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The effects of fractional microablative CO_2 laser therapy on sexual function in postmenopausal women and women with a history of breast cancer treated with endocrine therapy

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ABSTRACT

Purpose: To examine the outcomes of sexual function in postmenopausal women and women with a history of breast cancer treated with endocrine therapy who were experiencing the symptoms of GSM for which they were treated with fractional microablative CO_2 laser. **Materials and Methods**: From July 2015 to October 2016, a retrospective chart review of women who underwent fractional microablative CO_2 laser therapy (MonaLisa Touch, DEKA) for GSM was conducted. Several validated questionnaires were used to assess changes in symptoms and sexual function including the Female Sexual Function Index (FSFI), the Wong-Baker Faces Scale (WBFS), and the Female Sexual Distress Scale—Revised (FSDSR). Comparisons of mean symptom scores were described at baseline and six weeks after each treatment. **Results**: There was a statistically significant improvement in every domain of FSFI, WBFS, and FSDS-R when comparing baseline symptom scores to after treatment three symptom scores for all patients. The secondary outcome was to evaluate the differences, if any, in outcomes of sexual function between postmenopausal women and women with a history of breast cancer treated with endocrine therapy. Both groups had statistically significant improvements in many domains studied. **Conclusions**: Fractional microablative CO_2 laser therapy (MonaLisa Touch, DEKA) is an effective modality in treating the symptoms of GSM in postmenopausal women and women with a history of breast cancer treated with endocrine therapy.

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The genitourinary syndrome of menopause (GSM) is a physiological process affecting more than 50% of postmenopausal women and up to 70% of breast cancer survivors (1–3). The concert of signs and symptoms of GSM can arise after a significant decrease in estrogen and steroid hormones during menopause, bilateral oophorectomy or after endocrine or chemotherapy. Common symptoms of GSM include vaginal burning, itching, dryness, decreased lubrication, irritation, and dyspareunia. It can also include urinary symptoms such as urgency and dysuria. The mechanism of GSM is thought to be due to atrophy of the vaginal and vulvar mucous membranes, loss of vaginal elasticity and rugal folds, and loss of sebaceous glands (1,4). The combination of an aging population, a 1 in 8 lifetime risk of developing breast cancer in US women, and a 2 out of 3 chance of hormone-receptor positive breast cancer make GSM a potentially large public health risk, especially as more women are being offered treatments with endocrine therapies that can induce early menopause(5).

Several first-line therapies treating GSM are currently recommended by the North American Menopause Society and The Endocrine Society including vaginal moisturizers, continued sexual activity, and lubricants (6,7). When these first-line therapies are inadequate, local estrogen therapy or selective estrogen receptor modulators may be considered for suitable candidates. However, systemic hormonal therapy is contraindicated in women with hormonally responsive cancers, and the use of local estrogen therapy and selective estrogen receptor modulators in breast cancer patients being treated with endocrine therapy is currently not recommended (8,9).

Recently, the beneficial effects of fractional microablative CO_2 laser therapy seen in dermatology have been applied to treat the symptoms of GSM (10). A few early studies have shown fractional microablative CO_2 laser therapy to be effective in treating the symptoms of GSM in postmenopausal women (11–14). Even fewer studies have shown fractional microablative CO_2 laser therapy to be safe and effective in women with breast cancer (15,16). Given this background, we designed this study to examine the outcomes of sexual function in postmenopausal women and women with a history of breast cancer treated with endocrine therapy who were experiencing the symptoms of GSM for which they were treated with fractional microablative CO_2 laser.

Materials and methods

From July 2015 to October 2016, a retrospective chart review of women who underwent fractional microablative

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CO_2 laser therapy (MonaLisa Touch, DEKA) for GSM was conducted.

The research was conducted according to Good Practice Guidelines and was approved by the Drexel University Institutional Review Board.

Inclusion criteria included: women complaining of symptoms of GSM who either had a history of menopause or a history of iatrogenically induced menopause secondary to endocrine therapy for breast cancer.

Exclusion criteria included: prolapse of any kind beyond the hymen, a history of radiation to the vagina or colon, a history of reconstruction to vagina with mesh, a history of impaired wound healing, a history of keloid formation, a history of acute vaginal infection, and having not completed the provider recommended three treatments.

The primary outcome of the study was to evaluate the changes in sexual function in women treated for symptoms of GSM with fractional microablative CO_2 laser therapy.

The secondary outcome of the study was to evaluate the differences, if any, in outcomes of sexual function of postmenopausal women and women with a history of breast cancer treated with endocrine therapy.

All patients underwent vaginal exam prior to treatment. All patients had a documented negative Papanicolaou (PAP) smear prior to treatment.

Fractional microablative MonaLisa Touch CO_2 laser system (DEKA) was administered for three treatments, each spaced six weeks apart. The vaginal probe was gently inserted into the vaginal canal, and subsequently rotated to four quadrants of the vagina then withdrawn by 1 cm and repeated until there was complete treatment of the vaginal wall. Along with treatments number two and three, an external laser probe was used to treat the vulva.

Following each treatment, patients were monitored for complications and side effects. Patients were instructed to abstain from vaginal sexual activity for three days after each treatment.

Several validated questionnaires were used to assess changes in symptoms and sexual function including the Female Sexual Function Index (FSFI), the Wong-Baker Faces Scale (WBFS), and the Female Sexual Distress Scale—Revised (FSDS-R). Responses to each questionnaire were noted at baseline, prior to initiation of treatment, and six weeks after each treatment.

Comparisons of mean symptom scores from each domain of the FSFI (desire, arousal, lubrication, orgasm, satisfaction, pain, and total score), WBFS (pain, vaginal itching, dyspareunia, vaginal burning, vaginal dryness, and dysuria), and FSDS-R (total sexual distress) were described at baseline and six weeks after each treatment with student 2-tailed paired *t* tests. All *P* values of < 0.05 were considered statistically significant. These analyses were performed using the SPSS software version 24.0 (SPSS Science, Chicago, IL, USA).

Results

Thirty-one patients were eligible for the study. Six were excluded for having not completed the provider recommended three treatments. For the 25 patients included, mean age was 55.2 ± 9.5 years, average onset of menopause was 47.3 ± 6.3 years, and average duration of symptoms was 9.4 ± 7.6 years. Eight of the 25 patients treated had a history of breast cancer for which they all had received endocrine therapy. Four of the eight breast cancer patients were still being treated with endocrine therapy during the course of the study.

Table 1. Change in symptom scores of Female Sexual Function Index (FSFI) for all patients.

	Baseline to T x 1		T x 1 to T x 2		T x 2 to T x 3		Baseline to T x 3	
Symptom	Improvement	*P*	Improvement	*P*	Improvement	*P*	Improvement	*P*
Desire	0.37 ± 0.96	0.061	0.60 ± 0.86	0.002	0.17 ± 1.26	0.540	0.86 ± 1.42	0.012
Arousal	0.52 ± 1.61	0.112	0.93 ± 1.69	0.009	0.33 ± 0.99	0.147	1.73 ± 1.94	0.001
Lubrication	0.33 ± 1.72	0.330	1.19 ± 1.74	0.002	0.43 ± 1.02	0.068	1.79 ± 2.20	0.001
Orgasm	0.66 ± 2.06	0.114	0.97 ± 2.12	0.028	0.42 ± 0.54	0.002	2.11 ± 2.04	<0.001
Satisfaction	0.66 ± 1.43	0.026	0.80 ± 1.86	0.038	0.32 ± 1.24	0.247	1.68 ± 1.76	<0.001
Pain	0.91 ± 1.86	0.020	0.78 ± 1.66	0.024	0.74 ± 1.54	0.039	2.15 ± 1.67	<0.001
Total score	3.45 ± 6.84	0.016	5.28 ± 8.12	0.003	2.41 ± 3.63	0.006	10.3 ± 8.68	<0.001

Table 2. Change in symptom scores of Wong-Baker Faces Scale (WBFS) for all women.

	Baseline to T x 1		T x 1 to T x 2		T x 2 to T x 3		Baseline to T x 3	
Symptom	Improvement	*P*	Improvement	*P*	Improvement	*P*	Improvement	*P*
Pain	2.46 ± 3.45	0.001	0.08 ± 1.98	0.844	0.81 ± 2.36	0.131	3.71 ± 3.21	<0.001
Vaginal itching	1.58 ± 2.61	0.005	0.11 ± 1.34	0.664	0.29 ± 1.59	0.419	2.33 ± 3.12	0.003
Dyspareunia	3.11 ± 3.97	<0.001	0.12 ± 1.58	0.713	1.24 ± 1.64	0.002	5.00 ± 2.92	<0.001
Vaginal burning	1.88 ± 2.55	0.001	0.46 ± 2.21	0.298	0.09 ± 1.81	0.812	3.10 ± 3.70	0.001
Vaginal dryness	2.58 ± 2.99	<0.001	1.50 ± 2.77	0.011	0.19 ± 2.23	0.699	4.71 ± 3.38	<0.001
Dysuria	0.73 ± 1.87	0.057	0.12 ± 0.43	0.185	0.09 ± 0.44	0.329	1.14 ± 2.33	0.036

Table 3. Change in symptom score of Female Sexual Distress Scale—Revised (FSDS-R) for all women.

	Baseline to T x 1		T x 1 to T x 2		T x 2 to T x 3		Baseline to T x 3	
Symptom	Improvement	*P*	Improvement	*P*	Improvement	*P*	Improvement	*P*
Sexual distress	6.25 ± 7.95	0.001	6.25 ± 9.04	0.003	5.10 ± 7.56	0.007	16.7 ± 10.79	<0.001

Table 4. Change in symptom scores of FSFI for postmenopausal women.

	Baseline to T x 1		T x 1 to T x 2		T x 2 to T x 3		Baseline to T x 3	
Symptom	Improvement	*P*	Improvement	*P*	Improvement	*P*	Improvement	*P*
Desire	0.32 ± 0.88	0.155	0.49 ± 0.88	0.034	0.05 ± 1.02	0.874	0.55 ± 1.40	0.178
Arousal	−0.14 ± 1.07	0.595	1.16 ± 1.89	0.022	0.28 ± 0.98	0.326	1.32 ± 2.03	0.037
Lubrication	0.02 ± 0.88	0.935	1.36 ± 1.96	0.011	0.37 ± 1.18	0.282	1.64 ± 2.28	0.023
Orgasm	0.05 ± 1.68	0.909	1.13 ± 2.53	0.084	0.37 ± 0.50	0.021	1.63 ± 1.92	0.010
Satisfaction	0.26 ± 1.10	0.348	1.20 ± 1.79	0.014	0.15 ± 1.19	0.651	1.69 ± 1.74	0.004
Pain	0.52 ± 1.84	0.264	0.87 ± 2.03	0.096	0.98 ± 1.65	0.052	2.15 ± 1.79	0.001
Total score	1.02 ± 4.67	0.382	6.22 ± 9.35	0.014	2.20 ± 2.74	0.013	8.98 ± 9.27	0.004

Table 5. Change in symptom scores of FSFI for women with history of breast cancer treated with endocrine therapy. Change in symptom score of FSDS-R .

	Baseline to Tx1		Tx1 to Tx2		Tx2 to Tx3		Baseline to Tx3	
Symptom	Improvement	*P*	Improvement	*P*	Improvement	*P*	Improvement	*P*
Desire	0.38 ± 1.20	0.405	0.60 ± 0.64	0.033	0.375 ± 1.63	0.537	1.35 ± 1.42	0.032
Arousal	1.88 ± 1.85	0.024	0.11 ± 0.32	0.351	0.41 ± 1.10	0.323	2.40 ± 1.70	0.005
Lubrication	0.83 ± 2.81	0.434	0.68 ± 1.21	0.158	0.53 ± 0.75	0.087	2.03 ± 2.20	0.035
Orgasm	2.00 ± 2.40	0.051	0.40 ± 0.71	0.155	0.50 ± 0.63	0.060	2.90 ± 2.09	0.006
Satisfaction	1.50 ± 1.81	0.052	−0.45 ± 1.16	0.309	0.60 ± 1.35	0.250	1.65 ± 1.91	0.044
Pain	1.10 ± 0.73	0.004	0.70 ± 0.56	0.009	0.35 ± 1.36	0.490	2.15 ± 1.58	0.006
Total score	7.68 ± 8.61	0.040	2.04 ± 2.76	0.075	2.76 ± 4.96	0.159	12.48 ± 7.70	0.003

Table 1 displays the FSFI results for all patients. There was a statistically significant improvement in every domain when comparing baseline symptom scores to after treatment three symptom scores.

Table 2 displays the WBFS results for all patients. Statistically significant improvements were noted in every domain when comparing baseline symptom scores to after treatment three symptom scores.

Table 3 displays the FSDS-R results for all patients. There was a statistically significant decrease in sexual distress from each treatment to the next and from baseline symptom score to after treatment three symptom score.

The secondary outcome was to evaluate the differences, if any, in outcomes of sexual function between postmenopausal women and women with a history of breast cancer treated with endocrine therapy. Tables 4 and 5 display the FSFI results of these groups. Both groups had statistically significant improvements in total FSFI score from baseline to after treatment three. Additionally, for postmenopausal women, statistically significant improvements were noted in every domain except desire when comparing baseline symptom scores to after treatment three symptom scores. For women with a history of breast cancer treated with endocrine therapy, statistically significant improvements were noted in every domain when comparing baseline symptom scores to after treatment three symptom scores.

Tables 6 and 7 display the WBFS results for postmenopausal women and women with a history of breast cancer treated with endocrine therapy. For postmenopausal women, statistically significant improvements were noted in every domain except dysuria when comparing baseline symptom scores to after treatment three symptom scores. For women with a history of breast cancer treated with endocrine therapy, statistically significant improvements were noted in pain, dyspareunia, and vaginal dryness

Table 6. Change in symptom scores of WBFS for postmenopausal women.

	Baseline to T x 1		T x 1 to T x 2		T x 2 to T x 3		Baseline to T x 3	
Symptom	Improvement	*P*	Improvement	*P*	Improvement	*P*	Improvement	*P*
Pain	2.18 ± 3.68	0.027	0.29 ± 2.05	0.563	0.77 ± 2.83	0.347	3.77 ± 3.52	0.002
Vaginal itching	1.59 ± 2.37	0.014	0.24 ± 1.56	0.543	0.38 ± 1.56	0.391	2.69 ± 3.22	0.011
Dyspareunia	3.29 ± 3.80	0.003	0.06 ± 1.56	0.878	1.31 ± 1.80	0.022	5.46 ± 2.57	<0.001
Vaginal burning	2.00 ± 2.69	0.007	0.41 ± 2.40	0.489	0.00 ± 1.91	1.000	3.31 ± 3.90	0.010
Vaginal dryness	2.29 ± 3.39	0.013	2.18 ± 2.72	0.005	0.31 ± 1.89	0.568	5.62 ± 3.20	<0.001
Dysuria	1.12 ± 2.12	0.045	0.06 ± 0.24	0.332	0.15 ± 0.55	0.337	1.69 ± 2.81	0.051

Table 7. Change in symptom scores of WBFS for women with history of breast cancer treated with endocrine therapy.

	Baseline to T x 1		T x 1 to T x 2		T x 2 to T x 3		Baseline to T x 3	
Symptom	Improvement	*P*	Improvement	*P*	Improvement	*P*	Improvement	*P*
Pain	3.86 ± 2.73	0.010	−0.38 ± 1.99	0.612	0.88 ± 1.46	0.133	4.14 ± 2.67	0.006
Vaginal itching	1.75 ± 3.33	0.180	−0.13 ± 0.83	0.685	0.13 ± 1.73	0.844	1.75 ± 3.06	0.150
Dyspareunia	2.88 ± 4.79	0.134	0.25 ± 1.83	0.711	1.13 ± 1.46	0.065	4.25 ± 3.45	0.010
Vaginal burning	1.88 ± 2.47	0.069	0.63 ± 2.07	0.420	0.25 ± 1.75	0.699	2.75 ± 3.58	0.066
Vaginal dryness	3.00 ± 2.27	0.007	0.25 ± 2.71	0.802	0.00 ± 2.83	1.000	3.25 ± 3.33	0.028
Dysuria	0.00 ± 1.07	1.000	0.25 ± 0.71	0.351	0.25 ± 0.71	0.251	0.25 ± 0.71	0.351

Table 8. Change in symptom score of FSDS-R for postmenopausal women.

	Baseline to T x 1		T x 1 to T x 2		T x 2 to T x 3		Baseline to T x 3	
Symptom	Improvement	*P*	Improvement	*P*	Improvement	*P*	Improvement	*P*
Sexual distress	4.76 ± 6.77	0.010	6.06 ± 10.28	0.027	5.85 ± 8.79	0.034	15.6 ± 11.74	<0.001

Table 9. Change in symptom score of FSDS-R for women with history of breast cancer treated with endocrine therapy.

	Baseline to T x 1		T x 1 to T x 2		T x 2 to T x 3		Baseline to T x 3	
Symptom	Improvement	*P*	Improvement	*P*	Improvement	*P*	Improvement	*P*
Sexual distress	9.86 ± 9.92	0.039	4.83 ± 2.79	0.008	3.71 ± 4.79	0.086	18.7 ± 9.25	0.002

when comparing baseline symptom scores to after treatment three symptom scores.

Tables 8 and 9 exhibit the FSDS-R results for postmenopausal women and women with a history of breast cancer treated with endocrine therapy. Both groups independently had a statistically significant decrease in sexual distress when comparing baseline to after treatment three.

Discussion

The proposed mechanism of action of the fractional microablative MonaLisa Touch CO_2 laser system (DEKA) is that it induces ablation and coagulation of the superficial layer of the vaginal mucosa and, importantly, activates heat shock protein 47. Activation of heat shock protein 47 in turn induces cytokine production. These cytokines promote re-epithelization of the vaginal mucosa leading to a thicker epithelium, induce angiogenesis thereby increasing vaginal mucosa nourishment, and activate TGF-β, stimulating inactive fibrocytes to become active fibroblasts. These active fibroblasts increase production of the extracellular matrix, further promoting healthy vaginal mucosa (17,18).

Postmenopausal women experiencing the symptoms of the GSM have a variety of treatment options including vaginal lubricants, moisturizers, and local estrogen, as well as other therapies such as selective estrogen receptor modulators and systemic hormonal therapy. However, due to poor compliance, concerns about side effects, and contraindications to some therapies, many women are faced with difficult treatment decisions. According to the AGATA study (19), of women treated with any of the aforementioned or combination of aforementioned therapies, 62% discontinued treatment. In another study, the rate of compliance with estrogen creams was about 12% and the rate of compliance with vaginal estrogen tablets was about 42% (20). The REVIVE study (21) found that only 35% of postmenopausal women being treated for GSM with lubricants, moisturizers, local estrogen therapy, or a combination of these therapies were satisfied with treatment. The study also found that 41% of women cited long-term safety as concern for local estrogen therapy, while another 43% of women cited messiness with lubricants and moisturizers as their main concern (21). Additionally, because systemic hormonal therapy is contraindicated in women with hormonally responsive cancers and because the use of local estrogen therapy and selective estrogen receptor modulators in breast cancer patients being treated with endocrine therapy is currently not recommended, these difficult treatment decisions are extremely prevalent and important (8,9). Therefore, the need to evaluate the safety and efficacy of other treatment modalities is prudent.

This study is the first in the United States to examine the outcomes of sexual function for postmenopausal women and women with a history of breast cancer treated with endocrine therapy who were experiencing the symptoms of GSM for which they were treated with fractional microablative CO_2 laser. In contrast to compliance rates seen with other treatment modalities, in this study, there was greater than 80% compliance with the provider recommended three-treatment protocol. Furthermore, the procedure was safe with no adverse events having been documented. The results of this study demonstrate that in women who experience the symptoms of GSM, either postmenopausal women or women with a history of breast cancer treated with endocrine therapy, fractional microablative CO_2 laser therapy is effective in significantly improving sexual function.

The limitations of the study include a small sample size, absence of a control group, and lack of long-term follow-up. Due to size of the groups, we were unable to compare the postmenopausal women directly with the women with a history of breast cancer treated with endocrine therapy. Randomized controlled trials comparing fractional microablative CO_2 therapy with other existing therapies or even sham laser treatments are needed, as are studies evaluating the long-term efficacy of treatment.

Conclusions

Fractional microablative CO_2 laser therapy (MonaLisa Touch, DEKA) is an effective modality in treating the symptoms of GSM in postmenopausal women and women with a history of breast cancer treated with endocrine therapy.

References

1. MacBride MB, Rhodes DJ, Shuster LT. Vulvovaginal atrophy. Mayo Clin Proc. 2010;85:87–94. doi:10.4065/mcp.2009.0413.
2. Palma F, Volpe A, Villa P, Cagnacci A. Vaginal atrophy of women in postmenopause. Results from a multicentric observational study: the AGATA study. Maturitas. 2016;83:40–44. doi:10.1016/j.maturitas.2015.09.001.
3. Lester J, Pahouja G, Andersen B, Lustberg M. Atrophic vaginitis in breast cancer survivors: a difficult survivorship issue. J Pers Med. 2015;5:50–66. doi:10.3390/jpm5020050.
4. Gandhi J, Chen A, Dagur G, Suh Y, Smith N, Cali B, Khan SA. Genitourinary syndrome of menopause: an overview of clinical manifestations, pathophysiology, etiology, evaluation, and management. Am J Obstet Gynecol. 2016;215:704–11. doi:10.1016/j.ajog.2016.07.045.
5. The American Cancer Society medical and editorial content team. Breast Cancer. American Cancer Society. https://www.cancer.org/cancer/breast-cancer.html. 2016.
6. Shifren JL, Gass ML. The North American menopause society recommendations for clinical care of midlife women. Menopause. 2014;21:1038–62. doi:10.1097/GME.0000000000000319.
7. Stuenkel CA, Davis SR, Gompel A, Lumsden MA, Murad MH, Pinkerton JV, Santen RJ. Treatment of symptoms of the menopause: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2015;100:3975–4011. doi:10.1210/jc.2015-2236.
8. Sousa MS, Peate M, Jarvis S, Hickey M, Friedlander M. A clinical guide to the management of genitourinary symptoms in breast cancer survivors on endocrine therapy. Ther Adv Med Oncol. 2017;9:269–85. doi:10.1177/1758834016687260.
9. Runowicz CD, Leach CR, Henry NL, Henry KS, Mackey HT, Cowens-Alvarado RL, Cannady RS, Pratt-Chapman ML, Edge SB, Jacobs LA, et al. American Cancer Society/American Society of Clinical oncology breast cancer survivorship care guideline. CA Cancer J Clin. 2016;66:43–73. doi:10.3322/caac.21319.
10. Hutchinson-Colas J, Segal S. Genitourinary syndrome of menopause and the use of laser therapy. Maturitas. 2015;82:342–45. doi:10.1016/j.maturitas.2015.08.001.
11. Salvatore S, Leone Roberti Maggiore U, Athanasiou S, Origoni M, Candiani M, Calligaro A, Zerbinati N. Histological study on the effects of microablative fractional CO2 laser on atrophic vaginal tissue: an ex vivo study. Menopause. 2015;22:845–49. doi:10.1097/GME.0000000000000401.
12. Zerbinati N, Serati M, Origoni M, Candiani M, Iannitti T, Salvatore S, Marotta F, Calligaro A. Microscopic and ultrastructural modifications of postmenopausal atrophic vaginal mucosa after fractional carbon dioxide laser treatment. Lasers Med Sci. 2015;30:429–36. doi:10.1007/s10103-014-1677-2.
13. Salvatore S, Nappi RE, Parma M, Chionna R, Lagona F, Zerbinati N, Ferrero S, Origoni M, Candiani M. Leone Roberti Maggiore U. Sexual function after fractional microablative CO_2 laser in women with vulvovaginal atrophy. Climacteric. 2015;18:219–25. doi:10.3109/13697137.2014.975197.
14. Perino A, Calligaro A, Forlani F, Tiberio C, Cucinella G, Svelato A, Saitta S, Calagna G. Vulvo-vaginal atrophy: a new treatment modality using thermo-ablative fractional CO2 laser. Maturitas. 2015;80:296–301. doi:10.1016/j.maturitas.2014.12.006.
15. Salvatore S, Nappi RE, Zerbinati N, Calligaro A, Ferrero S, Origoni M, Candiani M. Leone Roberti Maggiore U. A 12-week treatment with fractional CO2 laser for vulvovaginal atrophy: a pilot study. Climacteric. 2014;17:363–69. doi:10.3109/13697137.2014.899347.
16. Sokol ER, Karram MM. An assessment of the safety and efficacy of a fractional CO2 laser system for the treatment of vulvovaginal atrophy. Menopause. 2016;23:1102–07. doi:10.1097/GME.0000000000000700.
17. Filippini M, Farinelli M.Use of the MonaLisa Touch® Treatment on Cancer Patients. State Hospital – Republic of San Marino, Republic of San Marino; 2014.
18. Pieralli A, Fallani MG, Becorpi A, Bianchi C, Corioni S, Longinotti M, Tredici Z, Guaschino S. Fractional CO2 laser for vulvovaginal atrophy (VVA) dyspareunia relief in breast cancer survivors. Arch Gynecol Obstet. 2016;294:841–46. doi:10.1007/s00404-016-4118-6.
19. Palma F, Della Vecchia E, Cagnacci A. Medical and patient attitude towards vaginal atrophy: the AGATA study. Climacteric. 2016;19:553–57. doi:10.1080/13697137.2016.1240770.
20. Portman D, Shulman L, Yeaw J, Zeng S, Uzoigwe C, Maamari R, Iyer NN. One-year treatment persistence with local estrogen therapy in postmenopausal women diagnosed as having vaginal atrophy. Menopause. 2015;22:1197–203. doi:10.1097/GME.0000000000000465.
21. Kingsberg SA, Wysocki S, Magnus L, Krychman ML. Vulvar and vaginal atrophy in postmenopausal women: findings from the REVIVE (REal Women's VIews of Treatment Options for Menopausal Vaginal ChangEs) survey. J Sex Med. 2013;10:1790–99. doi:10.1111/jsm.12190.