

# Effects of Complementary Therapies on Clinical Outcomes in Patients Being Treated With Radiation Therapy for Prostate Cancer

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**BACKGROUND.** This pilot randomized controlled trial (RCT) examined the clinical effects of 2 complementary (CAM) therapies, relaxation response therapy (RRT) and Reiki therapy, in men being treated with external beam radiotherapy (EBRx) for prostate cancer. **METHODS.** Study participants were randomly assigned to weekly RRT, Reiki therapy twice weekly, or wait-list control. Well-validated instruments measured anxiety (STAI), depression (CES-D), and quality of life in cancer patients (FACT-G) at randomization and 3 subsequent time points. **RESULTS.** Fifty-four men were randomized, and 16 of 18 (89%) of RRT and 15 of 18 (83%) of Reiki patients completed the intervention protocol. No statistically significant difference was found between the RRT, Reiki, and control groups on total scores for the STAI, CES-D, or FACT-G instruments at any time point. However, at the end of the intervention, significant improvement was found on the emotional well-being subscale of the FACT-G quality of life scale in the RRT group compared with the Reiki and control groups ( $P = .01$ ). In participants who were classified as “anxious” at baseline, statistically significant improvement occurred in the RRT group ( $P = .02$ ), and a positive trend was found in the Reiki group ( $P = .10$ ). **CONCLUSIONS.** This pilot study documented the feasibility of conducting a RCT of CAM therapies in men undergoing EBRx for prostate cancer. Relaxation response therapy improved emotional well being and eased anxiety in participants. Reiki therapy also had a positive effect in anxious patients. A larger study to verify and better define the benefits of these therapies in men with prostate cancer is warranted. *Cancer* 2011;117:96–102. © 2010 American Cancer Society.

**KEYWORDS:** anxiety, clinical trials, energy medicine, mind-body medicine, prostate cancer, radiation therapy, Reiki, relaxation response therapy.

**Prostate** cancer is the most common cancer in men and is associated with high levels of anxiety and depression with respect to life-threatening risks and complications of treatment such as sexual dysfunction and disabling urinary tract symptoms.<sup>1-3</sup>

Increasing evidence supports the interconnectedness of mind and body and suggests important benefits of mind/body interventions in reducing the harmful effects of stress. Meditation, relaxation response therapy, and Reiki therapy are important among complementary and alternative medicine (CAM) techniques being examined. The popularity of CAM is amply demonstrated by the 2002 National Health Interview Survey, conducted by the National Center for Health Statistics, that found 36% of American adults used some form of CAM during the preceding 12 months.<sup>4</sup> In 2007, American adults spent 33.9 billion discretionary dollars on CAM therapies.<sup>5</sup>

The National Cancer Institute has found between 9% and 91% of surveyed oncology patients use some form of CAM,<sup>6</sup> including 63% to 83% of women with breast cancer.<sup>7</sup> Surveys of men with prostate cancer have indicated interest in CAM, but most data refer to nutritional therapies.<sup>8-14</sup>

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This study examined the effects of Reiki or relaxation response therapy (RRT) with cognitive restructuring in patients with prostate cancer who were undergoing external beam radiation therapy. Reiki is a type of energy therapy used to improve the body's ability to heal itself.<sup>15-18</sup>

A limited number of scientifically rigorous research studies have explored Reiki's effectiveness,<sup>19,20</sup> and a review suggests beneficial effects on pain, fatigue, mood, and quality of life.<sup>18,20</sup> RRT teaches subjects to evoke the relaxation response,<sup>21-23</sup> which helps them replace negative thoughts with less frightening and more positive images (cognitive restructuring). A recent meta-analysis examining autogenic training and self-relaxation demonstrated that each technique had positive effects in patients with tension headaches, coronary artery disease, asthma, pain, Raynaud syndrome, anxiety, depression, or sleeplessness.<sup>24</sup> Early studies suggest genomic changes may be induced by the relaxation response.<sup>25</sup>

This pilot randomized clinical study examined the willingness of men undergoing radiotherapy for prostate cancer to participate in a study of CAM therapies and tested the effects of Reiki and RRT on psychosocial and physiological outcomes. The study was not powered to obtain statistically significant results and, therefore, relies primarily on trends to describe clinical responses.

## MATERIALS AND METHODS

### *Study Population*

Male patients 30 years of age or older were eligible to participate if they had a biopsy-proven diagnosis of nonmetastatic prostate cancer, were not receiving chemotherapy, and had elected to receive external-beam radiation therapy (EBRx) at the Dana-Farber/Brigham and Women's Cancer Center. Patients were excluded if they were receiving ongoing psychotherapy, were receiving antidepressive medications, had had prior experiences with Reiki or RRT, or if they could not read, write, or understand English at an eighth-grade level.

### *Study Design*

This was a phase 2 randomized, intention-to-treat clinical trial that compared psychosocial outcomes in participants who received either Reiki or RRT/CR in comparison with wait-list controls. Patients were recruited between June 2005 and April 2007. Eligible patients were identified from the computerized medical records at Dana-Farber/Brigham and Women's Cancer Center. They were approached initially by their treating radiation oncologist at the time they opted for radiation therapy for their prostate cancer, were

given a detailed explanation of the study, and were invited to participate. The study was approved by the Dana-Farber/Harvard Cancer Center Institutional Review Board, and all participants signed an informed consent form. Participants were not charged for their CAM therapies, but received no financial incentives to participate.

All participants underwent the standard procedures for patients receiving EBRx, which included treatment planning and education for their diagnosis, discussion of the prognosis, and description of the EBRx treatment protocol. EBRx was delivered 5 days per week for 8 or 9 consecutive weeks. In patients who received androgen-suppression therapy (AST), EBRx commenced 8 weeks after AST was begun.

Participants provided information on their demographics, medical history, and current health status at the time of enrollment. They also completed psychosocial instruments and physiological testing at the time of randomization, after 4 and 8 weeks of EBRx, and at their postradiation visits 8 to 12 weeks after EBRx was concluded. At each time point, the instruments were administered in a quiet room after the EBRx treatment or physician visit had been completed.

### *Randomization*

Subjects were randomized before starting EBRx using a computer-generated randomization list derived from permuted blocks in equal proportions to the Reiki, RRT/CR, or wait-list control groups. Participants who were randomized to the control arm were given the option of receiving either Reiki or RRT/CR free of charge at the end of the study. Two of 18 control patients elected to receive Reiki after completing the study.

### *Interventions*

External-beam radiotherapy was given 5 days per week for 8 or 9 weeks with sessions averaging 15 minutes in length. Reiki or RRT sessions were scheduled on the same day as an EBRx treatment and usually preceded it. Appointments, space, and credentialing for CAM treatments were facilitated by the hospital's integrative therapies center and radiation oncology department.

Reiki sessions were given in a quiet, private room twice weekly for 8 consecutive weeks for a maximum total of 16 sessions. Twice weekly sessions were recommended by the Reiki practitioners as a reasonable norm of practice and to counterbalance the RRT, which was given only once per week but included recommended daily practice of the relaxation response and journaling. Sessions were given by 1 of 3 nurses who were very experienced master

level Reiki practitioners and lasted approximately 50 minutes. During the session, the patient lay comfortably on a massage table, fully clothed. The practitioner placed her hands on the subject in 12 designated areas of the body with the intent to balance the subject's *chi* (life energy). A standardized protocol was followed to minimize variability among practitioners. The practitioners met periodically to review the protocol for practitioner consistency and discuss other study procedures.

In accordance with standard protocols, RRT/CR sessions were conducted weekly for 8 consecutive weeks (total of 8 sessions) in a quiet, private room by a psychologist (AW). At the beginning of each 60-minute session, the therapist guided the subject to evoke the relaxation response using a standardized script. The remainder of the session was devoted to cognitive restructuring using a systematic and replicable methodology involving 5 standardized steps: self-monitoring using a home diary; recognizing how thoughts are distorted, illogical or untrue; challenging the negative thoughts; replacing negative thoughts with more rational responses; and training to practice the new internal dialogue in the outside world. The therapist's goal was to aid the patient in developing skills that would help him cope with negative thoughts and life's stresses. In this arm, subjects were encouraged to practice RRT/CR techniques daily between sessions and to document these in a home journal.

### Outcome Measures

Psychosocial tests included the following:

- Spielberger State Anxiety Inventory (STAI)<sup>26</sup>;
- Center for Epidemiologic Studies Depression (CES-D) scale<sup>27</sup>; and
- Functional Assessment of Cancer Therapy-General (FACT-G) Scale.<sup>28</sup>

The STAI consists of 20 items, each scored from 1 to 4 on a Likert scale ranging from "never" to "almost always" this metric has a maximum score of 80, with higher scores indicating greater anxiety. Responses with 1 or 2 missed items were included, and the total score was weighted accordingly. Responses with 3 or more missing responses were purged. *Anxiety* is defined by a STAI score of 42 or higher.

The CES-D is a 20-item instrument that measures the frequency of depressive affect, somatic symptoms, positive affect, and interpersonal relations during the previous week on a 4-point scale from 0 ("rarely or none of the time") to 3 ("most of the time"). The maximum score is 60,

and higher scores indicate more severe depression. A cutoff score of 16 is used to define clinically significant depression.

The FACT-G (version 4.0), developed by Cella and colleagues,<sup>15</sup> is a cancer-specific quality of life questionnaire that consists of a 27-item core quality-of-life measure grouped into 4 subscales: physical well being, social/family well being, emotional well being, and functional well being. Most items are rated on 5-item Likert scales ranging from 0 for "not at all" to 4 for "very much." Higher scores indicated worse functioning on the overall instrument, but on the emotional well-being subscale higher scores reflect better functioning. Responders needed to have answered at least 80% of all questions for the total FACT-G score to be calculated.

### Analysis Plan

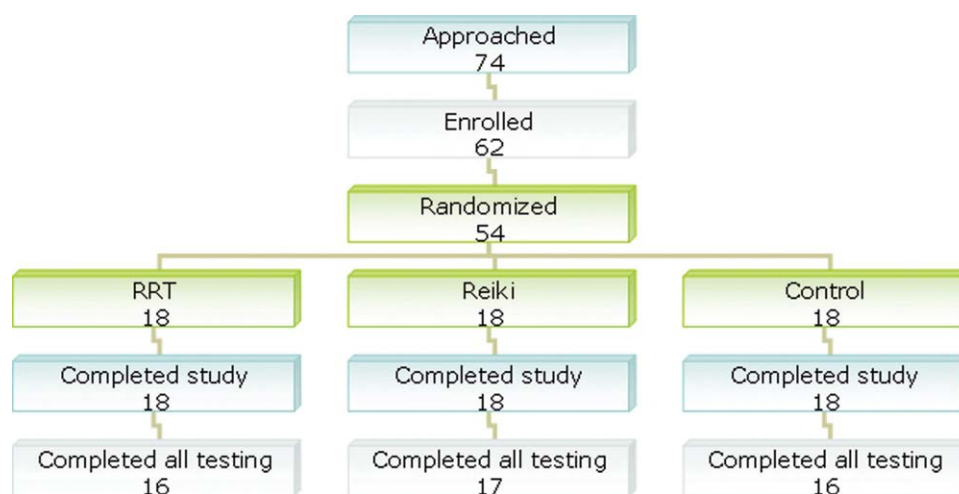
The study's aims were to assess success in enrolling men into the study, monitor adherence to study protocols, and examine the effects of Reiki and RRT/CR on psychosocial outcomes.

The primary outcomes were state anxiety measured by the STAI, depression as measured by the CES-D, and functional status measured by the FACT-G. Change scores were calculated for each outcome measure. Because changes over time were not linear, area-under-curve (AUC) analyses were used to compare differences between treatment arms. For each study outcome, AUC was calculated for the active treatment period (3 time points) and the entire study period, including post-treatment follow-up (4 time points). ANOVA<sup>29</sup> was used to test for differences among study arms. The Wilcoxon<sup>30</sup> signed-rank test was used to gauge whether anxious or depressed patients were significantly improved at the end of treatment. The Wilcoxon rank sum test was used to determine whether participants who were classified as *anxious* or *depressed* at baseline benefited more or less than those who were not. A Bonferroni-adjusted *P*-value of .017 was considered statistically significant for all 3-way comparisons.

## RESULTS

### Study Population

Seventy-four men satisfied eligibility requirements and were approached. Of these, 62 completed enrollment questionnaires and 54 were ultimately randomized into the study (Fig. 1). Reasons given for refusals to complete enrollment questionnaires included the time commitment and conflicts with work (6 participants), concerns over participating in any study (4 participants), disease progression,<sup>1</sup> and an unexpected family emergency.<sup>1</sup> Six men did not give a specific reason for not participating.



**Figure 1.** A consort diagram depicts the study population.

**Table 1.** Study Population: Baseline Demographic and Clinical Characteristics

Intervention Group	Reiki n=18 No. (%) [Range]	RRT n=18 No. (%) [Range]	Control n=18 No. (%) [Range]
Age, y (median and range)	62 [50-77]	66 [46-91]	65 [56-77]
<b>Age, y</b>			
<65	12 (67)	11 (61)	9 (50)
≥65	6 (33)	7 (39)	9 (50)
Race (white)	17 (94)	16 (89)	16 (89)
Marital status (married)	14 (78)	14 (78)	16 (89)
Education (college degree or more)	13 (72)	12 (67)	15 (83)
ECOG performance status (fully functional)	17 (94)	18 (100)	17 (94)
<b>Treatment category</b>			
Radiation therapy without AST	2 (11)	1 (6)	2 (11)
Radiation with AST	16 (89)	17 (94)	16 (89)
Prior prostatectomy	3 (17)	2 (11)	3 (17)

RRT indicates relaxation response therapy; ECOG, Eastern Cooperative Oncology Group; AST, androgen-suppression therapy.

The 3 treatment groups were similar in their baseline demographic and clinical characteristics (Table 1). Participants had a median age of 64 years; 91% were white, 82% were married, and more than three-quarters had received at least a college degree. Ninety-one percent were taking androgen suppression therapy (AST) at the time of randomization. Eight participants had undergone a prior prostatectomy.

#### **Adherence to the Study Protocol**

In the RRT group, 16 of 18 (88%) participants attended all weekly sessions. Regular attendance at twice weekly Reiki sessions occurred in 15 of 18 (83%) participants. Psychological and physiological testing was completed by

80% to 100% of participants at different experimental time points, and 86% completed the follow-up assessment.

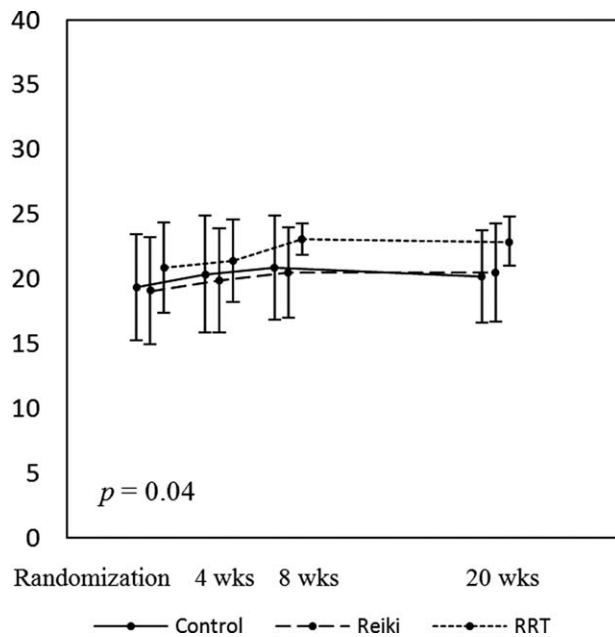
#### **Psychosocial Outcomes**

No statistically significant differences were found among study arms on any of the 3 major psychological outcome measures (STAI, CES-D, or FACT-G) either at the end of the intervention period or at the end of follow-up. Interpretation of this result, however, needs to take into account that this pilot study was not powered to detect significant differences between study groups. Trends favoring the intervention groups in area under the curve (AUC) analyses using ANOVA were found on the STAI anxiety scale ( $P = .08$ ) and the FACT-G quality of life scale ( $P = .13$ ).

**Table 2.** Effects on Levels of Anxiety in Anxious and Nonanxious Participants (Wilcoxon Rank-Sum Test)

STAI Score	Condition at Baseline	No. at Baseline	No. at End of Study	Average Score at the Start	Average Score at the End	Average Difference End-Start	P
RRT	Anxious	6	4	51	30	-19	.02
	Normal	12	12	27	26	-2	
Reiki	Anxious	5	5	49	40	-9	.10
	Normal	12	11	28	26	-2	
Control	Anxious	5	5	49	45	-4	.19
	Normal	13	11	28	31	3	

STAI indicates State-Trait Anxiety Inventory; RRT, relaxation response therapy.



**Figure 2.** Reiki therapy and control groups on the emotional well-being subscale of the FACT-G scale are compared for response to relaxation technique.

### Effects in Anxious Participants

Subgroup analyses compared the effects of RRT and Reiki therapy on participants who were *anxious* at baseline as indicated by STAI score of 42 or higher. Effects of RRT were significantly positive ( $P = .02$ ), and a positive trend was found in the Reiki group ( $P = .10$ ). Table 2. ANOVA indicated that, overall, the presence of anxiety at baseline was significantly associated with favorable changes in the STAI scores ( $P = .0004$ ).

### Functional Assessment of Cancer Therapy

#### Effects on emotional well-being

Although neither intervention had statistically significant effects on overall FACT-G scores, analysis of the emotional well-being subscale of this instrument indi-

cated statistically significant effects of the RRT intervention over the Reiki arm ( $P = .02$ ) and the control arm ( $P = .01$ ).

#### Depression scores

Effects on depression were characterized by CES-D scores. Results need to be interpreted in light of the decision to exclude from the study patients who were receiving treatment for depression. Although no overall improvement was found, a statistically significant decrease was identified in the 7 participants who were *depressed* at baseline (CES-D scores of 16 or higher) [ $P = .05$ ]. These individuals were divided evenly among the 3 intervention groups.

### DISCUSSION

This pilot study found that men with prostate cancer were indeed interested in participating in controlled trials of CAM treatments. The study yielded encouraging results suggesting that RRT and Reiki therapy may improve outcomes in such patients. Principal findings were: 1) reductions in anxiety in both treatment groups in patients who were anxious at baseline, 2) reductions in depression scores in men who met CES-D criteria for major depression at baseline, and 3) statistically significant improvements in the sense of emotional well-being in men who received RRT.

A carefully performed meta-analysis of 37 controlled studies of psychosocial interventions, ranging from patient education to coping skills training and psychotherapy in 3120 adult cancer patients, found a statistically significant overall effect size.<sup>31</sup> The single most important moderating variable was the length of the intervention, with durations of more than 12 weeks being more effective. Males responded at least as well as females. Only 2 controlled studies of CAM therapies have focused on men with prostate cancer.<sup>32,33</sup> In one, 30 subjects were

randomized to either observation, acupuncture, or sham acupuncture.<sup>32</sup> No significant differences in outcomes were found between groups in this small study. The other study included 191 men and examined a 10-week group-based, cognitive-behavioral stress management intervention compared with an education-only control group.<sup>33</sup> Quality of life, measured by the Functional Assessment of Cancer Therapy (FACT) instrument, was significantly better in the intervention (treatment) arm ( $P < .01$ ). These published studies, together with our own study, underscore the need for larger, well-designed clinical studies that define the appropriate role of CAM therapies in men with prostate cancer undergoing active conventional treatment.

The strengths and limitations of our clinical study need to be emphasized. Strengths included the careful attention given to study design, such as patient selection criteria, the choice of well-validated instruments to measure key outcomes, and randomization strategies. The high enrollment rate for men who met eligibility criteria (84% enrolled and 73% randomized) and high rates of adherence support the external and internal validity of these findings, respectively. The major limitations of the study are its relatively small sample size and the finding that participants were predominantly well-educated white men. Hence, the study's results may not be generalizable to more sociodemographically heterogeneous populations. A larger randomized trial in a more diverse population will be needed to verify and extend the study's findings.

## CONFLICT OF INTEREST DISCLOSURES

Research support for this study was provided by the Advanced Medical Research Foundation, Boston, Massachusetts.

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