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# Abstract Book

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**THE ASSOCIATION BETWEEN MAMMOGRAPHIC CALCIFICATIONS AND INVASIVE BREAST CANCER PROGNOSTIC FACTORS IN A POPULATION-BASED MAMMOGRAPHY REGISTRY.** Sarah J. Nyante*, Thad Benefield, Tiffany Hoots, Louise M. Henderson (Department of Radiology, University of North Carolina at Chapel Hill)

Mammographic calcifications are often associated with ductal carcinoma in situ (DCIS), but their role in invasive breast cancer is less understood. Studies of patient subgroups have linked calcifications with poor survival. We examined calcifications in the population-based Carolina Mammography Registry to determine their association with breast cancer prognostic markers in a broader population. Demographics and health history were self-reported and mammographic findings were recorded prospectively by a radiologist. Cancer diagnosis data was obtained by linkage to state cancer registry and hospital-based pathology records. We included all screen-detected unilateral primary invasive breast cancers diagnosed from 1996-2011 where calcification data was recorded (N=6,797). Associations between tumor characteristics and the presence of calcifications were estimated using logistic regression. Calcifications were observed in 8.6% of cases. The presence of calcifications was associated with heterogeneously dense or extremely dense breast tissue, prior breast biopsy and use of screen-film mammography (all $\chi 2$ $P<0.01$); there was no association with age, race, menopausal status or hormone use. Calcifications were detected more often with estrogen receptor (ER)- (vs. ER+, OR=1.32, 95%CI 1.03-1.68), high grade (vs. low, OR=1.54, 95%CI 1.15-2.07) or ≤5mm (vs. >5, OR=2.91, 95%CI 2.38-3.57) tumors. Estimates were similar when adjusted for breast density, prior biopsy and mammogram type, but the association with grade was slightly weakened when we excluded cases with associated DCIS. Stage at diagnosis, progesterone receptor expression, lymph node positivity and histology were not associated with calcifications. Our results suggest that calcifications are associated with both poor (ER-, high grade) and good (≤5mm) prognostic factors in screen-detected invasive breast cancer. Analysis of calcification morphology and distribution is needed to better understand these associations.

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**ANTI-MÜLLERIAN HORMONE CONCENTRATIONS IN PREMENOPAUSAL WOMEN AND BREAST CANCER RISK**. Hazel Nichols*, Donna Baird, Frank Stanczyk, Anne Steiner, Melissa Troester, Kristina Whitworth, Dale Sandler (University of North Carolina Gillings School of Global Public Health)

In laboratory models, increasing anti-Müllerian hormone (AMH) concentrations reduces breast tumor development. Human studies are lacking; one study (N=105 cases, 204 controls) with prospectively-collected serum reported the opposite—a ~10-fold increase in breast cancer risk comparing 4th to 1st quartile AMH levels. We investigated the relation between serum AMH levels and breast cancer risk within the Sister Study prospective cohort. We conducted a nested case-control (N=452 cases, 902 controls) study within the Sister Study cohort of 50,884 women. At enrollment, participants were ages 35-54, premenopausal, and completed questionnaires on medical and family history, lifestyle factors, and demographics. AMH (ng/ml) was measured by ultrasensitive ELISA in serum collected at enrollment and log-transformed for analysis. Multivariate conditional logistic regression was used to calculate ORs and 95% CIs to account for matching on age and enrollment year. Mean age at enrollment was 46.8 years with an average 2.9 years from blood draw to breast cancer diagnosis (SD=1.9). AMH concentrations were below the limit of detection (0.003 ng/ml) for ~25% of samples. Compared with samples below the LOD, women with AMH >2.84 ng/ml (90th percentile among controls) had a 2.25-fold increase in breast cancer odds (95% CI: 1.26-4.02). For each 1-unit increase in lnAMH, overall breast cancer odds increased by 8% (OR=1.08; 95% CI: 1.02-1.15) and ER-positive, invasive disease increased by 15% (OR=1.15; 95% CI: 1.05-1.25). In our study, AMH was positively associated with breast cancer risk. Prior laboratory studies used basal-like breast cancer models such as the C3Tag mouse model or the MCF10A cell line and therefore may not generalize to more common ER-positive breast cancers. A larger study with a younger age distribution or higher proportion of basal-like tumors is needed to conclusively address possible protective effects of AMH on breast cancer.

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**REPRODUCTIVE RISK FACTORS IN RELATION TO MOLECULAR SUBTYPES OF BREAST CANCER**. Julia S. Sisti*, Rulla M. Tamimi, Bernard A. Rosner, A. Heather Eliassen (Harvard T.H. Chan School of Public Health, Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School)

**Background:** Several intrinsic breast cancer subtypes have been identified on the basis of unique gene expression profiles; these subtypes may represent different etiologic processes. Previous studies have suggested that associations of breast cancer with reproductive risk factors, particularly parity and lactation, may vary by subtype. **Methods:** We used multivariate-adjusted Cox proportional hazard models to examine relationships between age at menarche, parity, age at first birth, age at menopause and postmenopausal hormone (PMH) use and risk of breast cancer subtypes in the Nurses' Health Studies. We also examined whether a derived birth index, incorporating age at each birth, was differentially associated with subtypes. **Results:** Over 4,853,825 person-years of follow-up, we identified 2114 luminal A, 1064 luminal B, 245 HER2-type, 396 basal-like and 118 unclassified tumors. Age at menarche (HR >14 v. <12 years=0.73, 95% CI: 0.61-0.88, ptrend<0.0001) was inversely associated with risk of luminal A tumors only. Increasing age at menopause and current use of both estrogen-only and estrogen + progestin PMH appeared most strongly associated with luminal subtypes. Parity was not associated with risk of any subtype, though increasing age at first birth was associated with risk of luminal A tumors (HR per 1-year increase=1.04, 95% CI: 1.02, 1.05). Birth index was also inversely associated with risk of luminal A tumors, suggesting a protective effect of many births at younger ages. Duration of lactation was inversely associated with risk of basal-like tumors only (HR never v. 7+ months v. never: 0.64, 95% CI: 0.48, 0.84, ptrend=0.02). **Conclusion:** Associations between reproductive risk factors and breast cancer risk appeared to vary by subtype, with several appearing most strongly associated with luminal A. Our results support previous reports that lactation may be protective against basal-like tumors, representing a potential modifiable risk factor for this aggressive subtype.

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**A PROSPECTIVE STUDY OF ENDOMETRIOSIS AND RISK OF BREAST CANCER**. Leslie V. Farland*, Rulla M. Tamimi, A. Heather Eliassen, Donna Spiegelman, Susan E. Hankinson, Stacey A. Missmer (Department of Epidemiology, Harvard School of Public Health)

**Background:** Endometriosis, a gynecologic condition that affects approximately 10% of women, has been associated with altered systemic hormonal and inflammatory environments. Previous studies on endometriosis and breast cancer report mixed results, potentially due to limited data on confounding and mediating factors. Additionally, no study has addressed breast cancer heterogeneity across tumor hormone receptor types. To overcome these limitations, we evaluated the association between endometriosis and breast cancer among participants in the Nurses' Health Study II across >20 years of follow-up. **Methods:** We used laparoscopy, the clinical gold standard for endometriosis diagnosis, to define our exposure. Cox proportional hazard models, adjusted for a priori confounding factors, were used to calculate hazard ratios (HR) and 95% confidence intervals (CI). We assessed potential mediators: hysterectomy, oophorectomy, and postmenopausal hormone use. Breast cancer was further classified by menopausal status and tumor hormone receptor status. **Results:** Women with endometriosis were not at higher risk for overall (HR:1.04 [0.94-1.16]), premenopausal (HR:1.10 [0.93-1.29]) or postmenopausal breast cancer (HR:0.97 [0.82-1.15]). However, associations varied significantly by tumor hormone receptor status (P-value, test for heterogeneity: 0.0006). While women with endometriosis were not at increased risk of estrogen/progesterone receptor positive (ER+/PR+) tumors (HR:1.02[0.88-1.17]) or ER-/PR- tumors (RR:0.81 [0.59-1.11]), endometriosis was associated with significant risk of ER+/PR- breast cancers in crude and final models adjusted for confounders and mediators (RR:1.84 [1.36-2.49]). **Conclusions:** A hormonal environment high in estrogen and low in progesterone has been proposed in the pathogenesis of endometriosis, thus this shared environment may contribute to increased risk in ER+/PR- breast cancers. Future work should focus on disease heterogeneity and confirm these relationships.