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Review Article

EFFICACY OF FRACTIONAL LASERS- ABLATIVE AND NON-ABLATIVE IN TREATING PHOTO AGEING, A SYSTEMIC REVIEW

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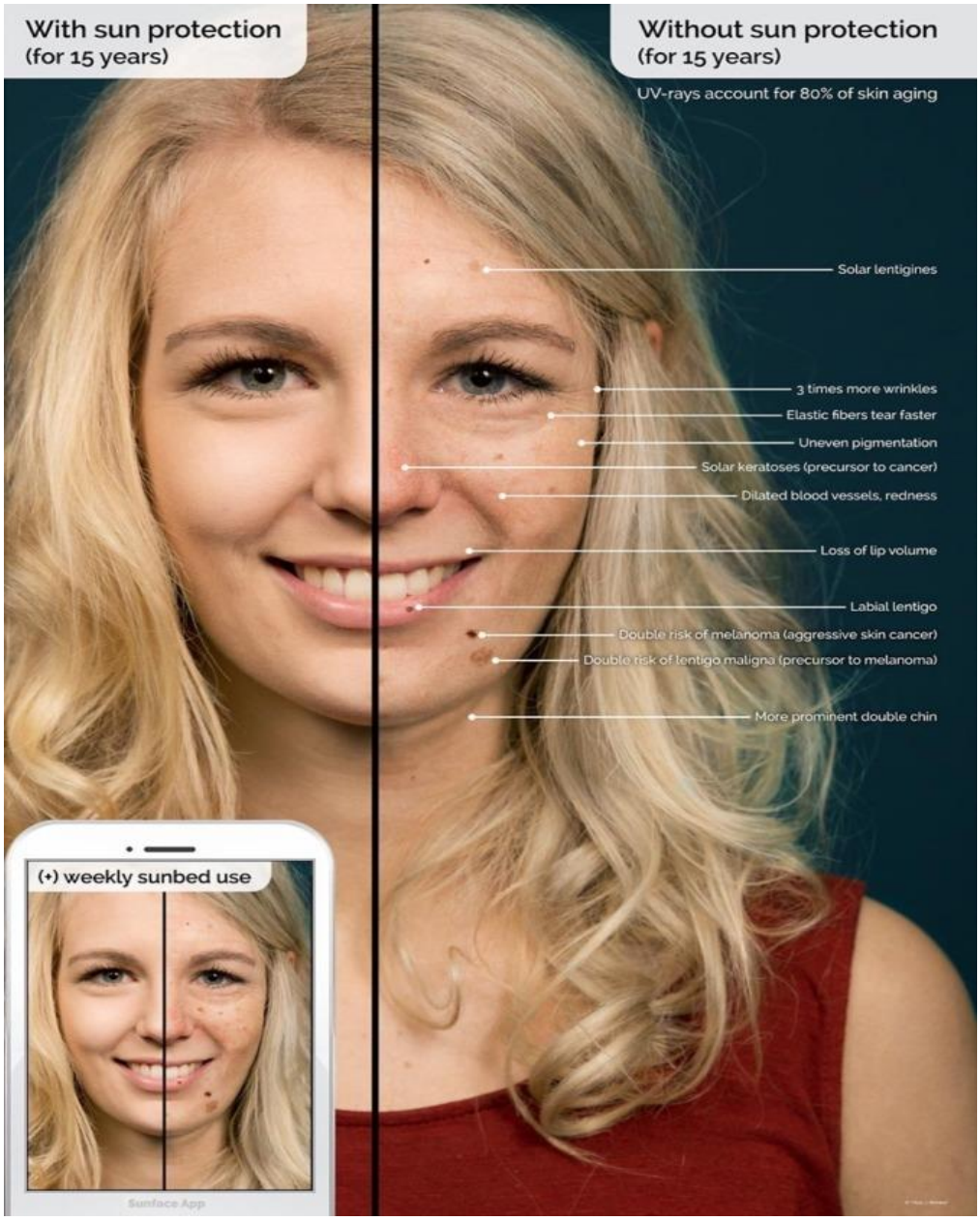
ABSTRACT

Photo ageing also known as dermatoheliosis is a term used for the characteristic changes to skin induced by chronic UVA and UVB exposure. The deterioration of biological functions and ability to manage metabolic stress is one of the major consequences of the aging process. It affects people of all ages regardless of age, sex or race. Roughness, Wrinkles, Pigment, Laxity and Pore size of skin are the consequences of photo damage. Which is a major concern in esthetic point of view. As the advancement in laser technology many devices have been developed which made the patient as well as the practitioner to decide which the most appropriate device for concerned issue is. The review provides an up-to date test of the efficacy of the two interventions in treating photo-ageing and also promotes sun protective behaviors to reduce UV exposure and consequent sunburn experience amongst adults and youths.

Keywords: Ablative Fractional Laser, Non Ablative Fractional Laser, Laser Resurfacing, Photo-ageing.

INTRODUCTION

Photo ageing is caused due to continuous, long-term exposure to ultraviolet (UV) radiation of approximately 300-400nm. [1] Which results in Roughness, Wrinkles, Pigment, Laxity, increase in elastin and collagen damage and increased Pore size of skin leading to a major esthetic concern affecting peoples' Physiological and Psychological wellbeing. Skin is the outermost layer of the body and the epidermal layer does not contain any blood vessels or nerve endings but melanocytes and basal cells are embedded in this layer. UV rays are of two types UVA and UVB, UVA rays are able to penetrate deeper into the skin as compared to UVB rays. UVB cause the formation of freckles and dark spots, both of which are symptoms of photo aging. Whereas, UVA rays affects the epidermal layer and the dermal layer causing the epidermis to start drooping off the body and can lead to dilated or broken blood vessels which are most commonly visible on the nose and cheeks. Treatment and intervention for photo aging can be classified into a unique paradigm based on disease prevention. Primarily it can be treated by sun avoidance, sun protective clothing, and sunscreens. Secondarily, by using Retinoid (e.g. tretinoin), Antioxidants (e.g. topical vitamin C, oral supplements, CoQ10, Lipoic acid), Estrogens, and Growth factors and cytokines and Teritiarily by Chemical peels, Resurfacing Technologies (e.g. micro-dermabrasion), ablative or non-ablative laser resurfacing, radio-frequency technology, soft tissue augmentation (also known as fillers) [2], and botulinum toxins.



Signs, Symptoms and histopathology:

Early symptoms of photo aging:

- Dyspigmentation and the formation of wrinkles around regions of skin commonly exposed to sun, namely the eyes, mouth and forehead. [3]
- Spider veins on face and neck
- Loss of color and fullness in lips

Symptoms of photo aging attributed to prolonged exposure to UV:

- Wrinkles deepen and forehead frown lines can be seen even when not frowning.
- Telangiectasia's (spider veins) most commonly seen around the nose, cheeks and chin.

- Skin becomes leathery and laxity occurs.
- Solar lentigines (age spots) appear on the face and hands.
- Possibly pre-cancerous red and scaly spots (actinic keratosis) appear.
- Cutaneous malignancies

In this article we are discussing about Tertiary treatment of Photo aging with Resurfacing Technologies (micro-dermabrasion) with Fractional ablative lasers (AFL) and non-ablative fractional lasers (NAFL) and to find which is more efficient.

Fractional Laser Technology: Fractional laser treatment works by targeting both the epidermis and dermis. It does this by delivering a laser beam that is divided into thousands of tiny but deep columns of treatment into the skin. These are called micro thermal treatment zones (MTZs). [13] Within each MTZ old epidermal pigmented cells are expelled and penetration of collagen in the dermis causes a reaction that leads to collagen remodeling and new collagen formation. By using MTZs, the laser targets and treats intensively within the zone whilst surrounding healthy tissue remain intact and unaffected and helps heal the wound. This fractional treatment results in a faster healing process than if all tissue in the treatment area was exposed to the laser.

Non-Ablative Fractional Laser Technology: Non-ablative lasers such as Cool Touch, Fraxel Restore and N-lite are far less invasive than ablative treatments. They work by heating up the targeted tissue, without actually destroying it. [4] This process stimulates body's collagen production to fill in unwanted skin imperfections such as fine lines or wrinkles. [4]

Nonablative Fractionated Lasers

Wavelength & Type	Manufacturer & Product	Key Features
1410 nm	Solta Fraxel re:fine	700 μm depth; 20 mJ / MTZ
1440 nm Nd:YAG	Cynosure Affirm	1,000 micro-pulses / 10-mm spot
	Palomar StarLux	Includes both 1440- and 1540-nm handsets
1540 nm	Palomar StarLux	Includes both 1540- and 1440-nm handsets
	Palomar Icon	Includes 2940 nm fractional ablative handset
1550-nm Erbium glass and 1927-nm thulium fiber	Solta Fraxel re:store and re:storeDUAL	1550 nm:1.4 mm depth; 70 mJ / MTZ 1927 nm:0.23 mm depth; 20 mJ / MTZ

MTZ, microscopic treatment zone.

1550 nm erbium glass non-ablative fractional laser

Ablative Fractional Laser Technology:

Ablative Fractional Lasers are more invasive and they work by vaporizing the outer layer of skin, this process causes the skin to heal and restructure, and increases collagen production. [5]

In 2007, Hantash et al. [6] first described the use of an "ablative" CO2 fractional resurfacing device (AFP), which produces an array of micro thermal zones of a customizable density and depth, with a confluent pattern of ablation and coagulation extending from the stratum corneum through the dermis [6]. In the initial in vivo studies demonstrating the histologic and clinical effects of this device, Hantash et al. confirmed with immunohistochemistry that collagen remodeling occurred for at least 3 months post treatment [6].

Ablative Fractionated Lasers

Wavelength and type	Manufacturer & Product	Key Features
10,600-nm fractional CO_2	Alma Lasers, Inc. Harmony Platform Pixel CO_2	Short/medium/long pulses; 300–2,500 mJ/p; multiple "pixel" tips
	Cynosure, Inc. SmartSkin	150–20,000-μs pulses; up to 30 W power; multiple scanning patterns
	DEKA SmartXide DOT 30 W/50 W	0.2-μs–80-μs pulse; 150 W to tissue; multiple scanning modes
	Ellman International, Inc. Elluminé Fractional CO_2 laser system	2–7-ms pulse; up to 105 mJ
	Focus Medical NaturaLase CO_2	Up to 10-ms pulse; 50 W
	Hironio Co., Ltd. MIXEL	Up to 5000-μs pulse; 60 mJ; 2- × 2- to 20- × 20-mm scan size
	ILOODA CO., Ltd. Fraxis	0.1–5-ms pulse; up to 30 W
	Lasering USA Slim Evolution II MiXto Pro	2.5–16-ms CW chopped pulse; 0.5–30 W; 180-μm or 300-μm spot size
	Lumenis Ultrapulse Encore (Active FX/ Deep FX/ Total FX)	<1-ms pulse; 240 W to tissue; Active FX mode with 1.3-mm spot size; Deep FX with 0.12-mm spot size; Total FX combining Active FX and Deep FX
	Lumenis AcuPulse MultiMode	CW scanning robot-assisted laser; 0.01–1.00-s pulse; 30 W and 40 W models available; 1.3-mm and 0.12-mm spot sizes in one handpiece
	Lutronic eCO_2	2–240 mJ; "controlled chaos technology" promotes heat dissipation
	Solta Fraxel re:pair	Up to 70 mJ/MTZ; "intelligent optical tracking system"
	Syneron & Candela CO2RE	60 W; 7 different treatment modes

10 600 nm CO2 fractional ablative laser

However, the comparison of the effectiveness of Ablative fractional lasers and non-ablative fractional lasers were not always consistent. Therefore, a systematic review and meta-analysis are needed to deal with this issue.

MATERIAL AND METHOD

A systematic literature search for Specified question was formulated according to the Population, Intervention, Control and Outcome (PICO) format was used to define Is Ablative Fractional laser (AFL) more efficient than the Non Ablative Fractional Laser (NAFL) in Biological and Esthetic point of view to treat Photo

damage also called as photo aging of Skin? A comparative clinical studies involving Patients treated with Photo damage of skin (P) with different Fractional lasers (I) Ablative fractional Laser or Non ablative Fractional laser (C) and the Outcome Concerning their efficiency in treating Roughness, Wrinkles, Pigment, Laxity and Pore size of skin (O)

Different protocols, patient selection, treatment techniques, and complications are discussed for each system.

Study subjects:

An Electronic search of the PUBMED,ELSILVER, OVID and Cochrane library databases was performed using specific search terms using Boolean logic which is combining Medical subject Headings (Mesh), and looked up the words in text word, abstract, title, and combined Mesh with all word, abstract and title like this Ablative[TIAB] AND "Non-ablative"[TIAB], Ablative[TIAB] AND "Non-ablative"[TIAB] AND Meta-Analysis[ptyp], ("fractional lasers"[TIAB] OR "fractional laser"[TIAB]) AND (Photo aging[TIAB] OR rejuvenation[TIAB] OR ageing[TIAB] OR aging[TIAB] OR “resurfacing” [TIAB]), ("fractional lasers"[TIAB] OR "fractional laser"[TIAB]) AND (Photoaging[TIAB] OR rejuvenation[TIAB] OR ageing[TIAB] OR aging[TIAB]) AND Meta-Analysis[ptyp]. Published in English up to December 2018 according to stated, scientific research methods, and designed to minimize biases and errors inherent to traditional, narrative reviews.

The study also used explicit and justified criteria for the inclusion or exclusion of any study according to the criteria and did a clear presentation of characteristics of each study which is included in our thesis and an analysis of methodological quality was performed as well.

INCLUSION CRITERIA:

Published randomized controlled trials (RCTs), cluster randomized controlled trials (CRTs), and non-randomized controlled before-after studies (CBAs) comparing either two or more types of interventions with each other or one or more intervention with no intervention or standard practice (control group) were included in this review.

We will be reviewing abstracts of the retrieved studies with the following criteria:

1. Patients who had received treatment of Photo ageing with ablative Fractional laser.
2. Patients who had received treatment of Photo ageing Non ablative Fractional laser.
3. RCTs comparing photo ageing treatment with ablative fractional laser with non-ablative fractional laser.
4. Studies containing sufficient raw data reporting photo ageing treatment of Ablative or Non ablative Fractional laser for the weighted mean difference (WMD) with 95 % confidence intervals.

Exclusion Criteria:

1. The use of any other medication for the treatment,
2. Any Existing skin pathology,
3. or animals research and,
4. If there is any incorrect data reported.

RESULT

In the initial screening 216 articles were found, of which 45 studies were selected and after an evaluation of their titles and abstracts. Full articles were analyzed, the search results of 19 articles studies (10 AFL, and 9NAFL) were involved comprising of 383 subjects according to our inclusion criteria are considered eligible in the review. Reasons for the exclusion of articles that did not fulfill the inclusion criteria are clearly explained above. There are many limitation in this review that are different frequency and number of settings for treatment.

Comparison and assessment of Parameters (wrinkle, Roughness, Pigmentation, Laxity, Pore size) is performed in both the Fractional lasers (AFL and NAFL)

Study characteristics:

The main characteristics of included studies are detailed in Table1.

Study	Total	Female	Male	skin type	mean age	laser
1 H. M. Lee et al.	29	28	1	III-IV	41.6 years	Fractional erbium: YAG laser (2,940nm)
2 LAPIDOTH ET AL	28	27	1	II-IV	54.2 year's	Fractional erbium: YAG laser (2,940nm)
3 F. Prignano et al	18	18	0	N/R	55 years	Fractional carbon dioxide laser (SmartXide DOT, DEKA M.E.L.A)
4 G. H. Sasaki et al.	72	65	7	III-IV	58.4 years	Ultra Pulse® CO2 Laser System (Lumenis Inc., Santa Clara, CA, USA)
5 El-Domyati et al	6	3	3	III-V	44years	Fractional Er: YAG 2940 nm Dualis XS
6 Stebbins & Hanke et al	10	10	0	I-III	57.7 years	DOT AF CO2 laser
7 AVRAM ET AL	5	5	0	I-II	57 years	Fractional carbon dioxide laser
8 M. T. Clementoni et al	24	24	0	II-III	47.3 years	Fractional carbon dioxide laser
9 KARSAI ET AL	28	26	2	I-III	46.1 years	Fractional carbon dioxide laser & Er: YAG 2940
10 Francesca Prignano et al	12	12	0	II-III	55 years	Fractional carbon dioxide laser
11 BOEN ET AL	4	0	4	II-III	54+/-11 years	Fractional 1,927nm thulium fiber laser
12 S. M. Lee et al	52	50	2	III-IV	34.1 years	(1550-nm erbium-doped laser/ 1927-nm thulium fiber) fractional laser
13 MARMON ET AL	10	10	0	III-V	30.6 years	1,440-nm diode-based

fractional laser						
14 SUKAL ET AL	31	N/R	N/R	I-IV	55.3 years	Fractionated1, 550-nm erbium-doped fiber laser
15. N. S. Sadick & B. Smoller	9	N/R	N/R	I-III	57years	Fractionally delivered 1550 nm erbium-diode fiber laser
16. P. L. Bencini et al.	18	18	0	N/R	(50.1years	Fractionated 1540-nm erbium-glass fiber laser
17 Regia Celli Patriota de Sica1 et al	15	15	0	II-III	56.4 years	Fractionated 1550 nm Erbium Glass Laser
18. FRIEDMANN ET AL	16	16	0	II-IV	49.6 years	Novel 1,565nm Non-Ablative Fractional Erbium-Doped Fiber Laser
19. M. W. Kroon et al.	14	14	0	II-V	35+/-4 years	Non-ablative 1550 nm fractional laser
19 studies	387 subjects 367females 20males					

N/R- not reported.

Table 1: Baseline Characteristics of subjects (N=684)

DISCUSSION

As the world is modernizing demand of interventions to treat photo damage caused by UV rays has increased tremendously which resulted in development of many interventional devices like Ablative and non-ablative lasers and later development of fractional technology which bridged the gap between these two interventions has made patients researchers as well as practitioners a bit confused as which intervention is more efficient with less adverse effects to treat photo ageing. As Clear and complete reporting is a key condition for replicable and cumulative science [7] If the attempt to tackle photo ageing through laser intervention is to be taken seriously, methodology and reporting was needed to improve. Better reporting will make it easier at the stage of evidence synthesis to conclude what is more effective.

We have performed a systematic review of the different types of laser currently employed for Fitzpatrick skin I-VI rejuvenation with fractionated technology either ablative or non-ablative in different regions of the body like head, neck, facial, hand, peri orbital region in both the sex male and female in different races Caucasians, African as well as Asians and evaluated as well as analyzed the outcomes of each study to report which fractionated laser technology is more efficient to treat photo ageing and reporting of adverse effect post treatment was also included.

Total 19 articles were included after inclusion and exclusion criteria which matched our requirement for the evaluation and analysis. There were 367 females and 20males in our study amounting to 387 subjects.

Subjects who took AFL treatment were total 214 of which 203 were females and 11 were male in 10 studies, whereas subjects who undertook NAFL were 169 studies of which 163 were females and 6 were male in 9 studies.

As flaws in the design, conduct and analysis of RCT (Randomized control trial) can lead to bias, we appropriately considered risk of bias when assessing studies.

AFL resurfacing was performed using fractional erbium: YAG laser (2,940nm), and fractional carbon dioxide laser whereas NAFL was performed using fractional 1,927nm thulium fiber laser, 1550-nm erbium-doped laser, 1,440-nm diode-based fractional laser, Fractionated 1540-nm erbium-glass fiber laser and Novel 1,565nm Non-Ablative Fractional Erbium-Doped Fiber Laser.

Different protocols, patient selection, treatment techniques, and complications are discussed for each system in the result section. Parameters assessed were Roughness, Wrinkles, Pigmentation, Laxity, Skin Pore size, PIH in each study.

Post-inflammatory hyper pigmentation (PIH) is the most common complication of fractional laser resurfacing. Appropriate pre-operative and post-operative skin care and selection of lower density settings over a greater number of treatments while allowing for full recovery between sessions play a critical role in decreasing this complication.

We found from one of the articles that Hypertrophic scarring (HS) is a significal potentially Permanent complication of ablative Fractional C02 laser particularly on the neck and Subjects who underwent a higher energy but low density treatment had a lower risk of getting PIH, than those who underwent a lower energy and higher density treatment. Therefore, use of adequate parameter laser, the risk of PIH in darker skin can be significantly reduced. Regarding scalp, the male scalp undergoes extensive photo damage due to high prevalence of androgenic alopecia and exposure to UV Radiation present as solar lentigens, fire rhytides and keratosis.

Regarding hand skin rejuvenation paucity of pilosebaceous units and superficial dermal vessels located on the dorsum of the hand [8]**.** Additionally, the dermis of the hand has an estimated thickness of 1.2 mmatage25, decreasing to 0.75 mm by the age of 70 [9]. This is in comparison to a dermal thickness of facial skin approximating 1.375 mm on the forehead and 0.975 mm on the mental region [10] Thus, the lower number of pilos sebaceous units and a thinner dermis of the hand are believed to contribute to protracted wound healing as well as the potential for scarring and pigmentary alterations after treatment settings that would normally be well tolerated by facial skin.

Non-ablative fractional methods have been reported to be effective and to have limited side effects, but they failed to achieve results comparable to those of conventional Ablative techniques, which finally led to the development of ablative fractional devices. [**11]** laser that can be used to create both small diameter (120 μ m) deep columns of ablation and superficial large (1.3 mm) ablation can lead to good results on A clear statement of review's essential findings is given by summarizing via tables which aims to prove the efficiency

of the two lasers and help the people make better informed decisions in choosing one for the treatment of photo ageing.

The safety of the use of a skin resurfacing laser in darker skin types (type IV–VI) is always a controversial issue. As the risk of complications is greater than in skin type's I–III, due to trapping of the laser energy by the melanin pigment causing the generation of thermal energy in the epidermis. This leads to a greater risk of post-inflammatory hyper pigmentation and skin burns in darker skin types. The reduced risk of hyper pigmentation seen with fractionated non ablative lasers compared with fractional ablative lasers enables the safe application of laser technology for skin resurfacing in Fitzpatrick skin types IV–VI.

Ablative FLT may induce fibrosis, whereas treatment with non-ablative FLT does not. Whether formation of fibrosis has to be regarded as dermal remodeling or a subtle subclinical form of scarring should be investigated in future research

Appendices were created which can be considered supplementary material when published which expose the detailed search strategies, detailed statistical methods used, and Data Extraction forms.

Limitation of study:

The study has limitations as fractional lasers differ in terms of wavelength, spot size, pulse duration, intensity, density, and cooling mechanism, which influences the histological depth difference extents with respect to the dosage and depth achieved, It is important to realize that different patients have different morphological types and grades and it is difficult to get satisfactory treatment in single treatment option and multiple settings is required.

Most studies did not provide sufficient information about intervention procedures and components, and, therefore, it was difficult to determine exactly what interventions consisted of. One limitation to this review is the exclusive focus on published trials. While standard tests (e.g., funnel plot inspection;

Egger's regression shift with the inclusion of un published materials. Moreover, more sophisticated analyses of the effect of methodological quality on effect sizes would be desirable. But the level of reporting and the limited test) do not show evidence of possible publication bias, it is possible that the effect size estimates would number of high quality trial included in this review did not allow for such analyses.

CONCLUSION

Utilizing the correct treatment plan and respecting the unique characteristics of each skin type will allow the laser surgeon to safely and effectively treat photo damage of skin with both non-ablative and ablative fractional Laser resurfacing technique. In general, a greater number of lower density NAFL treatment administered over a longer time period should be the primary therapeutic modality for the Asian patient. Ablative options should be chosen only for those patients who fail to achieve satisfaction following non-ablative treatment. We observed that Both fractional Non Ablative laser as well as fractional ablative laser are effective and safe modalities for the treatment of photo ageing, However, these data analysis suggests better clinical

efficacy with the use of ablative laser, but it is found to be taking more time for recovery and with higher side effects.

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