Special Topic

Aesthetic Surgery Journal
2017, 1–10

DOI: 10.1093/asj/sjx138
www.aestheticsurgeryjournal.com
OXFORD
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Nonsurgical Vulvovaginal Rejuvenation With Radiofrequency and Laser Devices: A Literature Review and Comprehensive Update for Aesthetic Surgeons

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Abstract

Nonsurgical vulvovaginal rejuvenation (NVR) is growing in popularity as a treatment for restoration of youthful female genitalia. Numerous radiofrequency (RF) and laser devices have entered the market claiming improvement in vaginal laxity and genitourinary syndrome of menopause. There is a paucity of evidence existing concerning the effectiveness of these devices for both pre- and postmenopausal women with laxity and/or atrophy at the histologic and clinical level. Therefore, the goal of this review is to scrutinize the peer-reviewed data on NVR with RF and laser devices, identify gaps in existing literature, and propose opportunities for further investigation.

Editorial Decision date: July 4, 2017.

Nonsurgical vulvovaginal rejuvenation (NVR) is an option for women desiring restoration of youthful appearance and function of their genitalia. A plethora of nonsurgical devices using radiofrequency (RF) and laser technology have inundated the market prompting a desire for greater clarity regarding the indications, treatment options, and expected results for patients and their providers. Dermatologists, gynecologists, and plastic surgeons all perform NVR. However, because treatment options for both the external genitalia and vagina exist, we propose the term nonsurgical *vulvovaginal* rejuvenation (NVR) *in lieu* of "vaginal rejuvenation" alone to better characterize the scope of potential treatment areas with nonsurgical devices. These devices may serve as an alternative or adjunct to more invasive surgical options with greater downtime, discomfort or cost.

NVR can be used for both aesthetic and functional problems of the female genitalia and urinary tract. In general, patients seeking NVR may have vaginal laxity (VL), genitourinary syndrome of menopause (GSM), or both. Vaginal laxity is associated with stretching and expansion of the vaginal introitus, often attributed to vaginal childbirth and can be experienced by both pre- and postmenopausal women.[1-3] With childbirth and aging, the vaginal muscle tone can decrease and lead to orgasmic dysfunction, changes in genital sensation, and even urinary incontinence. It differs from GSM, which is a myriad of symptoms associated most commonly with postmenopausal hormonal changes in estrogen and includes changes beyond laxity and involves urinary symptoms.[3]

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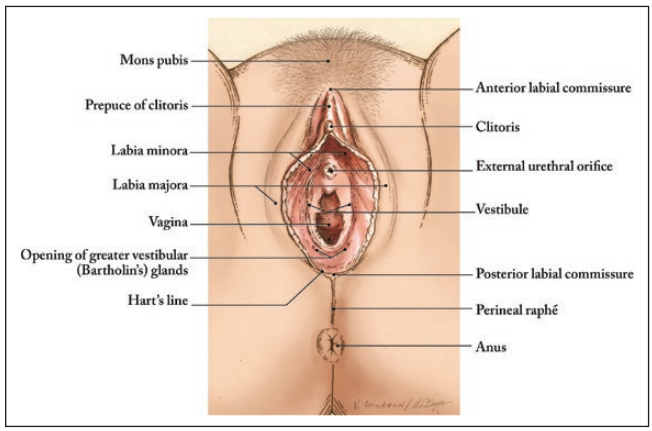

Figure 1. Anatomy of female genitalia.

Both diagnoses are different from pelvic organ prolapse in which pelvic organs like the bladder and rectum can bulge into and even out of the introitus.[2] Patients with severe pelvic organ prolapse may not be ideal candidates for NVR with RF or laser devices and are often treated by clinicians like urogynecologists with special training in prolapse. Patients with VL and GSM may also have stress urinary incontinence (SUI), recurrent urinary tract infections and even pain with urination.[4]

Plastic surgeons and aesthetic practices are suited to provide NVR as a part of comprehensive rejuvenation of the genitalia in a multidisciplinary way. Plastic surgeons are increasingly meeting the requests of patients with surgical vaginal rejuvenation with their technical skills and aesthetic intuition. The 23% rise in volume of labiaplasties from 2015 to 2016 performed is a testament to this growing field within aesthetic plastic surgery.[5] Furthermore, many patients seeking NVR may already be patients who have availed other nonsurgical procedures of the face and body.[6] Others, such as breast cancer patients who have undergone reconstruction, may already be patients of a practice. Aesthetic plastic surgery provides comprehensive care to patients aimed at improving wellness and health and NVR is a natural extension of that ethos.

The goal of the present review is to critically assess the peer-reviewed data on NVR with RF and laser devices. We identify gaps in the literature and propose opportunities for potential research in this evolving field.

Anatomy

Female genitalia include both internal and external structures that are amenable to NVR (Figure 1). The vagina is a part of the internal female genitalia while the vulva, or external genitalia, consists of the mons pubis, labia minora, labia majora, and clitoris. The urethral meatus is inferior to the clitoris and frenulum of the clitoris. Sensory innervation to the external genitalia is through the pudendal nerve which branches into the superficial and deep perineal nerves. Blood supply to the region is through branches of the internal pudendal artery with the dominant supply to the labia minora entering posteriorly. Several pudendal artery perforators exist in the labia majora.

Histologically, the vaginal wall consists of a superficial layer of nonkeratinized, squamous epithelium with a high water content. Deeper layers of the vaginal wall contain dense connective tissue, smooth muscle, collagen, and elastin, which give the vaginal wall strength and elasticity.[1] Vaginal mucosa is estrogen dependent and responds to cyclic changes associated with the menstrual cycle.[2] With aging, estrogen production decreases and this in turn causes changes in the genital tract with the decreased vaginal elasticity and thinning of the vaginal walls.[2,3] The vagina can lose its rugation with loss of estrogen. Decreased collagen and elastin lead to laxity and thinning. Blood flow and secretions in the vagina also decrease as a result of decreased estrogen levels. Postmenopausal vaginal mucosa differs from premenopausal mucosa in that it has a lower water content, which may have consequences on modalities of treatment like lasers that use water as their chromophore.[3]

The vulva including the labia majora becomes atrophic and may be prone to many symptoms experienced by postmenopausal woman as these tissues also express estrogen receptors.[7] The composition of the skin of the external genitalia is different from that of the vagina as the mons and labia majora have layers of epidermis, dermis, and subcutaneous tissue similar to skin that is targeted in nonsurgical rejuvenation in the face, hands, or chest.[1] Such skin has stratified squamous epithelium that is keratinized with dermis containing collagen and elastin. The labia majora have dry skin while the labia minora have moist, nonkeratinized epithelium with sebaceous and mucous producing glands.[1] Hart's line marks the transition from the moist mucous epithelium of the labia minora and the dry, fully keratinized epithelium of the labia majora.

Evaluation

A thorough history, examination, and discussion of goals of treatment can help identify suitable candidates for NVR. Patients with GSM report symptoms of laxity, dryness, itching, urinary incontinence, and even pain.[2,8,9] These patients tend to be menopausal women, though GSM can occur at any age.[10] Patients with VL will report experiencing vaginal laxity during intercourse and largely remains a self-reported condition.[11] They are often premenopausal women with a history of vaginal childbirth. It is important to note that not all patients with VL will have changes of the vulva. Conversely, patients with vulvar changes may or may not have VL.

Table 1. Questionnaires Used in NVR Evaluation and Studies

Questionnaire	Validated	Aim of questionnaire
Female Sexual Distress Scale Revised (FSDS-R)	Yes	Distress with sexual dysfunction
Female Sexual Function Index (FSFI)	Yes	Multiple domains of sexual function
Incontinence Impact Questionnaire (IIQ-7)	Yes	Impact of urinary leakage on quality of life
Sexual Satisfaction Questionnaire (SSQ)	No	Sexual satisfaction
Urogenital Distress Inventory (UDI-6)	Yes	Assesses frequency of urination, urgency and incontinence
Vaginal Laxity Questionnaire (VLQ)	No	Degree of patient reported vaginal laxity
Vulvovaginal Symptom Questionnaire (VSQ)	Yes	Quality of life impact from vulvovaginal symptoms, emotional and sexual concerns

FSDS-R, Female Sexual Distress Scale Revised; FSFI, Female Sexual Function Index; IIQ-7, Incontinence Impact Questionnaire; SSQ, Sexual Situation Questionnaire; UDI-6, Urogenital Distress Inventory; VLQ, Vaginal Laxity Questionnaire; VSQ, Vulvovaginal Symptom Questionnaire.

Many patients may have complaints of urinary incontinence or orgasmic dysfunction. Previous assessments of urinary incontinence and a history of urodynamic testing in the past should be obtained. A surgical history including any specific urogynecologic or vaginal procedures should be documented. Patients with complaints of orgasmic dysfunction should also be assessed for any other concomitant diagnoses of sexual disorders including nonspecific pelvic pain, vulvodynia, or vaginismus as these patients may not tolerate NVR procedures, while patients with isolated orgasmic dysfunction may be suitable candidates.

Because hormone therapy can be used for the medical management of symptoms of GSM or hormonal imbalance, patients should be asked about hormone supplement use. Oral contraceptive use, pregnancy history, and current pregnancy in premenopausal women must be assessed. A sexual history including any active sexually transmitted diseases should be obtained as well as documentation of medications that are known to affect sexual function. Oncologic history specifically including history of breast cancer, treatment status, endocrine therapy, and surgical menopause should be elicited.

Patients may come as a referral from a primary care physician or obstetrician-gynecologist. A careful physical examination should be performed by a trained medical professional to rule out pelvic organ prolapse, in which internal organs will be found to push on the vaginal walls. The vulva should be assessed for signs of atrophy.

Objective methods of assessing vaginal wall biomechanics including laxity are currently lacking. pH measurement of the vagina can be used as an adjunct in diagnosis of vaginal atrophy as the pH increases outside the range of normal (pH 3.5-4.5) in atrophy. A urine pregnancy test should be performed to rule in or out pregnancy prior to the start of any therapy. Biopsies of the vaginal wall are unlikely to be necessary for the diagnosis of vaginal atrophy, but may be of benefit in the presence of abnormal or suspicious lesions or in a research setting to assess for histologic changes as a result of NVR.

Photographs can be taken to document pre- and post-procedure changes and can serve as an objective way to assess for changes from treatments particularly if the vulva is to be addressed. Patients should be positioned in the lithotomy position with photographs of the labia together and apart. Additionally patients should be photographed in the standing position. Photographs, however, have limited if any documentation benefit in the setting of internal aesthetic procedures such as when the introitus alone is treated.

Patient-Reported Questionnaires

In addition to examination, diagnosis of GSM or VL largely depends on patient-reported symptomatology. Several self-reported questionnaires exist that assess individual perceptions of VL and vulvovaginal symptoms (Table 1). The Vaginal Laxity Questionnaire (VLQ) uses a seven-point Likert scale from “very loose” to “very tight” and has been used in NVR research, though unvalidated.[12,13] The Vulvovaginal Symptom Questionnaire (VSQ) is a validated questionnaire that assesses quality of life impact of physical vulvovaginal symptoms (like dryness, pain, burning, and itching) in postmenopausal women as well as emotional and sexual concerns associated with GSM.[14]

The Female Sexual Function Index (FSFI) and Female Sexual Distress Scale Revised (FSDS-R) are also used as patient reported outcomes of sexual function and distress.[15,16] The FSFI is a validated questionnaire that assess the domains of desire, arousal, lubrication, orgasm, satisfaction, and pain. This differs from FSDS-R, also a validated questionnaire, which assess patients’ distress with sexual activity.

Urinary incontinence can also be assessed with validated questionnaires like the Urogenital Distress Inventory (UDI-6) and Incontinence Impact Questionnaire (IIQ-7).[17]

METHODS

A review of the literature was performed by the first author (A.A.Q.) using PubMed database in April 2017 and articles up to this point were considered. Keywords were searched and included: vaginal laxity, vaginal rejuvenation, vulvovaginal atrophy, genitourinary syndrome of menopause, lasers, radiofrequency, and nonsurgical vaginal rejuvenation. The review was limited to articles written in English. Articles that described techniques, outcomes, and safety profiles of laser or radiofrequency devices for the treatment of vaginal laxity, vulvovaginal atrophy, or genitourinary syndrome of menopause were included. Studies that include treatment of pelvic organ prolapse or urinary incontinence were excluded from the review as the focus of the review was not on these disease processes.

RESULTS

The initial criteria yielded 150 articles and a total of 33 were included in the present review after reviewing titles and abstracts and applying inclusion and exclusion criteria. Papers from 1995 to 2017 were included.

Technique Options

RF and laser devices are the two main technologies for NVR. The majority of these devices have been offered to patients who do not have major pelvic organ prolapse. Both have been extended to NVR after use in nonsurgical rejuvenation of the face and body.

Radiofrequency Devices and NVR

RF devices create an electrical field in the tissue that causes molecular motion of charged particles and thereby generate heat.[1,18] The amount of heat generated in the tissue is a direct result of the current and contact time between device and tissue. The energy produced is not absorbed by melanin. RF devices can be unipolar, monopolar, bipolar, or multipolar, which leads to differences in how the electric current passes from the device through the tissue and between the electrodes or back to a grounding pad (Table 2). At tissue temperatures between 40 to 45°C, RF can induce fibroblasts to produce collagen through activation of heat shock proteins and initiation of the inflammatory cascade.[19] Temperatures greater than 45°C have led to thermal injury and pain at the skin level with vaginal tissue tolerating temperatures up to 47°C without visible thermal injury.[1] Cooling probes are thought to cool cutaneous nerves that come in contact with the device and lead to less pain during treatments. They also create a reverse heat gradient so that deeper tissue is more likely to be treated than surface tissue, thereby reducing the likelihood of thermal injury to the skin or mucosa. ThermiVa (Thermi Aesthetics, TX) and Viveve (Viveve, CA) both have FDA 501(k) clearance for use in electrocoagulation and hemostasis in dermatologic and general surgical procedures. No device is currently FDA approved for the indication of treatment of vaginal laxity, though international agencies have varying levels of approval.

Table 2. Radiofrequency Devices for NVR

Device	Technology ype
Protégé Intima (BTL Industries, MA)	Monopolar RF with ultrasound, no cooling probe
ReVive (Viora, NY)	Bipolar RF, no cooling probe
ThermiVa (Thermi Aesthetics, TX)	Unipolar RF, no cooling probe
Viveve (Viveve, CA)	Monopolar RF with cooling probe

RF, radiofrequency.

Histologic Changes and RF

The histologic effects of RF on tissue have been studied. RF has been found to reduce skin laxity, improve the mechanical strength of skin, and induce neocollagenesis and elastogenesis.[1] RF aims at reducing tissue compliance without inducing true scar formation. NVR has been studied in the ovine model with Viveve. Biopsies of the ovine vaginal wall were obtained after a spectrum of RF doses at 1 week, 1, 3, and 6 months posttreatment. Fibroblast activation was found to vary with increased contact time and energy delivered. Increased collagen production was noted at 1 month in the submucosa with increased fibroblasts and was found to persist at 3 months.[20] Changes in elastin were not studied in the ovine model. The histological changes seen in patients treated with RF are unknown and warrant investigation.

Clinical Studies Using RF

A limited number of clinical studies have looked at RF devices in NVR (Table 3). Millheiser et al examined the use of Viveve in premenopausal women with self-diagnosed VL using the VLQ.[13] Patients had a screening physical and pelvic examination prior to treatment. All patients had a single treatment. The first three patients in the study received 60 J/cm^2 and because there were no adverse events, the next three patients received 75 J/cm^2. Because no adverse events occurred, the following 18 patients received 90 J/cm^2 with treatment times of 30 minutes. The authors extrapolated these energy setting from ovine studies with the device.[21] Approximately 20 cm^2 of the vagina was treated with the treatment device applied to the vaginal introitus from 1 to 11 o'clock positions while avoiding treatment to the urethra. The number of total

Table 3. Studies Using Radiofrequency Devices for NVR

Study	Device	Level of evidence*	No. of treatments (n, min)	Areas treated	Inclusion criteria	Number of patients	Follow up (mo)	Outcome of the study	Effect
Millheiser et al, 2010[13]	Monopolar RF with cooling probe (Viveve)	IV (case series)	1, 30	Vaginal mucosa	Premenopausal with at least one full term vaginal delivery, vaginal laxity	24	6	FSFI, FSDS-R, SSQ	Improved
Sekiguchi et al, 2013[12]	Monopolar RF with cooling probe (Viveve)	IV (case series)	1, 30	Vaginal mucosa	Premenopausal with at least one full-term vaginal delivery, vaginal laxity	30	12	FSFI, FSDS-R	Improved
Alinsod, 2016[22]	Unipolar RF, no cooling probe (ThermiVa)	IV (case series)	3, 25 1 month apart	External genitalia, vaginal mucosa	Self-reported anorgasmic or slow-to-orgasm	25	Not stated	Unvalidated questionnaire	Improved
Krychman, 2016[11]	Monopolar RF with cooling probe (Viveve)	II (randomized, controlled)	1, 30	Vaginal mucosa	Premenopausal with at least one full-term vaginal delivery, vaginal laxity	123	6	FSFI, FSDS-R	Improved

FSDS-R, Female Sexual Distress Scale Revised; FSFI, Female Sexual Function Index; SSQ, Sexual Situation Questionnaire; RF, radiofrequency. *Levels of Evidence were determined by the authors of this paper.

pulses administered is not reported. Patients underwent pelvic examinations at 1 and 3 months posttreatment and had completed the modified female sexual function index (mv-FSFI) and FSDS at 6 months. Patients reportedly tolerated the procedures well, noting a sense of warmth during treatment but no pain. No patient reported pain with posttreatment vaginal intercourse. Self-reported vaginal laxity based on the VLQ improved significantly at 1, 3, and 6 months, independent of treatment settings. The authors also looked at the Sexual Situation Questionnaire (SSQ) and found significant improvements in sexual satisfaction in those patients who had a diminished level of sexual satisfaction after vaginal deliveries while those patients who had no change or an increase in satisfaction after childbirth did not experience improvements that were significant. Based on the mv-FSFI, patients had significant improvements in arousal, lubrication, and overall scores at 1 month and arousal, orgasm, and satisfaction. At 3 and 6 months, arousal, orgasm, satisfaction and overall scores remained significantly improved but lubrication did not. Patients also had significant improvements in sexual dysfunction as measured by the FSDS-R at 6 months. The authors hypothesized that the RF device may stimulate neocollagenesis and neoelastogensis in the vagina leading to improvements in vaginal laxity. They also cite the lack of major complications including ulceration, necrosis, and scarring at 6 months to suggest the safety of the treatment. The study had limited long-term follow up. The authors did not explain the transient improvement in lubrication which may be a source of distress for patients and was limited to premenopausal patients. There was no objective measurement of changes that may have occurred in the vaginal wall. The authors explain this limitation is because there is no current standard measuring device for such changes in the vaginal wall. Additionally, the authors acknowledge the possibility that the outcomes were a result of a placebo effect and recommended further comparison studies with a sham group.

An almost identical study was performed in Japanese premenopausal women by Sekiguchi et al but with 1 year follow up using Viveve.[12] The vaginal introitus was treated in a single session at 90 J/cm^2 with a maximum of 105 pulses with average treatment time of 26 minutes. They reported significant improvements in vaginal laxity based on the VLQ within 1 month and sustained through their 1 year follow up. Like Millheiser et al, Sekiguchi et al found significant improvements in sexual satisfaction in patients with diminished sexual satisfaction after vaginal deliveries until 6 months but this improvement disappeared at 12 months. Patients with no change or increase in satisfaction after childbirth did not experience improvements that were significant at any time point in the study. Based on the FSFI, patients reported significantly increased improvement in pain at 1 month. Patients did not experience the improvements that Millheiser et al found in arousal, orgasm, or satisfaction, but did have significantly improved overall scores. At 3 months, patients had increased orgasm, satisfaction, pain, and overall scores. At 6 months, improvements in arousal, lubrication, orgasm, and overall score were seen while the improvement in satisfaction diminished. At 12 months, there were no sustained improvements seen in desire, arousal, lubrication, orgasm, satisfaction, pain, or total scores. The FSDS-R was used to assess for distress during the study period; the authors reported that significantly decreased levels of distress were sustained at 1 year. The authors hypothesized that RF treatment stimulated connective tissue activation leading to vaginal rejuvenation. The study was limited to Japanese women. The authors do not explain why specific improvements in FSFI are seen at 3 or 6 months when

compared to baseline. At 12 months, no changes in FSFI were statistically significant. It is important to note this may be because only 22 of the 30 patients had follow up at one year.

A recent multicenter prospective, randomized, single-blinded with sham-control study was performed assessing Viveve for treatment of self-reported vaginal laxity based on VLQ (VIVEVE I trial, NCT 02261974).[4] The primary endpoint was "no vaginal laxity" on the VLQ at 6 months. No vaginal laxity was a score of 5 to 7 on the VLQ, and laxity was a score of 1 to 3. Patients were randomized to receive single treatment of active (90 J/cm^2) or sham (1 J/cm^2) treatment circumferentially to the vaginal introitus with avoidance of the urethra. The introitus was treated with up to 110 total pulses. Subjects were blinded to treatment. Pelvic examinations were performed at 10 days, 1 month, and 3 months with a study exit interview at 6 months. 43.5% of patients in the active group had no vaginal laxity while 19.6% in the sham group had no vaginal laxity. This difference was significantly different. Patients in the active group also had significantly greater improvements in FSFI total scores at 6 months versus the sham group with specific improvements in arousal and lubrication. This parallels some of the findings by Sekiguchi and Millheiser.[12,13] Improvements in sexual distress based on FSDS-R were not significantly different at 6 months, which contrasts the findings by Sekiguchi and Millheiser.[12,13] The study was powered based on efficacy endpoints, but not safety and complications. 32.5% in the active and 35.1% in the sham groups reported adverse events but were not significantly different. These included vaginal discharge, vaginal discomfort and feeling "hot." There was only one serious adverse event in the sham group, which is not explicitly stated in the study. Only one patient in the active group reported pain and discomfort that lead to early termination of the treatment procedure. The authors note that the placebo effect was greater than expected. Because of the magnitude of the placebo effect, carefully designed crossover studies may be warranted to better understand the placebo effect. The placebo effect in NVR may not be unique to this device but may also be seen with other devices and technologies.

Alinsod recently performed a case series study of 25 sexually active patients with self-reported anorgasmia or slow-to-orgasm.[22] Patients received three treatments, one month apart for on average 25 minutes with ThermiVa. The study did not include a sham control. The treatment areas including both the vagina including the area of the vagina with maximum sensitivity and external genitalia including the labia majora, labia minor, mons, perineal body, clitoral hood, and clitoris. Of the patients, 76% reported reduction in time to orgasm by at least 50% with all patients who had anorgasmia reporting the ability to achieve orgasm. They also reported vaginal tightening, lubrication, and clitoral sensitivity. The author did not use a validated questionnaire to assess outcomes. Follow-up time is unclear from the study as well as longevity of improvements reported by patients. The author suggests that treatment benefits can last 9 to 12 months and recommends yearly maintenance but does not provide any data to support this statement. The study hypothesizes that improved blood flow may be responsible for improved sexual response. The study fails to study the placebo effect with a control or sham group. Two patients without improvement in symptoms had previous pelvic reconstructive surgery and the author hypothesizes that previous surgery may have affected blood flow or innervation to the area altering the ability to achieve orgasm.

Table 4. Laser Devices for NVR

Device	Technology type
CO2RE Intima (Syneron, MA)	Digital superpulse CO_2 laser (RF-excited, 10,600 nm)
diVa (Sciton, CA)	Hybrid fractional laser (2940 and 1470 nm)
diVaTyte (Sciton, CA)	Intense pulsed light (500-1400 nm)
DivaTight (Quanta System, Italy)	Dual wavelength laser (1540 and 10,600 nm)
FemiLift (Alma Lasers, IL)	Superpulse CO_2 laser (10,600 nm)
FemTouch (Lumenis, Israel)	Superpulse CO_2 laser (10,600 nm)
IntimaLase (Fotona, CA)	Er:YAG laser (2940 nm)
MonaLisa Touch (Cyanosure, MA)	Digital superpulse, fractional CO_2 laser (10,600 nm)
Petit Lady (Lutronic, MA)	Er:YAG laser (2940 nm)

Lasers and NVR

Several fractional ablative and nonablative lasers have emerged for NVR including CO_2 (10,600 nm), Er:YAG (2940 nm), and hybrid fractional lasers (2940 and 1470 nm) (Table 4).[23] To our knowledge, there are no laser devices that are FDA approved or have 501(k) approval specifically for the treatment of VL or GSM. Many lasers use technology that have FDA 501(k) clearance have been used in gynecology for other indications including incision, excision, ablation, and vaporization of soft tissues in surgical procedures for coagulation and hemostasis.[24] International agencies, however, have different approvals for these devices.

Carbon Dioxide Lasers and NVR

Fractional CO_2 lasers (10,600 nm) allow for focused energy delivery and targeted ablative islands surrounded by adjacent healthy tissue with water as the chromophore.

The energy leads to heating of underlying tissues to 45 to 50°C and induces shrinkage of collagen and stimulates fibroblasts to produce new collagen in the treated tissue. Superpulsed CO_2 lasers provide more precise depth of ablation because they combine short pulse duration and higher power. The depth of penetration ranges from 20 up to 125 μm.[1]

Histologic Changes and CO_2 Lasers

CO_2 lasers initiate an inflammatory and wound healing pathway in skin that stimulates the underlying tissues to heal with both increased elastin and collagen.[25] Changes in vaginal biopsies treated with CO_2 laser and platelet-rich plasma were first demonstrated in 2011 by Gaspar et al with visible changes in all layers of the vaginal wall.[26] Ex vivo histologic studies of CO_2 laser treated vaginal walls have showed thickening of mucosa, increase in fibroblasts and collagen deposition and vascularity in atrophic vaginal tissue.[27,28] Premenopausal vaginal mucosa with its increased water content may respond differently to CO_2 than postmenopausal mucosa. Studies of CO_2 laser in postmenopausal vaginal mucosa have demonstrated histologic changes that resemble premenopausal vaginal mucosa, suggesting that CO_2 lasers can rejuvenate the vaginal mucosa at the histologic level.[29]

Clinical Studies Using CO_2 Lasers

Salvatore et al looked at MonaLisa Touch (Cyanosure, MA) for GSM in 50 postmenopausal women treated three times, one month apart.[29] Authors looked at the Vaginal Health Index (VHI) and GSM symptoms. VHI is a clinically objective assessment of vaginal health and assesses elasticity, secretions, pH, mucosa, and moisture.[30] VHI and dysuria was significant improved compared to baseline and each follow up time point. Vaginal dryness, itching and dyspareunia was significantly improved at all time points compared to baseline but not significantly improved from 8 weeks to 12 weeks. Authors reported patients tolerated procedures well with mild pain during probe insertion but no other adverse events were reported. A separate study of these patients looked at five patients who had vaginal biopsies performed before and after the first treatment. The histologic study found restored vaginal epithelium with increased glycogen, fibroblasts, and deposition of extracellular matrix similar to premenopausal vaginal samples.[28]

In a similar study of 48 postmenopausal women with GSM treated with MonaLisa Touch, patients underwent three treatments 30 days apart.[31] Outcomes included VHI, patient reported intensity of GSM and satisfaction with treatment and were followed for 30 days after their last treatment. Mean treatment time was 6 minutes. Patients had significantly higher VHI scores and significant improvements in dryness, burning, itching, and dyspareunia. Of patients, 91.7% were satisfied. The study is limited by its follow-up period and no conclusions about the longevity of improvements can be made. It also did not use validated scales beyond the VHI for evaluation of patient's symptomatology.

In a prospective study of 77 patients with GSM treated with MonaLisa Touch treated three times 1 month apart, FSFI scores significantly improved at 12 weeks in all domains of desire, arousal, lubrication, orgasm, satisfaction, and pain. Some patients who were sexually inactive prior to treatment being able to resume sexual activity at follow up.[32]

The largest study to date by Filippini et al of 386 menopausal women with GSM underwent three MonaLisa Touch treatments at unspecified time intervals.[33] The vulva and vaginal introitus were both treated. Main side effects were pain with insertion of the probe, discharge, and burning after treatment. Patients reported improvement in dryness, burning, dyspareunia, itching, soreness, and pain at follow up of 2 months after the last treatment. A validated questionnaire was not used. Half the patients reported an improvement in urinary symptoms, which was not an endpoint of the study.

There is wide variability between CO_2 lasers that have been marketed and studied for GSM. CO_2 lasers can differ by power delivered, dwelling time, and interval between treatment sessions among other variables. Because of the large number of parameters and CO_2 laser types that exist, it is difficult to compare whether these differences have clinically meaningful endpoints for patients and whether one type of CO_2 laser is superior to another. Some studies have explained their protocol development for treatment albeit in a limited fashion, but the number of treatments and specifics of each treatment type will largely vary on the device and need to be studied more rigorously.[25,29,31] None have specifically looked at VL improvement in a rigorous fashion.

Er:YAG and Hybrid Fractional Lasers and NVR

Er:YAG (2940 nm) is a nonablative laser that has a coefficient of absorption that is 16 times that of CO_2 for water.[1] In turn, it has a lower depth of penetration of 1 to 3 μm leading to minimal thermal injury to surrounding tissue and less pain, discomfort, swelling, and erythema.[1] Histology of vaginal mucosa treated with Er:YAG demonstrated increased vaginal thickness and denser connective tissue with increased collagen and elastin.[34] Some studies have noted secondary changes in VL after treatment with Er:YAG but have included patients with pelvic organ prolapse with primary outcomes being urinary incontinence and pelvic organ prolapse.[35-38] Because the treatment of pelvic organ prolapse and urinary incontinence with

Er:YAG lasers are beyond the scope of the present review and met exclusion criteria, they were not reviewed here.

Hybrid fractional lasers (HFL) uses 2940 nm and 1470 nm wavelengths to target tissue. However, no studies currently exist in the peer-reviewed literature that have looked at HFL in vaginal tissue.

Complications and Safety Issues

Studies of all treatment types in NVR using RF or laser therapy have not reported any major complications that required operative intervention. Both modalities of treatment have generally reported patient tolerability of in-office procedures with a feeling of warmth commonly reported regardless of modality during treatment. Discomfort with probe insertion seems to be greater for laser therapy than RF device and may be a function of device design rather than treatment modality.

DISCUSSION

Among the options for genital rejuvenation offered by plastic surgeons and aesthetic practices, NVR with RF and laser devices can be used for the treatment of VL and/or GSM with anecdotal evidence of improvement in stress urinary incontinence. A limited number of studies have look at patient reported improvements for these diagnoses using both validated and unvalidated questionnaires. They are limited by their follow up. Based on the existing data, it remains unknown whether clinical and histologic changes persist beyond 6 months. This suggests that NVR may require maintenance treatments after an initial treatment or set of treatments, unlike surgical treatments for female genital rejuvenation. NVR interventions may be akin to neurotoxin or soft tissue filler in facial rejuvenation versus surgical options like facelift and necklift procedures. No analysis in the current literature helps define treatment protocols or ideal device based on menopausal status or even attempts to answer whether menopausal status is relevant. Additionally, studies comparing NVR to surgical options like labiaplasty or vaginoplasty along with cost will help inform providers and patients about cost effectiveness.

Studies have looked at the distress and impact of physiologic and anatomic changes of female genitalia and sexual function. Changes in vaginal laxity are related to alterations in sexual function. Studies have found sexual gratification to be directly related to frictional forces during intercourse with friction directly proportional to vaginal diameter. Increases in the diameter of the vagina and subsequent vaginal laxity would in turn decrease frictional forces and in turn sexual gratification.[22] Hence, NVR aimed at reducing the diameter and laxity of the vagina have been thought to improve sexual functioning. VL means different things to different patients and the VLQ is an unvalidated scale. An objective, reproducible way or device to measure vaginal laxity or changes after treatment using NVR does not exist; this would enhance research and clinical tracking of changes experienced by patients. Additionally, some studies have found urinary incontinence to improve though these were not primary endpoints of the studies examined in this review. Other studies have looked at the role of laser therapy in urinary incontinence when the periurethral tissue and urethra itself are treated. This area is beyond the focus of the present review.

Treatment protocols and techniques are largely device dependent, and variability between devices has led to difficulty in standardization and comparison of devices and treatment protocols for both RF and laser devices. Additionally, RF devices like ThermiVa have been used on the external genitalia while Vivive has not. Little has been published on the use of RF on the vulva. Further investigation is warranted with histologic and even gene expression studies to better understand how NVR affects the areas being treated. The placebo effect of treatments with both technologies needs specific investigation.

NVR may be a unique treatment modality for many breast cancer patients who undergo surgical, endocrine, or age-related menopause and are not candidates for hormone therapy. Plastic surgeons have a unique opportunity to help these patients as many breast cancer patients undergo reconstruction and already have a relationship with a plastic surgeon. The true prevalence of vaginal laxity and GSM in breast cancer patients is unknown and warrants investigation. Because estrogen therapy only targets vaginal mucosa and not deeper layers, more studies that compare medical therapy to NVR should be performed. The oncologic concerns or risks associated with these treatments remains unknown.

Our review has limitations. There are a lack of data with inconsistency of outcome metrics making it difficult to compare devices and technology types. The multitude of parameters inherent to laser therapies also makes comparison of treatment regimens among lasers difficult which we were unable to perform. While there is some, more translational histology to clinical data will help us understand the changes happening in the tissues and how this correlates to clinical changes in symptomatology of VL and GSM. Currently, the mechanisms of action such as increased collagen production, changes in the angle of the urethra, and increased lubrication due to blood flow are largely speculative. Much of the research is being driven by industry as different devices seek to claim a niche within NVR while the indications are currently quite broad. Our review excluded studies where pelvic organ prolapse and urinary incontinence were the primary diseases being treated. Many patients seeking NVR may have these comorbidities

and the impact of these diseases on changes in VL remain unknown.

CONCLUSIONS

Providing a range of services in an aesthetic practice that includes NVR will only enhance the ability of plastic surgeons to provide comprehensive, holistic care to patients aimed at improving health, and wellness. Plastic surgeons are suited to provide this service to appropriate candidates desiring genital rejuvenation in a multidisciplinary approach.

Acknowledgments

The authors would like to thank Vicki Friedman and Mary Lynn Brophy for their medical artistry and illustration included in this paper.

Disclosures

Drs. Tenenbaum and Myckatyn serve on the advisory board for Viveve® (Sunnyvale, CA). Dr Qureshi declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

Funding

The authors received no financial support for the research, authorship, and publication of this article.

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