Laser-Assisted Delivery to Treat Facial Scars

Jill S. Waibel, MD[a,b,c,*], Ashley Rudnick, BS[d]

KEYWORDS

• Laser assisted drug delivery • Ablative fractional laser • Facial scars

KEY POINTS

- The treatment of disfiguring facial scars has been reinvigorated with recent advances in technology.
- Laser-assisted drug delivery (LAD) is an emerging technology to achieve greater penetration by existing topical medications and drugs to reach desired targets in the skin.
- LADs allows us to alter the stratum corneum, epidermis and/or dermis to facilitate increased penetration of a drug or device to a specific target.
- This emerging concept is bridging medicine with technology; however, the drugs have not been formulated for this type of delivery and so this science is "off-label."

INTRODUCTION

Facial Scars

There are few medical situations as distressing as that of a child or adult whose life has been permanently altered by tragedy. The profound physical, mental, financial, and psychological damage brought on by such calamitous events often are accompanied by significant scarring. When the scarring is on the face, patients have severe physical and psychological stress. The treatment of facial scars is a multispecialty endeavor for optimal patient recovery.

Current Treatments

Scar rehabilitation is the restoring of form and function in scar patients. There are multiple therapeutic approaches have been used in scar management, including surgery (z-plasty), physical therapy, compression, silicone sheeting, corticosteroid therapy, and laser therapy. Leading the way in scar treatments are lasers, which are a scientifically precise and effective treatment modalities to rehabilitate and improve scars. Laser has added a powerful tool to improve scar symptoms and deformities. Given the established benefit of lasers with scars[1,2] new methods to synergistically improve scars are being studied. At the forefront is laser-assisted delivery (LAD) of drugs, molecules and cells for scar rehabilitation. LAD is a new delivery system (vs oral, intravenous) that enables physician to uniformly distribute drug, cell, or cosmeceutical in microscopic channels to desired depth in cutaneous tissue. Without exception thus far, ablative fractional laser has been found to enhance the local uptake of any drug or substance applied to the skin through any fractional ablative tunnels can be used for LAD systems of a variety of drugs, topical agents, and other living tissue. These zones may be used immediately postoperatively to deliver drugs and other substances to synergistically create an

Disclosure Statement: J.S. Waibel, disclose the following "relevant financial relationship(s)" with commercial or financial conflicts of interest and any funding sources. Serve as a consultant: MiraDry, Lumenis, Sciton. Speaking Honoraria: Lumenis, Sciton, Syneron/Candela. Research Grant: Galderma, Lumenis, Lutronics, Sciton, Syneron/Candela.

[a] Private Practice: Miami Dermatology and Laser Institute, 7800 Southwest 87th Avenue, Suite B200, Miami, FL 33173, USA; [b] Baptist Hospital, Miami, FL, USA; [c] Dermatology Faculty, Miller School of Medicine, University of Miami, Miami, FL, USA; [d] 7800 Southwest 87th Avenue, Suite B200, Miami, FL 33173, USA
* Corresponding author. 7800 Southwest 87th Avenue, Suite B200, Miami, FL 33173.
E-mail address: jwaibelmd@miamidermlaser.com

Facial Plast Surg Clin N Am 25 (2017) 105–117
http://dx.doi.org/10.1016/j.fsc.2016.08.010
1064-7406/17/Published by Elsevier Inc.

enhanced scar therapeutic response to drug or substance applied to the skin.

History of Laser-Assisted Delivery

Topical drug delivery is essential in the treatment of many cutaneous conditions. The efficacy of topical therapy depends on the penetration of viable skin. However, therapeutic benefit is ultimately limited by absorption of the medication through the skin's inherent barrier properties. The stratum corneum, the outermost layer of the skin, serves as the rate-limiting step for percutaneous penetration and only 1% to 5% of topically applied drugs absorb into the skin.[3]

Drugs that are semilipophilic (uncharged/nonpolar) and small (<500 Da) may pass through the stratum corneum because the corneocytes are embedded in a lipid matrix. Drugs that are lipophilic and large hydrophilic drugs are not suited for delivery through intact skin. Furthermore, many medications are too large to penetrate and currently require either an injectable or systemic delivery.

Strategies to enhance topical drug delivery include chemical (solvents, surfactants), biochemical (nanoparticle, lipid synthesis inhibitors), and physical methods (tape stripping, sonophoresis, microneedling). The most commonly used in today's topical drug world is chemical modifications. These approaches are used to remove or alter the stratum corneum and have had variable success with improving drug delivery.

When a drug enters the skin and remains within the skin it is called *penetration*; this is how most dermatology drug targets within the skin and function to improve disease. *Transdermal delivery* and absorption means a drug has crossed the skin barrier and entered the bloodstream.[3] Transdermal patches have been used since the 1970s, but are limited to drugs with a low molecular mass (<500 Da) and high lipophilicity.[3–5]

Laser-assisted drug delivery

Laser-assisted drug delivery is an evolving modality first published in 2002,[6] which may allow for a greater precision of depth penetration by existing topical medications and more efficient transcutaneous delivery of drug molecules. Fractional ablative lasers, either carbon dioxide (CO_2) or erbium:YAG (Er:YAG), provide a novel way to create a conduit in the stratum corneum, epidermal, and dermal layers in a predictable and controlled pattern resulting in the potential for increased penetration of topically applied molecules. Both CO_2 and Er:YAG are infrared lasers that heat skin tissue to greater than 100°C and cause vaporization. The Er:YAG has an absorption coefficient of 2×10^7/cm and owing to high absorption of water it takes less energy to ablate tissue. The CO_2 has an absorption coefficient 2×10^6 cm^{-1} m^{-1} and takes higher energies to ablate tissue resulting in increased thermal damage compared with the Er:YAG laser.

Ablative fractional resurfacing creates vertical channels of ablation surrounded by thin layers of coagulated tissue known as microthermal zones (MTZ).[5] The creation of these channels theoretically serves as access points for drug delivery and allow for transport of actives deeper into the skin.

LAD is a more efficient transcutaneous delivery of large drug molecules, and potentially a way of delivering systemic medication via a transcutaneous route.[3] Topical drug delivery has many advantages over traditional oral medication. With dermatologic disease, topical administration of therapies directly to the skin limit systemic toxicity. In addition, drug degradation by the gastrointestinal system and first-pass liver metabolism can be avoided with laser cutaneous delivery.

The goals for a cutaneous delivery system include increasing the ability to attain a therapeutic target, decreasing amount of drug needed to deliver, decreasing adverse events to other organs and ease of use for patients. LAD is a new emerging concept bridging medicine with technology to improve health care.

Clinical Applications of Laser-Assisted Delivery

Various dermatologic conditions have been studied with LAD including dysplasia, nonmelanoma skin cancer, psoriasis, inflammatory conditions, local anesthesia, and scars. Studies of LAD have shown without exception that ablative fractional laser pretreatment has been found to enhance the local uptake of any drug or substance applied to the skin.

Investigated dermatologic drugs included lidocaine, 5-aminolevulinic acid (ALA), methyl-5-amnolevulinate (MAL), 5-fluorouracil (5-FU), ascorbic acid, diclofenac, ingenol mebutate, imiquimod, methotrexate, and vaccinations.[7–18] Specifically in the arena of LAD of scars, compounds studied include corticosteroids, ascorbic acid, 5-FU, platelet-rich plasma, and stem cells.[8,19–21]

Which Laser Is the Best Laser-Assisted Delivery?

Haedersdal and colleagues[22] studied a variety of physical techniques that disturbed the stratum corneum to study which modality best enhanced protoporphyrin IX accumulation. Modalities studied included nonablative fractional laser, ablative fractional laser, microneedling, microdermabrasion,