Case Study: Laser Therapy of Port Wine Stain (PWS) Birthmarks

Bernard Choi
Virtual Photonics Workshop
21 Aug 2009
Objective of Case Study

Show how computational modeling has played a role in the evolution of laser technology for treatment of PWS birthmarks
What is a port wine stain (PWS)?

- Birthmarks
- Low-flow capillary malformations
- Progressive enlargement of superficial vessels
- 0.3% of all births (400,000 children worldwide)
- Most commonly on face and neck
- Asymmetric
- Present on all patients with Sturge-Weber Syndrome (neurological deficit)
Examples of PWS Lesions

Minkis et al., LSM 2009; 41:423
Histology of a PWS birthmark

Epidermis: 50-100 mm

Mean vessel diameter of ~50 mm

Barsky et al., J Invest Dermatol 1980; 74:157
• Maximize absorption of light in target
• Minimize absorption elsewhere
• Ignoring heat diffusion:

\[ \Delta T(x, y, z) = \frac{\mu_a \Phi(z) t}{\rho c} \]

Volumetric heat generation [J cm\(^{-3}\)]

Characteristic volumetric heat generation required to elevate temperature by one Kelvin [J cm\(^3\) K\(^{-1}\)]
Absorption spectrum of blood constituents

http://omlc.ogi.edu/spectra/hemoglobin/index.html
What is the best wavelength to use to destroy blood vessels?

http://omlc.ogi.edu/spectra/hemoglobin/index.html
Early theoretical modeling\(^1\) suggested \(577\) \(nm\) to be the optimal wavelength.

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Why 577 nm? Why not 418 nm?

1. Epidermal melanin absorption (i.e., unwanted absorber) decreases as wavelength increases

2. Inverse relationship exists between dermal scattering and wavelength
Epidermal absorption of light is unavoidable

Epidermis: 50-100 mm

Mean vessel diameter of ~50 mm

Barsky et al., J Invest Dermatol 1980; 74:157
Epidermal melanin absorption (i.e., unwanted absorber) decreases as wavelength increases.

418 vs. 577 nm
- 9x reduction in blood absorption
- 3x reduction in epidermal melanin absorption

http://omlc.ogi.edu/classroom/ece532/class3/muaspectra.html
Inverse relationship exists between dermal scattering and wavelength.
The SPTL-1a laser from Candela – 577 nm laser for vascular lesion treatment

SPTL – “selective photothermolysis”
Clinical finding

• Tan et al. (Plast Reconstr Surg 1985) showed that 585 nm produced a greater depth of vascular injury than 577 nm, and therefore 585 nm produces better clinical results than 577 nm.

• Unexpected outcome
  – Similar scattering coefficient at both wavelengths → no difference in the depth of light penetration in the (bloodless) dermis
  – In contrast to the clinical results, 577 nm was still predicted to provide the greatest heat confinement to the target blood vessel.
Key question

• Can computational modeling help explain this unexpected finding?

Modeling the effect of wavelength on the pulsed dye laser treatment of port wine stains

Wim Verkruysse, John W. Pickering, Johan F. Beek, Marleen Keijzer, and Martin J. C. van Gemert

1 February 1993 / Vol. 32, No. 4 / APPLIED OPTICS 393
Modeling geometry for Monte Carlo modeling

Homogeneous distribution of blood within dermis
Optical properties of the “bloody” dermis

\[ \mu_{\text{bloody-dermis}}(p\%) = \frac{p \mu^{\text{blood}} + (100 - p) \mu^{\text{dermis}}}{100}, \]

- \( p \) = volume fraction of blood
- \( m \) = absorption coefficient, scattering coefficient, or anisotropy factor
Optical properties of blood

<table>
<thead>
<tr>
<th>Wavelength (nm)</th>
<th>Absorption Coefficient (mm⁻¹)</th>
<th>Scattering Coefficient (mm⁻¹)</th>
<th>Anisotropy Factor</th>
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<td>48.0</td>
<td>0.995</td>
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<td>35.4</td>
<td>46.8</td>
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<tr>
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<td>19.1</td>
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<td>Epidermis b</td>
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Defining safe depth of vascular injury

- **Goal of treatment**: Photocoagulate vessels, spare epidermis
- **Assume**
  - Temperature rise is proportional to volumetric rate of heat generation $[\text{W/cm}^3]$.
  - Volumetric rate of heat generation $= m_a \Phi$
- **Define threshold for safe injury as**:

\[
\mu_a^{\text{epidermis}} \Phi(z_{\text{epi}|\text{derm}}) = \mu_a^{\text{blood}} \Phi(z, z_{bl}).
\]
Effects of blood volume fraction on maximum depth of vascular injury

1. Bloodless dermis → optimal wavelengths of 415, 542, or 577 nm

2. Progressive red shift with increasing blood volume fraction
Maximum depth of vascular injury **red shifts** with increasing blood volume fraction

- Depth of vascular injury defined as:
  - $Q_{\text{center of vessel}} > Q_{\text{epidermal-dermal junction}}$
What modeling tells us

- **Key question**: Can computational modeling help explain why laser therapy with 585 nm light results in deeper vascular photocoagulation than 577 nm?

- **Key modeling results**
  - Bloodless dermis $\rightarrow$ optimal wavelengths of 415, 542, or 577 nm (UNREALISTIC GEOMETRY)
  - Progressive red shift with increasing blood volume fraction
  - “...the model shows a greater coagulation depth at 585 nm than at 577 nm in all conditions of blood content, vessel size, and epidermal pigmentation.” (NOT SHOWN HERE)
The SPTL-1b laser from Candela – 585 nm light source for vascular lesion treatment
Revisiting predictions of vascular injury

• **Goal of treatment:** Photocoagulate vessels, spare epidermis

• Assume
  – Temperature rise is proportional to volumetric rate of heat generation \([W/cm^3]\)
  – Volumetric rate of heat generation = \(m_a\)

• Define threshold for safe injury as:

\[
\mu_a^{\text{epidermis}} \Phi(z_{\text{epi}|\text{derm}}) = \mu_a^{\text{blood}} \Phi(z, z_{bl}).
\]

*Time during which temperatures remain elevated, is not considered*
Thermal injury is a temperature-time phenomenon

Pfefer et al, LSM 2000; 26:145
Key questions

• With use of a realistic PWS geometry, what can we learn about PDL therapy?

• What is the effect of laser pulse duration on the degree of thermal injury?
Modeling Laser Treatment of Port Wine Stains With a Computer-Reconstructed Biopsy

T. Joshua Pfefer, MS, Jennifer Kehlet Barton, PhD, Derek J. Smithies, PhD, Thomas E. Milner, PhD, J. Stuart Nelson, MD, PhD, Martin J. C. van Gemert, PhD, and Ashley J. Welch, PhD
Computational Modeling Flowchart

Material Grid $M(x,y,z)$

Energy Deposition Rate $S(x,y,z)$

Temperature $T(x,y,z,t)$

Thermal Damage $\Omega(x,y,z,t)$

PWS biopsy and reconstruction

Monte Carlo optical model (MAGNUM)

Finite difference thermal model

Arrhenius rate process integral
Digitization of Histology Sections

Smithies et al, PMB 1997; 42:1843
Computational Modeling Flowchart

Material Grid \( M(x,y,z) \)

Energy Deposition Rate \( S(x,y,z) \)

Temperature \( T(x,y,z,t) \)

Thermal Damage \( \Omega(x,y,z,t) \)

PWS biopsy and reconstruction

Monte Carlo optical model (MAGNUM)

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Arrhenius rate process integral
Modular Adaptable Grid Numerical Model (MAGNUM)

Top view

Longitudinal cross-section

Pfefer et al, IEEE JSTQE 1996; 2:934
Compute rate of heat generation using MAGNUM Monte Carlo model
Computational Modeling Flowchart

Material Grid $M(x,y,z)$

Energy Deposition Rate $S(x,y,z)$

Temperature $T(x,y,z,t)$

Thermal Damage $\Omega(x,y,z,t)$

PWS biopsy and reconstruction

Monte Carlo optical model (MAGNUM)

Finite difference thermal model

Arrhenius rate process integral
Compute evolution of temperature field

- Use same material property grid for both optical and thermal models
- Method of **finite differences** to approximate solution of **heat diffusion equation** with **convective surface boundary condition**

\[
\rho c \frac{dT}{dt} = \frac{\partial}{\partial x}\left(k \frac{\partial T}{\partial x}\right) + \frac{\partial}{\partial y}\left(k \frac{\partial T}{\partial y}\right) + \frac{\partial}{\partial z}\left(k \frac{\partial T}{\partial z}\right) + S,
\]

\[
-k \frac{dT}{dz}\bigg|_{surface} = h(T_{air} - T_{surface}),
\]
Effect of pulse duration on temperature field

0.5 ms

5 ms

10 ms
Computational Modeling Flowchart

Material Grid $M(x,y,z)$

Energy Deposition Rate $S(x,y,z)$

Temperature $T(x,y,z,t)$

Thermal Damage $\Omega(x,y,z,t)$

PWS biopsy and reconstruction

Monte Carlo optical model (MAGNUM)

Finite difference thermal model

Arrhenius rate process integral
Compute evolution of thermal injury field

- Numerical integration of Arrhenius rate process integral

\[ \Omega(t) = A \int_{0}^{t} \exp \left[ - \frac{E_a}{RT(\tau)} \right] d\tau, \]

- Several examples of good agreement between model predictions and experimental measurements of thermal injury
Realistic tissue geometry $\rightarrow$ shielding effect
Effect of pulse duration on thermal injury field

0.5 ms

5 ms

10 ms

Uh-oh...
Cryogen spray cooling (CSC)

- Developed by Stuart Nelson, Lars Svaasand, and Tom Milner, at BLI
The Dynamic Cooling Device (DCD) from Candela
Simulated effects of CSC on thermal injury field

2 ms pulse duration
No cooling

2 ms pulse duration
20 ms cryogen spurt

Pfefer et al, LSM 2000; 26:145
ScleroPlus laser from Candela – 585 or 595 nm light, 1.5 ms pulse duration, integrated with DCD
Interspersed cryogen spurts and laser pulses (MCS-MTWLP)

Jia et al, LSM 2007; 39:494
Dualis by Fotona – MCS-MTWLP
Take-home message

• Computational modeling has played an important role in enabling the development of safe laser treatment protocols for PWS birthmarks

• Biological response is next modeling frontier for phototherapeutics
  – Vascular repair pathways
  – Transport of growth factors – use random-walk models?