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## Fractional CO<sub>2</sub> laser treatment for vaginal rejuvenation: a narrative review and comprehensive update

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### ABSTRACT

Vulvovaginal atrophy (VVA) and genitourinary syndrome of menopause (GSM) are common conditions affecting postmenopausal women, leading to symptoms such as dryness, itching, and dyspareunia. Traditional treatments include hormonal therapies and lubricants, but non-hormonal options have newly emerged. Vaginal rejuvenation has gained popularity in recent years, addressing a range of conditions related to aging, childbirth, and hormonal changes. Fractional carbon dioxide (CO<sub>2</sub>) laser treatment offers a minimally invasive approach to improve vaginal health, promoting collagen synthesis and enhancing tissue elasticity. Fractional CO<sub>2</sub> lasers work by delivering controlled thermal energy to the vaginal tissue, creating micro-injuries that stimulate the body's natural healing processes. These changes correlate with clinical improvements in vaginal hydration and pH levels. We emphasize the significant role of fractional CO<sub>2</sub> laser treatment in vaginal rejuvenation in postmenopausal women with GSM. It offers a safe, minimally invasive, and effective option to improve their quality of life and sexual health. This review explores the mechanisms, clinical applications, safety, and patient satisfaction associated with fractional CO<sub>2</sub> laser therapy, aiming to comprehensively understand its role in contemporary gynaecological practice.

### INTRODUCTION

Vaginal health is integral to overall quality of life, with many women experiencing vulvovaginal atrophy (VVA) issues such as dryness, burning, or itching, particularly after menopause, owing to estrogen insufficiency. These symptoms are often progressive and increase over time as hypoestrogenism persists. However, it is sometimes referred to

as a “silent symptom of menopause”. VVA can also be caused by iatrogenic events such as surgery and radio or chemotherapy in cancer cases. The medical term “vulvovaginal atrophy” has been replaced by the most recent “genitourinary syndrome of menopause” (GSM) to cover other vaginal, sexual, and urinary symptoms caused by the estrogen insufficiency such as dysuria, urinary frequency, urethral discomfort, haematuria, sexual discomfort

or dyspareunia. This disorder affects up to 60% of postmenopausal women, and it has a significant impact on quality of life and sexual function, being frequently overlooked and undertreated [1-3].

Traditional non-surgical treatments include systemic hormones and topical hormonal and non-hormonal treatments. For moderate to severe symptoms, estrogen treatment is the most effective therapeutic option; non-hormonal remedies relieve minor symptoms as well as other menopausal symptoms [4]. Systemic estrogen therapy is sometimes used; however, many women prefer not to use hormonal treatment due to adverse effects, for example, increased symptoms of urine incontinence. Moreover, 10% - 20% of women may have remaining GSM symptoms. Local estrogen treatment remains controversial as it appears to recover symptoms more efficiently. However, there is insufficient evidence to prove the safety of local estrogen, and endometrial safety has not been explored in long-term clinical investigations, especially in breast cancer patients. On the other hand, non-hormonal local moisturizers and lubricants can be safe and efficient in relieving GSM symptoms; however, they must be used on a regular basis for maximum results [5-9].

Traditional surgical options, while effective, can be invasive and carry significant recovery times. Vaginal rejuvenation encompasses a variety of procedures aimed at enhancing the function, appearance, and overall health of the vaginal area. Light amplification by stimulated emission of radiation (LASER) technology emerges as a promising alternative treatment for postmenopausal vaginal symptoms, offering minimal downtime and a less invasive approach, especially in women who are pursuing non-hormonal alternatives. Studies reveal that laser technology may also aid people who suffer from vulvar *Lichen sclerosus* (LS) [10, 11].

Laser methods to treat vulvovaginal problems employ a wavelength that may significantly absorb water, such as the 10,600 nm of the carbon dioxide (CO<sub>2</sub>) laser, in order to coagulate and ablate the vulvar and vaginal tissues. Through thermal diffusion, the Er-YAG laser also produces non-ablative photothermal effects in the vaginal walls. Heating sets off a wound response that causes atrophied skin to restructure and produce new collagen and elastic fibres [12, 13]. The vulvovaginal complex's supporting tissues are then tightened to restore vaginal muscle tone. CO<sub>2</sub> laser therapy has already been shown to significantly alleviate GSM symp-

toms in postmenopausal women. Fractional CO<sub>2</sub> laser treatment has also been proven to improve vaginal mucosa structure in postmenopausal or non-estrogenised women [14-18].

Although fractional CO<sub>2</sub> laser treatment may exert minimal adverse effects, it provides a safe therapeutic approach for VVA. Patients are usually pleased and express a desire to have laser therapy again because serious issues rarely occur, especially with trained professionals performing procedures, and the incidence of moderate problems is small and usually resolved without the need for therapy. Therefore, the safety profile of fractional CO<sub>2</sub> laser is generally favourable [19].

This study explores the use of fractional CO<sub>2</sub> laser for vaginal rejuvenation in cases of GSM, focusing on its mechanism, associated histological changes, clinical applications, efficacy, safety, and patient satisfaction.

## MECHANISM OF ACTION

Fractional CO<sub>2</sub> lasers utilize a specific wavelength of light to target the vaginal mucosa, inducing thermal injury in a controlled manner. This stimulates fibroblast activity and collagen production, leading to tissue tightening and rejuvenation. Unlike conventional lasers, fractional delivery allows for the preservation of surrounding tissues, reducing recovery time and discomfort [20].

The application of fractional CO<sub>2</sub> lasers in gynaecological procedures has been shown to improve symptoms related to vaginal atrophy, urinary incontinence, and overall vaginal health [21]. Clinical studies have demonstrated significant improvements in patient-reported outcomes, indicating the efficacy and safety of this minimally invasive treatment option [22].

Fractional CO<sub>2</sub> lasers deliver controlled thermal energy to the vaginal tissue, creating micro-injuries that trigger the natural wound-healing response of the body. This technology has been widely researched and is recognized for its effectiveness in promoting vaginal rejuvenation and overall tissue health. The key mechanisms include:

### 1. Thermal energy delivery:

- **Micro-injuries:** the laser creates microscopic columns of thermal damage in the vaginal mucosa, sparing surrounding tissue and promoting rapid healing. This process is essential as it stimulates the natural healing pro-

cesses of the body, leading to the production of new collagen and elastin fibres, which are crucial for maintaining the structural integrity and elasticity of vaginal tissue [15].

- **Controlled ablation:** this process removes damaged tissue and stimulates healthy tissue regeneration. The controlled ablation facilitated by the CO<sub>2</sub> laser ensures the precise removal of aged or damaged cells while minimizing the risk of adverse effects. Therefore, it stimulates cellular turnover and enhances tissue quality and function [23].
2. **Collagen production:**
    - **Stimulation of fibroblasts:** the thermal effect of laser activates fibroblasts to produce collagen and other extracellular matrix components, playing a vital role in tissue repair and regeneration [24].
    - **New collagen fibres:** increased production of collagen fibres enhances tissue elasticity and firmness. Collagen is a key structural protein in the skin and other connective tissues, providing strength and support [24].
  3. **Tissue remodelling:**
    - **Wound healing response:** the micro-injuries trigger a wound healing response, leading to healthy tissue regeneration. This process involves the activation of various cellular and molecular pathways that promote tissue repair and regeneration [25].
    - **Angiogenesis:** enhanced blood flow and new blood vessel formation improve tissue oxygenation and nutrient delivery. Angiogenesis is a critical component of the healing process, as it ensures that the newly formed tissue receives adequate oxygen and nutrients for optimal growth and repair [26, 27].
  4. **Improved lubrication and vaginal secretions:** enhanced blood flow and collagen production lead to better lubrication, reducing dryness and discomfort. The increased blood flow and collagen production stimulate the production of vaginal secretions, which helps in maintaining proper lubrication and alleviating symptoms of dryness and discomfort [20].

## HISTOLOGICAL CHANGES

Histological studies have provided insights into the tissue-level changes induced by fractional CO<sub>2</sub> laser treatment:

1. **Collagen and elastin:**
  - **Increased staining:** studies have shown increased staining for collagen and elastin fibres, enhancing tissue strength and elasticity. This increased staining reflects the higher presence of these structural proteins, which are essential for maintaining skin resilience and flexibility [28].
  - **New collagen fibres:** the treatment stimulates the production of new collagen fibres, contributing to improved tissue structure. The formation of new collagen fibres is a key factor in the rejuvenation process, as it helps restore the integrity and firmness of the treated tissue [29].
2. **Epithelial thickness:**
  - **Thicker epithelium:** the treatment leads to a thicker epithelium, which correlates with improved vaginal hydration and pH levels. This increase in epithelial thickness is associated with better tissue health and function [30].
  - **Increased cell layers:** histological findings show increased cell layers and a better degree of surface maturation. This indicates a more robust and well-structured epithelial layer, contributing to overall tissue integrity [31].
3. **Angiogenesis:**
  - **New blood vessels:** enhanced blood flow and new blood vessel formation improve tissue oxygenation and nutrient delivery. This process is essential for maintaining healthy tissue and promoting healing [26, 27].
  - **Improved vascularization:** the treatment promotes angiogenesis, which is crucial for tissue health and repair. Increased vascularization ensures that the treated area receives adequate oxygen and nutrients, supporting healing [26, 27].
4. **Improved surface maturation:** the treatment enhances the surface maturation of the vaginal epithelium, contributing to better overall vaginal health. This improved maturation results in a more robust and well-structured epithelial layer, essential for maintaining tissue integrity and function [20].

## CLINICAL APPLICATIONS AND EFFICACY

Studies have shown that fractional CO<sub>2</sub> laser treatment can effectively improve symptoms of vaginal atrophy, enhance sexual function, and even reduce

urinary incontinence. These studies have demonstrated significant improvements in vaginal health scores, with many patients reporting enhanced satisfaction in their intimate relationships.

Gaspar *et al.* (2011) studied the effect of combined CO<sub>2</sub> laser, platelet-rich plasma (PRP), and pelvic exercise (study group) *vs* combined PRP and pelvic exercise (control group) on vaginal dryness, dyspareunia, and itching. They found significant improvement in vaginal mucous histology and sexual function in most cases in the study group [22].

A study was conducted by Arroyo in 2017 on 21 perimenopausal women with VVA symptoms. They received three sessions of fractional CO<sub>2</sub> laser for resurfacing and coagulating the mucosal lining of the vagina and the introitus. Vaginal health index (VHI) scores and visual analogue scale (VAS) showed an improvement in vaginal health and relief of the vulvovaginal symptoms as well as improved sexual function in perimenopausal women [20].

Ruanphoo and Bunyavejchevin (2020) conducted a randomized double-blinded sham-controlled trial on 88 postmenopausal women with moderate to severe symptoms of vaginal atrophy. They received either microablative fractional CO<sub>2</sub> laser or sham procedures three times four weeks apart. After 12 weeks of treatment, the VHI and VAS scores were significantly improved in the laser group compared to the control group [32].

Salvatore *et al.* (2021) studied the effect of microablative fractional CO<sub>2</sub> laser for treating vulvovaginal symptoms in 40 women with a history of breast cancer. There was marked improvement in vulvovaginal symptoms and sexual function, with a significant decrease in VAS score and a significant increase in vaginal health index score (VHIS) and female sexual function index (FSFI). Their prospective cohort study concluded that microablative fractional CO<sub>2</sub> laser is a safe and effective treatment option for women on endocrine therapy, either previously or currently [33].

Gardner and Aschkenazi (2021) conducted a retrospective study on 139 menopausal women with breast cancer and *Lichen sclerosus* and vulvovaginal symptoms after CO<sub>2</sub> laser therapy every six weeks for three sessions. They concluded that treatment for VVA with fractional CO<sub>2</sub> laser is safe and successful as they found that all FSFI and VAS scores showed significant improvement with no major harmful events reported [34].

A systematic review was conducted by D'Oria *et al.* (2022) to evaluate the therapeutic efficiency of fractional CO<sub>2</sub> laser for VVA in young women with a history of gynaecological cancer. They concluded that fractional CO<sub>2</sub> laser is an effective and safe therapeutic choice for young women with a history of gynaecological cancer, as it improves the quality of life and sexual satisfaction [35].

Donato *et al.* (2022) conducted a cohort study on 92 menopausal women with VVA to assess the efficacy of fractional CO<sub>2</sub> laser therapy. They concluded that fractional CO<sub>2</sub> laser improves vaginal health as well as GSM-related signs and symptoms while also dramatically increasing the quality of life and sexual functioning in postmenopausal symptomatic women [36].

Jankovic *et al.* (2024) conducted a cohort study on 84 sexually active postmenopausal women to assess the effects of fractional CO<sub>2</sub> laser on the clinical symptoms of VVA (evaluated by VAS and VHIS) and the sexual function (evaluated by FSFI). They found a significant decrease in VAS score and a significant increase in VHIS and FSFI, denoting marked improvement in symptoms of VVA and sexual function [37].

Adabi *et al.* (2024) conducted a prospective study on 140 postmenopausal women with vaginal atrophy to assess the impact of the fractional CO<sub>2</sub> laser on their quality of life, vaginal atrophy symptoms, and urinary incontinence. They found significant improvement in the quality of life regarding somatic, social function, and mental health. In addition, sexual arousal, satisfaction, and urinary symptoms showed marked improvement [38].

On the contrary, Li *et al.* (2021) conducted a double-blinded randomized clinical trial to examine the efficacy of CO<sub>2</sub> laser therapy on vaginal symptoms related to menopause in 90 women with postmenopausal symptoms. They found no significant difference after 12 months between the CO<sub>2</sub> laser group and the control group in the change in VAS score for total vaginal symptoms, mean quality of life score, and VHIS [39].

## SAFETY AND COMPLICATIONS

While generally considered safe, fractional CO<sub>2</sub> laser treatment can have side effects, including transient discomfort, edema, and, rarely, infections. The safety profile of fractional CO<sub>2</sub> laser treatment is generally favourable, with most studies reporting



minimal adverse effects. A thorough review of existing literature highlights a low incidence of severe complications, particularly when trained professionals perform procedures.

For example, a study by Gaspar *et al.* (2011) reported that 30% of patients experienced transient discomfort and edema following fractional CO<sub>2</sub> laser treatment for vaginal rejuvenation that resolved within 5 days of applying diclofenac gel locally once daily [22]. Another study by Arroyo (2017) noted that only one case had a mild urinary infection after fractional CO<sub>2</sub> laser, and she completely recovered by using antibiotics orally for one week [20]. Additionally, in 2020, Di Donato concluded in his study that fractional CO<sub>2</sub> laser provides a safe therapeutic approach for VVA. They found that 94.9% of patients were pleased and expressed a desire to have laser therapy again. This could be attributed to rare serious issues, especially with trained professionals performing procedures, and the incidence of moderate problems was small and resolved without needing therapy [19].

On the other hand, women who received traditional surgical interventions may carry a higher risk of infection that may require additional treatment. In addition, surgical procedures often require a longer recovery period, during which patients may experience pain and limited mobility. However, Surgical interventions, such as vaginoplasty and perineoplasty, could be more efficient for severe to moderate degrees of vaginal laxity. Therefore, the severity of vaginal laxity should be considered before selecting the appropriate approach for vaginal rejuvenation [40].

## PATIENT SATISFACTION

Patient satisfaction with fractional CO<sub>2</sub> laser treatment is generally high, with many women reporting significant improvements in symptoms and quality of life. Research indicates high patient satisfaction following treatment, and many women report improved self-esteem and quality of life. Patients often experience enhanced sexual function, reduced discomfort, and improved overall well-being. Furthermore, it was reported that patient satisfaction remains high even 12 months post-treatment, highlighting the long-term benefits of the fractional CO<sub>2</sub> laser treatment. Factors such as pre-treatment counselling and realistic expectation setting play crucial roles in overall satisfaction.

A study by Woźniak *et al.* (2023) evaluated the clinical effectiveness of fractional CO<sub>2</sub> laser in treating GSM symptoms and used a treatment satisfaction questionnaire. The results showed significant symptom improvement and high patient satisfaction [41]. Another randomized clinical trial was conducted by Mension *et al.* (2023) on 84 patients with GSM and a history of breast cancer. This study reported high levels of patient satisfaction with the fractional CO<sub>2</sub> laser treatment [42]. A systematic review has also discussed the efficacy and patient satisfaction with fractional CO<sub>2</sub> laser treatment for vulvovaginal rejuvenation, often used to treat symptoms of GSM [43].

## CONCLUSIONS AND RECOMMENDATIONS

Fractional CO<sub>2</sub> laser treatment represents a significant advancement in vaginal rejuvenation, offering a safe, minimally invasive, and effective option for many women experiencing symptoms associated with GSM. Fractional CO<sub>2</sub> laser therapy should be the mainstay in gynaecological practice, at least in postmenopausal women with mild GSM and breast or gynaecological cancer survivors who suffer from VVA and are not eligible for hormonal treatment.

While current literature demonstrates the efficacy of fractional CO<sub>2</sub> laser therapy for vaginal rejuvenation, there is a need for further research to establish definitive treatment protocols for different severity of VVA and menopausal stages and identify the most suitable device. Additionally, clinical trials with long-term follow-up are needed to compare fractional CO<sub>2</sub> laser therapy with the other surgical options, such as labiaplasty or vaginoplasty, regarding the outcome and cost-effectiveness to ensure that women receive the most appropriate and beneficial treatment for their individual needs.

## COMPLIANCE WITH ETHICAL STANDARDS

### *Authors' contribution*

M.A.E.: Conceptualization, supervision, writing – review & editing. D.O.A., M.A.R.: Data curation, investigation, validation, writing – original draft, writing – review & editing.

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N/A.

**Disclosure of interests**

The authors declare that they have no conflict of interests.

**Ethical approval**

N/A.

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**Data sharing**

N/A.

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