

## **National Cancer Institute Breast Implant Study: Fact Sheet**

In 1992, researchers at the National Cancer Institute (NCI) initiated a study on the long-term health effects associated with silicone breast implants. It is estimated that between 1.5 million and 2 million women in this country have had breast implants since they first appeared on the market in 1962.

One of the longest and largest studies to date on the health effects of implants, the NCI report involves 13,500 women with an average follow-up time of 13 years. Most previous investigations have looked at the health effects over a shorter time period, typically less than 10 years, and have been too small to evaluate uncommon diseases.

In addition, earlier reports did not include detailed information about types of implants or risk factors affecting health, such as medical history, screening practices, and lifestyle behaviors all of which are included in the current study.

Another unique feature of the NCI study is that the investigators compared the health risks of the implant patients to both the general population and other plastic surgery patients. Prior reports have used only the general population as a comparison group.



The purpose of the NCI study is to evaluate the effect of implants on the risk of:

- Developing breast cancer;
- Developing cancers other than breast;
- Dying from all causes of mortality; and
- Developing connective tissue disorders.

The results will be published in various scientific journals. As the publications appear in the literature, the findings will be summarized at the end of this fact sheet.

## **Background**

Breast implants were first marketed in the early 1960s, before the 1976 Medical Device Amendments to the Food, Drug and Cosmetic Act required that medical devices be shown to be safe and effective. Silicone was initially assumed by manufacturers to be biologically inactive and, therefore, to have no harmful effects. However, cases of connective tissue disorders and cancers were reported in several short-term studies.

Because there were few reports on the long-term safety of implants, in 1992, the Food and Drug Administration (FDA) restricted the use of silicone gel breast implants to controlled clinical trials of women seeking breast reconstruction. That year, Congress also directed the National Institutes of Health to undertake a large follow-up study to assess the long-term health effects of exposure to silicone breast implants.

### ***Types of Implants***

Implants are soft silicone sacs or shells, inflated with either saline solution (salt water) or a synthetic silicone gel. Until the FDA ban in 1992, 90 percent to 95 percent of the implants contained the silicone gel because it had a more pleasing look and feel than the saline-filled implants. Since the 1992 ban, 90 percent to 95 percent of the implants have been saline-filled.

Currently, it is not known how many women have silicone vs. saline implants, but women with both types are included in the NCI study.

### ***Previous Studies***

About 80 percent of breast implants in the United States are for cosmetic reasons and 20 percent for breast reconstruction after breast cancer surgery. The majority of previous studies have focused on women who received implants for cosmetic reasons.

#### **1. *Breast Cancer Risk***

A number of previous studies have evaluated the relationship between breast implants and subsequent breast cancer risk. Most have shown that the risk of developing breast cancer is less among women with implants compared to women without implants. In several of the studies, the size of the reduced risk was as much as 50 percent to 60 percent. However, the vast majority did not have enough detailed information on patient characteristics that could affect the development of breast cancer, and had follow-up times of less than 10 years.

#### **2. *Stage at Diagnosis of Breast Cancer***

Some clinical studies have suggested that women with breast implants have more advanced breast cancer at diagnosis than women without breast implants. This is because implants have been reported to decrease the ability to detect breast lesions, with either clinical examination or mammography. However, in two larger epidemiologic studies, there did not appear to be differences in stage at diagnosis or survival rates among the two groups.

### 3. *Mortality*

No prior studies have evaluated all causes of mortality of breast implant patients but, instead, have limited their analyses to mortality from breast cancer. Compared to the general population, no increased risk in breast cancer mortality for implant patients was observed.

### 4. *Types of Implant*

Because earlier reports did not include detailed information about the types of implants, an evaluation of the effect of the implant type on the health risks of the patients has not been possible.

### 5. *Connective Tissue Disorders*

Anecdotal reports have suggested increased risks of certain connective tissue disorders, including scleroderma, systemic lupus erythematosus, rheumatoid arthritis, and Sjogren's syndrome. The size of the studies, however, has not been large enough to draw any definite conclusions.

### 6. *Women who receive implants for breast reconstructive surgery*

One small study reported no increase in the development of second primary breast cancer in women with silicone implants following mastectomy compared to women who received mastectomies without implants. The small size of the study, however, limits the conclusions.

Note: Any study of the risks of breast cancer or other cancers with women who receive reconstructive implants is more complicated than one involving women with cosmetic implants because it needs to take into account the effects of different breast cancer treatments. A study with breast cancer patients would best be done in the context

of a clinical trial where comparisons can be made between women who choose to have reconstruction and those who do not, but who otherwise have received identical treatments.

### **Patient Population in the NCI Study**

The participants include 13,500 women who had implant surgery for cosmetic reasons in both breasts before 1989. For comparison, about 4,000 women similar in age who had some other type of plastic surgery, such as removal of fat from the stomach or wrinkles from the face or neck, were identified. All participants were from 18 plastic surgery practices in six geographic areas (Atlanta, Ga.; Birmingham, Ala.; Charlotte, N.C.; Miami and Orlando, Fla.; and Washington, D.C.). The practices were chosen because the plastic surgeons had performed large numbers of cosmetic breast implant surgeries prior to 1989 and were willing to give the investigators access to their records. The health effects of the implant patients were also compared to the general population.

Half (49.7 percent) of the participants received silicone gel implants, 34.1 percent double lumen implants, (these have two shells; the inner sac is filled with silicone gel and the outer one with saline), 12.2 percent saline-filled implants, 0.1 percent other types of implants, and 3.8 percent unspecified types of implants.

The study participants had cosmetic surgery between 1962 and 1988 during a time when a great number of changes were taking place in the manufacturing of breast implants such as the shell thickness, the type of shell coating, and the silicone gel composition. There were no women included in the study who received implants following a diagnosis of breast cancer.

## **Study Design**

The medical records from the plastic surgery practices were reviewed to identify patients who were eligible for the study. For eligible patients, trained medical records abstractors collected information about the surgical procedures, the type of implant, any complications, and factors which might affect health status, such as weight or medical history.

Patients were then traced through a variety of sources. Living subjects were asked to complete a mailed questionnaire to collect information about their health status, including whether they had subsequent plastic surgery, as well as lifestyle factors that could affect their health (menstrual, pregnancy, and breast-feeding history, weight, hormone use, cigarette smoking, alcohol consumption, and medical history). Extensive data on the potential short-term (rupture) and longer-term complications (cancer, connective tissue diseases, symptoms of connective tissue disease) were also obtained through the questionnaire.

No clinical examinations were done on the living patients for this study. Attempts were made to verify patient reports of cancer and connective tissue diseases from the medical records of physicians who had diagnosed or treated these diseases. To verify the causes of death, death certificates were collected for the patients who had died. About 80 percent of the original 13,500 implant patients and 4,000 controls were successfully traced. About 70 percent of those traced as alive completed the questionnaires. These percentages are similar to other comparably designed epidemiologic studies.

## Special Issues

Because of the highly controversial and political nature of the study, maintaining objectivity was a particularly important issue. The following steps were taken to ensure scientific objectivity:

- The study was funded entirely by the government, not by plastic surgeons, implant manufacturers, or other special interest groups.
- Government scientists, not manufacturers of implants or plastic surgeons, designed and provided scientific oversight for the study.
- To participate in the study, plastic surgeons had to agree to allow investigators to see all of their records, not just records for selected patients. The investigators obtained detailed information on factors which could affect health status.
- Information gathered through the participant questionnaire about diseases such as cancer or connective tissue disorders was confirmed by the medical records of oncologists, rheumatologists, and other physicians who had seen the study respondents for these illnesses.
- Death certificates were collected for the patients identified as deceased to verify the causes of death.
- Scientific oversight for the study has been provided by NCI's Board of Scientific Counselors and its Breast Implant Study Advisory Panel, a multidisciplinary panel of academic scientists, including oncologists, plastic surgeons, rheumatologists, and epidemiologists, as well as patient advocates and consumer representatives. The panel meets regularly with NCI researchers to address issues involving data analysis and interpretation, and reports to NCI's Board of Scientific Counselors.
- A number of professional plastic surgery organizations, including the American Society of Plastic and Reconstructive Surgeons and the American Aesthetic Society, were consulted to help identify long-standing practices in which at least 500 cosmetic operations were done prior to 1989 and in which the surgeons retained complete records and were willing to give the researchers complete access to them. The NCI investigators performed their own review of the patient records.

## **Investigators**

Louise A. Brinton, Ph.D., is chief of the Environmental Epidemiology Branch in NCI's Division of Cancer Epidemiology and Genetics (DCEG). Additional NCI investigators are Jay H. Lubin, Ph.D., and Robert N. Hoover, M.D., also from DCEG. S. Lori Brown, Ph.D., is a research scientist from the FDA's Center for Devices and Radiological Health in Rockville, Md. Theodore Colton, Sc.D., from the Department of Epidemiology and Biostatistics at the Boston University School of Public Health in Massachusetts, was under contract with the study team, as was Mary Cay Burich from Abt Associates Inc., in Chicago, who assisted with specific data collection tasks.

## **Results/Publications**

- **The authors showed that other plastic surgery patients are a more appropriate comparison group than women in the general population for studies of the health effects of breast implants.**

In analyzing the data from the 7,447 breast implant patients and 2,203 patients with other types of plastic surgery, there were no differences between the two groups with respect to family income, number of pregnancies, alcohol consumption, cigarette smoking, histories of previous gynecologic operations, or operations for benign breast disease.

*Reference:* Brinton LA, Brown SL, Colton T, et al. Characteristics of a Population of Women with Breast Implants Compared with Women Seeking Other types of Plastic Surgery. *Plastic and Reconstructive Surgery* 2000;105(3):919–27.



- **The NCI researchers found no association between breast implants and the subsequent risk of breast cancer.**

In addition, they found no link between breast cancer risk and number of years of follow-up, nor with any particular type of implant. They did, however, see a shift toward somewhat later detection of breast cancers among the implant patients compared to the controls. Even though the differences were not statistically significant, there were consistently smaller percentages of in situ (early-stage) cancers among the implant patients. However, there was no significant difference in breast cancer mortality between the implant and comparison patients.

*Reference:* Brinton LA, Lubin JH, Burich MC, et al. Breast Cancer Following Augmentation Mammoplasty (United States). *Cancer Causes & Control* 2000; 11(9):819–827.

- **Women with implants were not at increased risk for most cancers with the exception of respiratory and brain cancers. The significance of the increased risks is not clear.**

NCI researchers did not find increased risks for cancers of the stomach, large intestine, cervix, uterus, ovary, bladder or thyroid. Likewise, neither connective tissue nor immune system cancers such as soft tissue sarcomas, lymphoma, and multiple myeloma, developed at higher rates. These cancers were previously linked to implants in smaller studies. The cancer rates for brain and respiratory cancers, however, were two to three times greater in the implant patients compared to other plastic surgery patients; only the rates of respiratory cancers reached statistical significance. The significance of the findings is not clear. It is possible that the higher risks observed for respiratory and brain cancers are not related to exposure to silicone, but are due to either chance findings or to factors common to women who choose to have implants.

*Reference:* Brinton LA, Lubin JH, Burich MC, et al. Cancer Risk at Sites Other than Breast Following Augmentation Mammoplasty. *Annals of Epidemiology* May 2001;11(4):248–256.

- **Women with implants were not at increased risk for most causes of death compared to the control group. The exceptions were deaths from suicide, and brain and respiratory cancers, but the significance of these increased risks is not clear.**

The researchers found that nearly every cause of death, including all cancers, circulatory and digestive system diseases, and endocrine, nutritional, metabolic and immune diseases, was decreased among implant patients compared to the general population. However, implant patients were three times more likely to die from respiratory tract cancer, two to three times more likely to die from brain cancer, and four to five times more likely to die from suicide than the comparison group; only the rates for respiratory cancers reached statistical significance. It is possible that these higher risks are not related to exposure to silicone, but are due to either chance findings or to factors common to women who choose to have implants.

*Reference:* Brinton LA, Lubin JH, Burich MC, et al. Mortality Among Augmentation Mammoplasty Patients. *Epidemiology* May 2001;12(3):321–326.

- **Women with breast implants were not at an increased risk for connective tissue disorders when their records were reviewed by two independent rheumatologists who did not know if the women had an implant or not.**

According to initial reporting by an implant patient questionnaire, there appeared to be a two fold increased risk for developing rheumatoid arthritis, scleroderma, systemic lupus erythematosus, and Sjogren's syndrome in this population. NCI researchers were able to access only 34–40% of these patients' records who reported being diagnosed with a connective tissue disorder. When these records were reviewed by two independent, board-certified rheumatologists who did not know if the patient had an implant or not, the rheumatologists found between 17–30% of the diagnoses likely. As a result, the risk for developing a connective tissue disorder due to breast implants, while still somewhat elevated, became statistically

non-significant. Further research including records linkage, standardized diagnostic criteria for rheumatoid disorders, and clinical exams, is needed to understand if a relationship exists.

*Reference:* Brinton LA, Buckley LM, Dvorkina O, et al. Risk of Connective Tissue Disorders among Breast Implant Patients. *American Journal of Epidemiology*; 2004;160; 619–627.

- **In an extended mortality follow-up study, a number of the previously observed excesses were attenuated. The risk of suicides continued to be of concern; in addition, a new excess risk among implant patients of deaths from motor vehicle accidents emerged.**

Participants in this study were followed for an additional 5 years to further examine mortality rates. Breast implant participants, in comparison to patients with other types of plastic surgery, were 1.6 times as likely to die from respiratory cancer, two times as likely to die from brain cancer, and 2.6 times as likely to die from suicide. No additional deaths from brain cancers were found during the extended follow-up period. New findings include the excess risk of death (1.7 times as likely) from motor vehicle accidents. The researchers suggest that some of the accidents may not have been totally accidental, or may have reflected alcohol/drug dependencies since higher rates of death due to these dependencies were also observed among implant patients. It is possible that the elevated mortality risks observed during this extended followup are not related to exposure to silicone, but are due to either chance findings or to factors common to women who choose to have implants.

*Reference:* Brinton LA, Lubin JH, Murray MC, et al. Mortality Rates Among Augmentation Mammoplasty Patients: An Update. *Epidemiology* March 2006; 17(2): 162–169.

## Related Links:

NCI news Web site for press releases about breast implants: Oct. 2, 2000 for breast implants and breast cancer risk; April 23, 2001 for press releases on risk of other cancers; April 27, 2001 for causes of mortality release. <http://www.cancer.gov>

FDA Web site on breast implants: <http://www.fda.gov/cdrh/breastimplants/>.

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## Related NCI materials and Web pages:

- Breast Cancer Home Page (<http://www.cancer.gov/cancertopics/types/breast>)
- Cancer Causes and Risk Factors Home Page (<http://www.cancer.gov/cancertopics/prevention-genetics-causes/causes>)
- *What You Need To Know About™ Breast Cancer* (<http://www.cancer.gov/cancertopics/wyntk/breast>)
- *What You Need To Know About™ Cancer* (<http://www.cancer.gov/cancertopics/wyntk/overview>)

## How can we help?

We offer comprehensive research-based information for patients and their families, health professionals, cancer researchers, advocates, and the public.

- **Call** NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237)
- **Visit** us at <http://www.cancer.gov> or <http://www.cancer.gov/espanol>
- **Chat** using LiveHelp, NCI's instant messaging service, at <http://www.cancer.gov/livehelp>
- **E-mail** us at [cancergovstaff@mail.nih.gov](mailto:cancergovstaff@mail.nih.gov)
- **Order** publications at <http://www.cancer.gov/publications> or by calling 1-800-4-CANCER
- **Get help** with quitting smoking at 1-877-44U-QUIT (1-877-448-7848)

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