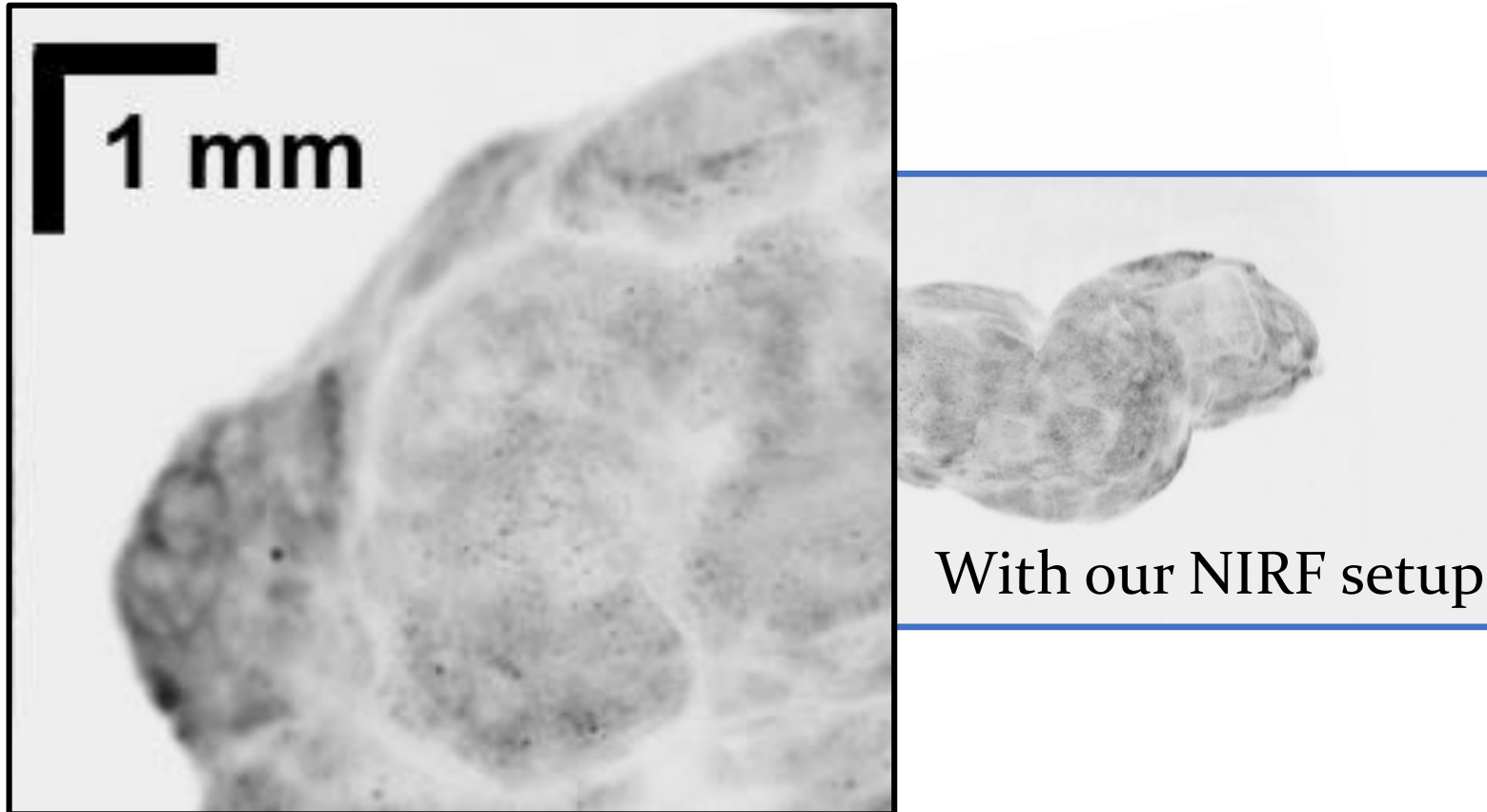


NIRF + Cross sectional OCT



NIRF

Our NIRF images show that tumors are highly heterogeneous
(Human cancer cell line in mouse model, fluorescently labeled with
labetuzemab)

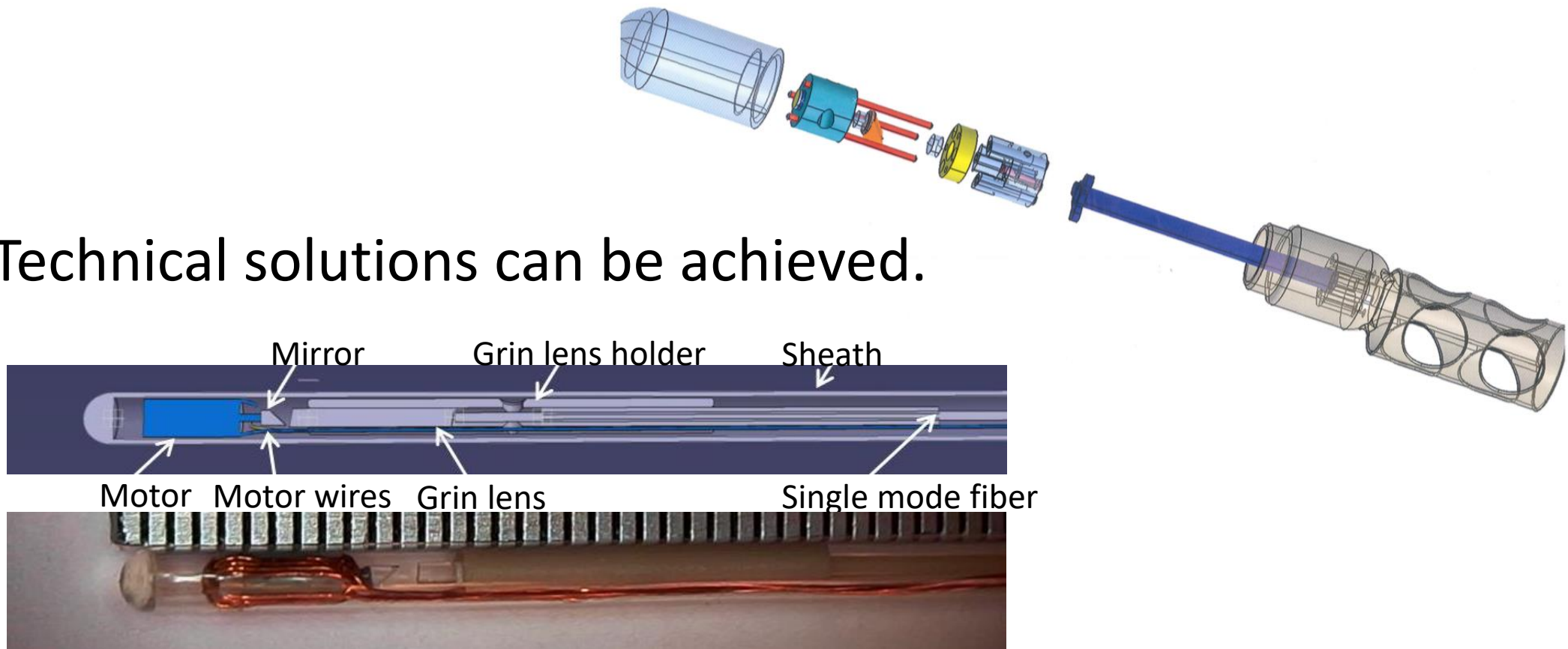


Feroldi *et al.* Biomed. Opt. Express 9, 6186-6204 (2018)

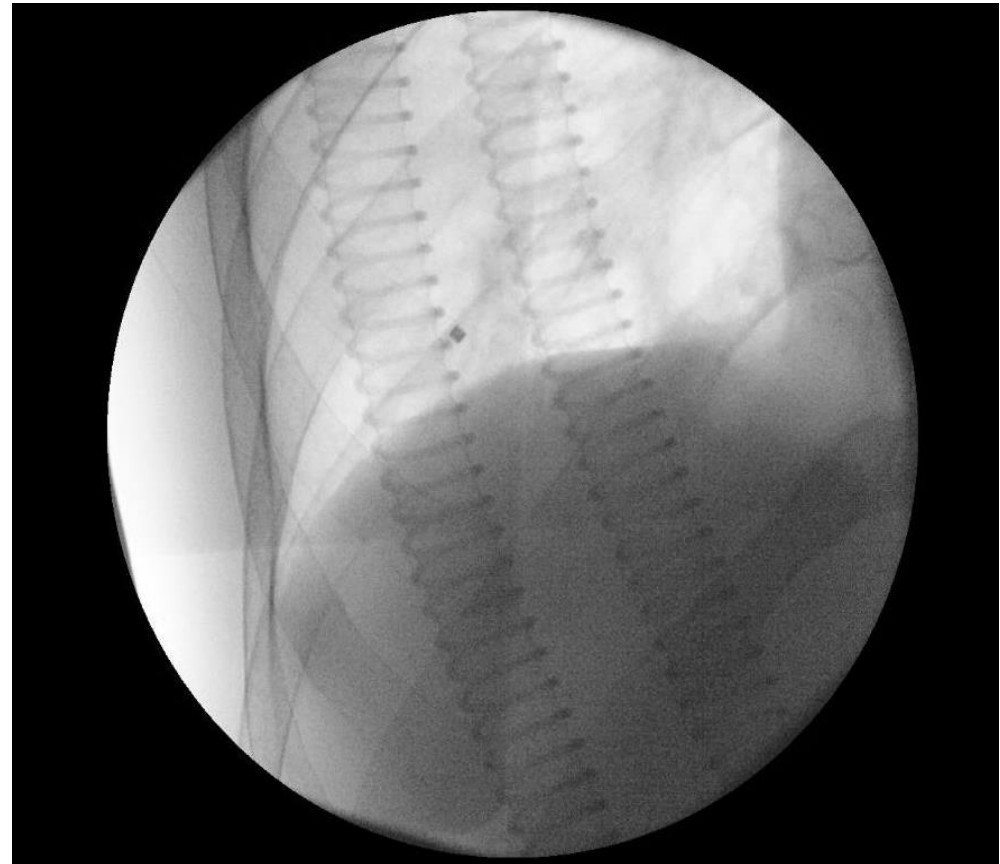
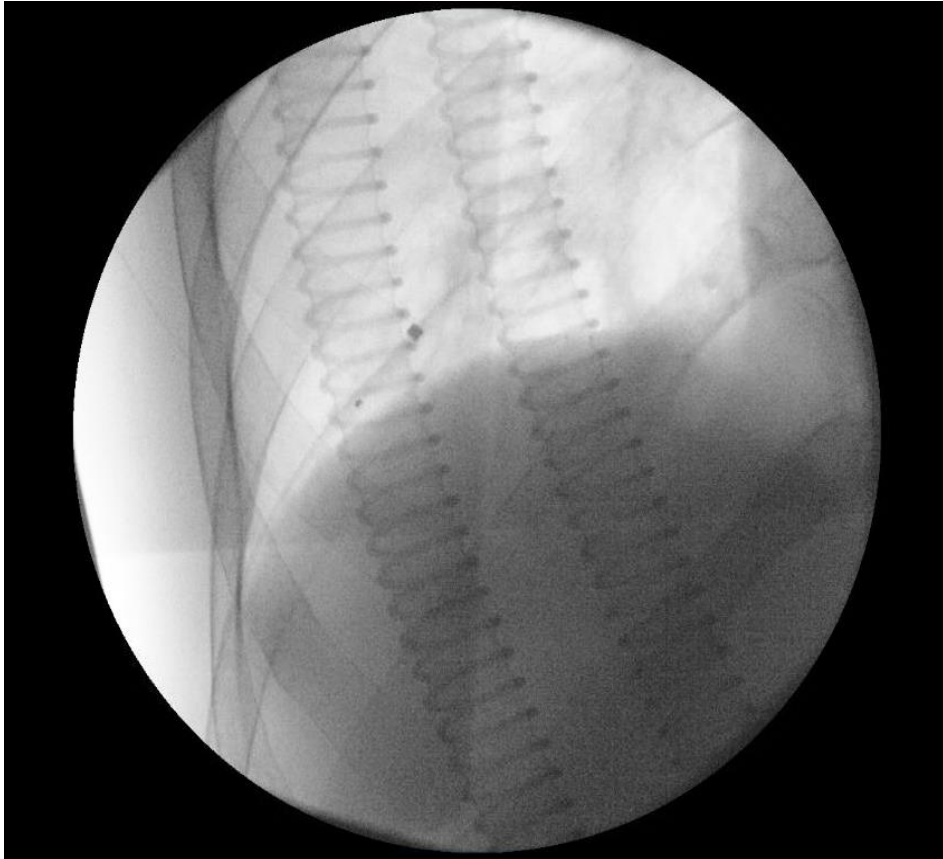
High resolution is needed to tell if the tumor or disease will respond to therapy - > Molecular imaging drives treatment decision

Scan probes for Lung, esophagus and rectum

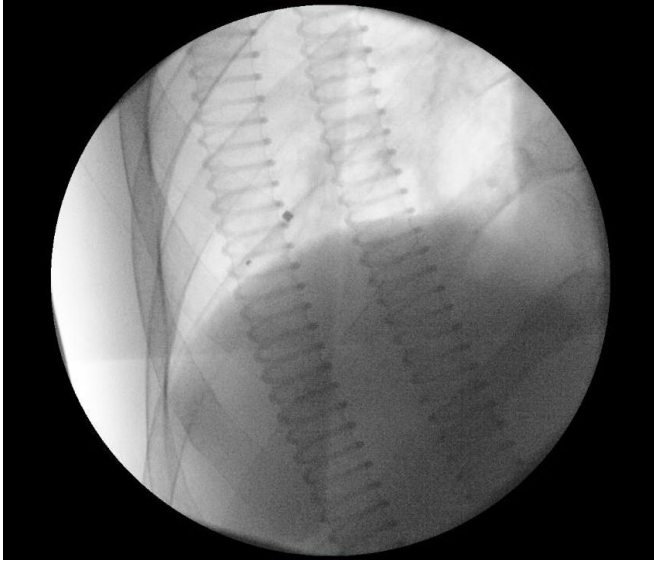
Technical solutions can be achieved.



In vivo patient #3 (Collaboration with Hans Daniels, VUmc)



In vivo patient #3



~10 cm

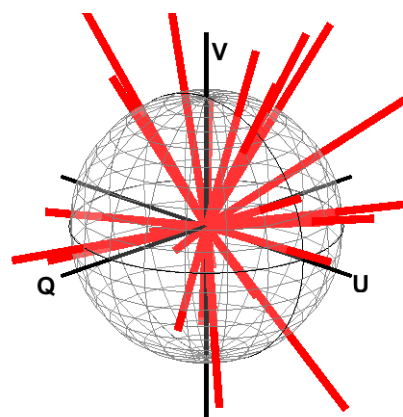


1800 μm

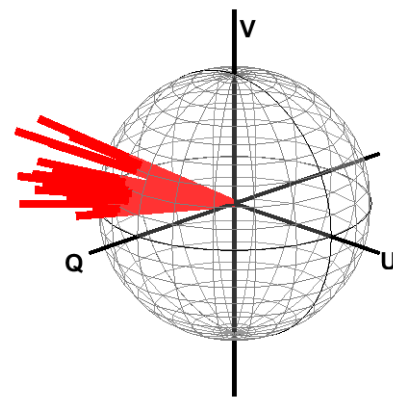
The birefringence vector – Associated with fibrous structures

$$\mathbf{\Gamma} = \begin{pmatrix} \eta \\ \nu \\ \mu \end{pmatrix}$$

$$\Delta\varphi = \|\mathbf{\Gamma}\|$$

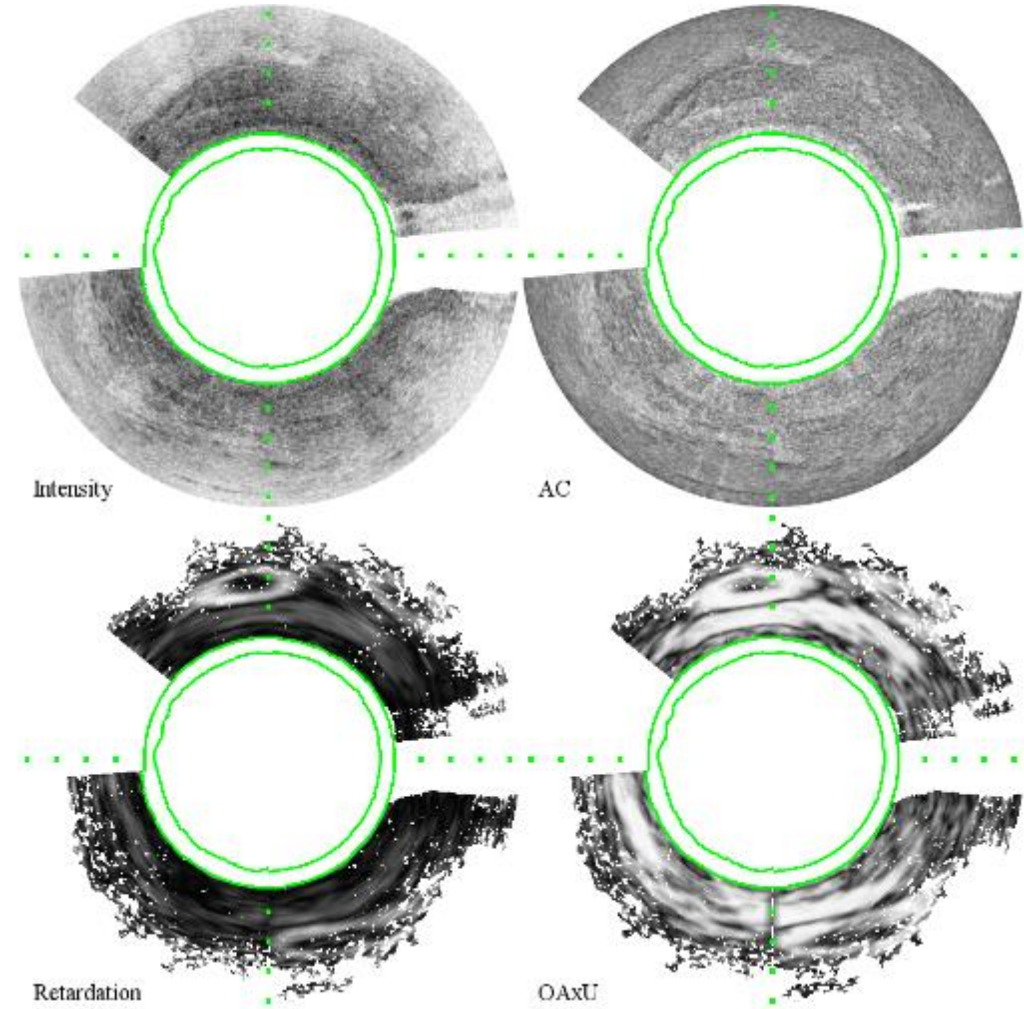
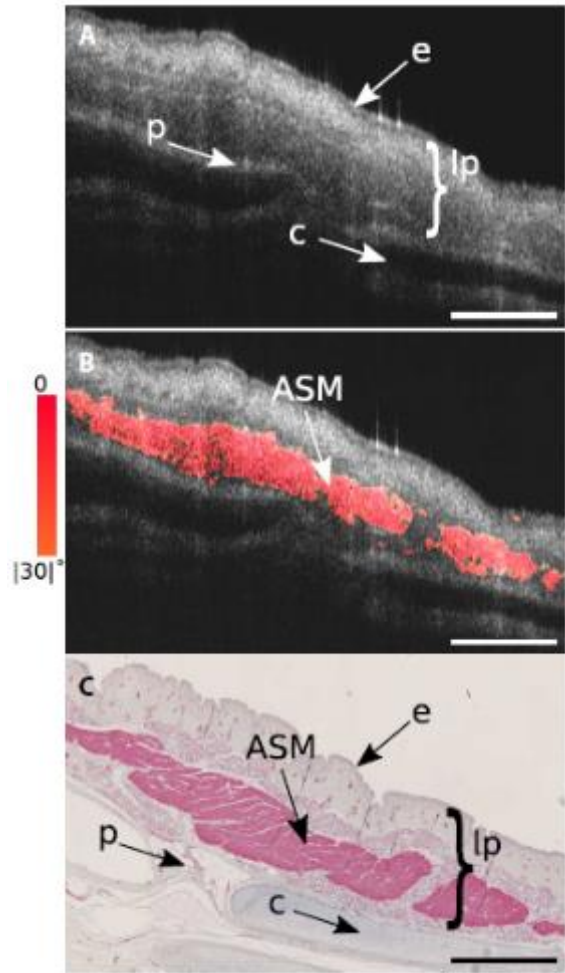


noise region
region



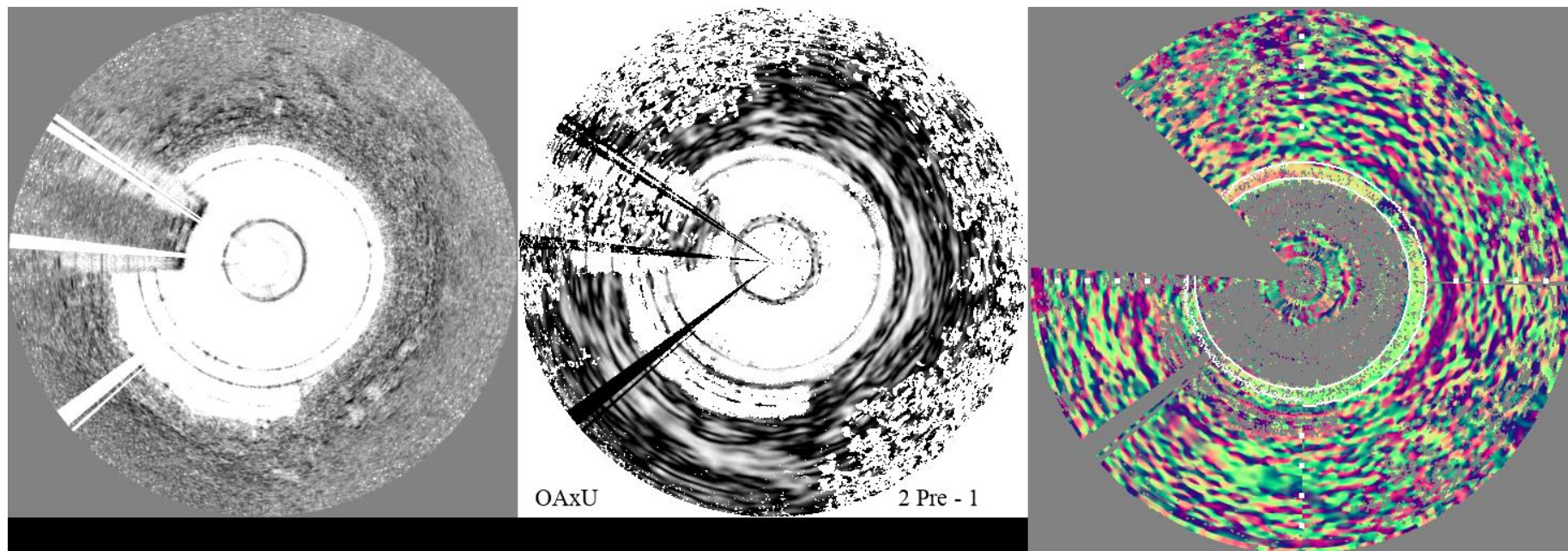
signal

Birefringence / PS - OCT platform



Images acquired in-vivo in lungs

Patient imaged 8/11/2017
Rll 8 pre – BT



Amsterdam Biophotonics environment

- Results will change drug development and treatment



EMA headquarter in the Netherlands



MEDPHOT Goal:

- Developing the optical analog of PET/CT or PET MRI
- CT/MRI -> OCT
- PET -> Near Infra Red Fluorescence
- Optical approach has a 10-100 times higher resolution

The background features a light blue gradient. Scattered across the scene are several stylized keys, each with a circular head and a rectangular bit. Each key is surrounded by a starburst of eight pinkish-red rays. At the bottom, a blue, wavy line represents a horizon or ground. On the left, a large, faint, light blue arrow points towards the right.

Thank you

Johannes de Boer, Professor, Vrije Universiteit

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