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14. **ABSTRACT** The purpose of this study is to use information collected from the parent study, the Women's Breast and Bone Density study (WBBD) to investigate the relationship between breast density and IGF levels in pre and postmenopausal Hispanic and non-Hispanic White women. The parent study was completed by the May 31, 2003. In all, recruitment was a lower than expected for the Hispanic women, but all recruitment goals were either met or exceed in the non-Hispanic White women. The total numbers are: 60 premenopausal Hispanic women, 75 premenopausal non-Hispanic White women, 28 postmenopausal Hispanic women, and 78 postmenopausal White women. The serum and plasma samples have been collected for the Insulin-like Growth Factor (IGF) and Insulin-like Growth Factor Binding Protein (IGFBP) assays used in this study (including IGF-1, IGFBP-3, and Free IGF-1), however, the actual analysis will be completed in October 2003 – November 2003. The mammographic density measurements are currently being finalized and will be merged with the data collected from questionnaires, physical measurements, and the dual energy x-ray absorptiometry (DXA) scan. When the laboratory analyses are complete, the results of those tests will be merged with the clean WBBD data so that the analysis can be completed and manuscripts written.

15. SUBJECT TERMS
Breast Cancer, Mammographic Density, Insulin-like Growth Factors, Ethnicity

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Introduction

Breast cancer is one of the most common cancers among Hispanic and non-Hispanic White women, although Hispanic women have considerably lower incidence rates. Many laboratory studies have focused on the role of Insulin-like Growth Factors (IGFs) in breast cancer development and progression. Recently, epidemiological studies have begun to investigate the association between breast cancer risk and circulating levels of IGFs and their binding proteins (IBFBPs). One study investigated the relationship between IGF levels and mammographic density, a known predictor for breast cancer, in a primarily Caucasian population. Most studies conclude that there is an association between circulating IGF and IGFBP levels and breast cancer risk in premenopausal women, but not in postmenopausal women. It has been proposed that free IGF-1 (or unbound IGF) is a stronger risk factor for breast cancer. However, these studies are still controversial and more research needs to be conducted in this area to elucidate the extent of this relationship. Specifically, there are many potential confounding factors and it is necessary to investigate the association between IGF and breast cancer risk after controlling for these factors. This study proposes to investigate the relationship between total IGF-1, free IGF-1, and IGFBP-3 and mammographic density with the ability to control for menopausal status, ethnicity, physical measurements, and precise body composition measurements as derived from dual energy x-ray absorptiometry (DXA).

Body

A one-year no-cost extension was granted from the sponsor on this project in regards the reviewer's comments from last year. In the previous year, I have focused on merging the results of the laboratory data with the results from the parent study and data analysis. Preliminary results were presented at the Era of Hope conference in June, 2005. At the Era of Hope conference I was able to interact with other researchers and continue my training by seeing very up to date research in the field of breast cancer research. The final data analysis and manuscript preparation is currently in progress.

Key Research Accomplishments

- **Conference Presentations:**
    - **L. Arendell**, D. Deshpande, R. Bruhn, T. Bassford, M. Maricic, Z. Chen. The Relationship between Bone Mineral Density and Breast Cancer in Hispanic and non-Hispanic White Postmenopausal Women – An Ancillary Study of the Women's Health Initiative. Poster presented at the American Society for Bone and Mineral Research Annual Meeting 2004, Seattle, Washington, October 4, 2004.

    - **L. Arendell**, Z. Chen. Relationship between Mammographic Density and IGF Levels among Hispanic and non-Hispanic White Women. Presented at the Era of Hope – Department of Defense Breast Cancer Research Program Meeting, June 9, 2005.

Reportable Outcomes

Abstract from Era of Hope Conference:

Introduction: Insulin-like growth factor-1 (IGF-1) and its binding proteins have been shown to be associated with breast cancer in several previous studies, however the relationship between IGF-1 and mammographic density, the strongest predictor of breast cancer has been studied much less frequently. The primary aim of this

study was to examine the relationship between IGF-1 and mammographic density and to explore if this relationship varies by ethnicity and/or menopausal status.

Methods: This cross-sectional study investigated the association between IGF-1 and IGFBP-3 and mammographic density among 223 Hispanic and non-Hispanic White women between the ages of 41-50 (premenopausal) and 56-70 (postmenopausal) in Southern Arizona. Physical measurements were taken. Mammographic density was measured using a computer-assisted methodology at the University of Hawaii. The premenopausal group was 45% Hispanic White and had a mean age of 44.8 years, while the postmenopausal group was 26% Hispanic and had mean age of 60.3 years. Linear regression analysis was used to investigate the association between IGF-1 and mammographic density and the role of menopausal status and ethnicity in this relationship.

Results: The results from this study show that there is a significant association between IGF-1 and mammographic density after adjusting for menopause, however, there is not a significant association between IGFBP-3 and mammographic density in this population.

Table 1: Results of Linear Regression Analysis: Association between circulating levels of IGF-1 and mammographic density.

	β Coefficient	p Value	R2
IGF-1 (ng/mL)	0.07	0.026	0.27
Postmenopausal Status	-21.42	< 0.001	

The association between IGF-1 and mammographic density did not differ significantly by menopausal status. Although, in stratified analyses the relationship between IGF-1 and mammographic density was significant among the Hispanic White women (b=0.13, p=0.005), but not non-Hispanic White women (b=0.03, p=0.571), the association between IGF-1 and mammographic density was not significantly different between the two ethnic groups.

Conclusions: Our preliminary results support the previous findings of an association between circulating IGF-1 levels and mammographic density. This association did not differ significantly by menopausal status or ethnicity, although the association between IGF-1 and mammographic density did seem a little stronger in the Hispanic women. To our knowledge, this is the first study to investigate this association in Hispanic and non-Hispanic White women. Further research with larger sample sizes are needed to elucidate the role of ethnicity in the relationship between mammographic density and IGF-1. The findings this study help us to understand the underlying mechanism of the association between IGF-1 and mammographic density, which can be used as an intermediate biomarker of breast cancer risk in intervention studies. This will allow us to test if intervention strategies that lower IGF-1 levels can reduce mammographic density.

Conclusions

From our preliminary analyses, we concluded that after adjusting for menopausal status, serum IGF-1 level and the ratio of IGF-1:IGFBP-3 were positively and significantly associated with mammographic density. Further analyses are in progress to investigate the complex associations between the IGF axis, mammographic density and body composition.

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