Although many factors influence cancer-related outcomes, the potential relevance of psychosocial variables such as quality of life (QOL) and stress is becoming increasingly recognized (Gotay, Kawamoto, Bottomley, & Efficace, 2008; Montazeril, 2009). Reviews have suggested a positive relationship between QOL (Montazeril, 2009) and cancer survival, as well as a negative relationship between stress and cancer-related outcomes (Chida, Hamer, Wardle, & Steptoe, 2008). In addition, poor QOL and high stress can contribute to long-term life disruption and emotional distress that can last well into survivorship (Andersen, 2002).

Mediators of the relationships between QOL, stress, and cancer-related outcomes include health behaviors and compliance with medical care (Andersen, Kiecolt-Glaser, & Glaser, 1994). Andersen et al. (1994) conceptualized many of these pathways in the Biobehavioral Model of Cancer Stress and Disease Course. The model posits that high levels of stress and poor QOL have negative effects on health behaviors and compliance to medical care. In turn, poor health behaviors and compliance to medical care can negatively affect cancer-related outcomes. Reviews of observational and experimental studies in patients with cancer and other populations provide preliminary support for the pathways in the Biobehavioral Model of Cancer Stress and Disease Course (Andersen, 2002; Andersen et al., 1994).

Many studies show support for the Biobehavioral Model of Cancer Stress and Disease Course (Andersen, 2002; Andersen et al., 1994), but have only tapped into state-type measures of stress (i.e., stress level at a particular moment in time) through instruments such as the State-Trait Anxiety Inventory (Spielberger, Gorsuch, & Lushene, 1970) and the Profile of Mood States (McNair, Lorr, & Droppleman, 1971). However, given the transient nature of stress, examining stress reactivity—a measure of an individual’s response to stressful situations and indicative of the more stable trait anxiety—also is logical. Past research indicated that high levels of trait anxiety were associated with greater psychological distress in cancer survivors at all points of the cancer trajectory, from diagnosis to survivorship (Bleiker, Pouwer, van der Ploeg, Leer, &...
measurement of stress reactivity gives an indication of how an individual will react to stressful situations, including the stress associated with a cancer diagnosis, treatment, and survivorship, rather than merely during a single moment in time.

One method of examining stress reactivity is through the elicitation of an acute stress response within a laboratory environment using the Trier Social Stress Test (TSST) (Kirschbaum, Pirke, & Hellhammer, 1993; Kudielka, Hellhammer, & Kirschbaum, 2007). The TSST features the use of public speaking and math tasks to create a situation with a high level of social evaluative threat as well as a feeling of uncontrollability. The acute stress response elicited by the TSST is indicative of individual stress reactivity and can be measured objectively by techniques such as heart rate variability (HRV) (Aubert, Seps, & Beckers, 2003) and salivary cortisol (Marques, Silverman, & Sternberg, 2010). Generally, HRV is found to decrease as arousal increases (Zhong et al., 2005). Salivary cortisol also may serve as an indicator of stress response by indicating activity of the hypothalamic-pituitary-adrenal (HPA) axis. In high-stress situations, the corticotrophin-releasing hormone and adrenocorticotropic hormone are released from the HPA axis, resulting in increased levels of salivary cortisol (Marques et al., 2010).

The purpose of the current study was to examine the relationships between stress reactivity (measured by HRV, salivary cortisol, and questionnaire), QOL, compliance to medical care, and health behaviors in a sample of post-treatment breast cancer survivors in the pathways outlined by the Biobehavioral Model of Cancer Stress and Disease Course. The authors hypothesized that breast cancer survivors showing higher levels of stress reactivity and poor QOL would practice the poorest health behaviors and show the lowest compliance to medical care. Those same participants were expected to indicate the poorest QOL.

Methods
Sample
Study approval was obtained from the University Medical Center Institutional Review Board at East Carolina University in Greenville, NC. Potential participants were recruited from an outpatient radiation oncology clinic in Greenville for follow-up appointments. Staff helped identify potentially eligible participants. Potential participants were informed about the study and provided informed consent if interested. Eligibility criteria included (a) being a female breast cancer survivor within five years of diagnosis, (b) being aged 18 years or older, (c) having no cognitive impairment, and (d) being able to provide written, informed consent.

Instruments
Diet: Dietary assessment was determined by the Dietary Risk Assessment (Jilcott et al., 2007). Participants were required to respond to 54 questions recalling average weekly consumption of a variety of foods. Scores of individual items were summed to create an overall Dietary Risk Assessment score ranging from 0–108; higher scores are indicative of a less healthful diet in terms of lower vegetable, fruit, and fiber intake and higher saturated fat content. The Dietary Risk Assessment has been found to be valid compared to food frequency questionnaires and analysis of serum carotenoids (Jilcott et al., 2007).

Physical activity: Physical activity was measured by the Seven-Day Physical Activity Recall (PAR) questionnaire (Sallis, 1997). The PAR requires participants to recall hours spent in moderate, hard, or very hard activity as well as hours of sleep in the past seven days. Total weekly energy expenditure was calculated by summing the product of hours at each activity level multiplied by their respective metabolic equivalent task (MET) value (i.e., sleep = 1 MET per hour; moderate = 4 METs, hard = 6 METs, and very hard = 10 METs). The PAR questionnaire has been found to be reliable according to a number of studies assessing test-retest and validity compared to a number of objective measures (Sallis, 1997).

Smoking: History of smoking was assessed by self-report recall of the average number of cigarettes smoked per day in the past seven days.

Alcohol consumption: A person’s alcohol consumption was measured by self-report recall of the number of alcoholic beverages consumed on each day in the past week.

Quality of life: The Functional Assessment of Cancer Therapy–Breast (FACT-B) scale (Brady et al., 1997; Cella et al., 1993) was used to measure QOL. The FACT-B consists of five subscales: physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB), functional well-being (FWB), and additional concerns (AC). All items were rated on a five-point Likert scale ranging from 0 (not at all) to 4 (very much). Higher scores are indicative of higher QOL. The FACT scales have been found to be high in convergent validity when compared to another measure of QOL (r = 0.87), low in divergent validity when compared to a measure of social desirability (r = 0.07), and have acceptable internal consistency (Cronbach alpha = 0.9) and test-retest reliability (r = 0.85) (Brady et al., 1997; Cella et al., 1993).

Self-report state and trait anxiety: State and trait anxiety were measured using the State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1970). The STAI is a 20-item self-report questionnaire that assesses trait and state anxiety on a four-point Likert scale ranging from 1 (not at all) to 4 (very much so), with higher values indicating higher levels of anxiety. The STAI scale
Levels of salivary cortisol were found to have high intercorrelation of items (r = 0.7), high retest reliability for the trait scale (r = 0.8) and low for the state scale (r = 0.35), and high concurrent validity when compared with other measures of anxiety (r = 0.73–0.83) (Spielberger et al., 1970; Spielberger, Reheiser, Ritterband, Sydeman, & Unger, 1995).

Heart rate variability: HRV was assessed using an HRV analysis system scanner via an ear piece sensor. The manufacturer’s instructions for data collection were followed. HRV provides a quantitative multidimensional measure of autonomic, sympathetic (SA), and parasympathetic (PS) modulation of cardiac function. HRV is a nonspecific marker of autonomic nervous system function and, therefore, is a good measure of stress response. Standard deviation of normal-to-normal (SDNN) heartbeats represents a general indicator of HRV and acute stress response. The authors hypothesized that, as stress increased, SDNN would decrease (i.e., lower HRV).

Salivary cortisol: Levels of salivary cortisol were measured using saliva samples obtained on cotton swabs. During each sampling, participants were asked to insert a cotton swab into the mouth and hold it under the tongue for about one minute. The saturated swab was deposited into a microfuge tube that was capped and stored in a −80°C freezer with a numeric indicator on it. Tubes were mailed to and analyzed by Salimetrics in State College, PA. Because of diurnal variation in cortisol as well as the influence of other factors on cortisol levels, such as age and adiposity (Larsson, Gullberg, Rastam, & Lindblad, 2009), time of awakening (Edwards, Evans, Hucklebridge, & Clow, 2001), and cancer-related fatigue (Bower et al., 2005), intra-individual differences between basal and post-TSST values were used for all analyses. Greater increases in salivary cortisol readings in response to the TSST were interpreted as a higher stress response (Marques et al., 2010).

Compliance with medical care: How a participant was in compliance with medical care was determined retrospectively from medical records of missed and attended appointments at the cancer center from diagnosis to the date of recruitment. Appointments following diagnosis and treatment are important for monitoring treatment, detecting recurrence, addressing side effects and late effects from treatment, providing supportive care, and managing psychosocial issues (Rose & Watson, 2009). Attendance of scheduled appointments was therefore used as a measure of compliance to medical care, given its importance for ensuring optimal prognosis and well-being for cancer survivors.

Disease information: Information about each participant’s disease was assessed from health records and self-report and consisted of information on stage, treatment received, date of diagnosis, height, and weight. Height and weight were used to calculate body mass index.

Demographic information: Information about age, ethnicity, education, income, and marital status was collected by self-report.

Procedures

After consent was obtained, participants took home a questionnaire package consisting of the STAI and demographic information and made an appointment time for the Visual Motor Laboratory (VML) at East Carolina University. Participants were asked to refrain from eating or drinking anything except for water for 1.5 hours before the appointment and to not drink any caffeinated beverages for three hours prior to the appointment. Upon arrival at the VML, participants rested for five minutes, then completed the state-anxiety portion of the STAI, provided a saliva sample, and completed a five-minute interval of resting heart rate recording.

To induce a stress response, participants were subjected to the TSST (Birkett, 2011). For the talk stressor, participants were asked to prepare a five-minute speech that they would give if they had a traffic violation that had to be defended in court. Participants were given five minutes to prepare the speech and were told that their performance would be videotaped and later evaluated for content, style, and believability by a panel of professionals. Although a video camera on a tripod was situated in front of the participant, no actual videotaping occurred. Following the speech, participants then were asked to complete the math stressor. This task involved counting aloud backwards from 2,083 to 0 in 13-step sequences in time to a metronome. Participants were told that their performance was being documented and would later be compared with other participants in the study. Once five minutes of the math calculation task had elapsed, the subtraction task was terminated.

A saliva sample was taken following the speech task and again following the math task. Heart rate was recorded during the five-minute speech task and again during the five-minute math task. Participants also completed the state anxiety portion of the STAI at the conclusion of the math task. After all measurements were taken, participants were debriefed about the study.

Participants were asked to complete and mail in the follow-up questionnaire (PAR, the modified Dietary Risk Assessment Tool, smoking behavior, and alcohol use) in the provided stamped envelope one week after the testing session. A reminder telephone call was made to all participants to complete and mail in the questionnaire.

Statistical Analyses

Means, standard deviations, and frequencies of demographic, medical, and outcome variables were assessed with descriptive statistics. Differences in
stress response based on demographic and medical variables were examined using independent t tests and chi square analyses.

To determine the effectiveness of the TSST in causing an acute stress response as measured by (a) the STAI, (b) cortisol, and (c) HRV, a 2 (group) x 3 (time) repeated-measures multivariate analyses of variance (MANOVAs) were employed.

A discriminant analysis was conducted to classify participants into either higher or lower stress response groups based on changed scores in the STAI (Spielberger et al., 1970), HRV, and salivary cortisol response to the TSST.

Separate one-way ANOVAs were conducted to indicate differences in each of the health behaviors, FACT-B, and each of its subscales based on the stress response group. Additional one-way ANOVAs were performed to test for differences in stress response as determined by the (a) STAI, (b) HRV, and (c) salivary cortisol response based on compliance to medical care. For these analyses, median splits were used to dichotomize compliance to medical care into higher and lower groups. Stress responses were used as continuous variables. Additional linear regression analyses were conducted to examine relationships between stress response scores and compliance to medical care.

### Results

A total of 25 participants entered and completed the study. Descriptive statistics revealed that the mean age was 56 years, the mean body mass index was 31.8, and the average months since diagnosis was 26.7. Most participants had been diagnosed with early-stage cancer and all reported receiving radiation therapy. The majority of the participants were Caucasian, not married, and had obtained a post-secondary education or higher. In addition, most reported not working and having an annual household income of less than $40,000 (see Table 1). No significant differences in anxiety levels were noted based on any of the demographic or medical variables (all p < 0.05).

Details of descriptive statistics of stress response outcomes, QOL, and health behavior variables are displayed in Table 2. In brief, the mean overall HRV at baseline was 150.8 and dropped to 107.5 during the talk stressor and 103.4 during the math stressor. Salivary cortisol rose from 0.186 mcg/dl during baseline to 0.196 mcg/dl during the talk stressor and 0.252 mcg/dl during the math stressor. State anxiety score was 36.16 at baseline and 45.66 during the talk and math stressors. The mean score for trait anxiety was 45.6, the average score on the FACT-B was 108.7, an average of 74% of appointments were attended, the mean weekly energy expenditure was 281.5 kcal/kg, less than one cigarette was smoked on average per day, 1.1 alcoholic beverages were consumed in the prior week, and the dietary risk assessment score was 31.1.

Results of the discriminant analysis indicated that the overall Wilk’s lambda was significant (λ = 0.62, χ² [4, N = 25] = 9.74, p < 0.01), suggesting that the predictors significantly differentiated two stress response groups: higher and lower. The authors were able to classify 14 (56%) participants into the higher stress response group and 11 (44%) into the lower stress response group.

The MANOVA examining the acute stress response test revealed a significant main effect for time (Wilk’s λ = 0.678, F₃,₁₆ = 8.86, p < 0.05, η² = 0.596). Follow-up 2 (group) x 3 (time) univariate ANOVA with repeated measures on the last factor were conducted on HRV, cortisol, and state anxiety. Analysis of HRV data indicated a significant time main effect (F₂,₁₈ = 8.86, p < 0.001, η² = 0.33). Both groups demonstrated a change in HRV from baseline following the laboratory stress manipulations. Salivary cortisol also increased during the TSST, although no significant differences were found (p > 0.05).

The 2 (group) x 2 (time) univariate ANOVA for state anxiety (STAI) indicated a significant main effect for time (F₂,₁₈ = 10.86, p < 0.001, η² = 0.33). Simple effects analysis

### Table 1. Demographic and Medical Characteristics of the Study Sample (N = 25)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>X</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56</td>
<td>12.6</td>
</tr>
<tr>
<td>Body mass index</td>
<td>31.8</td>
<td>7.9</td>
</tr>
<tr>
<td>Months since diagnosis</td>
<td>26.7</td>
<td>13.1</td>
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</table>

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage (N = 23)</td>
<td></td>
</tr>
<tr>
<td>In situ</td>
<td>3</td>
</tr>
<tr>
<td>I</td>
<td>10</td>
</tr>
<tr>
<td>II</td>
<td>6</td>
</tr>
<tr>
<td>III</td>
<td>4</td>
</tr>
<tr>
<td>IV</td>
<td>4</td>
</tr>
<tr>
<td>On hormone therapy</td>
<td>12</td>
</tr>
<tr>
<td>Received chemotherapy</td>
<td>25</td>
</tr>
<tr>
<td>Received radiation therapy</td>
<td>25</td>
</tr>
<tr>
<td>Ethnicity</td>
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<tr>
<td>Caucasian</td>
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</tr>
<tr>
<td>African American</td>
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</tr>
<tr>
<td>Marital status</td>
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<td>12</td>
</tr>
<tr>
<td>Not married</td>
<td>13</td>
</tr>
<tr>
<td>Yearly household income ($) (N = 24)</td>
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</tr>
<tr>
<td>Less than 40,000</td>
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<tr>
<td>40,000 or greater</td>
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<tr>
<td>Employment (N = 24)</td>
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<td>Education</td>
<td></td>
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<td>High school or less</td>
<td>6</td>
</tr>
<tr>
<td>Post-secondary or higher</td>
<td>19</td>
</tr>
</tbody>
</table>
revealed that both groups increased significantly from baseline (higher stress: $X = 35.15, SD = 5.77$; lower stress: $X = 37.36, SD = 5.65$) to following the TSST (higher stress: $X = 44.76, SD = 5.34$; lower stress: $X = 46.72, SD = 6.95$).

Significant differences were found in QOL based on the stress response groups. Specifically, the lower stress response group indicated higher scores on the FACT-B ($F_{1,20} = 8.72, p < 0.05, \eta^2 = 0.3$) and FWB ($F_{1,20} = 11.18, p < 0.01, \eta^2 = 0.36$), PWB ($F_{1,20} = 6.65, p < 0.01, \eta^2 = 0.24$), and AC subscales ($F_{1,20} = 9.86, p < 0.01, \eta^2 = 0.33$) (see Figure 1). No significant differences were noted in any of the health behaviors between stress response groups (all $p > 0.05$).

Participants high in compliance to medical care indicated a lower stress response as determined by HRV ($X = 64.74, SD = 22.02$) compared to participants low in compliance ($X = 148.27, SD = 90.96$; $F_{1,19} = 7.78, p < 0.01, \eta^2 = 0.29$). Similarly, state anxiety levels varied as a function of compliance to medical care ($X = 39.31, SD = 4.64$ for low compliance; $X = 42.7, SD = 7.1$ for high compliance; $F_{1,19} = 4.612, p < 0.05, \eta^2 = 0.18$).

A linear regression analysis was conducted to evaluate how HRV response to an acute stressor predicted compliance to medical care. The scatterplot for the two variables (see Figure 2) demonstrates that the two variables are linearly related such that as stress response to an acute stress increases, so does the likelihood of low compliance to medical care: $HRV = -82.18$ low compliance + 157.366 (F $p < 0.01$). HRV accounted for 31% of the variance in compliance to medical care. No significant relationships were noted between (a) the FACT-B and its subscales, and (b) compliance to medical care with health behaviors (all $p > 0.05$).

**Discussion**

In the current study, FACT-B scores differed by 15 points between higher stress response and lower stress response groups. That finding is clinically meaningful given that differences of 7–8 points in the FACT-B constitute minimally important differences based on performance status and pain anchors (Eton et al., 2004). In addition, QOL issues are a major concern in breast cancer survivorship given the prevalence of QOL disturbances such as mood, fatigue, lymphedema, cognitive dysfunction, and reproductive and menopausal symptoms (Pinto & de Azambuja, 2011).
Although past studies have indicated a relationship between markers of stress (e.g., perceived stress, life events) and QOL (Beatty, Lee, & Wade, 2009; Golden-Kreutz et al., 2005), the current study was the first to indicate a similar relationship using stress reactivity. The results suggest the importance of considering not only the role of acute stress in QOL endpoints in breast cancer survivors, but the additional role of stress reactivity.

In line with the biobehavioral model and with the authors’ hypotheses was the inverse relationship between compliance to medical care and stress reactivity. Previous research of noncancer populations has suggested that individuals indicating high levels of stress are less likely to comply with medical care, such as preventive care (Thorpe, Kalinowski, Patterson, & Sleath, 2006), antiretroviral therapy (Royal et al., 2009), and follow-up after benign breast biopsy (Andrykowski et al., 2001).

To date, very little research has examined compliance with medical care in cancer populations; however, adherence to medical procedures and appointments in patients with cancer is critical for ensuring the best possible outcomes (Van der Meer & Loock, 2008). In cancer survivorship, follow-up cancer care also is important to check for recurrence and new cancers as well as address the many concerns relevant to survivorship, such as treatment or cancer-related side effects and other changes in physical or mental health (National Cancer Institute, 2010). The National Cancer Institute (2010) has recommended that all cancer survivors receive follow-up cancer care, generally every three to four months for the first two to three years after treatment and then once or twice a year in the following years to ensure optimal surveillance and the best QOL outcomes. Based on the results of the current study and those in other populations, clinicians may be advised to identify breast cancer survivors with high stress reactivity and provide additional support to maximize compliance to medical care.

Contrary to the biobehavioral model and the authors’ hypotheses, health behaviors in the current study were not associated with stress reactivity. In contrast, many studies have indicated that stress may have a negative impact on health behaviors marked by appetite disturbances, the desire to self-medicate using alcohol or tobacco, as well as a diminishment in physical activity (Andersen et al., 1994). A review of psychological factors and behavior change in cancer survivors, however, suggested that cancer-related distress may facilitate positive health behavior change while general distress may negatively impact health behaviors (Park & Gaffey, 2007). The findings suggest that the type of stress determines the influence on health behaviors. Given the authors’ measure was of stress reactivity, how much stress and the type of stress that was present during the week after testing (i.e., during the week information on health behaviors was collected) is unknown. In addition, given that all participants were at varying points in cancer survivorship, the authors also are uncertain how much cancer-related stress was affecting participants at the time of assessment. Future research addressing stress reactivity, life events, and state anxiety during the time of the assessment of health behaviors in cancer survivors may yield different results.

Contrary to the authors’ hypotheses was the finding that QOL was not related to any of the health behaviors or compliance to medical care. That finding is surprising given the significant positive relationships between QOL and positive health behaviors in other studies of cancer survivors (Park & Gaffey, 2007). For example, interventional and cross-sectional studies have repeatedly shown that physical activity and diet

![Figure 1. Quality-of-Life Scores in Higher and Lower Stress Response Groups](image)

![Figure 2. Relationship Between Heart Rate Variability and Compliance to Medical Care](image)
are positively associated with improved QOL in cancer survivors, both during treatment and in survivorship (Demark-Wahnefried, Morey, Sloane, Snyder, & Cohen, 2009; Speed-Andrews & Courneya, 2009). Similarly, smoking (Gritz, Dresler, & Sarna, 2005) and excessive alcohol use (Llewellyn, McGurk, & Weinman, 2005) after cancer diagnosis have been associated with reduced QOL. Possibly, in the current study, QOL was not related to some of the health behaviors because of the relatively small number of participants engaging in poor health behaviors. For example, the mean number of cigarettes smoked per day and the average number of alcoholic drinks per day were around one. Similarly, energy expenditure was fairly high on average and the mean dietary risk assessment score was relatively low. Therefore, lack of variability in health behaviors may have contributed to lack of association between health behaviors and QOL.

Limitations

The main limitation of this study is the small sample size. A larger sample may have increased power and sensitivity to detect differences, as well as reduced the rate of detecting a false positive. A larger sample also may have provided greater variability in health behaviors that may have yielded different findings in terms of relationships between stress reactivity and health behaviors. Another limitation is the self-report nature of the health behaviors measured. Participants may have been subject to social desirability bias and provided more favorable responses in terms of their health behaviors. Alternatively, the sample may have been practicing better health behaviors than expected because of the self-selection of the sample.

Conclusions

The data suggest that breast cancer survivors who indicate the greatest acute stress response to a laboratory stressor and possibly to other stressors tend to have the poorest compliance to medical care. Because adherence to medical treatment and follow-up visits is important for effective cancer control, knowledge of variables that influence compliance to medical care is important for optimizing patient care. Contrary to the authors’ hypotheses, stress reactivity was not found to be related to any health behaviors. Also, unexpectedly, the findings indicated that QOL was not associated with any of the health behaviors or compliance to medical care. Additional research with a larger sample may be needed to better understand the relationships between stress reactivity, QOL, compliance to medical care, and health behaviors.

Implications for Nursing

High stress reactivity may have negative implications for compliance to medical care and QOL in breast cancer survivors. Therefore, it may be prudent for oncology nurses to provide extra care or references for auxiliary help and support to patients who indicate high levels of stress reactivity. In practice, stress reactivity can be approximated by the use of brief clinical screening tools such as the Distress Thermometer (National Comprehensive Cancer Network, 2005). Ultimately, intervention strategies that provide additional support to breast cancer survivors indicating high stress reactivity may be needed for ensuring optimal compliance to medical care and QOL.

Kristina H. Karvinen, PhD, is an assistant professor in the School of Physical and Health Education at Nipissing University in North Bay, Ontario, Canada; Nicholas P. Murray, PhD, is an associate professor in the Department of Kinesiology, and Hyder Arastu, MD, is a clinical professor in the Department of Radiation Oncology in the Brody School of Medicine, both at East Carolina University in Greenville, NC; and Ron R. Allison, MD, is the medical director for 21st Century Oncology in Greenville, NC. No financial relationships to disclose. Karvinen can be reached at kristinak@nipissingu.ca, with copy to editor at ONFEditor@ons.org. (Submitted April 2012. Accepted for publication July 10, 2012.)

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