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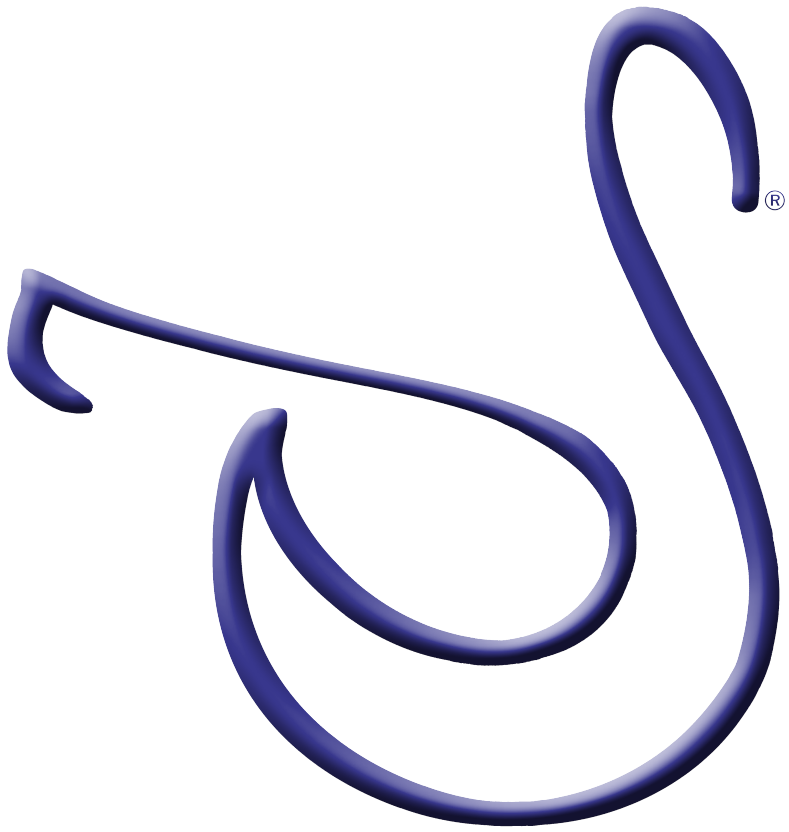
Post-marketing clinical safety study on mammary implants

Annual report 2016 of ongoing study since 2007

by Dr. Luana Clerico, Dr. Oliver Bögershausen

(edited excerpt)



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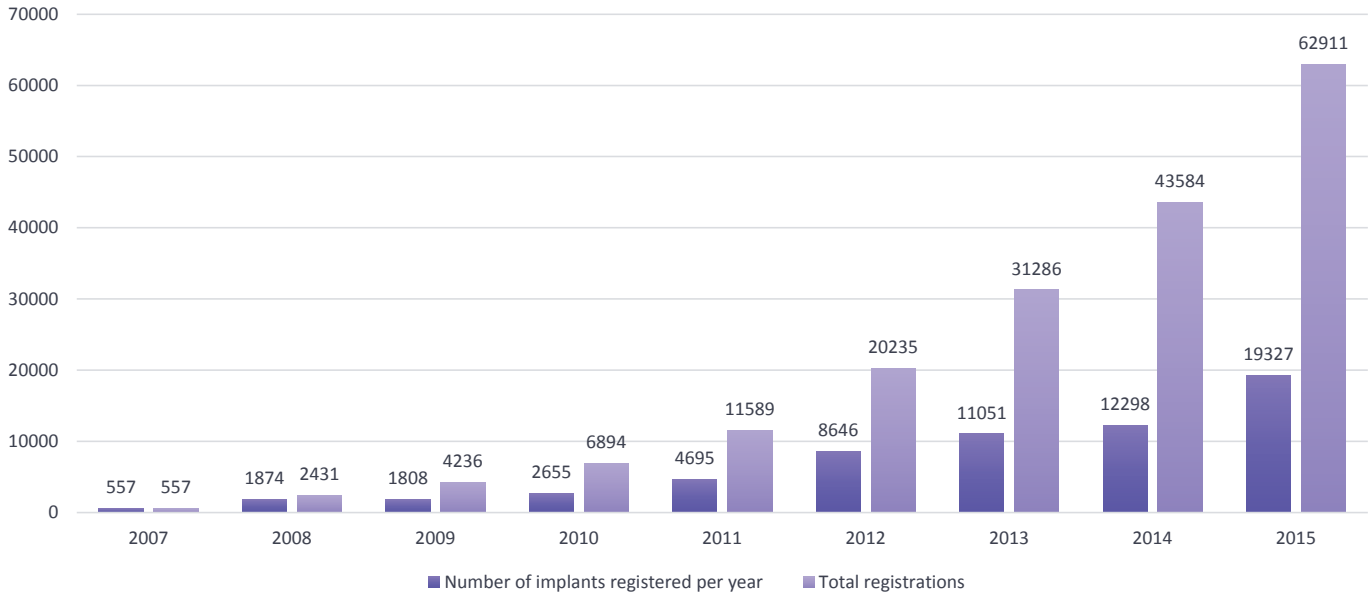
Since the introduction of breast implants in plastic surgery in the early 1960s, these devices have been comprehensively refined by modifying their composition, surface, and shape.[1-3] The implant shell may be smooth, textured, or coated with polyurethane foam. Saline solution or silicone gel are used for implant filling, though nowadays, implants filled with a highly cohesive silicone gel are the most widely used implant type.

Despite the progress achieved by different manufacturers, there are still some complications generally associated with the use of breast implants. Capsular contracture (CC) is one of the most frequent adverse events resulting in a relatively high percentage of reoperations, as described by recent core studies.[4-6,8,9] Plastic surgeons tend to recommend the use of implants associated with lower complication rates.

For all these reasons, it is crucial to gather as much long-term information as possible regarding the performance of breast implants. Therefore, in 2007 POLYTECH Health & Aesthetics launched a program called Implants of Excellence. The aim of this program is to further improve the post-market surveillance of breast implants and to extend the scope of clinical data.

The Implants of Excellence program is open to all patients undergoing breast surgery with implants manufactured by POLYTECH Health & Aesthetics. Patients participating in this program benefit from free replacement implants in case of shell rupture (lifetime, for all types of breast implants), and Capsular Contracture (10 years post-op for Microthane implants). In return, they are requested to complete a questionnaire at regular intervals. The acceptance of the program has been rising constantly over the

F1 **Implants of Excellence Registrations 2007–2015**



years (see table **F1**: Implants of Excellence Registrations 2007–2015; in 2016, 13,300 new patients – corresponding to approx. 26,600 implants – registered for the program, evaluation of their data still in process).

Data Evaluation

The systematic gathering of all adverse events reported in the questionnaires and the statistical data analysis form an integral part of an ongoing clinical study. The present document is an edited excerpt of the original paper, which presents an update of this post-marketing study.

This safety study includes patients from Europe, CIS-countries (former countries of the USSR), and Turkey that have undergone breast reconstruction, breast augmentation or revision breast surgery. Data were analysed without distinguishing between different surgical techniques. Women registered with the Implants of Excellence program are contacted once a year via email and asked to complete a digital questionnaire, if necessary after consultation with a surgeon. The invitation to the annual survey and the respective access data to the personalized questionnaire are sent to the above defined group of registered patients by email, including general information and detailed instructions on how to access the questionnaire.

Right from the start of the Implants of Excellence program in 2007, all women having undergone breast surgery with implants manufactured by POLYTECH Health & Aesthetics were invited to sign up. The first survey was carried out in 2009 and since then annually, the response rate of the current survey amounted to 9.4%.

The evaluation mainly focuses on the occurrence of capsular contracture (CC) Baker grade III and IV (grade III CC corresponds to a hard breast and noticeable implant; grade IV describes a rigid implant with stretched skin, pain and change of breast shape), revision surgery, implant removal, dislocation, hematoma, seroma, and open wounds. The occurrence of non-specific complications was also taken into consideration.

The occurrence of a complication largely depends on the impact of the different surface types, regardless of the surgery indication. The present update of the POLYTECH Health & Aesthetics post-marketing clinical safety study includes 5,619 breast implants (from 2,939 patients) distinguished according to the implant surface: 4,001 POLYtxt® implants with standard textured surface, 1,267 Microthane® implants covered with micropolyurethane foam, 299 MESMO®*sensitive* implants with micro-textured surface, and 52 POLYsmooth™ implants with smooth surface. All these implants are filled with a highly cohesive silicone gel, and more than 85% have a volume ranging from 200ml to 400ml.

The mean follow-up time was 35.9 months (standard deviation 18.9 months), and the median follow-up was 31.5 months (range, 2–147 months). More than 1,800 breast implants (32%) of this cohort had an in-situ period of less than two years, whilst less than a hundred implants (1.8%) had an in-situ period of more than 8 years.

The statistical analysis of data reported by patients having registered with the Implants of Excellence program over time resulted in the identification of the principal adverse events occurred following the insertion of POLYTECH Health & Aesthetics implants. The average occurrence of complications and possible consequences were as follows: CC Baker grade III and IV 1.5%, revision surgery 5.2%, implant removal 2.7%, implant dislocation 2.4%, hematoma 1.1%, seroma 1.6%, open wounds 0.6% and non-specific complications 12.8%.

Major part of the implants covered by this report (93.7%) were implants with the standard textured surface (POLYtxt®) and implants covered with micropolyurethane foam (Microthane®). The occurrence of each complication was analysed according to surfaces (see table **F2**: Complications per Surface Type). This update for the first time also shows the preliminary outcomes concerning a micro-textured surface (MESMO® *sensitive*).

The rate of capsular contracture (CC) with Microthane® implants was 0.6%, whereas with POLYtxt® implants it was triple as high (1.8%). The revision surgery rate was 3.0% for Microthane® and twice as high for POLYtxt® implants with a rate of 6.2%. The dislocation rate was not fundamentally different between the two surface types (2.8% versus 2.6%). As expected, the total of all complications not having been categorized with a precise diagnosis appeared to be lower with Microthane® implants than with POLYtxt® (9.3% versus 14.7%).

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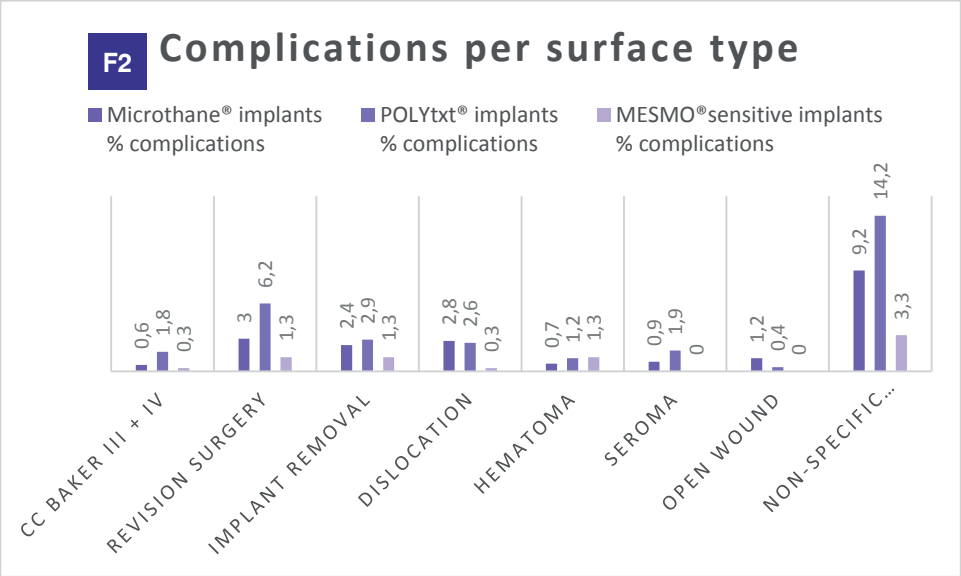
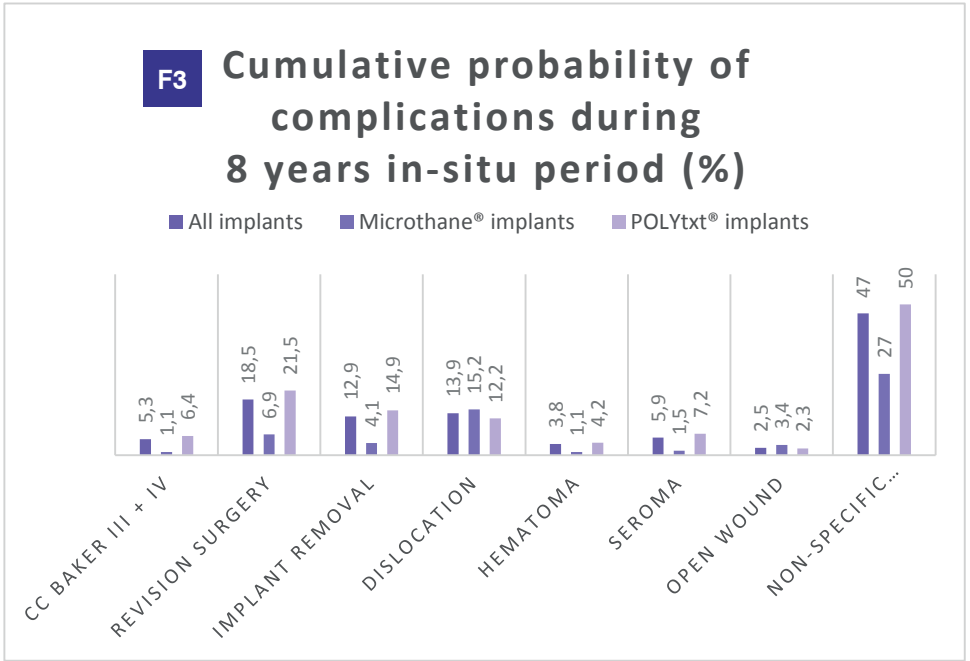


The first available data regarding the occurrence rates of adverse events with MESMO® *sensitive* implants are as follows: 0.3% CC; 1.3% revision surgery; 0.3% dislocation and 3,3% non-specific complications.

These data, however, just show the general relation between the number of complications and the number of implants in the study, they do not describe the real risk rates. This is because they do not take into consideration the time the implants have remained in the body. To put it simply: it makes a difference, if a complication occurs with 10 implants out of 1000 after only one year or if it occurs after a longer period of time. The same applies to the different implant types – they can only be compared properly if the time in the body is the same for all groups. That is why the Kaplan-Meier survival analysis is the means of choice to eliminate the weaknesses of the simplified evaluation.

The Kaplan-Meier survival analysis was used to show the likelihood of complications over time. The results demonstrate the relative risk to develop any complication during the in-situ period of 8 years according to this statistical method (see figure **F3**: Cumulative Probability of Complications During 8 Years In-situ Period). The probability of the occurrence of capsular contracture is 5.3%, whilst rates concerning other complications are as follows: revision surgery 18.5%, implant removal 12.9%, dislocation 13.9%, hematoma 3.8%, seroma 5.9%, open wounds 2.5%, and non-specific complication 47%. The same analysis was carried out splitting the data for Microthane® and POLYtxt® implants (see table below). For implants with MESMO® *sensitive* surface, no Kaplan-Meier survival analysis was carried out, as the number of available data is still too small.

In addition to the above data, Kaplan-Meier curves show that the occurrence of an adverse event rises almost linearly with the in-situ period of the implant. The obtained results demonstrate the increase of a risk for capsular contracture, revision surgery, implant removal, dislocation, hematoma, seroma, open wounds, and non-specific complications in relation to a longer in-situ period for all used implants.



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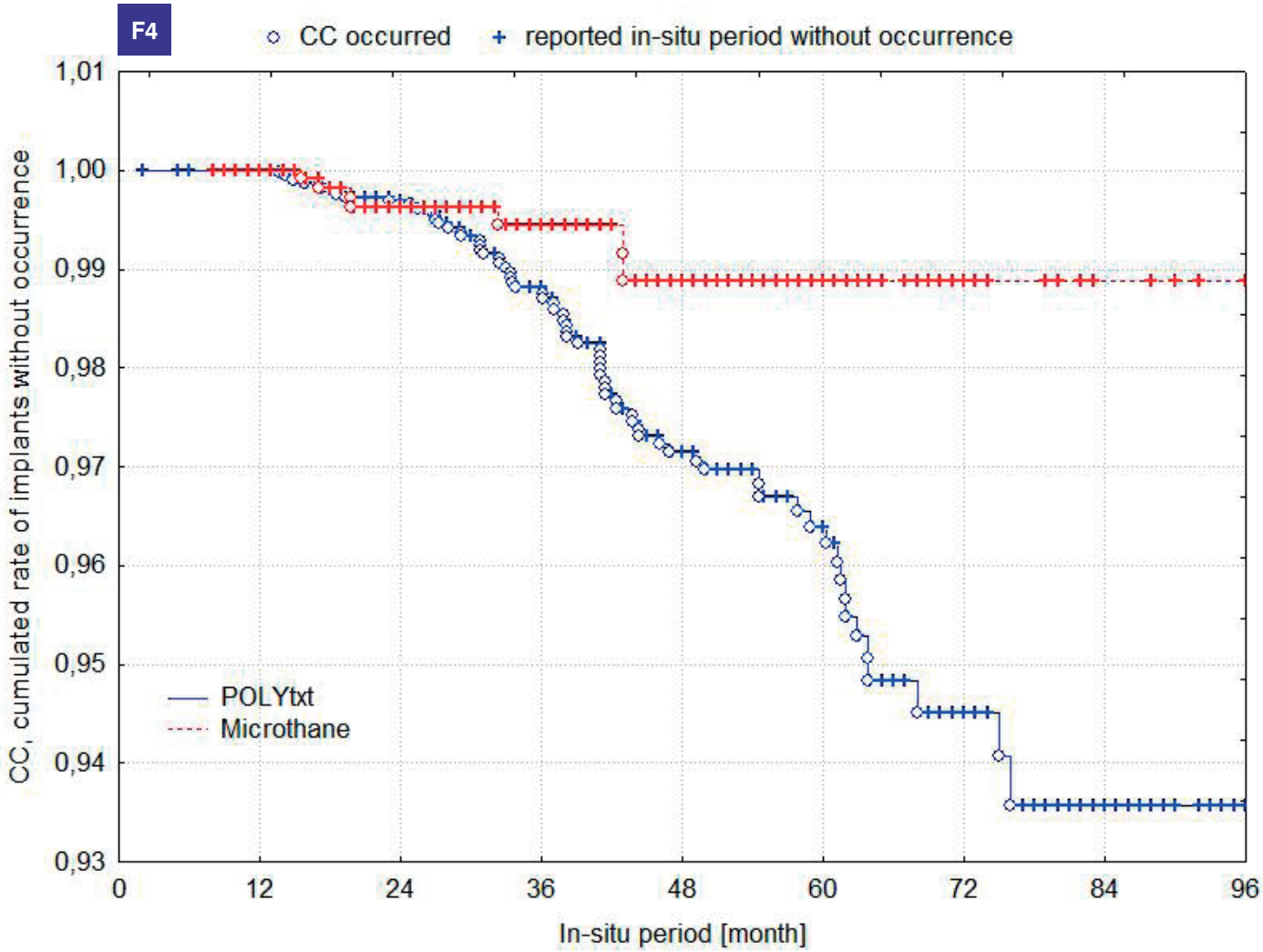

Capsular Contracture

The cumulative capsular contracture rate of Microthane® implants increases up to approximately 1.1% during the first 8 years after implantation. The cumulative capsular contracture rate of POLYtxt® implants is about six times higher (6.4%) than for Microthane® implants. Whilst with POLYtxt® implants the occurrence of capsular contracture was observed over the whole 8 years period, no capsular contracture case was reported with Microthane® implants after 3 and a half years (see figure **F4**).

Revision surgery

8 years after the insertion of POLYtxt® implants, the cumulative rate of revision surgery was 21.5%, i.e. three times higher than the cumulative rate observed for Microthane® implants (6.9%).

Implant Removal

An analysis of the occurrence of an implant removal with the Kaplan-Meyer method during the 8-year observation period, shows that the cumulative rate for POLYtxt® implants (14.9%) is three times higher than the rate reported for Microthane® implants (4.1%). The data, however, do not reflect the reason for removal. This means, they also include removal due to cosmetic reasons, i.e. if the patient wanted to change size. This may mean that women with Microthane implants generally tend to be more satisfied with their outcome than women with textured implants.

Implant Dislocation

The cumulative rate of implant dislocation with Microthane® implants after an in-situ period of 8 years (15.2%) is slightly higher compared to the cumulative rate observed for POLYtxt® implants (12.2%). This unexpected result, contrasting with the documented benefits of the polyurethane foam, can be explained with incorrect surgical procedures.

The occurrence of an implant dislocation is overall low and shows that POLYTECH Health & Aesthetics

implants are effective. However, the occurrence associated with Microthane® implants was not lower than the one with POLYtxt® implants, as it would have been expected by reading the international literature. The micropolyurethane foam strongly adheres to tissues of the breast pocket, making the implant resistant to a rotation or lowering movements, whilst a textured surface lacks this feature.[14,15] Most likely, major part of the reported cases referred to an intraoperative implant malposition, rather than to implant dislocations over time. If a polyurethane implant is incorrectly placed, due to the lack of experience of the surgeon, some patients could misinterpret this surgical malposition with a subsequent implant dislocation.

Hematoma

The cumulative rate of a hematoma with the use of Microthane® implants increases up to about 1.5% during the first 3 years after implantation, and remains constant. No hematoma case was reported afterwards. Whilst the cumulative rate of hematoma with POLYtxt® implants during the first 3 years is similar to the rate observed for Microthane® implants, for POLYtxt® implants it continuously increases and reaches nearly 4.2% after 8 years.

Seroma

The cumulative rate of seroma with Microthane® implants increases up to 1.5% during the entire observation period (8 years after implantation). The seroma rate related to POLYtxt® implants is about five times higher (7.2%).

Open wounds

The cumulative rate of open wounds for Microthane® implants after an in-situ period of 8 years (3.4%) is slightly, but not significantly, higher compared to the cumulative rate for POLYtxt® implants (2.3%).

Non-specific complications

The cumulative rate of non-specific complications after an in-situ period of 8 years increases with the use of Microthane® implants to about 27%, i. e. a rate that almost doubles with the implantation of POLYtxt® implants (50%).

Relevance of the Results

The outcome of this safety study originates from an ongoing survey with a prospective design, covering a period of more than 8 years with an annual data collection. The importance of this post-marketing surveillance is clear, especially after the most recent issues associated with breast implants having attracted the attention of the scientific community and prestigious indexed journals, including the public opinion.

POLYTECH Health & Aesthetics, having a farsighted and cautious vision, established this program for patients with the aim to identify the most common complications occurring after breast implant insertion, and to gain sufficient clinical data to release any significant findings. Moreover, a thorough, long-term investigation allows the company to constantly improve the manufactured products in order to enhance women‘s quality of life.

Since the introduction of breast implants more than 50 years ago, the international literature has reported several adverse events associated with these devices. All these studies, even long-term studies on breast augmentation or breast reconstruction, only focused on one surface type at a time.[7-9] POLYTECH Health & Aesthetics, being the only company in the market manufacturing breast implants with four different surfaces, is able to simultaneously analyse and compare different types of implants, especially textured versus polyurethane-coated implants.

F5	All types of breast surgery Clinical Safety Study		Primary Augmentation Core Study	
In-situ period 8 years	POLYtxt® implants POLYTECH	Microthane® implants POLYTECH	Textured implants ALLERGAN	Textured implants MENTOR
Capsular contracture	**6.4%**	**1.1%**	**6.9%**	**3.2%**
Revision surgery	**21.5%**	**6.9%**	**24.8%**	**19.5%**
Implant removal	**14.9%**	**4.1%**	**14.8%**	**7.6%**
Dislocation	12.2%	15.2%	no data available	no data available
Hematoma	4.2%	1.5%	no data available	no data available
Seroma	7.2%	1.5%	no data available	no data available
Open wounds	2.3%	3.4%	no data available	no data available
Non-specific complications	50.0%	27.0%	no data available	no data available

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The present update of our ongoing clinical safety study revealed important information. To start with, we were able to determine that the occurrence of the most severe complications related to breast implants are consistent with, if not lower than the occurrence reported in literature after similar investigations, even with implants from different manufacturers.[4-9]

The occurrence of a capsular contracture, a major cause of complication and a frequent cause of a reoperation following implant surgery, reaches a rate as high as 50% according to publications in scientific literature. In our study, we observed a cumulative capsular contracture occurrence of 6.4% for POLYtxt® implants and of 1.1% for Microthane® implants. We would like to point out that the reported rates are extremely positive considering that the patients of our cohorts underwent not only breast augmentation but also revision surgeries or breast reconstruction, a condition which, if combined with radiation therapy, most likely will result in a severe capsular contracture grade.[10,11]

As the present study covers 2,939 patients with a total of 5,619 implants, this means that 259 patients received a unilateral breast implantation (9%), whilst 2,680 patients underwent bilateral breast implantation (91%). We compared the present findings for POLYTECH Health & Aesthetics implants with data reported within the core studies for implants by U.S. American manufacturers having similar follow-up times and smaller cohorts of patients (core studies[12,13], see figures **F5** and **F6;** NOTE: in the core studies data are analysed separately for breast augmentation and breast reconstruction). As a result of this comparison, it can be seen, that POLYTECH Health & Aesthetics devices are particularly attractive to ensure the safety of patients, regardless of the severity of the surgery.

Similarly to the occurrence of a capsular contracture, Microthane® implants performed better than POLYtxt® regarding the occurrence of a revision surgery. The occurrence of a revision surgery is considered as a crucial safety marker. A revision surgery is common following a breast surgery with implants. Patients request revision surgery if complications lead to a loss in the cosmetic appearance or a risk for their health. According to the analysis of clinical studies, surgeons will most likely choose the breast implant, which shows the lower occurrence rate for a revision surgery. The present clinical study proved that this

F6	**All types of breast surgery Clinical Safety Study**		**Primary Reconstruction Core Study**	
In-situ period 8 years	POLYtxt® implants POLYTECH	Microthane® implants POLYTECH	Textured implants ALLERGAN	Textured implants MENTOR
Capsular contracture	**6.4%**	**1.1%**	**11.3%**	**12.0%**
Revisional surgery	**21.5%**	**6.9%**	**48.4%**	**46.1%**
Implant removal	**14.9%**	**4.1%**	**31.4%**	**28.5%**

cumulative occurrence is very low (21.5% for POLYtxt® and 6.9% for Microthane®) with POLYTECH Health & Aesthetics implants.

In addition, according to the most recent literature, this post-marketing clinical safety study confirmed that Microthane® implants definitely turned out to be the safest devices for breast surgery, with overall very low complication rates, which do not appear to reduce over time (14,15)

The cumulative occurrence of a hematoma, a seroma and open wounds with POLYTECH Health & Aesthetics implants did not present a problem for the safety of women at long term.

All adverse events, not classified as a specific disease, combined with patients‘ dissatisfaction, were gathered under the category of „non-specific complications“. For this reason, 718 implants were involved. Considering everything, the cumulative occurrence rate was assessed as normal.

Following an increasing demand on the market, POLYTECH Health & Aesthetics has provided the surgeons with a series of implants with a microtextured surface (Mesmo®-sensitive) since 2011. Considering the usual high level of quality for production and control of POLYTECH Health & Aesthetics devices, this specific surface performs behave equally well – if not even better – compared to the standard textured surface (POLYtxt®) in terms of complication occurrences.

Further updates on this ongoing post-marketing clinical safety study are scheduled.

Conclusions

The safety of POLYTECH Health & Aesthetics breast implants has been proven in clinical practice for more than three decades. The Implants of Excellence program helps the company to constantly improve their post-market surveillance. The results of this ongoing clinical study confirm the long-term safety of our products. Furthermore, this study stresses the superiority of Microthane® breast implants, and shows that these devices provide patients undergoing breast surgery and the surgeons alike with the overall safest choice.

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The unabridged paper by Dr Luana Clerico may be requested at POLYTECH Health & Aesthetics: info@polytechhealth.com

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