Over the past 50 years, breast implants have been available for breast reconstruction and augmentation; extra high–profile devices have been available for the past 10 years.1,2 Despite many years of experience in breast implant surgery, there is a paucity of clinical data concerning the potential risks and benefits associated with the use of high- and extra high–profile breast implants. Substituting for this data gap have been personal and anecdotal experiences of plastic surgeons, some of whom have suggested that high- and extra high–profile breast implants may be associated with higher risks of adverse events (AE) such as chest wall deformity, breast ptosis, tissue thinning, parenchymal atrophy, capsular contracture (CC), malposition, or need for secondary surgery.2,3 Despite these suggestions, patients generally
tolerate high-profile implants without issue.\(^4\) Moreover, similar AE have also been reported with mid- and low-profile breast implants.\(^4\) Overall, variables other than—and/or in addition to—breast implant projection, such as patient soft-tissue quality (eg, ptotic breasts or inelastic skin), patient age and childbearing history, or a history of significant weight loss, may affect the risk of AE in breast implant surgery.\(^5\) In general, the risk of AE, particularly CC and malposition, can be reduced by considering appropriate implant profile, base diameter, and implant volume in relation to the dimensions and soft-tissue quality of the patient.\(^2\) Capsular contracture is the most common risk associated with breast implant augmentation and reason for secondary surgery. The 10-year cumulative incidence rates of CC (Baker grades 3 and 4) for Allergan silicone breast implants (Allergan, Inc, Irvine, California) range from 6.7% to 27.5%, depending on the indication for the implant.\(^5\) Cumulative incidence rates for other AE have also been reported.\(^5\) The incidence of CC with silicone-filled breast implants has been reported to be similar to those with saline-filled implants, although there is a lack of properly designed and adequately powered prospective data.\(^6\) Overall, the existing data are equivocal, and it is unclear if implant position, textured or smooth surface, or saline or silicone-fill confers reduced risk of CC.\(^7-10\) The causes of CC are not clearly understood, but clinical data have demonstrated that subclinical bacterial infection (“biofilm”) can be a significant cause.\(^11,12\)

The causes of malposition are also poorly characterized but may be associated with surgical technique and postoperative management. Inappropriately large implant pocket sizes or excessive postoperative activity may prevent the development of connective tissue integration between a textured implant surface and the surrounding breast tissue, thereby allowing subsequent malrotation.\(^1,13,14\)

The lack of definitive clinical data on risks and benefits of high- and extra high–profile breast implants relative to moderate- or low-profile implants has led to calls for data from clinical trials.\(^2\) In response, we report on the risk-benefit profile for high- and extra high–profile breast implants by analyzing risks of CC, moderate to severe malposition, and secondary surgical outcome relative to moderate- or low-profile implants in patients registered in pooled long-term clinical trials.

**METHODS**

**Study Protocols**

The Core (NCT00689871) and 410 (NCT00690339) studies described in this report were interventional, nonrandomized, open-label clinical studies designed to evaluate long-term safety and efficacy of breast implants. Publications presenting 6-year data from the Core and 410 studies have reported high levels of safety and patient satisfaction.\(^15,16\) Patient inclusion and exclusion criteria were detailed in previously described study protocols.\(^15,16\) Magnetic resonance imaging (MRI) was obtained periodically, per protocol, to assess “silent” implant rupture but not soft-tissue thickness.

All study protocols were approved by applicable institutional review boards. There were a variety of institutional review boards involved in the various implant studies. Patients provided written informed consent. These studies were performed in accordance with Good Clinical Practice and were initiated to obtain US Food and Drug Administration (FDA) approval via a Premarket Approval (PMA) regulatory pathway. The clinical sites were carefully selected and data were collected using a systematic approach.

**Breast Implant Devices**

The breast implants used in the Core study were silicone-filled, round implants with a smooth or aggressively textured surface. The breast implants used in the 410 study and 410 Continued Access studies were silicone-filled (highly cohesive) and anatomically shaped with an aggressively textured surface. Patients participating in the primary augmentation cohorts of the Core study received low- to moderate-profile (style 40, 110) and high-profile (style 45, 120) implants. Patients participating in the primary augmentation cohort of the 410 studies received low-profile (style FL, ML), midrange-profile (style FM, MM, LM), and full/high/extra high–profile (style FF, MF, LF, FX, MX, LX) implants.

**Analysis Parameters**

This analysis included active follow-up of patients in primary augmentation cohorts from the Core and 410 studies to investigate the effect of breast implant profile size on risk of CC, moderate to severe malposition, secondary surgical procedures due to AE, and mastopexy. Details of patients, follow-up, devices, and procedures for Core and 410 studies are shown in Table 1. Pooling of the Core and 410 studies was performed to increase sample size and variability of device types and was done on the basis of comparable patient populations and standardized patient follow-up and outcome assessment between studies. Specifically, combining the studies increased the range of surface types, device profiles, and statistical power to evaluate profile as an independent predictor for the target outcomes. To determine whether the associations between device profiles and target outcomes were restricted to a particular study or device type, sensitivity analyses were performed within the Core study, which had longer accrued patient follow-up and was limited to the round, silicone-filled devices. The results for the Core study are therefore also presented separately.

Capsular contracture was measured using the Baker grade.\(^17,18\) The degree of malposition was recorded by the investigators on a 5-point scale (none, very mild, mild, moderate, severe). Outcomes are a function of many clinical input variables that need to be controlled to parse the contributor of each to the measured event. Patients undergoing revision augmentation or reconstruction procedures were not included in the analysis.
Parameters measured included patient age at surgery, body mass index (BMI), breast implant profile, breast implant size (volume or weight), device surface, device fill, placement, incision site, use of parenteral antibiotics and/or steroids, pocket irrigation with antibiotics and/or steroids, use of drains, and preoperative breast measurement.

Table 1. Core Study and Combined Core and 410 Studies Primary Augmentation Cohorts: Patients, Devices, and Procedures

| Characteristics                        | Core Study, No. (%) | Combined Core and 410 Studies, No. (%) |
|----------------------------------------|---------------------|----------------------------------------|
| Patients enrolled                      | 454                 | 4412                                   |
| Age, y, mean (SD); min-max              | 34.4 (8.2); 18-57    | 35 (8.6); 18-82                        |
| Body mass index, mean (SD); min-max    | 20.2 (2.3); 15-31    | 20.7 (2.6); 13-40                      |
| Devices implanted, No.                 | 907                 | 8811                                   |
| Dates of enrollment                    | January 6, 1999, to June 30, 2000 | 1999 to 2009                           |
| Scheduled follow-up postoperative visits| 0-4 wk, 6 mo, annually years 1-10 | 6 mo, annually years 1-10              |
| Duration of follow-up, mo, mean (SD); min-max | 86 (38); 0-124 | 37 (32); 0-124                        |
| Person-years of follow-up              | 3669                | 14 528                                 |
| Device fill, No. (%)                   |                     |                                        |
| Silicone                                | 907 (100.0)         | 907 (10.3)                             |
| Highly cohesive (410) silicone         | —                   | 7904 (90.7)                            |
| Device surface, No. (%)                |                     |                                        |
| Smooth                                 | 536 (59.1)          | 536 (6.1)                              |
| Aggressively textured                  | 371 (40.9)          | 8275 (93.9)                            |
| Device shape, No. (%)                  |                     |                                        |
| Round                                  | 907 (100.0)         | 907 (10.3)                             |
| Anatomically shaped                    | —                   | 7904 (90.7)                            |
| Incision site, No. (%)                 |                     |                                        |
| Periareolar                            | 355 (39.1)          | 981 (11.4)                             |
| Axillary                               | 122 (13.4)          | 132 (1.5)                              |
| Inframammary                           | 417 (46.0)          | 7526 (87.1)                            |
| Unknown                                | 13 (1.4)            | —                                      |
| Profile (style), No. (%)               |                     |                                        |
| Low/moderate (FL, ML, 40, 110)         | 659 (72.7)          | 678 (7.7)                              |
| Midrange (FM, MM, LM)                  | —                   | 4027 (45.7)                            |
| High/full/extra high (FF, MF, LF, FX, MX, LX, 45, 120) | 248 (27.3) | 4106 (46.6)                           |
| Placement, No. (%)                     |                     |                                        |
| Subcutaneous                           | 6 (0.7)             | 10 (0.1)                               |
| Subglandular                           | 269 (29.7)          | 1213 (13.8)                            |
| Subpectoral-partial                    | 546 (60.2)          | 7306 (82.9)                            |
| Subpectoral-complete                   | 86 (9.5)            | 282 (3.2)                              |
| Preoperative breast measurement, cm, mean (SD); min-max | 17.4 (3.9); 10.0-38.0 | 17.2 (3.7); 4.3-39.0 |
(the breast mound, measured as the distance between the point at which breast mound began laterally across the nipple to where it ended medially).

Statistics

Hazard ratios (relative risk, RR) and 95% confidence intervals (95% CI) for time to first event of Baker grade 3 to 4 CC, moderate to severe malposition, secondary surgical procedures due to AE, or mastopexy following enrollment surgery were estimated using Cox proportional hazards regression. The outcome of clinical studies is commonly described by using time-to-event curves analyzed by Cox proportional hazards regression. This methodology has the advantage of using all available information, including patients who fail to complete the study.\textsuperscript{19} A censoring event is the last recorded follow-up for the patient where the outcome was not observed. In this analysis, patients who failed to complete the study or who had not yet reached the end of the study can be included in order to provide information. In other words, these patients were observed to not have the outcome of interest up to the time of censoring, yet no assumptions were made about whether the outcome occurred after the censoring event. This method allowed for comparisons between patients with follow-up in each group at multiple points in time.

The unit of analysis was each device. This time-to-event analysis was performed to adjust for multiple covariates that could influence the outcomes under study, and censoring events included last follow-up visit, explant (except in analyses of secondary procedure where explant was considered an event), study discontinuation, or death. For the analysis of mastopexy, additional censoring events included other surgical procedures due to AE (eg, capsulectomy). Independent variables examined included age at implant surgery (years, continuous), BMI (kg/m\textsuperscript{2}, continuous), implant size (50-cc or 50-g increases), implant profile (low to moderate, midrange, or full/high/extra high), implant placement (subglandular, subpectoral), incision site (periareolar, axillary, inframammary), use of parenteral antibiotics (no, yes), use of parenteral steroids (no, yes), pocket irrigation with antibiotics (no, yes), pocket irrigation with Betadine (no, yes), and use of drains (no, yes). Adjusted models included all independent variables in addition to device surface (smooth, aggressively textured) and device fill (silicone, highly cohesive silicone). Preoperative breast measurement (<17 cm, ≥17 cm) was used for stratified analyses to investigate whether the effect of implant profile on CC, malposition, and secondary procedure was modified by preoperative breast size. The assumption of proportional hazards for the Cox model is that the hazard ratios (or relative risks) are proportional over the follow-up period. To correct violations of the proportional hazard assumption, all time-interaction terms were tested.\textsuperscript{20-23} The final models included only those interaction terms with $P < .001$. There was no adjustment for multiple comparisons, and $P < .05$ was considered statistically significant. Kaplan-Meier plots were generated to estimate the survival function for each outcome by implant profile over months of follow-up. All analyses were performed using SAS version 9.1 (SAS Institute, Cary, North Carolina).

RESULTS

The primary breast augmentation cohort of the Core study, with a mean follow-up of 7.2 years (3669 person-years), included 454 patients with 907 breast implants (Table 1). To broaden the types of devices studied, the primary breast augmentation cohorts of the Core and 410 studies were combined with a mean follow-up of 3.0 years (14 528 person-years), including 4412 patients with 8811 breast implants with follow-up attained through August 2009 (Table 1). Baseline characteristics are detailed in Table 1.

The minimum breast implant device volumes used in the primary augmentation cohorts of the Core study and combined studies were in the 50- to 99-cc range; the maximum device volumes were 650 to 699 cc for the Core study and 700 to 749 cc for the combined studies (Table 2). The most common breast implant devices in the Core study and combined studies were in the 300- to 349-cc range (40.5%) and 350- to 399-cc range (28.1%), respectively (Table 2). The median breast implant size in the combined studies was 325 cc. Increasing implant volume

| Device Volume, cc (or g) | Core Study, No. (%) | Combined Core and 410 Studies, No. (%) |
|-------------------------|--------------------|--------------------------------------|
| 50-99                    | 3 (0.3)            | 3 (0.03)                             |
| 100-149                  | 2 (0.2)            | 2 (0.02)                             |
| 150-199                  | 21 (2.3)           | 77 (0.9)                             |
| 200-249                  | 93 (10.2)          | 683 (7.9)                            |
| 250-299                  | 143 (15.8)         | 1906 (21.6)                          |
| 300-349                  | 367 (40.5)         | 2292 (26.0)                          |
| 350-399                  | 143 (15.8)         | 2477 (28.1)                          |
| 400-449                  | 99 (10.9)          | 809 (9.2)                            |
| 450-499                  | 19 (2.1)           | 363 (4.1)                            |
| 500-549                  | 9 (1.0)            | 115 (1.3)                            |
| 550-599                  | 2 (0.2)            | 44 (0.5)                             |
| 600-649                  | 1 (0.1)            | 9 (0.1)                              |
| 650-699                  | 2 (0.2)            | 11 (0.1)                             |
| 700-749                  | —                  | 2 (0.02)                             |
| Missing                  | 3 (0.3)            | 8 (0.09)                             |
was modestly associated with reduced risk of malposition, secondary procedure, and mastopexy in the Core study but not the combined studies in the adjusted models (Tables 3 and 4).

### Risk of CC

In the Core study, 126 events of Baker grade 3 or 4 CC were recorded. The risk of CC was significantly lower in patients with high-profile versus low- to moderate-profile breast implants using the adjusted model (RR, 0.21 [95% CI, 0.10-0.45], \( P < .01 \)) (Table 3). In the combined studies, there were 317 events of CC. Time in months to CC by implant profile is presented in Figure 1. The risk of CC was also significantly lower in midrange-profile and full/high/extra high-profile versus low- to moderate-profile breast implants in the adjusted model (midrange: RR, 0.49 [95% CI, 0.28-0.84], \( P < .05 \); full/high/extra high: RR, 0.55 [95% CI, 0.35-0.87], \( P < .05 \)) (Table 4).

The risk of CC was reduced with subpectoral (partial or complete) versus subglandular placement in the combined studies (Table 4). The risk of CC was higher with increased patient age in the Core and combined studies (Table 3).

### Risk of Moderate to Severe Malposition

In the Core study, 40 events of moderate to severe malposition were recorded. The risk with high-profile versus low- to moderate-profile breast implants was not significantly different in the adjusted model (RR, 0.58 [95% CI, 0.22-1.51]) (Table 3). However, the risk of moderate to severe malposition was modestly reduced with increasing implant size (RR, 0.76 [95% CI, 0.58-1.00], \( P < .05 \)) (Table 3). In the combined studies, 156 moderate to severe events of malposition were recorded. Time in months to malposition by implant profile is presented in Figure 2. The relative risk of moderate to severe malposition was not significantly different with full/high/extra high-profile versus low- to moderate-profile breast implants using the adjusted model (RR, 0.72 [95% CI, 0.31-1.70]) (Table 4). The relative risk of moderate to severe malposition in the combined studies was significantly reduced with

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### Table 3. Core Study: Risk of Capsular Contracture, Malposition, Secondary Procedure Due to Adverse Event, and Mastopexy

| Risk of Capsular Contracture (Baker Grade 3-4) | Malposition (Moderate-Severe) | Secondary Procedure | Mastopexy as Secondary Procedure |
|-----------------------------------------------|--------------------------------|---------------------|----------------------------------|
| | Unadjusted RR (95% CI) | Adjusted RR\(^a\) (95% CI) | Unadjusted RR (95% CI) | Adjusted RR\(^a\) (95% CI) | Unadjusted RR (95% CI) | Adjusted RR\(^a\) (95% CI) | Unadjusted RR (95% CI) | Adjusted RR\(^a\) (95% CI) |
| Patient age at surgery, continuous, y | 1.04 (1.02, 1.07) | 1.03 (1.01, 1.06) | 1.02 (0.98, 1.05) | 1.01 (0.98, 1.05) | 1.00 (0.96, 1.02) | 1.00 (0.98, 1.02) | 1.06 (1.02, 1.10) | 1.02 (0.99, 1.07) |
| Patient BMI (continuous) | 1.09 (1.02, 1.16) | 1.06 (0.98, 1.14) | 0.98 (0.85, 1.12) | 1.02 (0.88, 1.18) | 1.01 (0.95, 1.07) | 1.03 (0.97, 1.10) | 1.09 (0.87, 1.22) | 1.07 (0.94, 1.21) |
| Implant size (volume in 50-cc increases) | 0.83 (0.73, 0.94) | 0.88 (0.76, 1.03) | 0.76 (0.61, 0.95) | 0.76 (0.58, 1.00) | 0.79 (0.71, 0.87) | 0.77 (0.69, 0.86) | 0.65 (0.53, 0.81) | 0.58 (0.44, 0.77) |

Profile (style)

| | Low-moderate | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| High | 0.73 (0.48, 1.10) | 0.21 (0.10, 0.45) | 0.46 (0.19, 1.10) | 0.58 (0.22, 1.51) | 0.51 (0.46, 0.73) | 0.53 (0.36, 0.79) | 0.13 (0.03, 0.53) | 0.18 (0.04, 0.77) |

Placement

| | Subglandular | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Subpectoral | 0.55 (0.39, 0.79) | 0.64 (0.41, 1.01) | 1.12 (0.56, 2.23) | 0.69 (0.29, 1.62) | 0.76 (0.57, 1.01) | 0.74 (0.52, 1.07) | 0.28 (0.15, 0.54) | 0.35 (0.15, 0.83) |

BMI, body mass index; CI, confidence interval; Ref, reference group; RR, relative risk.

\(^a\)Multivariate models adjusted for variables in the table in addition to time interaction terms as described in the Methods section, device fill, device surface, incision site, parenteral antibiotics, parenteral steroids, pocket irrigation with antibiotics, pocket irrigation with Betadine, and use of drains.

\(^\) \( P < .001.\)

\(^\) \( P < .01.\)

\(^\) \( P < .05.\)
Risk of Secondary Surgical Procedures Due to AE

In the Core study, 207 devices underwent secondary procedures. The relative risk of secondary procedures was significantly lower with high-profile versus low- to moderate-profile breast implants using the adjusted model (RR, 0.53 [95% CI, 0.36-0.79], P < .01) (Table 3). In addition, increasing implant size was associated with reduced risk of secondary procedure (RR, 0.77 [95% CI, 0.69-0.86], P < .001) (Table 3). In the combined studies, 8.8% (n = 774) of implants underwent secondary surgical procedures due to AE. Time in months to secondary procedure by implant profile is presented in Figure 3. Secondary procedures included mastopexy (n = 134), capsulotomy or capsulectomy (n = 79), and aspiration of seroma or hematoma (n = 25). Five hundred four patients

Table 4. Combined Core and 410 Studies: Risk of Capsular Contracture, Malposition, Secondary Procedure Due to Adverse Event, and Mastopexy

| Capsular Contracture (Baker Grade 3-4)* | Malposition (Moderate-Severe)b | Secondary Procedurec | Mastopexy as Secondary Procedured |
|----------------------------------------|--------------------------------|----------------------|----------------------------------|
| **Unadjusted RR (95% CI)**             | **Adjusted RR* (95% CI)**     | **Unadjusted RR (95% CI)** | **Adjusted RR* (95% CI)**    |
| Patient age at surgery, continuous, y  | 1.02 (1.01, 1.04)             | 1.02 (1.01, 1.03)      | 1.00 (0.98, 1.02)             | 1.01 (1.00, 1.02)          |
| Patient BMI (continuous)               | 1.03 (0.99, 1.08)             | 1.02 (0.98, 1.07)      | 0.97 (0.91, 1.03)             | 1.01 (0.98, 1.04)          |
| Implant size (volume in 50-cc increases)| 0.91 (0.84, 0.99)f            | 0.95 (0.87, 1.03)      | 0.95 (0.85, 1.06)             | 0.93 (0.83, 1.05)          |
| Profile (style)                        |                                |                      |                                  |                                |
| Low-moderate                           | 0.35 (0.26, 0.47)l            | 0.49 (0.28, 0.84)l    | 0.30 (0.19, 0.48)l             | 0.56 (0.46, 0.69)l          |
| Midrange                               | 0.30 (0.19, 0.48)l            | 0.33 (0.13, 0.84)l    | 0.37 (0.25, 0.55)l             | 0.31 (0.19, 0.49)l          |
| Full/high/extra high                   | 0.42 (0.32, 0.56)f            | 0.55 (0.35, 0.87)d    | 0.63 (0.42, 0.96)f             | 0.66 (0.54, 0.80)f          |
| Placement                              |                                |                      |                                  |                                |
| Subglandular                           | 0.39 (0.31, 0.50)f            | 0.43 (0.33, 0.56)f    | 0.68 (0.46, 1.00)f             | 0.85 (0.71, 1.02)          |
| Subpectoral                            | 0.39 (0.31, 0.50)f            | 0.43 (0.33, 0.56)f    | 0.68 (0.46, 1.00)f             | 0.85 (0.71, 1.02)          |

BMI, body mass index; CI, confidence interval; Ref, reference group; RR, relative risk.

*P < .001.

**P < .01.

***P < .05.

Figure 1. Kaplan-Meier plot of time (months) to capsular contracture (Baker grade 3-4) analyzed by implant projection in the primary augmentation cohorts of the combined Core and 410 studies.

subpectoral (partial or complete) versus subglandular placement (Table 4).
underwent the explant procedure, including explants with mastopexy, with the largest subgroup being patients receiving replacement implants with or without other procedures (excluding explants for size change; Table 5).

In the combined studies, the relative risk of secondary procedures was significantly lower with midrange-profile (RR, 0.37 [95% CI, 0.25-0.55], \( P < .001 \)) and with full/high/extra high-profile (RR, 0.46 [95% CI, 0.32-0.66], \( P < .001 \)) versus low- to moderate-profile breast implants in the adjusted model (Table 4).

### Risk of Mastopexy

In the Core study, 40 mastopexy procedures were performed during follow-up, either alone or in combination with other procedures. Among low- to moderate-profile and high-profile implants, 38 (5.8%) and 2 (0.8%) patients, respectively, underwent mastopexy during follow-up. High-profile implants were associated with significantly reduced risk of mastopexy in the adjusted model (RR, 0.18 [95% CI, 0.04-0.77], \( P < .05 \)). Increasing implant size was also associated with reduced risk of mastopexy, as was subpectoral versus subglandular implant placement (Table 3).

In the combined studies, 134 mastopexy procedures were recorded during follow-up, either alone or in combination with other procedures. Among low- to moderate-profile, midrange-profile, and full/high/extra high-profile implants, 40 (5.9%), 39 (1.0%), and 55 (1.3%) patients, respectively, underwent mastopexy during follow-up. Time in months to mastopexy by implant profile is presented in Figure 4. Midrange- and full/high/extra high-profile implants were associated with significantly reduced risk of mastopexy in adjusted models (midrange: RR, 0.07 [95% CI, 0.02-0.17], \( P < .001 \); full/high/extra high: RR, 0.11 [95% CI, 0.04-0.29], \( P < .001 \)).

### Analyses Stratified by Preoperative Breast Measurement

In the combined studies, 8687 breasts had preoperative measures available, with 3989 < 17 cm and 4698 ≥ 17 cm. Among devices with a preoperative breast measurement < 17 cm, there were 123 events of CC Baker grade 3 or 4, 54 events of moderate to severe malposition, 280 events of secondary procedure due to AE, and 33 events of mastopexy as
specifically as compared with low- or moderate-profile CC, secondary procedures due to AE, and mastopexy. Implants of either type are associated with reduced risk of large, prospective clinical studies suggest that high-profile (form-stable) devices (410 studies). The results of these combined with the shaped, highly cohesive, silicone-filled silicone-filled devices alone (Core study) or when combined studies—including patients with shaped, extra high–profile implants were associated with reduced risk of mastopexy as compared with low- to moderate-profile devices and combined studies were on average thin, with baseline BMI professional planning and soft-tissue quality assessment—suggests that use of high- or extra high–profile implants is not associated with a greater risk of CC or secondary procedures. The median breast implant volume in the combined studies was 325 cc, with the largest implant volumes in the 650- to 749-cc range.

Breast ptosis is reported to be a potential AE of high-profile breast implants. In the combined studies, 134 (1.5%) implants underwent mastopexy secondary surgery either with or without other procedures, suggesting a low incidence of ptosis. Time-to-event analyses revealed a clinically important observation—that full/high/extra high–profile implants were associated with a significantly reduced risk of mastopexy in both round silicone gel and shaped form-stable implants. Patients in the Core and combined studies were on average thin, with baseline BMI in the 20- to 21-kg/m² range. In this analysis, BMI and age were regarded as proxy measures of soft-tissue quality and were included as covariates in multivariate analyses to adjust for the potential effects of these factors.

The authors submit that the problem of breast implant AE is multifactorial in nature and may involve patient age, size, breast volume, genetics, soft-tissue quality and stretch, weight change, childbearing history, and the inexorable effects of gravity. Unfortunately, some of these factors were not considered in the design of these observational clinical trials and therefore should be viewed as limitations that cannot be assessed in the data presented here. As patients did not undergo MRI evaluation before surgery, comparison between preoperative and postoperative soft-tissue quality cannot be made. Additional considerations include the normal asymmetry of soft-tissue quality between patients’ breasts, which may also affect success of breast implantation.

A limitation of the studies described and the conclusions drawn here is that the studies were observational; a randomized study comparing high- and extra high–profile versus

**DISCUSSION**

Analyses of the primary augmentation cohorts of the Core and combined studies—including patients with shaped, highly-cohesive (410) silicone-filled devices—demonstrated that high- and extra high–profile breast implants were associated with a significantly lower risk of CC and secondary surgical procedures versus low- or moderate-profile implants when results were considered for round silicone-filled devices alone (Core study) or when combined with the shaped, highly cohesive, silicone-filled (form-stable) devices (410 studies). The results of these large, prospective clinical studies suggest that high-profile implants of either type are associated with reduced risk of CC, secondary procedures due to AE, and mastopexy specifically as compared with low- or moderate-profile implants after adjusting for patient, surgical procedure, and additional device characteristics.

Multiple variables have potentially protective and contributory effects on the reporting of CC, moderate to severe malposition, and secondary surgery. To control for these complex interactions and minimize the potential for confounding bias, adjusted (multivariate) time-to-event regression analyses were performed. These statistical methods provided a comprehensive assessment of the potential of high- and extra high–profile implants to contribute to risk of AE.

This report represents the first comparative analysis of the risk of AE associated with high-profile as compared with low- to moderate-profile breast implants and contributes to addressing a data gap acknowledged in the literature. In general, we recommend that surgeons stay within the biodimensional limits of the patient, considering factors such as patient size, skin elasticity, and breast tissue quality when selecting breast implants. Some surgeons have attempted to define insertion of high- or extra high–profile breast implants with a volume greater than 350 cc as inappropriate; however, the data presented in our report—adjusted for multiple variables, stratified by preoperative breast measurement, and driven by biodimensional planning and soft-tissue quality assessment—suggests that use of high- or extra high–profile implants is not associated with a greater risk of CC or secondary procedures. The median breast implant volume in the combined studies was 325 cc, with the largest implant volumes in the 650- to 749-cc range.

Breast ptosis is reported to be a potential AE of high-profile breast implants. In the combined studies, 134 (1.5%) implants underwent mastopexy secondary surgery either with or without other procedures, suggesting a low incidence of ptosis. Time-to-event analyses revealed a clinically important observation—that full/high/extra high–profile implants were associated with a significantly reduced risk of mastopexy in both round silicone gel and shaped form-stable implants. Patients in the Core and combined studies were on average thin, with baseline BMI in the 20- to 21-kg/m² range. In this analysis, BMI and age were regarded as proxy measures of soft-tissue quality and were included as covariates in multivariate analyses to adjust for the potential effects of these factors.

The authors submit that the problem of breast implant AE is multifactorial in nature and may involve patient age, size, breast volume, genetics, soft-tissue quality and stretch, weight change, childbearing history, and the inexorable effects of gravity. Unfortunately, some of these factors were not considered in the design of these observational clinical trials and therefore should be viewed as limitations that cannot be assessed in the data presented here. As patients did not undergo MRI evaluation before surgery, comparison between preoperative and postoperative soft-tissue quality cannot be made. Additional considerations include the normal asymmetry of soft-tissue quality between patients’ breasts, which may also affect success of breast implantation.

A limitation of the studies described and the conclusions drawn here is that the studies were observational; a randomized study comparing high- and extra high–profile versus

**Figure 4.** Kaplan-Meier plot of time (months) to mastopexy analyzed by implant projection in the primary augmentation cohorts of the combined Core and 410 studies.
Table 6. Combined Core and 410 Studies: Risk of Capsular Contracture, Malposition, Secondary Procedure Due to Adverse Event, and Mastopexy, Stratified by Preoperative Breast Measurement

| Preoperative breast measurement <17 cm | Capsular Contracture (Baker Grade 3-4)* | Malposition (Moderate-Severe)b | Secondary Procedurec | Mastopexy as Secondary Procedured |
|--------------------------------------|----------------------------------------|-------------------------------|---------------------|----------------------------------|
|                                      | Unadjusted RR (95% CI) | Adjusted RR* (95% CI) | Unadjusted RR (95% CI) | Adjusted RR* (95% CI) | Unadjusted RR (95% CI) | Adjusted RR* (95% CI) | Unadjusted RR (95% CI) | Adjusted RR* (95% CI) |
| Patient age at surgery, continuous, y | 1.04 (1.02, 1.06) | 1.04 (1.02, 1.07) | 1.00 (0.97, 1.04) | 1.01 (0.97, 1.04) | 1.04 (1.02, 1.05) | 1.04 (1.02, 1.05) | 1.06 (1.02, 1.11) | 1.06 (1.02, 1.11) |
| Patient BMI (continuous)             | 1.01 (0.93, 1.10) | 1.04 (0.96, 1.13) | 0.95 (0.84, 1.09) | 0.94 (0.82, 1.08) | 1.00 (0.95, 1.06) | 0.99 (0.94, 1.05) | 1.03 (0.88, 1.20) | 0.92 (0.78, 1.09) |
| Implant size (volume in 50-cc increases) | 0.85 (0.74, 0.99) | 0.85 (0.73, 0.99) | 1.05 (0.86, 1.29) | 1.04 (0.84, 1.29) | 1.04 (0.95, 1.14) | 1.02 (0.93, 1.12) | 1.38 (1.07, 1.78) | 1.50 (1.16, 1.94) |
| Profile (style)                      |                          |                              |                          |                              |                          |                              |                          |                              |
| Low-moderate                         | Ref                      | Ref                           | Ref                      | Ref                           | Ref                      | Ref                           | Ref                      | Ref                           |
| Midrange                             | 0.35 (0.21, 0.56) | 0.69 (0.29, 1.63) | 0.51 (0.20, 1.33) | 0.41 (0.08, 2.15) | 0.65 (0.45, 0.93) | 0.58 (0.31, 1.09) | 0.30 (0.12, 0.77) | 0.01 (0.00, 0.15) |
| Full/high/extra high                 | 0.50 (0.31, 0.80) | 0.84 (0.41, 1.71) | 1.24 (0.50, 3.03) | 1.02 (0.22, 4.66) | 0.88 (0.61, 1.25) | 0.78 (0.45, 1.36) | 0.58 (0.24, 1.41) | 0.01 (0.00, 0.27) |
| Placement                            | Subglandular             | Ref                           | Ref                      | Ref                           | Ref                      | Ref                           | Ref                      | Ref                           |
| Subpectoral                          | 0.38 (0.25, 0.58) | 0.36 (0.22, 0.58) | 0.31 (0.16, 0.58) | 0.23 (0.12, 0.47) | 0.80 (0.55, 1.15) | 0.85 (0.57, 1.26) | 0.39 (0.17, 0.91) | 0.28 (0.10, 0.77) |
| Preoperative breast measurement ≥17 cm |                                      |                              |                          |                              |                          |                              |                          |                              |
| Patient age at surgery, continuous, y | 1.01 (0.99, 1.03) | 1.01 (0.99, 1.03) | 0.99 (0.97, 1.02) | 1.00 (0.97, 1.02) | 0.99 (0.98, 1.00) | 0.99 (0.98, 1.00) | 1.01 (0.98, 1.03) | 1.00 (0.97, 1.02) |
| Patient BMI (continuous)             | 1.03 (0.98, 1.09) | 1.03 (0.97, 1.09) | 0.94 (0.87, 1.02) | 0.97 (0.90, 1.06) | 0.99 (0.95, 1.02) | 1.00 (0.97, 1.04) | 1.03 (0.96, 1.11) | 1.04 (0.96, 1.12) |
| Implant size (volume in 50-cc increases) | 0.91 (0.82, 1.01) | 0.95 (0.85, 1.06) | 0.87 (0.75, 1.00) | 0.86 (0.74, 1.00) | 0.95 (0.90, 1.01) | 0.94 (0.88, 1.01) | 0.94 (0.82, 1.07) | 0.93 (0.80, 1.08) |
| Profile (style)                      | Low-moderate             | Ref                           | Ref                      | Ref                           | Ref                      | Ref                           | Ref                      | Ref                           |
| Midrange                             | 0.40 (0.27, 0.61) | 0.53 (0.25, 1.14) | 0.25 (0.14, 0.44) | 0.26 (0.07, 0.96) | 0.59 (0.45, 0.76) | 0.34 (0.19, 0.60) | 0.35 (0.20, 0.60) | 0.11 (0.04, 0.36) |
| Full/high/extra high                 | 0.42 (0.29, 0.61) | 0.52 (0.27, 1.02) | 0.43 (0.26, 0.70) | 0.49 (0.14, 1.69) | 0.62 (0.48, 0.80) | 0.40 (0.23, 0.67) | 0.46 (0.26, 0.78) | 0.17 (0.06, 0.52) |
| Placement                            | Subglandular             | Ref                           | Ref                      | Ref                           | Ref                      | Ref                           | Ref                      | Ref                           |
| Subpectoral                          | 0.40 (0.30, 0.54) | 0.44 (0.31, 0.61) | 0.96 (0.59, 1.56) | 0.95 (0.57, 1.59) | 0.90 (0.72, 1.11) | 0.93 (0.74, 1.19) | 0.94 (0.58, 1.51) | 1.33 (0.77, 2.31) |

BMI, body mass index; CI, confidence interval; Ref, reference group; RR, relative risk.

* n = 123 events of capsular contracture, Baker grade 3 to 4 where preoperative breast measurement <17 cm; n = 181 events of capsular contracture, Baker grade 3-4 where preoperative breast measurement ≥17 cm.

* n = 54 events of moderate to severe malposition where preoperative breast measurement <17 cm; n = 97 events of moderate to severe malposition where preoperative breast measurement ≥17 cm.

* n = 280 events of secondary procedure due to adverse event where preoperative breast measurement <17 cm; n = 459 events of secondary procedure due to adverse event where preoperative breast measurement ≥17 cm.

* n = 33 events of mastopexy as secondary procedure with or without other procedures where preoperative breast measurement <17 cm; n = 97 events of mastopexy as secondary procedure with or without other procedures where preoperative breast measurement ≥17 cm.

* Multivariate models adjusted for variables in the table in addition to time interaction terms as described in the Methods section, device fill, device surface, incision site, parental antibiotics, parenteral steroids, pocket irrigation with antibiotics, pocket irrigation with Betadine, and use of drains.

* P < .001.

* P < .01.

* P < .05.
CONCLUSIONS

In conclusion, these are the first data from prospective observational clinical trials that describe the relative risk of breast implant profile and size on the risks of CC, malposition, and secondary surgery, including mastopexy. Existing views on the potential increased risk of AE related to greater breast implant profile are based on personal experience and therefore difficult to generalize to a broader patient population. In contrast, the prospective data from clinical trials presented herein provide support that the incidence of CC and secondary procedure in high- and extra-high-profile breast implants is lower than with low- or moderate-profile implants. These findings indicate that a full range of breast implant profiles (projection and size) can be considered by the patient and surgeon and that appropriate choice and selection should be made based on the patient’s biodimensional limits and soft-tissue quality.

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Disclosures

Dr Largent is an employee and holds stock (and options) at Allergan, Inc (Irvine, California), the manufacturer of products discussed in this study. Drs Kaplan and Oefelein are former employees of Allergan, Inc. Dr Reisman has received honoraria from Allergan, Inc and LifeCell Corporation (Branchburg, New Jersey). Dr Jewell is a paid adviser to Allergan (Irvine, California), Excaliard Pharmaceuticals (Carlsbad, California), Keller Medical (Stuart, Florida), Medicis Pharmaceutical Corporation (Scottsdale, Arizona), New Beauty Magazine (Boca Raton, Florida; unpaid consultant), and Sound Surgical Technologies LLC (Louisville, Colorado; unpaid consultant). He is also a principal investigator for FDA-approved clinical studies for Allergan, Excaliard Pharmaceuticals, Medicis Pharmaceutical Corporation, and Mentor Worldwide LLC (Santa Barbara, California).

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