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
Light – ancient medicine

- Psoriasis
- Vitilago
- Skin Cancer
- Rickets

Helios – the god of the sun

Vitilago

Rickets
Photosensitive chemical

- Used by medicine men
- Psoralen + UVA = efficient light treatment (PUVA)
- Start of development of Photodynamic therapy (PDT)
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
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
What to look out for...

Basal Cell Carcinoma

Squamous Cell Carcinoma
What to look out for...

Bowen’s Disease

Actinic Keratosis
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

Tumour

Photosensitiser

3h

Light illumination

~ 15min

Photosensitiser accumulated in tumour
- Light illumination from above

- Light interaction with photosensitiser generated toxic singlet oxygen
  -> Cell death!
Jablonski diagram of PpIX

- **S₀**
  - a - excitation
  - b - internal conversion/vibrational relaxation
  - c - fluorescence

- **S₁**
  - d - intersystem crossing

- **T₁**
  - e - phosphorescence

- **³O₂**
  - f - excitation of oxygen

- **¹O₂**
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?
How do we find out

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

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

$\psi$=Fluence rate [W/cm$^2$]
$L$=Luminosity [W]
$N$= number of MCRT photons
$\Delta V$=volume of one grid cell [cm$^3$]
$S_i$ = distance along the photon path in one cell [cm]
Photobleaching

- Concentration of photosensitiser changes during treatment

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

- \( C_{\text{new}} \) = concentration at time t in each grid cell
- \( C_0 \) = Initial concentration in each grid cell
- \( \psi \) = fluence rate [W/cm\(^2\)]
- \( t \) = elapsed treatment time [sec]
- \( \beta \) = photobleaching constant [J/cm\(^2\)]

Can be determined experimentally
What wavelength to choose...
Optical Properties: Skin

Optical Properties: PpIX

Absorption coefficient [cm\(^{-1}\)]

Wavelength [nm]
Is the treatment effective?

- Light dose = $I \times t$ [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: $8.6 \times 10^{17}$ photons/cm$^3$
  - Absorbed photons required for necrosis (cell death)
  - Patterson et al (1990)

Add up energy of absorbed photons (by the photosensitiser)
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
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
Spectra

![Graph of normalized spectral emission against wavelength (nm)](image)
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
Photodynamic dose

Assuming same surface irradiance of 82mW/cm²
Beam diameter

- After 2 J/cm\(^2\)
- Beam diameters:
  - 10, 20, 50 mm
Beam diameter

- After 75 J/cm²
- Beam diameters:
  - 10, 20, 50 mm
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Motivation for daylight PDT

- Reduces pressure on the clinics
- More convenient for patients
- Less painful
- Possible to treat larger area
Daylight PDT
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 do one have to sit outside?
  • Under what conditions is it effective?
Sunlight vs. LED

![Graph showing spectral irradiance comparison between sunlight, Aktilite, and PpIX absorption.](image-url)
Fluence rate

- 630 nm
- 405 nm

Fluence Rate $\psi/\psi_0$ vs. Depth [mm]
Photodynamic dose

The graph illustrates the Photodynamic Dose (PDD) in photons/cm³ as a function of depth in millimeters. The graph shows curves for different light doses: 10, 20, 40, and 75 J/cm², indicated by the labels 4min, 30min, 2min, and 15min, respectively. The curves represent daylight and Aktilite conditions. The toxic threshold is also marked on the graph.
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

![Graph showing fluence rate versus depth for daylight (clear), Aktilite, and daylight (overcast).]
Photodynamic dose

![Graph showing photodynamic dose vs depth with various conditions: Daylight (clear), Daylight (overcast), and Aktilite. The graph indicates parameters such as 2 min, 15 min, 21 min, 31 min, and 156 min, and the toxic threshold at 10 and 75 J/cm².]
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
Other medical applications of the code

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

- Light therapy has been around for over 3500 years
- Photodynamic therapy
  - Light treatment for skin cancer
  - Light + PpIX = cell destruction
- MCRT can be 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