MCRT of Photodynamic therapy (PDT)

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Overview

• Photodynamic Therapy (PDT)
• Major challenges
• Some of my projects
• Other areas where MCRT can be applied
Skin

- Largest organ in our body
  - 11 kg
  - 1.8 m²
- Important function
  - Protection against external environment
  - Regulates body temperature
- Complex structure, with several defined layers
  - Blood vessels, hair follicles, sweat glands, fibers etc
Basal Cell Carcinoma (BCC)

Cause: overexposure to the sun
Motivation for treatment: possible extensive local damage
Actinic Keratosis (AK)

**Cause:** overexposure to the sun

**Motivation for treatment:** if not treated can develop into...
...this...
Cosmetically inconvenient
How do you treat this?

• Photodynamic Therapy
  • Non invasive
  • Good cosmetic outcome
  • Selective
  • Large area treatment

• Disadvantages
  • High experienced pain
  • Relative high recurrence rate

Alternative treatment methods
• Cryosurgery
• Curettage
• Surgical excision
Photodynamic Therapy

Cream: pro-drug -> Protoporphyrin IX (PpIX) (in tumour cells)

Supplied by the blood within the skin tissue

Selective accumulation in the tumour tissue

Photosensitiser + Oxygen + Light

Externally applied

Selectively tissue destruction through apoptosis, necrosis or vascular damage

Cell destruction
Jablonski diagram of PpIX

S₂
S₁
S₀

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

Cytotoxic -> cell destruction

¹O₂
³O₂
Appropriate wavelength
Appropriate wavelength

Skin tissue
Light sources

- Lasers – mostly used for internal applications
- LED – most commonly used for topical application (Aktelite,LINCE)
- Lamps – Photocure, Paterson, Waldman 1200
- Ambulight – Low fluence light source
  - Lower intensity for longer treatment time
- Daylight
Patient Experience – Week 1

1. Curettage
2. Cream application
   - Prodrug
3. Occlusive dressing
   - Prevents ambient light to interact with PpIX
4. Wait 3 hours
   - Diffusion of cream and production of PpIX
5. Remove dressing
6. Light illumination
   - Typically for about 15 min
Patient Experience – Week 2

1. Curettage
2. Cream application
   • Prodrug
3. Occlusive dressing
   • Prevents ambient light to interact with PpIX
4. Wait 3 hours
   • Diffusion of cream and production of PpIX
5. Remove dressing
6. Light illumination
   • Typically for about 15 min

Repeat previous week
Patient Experience – 5 weeks

• Lesion cleared!
• Colour change will recover with time
My project

- Monte Carlo Radiation Transfer modelling of Photodynamic Therapy
- Combine clinical data and mathematical modelling
- What happens under the surface of the skin
- How deep does the light penetrate?
- How much light is absorbed by the photosensitiser?
- What is an optimal treatment time?
- How is the treatment affected by different light sources?
Modelling technique

- Monte Carlo Radiation Transfer modelling
  - Light through highly scattering media
  - Frequently used in Astronomy
- Absorption and Scattering events are determined by optical properties of skin tissue
- MCRT uses the probabilistic nature of photons to determine the photon propagation
Main challenges

- Variation in published data
- Accurate skin phantoms
- Limited in vivo data
- There is no such thing as a generic patient
Some of my projects
Daylight as a potential light source?

- Reduces pressure on the clinics
- More convenient for patients
- Less painful
- Possible to treat larger area
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\(^2\)]
  (wavelength dependent)

Can be determined experimentally
Photodynamic Dose

• **Definition:** Number of absorbed photons by the PpIX / cm$^3$

• Combines light distribution, absorption probabilities and photobleaching

• Depends on wavelength, light source and treatment time
  • Builds up with time

• Increases with total irradiation time
  • Typical light dose: 75 J/cm$^2$
    • **Light dose = I * t**
Photodynamic Dose

Light Dose = I * t

![Graph showing photodynamic dose over depth and light dose with lines for Aktilite, Daylight (clear), and Daylight (overcast) with specific times for different depths and light doses of 10 and 75 J/cm².](image-url)
Non-uniform distribution of PpIX

Conventional PDT
- Before light treatment: 3h
  - Cream is removed
- Light application:
  - Aktilite (630nm)
  - High intensity
- PpIX conc:
  - Photobleaching

Daylight PDT
- Before light treatment: 30 min
  - Cream is not removed
- Light application:
  - Daylight (wide spectrum)
    - Clear/Overcast
    - Low intensity
      - Depends on weather condition
- PpIX conc:
  - Photobleaching
  - +continuous build up

Photobleaching: degrades PpIX with time
More knowledge needed....

- Clinical study
- More knowledge on build up and accumulation of PpIX
- How does it change with:
  - Skin type
  - Lesion type
  - Location
  - Etc
Study design

- Measure fluorescence signal during occlusive treatment
- Indication of PpIX amount
- Include in models to get more of a handle of the distribution of PpIX
Fluorescence signal
• ~ 50 patients with NMSC or dysplasia
• Measure PpIX fluorescence at regular interval
• Results indicates a linear increasing signal
Fluorescence modelling

- Compare the theoretical model with clinical data
- Gain more understanding about the distribution of PpIX

Diameter: 600 um

NA: 0.22

Collected region Diameter: 600 um
Normalised Fluorescence

MCRT results

clinical results
Skin Ageing

• Thinning of layers
• Less blood and melanin (strong absorbers)
• Dry rougher skin
Skin classification

I
Always burns, never tans

II
Often burns, minimal tanning

III
Burns sometimes, average tanning

IV
Slight burns, more than average tanning

V
Rarely burns, strong tan

VI
Never burns
Increased penetration with skin type

Reduced penetration with age

Skin type I

Skin type III

Skin type VI

Age 30

A
g
e 30

Age 80

Reduced penetration with skin type

Increased penetration with age
Other things you can do with MCRT in Medicine

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

• Photodynamic therapy
• Theoretical modelling important to understand light interaction with skin tissue
• Daylight as an alternative light source
• Combine with clinical data
• Effects of skin type

Use plenty of Sunscreen
Questions?