

cal antipsychotic medications . . . unless they have been initiated by a psychiatrist.” Aripiprazole and quetiapine are both approved by the US Food and Drug Administration for augmentation pharmacotherapy of major depressive disorder. Given a shortage of psychiatrists,<sup>5</sup> and wait times of up to 3 months to see a psychiatrist, and in an age when psychiatric disorders are the leading source of medical disability, it is imperative for primary care physicians to learn how to safely use any and all available interventions, including the appropriate use and monitoring of atypical antipsychotics.

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**In Reply:** Drs Karp and Whyte raise 2 important points regarding the management of depression in primary care settings. First, depressive symptoms can overlap with those of OSA. Therefore, in a patient with OSA, it is important to inquire about compliance with the CPAP device, verify proper mask fit, and consider modafinil if excessive daytime sleepiness persists despite appropriate therapy.

Second, patients with depression have a high prevalence of comorbid anxiety disorders, and screening with the 2-item Generalized Anxiety Disorder scale can improve case identification. Whether routine screening for anxiety disorders benefits primary care patients has not been determined. However, first-line therapies (cognitive behavioral therapy and selective serotonin reuptake inhibitors) are the same for both depression and anxiety disorders,<sup>1-3</sup> so patients treated for major depressive disorder will usually receive therapy for both conditions.

Karp and Whyte also are concerned about my statement that “Primary care physicians should not prescribe atypical antipsychotic medications . . . unless they have been initiated by a psychiatrist.” They suggest there are cases when it might be appropriate for a primary care

physician to initiate an atypical antipsychotic as an augmentative pharmacotherapy. Atypical antipsychotics are indeed effective augmentation agents for treatment-resistant major depressive disorder. However, they have a high risk of adverse effects, such as the metabolic syndrome and extrapyramidal symptoms, and have been associated with rare but serious complications, such as tardive dyskinesia and neuroleptic malignant syndrome.<sup>4</sup> There is no evidence that atypical antipsychotics are more effective than tricyclics, lithium, thyroid hormone, or other available augmentation therapies for major depressive disorder.<sup>5</sup> Therefore, unless a primary care physician has the expertise to select one of these strategies for a patient who has experienced failure with all first- and second-line therapies (psychotherapy, selective serotonin reuptake inhibitors, bupropion, serotonin nor-epinephrine reuptake inhibitors, and mirtazapine), I believe that a psychiatrist should be consulted.

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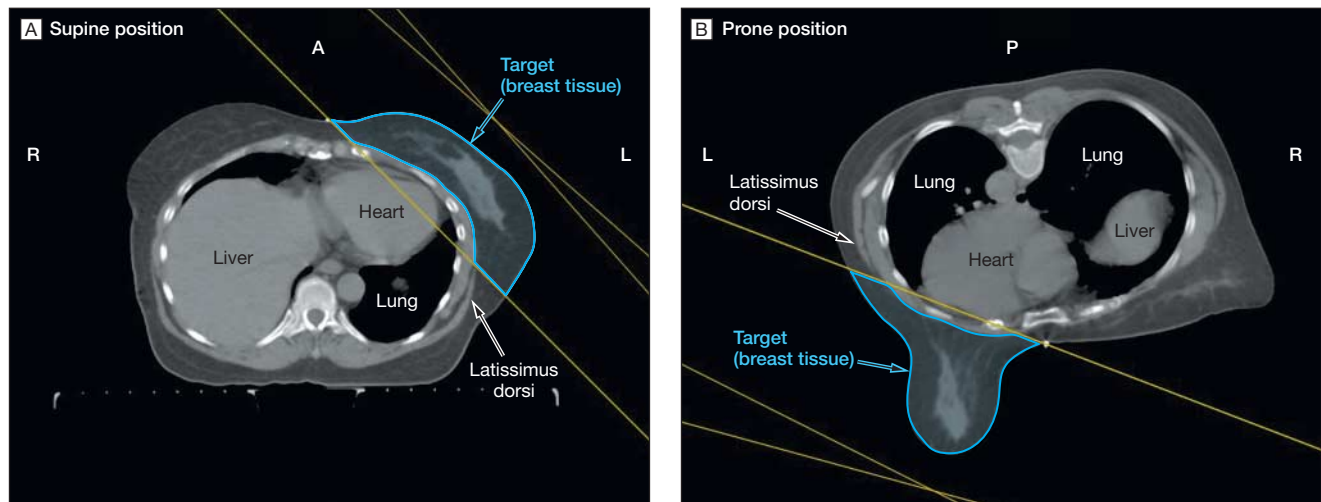
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## RESEARCH LETTER

### Prone vs Supine Positioning for Breast Cancer Radiotherapy

**To the Editor:** Adjuvant radiotherapy to the breast contributes to improved outcomes in breast cancer patients after breast preservation surgery.<sup>1</sup> However, whole breast radiotherapy is associated with damage to the heart and lung, increased cardiovascular mortality, and lung cancer development, with risks that remain 15 to 20 years after treatment.<sup>2</sup> These consequences occur when breast cancer patients are treated supine. Preliminary data on prone positioning suggest that radiation exposure to the heart and lung can be reduced compared with supine positioning<sup>3,4</sup> with similar efficacy.<sup>5</sup> To test the hypothesis that prone positioning is superior to standard supine positioning, we compared the volume of heart and lung within the radiation field in a pro-

**Figure.** Example of a Patient With Better Exclusion of the Heart and Lung When Prone

Placing the posterior edge of the fields on a plane connecting the midline to the anterior extent of the latissimus dorsi muscle ensures comparable breast coverage.

spective study of patients who underwent simulation in both positions.

**Methods.** From November 15, 2005, to December 26, 2008, patients with stage 0-IIA breast cancer, segmental mastectomy, negative surgical margins, and 3 or fewer involved lymph nodes referred to New York University Radiation Oncology were eligible for the study. Each patient underwent 2 computed tomography (CT) simulation scans, first supine and next prone. The dose from the second CT was justified ethically because additional imaging enabled the treating physician to choose the position that best spared heart and lung. The treating physician contoured target and normal structures and placed the treatment fields. Comparable coverage of the breast regardless of position was ensured by placing the posterior edge of the field on a plane connecting the midline to the anterior extent of the latissimus dorsi muscle, visualized at CT (FIGURE). In-field heart and lung volumes were then measured by 2 physicists (J.K.D. and G.J.) as reliable surrogates for dose.<sup>4</sup> Three breast volume groups were defined (<750 cm<sup>3</sup>, 750-1500 cm<sup>3</sup>, and >1500 cm<sup>3</sup>).

Two hundred patients per stratum (left and right breast cancer) were enrolled to detect differences smaller than  $\pm 0.30$  SD for each volume parameter between the supine and prone positions, using paired *t* tests with a 2-sided  $\alpha$  of .05 and power of 80%. Differences in in-field lung and heart volumes (and 95% confidence intervals) between the supine and prone positions for patients with left breast cancer and in lung volumes for patients with right breast cancer were estimated. Data analysis was performed using SAS software version 9.2 (SAS Institute Inc).

All patients provided written informed consent. The New York University institutional review board approved the study.

**Results.** Four hundred consecutive patients were prospectively accrued, approximately 60% of those eligible. Median age was 56.3 years (range, 30.7-94.3 years). Ethnicity was 322 (80.5%) white, 22 (5.5%) black, 21 (5.2%) Hispanic, 28 (7%) Asian, and 7 (1.7%) of other ethnicity. The primary insurance carrier was private in 310 (77%) patients, Medicare in 76 (19%), and Medicaid in 14 (4%). Eighty-six (21.5%) patients had ductal carcinoma in situ. Among the 314 (78.5%) patients with invasive breast cancer, 47 (14.96%) had involved sentinel or axillary lymph nodes.

In all patients, the prone position was associated with reduced in-field lung volumes compared with supine (TABLE) (mean difference: 104.6 cm<sup>3</sup> [95% CI, 94.26-114.95 cm<sup>3</sup>], an 86.2% reduction for right breast cancer; 89.85 cm<sup>3</sup> [95% CI, 80.16-99.55 cm<sup>3</sup>], a 91.1% reduction for left breast cancer). In patients with left breast cancer, the prone position was associated with a reduction of in-field heart volumes compared with supine (mean difference: 7.5 cm<sup>3</sup> [95% CI, 5.16-9.85 cm<sup>3</sup>], an 85.7% reduction). However, in 15% of patients with left breast cancer, the supine position was associated with less in-field heart volume compared with prone (mean difference: 6.15 cm<sup>3</sup>; 95% CI, 2.97-9.33 cm<sup>3</sup>). These reductions were statistically significant regardless of breast volume (with the exception of heart in women with breast size <750 cm<sup>3</sup>).

**Comment.** Prone positioning was associated with a reduction in the amount of irradiated lung in all patients and in the amount of heart volume irradiated in 85% of patients with left breast cancer.

The study is limited to a single institution. A multi-institutional prospective trial with outcome measures is warranted to confirm these findings. If prone positioning better protects normal tissue adjacent to the breast, the risks

**Table.** Differences in Volumes of Heart and Lung Between Supine and Prone Positions by Breast Volume and Right vs Left Breast Cancer

Breast Volume, cm <sup>3</sup>	Right Breast Cancer <sup>a</sup>				Left Breast Cancer						
	No.	In-Field Lung Volume, Mean (95% CI), cm <sup>3</sup>			No.	In-Field Lung Volume, Mean (95% CI), cm <sup>3</sup>			In-Field Heart Volume, Mean (95% CI), cm <sup>3</sup>		
		Supine	Prone	Difference of Supine Minus Prone <sup>b</sup>		Supine	Prone	Difference of Supine Minus Prone <sup>b</sup>	Supine	Prone	Change From Supine to Prone <sup>b</sup>
<750	73	122.80 (106.90 to 138.71)	20.91 (15.54 to 26.29)	101.89 (87.05 to 116.73)	78	90.64 (76.80 to 104.47)	17.56 (10.59 to 24.54)	73.07 (60.42 to 85.72)	3.09 (1.56 to 4.61)	2.60 (1.17 to 4.02)	0.49 (-1.62 to 2.60)
750-1500	91	120.71 (105.31 to 136.11)	17.47 (11.19 to 23.74)	103.24 (88.91 to 117.58)	84	110.44 (94.28 to 126.57)	3.65 (1.93 to 5.38)	106.78 (90.75 to 122.82)	10.38 (7.19 to 13.57)	0.57 (0.22 to 0.92)	9.81 (6.60 to 13.02)
>1500	36	120.20 (84.11 to 156.28)	6.66 (0.96 to 12.36)	113.54 (78.58 to 148.49)	38	88.68 (63.63 to 113.73)	1.81 (-1.55 to 5.17)	86.87 (61.50 to 112.23)	16.80 (8.46 to 25.13)	0	16.79 (8.45 to 25.13)
Total	200	121.38 (110.44 to 132.32)	16.78 (13.15 to 20.41)	104.60 (94.26 to 114.95)	200	98.58 (88.77 to 108.39)	8.73 (5.72 to 11.74)	89.85 (80.16 to 99.55)	8.75 (6.53 to 10.97)	1.25 (0.66 to 1.84)	7.50 (5.16 to 9.85)

<sup>a</sup>There was no in-field heart volume in any of the patients with right breast cancer.

<sup>b</sup>The 95% CIs are based on paired *t* statistics.

of long-term deleterious effects of radiotherapy may be reduced.

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**Author Contributions:** Dr Formenti had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Formenti, DeWyngaert, Goldberg.

**Acquisition of data:** Formenti, DeWyngaert, Jozsef.

**Analysis and interpretation of data:** Formenti, DeWyngaert, Goldberg.

**Drafting of the manuscript:** Formenti, DeWyngaert, Goldberg.

**Critical revision of the manuscript for important intellectual content:** Formenti, Jozsef, Goldberg.

**Statistical analysis:** Jozsef, Goldberg.

**Administrative, technical, or material support:** Formenti, DeWyngaert.

**Study supervision:** Formenti, Goldberg.

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**Role of the Sponsor:** The funding agency of the feasibility study on prone breast radiotherapy that permitted the current trial had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

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## CORRECTION

**Incorrect Author's Name:** In an Editorial entitled "The JAMA Network Journals: New Names for the Archives Journals," published in the July 4, 2012, issue of *JAMA* (2012;308[1]:85), one of the names in the byline had the wrong middle initial. The name should have appeared as Rita F. Redberg, MD, MSc. The article has been corrected online.