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The clinical role of LASER for vulvar and vaginal treatments in gynecology and female urology: An ICS/ISSVD best practice consensus document

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BACKGROUND: The clinical role of LASER for vulvar and vaginal treatments in gynecology and female urology is controversial.

AIMS: In this best practice document, we propose recommendations for the use of LASER for gynecologic and urologic conditions such as vulvovaginal atrophy, urinary incontinence, vulvodynia, and lichen sclerosus based on a thorough literature review.

Roger Dmochowski led the peer-review process as the Associate Editor responsible for the paper.

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MATERIALS & METHODS: This project was developed between January and September 2018. The development of this document followed the ICS White Paper Standard Operating Procedures.

RESULTS: Most of the available studies are limited by their design; for example they lack a control group, patients are not randomized, follow up is short term, series are small, LASER is not compared with standard treatments, and studies are industry sponsored. Due to these limitations, the level of evidence for the use of LASER in the treatment of these conditions remains low and does not allow for definitive recommendations for its use in routine clinical practice. Histological evidence is commonly reported as proof of tissue regeneration following LASER treatment. However, the histological changes noted can also be consistent with reparative changes after a thermal injury rather than necessarily representing regeneration or restoration of function. The use of LASER in women with vulvodynia or lichen sclerosus should not be recommended in routine clinical practice. There is no biological plausibility or safety data on its use on this population of women.

DISCUSSION: The available clinical studies do not present convincing data regarding the efficacy of LASER for the treatment of vaginal atrophy or urinary incontinence. Also, while short-term complications seem to be uncommon, data concerning long-term outcomes are lacking.

CONCLUSION: At this point, LASER is not recommended for routine treatment of the aforementioned conditions unless part of well-designed clinical trials or with special arrangements for clinical governance, consent, and audit.

KEYWORDS

genitourinary syndrome of menopause, ICS, ISSVD, LASER, lichen sclerosus, urinary incontinence, vulvovaginal atrophy, vaginal laxity

1 | INTRODUCTION

"Light Amplification by Stimulated Emission of Radiation" (LASER) has been widely used in gynecology and urology for more than 40 years. It is well established in the management of HPV-related genital lesions, prostate vaporization, and lithotripsy.[1,2] More recently the use of trans-vaginal or vulvar LASER has escalated to be used as a panacea for several urological and gynecological conditions, such as: lichen sclerosus, vulvodynia, "vaginal laxity", overactive bladder, and pelvic organ prolapse.

Limited ex-vivo studies have suggested that LASER has the potential to modify tissue characteristics. Clinically it has already been adopted for tissue remodeling of non-mucosal scars and wrinkles with relative success. These findings have led to the concept that LASER technology could be used in the treatment of vaginal atrophy[3] and has already been utilized and marketed as a "treatment" or therapy for vaginal "rejuvenation" and "Designer LASER Vaginoplasty" by the aesthetics industry.

Several published studies have suggested that fractional microablative CO_2 and Er:Yag LASER effectively treat not only atrophic vaginal mucosa (2014)(3), but also improve urinary incontinence (2015).[4] From the initial studies, the jump to aggressive marketing and widespread adoption of the LASER technology was quick. However, the studies failed to provide definitive evidence of its safety and effectiveness. Flaws of these studies include short follow-up time, absence of control groups, lack of standardized outcome measures, and the involvement of industry sponsorship.

Vaginal atrophy related to hypoestrogenism is recognized as a prevalent and significant cause of morbidity in the postmenopausal population.[5] In 2014 it was integrated into the broader definition of "genitourinary syndrome of menopause" (GSM).[6] GSM classifies an extensive list of signs and symptoms common to the natural process of female menopause as a syndrome. This umbrella term also carries the risk of classifying true disease (ie, lichen sclerosus) as GSM.[7]

Despite the lack of a true functional or anatomical definition, the use of the term "vaginal laxity" has become more widespread.[8] The term has been defined by the International Urogynecological Association (IUGA) and the International Continence Society as a feeling of vaginal looseness,[9] a woman's subjective sensation of vaginal "looseness." "Vaginal rejuvenation" with LASER is targeted to women with "vaginal laxity" as a procedure to improve the sensation of laxity and thus enhance sexual function in those with decreased vaginal sensation.[10]

In 2007 the American College of Obstetrics and Gynecology (ACOG) included "vaginal rejuvenation" and "designer vaginoplasty" in a list of procedures that were "not medically indicated" due to a "lack of evidence confirming safety and effectiveness."[11] However the US Food and Drug Administration (FDA) licenced the CO_2 LASER systems for "incision, excision, ablation, vaporization, and coagulation of body soft tissues and was used by specialities such as aesthetics (. . .), otolaryngology (. . .), gynecology, neurosurgery, and genitourinary surgery" in 2010.[12] Other LASER manufacturers requested FDA approval in 2014, with similar licence terms approved.[13] Er:YAG LASERs were licensed for dermatologic uses: coagulation, vaporization, ablation, or cutting of skin in dermatology and plastic/aesthetic surgery (2011).[14] The Nd:YAG had a similar approval in 2014.[15]

Treatment of vaginal atrophy and other gynecological disorders with LASER devices gained popularity and was marketed for this purpose. In response to this surge, ACOG issued a warning in 2016 clarifying that the FDA had not approved the use of these devices for the treatment of vulvovaginal atrophy.[16] Despite this announcement, claims that the devices had received FDA approval for such conditions were circulated.[17,18]

Several authors[19,20] and groups, such as the International Society for the Study of Vulvovaginal Disease (ISSVD)[10] and the Society of Obstetricians and Gynecologists of Canada (SOGC),[21] have raised concerns about the lack of evidence sustaining the use of LASER technologies for these gynecological indications. Finally, on the July 30th, 2018, the FDA issued a warning that the effectiveness and safety of energy-based devices (LASER and radiofrequency) for urinary incontinence, vaginal "rejuvenation" or cosmetic vaginal procedures has not been established.[22]

The executive council of the International Society for the Society for the Study of Vulvovaginal Disease (ISSVD) and the board of trustees of the International Continence Society (ICS) acknowledge the need to establish scientifically based recommendations on the new uses of LASER in their fields. This best practice document has therefore been developed to provide guidance on the use of LASER for the treatment of gynecological and urogynecological conditions and to educate providers about the weaknesses of the available data.

2 | MATERIAL AND METHODS

The ISSVD and the ICS identified and invited members to develop this project; participants were assigned a specific topic to be thoroughly researched and summarized in order to produce recommendations. The project was developed between January and September 2018. The development of this document followed the ICS White Paper Standard Operating Procedures.[23]

Literature searches were performed using Pubmed, Google Scholar, Ovid, Cochrane, and Embase to identify relevant papers. Search results were limited to papers written in English and published prior to June 2018.

Search strings for each topic were:

1. Vaginal atrophy/"rejuvenation":
   a. "genitourinary syndrome of menopause," "vulvovaginal atrophy," "atrophic vaginitis," "vaginal atrophy," "vaginal rejuvination," "menopause" and "LASER."
2. Urinary incontinence and/or pelvic organ prolapse:
   a. "urinary incontinence," "incontinence," "prolapse," "POP," "pelvic organ prolapse," "cystocele," "rectocele," "hysterocele," and "LASER."
3. Vaginal laxity:
   a. "vaginal tightening," "vaginal laxity syndrome," and "LASER."
4. Vulvodynia:
   a. "vulvodynia," "vestibulodynia," and "LASER."
5. Lichen sclerosus:
   a. "lichen sclerosus" and "LASER."
6. Other possible uses of LASER:
   a. "bleaching," "whitening," "brightening" "labiaplasty," "labioplasty," "nymphoplasty" and "LASER."

Evidence was graded according to the Center of Evidence Based-Medicine's "Levels of Evidence for Therapeutic Studies" and recommendations according to the American Society of Plastic Surgeons' "Grade Practice Recommendations."[24]

After discussion and consensus among all participants, the final version of the text was approved by the Executive Council of the ISSVD and the Board of Trustees of the ICS.

3 | BASIC SCIENCE EVIDENCE

3.1 | Proposed mechanism of action of LASER on skin and vaginal tissue

Human skin is comprised of three layers: the epidermis, the dermis, and the subcutaneous fat.[25] Currently, the hypothesized mechanism by which the LASER rejuvenates the vaginal mucosal epithelium has been developed based on the effects of LASER on epidermal skin epithelium. The LASER is believed to induce controlled injury to the epithelial layer of the skin, which stimulates tissue repair and remodeling.[26]

Wound repair in skin epithelium is a well-defined process characterized by inflammation, proliferation leading to tissue restoration, and tissue remodeling.[27] LASER is believed to normalize the cycle of collagenesis and collagenolysis[28–30] by inducing break down of disorganized collagen fibrils,[31] creating more organized collagen bundles, and decreasing collagen bundle thickness and density.[32]

Similar to skin, the vaginal wall is composed of three histologically unique layers. The most superficial layer of the vaginal mucosa is made up of stratified squamous epithelium but, unlike the skin epidermis, is devoid of keratinocytes and is therefore non-keratinized. Also unlike skin, vaginal tissue undergoes a number of discrete histologic changes during menopause. Thinning of the vaginal epithelium, reduced vaginal blood flow, diminished lubrication, increased pH, and a change in the vaginal microbiome, as well as decreased elasticity of the vaginal wall can occur.[33]

Neocollagenesis and restoration of the trabecular architecture of collagen is the proposed basis for vaginal rejuvenation with CO_2 LASER treatment. Investigators have hypothesized that the molecular and histologic changes demonstrated in the skin in response to LASER treatment can be recreated in the vaginal wall. However, given the differences in anatomy as well as histologic changes in response to hormone balance, such as those seen during menopause, it is unclear whether the effects of the LASER on skin could be expected for the vaginal wall.

In 2011, Gaspar et al[34] demonstrated that vaginal fractional CO_2 LASER treatment increased the thickness of the vaginal epithelium and increased the fibrillary component of the extracellular matrix. In 2015, Salvatore et al[35] described fibrillogenesis and neocollagenesis of vaginal tissue following vaginal LASER treatment in postmenopausal women. Zerbinati et al[36] in 2015 carried out a similar study and examined the tissue of postmenopausal patients with severe symptoms of GSM following CO_2 LASER treatment. They concluded that the histological changes seen support the theory that the LASER stimulates fibroblasts to produce collagen. It is unclear, however, if these histologic changes following LASER treatment can be directly correlated with improvement of clinical symptoms, as no control group was used (discussed in section 3.2).

TABLE 1 The use of LASER in the vagina for the treatment of atrophy/rejuvenation

	Level of evidence	Grade of recommendation
The mechanism of action of LASER on vaginal tissue in normal or diseased states is not known and cannot be used to justify treatment results	3b/4	C

Current published literature on the specific use of LASER in the vagina for the treatment of GSM is limited in the basic science results as well as clinical outcomes and the potential correlation to the histology findings (level of evidence 3b/4, grade of recommendation C). Thus, clinical conclusions drawn from these studies are highly speculative (Table 1).

3.2 | Histological effects

There is little known about the histology of the vaginal mucosa after LASER therapy for vaginal rejuvenation or functional remodeling. What is reported is based on small studies of patients over a short period of time.

Salvatore et al[37] described a single case, with a post-treatment biopsy performed 1 hour after the CO_2 fractional LASER treatment. The biopsy showed superficial epithelial desquamation. In comparison, animal skin burn studies report signs of injury to include desquamation. Desquamation therefore cannot be interpreted as beneficial remodeling.[38]

In a prospective study from the same group,[35] the authors compared treated vaginal mucosa with mucosa out of the field of therapy from the same patient. They noted neovascularization, neocollagenesis, and restoration of the trabecular architecture of collagen in the treated mucosa, which was interpreted as remodeling changes. These biopsies however were taken at the time of the LASER procedure, which would have provided insufficient time for remodeling to occur. In comparison, skin studies have shown changes of wound healing in the first few days after LASER therapy, while restorative changes ensue weeks later.[39] The histology images in the paper mentioned show denuding of the epithelium and different degrees of tissue coagulation, which are consistent with thermal injury.

Zerbinati et al[36] biopsied five patients before vaginal treatment, and at 1 and 2 months after treatment, which would allow early changes to be appreciated. At 1 and 2 months, changes were similar, noting thickened epithelium with superficial shedding, increased dermal papilla with elongated capillaries, giving the epidermal-dermal junction an undulating pattern, increased glycogen in the epithelial cells, and an increase in fibroblast activity. Increased collagen and ground substance have also been described in existing studies.[35,36] The illustrations in Zerbinati's paper show epidermal thickening with acanthosis, and some show parakeratosis and increase in dermal chronic inflammatory cells.[36] These changes are consistent with repair, as might be seen in lichen simplex chronicus, and alone do not indicate functional remodeling.

Histology changes to the vaginal muscosa following intravaginal LASER therapy have also been compared to a healing vaginal wound at the 2-month time point. A lack of significant capillary density and the increase in cellularity of connective tissue is consistent with this. It has not been confirmed if these changes are favorable for functional

TABLE 2 The histology of vaginal LASER "rejuvenation"

	Level of evidence	Grade of recommendation
The histological changes present after LASER therapy are consistent with reparative changes after a thermal injury. They do not necessarily represent restoration of function, and cannot be used to justify treatment results.	4	C

TABLE 3 Impact on the vaginal microbiome

	Level of evidence	Grade of recommendation
LASER cannot be recommended as a means to improve the vaginal microbiome.	2b	B
The use of CO_2 LASER does not negatively impact the vaginal microbiome.	2b	B

remodeling or if they would be sustained at the 6 and 12 month marks.[21]

Interpretation of available studies overall is limited by the lack of long-term follow-up, and hence complications such as scarring may not have been detected.[40] In addition, in a review of the literature on LASER therapy for treating GSM, the authors noted that in one pilot study, the maturation index (a ratio obtained by performing a random cell count of the three major cell types shed from the vaginal squamous epithelium: parabasal, intermediate, and superficial cells) was not considered.[3,40]

In summary, the histology of vaginal LASER "rejuvenation" is not well studied. Only small series have been published, with short follow-up. The changes present after therapy are consistent with reparative changes after a thermal injury. Whether they represent restoration of function has not yet been demonstrated by the histology. Further study is needed (level of evidence 4, grade of recommendation C). Further study is needed (Table 2).

3.3 | Impact on the vaginal microbiome

In postmenopausal women, lactobacilli concentration and diversity tend to be lower, while there is a higher diversity of other species.[41–43] These changes have been correlated to the severity of vulvovaginal atrophy symptoms with normalization using hormonal replacement therapy (HRT) associated with symptom improvement.[44] Based on the limited and controversial evidence demonstrating that vaginal LASER improves sexual health, vaginal glycogen, and vaginal epithelial thickness, its impact on the vaginal microbiome was evaluated in two studies.

Athanasiou et al[46] enrolled 53 women with at least one moderate or severe symptom of GSM. The methodology is insufficient as it assumes that one symptom can be used as a surrogate of an entire syndrome[45] and does not describe which scale of severity was used.

Following vaginal LASER treatment, the authors report a significant decrease in vaginal pH, but only one third reached a pH lower than 4.5. This decrease was accompanied by an increase in the number of lactobacilli although the techniques used to estimate the lactobacilli population are known to produce an inaccurate estimation. Interestingly, with an inclusion criteria of vaginal pH in the range 4.5-5 at baseline, nearly half of the women had normal vaginal flora according to Nugent and Ison-Hay scores. Following treatment and at the end of the study, this increased to approximately 90%. Colonization by *Candida* was very low (1.9%) and remained stable. The vaginal maturation index improved, but no changes regarding the presence of leukocytes in the vagina were noted.

Becorpi at al[47] studied the vaginal microbiome in 20 breast cancer survivors treated with two sessions of CO_2 LASER. The study reported an almost unchanged microbiome following treatment. The authors suggested that any possible benefits would be derived from a possible anti-inflammatory effect.

While LASER cannot be recommended as a means to improve the vaginal microbiome, it does not seem to have a deleterious effect on it (level of evidence 2b, grade of recommendation B) (Table 3).

4 | "GENITOURINARY SYNDROME OF MENOPAUSE" AND VAGINAL ATROPHY

GSM and vulvovaginal atrophy (VVA) are commonly seen in women after menopause. Nearly 50% of postmenopausal women report a vaginal symptom.[48] These symptoms have a significant impact on the quality of life, interfering with the ability to be intimate, and enjoy sexual intercourse in 60-70% of sexually active postmenopausal women.[49,50] However, many women consider their symptoms to be a natural part of aging. A survey of American women with a median age of 58 years revealed that 81% did not think VVA was a medical condition, of whom 71% had never sought treatment.[5]

A total of 24[51–74] clinical studies were identified that investigated transvaginal LASER in women with GSM/VVA. Two studies appeared to include the same study population (separate analyses).[55,67] The vast majority of the studies used

either Er:YAG or fractional, micro ablative CO_2 LASER. Some studies used ablative Er:YAG LASER.[62] All studies but four were prospective or retrospective case series without a control group. There was one randomized placebo/estriol controlled study[74] (level of evidence 2b) and three prospective, non-randomized studies using estradiol gel (or lubricant) as the comparative arm (level of evidence 3b).[51,53,69]

The clinical outcomes measured were inconsistent throughout the studies. Both subjective non-validated outcome measures and validated clinical outcomes scores were used to assess symptoms, quality of life impact, and general health. Samples taken varied from vaginal punch biopsy after treatment in one study,[75] to cytology, and pH evaluation[66] in others. Most studies had a follow up period of less than 12 months, although three studies presented 18-24 month follow up data. In addition, conflicts of interest were not always clearly specified and adverse events were rarely specifically outlined.

LASER treatment for women with a history of breast cancer and vaginal atrophy was investigated in one paper. In this group of women hormonal treatment is either contra-indicated or patients are reluctant to take low dose topical estrogens for symptoms of GSM. This limited study drew similar conclusions to those reached for other women and was hindered by similar study design flaws.[70,71,76]

Recent developments for the use of LASER in women with GSM/VVA include an international multicenter observational study aiming to evaluate 1500 women treated with vaginal Er:YAG LASER.[77] There is also an ongoing randomized study comparing the effects of CO_2 LASER to vaginal estrogen treatment. This study aims to enrol nearly 200 patients and is expected to finish by the end of 2018.[78] However there is still a need for a prospective randomized controlled trial with a placebo or sham control arm to understand the differences. For example a recent meta-analysis demonstrated that 67.7% of the treatment effect for female sexual dysfunction is accounted for by placebo.[79]

The available studies on the use of LASER to treat vaginal atrophy have overall not provided sufficient evidence of efficacy and long term safety (level of evidence 2b/3b, grade of recommendation C) (Table 4).

TABLE 4 "Genitourinary syndrome of menopause" and vaginal atrophy

	Level of evidence	Grade of recommendation
There is currently not enough scientific data demonstrating efficacy and safety of LASER for treating vulvovaginal atrophy.	2b/3b	C

5 | STRESS URINARY INCONTINENCE AND/OR PELVIC ORGAN PROLAPSE

Some evidence on the role of vaginal LASER exists for its use in urinary incontinence and pelvic organ prolapse.[4,34,77,80–86] The data on its use in stress urinary incontinence comprises mainly short-term observational studies. Participants varied from 19 to 205 women. Treatment response was usually assessed with validated questionnaires and showed favorable outcomes in terms of improvement of symptoms, but only one study followed patients for 24 months. None of the studies had a control or placebo group.[4,34,80–83]

There is minimal published data on the use of LASER in treating female pelvic organ prolapse. Its use has been described in women with grade II (prolapse to the hymen) to IV (maximum descent) cystoceles and follow up at 12 months has demonstrated an improvement in prolapse grade, with some patients sustaining the effect at 36 months.[86]

While the use of LASER to treat stress urinary incontinence and/or pelvic organ prolapse may seem appealing, the lack of good quality evidence in the form of multi-center randomized placebo-controlled trials is concerning.

Use of LASER may lead to serious adverse events such as vaginal burns, scarring, dyspareunia, and chronic pain. Although reports of adverse events in the literature is minimal, the sample sizes are small hence minimal reassurance can be taken from this.[87] The histological effects of LASER to the vaginal wall remain unclear leaving further questions regarding the effect of LASER therapy on surgical dissection and outcomes in women who may eventually require reconstructive pelvic or anti-incontinence surgery.

A recent review article looking at the evidence relating to the risks and benefits of intravaginal LASER technology in the management of stress urinary incontinence confirmed that despite the short-term observational studies of small patient numbers demonstrating improvements, there is still insufficient evidence to offer it as an effective modality for the treatment of stress urinary incontinence over alternative managements, such as pelvic floor physiotherapy, incontinence pessaries, or continence surgery.[21] Similarly there is insufficient evidence to offer intravaginal LASER therapy for vaginal prolapse (level of evidence 4, recommendation grade D) (Table 5).

6 | VAGINAL LAXITY SYNDROME

Vaginal laxity as a subjective patient complaint has been described by IUGA and ICS as a feeling of vaginal looseness.[9] Its anatomical definition, quality of life impact and treatment are poorly understood[88] and not widely recognized. "Vaginal laxity syndrome" (VLS) or even

TABLE 5 Stress urinary incontinence and/or pelvic organ prolapse

	Level of evidence	Grade of recommendation
There is limited evidence supporting the use of LASER for stress urinary incontinence	4	D
There is limited data concerning the safety of LASER for stress urinary incontinence	4	D
The evidence supporting the use of LASER for pelvic organ prolapse is limited	4	D
The data concerning the safety of LASER for pelvic organ prolapse is limited	4	D

"vaginal hyperlaxity syndrome" are concepts and marketing terminology with a lack of a standardized definition.

Some believe that VLS is an evolution of the aesthetic designation of "vaginal rejuvenation."[89] It is described as a disorder derived from the excessive laxity of the vaginal walls, leading to a sensation of looseness, diminished sensation of penile friction, and may be associated with urinary incontinence (urgency or stress).[61] VLS is considered a consequence of aging and related to having had vaginal deliveries. The term VLS and therefore its therapy, vaginal rejuvenation, is not endorsed or formally defined by the leading gynecological societies.[11] However, management of the symptoms have evolved from techniques involving sutures and the adaptation of traditional urogynecological procedures to the use of LASER[61,90] and radiofrequency procedures.[91–99]

In 2011, there was an attempt to restore the *rugae* of the vagina in postmenopausal women ("vaginal rugation rejuvenation"), by vaporization of the vaginal wall in order to create parallel grooves. The procedure was performed in women with a sensation of a loose or smooth vagina. In a small observational trial (10 patients in each arm), there was an apparent improvement of sexual function and no complications. The design and small sample size did not allow the authors to draw conclusions from the study.[90]

In 2014, Lee evaluated two different protocols (15 patients in each arm), using Er:YAG LASER. Women in both groups were evaluated 2 months after the procedure. There were no complications or adverse effects, although mild heating of the vagina and ecchymosis were reported. There was an objective (perineometer) and subjective improvement for 70% of the subjects with 76.6% of their partners reporting an improvement in sexual function. No validated scales were used for evaluation of the sexual function. A histological improvement was also suggested, but no analysis was shown in Ref.[61]

TABLE 6 "Vaginal Laxity Syndrome"

	Level of evidence	Grade of recommendation
There are no data supporting the recommendation of performing "vaginal rugation rejuvenation" or showing its safety	4	D
Er:YAG LASER for vaginal looseness or laxity has not been shown to be safe or efficacious	4	D

In total, two small studies on the use of LASER in vaginal relaxation syndrome comprising 51 women showed non-validated patient-reported improvements in sexual experience after LASER treatment but follow up was short term.[84,85] We could not find any study in the literature evaluating the role of CO_2 LASER for vaginal tightening specifically. Several studies have arisen using radiofrequency. The available data, in comparison to that for LASER use, are more robust and sustained by studies with a better design. So far, there has been no comparison between the different types of energy. There are no data supporting the recommendation of performing "vaginal rugation rejuvenation" or showing its safety (level of evidence 4, grade of recommendation D) (Table 6).

7 | VULVODYNIA

Vulvodynia is a chronic, complex pain disorder of multifactorial aetiology that can be difficult to manage. It is common, affecting more than 4-16% of women and can occur at any age, including postmenopausal women, particularly among those who remain sexually active.[100,101]

In 2015, the ISSVD, the International Society for the Study of Sexual Health of Women (ISSWSH) and the International Pelvic Pain Society (IPPS) adopted new terminology for vulvar pain and vulvodynia.[102] It is classified according to the site of pain (generalized or localized), the need of a stimulus (provoked, not provoked [spontaneous], or mixed), and the onset (primary or secondary). Treatment is difficult, and rapid resolution is unusual even with proper treatment. Decrease in pain may take weeks to months and may not be complete. No single treatment is successful in all women.[103] The vulvodynia treatment algorithm includes vulvar skin care guidelines, topical, oral, and injectable medications, pudendal nerve block, biofeedback, physical therapy, dietary modifications, cognitive behavioral therapy, sexual counseling and surgery, as well as alternative therapies such as acupuncture and hypnotherapy.[104]

Few studies have been conducted evaluating the usefulness of LASER therapy in the treatment of vulvodynia.[59,105,106]

A retrospective study indicated less pain with sexual intercourse among 24 of 37 women treated with LASER pulse therapy for vestibulodynia. However, 35% of the patients in the study required a vestibulectomy to control the symptoms.[105]

In 2016, in a study involving 70 patients who underwent fractional micro-ablative CO2 LASER treatment for vestibular pain plus vestibulodynia ($n = 37$) or menopausal patients (age > 50 years) who presented with vulvar pain secondary to GSM/VVA ($n = 33$), showed statistically significant improvement of dyspareunia and pain scores, with gradual improvement over each time point persisting through 4-month follow-up. Average overall vestibular health index score (a non-validated score, that intends to assess vestibular atrophy) improved significantly in the two groups after each of the three individual treatments. There was no statistically significant difference in outcomes between the two study groups.[59]

More recently, a placebo-controlled, double-blinded, randomized clinical trial involving 34 women aged 19-46 years old using low-level LASER therapy (LLLT) versus placebo showed *Clinical Pain Report* improvement in 78% in the LLLT group and 44% in the placebo group. Nevertheless, other measurable parameters (Q-tip test, intercourse pain on the Visual Analog Scale, and tampon tests before and after treatment, severity of discomfort in daily activities and/or in daily pain intensity) did not show a difference between groups. Although none of the patients reported side effects during the study, recurrence of pain was evidenced in 33% of the LLLT group.[106]

Interestingly, LASER (pulse or scan), used to treat vulvar mucosa disease (warts or vulvar HSIL) has been shown to be a possible cause of chronic vulvar pain.[107]

The few available studies concerning the treatment of vulvodynia with LASER have not proven it to be efficacious or safe, therefore its use should not be considered in these patients (level of evidence 2b, grade of recommendation B) (Table 7).

TABLE 7 Vulvodynia

	Level of evidence	Grade of recommendation
LASER therapy cannot be recommended as a means to improve pain in vulvodynia.	2b	B
The use of low-level LASER does not negatively impact symptoms in vestibulodynia.	2b	B

8 | LICHEN SCLEROSUS

Lichen sclerosus (LS) is a complex chronic inflammatory autoimmune dermatosis that can be found in patients of any age and race.[108] It is 10 times more common in females.[109] The incidence rate is around 10 per 100 000 woman-years, rising to over 30 per 100 000 woman-years in women older than 55.[110] The main symptoms are itching, burning, and dyspareunia, with impact on health-related quality of life.[111]

Vulvar LS (VLS) clinical aspects can vary significantly. Differentiated (dVIN), the HPV-independent pathway to vulvar carcinoma, must be suspected and biopsied promptly in treatment-resistant cases, and in the presence of erosion or hyperkeratotic plaques in a field of VLS.[112] The risk of vulvar cancer in VLS is estimated to be 2-5%, with higher risk in older women and with longer duration of disease.[110,113,114] Long term therapy, however, seems to be protective.[115,116] Current guidelines recommend the use of super-potent topical corticosteroids as first-line. Both the risk of cancer and the need of long term follow up must be taken into account when new treatment options are presented for LS, given the proven efficacy of topical corticosteroids.[117–120]

In 1991 a Canadian study reported seven women with LS refractory to topical testosterone who became asymptomatic following LASER ablation (600-900 W/cm^2 depth of tissue destruction 2 mm under general anesthesia). No biopsy after treatment was performed to confirm histological changes.[121] Similar results and depth of tissue vaporization was described by Kartamaa and Reitamo[122] in two patients with VLS. The aim to "remove the epithelium and papillary dermis involved in LS" for resolution of symptoms was reported in another two cases study in the absence of post treatment biopsies.[123]

In a recent case series,[124] five women underwent fractional CO_2 LASER treatment for hyperkeratotic VLS not responding to topical clobetasol. After 1-3 treatments with CO_2 LASER, energy 140-170 MJ and treatment depth 150 μm, symptoms had complete resolution in three, partial in one, and one was asymptomatic before treatment. Median follow up was 9 months (range 6-48). Re-epithelialization occurred in 3-4 weeks in all cases. Hyperkeratosis recurred after 6-8 months. In all patients, maintenance treatment was clobetasol. The objective to ablate the improper function of dermal epidermal zone, creating a new zone with proper function, is not supported by the published data.

All the papers considered are studies with very small series of patients, who did not undergo randomization, with short follow-up time. Neither visual acuity scale (VAS) for symptoms, nor details of pre/post treatment vulvar lesions were reported. The lack of description of the corticosteroid regimen utilized is another common weakness in the reported studies that prevent correct analysis of CO_2 LASER-treated patients and interpretation of its true efficacy. Furthermore, injuries (mechanical, chemical, burning, etc.) can be a cause

TABLE 8 Lichen sclerosus

	Level of evidence	Grade of recommendation
There are no data supporting the use of CO_2 LASER in VLS	4	C
There are no data concerning the long term safety of the use of CO_2 LASER in VLS treatment	4	C

of isomorphic or Koeber phenomenon in LS patients.[125] Currently, there is no evidence that fractional LASER is exempt from this risk in LS patients. Up to now the description of CO_2 LASER as a safe and effective therapy for recalcitrant VLS has no evidence within the literature data (level of evidence 4, grade of recommendation C) (Table 8).

9 | OTHER POSSIBLE USES OF LASER (VULVAR BLEACHING/ WHITENING/BRIGHTENING, LABIAPLASTY)

While the labia tend to be more pigmented than the surrounding structures, some women have the desire to whiten it. It can represent up to 6.8% of the patients consulting a gynecological aesthetical unit.[126] This procedure, using LASER, is commonly offered, but there are no studies showing its efficacy or safety. We could only find reference to it in one study, but LASER was done in combination with other procedures, such as labiaplasty, augmentation of the labia *majora*, *mons pubis* liposuction, or vaginal tightening.[127] Of note, even the use of LASER for hair removal has been related to serious urogynecologycal complications, such as labial adhesion with cryptomenorrhea, and acute urinary retention.[128] In one survey, 85.9% of physicians stated that there is no medical indication for the performance of such procedures.[129]

Labiaplasty is one of the most performed female cosmetic genital procedures worldwide. There are several techniques described, some with the use of LASER. Despite the misleading anatomical description, the procedure coined "Designer LASER Vaginoplasty" is also a form of labiaplasty.[130] Of note, this procedure has been considered unethical by the American College of Obstetricians and Gynecologists, due to the lack of supporting evidence.[11]

In 2006, the use of Nd:YAG LASER for the treatment of hypertrophy of the labia *minora* was reported. In a series of 55 women (including 4 children 10-15 years old), of whom 11 (20%) lacked the authors' established criteria of hypertrophy of the labia *minora* (>2 cm of width), there were no intraoperative complications, dehiscence occurred in 5.4%, and there was no pain after 7 days. Satisfaction rates were very high (>90%).[131] In another series, comprising 231 women who underwent reduction of the labia *minora* using CO_2 LASER to make a lambda shaped incision, a 100% satisfaction rate was reported, along with a low complication rate (11 wound dehiscence, 3 hematomas, 1 acute bleed requiring return to the operating room); however, there is no reference to the duration of follow up.[132] More recently, in a study involving 112 women aged 15-62 years old using CO_2 LASER, improvement in overall satisfaction and comfort during intercourse were reported. The rate of complications and the duration of follow-up were not mentioned.[133]

None of the studies have included a control group. In at least two of the studies children were enrolled. In at least one study, women did not meet the (controversial) study definition of hypertrophy of the labia *minora*. There appears to be no sufficient good quality data showing the safety of or justification of the use of LASER for cosmetic indications.

There is no universally accepted definition of hypertrophy of the labia minora; some authors have described it as a width superior to 4 or 5 cm, or protruding beyond the labia majora133. There is no correlation between the size of the labia minora and the ability to feel sexual pleasure or orgasm134. Brodie et al evaluated normal adolescents and pointed that there can be significant variance in the size of labia minora, according to being stretched or non-stretched (1-13 mm), that asymmetry is common (>50% of adolescent women), and that the mean width of labia minora was 10 mm (3-70 mm) (unstretched) and 20.5 mm (5-62 mm) (stretched) 135. If those definitions were applied to adolescents, a significant number would be considered "abnormal"!

There appears to be no sufficient good quality data showing the safety of or justification of the use of LASER for gynecological cosmetic indications in general (level of evidence 4, grade of recommendation C). It appears, however, to be safe for labiaplasty (level of evidence 3b grade of recommendation C) (Table 9).

TABLE 9 Other possible uses of LASER (vulvar bleaching/ whitening /brightening, labiaplasty)

	Level of evidence	Grade of recommendation
There is no medical indication for the use of LASER for vulvar bleaching	4	C
There are no data concerning the safety of the use of LASER for vulvar bleaching	4	C
Nd:YAG and CO_2 LASER appear to be safe options for labiaplasty	3b	C
There is no data supporting the use of LASER labiaplasty to enhance sexual function	4	C

10 | CONCLUSIONS

Advances in science, including medicine, are often questioned. However, as science evolves, we must remain committed to maintaining a high ethical standard. The four pillars of ethics—autonomy, beneficence, non-maleficence, and justice[134]—must guide medicine in both clinical practice and research.

The lack of quality studies regarding the use of transvaginal and vulvar LASER for gynecology and urology raises the question of whether such therapy provides beneficence and absence of maleficence; its use also hinders the patient's autonomy and choice. In order to give truly informed consent, there is need for clear and definitive information. Many questions remain unanswered from the safety profile of the therapies, comparison to current treatments, and long-term effects on tissues. Interestingly, the majority of LASER research carried out so far has been industry-funded, leading to significant risk of bias. There is an attraction to this office procedure which is profitable to the individual provider, however this should not drive un-guided practice.

Controversial applications regarding the use of LASER that have been promoted recently without rigid scientific validation, regulation, or oversight include the reconstructive therapy for "vaginal rejuvenation," and design LASER vaginoplasty.[130] The deceptive marketing of unproven treatments may not only cause injuries but may also keep patients from accessing appropriate and recognized therapies. It is imperative that providers protect patients from potential unknown harm due to the understudied clinical application of LASER technology and protect themselves from potentially indefensible lawsuits.

While there is potential for utilization of LASER to treat some proposed clinical conditions, most commonly vaginal atrophy and stress urinary incontinence, the scientific evidence remains exploratory. The existing literature is almost all post-marketing, in the setting of daily practice, rather than within controlled clinical trials. As with other innovations this is unacceptable, as safety must be proven before reaching the consumer. LASER has been available for use and disseminated among clinicians before sufficient data regarding quality, safety, and efficacy were provided.[135] Use of this technology prior to rigorous scientific examination may end in adversity, as has been demonstrated by previous technologies such as vaginal mesh for prolapse repair and power tissue morcellation.[136]

Although LASER technology seems promising for select indications, long-term efficacy and safety data are lacking. In order to elucidate its optimal clinical application, LASER therapy must be evaluated in rigorous, well-designed studies that are of appropriate time scale, randomized and sham-controlled, to evaluate safety and efficacy. Therefore, despite its appeal to clinicians and women, assumptions cannot yet be made regarding the durability of this treatment nor its long-term effects, either positive or negative to date. Until further literature emerges, this technology should be considered experimental and remain within the domain of clinical trials or with special arrangements for clinical governance, consent, and audit.

11 | RECOMMENDATIONS

Based on the available scientific evidence, with no supporting long term follow-up data, the use of LASER should, at present, not be recommended for the treatment of vaginal atrophy, vulvodynia, or lichen sclerosus. The data for the role of LASER for stress urinary incontinence and vaginal laxity are inadequate to draw any conclusions or safe practice recommendations. Therefore based on the available scientific evidence and on the lack of long term follow-up, the use of LASER should, so far, not be recommended for the treatment of vaginal atrophy, vulvodynia, lichen sclerosus, stress urinary incontinence, vaginal prolapse, or vaginal laxity.

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CONFLICT OF INTEREST

No conflicts of interest to declare.

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