



MonaLisa Touch
Fractional Co2 Laser
Scientific Update
2024

THE GENITOURINARY SYNDROME of MENOPAUSE (GSM)

The term (GSM) was adopted by the International Society for the Study of Women's Sexual Health and the North American Menopause Society. It is also known as atrophy.

The problem: GSM is characterized by genital, urinary and sexual symptoms in menopausal women due to lack of oestrogen. Symptoms include vaginal dryness, itching, burning, dyspareunia (painful intercourse) and urinary problems.

Treatments include vaginal moisturisers, lubricants and gels; DHEAS / oestrogen (hormonal preparations), and vaginal laser.

This presentation is designed to give up to date evidence as to the laser, specifically the CO2 laser

Fractional CO2 laser treatment has been used worldwide since 2008 for managing symptoms of vaginal atrophy after menopause.

The results and outcomes continue to be positive for patients. In 2022, a published analysis of 52 000 patients who have had the treatment (combining published data from over 100 published studies) reported women experienced a significant improvement after exposure to vulval or vaginal laser across all indications, with no serious adverse events. (*Acta Obstet Gynecol Scand* 2022:00: 1-36).

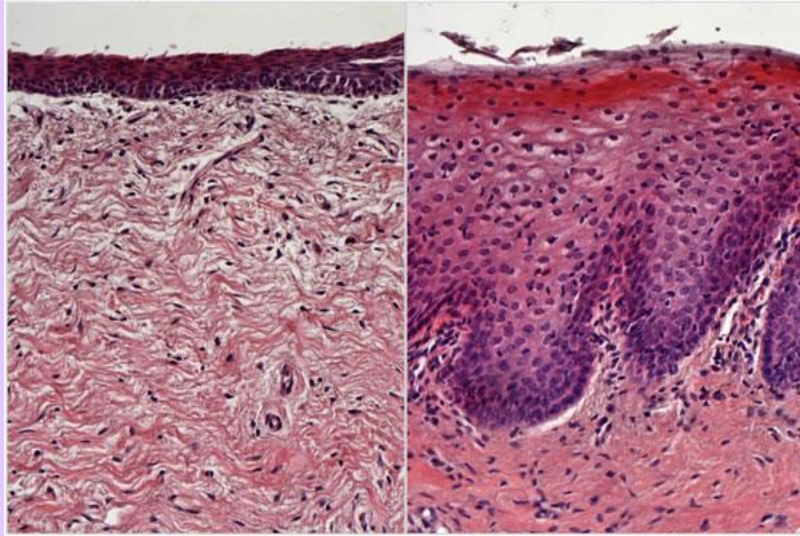
Your specialist will assess your own circumstances to determine your clinical signs and symptoms to determine the most appropriate management plan.

This document is **not** designed to replace a clinical consultation, but rather to summarize the Scientific Research. Not every patient who seeks this treatment is suitable or might benefit.

MECHANISM OF ACTION - CO2 LASER

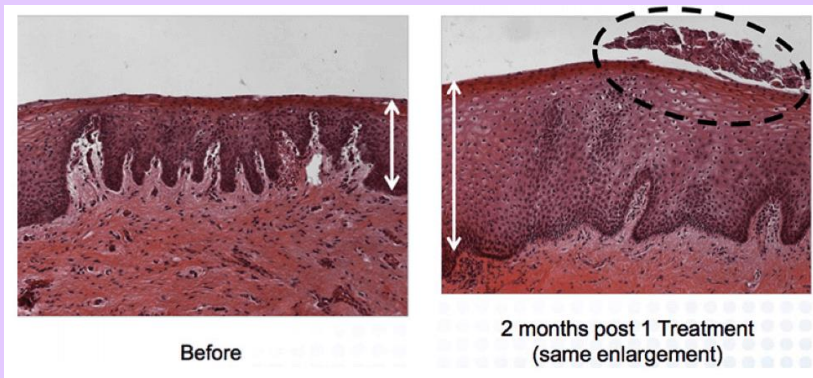
Evidence of the efficacy and safety of energy devices for atrophy is growing constantly. The CO2 laser (wavelength 10 600 nm) is absorbed by water, thus having a superficial effect. Also the fractional delivery (due to pulse emission, dot spacing and dwell time) avoids secondary damage due to overheating (Curr Opin Obstet Gynecol 2015; 27(6)). The fast-pulsed energy stimulates DNA and RNA expression for proteins which initiate temporary changes in cellular metabolism, resulting in the release and production of growth factors and increased cell proliferation. This results in new collagen and restoration of the trabecular architecture of the collagen in vaginal tissues following treatment.

PATHOLOGY STUDIES - Tissue changes- before and after vaginal fractional laser



The photomicrographs on the left (pre treatment) show thin, atrophic vaginal mucosa.

The right (post treatment) demonstrate images at the same magnification. The surface now has thicker epithelium, more glycogen (moisture) in the cells with more active tissue and cell turnover.



PATHOLOGY STUDIES - Tissue changes- before and after vaginal fractional laser

- Zerbinati et al. *Lasers Med Sci.* 2015 30:429-436 -Fibroblast improvement, r- ER. Improved epithelial thickness. Large amount of glycogen. Improved blood flow
- Salvatore et al. *Menopause* 2015;22. 845-9 -Changes in epithelium and lamina propria. Fibroblasts activated. Positive effects on collagen and elastin.
- Athanasidou et al. *Climacteric.* 2016: 19:512-518 -Increased lactobacillus to improve vaginal pH and vaginal epithelium
- Salvatore et al. *Maced J Med Sci.* 2018: 6: 6-14-Thicker epithelium. Connective tissue improved fibroblasts and blood vessels.
- Becorpi et al *Lasers Med Sci* 2018:33:1047-1054 -
High remodelling status in vagina epithelium. Changes in cytokines
- Pagnano et al *Lasers Surg Med* 2021:53:521 – 518-Improved vulvar epithelium, remodelling of connective tissue, new blood vessels
- Benitz- Roig et al *Lasers Med Sci* 2023 Sept 8

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PATHOLOGY STUDIES - Tissue changes Long Term

Casiraghi et al *Climacteric* 2023 Aug 21 (<https://doi.org/10.1080/13697137.2023.2246886>).

‘Long-term clinical and histological safety and efficacy of the CO2 Laser for treatment of GSM..’

This European study evaluated patients 4 weeks after the last treatment in women who had been undergoing annual laser treatment cycles.

VAGINAL HEALTH – using histology, light microscopy (taking great care the embedding technique of samples to avoid incorrect measurements), Haematoxylin and Eosin, Masson trichrome (test for reticular and fibrillar collagen, PAS (for glycogen staining), immunohistochemistry for CD34+cells (cells destined to become new blood vessels in the connective tissue.

GSM SYMPTOMS – at 4 weeks after the last treatment the vaginal health index symptoms were significantly increased

They observed a ‘statistically significant increase in the number of epithelial cell layers with a consequent increase in epithelial thickness (vaginal wall thickness), in the number of glycogen-filled cells (moisture) and the number of papillae (folds rich with blood supply)...with neovascularization(new blood supply) in each woman’. They concluded ‘tissue changes always leading to regenerative results without any sign of fibrosis’(no scarring).

(purple font describes in lay terms the findings).

Clinical Trials – Atrophy, Genitourinary Syndrome Menopause

During the last decade, evidence about the efficacy and safety of thermal energies vaginally administered in women suffering GSM is growing (*Benini et al Medicina 2022, EUGA, Climacteric 2023*).

This is of particular interest to women and their health care providers when they are non-responsive to first line therapies (moisturisers, hormone treatments or pessaries), or those who have contraindications to hormone treatment (breast cancer survivors etc).

The EUGA European Urogynaecological Association (EUGA) has formed a working party have published extensive data supporting ongoing research in this important space.

Cohort Trials This is just a small selection of publications from 2017 to 2022.

Alexiades. *Lasers Surg Med* 2021:53 (USA). N= 18. Significant improvement VHI (vaginal health index) and FSFI (female sexual function index) at 12 months

Bretas et al *Climacteric* 2022 :25 (Brazil) N=14. Significant improvement in VHI and FSFI

Gardner & Aschkenazi *Menopause* 2021:28 (USA) N=139. Significant improvement in FSFI , improved scores for intercourse and less dryness

Li et al *Lasers Surg Med* 2021:53 (China) N= 162. Both laser and vaginal oestrogen cream (compared) improved vaginal health at 12 months in both the laser and the vaginal oestrogen treated groups

Luvero et al *Lasers Med Sci* 2021;36 (Italy) N=44. The laser group (compared to the no treatment group) had significant improvement in all symptoms

Quick et al *Menopause* 2021:28 (USA) N=67. Significant improvement in FSFI. At 12 months some problems with Sexual intercourse still present.

Roser-Tenerowicz et al *Ginekol Pol* 2021 (Poland) N=205. Significant improvement in VHIS and VAS(Visual analog scores)

Ruffolo et al *Lasers Surg Med* 2021 :53 (Italy) N=61. Significant improvement in vulvovaginal atrophy symptoms.

Salvatore et al *Clin Breast Cancer* 2021:21 (Italy) N=40. Effects of laser comparing past users of hormone treatment. Study found both patients who had or had not previously used estrogen had a significant improvement in VAS and VHI . Both groups had the same benefit.

Silinqui et al *Breast J* 2021:27 (Italy). N=135 . Laser improved dryness and dyspareunia in patients both with and without a history of breast cancer.

Sindou-Faurie et al *Arch Gynecol Obstet* 2021:303. (France) N=46. Significant improvement in dryness and stress urinary incontinence

Veron et al *Breast Cancer Res Treat* 2021:188 (France) N = 46 Improved cell maturity and vaginal pH. Improved FSFI

Adabi et al *J Lasers Med Sci* 2020:11.(Iran) N=140. Significant improvement arousal, vaginal elasticity, fluid, satisfaction

Angioli et al *Int J Gynecol Cancer: 2020; 30*(Italy) N=165.Improved vulvovaginal atrophy symptoms on visual analog scale

Di Donato et al *Matuitas* 2020 (Italy) N=53. High satisfaction in 89%

Filippini et al *Menopause* 2020:27 (Italy) N=645. Significant improvement in dryness, dyspareunia, burning, pain, itching

Ghanbari et al *J Fam Reprod Health* 2020:14 (Iran) N=47 Significant improvement in Visual Analog Scale for Vulvovaginal atrophy symptoms.

Hersant et al *Ann Chir Plast Esthet* 2020: 65 (France) N=20. Significant improvement vaginal elasticity, fluid volume, epithelial integrity and moisture

Marin et al *J Gynecol Otstet Hum Reprod* 2020:49.(France) N=50 Significant improvement FSFI (female sexual function index) and quality of life

Mezzana et al *Dermatol Thera* 2020:33 (Italy) N= 40. Significant improvement in FSFI and stress urinary incontinence

Takecs et al *Lasers Surg Med* 2020:52 (USA) N=52 Significant improvement in visual analog scores and vaginal maturation

Athansiou et al *Menopause* 2019:26 (Greece).N=94 Significant improvement in VAS(visual analog scale) and FSFI(female sexual function index) after 3, 4 or 5 treatment sessions. 5 sessions had similar results to 4 sessions.

Eder et al *Laser Ther*2018:28 (USA) N=28. Significant improvement in VHI (Vaginal Health Index) from baseline to 6 months

Eder et al *Laser Ther* 2019:28 (USA) N=20. Significant improvement in VHI (Vaginal Health Index) at 12 15 and 18 months

Gittens et al *J Cosmet Laser* 2019:21(USA) .N=25 . Significant improvement in every domain of FSFI

Murina et al *Gynecol Endocrinol* 2019:36 (Italy) N=72. Significant improvement in dryness with laser patients as well as laser +ospemifene patients (laser +ospemifene– not available in Australia – better than laser alone

Pearson et al *Breast Cancer Res Treat: 2019;178 (Australia)* N=29 Significant improvement in dryness, burning and dyspareunia

Quick et al *Support Care Cancer :2019 :28.(Germany)* N=64. Improvement in VAS FSFI and Urinary Diary

Samuels et al *Aesthet Surg J:2019:39 (USA)* N=40 Significant improvement in VHI at 6 months, and in all evaluations

Singh et al *J Gynecol Surg* 2019:35 N=45. 90% of patients improved dryness, 89.5% improved dyspareunia

Tovar-Huamani et al *Lasers Surg Med* 2019:51. N=60. Improvement in VAS for genitourinary syndrome of menopause

Athansiou et al *Maturitas* 2017:104 (Greece) N=55 Significant improvement after 3rd session

Arroyo et al *Int J Womens Health*2017:9 (Spain) N=21 Significant improvement in VHI (vaginal health index) 12 weeks and 24 weeks after last treatment

Behnia-Willison *Eur J Obstet Gynecol Reprod Biol* 2017 :213 (Australia) N=102 Significant improvement in GSM (Genitourinary syndrome of Menopause) symptoms at 2, 4, 12 and 24 months

Filippini Et al *Photomed Laser Surg*2017:35 (Italy) N=386 2 months after last treatment patient reported improvement

Lang et al *Lasers Surg Med* 2017:49 (USA) N=368 Significant improvement in dryness ; reported satisfaction 86%

Pitsdouni et al *Lasers Med Sci*2017:32 (case control study) within group improvement significant

Pagano et al *Menopause :2017:25*(Italy) N=82 Significant reduction vulvovaginal symptoms. No improvement in laxity.

Pieralli et al *Arch Gynecol Obstete* 2017:296 (Italy) N=184 92% satisfaction at 6 months, 25% satisfaction at 24 months

Siliquini et al *Climacteric* 2017: 20 ((Italy) N=91 Significant improvement in VHI VAS at 15 month follow up

Sokol et al *Menopause* 2017:24 (USA) N=30. Significant improvement in VAS in first year (except dysuria

Randomised Controlled Trials – Atrophy, Genitourinary Syndrome Menopause

Cruz et al. *Menopause*. 2018 25:21-28

(Brazil) Comparison of estriol(E) v laser(L) v laser with estriol(L+E)

Politano et al. *Menopause*. 2019.26 -833-840.(Brazil)

Comparison Co2 Laser(L) v estrogen cream(E) v lubricant(Gel)

Ruanphoo *Menopause*. 2020:27: 858-863 (Thailand)Laser v Sham laser

Paradiso et al ‘Velvet trial’ *Menopause*. 2020;27:50-56 (USA)Laser v Vaginal Estrogen

Salvatore et al. *Climacteric*:2020:24:187-193 (Italy)Laser V Sham Laser

Dutra et al. *Menopause* : 2021 :28: 756-763 (Brazil)Laser v Vaginal Estrogen

Li et al. *JAMA*. 2021:326:1381-1389 (Australia)Laser v Sham Laser

Cruff et al(*J Sex Med*:2021: 18:761-769 (USA)Laser v Sham Laser

Quick et al. *Maturitas*. 2021:144: 37-44Laser v Sham Laser

Gold D, Nicolay L, Avian A, et al. Vaginal laser therapy versus hyaluronic acid suppositories for women with symptoms of urogenital atrophy after treatment for breast cancer: A randomized controlled trial. *Maturitas*.2022;167:1-7.

<https://pubmed.ncbi.nlm.nih.gov/36279690/>

A randomized clinical trial comparing vaginal laser therapy to vaginal estrogen therapy in women with genitourinary syndrome of menopause: The VeLVET Trial.

<https://www.ncbi.nlm.nih.gov/pubmed/31794500/>

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Randomized Controlled trials. Systematic Reviews(1).

JAMA Network Open. 2022, 5(9): e2232563. Jang et al

A total of 6 RCTS with 270 women were included. 135 were randomized to laser and 135 to estrogen treatment.

The importance : *'Vaginal estrogen for genitourinary syndrome of menopause (GSM) should be used with caution in women with contraindications, highlighting the need for effective treatment alternatives.'*

The findings : *'This systemic review and meta-analysis of RCTs found that vaginal laser treatment is associated with similar improvement in genitourinary symptoms as vaginal estrogen therapy.'*

European J of Obstetrics & Gynaecology and Reproductive Biology 227(2022) 84-89

A systemic review of CO2 laser treatment of vulvovaginal atrophy and gynaecologic cancer survivors, and major US Society Guidelines .

The importance: *'One of the most common adverse events reported by gynaecologic cancer survivors with spontaneous or iatrogenic menopause is vulvovaginal atrophy...induced by cancer therapies'*

The findings: *'According to the best evidence available, fractional CO2 laser treatment for VVA is an effective and safe therapeutic option for gynaecologic cancer survivors, improving sexual life and quality of life.'*

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Randomized Controlled trials. Systematic Reviews (2)

Efficacy of CO₂ laser treatment in postmenopausal women with vulvovaginal atrophy: a meta-analysis. Liu et al. *Int J Gynaecol Obstet.* 2021 Oct 8. doi: 10.1002/ijgo.13973.

PubMed, Embase, Cochrane Library and Web of Science were searched to June 9th, 2020. Prospective studies on the efficacy of CO₂ laser treatment were included. Twelve literatures including 459 participants were enrolled. Compared to baseline, VHIs were significantly higher at 1-, 3-, 6-, and 12-month follow-ups (P<0.001). For VVA severity, VAS scores in vaginal dryness at 1-, 3-, 6-, and 12-month follow-ups (P<0.050), in vaginal burning, itching and dysuria at 1-month follow-up (P<0.001), and in dyspareunia at 1-, 3-, 6-, and 12-month follow-ups (P<0.001) were all significantly lower. For FSFI, total scores at 1-, 3-, 6-, and 12-month follow-ups (P<0.001), and the scores in desire, arousal, lubrication, orgasm, satisfaction, and pain at 1-month follow-up (P<0.050) were all significantly higher. For QoL, PCS12 and MCS12 scores were all significantly higher (P<0.050) at 1-month follow-up.

They concluded “CO₂ laser treatment may be effective for post-menopausal women with VVA symptoms in improving QoL and sexual function.”

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Randomized Controlled trials. Systematic Reviews (3)

Vaginal Laser therapy for GSM?VVA: where we stand now - a review by the EUGA Working Group on Laser. *Climacteric*, 26:4, 336 -352 , DOI 10.1080/13697137.2023.2225766

‘Ten RCTs compared the microablative CO2 laser with the sham or with vaginal oestrogen, with conflicting results at the 1-month to 12-month follow-up. Five RCTs including 278 women compared the fractional microablative CO2 laser with the sham; considering that one RCT was unpowered for the study purpose, two RCTs concluded CO2 vaginal laser treatment to be superior to the sham both in improving VVA symptoms and sexual function while the other two RCTs reported a comparable improvement for the treatment and the sham. In five RCTs including 254 women and comparing the fractional microablative CO2 laser to vaginal oestrogen, three RCTs demonstrated similar efficacy in improving vaginal health, VVA symptoms and sexual function, excepting two trials that reported a vaginal laser superiority in VVA and sexual function improvement.

Monalisa Touch trials. Systematic Reviews (4)

AUGS (American Urogynaecology Society) Clinical Consensus Statement. Ashliek et al

Female Pelvic Medicine & Reconstructive Surgery. Vol 26, Number 5, May 2020.

https://www.augs.org/assets/1/6/Vaginal_Energy_Based_Devices.3.pdf

This well researched article from the American Urogynaecology Society looks at **all** energy based vaginal devices (EBD), and acknowledge the significant differences between non-ablative devices, fractional CO2 laser (eg Monalisa Touch smartxide DEKA) , hybrid lasers, and the different category of radiofrequency devices. In total 28 statements reached consensus by the working parties; the 12 statements that did not reach consensus were a result of an absence of evidence.

Listed are some of the consensus statements.

EFFICACY: A statement that reached consensus is that ‘EBD therapy has shown promise in treatment of VVA, vaginal dryness, and menopausal dyspareunia’. **The statement concluded that ‘overall most published articles are small, short case series that measure a variety of outcomes’.**

TIMING: ‘The AUGS EBD writing group reached consensus that the benefits of fractionated laser therapy to treat menopausal dyspareunia may last up to 1 year’, and ‘vaginal CO2 laser therapy has been shown to be effective in treatment of VVA in several studies up to 20 weeks’.

COST-EFFICACY DATA: ‘There are no comparative cost-efficiency data for EBD therapy versus available medical and surgical therapies for GSM/VVA’.

OTHER THERAPIES: ‘Pretreatment criteria for EBD therapy may include inability to use vaginal estrogen treatment for menopausal dyspareunia, VVA or vaginal dryness...But there are insufficient data to demonstrate the safety of vaginal oestrogen for women with breast cancer’.

SAFETY: All 6 drafted statements on the safety of vulvovaginal EBD therapy achieved consensus....the AUGS EBD writing group largely agreed that.. (these) therapies have a favorable safety profile’, but ‘the long-term sequelae of vulvovaginal EBD therapy are unknown’.

WHAT IS THE RISK OF HORMONE TREATMENTS WITH A HISTORY OF BREAST CANCER ? WHAT IS THE ALTERNATIVE TO LASER ?

NAMS Position Statement. The 2020 genitourinary syndrome of menopause position statement of the North American Menopause Society. *Menopause* 27 (9). pp976-992

<https://www.menopause.org/docs/default-source/default-document-library/2020-gsm-ps.pdf>

This document contains some helpful data on treatment options **other than laser**, and stresses that ‘there is insufficient data at present to confirm the safety of vaginal estrogen or DHEA in women with breast cancer’; recommends ‘non-hormonal therapies for women with mild symptoms’; and calls for ‘more placebo-controlled trials..of laser(therapies)’.