



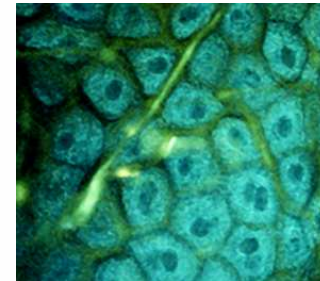
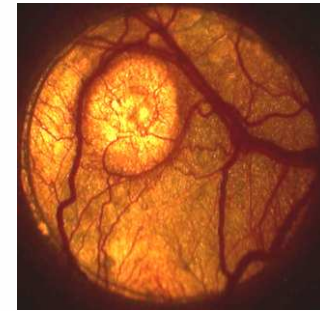
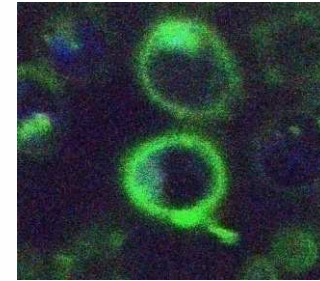
Center for Optical Diagnostics and Therapy

Dominic J. Robinson

Department of Radiation Oncology

Erasmus Medical Center Rotterdam

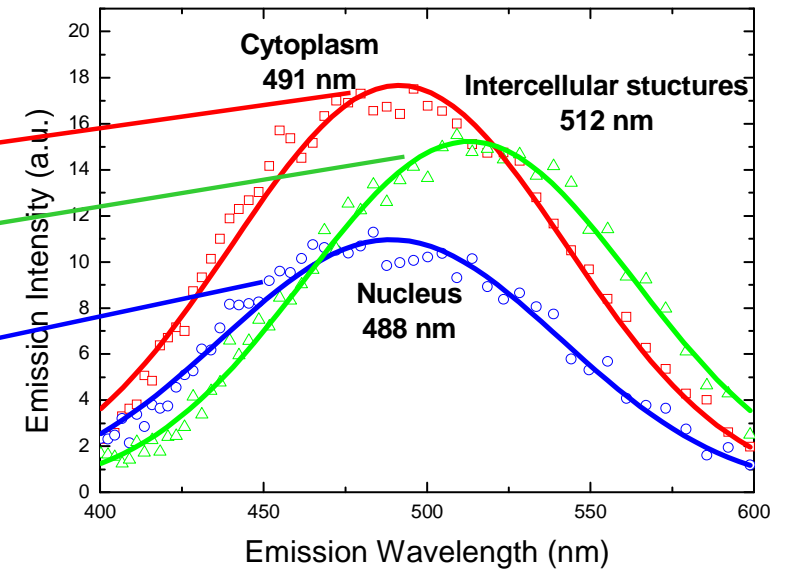
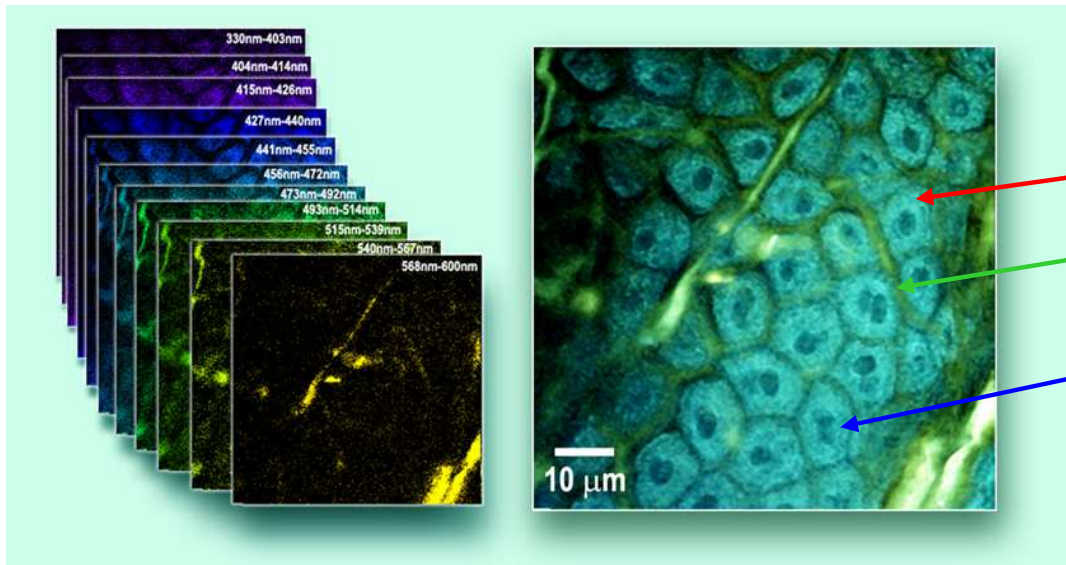
The Netherlands



Overview

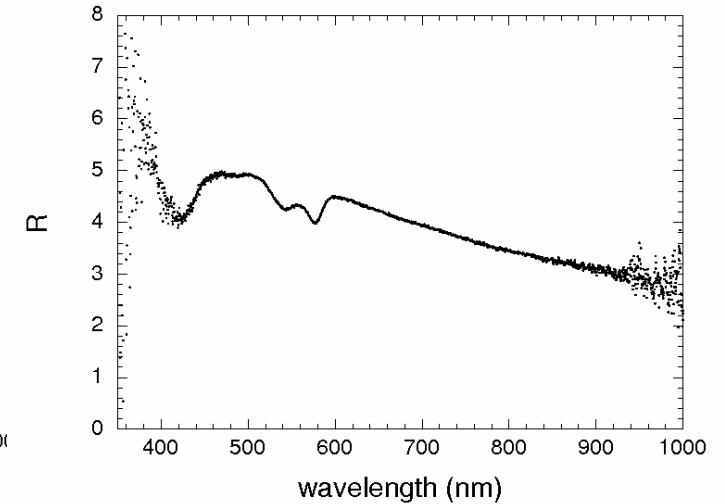
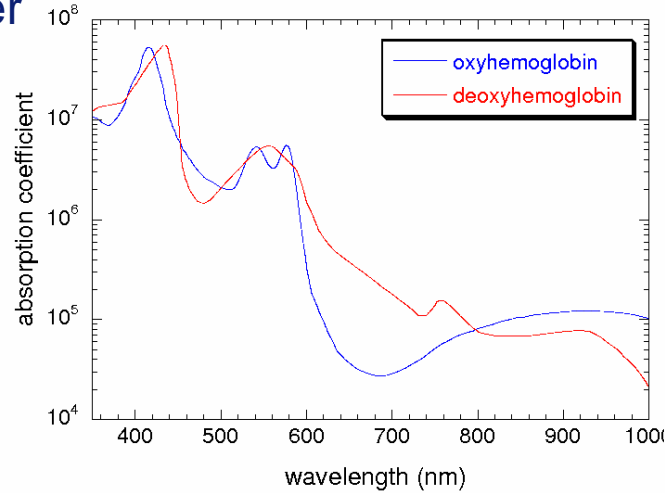
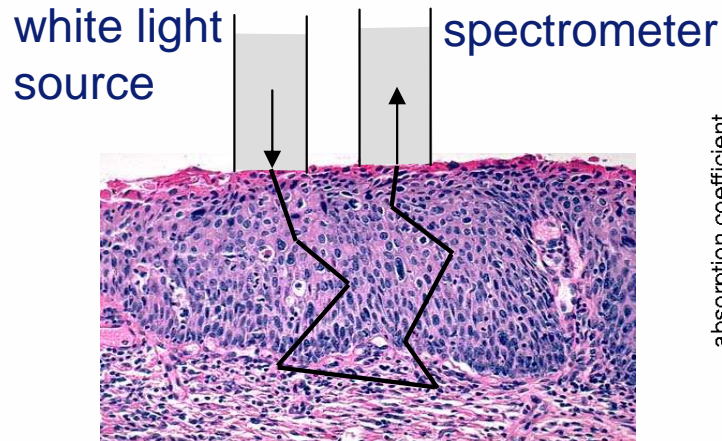
- Optical diagnostics
 - Quantitative Reflectance spectroscopy
 - In-vivo multi-photon imaging
- Photodynamic Therapy
 - Application areas
 - Cost effective solutions
 - Problems
- Targeted PDT
 - Small peptide: Somatostatin
 - Problems
- Solutions
 - Nano-photo-medicine
 - Amrita Center for Nanoscience

Optical Diagnostics: Non-linear Imaging



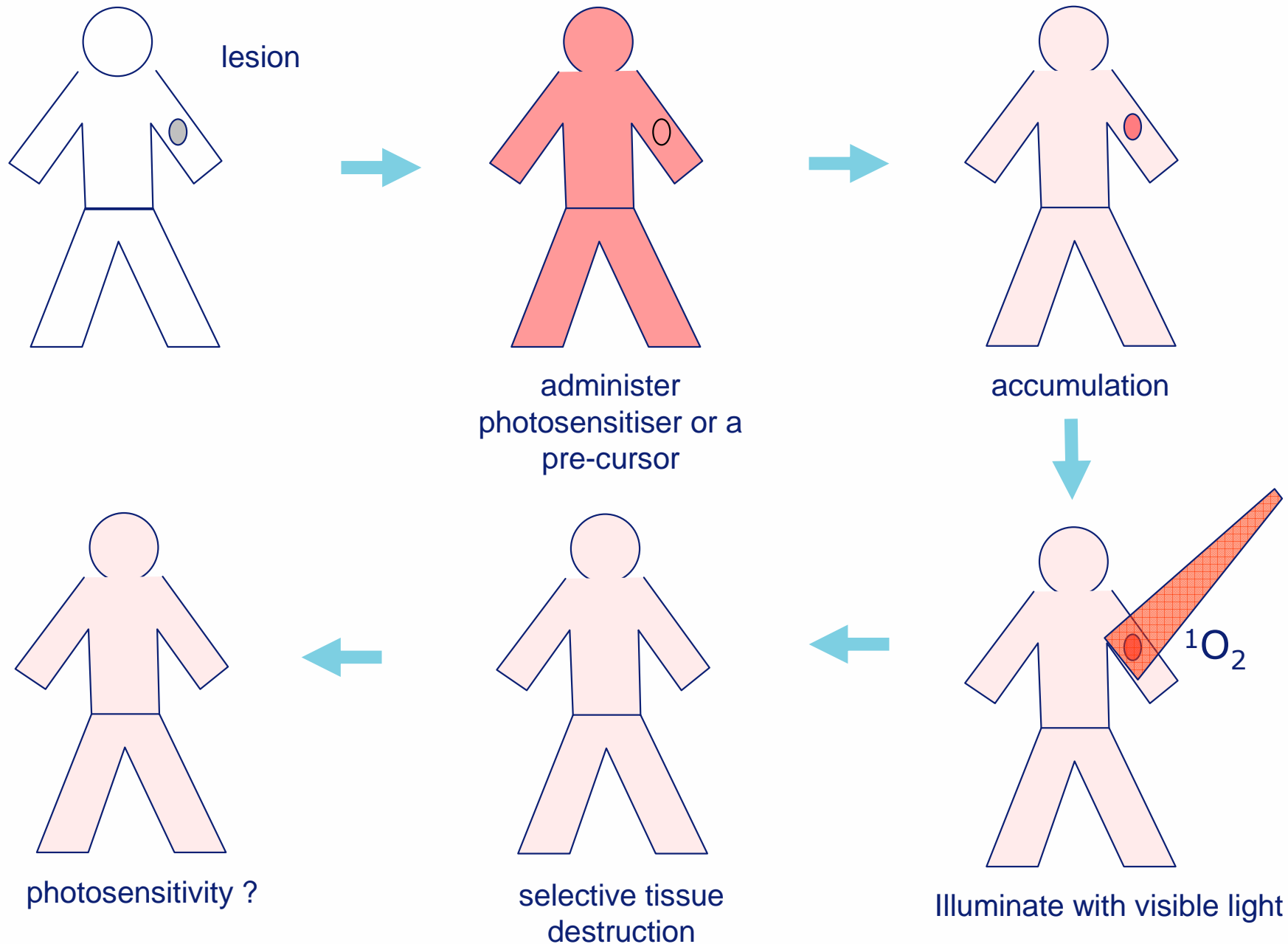
- In-vivo multi-photon microspectroscopy
- Normal mouse skin
- Clinical applications
 - Oral Cavity
 - Skin
 - Breast duct tumors
 - Solid organs
 - Prostate
 - Brain

Quantitative Reflectance Spectroscopy



- Differential pathlength spectroscopy (DPS)
- Clinical applications
 - Bronchial tract
 - Oral Cavity
 - Bladder function
 - Lymph node staging
 - Breast
 - Brain

Photodynamic Therapy



Why is PDT potentially important

- Single curative treatment
 - Cost effective
 - Outpatient clinics
 - Developing countries
 - India, Indonesia, China, Brazil...

- Targeted therapy
 - Chemotherapy
 - Dark toxicity outside the target volume
 - PDT
 - Light is like the remote control
 - No dark toxicity for internal organs

Clinical PDT

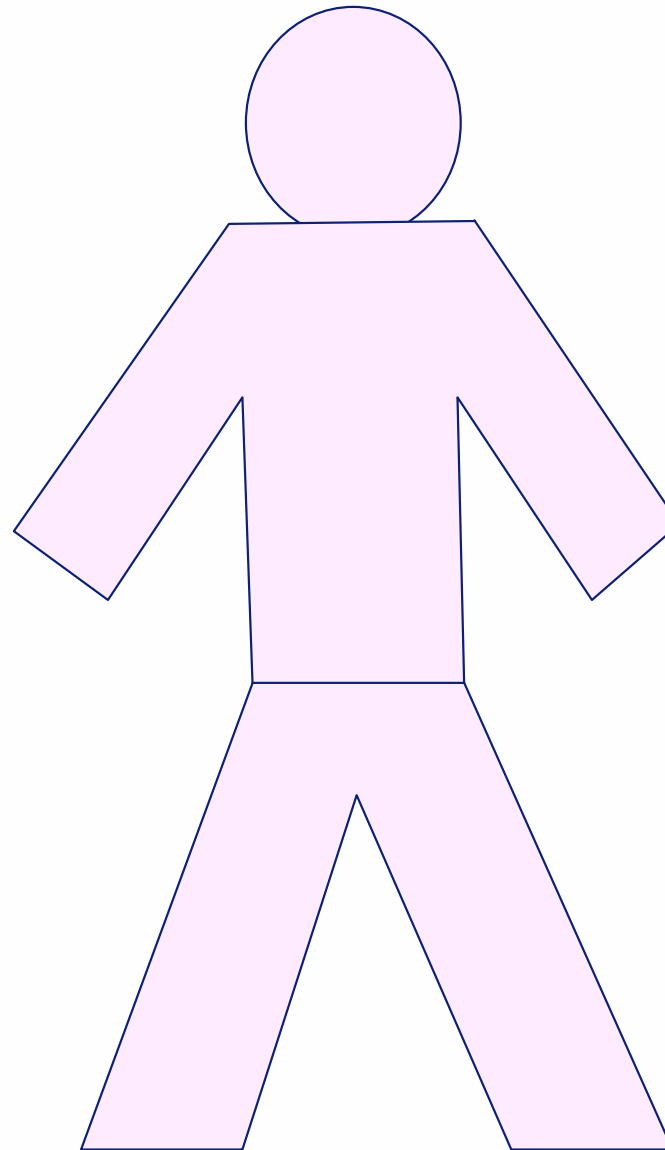
Head and Neck SCC
Nasopharynx
Oral cavity
Tongue base

Esophagus
Stomach
Pancreas/Bile Duct
Colon
Anal Cavity

Prostate

Vasculature
Bone metastasis

Skin (NMSC)



Glioblastoma multiform
Pituitary adenoma

AMD

Larynx
Bronchial tree
Pleural cavity

Breast CA

Endometrial ablation
Ovarian CA
CIN

Antimicrobial PDT

Clinical PDT

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Oral cavity
Tongue base

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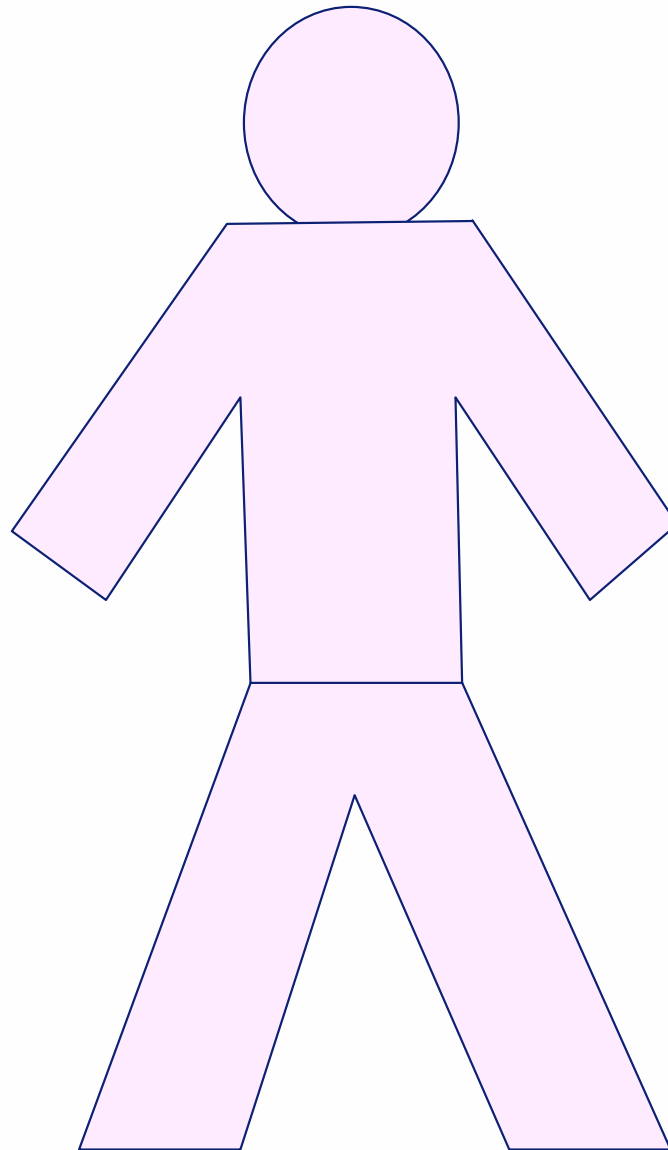
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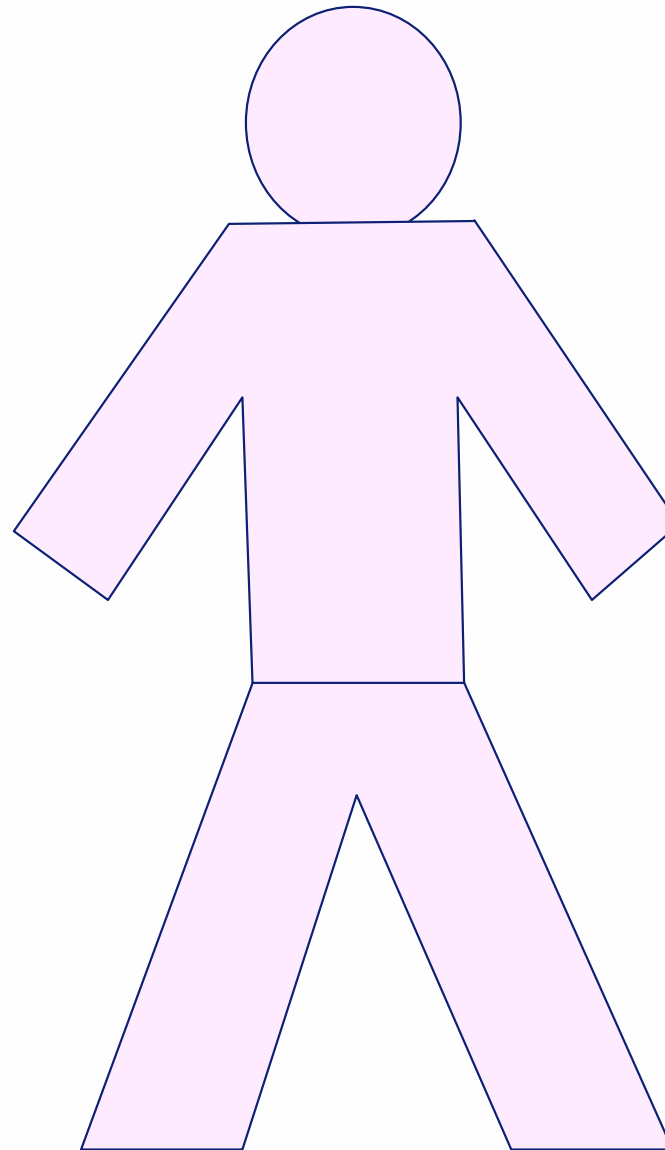
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Clinical perspective

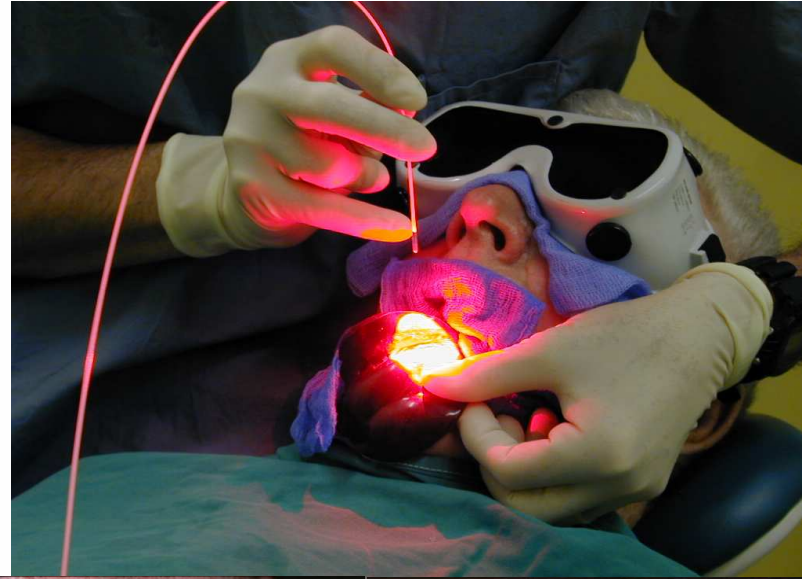
ALA-PDT

basal cell carcinoma

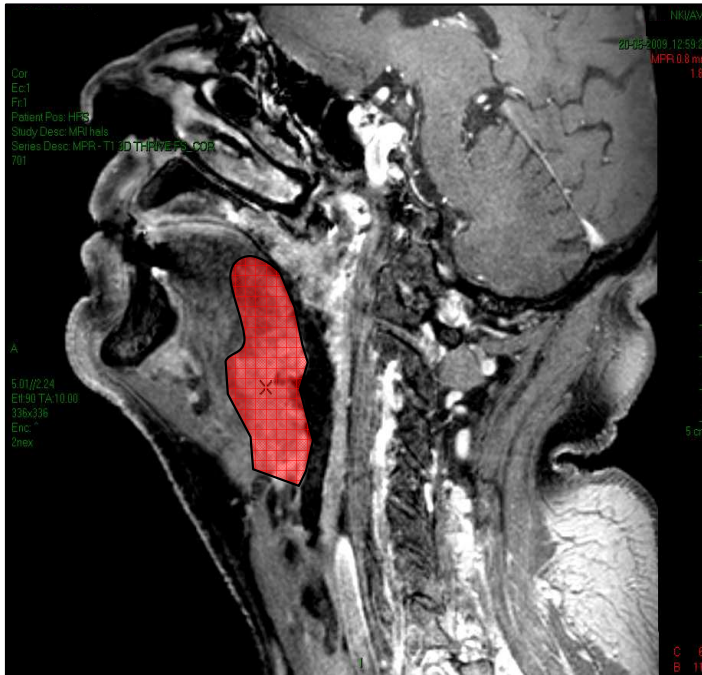


mTHPC-PDT

squamous cell carcinoma



Interstitial PDT Head and Neck Cancer



Cost effectiveness and optimization

NL: 3 nationally coordinated studies investigating cost effectiveness and treatment optimization in Head and Neck Cancer



ZonMw

I. B. Tan et. al. The cost effectiveness of m-THPC-PDT for recurrent Head and Neck cancer compared to current standard of care:
Surgery, radiotherapy and chemotherapy



R. P. L. van Veen Optimizing light dosimetry for PDT in Head and Neck cancer



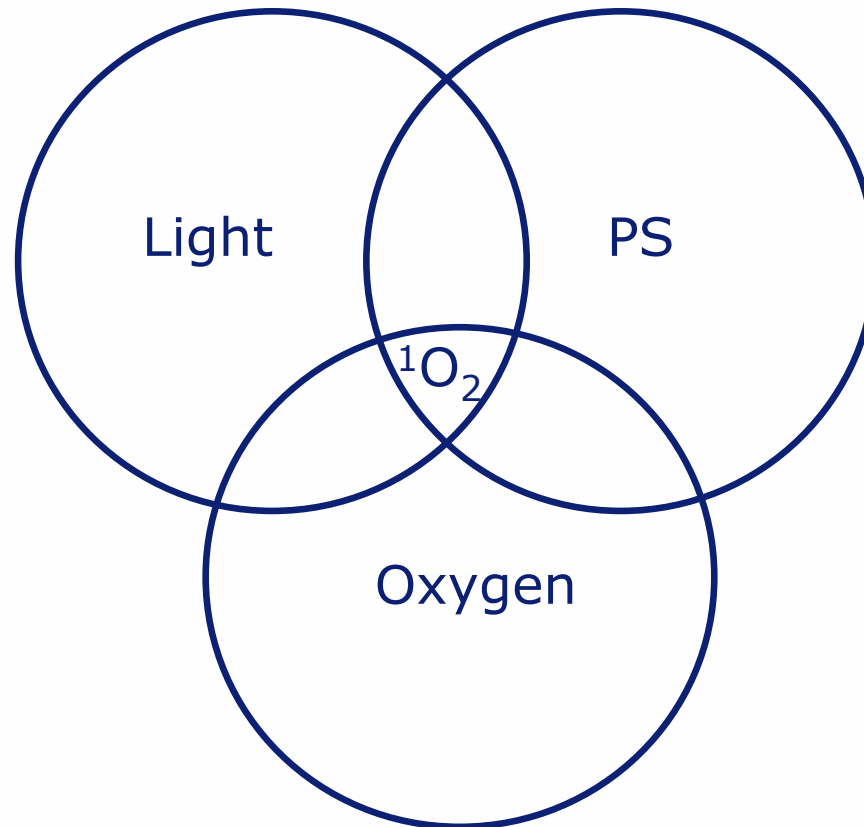
ZonMw

D. J. Robinson et. al. Optimizing m-THPC-PDT dosimetry in Head and Neck cancer

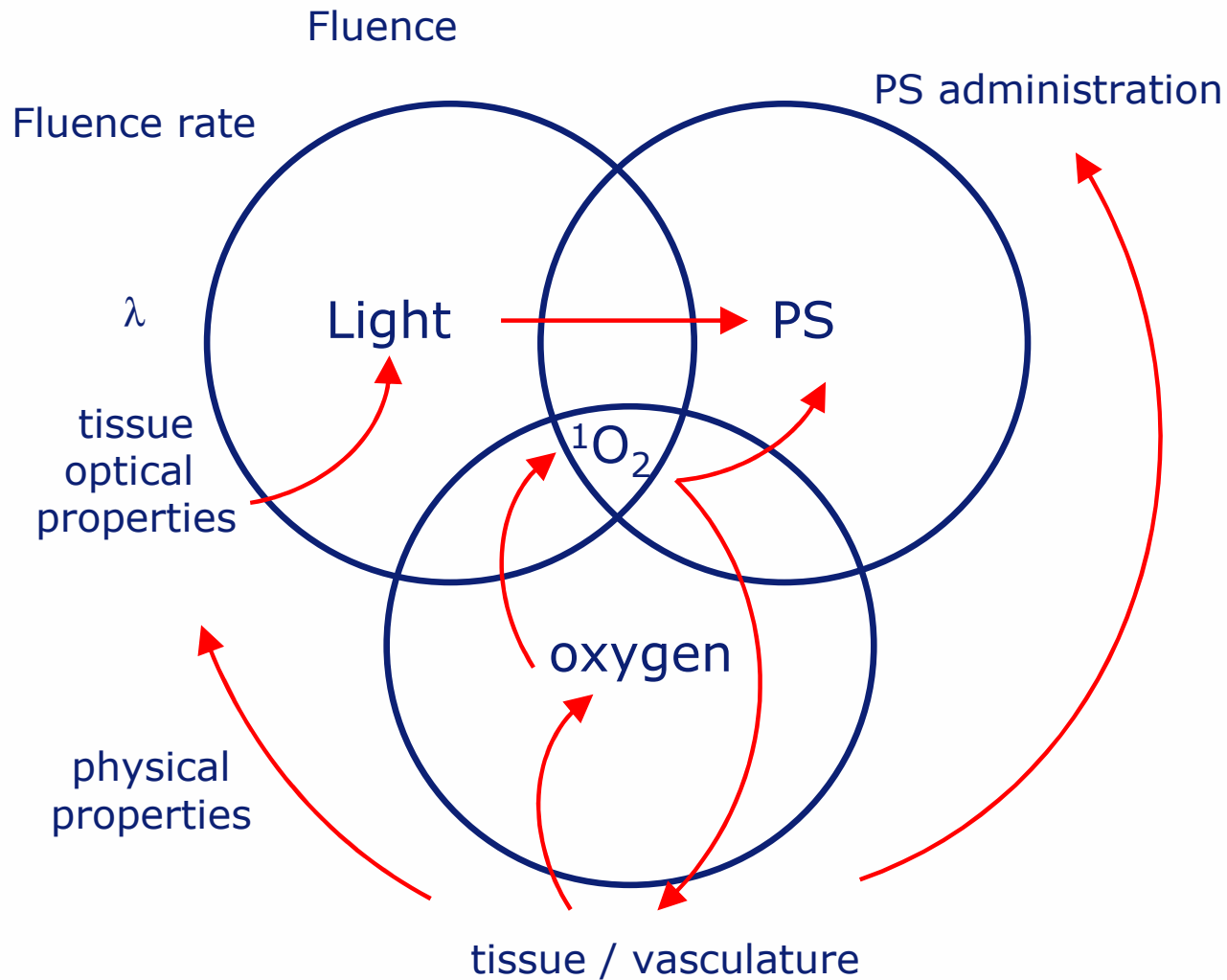
Its **even** cost effective in the Netherlands!

South Asia, East Asia and in China - large patient population

Problems with PDT



PDT dosimetry is complex



Selectivity \longleftrightarrow Complexity

Photosensitisers

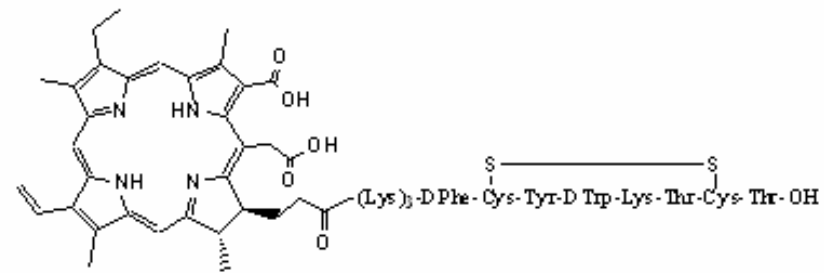
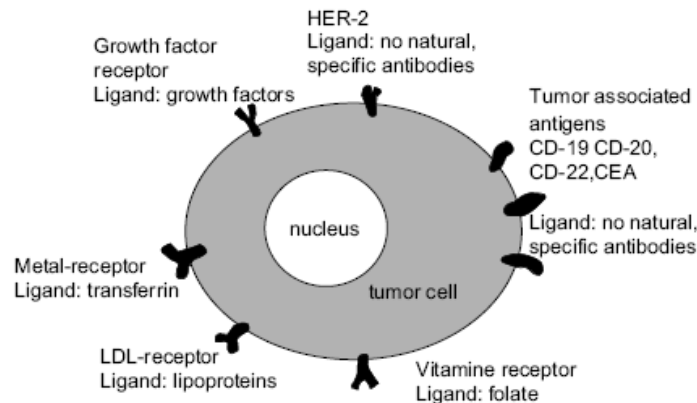
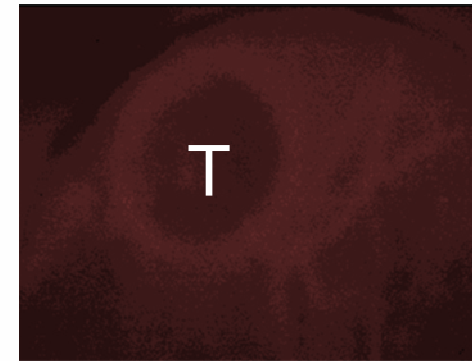
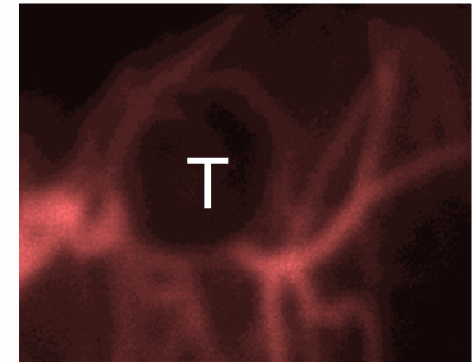
- Photosensitiser pre-cursors
 - porphyrin precursors (esters-) ALA
- Pre-formed photosensitiser
 - Porphyrins (Photofrin)
 - Chlorins (Ce6, Foscan)
 - Phthalocyanines
 - Bacteriochlorins
 - Methylene blue derivatives



Traditional photosensitisers

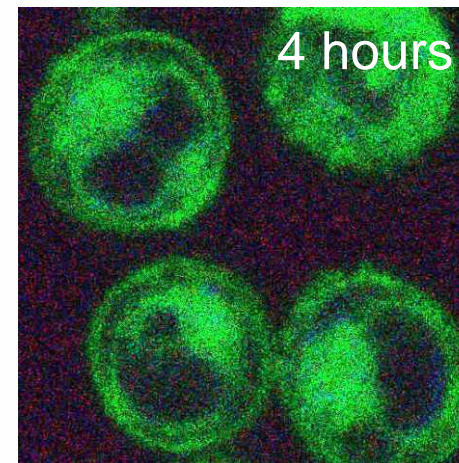
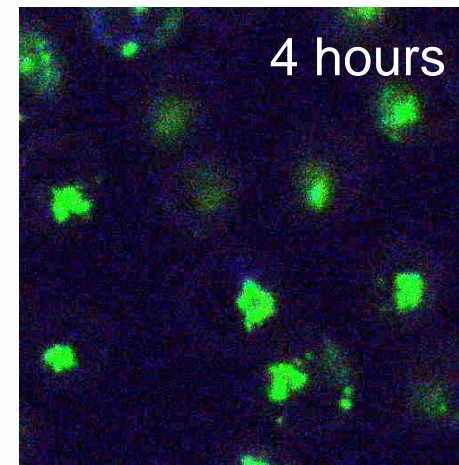
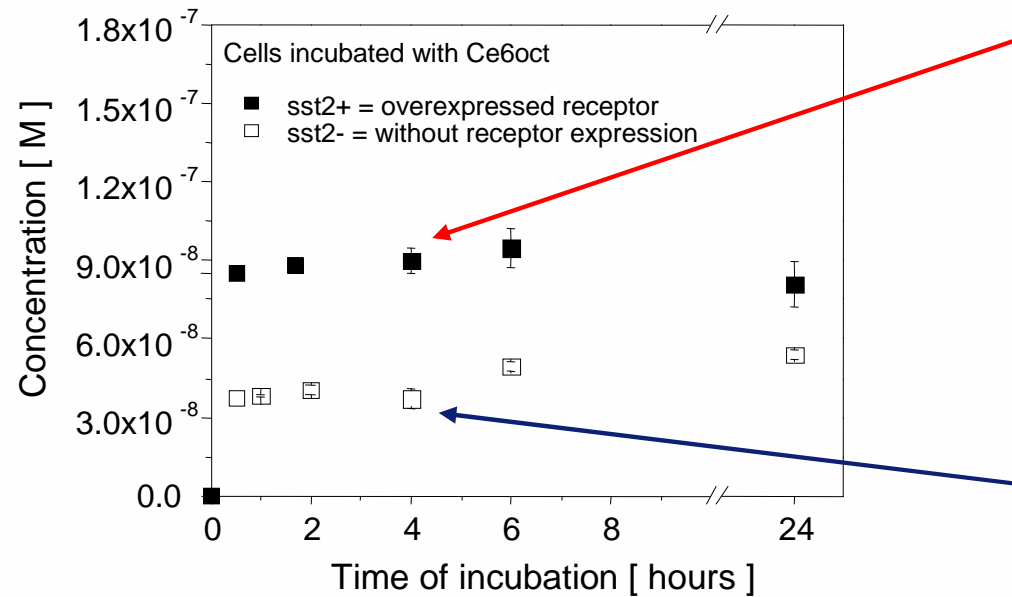
- Not very specific for tumour cells/tissue
 - Normal tissue damage limits dose to tumour
- Are normally very hydrophobic
- Aggregate in-vivo at high concentrations
- Retained in skin
 - Prolonged skin photosensitivity (weeks/months)

- Targeted PDT



Ce6-KKK-octreotate

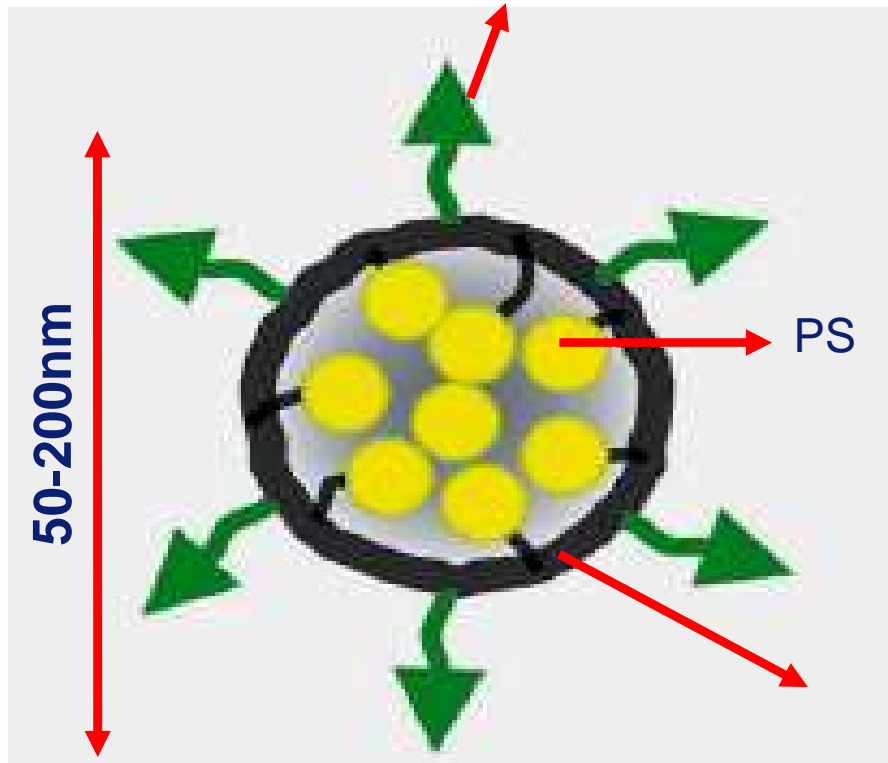
Problems!



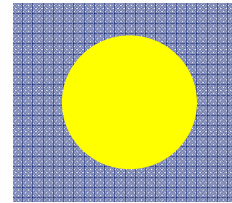
- In-vivo testing under way
- Conjugate structure is critical & interaction with cells difficult to predict
- **Hydrophilicity is most important in specific targeted PDT**
- Only one/few photosensitiser per ligand
- Do we have sufficient selectivity?
- Can lipophilic photosensitisers be shielded from their environment?
- High photosensitiser concentrations without aggregation?

Solutions

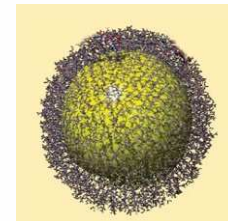
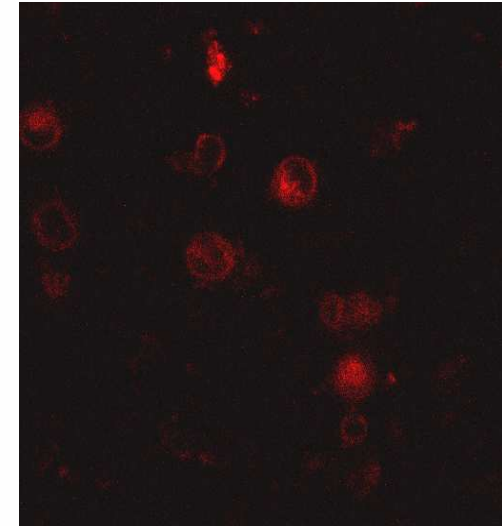
Cancer targeting ligands



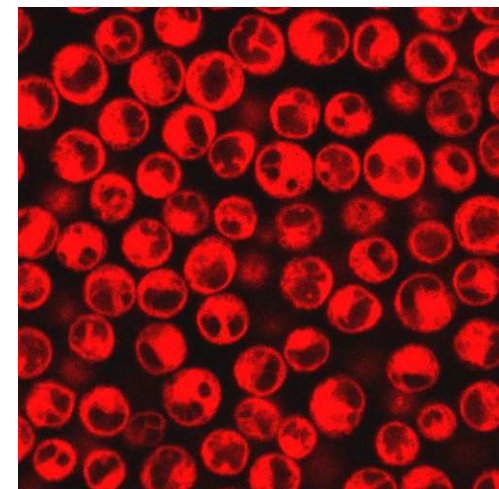
Porous silica and/or polymeric based nano-delivery vehicles



mTHPC@SiO₂



mTHPC@SiO₂-Octreotate



Acknowledgements

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