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TITLE: Hormonal Determinants of Mammographic Density

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**Abstract**

Hormone Replacement Therapy (HRT) has been shown to increase breast cancer risk as well as to increase breast density. Breast density, a reflection of the histologic composition of the breast, is one factor shown to affect mammographic sensitivity and specificity, and it is predictive of breast cancer risk. Thus, the use of HRT, through its effect on breast density, may compromise the well-established reduction in mortality gained by mammographic screening. However, not all women on HRT will experience an increase in breast density. We propose a novel hypothesis to explain in part the individual variability in breast density seen among women on HRT: differences in breast density are associated with differences in estrogen metabolism, and this association may be attenuated by individual factors such as body mass index and HRT regimen. Our work and the work of others provide compelling evidence to support this hypothesis. To date 50 cases and 180 healthy postmenopausal women have been enrolled in this study.
Introduction
The specific objective of this proposal is to begin to understand factors associated with individual variability in breast density including HRT, BMI and estrogen metabolism. Our rationale is that by understanding factors that affect breast density, we can improve breast cancer screening as well as to identify women at an increased risk of breast cancer. We will accomplish this objective by pursuing the following specific aim: to determine the effects of serum markers of estrogen metabolism, body mass index (BMI), and hormone replacement therapy (HRT) on postmenopausal breast density. This is an observational study within an ongoing study of the relationship between HRT, estrogen metabolism and breast cancer (PA State 2777693, Modugno, PI). We will measure estrogen metabolite levels and mammographic density in a group of 300 postmenopausal women (150 HRT users, 150 non-users), and correlate metabolite levels with qualitative and quantitative measures of breast density.

Body
Work Plan: Research Proposal

We currently have recruited 230/300 of the planned participants for this proposal from the Magee-Womens Hospital system. Recruiting women currently on hormone replacement therapy (HRT) continues to be an issue as another recent Women’s Health Initiative (WHI) publication revealed risks of HRT use. We continue to recruit women from the Magee-Womens Hospital system and will attempt to recruit those women still taking HRT to ensure that we have adequate representation of non-users, estrogen only, and estrogen + progesterone users. For all women recruited, blood has been processed and stored, mammographic films have been collected and a take home questionnaire was given to each subject. All data forms for women recruited to date have been entered. Upon receipt of the questionnaire, it is reviewed for any discrepancies or blanks. If needed, the subject is called for clarification. All data has been entered into the database and after the first key entry, a set of edit checks are run to identify data entry errors as well as inconsistent responses. The edit checks are then addressed and a second key entry is performed. Finally, the two data sets are compared and reconciled. To date all 230 subjects’ data has been entered and cleaned. As our main concern continues to be lack of HRT use among subjects, an initial query of the database reveals approximately 30% of women were on HRT at the time of enrollment. Further analysis of the database is currently in progress.

All serum samples to date have been sent to Immuna Care for estrogen metabolism testing with blinded duplicates to check for reproducibility. Results are pending at this time. All samples were given random numbers and were placed in a randomly generated order in boxes to ensure that the processing of the samples is blinded. We continue to obtain mammographic films. To date we have 78% of the participant films. All films have been sent to Martine Salane for evaluation. Of the films that have been read utilizing Wolfe’s method, 7.7% are N1, 33.1% are P1, 58.5% are P2, and 0.8% are DY.
Work Plan: Training Proposal
Once the estrogen metabolism results, mammographic reading and questionnaire data are received, abstracts will be completed. As outlined, I have attended the weekly Cancer Prevention Journal Club to discuss topics in cancer prevention, gain experience in presenting research results, and practice presentations for national meetings as well as for preparation for my defense presentation. I have also attended the annual UPCI retreat to learn about ongoing research within the university environment and those clinical grand rounds that focus on breast cancer. I applied and was accepted to the New Investigator Workshop that took place at the annual American Society of Preventative Oncology (ASPO) in March 2004. This gave me experience in presenting my research plan to a panel of experts in Epidemiology and to receive constructive criticism from well-known experts in the field of Epidemiology. Furthermore, I successfully completed my oral comprehensive exam and am now in the process of preparing my dissertation documents.

Key Research Accomplishments
- 77% of planned recruitment completed from the Magee-Womens Hospital System
- All serum samples to date have been sent for estrogen metabolism analysis
- All mammographic films received to date have been sent for breast density reading
- All data forms double key entered and reconciled
- Study remains in progress at current time

Reportable Outcomes
None to date

Conclusions
N/A – study in progress
References
References


64. Colditz GA Relationship between estrogen levels, use of hormone replacement therapy, and breast cancer. Journal of the National Cancer Institute, 87: 190-197, 1998.


