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ORIGINAL ARTICLE

The effects of a real-time temperature monitoring non-ablative monopolar radiofrequency technology on vulvovaginal atrophy symptoms in postmenopausal Chinese women

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Abstract

Background: Vulvovaginal atrophy (VVA) includes a wide range of conditions affecting the reproductive and urinary systems, often requiring careful evaluation and management for optimal health.

Aims: This study aims to evaluate the symptom management effects of a real time temperature-monitored non-ablative RF device for the treatment of postmenopausal Chinese women with VVA symptoms.

Methods: This pilot study involved 24 postmenopausal Chinese women with one or more VVA symptoms, who wished to remain sexually active. VHIS, VAS, and FSFI were used to track and evaluate various aspects of the patient's condition. Analyses were conducted at the end of the study to verify the statistical significance of the treatment's results.

Results: All patients reported substantial, statistically significant, improvements on every VVA symptom tracked. Approximately 80% of the patients reported total symptom reversal at 12-week post-treatment follow-up.

Conclusion: This pilot study demonstrated that non-ablative, monopolar RF technology equipped with real time temperature monitoring is feasible and safe in the treatment of postmenopausal women with VVA symptoms, and efficacious at up to 12 weeks post-treatment.

KEYWORDS
energy-based vaginal rejuvenation, GSM, menopause, radiofrequency, vulvovaginal atrophy

1 | INTRODUCTION

Natural menopause occurs at the average age of 51 amongst Hong Kong women.[1,2] Boasting the world's highest life expectancy at 88 years,[3] these women spend more than half their adult lives in a postmenopausal state.[4] With a rapidly aging population, Hong Kong is the home to approximately 1.7 million post-menopausal women, constituting 23% of the city's total population.[5] This segment is projected to comprise more than one-quarter (27%) of the city's total population by 2030, representing almost half (49%) of the entire female population in Hong Kong.[5]

In contrast to the more commonly discussed vasomotor symptoms such as hot flushes and night sweats, vulvovaginal atrophy (VVA) is the most long-lasting symptom of menopause,[6–8] yet is

given little attention and the topic is rarely discussed in the relatively conservative Chinese society. While this prevalent condition is non-life threatening, it seriously impacts the physical and mental health, well-being, couple's intimacy, and the overall quality of life of postmenopausal women.

VVA is an involution of the mucous membranes and tissues of the vulva and vagina caused by the drop in estrogen that occurs in women during menopause.[9–12] Recent reviews[12–14] on the prevalence of VVA symptoms indicate that about 50% of postmenopausal women report at least one symptom associated with the condition. Patients with VVA complain of vaginal burning, discharges, itching, dryness, irritation, dysuria and dyspareunia.[12,15–18] Moreover, the weakened tissues are more prone to develop trauma, tears, bleeding, and infections.[12,19,20]

Atrophy of the vulva, introitus, and vagina can be especially problematic for women who want to stay sexually active, but experience dyspareunia during sexual intercourse due to vaginal dryness and atrophic changes.[7,19,21–25] According to community studies, the prevalence of sexual dysfunction amongst postmenopausal women is 91.2%.[26] Some vulvovaginal symptoms can be alleviated by the use of vaginal lubricants or moisturizers; however, such solutions offer limited and temporary relief only.[27] In addition, emerging data suggest that lubricants may adversely affect the vaginal epithelium, lamina propria, and the vaginal microbiota.[27–31]

Hormonal replacement therapy (HRT) may be considered for climacteric symptoms in the absence of contraindications, whereas local estrogens are primarily indicated to alleviate symptoms and reverse atrophic changes in cases where VVA represents the sole menopausal complaint.[12,32,33] Although local estrogen therapies are effective and safe at very low doses,[32,34,35] medication adherence is quite variable (52%–74%),[36] mainly due to safety concerns, inconvenience, and inadequate symptom relief from treatment.[12,37,38]

More recently, energy-based vaginal rejuvenation modalities such as lasers, fractional CO_2,[39] fractional Er: YAG, and radiofrequency (RF) devices,[40–42] have brought new hope to patients suffering from VVA symptoms. RF has gained significant popularity in recent years due to its non-invasiveness and rapid results. The mechanism of action is based on elevating the temperature of the treated tissue to initiate biological changes.[43] RF energy heats the connective tissue of the vaginal wall to 40–45°C, triggering microinflammatory stimulation of fibroblasts to stimulate collagen contraction, neocollagenesis, and neoelastogenesis to revitalize and restore the strength, elasticity, and moisture of the vaginal mucosa.[27,44] However, a long-standing disadvantage of some RF devices has been their constrained application due to limitations in application area where the whole vaginal canal is unable to be treated at once. Nowadays, there are solutions employing 360 degrees of RF energy emission, simplifying the procedure.

A number of qualitative studies exist to demonstrate the therapeutic efficacy of RF-based devices in improving VVA symptoms, stress urinary incontinence (SUI), and sexual functions. Treatment effects on postmenopausal Chinese women are, however, lacking. This study aims to evaluate the symptoms management effects of a real-time temperature-monitored non-ablative RF device in the treatment of postmenopausal Chinese women with VVA.

1.1 | Terminology

The term Genitourinary Syndrome of Menopause (GSM)[34,45] emerged following a consensus conference by the International Society for the Study of Women's Sexual Health (ISSWSH) and the North American Menopause Society (NAMS) held in 2013. GSM is a chronic, progressive vulvovaginal, sexual, and lower urinary tract condition.[46] In the absence of medical intervention, this condition does not improve.

While GSM is a more descriptive term than VVA, the term does not necessarily imply pathology. There are some concerns that the term GSM may be overly all-encompassing, as it refers not only to the symptoms resulting from estrogen deficiency but also those arising from the effects of aging and other processes on the bladder and pelvic floor.[47] As the focus of this pilot study is centered specifically on the effect of non-ablative monopolar RF technology on VVA symptoms, precluding other urogynecological symptoms except dysuria, the term VVA will be used throughout this paper.

2 | METHODS

2.1 | Study design

This pilot study was conducted over a period of 18 months between October 2021 and April 2023, involving 24 postmenopausal women of Chinese origin living in Hong Kong. All subjects suffered one or more VVA symptoms of various severity and harbored the wish to remain sexually active. The subject selection for this study was designed to be monoethnic in nature to evaluate the therapeutic efficacy of RF-based devices on Chinese women with VVA symptoms—an area that has not been sufficiently addressed in previous studies. Given the strong association between vaginal microbiota species composition and VVA,[27] and that the former is known to be influenced by the host's race, internal and external factors, and to some extent, diet, medication, and lifestyle habits,[44,48] this study with its monoethnic subject group serves to assess the treatment efficacy on VVA patients and to provide treatment expectations that are more relevant and meaningful to the vast population of postmenopausal women in Hong Kong.

2.2 | Subject selection

Postmenopausal Chinese women seeking the treatment of VVA were recruited for the study from the existing Investigator's

pool. All subjects were required to be in a postmenopausal state, as defined as the absence of menstruation for a continual 12 months or more,[49] at the time of the subject recruitment process, and have to suffer at least one symptom of VVA, such as dryness, burning, itching, dyspareunia, and/or dysuria, and wished to remain sexually active. Exclusion criteria included: the use of any HRT (either systemic or local, within the 6 months prior to inclusion in the study), antibiotics, probiotics, or prebiotics (either systemic or local, within the 3 months prior to inclusion in the study), vaginal moisturizers, lubricants or any other local preparation (within the 30 days prior to inclusion in the study); the use of any immunosuppressants, steroids or NSAIDs (within the 3 months prior to inclusion in the study); acute or recurrent urinary tract infections, active genital infections; pelvic organ prolapses, previous pelvic reconstructive surgery, serious diseases or chronic conditions, psychiatric disorders; pacemakers, defibrillators, or any metal implants; and/or other contraindications listed on the device manual (Appendix S1).

Prior to commencement, the study protocol was reviewed and approved by the University Institutional Review Board. The study's conduct adhered to the ethical principles of the 1975 Declaration of Helsinki. The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been followed. Each patient was assigned a unique subject identification number for anonymization. The patient's medical, obstetric, and gynecological history was thoroughly reviewed during the initial consultation with a clinician. An informed written consent was obtained before the patient was entered into the study.

Each participant underwent a standardized gynecological examination. The clinician also performed a speculum-assisted examination as well as pH testing with pH test strips.

A summary of the demographic and clinical profile of the subjects is presented in Table 1.

When the gyneco-obstetric features of women in the study group were examined, 66.7% had given birth, and one-third of the subjects had no child-bearing experience. 16.7% of the patients had one pregnancy, 41.7% had two, and 9.3% had three or more pregnancies. 41.7% of the subjects had vaginal deliveries, 20.8% had cesarian deliveries, and 4.2% had both. Of those who had given birth, 87.5% had the first delivery at or before the age of 35.

At the time of the study, 33.3% of the patients had been in the menopausal state for 1–4 years, half of the women had been in menopause for 5–9 years and 17% for 10 years or more.

TABLE 1 Demographic & clinical profile of the study cohort ($n = 24$).

Personal history	N	Mean ± SD or %
Age (years)	24	55.9 ± 4.1
Age at menopause (years)	24	50.4 ± 3.2
Time-lapse since menopause (years)	24	6.5 ± 3.4
Sexually active[a] in the last 6 months	19	79%
Sexually inactive	5	21%
Nulliparous	8	33%
Childbirth	16	67%
Childbirth history		
Caesarean section only	5	31%
Vaginal delivery only	10	63%
Vaginal & caesarean	1	6%
Smokers	0	0
BMI	24	22.8 ± 4.9
Previous treatment		
No treatment	12	50%
Lubricant/moisturizer	9	38%
HRT	0	0
Other (topical medication, pre−/probiotics)	3	12%

[a]"Sexually active" is defined as having engaged in sexual activities at least once every month.

2.3 | Treatment protocol

The machine used in this pilot study was the Exion BTL-785F, with an EMFEMME 360 applicator (BTL Industries Ltd). The device emits RF energy in 360 degrees, thus treating the entire vaginal canal at once. It also uses a built-in temperature sensor for real-time temperature tracking.

Each patient underwent four weekly treatment sessions, carried out as an outpatient procedure by a clinician with the assistance of a designated clinic personnel. The procedure involved 8 min of intra-vaginal RF treatment and 12 min of extra-vaginal RF treatment. The patients were treated in a lithotomy position on a gynecology bed. No anesthesia was required for this non-ablative monopolar RF procedure. A grounding pad was firmly attached to the subject's musculus gluteus maximus area during the entire treatment.

Real-time temperature was monitored through the infrared thermal sensor on the handpiece. All applicator tips used were for single use only and were properly disposed of after each treatment.

During the treatment, RF energy was emitted through a 360-degree metal ring located at the upper part of the intra-vaginal applicator, while the plastic cap covering the top of the applicator prevented the RF energy from reaching the cervix. Within 90 s into the intra-vaginal treatment, the vaginal tissue was gradually heated to the therapeutic level of 40–45°C. As for the extra-vaginal session, the treatment areas including the labia majora, labia minora, introitus, and perineum,[50] reached the therapeutic temperature of 40°C within 60 s. Patients could return to their normal activities immediately afterwards and did not need to avoid coital sexual activity after the procedure.

Follow-up appointments were arranged 4 weeks (R1) and 12 weeks (R2) after the last treatment session. Treatment safety and experience, with special attention to heat, pain, and discomfort, were assessed at each visit.

2.4 | Data collection & analysis

Three evaluation systems, namely the Vaginal Health Index Score (VHIS), the 10-cm Visual Analog Scale (VAS), and the Female Sexual Function Index (FSFI), were used concurrently in this pilot study. The patients' conditions were evaluated with VHIS and VAS at the initial visit (baseline), at each of the weekly treatment visits, and during the two follow-up appointments. As the FSFI measures sexual function in six domains over the previous 30 days,[51] the patients were asked to complete the FSFI questionnaire during their initial visit (baseline), at the 4th treatment visit, and at the two follow-up appointments.

2.4.1 | VHIS

At each point of time during the study, the patients were evaluated using the VHIS. The system consists of five parameters: Elasticity, Fluid volume, pH, Epithelial Integrity, and Moisture. Each parameter is graded from 1 to 5, with 1 being the least desirable and 5 being the most satisfactory; if the total score is <15 out of a total score of 25, the vagina is considered atrophic.[52] Assessment of clinical changes related to vaginal atrophy was evaluated through clinical examination and the VHIS system developed by Gloria Bachman et al.[53]

2.4.2 | 10-cm VAS

Using VAS, the intensity of VVA symptoms (vaginal burning, vaginal itching, vaginal dryness, dyspareunia, and dysuria) were evaluated by patients themselves, with the left extreme of the scale (0) indicating *"absence of symptom"* and the right (10) indicating *"symptom as bad as it could be"*.[54] The VVA symptoms evaluations were conducted before the first RF application (baseline), at every subsequent treatment visit, and again at the 4-week and 12-week follow-up.

2.4.3 | FSFI

FSFI is a broadly used and highly reliable instrument for assessing female sexual functions; the system was recently validated for use amongst Chinese women,[55,56] and was used in this study. The FSFI questionnaire consists of 19 items across six domains, namely, Sexual desire, Arousal, Lubrication, Orgasm, Satisfaction, and Pain.[57] This self-report system uses a 5-point Likert scale ranging from 0 to 5 or 1–5 with higher scores indicating greater levels of sexual functioning on the respective item.[58,59] The scores are then summed up within each domain and multiplied by a domain factor ratio to yield the individual domain scores.[56] The total FSFI score is the sum of the six domain scores, which ranges from 2 to 36; a higher FSFI score is associated with a lesser degree of sexual dysfunction.[60] A total score below 26.55 indicates sexual dysfunction.[61] Use of FSFI in postmenopausal women suggests that a lower threshold of 20 may be appropriate for identifying women with sexual dysfunction.[62]

Statistical analyses were conducted using the Minitab® Statistical Software to evaluate: the statistical significance of the differences (improvements) between the scores at baseline and at 12-week follow-up. In view of the relatively small sample size and the data type, we have opted for a combination of One-Way ANOVA tests and Two-Sample *t*-Tests in our statistical analysis.

3 | RESULTS

Twenty-four postmenopausal Chinese women (47–64 years, BMI $22.8 \pm 1.0\,kg/m^2$) were recruited for the study from the existing Investigator's pool.

3.1 | VHIS

At baseline, 100% of the patients scored 1 or 2 on the Fluid Volume and Elasticity. 75% and 46% of the patients scored 1 or 2 on the parameters of pH and Epithelial Integrity respectively, and 71% on Moisture. The distribution is shown in Figure 1A.

At the 3-month post-treatment follow-up, vaginal conditions of Moisture and Elasticity were reversed in all 24 patients. On the Fluid Volume measure, 18 out of 24 subjects (75%) showed moderate or normal amounts of fluid volume in vagina (scored 4 or 5). While 71% of the patients still scored 1–3 on the pH, which is equivalent to a pH value of 5.1 or above—an elevated level that increases the patients' susceptibility to vaginal infections. The distribution is shown in Figure 1B.

Both the VHIS total score as well as the scores on individual parameters recorded marked improvements after the completion of four treatment sessions. The improvement in pH, however, was quite unremarkable. It is interesting to note that while all five parameters improved steadily over the six measurement points, the improvement in pH did not follow the same pattern. After a relatively dramatic initial improvement recorded following the first treatment, further improvement as measured by pH at subsequent visits was notably lacking.

The charts showing the improvement trends of the VHIS average score and the VHIS improvements by measure are shown in Figure 2A,B. Trend charts showing the improvement trends on the five measures are shown in Appendix S1.

The average VHIS score increased from 9.42 ± 2.36 (baseline) to 21.00 ± 2.43 (3-month follow-up), representing a 123% improvement. When the two sets of data were compared, the difference

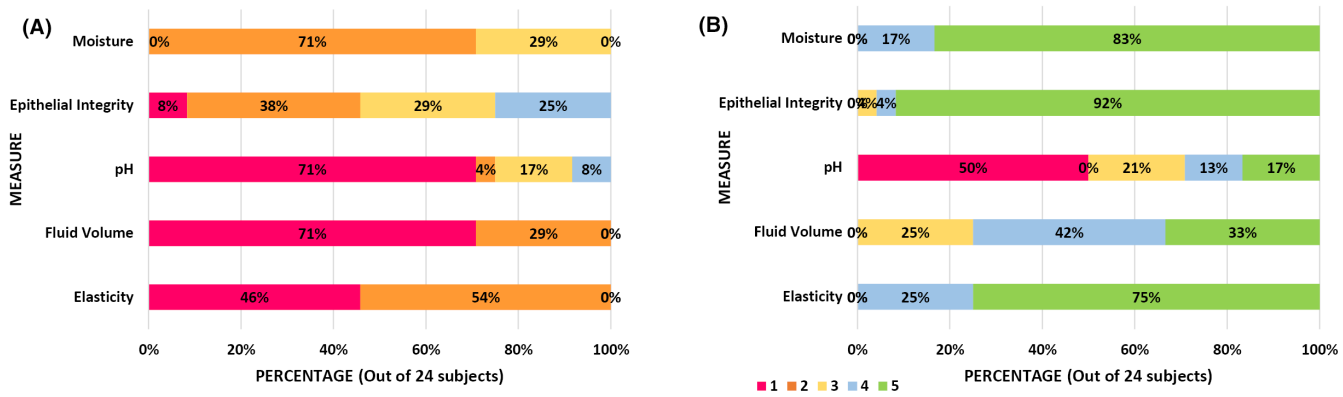


FIGURE 1 VHIS baseline score by measure (left) and VHIS Score at 3-Month f/u by measure (right).

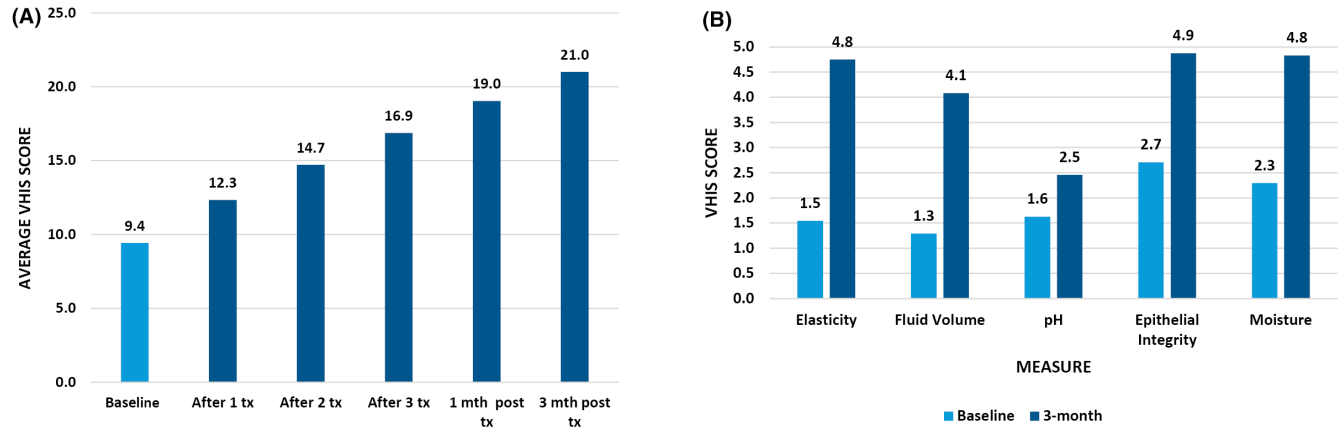


FIGURE 2 Average VHIS at each f/u (left) and comparison of VHIS score by measure (24 subjects) at baseline versus 3 months post-treatment (right).

TABLE 2 Summary of VHIS scores.

VHIS	Baseline	3-Mth f/u	% Increase	*p*-Value
Average	9.42 ± 2.36	21.00 ± 2.43	123%	0.000
Elasticity	1.54 ± 0.54	4.75 ± 0.44	208%	0.000
Fluid volume	1.29 ± 0.46	4.08 ± 0.78	216%	0.000
pH	1.63 ± 1.06	2.46 ± 1.61	51%	0.041
Epithelial integrity	2.71 ± 0.96	4.88 ± 0.49	80%	0.000
Moisture	2.25 ± 0.44	4.83 ± 0.38	115%	0.000

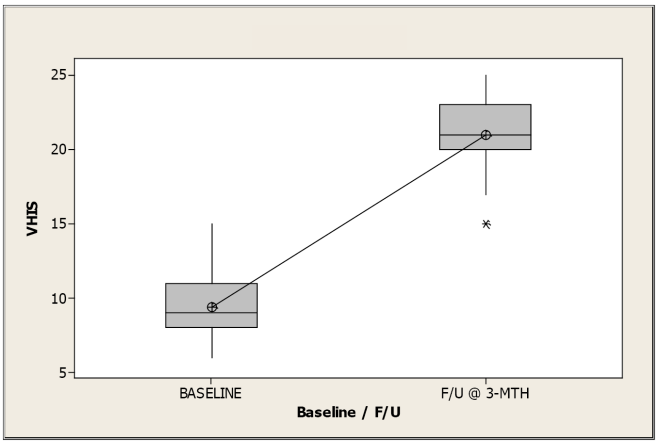
(improvement) was shown to be statistically significant (p-value <0.05), with a p-value of 0.000. All five parameters also logged drastic, statistically significant improvements. The results are summarized in Table 2. The Two-sample t-Test boxplot and the corresponding statistical analysis of the VHIS Total Score are shown below in Figure 3; the analyses on the five measures are presented in Appendix S1.

It is interesting to note that while the analyses on VHIS Total Score and the parameters of elasticity, fluid volume, epithelial integrity, and moisture all showed very strong evidence (p-value = 0.000) that the post-treatment improvements were statistically significant, the pH parameter was borderline with a p-Value of 0.041. This is consistent with our previous observation that pH improved after the first treatment but subsequently plateaued.

3.1.1 | 10-cm VAS

Based on the average scores at baseline, dyspareunia, and dryness were the top two highest-scoring VVA symptoms, with average scores of 7.0 and 5.5 respectively. At the 12-week follow-up visit, the average scores of dyspareunia and Dryness were 1.5 and 0.6 respectively, representing a decrease of 78.6% and 89.1%. The average scores of all 5 VVA symptoms also recorded improvements. Comparisons of the scores at baseline (Before) and the score at 12-week follow-up (After) are summarized in Figure 4.

Prior to treatment at baseline, 83% of the patients had a dyspareunia score of >5.0, more than 67% of the patients had a Dryness score >5.0, and 46% had an Itchiness score >5.0. The distribution



Two-Sample T-Test and CI: VHIS, Baseline / F/U

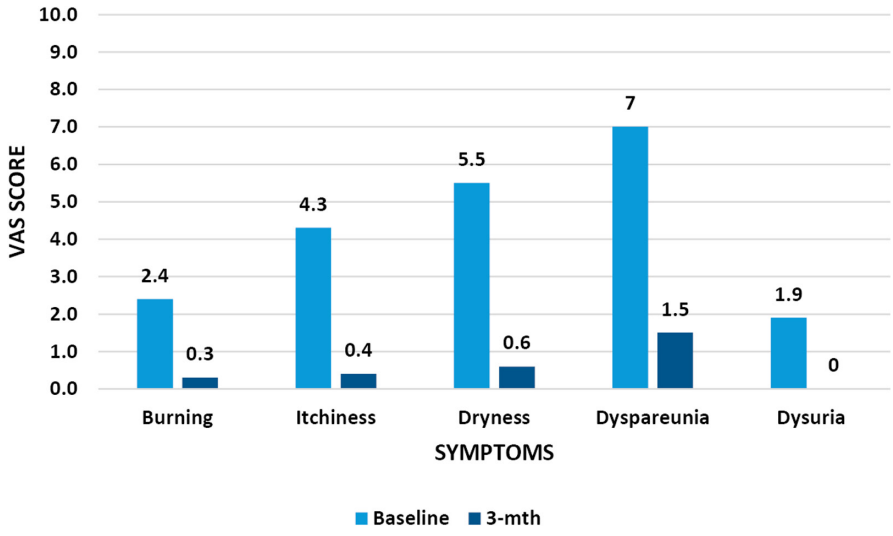
Two-sample T for VHIS

Baseline / F/U	N	Mean	StDev	SE Mean
BASELINE	24	9.42	2.36	0.48
F/U @ 3-MTH	24	21.00	2.43	0.50

Difference = mu (BASELINE) - mu (F/U @ 3-MTH)
Estimate for difference: -11.583
95% CI for difference: (-12.976, -10.191)
T-Test of difference = 0 (vs not =): T-Value = -16.75 P-Value = 0.000 DF = 45

FIGURE 3 Boxplot of VHIS score at baseline and 3-month f/u and its statistical description.

FIGURE 4 VVA Symptoms average score before & after (baseline vs. 3-Month f/u).



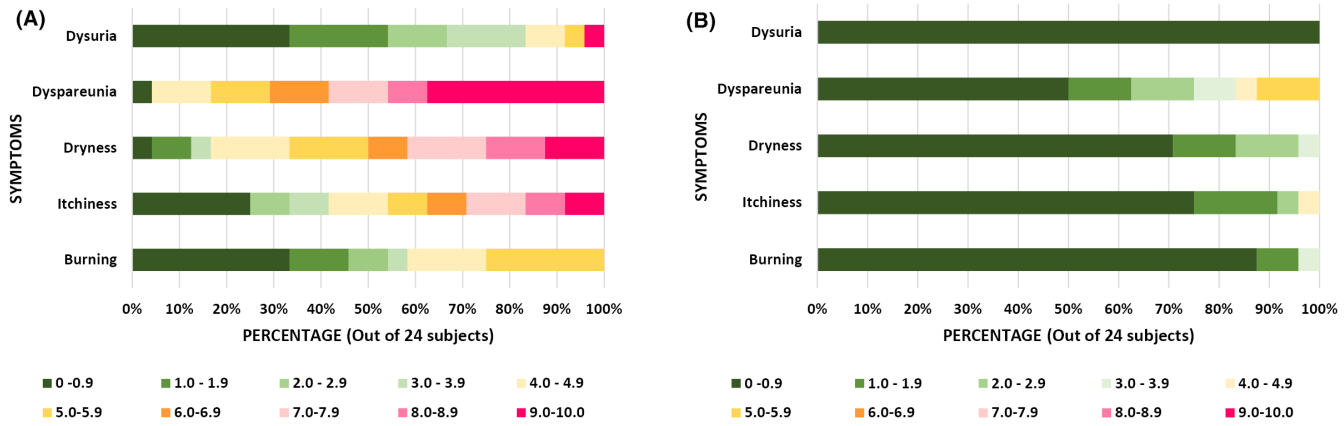


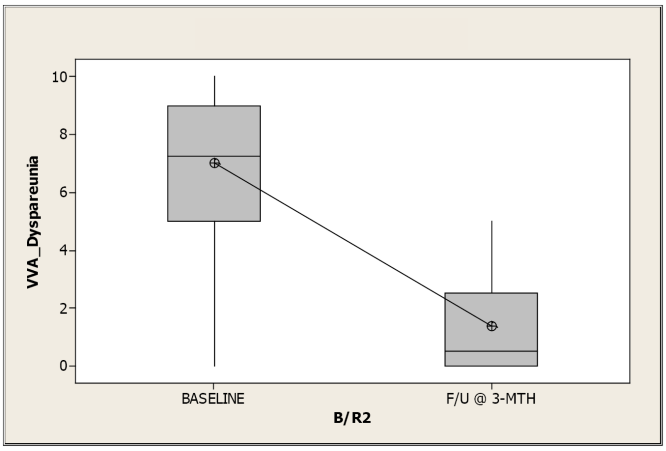
FIGURE 5 VVA Symptoms at baseline (left) and at 12-week f/u (right)—24 subjects.

is shown in Figure 5A. At the 12-week post-treatment follow-up, all 5 VVA symptoms recorded marked improvements. Issues of Burning, Dryness, and Dysuria were resolved; only one patient still suffered Itchiness (scored 4), and four subjects still suffered Dyspareunia scores of 4.0–5.9 after treatment. The distribution of VVA Symptoms Severity at 12-week post-treatment follow-up is shown in Figure 5B.

Using the data on the patient's VAS scores at baseline (BASELINE) and the corresponding VAS scores after treatment at 12-week follow-up (F/U@ 3-MTH), analysis showed that the differences were

TABLE 3 Summary of VAS scores.

VVA Symptom	Baseline	3-Mth f/u	% decrease	*p*-Value
Burning	2.35 ± 2.12	0.26 ± 0.66	88.9%	0.000
Itchiness	4.25 ± 3.23	0.44 ± 0.924	89.6%	0.000
Dryness	5.54 ± 2.57	0.58 ± 0.86	89.5%	0.000
Dyspareunia	7.00 ± 2.57	1.38 ± 1.74	80.7%	0.000
Dysuria	1.94 ± 2.29	0.00 ± 0.00	100%	0.000



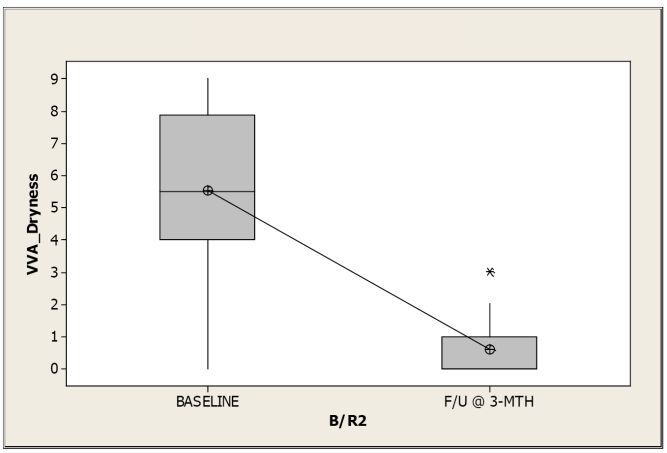
Two-Sample T-Test and CI: VVA_Dyspareunia, B/R2

Two-sample T for VVA_Dyspareunia

B/R2	N	Mean	StDev	SE Mean
BASELINE	24	7.00	2.57	0.52
F/U @ 3-MTH	23	1.38	1.74	0.36

Difference = mu (BASELINE) - mu (F/U @ 3-MTH)
Estimate for difference: 5.617
95% CI for difference: (4.329, 6.906)
T-Test of difference = 0 (vs not =): T-Value = 8.81 P-Value = 0.000 DF = 40

FIGURE 6 Boxplot of symptom "dyspareunia" at baseline and 3-month f/u and its statistical description.



Two-Sample T-Test and CI: VVA_Dryness, B/R2

Two-sample T for VVA_Dryness

B/R2	N	Mean	StDev	SE Mean
BASELINE	24	5.54	2.57	0.53
F/U @ 3-MTH	24	0.583	0.856	0.17

Difference = mu (BASELINE) - mu (F/U @ 3-MTH)
Estimate for difference: 4.958
95% CI for difference: (3.824, 6.093)
T-Test of difference = 0 (vs not =): T-Value = 8.95 P-Value = 0.000 DF = 28

FIGURE 7 Boxplot of symptom "dryness" at baseline and 3-Month f/u and its statistical description.

statistically significant across all 5 symptoms, with *p*-value = 0.000. A summary of the VAS scores is shown in Table 3.

The Two-sample *t*-Test boxplot and statistical outputs of Dyspareunia and Dryness—the top two scoring concerns—are shown below as Figures 6 and 7 respectively; the Minitab® outputs on Burning, Itchiness, and Dysuria are shown in Appendix S1.

3.1.2 | FSFI

Scoring may not be accurate in circumstances where the patient did not engage in sexual intercourse attempting vaginal penetration in the 4 weeks prior completing the FSFI questionnaire,[52] since the absence of sexual activity is not necessarily attributable to sexual dysfunction, although the assigned FSFI score is identical (zero) for either.[52,62] In view of this, we have excluded five patients from our FSFI analysis. These patients did not engage in sexual intercourse during the course of this pilot study and thus, could not provide fair evaluations. Nevertheless, they entertained the wish to remain sexually active in the future. Information on the five patients is shown in Appendix S1.

Prior to treatment at baseline, the average FSFI score of the 19 patients was 15.05 ± 6.07. The score improved after three weekly treatments by 53.9% to 23.16. At 3 months post-treatment, the

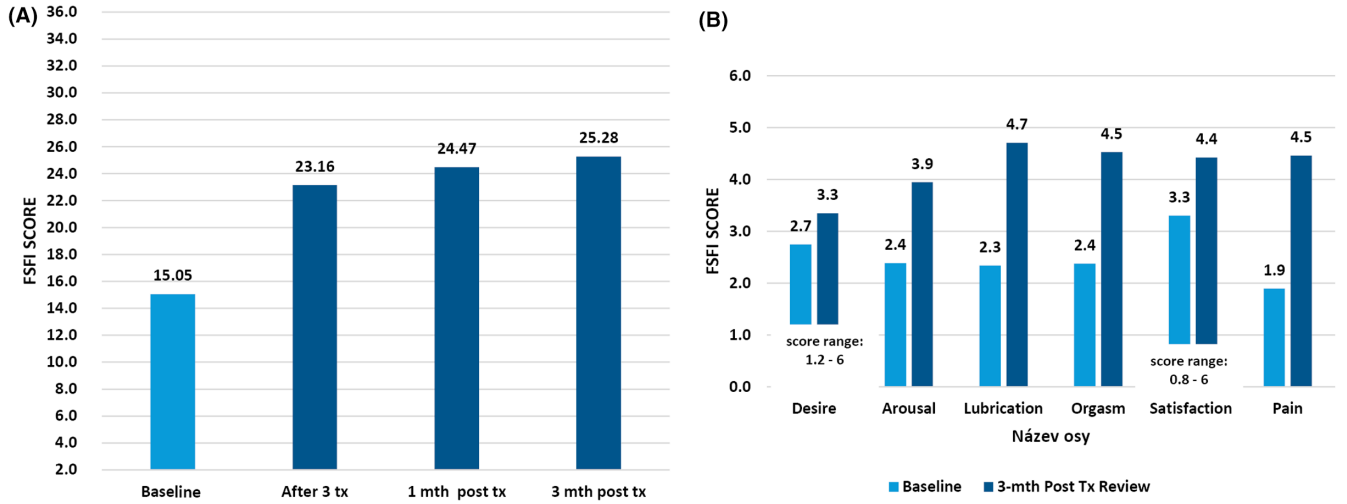


FIGURE 8 Average FSFI score (19 subjects) at each f/u (left) and FSFI average score by domain (19 subjects) before & after (baseline vs. 3-month f/u) (right).

average FSFI score was 25.28, representing a 68.0% increase (Figure 8A) from baseline.

At 12 weeks post-treatment, all six domains recorded drastic improvements. Pain—the lowest scoring domain at baseline—recorded the most significant improvement; the average score logged a 136% increase from 1.89 to 4.46. Only 16% (3) of subjects still experienced some pain (score 0–3). Other domains, namely Arousal, Lubrication, and Orgasm also logged improvements, at 66.0%, 101.3%, and 90.3% respectively. It is interesting to note that at 21.8% and 33.5% respectively, the improvements on Desire and Satisfaction were relatively modest. Psychological factors may play a more significant role in these two domains.

The FSFI average score by domain is shown in Figure 8B.

Despite the substantial improvements and symptom relief recorded, the average FSFI score did not reach the FSFI cutoff score of 26.55. Only 8 out of 19 patients, representing 42.1%, reported FSFI scores above the optimal cutoff score of 26.55 at the 12-week post-treatment follow-up, and are qualified as being without sexual dysfunctions.[52,61] However, at the lower threshold suggested for peri- and post-menopausal women, 18 out of 19 patients, representing 94.7%, met the cutoff score of 20.0 and were qualified as being sexually functional. The distribution of the patients' FSFI scores at baseline (Before) and at 12-week follow-up (After) is shown in Figure 9.

The Average FSFI score increased from 15.05 ± 6.07 at baseline to 25.28 ± 4.69 at the 3-month follow-up, representing a 68.0% improvement. When the two sets of data were compared, the difference (improvement) was shown to be statistically significant, with a *p*-value of 0.000. The Two-sample *t*-Test boxplot and the corresponding statistical analysis are shown in Figure 10. All domains logged strong, statistically significant, improvements; the domain Desire exhibited a borderline *p*-value of 0.05. The results are summarized in Table 4. The Minitab® outputs on the six domains are shown in Appendix S1.

4 | DISCUSSION

In contrast to the more commonly discussed vasomotor symptoms, VVA is the longest-lasting symptom of menopause.[6,7] Large cohort studies have depicted a 27%–55% prevalence of vaginal atrophy in menopausal women.[56,63,64] Contrary to the vasomotor symptoms, which tend to be milder over time, VVA symptoms rarely resolve spontaneously and, in most cases, deteriorate if left untreated, thereby negatively affecting patients' confidence and intimacy with their partners.[21,32,46,65] Despite the prevalence of VVA symptoms and their long-term effects affecting both the patients' quality of life and couples' intimacy, it is estimated that only 1 in 4 women experiencing VVA symptoms seek medical attention.[32,56]

With the loss of follicular activity, ovarian estrogens reduce dramatically, leading to significant changes in the structure of the vaginal mucosa, and consequently, the impairment of numerous physiological functions.[66] After menopause, a woman's estrogen level in plasma decreases from 129 ng/L during her reproductive period to 18 ng/L.[67] This drastic drop in the level of estrogen—a vasoactive hormone—decreases blood flow to vagina and vulva, leading to reduced vaginal lubrication and loss of libido.[68]

Estrogen deficiency also impacts mucosal elasticity through matrix glycosaminoglycan depletion and the hyalinization, fragmentation, and fusion of collagen and elastin fibres.[17,32] Such changes are represented by the progressive loss of elasticity and the rugal folds of the vaginal lining becoming thinner with potential petechiae.[12] Rugae aids in expandability, distensibility, and lubrication of the vagina during sexual stimulation. These pro-lubricative and pro-elastic functions are lost due to diminished collagen, elastin, and hyaluronic acid content, leading to thinned epithelium, impaired smooth muscle proliferation, denser connective tissue arrangement, and loss of vascularity.[14] In more persistent cases, the vagina becomes narrower and shorter and the introitus can constrict.[12,32,69]

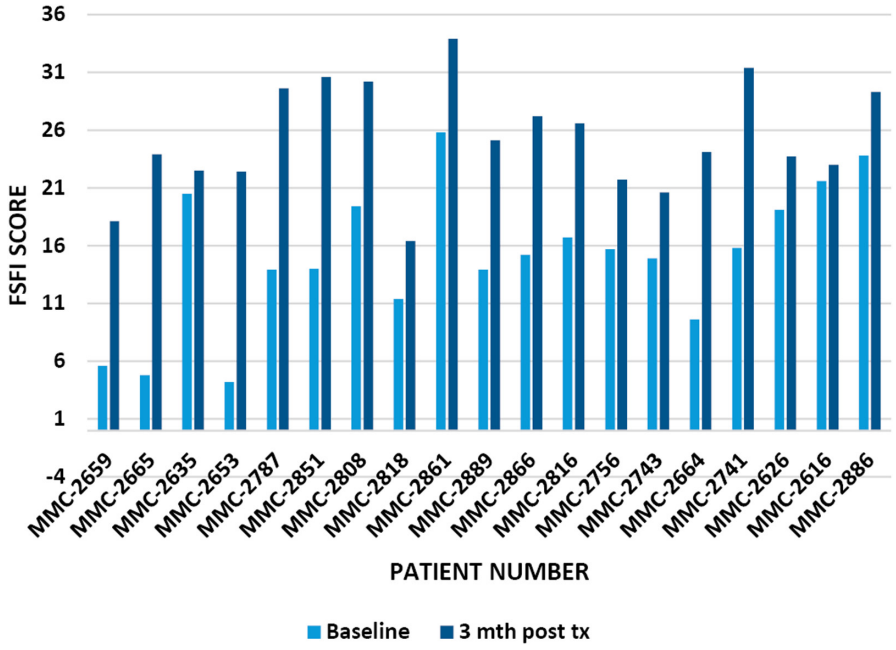
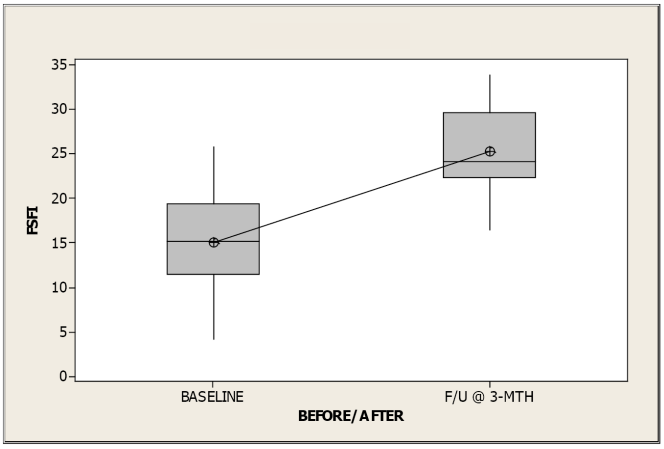


FIGURE 9 FSFI total score before & after (19 subjects).



Two-Sample T-Test and CI: FSFI, BEFORE/AFTER

Two-sample T for FSFI

BEFORE/AFTER	N	Mean	StDev	SE Mean
BASELINE	19	15.05	6.07	1.4
F/U @ 3-MTH	19	25.28	4.69	1.1

Difference = mu (BASELINE) - mu (F/U @ 3-MTH)
Estimate for difference: -10.23
95% CI for difference: (-13.81, -6.65)
T-Test of difference = 0 (vs not =): T-Value = -5.81 P-Value = 0.000 DF = 33

FIGURE 10 Boxplot of symptom FSFI at baseline and 3-month f/u and its statistical description.

Increased sexual activity is advised for maintaining robust vaginal muscle condition. Sexual activity, with or without a partner, improves blood circulation to the vagina.[70] A positive link between sexual activity and the maintenance of vaginal elasticity, pliability, and lubricative response to sexual arousal has been demonstrated.[71] With heterosexual intercourse, the seminal fluid contains sexual steroids, prostaglandins, and essential fatty acids, which serve to maintain the vaginal tissues.[72] Deficiency of estrogen and androgen in postmenopausal women is often associated with a loss of libido.[73] Decreased frequency or sexual abstinence exacerbates vaginal atrophy,[74,75] leading to unpleasant sexual experiences due to vaginal dryness and dyspareunia, which further disrupt the intimacy-based sexual response cycle.[76]

4.1 | Vaginal dryness and dyspareunia

The most predominant complaints of sexually active, postmenopausal women are vaginal dryness and dyspareunia.[46] Defined by genital pain that can be experienced before, during, or after intercourse, dyspareunia can have a significant effect on physical and emotional health. Since the condition affects the patient's partner and couples' intimacy, this condition is the primary reason VVA patients seek medical attention.

Vaginal lubrication is caused by fluid transudation from blood vessels, and from endocervical and Bartholin glands. With the drastic reduction in estrogen after menopause, sebaceous glands reduce the production of secretions and therefore, during sexual activity, lubrication is decreased and delayed.[12,19,35,71] Postmenopausal women have a total estimated volume of vaginal fluid of 0.0825 g per 15-min collection, compared to 0.214 g in fertile women. The majority of vaginal fluid in postmenopausal women appears to be secreted from the vaginal epithelium.[12,77]

The prevalence of vaginal dryness and dyspareunia has been reported to be 90% and 80% respectively.[46] Data from this pilot study validated the trend, although dyspareunia seemed to be more prevalent amongst the study subjects. Based on our records, 96% of

TABLE 4 Summary of FSFI scores.

FSFI	Baseline	3-Mth f/u	% Increase	*p*-Value
Total	15.05 ± 6.07	25.28 ± 4.69	68%	0.000
Desire	2.75 ± 0.92	3.35 ± 0.90	22%	0.050
Arousal	2.38 ± 1.41	3.95 ± 1.09	66%	0.001
Lubrication	2.34 ± 1.33	4.71 ± 0.85	101%	0.000
Orgasm	2.38 ± 1.41	4.53 ± 1.16	90%	0.000
Satisfaction	3.31 ± 1.13	4.42 ± 0.76	34%	0.001
Pain	1.89 ± 1.35	4.46 ± 1.39	136%	0.000

the 24 subjects recruited for this pilot study suffered dyspareunia of various severities prior to treatment. The FSFI data also showed "Pain" as the domain with the lowest score at baseline. With regard to reduced lubrication, the data obtained from this pilot study indicated that 84% of the patients suffered vaginal dryness of various severities. RF was shown to be an effective approach for the treatment of these symptoms of VVA.

The minimal clinically important difference (MCID) was introduced to determine the least threshold of beneficial outcomes. Previous research identified that the MCID for the FSFI questionnaire may lie in the range of 2.1–4.0[78] points which was notably overstepped by the results documented in this study (+9.3 points) and therefore can be considered clinically significant. For the VAS scores used as the primary mode of assessing response to treatment in this study, there has not been a well-established MCID yet. For VHI, the cutoff value (<15) is used instead of MCID. This threshold was surpassed on average since the 4th treatment and gradually reached the 3-month follow-up value of 21.1 points.

4.2 | Increased pH in menopause

Besides subject symptoms, low estrogen levels are associated with unfavorable changes in the bacterial flora colonizing the vagina, which leads to elevated vaginal pH and a heightened risk of infection with pathogenic bacteria in postmenopausal women.[79,80]

The vaginal flora composes of a variety of aerobic and anaerobic, gram-positive, and gram-negative bacteria.[72] In fertile women, *Lactobacilli* metabolize glucose into lactic acid and acetic acid, thus lowering the vaginal pH. The normal acidity of an estrogenized vagina is usually moderately acidic, favoring *Lactobacilli*. A lactobacillus-dominant flora protects its host against vaginitis and urogenital tract infections through the maintenance of an acidic vaginal pH in the range of 3.6–4.5.[56,81] Elevated vaginal pH higher than 4.5 is associated with vaginitis, which causes various vaginal symptoms.[56,82]

In post-menopausal women, low estrogen levels and a decrease in the epithelium glycogen concentrations hinder the production of lactic acid by *Lactobacilli*.[56,75] The more alkaline pH leads to a shift in the vaginal flora toward more coliforms and, together with other atrophic changes, is responsible for increased susceptibility to and frequency of infections, malodors, and exacerbation of vaginal symptoms associated with VVA.[12,62,83,84]

4.3 | RF for VVA

The present pilot study demonstrated that RF technology with real-time temperature control monitoring is an effective treatment option for postmenopausal women with VVA symptoms. Data from the study showed that all patients reported substantial symptom alleviation after 4 weekly treatment sessions. Patients' VVA symptoms on all dimensions recorded statistically significant improvements. More than 90% of the patients experienced total symptom relief from dyspareunia and vaginal dryness—the most prevalent and concerning VVA symptoms both globally and amongst our subjects.

Study procedures were conducted without incident. No thermal burns or injuries occurred, and according to treated patients, procedures were painless and the temperature emitted by the device was acceptable. No adverse effects were reported during or after treatments.

RF has been established as an excellent modality for tissue tightening via stimulation of neocollagenesis, denaturation of collagen, contraction, and activation of the healing cascade.[47] Numerous studies in dermatology[47,82] have demonstrated tissue contraction and have determined a therapeutically ideal temperature range of 40–45°C. Neocollagenesis is stimulated without causing unnecessary damage to the skin or integral tissue structures.[85,86] The same treatment concept applies in the application of RF for vulvovaginal rejuvenation.

The RF device used in this pilot study is equipped with real-time temperature monitoring and regulation, ensuring the therapeutic temperature is reached, but more importantly, that the temperature is maintained throughout the treatment timeframe. The goal of treatment is to heat vaginal and vulvar epithelium to approximately 40–45°C, for 20 min (8-min intra-vaginal, 12-min extra-vaginal). This temperature has been shown to be necessary to stimulate fibroblast activity, which contributes to the production of new connective tissue matrix molecular components.[87] The biostimulative effect of RF restores most vaginal functions such as secretion, absorption, elasticity, lubrication, and vaginal epithelium thickness.[88]

Several studies have investigated different modalities for VVA, including hormonal and nonhormonal approaches. Hormonal treatments like estrogen creams or tablets have been widely studied and shown effectiveness in alleviating VVA symptoms by replenishing estrogen levels.[89] They've demonstrated improvements in

vaginal health, moisture, and pH balance.[89] However, some patients are cautious about hormonal treatments due to concerns about potential side effects, especially for those with a history of hormone-sensitive cancers or conditions.[89] Nonhormonal options, including lubricants, moisturizers, and medical devices like vaginal dilators or lasers, offer alternatives for those who prefer to avoid hormonal interventions.

The study conducted by Pacik and Geletta[90] focused on the use of vaginal dilators in postmenopausal women with VVA have suggested that regular use of dilators helped alleviate pain during intercourse. Further, laser therapy, similar to the RF technology used, has reported similar improvements in VVA symptoms such as dryness, elasticity, and pain (fractional CO2 lasers have shown positive outcomes in vaginal health, aligning with the RF study's focus on VHIS).[91]

However, the use of both, dilators or lasers, can be discomforting, and time-consuming, raising safety concerns, while also lacking comprehensive long-term data on its efficacy and accessibility, posing adherence challenges, potentially leading to limited effectiveness and psychological barriers for some individuals.[91,92]

The provided study on RF technology for treating VVA shows promising results, especially in safety and improving symptoms like dryness, dyspareunia, and VHISs. The novel device delivers RF energy at 360° simultaneously which increases the comfort of the patients and minimizes the therapy time. However, more research is needed to solidify the long-term effects, optimal treatment protocols, and comparisons with other therapies are areas requiring further exploration.

Results from this pilot study validated the effectiveness of RF in the reversal of vaginal symptoms. At the 12-week follow-up, the majority of women were satisfied with the treatment, and no related adverse events were recorded.

The potential systematic biases could occur during the selection of the patients from the Investigator's pool and could affect the results. To prevent potential systematic biases, a set of objective selection criterion and exclusion criterion were devised prior to the selection process. Patient selection for the study was conducted with strict adherence to these criteria. In addition, a unique 4-digit patient number was assigned to each patient upon her arrival for the initial visit. The patient number was used in place of the patient's given names on all patient records for this study. This served to protect the patient's data privacy, as well as a mean to “blind” the selector during the selection process.

The generalizability of the finding is partly limited by the study's focus on postmenopausal Chinese women only. Different ethnic groups can exhibit variations in genetic makeup, hormonal profiles, lifestyle, and environmental factors, all of which can influence the manifestation and progression of VVA.[93–95] Further, variations in menopausal symptoms, hormonal profiles, cultural attitudes toward menopause and sexual health, as well as lifestyle factors such as diet, physical activity, healthcare access, and, in the end, responses to treatment alone can occur. Therefore, results derived from a monoethnic cohort might not apply to women from other ethnic backgrounds.

Similar findings were observed in Spanish postmenopausal women with GSM in Aznar et al study[96] evaluating the safety and efficacy of a 360° energy distribution RF device for non-invasive treatment of dyspareunia and demonstrating positive effects on the nonhormonal restoration of the vulvovaginal tissue.

The absence of a control group might lead to an overestimation of the treatment's effectiveness. Participants knowing they are receiving some form of treatment (and not a placebo) might report improvements due to psychological factors rather than actual physiological changes. Further, a control group could help with an objective comparison within ethnicity. Despite these factors, the study can still be compared to other studies with different ethnicities using the same validated questionnaires and although the sample size is small, it is still sufficient for the statistical analysis. On the other hand, this study can help to understand the outcomes of underrepresented Asian ethnicities in the population, a cohort that presents considerable recruitment challenges for VVA-related studies. When considering the questionnaire, the incorporation of subjective patient assessment could help the patient to participate more in the treatment and could increase the probability of active treatment participation.

The missing nonfunctional measurements could also have helped us analyze tissue composition and have a more exact description of the patient's condition at baseline, after therapy, and at follow-up visits. Obtaining the patient's consent to participate could, however, be extremely challenging. The length of follow-up period is always disputable according to the patient's comfort and the importance of long-term observation of the changes induced by the treatment.

This pilot study demonstrated that non-ablative, monopolar RF technology equipped with a real-time temperature monitoring system is feasible, and safe for the treatment of postmenopausal Chinese women with VVA symptoms, and efficacious up to 12-week post-treatment.

Given the limitations, the study's conclusions regarding the efficacy and safety of RF treatment for VVA in postmenopausal women may not fully represent the broader population. The findings are, however, valid for the specific group of Hong Kong postmenopausal women, caution should be exercised when extrapolating these results to other ethnic groups or a more diverse population. Future studies with unbiased patient selectors, long-term data, and more diverse ethnic representation with a larger sample size and a robust control group are needed to validate these findings universally. Additionally, nonfunctional measurements including histological analysis, CHIP cytometry, or VMI analysis should be included as well as the patient experience and treatment perception monitoring.

4.4 | Study limitations

Small sample size, no nonfunctional measurement (e.g. histological analysis, CHIP cytometry, etc) no patient experience and treatment perception questionnaire, long-term follow-up, monoethnic focus,

and the absence of a comparator (sham procedure, placebo, or other active treatment) are some of the known limitations of this pilot study.

AUTHOR CONTRIBUTIONS

Vivian Cheng contributed to the study design and performed all the treatments together with a designated Clinic Assistant, Ms. Rita Lee. Dr. William Tai provided advice on the scientific part of the whole research. Ms. Athena Lee was responsible for statistical analyses of the data.

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CONFLICT OF INTEREST STATEMENT

The authors did not report any potential conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

This study was approved by the PolyU Institutional Review Board (The Hong Kong Polytechnic University) for ethical review for research involving human subjects for a period from 01-Aug-2021 to 01-Aug-2023, reference number HSEARS20210625001.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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