

CASE REPORT**Fluorescent light energy: Treating rosacea subtypes 1, 2, and 3**

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Key Clinical Message

Kleresca® biophotonic platform utilizing fluorescent light energy effectively decreased the inflammatory and erythematous reaction common in rosacea subtypes 1, 2, and 3. Kleresca® may be considered as a single treatment for rosacea, targeting multiple features, or combined with invasive methods for an enhanced normalizing and healing profile of the skin.

KEYWORDS

biophotonic platform, chromophore, erythema, fluorescent light energy, inflammation, rosacea, subtype 1, 2, and 3

1 | INTRODUCTION

Rosacea is a chronic inflammatory skin condition that primarily affects the central face and eyes. Its prevalence is increasing, with 5% of women and almost 4% of men in the 45–60 age group affected, and greater incidences in Fitzpatrick phenotypes I–II.¹ This is a complex disorder with many predominant features including: transient or persistent erythema, flushing, telangiectasia, inflammatory pustules/papules, and phyma.² As many features of rosacea often occur together, upon clinical examination they are usually grouped into subtypes.³

Subtype 1 - erythematotelangiectatic rosacea (ETR) - is characterized by flushing and persistent erythema with visible telangiectasias. Inflammatory papulopustular rosacea (PPR) with persistent erythema and occasional papules and pustules is typical of subtype 2. Subtype 3, the least common form of rosacea, is known as phymatous rosacea (PHR), characterized by skin thickening, often of the nose, which can be grossly disfiguring. Ocular rosacea (OR), or subtype 4, leads to dry eyes, tearing, blurring, and swelling.³ ETR and PPR are the most common of the four subtypes.⁴

Within a given subtype, the key clinical symptoms can be mild, moderate, or severe, and can be progressive, with the development of additional features.⁵ The overlap of rosacea features among subtypes^{6,7} shows that irrespective of the subtype, most patients at some point will present with transient or persistent erythema.⁴ Indeed, this is a key diagnostic sign of rosacea when we consider the updated classification system.^{7,8} Furthermore, although inflammation may not be clinically visible in all presentations of rosacea, it is reported to be biochemically detectable underpinning the continuum of the condition.⁸

While the etiology of rosacea is still not completely understood, exaggerated responses to “triggers” (eg ultra violet light, wind, alcohol, spicy food and stress), altered immunity and aberrant vascular control are known to play a role in the pathophysiology of this condition.⁹ In addition to trigger avoidance, the most common treatment for rosacea is pharmacological intervention, including systemic and topical agents. To target certain features such as erythema and telangiectasia energy-based devices are often applied, including laser and intense pulsed light treatment. While these have been beneficial in treating some features of rosacea, no single treatment is completely effective.^{6,10}

Recently, a novel biophotonic platform - Kleresca® biophotonic platform (consisting of a multi-light emitting diode (LED) lamp and proprietary chromophore containing gel) utilizing fluorescent light energy (FLE) - has emerged as a new therapy for treating inflammatory skin conditions.¹¹⁻¹⁵ Beneficial effects of FLE, such as reducing inflammation and associated redness have been reported in acne vulgaris¹³⁻¹⁵ and PPR.¹² Further, FLE also has skin healing and rejuvenating properties as a stand-alone treatment¹⁶ or when used as a post interventional therapy.¹⁷

This study sought to expand the original reports of the benefit of FLE in PPR to other 'subtypes' of rosacea. We investigated a role for FLE in targeting inflammation and erythema in rosacea subtype 1, 2, and 3.

2 | MATERIALS AND METHODS/ CASE REPORTS

All procedures were carried out with prior, informed consent and in accordance with the Declaration of Helsinki and the International Conference of Harmonization (ICH) Guidelines for Clinical Practice.

2.1 | Case report 1: erythematotelangiectatic rosacea

A 52-year-old female patient with ERP was treated with the Kleresca® biophotonic platform. Briefly, a 2 mm-thick layer of the photoconverter chromophore gel (Kleresca® Acne treatment) was applied to the patient's cleansed face and subsequently illuminated with a blue multi-LED Kleresca® lamp (Kleresca® Light, Ballerup, Denmark) using the therapeutic mode of the lamp (wavelengths of 415 and 447 nm) for 9 minutes.¹² Two successive treatments were completed in one session, once per week for three consecutive weeks.

2.2 | Case report 2: papulopustular rosacea

A 36-year-old female patient with PPR who had previously been unsuccessfully treated with topical metronidazole and topical ivermectin underwent the FLE treatment as described in case 1.

2.3 | Case report 3: phymatous rosacea

A 54-year-old male patient with PHR was treated with FLE as described. This patient received two successive treatments in one session, once per week for eight consecutive weeks.

In all cases, standardized photographs were taken with a multispectral camera with fixed settings and in a constant diffused light environment. Photographs were taken before the treatments commenced and during the full course of

treatment (ie once a week). The photographs were analyzed using a color balance threshold with ImageJ v.1.51u (NIH, USA).¹⁷ The percentage area of inflammation/redness was masked out and measured (Figure 1).

The percentage of inflammation/redness was calculated before and after treatment. Based on this, the percentage decrease in inflammation was calculated.

3 | RESULTS

In all cases, there was an overall reduction in inflammation and erythema (Figures 2-4 and Table 1). In case 1, there was a clear reduction in facial erythema following FLE treatment (Figure 2A), which was most visible on the cheeks (Figure 2A-C). The erythema and inflammatory papules and pustules in case 2 showed a marked reduction (Figure 3). For case 3 there was also a generalized decrease in the inflammatory reaction with a reduction in facial erythema (Figure 4). While the phyma of the nose was still present in case 3 after treatment with FLE, there was a clear reduction in the associated erythema (Figure 4A). Additionally, in all cases there was a visible improvement in the skin with a generalized normalization and smoothening of the skin's texture (Figures 2-4).

4 | DISCUSSION

We have previously reported a beneficial effect of the Kleresca® biophotonic platform in treating papulopustular rosacea (subtype 2), where FLE reduced the inflammatory reaction and enhanced the skin's texture.¹² This study sought to demonstrate the application of FLE beyond subtype 2 and investigated its applicability to all three subtypes of rosacea.

Here we report a positive effect of FLE in reducing erythema and inflammation notable in each of the three reported cases. Conventional treatments for rosacea often include a multi-method approach to target the many clinical features. Topical ointments including metronidazole or

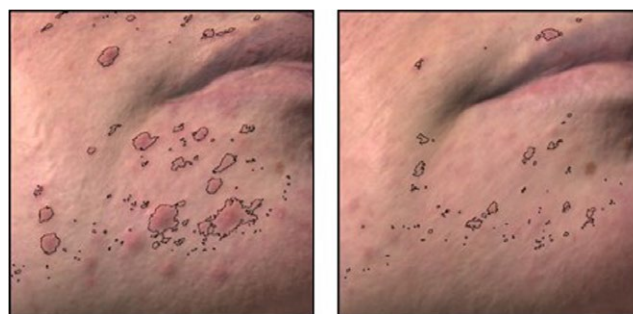


FIGURE 1 Inflammation was masked and measured before (left), and after (right) fluorescent light energy treatment using ImageJ v.1.51u (NIH, USA) for each clinical case

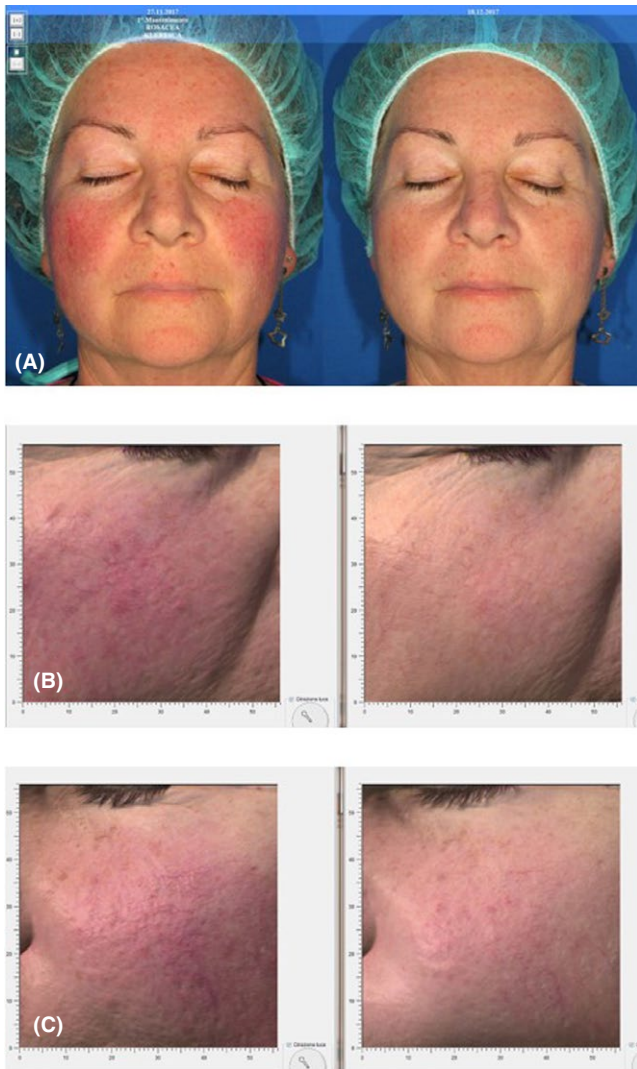


FIGURE 2 Clinical case report of a female patient with erythematotelangiectatic (subtype 1) rosacea. A, shows the full face before (left) and after (right) fluorescent light energy treatment. B, left cheek and C, right cheek, before and after treatment. All images show a marked reduction in erythema (redness) and a notable improvement in the skin texture

ivermectin are often a first-line treatment, however additional treatments are often required, depending on the subtype.¹⁰ We have shown that FLE is effective in targeting not just subtype 2, but also had beneficial effects in rosacea subtype 1 and 3. While the exact pathophysiological mechanisms of rosacea remain unclear, an aberrant immune response has been noted as a key contributory factor,⁵ and although this is a multivariable disease, inflammation is thought to underpin its many features.⁸ This report shows that FLE reduced the inflammatory reaction and associated erythema in each of the clinical cases investigated. FLE is a relatively new technology with a broad utility, including treating inflammatory skin conditions.¹⁵ Previous clinical work has shown that FLE can successfully target inflammation, reduce redness, and the associated lesions in acne

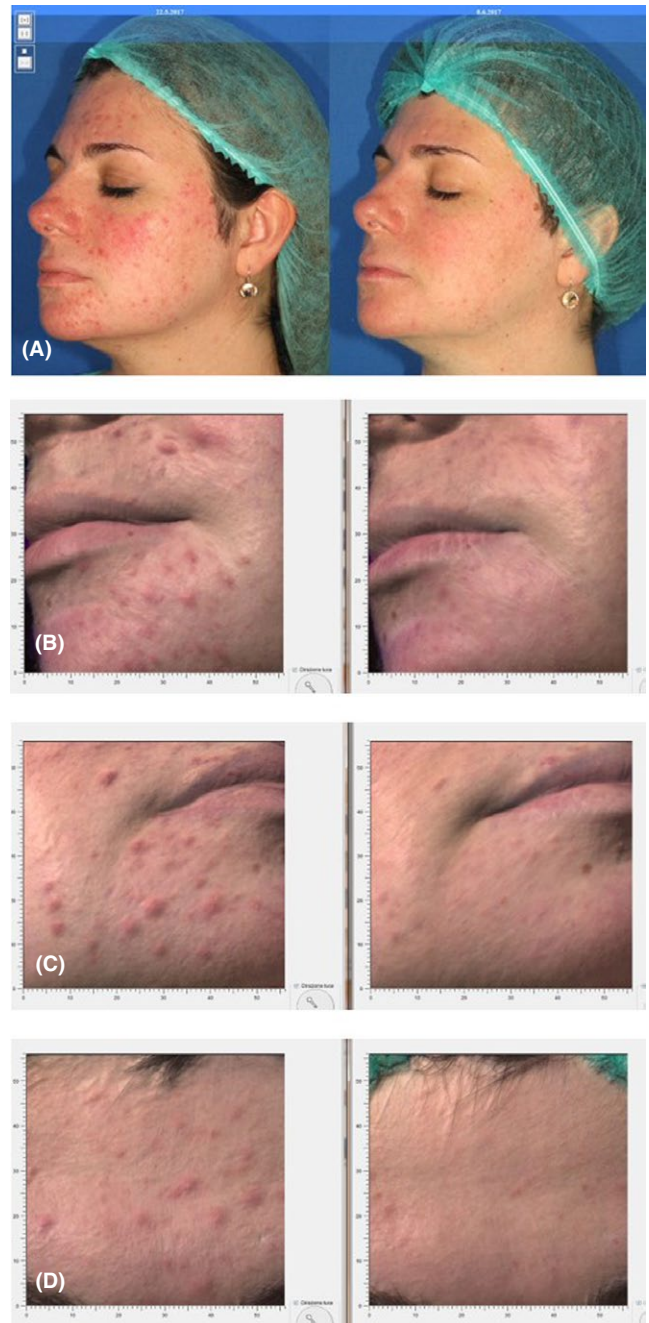


FIGURE 3 Clinical case report of a female patient with papulopustular (subtype 2) rosacea. A, shows the full face before (left) and after (right) fluorescent light energy treatment. B, left chin; C, right chin; and D, forehead, before and after treatment. All images show a marked reduction in inflammatory papules and pustules and associated erythema (redness)

vulgaris,¹³⁻¹⁵ as well as targeting inflammation and erythema in PPR, where topical treatment with metronidazole and ivermectin was ineffective.¹²

Recent work has explored some of the cellular mechanisms of FLE.¹⁵ It has been shown to enhance collagen production from human dermal fibroblasts, attenuate the inflammatory signature of a variety of cutaneous cells, and

TABLE 1 Summary of percentage of inflammation/redness

Facial area	Percentage area of inflammation - subtype 1 (%)	Percentage decrease - subtype 1 (%)	Percentage area of inflammation - subtype 2 (%)	Percentage decrease - subtype 2 (%)	Percentage area of inflammation - subtype 3 (%)	Percentage decrease - subtype 3 (%)
B before	4.28	83	4.27	78	1.62	54
B after	0.71		0.95		0.75	
C before	0.84	76	2.83	68	4.08	91
C after	0.21		0.92		0.39	
D before			4.21	46	2.30	20
D after			2.26		1.85	

B, C, and D refer to the photographs above for each subtype. The percentage of inflammation was calculated using ImageJ v.1.51u (NIH) to capture the redness before and after FLE treatment as described by Scarcella et al (2018). The percentage decrease was calculated by expressing the difference (before-after)/initial $\times 100$.

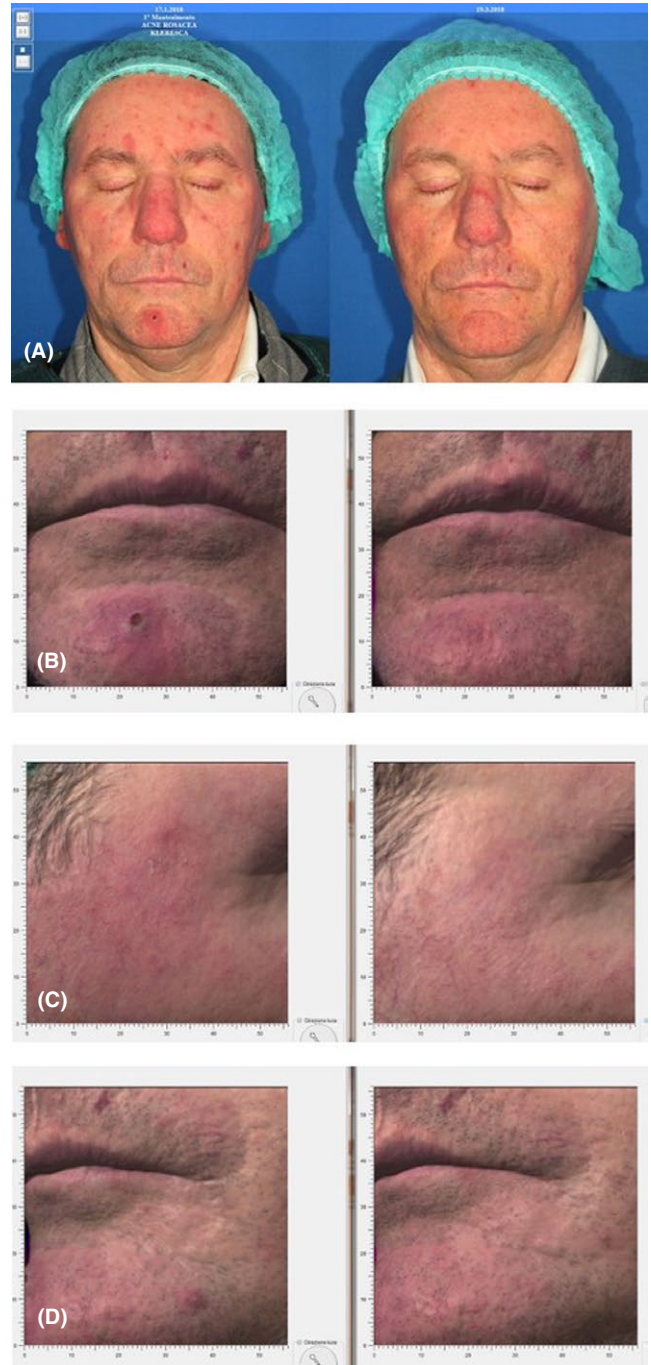


FIGURE 4 Clinical case report of a male patient with phymatous (subtype 3) rosacea. A, shows the full face before (left) and after (right) fluorescent light energy treatment. B and D, chin and; C, right temple, before and after treatment. All images show a marked reduction in erythema (redness), and pustules as well as notable improvement in the overall texture of the skin

induce neovascularization *in vitro*.¹⁵ The ability of FLE to turn down the cutaneous inflammatory response has implications for the presence of papules and pustules as well as the erythematous reaction observed in rosacea. Further, enhanced vascularization in rosacea may offer benefits to the distribution of blood flow and the flushing response.¹⁵

In addition to a reduction in inflammation and associated redness, there was an apparent improvement in skin texture in all three subtypes following treatment with FLE. Indeed, FLE has previously been shown to rejuvenate the skin.¹⁶ Following only 4 weeks of FLE-treatment, there was an increase in collagen production, a reduction in the appearance of fine lines, wrinkles as well as the size of skin pores, leading to an overall improvement in the skin's texture and appearance.¹⁶ In all three cases reported here, there was an enhanced normalization and smoothing of the skin, which improved the skin texture. Highlighting, FLE is not just of therapeutic benefit but it also provides an aesthetic reward to patients, which is beneficial especially when considering the huge psychosocial burden of the disease.⁷

Further, this biophotonic treatment targets the whole face in one treatment, maximizing the effects and minimizing the discomfort, especially when one considers that dry skin, edema, and stinging are secondary features experienced by many rosacea sufferers.⁸

Laser therapy is typically the treatment of choice for our third case report with PHR where there is a persistence of the phyma.¹⁰ While FLE did not alter the bulbous appearance of the nose, there was a notable improvement of the skin's texture. For these specific cases, FLE could be used in combination with laser treatment to achieve an enhanced overall appearance of the skin. Indeed, we recently reported a combination of FLE with picosecond laser in the treatment of solar lentigines, which produced enhanced effects.¹⁷

5 | CONCLUSION

The Kleresca® biophotonic platform may be a suitable treatment option for targeting inflammation and erythema, common features of rosacea that usually present in all subtypes. In addition to the therapeutic outcome of FLE, it also enhanced the overall texture of the skin, offering an additional aesthetic benefit. FLE may be used as a stand-alone treatment, or in combination with other rosacea therapies for an enhanced outcome.

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CONFLICTS OF INTEREST

MCE Nielsen is an employee of FB Dermatology Denmark Limited Aps.

AUTHORS' CONTRIBUTION

MS: study design; patient selection; data generation; GL: study design; patient selection; data generation, data gathering; MWD: advanced image analysis; statistical analysis; SPN: patient selection; patient follow-up management; GC: patient selection; patient follow-up management; MCEN: study design; advanced image analysis; statistical analysis; drafting of the original manuscript. All the authors listed have reviewed and approved the final version of the manuscript.

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