Laser Induced Fluorescence Spectroscopy and Molecular Imaging as Tools for Tumor Detection *in vivo*

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Outline:

- **Spectroscopic identification of malignant regions in the gastrointestinal tract**
- **Receptor-targeted fluorescence imaging of animals**
- **Demarcation of lymph nodes by fluorescence imaging**
- **Spatial resolution in fluorescence imaging**
- **Fluorescence reference material**

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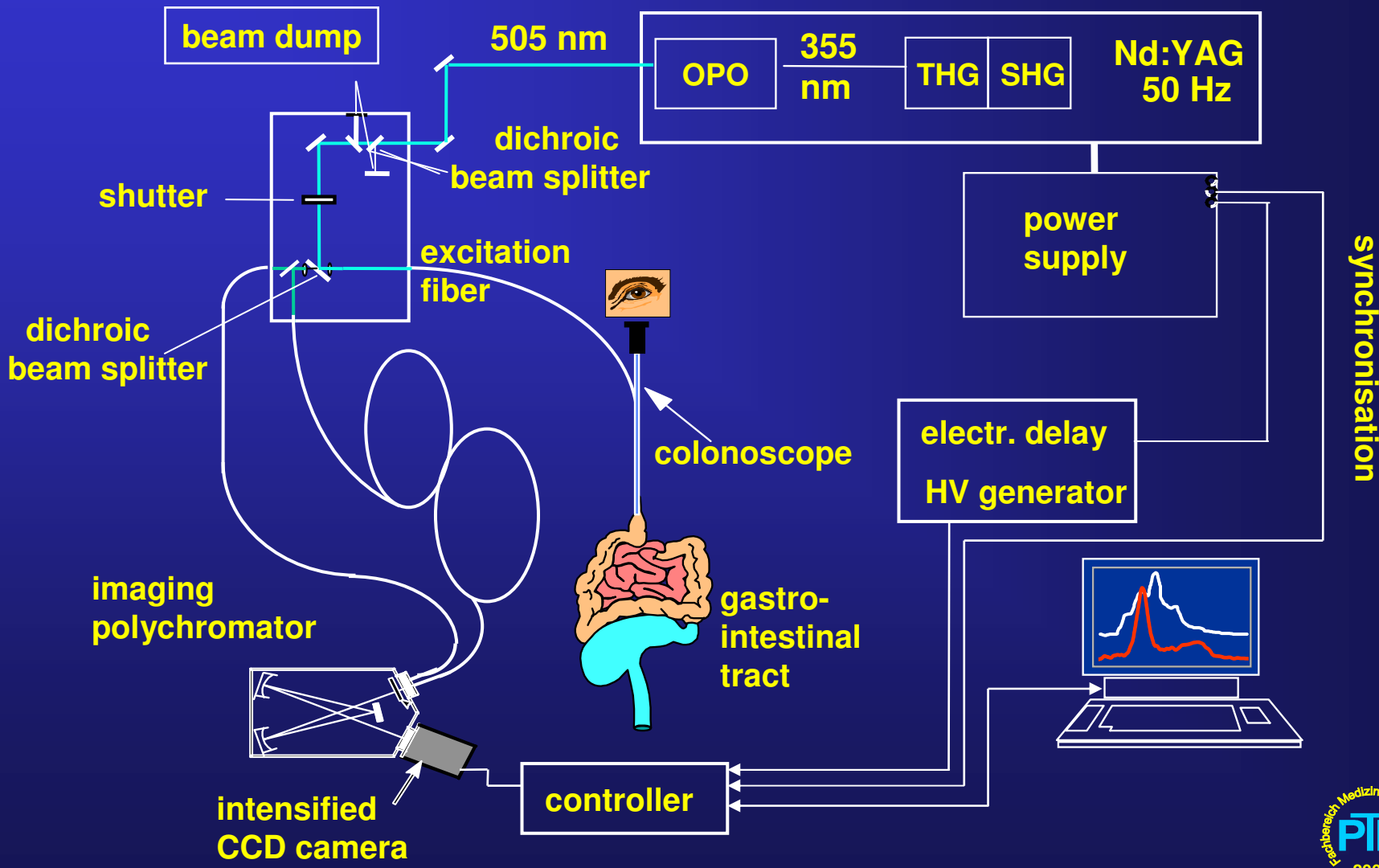
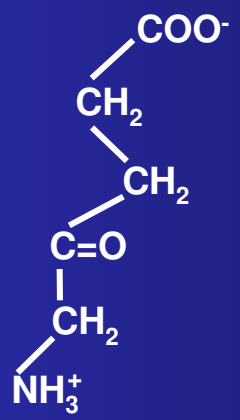
Fluorescence imaging of lymph nodes
Experimental setup



Heme biosynthesis

Succinyl-CoA + Glycine

→ 5 - Aminolevulinic acid (ALA)



2 mol ALA

↓

Porphobilinogen

↓

4 mol Porphobilinogen

↓

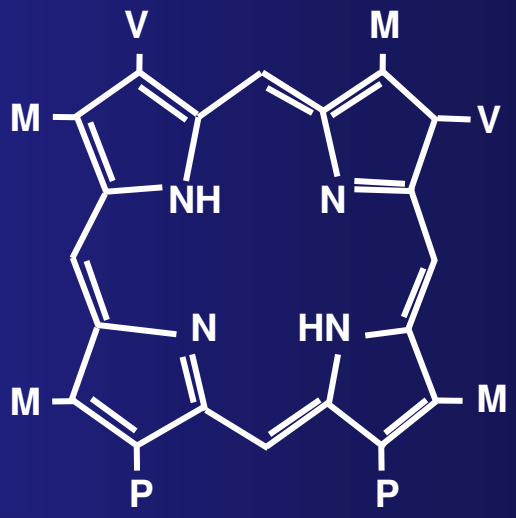
Uroporphyrinogen III

Coproporporphyrinogen

Protoporphyrinogen IX

↓

Protoporphyrin IX (PpIX)

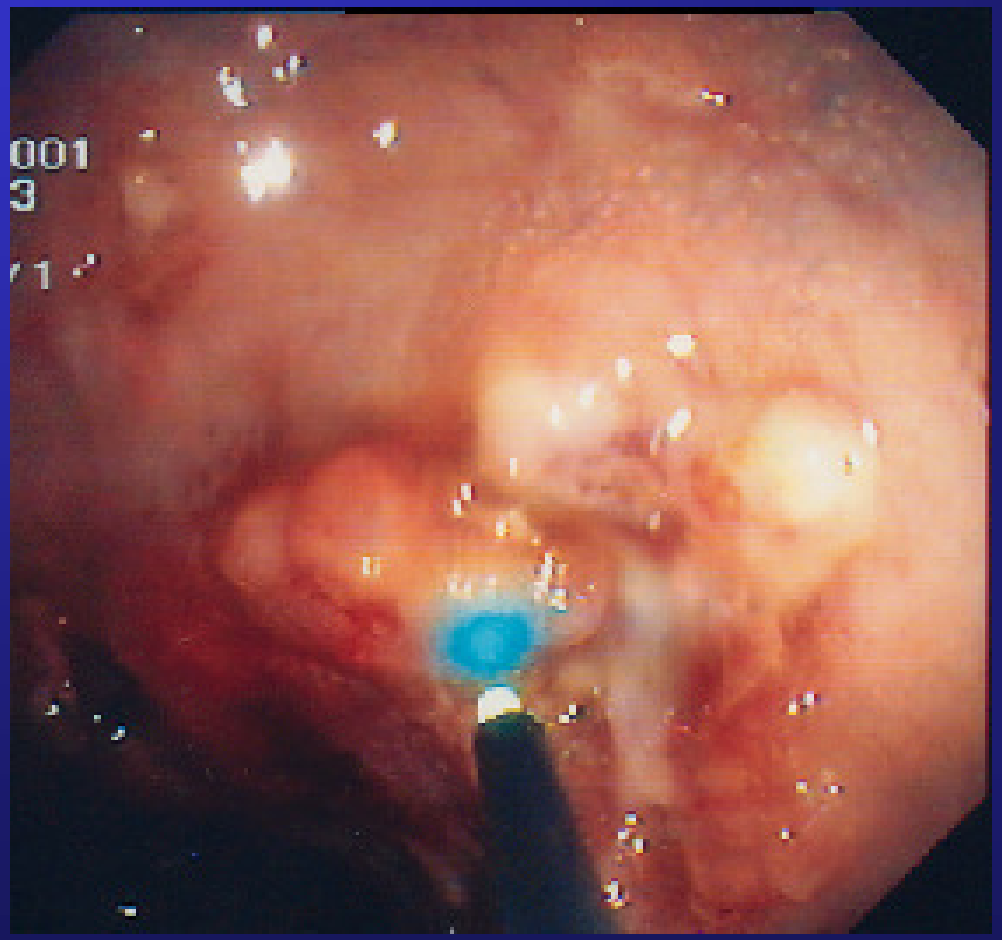


M: CH_3

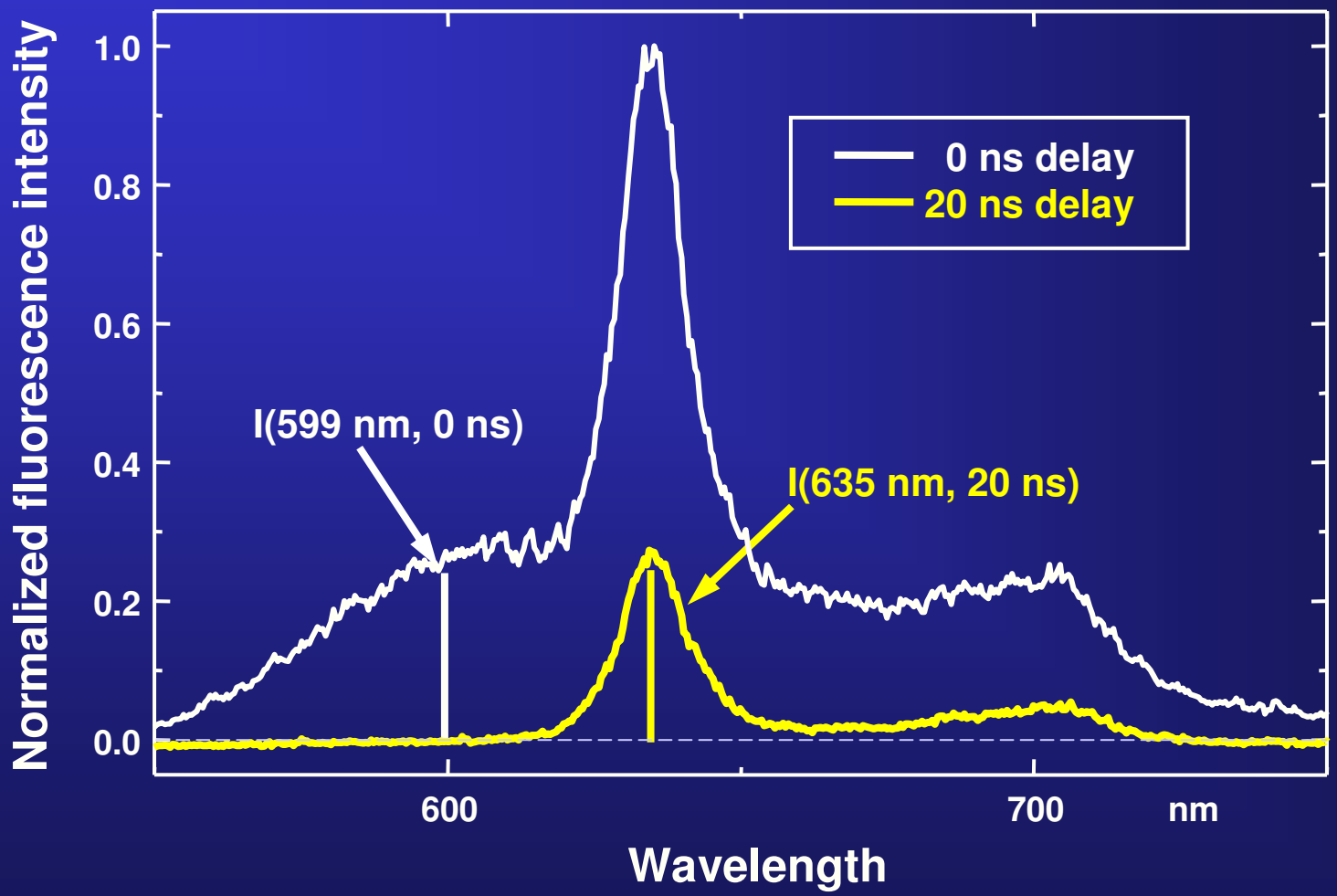
V: $CH=CH_2$

P: CH_2-CH_2-COOH

Fluorescence spectroscopy of tumors endoscopic view



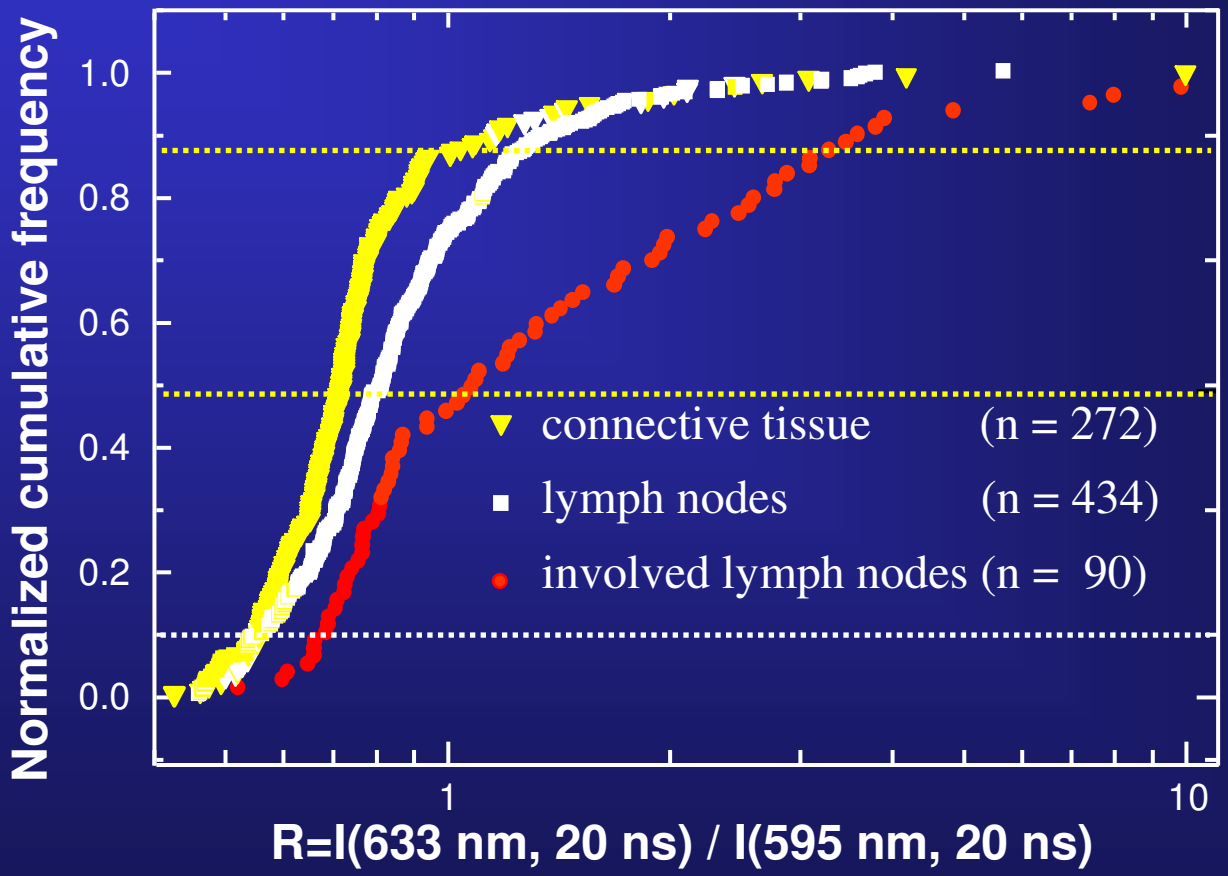
Fluorescence spectroscopy of malignant tissue



R= I(635 nm, 20 ns) / I(599 nm, 0ns)

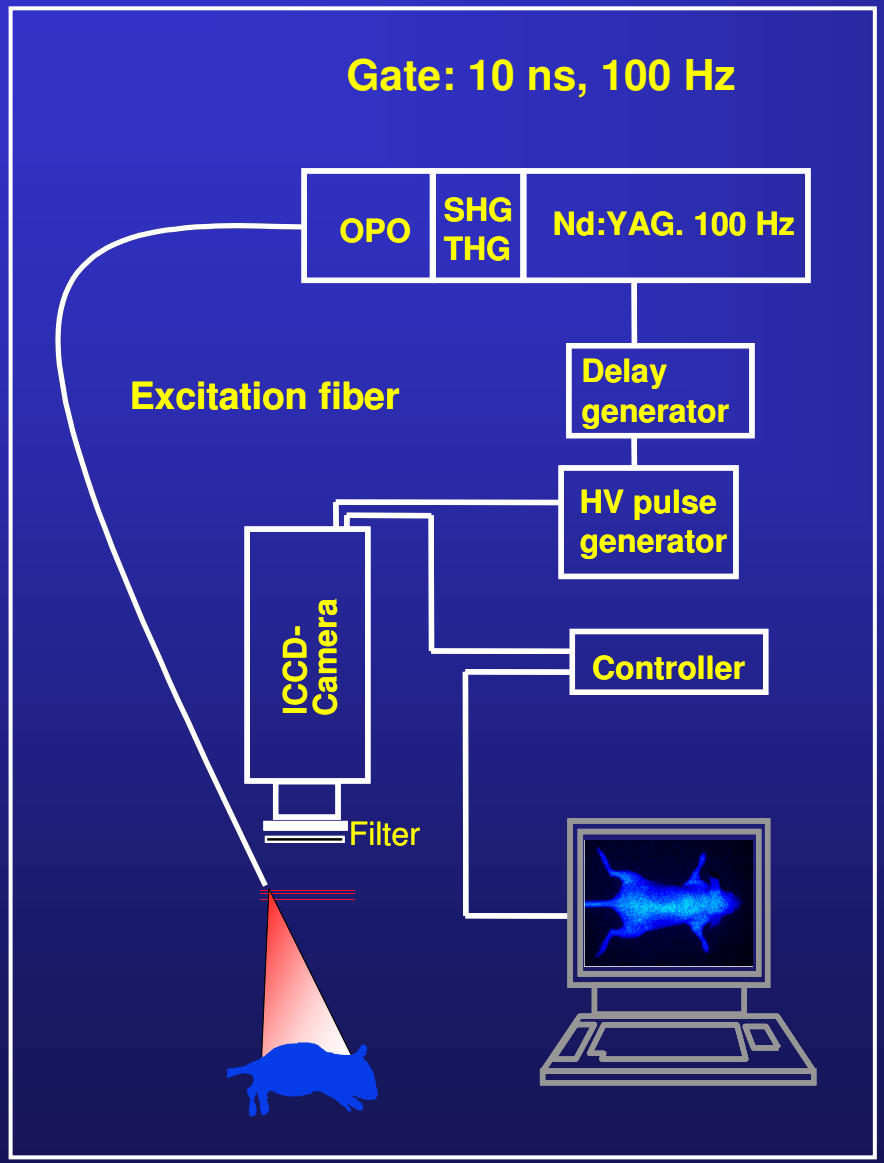
Fluorescence spectroscopy of lymph nodes

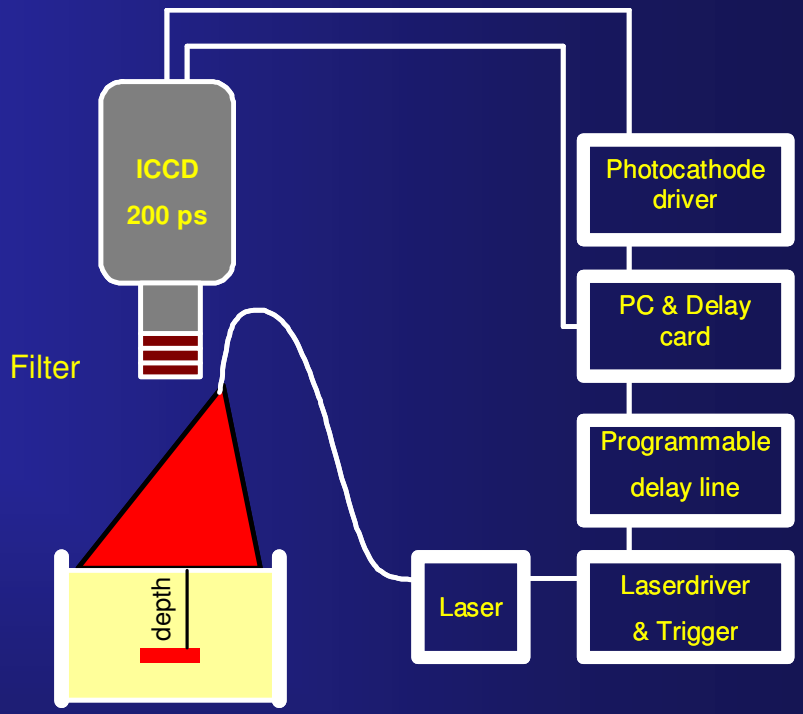
Comparison with histology (cumulative frequency)



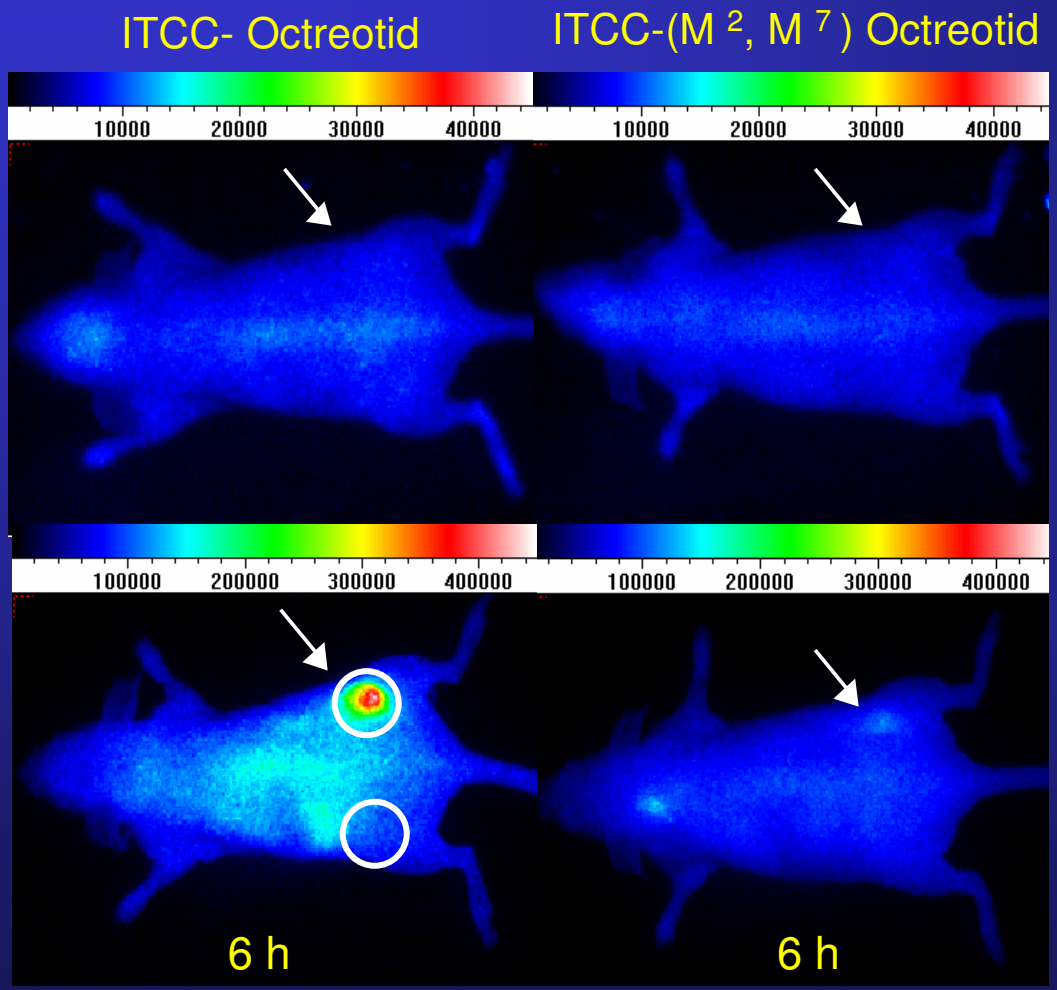
Cancer Research, 2001, 61, 991-999

Experimental setup: Gated fluorescence imaging





Receptor targeted NIR- imaging of mouse xenografts with fluorescent ligands



nature biotechnology, 2001, • 19, 327 - 331

In vivo fluorescence imaging of tumors

SSTR2 Tumor, NIR38: 20nmol /kg body weight

Octreotid

R = dPheCys-Phe-dTrp-Lys-Thr-Cys- Thr

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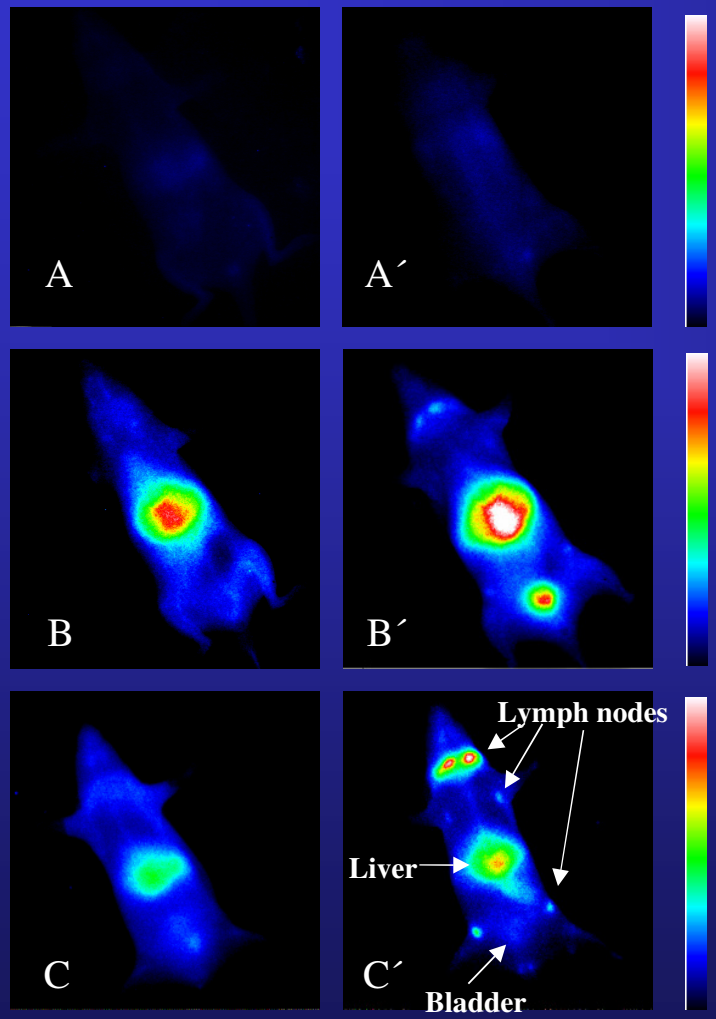
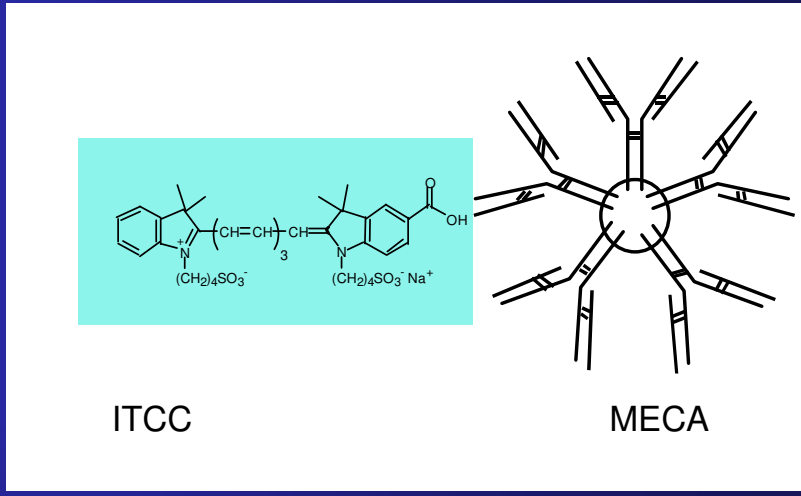
Optical molecular imaging of lymph nodes using a targeted vascular contrast agent





strong fluorescence in the liver consistent with the hepatobiliary elimination pathway

J Biomed Opt. 2005, 10(4):41205

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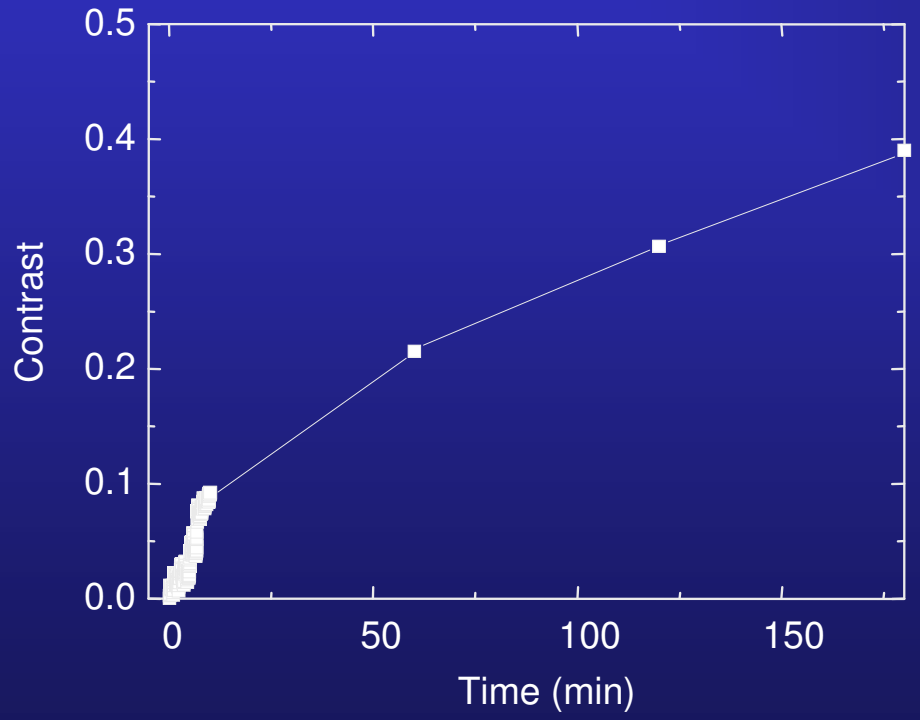
Optical molecular imaging of lymph nodes using a targeted vascular contrast agent

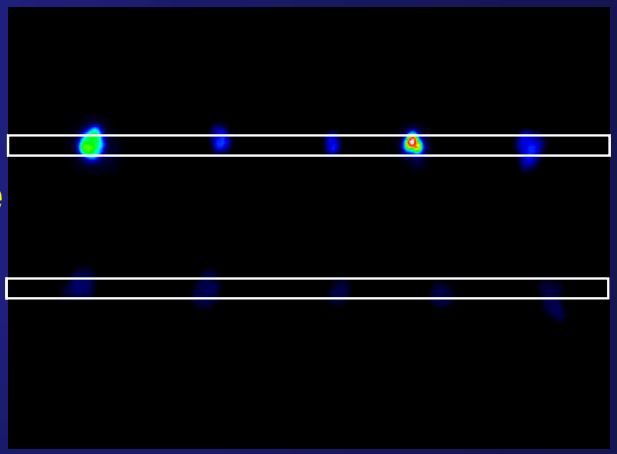
Contrast: $K = (I_{lymph} - I_{muscle})/I_{muscle}$



High sensitivity, requiring as little as 0.25 nmol dye per animal

MECA 79
Cyanine dye

Control
conjugate



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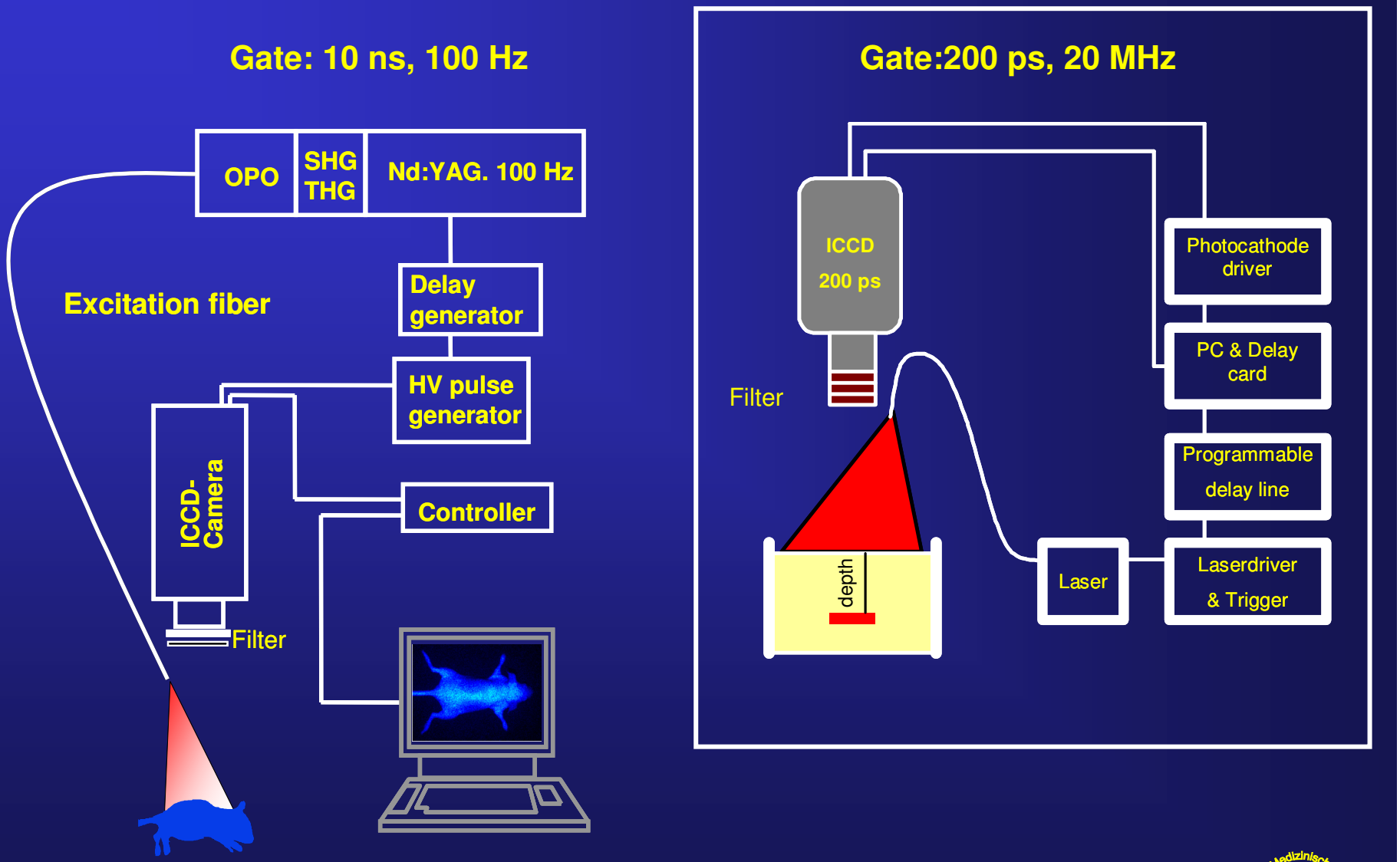
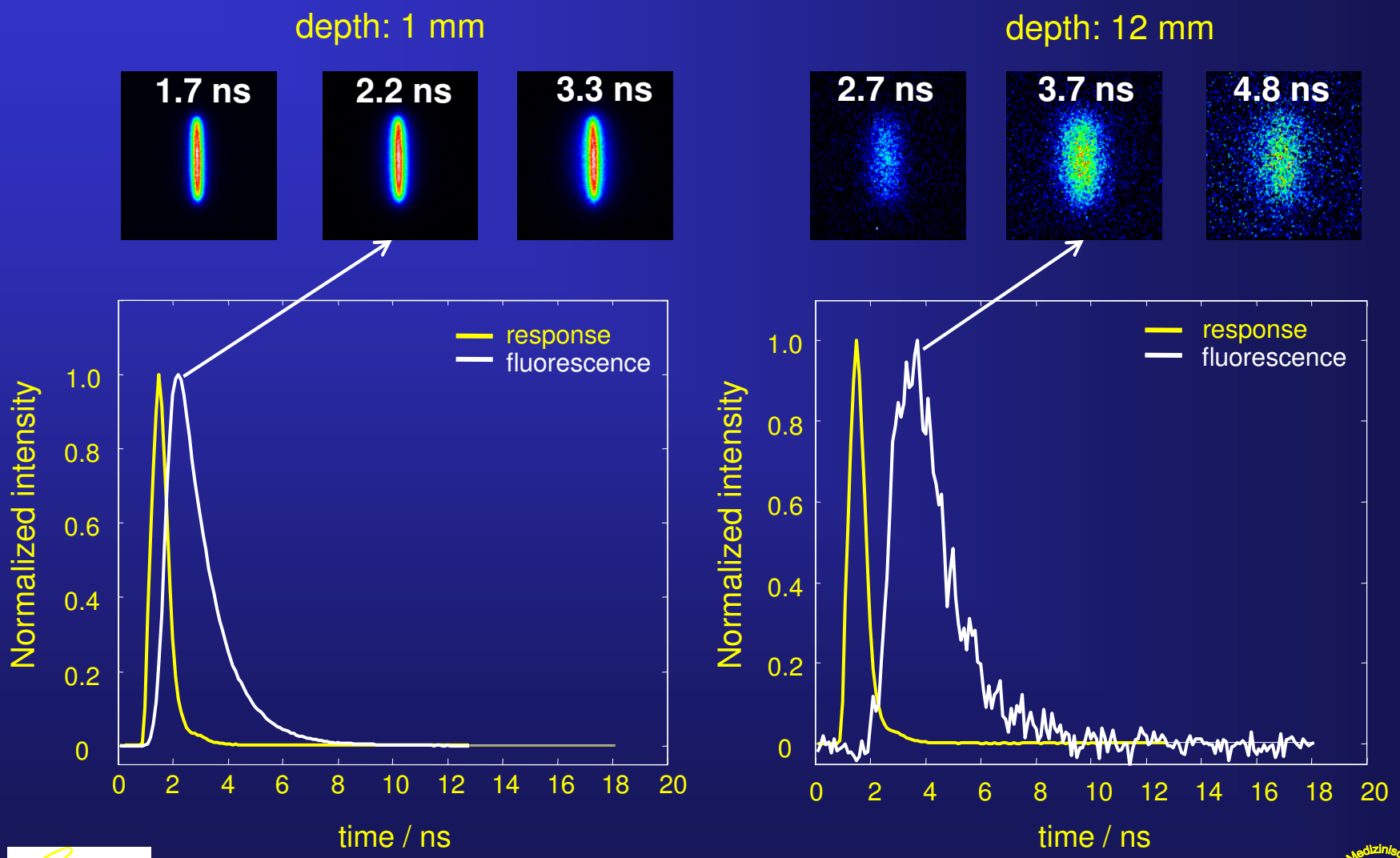
Experimental setup: Gated fluorescence imaging



Depth resolved fluorescence imaging

Fluorescent rod at different depth in a scattering solution $\mu'_s = 14\ cm^{-1}$



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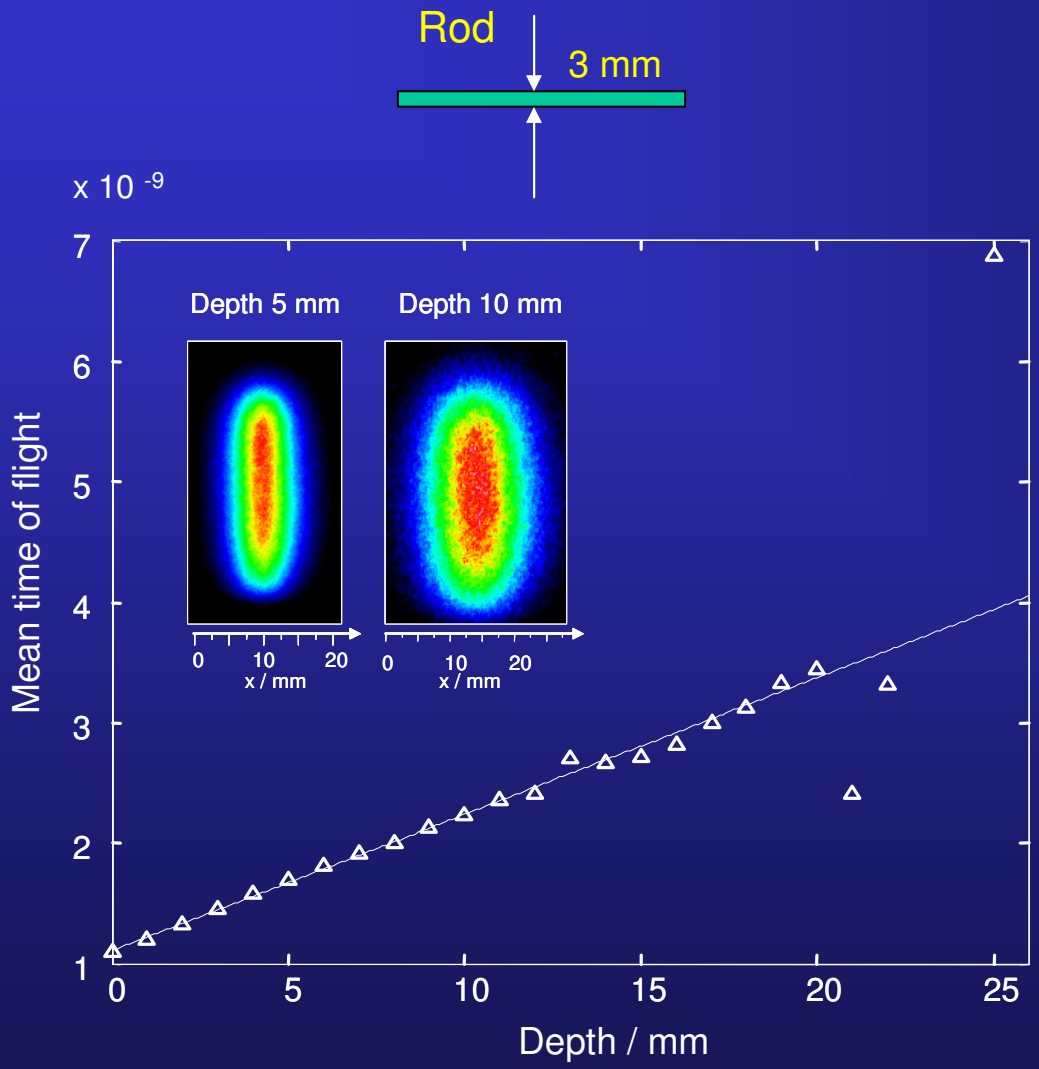
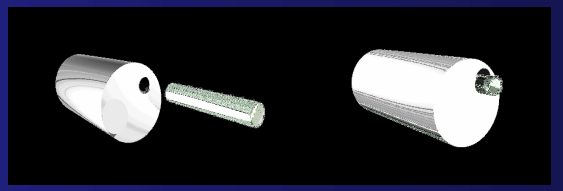
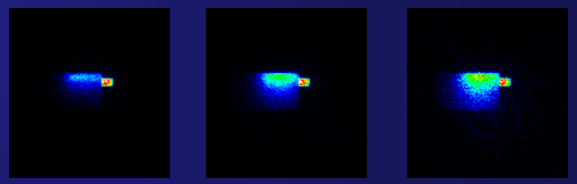


Influence of geometry

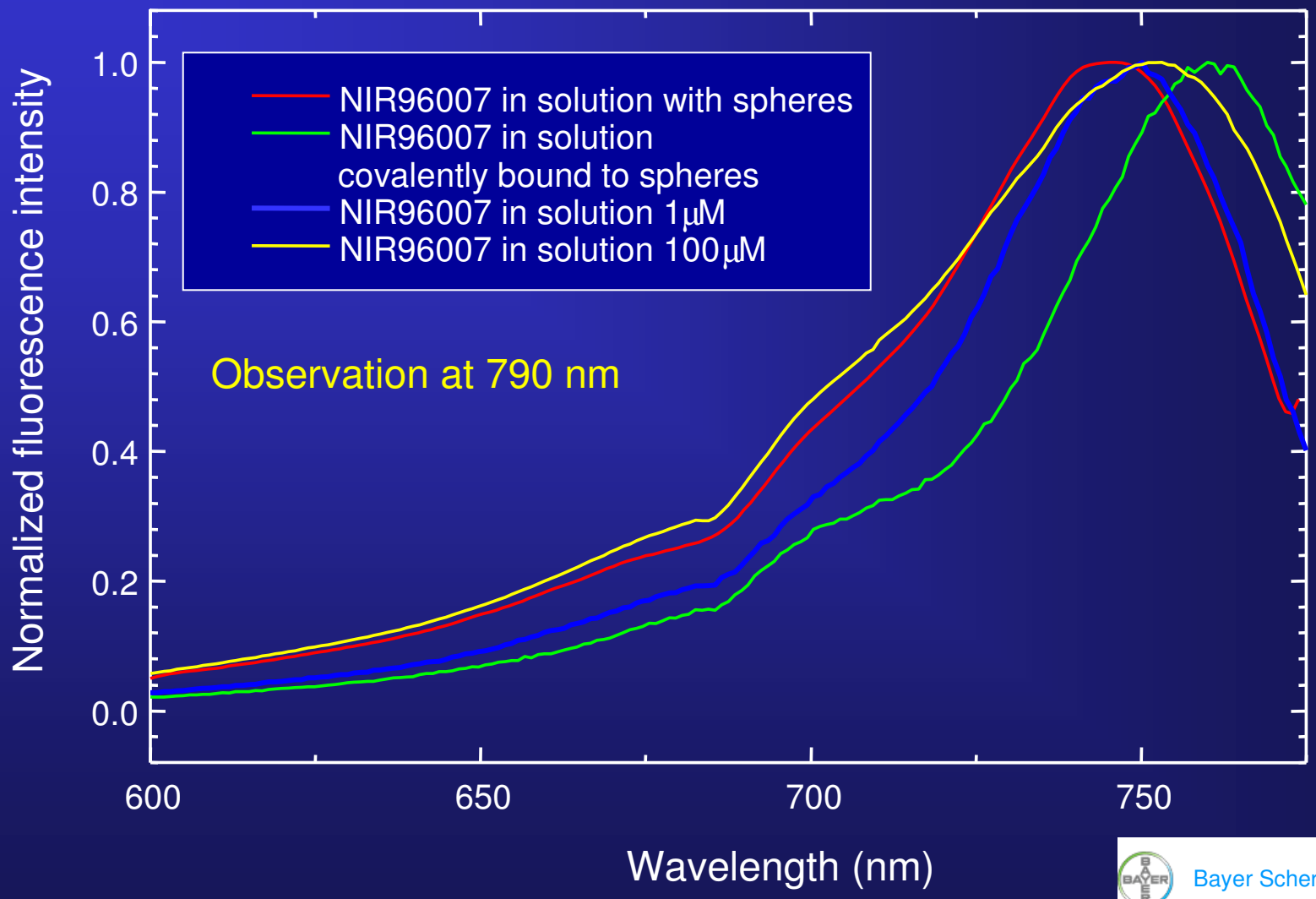


2.2 ns 2.85 ns 4.0 ns



Fluorescence reference material and application

Fluorescence excitation spectra



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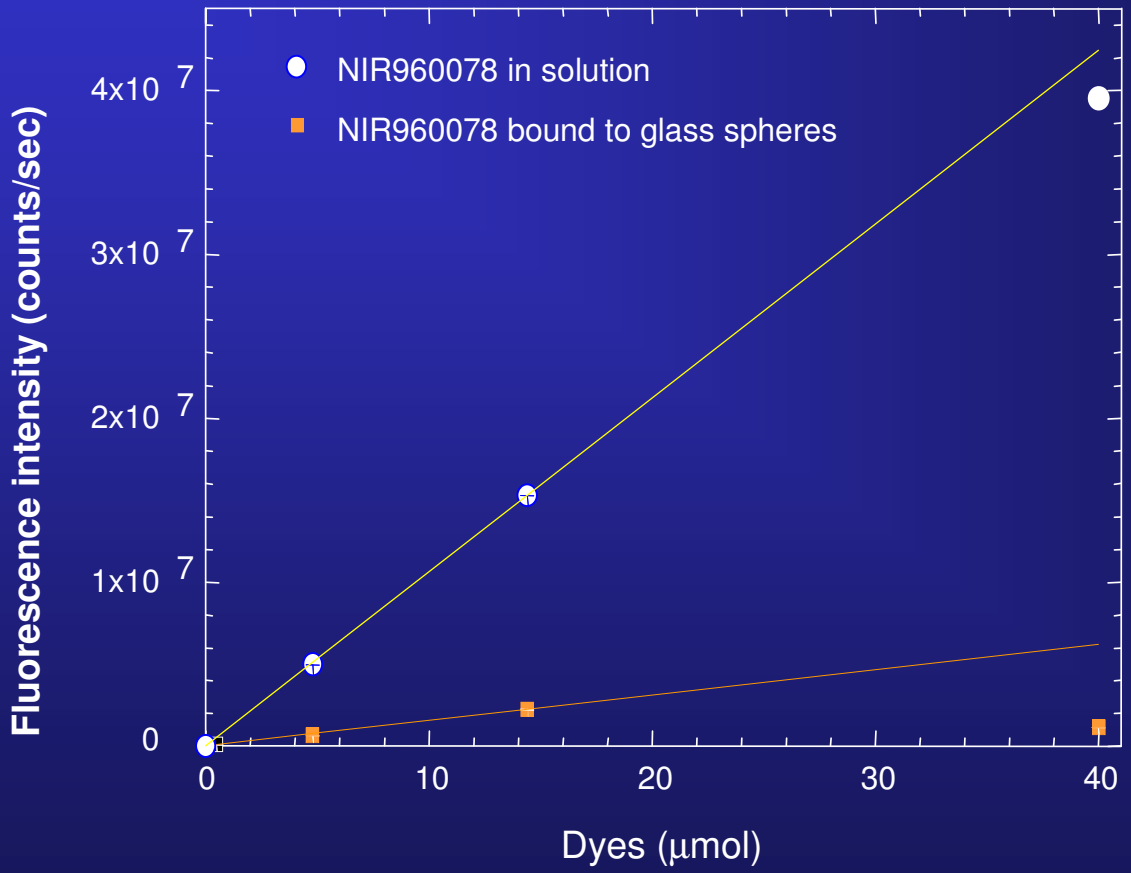
Fluorescence intensity in dependence on concentration of cyanine dye molecules



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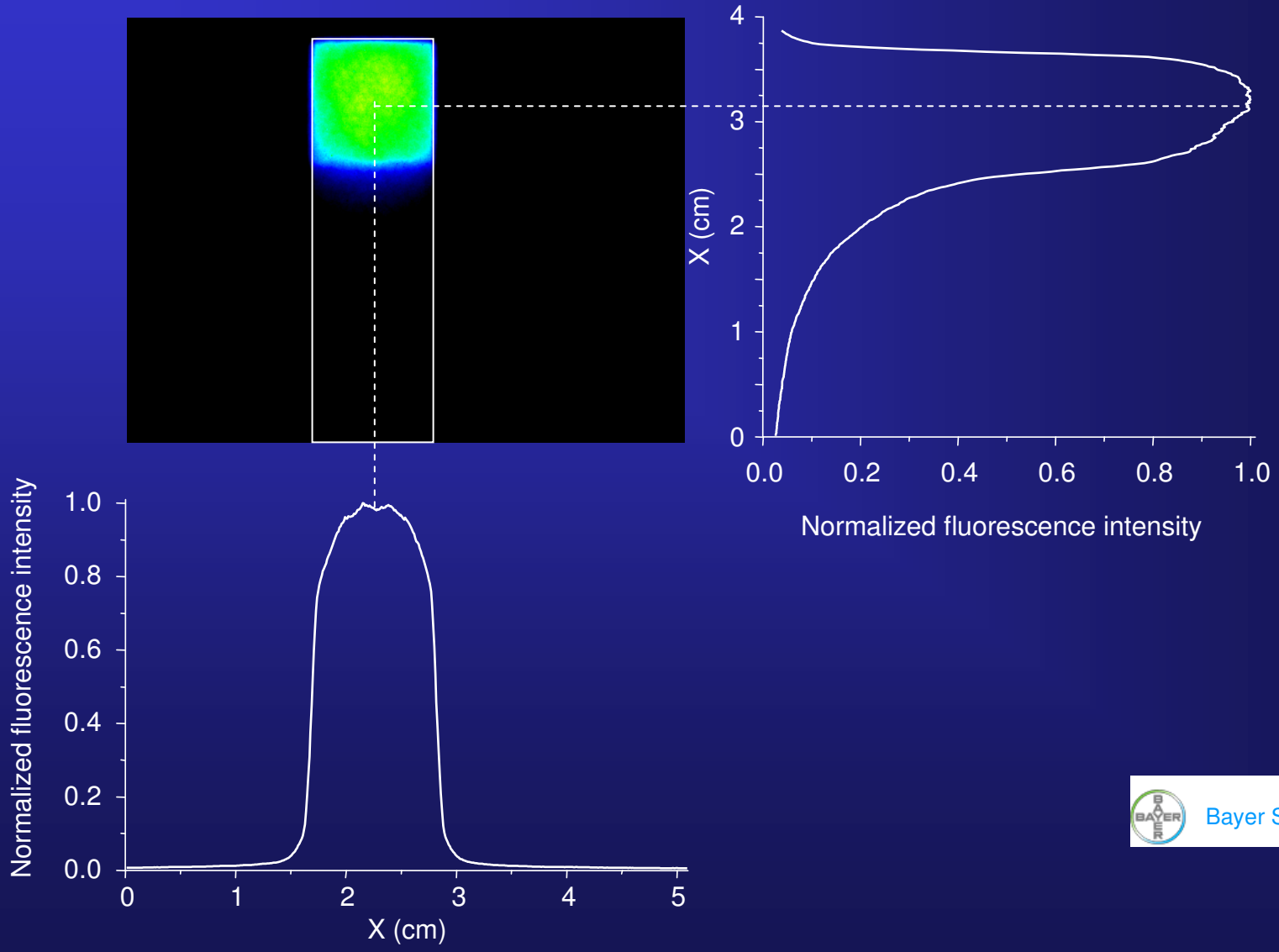
Scattering phantom with NIR96007, 2% on glass spheres



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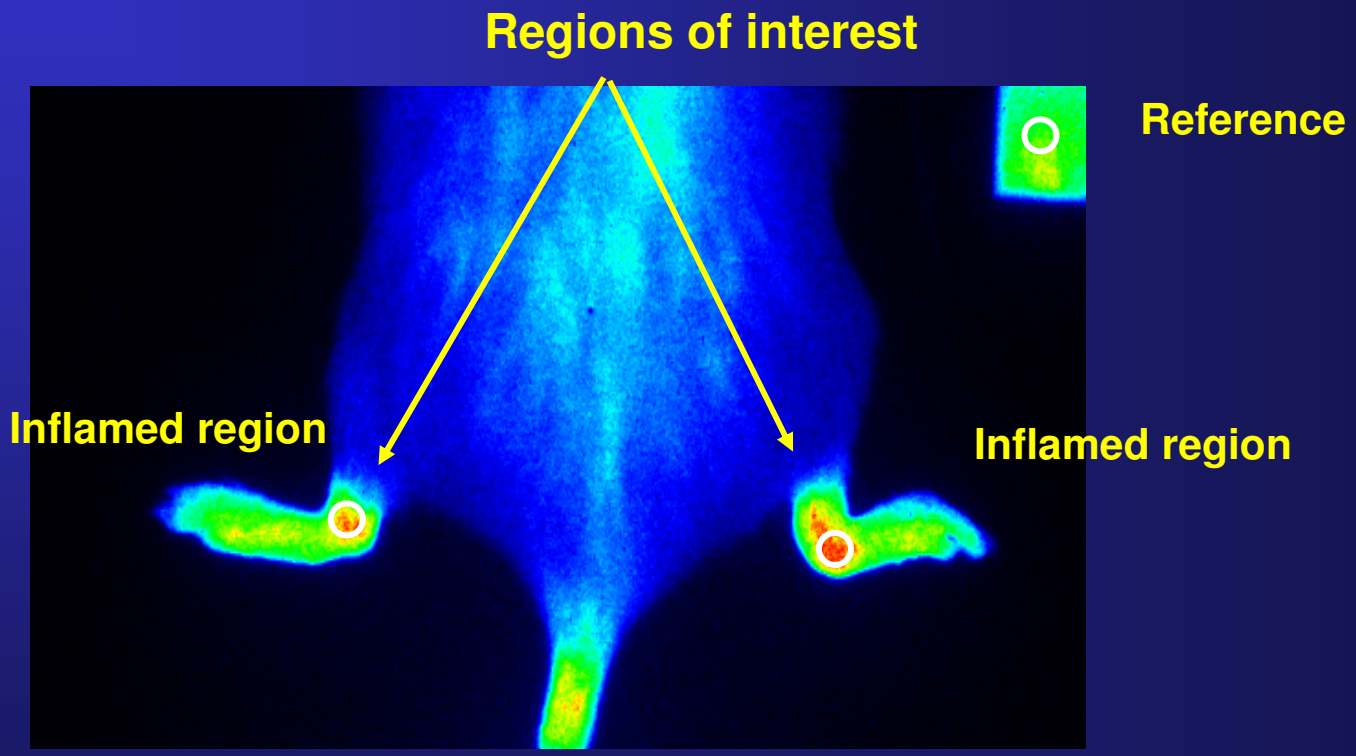
Monitoring of inflammation of ankle joints using cyanine dyes as contrast agents



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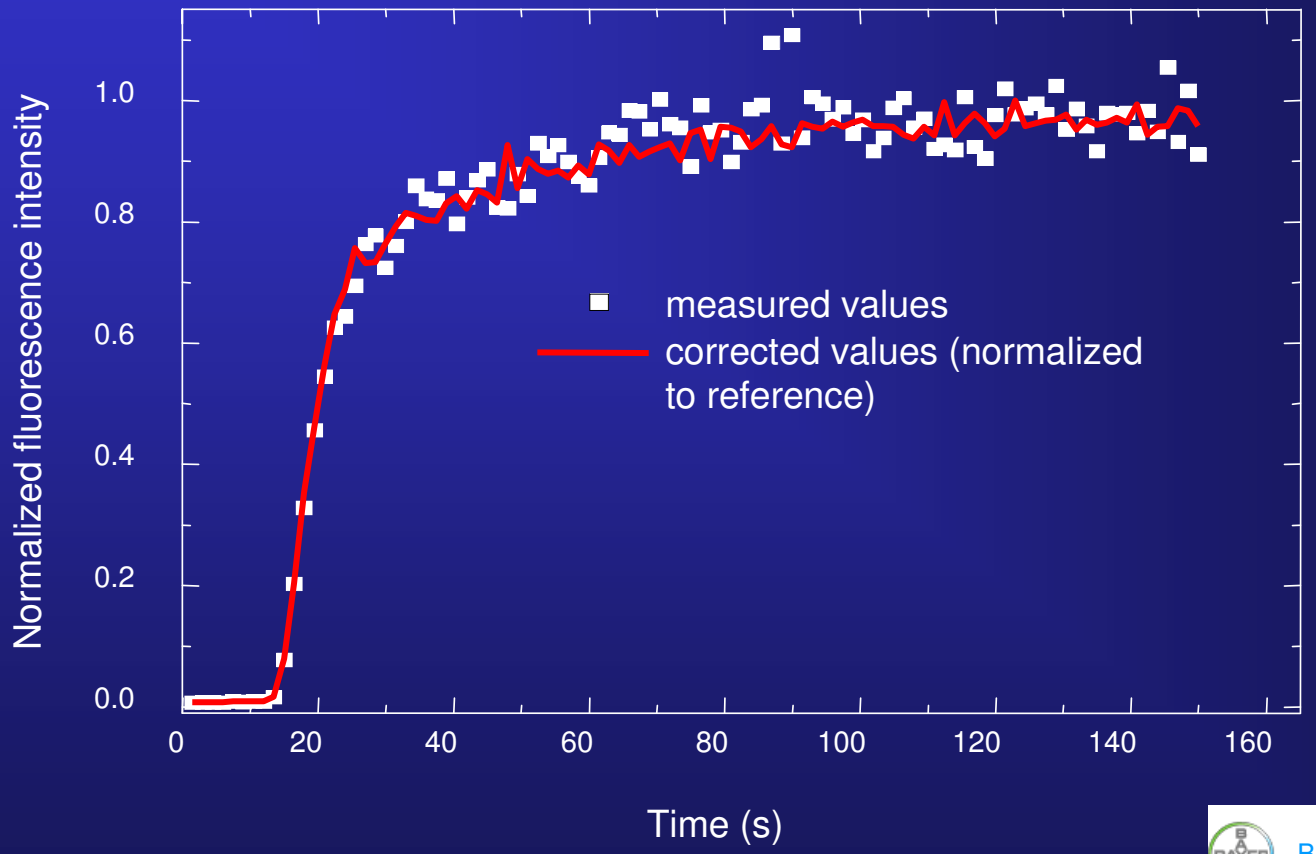
Increase of fluorescence intensity in the right ankle joint after i.v. application of a cyanine dye



J Fluoresc. 2005 15(3):337-62

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Conclusion

- ★ Small malignant regions (dysplasias) in the gastrointestinal tract can be identified.
- ★ Light sources with high pulse energy and low repetition rates are preferable to suppress ambient light
- ★ Succesful targeting of endothelial surface-expressed molecules - leukocyte homing
- ★ Determination of depth of inclusions by time resolved fluorescence imaging
- ★ Fluorescent phantoms are needed, however, to match optical properties of biological tissue is difficult