Natrelle Saline-Filled Breast Implants: A Prospective 10-Year Study

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BACKGROUND: Natrelle saline-filled breast implants (Allergan, Santa Barbara, CA) are in widespread use in the United States for both breast augmentation and reconstruction. The primary safety concerns are local complications and secondary surgeries.

OBJECTIVE: This study provides long-term data on complications and effectiveness.

METHODS: The study began as a prospective, multicenter study of 901 augmentation subjects and 237 reconstruction subjects implanted with Natrelle saline breast implants. After completing 5 years of annual visits with physician examinations, subjects were asked to enroll in a survey-based study for follow-up through 10 years. Survey questions encompassed the major safety outcomes of implant deflation, capsular contracture, breast pain, reoperation, and implant removal/replacement as well as subject satisfaction. Safety results were analyzed with Kaplan-Meier cumulative risk rates, and subject satisfaction was measured on a 6-point scale from definitely satisfied to definitely dissatisfied.

RESULTS: Of the 876 augmentation subjects and 194 reconstruction subjects who completed the 5-year study, 781 augmentation subjects (89.2%) and 170 reconstruction subjects (87.6%) consented to participate in the survey study. The survey response rate at 10 years was 91.4% for augmentation subjects and 85.9% for reconstruction subjects. Reoperation was the most frequent safety issue for both subject groups, and 90% of the implants remained intact at 10 years. Subject satisfaction was 87.5% for augmentation subjects and 86.3% for reconstruction subjects at 10 years.

CONCLUSIONS: This study demonstrates the long-term safety and effectiveness of Natrelle saline breast implants. The 10 years of data amassed in the clinical study provide a solid foundation to facilitate the informed decision process. (*Aesthetic Surg J 2008;28:19–25.*)

For more than 50 years, women have sought to enhance or restore the shape and appearance of their breasts with implants. In 1988, saline-filled breast implants were classified by the United States Food and Drug Administration (FDA) as class III devices—thereby requiring manufacturers to submit a premarket approval application to demonstrate the safety and effectiveness of the devices. In 1995, Allergan (Santa Barbara, CA; formerly Inamed) began a long-term prospective study of women implanted with saline-filled implants for breast augmentation or breast reconstruction. FDA approval was granted in 2000, and the devices branded as Natrelle saline-filled breast implants are currently in widespread use in the United States. Large bodies of data now support the safety of breast implants in general, with the main safety concerns being the potential for local complications and the need for secondary surgeries.

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The Allergan long-term study continued after FDA approval was granted, and this manuscript presents the full 10-year safety and effectiveness follow-up data.

METHODS

Study Design

The overall study was comprised of 2 phases. The first phase was a 5-year prospective, multicenter interventional clinical study designed to document short-term and intermediate-term safety and effectiveness via in-office visits. The second phase, for subjects consenting to continue, was a 5-year prospective, follow-up observational study performed via mailed questionnaires regarding specific complications and satisfaction with the implants.

After subject enrollment but before surgery, baseline information was obtained and subjects completed quality-of-life (QOL) questionnaires. Following breast surgery, office visits occurred at 0 to 4 weeks, 6 months, and annually for 5 years to assess the incidence of local complications and other safety factors. The effectiveness evaluation included changes in bra cup size from pre- to

postsurgery (augmentation subjects only), subject satisfaction with the implants, and QOL assessments (through 3 years). Upon completion of the 5-year in-office portion of the study, subjects were asked if they wanted to participate in the follow-up study. Subjects agreeing to participate signed a new informed consent form.

Two weeks before the sixth to tenth anniversaries of each subject's implantation surgery, a self-completion survey was sent by mail. The survey encompassed questions regarding reoperation, implant replacement/removal, breast pain, capsular contracture, implant deflation, and satisfaction with implants. For capsular contracture severity grading, subjects were provided with descriptions of the capsule grades which were later classified with Baker grade scores as follows: grade I (naturally soft), grade II (a little firm but looks normal), grade III (firm and looks abnormal due to capsular contracture), and grade IV (painfully hard and looks abnormal due to capsular contracture). These descriptions, coupled with the previous 5 years of office visits—in which investigators discussed capsular contracture as the predominant implant complication—provide reasonable expectations that subjects would appropriately classify the degree of contracture.

Subjects

The primary inclusion criteria for subjects were female, 18 years of age or older, adequate tissue to cover the implants, and no connective tissue or autoimmune disorders. Exclusion criteria included a medical history precluding suitability for surgery (eg, advanced fibrocystic disease or inadequate breast tissue), a previous history of breast augmentation or reconstruction, pregnancy or breastfeeding, any condition that might constitute an unduly high surgical risk, and psychological characteristics that might be incompatible with the surgical procedure or the implant.

Subjects were classified as either augmentation (hypoplasia, asymmetry, ptosis, aplasia, postlactational involution, or congenital deformity) or reconstruction (mastectomy for breast cancer or prophylactic mastectomy, plus contralateral augmentation if desired to match unilateral reconstructions). Both phases of the study obtained institutional review board approval and written informed consent from the subjects.

Devices

This study included the types of Natrelle saline-filled breast implants that were available in 1995, when the study began. Round implants with smooth (styles 60 or 68) or textured (style 168) surfaces and shaped implants with textured surfaces (styles 163, 363, and 468) were eligible for implantation in the study.

Statistical Analyses

Investigators used standardized case report forms to collect data prospectively before implantation and at scheduled follow-up visits as well as at unscheduled office visits. For those complications assessed with severity ratings, the "very mild" or "mild" severities or Baker grades I or II capsular contracture were not considered to be clinically significant problems, and therefore were not included in the analysis.

To determine the effect of implantation on breast size for augmentation subjects, bra size information was collected pre- and postimplantation. At each follow-up visit, subjects provided ratings of implant satisfaction utilizing a 6-point scale (definitely satisfied, satisfied, somewhat satisfied, somewhat dissatisfied, dissatisfied, or definitely dissatisfied). Subjects independently completed QOL questionnaires containing scales measuring general health concepts, self- and body esteem, and breast-related concepts.

The survey mailed to subjects included severity ratings for breast pain and capsular contracture and yes/no checkboxes for the other safety issues, along with checkboxes for common reasons for reoperation. The same 6-point satisfaction scale from the in-office study was included in the survey.

Kaplan-Meier survivorship was the primary analysis method for the safety data, while frequency distributions were employed for implant satisfaction data and reasons for reoperation and explantation. Descriptive statistics were used for breast size change results, and repeated analysis of variance measures were performed on the QOL results.

RESULTS

Subjects and Surgical Characteristics

A total of 1138 subjects enrolled in the study, consisting of 901 women (1800 implants) who underwent breast augmentation and 237 women (316 implants) who underwent breast reconstruction surgery. Of those 1138 subjects, 1070 (94%) completed the initial 5-year phase.

From the 1070 subjects who completed the in-office initial phase of the study, 88.9% consented to participate in the second 5-year phase. Specifically, 89.2% (781 of 876) augmentation subjects and 87.6% (170 of 194) reconstruction subjects enrolled in the mail-in survey portion of the study. At year 10, the surveys were completed by 91.4% of breast augmentation subjects (714 of 781) and 85.9% of reconstruction subjects (146 of 170).

Demographic data revealed that most subjects were white, married, and attended college (Table 1). The median age was 32 years for augmentation subjects and 47 years for reconstruction subjects. The implants used in augmentation subjects were most commonly round and were inserted submuscularly via a periareolar or inframammary incision; the implants used in reconstruction subjects were more frequently shaped and inserted submuscularly via the mastectomy scar (Table 2). Almost all of the reconstruction implants and two-thirds of the augmentation implants had a textured surface. Pocket irrigation with antibiotic or betadine solutions was common, and the vast majority of the implants

Table 1. Demographic data

Demographic	Augmentation (N = 901)	Reconstruction (N = 237)
Median age (yrs)	32	47
Range	18–66	25–77
Race [n (%)]		
White	793 (88.0%)	223 (94.1%)
African American	8 (0.9%)	7 (3.0%)
Other	82 (9.1%)	5 (2.1%)
Unknown	24 (2.7%)	2 (0.8%)
Marital status [n (%)]		
Single	257 (28.5%)	18 (7.6%)
Married	471 (52.3%)	181 (76.4%)
Widowed	5 (0.6%)	11 (4.6%)
Divorced	151 (16.8%)	25 (10.5%)
Other	25 (2.8%)	5 (2.1%)
Unknown	3 (0.3%)	0
Highest level of education [n (%)]		
High school graduate	196 (21.8%)	72 (30.4%)
Some college education	396 (44.0%)	60 (25.3%)
College graduate	240 (26.6%)	59 (24.9%)
Postgraduate education	50 (5.5%)	40 (16.9%)
Other	8 (0.9%)	5 (2.1%)
Unknown	11 (1.2%)	1 (0.4%)

Table 2. Device and surgical characteristics

Characteristic	Augmentation (N = 1800)	Reconstruction (N = 316)
Implant style [n (%)]		
Round	1311 (72.8%)	42 (13.3%)
Shaped	489 (27.2%)	274 (86.7%)
Implant texture [n (%)]		
Smooth	549 (30.5%)	6 (1.9%)
Textured	1251 (69.5%)	310 (98.1%)
Incision site [n (%)]		
Periareolar	822 (45.7%)	2 (0.6%)
Inframammary	629 (34.9%)	27 (8.5%)
Axillary	309 (17.2%)	7 (2.2%)
Mastectomy scar	–	279 (88.3%)
Other	40 (2.2%)	1 (0.3%)
Implant placement [n (%)]		
Submuscular	1420 (78.9%)	311 (98.4%)
Subglandular	380 (21.1%)	1 (0.3%)
Subcutaneous	0	4 (1.3%)
Pocket irrigation [n (%)]*		
N (subjects)	901	237
Antibiotic	431 (47.8%)	139 (58.6%)
Betadine	338 (37.5%)	85 (35.9%)
Steroid	54 (6.0%)	2 (0.8%)
None	188 (20.9%)	24 (10.1%)

*Totals more than 100% because some implants had more than 1 type of pocket irrigation.

were filled within the manufacturer recommended fill volume (80.0%) or less than 10% above the recommended fill volume (13.8%).

Safety

The data collected by physicians during in-office visits showed that through 5 years, the most common complications for augmentation subjects were breast pain (17.0%), wrinkling (13.7%), asymmetry (12.2%), and implant palpability/visibility (12.1%; Table 3). The most common complications for reconstruction subjects through 5 years were asymmetry (39.0%), capsular contracture (35.7%), implant palpability/visibility (27.1%), and wrinkling (24.6%). The risk of implant deflation through 5 years was 6.8% for augmentation subjects and 7.5% for reconstruction subjects.

The risk of reoperation (secondary surgical procedure to the breast) through 5 years was 25.9% for augmentation and 44.5% for reconstruction, with the most common reasons for augmentation reoperation being deflation or capsular contracture, and the most common reasons for reconstruction reoperation being capsular contracture or asymmetry. For those subjects who had their implants removed or replaced, the most common reasons for augmentation subjects were patient choice for style or size change (43.4% of 166 explants) or deflation (32.5% of 166 explants), and for reconstruction subjects capsular contracture (31.4% of 70 explants) or patient choice for style or size change (21.4% of 70 explants).

In the more limited safety items assessed at years 6 to 10 through the mailed survey, the most common occurrence for both augmentation and reconstruction subjects through 10 years was reoperation (36.5% and 54.6%, respectively; Table 4). Capsular contracture occurred in 20.8% of augmentation subjects and 51.7% of reconstruction subjects through 10 years. Less than one fourth of subjects experienced implant deflation (13.8% for augmentation; 22.5% for reconstruction), with overall implant survivorship (ie, 100% minus the Kaplan-Meier risk rate for by-implant deflation) of 90% after 10 years (Figure 1).

The 10-year risk rate for implant replacement/removal was 20.2% and 39.5% for augmentation and reconstruction subjects, respectively. The most common reasons for implant replacement/removal for augmentation subjects were patient choice for style or size change (41.3% of 300 explants) or deflation (33.3% of 300 explants), and for reconstruction subjects were also deflation (32.7% of 104 explants) or patient choice for style or size change (25.0% of 104 explants).

Table 3. Kaplan-Meier key risk rates by subject through 5 years

Key risk rates	Rate (95% confidence interval) Augmentation (N = 901)	Reconstruction (N = 237)
Reoperation	25.9% (23.0–28.9%)	44.5% (37.9–51.0%)
Implant replacement/removal	11.8% (9.6–14.0%)	28.0% (22.1–34.0%)
Implant deflation	6.8% (5.0–8.5%)	7.5% (3.8–11.2%)
Capsular contracture (Baker grades III/IV)	11.4% (9.2–13.5%)	35.7% (29.0–42.4%)
Additional risk rates occurring in >7% of subjects		
Breast pain	17.0% (14.5–19.5%)	17.7% (12.4–23.0%)
Wrinkling	13.7% (11.3–16.1%)	24.6% (18.6– 30.6%)
Asymmetry	12.2% (10.0–14.4%)	39.0% (32.1–45.8%)
Implant palpability/visibility	12.1% (9.8–14.3%)	27.1% (20.6–33.5%)
Loss of nipple sensation	9.9% (7.8–11.9%)	18.1% (12.5–23.8%)
Nipple hypersensitivity/paresthesia	9.8% (7.8–11.8%)	0.4% (0.0–1.2%)
Implant malposition	9.2% (7.3–11.2%)	16.9% (11.7–22.2%)
Skin hypersensitivity/paresthesia	7.6% (5.9–9.4%)	6.3% (2.9–9.6%)

Table 4. Kaplan-Meier risk rates by subject through 10 years

Risk	Rate (95% confidence interval) Augmentation (N = 901)	Reconstruction (N = 237)
Reoperation	36.5% (33.4–39.9%)	54.6% (48.1–61.5%)
Breast pain	29.7% (26.6–33.0%)	33.0% (26.4–40.7%)
Capsular contracture (Baker grades III/IV)	20.8% (18.1–23.8%)	51.7% (44.6–59.2%)
Implant replacement/removal	20.2% (17.7–23.1%)	39.5% (33.3–46.5%)
Implant deflation	13.8% (11.5–16.4%)	22.5% (16.8–29.7%)

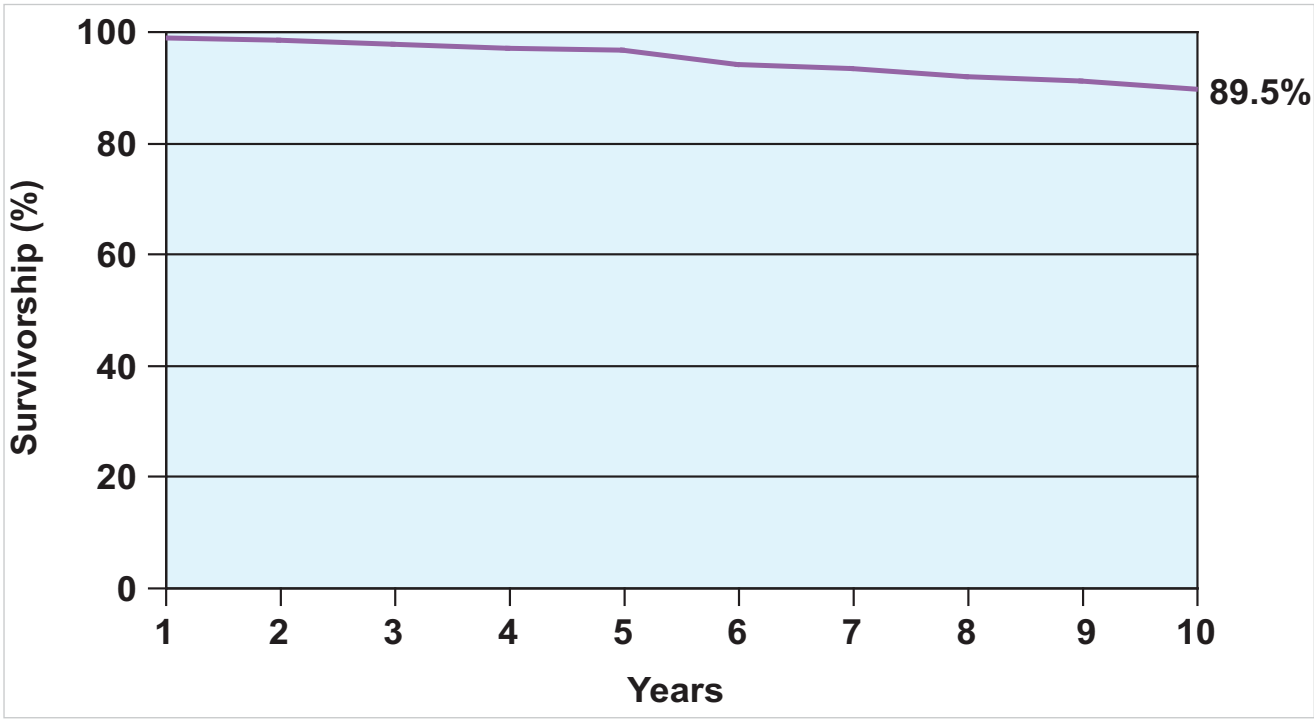

Figure 1. Rate of implant survivorship over 10 years.

Effectiveness

Most subjects who underwent augmentation increased breast size by either 1 (38%) or 2 (49%) cup sizes, with 9% having an increase of 3 cup sizes. The same cup size was maintained by 4% of subjects.

The mean QOL scores for augmentation subjects at 3 years postimplantation showed small but statistically significant decreases (worsening) over baseline in the general health concepts assessed by the Short Form 36 (SF-36) and most scales in the Body Esteem Scale (Table 5). Conversely, statistically significant improvements were seen in the Rosenberg Self-Esteem Scale and the Sexual Attractiveness scale of the Body Esteem Scale. However, aside from the improvement in the Sexual Attractiveness scale, the effect sizes were small, indicating that the changes were unlikely to be clinically significant. Dramatic improvement over baseline ($P < .001$) was evident in overall breast satisfaction and satisfaction with breast size, shape, and feel. Overall breast satisfaction for augmentation subjects increased from 3.8% at baseline to 91.9% at 3 years.

Ten years after their implant surgery, more than 85% of women (87.5% augmentation; 86.3% reconstruction) reported being satisfied with their implants (a response of either definitely satisfied, satisfied, or somewhat satisfied; Figure 2).

DISCUSSION

Until November 2006, when the FDA approved silicone gel-filled breast implants, saline breast implants were the de facto implant of choice in the United States. Now that the choices have been widened to include silicone implants, the question becomes how saline compares to silicone.

Comparing the 5-year office visit data from this saline study to Spear et al's report[1] of 6-year pivotal study data for Allergan (Natrelle) standard gel implants, we see similar results for the key risk rates of reoperation, implant removal/replacement, and implant rupture/deflation though a higher capsular contracture rate for reconstruction subjects with saline implants (15.9% for silicone versus 35.7% for saline). The real difference between the implant types comes down to the "look and feel" categories. Augmentation subjects with silicone implants had significantly lower rates for wrinkling (1.2% versus 13.7%), implant palpability/visibility (1.6% versus 12.1%), and asymmetry (3.0% versus 12.2%). Similar trends were seen for reconstruction subjects: wrinkling (10.2% versus 24.6%), implant palpability/visibility (4.1% versus 27.1%), and asymmetry (22.9% versus 39.0%).

The next-generation Natrelle highly cohesive silicone implants fare even better in comparison to the saline implants.[2] For augmentation subjects with highly cohesive implants, the 5-year pivotal study risk rate was less than 1% for wrinkling, implant palpability/visibility, and asymmetry. For reconstruction subjects at 5 years, wrinkling was 2.5%, implant palpability/visibility was 0%, and asymmetry was 9.1%.

These results quantify the commonly held belief espoused in continuing medical education articles on breast augmentation[3-4] and reconstruction[5] that saline implants are more prone to aesthetic complications,

Table 5. Quality of life assessments: Augmentation subjects

Assessment	Scale range	Baseline mean	3-yr mean	*P*	Effect size
General health concepts					
Role limitation caused by emotional problems (SF-36)	0–100	94.8	89.9	<.001	0.22
Role limitation caused by physical health problems (SF-36)	0–100	97.3	91.3	<.001	0.29
General health (SF-36)	0–100	90.7	87.3	<.001	0.22
Pain (SF-36)	0–100	92.6	88.3	<.001	0.23
Specific self-related concepts					
Self-esteem (Rosenberg)	10–40	35.3	35.7	.016	0.10
Body esteem: Total score (BES)	32–160	120.2	119.8	.002	0.11
Body esteem: Sexual attractiveness (BES)	13–65	48.9	51.0	<.001	0.36
Body esteem: Weight concern (BES)	10–50	34.1	33.1	<.001	0.02
Body esteem: Physical condition (BES)	9–45	37.0	35.5	<.001	0.10
Breast-related concepts					
Overall breast satisfaction	1–5	2.0	4.4	<.001	3.13
Satisfaction with breast size	1–5	1.8	4.3	<.001	3.25
Satisfaction with breast shape	1–5	2.6	4.4	<.001	1.58
Satisfaction with breast feel	1–5	3.6	4.0	<.001	0.36

BES, Body Esteem Scale; *Rosenberg*, Rosenberg Self-Esteem Scale; *SF-36*, Medical Outcomes Study 36-item Short-Form Survey.

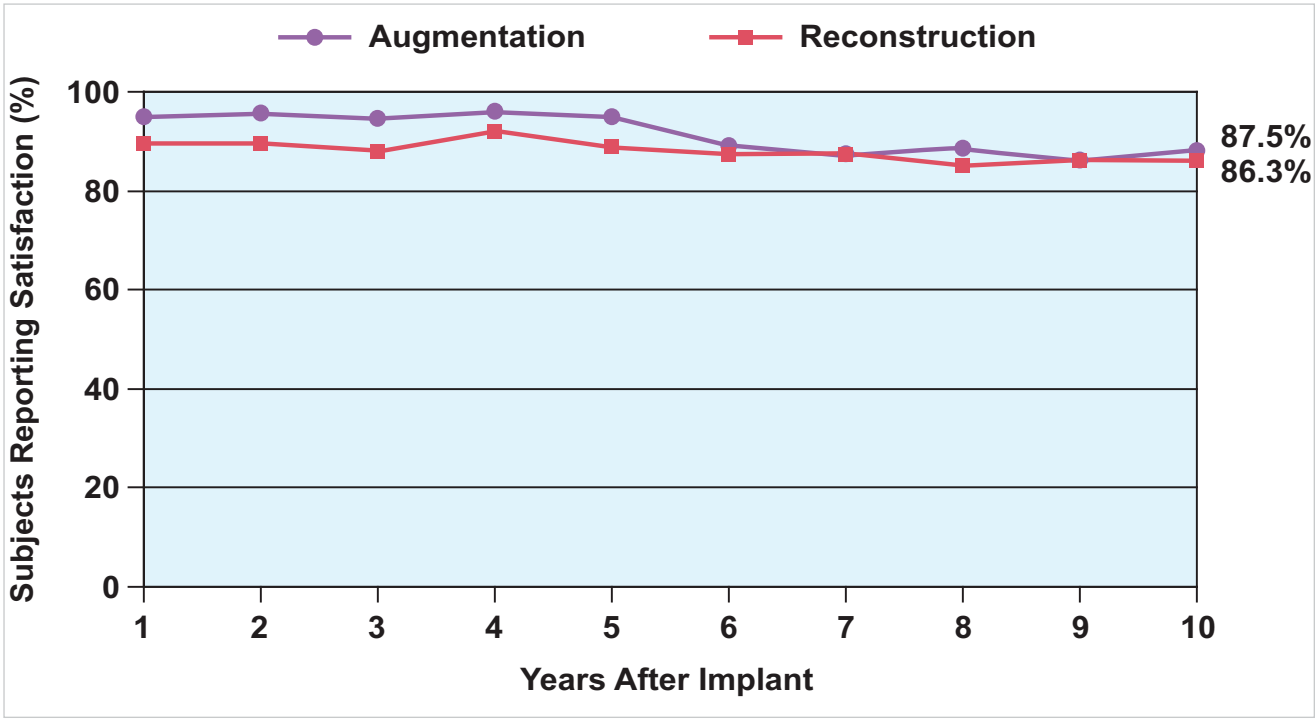

Figure 2. Proportion of subjects reporting satisfaction with their implants (ie, giving responses of definitely satisfied, satisfied, or somewhat satisfied).

such as wrinkling, palpability, visibility, and asymmetry. Saline implants also had a significantly greater risk of wrinkling (7.3% versus 2.1%; $P < .05$) in a study by Handel et al[6] that included 184 saline and 142 silicone implants.[6] An online survey by Young et al[7] of women who had undergone breast augmentation found that silicone implants were significantly more likely than saline implants ($P < .0001$) to be rated as "natural feeling."

In 2007, the first full year of silicone availability outside of clinical studies, 39.4% of the implantations used silicone implants,[8] up from 18.6% the previous year.[9] This proportion will likely increase over time, given the aesthetic benefits (natural look and feel) of silicone implants. However, saline implants remain a viable choice with their own aesthetic benefits (often a smaller incision).

Patients' satisfaction with saline breast implants is similar to their satisfaction with other cosmetic procedures. Sarwer et al's prospective study[10] of 100 subjects who underwent a variety of cosmetic procedures found that 1 year after the surgical procedure, 70% of participants were "extremely satisfied," a rating of 5 on a 5-point scale. Our saline data also show that 1 year postimplantation, 70% of augmentation subjects rated their satisfaction at the highest level on the scale (definitely satisfied). In comparison, the 1-year proportion of subjects definitely satisfied with their Natrelle silicone implants was 83% for standard silicone and 89% for highly cohesive silicone implants.[11] This greater percentage of subjects who are exceedingly satisfied with their implants is likely related to the natural look and feel benefits described above.

Overall satisfaction rates (including all levels of satisfaction on the rating scale) are extremely high for all of the implant types and remain so over time. The 3 pivotal Natrelle studies showed that satisfaction with augmentation implants was 88% at 10 years for saline implants, 95% at 6 years for silicone implants,[1] and 97% at 5 years for highly cohesive silicone implants.[2] The same studies found that satisfaction with reconstruction implants was similarly high at 86% for saline, 94% for silicone, and 92% for highly cohesive silicone. Therefore, it is not a question of which filler type is better—what is important is for the surgeon and prospective patient to draw upon the body of evidence available to them in order to select the right implant for that particular patient.

CONCLUSIONS

This study demonstrates the long-term safety and effectiveness of Natrelle saline breast implants. The 10 years of data amassed through a prospective clinical study provide a solid foundation of information to facilitate the informed decision process. ◗

ACKNOWLEDGMENTS

The authors would like to thank Maggi Beckstrand, MPH, for biostatistical assistance.

DISCLOSURES

Dr. Walker is an Allergan stockholder and former employee. Ms. Murphy and Ms. Walls are Allergan employees and stockholders. Financial support for this study was provided by Allergan. Allergan was also responsible for the study design and data analysis.

REFERENCES

1. Spear SL, Murphy DK, Slicton A, Walker PS. Inamed silicone breast implant core study results at 6 years. *Plast Reconstr Surg* 2007;120(7 Suppl 1):8S–16S.
2. Natrelle silicone-filled breast implants [package insert, Canada]. Santa Barbara, CA: Allergan; 2008.
3. Alpert BS, Lalonde DH. MOC-PS(SM) CME article: breast augmentation. *Plast Reconstr Surg* 2008;121(4 Suppl):1–7.
4. Spear SL, Bulan EJ, Venturi ML. Breast augmentation. *Plast Reconstr Surg* 2006;118(7 Suppl):188S–196S.
5. Sigurdson L, Lalonde DH. MOC-PS SM CME article: breast reconstruction. *Plast Reconstr Surg* 2008;121(1 Suppl):1–12.
6. Handel N, Jensen A, Black Q, Waisman JR, Silverstein MJ. The fate of breast implants: a critical analysis of complications and outcomes. *Plast Reconstr Surg* 1995;96:1521–1533.
7. Young VL, Watson ME, Boswell CB, Centeno RF. Initial results from an online breast augmentation survey. *Aesthetic Surg J* 2004;24:117–135.
8. American Society for Aesthetic Plastic Surgery Web site. 2007 cosmetic surgery national data bank statistics. (Accessed 5/22/2008, at http://www.surgery.org/download/2007stats.pdf.)
9. American Society for Aesthetic Plastic Surgery Web site. 2006 cosmetic surgery national data bank statistics. (Accessed 5/22/2008, at http://www.surgery.org/download/2006stats.pdf.)
10. Sarwer DB, Infield AL, Baker JL, Casas LA, Glat PM, Gold AH, et al. Two-year results of a prospective, multi-site investigation of patient satisfaction and psychosocial status following cosmetic surgery. *Aesthetic Surg J* 2008;28:245–250.
11. Gladfelter J, Murphy D. Breast augmentation motivations and satisfaction: a prospective study of more than 3,000 silicone implantations. *Plast Surg Nurs* (in press).

Accepted for publication September 30, 2008.

Presented in poster form at the American Society for Aesthetic Plastic Surgery, Inc. and the Aesthetic Surgery Education and Research Foundation Aesthetic Meeting 2007, April 19–25, 2007, New York, NY.

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1090-820X/$36.00

doi:10.1016/j.asj.2008.10.001