

# Efficacy of subcutaneous testosterone on menopausal symptoms in breast cancer survivors



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## Background

Menopausal symptoms can be quite severe in breast cancer survivors in whom estrogen therapy is contraindicated. Our previous proof-of-idea study demonstrated that 120 mg of testosterone (T) combined with 8 mg of anastrozole (A) in two subcutaneous implants provided therapeutic T levels without elevating estradiol<sup>1</sup>. Our current goal was to document the clinical effect of T + A combination implants (no estrogen) on menopausal symptoms in breast cancer survivors.

## Methods

This IRB approved study was designed to prospectively follow breast cancer survivors (stage 0-4) treated with subcutaneous T + A for breast cancer recurrence. As part of the study, the therapeutic effectiveness of T on the relief of psychological, somatic and urogenital symptoms and conditions was documented using the validated, self administered, 11-item Menopause Rating Scale<sup>2</sup>. Patients completed the survey prior to and following therapy. The statistical program R (R Development Core Team, 2009) was used for all data analysis. Paired Wilcoxon tests were used to compare the mean score values for each of the 11 categories Pre and Post T + A treatment.

Menopause Rating Scale (MRS)

Which of the following symptoms apply to you at this time?  
(X ONE Box For EACH Symptom) For Symptoms That Do Not Apply, Please Mark "None".

Symptoms:	none	mild	moderate	severe	extremely severe
Score	0	1	2	3	4
1. Hot flashes, sweating (episodes of sweating).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Heart discomfort (unusual awareness of heart beat, heart skipping, heart racing, tightness).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Sleep problems (difficulty in falling asleep, difficulty in sleeping through the night, waking up early).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Depressive mood (feeling down, sad, on the verge of tears, lack of drive, mood swings).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Irritability (feeling nervous, inner tension, feeling aggressive).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Anxiety (inner restlessness, feeling panicky).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Physical and mental exhaustion (general decrease in performance, impaired memory, decrease in concentration, forgetfulness).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Sexual problems (change in sexual desire, in sexual activity and satisfaction).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Bladder problems (difficulty in urinating, increased need to urinate, bladder incontinence).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Dryness of vagina (sensation of dryness or burning in the vagina, difficulty with sexual intercourse).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. Joint and muscular discomfort (pain in the joints, rheumatoid complaints).....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

English/US version of Menopause Rating Scale (MRS). 11 symptom categories with 5-point severity scale.

## Results

Over 1000 Testosterone + Anastrozole (T + A) pellet insertions have been performed in breast cancer survivors since 2006. Between April 2013 and May 2014, 72 patients had been enrolled in the study and were eligible for analysis.

T implant dosing is weight based<sup>3</sup>. Over 90% of patients were treated with 8 mg of A combined with T in the implant. A lower dose of A (4 mg) is occasionally used in smaller patients and/or patients with lesser or more remote disease. A higher dose of A (12 mg) is occasionally used in obese patients with advanced disease, or in the neo-adjuvant setting\*. Subcutaneous implants are inserted in the gluteal or inguinal area\*\* at 3-month intervals on average. Therapeutic T levels were confirmed without elevation of estradiol in any postmenopausal survivor.

There have been **no cancer recurrences** in up to 8 years of therapy. A single patient with active metastatic disease at enrollment developed ascites while on therapy, which responded to chemotherapy. T + A was continued throughout. Two patients had a decline of previously elevated tumor markers following initiation of T + A therapy.

Age at diagnosis (y)	50.04 ± 10.66 (31.25-90.26)
Age at first insertion (y)	57.17 ± 10.51 (31.74-90.28)
Treatment years	3.93 ± 2.41 (0.11-8.37)
BMI	26.03 ± 4.69
Testosterone dose (mg)	168.89 ± 32.25
Anastrozole dose (mg) (n)	4 (5), 8 (66), 12 (1)
Testosterone level (ng/dl)	354.42 ± 149.06
Stage-0, 1, 2, 3, 4 (n)	15, 25, 23, 6, 3
Disease recurrence (n)	0
Disease progression (n)	1

### Patient demographics.

\*Neo-adjuvant T+A patients were not included in this analysis

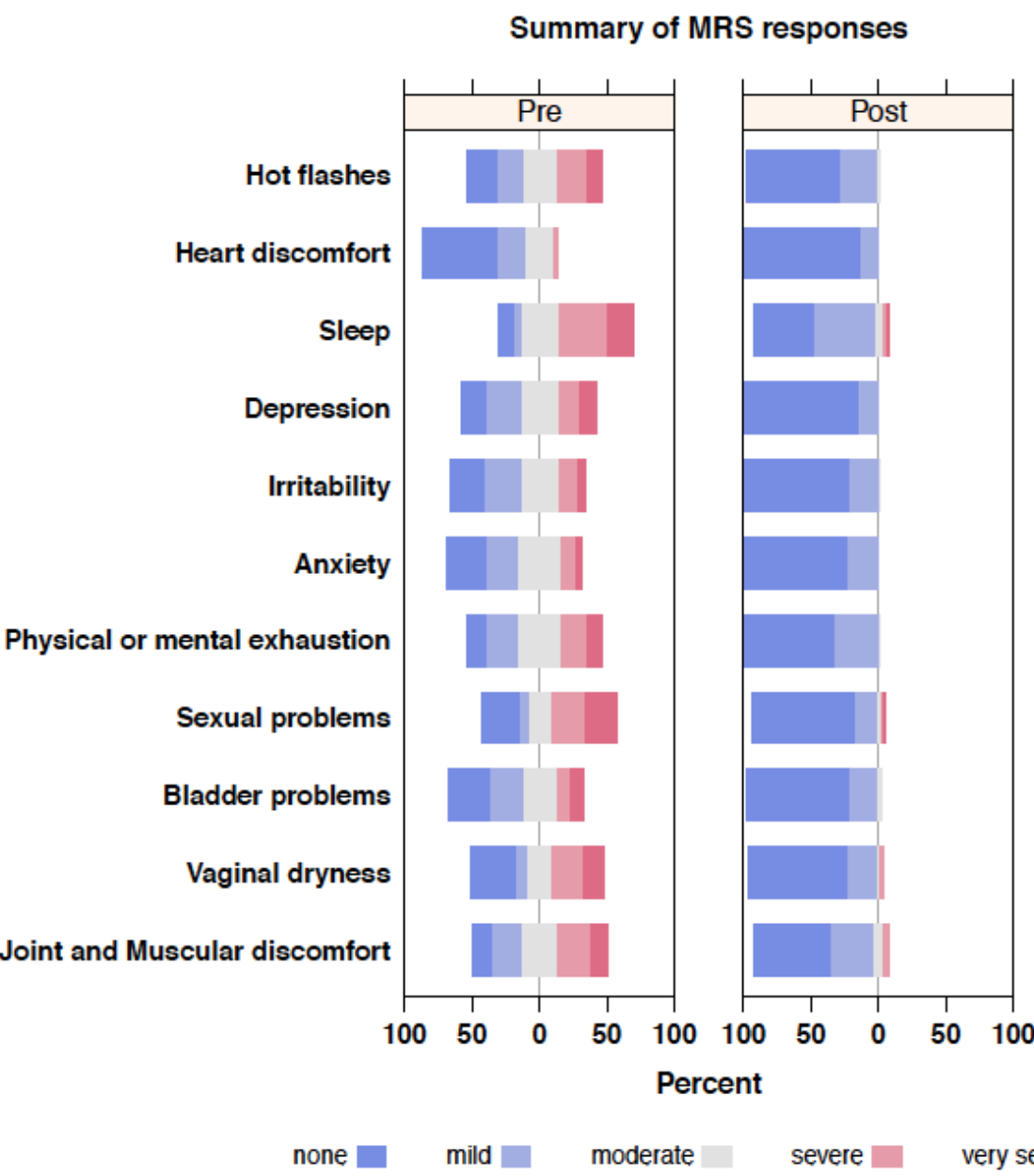
## Results

There was statistically significant improvement (P<0.0001) in MRS total score and all subscale scores including:

- **Psychological** (depression, irritability/aggression, anxiety)
- **Somatic** (hot flashes/sweating, heart discomfort, sleep problems/insomnia, physical exhaustion, impaired memory, joint/muscular pain)
- **Urogenital** (vaginal dryness, bladder problems/incontinence, sexual problems).

In addition, **all** individual symptoms/conditions, including hot flashes, improved on T + A implants (P<0.0001).

There have been **no adverse drug events** in any breast cancer survivor treated with parenteral T + A therapy.



**MRS results.** Summary of distribution of severity scores in each of the 11 categories Pre and Post T + A therapy.

## Conclusion

**Testosterone in combination with anastrozole**, an aromatase inhibitor, delivered by **subcutaneous implant**, was **extremely effective** for the relief of menopausal symptoms in breast cancer survivors. Furthermore, these findings support testosterone's **direct** (therapeutic) **effect** via the androgen receptor.

The lack of breast cancer recurrences and absence of adverse events support the **safety** of these doses of subcutaneous T + A therapy in breast cancer survivors.

Women with a history of breast cancer, or at increased risk for breast cancer, who are suffering from symptoms of hormone deficiency could be offered T therapy in combination with an aromatase inhibitor.

## Images



\*\*Simple 2-minute insertion procedure

### Poster Information

**Date and Time:** 9/4/2014 11:45AM - 1:30PM, 4:45PM - 6:00  
**Session Location:** Golden Gate Hall  
**Session Title:** General Poster Session A: Local/Regional Therapy, Survivorship and Health Policy D2  
**Poster Board:**

### References

1. Glaser R. Subcutaneous testosterone-anastrozole implant therapy in breast cancer survivors. American Society of Clinical Oncology Breast Cancer Symposium. 500; 2010:D:221.
2. Heinemann LAJ, DoMinhT, Strelow F, Gerbsch S, Schnitker J, Schneider HPG. The menopause rating scale (MRS) as outcome measure for hormone treatment? A validation study. Health and Quality of Life Outcomes 2004;2(1):67.
3. Glaser R, Kalantaridou S, Dimitrakakis C. Testosterone implants in women: Pharmacological dosing for a physiologic effect. Maturitas. 2013;74:179-184.

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