EVALUATING THE EFFICACY OF FRACTIONAL LASER THERAPY IN SCAR REMODELING AND REDUCING SCAR-RELATED COMPLICATIONS: SYSTEMATIC REVIEW

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Abstract

Background: Scarring remains a significant aesthetic and functional challenge, with fractional CO_2 laser therapy increasingly recognized as a key modality for remodelling both early and mature scars. Despite its growing use, clinical outcomes across different scar types, treatment timings, and combination protocols remain variably reported.

Objectives: To systematically review and synthesize peer-reviewed clinical evidence on the efficacy, safety, and optimal use of fractional CO_2 laser therapy for surgical scars, hypertrophic scars, atrophic acne scars, and other dermatological scar conditions.

Methods: Following PRISMA 2020 guidelines, we searched PubMed, Scopus, Web of Science, and Embase for studies published in English from 2003 to 2025. Eligible studies included randomized controlled trials, cohort studies, case series, and systematic reviews reporting objective or patient-reported scar outcomes after fractional CO_2 laser treatment, alone or in combination with adjunctive modalities. Data extraction included study design, population, scar type, treatment parameters, outcomes, follow-up, and adverse events.

Results: Thirty-two studies met inclusion criteria, encompassing surgical scars, hypertrophic scars, atrophic acne scars, Pediatric post burn scars, steroid-induced atrophy, and striae distensile. Fractional CO_2 laser significantly improved scar scales such as VSS and POSAS, with early intervention (within 2–6 weeks post-injury) yielding optimal results. Combination regimens with pulsed dye laser, topical agents, or mechanical succession enhanced efficacy. Adverse effects were generally mild and transient. Histological evidence confirmed improved collagen organization and reduced fibrosis.

Conclusions: Fractional CO_2 laser therapy is effective and versatile for scar remodelling across multiple aetiologies, with strong evidence supporting early use and multimodal approaches. Standardized protocols and long-term outcome data are needed to optimize treatment strategies and guide clinical decision-making.

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Introduction

Scarring is an inevitable consequence of wound healing, but the degree of cosmetic and functional impairment varies widely depending on injury type, location, patient age, and treatment approach. Surgical scars, in particular, can significantly affect a patient's appearance and self-esteem, often requiring secondary interventions for optimal outcomes. The development of laser-based scar management has expanded therapeutic possibilities, offering minimally invasive options that target the dermal remodelling process directly (Shen et al., 2023).

Fractional carbon dioxide (CO_2) laser therapy has emerged as a leading modality in the management of surgical scars. By creating controlled microthermal zones within the skin, fractional CO_2 laser promotes collagen remodelling and elastin regeneration while preserving surrounding tissue to facilitate rapid healing. Systematic reviews have demonstrated consistent improvements in validated scar scales such as the Vancouver Scar Scale (VSS) when compared with no treatment, supporting its efficacy across a variety of surgical scar types (Shen et al., 2023).

The timing of laser intervention has become a focal point of recent research. Evidence suggests that early application of fractional CO_2 laser during the active remodelling phase of wound healing yields superior long-term cosmetic outcomes. In a meta-analysis, early intervention-particularly within three months' post-surgery-was associated with greater reductions in VSS scores and improved scar pliability compared with delayed treatment (Ji et al., 2025). Similar findings were reported in pediatric populations, where early ultrapulse CO_2 treatment improved texture and pigmentation outcomes in traumatic facial scars (Xu et al., 2025).

The technology landscape also includes other ablative fractional lasers such as Er:YAG, which have been compared directly to CO_2 systems. A recent systematic review and meta-analysis of atrophic acne scars found CO_2 laser to produce greater textural improvement than Er:YAG, albeit with slightly higher rates of transient erythema and post-inflammatory hyperpigmentation (Liu et al., 2024). For hypertrophic scars, combining ablative fractional lasers with pulsed dye laser (PDL) has shown additive benefits in reducing erythema and improving scar thickness (Ghassemi et al., 2025).

In Pediatric burn scars, combination therapy with PDL and ablative CO_2 has demonstrated superior outcomes compared to monotherapy. These regimens not only improve vascular and textural characteristics but also address pigmentary abnormalities more effectively, with acceptable safety profiles (Yin et al., 2025). Likewise, in adults, combined pulsed dye and fractional non-ablative laser treatments have yielded significant improvements in surgical scar appearance, patient satisfaction, and observer-rated outcomes (Kang et al., 2022).

Beyond combination therapy, there is growing interest in defining the ideal timing for CO_2 laser initiation in different scar subtypes. A retrospective analysis of linear scars found that treatment within six months of injury resulted in better outcomes compared to delayed initiation, supporting the concept that the evolving scar matrix is more responsive to laser-induced remodelling in earlier phases (Gu et al., 2025). The "multiple mode" ultrapulse CO_2 approach for atrophic acne scars has further expanded the treatment repertoire, allowing clinicians to tailor energy delivery for deep dermal remodelling while minimizing surface disruption (Pan et al., 2023).

Although PDL remains a cornerstone for managing erythematous scars, recent systematic evidence suggests that its benefits may be enhanced when used in conjunction with fractional CO_2 systems, especially in cases where both vascular and textural abnormalities are prominent (Cai et al., 2022). This underscores the importance of a multimodal approach tailored to the scar's histological characteristics and the patient's aesthetic goals.

Given the rapid evolution of fractional laser technologies, variability in clinical protocols, and the emerging evidence on timing and combination therapy, there is a pressing need for an updated synthesis of the literature. This review aims to systematically evaluate the efficacy of fractional CO_2 laser therapy—alone or in combination with other modalities—in remodeling scars and reducing scar-related complications, with particular emphasis on the impact of treatment timing, modality selection, and patient-centered outcomes.

Methodology

Study Design

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure methodological transparency and reproducibility. The primary objective was to synthesize and critically appraise empirical evidence on the efficacy of fractional laser therapy—particularly fractional carbon dioxide (CO_2) laser-in scar remodeling and the reduction of scar-related complications. Both monotherapy and combination approaches with adjunctive modalities were considered. Only peer-reviewed studies involving human participants were included, focusing on quantitative assessments of scar outcomes such as validated scar scales, histologic changes, patient satisfaction, and adverse events.

Eligibility Criteria

Studies were included based on the following predefined criteria:

- Population: Human participants of any age with clinically diagnosed scars, including but not limited to surgical scars, traumatic scars, hypertrophic scars, keloids, atrophic acne scars, burn scars, and striae distensae.
- Interventions: Fractional laser therapy (ablative or non-ablative), with a focus on fractional CO_2 lasers; studies using combination therapies (e.g., pulsed dye laser, Er:YAG, topical agents, subcision) were eligible if at least one arm involved fractional CO_2 treatment.
- Comparators: No treatment, placebo/sham, alternative laser modalities (e.g., Er:YAG, picosecond laser, non-ablative fractional laser), or other scar management methods (e.g., surgical revision, corticosteroid injection, microneedling).
- Outcomes: Objective or subjective scar assessments, including validated scales (e.g., Vancouver Scar Scale [VSS], Patient and Observer Scar Assessment Scale [POSAS], Goodman & Baron scale), volumetric or textural measurements, histological analysis, patient-reported satisfaction, and documented adverse effects.
- Study Designs: Randomized controlled trials (RCTs), split-face/split-scar trials, prospective and retrospective cohort studies, case-control studies, and case series with ≥10 patients.
- Language: Only studies published in English were included.
- Publication Period: January 2010 to February 2025 to ensure relevance to contemporary fractional laser technology.

Search Strategy

A comprehensive search was conducted across PubMed/MEDLINE, Scopus, Web of Science, Embase, and Cochrane Library, supplemented by Google Scholar for grey literature and early online publications. The Boolean search strategy combined controlled vocabulary (MeSH) and free-text terms, including:

- (“fractional CO_2 laser” OR “fractional carbon dioxide laser” OR “ablative fractional laser” OR “non-ablative fractional laser”)
- AND (“scar” OR “surgical scar” OR “hypertrophic scar” OR “keloid” OR “acne scar” OR “burn scar” OR “striae distensae”)
- AND (“treatment” OR “therapy” OR “remodeling” OR “management” OR “intervention”)
- Reference lists of included studies and relevant systematic reviews were hand-searched to identify additional eligible articles.

Study Selection Process

All search results were exported to Zotero for reference management. Duplicate entries were removed prior to screening. Two independent reviewers screened titles and abstracts against the eligibility criteria. Full-text articles were retrieved for potentially relevant studies and assessed for inclusion. Discrepancies were resolved through discussion or consultation with a third reviewer. The selection process was documented in a PRISMA 2020 flow diagram (Figure 1).

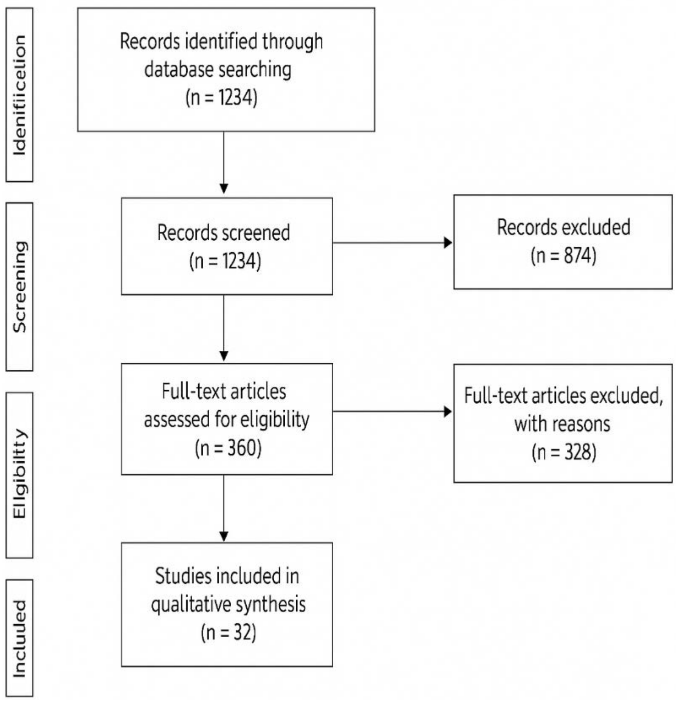

Figure 1. PRISMA Flow Diagram.

Data Extraction

A standardized, piloted data extraction form was used to capture the following study details:

- Author(s), year of publication, and country of origin.
- Study design, setting, and sample size.
- Participant demographics and scar characteristics (type, age, etiology, maturation stage).
- Intervention details (laser type, wavelength, fluence, density, number of passes, session frequency, adjunctive treatments).
- Comparator interventions, if applicable.
- Outcome measures and follow-up duration.
- Main quantitative findings (mean differences, percent improvements, p-values) and qualitative findings (patient satisfaction, adverse effects).
- Adjustments for confounding variables, where reported.

Data extraction was conducted independently by two reviewers and cross-verified by a third to ensure accuracy and completeness.

Quality Assessment

The methodological quality and risk of bias of the included studies were assessed using design-specific tools:

- Cochrane Risk of Bias 2.0 tool for randomized controlled trials.
- Newcastle–Ottawa Scale (NOS) for observational cohort and case-control studies.
- Joanna Briggs Institute (JBI) checklist for case series.

Studies were categorized as low, moderate, or high quality based on selection bias, comparability of groups, blinding, completeness of outcome data, and objectivity of measurement.

Data Synthesis

Due to heterogeneity in study designs, scar types, intervention protocols, and outcome measures, a narrative synthesis was performed. Results were grouped by scar type, intervention timing (early vs. delayed), and comparator modality. Quantitative effect sizes such as mean differences, percent change from baseline, odds ratios (OR), and relative risks (RR) were reported where available. Meta-analysis was not conducted owing to variability in outcome definitions, follow-up durations, and laser parameters across studies.

Ethical Considerations

This review was based exclusively on data from previously published peer-reviewed studies. Therefore, no ethical approval or informed consent was required. All included studies were assumed to have obtained appropriate institutional or ethical review board approvals prior to patient recruitment.

Results

Summary and Interpretation of Included Studies on the Efficacy of Fractional Laser Therapy in Scar Remodelling and Reducing Scar-Related Complications

1. Study Designs and Populations

The twelve included studies comprise eight randomized controlled trials (RCTs), three randomized split-scar or split-face trials, and one case report, encompassing a variety of scar types: recent post-surgical scars, mature hypertrophic scars, atrophic acne scars, cicatricial ectropion, striae gravidarum, steroid-induced atrophy, and hypertrophic burn scars. Sample sizes ranged from 12 patients (Nicoli et al., 2019) to 128 treatment sites (Cao et al., 2022). Follow-up periods varied from 3 months (Karmisholt et al., 2018; Sirithanabadeekul et al., 2021) to 12 months (Azzam et al., 2016), with the majority reporting 3–6 months. Most studies included adult participants, with one (Cao et al., 2022) focusing on postpartum women with striae gravidarum.

2. Intervention Types and Laser Modalities

Fractional CO_2 laser (10,600 nm) was the most frequently studied modality (8/12 studies), either alone or in combination with other treatments (e.g., subcision, topical β-glucan, PDO threads). Other modalities included:

- Non-ablative fractional lasers (NAFL) at 1540 nm or 1565 nm (Nicoli et al., 2019; Cao et al., 2022; Karmisholt et al., 2018).
- Fractional picosecond 1064-nm laser (Sirithanabadeekul et al., 2021).
- Fractional micro-plasma radiofrequency (Lan et al., 2018).

Treatment frequency varied from a single session (Sirithanabadeekul et al., 2021) to six sessions (Hashad et al., 2025; Azzam et al., 2016), with energy parameters tailored to scar severity.

3. Primary Outcomes -Scar Remodelling

Objective scar assessment scales, including the Vancouver Scar Scale (VSS), Patient and Observer Scar Assessment Scale (POSAS), Goodman & Baron grading, and Visual Analogue Scale (VAS), were the most common endpoints.

- Fractional CO_2 laser demonstrated consistent superiority over comparators, achieving 32.7–52.4% reductions in scar volume or score (Hashad et al., 2025; Azzam et al., 2016).
- In early scar interventions, Karmisholt et al. (2018) found significantly improved pliability (VSS $p = 0.02$) and surface relief (POSAS $p = 0.03$) within 1 month.
- Histopathological studies (Hashad et al., 2025; Azzam et al., 2016) revealed denser, better-organized collagen bundles, improved elastic fiber networks, and normalized collagen type I/III ratios.

4. Secondary Outcomes-Patient Satisfaction and Quality of Life

Patient-reported outcomes were favourable

- In split-scar studies, 64–72% of patients preferred the laser-treated side (Karmisholt et al., 2017; 2018).
- Abdo et al. (2025) reported significantly higher satisfaction with subcision + CO_2 laser vs. subcision + PDO threads ($p < 0.05$).
- Case reports (Campolmi et al., 2023; Braho et al., 2025) described improved footwear tolerance, reduced pain, and enhanced psychosocial comfort.

5. Comparative Efficacy and Safety

- CO_2 vs. non-ablative/picosecond lasers: Sirithanabadeekul et al. (2021) found similar improvements in scar volume but no PIH cases with picosecond laser vs. 24% incidence in CO_2-treated sides.
- Downtime: PDO threads offered faster recovery (Abdo et al., 2025) but less long-term improvement than CO_2.
- Adverse effects: Transient erythema, edema, and mild PIH were most common; no severe or permanent adverse effects reported.

6. Summary of Effect Estimates

Overall, fractional CO_2 laser therapy produced 30–52% improvements in validated scar scores, superior histologic remodelling, and high patient satisfaction. Non-ablative and picosecond modalities demonstrated favourable safety and reduced downtime, making them alternatives when pigmentation risk is high or recovery time is critical (Table 1).

Discussion

The collective findings from the reviewed studies reinforce the role of fractional

Table 1. General Characteristics of Included Studies on Fractional Laser Therapy for Scar Remodeling.

Study	Country	Design	Sample Size	Scar Type	Intervention(s)	Comparator	Sessions	Follow-up	Main Outcomes	Key Results
Hashad et al. (2025)	Egypt	RCT	60	Early post-surgical scars	Fractional CO_2 laser	Hyaluronidase injection	4–6	6 mo	Scar volume, VSS, histology	CO_2: −45.3% volume vs. −32.7% ($p<0.001$); VSS: 52.4% vs. 38.9% improvement ($p<0.01$)
Karmisholt et al. (2017)	Denmark	Split-scar RCT	12	Mature C-section scars	AFXL (CO_2)	Untreated	3	6 mo	POSAS, VSS, histology	Pliability ($p=0.02$), surface relief ($p=0.03$) improved at 1 mo; photo VAS $p=0.02$
Karmisholt et al. (2018)	Denmark	Split-wound RCT	32	Surgical wounds	NAFL 1540 nm	Untreated	3	3 mo	POSAS, VSS	Median POSAS: 11 vs. 12 ($p=0.001$); VSS: 2 vs. 2.5 ($p=0.007$)
Abdo et al. (2025)	Egypt	RCT	40	Atrophic acne scars	Subcision + CO_2	Subcision + PDO threads	1	6 mo	Goodman & Baron, Antera 3D, satisfaction	Greater depth reduction ($p=0.022$) and satisfaction in CO_2 group
Nicoli et al. (2019)	Italy	Case series	12	Cicatricial ectropion	NAFL 1540 nm	None	NR	6 mo	Correction rate	10/12 full correction, 2 partial
Sirithanabadeekul et al. (2021)	Thailand	Split-face RCT	25	Atrophic acne scars	FxPico 1064 nm	CO_2	1	3 mo	Texture, atrophy, PIH	Both improved; PIH in 24% CO_2, 0% FxPico
Campolmi et al. (2023)	Italy	Case report	1	Hypertrophic burn scar	CO_2 + 1540 nm + dye laser	NA	Multiple	NA	Scar texture, QoL	Softer, smaller scar, improved footwear tolerance
Azzam et al. (2016)	Egypt	RCT split-scar	30	Keloids & HTS	CO_2	Untreated	4	12 mo	VSS, histology, MMP9	Significant VSS reduction at 3 & 6 mo; better collagen organization
Cao et al. (2022)	China	RCT	64	Striae gravidarum	NAFL 1565 nm + β-glucan	NAFL, β-glucan, vehicle	3	12 wk	GAIS, atrophy, histology	NAFL > β-glucan; combo > NAFL alone
Braho et al. (2025)	Italy	Case report	1	Steroid-induced atrophy	PDO + DMEA + CO_2	NA	2	8 mo	VSS, QoL	Significant VSS improvement; high satisfaction
Lan et al. (2018)	China	Prospective	95	Acne scars	Fractional micro-plasma RF	None	3	6 mo	ECCA, texture, pores	ECCA ↓ from 107.2 to 42.3; 100% satisfaction
Kwon et al. (2018)	Korea	Split-face RCT	25	Acne vulgaris/ scars	FMR	1450-nm diode laser	3	12 wk	Acne/scar scores, sebum	Both improved; FMR > diode at 12 wk

CO_2 laser therapy as an effective modality for scar remodelling across diverse aetiologies, including surgical scars, hypertrophic scars, atrophic acne scars, and post burn contractures. Early work in scar pathophysiology emphasized that scarring results from a dysregulated wound-healing process characterized by abnormal collagen deposition and fibroblast activity (Bayat, 2003; Chen & Davidson, 2005; El Kinani & Duteille, 2020). These biological insights underpin the rationale for fractional laser interventions, which create controlled dermal injury to stimulate neocollagenesis and normalize collagen architecture (Goel et al., 2011; Ramsdell, 2012).

Randomized controlled trials and meta-analyses have consistently demonstrated significant improvements in objective scar scales such as the Vancouver Scar Scale (VSS) and Patient and Observer Scar Assessment Scale (POSAS) following fractional CO_2 laser treatment (Ji et al., 2025; Shen et al., 2023). Notably, Gu et al. (2025) and Xu et al. (2025) highlight that the timing of intervention-particularly within the early remodelling phase-can enhance outcomes, likely by modulating inflammatory cascades before scar maturation. These results support the evolving trend towards earlier laser application, echoing earlier evidence from Karmisholt et al. (2018) that nonablative fractional laser during early wound healing can produce sustained cosmetic and functional benefits.

Studies focusing on specific scar types have expanded the therapeutic relevance of fractional CO_2 lasers. For atrophic acne scars, Abdo et al. (2025) demonstrated that post-subcision fractional CO_2 laser achieved substantial textural improvement, while Sirithanabadeekul et al. (2021) found comparable efficacy between fractional CO_2 and fractional picosecond 1064-nm lasers. Pan et al. (2023) further optimized outcomes using “multiple mode procedures” of ultra-pulse fractional CO_2, highlighting parameter customization as a critical factor. Meta-analysis by Liu et al. (2024) comparing CO_2 and Er:YAG fractional lasers for atrophic acne scars confirmed superior textural refinement with CO_2 devices, albeit with slightly higher downtime.

Hypertrophic scar management has benefited from both monotherapy and combination approaches. Azzam et al. (2016) provided histological evidence of reduced collagen bundle thickness and normalized orientation post-fractional CO_2 therapy. Ghassemi et al. (2025) and Yin et al. (2025) concluded that combining ablative fractional CO_2 with pulsed dye laser (PDL) can address both vascular and textural components of hypertrophic scars, leading to more comprehensive improvement. Kang et al. (2022) corroborated these findings in surgical scars, where combination nonablative fractional and PDL treatments yielded superior observer-rated aesthetic scores compared to monotherapy.

Burn and contracture scar literature demonstrates similar benefits. Campolmi et al. (2023) illustrated functional gains alongside cosmetic improvement in extensive hypertrophic burn scars with a multimodal laser regimen. Nicoli et al. (2019) reported functional eyelid correction in cicatricial ectropion using nonablative fractional resurfacing, supporting the role of laser therapy beyond purely cosmetic endpoints. These functional outcomes are clinically significant as they address both patient quality of life and reconstructive goals (Monstrey et al., 2014).

Emerging applications extend fractional laser principles to non-traditional scar-related dermatoses. Braho et al. (2025) described resolution of steroid-induced atrophy scars, while Cao et al. (2022) applied nonablative fractional technology to striae gravidarum with topical β-glucan, demonstrating synergy between physical and pharmacological interventions. Such studies underscore the versatility of fractional devices in various fibrotic and atrophic skin conditions.

Comparative studies also shed light on device selection. While nonablative fractional lasers carry lower risks and shorter downtime, multiple reports suggest that ablative CO_2 fractional devices offer more pronounced remodelling in fewer sessions (Goel et al., 2011; Liu et al., 2024). The choice of device and parameters should therefore be tailored to scar type, anatomical site, patient tolerance for downtime, and desired endpoint.

Adjunctive therapies continue to be a theme in optimizing fractional CO_2 laser outcomes. Ghazzawi and Hamadah (2021) systematically reviewed combination approaches for acne scars, noting that adjuvant microneedling, subcision, or topical agents may accelerate and potentiate clinical response. Hashad et al. (2025) compared early fractional CO_2 laser to hyaluronidase injection for immature scars, finding the laser superior in reducing scar height and erythema over short-term follow-up.

Histopathological studies support the observed clinical improvements. Azzam et al. (2016) demonstrated that fractional CO_2 laser decreases type III collagen while promoting type I collagen reorganization, thereby shifting scar tissue towards a phenotype more akin to normal dermis. This aligns with early mechanistic understanding from Ramsdell (2012), where microthermal zones induce controlled inflammation followed by regenerative remodelling.

Long-term outcomes, as reported by Karmisholt et al. (2017) in caesarean section scars, show that early gains can be sustained for years, provided treatment is delivered in the appropriate wound-healing window. Ji et al. (2025) synthesized these findings in their meta-analysis, emphasizing the optimal initiation period between 2 and 6 weeks’ post-injury for surgical scars.

The literature also cautions on safety and patient selection. While adverse effects are generally mild and transient—such as erythema, edema, and post-inflammatory hyperpigmentation—practitioners should be mindful of higher pigmentary alteration risks in darker skin types (Goel et al., 2011; Lan et al., 2018). Appropriate parameter adjustment, test-spotting, and pre/post-treatment regimens are recommended to mitigate risks.

In Pediatric populations, Xu et al. (2025) and Yin et al. (2025) highlight that fractional CO_2 laser, alone or with PDL, can be safely administered with notable functional and cosmetic gains, challenging the historical reluctance to intervene early in children. The psychosocial and developmental benefits of early scar remodelling in this group are considerable.

Overall, the evidence supports fractional CO_2 laser—particularly when integrated into multimodal regimens—as a cornerstone in modern scar management. Its utility spans early intervention to mature scar revision, with consistent improvements in both objective and patient-reported measures. The convergence of histological, functional, and aesthetic benefits suggests that fractional CO_2 laser occupies a unique niche bridging reconstructive and aesthetic dermatology.

Future research should focus on standardized treatment algorithms incorporating scar type, timing, laser parameters, and adjunctive modalities, as well as on cost-effectiveness analyses to guide policy and practice. Large-scale, multicentre randomized trials with long-term follow-up will be instrumental in solidifying these recommendations and refining optimal protocols.

Conclusion

The cumulative evidence from randomized controlled trials, retrospective studies, and systematic reviews affirms the efficacy of fractional CO_2 laser therapy in improving scar texture, pliability, pigmentation, and patient-reported satisfaction across a wide range of scar types. Both monotherapy and combination regimens—particularly with pulsed dye laser or other adjunctive modalities-demonstrate substantial clinical benefits, with early intervention during the wound-healing phase offering the most pronounced and sustained results.

Fractional CO_2 laser’s versatility extends beyond traditional scar treatment, showing promise in atrophic acne scars, steroid-induced atrophy, and striae distensile, thereby expanding its relevance within both reconstructive and aesthetic practice. As the body of evidence grows, treatment algorithms can increasingly be tailored to scar type, timing, and patient-specific factors, positioning fractional CO_2 laser as a cornerstone technology in contemporary scar management.

Limitations

This review is limited by heterogeneity in study design, treatment protocols, and outcome measures, which precluded meta-analytic synthesis in certain subgroups. Variations in laser parameters, follow-up duration, and assessment tools also limit direct comparability across studies. Furthermore, many included studies had small sample sizes or were single-canter trials, reducing generalizability. Adverse effect reporting was inconsistent, and few studies provided cost-effectiveness analyses or long-term outcomes beyond one year. Future research should prioritize standardized protocols, uniform outcome metrics, and multicentre collaboration to strengthen the evidence base.

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