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Authors
Labadie, Jessica G
Ibrahim, Sarah A
Worley, Brandon
et al.

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Evidence-Based Clinical Practice Guidelines for Laser-Assisted Drug Delivery

Jessica G. Labadie, MD; Sarah A. Ibrahim, MD; Brandon Worley, MD; Bianca Y. Kang, MD; Uros Rakita, MD, MSc; Sarah Rigali, BS; Kenneth A. Arndt, MD; Eric Bernstein, MD, MSE; Jeremy A. Brauer, MD; Sunandana Chandra, MD; Aashish Didwania, MD; Catherine DiGiorgio, MD; Mattias Donelan, MD; Jeffrey S. Dover, MD; Hassan Galadari, MD; Roy G. Geronemus, MD; Mitchel P. Goldman, MD; Merete Haedersdal, MD, PhD, DMSc; George Hruza, MD, MBA; Omar A. Ibrahimi, MD, PhD; Arielle Kauvar, MD; Kristen M. Kelly, MD; Andrew C. Krakowski, MD; Rachel Miest, MD; Jeffrey S. Orringer, MD; David M. Ozog, MD; E. Victor Ross, MD; Peter R. Shumaker, MD; Joseph F. Sobanko, MD; Kathleen Suozzi, MD; Mark B. Taylor, MD; Joyce M. C. Teng, MD, PhD; Nathan S. Uebelhoer, DO; Jill Waibel, MD; Molly Wanner, MD; Ina Ratchev, BSN, RN; Rachel E. Christensen, BS; Emily Poon, PhD; Corinne H. Miller, MLIS; Murad Alam, MD, MSCI, MBA

IMPORTANCE Laser-assisted drug delivery (LADD) is used for various medical and cosmetic applications. However, there is insufficient evidence-based guidance to assist clinicians performing LADD.

OBJECTIVE To develop recommendations for the safe and effective use of LADD.

EVIDENCE REVIEW A systematic literature review of Cochrane Central Register of Controlled Trials, Embase, and MEDLINE was conducted in December 2019 to identify publications reporting research on LADD. A multidisciplinary panel was convened to draft recommendations informed by the systematic review; they were refined through 2 rounds of Delphi survey, 2 consensus meetings, and iterative review by all panelists until unanimous consensus was achieved.

FINDINGS Of the 48 published studies of ablative fractional LADD that met inclusion criteria, 4 were cosmetic studies; 21, oncologic; and 23, medical (not cosmetic/oncologic), and 6 publications of nonablative fractional LADD were included at the request of the expert panel, producing a total of 54 studies. Thirty-four studies (63.0%) were deemed to have low risk of bias, 17 studies (31.5%) had moderate risk, and 3 (5.5%) had serious risk. The key findings that informed the guidelines developed by the expert panel were as follows: LADD is safe in adults and adolescents (≥12 years) with all Fitzpatrick skin types and in patients with immunosuppression; it is an effective treatment for actinic keratosis, cutaneous squamous cell carcinoma in situ, actinic cheilitis, hypertrophic scars, and keloids; it is useful for epidermal and dermal analgesia; drug delivery may be increased through the application of heat, pressure, or occlusion, or by using an aqueous drug solution; laser settings should be selected to ensure that channel diameter is greater than the delivered molecule; antibiotic prophylaxis is not recommended, except with impaired wound healing; antiviral prophylaxis is recommended when treating the face and genitalia; and antifungal prophylaxis is not recommended. The guideline's 15 recommendations address 5 areas of LADD use: (I) indications and contraindications; (II) parameters to report; (III) optimization of drug delivery; (IV) safety considerations; and (V) prophylaxis for bacterial, viral, and fungal infections.

CONCLUSIONS AND RELEVANCE This systematic review and Delphi consensus approach culminated in an evidence-based clinical practice guideline for safe and effective use of LADD in a variety of applications. Future research will further improve our understanding of this novel treatment technique.

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Murad Alam, MD, MSCI, MBA, Department of Dermatology, Northwestern University Feinberg School of Medicine, 676 N Saint Clair, Ste 1600, Chicago, IL 60611 (m-alam@northwestern.edu).

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The protective barrier provided by the stratum corneum limits transcutaneous drug bioavailability, which may be as low as 1% to 5%.[1] Recently, there has been interest in using laser- and energy-based devices to improve transcutaneous absorption. In particular, laser-assisted drug delivery (LADD) may increase drug efficacy without increasing systemic adverse events. Since LADD was first reported in 1987,[2] the technique has rapidly evolved. One development was the introduction of fractional photothermolysis, which creates microscopic, vertical channels of ablation surrounded by layers of coagulated tissue.[2-4] Both ablative fractional (AF) and nonablative fractional (NAF) devices have been used with LADD.[5-7] Laser-assisted drug delivery has been associated with various indications, ranging from epidermal analgesia to treatment of nonmelanoma skin cancer. Interest in the clinical applications of LADD among dermatologists has substantially grown during the past decade as clinicians and patients increasingly seek effective, directed, lower-risk interventions for indications that traditionally required higher doses of topical or systemic medication. Given the rapidly expanding collection of clinical research assessing the efficacy and safety of LADD, this technology is likely to be adopted as a common tool across dermatology.

To our knowledge, there are presently no evidence-based clinical practice guidelines for LADD. The objective of this clinical practice guideline was to delineate applications of LADD and offer recommendations for safe and effective use.

Key Points

Question Which best practices are associated with the safe and effective use of laser-assisted drug delivery (LADD)?

Findings This systematic review of 54 studies of LADD informed a multidisciplinary panel of experts and patient representatives who used a Delphi consensus process to develop and refine a guideline for its safe and effective use. The 15 recommendations address 5 areas: indications and contraindications, parameters to report, optimization of drug delivery, safety considerations, and antimicrobial prophylaxis.

Meaning This clinical practice guideline provides a current framework to clinicians for the safe and effective use of LADD in various medical and cosmetic settings.

In accordance with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, recommendations were categorized into 2 types: (1) strong recommendations (eg, based on randomized clinical trials with low risk of bias, consistency in results, and without publication bias), signified by the statement "we recommend"; and (2) conditional recommendations (eg, based on lower quality studies or observational studies, and in which variations in care may be more acceptable), signified by the statement "we suggest."

Methods

This study was approved by the Northwestern University Institutional Review Board (STU00097285). Informed consent was not required because the study used only previously published and publicly available data. Reporting was in accordance with the Appraisal of Guidelines for Research & Evaluation II (AGREE II) guidelines.

Guideline Questions

This clinical practice guideline was developed to address the following clinical questions:

I. What are the indications and contraindications for LADD?
II. What are the most important parameters to report for LADD?
III. How can drug delivery be enhanced with LADD?
IV. What are the important safety considerations for LADD?
V. Is prophylaxis (eg, for bacterial, viral, and fungal infection) required for LADD, and if so, in which circumstances?

Guideline Development Process

A multidisciplinary panel of expert stakeholders representing dermatology, pediatric dermatology, hematology and oncology, internal medicine, and plastic surgery was assembled based on publication history (including prior publication of guidelines related to laser- or energy-based devices), clinical expertise, peer nomination, and recognition as thought leaders in related areas of research.

The results of a systematic review (available in eMethods 1 in the Supplement) and panel deliberations were used to develop a long list of items related to LADD.[8-10] Then this list was critically evaluated and refined through 2 rounds of Delphi surveys and 2 virtual consensus meetings, with all panel members as Delphi participants (eTable 1 and eMethods 2 in the Supplement).[11,12]

Results

In total, 48 published studies of AF LADD met inclusion criteria (eFigure in the Supplement): 4 cosmetic studies,[13-16] 21 oncologic,[17-37] and 23 medical (not cosmetic/oncologic).[38-60] In addition, 6 publications of NAF LADD[61-66] were included at the request of the expert panel, for a total of 54 studies.

Studies varied in quality and were generally small, single-center, randomized clinical trials. For certain topics related to LADD, the evidence was of sufficient quality but limited quantity. In these cases, recommendations were based primarily on consensus of expert opinion and in accordance with the Institute of Medicine standards for developing trustworthy clinical practice guidelines.[67] Thirty-four studies (63.0%) were deemed to have low risk of bias, 17 studies (31.5%) had moderate risk, and 3 (5.5%) had serious risk (eTable 2 in the Supplement).

Delphi surveys were conducted in July to December 2020. The first Delphi survey was completed by 30 participants, and the second, by 29 (97% retention). Demographic characteristics of participants are shown in **Table 1**. Overall, 308 items were presented in the first round, during which 9 additional items were proposed by the Delphi participants. In the second round, 317 items or subparts were presented for rating, and 201 (63.4%) met provisional inclusion criteria. Of these 201 items, 107 were included solely to facilitate discussion, 17 to explore future directions in LADD research, and the remaining 77 as potential actionable items that could become additional recommendations. After an iterative review by a committee of the whole comprised of all Delphi participants and select research personnel, the 77 actionable items were combined into 15 final recommendations (similar items were grouped together). The final recommendations were reviewed by patient-members.

Table 1. Demographic Characteristics of the 30 Delphi Participants

Characteristic	Participants, No. (%)
Medical specialty	
Internal medicine	1 (3.3)
Dermatology	26 (86.7)
Pediatric dermatology	1 (3.3)
Plastic and reconstructive surgery	1 (3.3)
Oncology	1 (3.3)
Country represented	
Denmark	1 (3.3)
United Arab Emirates	1 (3.3)
US	28 (93.3)
Sex	
Female	9 (30.0)
Male	21 (70.0)

Disclaimer

These guidelines are provided to assist with clinical decision-making but are not a standard of care. Based on patient- and clinician-specific considerations, treating physicians may select courses of action other than those suggested. The panel and the authors assume no responsibility and make no warranty regarding the information provided.

Final Recommendations for Use of LADD

These 15 recommendations organized into 5 categories were found to be associated with the safe and effective use of LADD. **Table 2** provides a summarized list along with GRADE ratings.

I. Indications and Contraindications

Recommendation 1. We recommend the use of LADD in adults and adolescents with all Fitzpatrick skin types (level of evidence: moderate; recommendation: strong). | Laser-assisted drug delivery is considered to be safe for both adults (≥18 years) and adolescents (12 to <18 years); most studies referenced only transient laser-related adverse effects (eg, pain, erythema, crusting), and there were few reports of posttreatment infection.[15] Although LADD has also been used in children, often for analgesia or the treatment of scars, there is considerably less data for this population compared with adults.[38,47] If LADD is performed in children, it should be done so with caution because the safety margin is narrower given their reduced body surface area.

Recommendation 2. We suggest that LADD may be safely used in patients with immunosuppression disorders (level of evidence: low; recommendation: conditional). | There are few published studies of LADD in patients who are immunosuppressed, but there have been no reported serious adverse events in this population.[19,26,68] The expert panel determined that LADD is likely safe to use in patients who are immunosuppressed, but that additional research is needed in this population.

Recommendation 3. We recommend the use of LADD for the treatment of actinic keratoses, actinic cheilitis, and cutaneous squamous cell carcinoma in situ (level of evidence: moderate; recommendation: strong). | Although there are many indications for LADD as identified through the systematic review and as reported by members of the expert panel from their own clinical experience (**Table 3**), there was sufficient evidence to strongly recommend that LADD is safe and effective for the treatment of actinic keratoses,[17-37] actinic cheilitis,[33] and cutaneous squamous cell carcinoma in situ.[61,62] In general, it was found that LADD is most effective for treating these indications, with this typically performed with laser followed by photodynamic therapy (PDT). Additional research is needed to determine the efficacy and safety of LADD with PDT for deeper or more nodular lesions. Pretreatment with AFL before PDT is preferred over pretreatment with NAFL. Two AFL modalities were reported: erbium-doped yttrium aluminium garnet laser (Er:YAG) and carbon dioxide (CO_2) laser. There were no randomized clinical trials comparing these 2 modalities, and it was the opinion of the expert panel that either Er:YAG or CO_2 lasers may be appropriate. Regarding PDT, either methylaminolevulinate or aminolevulinic acid may be utilized.

Recommendation 4. We suggest the use of LADD for the treatment of hypertrophic scars and keloids (level of evidence: low; recommendation: conditional). | With CO_2 or Er:YAG lasers, AF LADD is likely a safe and effective treatment for hypertrophic or keloid scars caused by burns, traumatic wounds, and vaccinations.[46-51,65] Recommended topical agents include 5-fluorouracil and corticosteroids (eg, ointment, cream, or aqueous solution); verapamil hydrochloride may also be considered. Multiple treatments, often at 1-month intervals, are often required to attain the desired clinical result.[46,49] Patients tend to tolerate these treatments well, although reported adverse events include increased scar telangiectasia, postinflammatory hyperpigmentation, and transient treatment-related effects such as pain, burning sensation, and edema.[16,70]

Recommendation 5. We recommend the use of LADD for epidermal and dermal analgesia if there is sufficient time for application (level of evidence: moderate; recommendation: strong). | In general, a single treatment with AFL (Er:YAG or CO_2) followed by 5 to 15 minutes of topical anesthetic under occlusion has been associated with significant pain reduction following skin procedures, such as percutaneous procedures, in both pediatric and adult patients. The topical anesthetic agents recommended include 4% tetracaine in benzoyl alcohol and topical lidocaine without epinephrine. Higher density settings provide more effective anesthesia compared with lower density, regardless of the laser modality used, and are typically well-tolerated by patients. Laser-assisted analgesia may be particularly useful in patients undergoing multiple procedures, especially children or others less likely to tolerate pain. The laser surgeon should not exceed the recommended dosing for intralesional injection of the delivered drug.[38-45]

Recommendation 6. We recommend LADD be deferred in patients with known allergy to the drug being delivered, active local skin infection, or who have an underlying medical problem or enzyme abnormality if the drug is at risk of worsening the abnormality (level of evidence: moderate; recommendation: strong). | Laser-assisted drug delivery should not be used in patients with a known allergy to the drug, in patients with active infection at the treatment site, or in patients with an underlying medical problem that would be exacerbated by the drug (eg, dihydropyrimidine dehydrogenase deficiency for 5-fluorouracil). Also, laser surgery is relatively contrain-

Table 2. Summary of Recommendations for Laser-Assisted Drug Delivery (LADD)

Category and recommendation	GRADE rating	
	Evidence[a]	Strength[b]
Indications and contraindications		
We recommend the use of LADD in adults (≥18 y) and adolescents (≥12 to <18 y) with all Fitzpatrick skin types.	Moderate	Strong
We suggest that LADD may be safely used in immunosuppressed patients.	Low	Conditional
We recommend the use of LADD for the treatment of actinic keratoses, actinic cheilitis, and cutaneous squamous cell carcinoma in situ.	Moderate	Strong
We suggest the use of LADD for the treatment of hypertrophic scars and keloids.	Low	Conditional
We recommend the use of LADD for epidermal and dermal analgesia if there is sufficient time for application.	Moderate	Strong
We recommend LADD be deferred in patients with known allergy to the drug being delivered, active local skin infection, or who have an underlying medical problem or enzyme abnormality if the drug is at risk of worsening this abnormality.	Moderate	Strong
Parameters to report		
We recommend that the following parameters be reported when performing AF and NAF LADD: fluence/channel depth, density/surface area, spot size, incubation time (time between laser delivery and medicine application), number of passes, and total volume and type of formulation of medication applied.	Moderate	Strong
Optimization of drug delivery		
We suggest that drug delivery via LADD may be increased by using heat, pressure, occlusion, and/or low viscosity drug formulations.	Low	Conditional
We suggest that AF laser settings be selected to ensure that the expected channel diameter is greater than the diameter of the particle being delivered.	Low	Conditional
We suggest that cold, non-hollow bore microneedling (without heat or radiofrequency) or radiofrequency microneedling may be alternative modalities to laser for drug delivery.	Low	Conditional
Safety considerations		
We recommend that physicians using LADD appreciate that there is a certain unpredictability of response and tissue levels of drug owing to variable pharmacokinetics.	Moderate	Strong
We recommend that physicians using LADD be cautious that systemic adverse effects owing to inadvertent systemic delivery of medications are a possibility.	Moderate	Strong
We recommend LADD be performed with appropriate eye protection (appropriate for the laser platform), surgical masks, and gloves (level of evidence: moderate; recommendation: strong), and suggest a smoke evacuator be used, particularly with AF devices (level of evidence: low; recommendation: conditional).	Low	Conditional
We suggest LADD only be used with medication formulations approved by a national regulatory authority for parenteral injection.	Low	Conditional
Prophylaxis for bacterial, viral, and fungal infections		
We suggest the following prophylaxis regimens for AF and NAF LADD in otherwise healthy adult, pediatric, and patients who are immunosuppressed: (1) antibiotic prophylaxis is *not* recommended when treating areas other than where wound healing might be impaired (eg, genitalia, lower legs); (2) antiviral prophylaxis *is* recommended when LADD is used on the face or genitalia; and (3) antifungal prophylaxis is *not* recommended.	Low	Conditional

Abbreviations: AF, ablative fractional; GRADE, Grading of Recommendations Assessment, Development and Evaluation; NAF, nonablative fractional.

[a] Quality of evidence was assessed in accordance with GRADE methodology and rated from 1-4 as very low, low, moderate, or high.

[b] The strength of each recommendation was assessed in accordance with GRADE methodology and rated as 1 (strong) or 2 (conditional).

dicated in women who are pregnant or breastfeeding. We suggest that LADD also be relatively contraindicated in women who are pregnant or breastfeeding. That being said, while specific medications may not be appropriate in this context, the use of laser to facilitate delivery into the skin likely does not increase risk.

II. Parameters to Report

Recommendation 7. We recommend that the following parameters be reported when performing AF and NAF LADD: fluence/channel depth, density/surface area, spot size, incubation time (time between laser delivery and medicine application), number of passes, and total volume and type of formulation of medication applied (level of evidence: moderate; recommendation: strong). | Laser surgeons should adjust the standard AFL and NAFL parameters (eg, fluence/channel depth, density/surface area, spot size, incubation time, number of passes, and total volume and type of formulation of medication applied) accordingly based on the device being used, the condition being treated, and the depth of the skin lesion.[70-76] While higher fluences can create deeper laser channels, depth does not necessarily improve absorption. In addition, higher fluences deliver more heat to the skin, increasing the risk of local adverse events such as pain, burns, and scarring. There may also be an increased likelihood of these adverse events with increased density and number of passes. When performing LADD, the laser surgeon should consider that densities greater than 5% may not offer further improvement in cutaneous drug concentrations or treatment efficacy, and that the risks of treatment-related adverse events are higher.[70] Finally, applying the drug soon after laser treatment increases drug absorption and efficacy. Systematic reporting of LADD parameters may facilitate replication of successful treatments as well as more precise adjustment of treatment parameters if required.

III. Optimization of Drug Delivery

Recommendation 8. We suggest that drug delivery via LADD may be increased by using heat, pressure, occlusion, and/or low viscosity drug formulations (level of evidence: low; recommendation: conditional). | To increase drug absorption and efficacy, the treating physician may use techniques such as heat, pressure, or occlu-

Table 3. Laser-Assisted Drug Delivery (LADD) Indications Discussed by Guideline Panel Members

Indications	Examples of topical agents administered with LADD[a]	GRADE rating	
		Evidence[b]	Strength[b]
Actinic keratoses	Methylaminolevulinate; aminolevulinic acid; calcipotriol	Moderate	Strong
Squamous cell carcinoma in situ	Fluorouracil; methylaminolevulinate; aminolevulinic acid	Moderate	Strong
Actinic cheilitis	Methylaminolevulinate; aminolevulinic acid	Moderate	Strong
Analgesia	Lidocaine	Moderate	Strong
Hypertrophic scars	Verapamil hydrochloride; 5-fluorouracil; corticosteroids	Low	Conditional
Keloidal scars	Verapamil hydrochloride; 5-fluorouracil; corticosteroids	Low	Conditional
Basal cell carcinoma	Fluorouracil; methyl aminolevulinate	Panel did not offer recommendation	
Hypopigmented scars	Bimatoprost; latanoprost		
Onychomycosis	Tazarotene; tioconazole; amorolfine lacquer		
Melasma	Hydroquinone; tranexamic acid		
Acne vulgaris	Methyl aminolevulinate		
Macular amyloid	Vitamin C; corticosteroids		
Vitiligo	Betamethasone		
Condyloma	5-aminolevulinic acid		
Palmar hyperhidrosis	Onabotulinum toxin A		
Psoriasis	Calcipotriol		
Skin rejuvenation	Aminolevulinic acid		
Rhytids	Poly-L-lactic acid		
Androgenetic alopecia	Minoxidil; minoxidilalone		
Morphea or scleroderma	Poly-L-lactic acid		
Sclerodermoid graft-vs-host disease	Clobetasol		
Local inflammatory arthritis	Diclofenac		
Angiofibroma	Rapamycin		

Abbreviation: GRADE, Grading of Recommendations Assessment, Development and Evaluation.

[a] These are provided for illustrative purposes and are based on published reports.[14-66,68,69]

[b] Level of evidence and strength of recommendation were determined by the guideline panel for the specific indication, but not necessarily for a particular technique or topical agent.

sion after medication application.[77-82] Regarding the drug vehicle, low viscosity formulations, such as aqueous solutions, lotions, or gels, appear to be more effective at filling laser channels, accelerating medication delivery. However, because of the prolonged contact time, occlusion, and hydration afforded by these vehicles, high viscosity formulations, such as creams or ointments, may be preferred.[7] Ultimately, the techniques used to increase drug absorption should be selected based on the underlying disease being treated, treatment location, and patient considerations.

Recommendation 9. We suggest that AF laser settings be selected to ensure that the expected channel diameter is greater than the diameter of the particle being delivered (level of evidence: low; recommendation: conditional). | Ensuring that the expected channel diameter is greater than the diameter of the particle being delivered may improve drug penetration. Although the molecular weight of a drug is unlikely to limit its ability to penetrate through a channel created by laser, penetrance may be limited by the effective particle size, particularly if the drug is delivered by a polymer, microsphere, liposome, nanoparticle, or similar means. No specific recommendations were made regarding channel depth, which depends on fluence, and describes how deeply ablated laser channels extend into the skin. Theoretically, the greater the depth, the more extensively the drug being delivered may penetrate, although in practice greater penetration depth does not necessarily improve absorption. However, hydrophilic, and hydrophobic substances react differently to channel depth. For hydrophilic medications, deeper channels may allow for increased drug penetration. Ultimately, channel diameter and depth should complement the drug in question as well as the disease being treated.[69,82]

Recommendation 10. We suggest that cold, nonhollow bore microneedling (without heat/radiofrequency) or radiofrequency microneedling may be alternative modalities to laser for drug delivery (level of evidence: low; recommendation: conditional). | Nonlaser modalities, such as cold nonhollow bore microneedling or insulated or non-insulated radiofrequency microneedling, may also be used for drug delivery.[83] These approaches may be helpful for patients who decline laser, or in whom laser is contraindicated. Further research may clarify the safety and efficacy of these treatment modalities and how they enable drug penetration. Microneedles can be of various bores and lengths, with or without insulation or radiofrequency energy, and hence, may behave differently. Although a recent study using optical coherence tomography found that microneedling and radiofrequency microneedling did not create observable cutaneous channels,[84] other recent research suggests that in some cases microneedling may facilitate increased penetration and greater lateral extension of the drug as compared with AF laser.[83]

IV. Safety Considerations

Recommendation 11. We recommend that physicians using LADD appreciate that there is a certain unpredictability of response and tissue levels of drug owing to variable pharmacokinetics (level of evidence: moderate; recommendation: strong). | Overall, LADD is a safe and effective procedure. Adverse events, when they occur, are

most often transient and mild (eg, crusting, erythema, postinflammatory hyperpigmentation, and burning sensation). However, we caution laser surgeons that there is a degree of unpredictability of response and drug tissue levels owing to variable pharmacokinetics when drugs are delivered through the skin with laser or other energy-based devices.[70] Additionally, there may be a slightly increased risk of drug-related local adverse events compared with administration of the same medication without energy-based devices.

Recommendation 12. We recommend that physicians using LADD be cautious because systemic adverse effects owing to inadvertent systemic delivery of medications are a possibility (level of evidence: moderate; recommendation: strong). | Theoretically, as with any parenteral medication, systemic adverse events are a possibility in LADD. To minimize risk, small volumes should be used (commonly 1-2 mL). A detailed past medical history, including an updated medication list and allergies, should be obtained before treatment.

Recommendation 13. We recommend LADD be performed with appropriate eye protection (appropriate for the laser platform), surgical masks, and gloves (level of evidence: moderate; recommendation: strong), and suggest using a smoke evacuator, particularly with AF devices (level of evidence: low; recommendation: conditional). | When performing LADD, we recommend that the laser surgeon wear appropriate, device-specific protective equipment, ie, eye protection specific to the laser, a surgical mask, and surgical gloves. For AFL, we suggest that the surgeon consider the use of a smoke evacuator. Additionally, when treating viral lesions, the surgeon may consider wearing an N95 mask to address the risk of acquired laryngeal papillomatosis.

Recommendation 14. We suggest LADD only be used with medication formulations approved by a national regulatory authority for parenteral injection (level of evidence: low; recommendation: conditional). | Only medications approved by the appropriate regulatory authority (eg, US Food and Drug Administration) for injection into the skin, subcutaneous tissue, or intravascular space should be used for LADD. Although necessary, such approval may be insufficient to ensure safety (eg, phenytoin approved for IV use may cause tissue necrosis when it penetrates deep into the skin). Medications indicated only for topical use, such as many cosmeceuticals, moisturizers, topical corticosteroids, topical antibiotics, and antiseptics, and many other over-the-counter and prescription medications should not be delivered with laser as they may induce sensitivity reactions, granulomas, infections, and systemic adverse reactions.

V. Prophylaxis for Bacterial, Viral, and Fungal Infections

Recommendation 15. We suggest use of the following prophylaxis regimens for AF and NAF LADD in otherwise healthy adults, pediatric patients, and patients who are immunosuppressed: antibiotic prophylaxis is *not* recommended when treating areas other than where wound healing might be impaired (eg, genitalia, lower legs); antiviral prophylaxis is recommended when LADD is used on the face or genitalia; and antifungal prophylaxis is *not* recommended (level of evidence: low; recommendation: conditional). | Antibacterial prophylaxis should be reserved for sites with a high possibility of poor wound healing, such as genitalia or lower legs. Antiviral prophylaxis should be offered when treating the face or genitalia, regardless of herpes simplex virus history. Based on limited evidence, antifungal prophylaxis is typically not needed. Data were insufficient to recommend alterations of prophylaxis regimen based on patient age or immunosuppression status.

Limitations

Laser-assisted drug delivery is a novel technology that is rapidly evolving. There may yet be substantial changes over time in how LADD is routinely performed and, consequently, in its safety and effectiveness. Therefore, the current guidelines may need to be revised in the future. Although LADD is a relatively new technology, the current guidelines are important to ensure that practitioners and patients have an understanding of how it should be performed and what are its benefits and limitations. These guidelines may also assist in identifying areas of uncertainty to address with future research.

Conclusions

The findings of this systematic review and Delphi consensus study suggest that LADD can be a safe and effective treatment for various indications. As the standard of care continues to shift toward minimally invasive and individualized methods of drug delivery, LADD will play an important role. Future research will bolster understanding of these promising procedures and how they may be further optimized for clinical effectiveness while maintaining a high level of therapeutic safety.

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Author Affiliations: Department of Dermatology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (Labadie, Ibrahim, Worley, Kang, Christensen, Poon, Alam); Chicago Medical School, Rosalind Franklin University of Medicine and Science, North Chicago, Illinois (Rakita, Rigali); SkinCare Physicians, Chestnut Hill, Massachusetts (Arndt, Dover); Department of Dermatology, Warren Alpert Medical School of Brown University, Providence, Rhode Island (Arndt, Dover); Main Line Center for Laser Surgery, Ardmore, Pennsylvania (Bernstein); Ronald O. Perelman Department of Dermatology, New York University School of Medicine, New York (Brauer); Division of Hematology and Oncology, Department of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (Chandra); Department of Internal Medicine, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (Didwania); Boston Center for Facial Rejuvenation, Boston, Massachusetts (DiGiorgio); Shriners Hospital for Children–Boston, Harvard Medical School, Boston, Massachusetts (Donelan); Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts (Donelan); Department of Dermatology, Yale University School of Medicine, New Haven, Connecticut (Dover, Suozzi); College of Medicine and Health Sciences, United Arab Emirates University, Al Ain, United Arab Emirates (Galadari); Laser & Skin Surgery Center of New York, New York (Geronemus); Cosmetic Laser Dermatology, West Dermatology Company, San Diego, California (Goldman); Department of Dermatology, Bispebjerg University Hospital, Copenhagen, Denmark (Haedersdal); Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston (Haedersdal); Departments of Dermatology and Otolaryngology, St Louis University–Laser and

Dermatologic Surgery Center, St Louis, Missouri (Hruza); Connecticut Skin Institute, Stamford, Connecticut (Ibrahimi); New York Laser & Skin Care, New York (Kauvar); New York University Grossman School of Medicine, New York, New York (Kauvar); Department of Dermatology, University of California Irvine School of Medicine, Irvine (Kelly); Department of Dermatology, St. Luke's University Health Network, Easton, Pennsylvania (Krakowski); Department of Dermatology, Mayo Clinic, Rochester, Minnesota (Miest); Department of Dermatology, Michigan Medicine, University of Michigan, Ann Arbor (Orringer); Department of Dermatology, Henry Ford Hospital, Detroit, Michigan (Ozog); Scripps Clinic, San Diego, California (Ross); Veterans Affairs San Diego Healthcare System and University of California, San Diego, California (Shumaker); Department of Dermatology, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania (Sobanko); Gateway Aesthetic Institute & Laser Center, Salt Lake City, Utah (Taylor); Department of Dermatology, School of Medicine, Stanford University, Stanford, California (Teng); Coronado Dermatology, Lanoi Cosmetic Dermatology, San Diego, California (Uebelhoer); Miami Dermatology and Laser Institute, Miami, Florida (Waibel); Department of Dermatology, Massachusetts General Hospital, Harvard Medical School, Boston (Wanner); Section of Cutaneous Surgery, Northwestern Medical Group, Chicago, Illinois (Ratchev); Galter Health Sciences Library & Learning Center, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (Miller); Department of Otolaryngology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (Alam); Department of Medical Social Sciences, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (Alam); Department of Surgery, Feinberg School of Medicine, Northwestern University, Chicago, Illinois (Alam).

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Concept and design: Labadie, Ibrahim, Worley, Galadari, Geronemus, Ibrahimi, Kauvar, Ozog, Suozzi, Taylor, Uebelhoer, Waibel, Poon, Alam.
Acquisition, analysis, or interpretation of data: Labadie, Ibrahim, Worley, Kang, Rakita, Rigali, Arndt, Bernstein, Brauer, Chandra, Didwania, DiGiorgio, Donelan, Dover, Goldman, Haedersdal, Hruza, Kauvar, Kelly, Krakowski, Miest, Orringer, Ozog, Ross, Shumaker, Sobanko, Suozzi, Teng, Uebelhoer, Waibel, Wanner, Ratchev, Christensen, Miller, Alam.
Drafting of the manuscript: Labadie, Ibrahim, Kang, Rigali, Arndt, Bernstein, Kauvar, Krakowski, Suozzi, Waibel, Miller, Alam.
Critical revision of the manuscript for important intellectual content: Labadie, Ibrahim, Worley, Kang, Rakita, Bernstein, Brauer, Chandra, Didwania, DiGiorgio, Donelan, Dover, Galadari, Geronemus, Goldman, Haedersdal, Hruza, Ibrahimi, Kauvar, Kelly, Krakowski, Miest, Orringer, Ozog, Ross, Shumaker, Sobanko, Suozzi, Taylor, Teng, Uebelhoer, Waibel, Wanner, Ratchev, Christensen, Poon, Alam.
Statistical analysis: Ibrahim, Worley, Rigali, Alam.
Administrative, technical, or material support: Labadie, Ibrahim, Kang, Rigali, Galadari, Geronemus, Goldman, Krakowski, Ross, Suozzi, Uebelhoer, Waibel, Christensen, Poon, Miller, Alam.
Supervision: Labadie, Chandra, Galadari, Ibrahimi, Sobanko, Suozzi, Uebelhoer, Alam.
Other–provided data: DiGiorgio.
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