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Energy-Based Devices for Functional Vaginal Problems: Issues and Answers

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Abstract
Vaginal rejuvenation is a marketing term that encompasses surgical and medical treatments for functional vaginal/vulvar problems including but not limited to genitourinary syndrome of menopause (GSM), sexual dysfunction, vaginal laxity, and stress urinary incontinence (SUI) and for esthetic concerns including dissatisfaction with vulvovaginal appearance. Multiple treatment options have become available for indications of functional vaginal problems. Noninvasive management options including the use of more novel treatments such as energy-based devices have gained interest. Previously, studies regarding the efficacy and safety of the energy-based devices for functional vaginal problems were mostly limited to cohort studies without sham treatment, control groups, randomization, or double blinding. As a result of this insufficient data in 2018, the FDA released a statement of warning against the use of energy-based devices in the treatment of functional vaginal problems or vaginal cosmetic procedures (Https://Www.Fda.Gov/Medical-Devices/Safety-Communications/Fda-Warns-Against-Use-Energy-Based-Devices-Perform-Vaginal-Rejuvenation-or-Vaginal-Cosmetic. 1–4, 2018).

Purpose of Review This article reviews the most current treatment modalities in the realm of vaginal rejuvenation therapy with an emphasis on the efficacy and safety of the energy-based devices.

Recent Findings In the most recent literature, there have been studies with improvements in study design that support the efficacy and the short-term safety of the energy-based devices.

Summary More recent studies with improved study design evidence that the use of energy-based devices results in improvements in functional vaginal problems and that serious adverse events appear to be rare. The availability of these devices as treatment options for functional vaginal problems has the potential to impact patient by improving their symptoms and quality of life. Caution still remains however regarding their safety following a longer period of time after their use.

Keywords Vaginal rejuvenation · Laser · Radiofrequency · Genitourinary syndrome of menopause · Vaginal laxity · Sexual dysfunction

Introduction

Vaginal rejuvenation is a nonmedical term that describes procedures that alter the cosmetic appearance of vulvovaginal tissue and may treat functional vaginal problems including vaginal laxity (VL), sexual dysfunction, genitourinary syndrome of menopause (GSM), and stress urinary incontinence (SUI). As so-called vaginal rejuvenation procedures can alter the cosmesis of the vulvovaginal tissues, these treatments may also be aimed at improving dissatisfaction with vulvovaginal anatomy [1–3]. All of these symptoms and syndromes are prevalent and have been noted to affect women's quality of life (QOL).

Women's interest in cosmetic genital procedures related to dissatisfaction with their vulvovaginal appearance has increased over recent years. This perception of inferior appearance is potentially a result of inaccurate information about normal variations in genital anatomy and depictions in the media [4]. Genitourinary syndrome of menopause includes signs of vulvovaginal atrophy (VVA), which describes the appearance of the vulva and the vagina secondary to post-

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menopausal effects of estrogen deficiency. GSM also includes the range of symptoms associated with the physical changes of the vulva and the vagina that include genital (irritation, dryness, burning), sexual (dyspareunia, discomfort), and urinary (recurrent urinary tract infections, urgency) [5]. GSM affects approximately 50% of women and has been shown to impact sex, relationships, and quality of life [6, 7]. Vaginal laxity (VL) is also a concern for many women. Vaginal laxity is a complex, multifactorial condition that is inadequately defined and not universally accepted. Despite the aforementioned complexity, VL has been studied and categorized by vulvovaginal anatomic location and symptomatology including functional or esthetic [8]. A relevant study showed that 50% of parous women were concerned about vaginal laxity, and 80% of these women did not discuss this concern with their obstetrician/gynecologist [9]. Vaginal laxity has been associated with patient reported sexual dysfunction, urinary incontinence, and decreased quality of life [10]. Sexual dysfunction has been shown to cause psychological distress in 43% of women during their lifetime [11]. The prevalence of urinary incontinence (UI) in women between the ages of 30–90 years old has been found to be 45%, with most of these women reporting SUI as the main component; UI has also been noted to impair women's quality of life [12].

Treatments under the umbrella term "vaginal rejuvenation" aim to correct and restore the vulvovaginal tissues to in turn alleviate the above signs and symptoms that women commonly experience [2]. The physiology of menopause, along with vaginal trauma from parturition, is one of the inciting factors that lead to GSM, VL, sexual dysfunction, SUI, and dissatisfaction with vulvovaginal appearance. Menopause results in estrogen deficiency which leads to diminished production of elastin and collagen in the vulvovaginal tissues, causing a decrease in vaginal elasticity and subsequent thinning of the vaginal epithelial lining [7, 13, 14]. Concentration of glycogen in the vaginal epithelium also declines as a result of hypoestrogenic status, which promotes changes in the normal vaginal flora and pH [14•]. Blood flow and secretions in the vagina also decrease as a result of lower estrogen levels [15].

Both surgical procedures and noninvasive therapies are included in treatment options for both functional vaginal problems and dissatisfaction with vulvovaginal appearance. Surgical and invasive options include labiaplasty, perineoplasty, vaginoplasty, and G-spot amplification, platelet-rich plasma (PRP), and lipofilling [16]. Noninvasive options include first-line treatments such as vaginal lubricants, moisturizers, and topical estrogen, while newer treatments include energy-based devices [2, 17]. This article reviews the most common treatments available under the array of "vaginal rejuvenation" with focus on the efficacy, safety, and current perspectives of the use of energy-based devices for functional vaginal problems. Surgical procedures and other invasive therapies will not be further discussed as they are beyond the scope of this review; however, Wilkie et al. [18] provide a thorough review of the literature.

Methods

We conducted a retrospective review of research related to the term vaginal rejuvenation, focusing on publications within the last 5 years, from 2016 to 2020. We aimed to describe this term based on the current evidence in the literature and discuss common and trending therapies under the umbrella of vaginal rejuvenation. Studies were identified by systematic search of PubMed, Google Scholar, and Cochrane Library. A combination of the following search terms were used: "vaginal rejuvenation," "vaginal tightening," "energy-based devices," "laser-based devices," "CO_2 laser," "radiofrequency," "vaginal laxity," "genitourinary syndrome of menopause," "vaginal cosmetic procedure," "safety," "FDA," "female genital cosmetic surgery," "vaginal treatment," "PRP," "platelet-rich plasma," "labiaplasty," "vaginoplasty." Articles were excluded if they were not in English or if they were out of the publication date range. A total of 66 articles retrieved through the database search and 10 additional articles ([19–28]) identified through citations within these sources were reviewed in detail by the authors.

Surgical Therapy

The term "vaginal rejuvenation" also encompasses genital procedures aimed to reduce vaginal laxity and enhance sexual function. Genital procedures include, but are not limited to, labiaplasty, perineoplasty, and vaginoplasty [29]. Additional surgical therapies include g-spot amplification (via injections of hyaluronic acid or autologous fat transfer) and vaginal rugation restoration. Newer procedure such as platelet-rich plasma (PRP) and lipofilling can also be considered in this category. Current research on these techniques is mostly expert opinion, case series, and case reports as they are newer techniques; thus, safety and efficacy profiles are very limited [16, 29]. Surgical interventions may alter the cosmesis of the genital tissue and/or act to eliminate some functional complaints. For example, women with elongated and asymmetrical labia may complain of poor cosmetic appearance (esthetic complaint); additionally, they may have functional complaints such as chaffing and or the labia dragged into the vagina during intercourse resulting in painful intercourse.

Other nonhormonal treatment options include PRP and lipofilling or fillers.

The use of lipofilling and PRP for functional vaginal problems has been described in case reports, but has not been widely studied. Lipofilling involves depositing autologous fat in the vulvovaginal tissues to restore the soft tissues; there is the potential for the fatty tissue to contain stem cells which may aid in tissue regeneration at the implantation sites. The process of PRP involves the injection of autologous plasma with high platelet fraction into the vulvovaginal tissues. The PRP which is rich in growth factors may promote tissue repair, angiogenesis, and inflammation [30].

Noninvasive Therapy

Noninvasive strategies for functional vaginal problems have the benefit of avoiding the potential morbidity of surgery. Current noninvasive standard of care treatment for GSM includes vaginal topical estrogen, moisturizers, and lubricants. Vaginal moisturizers are typically water-based products that are applied to the vaginal tissues regularly to treat vaginal dryness symptoms. Lubricants are applied to the genital tissue as needed to reduce symptoms of dyspareunia and decrease coital pain. Both moisturizers and lubricants are aimed at alleviation of symptoms of GSM as compared to vaginal estrogen which has the ability to revitalize the underlying vaginal tissues [6]. While topical estrogens are effective in some patients, there are groups of patients with contraindications to hormonal therapy and patients in which self-application of topical therapies is not feasible. Specifically, the use of topical estrogen is controversial in women with a history of breast cancer, estrogen sensitive tumors, including some gynecologic cancers, and thromboembolism due to the fact that these conditions are potentially responsive to serum estrogen levels [14•]. At this point, studies cannot conclude with certainty that topical estrogen does not increase serum estrogen level to a clinically significant degree of provocation in these diseases [31]. Most studies suggest that topical estrogen can be considered for patients with a history of breast cancer and some gynecologic cancers with shared decision-making when GMS is refractory to other treatment lines and without certain high risk features; however, it is stressed that there is insufficient high-quality evidence regarding the risks [31, 32]. Patients with breast cancer often have severe GSM as a result of hypoestrogenism following treatment with chemotherapy, GnRH agonists, or anti-estrogen therapy [33]. Alternative noninvasive methods that are nonhormonal may be the only option for some of the aforementioned patients with significant GSM and inability or reluctance to use topical estrogen.

Energy-Based Interventions

Energy-based devices apply the energy of radiofrequency (RF) or a laser to the vulvovaginal tissue to induce remodeling and revitalization of tissues [19•]. There are two types of lasers commonly used to treat vulvovaginal tissue, carbon dioxide (CO_2) and erbium:yttrium-aluminum-garnet (Er:YAG). All of the aforementioned devices have been used in dermatologic practice in rejuvenation of the face and neck with evidence for efficacy and safety [2]. Numerous studies have shown that the energy-based devices show promising efficacy in the treatment of GSM, vaginal laxity, sexual dysfunction, potentially SUI, and improvements in QOL; however, previously, very few of these studies reduced bias in the form of randomization, control groups, blinding, and sham treatments.

In addition to their promising efficacy, the energy-based devices have been shown to be cost-effective, and do not require sedation or downtime for patients. Wallace et al. [34] conducted a retrospective review study in 2020 comparing the cost-effectiveness of vaginal estrogen, ospemifene, and vaginal CO_2 laser therapy. All treatments were found to be cost-effective; however, they found vaginal CO_2 laser therapy to be the most cost-effective when assuming the following based on published data in their review of the research: typical adherence rates of the three treatment options, efficacy of the treatments, and patient costs for each treatment. While the findings are promising for the energy-based devices, it must be mentioned that the typical adherence rate for vaginal CO_2 laser therapy was assumed based on adherence rates to other in-office procedures such as percutaneous tibial nerve stimulation and on data from RCTs which is significant given the fact that the researchers found that the variable that most influenced the cost-effectiveness results was adherence to the treatment regimen. Additionally, the cost of each treatment was estimated based only on patient cost and did not evaluate physician office and hospital costs [34].

Another attraction to these devices is safety. Current data reports the energy-based devices to be well tolerated and result in limited and infrequent complications [35]. There remains limited data on long-term safety and currently there is unawareness of the optimal treatment duration and when to offer patients a repeat procedure. With the above benefits considered, the use of energy-based devices for the treatment of GSM, VL, sexual dysfunction, and urinary incontinence has become widespread. In a recent global survey conducted by Gambacciani et al. [36] among practitioners using the vaginal erbium laser, it was reported that among only 535 responding practitioners, a total of 113,174 patients spanning six continents were treated from 2012 to 2019.

Lasers

CO_2 Laser

The CO_2 laser produces heat which causes certain proteins to denature and trigger the expression of growth factors including TGF-beta, which is responsible for activation of the fibrogenic process. The efficacy of the CO_2 laser treatment in revitalizing the vulvovaginal tissues has been demonstrated in multiple histological studies. Gaspar et al. [20•] conducted a randomized control trial (RCT) in 2011 in women with GSM. The control group underwent treatment with platelet-rich plasma (PRP) and pelvic exercises, while the study group underwent treatment CO_2 laser therapy, PRP, and pelvic exercises. In the study group, histologic specimens showed an increase in fibroblast activity, fibrillar components, and neogenesis in the extracellular matrix, as well as improved thickness of the vaginal epithelium and the concentration of glycogen within the epithelium [20•]. In 2015, Zerbinati et al. [21] performed biopsies of vaginal mucosa on 50 post-menopausal women with GSM before and after treatment with CO_2 laser therapy. Following the treatment, they observed increased thickness of the vaginal epithelium with increased storage of glycogen within epithelial cells as well as activation of fibroblast synthesis of collagen in the lamina propria [21]. In comparison, topical estrogen therapy has predominantly shown only increased epithelial layers [22].

As previously mentioned, numerous studies have noted significant improvement in GSM, VL, sexual function, and QOL following treatment with vaginal CO_2 laser therapy (Table 1) [20, 22, 23, 38, 39, 42]. Improvement in urinary incontinence has not been reported with CO_2 laser therapy. Despite the large number of studies showing efficacy for GSM, VL, sexual function, and QOL, the majority of the studies previously performed were prospective cohort studies with limitations based on study design. These studies can be reviewed in Table 1. Here, studies that are more contemporary and have fewer limitations or new populations of patients not previously studied will be discussed.

Cruz et al. [14•] performed one of the first studies of vaginal CO_2 therapy for GSM treatment with a design that was randomized, controlled, and double-blinded with a sham treatment. Post-menopausal women (*N*=45) with GSM were randomly assigned for treatment groups including (laser + sham + vaginal estrogen), (laser + vaginal estrogen), or (vaginal estrogen + sham laser). A greater degree of GSM symptoms improved in the groups that received CO_2 laser therapy compared to the group that received only vaginal estrogen. Sexual function only improved in the group that received laser and vaginal estrogen therapy [14•]. In a recent study, Ruanphoo et al. [43•] performed a randomized control trial that was double-blinded and sham-controlled (*N*=88) with post-menopausal women experiencing GSM. The study group received laser treatment and the control group received a sham treatment. There were significant improvements in the Vaginal Health Index (VHI), which clinically evaluates vulvovaginal atrophy, and the Visual Analog Scale (VAS), which evaluates symptoms of GSM, compared to the control group, but there was no difference in urinary incontinence symptoms [43•]. In 2019, Paraiso et al. [37•] studied the effects of laser therapy versus vaginal estrogen in post-menopausal women with GSM in a randomized control trial that was single-blinded (*N*=62). Results showed improvement in GSM and sexual function in both groups, but did not find a significant difference between the two groups [37•]. Eftekhar et al. [41•] recently completed a randomized control trial (*N*=50) in which post-menopausal women with GSM received laser treatment or vaginal estrogen. This study found no significant improvement in VHI between the groups, but did find that there was greater improvement in sexual function in the laser group [41•].

Perrone et al. [40] conducted a prospective cohort study in which (*N*=43) patients suffering from vaginal shorting, atrophy, and stenosis following radiation therapy for gynecologic cancers received treatment with CO_2 laser therapy which showed improvement in vaginal length and VHI [40]. Moreover, Pieralli et al. [7] reported in a prospective cohort study improvement in VHI and VAS in patients (*N*=50) with a history of breast cancer and with resultant oncologic menopause following treatment with vaginal CO_2 laser therapy [7].

Erbium:Yttrium-Aluminum-Garnet

The Er:YAG laser has been used similarly for the indications of VL, and GSM; it has also been used more commonly than CO_2 laser for the indication of SUI and has recently been shown to improve QOL. This laser has a wavelength of 2940 nm that emits energy in the mid-infrared light spectrum [2]. The laser exposes the collagen tissue to heat which results in contraction of the collagen inducing the wound healing cascade which stimulates fibroblasts to synthesize collagen [19, 25, 44]. The efficacy of the Er:YAG laser on revitalizing the vulvovaginal tissue has been shown in histologic studies. Lapii et al. [44] conducted a study in which vaginal biopsies were obtained (*N*=18) from patients with SUI before exposure to Er:YAG laser and 1–2 months post-treatment with Er:YAG laser. Morphometric results showed increased epithelial glycogen content and epithelial layer thickness by 64.5%, increase in active fibroblasts and neocollagenogenesis, and increased density of capillaries [44].

Clinical studies of efficacy of Er:YAG for functional vaginal problems have primarily been limited to prospective cohort studies thus far. Multiple prospective cohort studies have reported effectiveness of the Er:YAG laser in management of vaginal laxity, GSM, sexual dysfunction, and SUI (Table 2) [19, 20, 25, 26, 48, 49]. One study performed by Gambacciani et al. [19•] compared Er:YAG laser to vaginal estrogen therapy for treatment of GSM (*N*=70). The study group received one treatment with the Er:YAG laser monthly for 3 months, while the control group received standard treatment with vaginal estrogen twice weekly for the 3-month period. On evaluation at 3 and 6 months post-treatment, VAS and VHI improved in both groups but significantly more improved in the group treated with laser [19•]. A more recent prospective cohort study by Reisenauer et al. [49] reported that among patients (*N*=30) receiving two treatments with Er: YAG laser therapy, patients reported a significant improvement in QOL, which had previously not been reported.

Table 1 Clinical studies using CO_2 lasers for vaginal rejuvenation

Type of study	*N* and inclusion criteria	Design	Outcome	Adverse events	Study
Controlled comparative study	92 Pre- and post-menopausal with GSM or dyspareunia	Study group: (*n*=40) PRP, laser, PF exercises Control group: (*n*=52) PRP, PF exercises 3 Txs, 1 Tx every 30 days Evaluated 30 days after last Tx Vaginal Bx pre-Tx and 30 days after Tx Sexual questionnaire	Sexual questionnaire with improvement in discomfort with sex Vaginal biopsies showed increased fibroblasts, neoangiogenesis, increased thickness of vaginal epithelium and glycogenic property Improvement in GSM symptoms	Minimal vaginal bleeding Mild discomfort during Tx	Gaspar et al. [20•]
Randomized control trial, double-blinded placebo control	45 Post-menopausal with GSM	(*n* = 15) Laser + sham vaginal estrogen (*n* = 15) laser + vaginal estrogen (*n* = 15) vaginal estrogen + sham laser Follow-up at 8 and 20 weeks VHI, FSFI	VHI was improved in all groups Laser and laser + estrogen showed improvement in dyspareunia, burning, and dryness Estrogen alone only showed improvement in dryness FSFI improved in laser + estrogen group	Dyspareunia with laser alone	Cruz et al. [14•]
Prospective cohort	50 Post-menopausal with GSM and dissatisfied with vaginal estrogen	3 Txs over 12 weeks Evaluated at 12-week follow-up VAS, VHI, SF-12, satisfaction	VAS improved VHI improved QOL improved on SF-12 84% satisfied with Tx	None	Salvatore et al. [23]
Prospective cohort	77 Post-menopausal with GSM	3 Txs of laser over 12 weeks Evaluated 12 weeks post-Tx VAS, VHI, SF-12	VAS improved VHI improved QOL improved on SF-12	None	Salvatore et al. [24]
Prospective cohort	48 Post-menopausal with GSM, failed vaginal estrogen	3 Txs over 30 days Evaluated 30 days post-Tx VHI, VAS, satisfaction	VHI improvement VAS improvement 91% satisfaction	None	Perino et al [22].
Prospective cohort	50 Post-menopausal with GSM	1 Tx Biopsies of vaginal tissue pre-Tx, and 2 months after Tx VHI	Improvement in VHI, improvement in GSM increased vaginal epithelial thickness and glycogen and increased fibroblast activation	None	Zerbinati et al. [21]
Prospective cohort	50 Hx of breast cancer and oncological menopause with GSM	3 Txs Evaluated 30 days post-Tx VHI, VAS	VHI improvement VAS improvement	Pain with probe insertion	Pieralli et al [7].
Randomized control trial Single-blinded	62 Post-menopausal with GSM	Study group: (*n*=30) laser, 3 Txs over 6 weeks Control group: (*n*=32) vaginal estrogen, Tx for 24 weeks Evaluated 6 months post-Tx VAS, VHI, FSFI, DIVA, UDI-6, VMI, PGI-I	Laser Tx and vaginal estrogen similar improvements in GSM, urinary symptoms and sexual function, and satisfaction	None	Paraiso et al [37•].
Prospective cohort	140 Post-menopausal with GSM	3 Txs Q month FSFI, SF-12, VHI, ICIQ	Improvement in sexual arousal, sexual satisfaction, urinary symptoms,		Adabi et al [38].

Table 1 (continued)

Type of study	*N* and inclusion criteria	Design	Outcome	Adverse events	Study
			vaginal dryness, itching, and dyspareunia		
Prospective cohort	84 Pre-menopausal women with VL and decreased sensation during intercourse	3 Txs Q month Evaluated 3 months and 6 months post-Tx VHI, FSFI	VHI and FSFI were improved at 3 months post-Tx, and decreased by 6 months post-Tx		Lauterbach et al [39].
Prospective cohort study	43 Patients with vaginal shortening, atrophy, and stenosis following RT for gynecologic cancer	3 Txs Q month Follow-up at 6 months Vaginal length, VHI, FSFI	Improvement in vaginal length, and VHI No changes in FSFI		Perrone et al [40].
Randomized control trial	50 Post-menopausal with VVA	Study group: (*n* = 25) 3 Txs, Q month for 3 months Control: (*n* = 25) vaginal estrogen 3 days per week for 3 months Evaluated 3 months post-Tx VHI, FSFI	VHI improvement in both groups, no difference between the two groups FSFI improvement in both groups, more improvement in laser group for arousal, satisfaction, desire, and dyspareunia		Eftekhar et al [41•].
Prospective cohort study	52 Pre-menopausal and post-menopausal with vaginal dryness	3 Txs Q month Vaginal smears obtained pre- and post-Tx Evaluated vaginal cytology and VAS	VAS improved in both pre- and post-menopausal groups No significant difference in parabasal, intermediary and superficial cells		Takacs et al [42].
Randomized control trial double-blinded sham-controlled	88 Post-menopausal with VVA	Study group (*n*=44) Q month Tx with CO2 laser 3 Txs Control group (*n*=44) Q month Txz x 3 with sham Participants and evaluators were blinded Evaluated 12 weeks after Tx VHI, VAS, ICIQ-VS, satisfaction	VHI, VAS, and vaginal dryness were improved ICIQ-VS no difference Study group more satisfied with Tx	No difference in adverse events	Ruanphoo et al [43•].

SFI, Female Sexual Function Index; ICIQ-VS, International Consultation on Incontinence Questionnaire; VAS, Visual Analog Scale; VHI, Vaginal Health Index

Table 2 Clinical studies using Er:YAG laser for vaginal rejuvenation

Type of study	*N* and inclusion criteria	Design	Outcome	Adverse events	Study
Pilot study	135 VL	1 Tx Evaluated at 1, 3, 6 months	90.4% reported satisfaction with vaginal tightening improvement	No	Rivera [25]
Pilot study	17	1 Tx PISQ-12 Evaluated at 1 month and 3 months after treatment	PISQ-12 improvement	Mild burns ($n = 1$)	Fistonic [45]
Pilot study	21 VL	2 Txs, Q 15 days to 1 month Evaluation at 3 months post-Tx LVT, POP-Q, PISQ-12, satisfaction	95% reported strong or moderate improvement in vaginal tightness, all partners reported improved tightness, 85% reported improved sensation Improvement in POP-Q No change in PISQ-12	None	Gaviria et al [26].
Prospective comparative cohort study	70 Post-menopausal with GSM Cohort with SUI	Laser group: (*n*=45) 1 Tx Er:YAG laser Q month for 3 months Control group: (*n*=25) 1g vaginal estrogen or 50mg of estriol twice weekly for 3 months Evaluated at 3 & 6 months VAS, VHI *N*= 19 with incontinence studied pre- and post-Tx with SUI ICIQ-UI SF	VAS improved in both groups, more improved in laser VHI improved in both groups, more improved in laser Improved ICIQ-SF	Mild discomfort with treatment	Gambacciani et al [19].
Retrospective cohort	60 Patient that underwent laser therapy	Telephone interviews using LVT	Average duration of effect was 16 months Improvement in SUI and prolapse 83% would repeat the therapy	Mild edema Tolerable heating sensation	Gaviria et al [46].
Prospective cohort study	98 SUI	2 Txs Q month Laser applied to anterior vaginal wall and urethral vestibule, biopsy of vaginal tissue pre- and post-treatment Evaluation 2 months post-Tx	Increase in density of blood capillaries and thickness of the epithelial layer increased fibroblasts		Lapii [44]
Prospective comparative cohort study	50 GSM	Study group: Er:YAG laser 2 Txs and vaginal estrogen Control group: vaginal estrogen Biopsies taken at 1, 3, 6, 12 months Evaluated at 12 months VAS, VMI	Improved VAS in both groups, more pronounced in the laser group Histology showed angiogenesis, congestion and restricting of the lamina propria in the laser group	Laser group = 4%, estriol group = 12%	Gaspar [47•]
Prospective cohort	24 Post-menopausal with history of breast cancer and GSM	3 Txs, Q month SPEQ, VHI	Improved SPEQ and VHI		Areas et al. [48]
Prospective cohort	33	2 Txs, Q month Evaluation at 4, 2, 6 months post-treatment ICIQ-SF QOL Likert scale	Significant improvement in QOL, improvement in ICIQ-SF	Vaginal discharge, spotting, burning; all transient	Reisenauer [49]

ICIQ, International Consultation on Incontinence Questionnaire, PISQ, Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire; SPEQ, Short Personal Experiences Questionnaire; VAS, Visual Analog Scale; VHI, Vaginal Health Index

Radiofrequency Therapy

In treatments of the vulvogaginal tissue with radiofrequency (RF) therapy, a device emits focused electromagnetic waves to generate heat that is applied to tissue. Heating of the tissue's collagen fibers leads to folding of its triple helix structure which causes the fibers to become thicker and shorter. Furthermore, this process causes a mild inflammatory response which activates fibroblasts for collagen and elastin synthesis [2, 50, 51]. The efficacy of this process has been shown histologically. Kent et al. conducted a study to evaluate histologic evidence of the efficacy of RF treatment on vulvovaginal tissue using an animal model of multiparous swine. The swine were administered RF treatment once per week for 3 weeks; biopsies were collected at baseline and at week four. The histology showed an increased density of elastin and collagen fibers after treatment with RF. A histologic study on post-menopausal women (*N*=20) by Leibaschoff et al. [52•] found that following three treatments with RF in the study group versus a sham treatment in the control group, biopsies of the study group showed increased concentration of collagen.

Regarding clinical studies, numerous prospective cohort studies have shown that RF is potentially effective as therapy for vaginal laxity, GSM, sexual dysfunction, improvement in QOL, and, notably, SUI [27, 28, 45, 51, 53–56]. In the past few years, there have been reports of efficacy for RF in treatment of functional vaginal problems as well as improvements in QOL in randomized control trials as well [52, 57, 58] (Table 3). Leibaschoff et al. [52•] performed a double-blinded randomized control trial in 2016 in which (*N*=20) post-menopausal women with SUI and vaginal laxity were randomized into either the study group which was administered 3 treatments with RF therapy, or randomized into the control group which was given 3 treatments with a sham device; a double-blinded method was used. Results showed improvement in SUI including 70% with negative post-treatment cough stress test, and improvement in VHI and VAS [52•]. In 2017, Krychman et al. [57•] performed a randomized placebo sham-controlled and blinded study in which pre-menopausal women (*N*=174) with VL were randomized to a study group which received 1 treatment with RF, and a control group which received 1 treatment with a sham device. At a 6-month evaluation, there was significant improvement in vaginal laxity and sexual function in the group treated with RF [57•]. Most recently, in 2020, Allan et al. [58•] completed a randomized control study in which (*N*=35) women with SUI were randomized to receive either one or two treatments with RF. When evaluated at 12 months post-treatment, both groups had improvements in SUI and QOL [58•].

Another interesting study regarding RF conducted by Sarmento et al. [59] in 2020 is a prospective cohort study in which post-menopausal women with GSM underwent 3 treatments with RF. At timepoints throughout the treatment course, vaginal smears were obtained and assessed. Compared to baseline, there was a significant increase in the concentration of lactobacillus species, a decrease in the vaginal pH, increased amount of parabasal cells and superficial epithelial cells, and improvement in VHI score and GSM [59].

Safety of Energy-Based Devices

Multiple prospective studies that were reviewed in which the energy-based devices were used for vulvovaginal treatments reported minimal or no adverse events, and none of the studies reported severe adverse events. The mild adverse events in the studies reviewed were dysuria, discomfort during treatment, urinary tract infection, vaginal discharge, edema, vaginal bleeding, vaginitis, and mild vaginal burn. Other sources report side effects may include itching, burning, or swelling that occurs immediately after the procedure and acutely resolves, bacterial vaginosis, UTI, and rarely the development of scarring [60, 61]. In a recent editorial, Delancey [62] voiced concern that while the tissue initially appears re-vascularized following laser or RF treatments over time the tissue would become avascular and form scar tissue similar to other wound healing processes.

The study by Wallace et al. [34] previously discussed found that there was less probability of side effects or complications when using CO_2 vaginal laser therapy compared to vaginal estrogen. Additionally, in a prospective cohort study conducted by Donato et al. [35] (*N*=53) to evaluate satisfaction and safety of treatment of GSM with CO_2 vaginal laser therapy, only acute and minor complications were reported including minor bleeding with insertion of the treatment probe and dysuria. After 30 days of treatment, no complications were reported, and no severe complications were reported during any time period. In Gaspar's [47•] study in 2017, the study group receiving Er:YAG laser therapy had less side effects (4%) than the control group that was treated with topical estrogen (12%).

While these results have shown promising safety profiles for the devices, a case series published by Gordon et al. [63] in 2019 reported four cases of adverse outcomes in patients following treatment with the CO_2 laser which included vaginal agglutination with resultant stenosis, and three cases of continued or worsening dyspareunia.

Ahluwali et al. [3•] published an analysis of the Manufacturer and User Facility Device Experience (MAUDE) database for events related to laser and energy-based devices for vulvovaginal problems. In review of the database, 45 adverse events had been reported, including (*N*=19) reporting vulvar, bladder, or urethral pain. Thirty-three of the patients reported that these adverse events involved chronicity including numbness, discomfort, bladder

Table 3 Clinical studies using radiofrequency for vaginal rejuvenation

Device	Type of study	*N* and inclusion criteria	Design	Outcome	Adverse events	Study
Transmucosal controlled radiofrequency heating device	Double-blinded randomized control trial	20 Post-menopausal with SUI on positive CST and VL	Study group: (n=10) laser Control group (n=10) sham 3 Txs Q month Evaluated at 3 months SUI assessment UDI-6 , ICIQ-UI SF, cough stress test VHI, VAS Biopsies at urethra vesical junction and of the vulva pre- and post-Tx	UDI-6 improvement, ICIQ-UI SF improvement and 70% had a negative cough stress test VHI and VAS Histology showed increased collagen	None	Leibaschoff et al [52•].
	Prospective cohort study	25 Pre- and post-menopausal women with difficulty achieving orgasm	3 Txs Q month Survey	23/25 reported reduction in time to orgasm, improved vaginal tightening, improved dryness and clitoral sensitivity	None	Alinsod et al [53].
Cryogen-cooled monopolar radiofrequency	Prospective cohort study	24 Pre-menopausal with VL	1 Tx Evaluated at 6 months Self-reported vaginal tightness FSFI, FSDS-R, sexual satisfaction	Vaginal tightness improvement in 67% Improved FSFI, FSDS-R improved, improvements in sexual satisfaction	None	Millheiser et al [27].
	Prospective cohort study	30 Pre-menopausal with VL	1 Tx Evaluated at 12 months FSFI, FSDS-R, VL questionnaire, sexual satisfaction questionnaire	FSFI improved FSDS-R improved improved vaginal laxity, improved sexual satisfaction	None	Sekiguchi et al [28].
	Randomized placebo sham-controlled, blinded study	174 Pre-menopausal with VL	Study group: (n=117) 1 laser Tx Control group: (n=57) 1 sham Tx Evaluated at 6 months VLQ, FSFI	VLQ score and FSFI improved more in RF group compared to the sham		Krychman et al [57•].
	Randomized control trial	35 SUI	Group 1: (n = 21) 1 CMRF Tx Group 2: (n = 14) 2 CMRF Tx Evaluated at 1, 4, 6, and 12 months post-Tx UDI-6, ILQ-7, ICIQ-UI-SF, pad weights	Both groups had improved pad weights and SUI symptoms and QOL 80% reported less leakage episodes	1 pt reported UTI	Allan et al [58•].
Bipolar radiofrequency	Prospective cohort	14 Post-menopausal with GSM	3 Txs WHOQOL questionnaire, FSFI, ICIQ-VS Satisfaction	WHOQOL showed improvement in health FSFI improvement in most categories ICIQ-VS Improvement in all 100% report satisfaction		Kamilos et al [54].
	Prospective cohort	30 VL symptoms	1 Tx Evaluated 2 months post-Tx	Improvement in vaginal laxity, sexual symptoms QOL, and SUI	None	Caruth [55]

Table 3 (continued)

Device	Type of study	*N* and inclusion criteria	Design	Outcome	Adverse events	Study
			ICIQ-VS, PFIQ-7, IIQ-7, ICIQ-UISF			
	Prospective cohort	55 Post-menopausal with GSM	3 Txs Vaginal smears were obtained during the treatments, VHI	Increase in lactobacillus, decrease in vaginal pH, increase in parabasal cells and superficial cells; VHI improved		Sarmento et al [59].
Monopolar radiofrequency	Prospective cohort	17 Pre- and post-menopausal with labial laxity	4 Txs weekly FSFI, VAS	Improved FSFI Improved VAS	Mild discomfort during Tx	Fistonic et al [45].
	Prospective cohort	27 SUI and VL	3 Txs, Q week ICIQ-UISF VVLQ	100% report improved VL 89% report improved SUI 93% report improved sexual satisfaction	None	Lalji et al [56].
	Prospective cohort	19	4 Txs weekly Images at baseline and 1month Evaluated vulvar appearance at 12 months, FSFI	Moderate change in vulvar appearance and laxity FSFI improved		Clark [51]

FSDS-R, Female Sexual Distress Scale Revised; FSFI, Female Sexual Function Index; ICIQ, International Consultation on Incontinence Questionnaire, VAS, Visual Analog Scale; VHI, Vaginal Health Index; UDI, Urogenital Distress Inventory; WHOQOL, World Health Organization Quality of Life

disturbance, scarring, dyspareunia, disfigurement, or worsening of previous gynecologic symptoms.

In summation, most of the information regarding the safety of the energy-based devices in their use for vulvovaginal problems supports that the energy-based devices are safe; however, there have been very few randomized control trials assessing their safety, and most studies to present day have not followed patient adverse events for a greater time period than 12 months.

Societies and Organizations

The positions of esteemed governing bodies including the US Food and Drug Administration (FDA), American College of Obstetricians and Gynecologists (ACOG), International Urogynecological Association (IUGA), the American Urogynecolgic Society (AUGS), and European Society for Sexual Medicine (ESSM) are essentially in agreement regarding the use of energy-based devices for vulvovaginal problems vaginal rejuvenation [64]. In July of 2018, the FDA issued a warning against the use of energy-based devices including laser and RF to perform vaginal rejuvenation procedures due to the fact that the safety and efficacy of the devices had not been established. The FDA stated that the devices had not been cleared for the treatment of GSM, SUI, and sexual dysfunction or for cosmetic purposes. This statement was invoked for concern that the energy-based devices could cause serious adverse events including burns, scarring, dyspareunia, and chronic pain [65•]. ACOG published a position stating that though the energy-based devices show potential utility they believed there was insufficient evidence for the efficacy and long-term safety of these treatments [66]. ACOG also published the opinion that women should be counseled about the lack of high-quality data supporting the effectiveness of vaginal rejuvenation or other female genital cosmetic surgery procedures and the potential complications including pain, bleeding, infection, scarring, adhesions, altered sensation, and dyspareunia [4]. IUGA further agreed with the previous opinions in their statement in September 2018. IUGA stated that there is necessity for randomized case control trials with long-term follow-up to further investigate efficacy and safety profile of the energy-based devices in the treatment of GSM, VL, sexual dysfunction, and SUI symptoms [60]. Most recently, AUGS stated that the energy-based devices have a favorable safety profile based on short-term data, while the long-term effects of the therapies are undetermined. AUGS also commented that the patient criteria for utilizing or having contraindications to the energy-based devices as well as the appropriate treatment regimen have not been established [61].

Conclusions

The concept of vaginal rejuvenation therapy has become more popular among patients and providers. As such, newer therapy modalities within this genre have been produced and pursued to treat functional vaginal problems such as GSM, VL, sexual dysfunction, and SUI. Among the noninvasive therapies, the energy-based devices have appealed to patients and providers. The energy-based devices show potential to offer another line of therapy for functional vaginal problems to patients that cannot utilize current first-line therapies, such as patients with certain cancers or other health limitations, or patients that simply prefer a different type of treatment. Previously, the efficacy and safety of the energy-based devices for functional vaginal problems had been mostly limited to prospective cohort studies. While essentially all of these studies reported significant efficacy and positive safety profiles, they were limited by their design. In more recent review of the literature, randomized control trials including treatment with CO_2 laser therapy and radiofrequency therapy have shown that these treatments are likely at least as effective in treating vulvovaginal problems as the standard treatment of topical vaginal estrogen and showed significant improvement compared to sham treatments [14, 37, 43, 52, 57]. No randomized control trials have been published evaluating the Er:YAG laser. While progress has been made in confirming the efficacy of these energy-based devices, future studies are needed to determine the long-term safety of these devices, as current studies have been limited to evaluation of their acute safety profiles.

Compliance with ethical standards

Conflict of Interest Alyssa Bujnak MD has no conflicts of interest.
Carly A Crowder MD has no conflicts of interest.
Michael L Krychman MD is a medical advisor for Viveve Medical.

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