

Association of the BellaGel® Breast Implant Scandal with the Poly Implant Prothèse Fraud: A Review of Literatures

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Abstract

Marketing defective breast implants (BellaGel®; HansBiomed Co. Ltd., Seoul, Korea) despite knowledge or reasonable cause to believe that the device is defective has been recently found in Korea, thus termed as the BellaGel® breast implant scandal. Evidence suggests that the HansBiomed Co. Ltd. previously participated in the Poly Implant Prothèse (PIP) fraud in Europe. Based on the fact that the manufacturer was previously involved in the PIP fraud, it would be mandatory to consider long-term safety outcomes of victims of the BellaGel® breast implant scandal.

Keywords: Breast; Implant; Implantation; Complications; Ultrasonography

Introduction

Since the emergence of a silicone gel-filled breast implant, its safety has been questioned. In 1977, the first lawsuit was filed by a woman who claimed that she presented with pain and other symptoms due to rupture of a breast implant; she finally won a lawsuit and received USD 170,000 settlement from the Dow Corning [1]. In the early 1980s, the Public Citizen Research Group reported that a silicone gel-filled breast implant would cause breast cancer [2]. Concerns regarding the safety of a silicone gel-filled breast implant were maximized in 1990 after a talk show “Face to face with Connie Chung” described terrible experiences with breast implants [3]. Public pressure on government to act on the use of a silicone gel-filled breast implant was increased, and the US Food and Drug Administration (FDA) banned its use to the effect that manufacturers had not adequately demonstrated its safety despite a lack of scientific evidence showing its causal relationship with diseases in January 6, 1992 [4]. During the accumulation of scientific data supporting the safety of a silicone gel-filled breast implant, patients have filed litigations and lawsuits against manufacturers. Thus, the Dow Corning faced almost 20 thousands lawsuits and approximately 410 thousands potential claims and finally got bankrupt in 1994 [1,5]. This was followed by considerable efforts to demonstrate the safety of a silicone gel-filled breast implant in an evidence-based manner [6-11]. This showed that it had no causal relationships with connective tissue diseases (e.g.,

Sjögren’s syndrome, systemic lupus erythematosus, scleroderma and rheumatoid arthritis), neurologic disorders and malignancies (e.g., breast cancer, cervical cancer, brain cancer, lung cancer and non-Hodgkin’s lymphoma) [6-11]. There was also a contradictory report showing lower incidences of breast cancer in women receiving a breast implant [12].

The first reported case of Breast Implant-Associated Anaplastic Lymphoma (BIA-ALCL) was published by Keech and Creech in 1997 [13]. BIA-ALCL is an extremely rare, non-Hodgkin’s lymphoma whose characteristics include abnormal growth of T lymphocytes and over-expression of protein cytokine receptor CD30. It annually occurs at an estimated incidence of approximately 3/100 million women in the United States [14]. Possible relationship between vulnerability to BIA-ALCL and placement of a textured breast implant was recently suggested. Cordeiro PG, et al. [15] prospectively enrolled a cohort of 3,546 women receiving 6,023 textured implants between 1993 and 2017, all of whom were surgically treated at a median age of 48 (range, 18-89) years old by the same single surgeon and then followed up during a median period of 7 (range, 3 days to 24.7 years). According to these authors, a total of 8 women developed BIA-ALCL after receiving textured implants during a median period of 11.2 (range, 8.3-15.8) years. The reported incidence corresponds to 1/433 women. According to these authors, 96.7% of textured implants were the BioCell® (Allergan Inc., Irvine, CA, USA) [16]. In December 2018, the CE mark for the Biocell® and Microcell® implants (Allergan Inc.)

was suspended by the Agence Nationale de Sécurité du Médicament (ANSM, formerly Agence Française De Sécurité Sanitaire Des Produits De Santé [AFSSAPS]). This has led to the removal of both products from 37 countries [16]. In April 2019, the use of all the macrot textured or polyurethane-coated breast implants was prohibited by the ANSM [15]. In the US in May 2019, however, the Food and Drug Administration (FDA) issued the letter to the effect that there was no sufficient evidence demonstrating a causal relationship between a textured device and BIA-ALCL; it finally announced that it would not ban it. In July 2019, the FDA updated the database reporting 573 cases of BIA-ALCL, including 116 new ones and 24 new deaths worldwide, since the previous communication dated March 2019. Then, it recommended a voluntary recall of Biocell® implants in the US, but this did not include Microcell® and smooth implants. This was followed by a global recall of Biocell® implants by the Allergan Inc. [17].

A breast implant is one of the most popular medical devices that are implanted in human body; the number of patients receiving it is estimated at approximately 5-10 million worldwide [18]. But breast implant failure is an inevitable phenomenon that occurs irrespective of its nature. There is a time-dependent increase in its probability [19,20]. Unlike breast implant failure, breast implant scandal is a case of fraud, as well illustrated in the Poly Implant Prothèse (PIP) fraud; the PIP breast implant scandal is one of the most significant patient protection failures [21,22]. In more detail, it is a type of medical device fraud; medical device fraud is defined as common violations of the False Claims Act, which is categorized into (1) off-label marketing, (2) defective medical devices, (3) kickbacks or referrals and (4) unnecessary billing [23]. Of these, marketing defective breast implants (BellaGel®; HansBiomed Co. Ltd., Seoul, Korea) despite knowledge or reasonable cause to believe that the device is defective has been recently found in Korea, which deserves special attention because it may endanger patients receiving an implant-based augmentation mammoplasty.

In this paper, we review the BellaGel® breast implant scandal and its potential harmful effects on the health and safety of patients receiving an implant-based augmentation mammoplasty.

The Manufacturer's Description of the Bellagel® Breast Implants

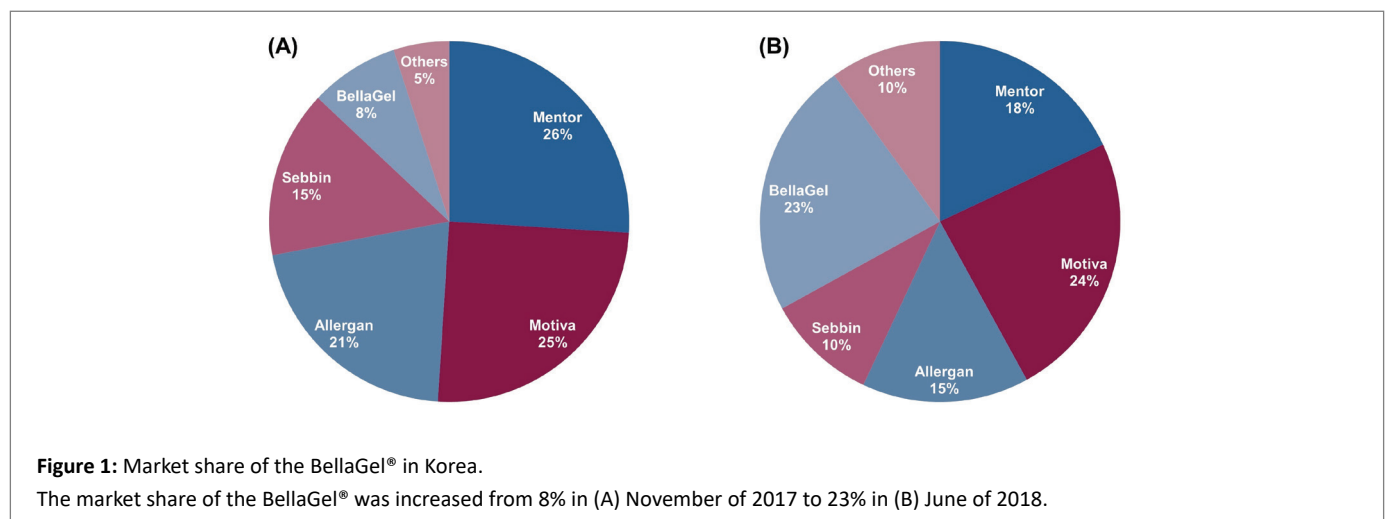
Diverse brands of a silicone gel-filled breast implant compete with each other in the Korean market. Of these, the BellaGel® is the only

product from a Korean manufacturer. According to the manufacturer, it is produced through a rigorous analysis of anatomical and anthropometric characteristics Korean women, thus addressing their needs. Approximately 300 different subtypes of the BellaGel® implants are available because there are three types of shape (round, anatomical and conical) and another three types of surface texture (smooth, textured and microtextured) [24]. Moreover, they are covered with five layers except for anatomical devices covered with six layers [25]. The BellaGel® was first developed in 2005 and then approved by the CE in 2008; it has become commercially available in 30 countries worldwide [26]. Previous studies have described the efficacy and safety of the BellaGel® [24-29]. Of these, a recent study showed that its safety profile was the most excellent among the six different brands of a silicone gel-filled breast implant [28]. It is allegedly reported that the BellaGel® implants are popular brands in Korea (Figure 1) [30,31].

The BellaGel® SmoothFine (formerly BellaGel® Micro) is the BellaGel® implant with a microtextured surface, and it is covered with five layers of shell, within which there is a barrier layer that efficiently prevents the leakage of a gel due to a rupture [32]. A previous study reported that the BellaGel® SmoothFine showed an almost 10-fold lower incidence of complications as compared with other brands of a silicone gel-filled breast implant [25].

Bellagel® Breast Implant Scandal in Korea in 2020

In November 3, 2020, a Korean news media reported that the HansBiomed Co. Ltd. was investigated by police for circulating defective devices, the BellaGel® implants, in the market. The manufacturer obtained the regulatory approval from the Korean Ministry of Food and Drug Safety (KMFDS, formerly the Korean Food and Drug Administration [KFDA]) in November of 2015 using the approved constituents, but it deliberately replaced them with unapproved materials during the manufacturing process. Such constituents are known to have detrimental effects on human health [33]. According to the news media, whistleblowers reported its unethical practices to the Korean Anti-Corruption and Civil Rights Commission (KACRC); former and current executives were involved in manufacturing and circulating breast implants with the use of 7-9700 and Q7-4850 (Dow Silicones Corporation, Midland, MI, USA), both of which were not approved for human use to the effect that "The product is not designed for, intended for and therefore not suitable for implantation of any duration in the human body." [33,34]. Their harmful effects were



also supported by the Korea Occupational Safety and Health Agency (KOSHA) [35].

In November 13, 2020, the KMFDS initiated the mandatory recall of the BellaGel® implants. According to the KMFDS, the HansBiomed Co. Ltd. has manufactured the BellaGel® implants using constituents whose use was not approved and then distributed approximately 70,000 products to medical institutions since December of 2015. A total of five constituents were not approved for use for manufacturing of the BellaGel® implants; these include 7-9700 (soft skin adhesive), Q7-4850 (liquid silicone rubber), MED2-6300 (silicone gel), MED-6400 (silicone dispersion) and MED2-4213 (skin adhesive) (Figure 2) [36]. Of these, 7-9700 is intended for wound care applications, including over-the-counter bandages and scar therapies, and Q7-4850 is intended for implantation in humans for less than 30 days [37,38]. The KMFDS noted that a finished product of the BellaGel® would not pose serious risk to human health, but recommended that patients receiving the BellaGel® implants be meticulously monitored at a regular follow-up [36].

A Criminal Connection between the Hansbiomed Co. Ltd., the Rofil Medical International B.V. and the PIP in Europe

The PIP fraud

Established in 1991, the PIP (La Seyne-sur-Mer, France) is allegedly known as the third-largest manufacturer of a silicone gel-filled breast implant from France [39]. Since then, for the next 20 years, it grew to annually produce approximately 100,000 implants and exported them to 65 countries worldwide, such as Brazil, Argentina, Britain, Germany, Spain, Australia, and the United States [40]. The PIP implants were approved by the CE in 1997 [41]. The number of patients receiving the PIP breast implants is estimated at approximately 400,000 [42]. In May 2000, the US FDA inspected manufacturing facilities of the PIP and then prohibited the marketing of the PIP breast implants in the US [43]. Then, two published studies showed defects in the PIP devices [44,45]. The PIP was found to use unapproved, industrial grade silicone, with a cost of only 10% of an approved gel [46].

In March 29, 2010, based on patients' complaints and rates of rupture and leakage of 10-11%, the ANSM suspended the marketing, distribution and use of the PIP breast implants illegally manufactured using unapproved, industrial grade gel fillers [43]. The PIP breast implants had no elastomeric shell, were vulnerable to oozing through an intact shell and caused local irritation [47,48]. This resulted in an increased risk of rupture and leakage and some rare cases of malignancies [49]. Patients receiving the PIP breast implants were recommended to be monitored for rupture of the device using ultrasound at a 6-month interval [43]. But they were not recommended to undergo surgery for removal of the device because there was a lack of conclusive scientific evidence concerning the toxicity of gel fillers [50]. In December 23, 2011, the French Ministry of Health recommended that 30,000 French patients receiving the PIP breast implants undergo prophylactic surgery for removal of the device because of the high rate of rupture. Before then, it was at surgeons' discretion whether patients receiving the PIP breast implants should undergo prophylactic surgery [42].

In 2013, executives of the PIP were prosecuted for fraud, aggravated deception and involuntary wounding. In addition, the owner and founder of the PIP, Jean-Claude Mas, was eventually sentenced to four years of imprisonment and fined EUR 75,000 for aggravated fraud by a court in Marseille [51,52].

Involvement of the HansBiomed Co. Ltd. in the PIP fraud

Between 2010 and 2012, a total of 78,000 breast implants were annually circulated in the French market. In France, a total of 12 manufacturers, including the HansBiomed Co. Ltd., were selling or were authorized to sell their products; foreign manufacturers accounted for 36% of total market shares [53,54]. It deserves special attention that the PIP breast implants had also been marketed under other brands such as the TiBreeze (GfE Medizintechnik GmbH; Nürnberg, Germany) and the M-Implants® (Rofil Medical International B.V.; Breda, Netherlands). The TiBREEZE was a titanium-coated implant containing the PIP components, and it was circulated between September 2003 and August 2004. Certain products of the M-Implants® (IMGHC-TX, IMGHC-MX and IMGHC-LS) were rebranded from the PIP breast

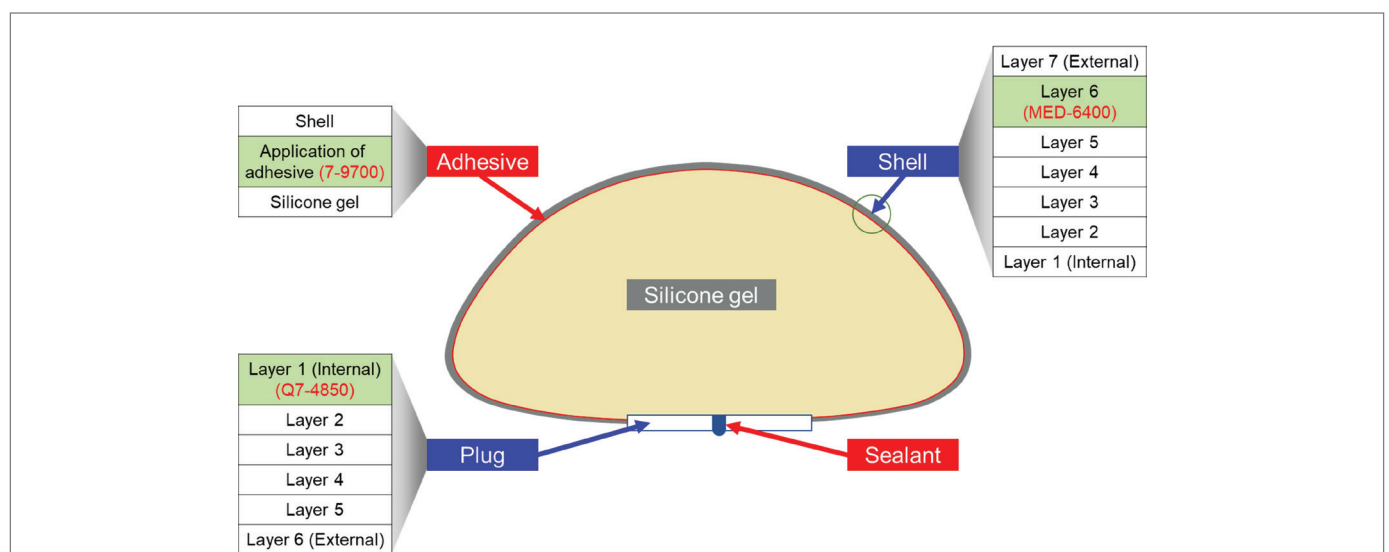


Figure 2: Use of unapproved materials for manufacturing of the BellaGel®.

A total of five constituents were not approved for use for manufacturing of the BellaGel® implants; these include 7-9700 (soft skin adhesive), Q7-4850 (liquid silicone rubber), MED2-6300 (silicone gel), MED-6400 (silicone dispersion) and MED2-4213 (skin adhesive).

implants in the UK, Netherlands and Estonia after they were withdrawn from the French market [43,55-57]. Interestingly, the HansBiomed Co. Ltd. was also involved in manufacturing the M-Implants as an Original Equipment Manufacturer (OEM), as requested by the Rofil Medical International B.V. That is, the M-Implants[®] were classified into the Rofil M-Implants[®] and the M-Implants[®] of HansBiomed origin. Indeed, Schott et al. revealed that the PIP implants were found in some lots of the Rofil-labeled device (Figure 3) [58]. In addition, Keizers PH, et al. [59] confirmed that the HansBiomed Co. Ltd. was involved in manufacturing M-Implants[®] by quoting "M-Implants of HansBiomed origin" [56,60]. In Europe, the HansBiomed Co. Ltd. was selling a silicone gel-filled breast implant under the three brand names of the BellaGel[®], M-Implants[®] and NatureShape[®], which were distributed by the European branch of the HansBiomed Co. Ltd., the Rofil Medical International B.V. and the Vital Esthétique (Paris, France), respectively [53,54].

Manufacturers of a silicone gel-filled breast implant in France were mandated to receive an inspection between September 2010 and December 2013 after the revelation of the PIP fraud, for which 20 initial inspections and 15 follow-up ones were performed. But the HansBiomed Co. Ltd. was the only manufacturer that did not pass the inspection. An on-site inspection was not accomplished because there were no breast implants at the European branch of the HansBiomed Co. Ltd. Meanwhile, M-Implants[®] and NatureShape[®] were sent to the ANSM laboratories for testing. This led to a conclusion that M-Implants[®] and NatureShape[®] were not of acceptable quality. The NatureShape[®] was not of primary concern because the Vital Esthétique was no longer involved in distributing it in France. But the ANSM took appropriate measures against both the Rofil Medical International B.V. and the HansBiomed Co. Ltd. The M-implants[®] were finally withdrawn from the French market because their gel fillers had octamethylcyclotetrasiloxane (D4) and decamethylcyclopentasiloxane (D5) of 2,200 ppm and 2,080-2,110 ppm, respectively. This was also

reported to the European Union health authorities. Lastly, samples of the BellaGel[®] were directly sent from the HansBiomed Co. Ltd. in Seoul, Korea to the ANSM. This showed that they contained D4 and D5 constituents at a concentration of <50 ppm [53,54]. Figure 4 shows a criminal connection between the HansBiomed Co. Ltd., the Rofil Medical International B.V. and the PIP in Europe.

Detrimental Health Effects of Defective Breast Implants

Physico-chemical characteristics of the PIP breast implants have been documented. According to the ANSM and a British NHS Expert Group, silicone gels of the PIP breast implants contain significantly higher levels of low-molecular-weight cyclic silicones (dimethylsiloxanes; D4, D5 and D6) as compared with medical grade silicone implants (≥ 10 -fold) [60,61]. But there is no evidence that chronic human exposure to siloxanes with levels found in the rupture condition of PIP implants is cytotoxic, genotoxic effects or carcinogenic [61-63]. It has also been reported that the PIP breast implants had a lack of the shell barrier preventing the leakage of silicone gel [59,64]. According to an extensive review of the previous published studies, patients receiving PIP breast implants had rates of rupture, ranging from 11.6% to 36% [42,55,65-68]. This is noteworthy because the leakage of silicone gel is associated with capsular contracture because of rupture or gel bleeding [69]. Bachour Y, et al. [70] showed that the shell of PIP breast implants was highly permeable and thereby caused a time-dependent increase or decrease in volume of the device. These authors added that there were antagonistic effects between capsular contracture and postoperative increase in the volume of device, thus reporting that the rupture of the device had a significant positive correlation with rates of capsular contracture [71].

There were cases of lymphoma in association with the PIP breast implants. Two women receiving PIP breast implants died of anaplastic large cell lymphoma, an extremely rare malignancy, in France and the UK [71,72]. More recently, Chen VW, et al. [73] reported a case of low-grade B-cell lymphoma in a 34-year-old woman with a 14-year-history of receiving bilateral breast augmentation using the PIP device; she also had a 7-year-history of T-cell lymphoma [74].

Patients receiving PIP breast implants also presented with unusual cases of complications; these include pain, swelling, deformity, axillary lymphadenopathy, erythematous rash, xanthoma, seroma, thoracic outlet syndrome, silicone granuloma and intramammary siliconomas [74-79,81-83].

Patients receiving PIP breast implants should be meticulously followed up. They had been warned of defects in the devices and possible complications, although some of them are still under follow-up for 10-20 years postoperatively. Surgeons should be aware of not only risks of complications but also the possibility that such complications would not be reported even in patients under long-term follow-up [49].

In January 1, 2012, the International Society of Aesthetic Plastic Surgery (ISAPS) recommended that patients receiving the PIP breast implants or M-Implants[®] distributed by the Rofil Medical International B.V. undergo surgery for removal or replacement with other safe devices even in the absence of any clinical signs of rupture for the purposes of avoiding further health risks [84].

Conflict of Interest (COI) as an Obstacle to Resolve Problems Arising from Bellagel[®] Breast Implant Scandal

The mandatory recall of the BellaGel[®] implants was initiated by the

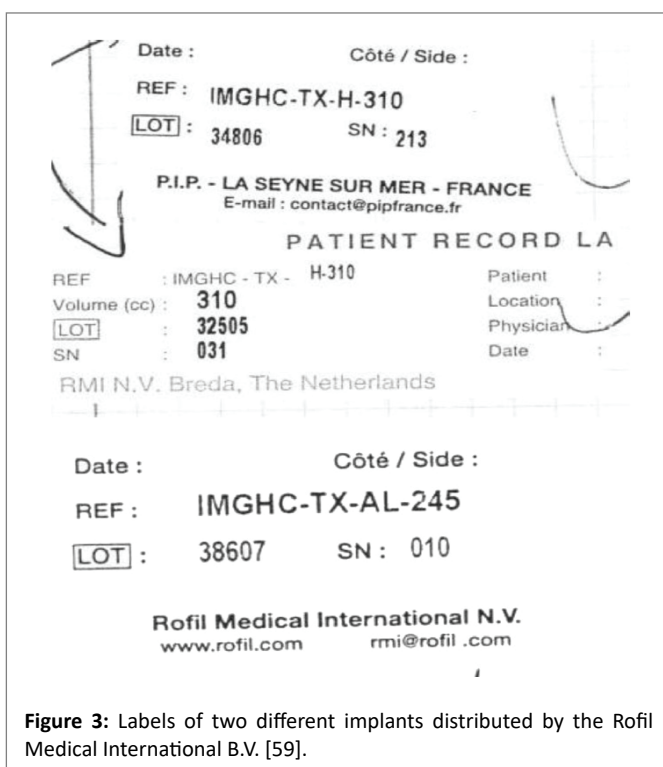
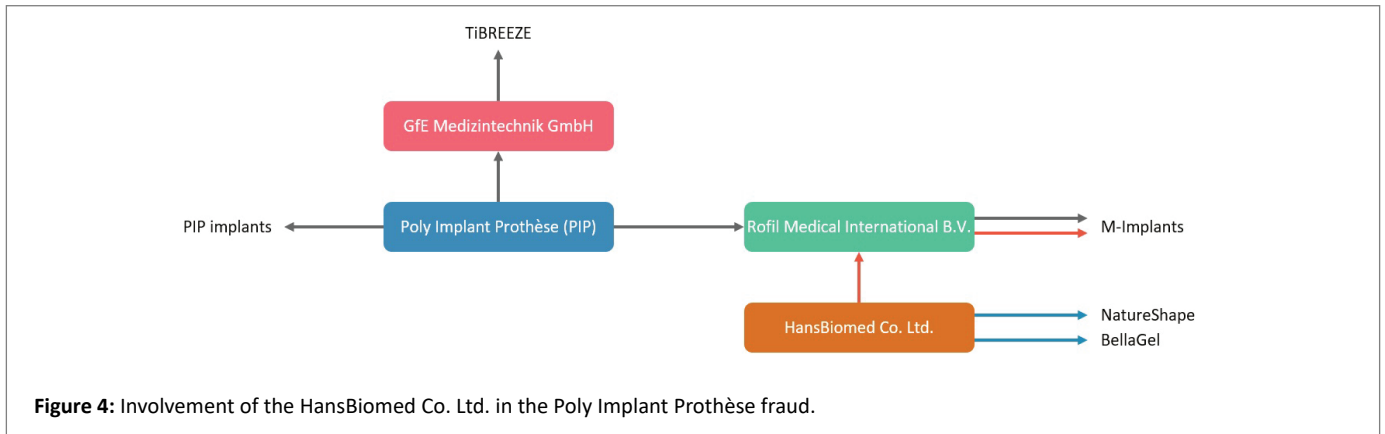


Figure 3: Labels of two different implants distributed by the Rofil Medical International B.V. [59].



KMFDS, accompanied by recommendations that patients receiving the device should be evaluated on long-term follow-up. But the KMFDS, the HansBiomed Co. Ltd. and surgeons shared the same opinions on the safety of the BellaGel[®] implants; a finished product of the BellaGel[®] would not pose serious risk to human health [36]. The safety of the BellaGel[®] implants has been well described in six manufacturer-sponsored studies whether they are prospective or retrospective in nature [25-29,85]. The HansBiomed Co. Ltd. even sponsored a 10-year prospective study and reported 6-year results. But this does not mean that 6-year safety outcomes ensure the safety of the device for six years postoperatively. Results of a manufacturer-sponsored study should be interpreted with caution [27]. Most of the published studies supporting the safety of a certain product have been authored by surgeons who had a financial relationship with the manufacturer [86-88]. Such authors commonly have favourable attitudes towards a single manufacturer, whose results could not be derived from an unbiased design [89]. Of the six studies supporting the safety of the BellaGel[®] implants, five have been published by medical advisors of the manufacturer [25,26,28,29,85].

COI is referred to a condition in which professional decision-making in research, involving a primary interest (e.g., patients' safety or welfare or the validity of its design or outcomes) is prone to influence by a secondary one (e.g., financial benefit) [90]. To date, concerns have been raised regarding its potential impacts on patient care, clinical practice and biomedical research; this has been well described in the literature [91,92].

In the US in 2007, biomedical and clinical studies were sponsored by industry, and the amount of funding exceeded USD 58 billion. But federal and private foundations paid only USD 36 billion for studies [93]. Moreover, there was a decrease in the amount of federal funding, but that of industrial one rose from 32% to 62% between 1980 and 2000 [94]. As a result, industry-sponsorship has become such a pivotal source of research funding that it has contributed to promoting the delivery of healthcare services and improving treatment outcomes [95]. This is closely associated with the fact that most of the industry-sponsored studies have shown positive findings about their products [96-101]. According to a meta-analysis, there was a significant correlation between industry sponsorship and pro-industry findings. Moreover, it was also shown that industry sponsorship had a close association [102].

Special attention should be paid to a relationship between plastic surgery and manufacturers of a breast implant. Still, there is a paucity of data suggesting the involvement of COI in designing studies

and producing their outcomes in the field of plastic surgery whose relationship with industry has been on the rise [103]. That is, possible impacts of commercial funding on positive findings of an industry-sponsored study cannot be denied [104,105].

A favourable relationship between plastic surgeons and manufacturers of a breast implant has also been found at the recent US FDA meeting; representatives of manufactures of a textured implant, such as the Allergan, Mentor and Sientra, maintained that their devices remained commercially available, and plastic surgeons did not recommend that such products be banned from the market [106]. Swanson lamented that plastic surgeons in the US defended a textured implant [107].

Discussion

In Korea, a silicone gel-filled breast implant was first approved as a medical device subject to tracking in July 2007. In the early 2012, the Replicon[®] (Polytech Health and Aesthetics, Dieburg, Germany), the Natrelle[®] 410 (Allergan Inc., Irvine, CA) and the Naturgel[™] (Groupe Sebbin SAS, Boissy-l'Aillerie, France) were approved by the KMFDS. This was followed by the approval of the Mentor[®] CPG[™] (Mentor Worldwide LLC, Santa Barbara, CA) and the Silimed (Sientra Inc., Santa Barbara, CA) [108,109]. Of these, however, the Natrelle[®] 410 and the Mentor[®] CPG[™] were approved by the US FDA before their commercial release in Korea.

Since the KMFDS approval of the BellaGel[®] in November 27, 2015, the HansBiomed Co. Ltd. has been the only Korean manufacturer of a silicone gel-filled breast implant [26,29]. In June 20, 2016, the Motiva Ergonomix[™] (Establishment Labs Holdings Inc., Alajuela, Costa Rica) was released in the Korean market. This opened the era of a microtextured device in Korea. Since then, the HansBiomed Co. Ltd. has competed with the Motiva Ergonomix[™] by releasing the BellaGel[®] SmoothFine in July 19, 2017; its advantages have been documented on six manufacturer-sponsored studies [25-29,85].

Before selling a silicone gel-filled breast implant in Korea, the HansBiomed Co. Ltd. manufactured the M-Implants[®] as an OEM, as requested by the Rofil Medical International B.V. that was a distributor of the PIP implants rebranded as the M-Implants[®]. Interestingly, we discovered a photograph showing the M-Implants[®] placed with the PIP implants in a box [110]. But there are no literatures suggesting whether there are differences in the composition between the M-Implants[®] rebranded from the PIP implants and those of the HansBiomed origin. Moreover, it also remains unanswered whether there are any differences in the composition between the BellaGel[®], the M-implants[®]

of HansBiomed origin and the NatureShape®. Furthermore, based on previous reports not only that it first developed a silicone gel-filled breast implant in 2005, obtained CE approval in 2008 and did the KMFDS approval in November 27, 2015 but also that defective breast implants of HansBiomed origin were withdrawn from the French market in 2013, it should be clarified whether, how, when and where the HansBiomed Co. Ltd. disposed defective breast implants of its origin [26,29,111]. Previous withdrawal of their products from the French market was also reported in a Korean news paper in November 3, 2014, which is based on a French newspaper article dated May 6, 2014 [111,112]. It remains uncertain whether Korean plastic surgeons were aware of the manufacturer's previous involvement in the PIP fraud. Of note, however, two authors of two articles sponsored by the HansBiomed Co. Ltd. were involved in the development and design of BellaGel® implants, one of whom is currently a non-executive medical director of the manufacturer [26,29,113,114].

According to 6-year interim results of a 10-year prospective study assessing the efficacy and safety of the BellaGel® implants, it started in August 24, 2010 [28]. It is therefore highly possible that some Korean patients might have received the BellaGel® implants that had been exported to Europe but whose composition had not been characterized. These patients should be further evaluated for whether they had signs and symptoms that are suggestive of rupture or gel bleed. Moreover, patients with rupture of the device after receiving the BellaGel® implants between August 24, 2010 and November 26, 2015 should also be further evaluated for the characterization of the composition on explantation study.

It was revealed that the HansBiomed Co. Ltd. illegally used 7-9700 to overcome the detachment between the shell and silicone gel since 2009 [33,34]. It was originally designed for use for a wearable monitoring device or wound dressing. Its biocompatibility was tested for cytotoxicity, skin irritation and skin sensitization, but there were no tests for mutagenicity/genotoxicity, pyrogenicity and system toxicity because it was not designed for *in vivo* use in humans [115]. It can therefore be inferred that the safety of a long-term *in vivo* presence of 7-9700 cannot be established.

Illegal use of Q7-4850 in the manufacturing process for the BellaGel® implants should also be considered serious in that its *in vivo* use for >30 days was prohibited [38]. But the reasons for the use of Q7-4850 remain unclear.

The recent recall of the BellaGel® implants because of fraudulent usage of unapproved materials, including 7-9700 and Q7-4850, has ignited the debate on the safety of a silicone gel-filled breast implant. Patients receiving the BellaGel® implants have visited physicians or surgeons. Following the manufacturer's position statement, however, most of these physicians or surgeons tend to deny any causal relationships between the BellaGel® implants and patients' complaints. Many patients even filed a lawsuit against the HansBiomed Co. Ltd. to get recognition for their health problems. Nevertheless, the HansBiomed Co. Ltd. maintained that a finished product of the BellaGel® implants would be safe even after the KMFDS initiated the mandatory recall of them because no toxic substances were detected from them although it admitted the illegal use of unapproved materials for manufacturing process [36]. But the KMFDS, the HansBiomed Co. Ltd. and physicians or surgeons should learn lessons from the PIP fraud. Bachour Y, et al. [71] estimated rates of gel bleed and rupture at 42% and 25%, respectively, in the PIP implants that were removed after a mean duration of 11 ± 2.1 years. Additionally, these authors also noted a significant correlation between the rupture and capsular contracture [71]. Unusual rupture rates of the PIP implants and their susceptibility

to rupture have been previously documented; their rupture rates at 10 years were estimated at 24-30% [42,116]. Studies have shown that the PIP implants were not equipped with the shell barrier preventing the leakage of silicone gel, a phenomenon termed as gel bleed that is observed in both intact and ruptured devices [48,117]. Moreover, a chemical analysis showed that the PIP implants contained a relatively higher proportion of low molecular weight silicones, D4 and D5, both of which are known to be associated with the early shell weakening and rupture [42]. Once released from the device, low molecular weight silicones may circulate throughout the body. This was well evidenced by a post-mortem analysis of tissues sampled from a patient with a 17-year-history of gel bleed after receiving a silicone gel-filled breast implant. The patient was characterized by the presence of plaques or droplets containing silicones in several organs and nervous tissue [118]. Over the past decades, the involvement of a silicone gel-filled breast implant in the pathophysiology of autoimmune inflammatory disorders. But its possible relationship with non-immune mediated diseases has also been suggested. These include chronic fatigue, fibromyalgia, xerophthalmia, xerostomia, xeroderma, dyspnea, recurrent infections, several neurological complaints and many other symptoms [119].

After the onset of the first Korean case of BIA-ALCL, reported in August 16, 2019, the clinical use of textured breast implants was prohibited by the KMFDS [120]. Therefore, there has been an interest in whether there is a possible causal relationship between a microtextured surface of the device and a risk of complications of an implant-based augmentation mammoplasty in Korea, as well illustrated in studies comparing between the BellaGel® SmoothFine and the Motiva Ergonomix™ [27,29,85]. With the revelation of the BellaGel® breast implant scandal, however, the KMFDS should consider the importance of rigorous inspection of manufacturing process when it approves a silicone gel-filled breast implant for clinical use.

Conclusions

The BellaGel® breast implant scandal and the PIP fraud share common traits that both products were approved by the CE although they were defective [31,39]. The KMFDS should therefore assess possible detrimental health effects of the BellaGel® breast implant scandal, which cannot be limited to *in vivo* toxic effects of 7-9700 and possible effects of Q7-4850, in consideration of the manufacturer's previous involvement in the PIP fraud. Moreover, it should also consider that the COI may negatively affect the manufacturer's social responsibility and plastic surgeons' duty, which is essential for ruling out the possibility of a moral hazard of both parties.

We, at the Korean Society of Breast Implant Research, propose the following recommendations:

- 1) A patient registry should be considered as an infrastructure for the standardized recording of data from patients receiving the BellaGel® implants. In 2019, when we noticed the first report of the Korean case of BIA-ALCL, we proposed that possible impacts of BIA-ALCL be rigorously analyzed and appropriate measures be taken as promptly as possible [120]. From similar contexts, we'll prospectively collect from patients receiving the BellaGel® implants and then track their outcomes and complications, thus endeavoring to ensure both high-quality care and patient safety. This should be accompanied by collaborations between patients receiving the BellaGel® implants and the KMFDS.

- 2) Patients receiving the BellaGel® implants should be meticulously monitored for rupture of the device. Lack of early detection of rupture of a breast implant may cause patients to be

vulnerable to silicone-induced axillary lymphadenopathy as well as extracapsular rupture [121,122]. This is serious because a complete resection of the mammary tissue involving silicone would not be achieved, a diagnosis of rupture of the device may be missed due to the residual presence of silicone even after explantation and silicone compounds may be present in breast milk [123,124]. Therefore, patients receiving the BellaGel® implants should be rigorously evaluated for the possible occurrence of rupture.

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