

# Fractional CO<sub>2</sub> Laser Treatment for Vulval Skin and Objective Quantifiable Effect on Vaginal pH

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The expanding long-standing role of lasers in the treatment of genitourinary (GU) conditions is supported by the growing body of objective quantifiable data demonstrating time-sensitive improvements in vulvovaginal health.<sup>1,2</sup> Recently, a cohort analysis demonstrated that early intervention post-menopause restores normal vaginal health indices (VHI) with a statistically significant difference when administered <3 as opposed to >3 years post-menopause, indicating a critical window for restoring normalcy.<sup>3</sup> Given the time-urgency for the >50% of post-menopausal women who suffer from GU conditions, important facts include that the external genitalia are lined by skin, the long-standing history of lasers to treat mucosa, and that quantifiable reproducible measures of vaginal health have been tested alongside randomized controlled comparisons to the gold standard, attaining level I evidence-based data.

## Lasers Treat Skin

The external genitalia—vulvae in women—are lined by skin, consisting of keratinized stratified squamous epithelium overlying the dermis connective tissue layer. Numerous lasers are approved for use for resurfacing of skin, including genital and perianal skin, therefore supporting the appropriateness of cutaneous laser application to the skin of this anatomic area.<sup>4</sup>

## Lasers Treat Mucosa

The vagina is lined by non-keratinized stratified squamous epithelium, which pre-menopause is glycogen-rich, whereas post-menopause, it becomes atrophic with diminished glycogen; the underlying lamina propria is the connective tissue layer, which declines in vascularity, cellularity and ground substance with age. Fractional ablative laser treatment stimulates glycogen-rich epithelial thickening, and lamina propria cellularity and vascularity.<sup>5,6</sup> In addition to over 40 years of GU application in the treatment of genital warts, myomectomy, and surgery, lasers are also extensively used to treat the oral mucosa.<sup>1,7</sup>

## Level I Evidence-Based Medicine

Fractional ablative lasers have been shown to be safe and

efficacious compared to the gold standard of topical therapy in randomized controlled trials for the treatment of the genital skin, including lichen sclerosus and atrophic vulvovaginitis, constituting level I of clinical evidence.<sup>8-10</sup>

## Alexiades Pathogenetic Theory

The metabolism of glycogen to lactic acid by the protective *Lactobacilli* bacteria creates the acidic environment (pH<4) in pre-menopausal vagina.<sup>11</sup> The inverse relationship between *Lactobacilli* populations and pH was shown by Athanasiou et al, underscoring its importance in GU syndrome of menopause (GSM).<sup>12</sup> In my theory, the loss of *Lactobacilli* due to diminishing glycogen levels in the face of post-menopausal hypoestrogenism results in the overgrowth of pathogenic microbes and yeast, leading to chronic vaginitis, *Candidiasis*, and lichen sclerosus in susceptible individuals. In the mid-2000s, Zerbinati and colleagues demonstrated that fractional CO<sub>2</sub> restores glycogen-rich vaginal epithelium, therefore providing the functional basis for restoration of the vaginal microbiome.<sup>5,6</sup>

## Objective Scientific Measures

Vaginal pH provides an objective quantifiable endpoint at the pathogenetic crux of GSM. In the Alexiades clinical trial of fractional CO<sub>2</sub> vulvovaginal treatment (ClinicalTrials.gov Identifier: NCT02704741, CO2RE, Candela Lasers), mean post-menopausal vaginal pH was 6.32. Following three monthly fractional CO<sub>2</sub> laser treatments, acidic mean vaginal pH was restored to 4.28 at 6 months follow up ( $P<0.0001$ ). pH levels began to slowly rise again between 6- and 12-months post-treatment, correlating with the recurrence of clinical symptoms.<sup>3</sup>

**FIGURE: Mean Vaginal pH Post-Fractional CO<sub>2</sub> Laser Treatment.** Vaginal pH was measured at baseline and following treatment with fractional CO<sub>2</sub> laser (CO2RE, Candela) to 12-month follow-up. ClinicalTrials.gov Identifier: NCT02704741.<sup>3</sup>



All timepoints statistically significant change from baseline,  $P<0.00001$   
Key: Rx=fractional CO<sub>2</sub> laser treatment, m=months post-treatment follow-up

In sum, the extensive background of lasers to treat skin and mucosa, and the growing body of clinical data and objective scientific findings support the appropriateness of the fractional lasers for the treatment of GU conditions. More randomized controlled comparative trials to the gold standard employing objective quantitative measures will continue to elevate the level of scientific rigor to this important area of therapeutic advances for women's health.

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