MCRT in Photodynamic Therapy

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Overview

- Light therapy in the past
- Photodynamic therapy (PDT)
  - What, How, Why?
- The aim with my project
- How can MCRT be used for light treatment for skin cancer
  - Simulating skin tissue
  - Important parameters
- Light sources
  - Conventional PDT
  - Sunlight PDT
- Other possible areas where code can be used

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Light – ancient medicine

- Psoriasis
- Vitilago
- Skin Cancer
- Rickets

Helios – the god of the sun

Vitilago

Rickets

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Photosensitive chemical

- Used by medicine men
- Psoralen + UVA = efficient light treatment (PUVA)
- Start of development of Photodynamic therapy (PDT)

Psoralea corylitolia

Getafix

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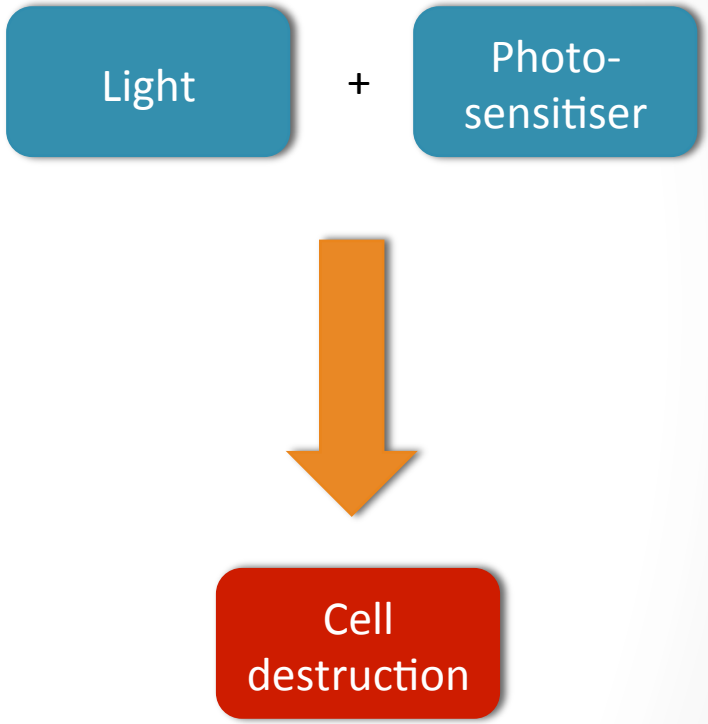
Photodynamic therapy

- Light treatment for skin cancer
- Cell death caused by the combination of light and photosensitive chemical.

- Raab (1900) discovered the interaction between dye and light caused cell destruction
- Von Tappeiner was the first to report PDT in humans



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What we treat

- Non-melanoma skin cancer (NMSC)
  - Main risk factor: sun exposure
  - Motivation for treatment:
    - Common on neck and head hence cosmetically inconvenient
    - Can spread and cause severe local damage
    - Can develop to more aggressive cancer types
  - Varied in type and size, main types:
    - Basal Cell Carcinoma - BCC
    - Squamous Cell Carcinoma – SCC
      - Most aggressive type, most common of all NMSC to cause mortality
    - Actinic Keratosis- AK
    - Squamous Cell Carcinoma in situ –Bowen's disease

] Precursor lesions of SCC

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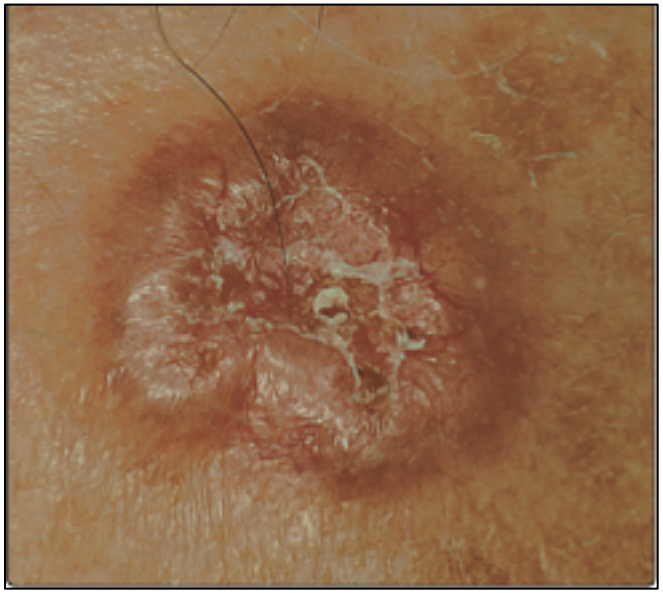
What to look out for…



Basal Cell Carcinoma

Squamous Cell Carcinoma

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What to look out for…

Bowen's Disease

Actinic Keratosis

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Why use PDT?

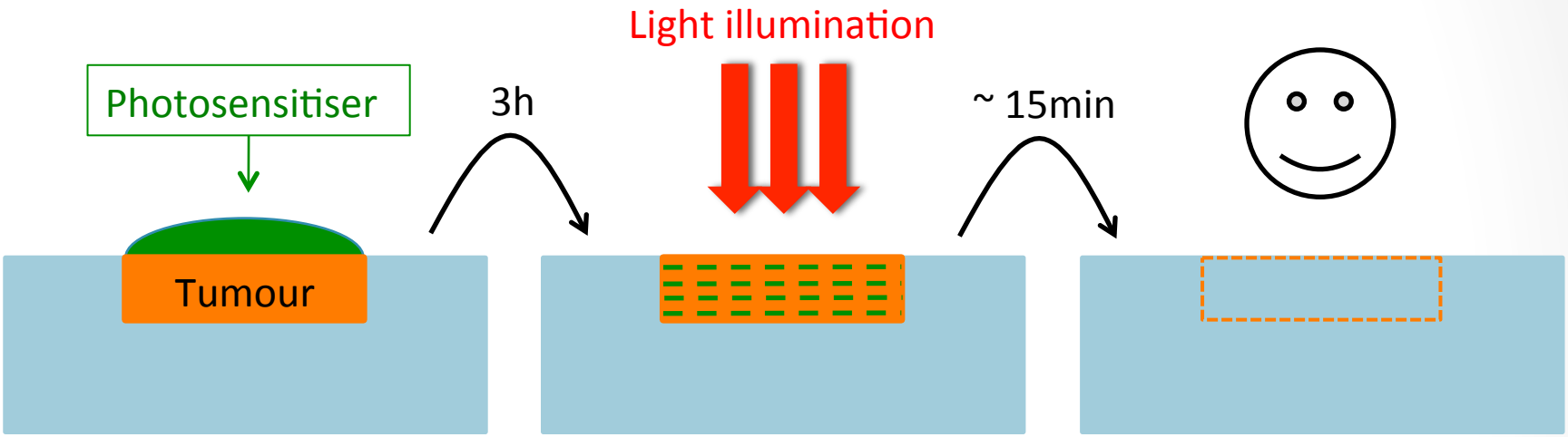
PDT

- Positive:
  - Excellent cosmetic outcome, no scarring
  - Non-invasive
- Negative:
  - Can be experienced as painful
  - Still a relatively high recurrence

Alternative treatment methods

- Cryosurgery
- Curettage
- Radiotherapy
- Surgical excision

Mechanism of Action



- Topical application of cream containing photosensitiser
- Cream diffuses into skin

- Photosensitiser accumulated in tumour
- Light illumination from above

- Light interaction with photosensitiser generated toxic singlet oxygen

-> Cell death!

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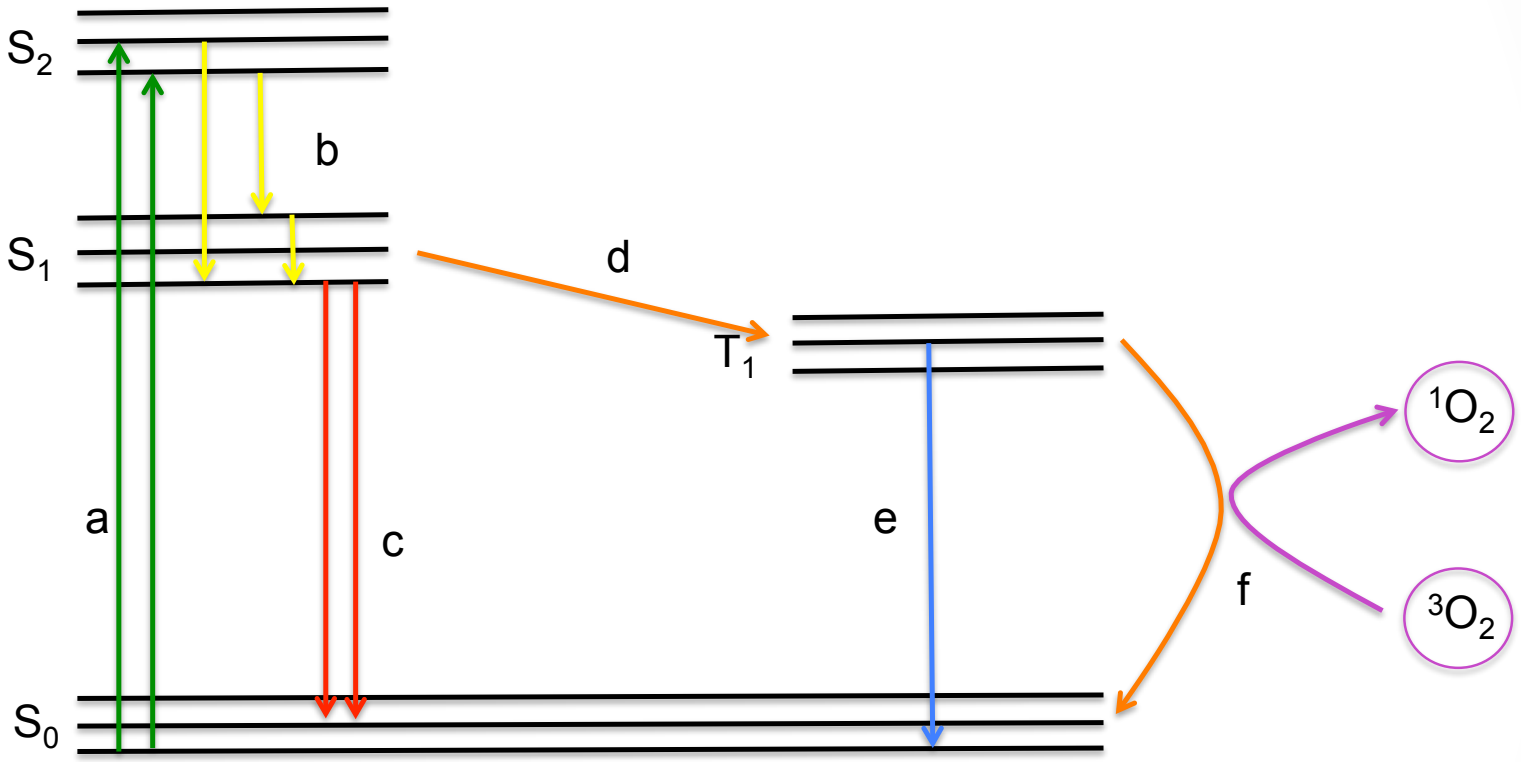
Jablonski diagram of PpIX



a- excitation
b- internal conversion/ vibrational relaxation
c- fluorescence
d- intersystem crossing
e- phosphorescence
f- excitation of oxygen

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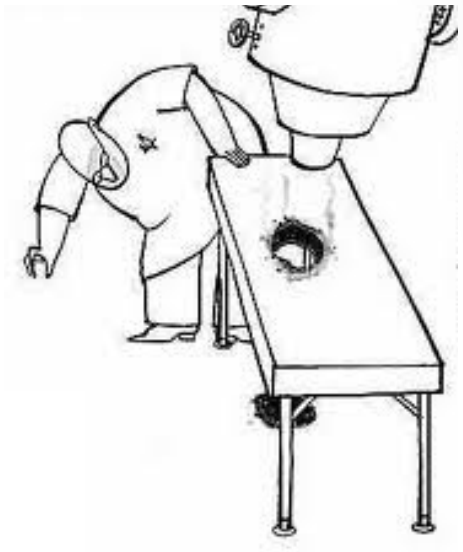
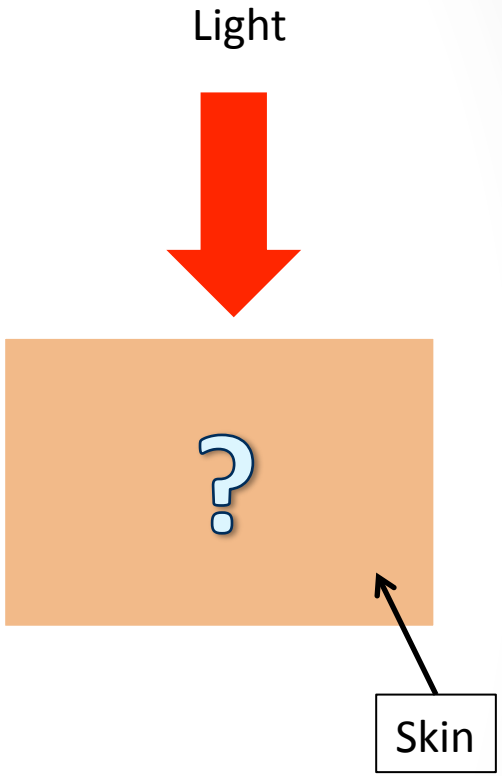
My project



- Biophysical aspects of PDT
- Tailor PDT
- Theoretical
  - Investigating different light sources
  - Efficiency of treatment methods
- Practical
  - Collaboration with Ninewells Hospital in Dundee
  - Measurements to include in MCRT code
  - Fluorescence measurements

What do we want to know?

- What happens under the skin?
- Tissue optics very important to optimise treatment
- How deep does the light penetrate?
- How does the light behave when entering the skin?
- How much light is absorbed by the photosensitiser?
- What is an optimal treatment time?
- How is the treatment affected by different light sources?



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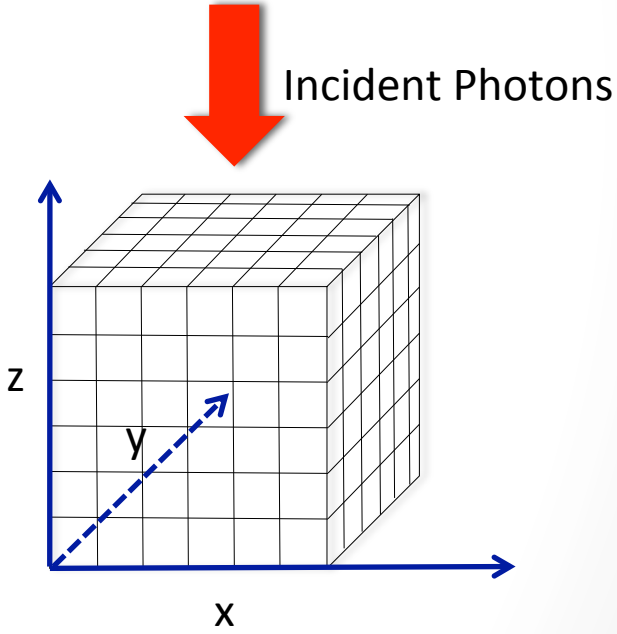
How do we find out

- Use MCRT code
- Develop code from Astronomy
  - Dimensions and optical properties will change
- Simulate skin tissue



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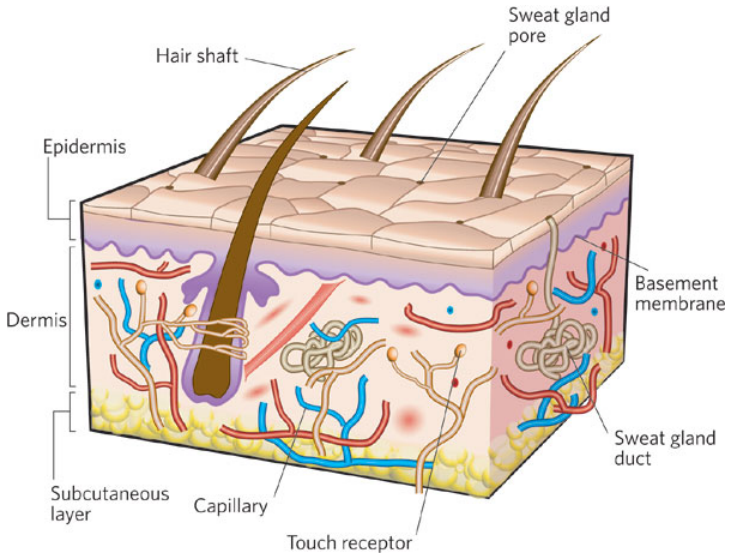
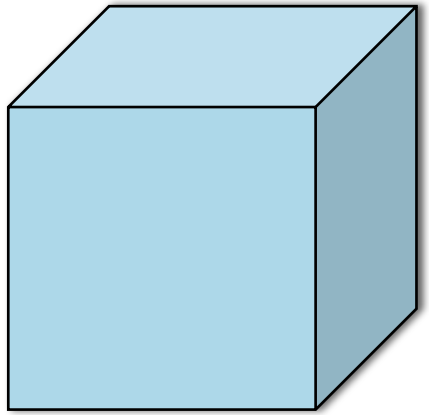
Skin tissue

What our skin actually looks like…



- Different structures and layers
- Rough surface

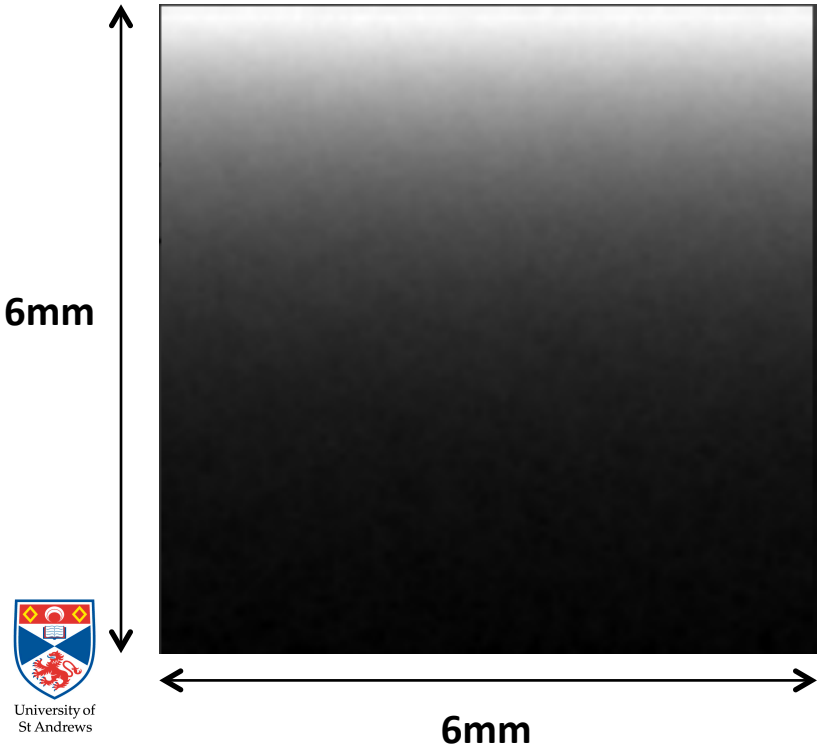
What we simulate…



- Uniform density
- One tissue type
- Smooth surface

Fluence Rate

- Light distribution through the tissue
- Determines penetration depth
- In Astronomy: Mean Intensity, J



$$\psi = \frac{L}{N\Delta V}\sum_i S_i$$

Ψ=Fluence rate [W/cm^2]
L=Luminosity [W]
N= number of MCRT photons
ΔV=volume of one grid cell [cm^3]
S_i = distance along the photon path in one cell [cm]

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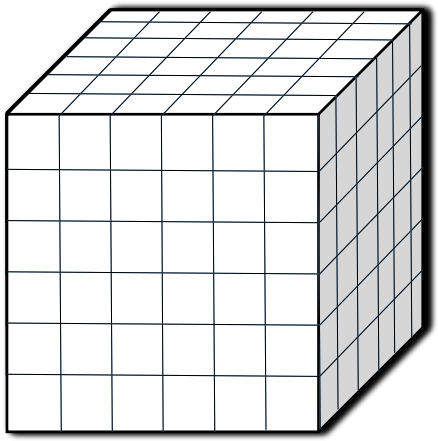
Photobleaching

- Concentration of photosensitiser changes during treatment

$$C_{new}(x,y,x,t) = C_0(x,y,x)e^{-\psi(x,y,z)t/\beta}$$



C_{new}= concentration at time t in each grid cell
C_0 = Initial concentration in each grid cell
Ψ = fluence rate [W/cm^2]
t = elapsed treatment time [sec]
β = photobleaching constant [J/cm^2]

Can be determined experimentally

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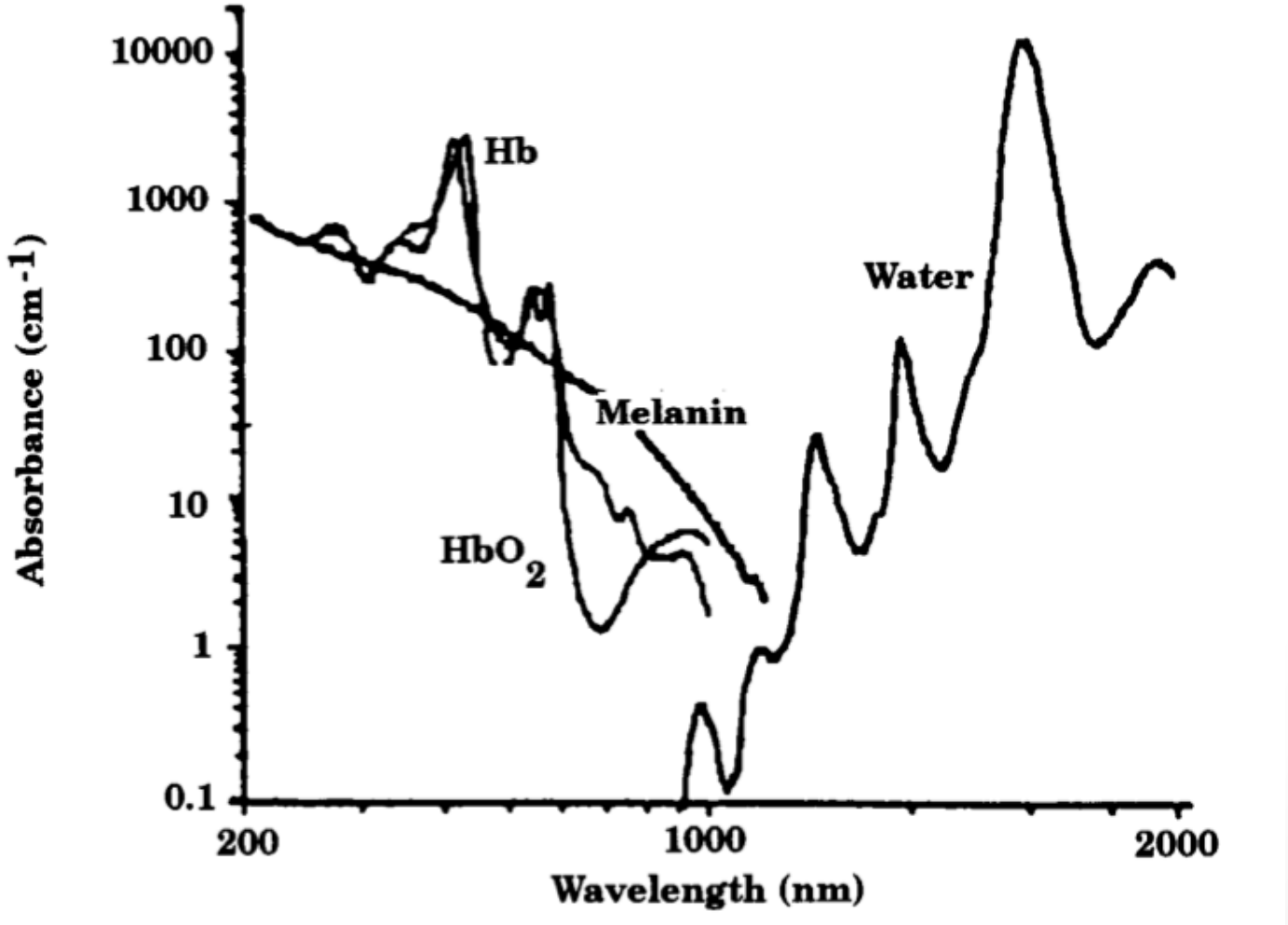
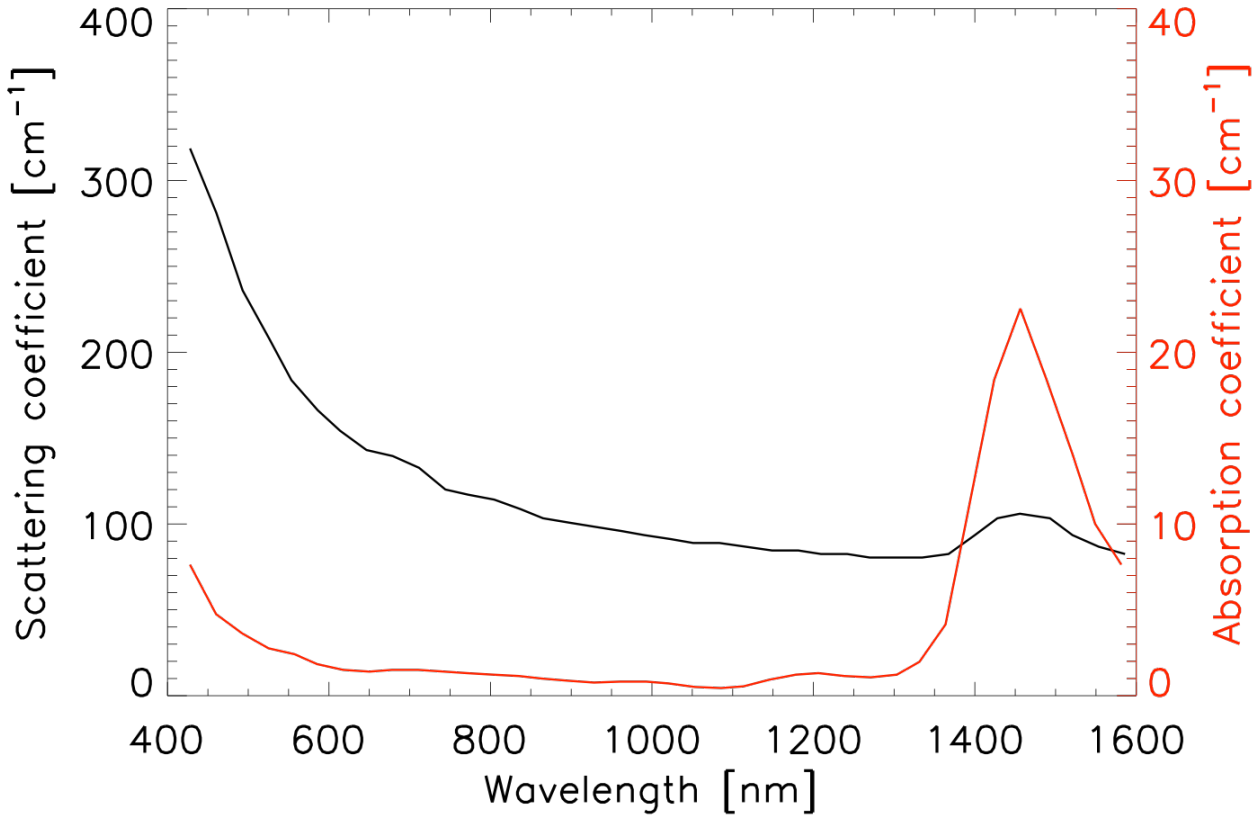
What wavelength to choose…



Optical Properties: Skin



Salomatina et al, Optical properties of normal and cancerous human skin in the visible and near-infrared spectral range', J Biomed Opt, 2006

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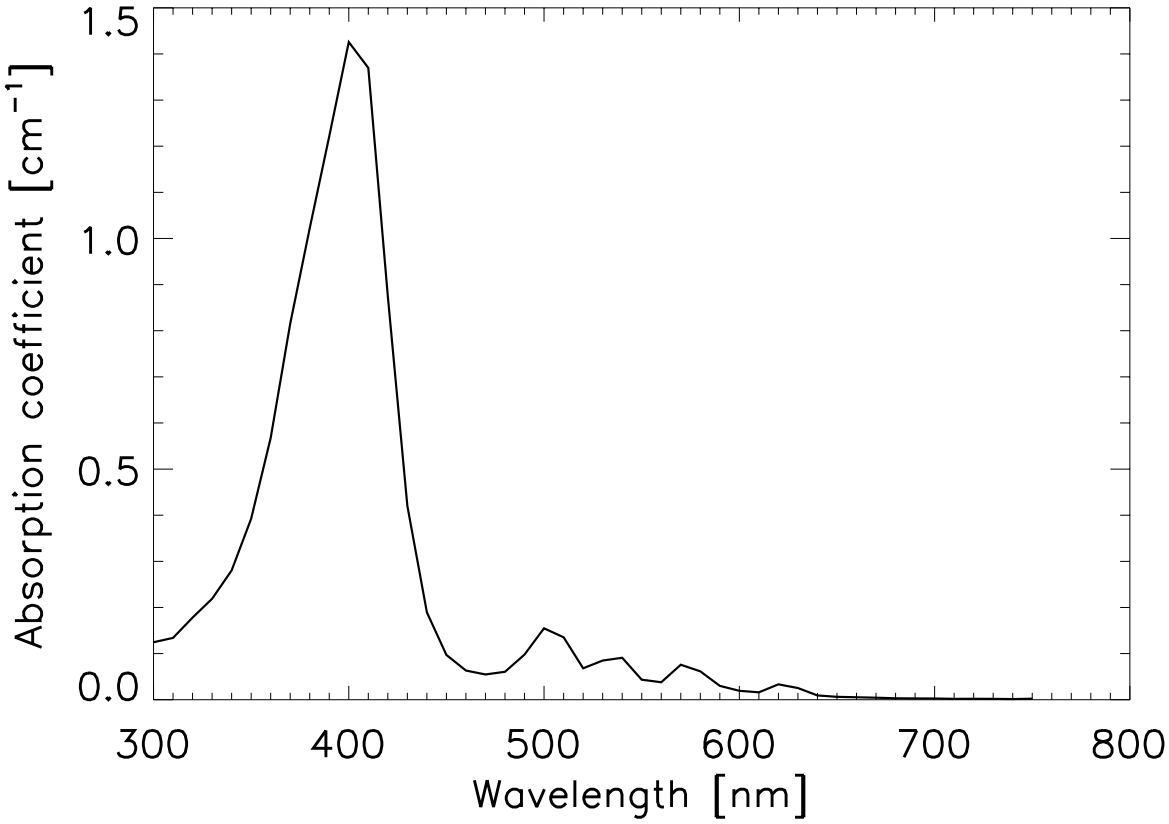
Optical Properties: PpIX



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Is the treatment effective?

- Light dose = I*t [J/cm^2]
  - I = Intensity [W/cm^2]
  - t = elapsed treatment time [sec]
  - Typical light dose for treatment: 75 J/cm^2
- **Photodynamic dose**
  - Number of absorbed photons per cubic centimeter by the photosensitiser
  - As a function of depth
- Toxic threshold: 8.6 x 10^{17} photons/cm^3
  - Absorbed photons required for necrosis (cell death)
  - Patterson et al (1990)

Add up energy of absorbed photons (by the photosensitiser)

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Light sources

- Lasers – mostly used for internal applications
- LED – most commonly used for topical application (Aktilite)
- Lamps – Photocure, Paterson, Waldman 1200
- Ambulight – Low fluence light source
  - Lower intensity for longer treatment time
- Daylight

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IOP PUBLISHING PHYSICS IN MEDICINE AND BIOLOGY

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Monte Carlo simulations for optimal light delivery in photodynamic therapy of non-melanoma skin cancer

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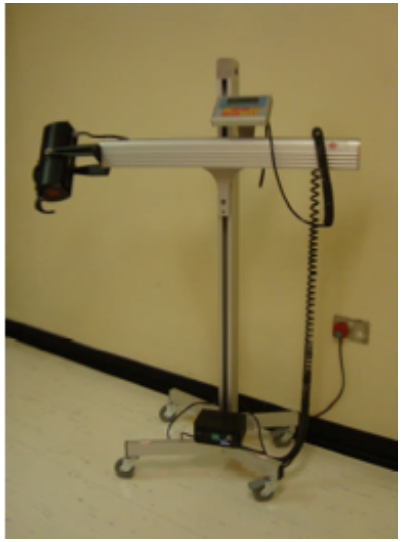
Light sources

Aktilite



Photocure

Paterson

Waldmann 1200

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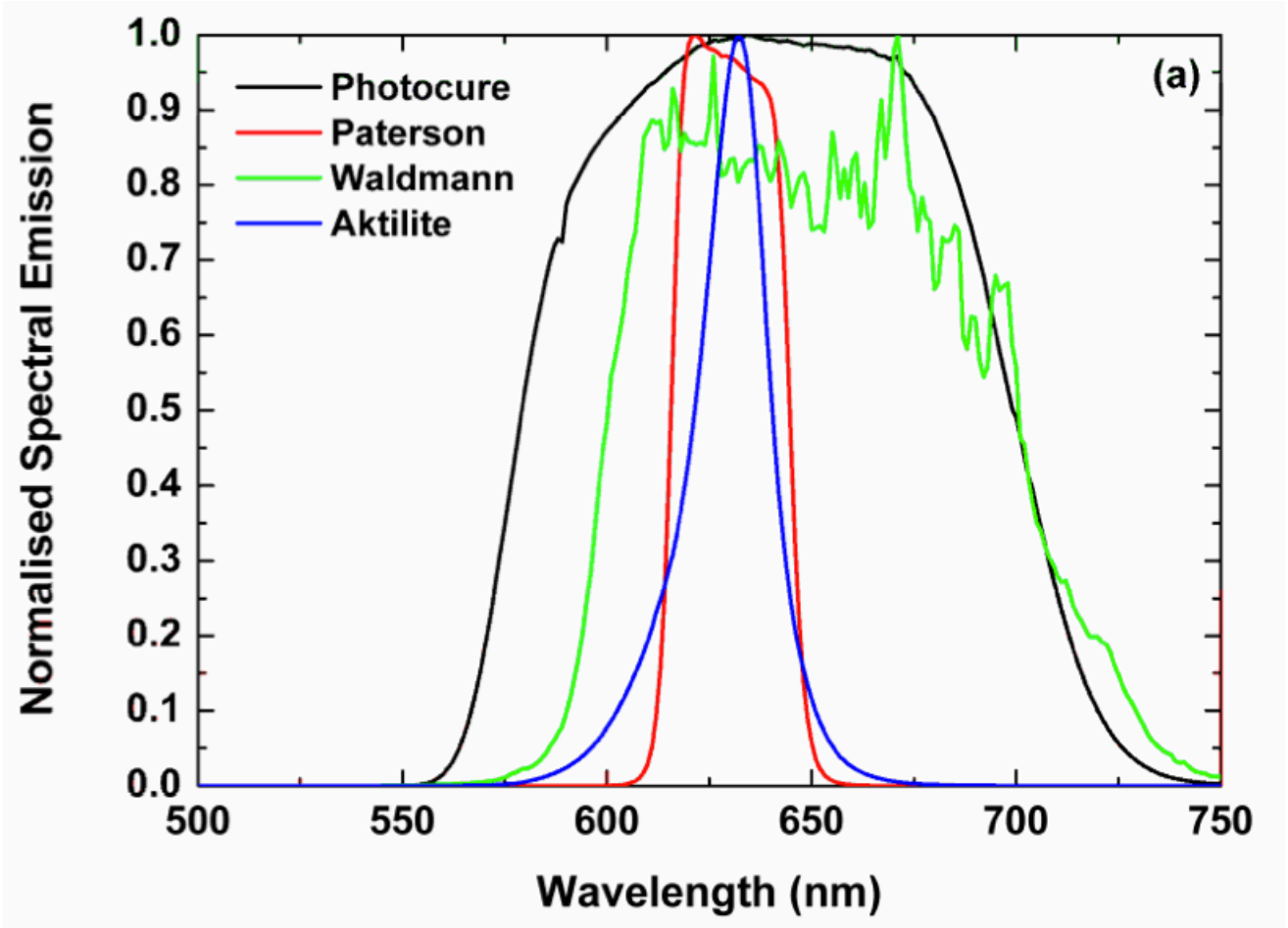
Spectra



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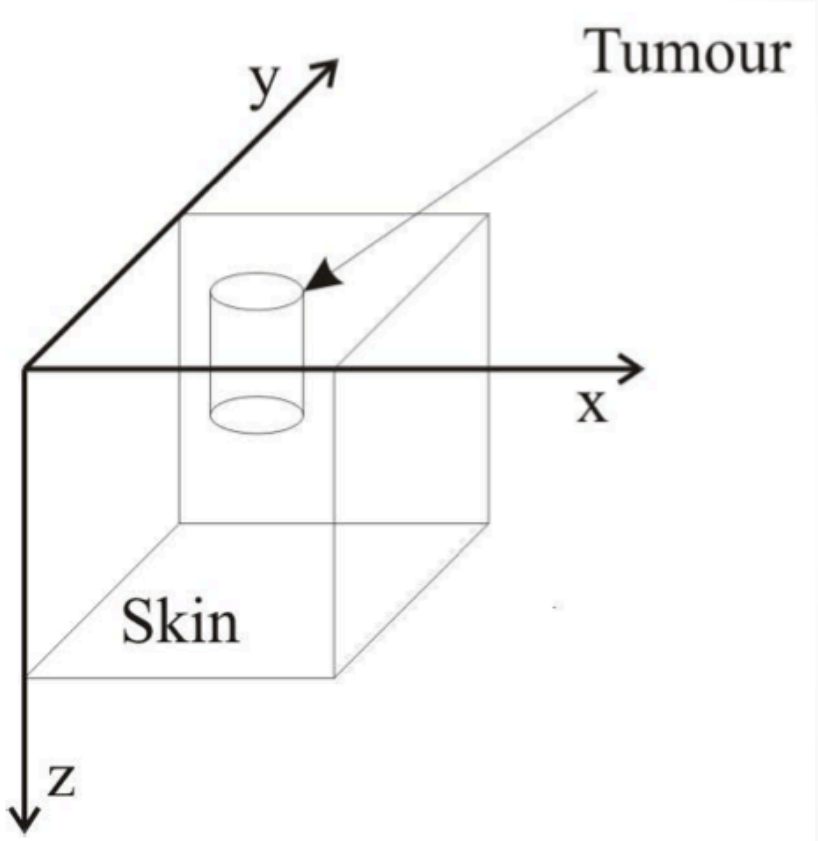
Skin Phantom

- Grid: 20 mm x 20 mm x 20mm
- Cylindrical tumour
- r: 5mm
- h: 4mm
- Placed at the centre of the normal skin tissue



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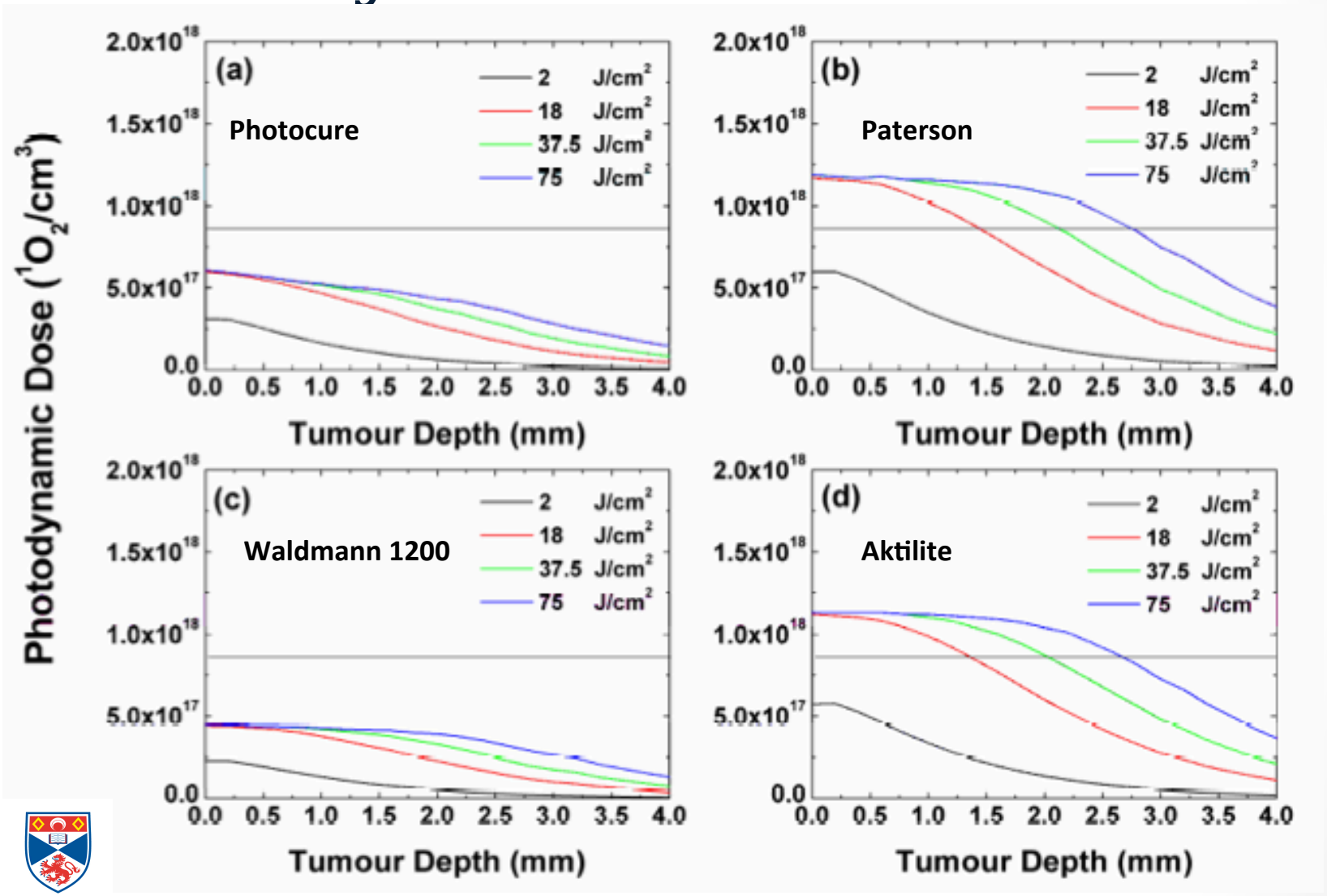
Photodynamic dose



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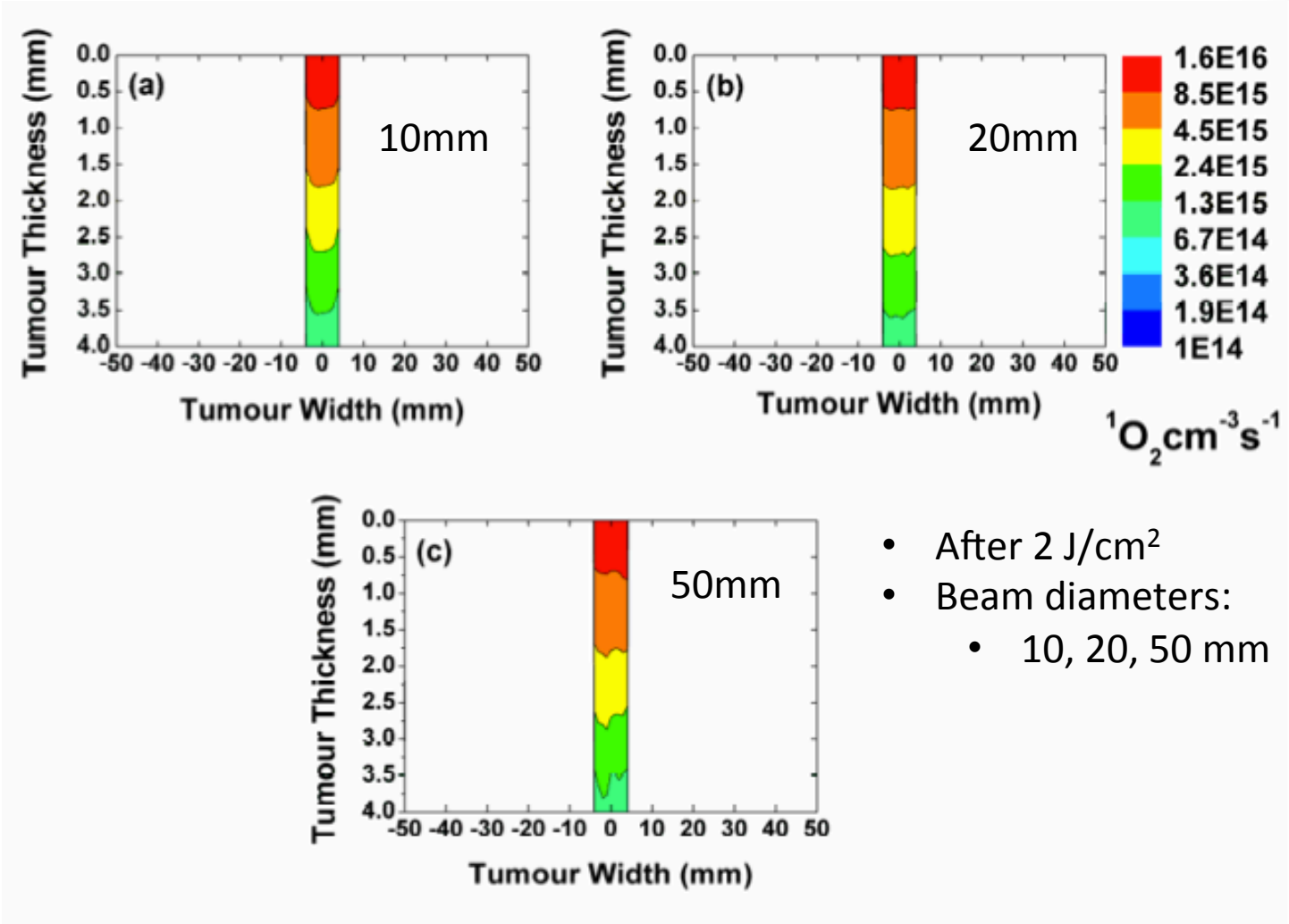
Assuming same surface irradiance of 82mW/cm^2

Beam diameter



- After 2 J/cm^2
- Beam diameters:
  - 10, 20, 50 mm

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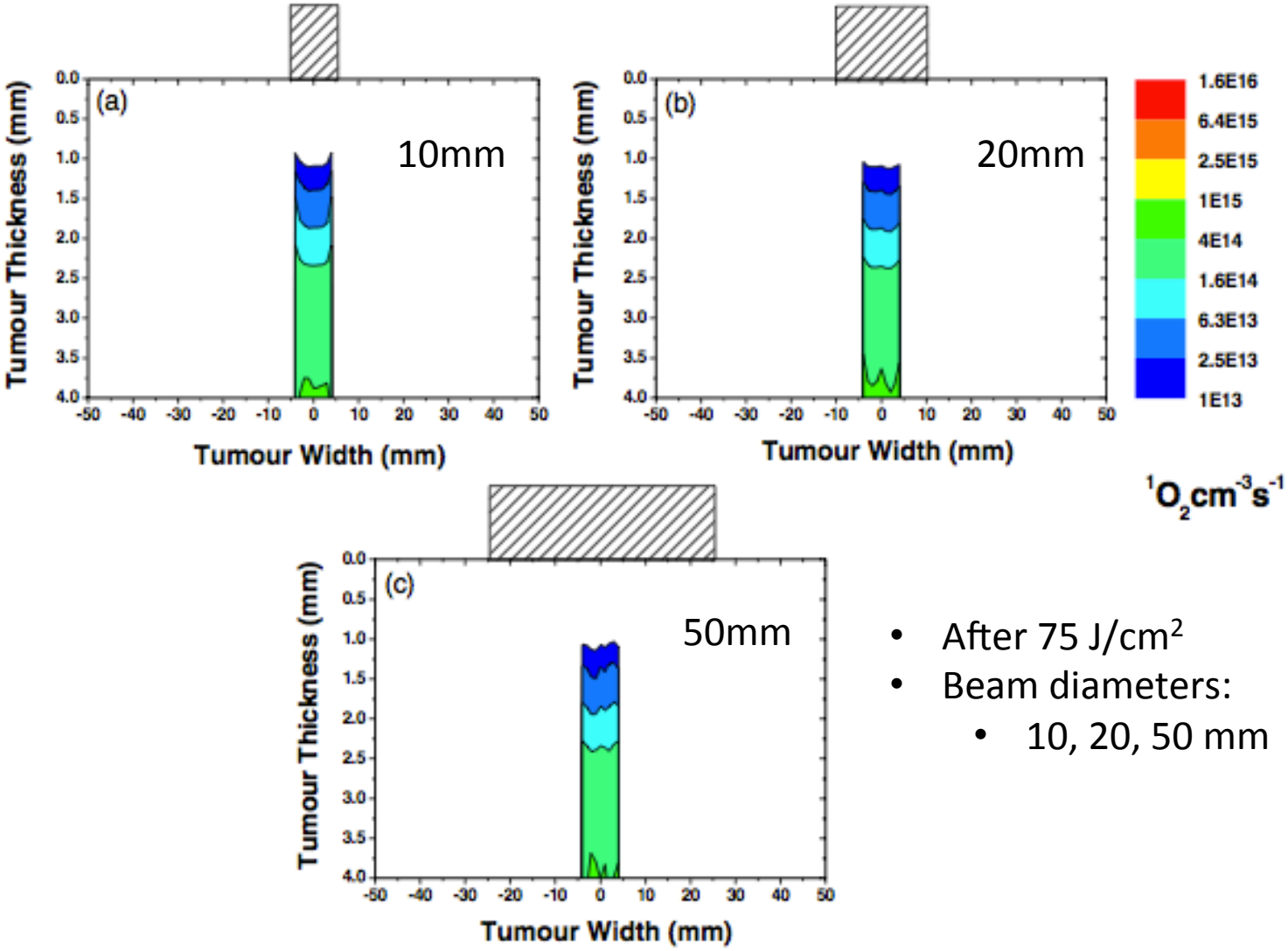
Beam diameter



- After 75 J/cm^2
- Beam diameters:
  - 10, 20, 50 mm

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Light sources

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- Lamps – Photocure, Paterson, Waldman 1200
- Ambulight – Low fluence light source
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- Daylight

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Motivation for daylight PDT

- Reduces pressure on the clinics
- More convenient for patients
- Less painful
- Possible to treat larger area

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Daylight PDT

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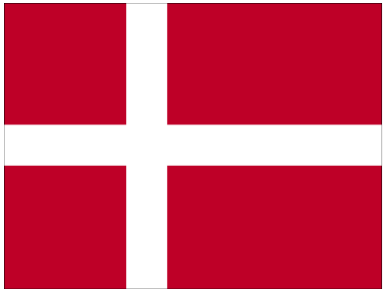
Previous results

- Several trials in Denmark
  - Successful results (mostly AKs)
  - As high as 94% response rate (higher than some reported response rates for conventional PDT)
  - At least 1.5h daylight exposure
  - 62% preferred daylight PDT
  - 14% preferred conventional PDT
  - Remaining had no preference
- No theoretical validation
  - How long dose one have to sit outside?
  - Under what conditions is it effective?



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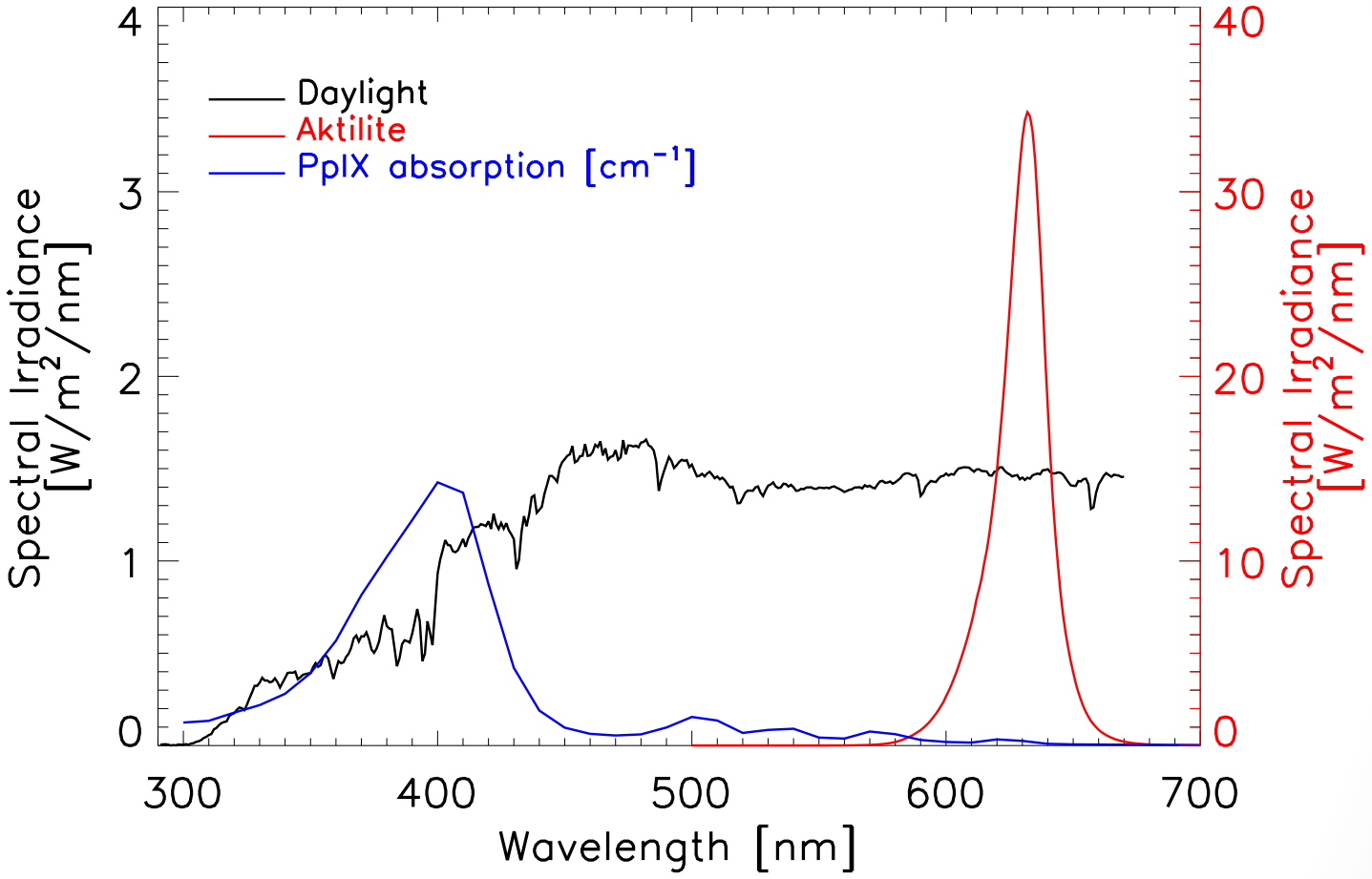
Sunlight vs. LED



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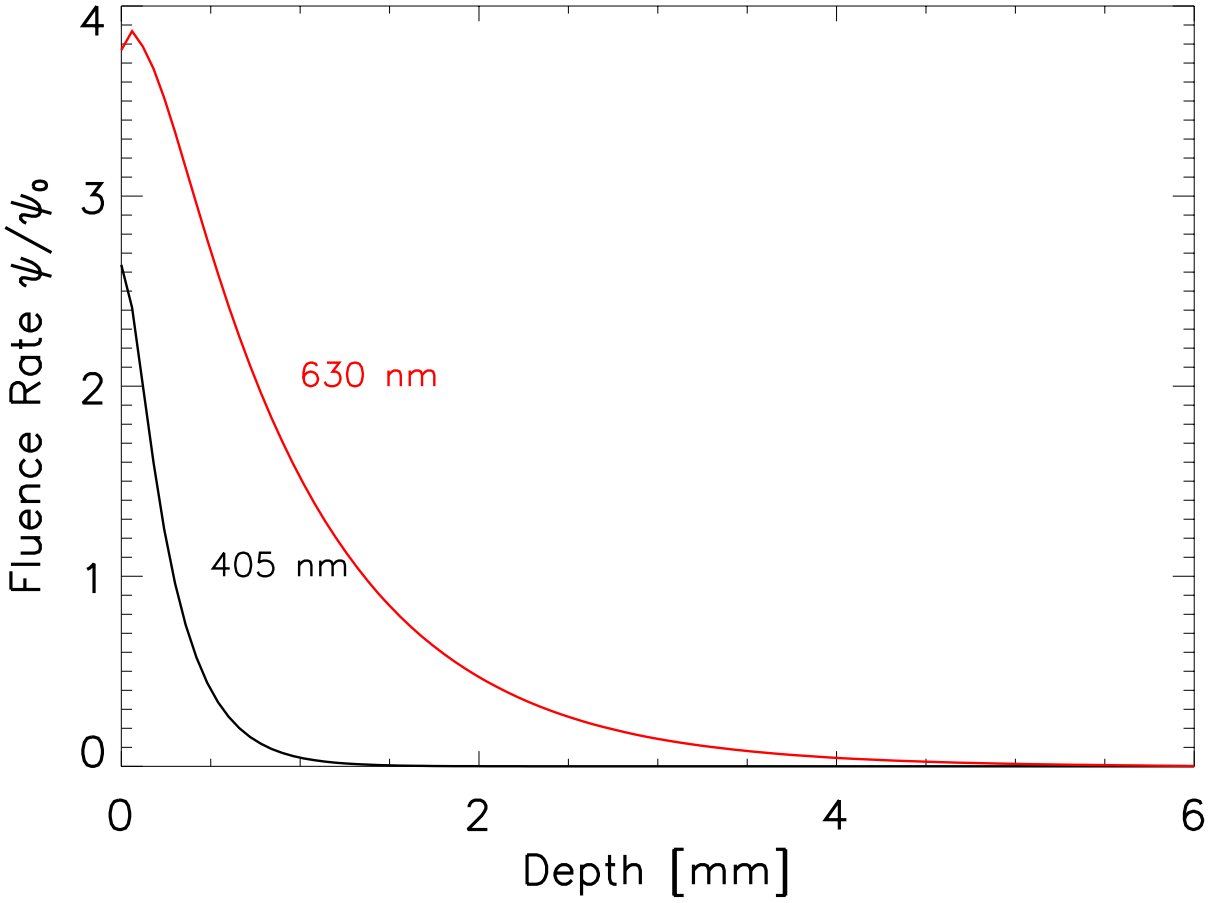
Fluence rate



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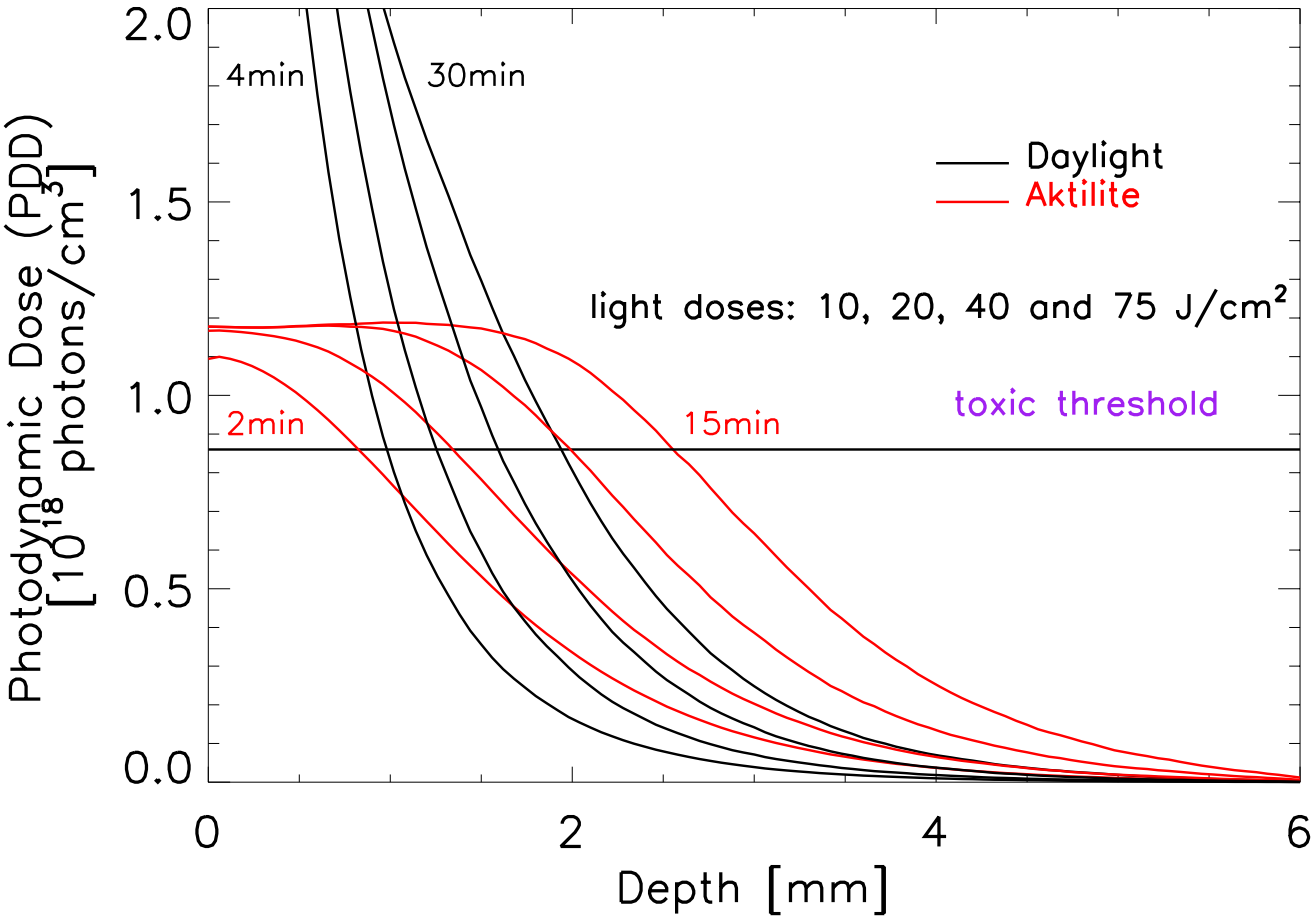
Photodynamic dose



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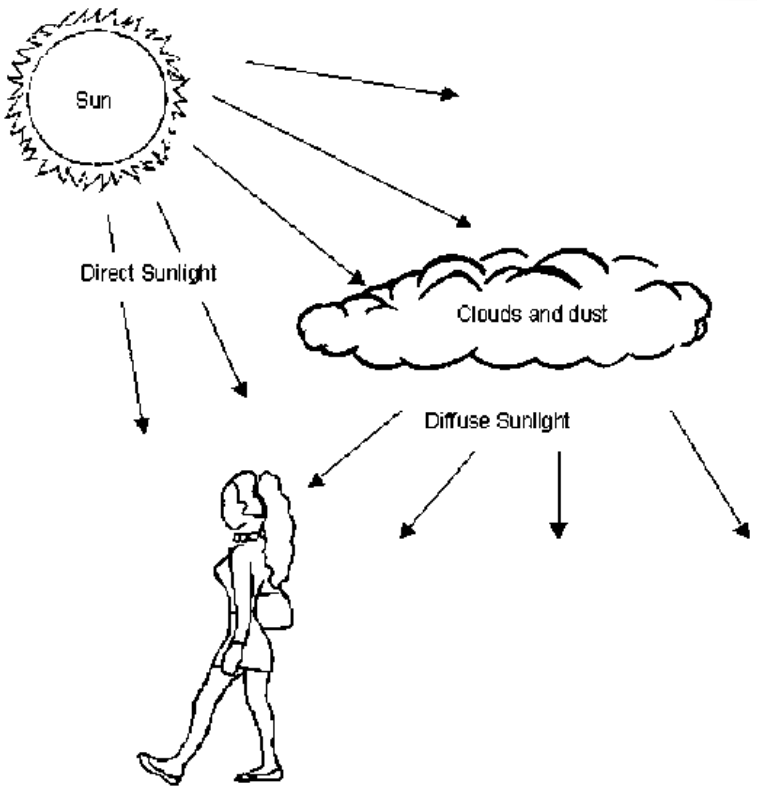
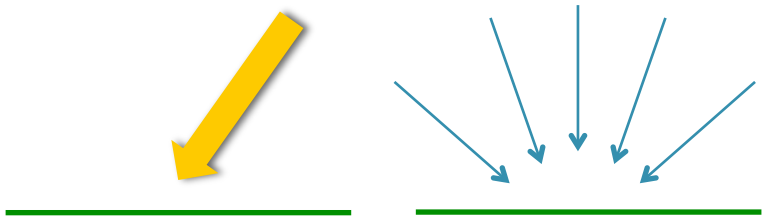
Daylight

- Clear summer day
  - Solar zenith angle ~ 30°
  - ~ 80% direct sunlight
  - ~ 20% diffuse sunlight
  - 100 000 lux
- Overcast summer day
  - 100% diffuse
  - 10 000 – 25 000 lux





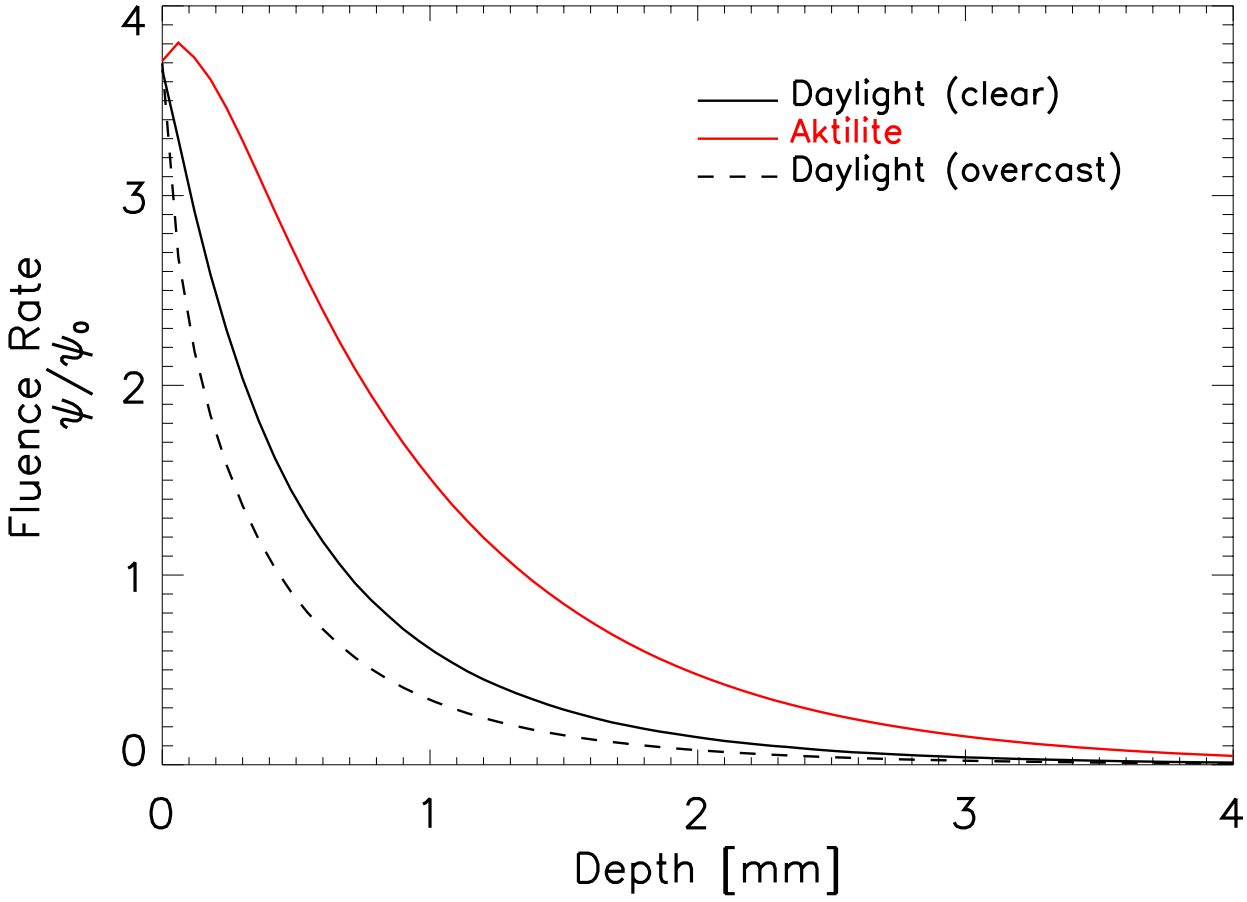
Direct light

defined direction

Diffuse Light

no defined direction

Fluence Rate



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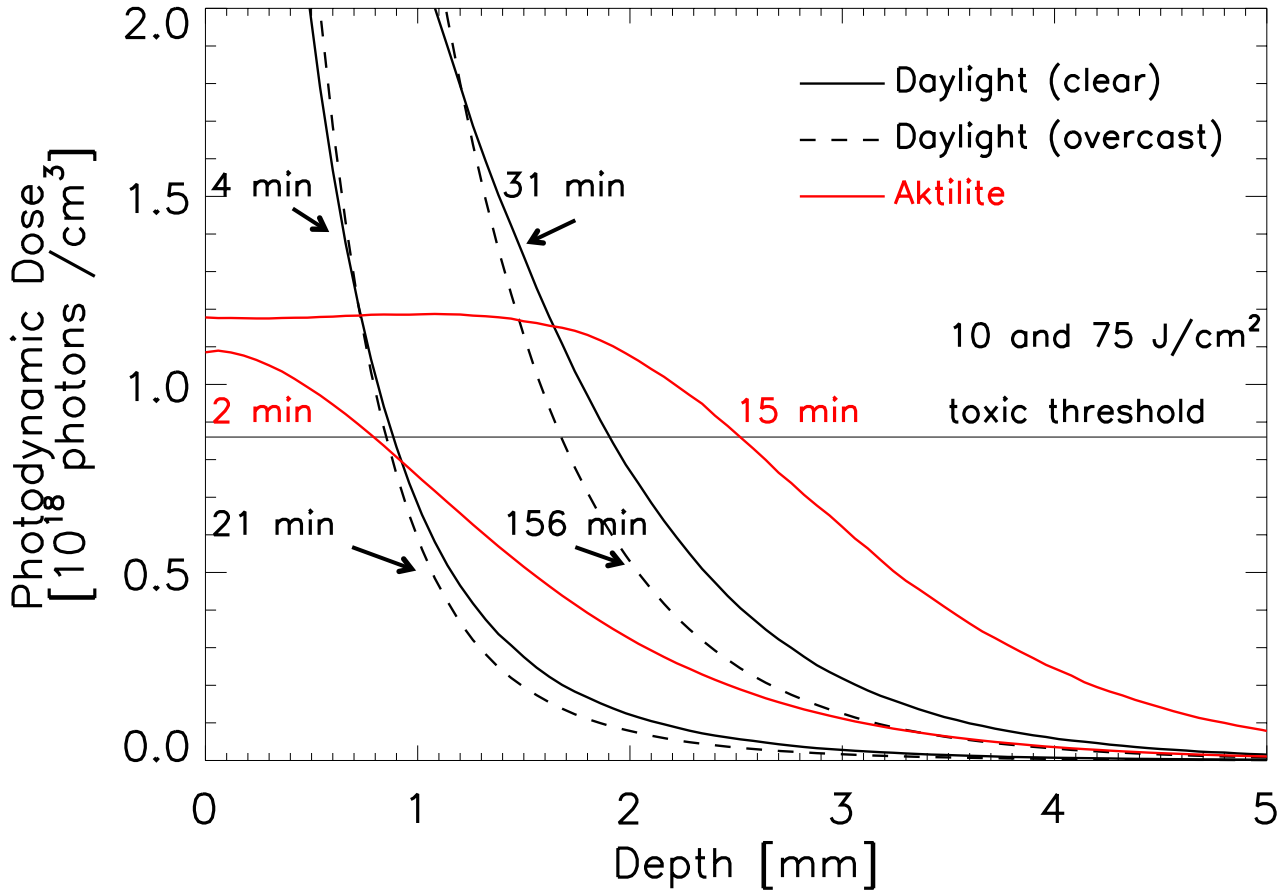
Photodynamic dose



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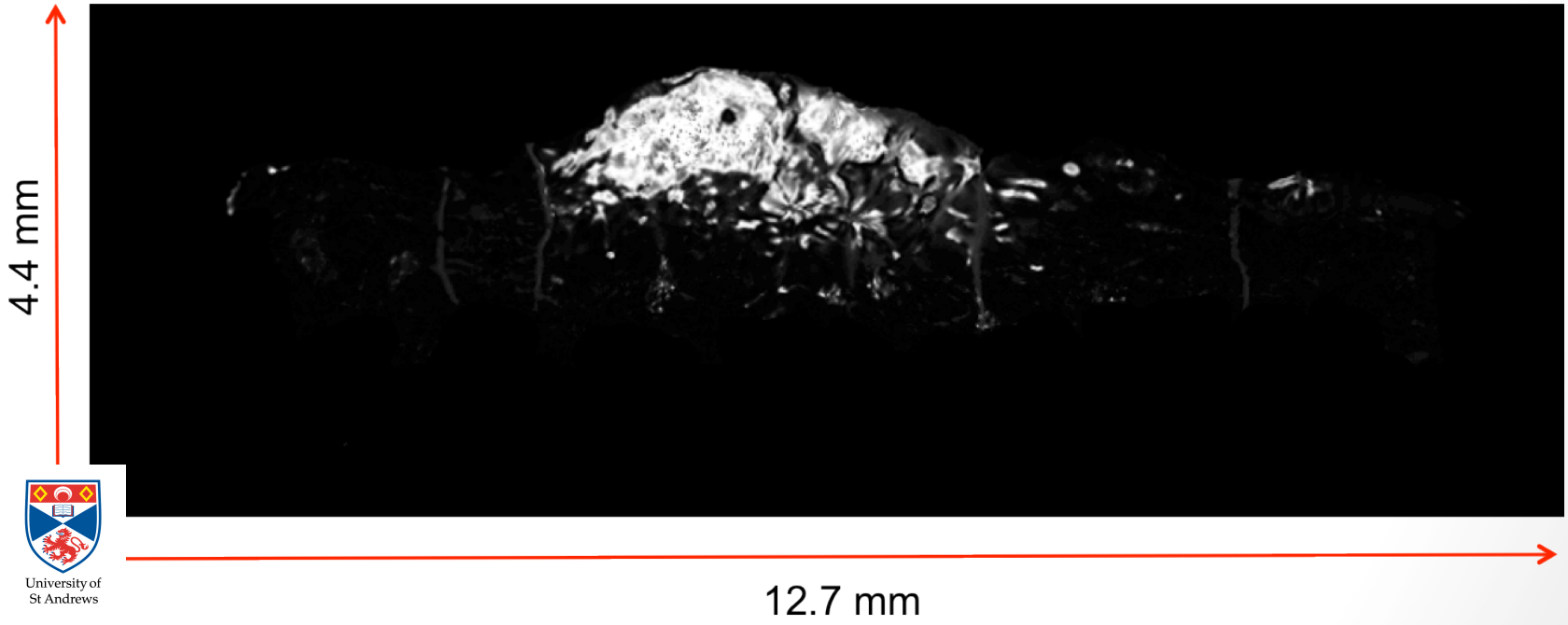
Future developments of code

- Add layers of skin
  - Layers with slightly different optical properties
  - Closer resemblance to actual skin
- Tumour shapes, not a uniform distribution



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Other medical applications of the code

- Internal PDT eg brain tumours
- Sun beds
- Laser hair removal
- Laser treatment for acne
- Tattoo removal using lasers

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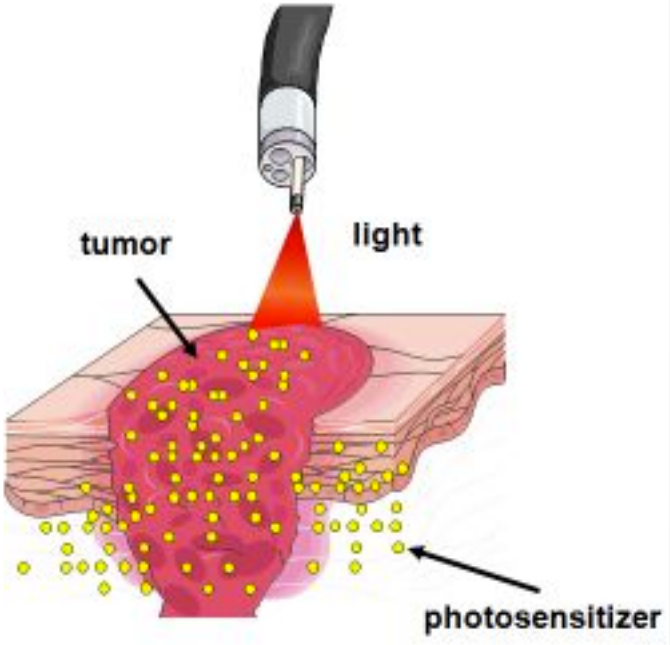
Summary

- Light therapy has been around for over 3500 years
- Photodynamic therapy
  - Light treatment for skin cancer
  - Light + PpIX = cell destruction
- MCRT can me used to model light travelling through skin
  - Different treatment methods and light sources
  - Results supports daylight PDT for various weather conditions
- Future developments include tumour structures
- MCRT can be used for other medical applications



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