

Laboratory Approaches for Therapy Modelling: Tissue Phantoms and Simulations

Maximilian Aumiller^{a,b}

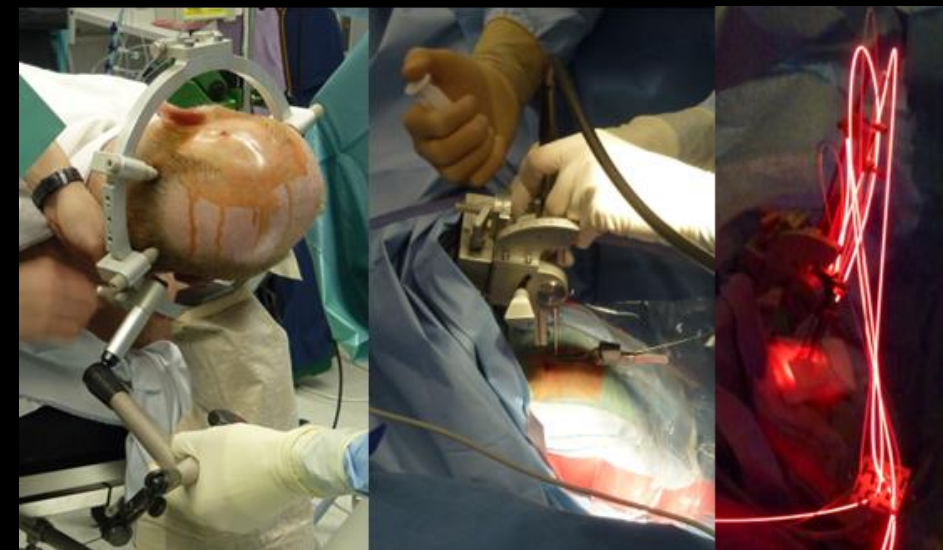
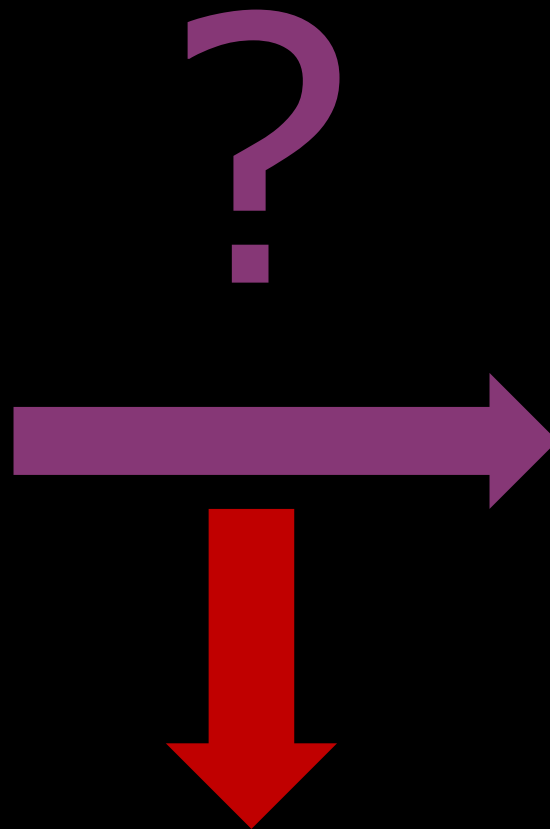
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GlioLighT Workshop

1st September 2026



Laboratory Investigations

The Laboratory Approach

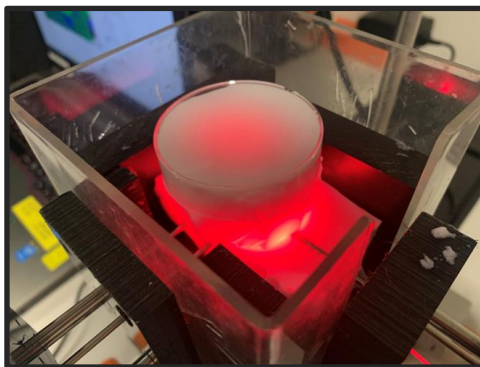
- Basic research
- Procedure evaluations
- (Side-)Effect investigations
- Feasibility testing
- Translational



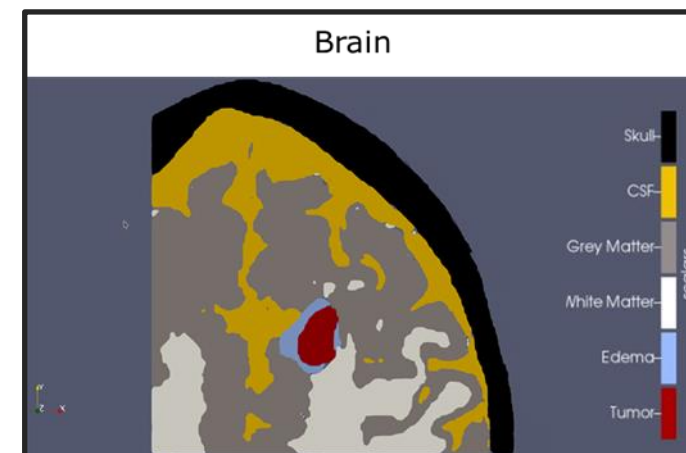
Some kind of test set-up / environment needed

The Laboratory Approach

Ex-vivo/in-vitro laboratory tests



Analytics and Simulation



None of the approaches stands alone.

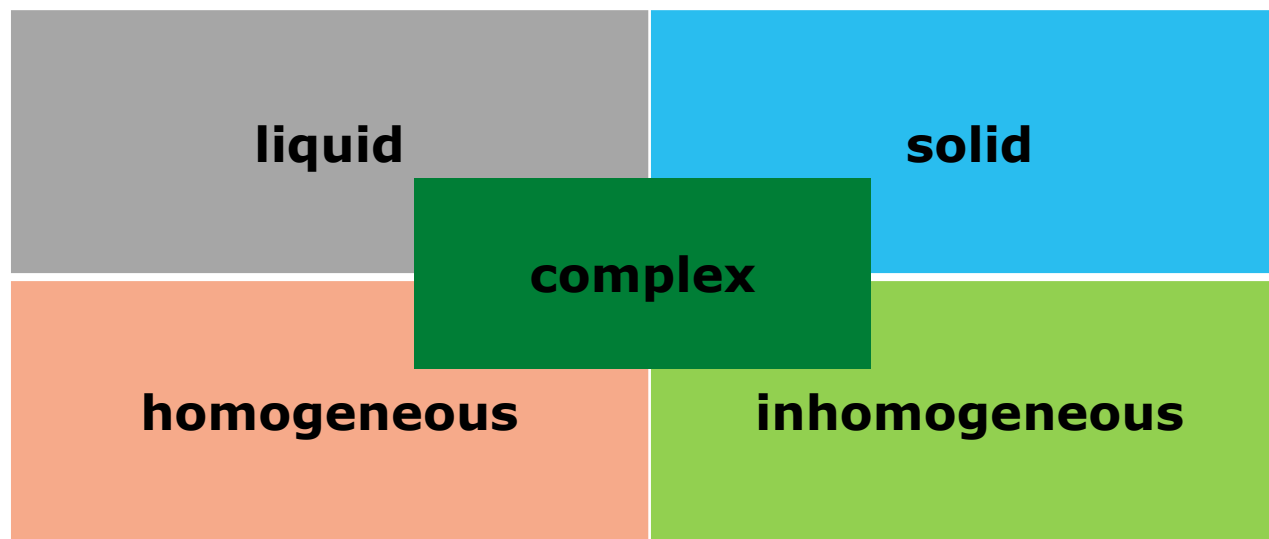
Analyse Laboratory Data
Validate Simulations with Lab-Data

Ex-Vivo/In-Vitro Laboratory Tests

- *Tissue phantoms*
- *Tissue tests*
- *(Cell culture)*

Tissue Phantoms

- **Def.:** Liquid or solid tissue-equivalent medium and object for simulating the interaction between biological objects and radiation
- **What is needed?**
- **What can be used?**



Tissue Phantoms - What do i need?

solid

optical tissue properties

mechanical tissue properties

conditional homogeneous

easy - complex fabrication

multilayer/
inhomogeneous



liquid

optical tissue properties

homogeneous

easy fabrication

What do i need?

- Phase dependent on matrix material

- Silicon

- Synthetic resin (e.g. epoxy)

} solid



setting lotions,
solidifiers,
binding agents

gelantine, Agar,
castor,
gypsum, cement



- Liquid buffer (PBS, water)

} liquid



Optical tissue phantoms

- Reminder - optical tissue properties: absorption, scattering, anisotropy
- At least 1 more ingredients next to matrix needed
 - Absorber material
 - Scattering material
- Choose of material by comparison with literature values
- Adjustment by mixing ratios and components

Tissue Phantoms

What is the most simple representation of the usage?

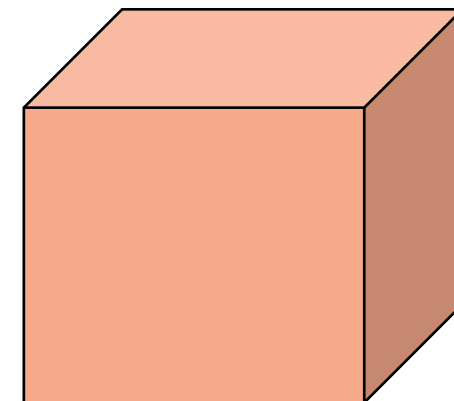
What do you want to show?

- In 99% of cases:

Homogeneous Block of tissue with well-known properties.

- **PDT/DLT GBM case:** Homogeneous Solid/Liquid Phantom with tumor-like properties.

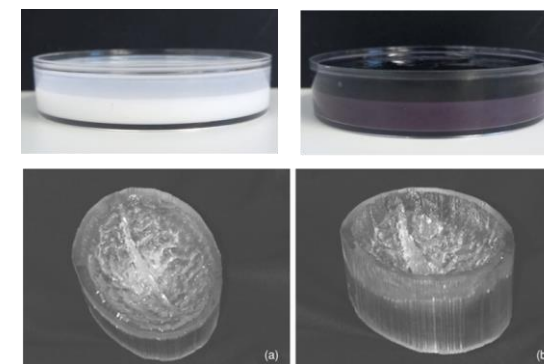
- Starting point to be modified after initial testing.



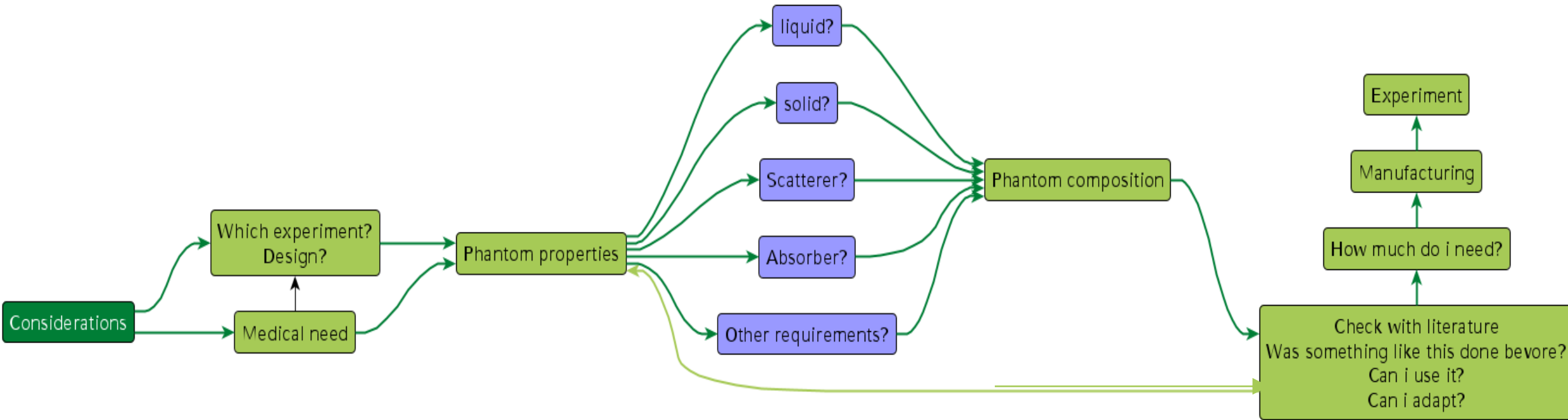
Tissue Phantoms

Increase complexity by

- adding special reagents
 - PpIX for fluorescence
 - Blood,
- alter the phantom geometry
 - inhomogeneities in the phantom (tumor within brain matter)
 - use molds for special shapes
 - inhomogeneous phantoms (mimic skin)
- Get animal tissue from the butcher (pork, cow, chicken,...)



Tissue Phantoms - Considerations



Ex-Vivo/In-Vitro Laboratory Tests

Pogue BW, Patterson MS.

Review of tissue simulating phantoms for optical spectroscopy, imaging and dosimetry.

J Biomed Opt. 2006 Jul-Aug;11(4):041102. doi: 10.1117/1.2335429. PMID: 16965130.

Optical Phantom Components

Matrix		Liquid		Agar		Silicone	
phantom properties		homogeneous		multi-layer, limited homogeneity		multi-layer, limited homogeneity	
biocompatible		-		yes		no	
fabrication		“easy”		time consuming			
radiation		all		all		non-interstitial	
Absorber	Blood	Ink	Fluorophores	C-Dots			
absorbance spectra	characteristic	type dependent	selective	Adjustable			
durability	low	high	Bleaching/irradiation time dependent	unknown			
special	PBS needed(liquid phantom)	problem: reproducibility	fluorescence, bleaching products	expensive, chemical modification for application			
Scattering media		Lipids		Microspheres		Metal oxides	
scattering		linear shape, easy to predict (literature, Mie-Scattering)					
durability		Low-medium		nonperishable		nonperishable	
special		scattering similar to biological tissue		expensive		problem: sedimentation	

Analytics and Simulation

- Analysis
- Monte Carlo
- Partial Differential Equation (PDE)

Analysis

- Get more information from the Laboratory Data
Theory or Self-Designed

RTE:

$$\frac{1}{c} \frac{\partial L(\bar{r}, \bar{s}, t)}{\partial t} = -\bar{s} \cdot \bar{\nabla} L(\bar{r}, \bar{s}, t) - (\mu_s + \mu_a) L(\bar{r}, \bar{s}, t) + \mu_s \int_{4\pi} p(\bar{s}, \bar{s}') L(\bar{r}, \bar{s}', t) d\Omega' + S(\bar{r}, \bar{s}, t)$$

**Diffusion
Approximation:**

$$\Phi(\bar{r}) = P \frac{\mu_{eff}^2}{4\pi \mu_a r} e^{-\mu_{eff} r}$$

F Martelli, Light Propagation Through Biological Tissue and Other Diffusive Media

Analytical Description

Complex solution

- Also very complex solutions for RTE available:

$$L(r, \hat{s} \cdot \hat{r}) = \frac{\exp(-(\mu_a + \mu_s)r)}{4\pi r^2} \frac{\delta(\hat{s} \cdot \hat{r} - 1)}{2\pi} + \frac{\phi(r, \hat{s} \cdot \hat{r})}{4\pi}$$

$$\phi(r, \hat{s} \cdot \hat{r}) = \frac{\mu_s}{4\pi} \sum_{\lambda_i > 0} \sum_{l=0}^N A_l^{(i)} \lambda_i^l \left[P_l \left(\frac{\mu_a + \mu_s}{\lambda_i} \right) \int_0^\infty \frac{e^{-\lambda_i \sqrt{r^2 + \xi^2 - 2r\xi(\hat{s} \cdot \hat{r})}}}{\sqrt{r^2 + \xi^2 - 2r\xi(\hat{s} \cdot \hat{r})}} e^{-(\mu_a + \mu_s)\xi} d\xi + (-1)^l \sum_{k=0}^l \frac{c_{kl}}{\lambda_i^k} \sum_{n=0}^{k-1} (-\mu_a - \mu_s)^{k-n-1} D(r, \hat{s} \cdot \hat{r}) \right]$$

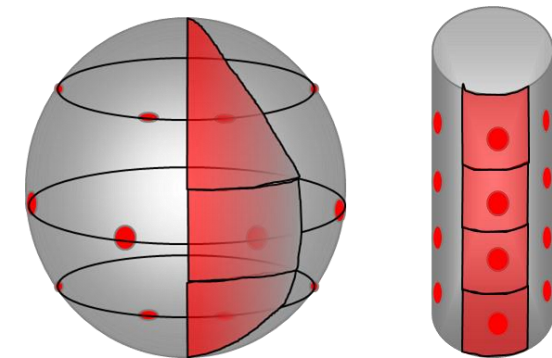
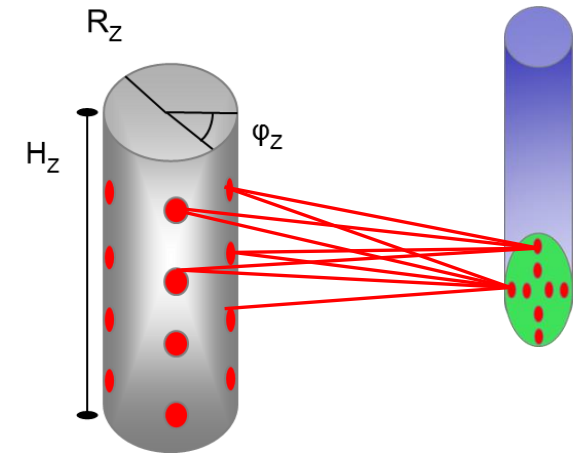
Liemert 2012, Journal of Quantitative Spectroscopy and Radiative Transfer

Analytical Description

RTE-Solutions Usage

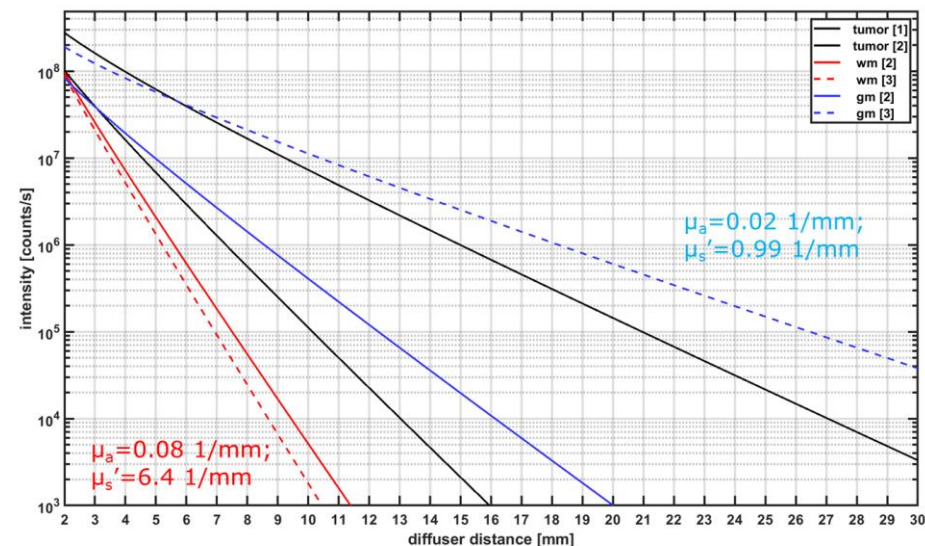
- Basic equation only point source vs. point detector
- Can be adjusted for different source and detector geometries:
 - Assumption of multiple point light sources / point detectors

$$I_{t,theo} = \frac{P_0 \cdot L_E}{N} \sum_i \sum_j \Phi_{ij}(r_{ij}, \mu_a, \mu'_s)$$

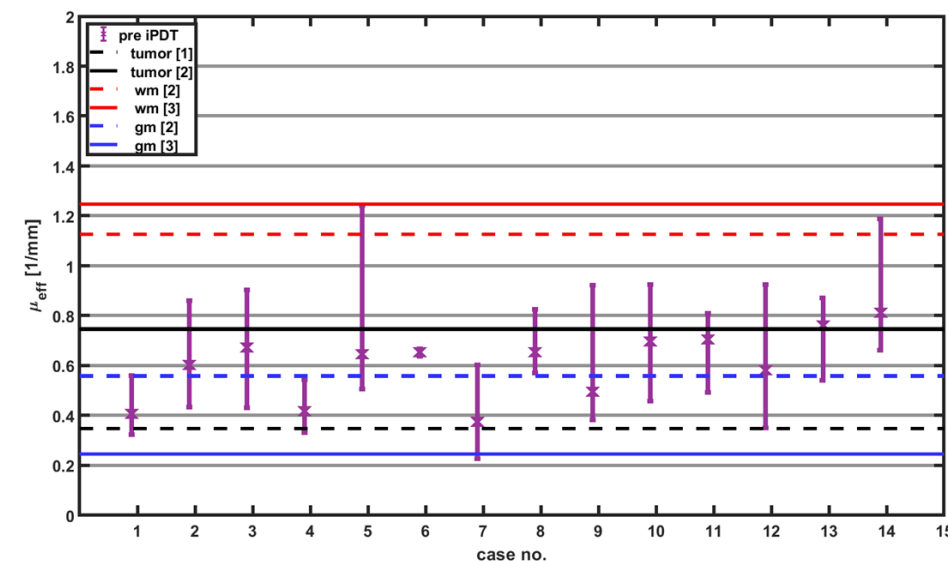
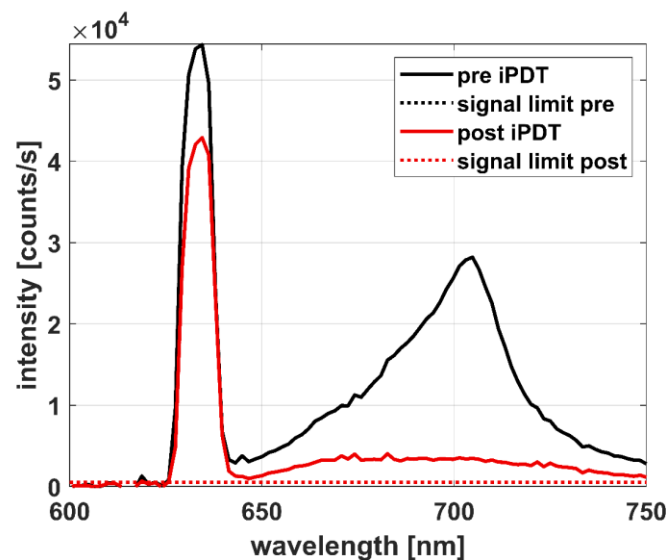


Analytical Description RTE-Solutions Usage

- Forward calculations for theoretical signal intensities



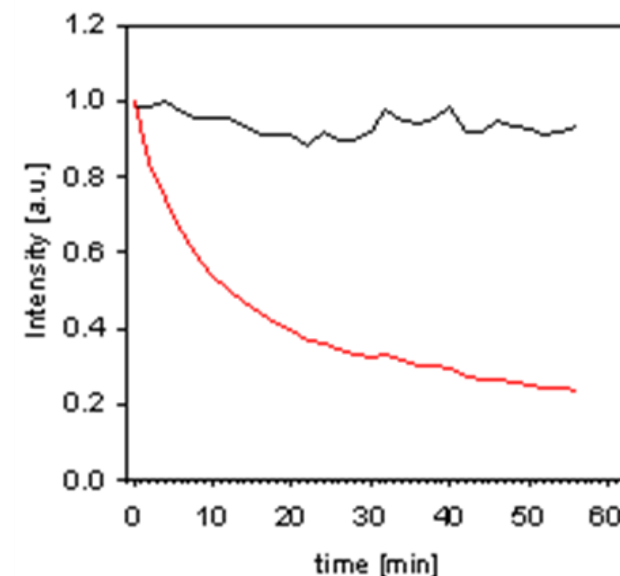
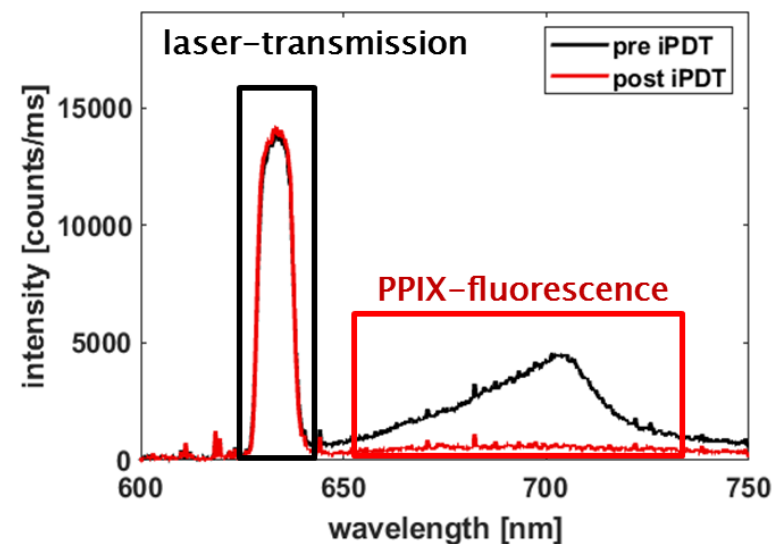
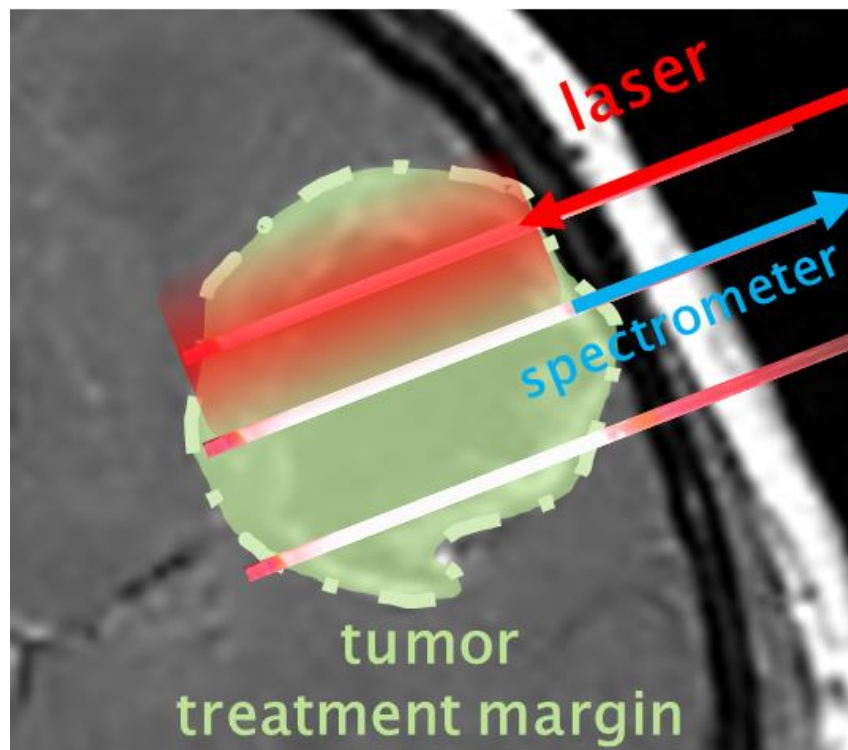
Extraction of optical coefficients



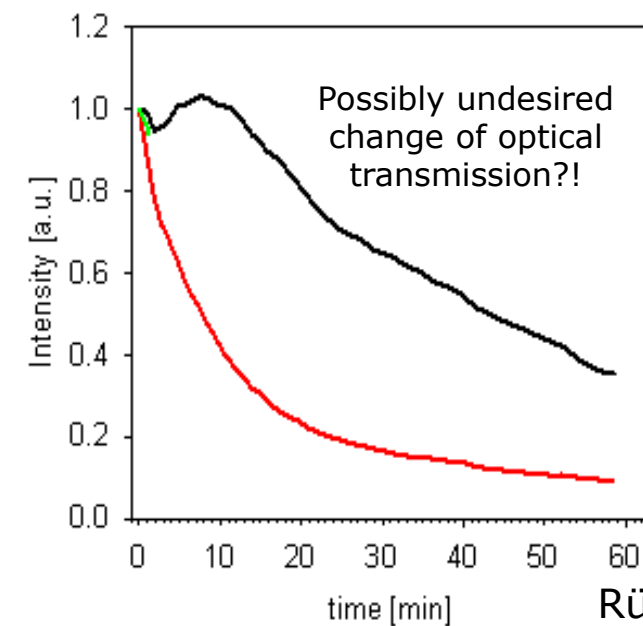
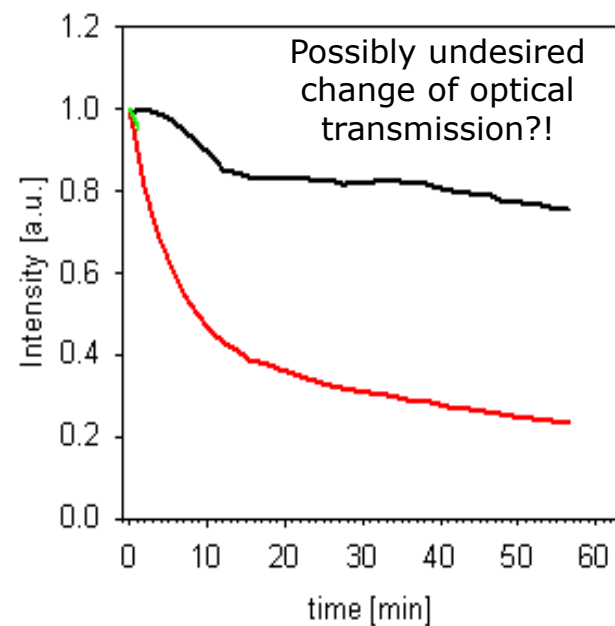
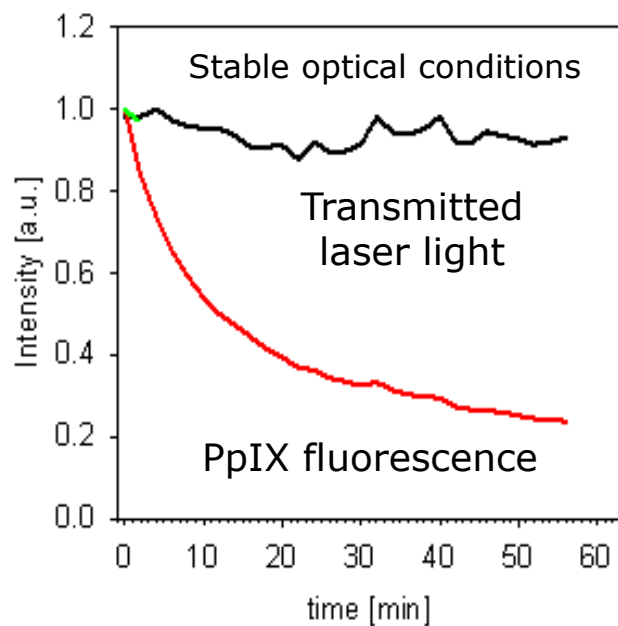
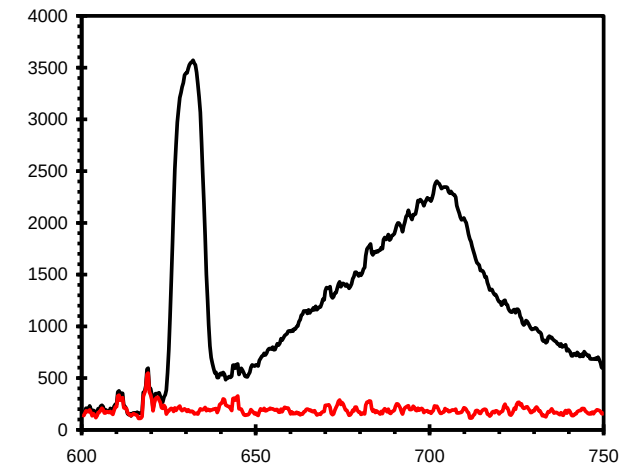
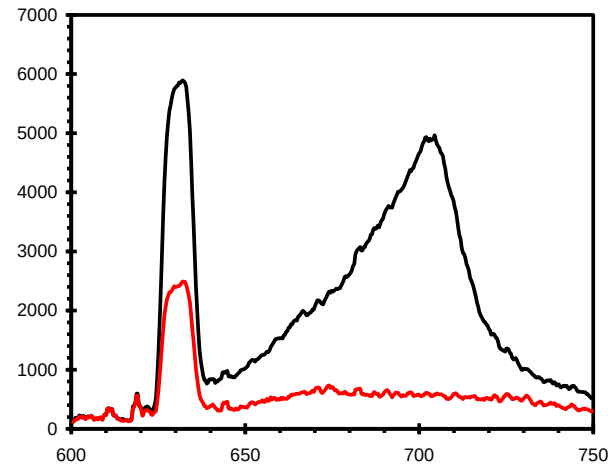
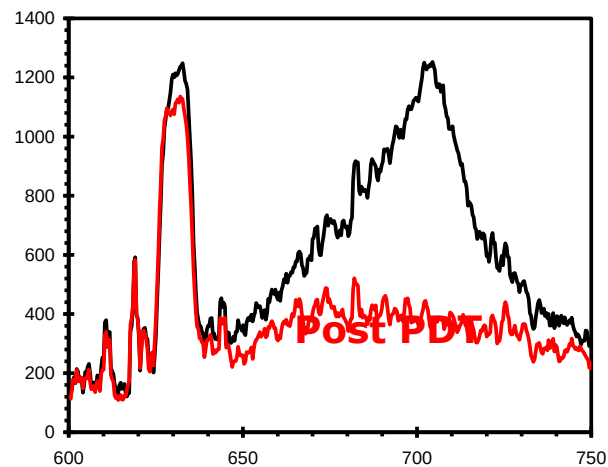
Aumiller 2021 Cancers Basel
Aumiller 2022 PDT Update

Example for Combination of Phantoms and Analysis Spectral Online Monitoring During iPDT

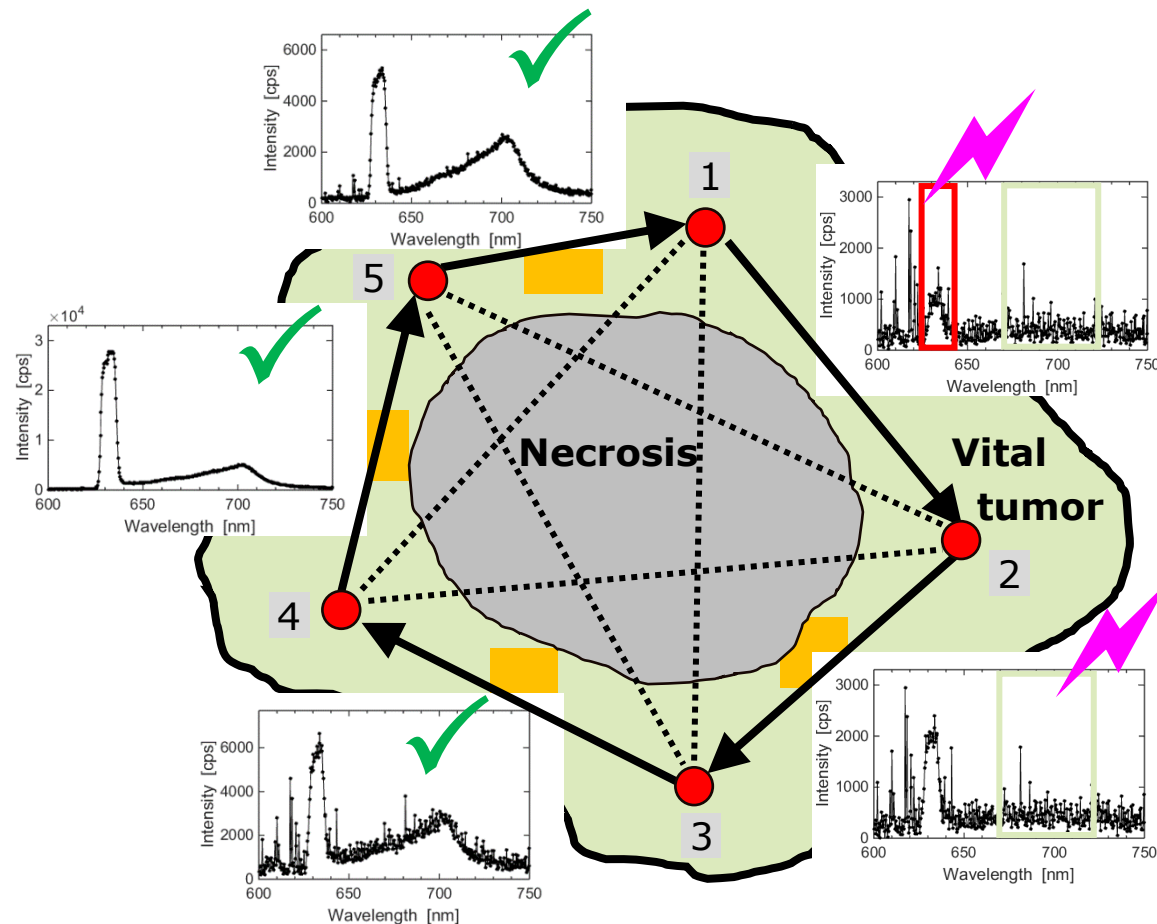
- Spectral measurements between light applicators before and after laser treatment



Spectral Online Monitoring – Problem Signal Changes



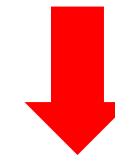
Spectral Online Monitoring – Problems Signal Changes



Problem 1

No **transmission** + **fluorescence**

→ Insufficient light dose !



No PDT effect!



Problem 2

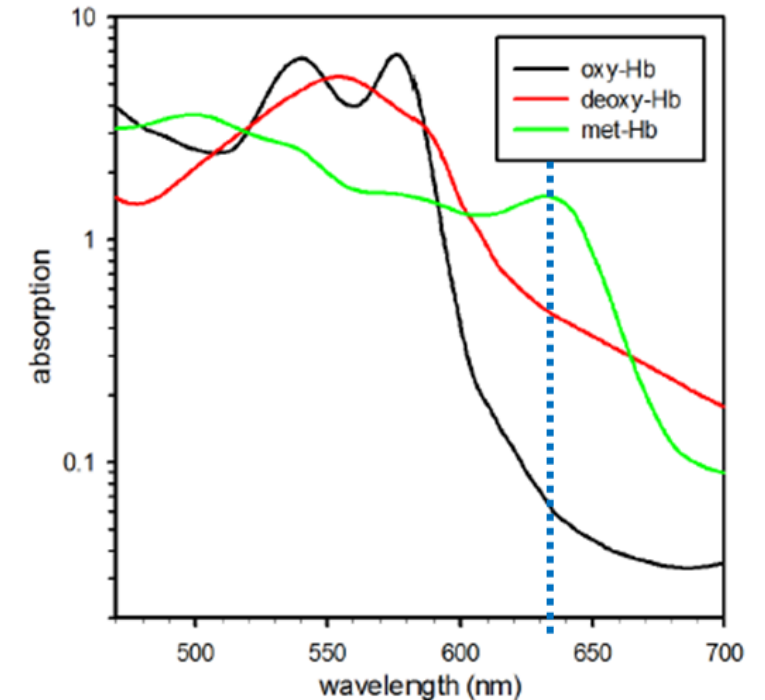
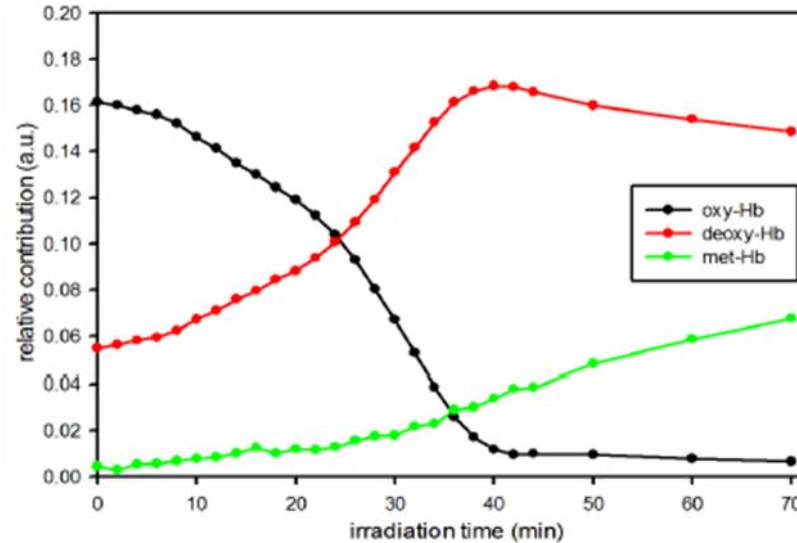
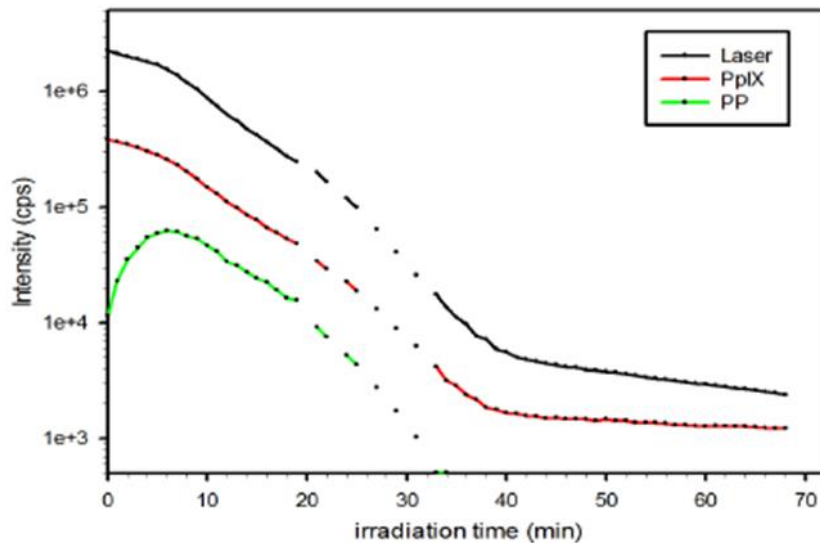
Transmission but no **fluorescence**

→ No PpIX accumulated !

A. Rühm, Proc. SPIE 89280E (2014)

Spectral Online Monitoring – Latest Research

- Different absorption of oxygenated, deoxygenated and methemoglobin
- If there is blood in the treatment volume, the absorption may change!
- → Avoid bleeding!

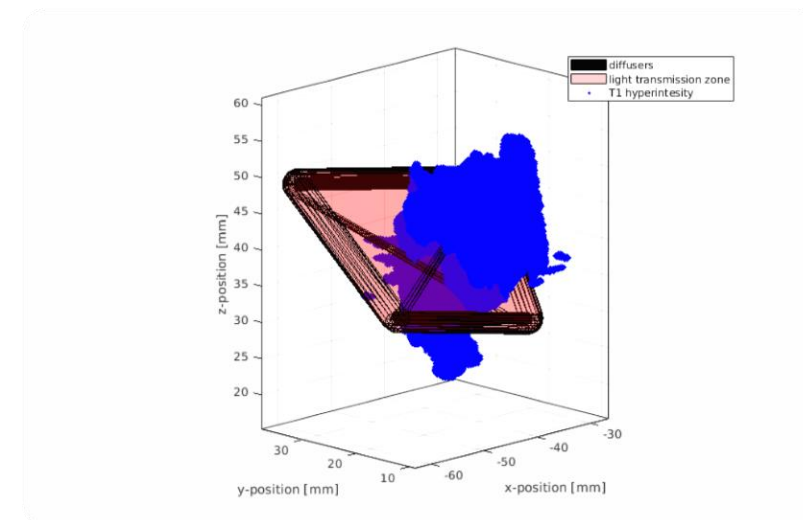
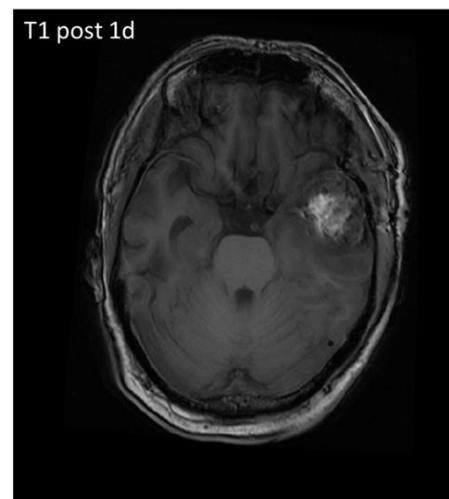
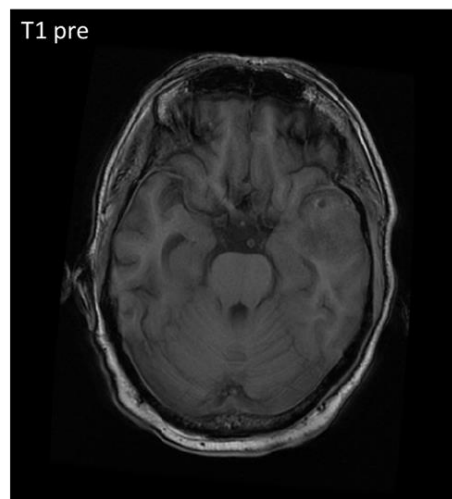
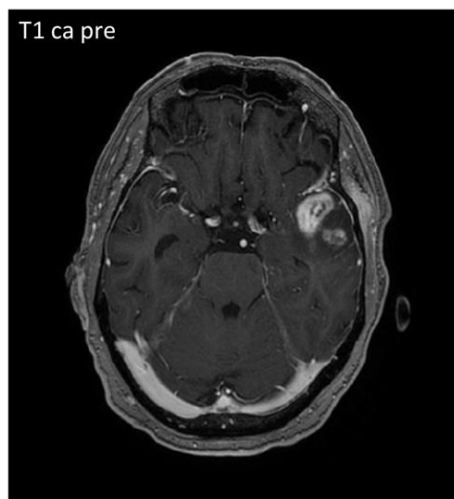
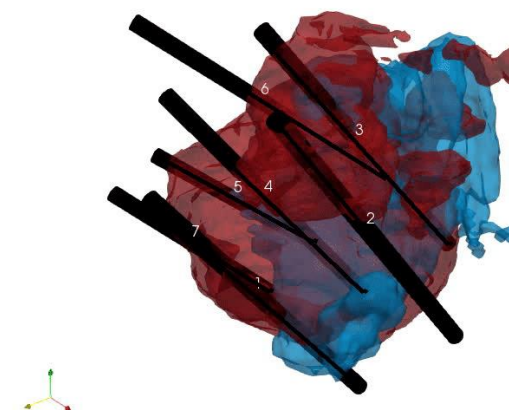


C. Heckl, PhotochemPhotobiol 2020

Spectral Online Monitoring

- Intrinsic T1 hyperintensity in treatment volume **after** iPDT
- 3D position analysis showed: light transmission signal decrease is related to intrinsic T1 hyperintensity

→ Signal decrease related to microhemorrhages in tumor

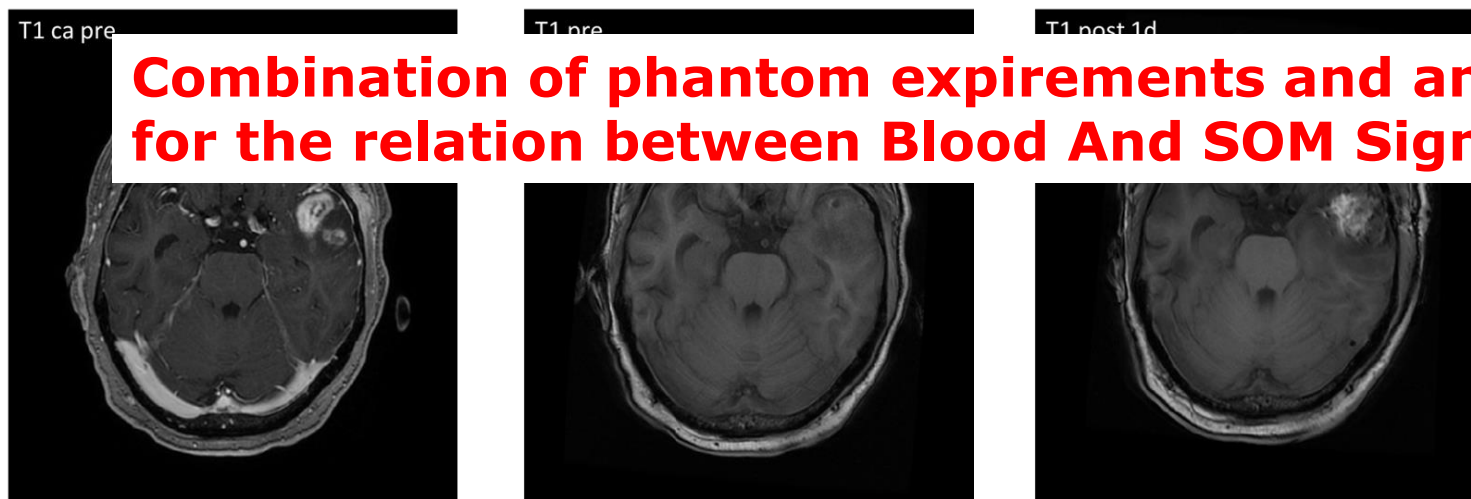
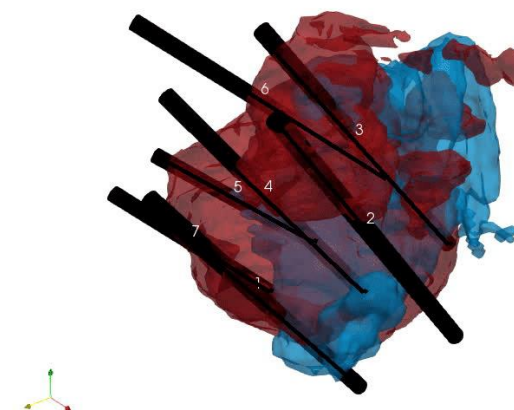


M. Aumiller, Cancers 2021

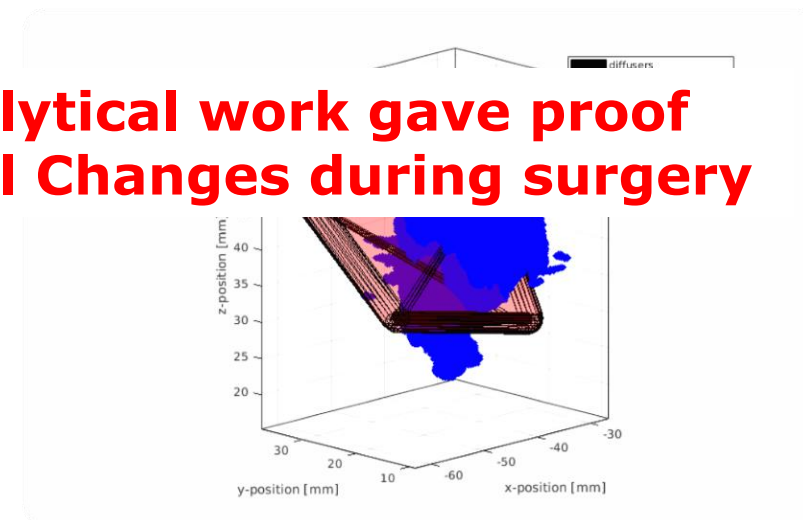
Spectral Online Monitoring

- Intrinsic T1 hyperintensity in treatment volume **after** iPDT
- 3D position analysis showed: light transmission signal decrease is related to intrinsic T1 hyperintensity

→ Signal decrease related to microhemorrhages in tumor



Combination of phantom experiments and analytical work gave proof for the relation between Blood And SOM Signal Changes during surgery



M. Aumiller, Cancers 2021

Simulation

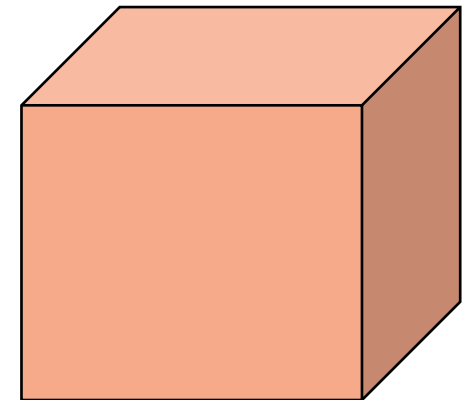
Overcome the limitations of the laboratory and analytical equations

„The only true solution to some problems in physics is the simulation“

What is the most simple representation of the usage?

What do you want to show?

- Simple version: testing if the basic physics approach works
- Go into complex modelling



System and properties must be well known – Simulation only as accurate as input.

Simulation

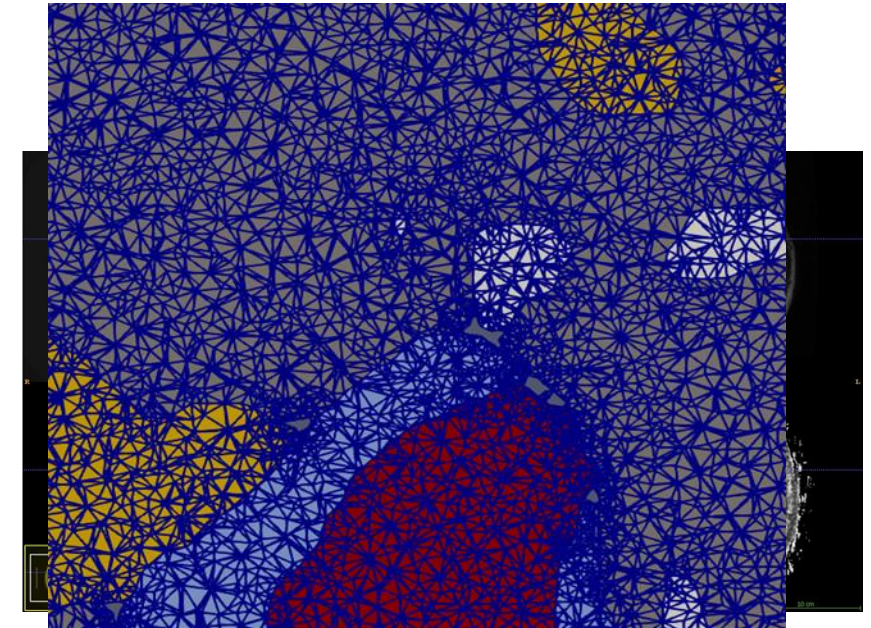
- 1) Geometry & Mesh Generation**
- 2) Setting Up and Running the Kernel**
- 3) Analysis – Comparison with Laboratory Data**

Simulation

1) Geometry & Mesh Generation

3D file generation – 1:1 ratio of reality

- CAD drawing
- Segmentation of Brain CT/MRI
- Meshing → Tetrahedron Mesh
 - Own Tool or Software built-in
 - Structure for simulating interactions



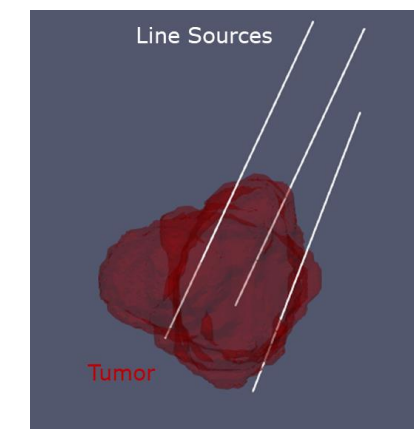
Simulation

2) Setting Up and Running the Kernel

- Set the environment:
Optical, thermal, physical, mechanical properties, for each tissue type
- Set up boundary conditions
- Set the interactions – for PDT/DLT Light Source Definition and Placement.
Cylindrical Diffusor: Line Source or Pseudo Cylinder?
- **Run the Kernel and the Simulation**

	μ_a/mm^{-1}	μ_s/mm^{-1}	g	n
Glioblastoma (blood free)	0.085	19.1	0,89	1,37
Blood (96% Ox)	0.35	364	0,99	1,33
Blood (75% Ox)	0.82	357	0,99	1,33

Tuchin 2015



Simulation

2) Setting Up and Running the Kernel

■ Run the Kernel and the Simulation

Reach the convergence point

- Statistical computation of probability experiments
- Law of large numbers (LLN)

Repetition of the Kernel is needed until the result statistically does not change anymore

For iPDT / DLT → several Million Photons

Limitation: Hardware defines precision and what you can actually do



Simulation

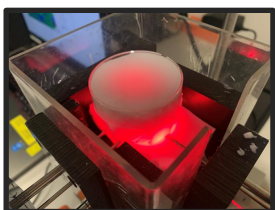
3) Analysis – Comparison with Laboratory Data

- Different types of investigation possible on the results
- Comparison with laboratory data or known datasets → Validate the simulation
- Where do the differences come from?

**Simulation is closest to the real physics,
but it is always the ideal and perfect case.**

Summary

Ex-vivo/in-vitro laboratory tests

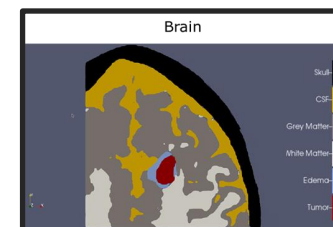


- Test procedures
- Reproduce clinical cases in the Lab
- Test the limitations of systems
- Simple and fast

- Metabolism missing
- Geometry and property limitations
- Not available/useful or everything
- Tissue: (Ethics?), reproducibility

**Validate
and
proof
each other**

Analytics and Simulation



- Analysis of Lab data
- Overcome boundary conditions
- Test the limitations of systems
- Biochemical effects

- Ideal perfect case
- Input vs. output
- Hard-/Software needed

Solve your problem

The Most Important

- Several Ways to solve Problems in Tissue Optics
 - Laboratory
 - Analytical
 - Simulation
- Knowledge of your setup is important
 - Input (Variables and Geometry)
 - Boundary conditions
 - Result only valid with the correct input

Use what best fits your problem

Go from simple to complex

Thank you very much.
Questions?

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