FIBROGLANDULAR TISSUE AND BACKGROUND PARENCHYMAL ENHANCEMENT ON BREAST MRI FOLLOWING BILATERAL-SALPINGO-OOPHORECTOMY

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By
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CERTIFICATION OF APPROVAL

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ABSTRACT

It has been well-studied that women with a BRCA1 or BRCA2 gene mutation have an increased risk for breast and ovarian cancer. One of the recommended interventions is a bilateral salpingo-oophorectomy (BSO), which decreases a BRCA1 or BRCA2 mutation carrier's risk of developing ovarian and breast cancer. Since ovaries produce natural hormones, which also stimulate breast cells, removal of ovaries and thus, removal of natural hormones, could decrease breast cancer risk. Two biomarkers, background parenchymal enhancement (BPE) and fibroglandular tissue (FGT), are reported on breast MRI images. Each has been studied as a qualitative way to determine a woman's residual breast cancer risk post-BSO. It is hypothesized that since BPE and FGT are influenced by hormones, a decrease in BPE and FGT could be interpreted as a decrease in breast cancer risk. To further investigate this phenomenon, we performed a retrospective study, reviewing medical records and collecting data of patients all from the University of California, San Francisco (UCSF) Cancer Center. BPE, FGT and breast density categories will be collected pre- and post- BSO. We plan to see a decrease in BPE, FGT and breast density post-BSO. In total, thirteen patients were identified that fit our inclusion criteria. Seven patients were analyzed in our study population for BPE. Analyzing BPE, the Wilcoxon Signed-Rank Test analysis did not find a significant decrease in BPE post-BSO ($Z=-0.276$, $p=0.783$). Thirteen patients were identified that fit our population inclusion criteria for FGT. The Wilcoxon Signed-Rank Test analysis did not find a significant decrease in FGT post-BSO ($Z=-1.000$, $p=0.317$). A secondary

analysis was conducted to assess whether breast density decreased post-BSO. We used the same inclusion criteria as BPE and FGT and obtained 19 women, 9 of which were previously analyzed for BPE and FGT. The results of the Wilcoxon Signed-Rank Test did not find significant results ($Z=0.378$, $p=0.705$). Additional studies are required before we are able to obtain enough evidence to incorporate BPE and FGT biomarkers as a qualitative approach to determining residual cancer risk post-BSO.

CHAPTER I

INTRODUCTION

The discovery of the breast cancer genes, BRCA1 and BRCA2, identified in 1994 and 1995 respectively, was an important milestone in genetics. The discovery provided an explanation for strong family histories of breast and ovarian cancer and allowed high-risk, asymptomatic women to be more proactive in their risk management. In the United States, BRCA1 and BRCA2 mutation carriers are estimated as 1 in 400 and 1 in 800 women (Whittemore et al.,2004; Eng et al.,2001), respectively. BRCA1 and BRCA2 genes are tumor suppressor genes that are important for DNA repair, cell cycle control and overall genomic stability (Venkitaraman, A.R., 2002). Therefore, a mutation in these genes can lead to an increase in cell error and ultimately cause cancer, specifically Hereditary Breast and Ovarian Cancer (HBOC) syndrome.

The average woman has a 12% risk of developing breast cancer and a 1.4% risk of developing ovarian cancer over her lifetime (Howlader et al., 2013). The risk increases significantly if a woman has a BRCA1 or BRCA2 mutation, although the estimated risk percentages vary slightly. In one study the average risk for a woman with a BRCA1 mutation to develop breast cancer is 65% by age 70, and ovarian cancer is 39% (Antoniou et al., 2003). In a BRCA2 mutation carrier, there is a 45% risk of developing breast cancer by age 70 and an 11% risk of developing ovarian cancer (Antoniou et al., 2003). A meta-analysis of ten studies has found a slightly lower cumulative breast cancer risk for BRCA1 mutation carriers, with a 57%

increased risk by age 70 years, but a similar breast cancer risk in BRCA2 mutation carriers of 49% by age 70 (Chen & Parmigiani, 2007). The ovarian cancer risks in this paper are similar to the previous studies, with BRCA1 mutation carriers at a 40% risk by age 70 and BRCA2 mutation carriers at an 18% cancer risk by age 70 (Chen & Parmigiani, 2007).

The conclusion is that all women who carry a BRCA1 or BRCA2 mutation have a significantly increased risk for developing breast and ovarian cancer compared to women without the mutations. Therefore, there are published guidelines for women who have tested positive for a gene mutation that outline early detection screening regimens, drug therapy options, and prophylactic surgical options to decrease cancer risk. As more is learned about the BRCA1 and BRCA2 gene mutations and technology improves, the guidelines and recommendations will continue to evolve.

When the BRCA1 and BRCA2 genes were first discovered, a recommended screening practice for breast cancer was increased mammography, starting at younger ages (Warner et al., 2004). Currently, the American Cancer Society and National Comprehensive Cancer Network added annual magnetic resolution imaging (MRI) to be used in adjunct with annual breast mammography (Smith et al.,2003; National Comprehensive Cancer Network [NCCN], 2015), because MRI has been shown to detect breast cancer at an earlier stage than mammography in high risk patients (Kriege et al., 2004). Multiple studies have been conducted regarding the sensitivity of MRI versus mammograms. Most studies have found that the sensitivity of MRI ranged from 71%-100% versus 16% to 40% in mammogram sensitivity in high risk

populations (Smith et al.,2003). It is agreed that MRI is an effective screening tool for BRCA1 and BRCA2 mutation carriers for detecting early breast cancer (Kuhl et al.,2005;Watern et al.,2004; Saslow et al.,2009; Kriege et al.,2004) and is now incorporated as a standard of practice in breast cancer screening recommendations. Although there are published screening guidelines for ovarian cancer, many studies have shown that current screening methods have been ineffective. Common methods of ovarian cancer screening include the use of blood testing for CA-125 levels and transvaginal ultrasound (TVU). Unfortunately, though, both of these tests have been shown to be ineffective at detecting early stage ovarian cancers (Woodward et al.,2007). Oral contraceptives have also been recommended and have been reported to decrease ovarian cancer risk in some studies, but not all studies (Narod et al.,1998; Modan et al.,2001). Therefore, prophylactic bilateral salpingo-oophorectomy (BSO; surgical removal of both ovaries and fallopian tubes) is recommended to decrease ovarian cancer risk (National Comprehensive Cancer Network [NCCN], 2015).

Although primarily aimed to decrease ovarian cancer risk, it has been observed that removing the ovaries also helps reduce breast cancer risk (Kauff et al.,2002; Rebbeck et al.,2002). It is believed that since ovaries produce natural hormones, removal of the ovaries during prophylactic BSO, decreases breast cancer risk. However, the conclusion that BSO decreases breast cancer risk is drawn from whether patients with a BRCA1 and BRCA2 mutation develop breast cancer after BSO surgery. In the study done by Kauff et al. (2002), although many women in the study did not develop breast cancer in the follow-up, there are women that still

developed breast cancer despite BSO. The exact cause of the breast cancers in women following risk-reducing BSO remains unknown. New studies have been looking at two specific biomarkers seen on breast MRI images that could potentially elucidate which women may still be at increased breast cancer risk and require continued high risk breast cancer screening post-BSO. These biomarkers are fibroglandular tissue (FGT) and background parenchymal enhancement (BPE). FGT and BPE have been observed to be influenced by hormones and thus, it has been proposed that decreases in BPE and FGT could be indicators for decreased breast cancer risk post-BSO (Price et al., 2014). The original study by Price et al., had a small sample size so further study is required to see if there is a significant relationship between prophylactic BSO, FGT and BPE in a larger, diverse population of women (Price et al., 2014).

This study plans to further explore the observation that since BPE and FGT are influenced by hormone levels and have been shown to be risk factors for breast cancer, a decrease in FGT and BPE post-BSO could indicate an overall decreased breast cancer risk (King et al., 2012b). A secondary observation is looking at mammographic breast density post-BSO, which is a known, independent risk factor for breast cancer (DeLeoIII et al.,2015). We plan to analyze MRI and mammogram image reports of BRCA1 and BRCA2 mutation carrier women who have had a BSO at University of California San Francisco (UCSF). BPE, FGT along with breast density categories will be collected pre- and post-BSO to determine if there is a change in measurement after surgery. We hypothesize a decrease in BPE and FGT levels and breast density post- BSO, which could indicate that breast cancer risk has

also decreased. If this relationship is confirmed with the support of additional studies, BPE and FGT biomarkers may be useful indicators on breast MRI images to determine which women remain high risk despite BSO and would therefore still require intensive breast screening. Ultimately, we hope that BPE and FGT can be another tool used to personalize individual patient cancer risk and decrease the number of BRCA1 and BRCA2 mutation carriers who develop cancer in the future.

CHAPTER II

REVIEW OF THE LITERATURE

There has been extensive previous studies conducted exploring various internal and external factors that influence breast cancer risk. Studies have also focused on high risk breast cancer patients and the effect of certain treatments in decreasing overall cancer risk, such as bilateral salpingo-oophorectomy (BSO). Although there have been many published studies that support BSO as a means of decreasing breast and ovarian cancer risk, research is now developing methods to make personal predictions of risk. Currently, fibroglandular tissue (FGT) and background parenchymal enhancement (BPE) biomarkers on breast MRI are being studied as a qualitative approach to assess for decreased breast cancer risk post-BSO.

In general, genetic risk factors for women that increase breast cancer risk include natural hormone production by the body affected by age of menarche, age of menopause, and age of first full pregnancy (Hsieh et al., 1990; MacMahon et al., 1970). For example, women who have undergone natural menopause after age 55 are twice as likely to develop breast cancer than women who go through menopause earlier (McPherson et al., 2000). It has also been reported that women with denser breast tissue have a three-to five-fold greater risk for breast cancer than women who have fatty breasts (King et al., 2011). There are also known external risk factors such as smoking, alcohol-use, increased BMI and the use of oral contraceptives and the use of hormone therapy, which all contribute to increased breast cancer risk (McPherson et al., 2000).

Alcohol has been a well-studied environmental component in regards to increasing breast cancer risk. One study showed that consumption of alcohol as low as 3-6 glasses of wine per week can be associated with a modest increase in breast cancer risk. A 10% increase in risk has been reported with each additional 10g per day of alcohol ingested (Chen et al., 2011). There has also been evidence that alcohol can raise estrogen levels (Chen et al., 2011).

Smoking is also another known environmental factor that increase breast cancer risk. In a meta-analysis conducted on 73,000 postmenopausal women, the study found that incidence of invasive breast cancer was higher in current or former smokers versus women who have never smoked (Guadet et al., 2013).

BMI has been shown to have an effect on breast cancer risk. A study that looked at various cohorts of women regarding height, weight and its relationship with breast cancer found a positive association between BMI and post-menopausal breast cancer in women (Van den Brandt et al., 2000). The Van den Brandt et al., study further concluded that there is a stronger association between BMI and breast cancer risk in older, post menopausal women as compared to younger, post menopausal women (Van den Brandt et al., 2000). It is also suggested that fat distribution may be better at predicting breast cancer risk than body mass because estrogen has been known to be produced by adipose tissue (Van den Brandt et al., 2000).

Studies have specifically focused on the effects of hormone therapy drugs on FGT and BPE, such as the use of aromatase inhibitors (e.g. anastrozole, letrozole, exemestane) (King et al., 2012a) and tamoxifen (King et al., 2012b). One study looked at the effects of tamoxifen on BPE and FGT on a group of women who have had breast cancer (King et al., 2012b). The results showed that BPE significantly decreased within the group, but a larger percentage of women saw a decrease the longer they were on tamoxifen (King et al., 2012b). FGT also saw a decrease, however it was greater in patients who have been on tamoxifen for a longer duration of time (King et al., 2012b). Another study concluded that the use of aromatase inhibitors in women who were at greater than average risk for second primary breast cancers showed a significant decrease in BPE category 6-12 months after treatment with these drugs (King et al., 2011). However, the study did not see as large of a decrease in FGT in the majority of women (King et al., 2011), but suggested that FGT may change with more time (King et al., 2011).

More extensive data exists assessing the direct relationship between the effects of BSO on breast and ovarian cancer risk in high-risk women. Ovaries are a source of endogenous estrogen and progesterone production so removal of these organs has proven to play a role in breast cancer risk (DeLeoIII et al., 2015). Most studies concluded that BSO significantly decreases breast and ovarian cancer risk (Kauff et al., 2002; Rebbeck et al., 2002). In one study a group of women with a BRCA1 or BRCA2 mutation decreased their ovarian cancer risk by 85% and their breast cancer risk by 25% following BSO (Rebbeck et al., 2002). The study

recommended prophylactic BSO as the best method to reduce ovarian cancer risk (Rebbeck et al., 2002). A second study had a smaller sample size, but also reported on similar findings (Kauff et al., 2002). The study evaluated BRCA mutation carriers who either chose to do ovarian cancer screening or prophylactic BSO. Five years post-BSO, the women were re-evaluated for breast cancer or gynecological cancers. The results showed that 94% of women who had undergone prophylactic BSO were cancer free as opposed to 69% of women who only did screening ($p=0.006$) (Kauff et al., 2002). This study also concluded that prophylactic BSO is the recommended option for decreasing breast and ovarian cancer risk.

However, not all study results uniformly support this recommendation. One study did not see a decrease in breast and ovarian cancer risk after a premenopausal prophylactic BSO (Fakkert et al. 2002). Although the study suggested that women who had used hormone replacement therapy drugs had an increased risk for new or recurrent breast cancer, previous studies have noted that short term use of hormone replacement therapy does not negate the protective effects of BSO on breast cancer risks in BRCA1 and BRCA2 mutation carriers (Rebbeck et al., 2005). In fact, higher mortality was seen in women who did not use hormone replacement therapy (Fakkert et al. 2002). Other studies have noted that the age at which a woman chooses to do BSO can also play a role in determining the protective effects of BSO on breast cancer. One study found that the greatest reduction in breast cancer risk in BRCA-1 and BRCA2 mutation carriers was 40 years old and younger (Eisen et al., 2005). A similar study that focused on BRCA1 mutation carriers, noted that BSO after the age

of 50 years old, no longer provided protective effects against breast cancer risk (Rebbeck et al., 1999).

Few studies have examined the relationship between FGT and BPE post-BSO to find a qualitative marker for hormone response, potentially reflective of breast cancer risk. Breast tissue is comprised of fatty tissue and fibroglandular tissue (FGT) and the more fibroglandular tissue, the denser the breast (Lee et al.,1997). On MRI imaging, FGT appears white and is a heterogeneous mixture of fibroglandular and adipose tissue (Lee et al., 1997). BPE refers to the intensity and volume of normal FGT enhancement during early phases of dynamic contrast enhanced examination (Price et al., 2014). As FGT and BPE are influenced by hormones, removal of ovaries with subsequent decrease in hormone levels may impact the FGT and BPE categories seen on breast MRI. It has also been observed that BPE decreases more rapidly than FGT in postmenopausal women (King et al., 2012a). However, most existing studies are restricted to small sample sizes. One study recruited 18 BRCA1 and BRCA 2 mutation carrier patients and analyzed their BPE and FGT levels pre and post prophylactic BSO (Price et al., 2004). It was found that a higher proportion of women had a decrease in BPE than FGT, however FGT decrease was still statistically significant (Price et al., 2004).

A second study found similar results using a slightly larger patient cohort. The study reported that the FGT categories stayed the same eight months post-BSO, and the proportion of women who developed breast cancer during a 4.8 year follow-up was consistent previously published data of around 16% post-BSO (DeLeoIII et al.,

2015). However, post-BSO BPE categories were overall higher in women who developed breast cancer compared to the women who did not develop breast cancer, suggesting these women may still be at increased risk for breast cancer (DeLeoIII et al., 2015). As for FGT, the study suggested that additional time may be needed before a change occurs. Overall, the study findings agree with Price et. al., suggesting that BPE and FGT may be important biomarkers to further investigate (DeLeoIII et al., 2015).

Given the paradigm of recommended MRI screening for BRCA1 and BRCA2 gene mutation carriers, the relationship between BPE and FGT to BSO is important to understand. Since BPE and FGT are suggested biomarkers that indicate physiologic changes in hormone production, decreased levels seen on a post-BSO breast MRI may be an indicator of decreased breast cancer risk. On the other hand, if BPE and FGT levels remain high post-BSO, this may be an indicator of residual breast cancer risk. If this is true, these two indicators can possibly become additional markers used for future assessment of breast cancer risk amongst women. A correlation between BPE/FGT and BSO will allow for better interpretation of breast MRI images, with the end goals of personalizing risk assessment for BRCA1 and BRCA2 mutation carriers and finding the most suitable screening and preventive options for each individual.

CHAPTER III

METHODOLOGY

Overview of the Study

This is a retrospective study involving the analysis of medical records of BRCA1 and BRCA2 mutation carriers from the University of California San Francisco (UCSF), Mt. Zion Cancer Genetics and Prevention Program database, UCSF Electronic Medical Record (APeX) and UCSF Department of Radiology for generated reports and interpretation of breast MRI and mammography images. UCSF Medical Center is ranked among the best hospitals in the country according to *US News and World Report* and is known for its research, education and patient care. Mt. Zion Cancer Genetics and Prevention Program is a hereditary cancer specialty clinic associated with the UCSF Medical Center Mt. Zion campus. The Cancer Genetics and Prevention Program services families with a history of cancer, providing individual risk management and recommendations for preventative measures. UCSF Medical Center and the Cancer Genetics and Prevention Program at Mt. Zion serves a large ethnically and socioeconomically diverse cancer patient population using the most up-to-date technology and recommendation guidelines.

Study Population

The study population was women over the age of 18, who have a documented BRCA1 or BRCA2 gene mutation and have had a breast MRI and/or mammogram at UCSF Radiology before and after an elective risk-reducing BSO. A list of women who have had a BSO at UCSF Medical Center from July 2000 to April 2014 and a

brief surgical note that contained patient MRN and surgical date were provided by the Cancer Genetics and Prevention Program. The medical record number (MRN) of each patient was included in the report. Each patient's medical chart was examined to see if they had either an MRI or mammogram before and after an elective BSO. Participants were excluded if they were pregnant or under the age of 18. It was also noted if patients had a documented history of postoperative hormone therapy use including, but not limited to, tamoxifen, raloxifene, and aromatase inhibitors.

There was minimal risk to the patient cohort being studied. All the patient information used from the database was already collected as a standard of care at the Cancer Genetics and Prevention Program. Furthermore, all personal identifying information was stripped and data was coded when results were compiled. Patient information and charts were stored on a secure UCSF server or locked in filing cabinets behind two closed, locked doors in a secured building at UCSF.

Data Collection

The information collected included patient: names, birthdates, height, weight, BMI, medical record numbers and/or pathology and radiology accession numbers, BRCA mutation status, BSO surgical date, pathology at BSO, ethnicity, last menstrual period (LMP), mammogram density, any cancer history, and current and past hormone therapy treatments. Dates of imaging, imaging reports, BPE and FGT category, Breast Imaging-Reporting And Data System (BI-RADS) information from mammograms and MRI images were also collected. Only information from the mammogram and MRI closest to BSO surgery date were used in the analysis. After

the information of the subjects of interest was compiled, analysis of the data began, with the explicit goal of comparing the FGT and BPE of BRCA1 and BRCA2 mutation carriers prior to and following an elective BSO. Secondary analysis was also conducted looking at changes of mammographic breast density before and after elective BSO as well as hormone therapy influences on BPE and FGT. Women from the initial analysis of BPE and FGT were used if they had mammographic breast density information as well as additional women who fit the inclusion and exclusion criteria, but only had mammogram imaging information.

MRI and Mammogram Imaging

The MRI images were obtained using either a 1.5 Tesla (T) scanner or a 3T scanner and were read by an experienced UCSF breast radiologist. The data collected was from the report generated by the radiologist in the patient's medical chart. The reports documenting breast imaging were written by different radiologists who work at UCSF. The radiologists follow strict guidelines and standards when generating reports. The reported BI-RADS categories for BPE were from 1 to 4: minimal, mild, moderate and marked. The reported BI-RADS categories for FGT were from 1 to 4: fatty, scattered, heterogeneously dense, or extremely dense. The reported BI-RADS categories of mammographic density for each breast were from 1 to 4: fatty, scattered, heterogeneously dense, or extremely dense. It was assumed that MRI examinations were performed following standard protocol, which meant all women should have had imaging 4-11 days after the women's menstrual cycle for the most optimal and accurate read as instructed at the time of scheduling per UCSF protocol.

Additionally, only MRI images that were performed after January 2008 were collected as the UCSF Breast MRI program had been substantially changed effective that time. MRI images prior to the date did not include the necessary information and used different imaging technology.

IRB approval

All information collected through UCSF Mt. Zion Cancer Genetics and Prevention Program database and UCSF Electronic Medical Record (APeX) was already obtained as part of standard of care. All patients gave consent to be enrolled in the UCSF Cancer Risk Program 20-Year Follow-Up Program per approval by the UCSF Committee on Human Research (CHR) (Protocol#10-04932). The UCSF CHR approval also covers the analysis of MRI imaging data (Protocol#10-04932). This study was also approved by the Institutional Review Board at the California State University, Stanislaus (Protocol#1415-007).

Statistical Analysis

Descriptive statistics (means, median, etc) were used to measure basic demographic information (ethnicity, BRCA status etc.). The relationship between BPE/FGT reported in MRI images pre- and post- BSO of BRCA1 and BRCA2 mutation carriers were analyzed using the Wilcoxon Matched-Pairs Signed Ranks Test to look for statistical significance. Statistical significance was considered to be achieved when $p<0.05$ with a confidence interval of 95%. A Wilcoxon Matched-Pairs Signed Ranks Test was used because the sample size is small with an unknown distribution. Analysis of BPE/ FGT categories of patient MRI images was conducted.

Of important note, women with an initial minimal BPE and initial fatty FGT where a decrease was not possible were excluded. Secondary outcomes from this study looked at women's mammographic density BI-RADS scores before and after BSO for any category changes. The Wilcoxon Matched-Pairs Signed Ranks Test was used. All data was exported into IBM SPSS Statistics 22 software for calculation.

CHAPTER IV

RESULTS

Description of Women with MRI Imaging

All demographic information of our study population is summarized in Table 1. Additional detailed information is broken down in Table 2a for an individual's demographics and Table 2b for an individual's characteristics included in the study population. After reviewing medical records of 347 women who had elected to do a BSO at UCSF, the final number of patients who met study criteria was 13. The median age was 55 years old (range:43.0-66.0) and a median body mass index (BMI) of 25.8 kg/m^2 (range: 21.0kg/m^2-31.6kg/m^2). There was a total of 5/13 (38.4%) BRCA1 mutation carriers and 8/13 (61.5%) BRCA2 mutation carriers. The majority of the population, 9/13 (69.2%) identified themselves as Caucasian (n=13) with 1/13 (7.6%) identifying as Ashkenazi Jewish, 3/13 (23.0%) identified as Asian and 1/13 (7.6%) identified herself as "Other." Although the majority of the patients declined smoking, drinking or drug use, 3/13 (23.0%) were former smokers, but quit before BSO surgery. Furthermore, 3/13 (23.9%) women have never been pregnant and 2/13 (15.3%) declined to state. The median time from the most recent MRI to pre-BSO was 1 month (range: 0.1-10.0) and the median time from the most recent MRI to post-BSO was 8 months (range: 2.0-21.0).

Table 1

Study Cohort Demographics and Characteristics: BPE and FGT

Demographics	**n (%)**
Race	
Caucasian	9.0 (69.2)
Non-Caucasian	4.0 (30.7)
Ethnicity	
Ashkenazi Jewish	1.0 (7.6)
Non-Ashkenazi Jewish	4.0 (30.7)
Asian	3.0 (23.0)
Other	1.0 (11.1)
BRCA 1 Mutation Carrier	5.0 (38.4)
BRCA 2 Mutation Carrier	8.0 (61.5)
Smoker	3.0 (23.0)
Former	3.0 (23.0)
Current	0.0 (0.0)
Pregnancy History	5.0(38.4)
No previous pregnancies	3.0 (23.0)
One or more pregnancies	9.0 (69.2)
Unknown	2.0 (15.3)
Characteristics	**Median (range)**
Age range (y)	55.0 (43.0-66.0)
BMI (kg/m2)	25.8 (21.0-31.6)
Most recent MRI pre-BSO (months)	1.0 (0.1-10.0)
Most recent MRI post-BSO (months)	8.0 (2.0-21.0)

BMI, body mass index; BSO, bilateral-salpingo oophorectomy.

Table 2a

Individual Demographics: BPE and FGT

Individual Woman	Race (Ethnicity)	BRCA1/BRCA2	Smoker	Alcohol	Pregnancy History
Woman 2	Caucasian	BRCA2	Former Smoker	No	0
Woman 6	Other	BRCA1	Former Smoker	No	2
Woman 8	Non-Caucasian (Asian)	BRCA2	No	No	N/A
Woman 9	Caucasian	BRCA2	No	Yes	1
Woman 10	Non-Caucasian (Asian)	BRCA1	No	Yes	1
Woman 11	Caucasian	BRCA1	No	No	0
Woman 12	Caucasian	BRCA2	Former Smoker	No	2
Woman 15	Caucasian	BRCA2	No	N/A	0
Woman 18	Caucasian	BRCA2	No	No	1
Woman 31	Caucasian	BRCA2	Former Smoker	No	2
Woman 34	Caucasian (Ashkenazi Jewish)	BRCA1	No	N/A	1
Woman 35	Caucasian	BRCA1	N/A	N/A	0
Woman 40	Non-Caucasian (Asian)	BRCA2	No	No	5

N/A: not asked

Table 2b

Individual Characteristics: BPE and FGT

Individual Woman	Age	BMI (kg/m^2)	MRI pre-BSO (months)	MRI post-BSO (months)
Woman2	52	26.4	5.0	8.0
Woman 6	62	31.6	1.0	2.0
Woman 8	66	22.1	1.0	11.0
Woman 9	45	23.8	0.1	12.0
Woman 10	57	22.9	4.0	8.0
Woman 11	51	27.4	8.0	3.0
Woman 12	55	23.0	10.0	2.0
Woman 15	58	25.8	1.0	14.0
Woman 18	50	21.0	0.9	11.0
Woman 31	61	28.6	3.0	7.0
Woman 34	50	27.8	7.0	21.0
Woman 35	43	25.3	0.9	4.0
Woman 40	62	29.9	0.5	5.0

BMI, body mass index; BSO, bilateral salpingo-oophorectomy

BPE and BSO

Women who had an initial minimal BPE were excluded in the final BPE analysis since category decrease was not possible. There was no significant change in BPE after BSO (Table 3). Six women had an initial minimal BPE and were therefore excluded, leaving seven subjects for analysis (n=7). There was 1/7 (14.2%) woman had a one-category decrease, 1/7 (14.2%) had a two-category decrease, 2/7 (28.5%) women had a one-category increase, and 1/7 (14.2%) woman had a two-category increase in BPE after BSO. The Wilcoxon Signed-Rank Test showed that BPE did

not significantly decrease in patients who had undergone a prophylactic BSO (Z= -0.276, p=0.783). The median BPE was 2.0 (range, 1-4) before BSO and 2.0 (range 1-4) after BSO. Additional detailed information about the woman who had a change in BPE is provided in Table 4.

Table 3

Change in BPE post-BSO

Baseline BPE	**n** (%)	Two-category decrease **n** (%)	One-category decrease **n** (%)	No category change **n** (%)	One-category increase **n** (%)	Two-category increase **n** (%)
Minimal (1)	6 (46.1)	NA	NA	6 (46.1)	0 (0.0)	0 (0.0)
Mild (2)	5 (38.4)	0 (0.0)	1 (7.6)	3 (23.0)	0 (0.0)	1 (7.6)
Moderate (3)	2 (15.3)	1 (7.6)	1 (7.6)	0 (0)	0 (0.0)	0 (0.0)
Marked (4)	0 (0)	0 (0.0)	0 (0)	0 (0)	NA	NA
Total	13 (100.0)	1 (7.6)	2 (15.3)	9 (69.2)	0 (0.0)	1 (7.6)

BPE, background parenchymal enhancement; BSO, bilateral salpingo-oophorectomy; NA, not applicable

Table 4

Environmental Descriptives of Women with a Change in BPE

Individual Woman	Age at BSO (years)	MRI post-BSO (months)	Pregnancies	Smoke, Drink Alcohol, Drugs	BMI Category	Breast or Ovarian Cancer	Initial BPE
Two-Category Increase							
Woman 12	50	2	2	Former Smoker	Normal	No	2
One-Category Increase							
Woman 18	43	11	1	No	Normal	Bilateral breast cancer	1
Two-Category Decrease							
Woman 2	51	5	0	Former Smoker	Overweight	No	3
One-Category Decrease							
Woman 34	43	7	1	No	Overweight	No	3
Woman 40	54	0.5	5	No	Overweight → Obese	No	2

BPE, background parenchymal enhancement; BSO, bilateral salpingo-oophorectomy; BMI, body mass index

FGT and BSO

All 13 patients were analyzed for FGT since there were no women with an initial fatty FGT (n=13) (Table 5). After analysis, 3/13 (23.0%) women had a one-category decrease, 1/13 (7.6%) woman had a one-category increase and 9/13 (69.2%) women had no change. The Wilcoxon Signed-Rank Test showed that FGT did not significantly decrease in patients who had undergone a prophylactic BSO (Z=-1.000, p=0.317). The median FGT was 2.0 (range 1-4) before BSO and 2.0 (range 1-4) after BSO. Additional detailed information about the woman who had a change in FGT is provided in Table 6.

Table 5

Change in FGT post-BSO

Baseline FGT	**n** (%)	One-category decrease **n** (%)	No category change **n** (%)	One-category Increase **n** (%)
Fatty (1)	0 (0.0)	NA	0 (0.0)	0 (0.0)
Scattered (2)	7 (53.8)	0 (0.0)	6 (46.1)	1 (7.6)
Heterogeneous (3)	5 (38.4)	2 (15.3)	3 (23.0)	0 (0.0)
Dense (4)	1 (7.6)	1 (7.6)	0 (0.0)	NA
Total	13 (100.0)	3 (23.0)	9 (69.2)	1 (7.6)

FGT, fibroglandular tissue; BSO, bilateral salpingo-oophorectomy; NA, not applicable

Table 6

Environmental Descriptives of Women with a Change in FGT

Individual Woman	Age at BSO (years)	MRI post-BSO (months)	Pregnancies	Smoke, Drink Alcohol, Drugs	BMI Category	Breast or Ovarian Cancer	Initial FGT
One-Category Increase							
Woman 11	46	3	0	No	Overweight	No	2
One-Category Decrease							
Woman 8	63	1	N/A	No	Normal	Left, stage 1 breast cancer	3
Woman 18	43	11	1	No	Normal	Bilateral breast cancer	4
Woman 40	54	0.5	5	No	Overweight → Obese	No	3

BMI, body mass index; BSO, bilateral salpingo-oophorectomy; FGT, fibroglandular tissue

It was also observed that 12/13 women who had undergone a prophylactic BSO (n=13) did not develop cancer after surgery at a median time interval of 59 months (range: 11.0-90.0). One woman developed a stage IIIC peritoneal carcinoma 12 months after her surgery. During her BSO, the pathology report stated that some atypical fimbriae cells and patchy P53 staining was noticed, but this was not enough

evidence to say whether this finding could be classified as an in situ carcinoma. Therefore, the diagnosis post-BSO of a stage IIIC peritoneal carcinoma was most likely not a new primary cancer, but a cancer that had unfortunately progressed from an earlier stage found at BSO. The woman had never been pregnant and stated that she drank three alcoholic beverages a week. There was no history of smoking or drug-use.

Population Description of Mammographic Breast Density

Additionally, we analyzed changes in mammographic breast density pre- and post- BSO (n=19) following the same inclusion and exclusion criteria as the women in the analysis of BPE and FGT. From the total, 9/19 women analyzed were also included in the BPE and FGT population. The rest of the women in the mammographic breast density group only had mammogram reports in the medical chart, but did not have MRI image reports. The descriptives are summarized in Table 7. Additional details were further broken down for each individual. Table 8a provides information about the individual's demographics and Table 8b provides information about the individual's characteristics. In summary, 68.4% of women were Caucasian (13/19) and 4/19 (21.0%) women were of Ashkenazi Jewish descent. Out of the six patients that were non-Caucasian, 2/19 (10.5%) were African American, 2/19 (10.5%) were Asian, 1/19 (5.2%) was Hispanic and 1/19 (5.2%) identified herself as "Other." Regarding environmental factor history, 3/19 (15.7%) were former smokers and 3/19 (15.7%) have never been pregnant. There was 10/19 (52.6 %) BRCA1 mutation carriers and 9/19 (47.3%) BRCA2 mutation carriers.

Table 7

Study Cohort Demographics and Characteristics: Breast Density

Demographics	**N (%)**
Race	
Caucasian	13 (68.4)
Non-Caucasian	6 (31.5)
Ethnicity	
Ashkenazi Jewish	4 (21.0)
Non-Ashkenazi Jewish	15 (78.9)
Asian	2 (10.5)
African American	2 (10.5)
Hispanic	1 (5.2)
Other	1 (5.2)
BRCA 1 Mutation Carrier	10 (52.6)
BRCA 2 Mutation Carrier	9 (47.3)
Smoker	3 (15.7)
Former	3 (15.7)
Current	0 (0.0)
Pregnancy History	
No previous pregnancies	5 (26.3)
One or more pregnancies	13(68.4)
NA	1(5.2)
Characteristics	**Median (range)**
Age range (y)	57 (45.0-69.0)
BMI (kg/m2)	24.6 (18.9-41.2)
BSO surgery date to closest post-mammogram (months)	7 (0.8-34.0)

BMI, body mass index; BSO, bilateral-salpingo oophorectomy; NA, not applicable

Table 8a

Individual Demographics: Breast Density

Individual Woman	Race (Ethnicity)	BRCA1/BRCA2	Smoker	Alcohol	Pregnancy History
Woman 2	Caucasian	BRCA2	Former Smoker	No	0
Woman 6	Other	BRCA1	Former Smoker	No	2
Woman 8	Non-Caucasian (Asian)	BRCA2	No	No	N/A
Woman 9	Caucasian	BRCA2	No	Yes	1
Woman 10	Non-Caucasian (Asian)	BRCA1	No	Yes	1
Woman 11	Caucasian	BRCA1	No	No	0
Woman 12	Caucasian	BRCA2	Former Smoker	N/A	2
Woman 15	Caucasian	BRCA2	No	Yes	0
Woman 18	Caucasian	BRCA2	No	No	1
Woman 24	Caucasian	BRCA1	No	Yes	1
Woman 27	Non-Caucasian (Black/African)	BRCA1	No	No	0
Woman 32	Caucasian	BRCA2	No	No	1
Woman 33	Caucasian	BRCA2	No	No	2
Woman 36	Caucasian (Ashkenazi Jewish)	BRCA1	No	Yes	5
Woman 37	Non-Caucasian (Black/African)	BRCA2	No	Yes	7
Woman 42	Caucasian (Ashkenazi Jewish)	BRCA1	No	No	3
Woman 44	Non-Caucasian (Hispanic/Latino)	BRCA2	No	Yes	3
Woman 45	Caucasian (Ashkenazi Jewish)	BRCA1	No	Yes	1
Woman 54	Caucasian (Ashkenazi Jewish)	BRCA1	Former Smoker	No	0

N/A: not asked

Table 8b

Individual Characteristics: Breast Density

Individual Woman	Age	BMI (kg/m^2)	Mammogram pre-BSO (months)	Mammogram post-BSO (months)
Woman 2	52	26.4	11	1
Woman 6	62	31.6	0.9	11
Woman 8	66	22.1	7	5
Woman 9	45	23.8	12	4
Woman 10	57	22.9	12	2
Woman 11	51	27.4	2	9
Woman 12	55	23.0	3	12
Woman 15	58	25.8	8	3
Woman 18	50	21.0	7	5
Woman 24	47	24.0	12	8
Woman 27	52	18.9	12	11
Woman 32	51	22.1	4	8
Woman 33	69	27.6	7	34
Woman 36	49	28.9	1	5
Woman 37	66	41.2	1	10
Woman 42	66	22.0	11	1
Woman 44	68	24.6	11	0.8
Woman 45	58	31.4	4	7
Woman 54	66	36.8	11	15

BMI, body mass index; BSO, bilateral salpingo-oophorectomy

Breast Density and BSO

The analysis showed that 4/19 (21.0%) women had a one-category decrease in breast density after BSO, 3/19 (15.7%) women had a one-category increase in breast

density after BSO and 12/19 (63.1%) women did not have any change. The findings are summarized in Table 9. The results of this analysis showed no significant changes of breast density after BSO (Z=-0.378, p=0.705). The median breast density, was 2.0 (range, 1-4) before BSO and 2.0 (range 1-4) after BSO. Additional detailed information about the woman who had a change in breast density is provided in Table 10.

Table 9

Changes in Breast Density Post-BSO

Baseline Breast Density	**n** (%)	One-category decrease **n** (%)	No category change **n** (%)	One-category increase **n** (%)
Fatty (1)	5	NA	3	2
Scattered (2)	7	1	5	1
Heterogeneous (3)	6	2	4	0
Dense (4)	1	1	0	NA
Total	19	4	12	3

NA: not applicable

Table 10

Environmental Descriptives of Women with a Change in Breast Density

Individual Woman	Age at BSO (years)	MRI post-BSO (months)	Pregnancies	Smoke, Drink Alcohol, Drugs	BMI Category	Breast or Ovarian Cancer	Initial Breast Density
One-Category Increase							
Woman 6	59	11	2	Former Smoker	Overweight	No	2
Woman 9	41	12	1	Drinks Alcohol	Normal	No	1
Woman 37	59	10	7	Drinks Alcohol	Obese	Right breast ductal carcinoma	1
One-Category Decrease							
Woman 32	47	8	1	No	Normal	No	3
Woman 33	63	34	2	No	Overweight	Right breast ductal carcinoma	2
Woman 45	48	7	1	Drinks Alcohol	Obese	Left breast ductal carcinoma	4
Woman 54	64	15	0	Former Smoker	Obese	Left breast adenocarcinoma	3

BSO, bilateral salpingo-oophorectomy; BMI, body mass index

Out of the 19 total patients, 12 have had a history of cancer before BSO surgery. Additionally, 4/12 women did not have a corresponding date of diagnosis for their personal cancer history, so it is unknown whether they developed cancer pre- or post-BSO. There was only one patient out of the 12 with a cancer date of diagnosis who had developed a right, triple negative breast cancer after BSO surgery. She had been pregnant three times and denied smoking, alcohol and drug-use.

CHAPTER V

DISCUSSION

The purpose of this study was to recreate a previous studied phenomenon involving BPE and FGT as potential biomarkers in reflecting hormonal decrease after prophylactic BSO (Price et al., 2014). The findings of this study were not consistent with previous studies, however it did bring up additional questions to be explored that would propel future studies on this topic.

The overall findings did not show a significant decrease in BPE and FGT categories consistent with previous published studies. In fact, this study had a similar number of women show an increase in BPE and FGT categories compared to women who had a decrease. Another observation was median BPE and FGT were identical pre- and post- BSO. Additional environmental factors were also reported, however due to the lack of scientific evidence between the relationship of environmental factors and their influence on BPE and FGT changes this paper could not make any definitive conclusions about how much of an effect these environmental components play in influencing BPE, FGT and breast density.

The results for changes in BPE were not significant. The negative z- score and small p-value upon analysis indicated that it was unlikely that there was any observable pattern in BPE categories pre- and post- BSO. There were three women who had a BPE category decrease and one women with a two-category BPE category increase. The woman with the BPE increase was a former smoker and had two pregnancies that resulted in two children. She declined to answer questions about the

use of alcohol and drugs. The time interval of her MRI post-BSO was two months. In the Price et al., study the median interval of time between MRI and post- BSO was 3.6 months. If given more time between MRI and post-BSO, it was possible the woman in this study could have a decrease in BPE based on evidence from other studies.

Other studies observed that BPE was a more sensitive biomarker for breast cancer risk and saw significant changes shortly after BSO (DeLeoIII et al.,2014). However, there were no studies that gave definitive time periods in which a change in BPE should be expected. Therefore, it could not be assumed that the BPE calculated for this study population would remain stagnant. Additional follow-up must be conducted to obtain more evidence.

This study did not see any patterns with increasing or decreasing BPE levels and risk factors. Some women who have had environmental risk factors for breast cancer showed a decrease in BPE levels, while some women did not see a change. Furthermore, although there have been many studies that have identified environmental risk factors for breast cancer risk such as smoking and alcohol consumption, there has not been much research looking at whether these environmental risk factors would directly be reflected in BPE category changes. In this study, no definitive conclusion regarding environmental factors influencing BPE could be drawn.

FGT was an additional biomarker that was analyzed. There were no significant results with a z-score approaching the middle of the distribution and a

large p-value. In this case, the majority of patients saw no change in the FGT. There were three women who had a decrease in FGT and one woman who had an increase in FGT. The median time interval between the MRI images taken after BSO was eight months. A previous study that looked at FGT category changes at a median time interval of eight months post-BSO did not observe any significant change in FGT (DeLeoIII et al., 2014). The study suggested that a change in FGT may require additional time for follow-up and women should be continually monitored for changes over a longer period of time (DeLeoIII et al., 2014). However, the study by Price et al., saw significant FGT changes after a median time of 5.6 months.

In this study, the only woman who had an increased FGT category had never been pregnant, smoked, drank alcohol or taken drugs and had a BMI of 27.4 kg/m^2 which was in the overweight category. Three women in the study had a decrease in FGT. Two of those patients have had a history of cancer before BSO, but a BMI in the healthy weight category. One patient was diagnosed with stage I, left breast cancer a little over three and a half months before BSO, but completed her cancer treatment and was in remission eight months after her diagnosis. The other patient had bilateral breast cancer ten years prior to BSO. The last patient did not have a history of cancer, but had a BMI of 29.9 kg/m^2, which approached the obese category. All three women reported that they have never smoked, drank alcohol, or taken drugs. It was observed that women who showed a decrease in FGT started out with a higher FGT with either a heterogeneously dense or dense FGT while the woman who had an increase in FGT started out with a scattered FGT. It was difficult to conclude whether

FGT was reflecting the decrease in hormone production post- BSO or more likely, due to the fact that there was more opportunity to have a decrease in FGT if someone had started out with a higher FGT. Similarly, two out of the three women in the decrease category had breast cancer. It was also possible that since these women had a higher FGT, imaging was more difficult to detect tumors on MRI, and therefore, undetected tumors could have led to the development of breast cancer in these women rather than breast cancer being a significant factor in influencing FGT changes. More follow-up for any changes in FGT needed to be monitored before any conclusions could be made.

Looking at the time interval of MRI post-BSO, the women who saw a decrease in FGT had a shorter amount of time between BSO and MRI imaging (0.5 months , 11 months, 1 month) while the woman with an increase in FGT had a slightly longer time interval of three months. This finding was contradictory to previous research that stated FGT may require more time to notice a significant change, specifically a decrease. It was unknown if FGT categories would increase or decrease given more time in both the patients who saw a change in FGT and in the patients that did not.

From previous studies we have seen that breast density could also be affected by BSO. This study planned to analyze patient data to see if a similar pattern could be determined. This study did not find any significant changes in breast density. A similar number of women had a decrease in breast density compared to the women who had an increase in breast density. The group with decreasing breast density had

three women with a history of breast cancer: a right breast IDC, left breast grade 3 triple negative ductal carcinoma, and a left breast adenocarcinoma. The group with increasing breast density had one woman with a right breast ductal carcinoma in situ. Since both groups of women with increasing and decreasing breast density had at least one woman with breast cancer, there was no conclusion that could be drawn regarding a relationship between breast cancer and changes in breast density. It was observed that women who had an increased breast density had an initial breast density of fatty or scattered and women who had a decrease in breast density had started with an initial heterogeneous or dense breast tissue. Similar to the discussion with FGT, having a higher breast density could allow for more opportunity for a decrease to happen and not necessarily be representative of a change due to BSO. Furthermore, the three women who had a FGT increase all had at least one environmental risk factor that could have increased their overall breast cancer risk, but there was no evidence that suggests these environmental risk factors would be reflected in changes of breast density.

With respect to the interval of time between BSO and post- BSO mammography, there was no consistent pattern. The women who saw an increase had a time interval of 11 months, 12 months and 10 months while the women who saw a decrease saw a time interval of 8 months, 34 months, 7 months and 15 months. The median interval period was longer in women who saw a decrease in breast density. Since breast density was shown to be positively correlated with FGT, it could indicate that additional time may be required to see additional changes in patient breast

densities (Wei et al., 2004). Further follow-up would be necessary to make definitive conclusions.

Limitations

A primary limitation to the study was a small sample size, which likely impacted the lack of significance in the study. Multiple factors influenced the small sample size. The standard of care for women with a BRCA1 or BRCA2 mutation used to be more frequent mammograms at earlier ages. However, it was not until the early 2000's that studies demonstrated that breast MRI was an even more effective tool in detecting early-onset breast cancer and was then added to standard guidelines. Therefore, many patients did not have MRI image reports in their charts either before or after prophylactic BSO and therefore these patients had to be excluded. It was also common practice for the Mt. Zion Cancer Genetics and Prevention Program patients to receive annual mammograms and MRI imaging at other institutions. Therefore, some patients had MRI images and mammogram reports that were "outside records," some of which were inaccessible. All these factors contributed to the decrease in number of patients that could be included in the study.

Furthermore, all MRI images prior to 2008 were also excluded for two reasons. The first reason was all MRI image reports that were documented prior to 2008 used a different MRI imaging protocol and therefore, the BPE and FGT readings could not be accurately compared to the BPE and FGT readings used in MRI images post-2008. Second, Mt. Zion Cancer Genetics and Prevention Program provided a consent form for all patients to opt-in to participate in research. It was not

until 2008 that the consent was revised to include the ability to use patient breast imaging reports and compare them at different time points.

Some women with a BRCA1 or BRCA2 mutation who chose prophylactic BSO, also chose to undergo a bilateral mastectomy during the same procedure. These women were also not included in the study because these women no longer have a sufficient amount of natural breast tissue to be imaged. Additionally, BRCA1 and BRCA2 mutation carriers were grouped together to be analyzed. There were slight differences with risk between the two gene mutations and at this moment, it is unknown whether or not these differences will play a role in affecting BPE and FGT category changes.

The study population was derived from electronic medical records from UCSF Mt. Zion Cancer Genetics and Prevention Program database and UCSF Electronic Medical Record (APeX). Although UCSF is located in the San Francisco Bay Area, an area known for its diversity more, than half of the patients in the current study were Caucasian. Since BRCA1 and BRCA2 mutations are more commonly found in the Eastern European population, it was not unexpected to have more Caucasian patients with this gene mutation compared to other races. This study was unable to control for demographic factors such as ethnic background.

This study relied entirely on retrospective review of patient data from online medical records. In most cases, it was impossible to verify the medical information that was listed in the patient charts. Although it was a standard protocol of UCSF to perform breast MRI 4-11 days after the patient's menstrual cycle for the most optimal

and accurate read, there was no way to verify this standard of practice. Furthermore, we relied on using the radiology reports to determine BPE, FGT and breast density for each patient. BPE, FGT and breast density were determined with a qualitative approach so it was possible that there could be differing interpretations of the biomarker categories depending on the radiologist.

It was also possible that patients could have received additional treatment and care from other institutions that would not be documented in the UCSF medical chart. Therefore, it is possible that some patients who were thought not to have used hormone therapy treatments, may have chosen not to report past treatments if treatments were conducted at other institutions. Additionally, information in patient charts regarding alcohol and drug use were patient reported. There was no way to confirm any of the information.

This study also included woman who have had cancer. Common treatments for breast cancer patients in the past was radiation of the breast tissue. Radiation has been known to quiet the breast tissue's responsiveness to hormone influence. The treatment plan to treat the breast cancer in the women in this study were not known, however if some of these women had undergone radiation as a potential treatment, there could be a possibility that this could have influenced the responsiveness of BPE and FGT.

A final limitation has to do the average age of the patient cohort. It has been studied that post-menopausal women produce less hormones than pre-menopausal women. Therefore, since the median age of this study is 55 years old, which was

considered an older age group, it is possible that effects of BSO may not be noticeable.

Future Direction

This study aimed to further provide evidence that decreasing BPE and FGT categories were two biomarkers that could be observed in breast MRI images to determine residual breast cancer risk post-BSO. This study did not support this finding, however due to a small sample size, additional research needed to be conducted in order to assess BPE and FGT as biomarkers for breast cancer risk.

Future studies focusing on the quantification of BPE and FGT would eliminate individual differences in interpretation of breast MRI images. If BPE and FGT are proven to be related to breast cancer residual risk post-BSO, it would be important to quantify risk with a more accurate and objective measurement of BPE and FGT and as a result, develop guidelines that determine sufficient breast cancer monitoring for each patient.

Previous studies have shown that higher levels of BPE both before and after BSO may indicate an increased risk for breast cancer. It would be interesting to follow patients long-term and compare BPE categories of patients to see whether or not patients with a higher initial BPE are at higher risk than patients with lower initial BPE levels.

There have been a few studies that have noted that FGT category changes may not be evident until longer time intervals post-BSO. Additional studies could focus on long term follow-up with previously studied patients to see if FGT levels have

changed after a longer time interval post-BSO. Ideally, it would be beneficial to know what the optimal time period would be for BPE and FGT category changes. Determining set time periods would make determining risk more accurate and predictable.

Hormone therapies have also been shown to impact BPE and FGT category changes. Although this study did not focus on patients on hormone therapy treatment, a similar study can be conducted looking at various hormone therapies and their effects on BPE and FGT. Similarly, studies can also look at the effects of various environmental factors on BPE and FGT and whether those changes would be significant in changing breast cancer risk.

Conclusion

Our study analyzed thirteen women with BRCA1 and BRCA2 mutations that chose to undergo prophylactic BSO. Based on MRI reports, there were no statistically significant results that BPE or FGT decreased post-BSO. Although this study was able to comment on some patterns and observations in individual women who had an increase or decrease in biomarker categories, the small sample size and various environmental factors made drawing strong conclusions difficult. However, the patterns seen in this study fuels additional research opportunities to provide more evidence to support significant findings in decreasing BPE and FGT biomarkers post-BSO. In order to confirm these findings, additional investigations with a different and larger cohort of women will be required. The hope is with further research, BPE and

FGT may be used as biomarkers in breast MRI imaging as indicators of residual breast cancer risk post-BSO, allowing women to receive personalized cancer risk.

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