Innovative Medical Uses of Lasers

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Disclosures

• No conflicts of interest for this lecture
• 100% of drugs and devices discussed are off-label
Overview

1. PDT treatment of skin cancer
2. Laser-assisted drug delivery
3. Laser management traumatic scars and fibrotic disorders
PDT for Skin Cancers

- 77 tumors (67 patients)
  - 44 superficial BCC
- 5 year f/u data
  - 2 year recurrence = 25%
  - 5 year recurrence = 30%

How to Enhance ALA Penetration?

• Rate-limiting step in topical drug absorption is penetration through the stratum corneum

• Disrupt the Stratum Corneum
  – Topical Pre-Treatment
    • Retinoid
    • 5-FU
  – Mechanical Disruption
    • Microdermabrasion
    • Tape-stripping
    • Curettage
    • Microneedling
  – Fractional Laser Ablation
Ablative Fractional Resurfacing

Immediately 48 hours 7 days 1 month 3 months
Laser-Assisted PDT

Skin Surface Fluorescence After Topical Application of Methyl 5-Aminolevulinic Acid (MAL)

<table>
<thead>
<tr>
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<th>90 minutes</th>
<th>180 minutes</th>
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<tbody>
<tr>
<td>MAL alone</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
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<tr>
<td>Fractional CO₂ laser + MAL</td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
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Laser-Assisted PDT

Fluorescence 3 hours after mALA application

- Ablative Fractional Laser
- Non-Ablative Fractional Laser
- Microneedling
- Dermabrasion

Image adapted from Bay et al. JAMA Dermatol 2017
Laser-Assisted PDT

Fluorescence 3 hours after mALA application

Ablative Fractional Laser
Non-Ablative Fractional Laser
Microneedling
Dermabrasion

Laser-assisted PDT for nodular BCC

- 39 patients randomized to either:
  - Conventional MAL-PDT (2 sessions)
  - Er:YAG + MAL-PDT (1 session)

- 3 month response rate (p=0.028)
  - MAL-PDT: 50.0%
  - Laser-assisted PDT 84.2%

- 12-month response rate
  - MAL-PDT: 22.2%
  - Laser-assisted PDT 78.9%
Laser-Assisted Drug Delivery (LAD)

• Candidate Diseases and Drugs
  – Actinic Keratoses and SCC/BCC: Photosensitizing drugs, 5-FU, imiquimod
  – Scars, Fibrosis: Corticosteroids\(^1\)
  – Anesthesia: Lidocaine\(^2,\,3\)
  – Hair Loss: Minoxidil, Latanoprost\(^4\), Corticosteroids
  – Atrophy: Poly-L Lactic Acid\(^5\)
  – Hyperpigmentation: (e.g. hydroquinone, azeleic acid)
  – Vaccinations\(^6\)
  – Hypo/Depigmentation: bimatoprost\(^7\)

LAD Repigmentation with Bimatoprost

• **Hypopigmented scars**\(^1\)
  - 79% of patients had >50% improvement after 2-10 treatments with a nonablative fractional laser protocol

• **Vitiligo**

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LAD Vaccination

- In vivo mouse study
- Mouse skin treated with fractional Er:YAG laser
- Skin vaccination with a lysozyme antigen
  - 129 amino acid molecule
  - Too large to penetrate stratum corneum
- Production of antibodies in the serum ↑ by 3x

LAD of stem cells resulting in functional chimeric mouse

- Immunosuppressed mice received radiation to ablate their bone marrow
- Skin was subsequently treated with AFR and donor stem cells
- Three weeks after this single treatment, post-procedure fluorescence-activated sorting demonstrated engraftment of the donor cells, along with functional recovery.

Future Directions for LAD

1) Depth
   - Would expect deeper channels to give greater absorption
   - However, data inconsistent

2) Density
   - Higher density is not always better
   - At very high densities dermal vasculature gets wiped out and drug absorption decreases

3) Coagulation
   - Laser-induced thermal coagulation enhances skin uptake
     - CO2 is best b/c it has a coag zone
     - Er:YAG intermediate
     - Microneedle holes offer the least penetration
   - No-coag may be better for systemic delivery
Advances in Laser Treatment of Traumatic Scars and Sclerotic Disorders
Scar Contractures

- Scar contractures across joints impair functional mobility
- Non-healing erosions can be painful and a source for infection
- May impede prosthetic rehabilitation
- Surgical interventions may be required for refractory or severe contractures
  - incision and release, skin grafting, flaps, and long-term splinting
  - unpredictable efficacy, high recurrence rates, and additional morbidity.
Scar Contractures

- 43 y.o. male Iraq war veteran with scar contracture of left knee after IED injury
- Scheduled for surgery to have scar release and skin grafting
- 3 days after 1st AFR procedure, had 12° increased ROM, resolution of non-healing erosion
- By 2 year f/u (after 2 AFR), had regained normal ROM

Linear Morphea

- 27 y.o. Hispanic woman, avid runner
- Treated with topical calcipotriene, intralesional triamcinolone injections, UVA phototherapy
- No response, contracture worsening

Bandlike sclerotic plaque extends across the left ankle to the mediodorsal foot, restricting patient ambulation
Linear Morphea

Pretreatment

Restricted plantar flexion of the left foot
(45° from neutral)

4 month followup

65° of plantar flexion from neutral
Microstomia of Systemic Sclerosis

- Intense-pulsed light
- Patients (n=4) treated with up to 5 monthly sessions
- 3 of 4 patients had 1mm ↑ in oral aperture

Scar Contractures – Summary & Approach

- Start Treatment Early – 2-4 months
- Ablative column depth should approximate full thickness of scar
- Low density: ~5%
- LAD with topical triamcinolone or 5-FU
  - Similar efficacy
  - TAC may have more AEs, including increased scar width and telangiectasias
- 3-5 sessions
- Lasers are not a monotherapy for traumatic scars
  - Physical and occupational therapy should be an ongoing part of rehabilitation to optimize scar remodeling and functional enhancement
  - May still require surgical revision
Fractional Laser – Mechanism

• Fenestration?
• Collagen remodeling? – shift from collagen I to collagen III
• Transepidermal elimination of elastic fibers?¹

Thank You

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