

Interpreting Beam Geometry and Repeated Exposure in Dermatologic Laser Therapy

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Abstract

Studies of spot size, beam profile, and repeated laser exposure often appear to support conflicting treatment choices. Some compare equal pulse energy, others match surface radiant exposure, and others adjust several settings to reach a clinical endpoint. This critical narrative review examines how those choices determine what can be concluded about efficacy and safety. A documented PubMed search through October 1, 2026, was supplemented by citation checking and a previously assembled bibliography. Seventeen primary reports underwent detailed extraction of exposure settings, controlled variables, measurement methods, experimental units, and outcomes. The review distinguishes evidence about an optical mechanism from evidence about a complete treatment strategy. A pigment treatment trial found similar observed clearance with fewer unwanted reactions when a larger spot, lower fluence, and absence of whitening were combined, but did not isolate the contribution of spot size. Studies of repeated vascular exposure reported both improved blanching and no additional benefit under different pulse sequences and cooling schedules. Small descriptive comparisons did not establish equivalence, and histologic depth could not establish clinical improvement or safety. In one resurfacing report, a cumulative depth was the sum of means from separate treatment groups rather than the measured depth after repeated passes. These examples support a practical approach to appraisal: define the contrast, identify how exposure was established, and interpret the outcome at the correct experimental level. The contribution is a critical explanation of what published comparisons support, rather than a new dose formula. Similar target response should not be taken to imply similar collateral injury or justify transfer of settings between devices.

Categories: Dermatology

Keywords: dermatology, lasers, laser therapy, radiation dosage, reproducibility of results, skin, treatment outcome

Introduction And Background

Selective photothermolysis linked wavelength, pulse duration, and exposure to selective tissue injury [1]. Yet the same displayed value in J/cm² can represent different illuminated areas, spatial peaks, pulse sequences, and cooling conditions. It also differs from the optical field within scattering tissue [2]. Clinically, these differences matter when a change intended to improve target clearance also changes the exposure of surrounding skin. A larger spot or an additional pass may alter both the treatment response and unwanted pigmentary or textural effects. Interpreting a comparison therefore requires identifying the intervention tested and the outcome measured.

The need to report more than fluence is established. Jenkins and Carroll specified dose and beam information needed to reproduce photomedicine studies. Shurab extended this guidance and explicitly distinguished manufacturer specifications from measurements and independently validated parameters. International Organization for Standardization (ISO) standards define methods for measuring spatial distributions and beam propagation [3-6]. A further parameter checklist, by itself, would add little to this work.

Park et al. linked engineering settings to clinical endpoints across dermatologic indications [7]. The author's related conceptual article, "Beyond millijoules," described multidimensional tissue exposure in fractional ablative carbon dioxide (CO₂) therapy [8]. The present review addresses a narrower question across vascular, pigment, and resurfacing studies: when does a comparison support attribution to a particular delivery variable, and when does it support only the combined treatment strategy? Table 1 distinguishes this purpose from existing guidance.

How to cite this article

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Prior work	Established contribution	Focus of the present review
Jenkins and Carroll [3]	Beam and dose reporting in photomedicine; measurement checks.	Use reported settings to assess the contrast in selected dermatologic studies.
Shurrab [4]	Reporting of laser parameters and the source and verification of values.	Examine attribution, independent observations, and outcome meaning in primary comparisons.
ISO standards [5,6]	Measurement of spatial distributions and beam propagation.	Distinguish optical measurements from modeled fields and tissue responses.
Park et al. [7]	Selection of parameters in relation to indication, skin type, and endpoints.	Distinguish effects of individual components from effects of a complete strategy.
Bigge [8]	A conceptual model of fractional ablative tissue exposure for planning and reporting.	Appraise comparative evidence across vascular, pigment, and resurfacing treatments.

TABLE 1: Relationship to existing guidance and reviews.

Scope and emphasis are compared here; no claim of bibliographic priority is made. The reporting aid adapts established recommendations.

ISO: International Organization for Standardization

Equal energy, equal radiant exposure, and a matched tissue response answer different questions. Reading the original comparisons on those terms helps explain apparent disagreements. The reporting aid developed here adapts existing recommendations to this task; it is not a validated clinical dosing rule.

Review

Literature identification and selection

This critical narrative review addresses a defined comparison question: what can be inferred when a study changes beam profile, spot geometry, focus, or the spatial and temporal pattern of repeated laser delivery? A new PubMed search, covering MEDLINE and other PubMed records, was executed on 1 October 2026. It combined MeSH and title/abstract terms for lasers and skin with terms for beam profile, spot size, beam diameter, focus, working distance, overlap, stacking, repeated pulses, multiple passes, and scanning. No language filter or substantive lower date limit was applied; the publication date cutoff was 1 October 2026. The query, its executed translation, retrieval time, all returned records, and screening decisions were retained in the search record.

The search retrieved 1,083 unique records. Titles were screened, with available abstracts examined unless the title established that the record was outside scope. A previously assembled bibliography of 42 references was retained as a separate source set, not counted as newly discovered studies. Backward and forward citation checks used six central studies spanning beam characterization, focused delivery, vascular overlap and stacking, and pigment treatment. Publisher and Crossref records were used to verify bibliographic identity and obtain primary reports. Appendix 1 gives the search strategy, sources, and selection record. No counts were reconstructed for earlier undocumented searches.

Primary candidates were comparative clinical studies, human or animal tissue experiments, phantoms representing skin, beam measurements, and optical or thermal models addressing the specified delivery variables. Bundled protocol comparisons were eligible but were not treated as isolated geometry tests. Diagnostic imaging without treatment, industrial processing, dental and ophthalmic applications, and studies without a relevant exposure comparison were outside the primary synthesis. Studies changing only energy or pulse duration at unchanged geometry and without a comparison of repeated delivery could inform background mechanisms but did not meet the focused primary criterion. Reviews and reporting guidance were classified separately; photobiomodulation guidance informed metrology rather than effects of treatments intended to injure tissue.

The screening classified 207 records as potentially relevant primary studies, 151 as background material, and 14 as unresolved; 711 were excluded. Detailed extraction was purposive. Sixteen reports from the retrieved primary candidates and two previously known reports outside the current retrieval were selected for closer assessment. All 18 targeted main reports were assessed in full. One report was not selected for the detailed matrix because inconsistent exposure descriptions prevented a sufficiently clear reconstruction of the relevant contrast [9]. The remaining 17 reports form the matrix in Appendix 2. Figure 1 adapts the PRISMA 2020 flow structure to this selection process [10]. It describes the detailed evidence panel, not exhaustive inclusion in a systematic review.

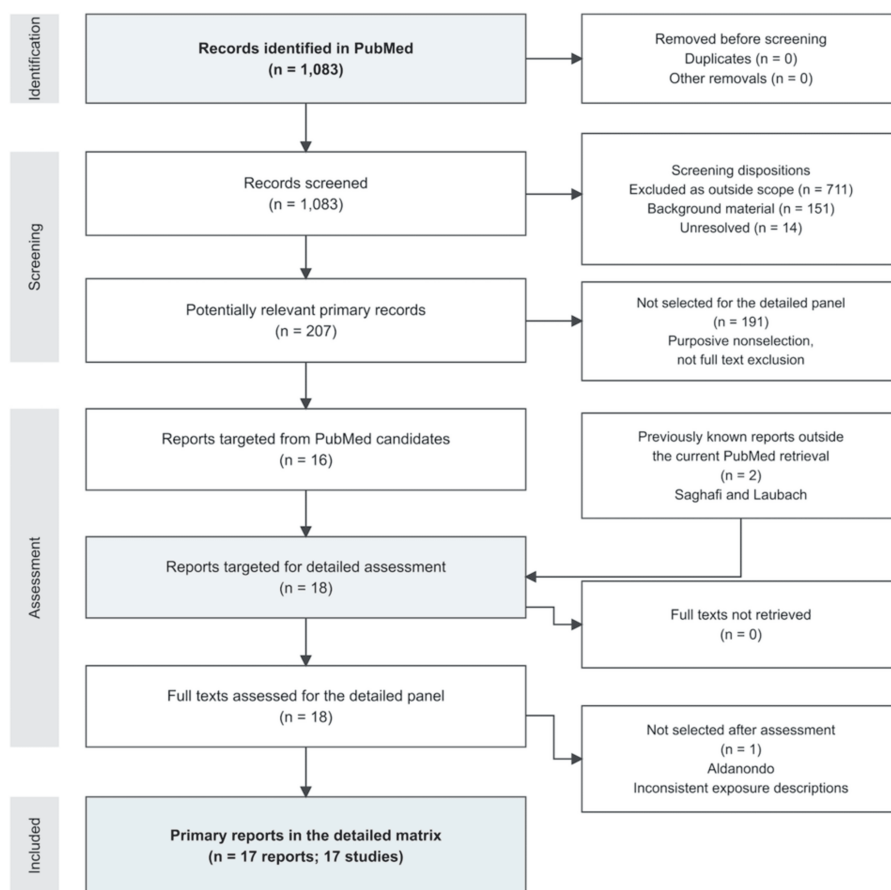


FIGURE 1: Identification and purposive selection of the detailed evidence panel

Adapted from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 flow structure [10] under the CC BY 4.0 license. Boxes report the actual screening and selection record for this narrative review. Previously held full texts are included in the assessment count. Background sources and other full texts used outside the panel are not represented as panel inclusions. This adaptation does *not* constitute a claim of systematic review or full PRISMA compliance. The panel is not an exhaustive set of eligible studies. The 42 seed references and 218 citation links overlap with PubMed records and are not added as separate unique studies. Selection does not imply independent human duplicate screening.

Fourteen records remained unresolved after screening: four had no available abstract, and 10 did not provide enough information to establish the relevant comparison or study design. They were not selected for full-text assessment; their eligibility remains open. They were not counted as full-text exclusions. The complete screening log is available from the corresponding author on reasonable request, as stated in the Data Availability Statement in Appendix 1.

Evidence appraisal

The search protocol recorded broad priorities before the October search: direct relevance to the comparison question, controlled clinical comparisons, measured beam or tissue effects, and coverage of distinct mechanisms and indications. Selection sought positive, null, and adverse findings. These priorities guided judgment; there was no predefined target of 17 studies, numerical ranking, or quota for a technology or indication. The first table in Appendix 2 explains the role of each selected report. The panel spans vascular and pigment treatment, hair removal, and resurfacing, using optical measurements, models, tissue experiments, and clinical comparisons. This breadth supports the comparison questions addressed here but does not establish representative coverage of all eligible evidence.

Laubach's experiment on starting skin temperature was retained as a contextual study of tissue conditions at unchanged laser settings, rather than as a direct test of geometry or repeated delivery. Other reports and reviews supplied context without entering the 17-study primary panel.

Extraction covered wavelength, pulse regime, energy or exposure, spot definition, beam characterization,

cooling, the independent experimental unit, and the outcome being compared. Numerical findings were checked against the main reports and their tables. An unavailable supplement was not treated as assessed. Bibliographic identifiers were checked against PubMed, publisher records, and Crossref; unresolved conflicts are documented in Appendix 1. No pooled effect estimate or formal risk-of-bias score was calculated.

Methodological strength was appraised qualitatively by considering allocation and masking, control and measurement of the exposure contrast, independent biological replication, pairing and repeated observations, missing data, and the relevance and timing of outcomes. These domains inform the study-specific interpretation and the comparative appraisal below; they are not a validated scoring instrument. A controlled tissue experiment can support a mechanism while providing little evidence about durable clinical benefit. A randomized clinical comparison can support a complete treatment strategy without separating the effects of its components.

Meaning of the displayed fluence

Surface Radiant Exposure and Tissue Fluence

The fluence displayed by a laser system commonly represents pulse energy (E_p) divided by a nominal beam area (A_{nom}):

$$H_{\text{nom}} = \frac{E_p}{A_{\text{nom}}}$$

This nominal value represents an area-averaged radiant exposure only when the pulse energy and beam area refer to the same defined aperture or integration region. Its interpretation therefore depends on how the beam area is defined. A Gaussian beam has no sharp boundary, and beam diameters based on full width at half maximum, the $1/e^2$ intensity level, second-moment measurements, or a manufacturer-specified aperture are not interchangeable. Substituting one diameter convention for another changes the area used in the calculation and thus the meaning of the reported value. Similarly, a threshold mark on burn paper does not, by itself, constitute a standardized beam-width measurement [5,6].

At a surface position $\mathbf{r}_s$, radiant exposure (H_s) is the local irradiance (E_e) integrated over the exposure duration:

$$H_s(\mathbf{r}_s) = \int E_e(\mathbf{r}_s, t) dt$$

Within tissue, fluence rate (Φ) is obtained by integrating radiance over all propagation directions. Integrating this fluence rate over the exposure duration gives tissue fluence (Φ). Although surface radiant exposure and tissue fluence are both expressed in J/cm^2 , they describe different physical quantities. Surface radiant exposure quantifies incident energy per unit surface area, whereas tissue fluence accounts for radiation propagating in all directions at a location within tissue. Their relationship depends on scattering, reflection, absorption, and source geometry [2,11]. Table 2 and Figure 2 summarize these distinctions.

Quantity	Unit	Meaning	Main limitation
Nominal radiant exposure, H_{nom}	J/cm ²	Pulse energy divided by a stated nominal area.	Not a measured spatial map.
Irradiance, E_e	W/cm ²	Instantaneous incident power per surface area.	Requires position and time.
Surface radiant exposure, H_s	J/cm ²	Local time integral of incident irradiance.	Does not specify tissue transport.
Tissue fluence rate, Φ	W/cm ²	Local radiance integrated over directions.	Depends on transport and boundary conditions.
Tissue fluence, Φ	J/cm ²	Time integral of tissue fluence rate.	Not identical to incident surface exposure.
Absorbed energy density, q_{abs}	J/cm ³	Local energy absorbed per tissue volume.	Does not alone specify the temperature history or injury mechanism.
Lesion geometry / clinical outcome	Specific to the endpoint	Ablation, coagulation, vessel clearance, pigment change, or other measured response.	Different endpoints cannot share an assumed universal threshold.

TABLE 2: Quantities that should not be treated as interchangeable.

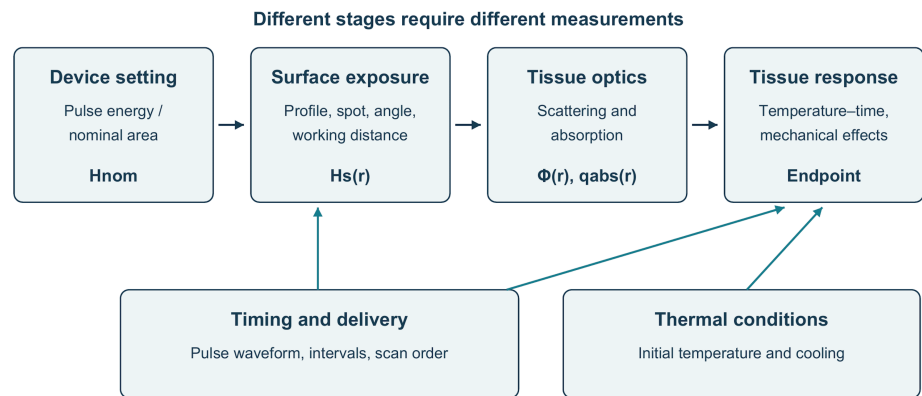


FIGURE 2: From a device setting to a tissue endpoint.

The optical chain and the timing/thermal inputs describe different parts of the problem. At unchanged optical delivery, cooling alters thermal conditions rather than incident exposure. Arrows indicate dependencies, not a validated predictive model. H_{nom} : nominal radiant exposure; H_s : surface radiant exposure; Φ : tissue fluence; q_{abs} : absorbed energy density.

For approximately monochromatic radiation, linear absorption, and optical properties that remain constant during exposure, the local absorbed energy density is:

$$q_{\text{abs}}(\mathbf{r}) = \mu_a(\mathbf{r}) \Phi(\mathbf{r})$$

Here, μ_a is the local absorption coefficient in cm⁻¹, and q_{abs} is the absorbed energy density in J/cm³. When the absorption coefficient varies during exposure or multiple wavelengths contribute, absorbed energy density is calculated by integrating the product of the wavelength- and time-dependent absorption coefficient and the spectral fluence rate ($\Phi\lambda$) over wavelength and time:

$$q_{\text{abs}}(\mathbf{r}) = \int \int \mu_a(\mathbf{r}, \lambda, t) \varphi_{\lambda}(\mathbf{r}, t) d\lambda dt$$

The resulting temperature change and tissue injury also depend on heat capacity, heat conduction, cooling, and, where relevant, perfusion, phase transitions, mechanical stress, or plasma formation. Dividing absorbed energy density by volumetric heat capacity provides an estimate of temperature rise only under approximately adiabatic conditions and in the absence of phase changes. Models that assume constant optical properties therefore require reassessment when applied to ablation or optical breakdown.

Sensitivity to the Diameter Convention

The area term makes nominal exposure sensitive to how a spot is defined. For equal pulse energies contained within circular regions defined by the same diameter convention, the ratio of their mean radiant exposures is:

$$\frac{H_2}{H_1} = \frac{d_1^2}{d_2^2}$$

Increasing the diameter from d_1 to $1.10d_1$ increases area by 21% and reduces the corresponding mean exposure to 0.8264 of its original value, a 17.36% decrease. This is a deterministic sensitivity calculation, not a measured calibration error or an uncertainty interval. It assumes that energy and area refer to matching integration regions; a change from a Gaussian $1/e^2$ diameter to a diameter measured at full width at half maximum violates that assumption. A measurement uncertainty estimate would additionally require the uncertainties and covariance of energy and diameter. The calculation says nothing about local peaks, tissue fluence, or clinical dose adjustment.

Thresholds Depend on the Endpoint

“Threshold” needs an endpoint. Vessel coagulation depends on the temperature history and vessel properties. Pigment treatment may involve melanosome disruption, pressure transients, and cavitation; visible whitening is not a direct measurement of clearance. Ablative depth and residual coagulation are separate outcomes. A threshold for one of these responses cannot be used as a universal threshold for skin injury [1,12,13].

Shimojo et al. combined measurements of isolated melanosomes with optical modeling at 755 nm. The laboratory disruption thresholds were 2.19 and 2.49 J/cm² for pulses of 550 and 750 ps, respectively [13]. These are experimental suspension thresholds, not recommended patient fluences. The study also illustrates why a visible epidermal reaction need not establish adequate treatment of a deeper pigment target. Later measurements at other wavelengths and phantom work extend the mechanistic basis, but retain assumptions about the model and specimen [14–16]. These measurements help explain why a visible surface endpoint may not track exposure at depth. Clinical threshold selection still requires evidence for the relevant tissue, device, and treatment outcome.

Beam profile and spot size

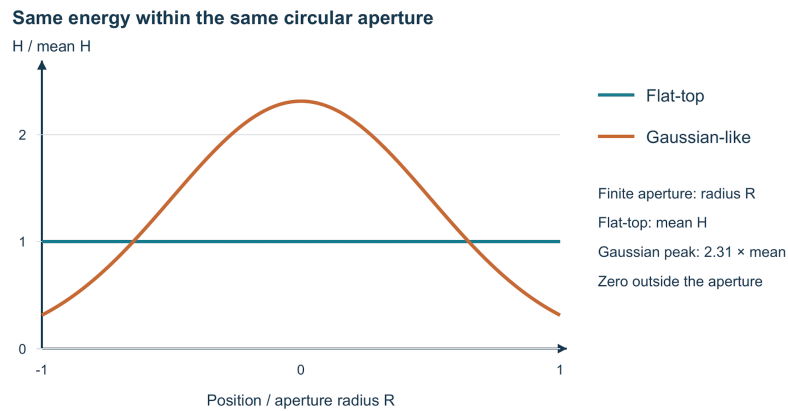
Measuring the Delivered Profile

A beam close to the fundamental transverse mode can yield an approximately Gaussian profile; multimode output and delivery optics may substantially alter it before it reaches skin. A flat-top label does not establish perfect uniformity or absence of local peaks. Wavelength and laser medium alone do not determine the delivered profile, and spatial profile must be distinguished from temporal pulse waveform.

Jackson et al. measured four pulsed dye lasers at 585 nm with nominal handpiece diameters of 5 mm [17]. Areas measured on burn paper differed from nominal by approximately +35%, +30%, –8%, and –4%; camera measurements showed approximately Gaussian and more flat-top distributions. Nominally similar equipment thus delivered different footprints and profiles. Because area, optics, and equipment also differed, the study did not isolate a clinical effect of profile alone.

Dinehart et al. sampled the output of one pulsed dye laser (PDL) at 585 nm through a nominal 5 mm applicator at 5.0 and 7.5 J/cm² [18]. Photodiode scans across the diameter showed a relatively flat central region and declining edges. The measurements supported the rationale for overlapping peripheral parts of adjacent spots, but did not establish a universal PDL profile or an optimal clinical overlap. Appendix 2 retains the measurement procedure and the source’s differing width conventions.

Figure 3 illustrates a simpler, explicitly defined comparison. An ideal flat-top beam and an approximately Gaussian beam truncated at the aperture deliver the same energy within the same circular aperture. The approximately Gaussian beam has a higher central exposure and lower peripheral exposure. Depending on the chosen threshold, either profile can expose a larger useful area. This construction explains why uniformity may help achieve consistent coverage, while a central peak may favor a localized threshold response. It does not establish that one profile is clinically safer or more effective.



Analytical illustration only; no measured beam or clinical threshold is shown.

FIGURE 3: An explicitly normalized profile comparison

A flat top beam and an idealized, radially symmetric Gaussian profile truncated at its $1/e^2$ radius R contain equal energy inside the same circular aperture. The truncated Gaussian profile is renormalized over that aperture, giving a central value of approximately 2.31 times the common area mean. Both are zero outside the aperture. The plotted curves are diameter cross sections; energy is normalized over the circular aperture. This analytical illustration is not a measured device profile or evidence of clinical superiority.

Saghafi et al. combined Monte Carlo transport with beam shaping using a copper vapor laser [19]. Their comparison of 5 and 10 mm spots at equal power gives the smaller spot a higher average irradiance and therefore answers a different question from a comparison at equal radiant exposure. The briefly described patient series cannot establish clinical superiority. A greater response depth defined by a threshold also differs from a change in intrinsic optical penetration length. Phantom coagulation studies provide experimental tests under specified phantom and exposure conditions [20].

For practice, a profile label or nominal diameter is therefore insufficient to assume that two devices deliver comparable exposure. The strongest evidence in this section concerns measured light distributions; the clinical consequences depend on the full treatment protocol.

Defining the Spot Size Comparison

At fixed pulse energy, increasing a circular spot's area decreases its nominal radiant exposure. At fixed radiant exposure, increasing area requires more pulse energy. The latter energy change is a necessary consequence of the defined contrast, not automatically a confounder. A useful comparison distinguishes changes that define the intervention and their mathematical consequences from additional treatments or uncontrolled differences. In scattering tissue, a wider incident field may reduce lateral photon escape relative to the illuminated region and increase central energy deposition; the magnitude depends on wavelength, optical properties, depth, and beam size [2,21,22].

Keijzer et al. modeled a vessel of 100 μm diameter beneath an epidermal layer at 577 nm [21]. Increasing beam width from 0.2 to 2 mm while reducing incident irradiance from 1.0 to 0.7 W/cm^2 kept mean epidermal deposition approximately unchanged and increased mean vessel deposition from about 22 to 65 W/cm^3 . This was a transport calculation using a simplified, infinitely extended rectangular cross section, not a randomized clinical study or a calculation of a complete temperature history. Its enduring contribution is the distinction between incident exposure and energy reaching a target.

Comparisons of tattoo treatment and hair removal illustrate how available spot size, achievable exposure, cooling, and target conditions jointly define a protocol [23-26]. Recent models and phantoms help interpret such contrasts when their optical inputs and assumptions are explicit [15,16,27]. Clinical safety remains specific to the tested regimen and indication.

Jo et al. provide a controlled clinical spatial comparison [26]. Ten women received axillary treatment with 10 $\times$ 10 mm or 10 $\times$ 30 mm handpieces, randomly allocated by side on the same 805 nm diode platform. Nominal fluence, pulse duration, cooling, session schedule, and intended overlap were matched. Three months after the third session, mean hair clearance was 38.7% with the smaller handpiece and 50.1% with the larger ($p = 0.028$); pain at the first session was also higher with the larger handpiece (3.1 versus 4.3, $p = 0.009$). One participant developed bilateral hyperpigmentation. The comparison supports a benefit for the larger handpiece under those conditions. Handpiece design and aspect ratio changed together, however, and spatial profiles were not independently measured.

Nehal et al. treated paired halves of 12 lesions in 11 patients with nominal 5.0 and 6.5 mm spots at 694 nm and 28 ns [28]. Nine lesions were tattoos and three were benign pigmented lesions. Fluences were described as similar within 6–10 J/cm², without exact paired values. Four to eight weeks after one treatment, photographic grades were identical in five lesions, favored the larger spot in five, and favored the smaller spot in two. Three lesions had adverse changes affecting both halves equally. This small, mixed series offered a descriptive comparison; no formal statistical or equivalence analysis was reported.

The Wang Trial as a Comparison of Strategies

Wang et al. randomized facial sides in 30 Asian patients with acquired bilateral nevus of Ota-like macules (ABNOM); 28 completed three treatments, six months apart, with final efficacy assessment 12 months after the last session [29]. Both sides received treatment with an alexandrite laser at 755 nm through the same zoom handpiece at 2.5 Hz and a single pass. The Discussion specifies pulses of 750 ps. The regimens were 4.5 to 5.0 mm at 1.02 to 1.26 J/cm² with an endpoint without whitening versus 2.5 to 3.0 mm at 2.83 to 4.07 J/cm² with immediate whitening. Spot size, exposure, and intended immediate endpoint defined the two strategies; a measured spatial profile was not reported.

Observed clearance was similar; equivalence or noninferiority was not formally tested. Postinflammatory hyperpigmentation occurred in four out of 84 observations of treated facial sides across sessions (4.8%) with the strategy using the larger spot versus 19 out of 84 (22.6%); scabbing occurred in eight out of 84 (9.5%) versus 52 out of 84 (61.9%). The reported p values were 0.0008 and <0.001. These are observations across treatment sessions from 28 patients, not risks per patient. The authors specified McNemar testing for categorical comparisons, but handling of dependence across repeated sessions is insufficiently described. No new inferential statistics are calculated here.

Randomized side allocation supports the comparison of the complete Wang regimens. Simulations and electron microscopy offer a mechanistic explanation without separating the clinical contributions of spot size, fluence, and endpoint [29]. Reported hyperpigmentation resolved over six to 12 months, whereas scabs resolved within one to two weeks. Similar observed clearance therefore did not imply the same burden of adverse effects; pigmentary changes lasted substantially longer than scabbing. This evidence concerns ABNOM treated with the specified picosecond regimens and cannot be transferred directly to vascular treatment.

Working distance and focus

Sensitivity to working distance depends on the optics. Small distance changes may scarcely affect a collimated macroscopic beam but substantially alter a focused microbeam. Distance holders, contact interfaces, and focus correction constrain geometry; curved or deformable surfaces can still change local distance and incidence angle.

Kositratna et al. tested one fractional CO₂ system on excised abdominal skin from two donors, at 50 mJ per microscopic treatment zone (MTZ), a nominal spot diameter of 120 µm, and deviations up to ±3 mm [30]. Optical propagation was characterized with scanning knife-edge measurements and modeling. Mean histologic depth and diameter were 1700 and 248 µm at the focal plane and 680 and 359 µm at +3 mm. These are lesion dimensions, not optical spot widths. The experiment establishes a distance effect under the tested focusing conditions; its numerical results do not provide a correction factor for other handpieces.

Improved distance holders have been evaluated for fractional treatment, and focused delivery can intentionally control the depth and pattern of skin injury [31,32]. A 2025 preclinical study combined pulses at 1030 nm lasting 400 fs with surface reconstruction and scanning with focus correction in porcine tissue and a rat model [33]. It supports the importance of geometry in precision delivery, but does not establish routine clinical benefit for dermatologic resurfacing. Figure 4 shows the geometric issue without implying that optical beam contours are histologic lesion boundaries.

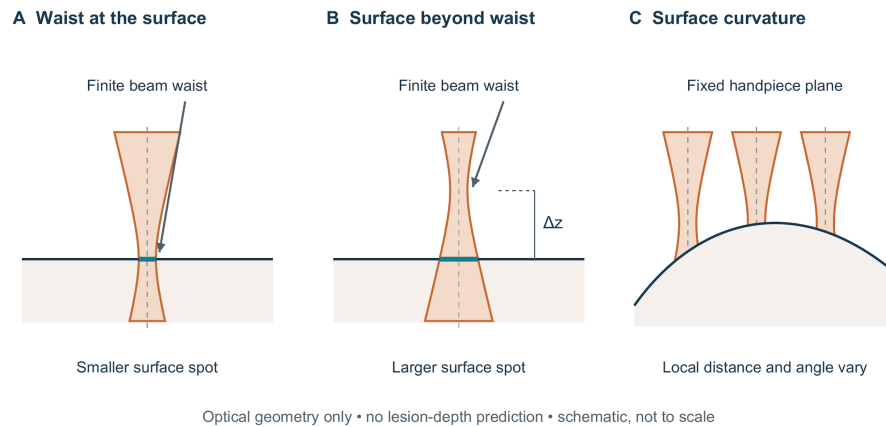


FIGURE 4: Working-distance geometry

(A) A finite waist lies at a flat skin surface. (B) The surface lies beyond the waist, increasing the local footprint for this focused beam. (C) Curvature can vary local distance and incidence angle across a fixed delivery plane. The outlines represent schematic beam envelopes, not injury margins, and do not model refraction or tissue transport. The magnitude of the effect depends on the optical system; small distance changes need not materially affect a collimated beam.

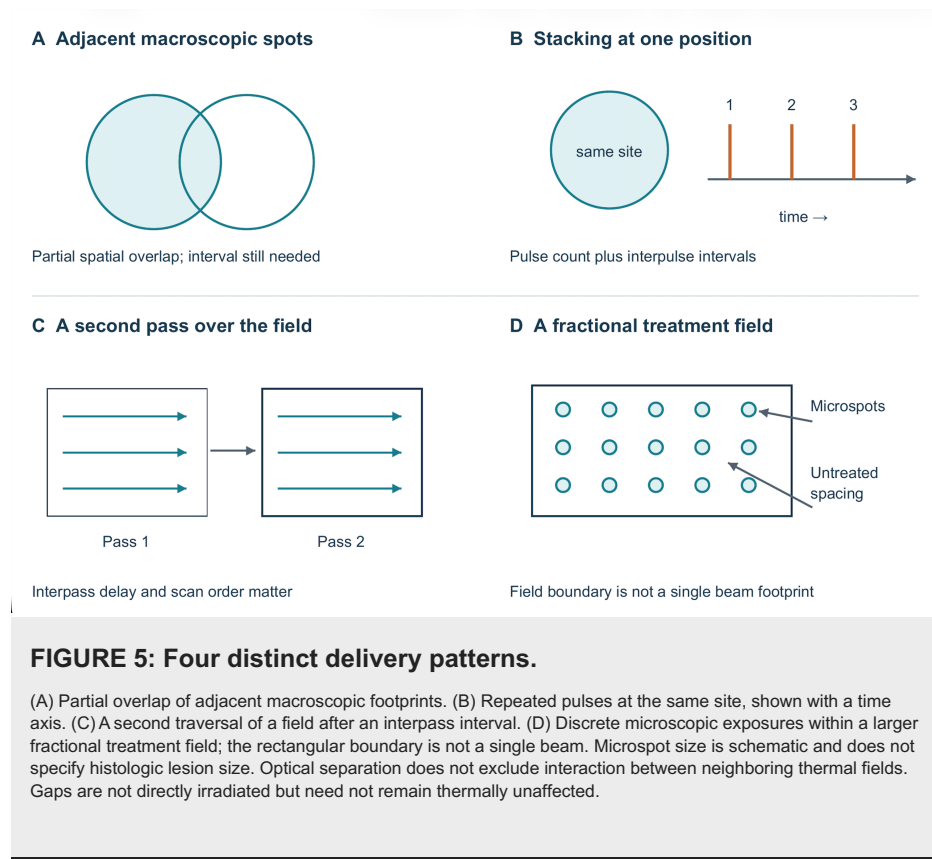
The practical implication is to preserve the delivery geometry used in a tested protocol and report departures from it. Evidence that focus changes microscopic injury is stronger than evidence that a particular distance-control method improves long-term clinical outcomes.

Overlap and repeated exposure

Spatial Patterns and Timing

Overlap describes spatial coincidence; stacking describes repeated exposure at approximately the same coordinates; a pass describes a traversal of a treatment field. Figure 5 distinguishes these patterns; none defines the pulse interval. For a set of incoherently combined exposures, the incident irradiance can be represented as:

$$E_{\text{field}}(\mathbf{r}, t) = \sum_i E_{e,i}(\mathbf{r} - \mathbf{r}_i, t - t_i)$$



Each exposure retains its position r_i and time t_i . Time integration gives a map of radiant exposure but removes the timing needed to estimate thermal accumulation. Equal integrated exposures may therefore produce different temperature histories. Biological damage is not additive in the same way as incident exposure, especially when treatment changes tissue optical or thermal properties.

Equal pulse energy and stated duration do not ensure equal peak irradiance, rise time, or subpulse structure. Q-switching describes pulse generation; fractionation describes spatial delivery, so the categories may coexist. High repetition rates can produce thermal accumulation even with femtosecond pulses [33].

Ablation and Residual Injury in Carbon Dioxide Resurfacing

Ross et al. examined pulsed and scanned CO_2 exposure in a porcine model [34]. Ordinary repeated passes and rapid overlapping scans did not produce interchangeable effects. Rapid repeat exposure could increase residual thermal injury and depth of cell death, whereas additional passes under other conditions did not consistently increase residual damage. The experiment used one animal and scanning and cooling intervals specific to the device. It supports reporting those intervals, not a general prohibition on overlap.

Fitzpatrick et al. studied excised human skin using CO_2 spots of 3 mm at 250 or 500 mJ, comparing passes with single, double, or triple pulses [35]. Stacked pulses were separated by 100 ms; passes were seconds apart and included debris removal. Ablation became less efficient while residual thermal injury could continue to increase. Pulse count or summed nominal fluence therefore cannot substitute for separate measurements of removal and residual injury. The independent donor count was not reported. Appendix 2 records the experimental units and exposure comparisons for these studies.

Grover et al. treated preauricular and postauricular skin in seven rhytidectomy patients with a CO_2 scanner at 300 mJ, approximately 7.5 J/cm^2 , a nominal spot diameter of 2.25 mm, and density settings corresponding to 30% or 60% overlap [36]. Their “cumulative depth” requires particular caution. At the preauricular sites treated with 30% overlap, mean depths for one, two, and three passes were 41, 52, and 86 μm . The reported cumulative value of 179 μm adds those three means from separately treated sites; it is not the measured depth after three passes. The latter is 86 μm . The corresponding means at 60% overlap were 43, 76, and 121 μm , not a measured depth after three passes of 240 μm . These sums should not be pooled with directly measured final lesion depths or used to predict incremental ablation per pass.

The same study assigned density by side rather than randomizing it and discarded two observations as presumed transcription errors, including the only site described as extending into the reticular dermis. Its broad safety conclusion is therefore less secure than its descriptive histology. The data remain informative

about specific scanner settings, but do not establish a general safety margin for repeated CO₂ exposure.

Together, these resurfacing studies show that tissue removal and residual thermal injury can respond differently to repeated delivery. Their value is mechanistic and histologic; none establishes a generally safe number of passes for patients.

Repeated Exposure in Vascular Treatment

The Dinehart report also reviewed 135 patients who underwent 362 treatments at 6.5–8.5 J/cm² [18]. Approximately 13% overlap of spot diameter was estimated geometrically to expose 18% of the lesion area twice. Two patients developed scarring or textural changes, nine had hyperpigmentation, and four had temporary hypopigmentation. A comparison of overlapping and nonoverlapping portions in 10 patients with port wine stains (PWS) reported no difference in adverse effects, but allocation, masking, paired event counts, and extended follow-up were insufficiently described. These observations did not determine optimal overlap.

Koster et al. examined normal human skin scheduled for excision, using pulsed dye exposure at 585 nm with pulses of 450 μs, a spot of 5 mm, and a fluence of 7 J/cm² [37]. In the overlap experiment, complete and approximately 30% overlap increased depth of vascular injury relative to a single pulse by 0.61 and 0.48 mm, respectively. No severe injury to dermal connective tissue was identified at that exposure. Pulses were delivered at 0.3 Hz, so overlap should not be described simply as almost simultaneous thermal stacking. The endpoint was histology in normal skin, not clearance of PWS, delayed scarring, or outcomes reported by patients.

Rohrer et al. compared a single pulse at 595 nm with two to four pulses at 1.5 Hz to vessel spasm, with matched settings for each pulse and dynamic cooling [38]. Of 25 patients with facial telangiectasias, 23 completed the comparison between facial sides. Photographic clearance at six weeks was 87.6% with stacking versus 67.4% with one pulse. No purpura, pigmentary change, or scarring was reported; one patient had marked edema on the stacked side. The pulse count and stopping endpoint defined the strategy for repeated exposure.

Peters et al. found no significant benefit from double passing in resistant PWS [39]. Sixteen of 17 participants completed a randomized within-person comparison of one pass at 595 nm and 12 J/cm² versus two passes at 11 J/cm² each, six minutes apart. Both used a 7 mm spot, pulses of 1.5 ms, and dynamic cooling. Outcomes three months after the second session did not favor double passing; one site receiving two passes developed a slightly atrophic scar still present at one year. The previously treated population and six-minute interval differ substantially from Rohrer's telangiectasia protocol.

Yu et al. compared one and two passes in 21 patients with previously untreated PWS, including 11 flat and 10 hypertrophic lesions [40]. Three sessions were given two months apart. The first pass used 595 nm and 1.5 ms at either 10 mm and 10 J/cm² or 7 mm and 12 J/cm². A second pass followed 30 minutes of ice-bag cooling and used 1 J/cm² less fluence. Both regimens used cryogen cooling. Colorimetry and photographs showed no additional improvement three months after the final session. Five patients developed blisters or crusts at double-pass sites; three had bilateral hyperpigmentation that resolved within six months. Immediate biopsies from two patients showed mean thrombus depths of 0.388 and 0.386 mm after one and two passes. That small histologic sample cannot establish equal injury depth.

Noormohammadpour et al. tested another sequence in 24 patients with untreated PWS, dividing each lesion into randomized portions [41]. A single pass at 1.5 ms and 11 J/cm² was compared with a 20 ms pass at 13 J/cm² followed, after 20 minutes of ice-pack cooling, by the same short-pulse pass. Both used 595 nm, a 7 mm spot, cryogen cooling, and nominal 10% overlap. One month after three monthly sessions, mean colorimetric blanching was 48% with two passes and 37% with one (p = 0.001). Crusting and purpura occurred in all patients. Hyperpigmentation affected both portions in one patient and only the double-pass portion in another. The positive result concerns the combined long-pulse, cooling, and short-pulse sequence. Appendix 2 gives the full cooling settings and notes the abstract's erroneous pulse-duration units.

Yang et al. pooled six trials involving 130 patients in their 2023 systematic review and meta-analysis and found no statistically demonstrable overall advantage of double-pass 595 nm PDL treatment [42]. The present appraisal complements that result by examining what the pooled label combines: short- and long-pulse sequences, intervals ranging from seconds to days, differences in exposure per pass and cooling, and different lesion histories. Peters and Yu reported no added benefit, whereas Noormohammadpour reported improved blanching with a long-pulse prepass and cooling interval [39–41]. This heterogeneity does not identify the cause of the differing results, but it limits transfer of a pooled conclusion to a particular exposure strategy. Neither nonsignificant pooled effects nor the small individual trials establish equivalence. Table 3 separates clinical comparisons from histologic evidence.

Study / population	Defined comparison	Outcome and timing	Supported inference
Dinehart 1994 [18] 135 patients; 362 treatments. Ten patients with paired lesion portions.	585 nm; nominal 5 mm. Clinical series: 6.5 to 8.5 J/cm ² ; paired comparison: 6.5 to 7.5 J/cm ² . Authors describe 13% diameter overlap; their geometric estimate gives 18% of lesion area treated twice.	Two patients had scarring or textural change, nine hyperpigmentation and four temporary hypopigmentation. Assessment at 6 to 8 weeks, followed by two further months. No adverse-effect difference reported in ten paired comparisons.	Retrospective experience plus a small paired comparison. Random allocation, masking and paired event counts not reported. No established safety equivalence or optimal overlap; 362 treatments are not 362 independent patients.
Koster 2001 [37] Normal skin histology; 10 subjects in overlap experiment	585 nm; 450 μs; 5 mm; 7 J/cm ² ; 0.3 Hz. Single pulse vs two fully or ~30%-overlapping pulses.	At 24 hours, depth of vascular injury increased by 0.61 mm (p = 0.0003) and 0.48 mm (p = 0.0019). No severe damage to connective tissue at this exposure.	Overlap deepened a histologic effect in the target tissue. Normal skin histology does not establish port wine stain clearance or long term safety.
Rohrer 2004 [38] Facial telangiectasias; 23 completed	595 nm; 10 ms; 10 mm; 7.5 J/cm ² ; cooling spray/delay 30/20 ms. One pulse vs 2 to 4 at 1.5 Hz to vessel spasm.	Six week clearance 67.4% vs 87.6%. One pronounced edema event with stacking; no reported pigment change, purpura or scarring.	Stacking benefited this regimen. Total energy and stopping rule changed; small sample and short follow up limit safety inference.
Peters 2012 [39] Resistant port wine stains; 16 clinical completers	595 nm; 1.5 ms; 7 mm; cooling spray/delay 30/20 ms. Single pass 12 J/cm ² vs double pass 11 J/cm ² each, six minutes apart.	No significant added benefit three months after session 2. One double pass site had a slightly atrophic scar persisting at one year.	No added improvement was detected. Per pulse exposure, pulse interval and resistant lesion population differ from Rohrer.
Yu 2018 [40] PWS; clinical n = 21, histology n = 2	595 nm; 1.5 ms. Single pass and first pass of the strategy using two passes: 10 mm at 10 J/cm ² or 7 mm at 12 J/cm ² . Second pass after 30 minutes of ice cooling at 1 J/cm ² less. Cryogen spray/delay 40/20 ms.	No added clinical benefit detected three months after three sessions. Blanching: 32.12% with one pass versus 30.73% with two. Five patients had blistering or crusts at sites receiving two passes.	No demonstrated equivalence. Biopsies from two patients cannot establish a universal depth limit. Extra exposure, cooling, and endpoint define the strategy.
Noormohammadpour 2021 [41] PWS; 24 patients	595 nm; 7 mm; nominal 10% overlap. Added 20 ms/13 J/cm ² pass, then 20 minutes of ice cooling, followed by the shared 1.5 ms/11 J/cm ² pass. Cryogen 40/20 ms.	One month after three sessions: blanching 48% with two passes versus 37% with one (p = 0.001). PIH in both portions in one patient and only the portion receiving two passes in another.	Positive result for this sequence, not an isolated pulse interval effect. Small sample and short follow up do not establish equal safety.
Wang 2026 [29] ABNOM; 30 randomized, 28 completed	755 nm; 750 ps; same zoom handpiece, 2.5 Hz, single pass. 4.5 to 5.0 mm / 1.02 to 1.26 J/cm ² / without whitening vs 2.5 to 3.0 mm / 2.83 to 4.07 J/cm ² / whitening.	Similar observed clearance 12 months after session 3. Larger spot/lower fluence versus smaller spot/higher fluence: PIH 4/84 vs 19/84; scabbing 8/84 vs 52/84 observations of treated facial sides across three sessions.	Complete strategy comparison; no isolated spot size or formal equivalence result. Denominators across repeated sessions are not patient level risks.

TABLE 3: Selected histologic and clinical comparisons of exposure strategies

PWS: port wine stain; ABNOM: acquired bilateral nevus of Ota-like macules; PIH: postinflammatory hyperpigmentation. Results are reported from the sources, not pooled estimates. Changes intrinsic to an assigned strategy, such as greater cumulative energy with more pulses, must be distinguished from uncontrolled additional treatments.

Early reactions and longer-term safety

Immediate endpoints such as vessel spasm or whitening, and early reactions such as purpura, edema, or crusting, must be distinguished from durable clearance and persistent pigmentary or structural change. Rohrer's six-week telangiectasia assessment and Noormohammadpour's one-month PWS assessment provide limited information on later scarring or texture [38,41]. In Peters, the scar observed at one year was follow-up of an adverse event, not a one-year assessment of the whole cohort [39]. Likewise, Yu's six-month resolution of hyperpigmentation concerns affected patients; the principal efficacy assessment was at three months [40].

Population and protocol also limit comparison: previously treated resistant PWS, untreated flat or hypertrophic PWS, and facial telangiectasias are different clinical settings. A favorable short-term response

in one cannot establish long-term safety in another. Wang's longer observation in pigmented skin provides useful information about the duration of hyperpigmentation, but concerns a different target and laser regimen [29]. Across the selected vascular studies, systematic long-term assessment of persistent pigment change, scarring, and texture remains limited. Absence of a reported event during short follow-up should not be interpreted as evidence that the event cannot occur.

Cooling and Fractional Exposure

At unchanged optical delivery, cooling changes the initial temperature and thermal boundary conditions rather than the incident radiant exposure. Any accompanying change in optical coupling requires separate characterization. Cooling timing also matters: Milanič et al. modeled optical transport, heat transfer, and injury for repeated pulses at 532 nm lasting 1 ms interleaved with cryogen spray [43]. Under the modeled conditions, this sequence could preserve vessel heating while limiting epidermal injury; it was not a clinically validated dosing schedule.

Laubach et al. tested cadaver skin with a fractional laser at 1550 nm and 10 mJ per MTZ [44]. Across starting temperatures from 0 to 45 °C, mean epidermal MTZ diameter increased from 93 to 147 μm. Two passes were delivered at 250 MTZ/cm² per pass; overlapping MTZs were excluded from measurement. Donor count was not reported. Within this ex vivo preparation, equal pulse energy produced different lesion areas at different starting temperatures.

Fractional coverage may describe optical spacing, delivered spot count, or observed injury area. Repeated passes can revisit MTZs or treat new locations, and thermal fields can interact despite optical separation [45-48]. The idealized fraction $1 - (1 - f)^n$ after n passes of fractional coverage f assumes independent placement. Actual scanners may repeat or deliberately offset positions, so that expression cannot be used as a general clinical coverage calculator.

Wenande et al. recently imaged fractional thulium exposure at 1927 nm with energies of 3 to 20 mJ with two tips in one healthy volunteer [49]. Tissue effects ranged from subepidermal changes to ablation. The tips differed in both nominal spot diameter and spot density, and imaging limitations affected depth assessment. The report is valuable morphological evidence, not a controlled clinical comparison of isolated spot size. It also cautions against treating the label "nonablative" as a guarantee of the tissue response at every setting.

Applying the appraisal to clinical literature

Information Needed to Interpret a Comparison

Table 4 adapts existing reporting recommendations [3,4,7] to the comparison question. It separates information available in a clinical record from measurements requiring manufacturer documentation or an optical laboratory. Unknown quantities should remain labeled unknown; a device name does not justify assigning a Gaussian or flat-top profile. Measurement of high-power beams requires appropriate expertise and safety controls.

Domain	Clinical record / study report	Additional characterization when available
Source and pulse	Device, handpiece, wavelength, pulse mode and stated duration; energy and its unit of delivery.	Calibrated pulse energy; waveform, subpulses and stability; calibration date and uncertainty.
Spot and profile	Nominal diameter; stated spot definition; contact or noncontact delivery.	Measured profile and beam width convention at the treatment plane; source of specification.
Geometry	Working distance, distance holder, focal adjustment, contact pressure and site curvature where relevant.	Focal tolerance, divergence and repeatability over the intended treatment range.
Field and timing	Scan pattern, passes, intended overlap, pulse count per site, repetition rate and pauses.	Microspot spacing and placement; actual revisit intervals; definition and measurement of coverage.
Cooling and tissue	Cooling method and timing; skin type, site and clinical endpoint; preparation and wiping between passes.	Starting temperature, cooling boundary conditions and tissue optical properties, if measured.
Outcome and provenance	Target response, adverse events, follow up and denominator: patients, sites or sessions. Identify each value as displayed, specified by the manufacturer, measured, estimated, or unknown.	Measured lesion dimensions separately from model estimates; explicit assumptions and independent validation of predictive claims.

TABLE 4: Information needed to interpret and reproduce an exposure comparison

The clinical record should identify the device and handpiece, settings, tissue and anatomical site, intended endpoint, cooling, passes, and pattern of repeated exposure. Energy must be linked to its unit of delivery: microbeam, pulse, or scanner field. A proprietary density setting requires the corresponding spacing or coverage definition before it can be compared across devices.

Engineering characterization adds the profile at the treatment plane, convention for spot width, calibrated energy, waveform, focal tolerance, and measurement uncertainty. Optical measurements, manufacturer specifications, model estimates, and observed tissue outcomes should be labeled separately. This provenance is essential when deciding whether a protocol can be reproduced or only approximately described.

Strength and clinical relevance of the evidence

The randomized within-person studies provide the most direct evidence for the clinical regimens they compare. Jo matched nominal fluence, pulse duration, and cooling, narrowing the attribution to a change of handpiece and footprint, although only 10 participants were studied [26]. Wang assessed clinical response 12 months after the final session and included 28 completers, but compared combined regimens and did not clearly describe how repeated session-level adverse events were handled statistically [29]. The vascular trials used within-person allocation and clinical outcomes, but their small samples, differing lesion populations, and efficacy follow-up ranging from one to three months constrain conclusions about durable benefit and uncommon harms [38–41].

The experiments offer stronger control of physical conditions than of clinical applicability. Keijzer isolates a transport problem within a simplified model; Kositratna combines controlled focal deviations with optical measurements and tissue histology [21,30]. These approaches support mechanisms. Their clinical reach is limited by model assumptions and, for Kositratna, two skin donors. Ross used one animal, Fitzpatrick did not report the independent donor count, and Koster measured acute injury in normal skin [34,35,37]. Multiple lesions or measurements improve description within those preparations without increasing independent biological replication.

Less controlled clinical observations carry less weight for causal conclusions. Nehal combined different lesion types with incompletely matched fluences; Dinehart’s overlap comparison lacked reported random allocation and paired event counts [18,28]. Grover’s side-based allocation, excluded observations, and unconventional cumulative-depth calculation weaken its broad safety claim [36]. These reports remain useful for identifying measurement and interpretation problems, but do not carry the same evidential weight as controlled clinical comparisons. The second and third tables in Appendix 2 retain the study-level details behind this appraisal.

For clinical reading, the practical sequence is to identify the assigned regimen, check whether the outcome measures the intended benefit or collateral injury, and then consider the design and follow-up needed to support that claim. The reporting aid itself has not been validated. Its first evaluation should test reporting completeness and agreement between readers before any claim that it improves care.

Limitations and research priorities

The evidence spans distinct mechanisms, devices, and clinical questions. It does not support a single pooled treatment effect across this review. A detailed comparison can clarify what a study tested without resolving weaknesses in the original design or missing measurements.

This narrative synthesis used PubMed and bounded citation checks and may miss relevant work, particularly engineering reports outside biomedical indexing. Selection was purposive: 191 potentially relevant records were not selected for detailed assessment, and 14 records remained unresolved without full-text assessment. The selected panel cannot establish comprehensive or proportionate coverage. No formal risk-of-bias instrument was applied. These limitations remain despite the detailed selection record and study matrix.

Future studies should define the intended contrast before matching energy, exposure, or endpoint, and measure the delivered beam where feasible. Factorial or carefully matched designs could distinguish strategy components. Clinical analyses should accommodate pairing and repeated sessions, with follow-up adequate for pigmentary change and scarring. Validation requires assessment of intended target response alongside collateral injury.

Conclusions

Comparisons of dermatologic laser treatments are most useful when the exposure contrast and the outcome are read together. A change in spot size at equal energy answers a different question from the same change at equal radiant exposure. Repeated pulses with different intervals or cooling histories are also different interventions. Clinical benefit from a combined strategy should therefore not be assigned to an individual setting without a design that separates its contribution.

The value of this review lies in applying these distinctions to the primary evidence. It identifies where optical measurements, tissue experiments, and clinical observations support a conclusion, and where missing delivery details or the unit of analysis limit it. For safety, intended target response and collateral injury require separate assessment. More complete reporting should improve interpretability, but whether the proposed appraisal aid changes treatment decisions or reduces complications remains to be tested.

Appendices

Appendix 1: Literature identification and selection

Search Question and Scope

The search concerned the interpretation of changes in beam profile, spot geometry, focus, working distance, spatial overlap, stacking, repeated pulses, multiple passes, and scanning in cutaneous laser treatment. Comparative clinical studies, tissue and phantom experiments, optical measurements, and models were eligible for consideration. Combined treatment strategies were permitted but were not treated as isolated geometry tests. Studies changing only energy or pulse duration at fixed geometry without a repeated delivery contrast could inform background mechanisms but did not meet the primary search criterion.

Diagnostic imaging without treatment, industrial processing, dental or ophthalmic applications, and studies without a relevant exposure comparison were outside scope. No language restriction was applied. Clearly irrelevant titles could support exclusion; otherwise available abstracts were examined. Uncertain records remained unresolved.

Search Record

PubMed via NCBI E-utilities was searched on October 1, 2026, at 05:19:28 UTC (07:19:28 Europe/Berlin). All 1,083 unique PMIDs were fetched by 05:19:55 UTC. Abstracts were available for 1,076 records and absent for seven. The protocol was saved and hashed before execution, but was informed by previous vocabulary development and was not preregistered. No earlier screening decision was reused. The publication date cutoff was October 1, 2026; indexing date and publication date differ, so later retrievals may change.

Submitted Query

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(laser*[Title/Abstract] OR "Lasers"[MeSH Terms] OR "Laser Therapy"[MeSH Terms]) AND (skin[Title/Abstract] OR cutaneous[Title/Abstract] OR dermatolog*[Title/Abstract] OR "port-wine"[Title/Abstract] OR tattoo*[Title/Abstract] OR "hair removal"[Title/Abstract] OR "Skin"[MeSH Terms] OR "Skin Diseases"[MeSH Terms]) AND ("beam profile"[Title/Abstract] OR "beam profiles"[Title/Abstract] OR "beam shape"[Title/Abstract] OR "beam shaping"[Title/Abstract] OR "spot size"[Title/Abstract] OR "spot sizes"[Title/Abstract] OR "spot diameter"[Title/Abstract] OR "beam diameter"[Title/Abstract] OR "focal plane"[Title/Abstract] OR "working distance"[Title/Abstract] OR "pulse stacking"[Title/Abstract] OR "spatial overlap"[Title/Abstract] OR "scan pattern"[Title/Abstract] OR "scanning pattern"[Title/Abstract] OR "distance holder"[Title/Abstract] OR "multiple pulses"[Title/Abstract] OR "double pass"[Title/Abstract] OR "double-pass"[Title/Abstract] OR
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"multipass"[Title/Abstract] OR "multi-pass"[Title/Abstract] OR "multiple pass"[Title/Abstract] OR "multiple passes"[Title/Abstract] OR "repeated pulse"[Title/Abstract] OR "repeated pulses"[Title/Abstract] OR overlap*[Title/Abstract]) AND ("1000/01/01"[Date - Publication] : "2026/10/01"[Date - Publication])

Executed PubMed Translation

("laser"[Title/Abstract] OR "Lasers"[MeSH Terms] OR "Laser Therapy"[MeSH Terms]) AND ("Skin"[Title/Abstract] OR "cutaneous"[Title/Abstract] OR "dermatolog*"[Title/Abstract] OR "port-wine"[Title/Abstract] OR "tattoo*"[Title/Abstract] OR "hair removal"[Title/Abstract] OR "Skin"[MeSH Terms] OR "Skin Diseases"[MeSH Terms]) AND ("beam profile"[Title/Abstract] OR "beam profiles"[Title/Abstract] OR "beam shape"[Title/Abstract] OR "beam shaping"[Title/Abstract] OR "spot size"[Title/Abstract] OR "spot sizes"[Title/Abstract] OR "spot diameter"[Title/Abstract] OR "beam diameter"[Title/Abstract] OR "focal plane"[Title/Abstract] OR "working distance"[Title/Abstract] OR "pulse stacking"[Title/Abstract] OR "spatial overlap"[Title/Abstract] OR "scan pattern"[Title/Abstract] OR "scanning pattern"[Title/Abstract] OR "multiple pulses"[Title/Abstract] OR "double-pass"[Title/Abstract] OR "double-pass"[Title/Abstract] OR "multipass"[Title/Abstract] OR "multi-pass"[Title/Abstract] OR "multiple pass"[Title/Abstract] OR "multiple passes"[Title/Abstract] OR "repeated pulse"[Title/Abstract] OR "repeated pulses"[Title/Abstract] OR "overlap*"[Title/Abstract]) AND 1000/01/01:2026/10/01[Date - Publication]

The lower archival date of year 1000 in the query is a search sentinel, not a substantive lower eligibility limit. PubMed omitted the unindexed exact phrase “distance holder” from the executed translation. The submitted query, translation, warning, PMID list, and individual decisions were retained. Publisher and Crossref checks were used for identity and access verification, not as independently screened databases. No separately logged Google Scholar database search is claimed.

Disposition	Records
Potentially relevant primary study	207
Background material	151
Outside scope	711
Unresolved	14

TABLE 5: Screening decisions for the 1,083 unique PubMed records

Title and abstract informed 828 decisions; title alone informed 255. The screening log includes PMID, title, decision, reason, screening basis, priority flag, and subsequent use. The 113 records flagged for priority full-text consideration were not a mandatory retrieval list or a ranked selection. The complete record-level log and dated protocol are available from the corresponding author on reasonable request.

The 14 unresolved records comprised four without an available abstract and 10 whose abstracts did not sufficiently establish the relevant comparison or study design. None entered the targeted full-text set or detailed panel. Their eligibility remains unresolved; they were not reclassified as ineligible or as full-text exclusions. This incomplete follow-up limits the coverage of the review.

Selection of the Detailed Primary Panel

Of the 207 potentially relevant primary records, 16 were selected for detailed assessment. The other 191 were not selected for this panel; this is purposive nonselection, not exclusion after full text assessment. Some sources outside the panel informed the narrative. Two previously known reports not returned by the current query, Saghafi and Laubach, brought the targeted set to 18. All 18 targeted main reports were available and assessed in full. Aldanondo [9] was not retained in the detailed matrix because inconsistent descriptions of the exposure contrast limited reconstruction. Its combined intervention was not, by itself, a reason for nonselection. The final panel contains 17 primary reports, each corresponding to one study.

The protocol recorded general selection priorities before execution of the fresh search: direct relevance, controlled clinical comparisons, measured beam or tissue effects, foundational mechanisms, and coverage across technologies and indications. Positive, null, and adverse findings were considered. There was no predefined number of 17 studies, ranking algorithm, or quota for each domain. The first table in Appendix 2 makes the rationale for each selected study explicit from the retained record and extraction; it is an explanatory account, not a retrospectively claimed prospective ranking. The panel covers beam measurement, transport models, focus, repeated CO₂ exposure, vascular and pigment treatment, hair removal, and the influence of starting skin temperature. Laubach was retained for the last contextual

question, although unchanged geometry places it outside the focused comparison criterion. The adapted PRISMA flow reports this restricted selection process, not all eligible studies or every source consulted [10].

Seed Bibliography and Citation Checks

Seed and PMID	Backward links	Forward links
Jackson 1996 8647964	11	6
Kositratna 2016 26842919	20	5
Koster 2001 11241527	11	17
Rohrer 2004 14756644	6	46
Peters 2012 22362420	37	12
Wang 2026 42214498	46	1

TABLE 6: Bounded citation checks using Europe PMC

The earlier bibliography contained 42 references, reconciled separately against primary bibliographic records. The six citation checks returned 131 backward and 87 forward links, corresponding to 186 distinct indexed source and identifier pairs plus 12 links without identifiers. These links overlap with PubMed and with one another and cannot be added as unique studies. One page of up to 1,000 links per seed and direction was requested; all returned counts were below that cap. Titles were prioritized for selective follow up, not subjected to an exhaustive independent eligibility screen. Reference lists in available main reports supplied additional anchors.

Source Access and Identification Limits

The full main reports by Nehal [28], Yu [40], Noormohammadpour [41], and Dinehart [18] were assessed on October 1, 2026, after they had initially been considered from their primary abstracts. Their access status was updated in the current selection record without altering the earlier screening history. Jo [26], already in the bibliography, had also received a new complete extraction. No main report remained unavailable within the deliberately selected set of 18. This does not imply that every potentially relevant record or background reference was assessed in full. Missing methods or safety findings were not supplied by inference.

The main Noormohammadpour report refers to an unavailable supplementary demographic table. Wang supplementary methods were not included in the source audit. Neither report is described as having all supplementary material assessed. Yu prints two different trial registry identifiers; this review does not choose between them or claim verified prospective registration. Nehal and Dinehart are scanned sources and were read visually. Supplier cover sheets and watermarks were preserved in the private archive.

Grover [36] is identified by the supplied primary title page, authors, journal pages, and PMID 11149794. PubMed attaches a DOI ending 00048, while Crossref attaches that identifier to another article. Crossref assigns Grover the ending 00050, which PubMed associates with another report. The supplied first page has no printed DOI. The reference therefore uses the verified bibliographic details and PMID URL without an unresolved DOI.

The complete main texts of Shurrab, Park, and the related Bigge conceptual article were assessed for scope and overlap. Jenkins and Carroll were checked through the primary abstract. This comparison establishes the documented scope of those publications; it is not an exhaustive priority search or a claim that no earlier author considered attribution.

During revision, Yang’s 2023 systematic review and meta-analysis was checked in full and added as contextual synthesis [42]. It does not add a primary report to the 17-study panel. Reference 8 was checked against the publisher on October 19, 2026: it was published online on September 2, 2026 and still lacked consistent final issue and pagination details. The original October 1 search counts have not been changed by these targeted checks.

Appendix 2: Detailed primary evidence matrix

Table 7 explains the inclusion rationale for each study. Tables 8, 9 use matching study identifiers for exposure details and outcomes. A measured beam width differs from a spatial intensity map, prescribed model profile, or nominal device specification. Changes intrinsic to a defined contrast are not automatically

confounders. Patients, donors, and animals are counted separately from repeated sites, lesions, and sessions. No aggregate quality score was assigned.

Study and setting	Comparison question	Reason for inclusion
Jackson 1996 [17] 585-nm pulsed-dye laser; beam measurement and normal-skin histology	Do equal displayed settings produce equal spatial exposure across devices?	Measured beam and tissue evidence directly tests the comparability of nominal settings.
Dinehart 1994 [18] 585-nm pulsed-dye laser; beam measurement, geometric coverage and vascular treatment	How does a measured peripheral intensity fall-off relate to overlapping spots?	Connects measured spatial delivery with the rationale for overlap and its limited clinical validation.
Saghafi 2006 [19] Copper-vapor laser; beam shaping and optical transport model	What does a spot-size comparison at equal optical power actually change?	Provides the equal-power comparison needed to distinguish irradiance changes from intrinsic optical penetration; the brief clinical series is treated separately.
Keijzer 1991 [21] 577-nm optical transport model of a cutaneous vessel	How does beam width affect target deposition when epidermal deposition is approximately matched?	Supplies a foundational matched-deposition contrast that differs from equal incident exposure.
Jo 2015 [26] 805-nm diode laser; axillary hair removal	Does a larger rectangular footprint change outcomes when nominal fluence, pulse duration and cooling are matched?	A randomized within-person clinical comparison with matched delivery settings and both clearance and pain outcomes.
Nehal 1996 [28] 694-nm Q-switched ruby laser; tattoos and benign pigmented lesions	What can be inferred from a small paired spot-size comparison with similar, incompletely matched fluences?	Adds a mixed clinical result and demonstrates the limits of interpreting descriptive similarity as equivalence.
Wang 2026 [29] 755-nm picosecond alexandrite laser; acquired bilateral nevus of Ota-like macules	Does a larger-spot, lower-fluence, non-whitening regimen differ from a smaller-spot whitening regimen?	A randomized clinical strategy comparison with clearance and collateral-injury outcomes; it tests the combined regimen.
Kositratna 2016 [30] Fractional CO2 laser; ex vivo human skin	How does focal deviation alter lesion geometry at unchanged pulse energy and scanner settings?	A controlled geometry experiment linking measured optical propagation to tissue injury.
Ross 1999 [34] Pulsed and scanned CO2 lasers; porcine resurfacing model	Do ordinary passes and rapid overlapping scans produce the same injury and healing?	Directly examines the interaction of spatial overlap, pass count and revisit timing with histology and healing outcomes.
Fitzpatrick 1999 [35] Pulsed CO2 laser; excised human skin	Do stacked pulses and separate passes produce proportional ablation and residual thermal injury?	Distinguishes ablation saturation from accumulating thermal injury under specified pulse and pass sequences.
Grover 1999 [36] Scanned CO2 laser; facial surgical skin	How do scanner density, pass count and the definition of cumulative depth affect interpretation?	Direct density/pass histology comparison in which the reported cumulative quantity requires source-level reconstruction.
Koster 2001 [37] 585-nm pulsed-dye laser; normal human skin	How does partial or complete overlap at a defined pulse spacing affect vascular histologic injury?	A within-subject exposure comparison connects overlap with injury depth while exposing the limits of normal skin as a disease model.
Rohrer 2004 [38] 595-nm pulsed-dye laser; facial telangiectasias	Does endpoint-guided pulse stacking improve clearance relative to one pulse?	A positive randomized clinical stacking comparison with clearance and collateral-effect outcomes.
Peters 2012 [39] 595-nm pulsed-dye laser; treatment-resistant port-wine stains	Does a second pass after six minutes improve response in previously treated lesions?	A controlled null clinical comparison provides a counterexample to a general benefit from repeated delivery.
Yu 2018 [40] 595-nm pulsed-dye laser; previously untreated port-wine stains	Does a second short-pulse pass after a cooled 30-minute interval improve clinical response or histologic injury?	A randomized null clinical comparison with a small histologic component tests a different repeated-delivery regimen and population.
Noormohammadpour 2021 [41] 595-nm pulsed-dye laser; previously untreated port-wine stains	Does a long-pulse prepass followed by cooling and a short-pulse pass improve blanching?	A positive randomized clinical counterexample shows why pulse sequence and cooling must be distinguished from pass number alone.

Laubach 2007 [44] 1550-nm fractional laser; ex vivo human skin	Can initial tissue temperature change lesion dimensions at unchanged laser settings?	A contextual tissue-state experiment tests a thermal boundary condition relevant to comparisons of cooling and repeated exposure.
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TABLE 7: Comparison question and reason for detailed inclusion

Study and independent units	Matched and changed conditions	Measurement and repeated observations
Dinehart 1994 [18] Optical characterization of one laser, idealized coverage geometry, a retrospective adverse-event series, and a ten-patient comparison of paired lesion portions; random allocation was not described. Independent units: One laser with a new fiber/applicator; 135 patients in the retrospective series. Ten patients underwent paired comparison; their membership in the larger series was not specified.	Matched: Same SPTL-1 laser at 585 nm and nominal 5 mm spot. Fresh dye, new fiber/applicator and approximately 30 minutes of warm-up for optical measurements. Clinical series: 6.5 to 8.5 J/cm ² ; paired portions: 6.5 to 7.5 J/cm ² . Exact paired fluences were not given. Changed: Optical measurements: nominal fluence. Clinical comparison: overlapping versus nonoverlapping delivery. The selected pattern used approximately 13% diameter overlap; the authors geometrically estimated 18% of lesion area exposed twice. These are different quantities, not measured achieved coverage. Coverage and repeated exposure changed together.	Measured relative intensity along one diameter at the treatment plane through an approximately 100 μ m aperture, at nominal 5.0 and 7.5 J/cm ² . Three scans with fiber repositioning; four pulses averaged at each 0.2 mm step. No complete spatial map or formal distribution fit. Repeated observations: Three diameter scans and four-pulse averages are technical repeats. The 362 treatments are nested in 135 patients. Paired lesion portions are not independent patients.
Jackson 1996 [17] Four-device optical comparison plus immediate histology in normal human skin; historical comparator for the other platform. Independent units: Four laser units (two of each platform); eight human volunteers for the Cynosure histology arm.	Matched: Nominal 585 nm and 5-mm handpieces for optical comparison; burn paper at 3 J/cm ² . Human histology single pulses at 3, 5 and 7 mm and 3, 5 and 7 J/cm ² . Changed: Laser unit, manufacturer/platform, handpiece optics, actual footprint and profile; clinical histology varied spot size and displayed exposure on one platform.	Measured by CCD camera/beam analyzer at the treatment plane after the handpiece, at 6 and 7 J/cm ² . Approximately Gaussian versus more flat top output. Burn-paper diameter/area at displayed 3 J/cm ² is a separate measurement. Repeated observations: Twenty camera recordings per fluence; 24 punch biopsies across eight volunteers.
Keijzer 1991 [21] Monte Carlo optical transport model of one representative blood vessel in layered tissue. Independent units: Not applicable: no patients, donors or animals.	Matched: For the focal comparison: 577 nm; 60 μ m epidermis; 100 μ m vessel 300 μ m below epidermis; fixed tissue optical properties. Width 0.2 to 2 mm with irradiance 1.0 to 0.7 W/cm ² approximately maintained average epidermal deposition. Changed: Beam width and, in the matched-epidermal-deposition comparison, incident irradiance; separate simulations varied scattering and wavelength.	Prescribed collimated source with infinitely extended rectangular cross-section for two dimensional computational geometry; not a measured clinical beam. Repeated observations: Repeated Monte Carlo estimates describe numerical uncertainty, not biological replication.
Saghafi 2006 [19] Optical beam-shaping analysis, Monte Carlo skin transport and briefly described uncontrolled PWS series. Independent units: No biological n for modeling; 25 patients mentioned for the clinical protocol without analyzable participant-level outcome reporting.	Matched: 5- versus 10-mm modeled spots compared at equal optical power within the same modeled tissue. Copper-vapor wavelengths 511/578 nm; experimental source at 10 kHz. Absolute power stated inconsistently as 12/15 W. Changed: Source profile and spot diameter; clinical settings selected according to lesion depth, size and shape.	Analytically prescribed Gaussian and homogenized profiles; physical homogenizer described. No reproducible instrument-based profile measurement or calibrated map reported. Repeated observations: Not adequately reported for clinical component.
Kositratna 2016 [30] Controlled ex vivo human-skin focal-deviation experiment plus	Matched: One DeepFX CO ₂ system; 50 mJ/pulse; nominal focal diameter 120 μ m; 1 x 1 cm scan, 169 MTZs, displayed 5%	Beam diameter measured by scanning knife-edge at seven exposure planes; Gaussian zero-order diffraction-limited mode prescribed in Zemax comparison. Measured beam described as 1.1

optical beam propagation measurement/model. Independent units: Two abdominal-skin donors.	coverage; approximately 25 °C tissue after thawing; perpendicular mounting and fixed scanner settings. Changed: Axial handpiece-to-tissue position from -3 to +3 mm, and consequently optical spot and lesion geometry.	times diffraction limited. No complete two dimensional irradiance map. Repeated observations: Four repeats of full experiment per donor; 64-102 measured MTZ lesions per distance setting (81 ± 7 average).
Ross 1999 [34] Within-animal comparison of pulsed and scanned CO ₂ exposure, overlap, pass count and timing with histology and healing follow up. Independent units: One farm pig.	Matched: Same animal; device-specific groups with fixed per pulse settings/power. UltraPulse used 300 mJ and 2.25-mm impacts, 200-Hz within-scan repetition; ordinary passes had wiping and about two-minute gaps, rapidly overlapping scans had 0.5-second intervals. SilkTouch used 16 W with 6-mm scans and varied on/off schedules. Changed: Delivery platform, scanner density/overlap, ordinary pass number, rapid scan repetition and cooling interval; ordinary pass-count comparisons also performed separately.	Nominal beam/scanner dimensions described; no independent spatial intensity-profile mapping reported. Repeated observations: Multiple treatment sites and repeated biopsies/measurements within the single animal; not independent animals.
Fitzpatrick 1999 [35] Ex vivo surgical-skin CO ₂ ablation and pulse-stacking experiment with partly blinded histologic measurements. Independent units: Number of skin donors not reported.	Matched: One UltraPulse 5000C system, handpiece and operator; <1-ms pulses; 4 x 3 impact rectangles with no more than 10% intended overlap. Stacks 100 ms apart; passes several seconds apart with saline-gauze wiping and drying. Tissue irradiated within 30 minutes after excision. Changed: Pulse energy 250/500 mJ, one to three impacts per spot, and one to ten passes; five specific energy/stack combinations, not every factorial combination.	Nominal 3-mm collimated beam; no independent spatial profile measurement reported. Repeated observations: Seventy treatment areas/biopsy specimens reported; two or three specimens per parameter set. These are not 70 independent patients.
Grover 1999 [36] In vivo surgical-site histology with fixed-side density assignment in rhytidectomy patients. Independent units: Seven patients aged 37-68 years.	Matched: One UltraPulse 5000/CPG device, 300 mJ, about 7.5 J/cm ² , nominal 2.25 mm, reported 60 W. Right ear received 30%, left ear 60%. Adjacent scan squares without overlap and moist-gauze wiping between passes; histologist blinded to treatment settings. Changed: Density/overlap (30% versus 60%), one/two/three passes, and preauricular versus postauricular site.	Nominal scanner spot and density supplied; no measured spatial profile or map at the treatment plane. Repeated observations: Twelve planned sites/patient, 84 planned observations; two data points excluded as presumed transcription errors.
Koster 2001 [37] Within-subject normal skin histology experiment before planned surgery; exposure-ranging phase followed by overlap comparison. Independent units: Eighteen women overall; ten subjects in the overlap experiment (seven breast-skin, three abdominal-skin).	Matched: Same Candela SPTL-1, 585 nm, 450 μ s, 5 mm, 7 J/cm ² per pulse, 0.3-Hz repetition; within-person comparisons; earlier phase selected exposure using 5-10 J/cm ² . Changed: Overlap comparison: single pulse, two fully overlapping pulses, two approximately 30%-overlapping pulses, or two separated by 1-2 mm.	Nominal circular 5-mm spot; independent intensity-profile measurement not reported. Repeated observations: Multiple exposure sites per person; paired comparisons across ten subjects, not independent laser spots.
Rohrer 2004 [38] Randomized split face comparison with blinded outcome evaluators for facial telangiectasias. Independent units: Twenty-five enrolled; twenty-three completed follow up.	Matched: Same 595-nm Vbeam system, 7.5 J/cm ² per pulse, 10 ms, 10 mm, cooling 30-ms spray/20-ms delay; stacked pulses at 1.5 Hz. Similar baseline telangiectasia density used for side selection. Changed: One pulse versus two to four stacked pulses, hence total exposure and endpoint-based stopping rule. Stacking stopped after vessel spasm or four pulses.	Nominal 10-mm spot; measured spatial profile not reported. Repeated observations: Two facial sides within each patient, measured at one and six weeks.
Wang 2026 [29] Prospective randomized evaluator-blinded split face trial of complete picosecond alexandrite protocols for ABNOM. Independent units: Thirty Asian participants, skin types III-V; twenty-eight completed all three sessions.	Matched: Same 755-nm PicoSure device and zoom handpiece, 750-ps pulse duration (stated in Discussion), 2.5 Hz, single pass, three sessions six months apart, topical anesthetic and postoperative moisturizer/sunscreen. Changed: Spot diameter, displayed exposure and therapeutic endpoint together: 4.5-5.0 mm/1.02-1.26 J/cm ² /without whitening versus 2.5-3.0 mm/2.83-4.07 J/cm ² /whitening.	Same zoom handpiece stated; no measured spatial profile in main report. The Discussion specifies a 750-ps pulse duration. Repeated observations: Eighty-four side treatment observations per arm (28 participants x 3 sessions), not 84 independent participants; paired facial sides and repeated sessions.
Peters 2012 [39] Randomized within-patient controlled		

comparison in non-hypertrophic PWS resistant to previous PDL treatment; blinded clinical assessment and reflectance spectroscopy. Independent units: Seventeen enrolled; sixteen completed the two treatments and clinical follow up; fifteen evaluable for spectroscopy after one technical failure.

Matched: Same 595-nm Vbeam device, 7-mm spot, 1.5-ms pulse duration, 30-ms cryogen spray/20-ms delay and 10% spot overlap. Two sessions planned eight weeks apart (mean nine); patients acclimatized for 30 minutes in a 21 °C room. Comparable within-lesion sites randomized using digital sequence and numbered sealed envelopes. Changed: Single pass at 12 J/cm² per pulse versus two passes at 11 J/cm² per pulse with a six-minute interval. Both pass number and per pulse radiant exposure differ; greater total exposure is intrinsic to the double pass regimen.

Nominal 7-mm spot; spatial intensity profile not independently measured in the report. Repeated observations: Two randomized 2 x 2 cm PWS areas per participant; two treatment sessions and paired within-patient outcomes. Three color readings averaged per test area.

Laubach 2007 [44] Ex vivo human-cadaver skin experiment varying initial temperature with blinded epidermal MTZ measurement. Independent units: Number of cadaver donors not reported.

Matched: Same 1550-nm Fraxel SR1 laser, 10 mJ/MTZ, two passes at 250 MTZ/cm²/pass; dye and 30% lidocaine ointment; wet gauze/thermal plate with infrared temperature checks immediately before and after exposure. Changed: Skin temperature 0, 5, 10, 15, 20, 25, 30, 35, 37, 40 and 45 °C.

Device specified; independent beam diameter/intensity-profile measurement not reported. Repeated observations: Forty-eight non-overlapping MTZs randomly selected per each of eleven temperature levels; two perpendicular diameters per lesion. These are lesion-level measurements, not independent donors.

Jo 2015 [26] Randomized, evaluator-blinded, within-participant left-right comparison of two 805-nm diode-laser handpiece sizes for axillary hair removal. Independent units: Ten Korean women, ages 24-50 years, Fitzpatrick skin types II-IV, with black axillary hair. All ten completed three sessions and the three-month follow up; only three were followed to six months.

Matched: Same Advantage 805-nm long-pulsed diode platform. Reported fluence and pulse duration were identical between paired axillae: 25-33 J/cm² (median 27) and 30-45 ms (median 40), respectively. Epidermal cooling temperature was set to 3 °C on both sides; room 20-22 °C. Three sessions at one-month intervals, each one pass with intended 10% overlap; same experienced dermatologist. Settings varied across the study population, so these ranges are not a single fixed regimen for every participant. Changed: Handpiece footprint changed from 10 x 10 mm (D1) to 10 x 30 mm (D3), altering area and aspect ratio. At matched nominal radiant exposure, the nominal pulse energy necessarily scales with area; this is intrinsic to the contrast, not an additional confounder. The two handpieces were not independently characterized as having otherwise identical spatial profiles.

Nominal handpiece footprints of 10 x 10 mm and 10 x 30 mm; independent spatial irradiance profiles, beam widths at the treatment plane, and calibrated pulse-energy measurements were not reported. Repeated observations: Two axillae per participant, treated three times; serial photographic hair counts independently assessed by three blinded evaluators and averaged. Twenty axillae and repeated photographs are paired/nested observations, not twenty independent participants.

Nehal 1996 [28] Prospective comparison of paired halves of 12 lesions in 11 patients; allocation randomization and assessor masking not reported. Independent units: 11 patients; one contributed two tattoos. Nine tattoos and three benign pigmented lesions.

Matched: Same ruby platform, 694 nm and 28 ns. Fluences described as similar, within 6 to 10 J/cm², not documented identical for each pair. Changed: Nominal spot diameter 5.0 versus 6.5 mm. Exact paired fluences and overlap not reported.

Nominal diameter only; no measured beam profile or output calibration. Repeated observations: 12 paired lesions, two halves per lesion and four reader scores. Main comparison follows one treatment.

Yu 2018 [40] Prospective randomized within-lesion, evaluator-blinded comparison of single pass and double pass 595-nm PDL, with an untreated adjacent control region; immediate histology in a two-patient volunteer subset. Independent units: Twenty-one patients for clinical outcomes; only two volunteer patients with flat purple PWS for histology. All 21 contribute the reported visual comparison (4 favor double pass, 4 favor single pass, 13 tied); no attrition is

Matched: Same 595-nm Vbeam platform, nominal 1.5-ms pulse duration and cryogen spray/delay 40/20 ms. Single-pass settings matched the first pass of the double pass region: 10-mm spot at 10 J/cm² or 7-mm spot at 12 J/cm². The double pass second exposure used the same stated spot option at 9 or 11 J/cm², respectively. Adjacent test regions had similar size and were in the same subanatomical region, with approximately 0.5 cm untreated separation. Three treatment sessions two months apart, with clinical assessment three months after the final session. Changed: One pass versus two passes, with a 30-minute interval containing ice-bag cooling; the second pass used 1 J/cm² lower radiant exposure than the first and a distinct intended endpoint (darkening existing purpura). Increased cumulative exposure is intrinsic to this strategy, not an uncontrolled confounder. The study does not isolate interval, cooling, or pulse number at equal cumulative energy.

Nominal spot diameters and commercial device reported; no independently measured spatial beam profile, energy calibration at the treatment plane, beam width convention or pulse waveform reported. Repeated observations: Two treated regions and an untreated region within each patient's lesion; three sessions per treated region. Histologic fields and vessels are nested within biopsies from two people; five randomly selected fields per specimen were averaged. These are not independent patients.

reported.

Noormohammadpour 2021 [41]

Randomized within-patient split-lesion comparison, described by the authors as double-blind; 24 treatment-naive PWS patients, three monthly treatment sessions and assessment one month after the final session. Independent units: 24 patients; each contributes paired single pass and double pass lesion portions. All 24 completed treatment.

Matched: Within-patient lesion comparison; same anatomical subregion intended; nominal 595 nm and 7-mm spot, 10% spot overlap and cryogen setting; short-pass 1.5-ms/11-J/cm² settings identical; three monthly sessions. Changed: Addition of a 20-ms/13-J/cm² first pass, total number of passes/nominal cumulative exposure, pulse-duration sequence, 20-minute interval and icepack cooling history.

Nominal settings only; no measured spatial profile or independent delivered-energy/diameter calibration. Repeated observations: Two paired portions of each PWS, repeated treatment over three sessions, and multiple photographs/dermoscopic views do not constitute independent patient replications.

TABLE 8: Design and exposure comparison

Study	Outcome and timing	Supported interpretation and limits
Dinehart 1994 [18]	Text gives FWHM 4.7 to 4.8 mm; source Figure Two labels 4.6 and 4.8 mm at 5.0 and 7.5 J/cm ² . Full widths at 1/e were 5.1 and 5.2 mm, not 1/e ² widths. Two patients had scarring or textural change, nine hyperpigmentation and four temporary hypopigmentation. Pigment changes were recorded at two months; Methods describes assessment at 6 to 8 weeks and two further months. The ten paired comparisons reported no adverse-effect difference without event counts or effect estimates.	Peripheral intensity decline provides an optical rationale for overlap on this platform. The clinical observations describe outcomes with the tested pattern and exposure ranges. Limit: No isolated profile comparison or demonstrated safety equivalence. The retrospective series had no concurrent control; the ten paired comparisons lacked random allocation, masking, event-count and uncertainty details. No quantified clearance comparison or injury-depth measurement. The authors did not establish an optimal overlap.
Jackson 1996 [17]	Optical footprint and spatial distribution; 2-mm biopsies immediately after exposure. Measured 5-mm nominal footprints 5.8, 5.7, 4.8 and 4.9 mm, with reported area differences about +35%, +30%, -8%, -4%.	Equal nominal settings do not guarantee equal delivered footprints/profiles across equipment. Limit: Neither the equipment comparison nor histology isolates profile shape as the cause of a clinical difference; actual area and other optical features differ. No matched randomized clinical profile comparison, no long term harm outcome. Source's area-to-fluence percentage interpretation should not be reused.
Keijzer 1991 [21]	Modeled deposition rates: vessel about 22.0 to 65.4 W/cm ² . No temporal temperature history, heat diffusion or biological follow up.	Source geometry and scattering alter target-to-epidermal optical deposition, even when surface irradiance is reduced. Limit: Not a pure equal-irradiance comparison in the cited matched-epidermis example; not a clinical dose prescription or a thermal injury simulation. Infinite rectangular cross-section differs from circular clinical spots.
Saghafi 2006 [19]	Modeled intensity distributions; qualitative clinical improvement claim in 25 patients treated at two-week intervals. No standardized quantitative clearance, adverse-event denominator or defined final follow up.	At equal power, narrowing a spot changes irradiance as well as the modeled spatial deposition; source geometry is a mechanistic variable. Limit: Not a controlled clinical demonstration of profile superiority. Equal power is not equal irradiance. Threshold-defined depth must not be interpreted as intrinsic tissue optical penetration length. No full thermal model.
Kositratna 2016 [30]	Lesion depth and diameter by NBTC histology after post-exposure freezing/processing the following day. At 0 versus +3 mm, total injury depth 1700 versus 680 µm and diameter 248 versus 359 µm. Optical propagation measured independently.	Controlled focal deviation changes injury geometry for this optical system at unchanged nominal pulse energy/scanner settings. Limit: Only two donors and nested lesions; frozen/thawed tissue, no perfusion or clinical follow up. Optical diameter, ablative diameter and combined ablation/coagulation diameter are distinct. Not a universal displacement conversion or patient complication estimate.
Immediate residual thermal-damage		

Ross 1999 [34]	histology; immediate and day-1 NBT viability; clinical/histologic healing on days 1, 5, 21 and 42. Rapid overlap increased residual injury/cell-death depth in several comparisons; ordinary 2-4 passes did not consistently increase residual thermal damage.	Spatial overlap and temporal revisit pattern jointly affect acute injury; ordinary passes cannot be equated with rapid re-exposure. Limit: One animal; site-level statistics cannot establish between-animal reproducibility. Several timing/density variables differ. No universal safe overlap level or human complication rate.
Fitzpatrick 1999 [35]	Biopsy immediately after final exposure. H&E-based crater/vaporization depth and residual altered-collagen depth. Ablation approached a plateau after about three to four passes while thermal injury increased with stacking.	Total pulse count/nominal exposure does not determine ablation and residual injury equivalently; treatment history matters. Limit: Unreported donor n, ex vivo tissue, incomplete independence, no patient healing or scarring endpoint. Stacking/pass comparisons entail timing and tissue-cleaning differences. Microscopist blinded to settings except pass count.
Grover 1999 [36]	Excisional biopsy during flap redraping at the same surgery; no quantified delay or long term endpoint. At separate preauricular 30% sites, means were 41, 52, 86 μ m for one/two/three passes; 60% sites 43, 76, 121 μ m. Published 'cumulative' values 179 and 240 μ m are sums of these separately treated-site means.	Density/pass regimens produced different measured acute histologic depths; the reported cumulative sums are not measured three-pass depths or incremental ablation values. Limit: Small n, fixed-side allocation, site heterogeneity, uncertain measurement reproducibility and exclusion of two observations including the only reported reticular-dermal injury. Histology cannot establish universal clinical safety.
Koster 2001 [37]	Histology 24 hours after laser treatment; depth from dermoepidermal junction to deepest necrotic vessel. Full versus single: +0.61 mm, 95% CI 0.37-0.85, p=.0003; 30% versus single: +0.48 mm, 95% CI 0.23-0.73, p=.0019. No destruction of dermal collagen/elastin at this exposure.	Overlap can deepen a vascular histologic effect without severe damage to connective tissue under this tested regimen. Limit: Normal skin differs from PWS target physiology; source itself discusses possible differing reactive hyperemia. No clinical clearance or delayed fibrosis assessment. Overlap changes repeat exposure and cumulative energy; 0.3 Hz is not near-instantaneous stacking.
Rohrer 2004 [38]	Two blinded investigators assessed vessel clearance/density at one and six weeks. Mean six week clearance 87.6% stacked versus 67.4% single. One marked edema on stacked side; no reported purpura, pigment change or scars.	The studied endpoint-guided stacked protocol improved observed short term clearance at the same per pulse settings. Limit: Small completed sample, short follow up, no supplied dispersion or paired clearance effect confidence interval. Higher cumulative exposure is intrinsic to the pulse-count intervention, not an extraneous confounder. The study does not compare with a higher-fluence single pulse or estimate an isolated pulse-interval effect at equal total energy; endpoint-based stopping also belongs to the tested protocol.
Wang 2026 [29]	Three blinded dermatologists graded photographic GAIS; final efficacy/satisfaction assessment 12 months after final treatment. No significant between-side clearance difference. PIH 4/84 versus 19/84, scabbing 8/84 versus 52/84, reported by the source p=.0008 and <.001 (larger/lower-fluence first). Adverse events recorded with daily first-week and then monthly photographs plus visit confirmation. PIH resolved over 6-12 months; scabs resolved within one to two weeks (primary report, journal p. 712).	The larger spot/lower-exposure/without whitening protocol had similar observed clearance and fewer reported adverse-event observations under the complete tested regimen. Limit: Not isolated spot size causation; no prespecified equivalence/noninferiority proof in main report. McNemar's test named for categorical outcomes, but handling of within-person repeated sessions in aggregated adverse-event denominators is not fully explained. Two noncompleters; effect precision cannot be reconstructed as if observations were independent.
Peters 2012 [39]	Two blinded dermatologists, patient global assessment and L*a*b reflectance spectroscopy at three months after the second treatment. No significant between-regimen difference in assessed clearance. One slightly atrophic scar occurred at a double pass site and persisted at one year; pigment changes occurred at both sites in five participants and resolved during follow up.	No additional improvement in measured clearance was detected with the tested six-minute double pass regimen in this selected treatment-resistant PWS population. Limit: Small selected sample, per-protocol analysis, fixed settings and two treatment sessions. No equivalence proof and no general conclusion that repeat exposure cannot benefit other vascular targets or timing regimes. Different per pulse exposure means it does not isolate interval alone at equal total dose.

Laubach 2007 [44]	Punch biopsies immediately after each exposure, overnight dispase and NBTC processing; epidermal injury diameter and area. Mean diameter 93 to 147 μ m from 0 to 45 °C; no healing follow up.	At unchanged nominal energy/density, initial tissue temperature alters epidermal lesion dimensions in this ex vivo setup. Limit: Unreported donor replication, no physiological thermal gradient/perfusion, no dermal three-dimensional lesion assessment and no clinical outcome. Excluding overlapping lesions may bias estimated total injured area. Cannot derive a universal cooling-energy conversion or efficacy recommendation.
Jo 2015 [26]	Whole-axilla photographic hair clearance was assessed by three evaluators blinded to participant, side and photograph chronology; paired Wilcoxon testing. At one month after session 3, mean clearance was 65.5% for D1 versus 77.4% for D3 ($p=.022$); at three months, 38.7% versus 50.1% ($p=.028$). Pain immediately after the first session was greater with D3: mean VAS 4.3 versus 3.1 for D1 ($p=.009$). One participant developed PIH bilaterally after session 3; no other serious adverse events were reported. Six-month observations were available in only three participants and are not full-cohort durability evidence.	At matched nominal fluence, pulse duration and cooling setting, the larger rectangular handpiece produced greater observed axillary hair clearance and more procedural pain in this small within-person comparison. This is a more tightly controlled clinical spatial-delivery contrast than protocols that simultaneously change fluence and endpoint. Limit: Small, single-indication population; limited full-cohort follow up and no blinded operator. The paper explicitly notes that operator-applied pressure may influence results. Random-sequence generation and concealment details were not reported. Area, aspect ratio and handpiece all change; measured beam-profile equivalence and independently verified optical output were not shown. The comparison does not establish a universal spot size effect across lasers or a fluence reduction rule giving equal efficacy. Higher pain and one bilateral PIH event preclude describing the larger handpiece as simply safer. Absence of rare harms in ten participants is not proof of safety.
Nehal 1996 [28]	At four to eight weeks after one treatment, mean ordinal lightening grades were equal in five lesions, higher with 6.5 mm in five and higher with 5.0 mm in two. Three lesions had equal adverse changes in both halves: hyperpigmentation in two; tattoo darkening and hypertrophy in one.	Small descriptive comparison with mixed direction of response; no demonstrated uniform advantage of larger spots. Limit: No formal statistical test, confidence interval or equivalence margin. Short follow up, mixed diagnoses, incompletely matched exposure, and subsequent treatment selected by early response.
Yu 2018 [40]	At three months after the third session, no statistically significant paired clinical advantage was detected for double pass: source-caption mean blanching 32.12% (SD 15.31) single versus 30.73% (SD 16.10) double, $p>0.05$; visual score 3.10 (SD 0.72) versus 3.10 (SD 0.77), $p>0.05$. Immediate first-session histology in two patients showed mean thrombus/thermal-damage depth 0.388 versus 0.386 mm, with qualitatively greater vessel-wall injury after double pass. Five patients had blistering/crusting at double pass sites, and three patients with extremity lesions had PIH at both treated sites that resolved within six months.	Under this 30-minute, actively cooled, short-pulse PDL strategy in previously untreated PWS, an added pass did not yield a detected clinical benefit despite qualitatively greater acute vessel-wall injury in a very small histology subset. This is a defined negative strategy comparison, not evidence that all repeated-pulse or double pass regimens fail. Limit: Small clinical sample, two histology donors, limited precision and no equivalence/noninferiority analysis. Mean histologic thrombus depth is not measured optical penetration depth or an intrinsic penetration limit of 595-nm light. Immediate biopsy cannot establish delayed vascular remodeling. Pulse count, second-pass exposure, endpoint and intervening cooling jointly define the assigned strategy; efficacy and harms cannot be generalized to different intervals, pulse durations, lesion histories or devices.
Noormohammadpour 2021 [41]	One month after three monthly sessions, mean colorimetric blanching was 48% with two passes versus 37% with one ($p = 0.001$); ordinal photographic improvement 3.79 versus 3.33 ($p = 0.008$). Crusting and purpura in all patients; hyperpigmentation in both portions in one patient and only the portion receiving two passes in another.	In this randomized within-patient study of treatment-naïve PWS, adding the specified long-pulse prepass plus 20-minute icepack interval to a short-pulse regimen improved one-month observed colorimetric and photographic blanching after three sessions. This is a particular repeated-delivery strategy effect, not a universal advantage of double passing. Limit: The study does not isolate interval, pulse duration, extra energy, number of passes or cooling; does not directly demonstrate increased penetration/coagulation depth; and does not establish equal long term safety. Dermoscopic linear-vessel patterns are surrogate morphology, not histological vessel-depth measurements. The proposed mechanism was not directly observed.

TABLE 9: Outcomes and limits of inference

MTZ: microscopic treatment zone; PWS: port wine stain; ABNOM: acquired bilateral nevus of Ota-like macules; PIH: postinflammatory hyperpigmentation. Results are reported from the sources, not pooled estimates. Session counts are not converted to individual patient risks. No clinical conversion factors are derived from the models.

Outcomes and Interpretation

Locations Within the Primary Reports

Journal and supplied PDF page numbers are distinguished because delivery covers may shift numbering. Locations for the open access Jo report refer to XML sections rather than an independently inspected PDF. Peters was assessed in the university thesis chapter reprint; the citation follows the published author order.

Dinehart 1994 [18]

Journal p. 277/PDF p. 4: identity, abstract and nominal 5-mm spot; p. 278/PDF p. 5: Figure One apparatus, full optical and clinical methods, FWHM body statement, central $\pm 5\%$ region, overlap rationale and clinical sample; p. 279/PDF p. 6: Figures Two-Four, graph-specific widths, idealized overlap patterns, clinical adverse events and ten-patient comparison; p. 280/PDF p. 7: explicit uncertainty about clinical significance, optimal overlap not determined, non-additivity assertion, and complete references.

Reporting limit: No reported pulse duration, temporal waveform, repetition frequency/inter-pulse interval, cooling setting, treatment-session spacing, lesion demographics/phototypes, exact achieved overlap, independent energy calibration, detector model/responsivity, or full 2-D profile. No independent replication across units or fibers. No randomized or blinded clinical comparison, patient level paired adverse-event counts, efficacy scale, power calculation or confidence interval. Completeness of extended follow up and the relationship of the 10 paired patients to the 135-person series are unclear.

Jackson 1996 [17]

Journal p. 1000/PDF p. 4: optical methods begin; p. 1001/PDF p. 5: eight volunteers, 24 biopsies, immediate timing and area Results; pp. 1002-1003/PDF pp. 6-7: limitations and profile figures.

Reporting limit: No waveform characterization; the source itself states pulse duration and wavelength were not evaluated as outcome determinants.

Keijzer 1991 [21]

Journal p. 602/PDF p. 5: geometry, footnote on rectangular source, numerical estimates; pp. 603-604/PDF pp. 6-7: 22.0 and 65.4 W/cm³; pp. 604-605/PDF pp. 7-8: no heat diffusion/coagulation modeled.

Reporting limit: No clinical outcome by design.

Saghafi 2006 [19]

Article/PDF pp. 1-2: abstract and 25 patients; p. 4: 12-W statement; pp. 5-9: analytic homogenizer and 15-W/10-kHz source; p. 10: equal-power 5/10-mm comparisons; p. 11: brief clinical protocol.

Reporting limit: Clinical allocation, baseline comparability, standardized endpoints, outcome distributions, harms and final follow up not sufficiently reported.

Kositratna 2016 [30]

Journal p. 556/PDF p. 5: two donors and exposure controls; p. 557/PDF p. 6: repeats, timing, definitions and knife-edge method; p. 558/PDF p. 7: lesion results and Gaussian/knife-edge analysis; p. 560/PDF p. 9: Figure Six and clinical limitation.

Reporting limit: Pulse duration/complete waveform and two dimensional profile at the treatment plane not reported in the compared experiment.

Ross 1999 [34]

Journal pp. 104-105/PDF pp. 5-6: animal, devices, Tables One, Two, schedule; p. 106/PDF p. 7: histologic definitions and viability; pp. 107-109/PDF pp. 8-10: injury, pass-count and healing tables.

Reporting limit: No independently measured profile at the treatment plane; limited independent biological replication.

Fitzpatrick 1999 [35]

Journal pp. 615-617/PDF pp. 4-6: sample counts, Table One, preparation/timing/blinding and endpoint definitions; pp. 618-621/PDF pp. 7-10: plateau and accumulating injury.

Reporting limit: Independent donor count, full spatial profile and patient outcomes absent.

Grover 1999 [36]

Journal pp. 2247-2248/PDF pp. 4-5: seven patients, allocation and methods; pp. 2248-2250/PDF pp. 5-7: results and Tables One, Two, sums and exclusions; pp. 2253-2254/PDF pp. 10-11: separate contemporaneous Burns discussion also questions variability and cumulative interpretation.

Reporting limit: Precise inter-pulse/inter-pass timing, independently measured beam profile and long term clinical safety not reported.

Koster 2001 [37]

Journal p. 177/PDF p. 5: participants, device and 24-hour sampling; p. 179/PDF p. 7: ten patient rows and tissue findings; p. 180/PDF p. 8: Table Two paired estimates; p. 181/PDF p. 9: normal skin/PWS and follow up limitations.

Reporting limit: No measured profile, clinical efficacy assessment or delayed follow up.

Rohrer 2004 [38]

Journal p. 164/PDF p. 5: allocation, device/cooling, two-to-four-pulse endpoint, follow up and withdrawals; p. 165/PDF p. 6: Table One, harms and four-pulse ceiling; p. 167/PDF p. 8: epidermal cooling and discussion.

Reporting limit: Random-sequence generation/concealment detail, spatial profile measurement and complete paired uncertainty estimates not supplied. The abstract states three/four pulses; this extraction follows the Methods, which specify two/three/four.

Wang 2026 [29]

Journal p. 709/PDF p. 5: enrollment, intervals, final follow up and allocation; p. 710/PDF p. 6: protocol and follow up methods; p. 711/PDF p. 7: statistical methods and completers; p. 712/PDF p. 8: Table One and outcome interpretation; p. 713/PDF p. 9: 750-ps pulse duration.

Reporting limit: Supplementary methods were not assessed. The main report describes blistering on higher fluence sides but later states that no blistering occurred. Those inconsistent statements do not establish absence of blistering.

Peters 2012 [39]

University of Amsterdam thesis Chapter 6 reprint: PDF p. 5/thesis p. 118: selection, allocation, settings, cooling and timing; PDF p. 6/p. 119: endpoints and paired Wilcoxon/per-protocol analysis; PDF p. 7/p. 120: participant table; PDF p. 8/p. 121: spectroscopy n=15, between-regimen null finding and scar follow up, visually verified; PDF p. 9/p. 122: limitations. Article metadata verified separately against PubMed and publisher-deposited Crossref: Lasers Surg Med 2012, 44(3), 199-204, published online 23 February 2012.

Reporting limit: The thesis chapter reverses the first two authors, who contributed equally. The reference follows the published PubMed and Crossref order, Peters followed by van Drooge.

Laubach 2007 [44]

Journal p. 15/PDF p. 2: full methods, temperature levels, 48 MTZs, overlap exclusion; p. 16/PDF p. 3: diameter/area results and figures; p. 17/PDF p. 4: explicit limitations.

Reporting limit: Independent donor count, beam metrology, pulse waveform and clinical outcomes not reported.

Jo 2015 [26]

Open-access Europe PMC JATS full text, retrieved 1 October 2026: MATERIALS AND METHODS / Subjects: independent n, ages, skin types and eligibility; / Laser hair removal in the axilla: random side assignment, both handpiece dimensions, fluence/duration ranges, cooling and delivery schedule; / Efficacy and safety assessment and / Statistics: blinded whole-axilla hair counts, pain timing and paired analysis. RESULTS /

Efficacy of hair removal with LPDL: one- and three-month clearance, six-month n=3; / Discomfort and adverse events: pain and bilateral PIH. DISCUSSION, limitations paragraph: operator nonblinding and pressure. Figure Two caption distinguishes n=10 through three months from n=3 extended follow up. Journal citation: *Ann Dermatol* 2015;27(5):517-522. Locators refer to XML sections, not visually checked PDF pages.

Reporting limit: No profile map at the treatment plane or independent output calibration; no detailed randomization/concealment method or paired effect confidence interval. Pulse waveform and actual overlap distribution were not measured. The demographic table is supplied as a raster image in the XML; demographic claims here use the explicit Methods text. Complete article prose, abstract, reference list and figure/table captions were read; no claims were inferred from unread image-only table values.

Nehal 1996 [28]

Journal p. 683/PDF p. 4: identity and abstract. p. 684/PDF p. 5: full protocol, Table One and Table Two. p. 685/PDF p. 6: Results and Figure One. p. 686/PDF p. 7: Discussion and references.

Reporting limit: No precise paired fluence table, beam measurement, overlap fraction, pulse timing, phototype distribution, allocation randomization or assessor masking. Patient 8 has an ambiguous later treatment count; the primary one treatment assessment is used.

Yu 2018 [40]

Journal p. 305/PDF p. 4: identity and abstract; p. 306/PDF p. 5: eligibility, randomization, Table One, laser parameters, cooling, biopsy and evaluation methods; p. 307/PDF p. 6: paired analysis, sample-size statement, demographics and Figure One numerical outcomes; p. 308/PDF p. 7: lesion distribution, clinical comparison and two-patient histology; p. 309/PDF p. 8: adverse events, untreated 0.5-cm buffer and discussion; p. 310/PDF p. 9: Figures Six, Seven histology; p. 311/PDF p. 10: limitations, conclusion, funding and disclosure; p. 312/PDF p. 11: publication dates and remaining references.

Reporting limit: No independently measured profile, delivered-energy calibration, repetition frequency, within-pass overlap, total pulses/treated area, spot-option allocation counts, or per-patient settings. No allocation-concealment detail, blinded histology statement, numerical histology paired uncertainty, exact between-arm p values or confidence intervals. Blistering/crusting count for the single-pass arm is not explicitly given. Full-cohort six-month follow-up is not documented, although the three PIH cases are said to recover within six months. Two different trial-registration identifiers are printed. Assessor specialty is described inconsistently as plastic surgeons in Methods and dermatologists in Results.

Noormohammadpour 2021 [41]

PDF p3/e122: title/DOI, abstract unit typo, trial description/registration. PDF p4/e123: eligibility, randomization, full laser/cooling/overlap protocol, endpoint scales, sample-size/statistical methods, participant numbers. PDF p5/e124: all numerical comparative outcomes, Figures One, Two, adverse events. PDF p6/e125: Figures Three-Five, mechanistic interpretation and limitations/conclusion. PDF p7/e126: references 1-19 completed.

Reporting limit: Small one-centre sample; treatment-naïve population unlike resistant-PWS comparisons; one-month final follow up; fixed settings despite lesion/phototype heterogeneity; unspecified device, measured beam parameters and achieved overlap; incomplete colorimetric/dermoscopic metric definitions; patient/operator masking and allocation concealment unspecified; supplemental demographics not available; no paired effect CI or adequately powered safety equivalence.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Stefan Bigge

Acquisition, analysis, or interpretation of data: Stefan Bigge

Drafting of the manuscript: Stefan Bigge

Critical review of the manuscript for important intellectual content: Stefan Bigge

Disclosures

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