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CLINICAL INVESTIGATION **Cervix**

CLITORAL THERAPY DEVICE FOR TREATMENT OF SEXUAL DYSFUNCTION IN IRRADIATED CERVICAL CANCER PATIENTS

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Purpose: The purpose of this pilot study was to evaluate the efficacy of the clitoral therapy device (Eros Therapy) in alleviating sexual dysfunction in irradiated cervical cancer patients.

Methods and Materials: Eligible patients had a history of cervical cancer treated with radiotherapy and self-reported sexual dysfunction of sexual arousal and/or orgasmic disorders. Patients used the noninvasive, nonpharmacologic clitoral therapy device using a hand-held, battery-powered vacuum to cause clitoral engorgement four times weekly for 3 months during foreplay and self-stimulation. Study instruments included the Female Sexual Function Index, Derogatis Interview for Sexual Functioning, and Dyadic Adjustment Scale. The outcome evaluation was performed at 3 months.

Results: Between 2001 and 2002, 15 women were enrolled and 13 completed the study. The median patient age and radiotherapy–enrollment interval was 43.5 years and 2 years, respectively. At baseline, all patients reported symptoms of sexual arousal and/or orgasmic disorders, and some also had sexual desire and pain disorders. At 3 months, statistically significant improvements were seen in all domains tested, including sexual desire, arousal, lubrication, orgasm, sexual satisfaction, and reduced pain. The median Female Sexual Function Index total score increased from 17 to 29.4 (maximal score, 36; $p < 0.001$). The median Derogatis Interview for Sexual Functioning total raw score increased from 46 to 95 (maximal score, 118; $p < 0.001$). At baseline, the Derogatis Interview for Sexual Functioning total T-score corresponded to the bottom 10th percentile of normal sexual functioning. At 3 months, the total T-score placed the patients at the normalcy cutoff. Gynecologic examinations revealed improved mucosal color and moisture and vaginal elasticity and decreased bleeding and ulceration.

Conclusion: Our results from this pilot study suggest that the clitoral therapy device may alleviate sexual dysfunction in irradiated cervical cancer patients. A randomized, controlled trial is warranted to assess the full benefits of this approach. **© 2005 Elsevier Inc.**

Cervical cancer, Radiotherapy, Sexual dysfunction, Clitoral therapy device, Eros Therapy.

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INTRODUCTION

Radiotherapy (RT) has long occupied a role in the management of cervical cancer. The first cervical cancer patient underwent RT a century ago (1). Today, RT is used as definitive (2, 3) and also adjuvant treatment before (4, 5) and after (6, 7) surgery in these patients.

A long-held concern with use of RT in cervical cancer, however, has been its adverse effects on sexual function. Numerous investigators have documented high rates of female sexual dysfunction (FSD) in irradiated cervical cancer patients (8–20). In a recent survey of early-stage cancer patients (most treated with RT) (21), insufficient vaginal lubrication, dyspareunia, and distress due to the symptoms were common. Others have documented problems with lubrication (8–20), sexual satisfaction (11, 17, 18, 20), and sexual desire (9–10, 12–16, 20). Such sequelae are not surprising, because cervical cancer is often diagnosed in young, sexually active women. Moreover, RT involves the delivery of high doses to the vagina and surrounding normal tissues, resulting in marked tissue and vascular changes (22–24).

Despite its known prevalence, no effective treatment has been developed for sexual dysfunction in these women. Some gynecologists administer hormonal replacement therapy (HRT) to these patients in an effort to address select symptoms. However, recent data from the Women's Health Initiative study have questioned this practice, with greater rates of cardiovascular disease and breast cancer seen in patients receiving HRT (25). Most patients today are simply given a vaginal dilator to minimize vaginal stenosis and select symptoms are addressed as they develop (e.g., vaginal estrogen or artificial lubricants for vaginal dryness). These traditional therapies are intended to help patients cope with compromised sexual function but are limited in ability to restore sexual function fully.

Recently, a new treatment for FSD known as the clitoral therapy device (CTD; Eros Therapy, Urometrics, St. Paul, MN) was introduced (Fig. 1). The CTD increases blood flow to the clitoris by creating gentle suction around the clitoris. It is placed over the clitoris, and the patient activates the battery-powered pump. A vacuum is created that draws blood into the clitoris, causing clitoral, and then vaginal, vascular engorgement, leading to increased vaginal lubrication and consequent stimulation of sensory nerve endings. Ultimately, vasocongestion of the genitalia lays the anatomic foundation for the so-called orgasmic platform, resulting in the physiologic expression of the orgasmic experience (26). Physiologic studies of clitoral and vaginal blood flow before and after the use of the CTD demonstrated a marked increase in the velocity of the blood in this region (27, 28).

The CTD has shown considerable promise in noncancer patients with FSD. Billups *et al.* (26) reported on 32 subjects, 20 with and 12 without FSD. After using the CTD for 3 months, the FSD subjects reported increased genital/clitoral sensation, vaginal lubrication, orgasmic ability, and sexual satisfaction. Normal subjects also noted improvements in all domains tested. Wilson *et al.* (29) reported comparable results. Recently, the U.S. Food and Drug Administration approved the CTD for the treatment of female sexual arousal disorder and orgasmic disorder.

In our study of postmenopausal women (30), we reported statistically significant improvements in all domains of sexual function tested (desire, arousal, lubrication, orgasm, sexual satisfaction) and reduced dyspareunia after using the CTD for 3 months. Gynecologic examinations also revealed improved mucosal color and moisture and vaginal elasticity. Billups *et al.* (31) reported similar results in diabetic women.

On the basis of these promising results, we initiated a clinical trial of the CTD in irradiated cervical cancer patients with sexual dysfunction. Our goal was to evaluate its ability to improve the sexual function of these patients. We present our clinical results and discuss the implications of our findings.

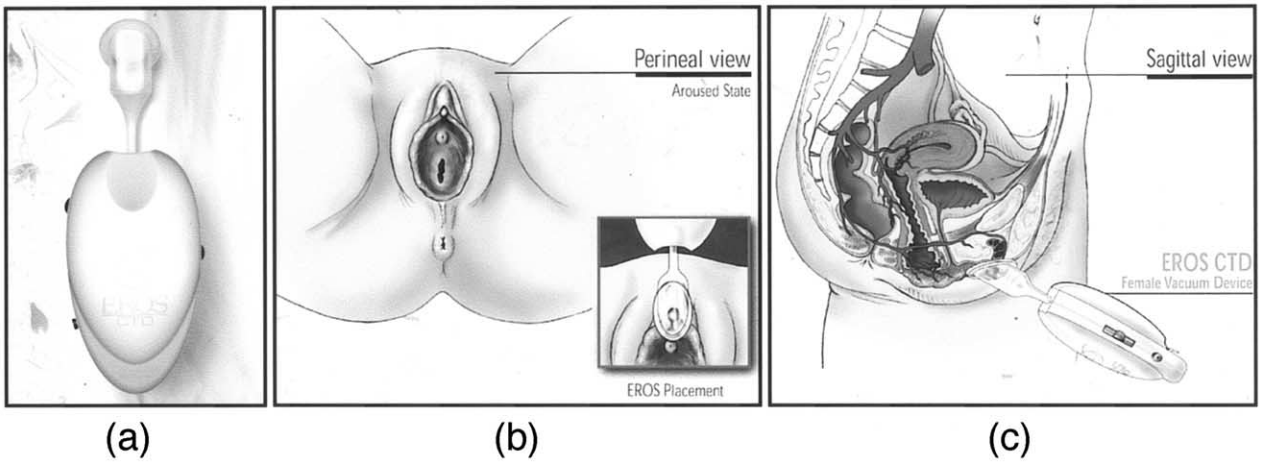

Fig. 1. (a) Clitoral therapy device (CTD) (Eros Therapy). (b) Perineal view of CTD placement. (c) Sagittal view of CTD placement. Courtesy of UroMetrics, Inc., St. Paul, MN.

METHODS AND MATERIALS

Study population

Eligible patients were aged ≥18 years who had been treated with definitive or adjuvant RT for cervical cancer with self-reported sexual dysfunction of sexual arousal and/or orgasmic disorders. The women could also have sexual desire and pain disorders. No patient had had evidence of disease recurrence for a minimum of 1 year, and all were in a stable heterosexual relationship and were comfortable with the idea of self-stimulation.

The exclusion criteria included metastatic disease, severe bowel or bladder sequelae, and significant comorbidities. Women with a history of preexisting FSD, sexual trauma or abuse, or undergoing current antidepressant therapy were excluded. The University of Chicago Institutional Review Board approved this study, and all participants provided written informed consent.

Study design

At baseline, all patients underwent a general medical history, sexual history, and physical examination, including a gynecologic examination. The gynecologic examination was done with integration of an educational sexologic examination (i.e., identifying the parts of the female genital anatomy and their function) by the principal investigator (M.S.), who is both a licensed, board-certified family nurse practitioner, and a board-certified, clinical sexologist. Each patient completed the Female Sexual Function Index (FSFI) questionnaire (32) and Dyadic Adjustment Scale (DAS) questionnaire (33) and underwent the Derogatis Interview for Sexual Functioning (DISF) (34). The pilot study's outcome evaluation of repeated measures was done after 3 months of CTD use to be comparable to the protocol used in the original research presented by the inventing company to the Food and Drug Administration for the initial approval of the device and other prior research.

The only treatment for FSD evaluated in the study was the CTD. No other medical treatments, psychosexual educational sessions, counseling, or therapies for FSD were given. As shown in Fig. 1, the CTD is a hand-held, battery-powered, mechanical device. It is noninvasive, nonpharmacologic, and used under the control of the patient. A small plastic cup is placed over the clitoris and the pump is activated by the woman, creating a gentle vacuum drawing blood into the clitoris and causing clitoral engorgement. Three suction levels are available: low, moderate, and high, with maximal vacuum at 9.8 in Hg. The suction can either be held steady or rapidly modulated or pulsated by the woman or her partner by placing a finger over the vacuum modulator.

The principal investigator gave instructions on use of the CTD, including demonstration, practice, and repeat demonstration of its proper use. The patient was shown the female genital anatomy, including the clitoris and where the CTD suction cup should be placed using anatomic diagrams and three-dimensional models. Initially, the patient was shown how the CTD functioned by operating it on the skin of the palm or arm before showing the positioning of the cup over the clitoris. Although the patients were given the option of their partners being included in the training session, all of them chose to teach their partners themselves when they were alone and at home.

Patients practiced using the device alone in our clinic to feel confident with its use and then in the presence of the principal investigator to verify correct use. During the training session, each cycle consisted of a 60-s engorgement period on low vacuum, followed by a 60-s rest period with the vacuum off. The engorgement period was repeated five times, with a 60-s rest period between cycles.

When at home during the 1-week adjustment period, the device was used once daily. When the engorgement/release cycle could be done on low vacuum without discomfort for five cycles, patients could increase the vacuum interval to 3 min. Once the patient could perform engorgement/release cycles on low vacuum, she could progress to moderate and then high vacuum using the same advancement protocol. The level of vacuum was determined by comfort and clinical response.

After the adjustment period, patients were instructed to use the device four times weekly for 3 months (as a part of partnered sex play twice a week and a minimum of two other times per week in self-stimulation). Each session was 15–30 min of intermittent use with up to 4.4 min of continuous use, which are the manufacturer's safety standards for time limits of use. The vacuum was either held at a steady level, rapidly modulated, or varied between these options according to the woman's preference.

During the 3-month study period, patients received telephone calls to assess their progress. At 3 months, the patients returned for the final assessment and underwent a history and physical examination, including a gynecologic examination. All patients completed the FSFI and DAS questionnaires and a repeat DISF.

Study instruments

The FSFI (32) is a 19-item, self-report questionnaire designed to assess six domains of female sexual function: desire, arousal, lubrication, orgasm, satisfaction, and pain. The answers are multiple choice, most with six choices arranged progressively from "abnormal" to "normal." For example, Item 7 asks the frequency of vaginal lubrication during intercourse. The possible answers are 0, no sexual activity; 1, almost never or never; 2, a few times (<50% of the time); 3, sometimes (50% of the time); 4, most times (>50% of the time); and 5, almost always or always. Each item receives 0–5 points depending on the response chosen. A scoring algorithm is used to determine individual domain and composite (total) scores. The maximal domain and composite scores are 6 and 36, respectively, with lower scores corresponding to poorer sexual functioning. The composite or full-scale score range is 2–36. The FSFI is a validated sexual function instrument widely used in the study of FSD. The questionnaire requires approximately 15 min to complete.

The DISF (34) is a 25-item semistructured clinical interview designed to measure the quality of an individual's current sexual functioning in quantitative terms. The DISF is arranged into five domains of female sexual function: I, Sexual Cognition and Fantasy; II, Sexual Arousal; III, Sexual Behavior and Experiences; IV, Orgasm; and V, Sexual Drive and Relationship. The answers are multiple choice using either a 9-point frequency scale or a 5-point satisfaction scale. For example, Item 2.3 asks the patient about the frequency of feeling sexually aroused with her partner. Possible answers based on the 9-point frequency scale are 0, not at all; 1, <1/mo; 2, 1–2/mo; 3, 1/wk; 4, 2–3/wk; 5, 4–6/wk; 6, 1/d; 7, 2–3/d; and 8, ≥4/d. Item 4.1 asks the patient about satisfaction with her ability to have an orgasm. The possible answers based on the 5-point satisfaction scale are 0, not at all; 1, slightly; 2, moderately; 3, highly; and 4, extremely. Each item receives a score from 0 to either 4 or 8. A scoring algorithm is used to calculate the individual domain and total (composite) scores. The maximal normative composite score is 118. The DISF also allows one to compare patient results on each domain and the total score with those of normal controls. The DISF raw score is converted using

a nomogram to a T-score, corresponding to percentiles of normal functioning. Area-T-scores are normalizing standardized transformations (of raw score distributions) with a mean of 50 and a standard deviation of 10. A T-score of 63 is taken as the normalcy cutoff, with 90% of normal subjects scoring within this range. The DISF requires approximately 15–20 min to complete.

The DAS (33) is a 32-item self-report questionnaire developed to assess Dyadic Consensus, Dyadic Satisfaction, Dyadic Cohesion, and Affectional Expression in marital or dyadic relationships. Dyadic Consensus assesses the extent of agreement on matters important to the relationship. Dyadic Satisfaction measures the overall amount of positive feeling in the relationship. Dyadic Cohesion assesses the common interests and activities shared by the couple. Only Affectional Expression items directly involve the expression of affection and sex in the relationship. The DAS instrument was included to assess the general quality of the relationships between patients and their partners. All items are multiple choice, most with six choices arranged progressively. For example, Item 26 asks patients how often they and their partners laugh together. Answers include never, less than once a month, once or twice a month, once or twice a week, once a day, and more often. The DAS yields a composite (total) score, providing an overview of the level of adjustment in the relationship, and four subscale scores, indicating areas of relationship conflict. The maximal total score is 151. The DAS has been widely used in research on the impact of major illnesses (including cancer) on relationships. The DAS questionnaire requires 15 min to complete.

Statistical analysis

For each measure of sexual function, the two-tailed Wilcoxon signed rank test was used to test the hypothesis that the CTD had no effect. The Holm step-down method was used to adjust the p values for multiple hypothesis testing. Tests for the effect of time on the difference in the pre- and posttest outcomes were performed with ordinary least squares regression. In this regression model, a unit change in the total FSFI or DISF score was assumed to be a linear function of the number of days after RT completion.

RESULTS

Patient population

Between January 2001 and July 2002, 19 potentially eligible irradiated cervical cancer patients were screened, 15 were enrolled, and 13 completed the study. Two women refused to participate in the study and two did not enroll for unrelated personal reasons (e.g., moving to a new home or changing jobs). A common reason for exclusion from the study was because of the lack of a stable sexual relationship owing to being divorced or abandoned after their cancer diagnosis and treatment. Two women did not complete the study as planned. One developed lung metastases and withdrew after initiation of chemotherapy. A second patient refused to complete the final evaluation despite multiple discussions with the principal investigator. Of note, both stated they had experienced improvements in their sexual function after use of the CTD.

Table 1 summarizes the characteristics of the patients who completed the study. One patient underwent intracavitary brachytherapy (40 Gy prescribed to Point A) followed by radical hysterectomy (5). Three patients were treated with adjuvant whole pelvic RT after radical hysterectomy because of adverse pathologic features (median pelvic RT dose 45 Gy). Nine patients received a combination of whole pelvic RT (45 Gy) followed by intracavitary brachytherapy. Of these, five were treated with definitive RT and received 40 Gy to Point A, and four underwent adjuvant simple hysterectomy and thus received 30 Gy to Point A. Of the 12 patients who underwent whole pelvic RT, 2 received intensity-modulated RT (35). Overall, 7 patients received concomitant chemotherapy (cisplatin, 40 mg/m^2/wk). The median RT completion–enrollment interval was 24 months (range, 12–144 months).

All patients were in a heterosexual relationship, with 8 patients married and 5 in long-term relationships. All 13 expressed sexual dissatisfaction since their cervical cancer diagnosis and treatment. Consistent with the inclusion criteria and based on their initial comprehensive evaluation, all subjects had sexual dysfunction that was an indication for the use of the CTD. Eleven patients had both sexual arousal and orgasmic disorders, one had sexual arousal disorder, and one had orgasmic disorder. Also, sexual dysfunctions that are not specific indications for CTD use were present; 11 patients had sexual desire disorder and 10 had dyspareunia, a sexual pain disorder. All patients had failed previous attempts at treatment of their sexual dysfunctions with traditional therapies (vaginal dilators, lubricants, or moisturizers). Past compliance with dilator use was poor. Nine had a

Table 1. Patient characteristics (n = 13)

Characteristic	
Age (y)	
Median	43 y
Range	33–58 y
Stage (n)	
IB	8
IIA	2
IIB	2
IIIB	1
Surgery (n)	
No	5
Yes	8
RT (n)	
Whole pelvic*	3
Intracavitary Brachytherapy†	1
Both	9
Chemotherapy	
Yes‡	7
No	6
RT–enrollment interval (mo)	
Median	24
Range	12–144

Abbreviation: RT = radiotherapy.

* After surgery because of high risk factors (e.g., positive nodes, deep cervical invasion).

† Before radical hysterectomy.

‡ All patients received concomitant cisplatin (40 mg/m^2/wk during pelvic RT).

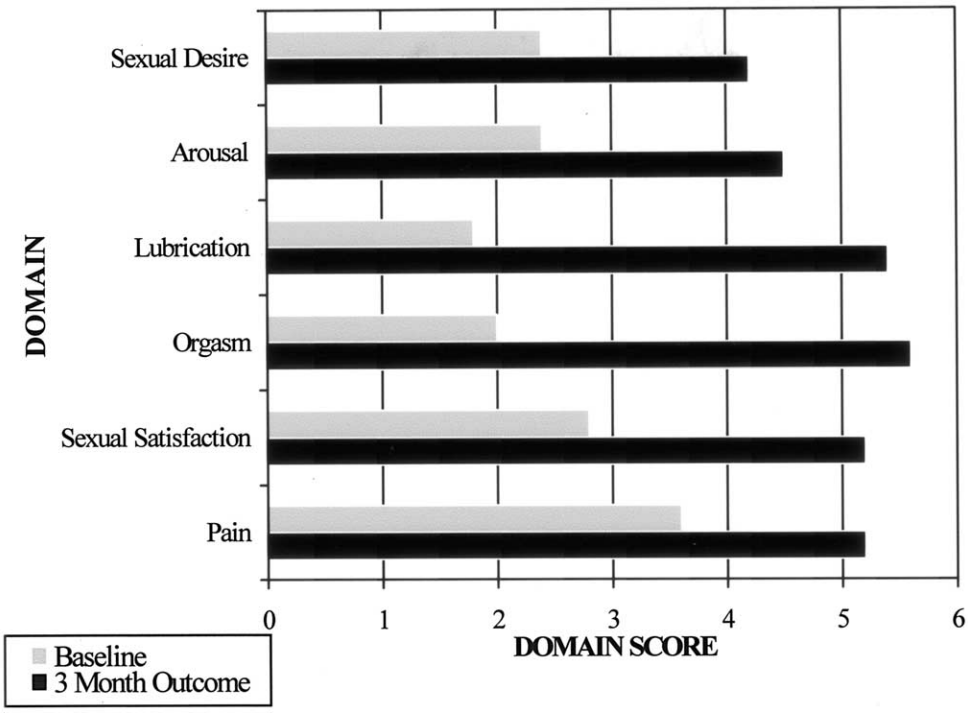

Fig. 2. Median Female Sexual Function Index (FSFI) domain (sexual desire, arousal, lubrication, orgasm, sexual satisfaction, and pain) scores (maximal possible score per domain 6; $n = 13$). All $p < 0.004$ (Wilcoxon signed rank test).

history of HRT, which had failed to resolve their FSD. Current HRT use was discontinued in all patients. Self-stimulation and vibrators had been tried without success by 5 women.

Compliance and adverse effects

All completed patients were able to use the device without problems. During the 3-month trial, none complained of discomfort at any level of suction or of other problems. None reported adverse effects related to device use, including skin irritation, hematomas, infection, or an allergic response.

FSFI scores

Figure 2 summarizes the FSFI domain scores at baseline and 3 months in the patients who completed the study. The median FSFI baseline domain scores were low, consistent with marked sexual dysfunction, with many patients reporting significant impairments in all domains tested. As shown in Fig. 2, statistically significant improvements were noted in all six domains at the 3-month evaluation, including sexual desire ($p = 0.004$), arousal ($p = 0.004$), lubrication ($p = 0.004$), orgasm ($p = 0.004$), sexual satisfaction ($p = 0.004$), and pain ($p = 0.004$). As seen in Fig. 3, the median total FSFI score increased from 17 to 29.4 (range, 2–36; maximal possible score 36; $p = 0.003$). The number of days between RT completion and enrollment in the study did not correlate with the change in the total FSFI score (ordinary least squares regression coefficient, −0.0353; 95% confidence interval, −0.123 to 0.0524).

DISF scores

The individual DISF domain T-scores at baseline and at 3 months are shown in Fig. 4. Consistent with the FSFI results, the median baseline DISF domain T-scores were low across all domains. At 3 months, statistically significant improvements were seen in Sexual Cognition and Fantasy

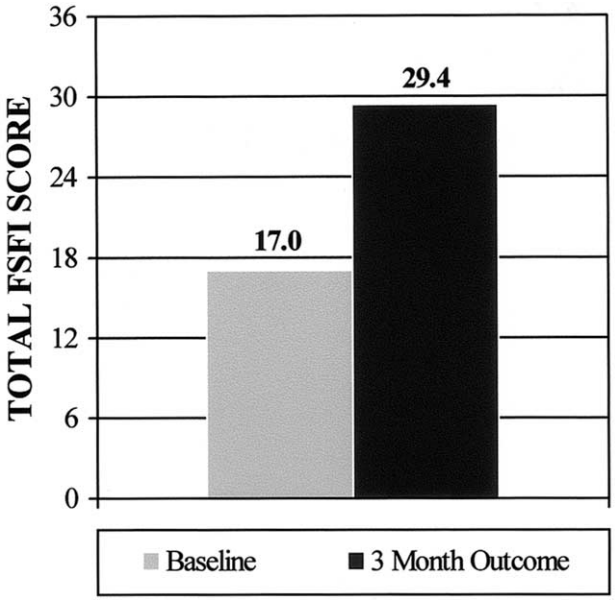

Fig. 3. Median Female Sexual Function Index (FSFI) total (composite) score (total score range, 2–36, maximum possible score, 36; $n = 13$). $p = 0.003$ (Wilcoxon signed rank test).

($p = 0.004$), Sexual Arousal ($p = 0.003$), Sexual Behavior and Experiences ($p = 0.004$), Orgasm ($p = 0.003$), and Sexual Drive and Relationship ($p = 0.003$). The median DISF total raw score increased from 46 to 95 (maximal score 118; $p = 0.003$). As with the total FSFI score, a statistically significant association between the change in total DISF raw score and the number of days between RT completion and enrollment in the study was not observed (ordinary least squares regression coefficient 0.142; 95% confidence interval, −0.0758 to 0.360). As seen in Fig. 5, the median total T-score at baseline was 33 and at 3 months had increased to 62. Although the baseline total raw score resulted in a T-score corresponding to the bottom 10th percentile of sexual functioning, the 3-month outcome T-score placed the subjects at the normalcy cutoff, suggesting resolution of their FSD.

DISF Item 5.4, which asks "In general, what would represent the best description of the quality of your current sexual functioning?," with answers on a 9-point scale (0, could not be worse; 1, very poor; 2, poor; 3, somewhat inadequate; 4, adequate; 5, above average; 6, good; 7, very good; and 8, could not be better), demonstrated the dramatically improved quality of sexual function in all 13 women. At baseline, the mean score for this item was 1.7, with all women rating themselves between "could not be worse" and "somewhat inadequate." At the 3-month outcome, the mean score for this item increased to 6.2, with all women rating themselves above the midpoint; specifically, 1 woman rated herself as "could not be better," 6 women as "very good," 2 as "good," 3 as "above average," and 1 as "adequate."

DAS scores

Although improvements were seen in all four DAS domains tested, the only difference that reached statistical significance was in terms of affectional expression ($p = 0.003$). The total DAS composite score increased from 104 to 111 (maximal possible score 151); however, this difference failed to reach statistical significance ($p = 0.13$).

Gynecologic examinations

At baseline, most patients exhibited vaginal changes consistent with their prior RT, ranging from mild telangiectasias to moderate stenosis. Seven had significant changes, including vaginal and/or cervical bleeding and ulceration, and five had vaginal stenosis as quantified using medical-grade vaginal dilators. At 3 months, improvements were noted in these women, most with complete or near complete resolution of ulceration and bleeding, increased size of the vaginal dilator and speculum admitted to the vagina, and decreased pain and tenderness on pelvic examination. At the beginning of the study, it was not possible to obtain satisfactory Papanicolaou smears in some patients, because it was too painful and excess blood was present in the vagina. After 3 months, the tissues had healed and satisfactory Papanicolaou smears could be performed. These changes

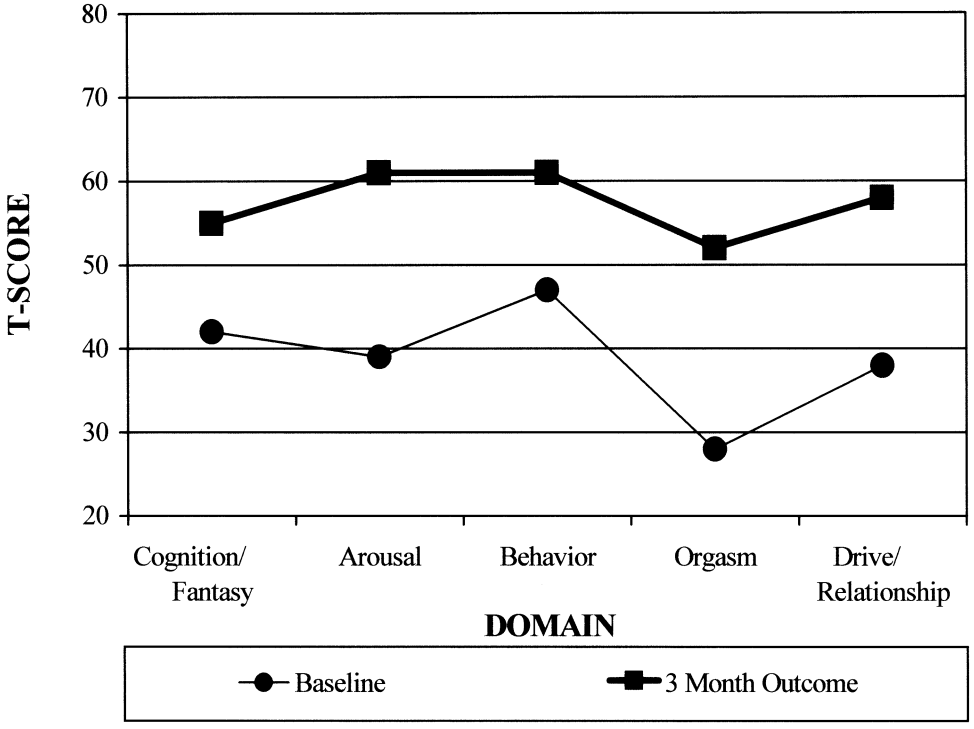

Fig. 4. Median Derogatis Interview for Sexual Functioning (DISF) domain (I, Sexual Cognition/Fantasy; II, Sexual Arousal; III, Sexual Behavior/Experiences; IV, Orgasm; and V, Sexual Drive/Relationship) T-scores. Area-T-scores are normalizing standardized transformations of raw score distributions, with mean of 50 and standard deviation of 10 (maximal possible T-score, 75, $n = 13$). All $p < 0.004$ (Wilcoxon signed rank test).

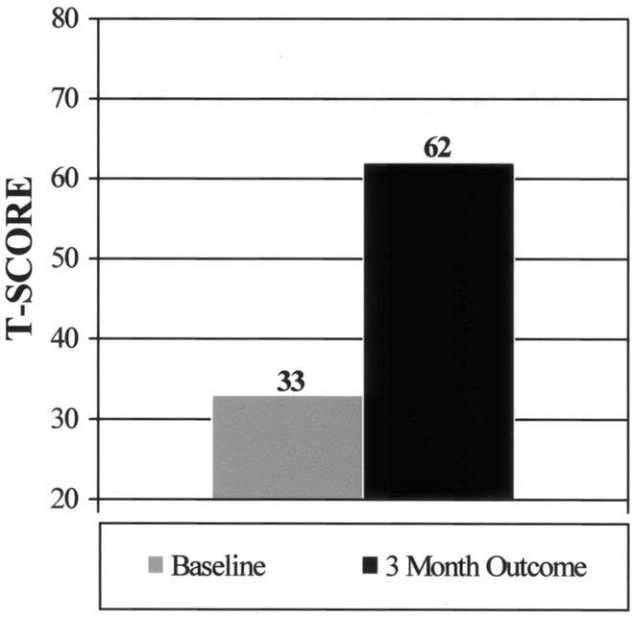

Fig. 5. Median Derogatis Interview for Sexual Functioning (DISF) total (composite) T-scores. Area-T-scores are normalizing standardized transformations of raw score distributions, with mean of 50 and standard deviation of 10 (maximal possible T-score 75; $n = 13$). $p = 0.003$ (Wilcoxon signed rank test).

were observed not only by the investigators during the study visits, but also by the patients' attending gynecologic oncologists during their regular follow-up examinations. No adverse effects from CTD use (i.e., genital or clitoral trauma or irritation) were observed during the gynecologic examination at the 3-month outcome visit. In addition, symptoms of urinary dysfunction (e.g., urgency, frequency) present in 5 women at baseline were spontaneously reported as resolved by the women on the 3-month outcome medical history. Because the effect on urinary function was not this study's primary objective, no detailed urinary assessment measures or tests had been used.

DISCUSSION

The purpose of this study was to evaluate the efficacy of a novel treatment of FSD known as the CTD in irradiated cervical cancer patients. Our results suggest that this approach resulted in significant improvements in all domains of sexual functioning. At baseline, our patients scored at the bottom 10th percentile of normal functioning. At 3 months, their functioning was at the normalcy cutoff. Objective improvements were seen on gynecologic examination, particularly in women with marked RT changes. Nonstatistically significant improvements were also noted in terms of marital and familial relationships.

This study was modeled after our earlier trial in noncancer patients (30). Using an identical study design, 22 postmenopausal women (none receiving HRT) completed the study. Statistically significant improvements were noted in all areas of sexual function, including sexual desire, arousal, lubrication, orgasm, sexual satisfaction, and reduced pain (all $p < 0.01$). The median FSFI total score increased from 16.7 to 28.3 ($p < 0.001$). The median DISF total score increased from 40.5 to 80 ($p < 0.001$). As in the current study, the gynecologic examinations revealed objective improvements in mucosal color, moisture, and vaginal elasticity. Others have reported equally favorable results in noncancer patients (26, 29, 31).

In many ways, it is remarkable that the CTD was effective at all, because many of our patients had received high doses of radiation to the vagina and surrounding tissues months to years before enrollment. We were skeptical that any response would be seen, given the well-described alterations in the pelvic soft tissues and vasculature in these women (21–24). Nonetheless, we not only saw a response, but a very significant one. The favorable changes in the irradiated vaginal tissues, particularly in women with ulcerations and bleeding, were also quite significant. Presumably, the improved tissue oxygenation due to increased blood flow promoted tissue healing.

Secondary clinical benefits of decreased urinary urgency and incontinence were reported during the trial with the CTD. This was without any other medical or surgical intervention for treatment of the urinary dysfunction. This phenomenon could have occurred because the clitoral and genital engorgement provided by the CTD may be stimulatory to the same afferent sacral nerves as the surgically implanted peripheral stimulators of the sacral nerve roots currently used to treat intractable urinary urge incontinence. The impact on urinary dysfunction seen in our study is now the focus of a separate, controlled clinical trial designed to compare the efficacy of the CTD to another medical treatment for urinary urge incontinence in women. That study will incorporate specific quantifications of urinary status (e.g., standardized questionnaires about urinary dysfunction, voiding diaries, and laboratory tests).

Our study had several limitations and, albeit promising, our results need to be interpreted with caution. First and foremost, this trial was limited in size with only 13 patients completing the study. Patients also had varying intervals between RT and enrollment, had undergone different primary therapies, had received different radiation doses, and complained of different FSD symptoms. Moreover, some had received chemotherapy. Patients also served as their own controls. It is possible that unidentified factors may have contributed to our results, including validation of the patients' complaints. The degree of improvement in reported sexual functioning due to the placebo effect of interested clinicians, sex education, and training in use of the CTD is nearly impossible to quantify. Another limitation was that the study was only conducted for 3 months; thus, long-term evaluation was beyond the scope of this pilot study. However, given the lack of any preliminary data and our skepticism of a response, we did not believe it was appropriate to begin with a randomized trial.

If validated, our findings will have major implications for

cervical cancer patients. The quality of life of patients with locally advanced cancer who must receive RT could be improved. In addition, the barrier to the use of RT in early-stage patients who could receive it may be reduced, hopefully obviating the unfortunate practice of withholding adjuvant RT in high-risk patients after surgery. The restorative effects on vaginal tissues may even augment the quality of follow-up examinations and Papanicolaou smears, improving the detection of tumor recurrence. Our results may also be applicable to noncervical cancer patients with RT-induced FSD, notably those with endometrial (17), rectal, or anal cancer. The latter group is particularly appealing, given the inclusion of the entire vagina in the anal cancer treatment fields.

Finally, our results beg the question of whether the CTD would be more beneficial immediately after RT completion before the development of chronic FSD symptoms in irradiated cervical cancer patients. The interval between RT completion and enrollment in the study did not seem to influence the outcome, suggesting that the CTD may be equally beneficial long after or immediately after RT completion. To answer this question, we have initiated a prospective trial in cervical cancer patients undergoing definitive or adjuvant RT. Patients begin to use the CTD at RT completion and are evaluated with the same instruments used in the present study. It is our hope that improved blood flow to the pelvic organs will help minimize the risk of not only sexual sequelae, but also RT-induced damage to other pelvic organs, including the bladder and rectum.

A larger, randomized, controlled clinical trial with long-term outcome evaluation at several points is warranted to assess the full benefits of this approach. The control arm participants in the randomized clinical trial would receive only "usual care," which is composed of counseling, education, and the use of vaginal dilators, lubricants, and moisturizers. The treatment arm participants would receive the "usual care" plus the additional treatment with the CTD. As new therapeutic modalities become available, studies should compare their efficacy to that of the CTD. Future studies could be improved by using more detailed, quantitative measurements in the gynecologic assessment (e.g., vaginal and clitoral blood flow measurements using Doppler ultrasonography, vaginal blood flow assessment with photoplethysmography, genital neurosensory testing using computerized instrumentation, and standardized, composite clinical assessment indexes) at baseline and outcome visits to yield objective evidence of therapeutic efficacy.

CONCLUSION

The results of this small pilot clinical trial suggest that the CTD may reduce symptoms of FSD in irradiated cervical cancer patients. On the centennial of the first use of RT for this disease (1), a possible means of alleviating one of its most common and distressing side effects may have finally been developed. Although our results are quite compelling, they remain preliminary and need to be validated in larger, controlled trials.

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