



Natrelle Silicone Breast Implant Follow-up Study: Demographics, Lifestyle, and Surgical Characteristics of More Than 5000 Reconstruction Subjects

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Background: A large, multicenter, 10-year observational study is comparing the long-term safety and effectiveness of Natrelle silicone breast implants versus saline implants or national norms.

Methods: Women who underwent primary augmentation, revision-augmentation, primary reconstruction, or revision-reconstruction were invited to participate. Enrolled subjects had completed surgery and received one implant or matching implants. Baseline demographics, health, lifestyle, and surgical characteristics are presented here for adult subjects who underwent primary reconstruction or revision-reconstruction.

Results: Of 5637 subjects who underwent reconstruction surgery (86.7% primary reconstruction; 13.3% revision-reconstruction), 5407 received silicone implants and 230 received saline implants; 72.9% received bilateral implants. Silicone implants were used in 96.2% who underwent primary reconstruction and in 94.1% who underwent revision-reconstruction. Median age was about 3 years lower in those who underwent primary reconstruction versus revision-reconstruction. Most subjects were white nonsmokers and had attended college. Hispanic subjects were more likely to receive saline implants for primary reconstruction. Across groups, the most common characteristics by implant type or procedure included smooth-surface implants (90.8%), mastectomy scar site (69.7%), and partial (59.2%) or complete (33.9%) submuscular placement. Implant size was larger for revision-reconstruction versus primary reconstruction, and incision size was larger for silicone versus saline implants in subjects undergoing primary reconstruction.

Conclusions: This study provides an unprecedented look at a large subject sample. The data offer surgeons an opportunity to make informed decisions regarding the most appropriate implant attributes and surgical approaches for women who desire breast implants for primary or revisionary breast reconstruction. (*Plast Reconstr Surg Glob Open* 2015;3:e489; doi: 10.1097/GOX.0000000000000406; Published online 25 August 2015.)

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Breast reconstruction is among the 10 most common reconstructive surgical procedures in the United States.¹ The number of procedures has increased steadily since 2000, with nearly 100,000 procedures performed in 2013 alone.¹ A primary, growing reason for breast reconstruction is to restore breasts to their presurgical form following mastectomy due to breast cancer.²⁻⁵ Breast reconstruction is also used to correct congenital deformities, malformations, and trauma to the breast.^{6,7} Natrelle silicone gel-filled breast implants (Allergan, Irvine, Calif.) are available in a range of implant options and are approved by the US Food and Drug

Administration (US FDA) for primary reconstruction and revision-reconstruction as well as for primary augmentation and revision-augmentation.⁸

The Breast Implant Follow-up Study (BIFS-001) is a large, multicenter, 10-year observational study being conducted as part of a US FDA requirement to provide postapproval data on safety concerns associated with the use of silicone-filled breast implants. The primary objective of this study is to compare the long-term safety and effectiveness of Natrelle silicone breast implants with those of saline implants or national norms in subjects who underwent primary augmentation, revision-augmentation, primary reconstruction, or revision-reconstruction. This ongoing study has enrolled more than 50,000 subjects. Although primary outcome data will continue to be collected over a 10-year period, available baseline data provide an opportunity to examine the demographic, health, lifestyle, and surgical characteristics of a large population of women requesting to undergo breast reconstruction. Because the analysis of safety endpoints in BIFS-001 will involve comparisons between silicone and saline implant groups that are self-selected rather than randomly assigned, it is especially important to understand how characteristics such as health and lifestyle factors that may potentially impact safety outcomes differ at baseline.

The current analysis consequently describes demographic, health, lifestyle, and surgical characteristics for subjects enrolled in BIFS-001 who underwent either primary reconstruction or revision-reconstruction surgery and baseline rates for some of the important safety outcomes. An analysis of subjects who underwent either primary augmentation or revision-augmentation surgery is reported separately. This analysis aimed to assess how characteristics of women undergoing primary

reconstruction procedures differ from those in the revision-reconstruction population and how women who select silicone implants differ at baseline from those who choose saline implants. Such differences may have important implications for the long-term safety profile of silicone implants in clinical practice.

METHODS

Study Design

BIFS-001 is a long-term observational study (ClinicalTrials.gov identification number NCT00443274) comparing outcomes between subjects who underwent primary augmentation, revision-augmentation, primary reconstruction, or revision-reconstruction procedures. Baseline information was collected upon each subject's decision to undergo an implantation procedure. Subjects must have received unilateral or bilateral silicone or saline implants during surgery, and all silicone implants were required to be Natrelle devices. All subjects agreed at enrollment to complete follow-up questionnaires via the Internet, telephone interviews, or postal mail once annually over 10 years.

The study followed Good Clinical Practice guidelines, was approved by the institutional review board covering each participating study site, conformed with World Health Organization guidelines, and was registered with the FDA at <http://www.clinicaltrials.gov> (NCT00443274). All participants provided written informed consent before enrollment.

Subjects

This analysis includes women aged 18 years or older who desired primary reconstruction or revision-reconstruction. Women screened for study eligibility were required to be fluent in English or Spanish. Enrolled subjects then completed surgery, receiving one implant or matching implants (matching implants were both silicone or both saline).

Subjects were ineligible for study participation if they were currently implanted with saline implants after having previously received silicone breast implants. Subjects were also excluded if they were transgender or if the investigator decided that a subject was not a suitable candidate for long-term observation.

Assessments

Assessments recorded at baseline included demographic characteristics (age, race, height, and weight) and subject-reported health and lifestyle characteristics (marital status, education, occupation, smoking status, alcohol use, and substance abuse history). Body mass index (BMI) was calculated based on height and weight. Surgical characteristics (implant type, placement location, style and size of implant,

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and incision size and site) were documented by investigators following surgery. Long-term safety outcome measures assessed at baseline included history of neurologic disease, connective tissue disease (eg, rheumatoid arthritis and fibromyalgia), cancer (basal cell/squamous cell, brain, breast, cervical/vulvar, and lung), suicide attempt or thoughts about suicide, and reproductive or lactation complications.

Statistical Analysis

Statistical analysis of the 10-year safety data will include comparisons of adverse event rates between women choosing silicone breast implants and those choosing saline breast implants. Therefore, baseline and surgical differences between the silicone and saline groups were analyzed. For primary-reconstruction and revision-reconstruction groups, comparisons between silicone and saline groups were based on a 2-sided *z*-test for continuous data and a 2-sided chi-square test for categorical data. Comparisons were also made between the primary reconstruction and revision-reconstruction populations, using descriptive statistics only.

RESULTS

Subjects

A total of 56,616 eligible subjects were enrolled in the BIFS-001 study from February 2007 through March 2010 (silicone, *n* = 41,163; saline, *n* = 15,453)

at 1116 sites. Of these, 5637 subjects underwent breast reconstruction procedures, including 4887 (86.7%) who underwent primary reconstruction and 750 (13.3%) who underwent revision-reconstruction. Most subjects in both the primary reconstruction and revision-reconstruction groups received silicone implants (96.2% and 94.1%, respectively).

Demographics

The median age in subjects in the primary reconstruction group was 50 years at implantation (range, 18–86 years), and the majority of subjects (82.9%) were white. Approximately half of the subjects (48.4%) had a normal BMI, whereas 46.2% were overweight or obese. Within the primary reconstruction group, silicone and saline groups differed statistically with regard to several demographic characteristics. Subjects selecting silicone implants were significantly older (*P* = 0.0024) and had a lower mean BMI (*P* = 0.0259) than subjects receiving saline implants (Table 1). Race/ethnicity distribution also differed significantly between implant groups (*P* = 0.0342), with a greater percentage of subjects in the silicone group versus the saline group being white and a greater percentage of subjects in the saline group versus the silicone group being Hispanic.

Relative to the primary reconstruction group, subjects in the revision-reconstruction group were older, with a median age difference of approximately 3 years (50 vs 53 years; Table 1). When divided by

Table 1. Subject Demographics by Procedure and Type of Implant

Characteristic	Primary Reconstruction		<i>P</i>	Revision-Reconstruction		<i>P</i>
	Silicone (<i>n</i> = 4701)	Saline (<i>n</i> = 186)		Silicone (<i>n</i> = 706)	Saline (<i>n</i> = 44)	
Age, y						
Mean (SD)	50.1 (10.97)	47.6 (13.09)	0.0024	53.1 (11.119)	50.9 (12.84)	0.2066
Median (min–max)	50 (18–86)	49 (18–80)		53 (19–86)	51 (27–76)	50 (18–86)
Age at implantation, <i>n</i> (%)						
18–21 y	74 (1.6)	11 (5.9)	<0.0001	7 (1.0)	0	0.0135
22–29 y	83 (1.8)	10 (5.4)		14 (2.0)	3 (6.8)	
30–39 y	534 (11.4)	25 (13.4)		47 (6.7)	7 (15.9)	
40–49 y	1603 (34.1)	53 (28.5)		193 (27.3)	11 (25.0)	
50–59 y	1495 (31.8)	52 (28.0)		242 (34.3)	14 (31.8)	
60–69 y	734 (15.6)	30 (16.1)		157 (22.2)	3 (6.8)	
≥70 y	176 (3.7)	3 (1.6)		45 (6.4)	6 (13.6)	
Unknown	2 (<0.1)	2 (1.1)		1 (0.1)	0	
Mean BMI, kg/m ² (SD)	25.8 (5.4)	26.7 (5.9)	0.0259	25.3 (5.0)	24.1 (3.9)	0.1295
BMI <18.5, %	2.3	1.0		2.5	2.3	
BMI = 18.5–24.9, %	48.5	45.2		50.0	56.8	
BMI ≥25, %	46.1	47.8		44.5	34.1	
Unknown, %	3.1	6.5		3.0	6.8	
Race, <i>n</i> (%)						
White	3907 (83.1)	144 (77.4)	0.0342	605 (85.7)	34 (77.3)	0.1754
Hispanic	263 (5.6)	17 (9.1)		28 (4.0)	2 (4.5)	
Black	235 (5.0)	7 (3.8)		36 (5.1)	4 (9.1)	
Asian	103 (2.2)	3 (1.6)		15 (2.1)	1 (2.3)	
Other	103 (2.2)	8 (4.3)		10 (1.4)	0	
Unknown	90 (1.9)	7 (3.8)		12 (1.7)	3 (6.8)	

10-year intervals, most subjects in both the primary reconstruction and revision-reconstruction groups received implants between the ages of 40 and 59 (Fig. 1). The mean BMI and BMI distribution were similar in the primary reconstruction and revision-reconstruction groups, although the percentage of subjects who were overweight/obese was lowest in the saline revision-reconstruction group. Among subjects undergoing primary reconstruction or revision-reconstruction, the age distribution at implantation differed significantly between the silicone and saline groups ($P < 0.0001$, primary reconstruction; $P = 0.0135$, revision-reconstruction). Subjects between the ages of 40 and 59 were more likely to receive silicone than saline implants, whereas subjects aged 39 years and younger were more likely to receive saline implants.

Lifestyle Characteristics

Between the primary reconstruction and revision-reconstruction groups, the lifestyle characteristics were generally similar (Table 2). Among all subjects, approximately 67% were married and more than 75% had attended college. Further, almost half of the subjects in both the primary reconstruction and revision-reconstruction groups held a professional occupation. About 50% of the subjects in both groups were nonsmokers, and fewer than 15% of subjects were current smokers. More than 86% of all subjects consumed 3 or fewer alcoholic drinks per week, including approximately 28% of subjects who did not drink at all. In both groups, fewer than 3% of subjects undergoing primary reconstruction or revision-reconstruction had ever been treated for substance abuse. In both the primary recon-

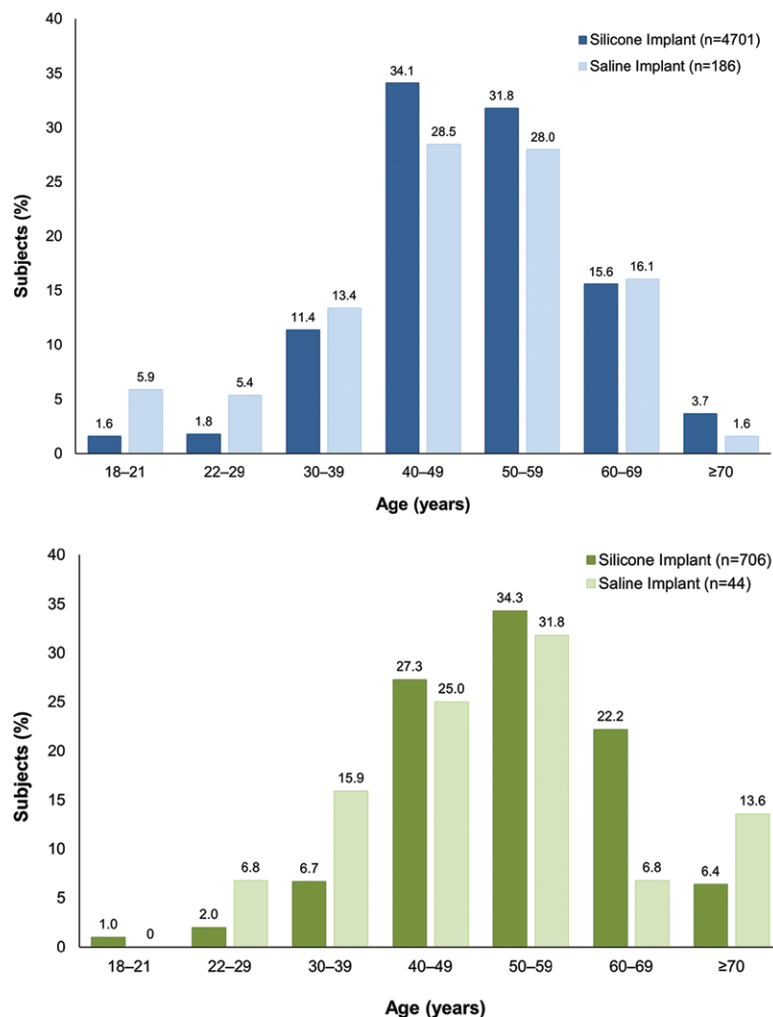


Fig. 1. Age distribution for primary reconstruction (A) and revision-reconstruction (B) subjects. Percentages of women selecting silicone implants were generally higher than percentages selecting saline implants in age groups over 40 years for primary reconstruction ($P < 0.0001$) and revision reconstruction ($P = 0.0135$).

Table 2. Lifestyle Characteristics of Subjects by Procedure and Type of Implant

Characteristic	Primary Reconstruction		<i>P</i>	Revision-Reconstruction		<i>P</i>		
	Silicone (<i>n</i> = 4701)	Saline (<i>n</i> = 186)		Silicone (<i>n</i> = 706)	Saline (<i>n</i> = 44)			
Education, <i>n</i> (%)								
High school*	963 (20.5)	44 (23.7)	0.1079	181 (25.6)	10 (22.7)	0.2223		
Some college	1357 (28.9)	59 (31.7)		202 (28.6)	15 (34.1)			
College graduate	1319 (28.1)	45 (24.2)		177 (25.1)	15 (34.1)			
Some postgraduate	260 (5.5)	8 (4.3)		43 (6.1)	1 (2.3)			
Postgraduate degree	675 (14.4)	20 (10.8)		85 (12.0)	1 (2.3)			
Unknown	127 (2.7)	10 (5.4)		18 (2.5)	2 (4.5)			
Marital status, <i>n</i> (%)								
Married	3176 (67.6)	118 (63.4)	0.1433	478 (67.7)	26 (59.1)	0.0170		
Never married	400 (8.5)	22 (11.8)		55 (7.8)	0			
Separated/divorced	735 (15.6)	23 (12.4)		111 (15.7)	7 (15.9)			
Cohabiting with partner	83 (1.8)	4 (2.2)		12 (1.7)	2 (4.5)			
Widowed	196 (4.2)	11 (5.9)		37 (5.2)	7 (15.9)			
Other/unknown	111 (2.4)	8 (4.3)		13 (1.8)	2 (4.5)			
Occupation, <i>n</i> (%)								
Professional	2266 (48.2)	85 (45.7)	0.3536	313 (44.3)	21 (47.7)	0.9520		
Homemaker	801 (17.0)	29 (15.6)		136 (19.3)	7 (15.9)			
Clerical	709 (15.1)	30 (16.1)		99 (14.0)	6 (13.6)			
Unemployed	287 (6.1)	9 (4.8)		52 (7.4)	5 (11.4)			
Trade	140 (3.0)	6 (3.2)		24 (3.4)	1 (2.3)			
Manual labor	120 (2.6)	4 (2.2)		15 (2.1)	1 (2.3)			
Student	73 (1.6)	7 (3.8)		11 (1.6)	1 (2.3)			
Unknown	305 (6.5)	16 (8.6)		56 (7.9)	2 (4.5)			
Smoking history, <i>n</i> (%)								
Nonsmoker	2780 (59.1)	99 (53.2)		0.0666	374 (53.0)		21 (47.7)	0.5298
Ex-smoker	1520 (32.3)	63 (33.9)	247 (35.0)		15 (34.1)			
Current smoker	295 (6.3)	15 (8.1)	72 (10.2)		6 (13.6)			
Unknown	106 (2.3)	9 (4.8)	13 (1.8)		2 (4.5)			
Alcohol consumption, <i>n</i> (%)								
Never drink	1344 (28.6)	59 (31.7)	0.3239	195 (27.6)	11 (25.0)	0.9246		
1–6 drinks/mo	2005 (42.7)	84 (45.2)		283 (40.1)	19 (43.2)			
1–3 drinks/wk	739 (15.7)	26 (14.0)		119 (16.9)	8 (18.2)			
1 drink/d	284 (6.0)	6 (3.2)		59 (8.4)	4 (9.1)			
≥2 drinks/d	121 (2.6)	1 (0.5)		25 (3.5)	0			
Unknown	208 (4.4)	10 (5.4)		25 (3.5)	2 (4.5)			
Treated for substance abuse, <i>n</i> (%)								
Yes	87 (1.9)	1 (0.5)	0.2667	15 (2.1)	0	0.4787		
No	4342 (92.4)	171 (91.9)		660 (93.5)	41 (93.2)			
Unknown	272 (5.8)	14 (7.5)		31 (4.4)	3 (6.8)			

*Includes vocational schools.

struction and revision-reconstruction groups, no significant differences were found between subjects receiving silicone versus saline implants with regard to any of the lifestyle factors examined, with the exception of marital status for women undergoing revision-reconstruction ($P = 0.0170$). Among women undergoing revision-reconstruction, a greater percentage of those receiving silicone versus saline implants were married, whereas a greater percentage of those receiving saline versus silicone implants were widowed.

Medical History

Baseline rates of selected medical diagnoses that are safety endpoints in BIFS-001 are presented for primary reconstruction and revision-reconstruction groups in Table 3. Among subjects undergoing primary reconstruction, there was a significantly high-

er overall rate of previous cancer diagnoses for the silicone group versus the saline group ($P < 0.0001$). The rate of breast cancer was significantly higher in the silicone group compared with the saline group at baseline ($P < 0.0001$), but no between-group differences were observed in previous basal cell/squamous cell carcinoma, brain, lung, or cervical/vulvar cancer rates. The percentages of women who reported previous suicide attempts or who had thoughts about suicide were similar in the silicone and saline groups. The percentage of subjects who were ever pregnant was similar between the silicone (89.2%) and saline (86.5%) groups. However, more than twice as many women in the silicone group who had been pregnant had tried to breastfeed ($P < 0.0001$) and, of those, the proportion of women who had difficulties in breastfeeding was significantly higher at baseline in women who chose saline versus silicone

Table 3. Selected Medical History by Procedure and Type of Implant*

Characteristic	Primary Reconstruction		P	Revision Reconstruction		P
	Silicone (n = 4650)	Saline (n = 182)		Silicone (n = 700)	Saline (n = 43)	
Neurologic diagnoses, n (%)	77 (1.7)	1 (0.5)	0.2453	11 (1.6)	0 (0.0)	0.4076
Cancer diagnoses, n (%)	3986 (85.7)	126 (69.2)	<0.0001	537 (76.6)	23 (53.5)	0.0007
Basal cell carcinoma or squamous cell carcinoma	213 (4.6)	6 (3.3)	0.4140	51 (7.3)	1 (2.3)	0.2159
Brain	3 (0.1)	0	0.7318	1 (0.1)	0	0.8041
Breast	3703 (79.6)	122 (67.0)	<0.0001	491 (70.1)	21 (48.8)	0.0034
Cervical/vulvar	50 (1.1)	3 (1.6)	0.4665	7 (1.0)	0	0.5100
Lung	12 (0.3)	0	0.4926	2 (0.3)	0	0.7256
Mental health, n (%)						
Attempted suicide	45 (1.0)	1 (0.5)	0.5686	11 (1.6)	0	0.4076
Thoughts about suicide	300 (6.5)	11 (6.0)	0.8260	44 (6.3)	0	0.0901
Ever pregnant, n (%)	3909 (89.2)	147 (86.5)	0.2537	598 (91.7)	38 (90.5)	0.7781
Tried to breastfeed, † n (%)	1665 (42.6)	30 (20.4)	<0.0001	223 (37.3)	7 (18.4)	0.0189
Difficulties in breastfeeding, ‡ n (%)						
None	929 (55.8)	10 (33.3)	0.0142	127 (57.0)	5 (71.4)	0.4456
Mastitis	215 (12.9)	7 (23.3)	0.0936	27 (12.1)	1 (14.3)	0.8622
Low milk production	297 (17.8)	6 (20.0)	0.7593	32 (14.3)	0	0.2801
Infertility, n (%)	432 (11.1)	14 (9.5)	0.5611	46 (7.7)	3 (7.9)	0.9638
Breast-related disease, n (%)	1870 (47.8)	47 (32.0)	0.0002	310 (51.8)	13 (34.2)	0.0351

*Based on the number of subjects who filled out the baseline questionnaire.

†Of those ever pregnant.

‡Of those who tried to breastfeed.

Table 4. Surgical Characteristics by Procedure and Type of Implant*

Parameter	Primary Reconstruction		P	Revision-Reconstruction		P
	Silicone (n = 4701)	Saline (n = 186)		Silicone (n = 706)	Saline (n = 44)	
Bilateral implants, n (%)	3439 (73.2)	138 (74.2)	0.7537	505 (71.5)	27 (61.4)	0.1496
Implant, n	Silicone (n = 8140)	Saline (n = 324)		Silicone (n = 1211)	Silicone (n = 71)	
Implant location, n (%)						
Submuscular–partial	4890 (60.1)	165 (50.9)	0.0012	682 (56.3)	30 (42.3)	0.1100
Submuscular–complete	2728 (33.5)	141 (43.5)		401 (33.1)	32 (45.1)	
Subglandular	445 (5.5)	13 (4.0)		110 (9.1)	7 (9.9)	
Unknown	77 (0.9)	5 (1.5)		18 (1.5)	2 (2.8)	
Surface type, n (%)						
Smooth	7488 (92.0)	235 (72.5)	NA	1069 (88.3)	57 (80.3)	NA
Textured	649 (8.0)	89 (27.5)		142 (11.7)	14 (19.7)	
Unknown	3 (<0.1)	0		0	0	
Implant style, n (%)						
10	514 (6.3)	NA	NA	101 (8.3)	NA	NA
15	1934 (23.8)	NA		344 (28.4)	NA	
20	4141 (50.9)	NA		452 (37.3)	NA	
40	32 (0.4)	NA		18 (1.5)	NA	
45	422 (5.2)	NA		47 (3.9)	NA	
110	81 (1.0)	NA		25 (2.1)	NA	
115	277 (3.4)	NA		63 (5.2)	NA	
120	363 (4.5)	NA		90 (7.4)	NA	
68HP	NA	60 (18.5)		NA	14 (19.7)	
68LP	NA	11 (3.4)		NA	2 (2.8)	
68MP	NA	85 (26.2)		NA	28 (39.4)	
168	NA	24 (7.4)		NA	7 (9.9)	
363LF	NA	52 (16.0)		NA	4 (5.6)	
468	NA	31 (9.6)		NA	8 (11.3)	
Unknown	376 (4.6)	61 (18.8)		71 (5.9)	8 (11.3)	

*n values refer to the number of implants.

NA, not applicable.

implants ($P = 0.0142$). The rate of breast-related disease was also significantly higher in the silicone group ($P = 0.002$).

As observed in the primary reconstruction subjects, revision-reconstruction subjects who selected silicone implants had a significantly higher overall rate of previ-

ous cancer diagnoses ($P=0.0007$) and a higher rate of previous breast cancer diagnosis ($P=0.0034$) at baseline, with rates of other cancer types included in the analysis not differing between the silicone and saline groups (Table 3). There was no difference between implant groups in the number of subjects reporting previous suicide attempts or thoughts about suicide. Among revision-reconstruction subjects, 91.7% of the silicone group and 90.5% of the saline group had ever been pregnant; of those, twice as many women in the silicone group compared with the saline group had tried to breastfeed ($P=0.0189$). The baseline rate of breast-related disease in subjects undergoing revision-reconstruction was higher for those receiving silicone versus saline implants ($P=0.0351$).

Surgical Characteristics

The majority of subjects received bilateral breast implants (Table 4). For those who underwent primary reconstruction, 73.2% and 74.2% received bilateral silicone and saline implants, respectively. Similarly, among subjects undergoing revision-reconstruction, 71.5% and 61.4% received bilateral silicone and saline implants, respectively. The majority of implants for primary reconstruction and revision-reconstruction were placed submuscularly, with partial submuscular placement occurring more frequently than complete submuscular placement for silicone implants (60.1% vs 33.5%, primary reconstruction; 56.3% vs 33.1%, revision-reconstruction). By contrast, saline implants were more evenly distributed between partial and complete submuscular placement for both primary reconstruction (50.9% vs 43.5%) and revision-reconstruction (42.3% vs 45.1%), respectively. The distribution of implant locations differed significantly only for subjects undergoing primary reconstruction ($P=0.0012$), in whom subglandular placement was more common and complete submuscular placement was less common for silicone versus saline implants. Although submuscular placement was also more common in subjects who underwent revision-reconstruction procedures, the frequency of subglandular placement of both silicone and saline implants was higher compared with that in primary reconstruction procedures (9.1% and 9.9% vs 5.5% and 4.0%, respectively).

Implant Styles and Sizes

The majority of silicone and saline implants were smooth in both the primary reconstruction and revision-reconstruction groups (Table 4). All silicone implants were round; Natrelle shaped implants were not available at the time of this study. The most frequently used silicone implant styles in both the primary reconstruction and revision-reconstruction

groups were, respectively, Natrelle style 20 (50.9% and 37.3%), which is considered high profile, and style 15 (23.8% and 28.4%), which is considered midrange profile. The most frequently used saline implant styles in both indications were, respectively, the moderate-profile Natrelle style 68MP (26.2% and 39.4%) and the high-profile style 68HP (18.5% and 19.7%).

In the primary reconstruction group, the most common implant size range for both silicone and saline implants was 400–499 cm³ (Fig. 2A). More specifically, the most commonly used implant size was 450–474 cm³, followed by 400–424 cm³, for both silicone and saline implants. The most common implant size range in the revision-reconstruction group was 300–399 cm³ for both silicone and saline implants (Fig. 2B). More specifically, the most commonly used implant size was 350–374 cm³ followed by 375–399 cm³ for silicone implants and a tie between 350–374 cm³ and 475–499 cm³ for saline implants. Size distributions differed significantly between the silicone and saline implant groups in subjects undergoing primary reconstruction ($P=0.0096$) but did not differ significantly in subjects undergoing revision-reconstruction ($P=0.3186$).

The percentage of women selecting saline implants was higher than the percentage selecting silicone for implant sizes from 200 cm³ up to 499 cm³ for primary reconstruction and for implant sizes up to 499 cm³ for revision-reconstruction. When subjects were divided by 10-year age intervals, the majority of subjects aged 50 years or older who underwent primary reconstruction received either 400–499 cm³ or 500–599 cm³ silicone or saline implants, whereas subjects aged 49 years or younger were more likely to receive either 300–399 cm³ or 400–499 cm³ for both silicone and saline implants. None of the subjects aged 18–21 years received saline implants for revision-reconstruction procedures.

When subjects were analyzed by BMI category, an association was observed between subject weight and implant size for those who underwent primary reconstruction procedures. Subjects who were underweight or within normal weight primarily received implants with volumes between 300 and 499 cm³. By contrast, overweight subjects mostly received 500- to 699-cm³ implants, whereas obese subjects primarily received 700-cm³ to greater than 800-cm³ implants. No size differences were noted between subjects receiving silicone or saline implants. A similar but less prominent trend was observed in subjects who underwent revision-reconstruction procedures.

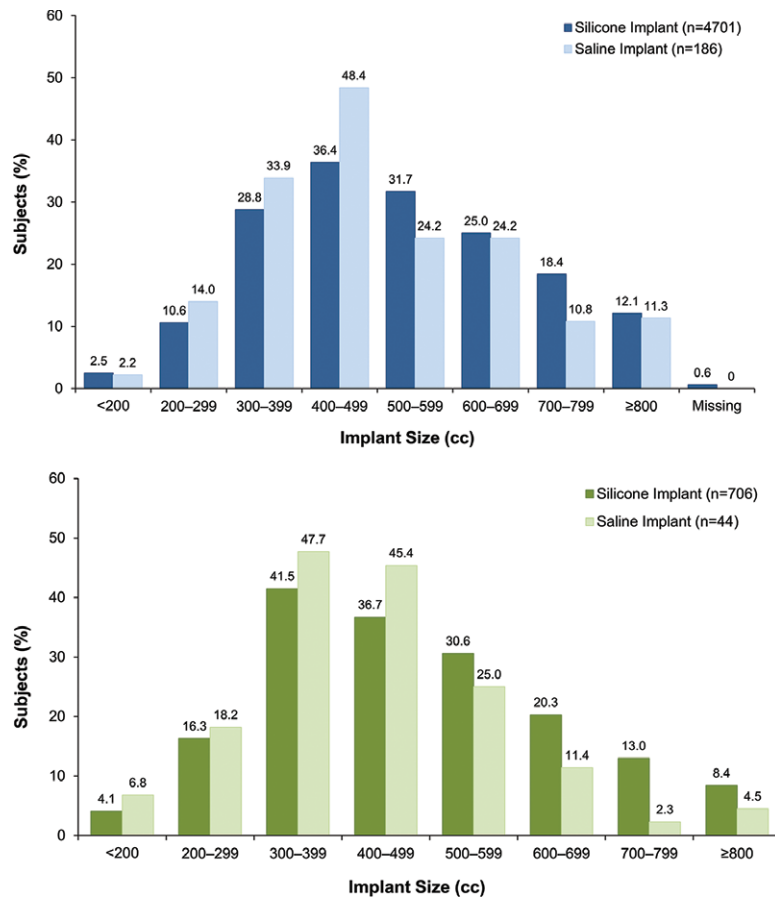


Fig. 2. Implant size for primary reconstruction (A) and revision-reconstruction (B) subjects. Size distributions differed significantly between the silicone and saline implant groups in subjects undergoing primary reconstruction ($P = 0.0096$) but were not significantly different in subjects undergoing revision-reconstruction ($P = 0.3186$).

Incision Sizes and Sites

In the primary reconstruction group, the majority of silicone implants required incision sizes of 5.0–5.9 cm or 6.0–6.9 cm (Fig. 3). Most saline implants required incision sizes of 4.0–4.9 cm or 5.0–5.9 cm. This trend was also evident in the revision-reconstruction group, wherein silicone implants more often required incision sizes of 5.0–5.9 or 6.0–6.9 cm. By contrast, the majority of saline implants required somewhat smaller incision sizes of 3.0–3.9 or 4.0–4.9 cm. The most frequently used anatomical incision site in both primary reconstruction and revision-reconstruction groups was the mastectomy scar, followed by inframammary incision. Although these were the 2 most common incision sites for both implant types in each indication, the percentage of subjects with each incision site differed significantly between silicone and saline implants for both primary and revision-reconstruction procedures (both $P < 0.0001$; Table 5).

DISCUSSION

The current analysis provides a detailed examination of the demographics, lifestyle, health, and surgical characteristics of a large number of subjects undergoing primary reconstruction and revision-reconstruction breast implant procedures. The majority of women in these populations received silicone implants. Women who underwent primary reconstruction procedures were slightly younger than those who underwent revision-reconstruction procedures, although other baseline demographics were similar. However, based on percentages, Hispanics were the second most common ethnic group to undergo primary reconstruction, whereas blacks were the second most common racial group to undergo revision-reconstruction. The majority of subjects who underwent primary reconstruction used a mastectomy scar as the incision site, with either silicone or saline implants placed most frequently in a partial or complete submuscular position.

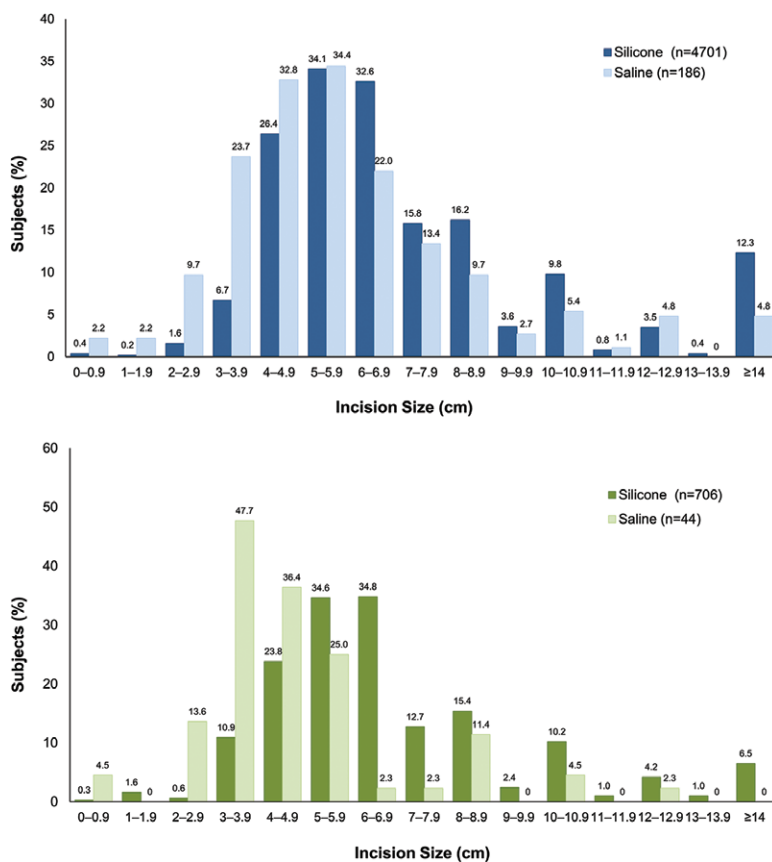


Fig. 3. Incision size for primary reconstruction (A) and revision-reconstruction (B) subjects.

However, subjects who underwent revision-reconstruction procedures were just as likely to have saline implants placed using an inframammary incision as a mastectomy scar incision. Subjects who received saline implants for either primary reconstruction or revision-reconstruction generally had smaller incision sizes compared with those who received silicone implants, most likely because saline implants are not filled until after insertion.^{9,10} In addition, subjects who underwent revision-reconstruction procedures received slightly smaller-

sized silicone and saline implants than did those who underwent primary reconstruction procedures.

Because subjects in this observational study were not randomly assigned but were self-selected into the silicone or saline implant groups, it will be critical to identify any differences between the populations choosing silicone versus saline implants so that these differences can be controlled statistically in the long-term safety analyses. Several significant differences observed between the silicone and saline groups at baseline could potentially influence

Table 5. Incision Site by Procedure and Type of Implant

Parameter	Primary Reconstruction		P	Revision-Reconstruction		P
	Silicone (n = 8140)	Saline (n = 324)		Silicone (n = 1211)	Saline (n = 71)	
Incision site, n (%)						
Mastectomy scar*	5908 (72.6)	169 (52.2)	<0.0001	688 (56.8)	24 (33.8)	<0.0001
Inframammary	1512 (18.6)	65 (20.1)		357 (29.5)	23 (32.4)	
Mastopexy incision with implant placement	455 (5.6)	66 (20.4)		83 (6.9)	10 (14.1)	
Periareolar	169 (2.1)	20 (6.2)		58 (4.8)	10 (14.1)	
Axillary	7 (0.1)	0		4 (0.3)	2 (2.8)	
Other	85 (1.0)	4 (1.2)		20 (1.7)	2 (2.8)	
Unknown	4 (<0.1)	0		1 (0.1)	0	

*Previous surgery without reconstruction.

the 10-year findings. Compared with women who chose saline implants, women who selected silicone implants for primary reconstruction were substantially older and had a lower mean BMI. Ethnicity patterns also differed significantly in this population, with a greater proportion of Hispanic subjects receiving saline versus silicone implants. Among subjects undergoing revision-reconstruction, those choosing saline implants were less likely to be married and were more likely to be widowed than were women receiving silicone implants. Such demographic and lifestyle characteristics may be associated with differential rates of BIFS-001 safety outcomes, including cancer,^{11–13} rheumatic and neurologic diseases,^{14,15} suicide attempts,^{16,17} and postoperative complications, such as capsular contracture and rippling.¹⁸ In the primary reconstruction population, the implant distributions were significantly skewed toward a larger size for silicone implants relative to saline implants. Although requiring confirmation, larger implant size may be a risk factor for breast implant rupture.¹⁹ Significant differences between the silicone and saline groups were also found among both primary and revision-reconstruction subjects for baseline rates of BIFS-001 outcomes, including previous cancer diagnoses, breast-related disease, and breastfeeding history and difficulties. There were also significant differences noted between silicone and saline implantation with regard to the percentage of subjects with each incision site.

The baseline data from BIFS-001 offer an opportunity to compare characteristics between a substantial cross-section of real-world reconstruction patients and populations previously enrolled in prospective, long-term clinical trials for silicone and/or saline implants. Subject demographic data and surgical characteristics reported for other breast reconstruction studies reveal similar baseline findings compared with those of the current study. In studies that reported demographic information, the majority of subjects were white, married, and had attended college; most subjects who underwent primary reconstruction procedures were aged in their late 40s, with those who had revision-reconstruction procedures being, on average, approximately 4 to 5 years older.^{20–26} With respect to surgical characteristics, the majority of subjects in these studies had breast implants placed submuscularly, using the mastectomy scar or other scar for the incision site.^{20–24,26} Incision sizes between 6.0 and 9.0 cm were favored for reconstruction procedures.^{23,24} Of the studies conducted solely using silicone implants, the majority (>70%) of subjects elected to undergo bilateral reconstruction procedures.^{22–24} One previously published study compared the base-

line demographic, lifestyle, and surgical characteristics of subjects undergoing postmastectomy breast reconstruction with silicone ($n = 306$) versus saline ($n = 176$) implants.²⁵ In that study, patients selecting silicone implants were significantly older at implantation (mean, 53.7 vs 51.3 years; $P = 0.017$) and were more likely to have bilateral placement (52.8% vs 39.9%; $P = 0.008$). No significant differences were observed between implant groups with regard to marital status, ethnicity, education level, or occupation, whereas the current analysis did identify differences in ethnicity between subjects choosing silicone versus saline implants for primary reconstruction.

BIFS-001 confirms many previously reported findings. However, as the sample size is considerably larger than the aforementioned studies, it offers an opportunity for surgeons to examine in greater depth the baseline characteristics of women receiving silicone or saline implants for breast reconstruction procedures. In addition, the BIFS-001 study assesses categories not described in recent breast reconstruction studies, including subject's medical history, history of substance abuse, the distribution of implant sizes by age and by BMI, and the distribution of incision sizes. In regard to BMI and implant size, there was a direct association between larger silicone and saline implant sizes and higher BMI for both breast reconstruction procedures, but this association was less prominent for subjects who underwent revision-reconstruction.

Several study limitations deserve mention. A primary objective of BIFS-001 is to compare the long-term safety of Natrelle silicone breast implants with that of saline implants. However, women who choose to receive silicone versus saline breast implants may potentially differ in clinically important ways that can affect safety outcomes. This analysis of the baseline characteristics of subjects selecting silicone or saline implants for primary reconstruction or revision-reconstruction addresses this limitation by identifying demographic and clinical differences between the implant types that must be addressed in all future safety analyses. Additionally, some of the data in the BIFS-001 study, such as lifestyle information, were self-reported. However, it is likely that the robust overall sample size may mitigate any reporting bias. The sample size for subjects with saline implants was small because individuals seeking reconstruction or revision-reconstruction typically favor silicone implants. Another limitation is that a substantial majority of the subjects were white ($n = 4690$), and relatively small numbers of Hispanic ($n = 310$), black ($n = 282$), and Asian ($n = 122$) subjects were included. This observation may reflect disparities in rates of postmastectomy reconstruction.^{27–29}

CONCLUSIONS

In conclusion, data derived from the BIFS-001 study offer surgeons an opportunity to make informed decisions and provide counseling with respect to the most appropriate implant attributes and surgical approaches for their patients who desire breast implants for primary or revisionary breast reconstruction. Further, these results identify baseline factors that will be critical when analyzing and interpreting the long-term safety outcomes for silicone-filled implants in BIFS-001.

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