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REVIEW ARTICLE

Light and energy-based therapeutics for genitourinary applications: Consensus on protocols and best practices

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Abstract

Background: Lasers and energy-based technologies have been developed for genitourinary applications over the past several decades.

Aims: This consensus article aims to categorize the published articles and clinical trial data that culminated in protocol development of technology for genitourinary applications, and to develop consistent parameters in future clinical trials.

Materials and Methods: The published articles and clinical trials data on lasers and energy-based devices applied to genitourinary conditions were categorized according to device and condition and consensus developed on protocols and parameters.

Results: The devices in genitourinary applications were classified as fractional lasers, radiofrequency and high-intensity focused electromagnetic field therapy. The consensus of the protocols and parameters based upon the published clinical trials of their application to the vaginal and urologic conditions associated with genitourinary syndrome of menopause was developed and organized according to device and condition.

Discussion: The status of FDA clearances and future pathways are discussed.

Conclusions: This consensus article categorizes and presents the protocols and practices for the main classes of lasers and energy-based devices for genitourinary applications in future clinical trials.

KEYWORDS

energy-based devices, genitourinary, HIFEM, lasers, menopause, pelvic, radiofrequency, urinary incontinence, vagina, vulvovaginal

HISTORY OF LASERS & ENERGY-BASED DEVICES FOR GENITOURINARY APPLICATIONS

Lasers and energy-based technologies have been developed for skin and genitourinary applications over the course of a half century.[1,2] A laser is an instrument that generates a beam of light of a single wavelength or color that is both highly collimated and coherent; the acronym stands for "light amplification by the stimulated emission of radiation."[3] In contrast, energy-based devices (EBDs) emit a different form of energy than a laser or light-based technology. Radiofrequency (RF) uses alternating current to generate an alternating electromagnetic field to heat and induce effects in the skin, while high intensity focused electromagnetic field (HIFEM) employs a rapidly moving magnet to generate an electric current to induce muscular contractions.[4,5]

Plastic surgeons and gynecologists pioneered the use of the carbon dioxide (CO_2) laser for ablation, coagulation, and incision, and reported the outcomes on cervical and vaginal pathologies dating back to the 1970s.[6–8] Lasers became an established treatment modality for genital warts, with beam alignment via micromanipulators connected to dedicated operating microscopes ("colposcopes").[9] Development of the laser laparoscope in the 1980s with rigid or flexible probes enabled laser vaporization treatment of endometriosis, fibroids, and adhesions; pelvic pain due to defects and adhesions; laser myomectomy; salpingolysis, laser resection of ovaries;

and cystectomy.[10] Alongside the CO_2 laser, the neodymium-YAG laser hysteroscope was also developed for endometrial ablation.[11]

Laser treatments of vulvovaginal atrophy, lichen sclerosus, and other genitourinary conditions were also pioneered in the 1980s. The CO_2 laser, which had been applied to rejuvenate atrophic body skin, was used to safely and effectively treat the atrophic vaginal conditions of pruritus vulvae and lichen sclerosus.[12–14] The first laser treatment of vulvodynia with the flashlamp-excited dye laser on a cohort of 175 subjects in 1995 reported a 92.5% response rate.[15] Esthetic laser treatment of the vulva, termed "laser labioplasty," was conducted in 2006; among 55 subjects, 91% reported being "very satisfied."[16] Laser laparoscopy ushered in a new era transitioning away from surgical toward less interventional treatments with consequently less morbidity and mortality. An editorial article in the journal *Fertility and Sterility* (2006) stated that "Landmark innovations in the 1980's involved the use of CO_2 lasers … triggered the transition from laparotomy to laparoscopy".[17] In 2007, one of the authors (A.G.) converted the use of the laser laparoscope with the defocusing coupler originally designed for beam alignment to test the concept of "vaginal rejuvenation" and triggered the design and assembly of a dedicated device.[18]

Laser and energy-based industries have developed a multitude of devices employing ablative and non-ablative fractional laser and RF technologies which largely differ in their method of thermal effects on live tissue.[3] Controlled wound-healing effects replaced irreversible tissue destruction to maximize long-term results, termed "skin rejuvenation." This approach was then translated from dermatology to gynecology to address gynecological needs.[19] Fractional laser resurfacing is a technology in which an array of microbeams of laser light creates microscopic columns of energy-mediated effects.[20,21] The microscopic lesions extend from the epidermal layer into the dermis, or from the vaginal epithelium into the lamina propria, to depths dictated by laser energy density up to 1.5 mm penetration depth.[20–22] Most fractional ablative devices use an optical scanner to deliver a very small laser spot across the tissue, and others employ a "pixelated" technology where an array of laser spots is "stamped" onto the target tissue through a micro-lens array or holographic beam splitter.[3,20,21]

Over the past 15 years, a growing body of published scientific and clinical reports has documented fractional CO_2 and Er:YAG laser applications for vulvovaginal dryness, dyspareunia, laxity, urinary incontinence, infections as well as other conditions related to genitourinary syndrome of menopause (GSM).[1,2] Clinical outcomes have been correlated with histologic changes such as reepithelialization, neovascularization, and improvement of collagen synthesis.[1,22,23] Beneficial effects have been reported on the urethra, improving urethral mucosal and submucosal trophism to decrease urinary symptoms using an intraurethral cannula.[24] Clinical reports have been compiled regarding the application of EBD such as RF and HIFEM technology.[1,25,26] Penetration depth of EBD varies considerably with a penetration depth of 4 mm demonstrated on histopathological analysis for RF devices in dermatologic applications.[27,28] In the case of HIFEM, penetration depths of up to 15 cm have been described.[29] However, the quality of evidence for application of these technologies to genitourinary conditions is inconsistent, and the aim of this editorial is to discuss treatment guidelines, optimal protocols, and best practices.

LASER AND EBD GENITOURINARY APPLICATIONS

The application of lasers and EBD to the genitourinary tract may be categorized according to device class, target anatomic site, and conditions treated. The first device category to be discussed is fractional lasers, including ablative (CO_2 and Er:YAG), non-ablative, and hybrid technologies. The second category is the EBD, including RF and HIFEM.

Fractional lasers

Fractional lasers employ the delivery of energy beams of laser light in microcolumns extending from the epidermis or epithelium into the dermal or lamina propria layer with intervening areas of untreated skin or tissue.[3,20,21] A fraction of the surface area is treated, which allows for intervening untreated tissue to facilitate wound healing and prevent complications such as scarring. Fractional devices may be subdivided into ablative, namely those that fully vaporize micron-level channels of tissue, and non-ablative, namely those that cause columns of thermal injury without vaporization.[3,20,21] The wound-healing response following fractional resurfacing induces reepithelialization and remodeling of deeper tissue, resulting in thickening of the epithelium, dermis, or lamina propria with denser connective tissue and neovascularization.[3,20–23]

Preoperative assessment

Before determining the course of therapy, pretreatment assessment includes the confirmation of the presence of a condition for which laser therapy is appropriate and elimination from consideration of any individuals with contraindications to laser surgery.

FDA clearance status of fractional devices for genitourinary tissues

The current FDA clearance status of lasers and EBD for genitourinary applications is shown in Table 1. Clearances are for general application and are not indicated for specified

TABLE 1 Current FDA approval status of devices in genitourinary applications[17]

Device	510K	Date	Indications
Joule Profile Multi-Platform System, diVA (Sciton), Er:YAG 2940 nm, 1470 nm	K060033 K101916	1/4/2006 3/18/2011	At 2940 nm: ablation, vaporization, and coagulation of soft tissue and for skin resurfacing and at 1470 nm: Ablation, vaporization, hemostasis, or coagulation of soft tissue.
Lumenis Femtouch, CO_2	K100415	4/12/2010	Vaporization, incision, excision, ablation or photocoagulation of soft tissue in the surgical specialties of ENT, Gynecology, Laparoscopic Surgery, including GYN Laparoscopy, Esthetic Surgery, Dental and Oral Surgery, Neurosurgery, Orthopedics, General Surgery and Podiatry.
SP DYNAMIS (Fotona), Er:YAG 2940 nm, Nd:YAG 1064 nm	K101817 K143723	11/22/2010 4/9/2015	Surgical applications requiring the ablation, vaporization, excision, incision, and coagulation of soft tissue in medical specialties, including aesthetic surgery (dermatology and plastic surgery), podiatry, gynecology, neurosurgery, orthopedics (soft tissue), arthroscopy.
Femilift (Alma), CO_2	K103501	1/14/2011	Laser incision, excision, ablation and/or vaporization and of soft tissue in gynecology for the treatment of conization of the cervix, including cervical intraepithelial neoplasia, vulvar and vaginal intraepithelial neoplasia; condylomna acuminate, including cervical, genital, vulvar, perineal, and Bowen's disease, (erythroplasia of Queyrat) and Bowenoid papulosa (BP) lesions; leukoplakia (vulvar dystrophies); incision and drainage of Bartholin's and nubuthian cysts; herpes vaporization; urethral caruncle vaporization; cervical dysplasia; benign and malignant tumors; hemangiomas.
ThermiVA (Thermi), RF	K130689	11/15/2013	For use in dermatological and general surgical procedures for electrocoagulation and hemostasis.
SmartXide2 CO_2, MonaLisa Touch, El En/ DEKA/Cynosure	K133895	9/15/2014	Incision, excision, vaporization and coagulation of body soft tissues in medical specialties, including aesthetic (dermatology and plastic surgery), podiatry, otolaryngology (ENT), gynecology, neurosurgery, orthopedics, general and thoracic surgery (including open and endoscopic), dental and oral surgery and genitourinary surgery. The use with the scanning unit is indicated for ablative skin resurfacing.
CORE Intima (Syneron), CO_2	K151655	9/14/2015	Surgical applications requiring the ablation, vaporization, excision, incision, and coagulation of soft tissue in medical specialties, including esthetic surgery (dermatology and plastic surgery), podiatry, gynecology, neurosurgery, orthopedics (soft tissue), arthroscopy.
HPM 6000UF	K181497	11/14/2018	Noninvasive electromagnetic stimulation of pelvic floor musculature for the purpose of rehabilitation of weak pelvic muscles and restoration of neuromuscular control for the treatment of male and female urinary incontinence
Emsella, BTL			https://www.accessdata.fda.gov/cdrh_docs/pdf18/K181497.pdf

Note: Modified from reference.[19]

genitourinary conditions. Off-label use as applied to medical devices is the application of the device for a purpose that is not included as an indication in the FDA-approved device labeling. When consenting patients, while explicit consent for off-label use is not a requirement by the FDA, a section may be included that specifies that the procedure is being used off label for a purpose that it is not included as an indication.

Conditions treated with fractional lasers

The conditions for which outcomes of fractional laser therapy have been published are listed in Table 2. Although published reports of outcomes for specified diagnoses and conditions are listed, the FDA clearances for these diagnoses and conditions have yet to be obtained at the time of this publication.

Severity assessments

The presence and severity of each genitourinary condition should be assessed through one or more of the validated genitourinary health grading scales. such as the Vaginal Health Index (VHI), Vulvovaginal Atrophy Questionnaire (VVA), Female Sexual Function Index (FSFI), Urinary Distress Inventory (UDI). Urinary Incontinence Severity Score (UISS), and Visual Analog Scale (VAS) (Addendum).

Contraindications

Contraindications to laser treatment include presence of intrauterine device, active urinary tract or genital infection, vaginal bleeding, current pregnancy, active or recent malignancy, electrical implant anywhere in the

TABLE 2 Fractional lasers and settings for vulvovaginal applications.

Device	Brand	Parameters	References
Fractional CO_2 10,600 nm	MonaLisa Touch, Cynosure	15–30 W, 1000 μs dwell time, 1000 μm dot spacing, unstacked or maximum 1–2 stacked, single pass, 3 monthly treatments	[30]
	CORE Intima, Candela	50 mJ, 283 J/cm^2, 60 W, 0.83 ms, 5% surface area, single pass, 3 monthly treatments	[31]
	FemiLift, Alma Lasers	40–120 mJ/Pixel, adjusted to patient's tolerance	[32–34]
	Femtouch, Lumenis	10 mJ and a spot density of 10%–15% 5 pulses every 60° in a 360° radius 1 cm apart	[35]
Fractional Er: YAG 2940 nm	Incontilase, intimalase, renovalase, fotona	1.75 J/cm^2, 250 ms, 7 mm spot Incontilase: vaginal canal	[36]
		(1) Angular extension (PS03X-GAc, 7 mm, 6 J/cm^2, 1.6 Hz, seven pulses, six adjacent longitudinal lines); (2) circular full laser beam (R11-GCc, 7 mm, 3 J/cm^2, 1.6 Hz, seven pulses, 2 passes); (3) external treatment, laser pulses on vestibule and introitus with a straight, patterned laser (PS03X, 7 mm, 10 J/cm^2, 1.6 Hz, two to three pulses, two passes). Intimalase: Vaginal canal (1) circular full laser beam (R11-GCc, 7 mm, 3 J/cm^2, 1.6 Hz, seven pulses, three passes), external treatment (2) laser pulses on vestibule and introitus with a straight, patterned laser (PS03X, 7 mm, 10 J/cm^2, 1.6 Hz, two pulses. Renovalase: Vaginal canal (1) circular full laser beam (R11-GCc, 7 mm, 1,75 J/cm^2, 1.6 Hz, seven pulses, 2–3 passes), external treatment (2) laser pulses on vestibule and introitus with a straight, patterned laser (PS03X, 7 mm, 10 J/cm^2, 1.6 Hz, 2 pulses. All procedures with a glass probe.	[37] [38]
	Petit Lady, Lutronic	3 treatments q 2 weeks, 15 mJ, 1.7 J per shot, 3 multishots, 250 μs,	[39]
	Diva, Sciton	Automated, 90°,190°, or 360°	NA
	Juliet, Cutera	360° sequential pulses, 1 cm apart; 2 passes 1st is ablative, 2nd is coagulative	[40]
Hybrid Er:YAG 2940 nm/ 1470 nm diode	Diva, Sciton	Automated tx, choose 90°,190°, or 360°	NA

body, significant concurrent illness, anticoagulative or thromboembolic condition or taking anticoagulation medications 1 week before and during the treatment course, immunosuppression/immune deficiency disorders or medications, prior pelvic lymph node dissection, history of keloid scarring, abnormal wound healing, radiation treatment to the area, collagen vascular disease or vasculitic disorders, use of isotretinoin within 6 months, systemic corticosteroid therapy, dysplastic nevi in the area, prolapse staged >II according to the pelvic organ prolapse quantification (ICS-POP-Q) system, or previous pelvic reconstructive surgery.

Preoperative preparation

Instruct the patient to avoid aspirin or any medications that contain aspirin for 7 days before your procedure. For patients who are menstruating, have them schedule their procedure for 1 week after their period. This will help distinguish between vaginal bleeding caused by the procedure and vaginal bleeding during the menstrual period. Instruct the patient to avoid intercourse the night before the procedure and if they may be pregnant, to alert the physician. Instruct the patient to reschedule if they have: a fever, chills, or vaginal bleeding or discharge.

Preoperative physical examination and testing

Before treatment with fractional lasers in the vaginal tract, a normal speculum examination and recent negative PAP smear by a trained gynecologist, urologist, or physician with a specialty in genitourinary care are required. A speculum examination of the entire vaginal vault and external examination with swab use to clear topical agents, if any, should be performed on the day of treatment before device insertion. For those of child-bearing potential, a pregnancy test is taken. Written and verbal informed consent should be obtained, including a discussion of all treatment options, risks, and benefits.

Anesthesia

No topical or local anesthetic is necessary for vaginal treatment, though topical lidocaine (EMLA or 5%

lidocaine gel) may be applied to the vulva for 10 min before external genital treatment with fractional devices and affords adequate pain control.

Perioperative laser methods

Vulvovaginal protocol

The settings on the device are provided by each manufacturer.[30–40] In general, the fluence (for microablative CO_2 laser) is in the low range of approximately 250–300 mJ/cm^2 and the spacing of the microbeams is approximately 1 mm apart. The handpiece is inserted fully into the vault. The laser-based devices applied to vaginal tissue with published settings are listed in Table 2. Pulses are administered circumferentially starting proximally at the vaginal vault and retracting the device until the entire vault is treated. Upon reaching the introitus, the device is removed, and the handpiece is exchanged for an external handpiece if external treatment is planned. External treatment with fractional resurfacing devices is associated with some discomfort. The introitus, labia minora and majora, and the clitoral hood may be treated with a single pass. Each technology provides parameters and precise protocols for treatment. Three treatments at 1-month intervals are recommended with maintenance treatments performed as a single treatment between 6- and 12-month follow-up based upon the duration of outcomes.[30–38]

Urinary protocol

Lasers used for the management of urinary symptoms have a specific chromophore, water. In postmenopausal women, tissue water retention decreases considerably, so before carrying out treatment for a condition that requires a greater energy fluence such as stress urinary incontinence, prior preparation of the tissue with topical estrogen, hyaluronic acid, or vaginal moisturizers is recommended to improve hydration in the weeks preceding laser treatment. This helps ensure a correct photothermal effect and good clinical results. A speculum examination with swab use to clear residual topical agents should be performed before probe insertion.

Stress urinary incontinence (SUI). The microablative CO_2 laser and the non-ablative long-pulse Erbium:YAG (Er:YAG laser have been demonstrated to be safe and effective in managing urinary symptoms for both urethral hypermobility (microablative CO_2 and non-ablative Er:YAG) and intrinsic sphincter deficiency (non-ablative Er:YAG) (Table 3).[30–34,41–43] Evidence to date has shown that the regenerative effect of laser light improves the mechanisms of continence, reinforcing the anterior vaginal wall and improving the trophism of the mucosal sphincter. The urethral laser protocol uses Er:YAG at 2940 nm delivered through a 4 mm cannula in a non-ablative manner at low fluence with caloric diffusion in the mucosa and submucosa, ensuring a congestive effect of the submucosal vascular plexus initially and angiogenic effect over time.[41,42] The intraurethral approach employs an intraurethral handpiece (e.g., RO92GU, Dynamis, Fotona, Table 3).[43] Non-ablative laser energy is deposited with four consecutive pulses delivered at 1.4 Hz, 4 mm spot size, and 1.5 J/cm^2 fluence. After full insertion, a train of four pulses are delivered; the cannula is pulled distally by 2.5 mm increments. Pulse delivery is repeated until the urethral orifice is reached. One treatment session consists of four passes.[43]

Overactive bladder. Overactive bladder (OAB) is characterized by urinary urgency and is often accompanied by frequent urination, nocturia, and urgency urinary incontinence. OAB symptoms are especially common

TABLE 3 Fractional lasers and settings for urinary applications.

Device	Power/energy/fluence	Pulse duration	Density/ spacing	Treatment sessions	Trade name	References
CO_2 10,600 nm	30 W	1000 µs	1000 µm	3 monthly	Mona Lisa, Cynosure	[30]
	60 W/50 mJ/283 J/cm^2	830 µs	5%	3 monthly	CO2RE Intima, Candela, Wayland, MA	[31]
	40–120 mJ/pixel			3 monthly	FemiLift, Alma Lasers, Cesarea, Israel	[32] [33] [34]
Er: YAG 2940 mm	1.5 J/cm^2 1st step angular extension 6 J/cm^2	1.4 Hz, 250 ms	7 mm spot	3 monthly	Dynamic, Fotona	[41]
	2nd step circular extension 3 J/cm^2					[42] [43]

among women suffering from GSM. If standard therapies do not improve OAB complaints, non-ablative Er:YAG and microablative CO_2 lasers can be considered to improve symptoms. Laser therapy has demonstrated comparable efficacy to outcomes reported with pharmaceutical agents by improving the blood flow in the vaginal wall, urethra, and bladder neck.

Postoperative management

Vulvovaginal management

Following vaginal ablative resurfacing with a CO_2 laser or vaginal non-ablative treatment protocol with Er:YAG laser, a 3-day recovery time is recommended with avoidance of intercourse during this period. Rarely, spotting or vaginal discharge may occur. Discomfort tends to be minimal or absent during treatment and minimal the first postoperative day. Any severe discomfort or burning may potentially signify infection and should prompt evaluation and possibly vaginal cultures. Instruct the patient to shower as usual but to avoid baths and strenuous activity for 3 days. Follow-up is performed monthly until three treatments are completed; maintenance treatment in a single session appears to be required between 6 and 12 months.

Urological management

Proper hydration of the vaginal mucosa before the use of non-ablative Er:YAG laser or microablative CO_2 is recommended to avoid symptoms of inflammation, bleeding, or pain immediately after the procedure. However, due to the inflammatory effect generated by excessive energy fluence deposited or low tissue hydration, urinary urgency and de novo urinary incontinence may occur. If these symptoms do worsen after treatment, they can typically be managed conservatively with improvement expected between 2 and 15 days postprocedure.

Return to normal sexual activity after a microablative CO_2 laser treatment for SUI is between 7 and 10 days and after a non-ablative Er:YAG laser treatment is 3 days. In elderly women, the use of hyaluronic acid, vaginal moisturizers, or local estrogen therapy may be recommended before and after the procedure to minimize the risk of these unwanted effects and to maximize positive outcomes.

RF devices

RF is defined by the oscillation rate of an alternating electric current or voltage or of a magnetic, electric, or electromagnetic field in the frequency range of approximately 20 kHz to 300 GHz, which is between the upper limit of audio frequencies and the lower limit of infrared frequencies.[4,27,28] RF heating of skin has been employed to result in dermal remodeling which correlates clinically with wrinkle and laxity reduction.[27,28] The transfer of the application of this technology to the vulva and vagina has been reported and reviewed.[44] RF heating of skin to internal temperatures of 65°C results in partial collagen denaturation, the triggering of a wound healing response, collagen, elastin, and hyaluronic acid synthesis, which correlate clinically with rhytid reduction and laxity reduction.[27,28]

Preoperative assessment

Contraindications

Contraindications and relative contraindications to treatment to be considered include the presence of metal implants or intrauterine device, urinary tract or genital infection, vaginal bleeding, active or recent malignancy, electrical implant anywhere in the body, significant concurrent illness, anticoagulative or thromboembolic condition or taking anticoagulation medications 1 week before and during the treatment course, immunosuppression/immune deficiency disorders or medications, uncontrolled hormonal imbalance, prior pelvic lymph node dissection, history of keloid scarring, abnormal wound healing, radiation treatment to the area, collagen vascular disease or vasculitic disorders, use of isotretinoin within 6 months, systemic corticosteroid therapy, dysplastic nevi in the area, prolapse staged >II according to the pelvic organ prolapse quantification (ICS-POP-Q) system, or previous pelvic reconstructive surgery.

Conditions treated with RF

RF is widely acknowledged as an effective noninvasive treatment for skin laxity.[27,28] In genitourinary applications, it is mainly employed for the targeting of vulvovaginal laxity. A vulvar laxity grading scale is in use and being validated to classify severity.[45] The Vaginal Laxity Questionnaire (VLQ), the Pelvic Floor Distress Inventory-20, the Female Sexual Function Index (FSFI), and the pelvic organ prolapse quantification (POP-Q) are used to assess vaginal laxity.[46]

Preoperative preparation

Instruct the patient to avoid aspirin or any medications that contain aspirin for 7 days before the procedure. For patients who are menstruating, have them schedule their procedure for 1 week after their period. This will help distinguish between vaginal bleeding caused by the procedure and vaginal bleeding during the menstrual period. Instruct the patient to avoid intercourse the night before the procedure and if they may be pregnant, to alert the physician. Instruct the patient to reschedule if they have: a fever, chills, or vaginal bleeding or discharge.

Preoperative physical examination and testing

Before treatment with fractional lasers in the vaginal tract, a normal speculum examination and recent negative PAP smear by a trained gynecologist, urologist, or physician with a specialty in genitourinary care are required. A speculum examination of the entire vaginal vault and external examination with swab use to clear topical agents, if any, should be performed on the day of treatment before device insertion. For those of childbearing potential, a pregnancy test is taken. Written and verbal informed consent should be obtained, including discussion of all treatment options, risks, and benefits.

Perioperative RF methods

RF devices include monopolar and bipolar types for vaginal application, shown in Table 4.

Monopolar RF

The monopolar technologies employ a handpiece that is inserted into the vagina with a grounding pad attached to the patient. Monopolar RF is painless when administered by mobile method and requires no anesthesia [Tables 3 and 4]. The target temperature for the surface of the vulva and vagina is similar to cutaneous applications at 40–45°C.[4,47] As coupling lubricants for RF may be device-specific, adhere to manufacturer specifications (Table 3).

Vulvovaginal protocol. Probe-delivered monopolar RF to the vulva and the vagina is administered with a hydrosoluble lubricating gel placed over the labia and inside the vaginal canal. The probe heating is delivered with the mobile technique until a uniform surface temperature of 40–45°C is attained, which correlates with clinical outcomes (Table 4).[47,48] Temperatures exceeding this level are associated with thermal burns and should be avoided. RF mobile delivery attainment of target temperature and maintenance for a 20–30-min period is associated with improved clinical outcomes.[47,48] Once the internal vaginal canal is fully treated, the RF may be delivered in the same manner to the vulva to improve tissue tightening and laxity reduction. Maintenance of a target temperature externally of 40–45°C for a total of 5 min is advised.[47,48]

Urinary protocol. A high-frequency radiowave of 0.5 MHz is connected to a monopolar active electrode with a diameter of 0.5 cm and a passive metal electrode, the return plate is attached to the patient (Table 4).[50] The electrode is inserted into the external urethral meatus and rotated in a circular motion. The active electrode is removed regularly to perform the temperature check. The temperature is monitored with an infrared thermometer, and after reaching 39–41°C, this temperature and the motions are maintained for 2 min. This protocol has been

TABLE 4 RF devices & parameters for genitourinary applications.

RF device	Brand	Parameters	Treatment sessions	References
Monopolar	ThermiVa, ThermiAesthetics	0.5 MHz, 40–45°C × 30 min, mobile delivery	3 monthly	[47] (see Erratum in: *Lasers Surg Med.* 2017 Sep;49(7):727).
	Viveve, Viveve Medical	6.78 MHz, 90 J/cm^2, each quadrant was treated with five consecutive passes of five locations of pulses for a total of 25 pulses per quadrant. Cryogen cooling.	3 monthly	[48]
	NuEra Tight, Lumenis	44–45°C × 25 min, mobile delivery	3 monthly	[49]
	IntraGen, Jeisys Medical	Stamping method	3 monthly	NA
	Protégé Intima, BTL Esthetics	RF and ultrasound		NA
	TempSure, Pelleve, Cynosure	4.0 MHz		NA
		Intraurethral		[50]
Bipolar	Facetite modified to Accutite, InMode	40 W, 1 MHz to 60°C internally, 37°C externally	3 monthly	[51]
	Fiore, Venus			NA

Abbreviations: NA, not applicable; RF, radiofrequency.

reported with five weekly sessions and improvement in the Oxford scale and Pad test (Table 4).[50]

Bipolar RF

Bipolar RF devices on skin employ a stamping or stationary method of delivery; this approach has been modified into a probe-delivered and skin surface application of electrodes.[51] A bipolar vulvar protocol employs the insertion of a probe cannula into each labium and an opposing probe placed externally so that the RF passes through the skin[31] (Table 4).[51] This method delivers volumetric heating or microcolumns of thermal injury are generated.

Vaginal protocol. During treatment with a bipolar RF device, the patient usually senses warmth while the vaginal canal is treated along the anterior vaginal compartment and pubocervical fascial regions. The vulvar vestibule and clitoral complex can be treated as well.[29]

Vulvar protocol. Pain control is required; patients are premedicated with oral diazepam and hydrocodone with acetaminophen. Oral antibiotics (cephalexin or ciprofloxacin) are given preoperatively. After standard prep and draping, the caudal aspect of each labium (majora and minora) is anesthetized with local 1% lidocaine with 1:200,000 epinephrine injection. A 14-gauge needle puncture is followed by 20-gauge spinal needle infiltration with 20–40 mL of tumescent solution per treatment site (50 mL of 2% lidocaine, 12 ml sodium bicarbonate, 1.5 mg epinephrine per liter of lactated ringers). Hydrosoluble lubricating gel is placed over the labia for the external port of the RF device to glide. RF settings included temperature-controlled cutoffs at 60°C internally and 37°C externally. The 40 W bipolar RF cannula is placed into the access port and moved in a radial cranio-caudal motion until the tissues reached target temperature across the labia (Table 4). Treatment is stopped ~1.5 cm from the access port to avoid repeat heating.[51]

Postoperative management

Following RF vaginal treatment, no specific post-operative care is required. Any significant discomfort or burning could potentially signify a thermal injury or infection and should prompt an evaluation and possibly vaginal cultures. Three monthly treatments are typically employed (Table 4).

HIFEM devices

Introduction

The "pelvic floor" refers to the group of muscles that form a sling or hammock across the floor of the pelvis, which hold the pelvic organs (the vagina, uterus, bladder, urethra, intestines, and rectum) in place so they can function correctly. Due to pregnancy and delivery and the loss of tissue structure during menopause, the pelvic floor weakens. This results in two major sets of conditions: pelvic organ dysfunction and urinary incontinence. Pelvic organ prolapse occurs when the uterus or rectum prolapses or herniates into the vagina. Urinary incontinence may result when the bladder has inadequate support and malfunctions.

Kegel exercises are a classic treatment for the pelvic floor. While pelvic muscle exercises have been shown to improve pelvic floor muscle tone and stress urinary incontinence, prospective, randomized trials unfortunately show no evidence that improvement of pelvic floor muscle tone leads to regression of pelvic organ prolapse. However, combining pelvic floor exercises with a pessary has been shown to work in reducing POP. An area of active research is high-intensity focused electromagnetic field (HIFEM) to stimulate the pelvic muscles.[5] Early results show potential for this modality to strengthen pelvic floor and return it to premenopausal function.[22] A systematic review of the published data on electromagnetic treatments concluded that the mechanism of action on muscle and adipose tissues are still not elucidated, and may suggest tissue edema rather than muscular hypertrophy, an ill-defined inflammatory response and adipocyte changes that require further investigation.[52] The device has FDA 510 K clearance for pelvic floor stimulation for urinary incontinence in men and women (Table 1).

Preoperative assessment

Pretreatment assessment includes the confirmation of the presence of pelvic floor prolapse or vaginal laxity and elimination from consideration of any individuals with contraindications (see RF: Contraindications)

HIFEM protocol

A flat spiral-shaped electrical coil is situated in a chair with an external power supply. Electromagnetic energy is directed upward toward the patient's perineum while the patient is seated in the chair. Six treatments at twice a week frequency are typically administered for the treatment of urinary incontinence due to pelvic floor weakness (Table 5).[26,27]

CURRENT STATUS OF CLEARANCES AND FUTURE PATHWAY

Devices for genitourinary application are FDA cleared generally for ablation, coagulation, or vaporization of genitourinary tissue; clearances for GSM and other

TABLE 5 The current device settings and applications for HIFEM in the genitourinary tract.

Device	Settings	Treatment sessions	Trade name	References
HPM 6000UF	2.5 T × 28 min	6–10 sessions at 2–3 × per week	Emsella, BTL Industries, Inc.	[25] [26]

Abbreviation: HIFEM, high intensity focused electromagnetic field.

gynecologic indications have not been granted by FDA and clinical trials or ongoing (Table 1).[2]

DISCUSSION

Surgical procedures are tested for safety and cost. Safety of lasers and EBD for various vulvovaginal-indications has already been confirmed in many clinical trials. Song et al.[53] searched the literature between 2012 and 2017 focusing on safety and efficacy. A total of 761 women underwent treatment for VV symptoms, and 408 for urinary incontinence. No moderate or severe, short or long-term adverse events (AE) were reported in these trials. Very few mild to immediate events were reported and ranged from mild discomfort, local irritation or edema, vaginal discharge, and short-term urinary urgency. AE reported on the US Food and Drug Administration Manufacturer and User Facility Device Experience (MAUDE) database reveal few minor events.[54–56]

Efficacy in clinically and statistically significant terms depends upon outcomes and the number of subjects treated. Several reviews and meta-analysis published in the last decade are summarized in similar terms: "It may reduce symptom severity, improve quality of life of postmenopausal women and restore the vaginal mucosa to premenopausal status. However, the quality of the body of evidence is 'low' or 'very low' and, thus, evidence-based modification of current clinical practice cannot be suggested".[57]

This consensus article is aimed at categorizing the published articles and clinical trial data that culminated in the protocol development of technology for genitourinary applications, and developing consistent parameters in future clinical trials. Data generated in similar treatment protocols may offer meaningful and comparable data. Future application of scientific tools with absolute parameters such as the new approach of noninvasive optical biopsy dedicated to the vaginal wall may reduce the number of subjects tested and increase the scientific merit of the generated data.[58]

Cost can be compared to other treatment modalities only if safety and efficacy are confirmed, and treatment protocols are optimized. Cost may vary in different parts of the world, based on reimbursement and governing body policies.

CONFLICTS OF INTEREST STATEMENT

Macrene R. Alexiades: Research investigator (Candela, Lumenis); Eric Sokol: Funding (National Institutes of Health Foundation for Female Health Awareness, Cook MyoSite, Watkins-Conti); Stock options (Pelvalon) and Yona Tadir: Consultant, Alma Lasers. The remaining authors declare no conflict of interest.

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REFERENCES

1. Tadir Y, Gaspar A, Lev-Sagie A, Alexiades M, Alinsod R, Bader A, et al. Light and energy based therapeutics for genitourinary syndrome of menopause: consensus and controversies. Lasers Surg Med. 2017 Feb;49(2):137–59.
2. Tadir Y, Iglesia C, Alexiades M, Davila GW, Guerette N, Gaspar A. Energy-based treatment for gynecologic conditions including genitourinary syndrome of menopause: consensus, controversies, recommendations, and FDA clearance. Lasers Surg Med. 2019;51:315–7.
3. Alexiades-Armenakas MR, Dover JS, Arndt KA. The spectrum of laser skin resurfacing: nonablative, fractional, and ablative laser resurfacing. J Am Acad Dermatol. 2008 May;58(5):719–40.
4. Alexiades-Armenakas M, Dover JS, Arndt KA. Unipolar versus bipolar radiofrequency treatment of rhytides and laxity using a mobile painless delivery method. Lasers Surg Med. 2008;40(7):446–53.
5. Alexiades M. High intensity focused electromagnetic field (HIFEM) devices in dermatology. J Drugs Dermatol. 2019 Nov 1;18(11):1088.
6. Bellina JH. Carbon dioxide laser in gynecology. Obstet Gynecol Annu. 1977;6:371–91.
7. Schellhas HF. Laser surgery in gynecology. Surg Clin North Am. 1978 Feb;58(1):151–66. https://doi.org/10.1016/s0039-6109(16)41442-8
8. Baggish MS. Carbon dioxide laser treatment for condylomata acuminata venereal infections. Obstet Gynecol. 1980;55:711–5.
9. Bellina JH, Ross LF, Voros JI. Colposcopy and the CO_2 laser for treatment of cervical intraepithelial neoplasia. An analysis of seven years' experience. J Reprod Med. 1983 Feb;28(2):147–51.
10. Weather Jr. L. Carbon dioxide laser laparoscopy in treatment of infertility and disorders associated with pelvic pain. J Natl Med Assoc. 1988 Feb;80(2):185–7.
11. Baggish MS. New laser hysteroscope for neodymium-YAG endometrial ablation. Lasers Surg Med. 1988;8(2):99–103.
12. Ovadia J, Levavi H, Edelstein T. Treatment of pruritus vulvae by means of CO_2 laser. Acta Obstet Gynecol Scand. 1984;63(3):265–7.
13. Simonsen EF. CO_2 laser used for cancer in situ/Bowen's disease (VIN) and lichen sclerosus in the vulvar region. Acta Obstet Gynecol Scand. 1989;68(6):551–3.
14. Stuart GC, Nation JG, Malliah VS, Robertson DI. Laser therapy of vulvar lichen sclerosus et atrophicus. Can J Surg. 1991 Oct;34(5):469–70.

15. Reid R, Omoto KH, Precop SL, Berman NR, Rutledge LH, Dean SM, et al. Flashlamp-excited dye laser therapy of idiopathic vulvodynia is safe and efficacious. Am J Obstet Gynecol. 1995 Jun;172(6):1684–701; discussion 1696–701. https://doi.org/10.1016/0002-9378(95)91400-5
16. Pardo J, Solà V, Ricci P, Guilloff E. Laser labioplasty of labia minora. Int J Gynecol Obstet. 2006 Apr;93(1):38–43.
17. Copperman AB, DeCherney AH. Turn, turn. Fertil Steril. 2006;85(1):12–3.
18. Gaspar A, Addamo G, Brandi H. Vaginal fractional CO_2 laser: a minimally invasive option for vaginal rejuvenation. Am J Cosmet Surgery. 2011;28(3):156–62.
19. Alexiades M. Device-based treatment for vaginal wellness. Semin Cutan Med Surg. 2018 Dec;37(4):226–32.
20. Alexiades-Armenakas M, Sarnoff D, Gotkin R, Sadick N. Multicenter clinical study and review of fractional ablative CO_2 laser resurfacing for the treatment of rhytides, photoaging, scars and striae. J Drugs Dermatol. 2011 Apr;10(4):352–62.
21. Alexiades-Armenakas MR, Dover JS, Arndt KA. Fractional laser skin resurfacing. J Drugs Dermatol. 2012 Nov;11(11):1274–87.
22. Salvatore S, Leone Roberti Maggiore U, Athanasiou S, Origoni M, Candiani M, Calligaro A, et al. Histological study on the effects of microablative fractional CO_2 laser on atrophic vaginal tissue: an ex vivo study. Menopause. 2015;22(8):845–9.
23. Zerbinati N, Serati M, Origoni M, Candiani M, Iannitti T, Salvatore S, et al. Microscopic and ultrastructural modifications of postmenopausal atrophic vaginal mucosa after fractional carbon dioxide laser treatment. Lasers Med Sci. 2015;30(1):429–36.
24. Gaspar A, Brandi H. Non-ablative erbium YAG laser for the treatment of type III stress urinary incontinence (intrinsic sphincter deficiency). Lasers Med Sci. 2017;32(3):685–91.
25. Samuels JB, Pezzella A, Berenholz J, Alinsod R. Safety and efficacy of a non-invasive high-intensity focused electromagnetic field (HIFEM) device for treatment of urinary incontinence and enhancement of quality of life. Lasers Surg Med. 2019;51(9):760–6.
26. Silantyeva E, Zarkovic D, Astafeva E, Soldatskaia R, Orazov M, Belkovskaya M, et al. A comparative study on the effects of high-intensity focused electromagnetic technology and electrostimulation for the treatment of pelvic floor muscles and urinary incontinence in parous women: analysis of posttreatment data. Female Pelvic Med Reconstr Surg. 2021 Apr 1;27(4):269–73.
27. Alexiades-Armenakas M, Rosenberg D, Renton B, Dover J, Arndt K. Blinded, randomized, quantitative grading comparison of minimally invasive, fractional radiofrequency and surgical facelift to treat skin laxity. Arch Dermatol. 2010 Apr;146(4):396–405.
28. Alexiades M, Berube D. Randomized, blinded, 3-arm clinical trial assessing optimal temperature and duration for treatment with minimally invasive fractional radiofrequency. Dermatol Surg. 2015 May;41(5):623–32.
29. Schwarz T, Prouza O. Aesthetic method of biological structure treatment by magnetic field, Aesthetic method of biological structure treatment by magnetic field. BTL Medical Technologies S.R.O., US patent number 10,549,109. 2018.
30. Behnia-Willison F, Sarraf S, Miller J, Mohamadi B, Care AS, Lam A, et al. Safety and long-term efficacy of fractional CO_2 laser treatment in women suffering from genitourinary syndrome of menopause. Eur J Obstet Gynecol Reprod Biol. 2017 Jun;213:39–44.
31. Alexiades MR. Fractional CO_2 laser treatment of the vulva and vagina and the effect of postmenopausal duration on efficacy. Lasers Surg Med. 2021;53(2):185–98. https://doi.org/10.1002/lsm.23247
32. Alcalay M, Ben Ami M, Greenshpun A, Hagay Z, Schiff E, et al. Fractional-Pixel CO_2 laser treatment in patients with urodynamic stress urinary incontinence: one year follow-up. Lasers Surg Med. 2021;53:960–7.
33. Franić D, Fistonić I, Franić-Ivanišević M, Perdija Ž, Križmarić M. Pixel CO_2 laser for the treatment of stress urinary incontinence—a prospective observational multicenter study. Lasers Surg Med. 2020 Sep 8;53:514–20. https://doi.org/10.1002/lsm.23319
34. Nalewczynska AA, Barwijuk M, Kolczewski P, Dmoch-Gajzlerska E. Pixel-CO_2 laser for the treatment of stress urinary incontinence. Laser Med Sci. 2022 Mar;37(2):1061–7.
35. Gao L, Wen W, Wang Y, Li Z, Dang E, Yu L, et al. Fractional carbon dioxide laser improves vaginal laxity via remodeling of vaginal tissues in Asian women. J Clin Med. 2022 Sep 2;11(17):5201.
36. Fistonić N, Fistonić I, Lukanovič A, Guštek ŠF, Turina ISB, Franić D. First assessment of short-term efficacy of Er:YAG laser treatment on stress urinary incontinence in women: prospective cohort study. Climacteric. 2015;18(suppl 1):37–42.
37. Gaviria JP, Korosec B, Fernandez J, Montero G. Up to 3-year follow-up of patients with vaginal relaxation syndrome participating in laser vaginal tightening. J Laser Health Acad. 2016;2016:1–6.
38. Gaspar A, Brandi H, Gomez V, Luque D. Efficacy of Erbium:YAG laser treatment compared to topical estriol treatment for symptoms of genitourinary syndrome of menopause. Lasers Surg Med. 2017;49(2):160–8.
39. Lee MS. Treatment of vaginal relaxation syndrome with an Erbium:YAG laser using 90° and 360° scanning scopes: a pilot study & short-term results. Laser Ther. 2014 Jul 1;23(2):129–38.
40. Liu M, Li F, Zhou Y, Cao Y, Li S, Li Q. Efficacy of CO_2 laser treatment in postmenopausal women with vulvovaginal atrophy: A meta-analysis. Int J Gynecol Obstet. 2022 Aug;158(2):241–51.
41. Ogrinc UB, Senčar S, Lenasi H. Novel minimally invasive laser treatment of urinary incontinence in women. Lasers Surg Med. 2015;47(9):689–97. https://doi.org/10.1002/lsm.22416
42. Fistonić I, Fistonić N. Baseline ICIQ-UI score, body mass index, age, average birth weight, and perineometry duration as promising predictors of the short-term efficacy of Er:YAG laser treatment in stress urinary incontinent women: a prospective cohort study. Lasers Surg Med. 2018;50(6):636–43. https://doi.org/10.1002/lsm.22789
43. Gaspar A, Maestri S, Silva J, Brandi H, Luque D, Koron N, et al. Intraurethral Erbium:YAG laser for the management of urinary symptoms of genitourinary syndrome of menopause: a pilot study. Lasers Surg Med. 2018;50(8):802–7. https://doi.org/10.1002/lsm.22826
44. Qureshi AA, Tenenbaum MM, Myckatyn TM. Nonsurgical vulvovaginal rejuvenation with radiofrequency and laser devices: A literature review and comprehensive update for aesthetic surgeons. Aesthet Surg J. 2018 Mar;38(3):302–11.
45. Motakef S, Rodriguez-Feliz J, Chung MT, Ingargiola MJ, Wong VW, Patel A. Vaginal labiaplasty: current practices and a simplified classification system for labial protrusion. Plast Reconstr Surg. 2015;135:774–88.
46. Polland A, Duong V, Furuya R, Fitzgerald JJ, Wang H, Iwamoto A, et al. Description of vaginal laxity and prolapse and correlation with sexual function (DeVeLoPS). Sex Med. 2021;9(6):100443.
47. Alinsod RM. Transcutaneous temperature controlled radiofrequency for orgasmic dysfunction. Lasers Surg Med. 2016;48:641–5. https://doi.org/10.1002/lsm.22537
48. Krychman M, Rowan CG, Allan BB, DeRogatis L, Durbin S, Yacoubian A, et al. Effect of Single-Treatment, Surface-Cooled radiofrequency therapy on vaginal laxity and female sexual function: the VIVEVE I randomized controlled trial. J Sex Med. 2017 Feb;14(2):215–25.
49. Alexiades M, and Dover, J. Randomized controlled three arm study comparing monopolar radiofrequency at 470 kHz, 1 MHz and 2 MHz for the treatment of abdominal circumference and skin laxity. Manuscript in preparation. 2023.

50. Lordelo P, Boas AV, Sodré D, Lemos A, Tozetto S, Brasil C. New concept for treating female stress urinary incontinence with radiofrequency. Int Braz J Urol. 2017 Sep-Oct;43(5):896–902.
51. Dayan E, Ramirez H, Theodorou S. Radiofrequency treatment of labia minora and majora: a minimally invasive approach to vulva restoration. Plast Reconstr Surg Glob Open. 2020 Apr;8(4):e2418.
52. Swanson E. A systematic review of electromagnetic treatments for body contouring. Ann Plast Surg. 2023;90(2):180–8.
53. Song S, Budden A, Short A, Nesbitt-Hawes E, Deans R, Abbott J. The evidence for laser treatments to the vulvo-vagina: making sure we do not repeat past mistakes. Aust N Z J Obstet Gynaecol. 2018;58:148–62.
54. Ahluwalia J, Avram MM, Ortiz AE. Lasers and energy-based devices marketed for vaginal rejuvenation: a cross-sectional analysis of the MAUDE database. Lasers Surg Med. 2019;51(8):671–7.
55. Guo JZ, Souders C, McClelland L, Anger JT, Scott VCS, Eilber KS, et al. Vaginal laser treatment of genitourinary syndrome of menopause: does the evidence support the FDA safety communication? Menopause. 2020;27(10):1177–84.
56. Wallace SL, Sokol ER, Enemchukwu EA. Vaginal energy-based devices: characterization of adverse events based on the last decade of MAUDE safety reports. Menopause. 2020 Sep 28;28(2):135–41.
57. Pitsouni E, Grigoriadis T, Falagas ME, Salvatore S, Athanasiou S. Laser therapy for the genitourinary syndrome of menopause. A systematic review and meta-analysis. Maturitas. 2017;103:78–88.
58. Miao Y, Sudol NT, Li Y, Chen JJ, et al. Optical coherent tomography evaluation of vaginal epithelial thickness during CO_2 laser treatment: a pilot study. J Bioiphotonics. 2022;15(11):e202200052. https://doi.org/10.1002/jbio.202200052

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