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Effect of Single-Treatment, Surface-Cooled Radiofrequency Therapy on Vaginal Laxity and Female Sexual Function: The VIVEVE I Randomized Controlled Trial

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ABSTRACT

Introduction: Vaginal laxity is a highly prevalent and undertreated medical condition.

Aim: To evaluate the efficacy and safety of surface-cooled, monopolar radiofrequency (RFc) therapy for the treatment of vaginal laxity in the VIVEVE I trial.

Methods: The VIVEVE I trial was a prospective, randomized, single-blinded, and sham-controlled study. Nine study centers in Canada, Italy, Spain, and Japan participated. Women presenting with vaginal laxity were screened and informed consent was obtained. Major study inclusion criteria were premenopausal status, age at least 18 years, at least one full-term vaginal delivery, and normal genito-pelvic examination results. Enrolled subjects were randomized (2:1) to receive RFc therapy (Active [90 J/cm^2] vs Sham [1 J/cm^2], respectively) delivered to the vaginal tissue.

Main Outcome Measures: The primary efficacy outcome was the proportion of randomized subjects reporting "no vaginal laxity" (Active vs Sham) at 6 months postintervention, which was assessed using the Vaginal Laxity Questionnaire. Treatment-emergent adverse events were evaluated in all treated subjects. Secondary efficacy end points included change on the Female Sexual Function Index (FSFI) and the revised Female Sexual Distress Scale (FSDS-R).

Results: No vaginal laxity was achieved by 43.5% and 19.6% ($P = .002$) in the Active and Sham groups, respectively. Differences in FSFI and FSDS-R total scores (Active vs Sham) were 1.8 ($P = .031$) and −2.42 ($P = .056$), respectively, in favor of Active treatment. Treatment-emergent adverse events were reported by 11.1% and 12.3% of subjects in the Active and Sham arms, respectively.

Conclusion: The VIVEVE I trial is the first randomized, controlled, blinded, clinical study of RFc for the treatment of vaginal laxity. A single treatment of RFc therapy was found to be safe and associated with both improved vaginal laxity and improved sexual function. The results from this trial support the use of a novel non-surgical therapy for vaginal laxity, a prevalent and undertreated condition. **Krychman M, Rowan CG, Allan BB, et al. Effect of Single-Treatment, Surface-Cooled Radiofrequency Therapy on Vaginal Laxity and Female Sexual Function: The VIVEVE I Randomized Controlled Trial. J Sex Med 2017;14:215−225.**

Key Words: Vaginal Laxity; Vaginal Looseness; Radiofrequency Therapy; Surface Cooled; Non-Surgical; Sexual Function

INTRODUCTION

Vaginal introital laxity or vaginal looseness is a poorly recognized and ill-defined condition that occurs in many women after pregnancy and vaginal childbirth. Trauma to the genito-pelvic musculature and stretching of the vaginal introitus during pregnancy and vaginal delivery can lead to permanent changes that can be worsened by multiparity, delivery of a large fetus, use of forceps, and age-related changes of vaginal connective tissue.[1,2] Long-term laxity of the vaginal introitus is differentiated from pelvic organ prolapse (POP), which primarily involves the collapse of

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internal genito-pelvic structures, whereas vaginal introital laxity (vaginal laxity) refers to looseness of the vaginal opening.

Vaginal laxity is associated with loss of physical sensation and decreased sexual satisfaction.[2,3] This poorly recognized, and frequently unreported, medical condition[4–6] negatively affects female sexual function, body image, and quality of life.[7–9] A recent study reported that 50% of parous women were concerned with vaginal laxity, yet 83% failed to discuss their concern with a health care professional.[4] Fifty-seven percent of urogynecologists viewed vaginal laxity as negatively affecting their patients' quality of life, sexual function, and relationship happiness. They further identified the vaginal introitus as the most frequently cited location of laxity, with symptoms arising from muscle and tissue changes.[4]

Therapeutic options for vaginal laxity include procedures and therapies targeted at the vaginal introitus and canal. The goal of these procedures is to restore sexual function. External cosmetic and gynecologic procedures of the vulva (eg, labioplasty) are performed primarily for esthetic enhancement, rather than to restore sexual function, and are not the focus of this research initiative. Restorative options for vaginal laxity include surgical procedures, physical therapy, and radiofrequency (RF) therapy.

Identifying an objective assessment of vaginal laxity remains elusive. A reliable correlation between vaginal length and introital caliber with sexual function has yet to be established.[10–14] Prior research of objective assessments such as introital diameter, genital hiatus, and vagina length have reported a poor correlation with women's perception of vaginal laxity and sexual function. The current standard of vaginal laxity assessment is the use of self-reported instruments.[1,15–17]

Surgical procedures (eg, vaginoplasty) intended to restore sexual function associated with vaginal laxity have been performed in women with decreased vaginal sensation, vaginal laxity, or a perception of a "wide vagina." These procedures, although controversial, involve reconstructive techniques aimed to decrease the caliber of the vaginal canal and introitus and can be conducted concomitantly with POP repair. Some studies of vaginoplasty repairs have reported improvements in sexual function.[10,18–20] However, the effectiveness of surgical approaches to restore vaginal tightness should be balanced by the risk involved in any surgery performed on vaginal tissue. Postsurgical recovery is substantial and includes the risk of scar formation and nerve damage, leading to fibrosis, dysesthesia, and dyspareunia.[20]

Pelvic floor muscle training and Kegel exercises are recognized therapies for vaginal laxity.[4] However, the heterogeneity of effectiveness evidence currently provides inconclusive scientific support for these therapies.[21,22] There is no scientific evidence to support the safe and effective use of over-the-counter products (eg, topical vaginal tightening products) for the treatment of vaginal laxity.

Non-surgical, monopolar RF therapy with cryogen surface cooling (RFc) provides a minimally invasive, outpatient modality to treat vaginal laxity. This hyperthermic therapy, originally developed to remodel epidermal tissue and treat stress urinary incontinence, activates fibroblasts to produce new collagen and stimulates remodeling of vaginal tissue without evidence of fibrosis or scarring.[23–31] Preclinical studies of RFc therapy delivered to the vaginal introitus reported non-fibrotic collagen deposition up to 6 months posttreatment.[23,24] Two published, single-arm pilot studies in women with vaginal laxity showed RFc therapy was safe and effective.[1,16] Before the data reported in this publication, there were no comparative effectiveness studies (ie, there were no controlled trials with a sham comparator arm) to support the safe and effective use of any RF therapy for the treatment of vaginal laxity.

The VIveve treatment of the Vaginal Introitus to EValuate Effectiveness (VIVEVE I) trial was the first randomized controlled trial of RFc therapy for the treatment of vaginal laxity. The VIVEVE I trial aimed to determine the efficacy and safety of RFc therapy for women with vaginal laxity. The trial was designed to demonstrate that Active treatment was superior to Sham treatment for the primary efficacy end point.

METHODS

Study Design and Research Subjects

The VIVEVE I was a multicenter, prospective, randomized, single-blinded, sham-controlled trial conducted at nine centers in Canada, Spain, Italy, and Japan. The VIVEVE I trial was registered at clinicaltrials.gov (NCT02261974). Subjects were recruited from January 1, 2015 through November, 1 2015.

Women presenting at the participating study centers with self-reported vaginal laxity were invited to participate in study screening. Written informed consent was obtained before screening. Local ethics committees or institutional review boards for each study center approved the overarching trial protocol, which adhered to the Declaration of Helsinki. The same assessments and procedures were carried out for all subjects, regardless of any site-specific required modifications (ie, one additional inclusion criterion and a reordering of efficacy assessments).

Study screening included collection of demographic data, medical and sexual history, physical and genito-pelvic examination, medication history, complete blood cell count and metabolic panel, Papanicolaou test results, and current and past pregnancy status. Women were screened using a detailed comprehensive interview to exclude those with severe psychiatric diagnoses (eg, body dysmorphic syndrome). Sexual function, sexual distress, and vaginal laxity questionnaires were administered in each subject's local language. Theses questionnaires required each subject to self-report on her vaginal laxity and sexual function and did not focus on her sexual partner's assessment.

The trial included premenopausal women (≥18 years of age) experiencing vaginal laxity during sexual intercourse who had at least one full-term vaginal delivery. Vaginal laxity was classified