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The effect of vaginal erbium laser treatment on sexual function and vaginal health in women with a history of breast cancer and symptoms of the genitourinary syndrome of menopause: a prospective study

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Abstract

Objectives: To assess the effects of vaginal erbium laser treatment on the vaginal health and sexual function of postmenopausal women with a history of breast cancer.

Methods: An open, prospective, therapeutic intervention study was conducted with 24 postmenopausal women with a history of breast cancer and vaginal dryness, and/or dyspareunia, who had not used vaginal hormone therapy for at least 6 months. The women were treated using a 2,940-nm Erbium: YAG laser (Etherea-MX, Athena, São Carlos, São Paulo, Brazil), with 90° and 360° scanning scopes, between August, 2017 and October, 2017 in a private clinic in a city of southeastern Brazil. Vaginal erbium laser treatment was performed at three sessions with a 30-day interval between each session. Sexual function was assessed before and 1 month after treatment using the Short Personal Experiences Questionnaire. Questions related to genitourinary symptoms were also applied. Vaginal health was assessed before each laser session using the Vaginal Health Index Score.

Results: Mean age was 53.7 years. Vaginal health improved, as shown by an increased overall score ($P < 0.001$). The effect size was large between pretreatment and post-treatment scores for vaginal elasticity, fluid volume, epithelial integrity, and moisture. The effect size was also significant for the overall sexual function score and for the score in the dyspareunia domain between pretreatment and 1 month after the final treatment session.

Conclusion: Vaginal erbium laser may represent a novel therapeutic option for improving vaginal health and sexual function in postmenopausal women with a history of breast cancer.

Key Words: Breast cancer – Dyspareunia – Erbium – Menopause – Sexual function – Vulvovaginal atrophy – YAG laser.

Breast cancer is one of the most common forms of cancer in women, with more than 2 million new cases occurring annually worldwide.[1] The survival rate for women with breast cancer is high[2]; however, many survivors also suffer cancer treatment side effects. Indeed, over 60% of survivors experience at least one urogenital symptom as a sequela of breast cancer treatment.[3] This prevalence is probably underestimated because the patient may be embarrassed to discuss these urogenital symptoms with her physician.[3]

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Women with a history of breast cancer are significantly more likely to present with sexual health problems compared with the general population.[4,5] Broekel et al[6] reported that sexual function was poorer in breast cancer survivors treated with adjuvant chemotherapy and/or aromatase inhibitors compared with women of a similar age with no history of cancer. The study also showed that vaginal dryness was one of the most important predictors of impaired sexual function in breast cancer survivors.

There are limitations in treating symptoms of vulvovaginal atrophy and dyspareunia in this group of women. Conventional treatments include vaginal moisturizers and lubricants that provide temporary relief.[7] When there is a consensus between patient and physician, the use of local vaginal hormone therapy may be an option for women whose symptoms fail to improve with nonhormonal treatments.[8] However, oncologists are often reluctant to prescribe local vaginal hormone therapy, as highlighted by Biglia et al[9] in a recent study conducted in Italy.

Therefore, novel approaches for the treatment of the genitourinary syndrome of menopause may offer better results for this group of women. Accordingly, the first trials on vaginal erbium laser treatment began in 2012,[10] and since then, many

publications have confirmed this approach as a feasible option for the treatment of the genitourinary syndrome of menopause.[11-13]

In a recent pilot study,[14] there was a statistically significant difference in dyspareunia, in vaginal dryness, and in the Vaginal Health Index Score between pretreatment and post-treatment with three sessions of vaginal erbium laser therapy in 43 postmenopausal breast cancer survivors with the genitourinary syndrome of menopause ($P < 0.05$). In that study, the women were followed up for 18 months; however, the differences only remained statistically significant for 12 months after the final laser session.

A systematic review and meta-analysis of observational studies[15] showed that sexual function improved consistently after treatment in all four available studies conducted to evaluate vaginal laser therapy in postmenopausal women with genitourinary syndrome. However, all those studies used the ablative fractionated CO_2 laser.

In a systematic review and meta-analysis of randomized clinical trials conducted in 2018,[16] only one of the trials included[17] had assessed the efficacy of the CO_2 laser compared with vaginal estriol and a combination of both treatments (laser + estriol). In the group of women using laser + estriol, there was a significant improvement in the overall Female Sexual Function Index (FSFI) score and in the individual domains of pain, desire, and lubrication. In contrast, in the group submitted to CO_2 laser treatment alone, there was a significant increase in the score for the pain domain of the FSFI. Many previous studies conducted with CO_2 laser have also reported this side effect,[18-23] with one possible explanation being the mode of action of the CO_2 laser. The main difference between the CO_2 laser and the Er: YAG laser lies in their ablative characteristics. Whereas the CO_2 laser works by vaporizing tissue columns,[18] the Er: YAG laser has a smooth-mode technique that creates heat pulses without damaging the mucosa.[24]

Only two recent nonrandomized studies[25,26] have assessed sexual function in women with a history of breast cancer after treatment with a CO_2 laser. Both studies reported an improvement in sexual function; however, one[25] included only eight women with breast cancer.

Study goals and hypotheses

The objective of the present study was to assess the effects of vaginal erbium laser on the vaginal health and sexual function of postmenopausal women with a history of breast cancer.

The initial hypothesis was that the treatment would improve the following parameters: the overall Vaginal Health Index Score; the individual vaginal health index parameters (vaginal elasticity, fluid volume, epithelial integrity, and moisture); the overall sexual function score; and the individual parameters of sexual function (dyspareunia, arousal, enjoyment, orgasm, and satisfaction with partner as lover) assessed using the Short Personal Experiences Questionnaire (SPEQ).[27,28]

METHODS

Study design

An open, prospective, therapeutic intervention study was conducted.

Participants

Thirty women with a history of breast cancer and complaints of dyspareunia and/or vaginal dryness were selected at gynecological and oncological clinics in a city of southeastern Brazil. The study investigators contacted these women by telephone, with 25 meeting the inclusion and exclusion criteria. One woman dropped out of the study for family reasons; therefore, the final sample consisted of 24 women.

Eligibility required a personal history of breast cancer, complaints of dyspareunia and/or vaginal dryness, and to have had no menstruation for at least 1 year. The exclusion criteria were: having used systemic or vaginal hormone therapy in the preceding 6 months, severe psychiatric problems, a history of vaginismus, vaginal bleeding or unexplained vulvar lesion, active or recent scars in the genital area (in the previous 30 days), a urinary tract infection in the preceding 30 days, having used lubricants or any local preparations in the previous 30 days, photosensitivity or use of photosensitizing drugs, second or third-degree genital prolapse according to the Pelvic Organ Prolapse Quantification System, and any chronic or severe disease that could compromise the study evaluation. Before their inclusion in the study, the eligible women were provided with information on the nature of the study in a private setting, were given the opportunity to ask any questions, and were then asked to sign an informed consent form.

The study protocol was approved by the institutional review board under registration number CAAE 60580316.0.0000.5143. All patients gave their written consent for participation in the study.

Therapeutic interventions and procedures

The women selected as possible candidates for inclusion in the study were invited by telephone to attend three vaginal laser sessions in a private clinic in a city in southeastern Brazil. The study was performed between August, 2017 and November, 2017.

Immediately before the first laser session, women completed a self-administered questionnaire containing 100 questions on their sociodemographic conditions, health habits, sexual aspects (SPEQ),[27,28] urogenital symptoms, and health issues. Next, two of the investigators together performed a speculum examination to calculate the woman's Vaginal Health Index Score. After this evaluation, the vaginal wall was anesthetized using a tampon soaked in 4% lidocaine for 30 minutes. The tampon was then removed and the excess anesthetic was washed away using saline solution.

The vaginal laser used was a 2,940-nm Erbium: YAG laser (Etherea-MX, Athena, São Carlos, São Paulo, Brazil), with 90° and 360° scanning scopes. After inserting the specific fenestrated speculum for the procedure, the 360° scanning scope was inserted into the speculum, hence not in direct contact with the vaginal mucosa. The vaginal wall was irradiated at 360° with four pulses every 5 mm (using the scale at the tip of the device). This procedure was repeated three times up to the entrance of the vaginal canal. The parameters used[29] for this collimated tip were: fluency (laser energy supplied per area unit) 2.0 J/cm^2, frequency 0.5 Hz, pulses using the smooth-mode technique (eight pulse trains of 50 ms totaling 400 ms), that is, long pulses with a very large quantity of photons, but low heat. This process does not generate vaporization; it merely heats the tissue and helps stimulate collagen production without causing necrosis.[24]

After removing the first scanning scope, the 90° scope was inserted into the speculum. The anterior vaginal wall was irradiated with four pulses every 10 mm (using the scale at the tip of the device). This procedure was repeated three times up to the entrance of the vaginal canal, rotating the speculum at the 11, 12, and 1 o'clock positions. The parameters used for this collimated tip were: fluency (laser energy supplied per area unit) 35 mJ/MTZ, frequency 0.5 Hz, pulses in accordance with the smooth-mode technique.

All women were submitted to three laser sessions (T0, L2, L3) at 30-day intervals. One month after the last session (L3 + 1), the women returned to the clinic to complete a further questionnaire on sexual function (SPEQ).[27,28]

Data collection and measurement instruments

Vaginal health

Vaginal health was assessed by speculum examination immediately before each laser session and, the Vaginal Health Index Score was calculated. The Vaginal Health Index Score assesses the vaginal mucosa (elasticity, fluid volume and consistency, pH, epithelial integrity, and moisture). Each parameter is rated from 1 to 5. If the total score is $\leq$15, the vagina is considered atrophic.[30] All the women were examined by the same two physicians, together, and a consensus was reached on all the parameters evaluated.

Sexual function

Sexual function was assessed just before the first laser session and again 1 month after the three sessions, using the self-administered SPEQ.[27,28] The sexual function score is calculated using the mean sum of the scores for enjoyment (a score of 1-6, where 1 = no enjoyment and 6 = maximum enjoyment); arousal (1-6); orgasm (1-6); frequency of intercourse (1-5, where 1 = never, 2 = less than once a week, 3 = once or twice a week, 4 = several times a week, and 5 = once a day or more); and desire (1-5). A score $\leq$7 was considered indicative of sexual dysfunction, whereas a score $>$7 indicated an absence of sexual dysfunction.[27,28] Each component of the sexual function score was also analyzed individually. In addition, other sexual variables were also assessed using this questionnaire: dyspareunia (a score of 1-6); satisfaction with partner as a lover (a score of 1-6); satisfaction with partner as a friend/human being (score 1-6); and partner's sexual problems (score 1-6).

Statistical analysis

Sample size was calculated using G*Power Version 3.1.2[31,32] and was based on a previous pilot study[14] conducted with women with a history of breast cancer. Calculation took into consideration the difference between a mean Vaginal Health Index Score of 8.1 ± 1.3 at baseline and 20.0 ± 1.0 after 4 months of treatment in a single group, for an alpha error of 0.05 and a beta error of 0.2.

The McNemar test of symmetry (for two categories) and the Bowker test of symmetry (for three or more categories) were used to compare categorical variables between the initial (pretreatment) and final (post-treatment) assessments. The Wilcoxon test was used to compare numerical variables between the initial and final assessments. The Friedman test was used to compare the Vaginal Health Index Score at the three evaluation moments. Significance level was defined at 5%. Cohen's d[33] was used to measure the effect size of the Vaginal Health Index Score parameters and SPEQ domains between baseline and post-treatment. Cohen's d and odds ratios (ORs) were used to evaluate the effect size of the overall SPEQ score between baseline and post-treatment.[33]

The SAS (Statistical Analysis System) software program for Windows, version 9.2 (SAS Institute Inc., 2002-2008, Cary, NC) was used throughout the statistical analysis.

RESULTS

All 24 women admitted to the study completed the three treatment sessions and were included in the analysis. The mean age of the women was 53.67 ± 9.66 years (±SD), and the mean number of years since menopause was 7.92 ± 5.94 years. Half the women had been diagnosed with breast cancer less than 5 years previously, 65% had undergone chemotherapy, and 60% were still undergoing cancer therapy. Of these, 60% were using tamoxifen, with 70% having used the drug for over a year.

The mean Vaginal Health Index Score increased significantly between pretreatment and the first and second laser sessions. The score changed from 11.88 ± 4.88 at baseline (immediately before T0) to 15.63 ± 3.75 after 30 days of the first laser session (immediately before L2) and further increased to 17.38 ± 4.55 after 30 days of the second laser session (immediately before L3) ($P < 0.001$; Fig. 1).

When each parameter of the vaginal health index was analyzed separately, a large effect size was found between baseline and 30 days after the second laser session (immediately before L3) for elasticity (Cohen's $d = 1.10$), fluid volume and consistency (Cohen's $d = 1.21$), epithelial integrity (Cohen's $d = 1.86$), and moisture (Cohen's $d = 1.24$) (Table 1).

The SPEQ sexual function score, dichotomized into $\leq$7 (sexual dysfunction) and $>$7 (no sexual dysfunction), and assessed before treatment (T0) and 1 month after the third

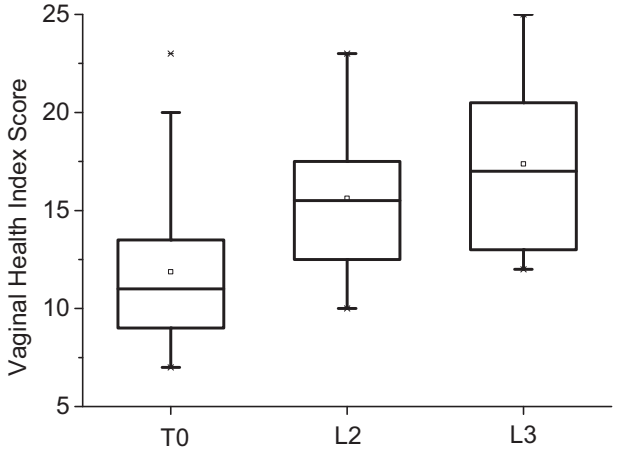

FIG. 1. Vaginal Health Index Score before and after two vaginal erbium laser sessions (n = 24). T0, immediately before the first session; L2, immediately before the second session; L3, immediately preceding the third session; VEL: vaginal Erbium laser; VHIS, Vaginal Health Index Score. $P < 0.001$: 1≠2, 1≠3, 2≠3. *P* value refers to Friedman test for comparison of VHIS between three sessions.

laser session (L3+1), showed a large effect size (Cohen's $d = 0.39$, OR 8.00) and a statistically significant improvement between pretreatment and post-treatment ($P = 0.04$) (Table 2).

Table 3 shows the individual analysis for each SPEQ component in which the baseline results were compared with those obtained following treatment. There was a large effect size (Cohen's $d = 0.95$) and a statistically significant improvement ($P = 0.01$) in dyspareunia. A medium effect size was found between pretreatment values and values found 1 month after the third laser session for: arousal (Cohen's $d = 0.73$), enjoyment (Cohen's $d = 0.62$), orgasm (Cohen's $d = 0.56$), and satisfaction with partner as a lover (Cohen's $d = 0.72$). In addition, there was a statistically significant improvement in these sexual parameters ($P < 0.05$).

Complications recorded during laser treatment included vaginal candidiasis (one woman) and acute cystitis (one woman) after the first session. These complaints were successfully treated before the second session.

DISCUSSION

According to the results of this study, the vaginal 2,n940-nm Erbium: YAG laser appears to exert a beneficial effect on vaginal health and sexual function in postmenopausal women with a history of breast cancer.

Vaginal health

Despite the small sample size in the present study, there were statistically significant differences and a large effect size between baseline results and those found 1 month after the second laser session for the vaginal health index parameters of vaginal elasticity, fluid volume and consistency, epithelial integrity, and moisture. Effect size is considered an essential complement of statistical significance because it differentiates between the significant statistical value and its practical importance.[34] There was a statistically significant improvement in vaginal atrophy, as measured by the Vaginal Health Index Score, between pre and post-treatment. These vaginal parameters were objectively analyzed by two trained medical doctors, who, working in conjunction, performed speculum examinations on all the women, thus providing much more reliable results and reducing any possible observation bias. Although there were three vaginal erbium laser sessions, as described in previous studies,[11-14] it proved impossible to assess vaginal health 1 month after the third session due to difficulties in scheduling another speculum examination. Some studies in the literature, however, suggest that the improvement in vaginal health is more significant 1 month after the third laser session.[11-14]

In the present study, no statistically significant difference was found in vaginal pH between baseline and the final laser treatment. As a decrease in vaginal pH depends on a cascade of events,[35] at the moment of evaluation, there had been insufficient time for the microbial lactobacillus flora to have been restored.

Hormonal changes during menopause may harm the standard structure and function of the genital tissues, with a consequent effect on vasoconstriction, lubrication, smooth muscle relaxation, and vaginal microbiota.[36] Mucosal hydration is reduced in the dermis, consequently reducing intercellular mucopolysaccharide and hyaluronic acid.[37] The laser has a photothermal effect, which could induce trophic changes in the vaginal mucosa, as shown by the histological findings reported by Gaspar et al.[38]

Sexual function

There was a large effect size in the overall SPEQ score between baseline and 1 month after the third vaginal erbium

TABLE 1. *Components of the Vaginal Health Index before and after two sessions of vaginal erbium laser (n = 24)*

	T0	L2	L3	Effect size	*P*
Vaginal elasticity	2.67 ± 0.87	3.04 ± 0.86	3.58 ± 0.72	1.10	<0.001
Fluid volume and consistency	2.0 ± 0.83	2.67 ± 0.92	3.17 ± 1.20	1.21	<0.001
Vaginal pH	2.25 ± 1.73	2.79 ± 1.67	2.63 ± 1.76	0.34	0.06
Epithelial integrity	2.58 ± 0.97	3.83 ± 0.64	4.21 ± 0.59	1.86	<0.001
Moisture	2.38 ± 1.21	3.29 ± 0.91	3.79 ± 0.98	1.24	<0.001

L2, immediately before the second session; L3, immediately preceding the third session; T0, immediately before the first session.
P value refers to Friedman test used to compare the vaginal health index components between the three laser sessions. Effect size for paired test: Cohen's *d*. Values are mean ± SD (standard deviation).

TABLE 2. *Short Personal Experiences Questionnaire (SPEQ) score before and after vaginal erbium laser treatment (n = 24)*

SPEQ score	T0, n (%)	L3 + 1, n (%)
≤7 (sexual dysfunction)	15 (62.5)	8 (33.3)
>7 (no sexual dysfunction)	9 (37.5)	16 (66.7)

L3 + 1, 1 month after the last vaginal erbium laser session; T0, before vaginal erbium laser.
$P = 0.04$ refers to the McNemar test for comparison of the SPEQ score between pre and post-treatment. Effect size refers to Cohen's $d = 0.39$ and odds ratio = 8.00.

laser session. There was also a significant effect size for the decrease in dyspareunia. A moderate effect size was found for arousal, enjoyment in sexual activities and orgasm, and with the woman's satisfaction with her partner as a lover. Such a positive effect is probably related to the restoration of genital tissues and consequent relief from urogenital symptoms.[18]

The clinical expression of sexual symptoms at menopause is influenced by several factors, ranging from significantly lower estrogen and androgen levels to intrapersonal and interpersonal factors.[39]The hemodynamic process of sexual arousal involves peripheral neurovascular function and pelvic floor muscles, and is closely linked to the biomechanical and viscoelastic properties of the vaginal wall.[40] In women with vulvovaginal atrophy, distention of the vaginal introitus is difficult, as is lubrication in response to sexual stimuli. Consequently, the vaginal canal is shorter and narrower, and these women may experience painful and/or unpleasant sexual intercourse.[41]

As reported in previous studies,[11-14] vaginal erbium laser reduces atrophy of the vaginal mucosa and restores genital tissues, relieving urogenital symptoms and exerting a secondary effect on these women's sexual function.

In the present study, laser treatment failed to improve sexual desire. However, laser treatment was not expected to directly affect libido because female sexual desire is complex and results from the interaction of biological (neuroendocrine) components, and also beliefs and values.[42]

In addition, vaginal erbium laser treatment had no effect on the frequency of sexual activity. A variety of factors have been associated with the frequency of sexual activity in menopausal women, suggesting that an individualized approach is needed for any improvement in sexual activity to be achieved.[43]

One of the limitations of the present study is that there is no control group. However, some previous studies[11,13,38] compared the use of vaginal erbium laser with the standard treatment for the genitourinary syndrome of menopause (vaginal estriol) in women with no history of breast cancer. The results achieved after laser therapy were similar to those obtained with the use of localized estrogen therapy, with the advantage that the results achieved in the laser group were maintained for 12 months after treatment discontinuation, unlike the results obtained by the women in the estriol group. It is also essential to recognize that the mechanism of action in laser therapy is probably different from that of estriol, resulting in the development of new vessels, reconstitution of the lamina propria, and, consequently, leading to long-lasting regeneration of the vaginal mucosa, even after the end of treatment.[38]

Another potential limitation of the present study is that it is impossible to guarantee that the women did not use any vaginal products during the study period, despite explicit instructions to avoid them. Postmenopausal women with symptoms related to the genitourinary syndrome of menopause widely use over-the-counter lubricants as a personal strategy to relieve pain during sexual intercourse.[39] The use of vaginal moisturizers or lubricants before the laser procedure could improve fluid retention in the tissues. As the erbium laser has a high affinity for water, previously hydrated mucosa could increase the thermal laser effect, with a consequently positive effect on results.

The follow-up period in the present study was short, only 30 days after the end of the final laser session; however, a published study with a 24-month follow-up[44] suggests that dyspareunia, vaginal lubrication, and improvements in vaginal health continue for up to 12 months. Based on that study[44] and because vaginal erbium laser is a safe and noninvasive procedure, treatment could be repeated annually or as soon as women begin to experience symptoms again, thus maintaining the beneficial effect on vaginal mucosa.

TABLE 3. *Components of the Short Personal Experiences Questionnaire before and after vaginal erbium laser (n = 24)*

	T0	L3+1	Effect size	*P*
Frequency of intercourse	2.17 ± 0.89	2.35 ± 0.88	0.35	0.219
Desire	1.96 ± 0.77	2.26 ± 0.86	0.43	0.092
Arousal	2.18 ± 1.56	3.23 ± 1.63	0.73	0.004
Enjoyment	2.73 ± 1.80	3.64 ± 1.73	0.62	0.012
Orgasm	2.59 ± 1.89	3.4 ± 1.82	0.56	0.022
Satisfaction with partner as lover	3.84 ± 1.86	4.74 ± 1.69	0.72	0.004
Satisfaction with partner as friend/human being	4.52 ± 1.60	4.90 ± 1.41	0.39	0.125
Partner's sexual problems	2.58 ± 1.84	2.74 ± 1.91	0.08	0.947
Dyspareunia	3.46 ± 1.66	2.23 ± 1.30	0.95	0.012

P value refers to Wilcoxon test; effect size for paired test: Cohen's *d* for comparison of pre and post-treatment values. Values are mean ± SD (standard deviation).
L3 + 1, 1 month after the last vaginal erbium laser session; T0, before vaginal erbium laser.

The maintenance of sexual activity is a component of life satisfaction and successful aging,[45] and, although laser therapy is not considered a definitive cure for the genitourinary syndrome of menopause, the results of this study suggest that this is a viable option for the treatment of vaginal atrophy and sexual dysfunction in women with a history of breast cancer. Furthermore, studies on laser therapy for the treatment of the genitourinary syndrome of menopause in women with this particular profile are few; therefore, one of the strengths of the present study is that it is the first to assess the effect of vaginal erbium laser therapy on the sexual function of women with a history of breast cancer.

CONCLUSIONS

The present study showed that vaginal applications of the 2,940-nm Erbium: YAG laser are associated with an improvement in sexual function and vaginal atrophy in postmenopausal women with a history of breast cancer. These results may have been achieved by improving the symptoms of the genitourinary syndrome of menopause. The long-term effects of the use of this technology on vaginal tissue should be investigated in future studies with longer follow-up periods and also in randomized clinical trials.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68:394-424.
2. National Cancer Institute. SEER Cancer Statistics Review 1975-2015; 2017. Available at: https://seer.cancer.gov/csr/1975_2015/. Accessed September 10, 2018.
3. Chin SN, Trinkaus M, Simmons C, et al. Prevalence and severity of urogenital symptoms in postmenopausal women receiving endocrine therapy for breast cancer. *Clin Breast Cancer* 2009;9:108-117.
4. Mortimer JE, Boucher L, Baty J, Knapp DL, Ryan E, Rowland JH. Effect of tamoxifen on sexual functioning in patients with breast cancer. *J Clin Oncol* 1999;17:1488-1492.
5. Farthmann J, Hanjalic-Beck A, Veit J, et al. The impact of chemotherapy for breast cancer on sexual function and health-related quality of life. *Support Care Cancer* 2016;24:2603-2609.
6. Broekel JA, Thors CL, Jacobsen PB, Small M, Cox CE. Sexual functioning in long-term breast cancer survivors treated with adjuvant chemotherapy. *Breast Cancer Res Treat* 2002;75:241-248.
7. Cohen PA, Brennan A, Marino JL, Saunders CM, Hickey M. Managing menopausal symptoms after breast cancer: a multidisciplinary approach. *Maturitas* 2017;105:4-7.
8. American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice, Farrell R. ACOG Committee Opinion No. 659: the use of vaginal estrogen in women with a history of estrogen-dependent breast cancer. *Obstet Gynecol* 2016;127:e93-e96.
9. Biglia N, Bounous VE, D'Alonzo M, et al. Vaginal atrophy in breast cancer survivors: attitude and approaches among oncologists. *Clin Breast Cancer* 2017;17:611-617.
10. Vizintin Z, Rivera M, Fistonic I, et al. Novel minimally invasive VSP Er: YAG laser treatments in gynecology. *J Laser Health Acad* 2012;1:46-58.
11. Gambacciani M, Levancini M, Cervigni M. Vaginal erbium laser: the second-generation thermotherapy for the genitourinary syndrome of menopause. *Climacteric* 2015;18:757-763.
12. Gambacciani M, Torelli MG, Martella L, et al. Rationale and design for the Vaginal Erbium Laser Academy Study (VELAS): an international multicenter observational study on genitourinary syndrome of menopause and stress urinary incontinence. *Climacteric* 2015;18 (Suppl 1):43-48.
13. Gambacciani M, Palacios S. Laser therapy for the restoration of vaginal function. *Maturitas* 2017;99:10-15.
14. Gambacciani M, Levancini M. Vaginal erbium laser as second-generation thermotherapy for the genitourinary syndrome of menopause: a pilot study in breast cancer survivors. *Menopause* 2017;24:316-319.
15. Pitsouni E, Grigoriadis T, Falagas ME, Salvatore S, Athanasiou S. Laser therapy for the genitourinary syndrome of menopause: a systematic review and meta-analysis. *Maturitas* 2017;103:78-88.
16. Pitsouni E, Grigoriadis T, Douskos A, Kyriakidou M, Falagas ME, Athanasiou S. Efficacy of vaginal therapies alternative to vaginal estrogens on sexual function and orgasm of menopausal women: a systematic review and meta-analysis of randomized controlled trials. *Eur J Obstet Gynecol Reprod Biol* 2018;229:45-56.
17. Cruz VL, Steiner ML, Pompei LM, et al. Randomized, double-blind, placebo-controlled clinical trial for evaluating the efficacy of fractional CO2 laser compared with topical estriol in the treatment of vaginal atrophy in postmenopausal women. *Menopause* 2018;25: 21-28.
18. Salvatore S, Nappi RE, Parma M, et al. Sexual function after fractional microablative CO2 laser in women with vulvovaginal atrophy. *Climacteric* 2015;18:219-225.
19. Salvatore S, Athanasiou S, Candiani M. The use of pulsed CO2 lasers for the treatment of vulvovaginal atrophy. *Curr Opin Obstet Gynecol* 2015;27:504-508.
20. Pieralli A, Fallani MG, Becorpi A, et al. Fractional CO2 laser for vulvovaginal atrophy (VVA) dyspareunia relief in breast cancer survivors. *Arch Gynecol Obstet* 2016;294:841-846.
21. Salvatore S, Nappi RE, Zerbinati N, et al. A 12-week treatment with fractional CO2 laser for vulvovaginal atrophy: a pilot study. *Climacteric* 2014;17:363-369.
22. Athanasiou S, Pitsouni E, Antonopoulou S, et al. The effect of microablative fractional CO2 laser on vaginal flora of postmenopausal women. *Climacteric* 2016;19:512-518.
23. Sokol ER, Karram MM. Use of a novel fractional CO2 laser for the treatment of genitourinary syndrome of menopause: 1-year outcomes. *Menopause* 2017;24:810-814.
24. Vizintin Z, Lukac M, Kazic M, Tettamanti M. Erbium laser in gynecology. *Climacteric* 2015;18 (Suppl 1):4-8.
25. Gittens P, Mullen G. The effects of fractional microablative CO2 laser therapy on sexual function in postmenopausal women and women with a history of breast cancer treated with endocrine therapy. *J Cosmet Laser Ther* 2018;1-5; doi: 10.1080/14764172.2018.1481510.
26. Becorpi A, Campisciano G, Zanotta N, et al. Fractional CO2 laser for genitourinary syndrome of menopause in breast cancer survivors: clinical, immunological, and microbiological aspects. *Lasers Med Sci* 2018;33:1047-1054.
27. Dennerstein L, Lehert P, Dudley E. Short scale to measure female sexuality: adapted from McCoy Female Sexuality Questionnaire. *J Sex Marital Ther* 2001;27:339-351.
28. Valadares AL, Pinto-Neto AM, de Sousa MH, Osis MJ. [Sociocultural adaptation of the short personal experiences questionnaire (SPEQ) in Brazil.]. *Rev Bras Ginecol Obstet* 2010;32:72-76.
29. Vydence medical. Guia de referência clínica Etherea-MX® Athena®, 1ª edição [Etherea-MX™ Athena™ Clinical Reference Guide, 1st Edition]. São Paulo; 2018.
30. Bachmann GA, Notelovitz M, Kelly SJ, Thompson C. Long-term nonhormonal treatment of vaginal dryness. *Clin Pract Sexual* 1992;8:3-8.
31. Faul F, Erdfelder E, Buchner A, Lang AG. *G*Power Version 3.1.2 [computer software]*. Germany: Universität Kiel; 2008.
32. Hulley SB, Cummings SR. *Designing Clinical Research*. Baltimore: Williams & Wilkins; 1988; pp. 148 and 215.
33. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*, 2nd ed. Hillsdale, NJ: Lawrence Earlbaum Associates; 1988.
34. Cano-Corres R, Sánchez-Álvarez J, Fuentes-Arderiu X. The effect size: beyond statistical significance. *EJIFCC* 2012;23:19-23.
35. Mac Bride MB, Rhodes DJ, Shuster LT. Vulvovaginal atrophy. *Mayo Clin Proc* 2010;85:87-94.
36. Palacios S. Managing urogenital atrophy. *Maturitas* 2009;63:315-318.
37. Calleja-Agius J, Brincat MP. Urogenital atrophy. *Climacteric* 2009;12: 279-285.
38. Gaspar A, Brandi H, Gomez V, Luque D. Efficacy of Erbium:YAG laser treatment compared to topical estriol treatment for symptoms of genitourinary syndrome of menopause. *Lasers Surg Med* 2017;49:160-168.

39. Nappi RE. New attitudes to sexuality in the menopause: clinical evaluation and diagnosis. *Climacteric* 2007;10 (Suppl 2):105-108.
40. Nappi RE, Palacios S. Impact of vulvovaginal atrophy on sexual health and quality of life at postmenopause. *Climacteric* 2014;17:3-9.
41. Sturdee DW, Panay N; International Menopause Society Writing Group. Recommendations for the management of postmenopausal vaginal atrophy. *Climacteric* 2010;13:509-522.
42. Kingsberg SA. The impact of aging on sexual function in women and their partners. *Arch Sex Behav* 2002;31:431-437.
43. Smith RL, Gallicchio L, Flaws JA. Factors affecting sexual activity in midlife women: results from the midlife health study. *J Womens Health* 2017;26:103-108.
44. Gambacciani M, Levancini M, Russo E, Vacca L, Simoncini T, Cervigni M. Long-term effects of vaginal erbium laser in the treatment of genitourinary syndrome of menopause. *Climacteric* 2018;21:148-152.
45. Woloski-Wruble AC, Oliel Y, Leefsma M, Hochner-Celnikier D. Sexual activities, sexual and life satisfaction, and successful aging in women. *J Sex Med* 2010;7:2401-2410.