Novel use of laser in pediatric patients

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Off-label uses will be discussed

**Kelly:** Drug donated by QLT, Light Sciences Oncology, Allergan
Light Sources donated by Solta; Syneron/Candela; Thermi RF
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Syneron-Candela, Allergan
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**Arkin:** Light sources donated by Syneron/Candela
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Learning objectives

1. Define the concept of selective photo-thermolysis
2. Review challenges and opportunities for laser treatment of port wine birthmarks (PWB)
3. Describe the potential utility of non-invasive imaging in the treatment of PWB
4. Offer pearls for laser treatment of vascular anomalies
“Laser Light has the same properties that you would wish for your own children…”

Rox Anderson, MD

“Energetic
Powerful, yet easy to control
Easily focused
On a well-defined wavelength
Coherent”
Selective photo-thermolysis creates precise, controlled damage while minimizing collateral injury

PDL

Laser energy preferentially absorbed by one structure (chromophore)
Surrounding tissue has low absorption

Critical parameters to spare surrounding tissue


1. Wavelength – selective absorption
2. Pulse duration – heat confinement
3. Fluence – exposure dose
Selection of Wavelength

Chromophores in human skin - Absorption spectra
Hemoglobin, melanin and water

Absorption spectra of Hemoglobin, Melanin, and Water across different wavelengths (nm): 400 to 10000.
Longer Wavelengths Penetrate Deeper

shallow

deep
Laser light must pass through pigmented epidermis to get to the targeted blood vessels

Shorter wavelengths have more melanin interaction
Wavelengths/Devices for Vascular Lesions

• Argon – historical
• Pulsed Dye Laser
• 532 nm Nd:YAG
• 755 nm Alexandrite
• 810 nm Diode
• 1064 nm Nd:YAG
• Intense Pulsed Light
• Combined Wavelength or Energy Devices
Increased ulceration risk with longer wavelength lasers
## Selection of Pulse Duration = Confinement of Thermal Energy

<table>
<thead>
<tr>
<th>Target</th>
<th>Size</th>
<th>( \tau_r )</th>
</tr>
</thead>
<tbody>
<tr>
<td>microvessel</td>
<td>10 ( \mu\text{m} )</td>
<td>90 ( \mu\text{s} )</td>
</tr>
<tr>
<td>blood vessel</td>
<td>200 ( \mu\text{m} )</td>
<td>1-10 ms</td>
</tr>
<tr>
<td>tattoo pigment</td>
<td>0.5-100 ( \mu\text{m} )</td>
<td>20 ns-3 ms</td>
</tr>
<tr>
<td>melanosome</td>
<td>0.5-1.0 ( \mu\text{m} )</td>
<td>20-40 ns</td>
</tr>
<tr>
<td>melanocyte</td>
<td>7 ( \mu\text{m} )</td>
<td>1 ( \mu\text{s} )</td>
</tr>
</tbody>
</table>

Increasing vessel diameter requires increased pulse duration

Capillary malformation (Heterogeneous)  Glomulovenous malformation  Venous malformation

A pulse width $\leq$ to TRT confines heat to target vessels during exposure
The treatment pulse width for non-uniformly pigmented targets should be longer than the TRT of the target.

Allows for heat diffusion from the primary chromophore to the rest of the target.

Vessel destruction requires heat diffusion from the blood (chromophore target) to the vessel wall endothelium.

Epidermal cooling prevents epidermal injury

Leaves the target vessels susceptible to laser induced thermal effects/injury
Epidermal cooling…

Allows the use of higher fluences
Allows safe treatment of darker skin types
Decreases treatment discomfort

Cryogen Spray Cooling
Contact Cooling
Air Cooling
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Affect up to 0.5% of newborns

Reduce QoL due to soft tissue overgrowth, nodularity, and life-altering, stigmatizing disfigurement
Histologic success with laser treatment

Damage to the vessel wall & vessel removal

Damage can be rupture (purpura) or wall injury & coagulation

Incomplete coagulation will generally not achieve the desired effect
Immediate blood vessel hemorrhage after pulsed dye laser treatment

Courtesy of D. Li, GX Wang, Y L He, W J Wu Z X Ying, YX Wang
Early treatment improves outcomes

Start as early as you can…

Hypothesized mechanisms for better early response:
1) Hemoglobin F in infants
2) Vessels less dilated in young
3) Less melanin interference
4) Skin thickness differences
5) Early treatment before pathway proliferation (more to come)…
Our Approach

• PDL for infants and children
• Mostly shorter pulse durations (caveat to come)
• Generally desired end point-purpura
• Often useful to change pulse durations over a course of treatment or do multiple passes in a single session in older patients with darker skin types
Optimizing the environment

Swaddle on parent’s lap
Sweet Ease
Music
Nursing support

Eye protection:
Laser Aid Eye pads
Overlying Gauze
Corneal shield if treating the eyelid
Damp abdominal pads if treating on lower face
Post-operative Care

- Ice and Elevation (sleep with an extra pillow in those old enough to sleep with a pillow)
- Mild analgesic – generally Tylenol if needed
- Emollient application
- Sun protection
Vascular stains are caused by mosaic mutations in genes that regulate the cell cycle

GNAQ, GNA11, PiK3CA >>> PIK3R1, MAP2K1, PTPN11
Mosaic mutations in both GNAQ and GNA11 can cause the clinical phenotype of SWS.

Forehead involvement predicts neurologic and ocular involvement.

Renovascular hypertension, macrocephaly, asymmetric growth are associated.

Waelchli et al, British Journal of Dermatology, 2014
Kinsler et al, British Journal of Dermatology
What if there were a more precise way to optimize vessel destruction?

Optical Coherence Tomography (OCT)
FDA approved in 2010
Calculates predominant vessel diameter and depth in a specific location
PWB with complex and heterogeneous vessel diameters on OCT, suggesting that treatment protocols could be individualized

Creating a precision-based approach for PWB

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Calculating Thermal Relaxation Time (TRT) and Pulse Duration (PD)

Thermal Relaxation Time = vessel diameter$^2$/16k

$k = 1.3 \times 10^{-3} \text{ cm}^2$

PD $\leq$ TRT (~1/2 of TRT)

Selective photothermolysis: precise microsurgery by selective absorption of pulsed radiation.
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Venous Malformations

- Mosaic Tie2 and PiK3CA

- Treatment options: sclerotherapy, excision, laser

- Long pulse 1064nm Nd:YAG due to high depth of penetration (5-6mm) in tissue and its coagulation potential

- 755nm alexandrite and 810nm diode lasers also used
Utility and tolerability of LP Nd:YAG for treatment of disfiguring vascular malformations in children and adolescents

- Retrospective review of 29 pediatric patients
- VMs of head and neck, particularly involving oral mucosa, responded the best to treatment
- Well tolerated treatment option for children with mucosal VMs

(J Am Acad Dermatol 2017;77:473-9.)
Targeted therapy in patients with PiK3CA-related overgrowth syndrome


Clinical and radiologic response in 100% of patients. No substantial adverse effects.
Topical PiK3CA inhibitors are effective in the treatment of PiK3CA associated VMs in mice

Take Away Points

• Earlier treatment improves outcomes in PWB.

• Integration of genotyping with vessel size may enable more targeted treatment parameters for PWB.

• Future therapies may integrate downstream inhibition of activated pathways in vascular anomalies including PWB.
Acknowledgements