What Effect, If Any, Does Soy Protein Have on Breast Tissue?

RM Fleming, MD, FICA, FACA, FASNC, FACP

Differences in breast tissue can be determined using breast-enhanced scintigraphy test (BEST) imaging. Minimal work in vivo has been done previously to determine the effects of soy protein on breast tissue. The authors' earlier work demonstrated reduction in inflammatory changes in breast tissue. This work was conducted to examine the effect of daily soy protein consumption on a larger group of women over the course of 1 year. Sixty-four premenopausal women were studied after initial BEST imaging evaluation revealed fibrocystic changes of the breast. Women were asked to consume a medical-grade soy protein on a daily basis, making no other dietary or lifestyle changes during that time. Each woman underwent BEST imaging 1 year later with the results compared to the initial findings. Women and their physicians reported a subjective reduction in both breast tenderness and fibrocystic disease (FCD). There was a nonstatistical reduction in both the average and maximal count breast activity following 1 year of daily soy consumption. There was a statistically significant reduction ($P < .01$) in variability of tissue activity following 1 year of soy protein treatment. This is the first in vivo study looking at the effect of soy protein on breast tissue health. The findings are promising and showed both objective and subjective findings consistent with a reduction in fibrocystic disease of the breast. Further research is needed to confirm these findings in a greater number of women and to determine if soy protein has the same beneficial effect in atypia and breast cancer.

Keywords: *Soy protein; breast cancer; fibrocystic disease of the breast; breast imaging; breast-enhanced scintigraphy test (BEST)*

Recent research[1] has demonstrated the ability to distinguish between normal breast tissue, breast tissue with inflammatory changes, breast tissue with precancerous cellular atypia, and breast cancer proper. The ability to distinguish between these different categories of breast tissue is dependent upon the ability of breast-enhanced scintigraphy test (BEST) imaging[2] to determine differences in vascularity (angiogenesis) and mitochondrial activity, which vary with tissue metabolic activity.[1-5]

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Although considerable debate has existed as to the effect of soy protein and its effect on breast tissue and possible carcinogenic or anticarcinogenic effects, little[6,7] research has been published on in vivo studies, and these have looked at the effect on normal breast tissue. There has been some research in animal models[8,9] discussing the effect of soy protein on mitochondrial activity, which supports the idea that BEST imaging could be used to monitor these changes in breast tissue. Our initial findings[10] supported the idea that soy protein, when added to the diet in sufficient quantity, could reduce mitochondrial activity seen in fibrocystic disease. Cellular differentiation between normal breast tissue and cancer can be made either by pathologic analysis or using BEST imaging[1,2,10] to determine mitochondrial activity and tissue vascularity as discussed in detail previously. Recent information[11,12] has shown that changes in normal breast tissue are first associated with increased metabolic activity. This metabolic activity is determined by measuring the average count activity (ACA) and maximal count activity (MCA) in the breast, along with measuring the variability (regional change in breast tissue) of metabolic activity within the breast, which signals the differentiation into hyperplasia or cellular atypia, which gives rise to cancer. Reductions in ACA, MCA, and tissue variability signal normalization of breast tissue away from cancer toward normal breast tissue. Armed with this knowledge regarding changes in metabolic activity and vascularity of breast tissue, one can not only determine differences in breast tissue but also follow the effect of treatment including soy protein consumption and treatment with chemotherapy, radiation therapy, estrogen receptor therapy, or other adjuvant treatments, upon breast health.

In an effort to extend our prior research and understanding of abnormal breast tissue and disease and to determine if soy protein effected any change in breast

RMF is at The Camelot Foundation, Omaha, Nebraska.

Correspondence: Prof. RM Fleming, MD, FICA, FACA, FASNC, FACP, The Camelot Foundation, 9290 West Dodge Road, Ste. 204, Omaha, NE 68114. E-mail: rfmd1@fhhi.omhcoxmail.com.

tissue, we measured ACA, MCA, and breast tissue varia-bility in 64 women with fibrocystic disease (FCD) using BEST imaging both before and after 1 year of daily soy protein consumption.

Methods

Patient Enrollment. Sixty-four women were enrolled in the study after an initial evaluation by BEST imaging revealed inflammatory changes of the breast, which were fibrocystic in character consistent with that provided either by prior tissue biopsy or by ob/gyn determination from physical examination. Participation in the study required that none of the women were taking hormone therapy. Subjects were all nonlactating, nonpregnant, and premenopausal for the duration of the 1 year they were enrolled. All participants signed informed consent forms approved by the institutional review board prior to participation in the study. Women were encouraged to perform monthly breast exams and report any change in breast tissue tenderness, nodularity, or other change.

BEST Imaging. Each woman underwent breast imaging[1,2,8] as described previously. Images acquired from BEST were analyzed to determine the total metabolic activity, measured as counts per pixel. The average and maximal/greatest metabolic activity was determined and quantified along with the standard deviation. The ACA represented the overall state of breast tissue metabolic activity and was derived from the mean number of counts per pixel for the entire breast image. The MCA represented the most metabolically active component of breast tissue and was derived from counts per pixel in areas of concern pointed out by the physician trained in nuclear imaging or the radiologist. A total of 2 studies were performed for each woman, 1 at the beginning and 1 at the end of the year of soy protein consumption.

Soy Protein. Each woman consumed one 20-gm packet daily of medical-grade soy protein supplement (Revival Soy) containing 160 mgs of isoflavones (genistein, daidzein, glycitein) and 1 gm of soy saponins. Because each packet contained between 130 and 260 calories (depending upon whether unsweetened or sweetened versions were used), participants were encouraged to mix the condensed powder thoroughly in cold water and use the liquid as a meal replacement to avoid increased calorie consumption. No other changes in medication or dietary consumption (eg, caffeine, chocolate, etc) or activity level were recommended or reported during the study.

Table 1. Differentiating the Effect of Soy Protein in 64 Women. Average and Maximal Count Activities Determined Using BEST Imaging

Category	$\overline{X} \pm \sigma$	*MCA* $\pm \sigma$
Before soy treatment	112.45 ± 40.40	249.60 ± 98.40
After soy treatment	103.66 ± 26.63	226.98 ± 59.22
P value	NS	NS

$\overline{X} \pm \sigma$ indicates average count activity (ACA) ± the standard deviation. MCA ± σ indicates maximal count activity (MCA) ± the standard deviation.

Statistical Analysis. The ACA and standard deviation in counts per pixel were determined for each BEST study along with the MCA and the associated standard deviation. Differences between groups were determined using Fisher's 2-tailed *t* test. Tissue variance was determined from standard deviation data and analyzed for differences using *F* ratio. Differences were determined to be statistically significant if and only if the *P* values were less than .05 as commonly defined.[13]

Results

Subjectively, women reported a reduction in both breast tenderness and nodularity and reported that their primary care physicians noticed a decrease in FCD changes on their yearly breast examination.

At the beginning of the study, the mean ACA of the women in the study, as measured using BEST imaging, was 112.45 ± 40.40. The mean MCA, representing the most metabolically active areas of breast tissue, was 249.6 ± 98.4. Following 1 year of daily soy protein consumption, the women showed a reduction in both average and MCA as shown in Table 1. Although a reduction in FCD as shown by these variables was noted, the difference was not statistically significant. Figures 1 and 2 show bar graph representations for the ACA and MCA values, respectively.

Changes in tissue variance were determined and analyzed both before and after 1 year of soy protein consumption using both the average and MCA findings. As shown in Table 2, the average variance before soy consumption was 1632, whereas the variance of MCA was 9682. The average (ACA) and maximal (MCA) metabolic activity was statistically ($P < .01$) reduced for both, showing final values of 709 and 3507, respectively.

Discussion

Subjective reporting from both the women and their physicians, as to a reduction in breast nodularity and FCD, is difficult at best to quantify. The findings are, however, consistent with the findings objectively noted on BEST imaging. The initial metabolic activity

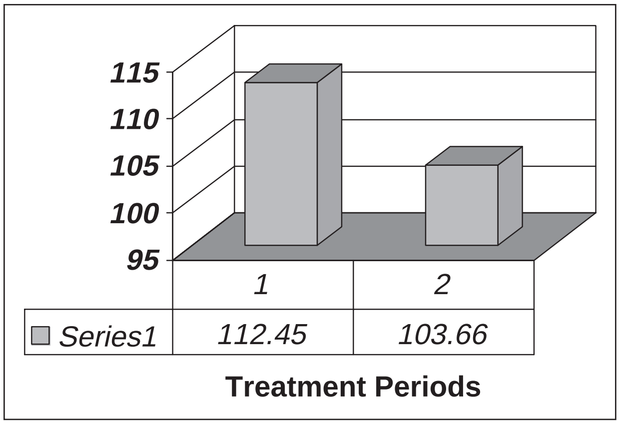

Figure 1 *Reduction in sestamibi activity in 64 women consuming soy protein. The x-axis indicates the results of average metabolic activity (ACA) in 64 women before (treatment period 1) and after (treatment period 2) 1 year of daily soy protein consumption. The average count decreased from (see Table 1) 112 to 104, which indicated an improvement that was not statistically significant.*

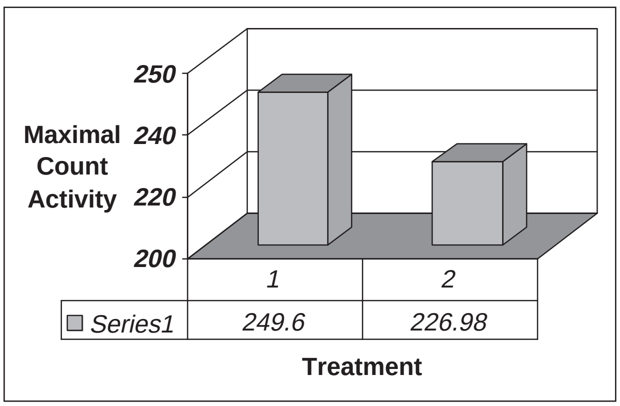

Figure 2 *Reduction in the maximal count activity (MCA) in women taking soy protein. As in Figure 1, the x-axis reveals the results before (period 1) and after (period 2) 1 year of daily soy protein consumption. The findings indicate a reduction in the maximal metabolic activity, which approached but did not reach statistical significance.*

measurements, with an ACA of 112.45 ± 40.40 and MCA of 249.6 ± 98.4, are consistent with inflammatory fibrocystic changes of the breast as previously documented.[1,2,8] Following 1 year of daily soy protein consumption, both the ACA and MCA had improved, suggesting a reduction in inflammation. The difference, which represented only 1 year's effect, was not statistically significant but did match what women and their physicians reported on monthly and yearly breast examinations, respectively. That is, there was less apparent FCD/nodularity of the breasts upon examination.

A statistically significant reduction in ACA and MCA tissue variability (variance) from the initial BEST imaging study to the final study was demonstrated.

Table 2. **Variability (Variance) in Breast Tissue Both Before and After Treatment**

Category	*ACA Variance (σ^2)*	*MCA Variance (σ^2)*
Before soy treatment	1632.16	9682.56
After soy treatment	709.16	3507.01
P value	< .01	< .01

These findings are consistent with the reduced nodularity of breast tissue reported by the women and their physicians during their monthly and yearly breast examinations, respectively.

Conclusion

The findings demonstrated a nonsignificant reduction in metabolic activity following 1 year of daily soy protein consumption. Subjectively, the women reported less breast tenderness, which would be consistent with reduced metabolic activity. In and of itself, this reduction in breast tenderness would be of tremendous benefit to the number of women who experience discomfort as a result of FCD. The reduction in breast tissue variability was statistically significant and corroborates the reduction in nodularity and enhanced homogeneity of breast tissue reported by both the women and their doctors on physical examination. Although only a small percentage of women with FCD may progress to cellular atypia and perhaps breast cancer, this study clearly demonstrated an improvement in breast health and breast tissue consistency associated with a reduction in breast cancer vulnerability in contrast to suggested increased risk of breast cancer. This is undoubtedly the effect of a weak estrogenic effect as well as anti-inflammatory components found within whole soy products, for example, L-arginine. Given these findings, concerned women may be able to reverse FCD using soy protein and avoid any progression toward the development of breast cancer. Further research is needed to corroborate these findings and to systematically investigate the effect of whole soy protein on women with atypia and/or cancer as a possible adjunct to current therapy.

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