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**TECHNOLOGICAL EVOLUTION IN THE
RADIOFREQUENCY TREATMENT OF
VAGINAL LAXITY AND MENOPAUSAL
VULVO-VAGINAL ATROPHY AND OTHER
GENITOURINARY SYMPTOMS:
FIRST EXPERIENCES WITH A NOVEL DYNAMIC
QUADRIPOLAR DEVICE**

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ORIGINAL ARTICLE

Technological evolution in the radiofrequency treatment of vaginal laxity and menopausal vulvo-vaginal atrophy and other genitourinary symptoms: first experiences with a novel dynamic quadripolar device

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ABSTRACT

BACKGROUND: This paper was a spontaneous, non-sponsored exploratory study to investigate the safety and efficacy of two schedules of thermal treatment with a new low-energy dynamic quadripolar radiofrequency (DQRF) device in: A) premenopausal women referring perception of vaginal introital laxity and related symptoms, with special reference to dysuria and urinary incontinence and unsatisfactory sexual activity (vaginal laxity arm of the study); B) postmenopausal women with vaginal atrophy and dryness and other vulvo-vaginal atrophy and *genitourinary syndrome of menopause* (VVA/GSM) related symptoms (VVA/GSM arm of the study).

METHODS: As for the vaginal laxity arm of the study, 12 women with perception of very to slightly loose vaginal introital laxity underwent five 20-min DQRF thermal treatment sessions every 14±1 days. A Vaginal Laxity Questionnaire (VLQ, certified Italian translation) and short form of the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12, Italian certified translation) were used to assess urinary incontinence, sexual gratification and the contribution of any concomitant pelvic organ prolapse. As for the VVA/GSM arm of the study, 13 women with objective evidence of VVA and vaginal dryness and/or dyspareunia rated as moderate/severe most bothersome symptoms underwent four 10-min DQRF sessions every 10±1 days. Specifically designed visual analogue scales (VAS) for VVA/GSM symptoms and overall satisfaction with sexual life were used.

RESULTS: No adverse effects, including thermal burns or injuries, were reported during or after treatments in either arm of the study. Eleven of the enrolled women completed the five planned DQRF treatment sessions in the vaginal laxity arm of the study; 12 women completed the four DQRF sessions planned in the VVA/GSM arm of the study. Clinically and statistically significant improvements in self-perceived sensation of looseness and symptoms like dysuria/urinary incontinence and sexual function in the vaginal laxity arm of the study as well as VVA/GSM symptoms and overall satisfaction with sexual life in the VVA/GSM arm of the study. Improvements were already reported at the first assessment visit before the end of the planned DQRF sessions of each arm of the study, after, respectively, 56±4 and 30±3 days.

CONCLUSIONS: The DQRF treatment was well tolerated, with no pain during the procedure and no untoward effect reported over the 2-month follow-up periods in both the vaginal laxity and VVA/GSM arms of the study. Improvements in self-reported VLQ and PISQ-12 scores (vaginal laxity arm) and VAS self-evaluation of VVA/GSM symptoms and overall satisfaction with sexual life (VVA/GSM arm of the study) were rapid and persistent. This suggests rapid and persistent vaginal rejuvenation as the basis of subjective improvement in symptoms and decreased sexual distress in both indications, including dysuria and urinary incontinence in menopausal women. Such promising exploratory findings deserve confirmation in larger studies.

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Key words: Pulsed radiofrequency treatment - Urinary incontinence - Menopause.

Well-defined clusters of events occur in all women in the weeks after vaginal childbirth and the months and years after menopause. The almost inevitable stretching during delivery of the dense connective tissue of the vaginal wall, introitus and labia majora, that then heals in varying degrees of laxity and worsens with each successive birth, may be considered physiological or quasi-physiological. Though distinct from vaginal and other genito-pelvic structures bulging into the vaginal canal and introitus more properly defined as prolapse, vulvovaginal laxity may seriously affect the woman's self-image, self-esteem and overall quality of life. This is due to compromised genital aesthetics and discomfort and irritation in everyday life, as well as to the negative impact on the woman's sexual experience and couple relationship. Much the same can be said of the menopausal estrogen drop associated with vulvar and vaginal involution and decreased circulatory engorgement, lubrication and elasticity, frequently leading to vulvo-vaginal atrophy (VVA) and related symptoms (dryness, irritation, itching, burning, discharge, dysuria).

Decreased genito-pelvic sensation during sexual activity is common in women with vaginal laxity. In a multinational survey of members of the International Urogynecological Association (IUGA), more than four out of five interviewed practitioners described vaginal laxity — mainly a delivery-related problem, though compounded by natural aging — as an under-reported and troubling condition that impacts the couple relationship. The interviewed IUGA members also described vaginal laxity as the most important change of body integrity experienced by women after vaginal delivery.¹

As regards VVA and genitourinary syndrome of menopause (GSM), symptoms may trouble up to 50% of postmenopausal women.^{2, 3} A 2015 survey in women with VVA symptoms found EQ-5D (EuroQol-5D) scores to be linearly related to symptom severity assessed with the Menopause Rating Scale. The decrements in EQ-5D scores associated with moderate to severe VVA symptoms were comparable to those observed in other serious

conditions such as arthritis, chronic obstructive pulmonary disease, asthma, and irritable bowel syndrome.⁴ The surveyed prevalence of VVA/GSM symptoms in the general menopausal population ranged between 40% (Germany) and 54.4% (Spain), with half of women reporting their symptoms as either moderate or severe.⁴ Vaginal dryness is the most commonly reported VVA symptom in Europe (70%), with 32% of women in Italy, Germany, Spain and the UK naïve to any kind of treatment.^{3, 5}

Besides impacting on the woman's quality of life and psychological wellbeing, introital and vaginal laxity after delivery and menopausal VVA/GSM frequently expose to unwelcome consequences in terms of long-term morbidity. Vaginal laxity is often detected in conjunction with atrophic vaginitis, stress incontinence and/or inappropriate micturition reflex with bladder instability. A lax vagina may in fact be the main determinant of both stress and urge female urinary incontinence.⁶ As regards VVA and GSM, recent vaginal infections were much more likely in a survey of a selected population of 722 women diagnosed with GSM out of 913 looking for routine gynecological examinations in Italian menopause health centers (OR 2.48, 50% CI: 1.33-4.62, vs. non-GSM controls). Itching and dysuria as risk factors for further morbidity were also highly prevalent (56.6% and 36.1%, respectively).⁷

The paper illustrates the outcomes, with special reference to safety, of the first study with the last technological evolution of non-ablative radiofrequency treatment in women with either vaginal laxity or VVA/GSM (see Appendix). The study, designed as a spontaneous, non-sponsored, short-term exploratory investigation, was carried out in a private outpatient setting and targeted to women experiencing quite severe quality of life disruption because of significant GSM- and vaginal laxity-related symptoms. Emphasis was on safety and the medical value of the new technology as elective procedure when either condition is a serious problem for the woman's wellbeing and quality of life.

The paper also discusses how the efficacy and safety outcomes of the study relate to the

biophysics of dynamic quadripolar application of highly targeted heat-generating radiofrequency fields to vulvar and vaginal subepithelial tissue layers.

Materials and methods

Study goal and design and study population

A spontaneous, exploratory, open-label investigation was prospectively conducted in outpatient office-based subjects at the investigator's private practice to probe the safety and efficacy of a newly developed dynamic quadripolar device as non-surgical, non-laser radiofrequency treatment in: A) women with subjective perception of laxity of vaginal introitus and other laxity-associated symptoms with special reference to urinary incontinence; B) postmenopausal women with subjective perception of vaginal dryness and other VVA/GSM-related symptoms. All study materials were appropriately peer reviewed for ethical problems. All candidate women gave full informed consent.

Candidate women with vaginal laxity were screened from early January to mid-May 2015; candidate women with VVA/GSM for enrolment from late mid-February to late May 2015. A total of 12 women with vaginal laxity and 13 with VVA/GSM were enrolled; follow-up of the last subjects ended in July 2015. The dimensions of the two samples were defined without any clear-cut indications from either published papers or systematic clinical experience about the value and role of the new radiofrequency technology in the two indications. The two schedules of thermal dynamic quadripolar radiofrequency (DQRF) treatment were designed based on the evidences of pre-clinical experiences in animal vaginal models.

Activities specific to the vaginal laxity arm of the study

SCREENING AND ENROLMENT PROCEDURES

Candidate women were to be less than 54 years old and premenopausal. They were to

have had at least one full-term vaginal delivery (more than 36 weeks gestation) completed at least one year before study enrolment and to currently have negative pregnancy tests and a normal Papanicolaou Smear Cytology Test (obtained no more than two months before enrolment). Candidate women were to be in a stable monogamous heterosexual relationship, to have reasonable sexual activity (at least two vaginal intercourses per month using an acceptable method of birth control), and to have no evidence of significant pelvic organ prolapse (*i.e.*, beyond the hymenal ring). Dosage of any medication, such as antihypertensives and psychotropics, known to affect sexuality should have been stable for at least 1 month prior to treatment with no dosage change likely or planned in the forthcoming weeks. Candidates should not have been taking medications known to affect collagen metabolism and healing such as non-steroidal anti-inflammatory drugs and steroids for at least one month. The vaginal canal, introitus and vestibule were to be free of injuries and bleeding. Previous pelvic surgery within four years also prevented enrolment.

Candidates were fit for enrolment if they reported a perception of vaginal introital laxity that they defined as "very loose", "moderately loose", or "slightly loose" on a certified Italian translation of the Vaginal Laxity Questionnaire (VLQ), a Likert-type Scale with seven levels of response ("Very loose", "Moderately loose", "Slightly loose", "Neither loose nor tight", "Slightly tight", "Moderately tight", "Very tight").⁸ Subjects with severe urinary incontinence with suspected intrinsic sphincteric deficiency (ISD) and positive empty bladder stress tests were excluded.

OUTCOME ASSESSMENT

VLQ was the main outcome measure instrument; the short form of the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12, Italian certified translation) was also used as a validated standard assessment instrument for symptoms like dysuria/urinary incontinence and for gratifi-

cation with sexual life as well as to discriminate the contribution of any concomitant pelvic organ prolapse.⁹ Categorical levels of response were translated into ordinal scores for statistical analysis (for the VLQ scale, for instance, “Very loose”=1, “Moderately loose”=2, “Slightly loose”=3, “Neither loose nor tight”=4, “Slightly tight”=5, “Moderately tight”=6, “Very tight”=7). After the first one, the 20-min DQRF sessions were repeated every 14±1 days for a total of 5 sessions.

Activities specific to the VVA/GSM arm of the study

SCREENING AND ENROLMENT PROCEDURES

Candidate women were to be more than 50 years old and to have experienced no menstruation for at least 12 months. A wish to maintain an active sexual life should have been coexisting with vaginal dryness and/or dyspareunia rated as moderate/severe most bothersome symptoms¹⁰ and objective evidence of VVA (thinning/loss of vaginal rugae, mucosal pallor, friability and/or petechiae, low vaginal pH, low vaginal maturation index). Any systemic or local hormonal replacement therapy should have been stopped for at least six months and no vaginal moisturiser, lubricant or any other local preparations should have been used in the previous month. Prolapse staged ≥II according to the pelvic organ prolapse quantification system¹¹ also prevented enrolment.

OUTCOME ASSESSMENT AND TIMING OF DQRF SESSIONS

Clinical severity of VVA/GSM symptoms (vaginal dryness, burning and itching, dyspareunia, dysuria) was self-assessed by the enrolled subjects using 10-cm visual analogue scales (VAS) with “No symptom” at the left extreme of the scale and “Symptom as severe as it could be” at the right extreme as previously reported in several VVA studies including breast cancer survivors.¹² The overall satisfaction with sexual life was similarly assessed by enrolled women using a 10-cm VAS with

“Worst level of satisfaction” at the left extreme of the scale and “Best level of satisfaction” at the right extreme. After the first one, the 10-min DQRF sessions were repeated every 10±1 days for a total of 4 sessions.

Screening and outcome assessment activities common to both arms of the study

Screening assessment included a physical and pelvic examination, demographics, and medical and obstetric/gynecological history. Exclusion criteria included pelvic surgery within four years of the study, acute or recurrent urinary tract infections, active genital infections, chronic vulvar pain or vulvar lesions or disease (dermatitis, human papillomavirus, herpes simplex, vulvar dystrophy), inadequate thickness of the recto-vaginal septum as assessed by pelvic examination. Any systemic condition or mood/psychiatric disorder interfering with informed consent and study compliance also prevented enrolment in either arm of the pilot study.

Basal assessment was performed immediately before the first DQRF procedure in both arms of the study immediately before the first DQRF session. Three office follow-up visits were planned: immediately before the last procedure (*i.e.*, after 56±4 days in women with vaginal laxity and after 30±3 in women with VVA/GSM) and after 30±1 and 60±1 days following this first follow-up assessment (Figure 1).

In-office safety assessment included recording of vital signs and adverse events with special reference to any experience of pain or discomfort during and after the procedure. Post-treatment safety assessments were carried out the next day by telephone calls and by questioning for any need of analgesics, anti-inflammatory drugs or other medications at the following DQRF session.

Statistical analysis

Descriptive statistics (means and standard deviations for continuous variables, frequency distributions and percentages for categorical

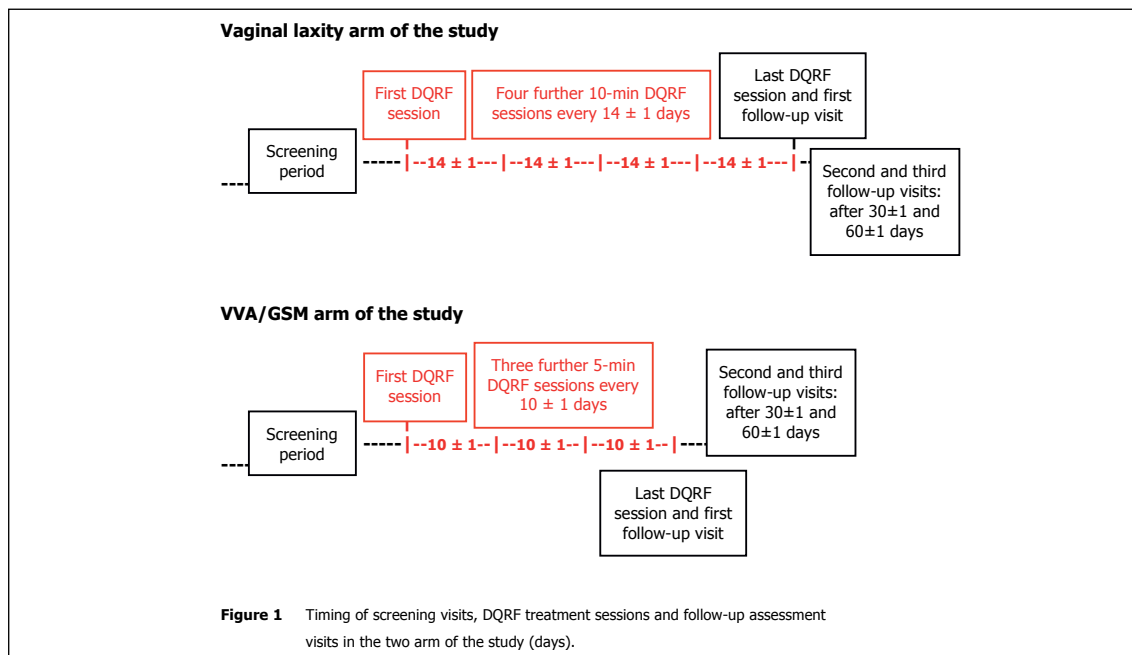


Figure 1 Timing of screening visits, DQRF treatment sessions and follow-up assessment visits in the two arm of the study (days).

Figure 1.—Timing of screening visits, DQRF treatment sessions and follow-up assessment visits in the two arm of the study (days).

variables) were generated for demographics, medical history, and physical examination findings. The nonparametric Wilcoxon Signed Rank Test for repeated measurements on a single population was applied to both repeated measures of ordinal data (VLQ, PISQ-12 and SF-12 mean scores) and continuous variables (VAS mean scores); the McNemar Test was used to test for differences in ordinal mean scores. Two-sided 95% confidence levels were used with $p < 0.05$ as cut-off for statistical significance.

Results

Eleven women completed the 5 planned sessions of DQRF treatment in the vaginal laxity arm of the study; 12 women completed the 4 planned sessions in the VVA/GSM arm of the study. One woman was lost to follow-up in each arm of the study without any further information. Table I illustrates the demographics and other characteristics relevant to the investigations of the two study populations at the screening visits immediately before the first treatment session.

TABLE 1.—Main characteristics of the two populations in the two arms of the study. SD, standard deviation; HRT, hormone replacement therapy.

Vaginal laxity arm, study population	
Women completing the five planned DQRF sessions	11
Age (years, mean ± SD)	41.7 ± 5.5
Body Mass Index (kg/m ² , mean ± SD)	24.1 ± 2.0
Parity (n, %)	
0	1 (9%)
1	3 (27%)
2	4 (36%)
3	3 (27%)
Current sexual activity (n, %)	11 (100%)
Frequency of sexual activity per week	1-4
VVA/GSM arm, study population	
Women completing the four planned DQRF sessions	12
Age (years, mean ± SD)	60.4 ± 6.5
Body Mass Index (kg/m ² , mean ± SD)	23.0 ± 1.8
Previous live births (n, %)	9 (75%)
Parity	1.7 (1-3)
Current sexual activity (n, %)	7 (58%)
Previous systemic HRT (n, %)	3 (25%)
Months of systemic HRT (months, range)	31 (3-54)

As regards evaluation of safety as the main goal of this explorative study, no burns, blisters or other complication were reported during or after treatments in both arms of the

study. All DQRF sessions were described as relaxing and comfortable in both arms of their study. All women were able to resume all everyday activities, including sexual life, immediately after each DQRF treatment session.

Vaginal laxity arm of the study

Secondary vaginal laxity-related conditions (orgasmic dysfunction, stress incontinence, atrophic vaginitis) were reported at the screening visit by 10 out of the 12 enrolled women with self-reported perception of vaginal laxity (9 out of the 11 subjects who actually completed the study).

Compared to basal assessment, VLQ mean scores as index of subjective perception of vaginal tightness significantly improved by at least one level in all women, as observed already at the first follow-up visit before the

end of the five DQRF sessions. Six out of the 11 women who completed the five planned DQRF sessions reported VLQ scores that were 2-4 levels higher than before treatment at the first assessment visit. A marginally non-significant trend to further improvement was apparent during the 2-month post-treatment follow-up, with 9 women reporting VLQ scores that were 2-4 levels higher than basal assessment after 60 ± 1 days (Figure 2A).

A statistically significant improvement in overall sexual function (mean Total PISQ-12 Score) could be demonstrated at the first evaluation visit, immediately before the last DQRF procedure, compared with basal assessment (34.5 ± 6.8 vs. 38.5 ± 6.1 , $P < 0.05$). Nine out of the 11 women who completed the five planned sessions showed an improvement of 2 to 4 points (Figure 2B).

Four individual PISQ-12 scores showed statistically significant improvements at the first assessment visit (Q2 or frequency of climax, Q6 or urinary incontinence related to sexual activity, Q7 or fear of urinary and stool incontinence, Q9 or emotional reactions during sex); four individual scores showed a tendency to improve (Q1 or sexual desire, Q3 or sexual excitation, Q4 or variety of sexual activities, Q8 or sense of vaginal bulging preventing sex.); for three PISQ-12 categories there was no change (Q5 or pain during intercourse, Q10 or partner's erection problems, Q11 or partner's premature ejaculation).

Similar mean total PISQ-12 scores were reported at the second and third assessment visit after 1 and 2 months of follow-up (40 ± 5.5 and 40.5 ± 5.6 , not significant compared to the first assessment visit, $P < 0.05$ compared with basal assessment).

Pain with intercourse subscores, already very low at screening, did not change over the follow-up period, meaning lack of even a very low-level of chronic inflammation induced, or anyway associated with the DQRF procedure. At the second visit, one woman missed more than two answers and was excluded from PISQ-12 assessment in accordance with PISQ-12 scoring instructions.⁹

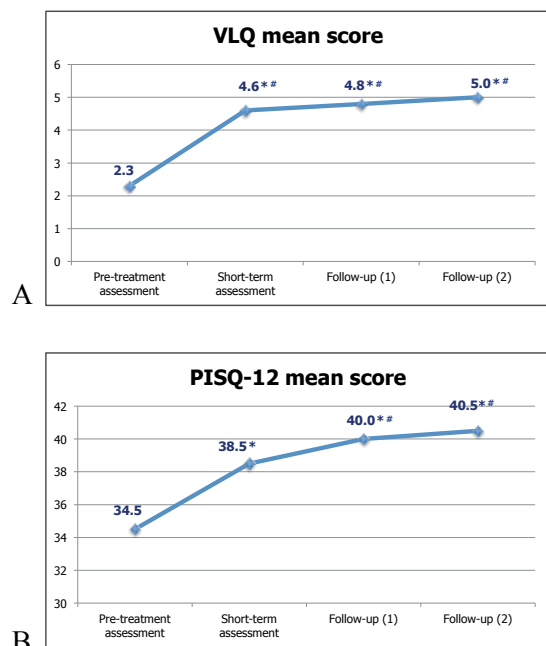


Figure 2.—Mean Vaginal Laxity Questionnaire (VLQ) scores (A), and mean Total Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12) scores (B) immediately before the first DQRF procedure (Pretreatment assessment), immediately before the last planned DQRF procedure (Short-term assessment) and after 30 ± 1 and 60 ± 1 days of post-treatment follow-up (Follow-up (1) and Follow-up (2)). * $P < 0.05$ vs. basal assessment; #non-significant vs. first assessment visit.

VVA/GSM arm of the study

Before treatment, 8 out of the 13 screened and enrolled women (61.5%) and 7 out of the 12 women who completed the four planned sessions (58.3%) were sexually active; 5 of the screened women reported to have had no sexual intercourse for at least three months due to severe VVA/GSM symptoms. As regards VVA/GSM symptoms, vaginal dryness was reported by all 13 enrolled women before treatment, vaginal itching and vaginal burning by 10, dyspareunia by 11, and dysuria/incontinence by 8.

At the first assessment visit before the first DQRF session, 10 of the enrolled women reported to have resumed coital sexual activity (83.3%). At the last follow-up visit 11 women reported to be variably but anyway sexually active; only one woman reported physical and emotional discomfort during a few attempts at having intercourse and would not consider herself sexually active.

Compared to basal assessment, clinically and statistically significant improvements were observed for mean VAS scores of most VVA/GSM symptoms and for the overall satisfaction with sexual life at the first evaluation visit before the last DQRF session. Further improvements for all scored items, or at least a tendency to further improvement, could be appreciated at the two post-treatment visits during the follow-up period (Table II).

The mean VAS score for overall satisfaction with sexual life improved from 4.3 ± 1.4 at baseline up to 7.0 ± 2.0 after 30 ± 3 days ("First assessment visit") and 7.7 ± 2.4 at the last fol-

low-up visit, 90 ± 4 days after the first DQRF session (Figure 3).

Discussion

The radiofrequency technology for non-surgical thermal treatment and vaginal rejuvenation in women with either vaginal laxity or VVA/GSM is well established and widely considered safe and effective.^{8,13}

In spite of the relative paucity of enrolled women with vaginal laxity and VVA/GSM, this exploratory study suggests that the novel dynamic quadripolar evolution of radiofrequency treatment is safe and well tolerated in both indications of vaginal rejuvenation with an excellent 2-month follow-up safety profile.

Even minimally invasive technologies may expose to bleeding, pain and burning.¹⁴ By minimizing the risk of thermal injuries, the new DQRF technology may offer further safety benefits over the current unipolar radiofrequency and laser technologies for non-surgical thermal treatment of introital and vaginal laxity and VVA/GSM.

Preclinical evidences provide convincing evidences of the biophysics of the DQRF concept. In infrared thermophotographs, the thermal effect in the treated genital areas appears to be highly localized onto the target mucosal surfaces and to rapidly dissipate after the end of the procedure without residual irritation or more severe injuries (Figure 4). The whole procedure has been usually reported by all women enrolled in the two arms of the study as painless and often devoid of any thermal sensation.

TABLE II.—*Detection and clinical severity of VVA/GSM symptoms in the study population of the VVA/GSM arm of the investigation. Mean scores (\pm standard deviation); data in cm assessed on 10-cm specifically designed visual analogue scales.*

	N.	Pre-treatment assessment	Short-term assessment	Follow-up (1)	Follow-up (2)
Vaginal dryness	12	8.8 \pm 2.4	4.3 \pm 1.8 **	3.4 \pm 1.7 ** °	3.2 \pm 1.9 ** °
Vaginal itching	10	7.5 \pm 2.7	3.7 \pm 1.9 **	3.0 \pm 1.6 ** °	2.6 \pm 1.3 ** °°
Vaginal burning	10	7.2 \pm 2.5	3.4 \pm 1.8 **	3.0 \pm 1.7 ** #	2.8 \pm 1.4 ** °
Dyspareunia	11	8.7 \pm 2.2	4.5 \pm 1.9 **	3.0 \pm 1.8 ** #	3.1 \pm 1.9 ** °
Dysuria/incontinence	8	5.5 \pm 2.6	3.0 \pm 1.9 *	2.9 \pm 1.6 ** #	2.6 \pm 1.5 ** °

N.: women reporting symptom; *P<0.05 vs. basal assessment; **P<0.01 vs. basal assessment; °P<0.05 vs. first assessment visit; °°P<0.01 vs. first assessment visit; # non-significant vs. first assessment visit.

Preclinical investigations relating to the time course and spatial distribution of the thermal effect in the subepithelial layers also suggested the tentative treatment schedules ad-

opted in this exploratory study. More formal dose-finding studies are warranted to fine-tune radiofrequency wavelengths and times of applications to maximize efficacy in both menopausal vaginal atrophy and laxity of the vaginal introitus and wall.

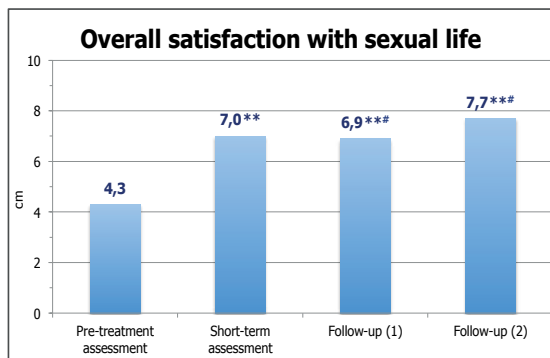


Figure 3.—Mean scores for overall satisfaction with sexual life (expressed as cm on a 10-cm visual analogue scale) before the first DQRF procedure (Pretreatment assessment) and at the first and second follow-up visit after 30±1 and 60±1 days of follow-up (Follow-up 1 and Follow-up 2). *P<0.05 vs. basal assessment; #non-significant vs. first assessment visit.

Somewhat different sets of biological effects should be pursued in the two conditions. As also suggested for other thermal therapy technologies, vaginal rejuvenation in introital and vaginal laxity implies re-activation of fibroblast and connective tissue function and development of new networks of collagen and elastin fibres in the subepithelial layers of introitus and vagina.^{13, 15}

Collagen re-activation is also the goal in vaginal rejuvenation in VVA/GSM, but possibly an even more important goal is vasodilatation. Increases of local blood flow facilitate the diffusion of the inactive sex steroid precursor dehydroepiandrosterone (DHEA) to vulvo-vaginal cells for local intracrine estrogen

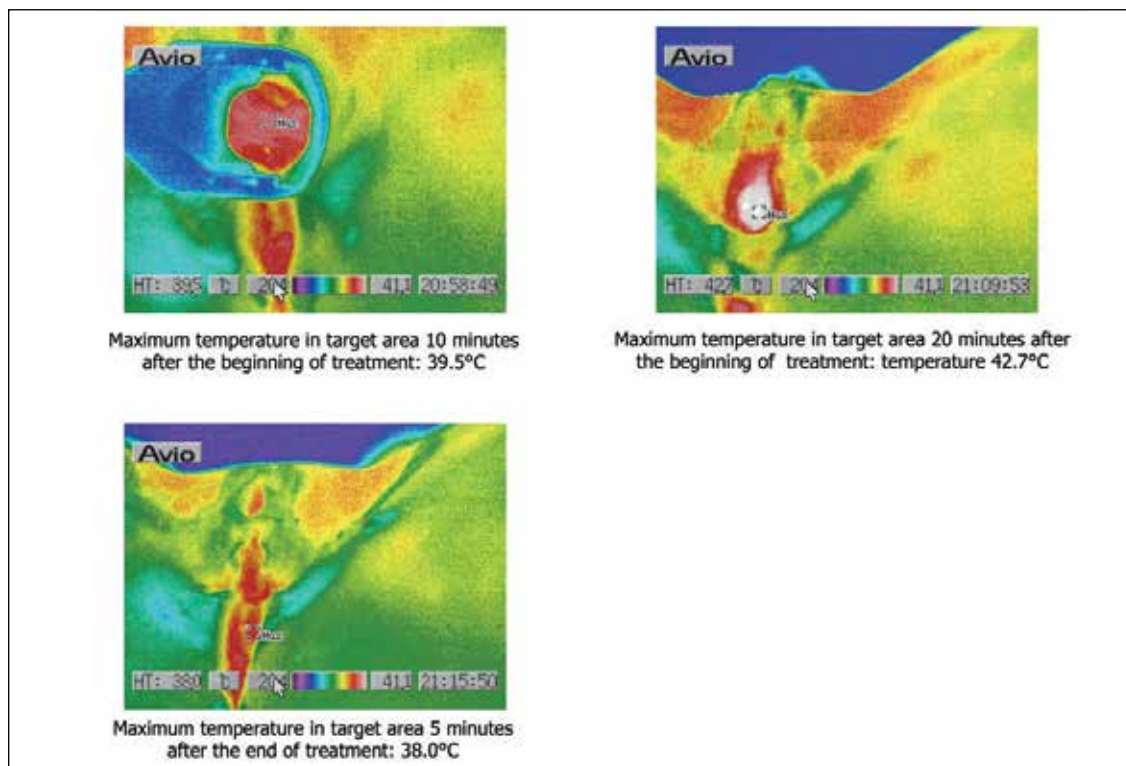


Figure 4.—Infrared temporised thermophotographs of the perineal, vulvar and vaginal areas of a woman enrolled in the vulvo-vaginal laxity arm of the study during her first 20-min DQRF session. Operational position: dorsal lithotomy position.

production. Thermally induced vasodilatation also facilitates the diffusion of DHEA-derived estrogens produced in local adipose tissue to the atrophic vaginal mucosa. From the time of menopause, DHEA from the adrenal glands becomes the only significant source of sex steroids for all hormone-dependent female tissues except the uterus. Ease of diffusion of DHEA and DHEA-derived sex steroids to vulvo-vaginal target cells may be crucial to counteract menopausal symptoms such as osteoporosis, muscle loss, vaginal atrophy, fat accumulation and hot flashes.^{16, 17}

The women with introital and vaginal laxity enrolled in the study defined their perception as “very loose”, “moderately loose”, or “slightly loose” on an internationally recognized self-assessment instrument as the VLQ. However few, as it is usually the case in exploratory studies, these women were a faithful sample of the universe of women with subjective perception of vaginal laxity in the gynecologist’s everyday clinical practice.

Improvements were rapid for both mean VLQ scores as index of vaginal laxity and PISQ-12 scores as index of overall sexual function and ancillary VVA-related disturbances like sex-related urinary and stool incontinence. Statistical and clinical VLQ and PISQ-12 improvements could be already shown at the first assessment visit immediately before the last DQRF procedure, only about 40 days after the first one, suggesting rapid onset of clinical benefits.

Improvements in VLQ and PISQ-12 scores vs. pre-DQRF basal assessment were similar at the first, the second and the third follow-up visits, suggesting persistence of clinical benefits with a base in anatomical re-modelling. Individual scores for intensity of orgasms and emotional experience during intercourse improved similarly to scores for dysuria and incontinence, confirming that anatomical re-modelling may be behind such ample benefits. Rapid and persistent improvement of vaginal laxity perception and laxity-related symptoms with DQRF treatment is in line with previous clinical evidences with highly effective unipolar radiofrequency and laser treatments.^{8, 13, 14}

When informally questioned during follow-up visits, women with pre-treatment introital vaginal laxity were usually happy to confirm gratifying, even unexpected, improvements in self-perceived sense of looseness, reduction of orgasmic dysfunction, better overall sexual satisfaction with a more relaxed couple relationship, as well as more pleasing genital aesthetics and improvement or disappearance of sex-associated stool and urinary incontinence. The operator also commonly referred visual improvements in looseness of labia majora, introitus and vagina: even at the first visit before the last planned DQRF treatment session.

As regards the VVA/GSM arm of the study, consistent improvements of all symptoms, as well as of sexual gratification, were reported by almost the whole VVA/GSM sample. Once again, the improvement of symptoms and the benefits for the sexual life were rapid — already after about a month and even before the end of the planned DQRF program — and persisted over the 2-month follow-up period.

The persistency of benefits once again suggests anatomical re-modelling and real correction of atrophy. Although no evaluation of thinning/loss of vaginal rugae, mucosal pallor and friability, low vaginal maturation index and other VVA-related symptoms was formally planned, anecdotic observations by investigators confirm anatomical rejuvenation. The menopausal fall of sex hormones, especially estrogens, impacts on mucosal elasticity by fusion, hyalinization and fragmentation of collagen and elastin fibers, and loss of highly hydrated matrix glycosaminoglycans.^{18, 19} As a consequence, urogenital atrophy-related symptoms develop in 40-57% of post-menopausal women and even in 15% of pre-menopausal ones.¹⁸

The benefits for vaginal health in menopausal women suggested by this exploratory study could even be indirectly self-sustaining over the long time. By letting the woman resume and maintain an active sexual life, DQRF vaginal rejuvenation may activate a series of physiological protective mechanisms that help to counteract the loss of mucosal elasticity and hydration associated with sex hormone depri-

vation.²⁰

However promising the results of this exploratory study with the new technologically advanced radiofrequency device in women with either vulvo-vaginal laxity or VVA/GSM, whether the benefits for wellbeing, self-esteem, sexual health and couple relationship are long-lasting remains an open question. Only further studies with a longer follow-up, hopefully in comparison with other effective non-surgical treatments, will be able to answer the question. Decreased sexual functioning in young breast cancer survivors as well as in pre-menopausal women with chemotherapy-related or surgical amenorrhea is another issue that this new technology could possibly contribute to relieve.²¹

Another field of application of non-surgical technologies for vaginal rejuvenation relates to the wish by many women, who have no real genitalia disorders, to obtain a more subjectively pleasing aesthetic appearance. This may indeed be the foremost field of application of non-surgical procedures for vaginal rejuvenation, and even for elective surgery.

Recent studies have shown that aesthetic reasons were behind the decision by 90% of patients to undergo elective surgery for vaginal tightening and perineal support.²² Labial reduction surgical procedures performed in the UK have doubled in the current decade,²³ whilst vaginal rejuvenation procedures increased by almost 30% in just one year in the USA in the last decade, from 793 in 2005 up to 1030 in 2006, according to the American Society of Plastic Surgeons.²⁴ The dynamic quadripolar evolution of the established radiofrequency technology is likely to have brilliant future also in aesthetic medicine, if the dynamic quadripolar concept — “persistent rejuvenation whilst minimising the risk of thermal injuries” — will survive the test of time. Well-designed dose-finding studies are a must also for any development in aesthetic medicine.

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Appendix.—DQRF device and procedure

The radiofrequency generator is driven by a patented dynamic quadripolar technology emitting radiofrequency DQRF with frequencies that vary between 1MHz and 1.3MHz and a maximum emitting power of 55W. The device is equipped with both a movement and a temperature detector sensor for high safety. Specifically designed treatment tips equipped with medically certified AISI Type 316 stainless steel dynamic quadripolar electrodes are mounted on anatomical probes used for intravaginal, introital and vulvar applications.

Procedures were office-performed with no need for previous preparations like analgesia or local anesthesia; subjects were placed on the examining table in dorsal lithotomy position. Vagina, perineum, and perianal area were cleansed using an alcohol-free cleanse. The treatment area, defined by a vaginal circumference at the hymenal ring of about 12 cm, was about 20 cm². The probe tipped by the dynamic quadripolar electrode system is applied onto the mucosa of the vaginal introitus starting behind the hymenal ring using a coupling gel to ensure the RF delivery. Radiofrequency energy is applied over the treatment area with circular and back-and-forth continuous movements, keeping the probe in contact

with the vaginal mucosal walls. The target temperature is reached setting the power from 15% to 18% according to the patient's sensitivity. The target range in VVA/GSM subjects is lower (40° C to 42° C) and is reached by setting a power between 12-15% according to the patient's sensitivity.

The new DQRF technology does not need a grounding pad attached on the subject's upper thigh, thereby leading to current flows through the thigh tissues and delivery of heavy energy loads because of Ohm's resistances in tissues. Electric fields generate only within the electrodes area. The configuration of the four electrodes is continuously and electronically controlled between alternating receiver and transmitter states. This allows repelling electric fields to form that, once in the ideal combination, direct energy deep in the subepithelial layers of the introitus, vagina and vulva. The operator can fine-tune the low-energy thermal effect generated by the localized electric fields both volumetrically and in terms of depth. Such fine-tuning is facilitated by a complete set of anatomically designed probes and tips equipped with the dynamic quadripolar electrode system.

