# A Systematic Review of Nonsurgical Vulvovaginal Restoration Devices: An Evidence-Based Examination of Safety and Efficacy

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**Background:** The efficacy and safety of vulvovaginal restoration devices were called into question in a U.S. Food and Drug Administration statement on July 30, 2018, claiming that women are being harmed by laser and other energy-based devices. The goal of this systematic literature review was to assess existing data, determine gaps in evidence, and propose opportunities for continued investigation pertaining to laser and energy-based vaginal restoration techniques.

**Methods:** A review of literature using PubMed, Cochrane Library databases, Embase, MEDLINE, and the Cumulative Index to Nursing and Allied Health Literature was conducted on January 9, 2019, and articles up to this point were considered. For inclusion, studies had to be available or translated in English and relate to clinical medicine, direct patient care, and nonsurgical energy-based vulvovaginal procedures.

**Results:** The authors found five level I studies, 19 level II studies, four level III studies, and 46 level IV studies that used 15 different devices. Various degrees of improvement of symptoms were reported in all studies. Adverse events/side effects were noted in two of the 13 radiofrequency device studies, 15 of the 23 erbium:yttrium-aluminum-garnet device studies, and 17 of the 37 carbon dioxide device studies. The majority of adverse events were considered mild.

**Conclusions:** The majority of studies resulted in mild to no adverse side effects. However, there is a large gap in level I evidence. As a result, the authors emphasize the necessity of supplemental data surrounding this subject and suggest that additional randomized sham-controlled studies be conducted to further investigate vulvovaginal restoration devices in an effort to address women's health issues. (*Plast. Reconstr. Surg.* 146: 552e, 2020.)

PATIENT SAFETY

Nonsurgical and minimally invasive vulvovaginal restoration has increased in popularity over the past 10 years.[1] Energy-based devices including radiofrequency and laser [carbon dioxide and erbium:yttrium-aluminum-garnet (YAG)] have been used successfully in aesthetic and restorative procedures.[2–9] These procedures are meant to improve and/or restore the function and structure of the vulvovaginal tissue. Studies have shown that they do so by stimulating neovascularization, improving natural lubrication, and accelerating collagen synthesis and reorganization.[10] There have been a number of

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*Received for publication August 19, 2019; accepted March 31, 2020.*

DOI: 10.1097/PRS.0000000000007236

**Disclosure:** *Dr. Preminger is a consultant for InMode. Ms. Kurtzman has no financial interests to disclose. Dr. Dayan is a consultant for InMode, receives book royalties from Thieme Publishers, is the developer and owner of coreaesthetics.com, and is a co-investigator for MTF, Allergan, and Galderma.*

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laser and radiofrequency devices developed in recent years, and each device differs in technology and method for penetrating and stimulating vulvovaginal tissue.[3,4,9–13]

The efficacy and safety of vulvovaginal restoration devices were called into question in a U.S. Food and Drug Administration statement on July 30, 2018. The U.S. Food and Drug Administration commissioner expressed concern that women are being harmed by laser and other energy-based devices marketed to remedy conditions such as menopause, urinary incontinence, and sexual function. The U.S. Food and Drug Administration stated, "we have not cleared or approved for marketing any energy-based devices to treat these symptoms or conditions (vaginal laxity, dryness, vaginal atrophy, itching, pain during urination, pain during intercourse, and or decreased sexual sensation), or any symptoms related to menopause, urinary incontinence, or sexual function."[14,15] Adverse side effects such as vaginal burns, scarring, pain during sexual intercourse, and recurring or chronic pain were mentioned in the report.

The North American Menopause Society issued a response citing the lack of research in this area, advocating for additional randomized trials to further investigate these devices.[16] The American College of Gynecologists recently reaffirmed their position statement on the matter, citing "preliminary observational data has shown some potential benefits with the use of this technology in treating patients with vulvovaginal atrophy, however, these observational trials do not evaluate the use of concomitant treatments, and they lack long term follow-up. Although early data indicate potential utility, additional data is needed to further assess the efficacy and safety of this procedure."[17] The goal of this systematic literature review is to address the U.S. Food and Drug Administration's claims by assessing existing data, determining gaps in evidence, and proposing opportunities for continued investigation pertaining to laser and energy-based vulvovaginal restoration techniques.

### Conditions

Conditions investigated included genitourinary syndrome of menopause, vaginal laxity, vulvovaginal laxity, vulvovaginal atrophy, vaginal dryness, atrophic vaginitis, orgasmic dysfunction, stress urinary incontinence, pelvic organ prolapse, overactive bladder, vaginal relaxation syndrome, mixed urinary incontinence, and urinary incontinence.

## MATERIALS AND METHODS

A review of the literature using PubMed, Cochrane Library databases, Embase, MEDLINE, and the Cumulative Index to Nursing and Allied Health Literature was conducted on January 9, 2019, and articles up to this point were considered. Duplicates were removed in Mendeley. Medical search terms in a variety of combinations were vaginal rejuvenation, nonsurgical vaginal rejuvenation, vaginal laxity, vulvovaginal atrophy, genitourinary syndrome of menopause, erbium laser, vaginal laser, fractional carbon dioxide laser, microablative fractional carbon dioxide laser, radiofrequency, vaginal dryness, atrophic vaginitis, decreased sensation during coitus, dissatisfaction with appearance of vagina, vulvovaginal laxity, labia majora laxity, orgasmic dysfunction, feminine rejuvenation, energy-based devices, safety, efficacy, patient satisfaction, monopolar, bipolar, and quadripolar. Two authors independently screened titles and abstracts in Mendeley. For inclusion, studies had to be available or translated in English, relate to clinical medicine, direct patient care, and nonsurgical energy-based vulvovaginal procedures. Exclusion criteria included conference abstracts and posters, letters, facial, dental, periodontal, cardiac, animal tissue, skin infections, neoplasia, surgical, hormonal, and low-level laser therapy studies. Studies meeting these criteria underwent full-text review. Disagreements were resolved through discussion.

## RESULTS

The initial search criteria produced 3326 results and a title/abstract review was performed. After review and subsequent resolution of conflicts, 91 articles were selected for inclusion. Articles from 1968 to January 9, 2019, were considered.

### Nonsurgical Energy-Based Treatment Options

Energy-based devices intended for vulvovaginal restoration summarized in Table 1[6,20–35] and included in this review are radiofrequency, carbon dioxide fractional laser, and erbium:YAG devices. Both laser and radiofrequency treatments induce neocollagenesis and neovascularization to restore thickness, elasticity, and moisture of the vaginal mucosa. The mechanism is believed to be secondary to activation of heat shock proteins and triggering of the inflammatory/proliferative cascade.[18] From our literature review, we identified six radiofrequency devices, five erbium:YAG devices, and four carbon dioxide devices that were used in the studies included in this article.

**Table 1. Energy-Based Devices**

| Device Name | Manufacturer | Type |
|---|---|---|
| ThermiVa[20] | ThermiAesthetics, Southlake, Texas | Temperature-controlled radiofrequency |
| Viveve Vaginal Laxity RF Therapy System[21] | Viveve, Inc., Sunnyvale, Calif. | Monopolar radiofrequency |
| Protégé Intima[22] | BTL Industries, Inc., Boston, Mass. | Focused monopolar radiofrequency |
| Exilis Ultra Femme 360[23] | BTL Industries | Monopolar radiofrequency |
| Votiva[24,25] | InMode MD Ltd., Lake Forest, Calif | Bipolar radiofrequency |
| Wavetronic 6000HF-FRAXX, Megapulse HF FRAXX system[26] | Loktal Medical Electronics, São Paulo, Brazil | Microablative fractional radiofrequency |
| FotonaSmooth XS[27] | Fotona, Dallas, Texas | 2940-nm nonablative erbium:YAG |
| FotonaSmooth XS Dynamis[28] | Fotona | 2940-nm nonablative erbium:YAG |
| FotonaSmooth SP Spectro[29] | Fotona | 2940-nm nonablative erbium:YAG |
| Action II[30] | Lutronic, Inc., Goyang, Republic of Korea | 2940-nm erbium:YAG |
| MCL 31 Dermablate[31] | Asclepion Laser Technologies, Jena, Germany | 2940-nm erbium:YAG |
| FemiLift[32] | Alma Lasers, Buffalo Grove, Ill. | Fractional carbon dioxide laser |
| SmartXide$^2$/SmartXide$^2$ V$^2$LR, MonaLisa Touch[33] | DEKA, Florence, Italy | Fractional carbon dioxide laser |
| CO2RE Intima[34] | Syneron Candela, Wayland, Mass. | Fractional carbon dioxide laser |
| AcuPulse System, FemTouch Handpiece[35] | Lumenis, Yokneam Industrial Park, Israel | Fractional carbon dioxide laser |

### Radiofrequency Devices

Radiofrequency devices use electromagnetic waves that generate heat in the vaginal tissue to stimulate collagen contraction, neocollagenesis, angiogenesis, and growth factor infiltration to restore the elasticity and moisture of the vaginal mucosa.[11] Temperatures of 40° to 45°C induce collagen production by fibroblasts, which leads to soft-tissue tightening. Temperatures exceeding 47°C have been associated with burns and pain following treatment, although vaginal tissue can tolerate temperatures up to 50°C without sustaining thermal burns.[10] Radiofrequency vulvovaginal restoration treatments typically last 15 to 30 minutes and require no anesthesia. Typically, downtime is minimal, and it is recommended that patients resume normal activity following treatment.[10]

### Clinical Studies Using Radiofrequency

ThermiVa (ThermiAesthetics, Southlake, Texas), Viveve (Viveve, Inc., Sunnyvale, Calif.), Exilis Ultra Femme 360 (BTL Industries, Inc., Boston, Mass.), Exilis Protégé Intima (BTL Industries), Votiva (InMode MD Ltd., Lake Forest, Calif.), and Wavetronic 6000HF-FRAXX, Megapulse HF FRAXX system (Loktal Medical Electronics, São Paulo, Brazil) were used in the clinical trials listed in Table 2.[1–112] Treatment results were evaluated using physician- and/or self-reported questionnaires. (**See Table, Supplemental Digital Content 1**, which documents the efficacy of radiofrequency device treatments in detail. List of scoring and self-reported questionnaires for radiofrequency studies are included, ***http://links.lww.com/PRS/E211***.) There are a total of two level I studies, one level II study, and 10 level IV studies included in Table 2. Varying degrees of improvement of symptoms were reported in all studies. Limited adverse events and/or side effects were reported in two of the 13 studies and included vaginal discharge, pain, discomfort, and erythema and edema that resolved within a few hours.[22]

### Erbium:YAG Devices

The erbium:YAG laser initiates tissue resurfacing by emitting light at a wavelength of 2940 nm. The erbium:YAG laser's penetration depth is approximately 1 to 3 μm of tissue per J/cm$^2$ allowing for precise skin ablation with minimal thermal damage to surrounding tissue.[10] FotonaSmooth possesses a proprietary "smooth-mode" that uses a fast sequence of low-fluence laser pulses inside an overall superlong pulse of several hundred milliseconds. This leads to nonablative heating at a depth of 100 μm that in turn tightens the vaginal canal by neocollagenesis. A secondary erbium:YAG laser, the Action II, has a dual mode that combines multiple micropulses with long-pulse modes automatically, which enables a deeper secondary thermal effect and the controlled heating of the target mucous membrane inside the vaginal canal.[10,11]

### Clinical Studies Using Erbium:YAG

FotonaSmooth (i.e., XS, SP Spectro, Dynamis, and Incontilase), Action II, and MCL 31 Dermablate were used in the clinical trials listed in Table 3. In each study, results were cited through self- and/or physician-reported questionnaires and scales. (**See Table, Supplemental Digital Content 2**, which documents the efficacy of erbium:YAG device treatments in detail. List of scoring and self-reported questionnaires for erbium:YAG studies included,

**Table 2. Radiofrequency Clinical Studies**

| Device Name | Type of Study | Adverse Side Effects |
|---|---|---|
| ThermiVa | Single-center, prospective; $n = 23$[38]; level IV | No |
| ThermiVa | Single-center, prospective; $n = 25$[36]; level IV | No |
| ThermiVa | Prospective, randomized, controlled trial; $n = 20$[39]; level I | No |
| ThermiVa | Prospective, nonrandomized; $n = 10$[40]; level IV | No |
| Vivieve | Pilot; $n = 24$[41]; level IV | No |
| Vivieve | Prospective, longitudinal, single-arm; $n = 30$[37]; level IV | No |
| Vivieve | Randomized, placebo, sham-controlled, blinded, multicenter; $n = 186$[42]; level I | Treatment-emergent adverse events were reported by 11.1% and 12.3% of subjects in the active and sham arms, respectively; adverse events included vaginal discharge, pain, and discomfort |
| Exilis Ultra Femme 360 | Nonrandomized, prospective, multicenter; $n = 27$[27]; level IV | No |
| Exilis Protégé Intima | Prospective cohort; $n = 17$[21]; level IV | Mild discomfort, erythema, and edema that resolved in a few hours were noted |
| Votiva | Pilot; $n = 30$[25]; level II | No |
| Dynamic quadripolar radiofrequency (device name not disclosed) | Spontaneous exploratory; $n = 25$ and 13[43]; level IV | No |
| Dynamic quadripolar radiofrequency (device name not disclosed) | 12-mo extension of previous spontaneous exploratory study; $n = 25$ and 32[44]; level IV | No |
| Wavetronic 6000HF-FRAXX, Megapulse HF FRAXX system | Pilot; $n = 14$[26]; level IV | No |

***http://links.lww.com/PRS/E212***.) There are a total of two level I studies, eight level II studies, one level III study, and 12 level IV studies included in Table 3. Varying degrees of improvement of symptoms were reported in all studies. Limited adverse events and/or side effects were reported in 15 of the 23 studies and included discomfort during treatment, a burning sensation, slight vulvar edema, warmth or prickling sensation during treatment, vaginal discharge, mild pain during treatment, dysuria, minimal hematuria, vaginal dryness, vaginal itching, vulva discoloration, pelvic pain, vaginal bleeding, mild vaginal ecchymosis, lower abdominal discomfort, and vaginal spotting. Fewer than 2 to 3 percent of patients discontinued because of side effects in three studies.[22,33,38] Urinary tract infections occurred in two patients in separate studies; both were treated with antibiotics.[45,46] There is a large multicenter study currently being conducted; however, it does not include a control group.[47]

### Carbon Dioxide Devices

The carbon dioxide laser ablates tissue by emitting light at a wavelength of 10,600 nm that is absorbed by water in the tissue. Carbon dioxide devices differ from erbium in terms of depth of vaporization, crater base carbonization, and thermal coagulation based on the quantity of energy released within a certain period. These devices have the ability to penetrate approximately 20 to 30 μm of tissue in shorter than 1 msec, and the ability to confine the targeted area of thermal damage to a 100- to 150-μm-thick section of tissue.[10] Carbon dioxide lasers function by applying heat to a confined region of the epidermal and or dermal tissue while leaving proximal regions untouched. The affected areas experience tissue healing and collagen stimulation. When put into practice, carbon dioxide lasers act to stimulate the alteration of vaginal mucosa.[18,69]

### Clinical Studies Using Carbon Dioxide Lasers

FemiLift, SmartXide² V²LR/SmartXide², MonaLisa Touch, AcuPulse System, FemTouch Handpiece, and CO2RE Intima were all used for clinical trials summarized in Table 4. Results were evaluated using self- and/or physician-reported questionnaires. (**See Table, Supplemental Digital Content 3**, which documents the efficacy of carbon dioxide device treatments and 1 comparative study in detail. List of scoring and self-reported questionnaires for carbon dioxide studies included, ***http://links.lww.com/PRS/E213***.) There is a total of one level I study, nine level II studies, three level III studies, and 24 level IV studies included in Table 4. Varying degrees of improvement of symptoms was reported in all studies. Limited adverse events and or side effects were reported in 17 of the 37 studies and included: itching, discomfort, mild swelling, moderate burning with urination, moderate soreness, moderate spotting, mild to moderate pain, minor bleeding, mild irritation at the introitus during the procedure, dyspareunia,

**Table 3. Erbium:YAG Clinical Studies**

| Device Name | Type of Study | Adverse Side Effects |
|---|---|---|
| FotonaSmooth (XS) | Prospective, cohort, pilot, longitudinal; $n = 45$[48]; level II | Less than 3% of patients discontinued because of adverse side effects, including discomfort during treatment and a burning sensation starting 36 hr after treatment |
| FotonaSmooth (XS Dynamis) | Prospective, cohort, single-center; $n = 73$[49]; level II | No major adverse side effects were noted; one patient experienced a slight vulvar edema that resolved within 48 hr; patients reported warmth or prickling sensation during treatment |
| FotonaSmooth (SP Spectro) | Prospective, single-center, nonrandomized, pilot; $n = 175$[50]; level II | No major adverse events; patients reported mild discomfort |
| FotonaSmooth (XS Dynamis) | Pilot; $n = 31$[51]; level IV | Slight vulvar edema that disappeared within 48 hr, vaginal discharge, and a sensation of warmth were reported |
| FotonaSmooth (XS) | Prospective, longitudinal, pilot; $n = 42$[52]; level IV | Mild pain during treatment |
| FotonaSmooth (XS Dynamis) | Prospective, cohort, pilot, comparative; $n = 50$[53]; level II | A sensation of warmth, mild to moderate pain, and slight vulvar edema was noted in 4% of patients in the laser group; one patient developed transitory pain and spotting after the laser treatment; in the estriol group, 8% of patients experienced spotting, 4% experienced mastodynia, and 12% experienced abdominal pain |
| FotonaSmooth (XS) | Prospective, longitudinal, pilot; $n = 43$[54]; level IV | No |
| FotonaSmooth (IncontiLase) | Prospective; $n = 98$[55]; level IV | Not specified |
| FotonaSmooth (IncontiLase) | Retrospective (continuation of above study); $n = 18$[56]; level IV | Not specified |
| FotonaSmooth (SP Spectro) | Prospective, pilot; $n = 29$[45]; level IV | Dysuria and minimal hematuria were observed in four patients; one patient contracted a urinary infection and was treated with antibiotics |
| FotonaSmooth (XS Dynamis) | Prospective, pilot; $n = 33$[57]; level II | No |
| FotonaSmooth (IncontiLase) | Prospective, single-center; $n = 65$[58]; level IV | Less than 2% of patients discontinued treatment because of adverse events; adverse events not specified |
| FotonaSmooth (IncontiLase) | Randomized, controlled; $n = 114$[59]; level I | Patients reported minimal discomfort and sensation of warmth; increased vaginal discharge lasting up to 3 wk was reported by 49 patients in the laser group and six in the sham group; one patient in the laser group reported increased vaginal dryness after treatment |
| FotonaSmooth (IncontiLase) | Prospective, single-center; $n = 35$[60]; level IV | No |
| FotonaSmooth (SP Spectro) | Randomized, placebo-controlled; $n = 120$[61]; level I | Minimal treatment discomfort |
| FotonaSmooth (SP Spectro) | Pilot; $n = 22$[62]; level IV | One patient reported pelvic pain and two reported dysuria; both resolved within 24 hr of the procedure |
| FotonaSmooth (XS) | Prospective, longitudinal; $n = 205$[63]; level II | Less than 3% of patients discontinued treatment because of adverse events; adverse events included discomfort after the first application |
| FotonaSmooth (XS Dynamis) | Prospective; $n = 30$[64]; level IV | Mild but tolerable pain and burning sensation were noted; there were four reported cases of vaginal itching, seven cases of increased vaginal discharge, seven cases of vulva discoloration, and two cases of abnormal vaginal bleeding; the symptoms resolved in several days |
| Action II) | Prospective, cohort, randomized; $n = 30$[65]; level II | Very few patients felt mild vaginal ecchymosis with a mild burning sensation that lasted 24–48 hr |
| MCL 31 Dermablate | Prospective; $n = 37$[66]; level II | No |
| MCL 31 Dermablate | Retrospective, single-center, cohort; $n = 71$[48]; level III | There was one case of a urinary tract infection that was treated with antibiotics; one patient reported lower abdominal discomfort and vaginal spotting for 2 days |
| MCL 31 Dermablate | Prospective; $n = 16$[67]; level IV | No |
| FotonaSmooth (XS Dynamis) | Retrospective, telephone follow-up to overview results; $n = 103$[68]; level IV | A mild and transient edema and a tolerable heating sensation occurred in a few cases (exact number not specified by author) |

bruising, twinging sensation, numbness, purpura, mild irritation, vaginal discharge, lower pelvic pain, possible yeast infection, mild urinary infection, minimal blood serum secretion, postcoital urinary tract infections, and postmenopausal bleeding. One patient (who failed to disclose her medical history of genital herpes) had a genital herpes breakout following treatment[69] (Table 5).

**Table 4. Carbon Dioxide Laser Clinical Studies**

| Device Name | Type of Study | Adverse Side Effects |
|---|---|---|
| SmartXide² V²LR; MonaLisa Touch | Retrospective, cohort; $n = 94$[70]; level III | No |
| CO2RE Intima | Prospective, investigational; $n = 40$[71]; level IV | Two cases of mild itching and discomfort, one case of mild swelling, two cases of moderating burning with urination, one case of moderate soreness and spotting, one case of major itching, and one case of a possible yeast infection; these were reported within a 1-wk follow-up period |
| SmartXide² V²LR; MonaLisa Touch | Prospective, cohort; $n = 184$[72]; level II | Not specified |
| SmartXide²; MonaLisa Touch | Pilot; $n = 30$[73]; level IV | Two women reported mild to moderate pain lasting 2–3 days and two reported minor bleeding lasting <1 day; none were discontinued because of the occurrence of adverse events |
| SmartXide² V²LR; MonaLisa Touch | Prospective; $n = 55$[74]; level IV | Some participants reported a mild irritation at the introitus during the procedure and/or immediately after that resolved spontaneously |
| AcuPulse System, FemTouch Handpiece | Prospective; $n = 28$[75]; level IV | Adverse events reported during the study were of moderate severity and were unrelated to the procedure; one case of vaginal bleeding was reported 1 mo after the last treatment; no subjects were discontinued because of an adverse event |
| SmartXide²; MonaLisa Touch | Retrospective, chart review; $n = 31$[76]; level IV | Not specified |
| SmartXide²; MonaLisa Touch | Prospective, cohort; $n = 45$[77]; level II | Discomfort during probe insertion and vaginal soreness for 1–2 days after the procedure |
| FemiLift | Prospective, comparative; $n = 33$[78]; level II | No |
| SmartXide² V²LR; MonaLisa Touch | Prospective, comparative; $n = 87$[79]; level II | Not specified |
| SmartXide² V²LR; MonaLisa Touch | Prospective; $n = 20$[80]; level IV | Not specified |
| SmartXide²; MonaLisa Touch | Case series; $n = 112$[81]; level IV | No |
| SmartXide² V²LR; MonaLisa Touch | Prospective, descriptive, cohort; $n = 50$[82]; level II | No |
| SmartXide²; MonaLisa Touch | Retrospective cohort; $n = 122$[83]; level III | Five patients reported urinary tract symptoms, two reported vagina pain/burning, one reported vaginal itching, and one reported dyspareunia |
| CO2RE Intima | Prospective; $n = 21$[84]; level IV | Immediate responses included burning (20%), itching (20%), bruising (4%), swelling (4%), twinging sensation (4%), numbness (4%), and purpura (2%); one patient experienced a mild urinary tract infection that resolved after a weekly course of antibiotics |
| SmartXide²; MonaLisa Touch | Pilot, comparative; $n = 70$[85]; level II | Transient burning sensation that resolved within 5–6 days |
| SmartXide² V²LR; MonaLisa Touch | Prospective, observational; $n = 10$[86]; level IV | Not specified |
| SmartXide²; MonaLisa Touch | Case series; $n = 386$[87]; level IV | Mild discomfort with insertion of the probe, minimal blood-serum secretions for 1–2 days, and mild burning sensations for 1–2 hr after treatment were reported |
| SmartXide² V²LR; MonaLisa Touch | Observational, retrospective; $n = 26$[88]; level IV | Discomfort with insertion of the probe |
| SmartXide² V²LR; MonaLisa Touch | Retrospective; $n = 82$[89]; level IV | Three subjects discontinued treatment after two cycles because of persistent procedure-related discomfort; mild pain with insertion of probe |
| SmartXide² V²LR; MonaLisa Touch | Prospective, observational, pilot; $n = 30$[90]; level IV | No |
| SmartXide² V²LR; MonaLisa Touch | Pilot; $n = 15$[91]; level IV | No |
| SmartXide² V²LR; MonaLisa Touch | Prospective, cohort; $n = 40$[92]; level II | No |
| SmartXide² V²LR; MonaLisa Touch | Prospective, observational; $n = 53$[93]; level IV | Temporary mild irritation to the introitus that lasted up to 2 hr after treatment |
| SmartXide² V²LR; MonaLisa Touch | Retrospective, case control; $n = 50$[94]; level III | Adverse events in both groups related to the treatment were irritation and burning sensation with mild intensity at the introitus; serious adverse events were not present in any of the participants of either group |
| SmartXide² V²LR; MonaLisa Touch | Pilot; $n = 50$[95]; level II | Not specified |
| FemiLift | Prospective; $n = 15$[96]; level IV | Not specified |
| SmartXide²; MonaLisa Touch | Randomized, double-blind, placebo-controlled; $n = 45$[97]; level I | No |

(*Continued*)

**Table 4. *Continued***

| Device Name | Type of Study | Adverse Side Effects |
|---|---|---|
| SmartXide$^2$ V$^2$LR; MonaLisa Touch | Prospective; $n = 102$[69]; level IV | Three subjects experienced postcoital urinary tract infections and two experienced vaginal discharge/infection; three subjects experienced lower pelvic pain for 2–3 days; one patient (who failed to disclose her medical history of genital herpes) had a genital herpes breakout following treatment; two women presented with postmenopausal bleeding following their third laser treatment (at 4 mo and 6 mo, respectively) |
| SmartXide$^2$ V$^2$LR; MonaLisa Touch | Prospective; $n = 77$[98]; level IV | Not specified |
| SmartXide$^2$ V$^2$LR; MonaLisa Touch | Observational, pilot; $n = 48$[99]; level IV | No |
| SmartXide$^2$; MonaLisa Touch | Two-center, prospective; $n = 30$[100,101]; level IV | Mild to moderate pain following treatment was reported in two patients; pain resolved within 2 or 3 days; slight bleeding for <1 day occurred in two patients |
| SmartXide$^2$; MonaLisa Touch | Case control, observational; $n = 92$[102]; level II | Six cases of vaginal bleeding occurred with the application of PRP; 30% of patients reported mild discomfort such as pain or a burning sensation with the vaginal scanner application |
| SmartXide$^2$ V$^2$LR; MonaLisa Touch | Prospective; $n = 53$[103]; level IV | No |
| SmartXide$^2$ V$^2$LR; MonaLisa Touch | Pilot study; $n = 50$[104]; level IV | No |
| SmartXide$^2$ V$^2$LR; MonaLisa Touch | Prospective; $n = 386$[87]; level IV | A burning sensation, discomfort during handpiece movement, vulvar introitus burning/pain, and vulvar pain were reported |
| SmartXide$^2$ V$^2$LR; MonaLisa Touch | Prospective; $n = 161$[105]; level IV | No |

PRP, platelet-rich plasma.

**Table 5. Comparative Study**

| Device Name | Study | Adverse Side Effects |
|---|---|---|
| FotonaSmooth (XS Dynamis), and SmartXide$^2$; MonaLisa Touch | Prospective; $n = 31$[106]; level II | Mild irritation of the introitus was noted during the procedure but resolved spontaneously after therapy (side effects per specific device were not distinguished) |

## DISCUSSION

The first energy-based vulvovaginal restoration device became available in Europe in 2008. Less than 10 years later, there were an estimated more than 500,000 procedures performed annually.[107,108] The American Society of Plastic Surgeons estimated a 39 percent increase in plastic surgeons performing vulvovaginal restoration procedures (surgical and nonsurgical) in the United States from 2015 to 2016.[1] In fact, nonsurgical and minimally invasive vulvovaginal restoration has been one of the fastest growing areas in plastic surgery and urogynecology over the past decade.[12] This is thought to be a reflection of decreased stigmatization of female health issues[3,4,9,10,12,13] and demonstrated safety and efficacy of energy-based devices.[5,8,12,20,36,41,109,110] Despite this, there are barriers preventing sound scientific evaluation of these devices, including lack of objective outcome measures, use of unvalidated surveys, paucity of case/control studies, and inadequate follow-up.

A number of energy-based devices, including radiofrequency and laser (carbon dioxide and erbium:YAG) have reportedly improved external genital appearance, vaginal laxity, and stress incontinence.[8,10,12,20,37,41,110] Patients and clinicians often view these nonsurgical options as more attractive than invasive surgical treatments, with less downtime, discomfort, and expense.

Laxity of the female vulvovaginal tissue can occur for a variety of reasons, including natural aging, childbirth, genetics, and trauma. These events often lead to generalized symptoms of genitourinary syndrome of menopause, stress urinary incontinence, atrophic vaginitis, orgasmic dysfunction, and dissatisfaction with appearance.[11] Currently, 50 percent of women exhibit symptoms of genitourinary syndrome of menopause, and in most cases, this is a chronic condition that worsens when untreated.[10] In addition, stress urinary incontinence has estimated prevalence rates ranging from 4 to 35 percent of all adult women,[51] and an estimated 76 percent of women have symptoms of sexual dysfunction that significantly affect their quality of life.[111] The prevalence of these

conditions increases significantly with age, with a lifetime likelihood of undergoing a single operation for prolapse or incontinence of 11 percent and a reoperation rate of 30 percent.[2,3] Given the widespread presence of these symptoms, these are public health issues that deserve attention. Current treatment options are limited and include biofeedback, laser, electrical muscle stimulation and, in certain cases, operative intervention.[2–9] The purpose of this review was to address the claims made by the U.S. Food and Drug Administration by examining all relevant literature and identifying areas in which data may be lacking in the area of energy-based devices for vulvovaginal restoration.

Based on the evidence we found through our research, and according to the American Society of Plastic Surgeons Evidence Rating Scale for Therapeutic Studies,[112] we found five level I studies, 19 level II studies, four level III studies, and 46 level IV studies that used 15 different devices. The majority of studies indicated overall satisfaction with treatment, and 100 percent of studies reported differing degrees of improvement of symptoms. One large study confirmed that patients felt the out-of-pocket expense was worth the expenditure.[83] It is clear that the number of level I, sham-controlled, randomized studies is lacking; however, a large majority of our comprehensive list of studies conducted to date yielded mild to no adverse events and/or side effects as a result of treatment.

Adverse events and/or side effects associated with radiofrequency devices were noted in two of the 13 studies and included vaginal discharge, pain, discomfort, and erythema and edema that resolved within a few hours.[22] Adverse events and/or side effects associated with erbium:YAG devices were noted in 15 of the 23 studies and included discomfort during treatment, a burning sensation, slight vulvar edema, warmth or prickling sensation during treatment, vaginal discharge, mild pain during treatment, dysuria, minimal hematuria, vaginal dryness, vaginal itching, vulva discoloration, pelvic pain, vaginal bleeding, mild vaginal ecchymosis, lower abdominal discomfort, and vaginal spotting. Urinary tract infections occurred in two patients in separate studies; each was treated with antibiotics.[45,46] Adverse events and/or side effects associated with carbon dioxide devices were noted in 17 of the 37 studies and included itching, discomfort, mild swelling, moderate burning with urination, moderate soreness, moderate spotting, mild to moderate pain, minor bleeding, mild irritation at the introitus during the procedure, dyspareunia, bruising, twinging sensation, numbness, purpura, mild irritation, vaginal discharge, lower pelvic pain, possible yeast infection, mild urinary infection, minimal blood serum secretion, postcoital urinary tract infections, and postmenopausal bleeding. One patient (who failed to disclose her medical history of genital herpes) had a genital herpes breakout following treatment.[69] It is also important to note that in one study, which monitored vaginal bacteria before and after carbon dioxide laser treatment, there were no symptoms of bacterial vaginosis, aerobic vaginitis, or candidiasis detected in any subjects following treatment. There was, however, an increase of *Lactobacillus* and normal flora noted in subjects following treatment.[103] Although there are fewer radiofrequency studies included in this article, there is a significantly smaller correlation between adverse events and/or side effects and radiofrequency treatments compared to erbium:YAG and carbon dioxide devices.

Improvement after radiofrequency device treatment regarding symptoms of vaginal laxity, stress urinary incontinence, vulvovaginal atrophy, atrophic vaginitis, pelvic organ prolapse, genitourinary syndrome of menopause, urinary incontinence, and sexual distress in addition to increased sexual satisfaction, reduction in time to orgasm, ability to orgasm, increased vaginal moisture, improved sexual function, improved vulvar appearance, and/or improved quality of life was reported in 13 of the 13 studies included. Improvement after erbium:YAG device treatment regarding symptoms of vaginal dryness, dyspareunia, genitourinary syndrome of menopause, stress urinary incontinence, mixed urinary incontinence, pain, pelvic organ prolapse, dysuria, urgency, sexual function, vulvovaginal atrophy, vaginal wall relaxation, vaginal health, and sexual satisfaction in addition to vaginal tightening and/or perineometry variable improvement was reported in 23 of the 23 studies included. Improvement after carbon dioxide device treatment regarding symptoms of genitourinary syndrome of menopause, dyspareunia, vaginal dryness, sexual function, vaginal health, itching, menopause, pain, burning, dysuria, vulvovaginal atrophy, painful intercourse, sexual distress, stress urinary incontinence, quality of life, sexual satisfaction, vestibular pain, vulvodynia, sensitivity during sexual intercourse, pelvic organ prolapse, atrophic vaginitis, bladder function, vaginal sensation, vaginal lubrication, and/or urge incontinence was reported in 37 of the 37 studies included.

Histologic results from two radiofrequency device studies reported positive histologic changes

in women suffering from postmenopausal vaginal atrophy and/or increases in collagen, elastin, vascularity, and small nerve fibers.[39,40] Histologic results from four erbium:YAG treatment studies revealed changes in the tropism of the vaginal mucosa, angiogenesis, congestion and restructuring of the lamina propria, an increase in neoangiogenesis, evidence of tissue regeneration, neocollagenesis, remodeling of vaginal mucosa, an improvement of structural organization of the epithelium, and/or better elasticity of the vaginal wall.[53,55,56,65] Histologic findings from four carbon dioxide studies revealed increased collagen and elastin, thicker epithelium, an increased number of cell layers, a better degree of surface maturation, restoration of the epithelial and subepithelial structures, restoration of the vaginal thick squamous stratified epithelium, significant storage of glycogen in the epithelial cells, a high degree of glycogen-rich shedding cells at the epithelial surface, significant increase in the fibrillar component of the extracellular matrix and fibroblast activity bins, and/or neoangiogenesis after laser treatment.[71,78,95,102]

Further investigation in the form of head-to-head comparison of level I, sham-controlled, randomized trials is needed to accurately assess the effects, outcomes, and limitations of treatments using radiofrequency, carbon dioxide, and erbium:YAG devices. We saw that the placebo effect that was manifested in one of the few sham-controlled studies was proven to be an influential factor in the results,[42] and this should be expanded on in future studies. In addition to conducting additional studies, when extrapolating current data pertaining to the efficacy and safety of energy-based vulvovaginal restoration devices, there are a variety of key limitations to consider.

The lack of standardization in both patient inclusion criteria and measuring posttreatment outcomes poses a significant barrier to data interpretation. Standard baseline values for symptoms treated with radiofrequency and laser devices should be determined to effectively cross-compare evidence. Objective standards pertaining to time to orgasm, vulvovaginal appearance, vaginal laxity, vaginal lubrication, and changes that occur in the vaginal wall are also lacking. Standardization regarding the severity of adverse events is also necessary for future investigation to effectively compare outcomes. The language surrounding adverse event classification in this article is transcribed from individual studies; however, there is a lack of prescribed terminology, which must be taken into account when analyzing results. A majority of past studies were built on self-reported validated and unvalidated questionnaires. Key terms listed on questionnaires such as the unvalidated Vaginal Laxity Questionnaire can have different meanings to different patients, making it difficult to compare results. Studies performed also have very limited long-term follow-up. With the standard follow-up averaging 6 to 12 months, there is a gap in knowledge regarding the lasting effects of radiofrequency and laser treatments.

It is also important to consider that energy-based vulvovaginal restoration devices differ greatly from one another. Radiofrequency, carbon dioxide, and erbium:YAG use different methods and have differing settings, heat capacity, and operation standards. As a result, we must exercise caution when categorizing these devices together. Furthermore, we were able to identify only one comparison study between device categories. More of such studies are needed to assess the efficacy and safety of the devices and to also determine which devices are best suited for different indications. A potential source of funding for future studies is device companies themselves; however, there is inherent bias that must be taken into account when financial interests are at play. We must also ensure that in future studies, experienced professionals in core-related specialties are at the forefront of the use of these technologies to ensure quality control.

## CONCLUSIONS

After a systematic review of the literature regarding energy-based vulvovaginal restoration, the authors have found that a majority of studies conducted resulted in mild to no adverse side effects. In addition, various degrees of beneficial effects were reported in 100 percent of the studies included. However, to date, there is a large gap in level I evidence in this field. As a result, the authors emphasize the necessity of supplemental data surrounding this subject and suggest additional head-to-head, randomized, sham-controlled studies be conducted to further investigate vulvovaginal restoration devices in an effort to address women's health issues at large. The authors have found that public academic literature does not support the U.S. Food and Drug Administration commissioner's claims, although we must consider the possibility of a private data source to which the U.S. Food and Drug Administration may have potential access.

It is critical that we not create fear for women seeking treatment for vulvovaginal health issues

and that we do not discourage patients from participating in additional studies that will advance our knowledge surrounding the safety of these devices. Energy-based vulvovaginal restoration may have the potential to advance female sexual wellness and the manner in which women can seek medical attention for vulvovaginal symptoms. We advocate for further investigation so that, if proven to be safe, treatment can be made accessible to women.

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