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Breast

Measuring Platinum Levels in Hair in Women with Silicone Breast Implants and Systemic Symptoms

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Background: It has been suggested that compounds present in silicone breast implants (eg, silicone particles or heavy metals such as platinum) migrate into the body and can cause systemic symptoms in susceptible women, causing what is known as breast implant illness. This pilot study investigates possible associations between hair platinum levels in patients with breast implants and breast implant illness, and evaluates its possible use for diagnostic purposes.
Methods: Patients were included from the silicone outpatient clinic at Amsterdam University Medical Centre. Platinum concentration in hair samples of 10 women with breast implants and systemic symptoms (group A) was compared with that in 10 women with breast implants but no symptoms (group B), and a control group of 10 women without implants or symptoms (group C), using laser ablation inductively coupled plasma mass spectrometry. Radiological imaging was used to assess implant ruptures or silicone leakage.
Results: A median platinum concentration of 0.09 µg per kg [IQR 0.04–0.15] was found in group A, 0.08 µg per kg [IQR 0.04–0.12] in group B, and 0.04 µg per kg [IQR 0.02–0.13] in group C, with no statistical significant difference between the groups (Kruskal-Wallis test, $P = 0.43$). No correlation between radiologically proven implant leakage and platinum level was found.
Conclusions: There was no statistically significant difference in hair platinum levels in women with or without silicone breast implants or breast implant illness. Therefore, based on this pilot study, we do not recommend this test for clinical use. Given the small sample size, more research is required to fully assess its possible use for diagnostic purposes. *(Plast Reconstr Surg Glob Open 2022;10:e4373; doi: 10.1097/ GOX.0000000000004373; Published online 10 June 2022.)*

INTRODUCTION

The safety of silicone breast implants has been a subject of debate for decades. The U.S. Food and Drug Administration issued a moratorium in 1992 that lasted for nearly 15 years, because of emerging reports of women with systemic symptoms attributed to silicone breast implants.[1] This set of symptoms is presently referred to as breast implant illness and shows similarities to autoimmune syndrome induced by adjuvants.[2–4] In 2006, silicone breast implants were re-approved because of insufficient conclusive data proving a causal relationship between silicone breast implants and systemic disease.[1,5–7] The debate reignited in 2019, after silicone breast implants were shown to be associated with a rare type of T-cell lymphoma: breast implant associated-anaplastic large cell lymphoma, raising new concerns regarding silicone breast implant-induced inflammation.[8] Moreover, multiple studies showed significant improvement of systemic symptoms in women after removal of the silicone breast implants.[9–11] However, the pathogenesis of breast implant illness remains to be elucidated, and no clear classification system is yet available. It has been proposed that, in those who are susceptible, an inflammatory process may be triggered by leakage of

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silicone particles (gel-bleed) or other compounds in the implants, such as platinum.[9,12–15]

Silicone gel-filled breast implants are made from a silicone elastomer shell surrounding a core of silicone gel. Silicone is widely used for medical devices and is presumed to be biologically inert. Although rare, hypersensitivity-like reactions to silicone have been described before.[16–22] Platinum, ranging in a dose from 0.1 to 10 mg per two implants, is used as a catalyst in the hydrosilylation reaction for the crosslinking of silicone elastomers.[23] A single silicone gel-filled breast implant contains an estimate of 7–14 µg per kg platinum, whereas a saline-filled breast implant contains a platinum level ranging from below detection limit up to 3 µg per kg.[24] Concern was raised after studies showed platinum migration into the surrounding tissue in both ruptured and intact implants.[25–27] Platinum salts in general are considered potent allergens and have been associated with serious health hazards.[28–32] One study proposed that platinum salts may be present in silicone gel-filled breast implants and pose a health risk through platinum toxicity.[12] Platinum toxicity is dependent on the platinum species. Metallic platinum has a oxidation state of zero, and is considered a nonallergenic and nontoxic complex.[33] One study reported platinum in silicone breast implants to exist in harmful reactive oxidation states of +2, +4, and +6.[12] However, this study received heavy criticism because of an insufficiently detailed explanation for their unusual findings. Furthermore, it was argued that various techniques showed platinum at the end of the hydrosilylation reaction to be in the zero-oxidation state.[23,34,35] It should, however, be noted that these studies analyzed silicone precursor materials, and not silicone breast implants or explants.[36–40] A case series and one case study identified symptoms of platinum salt hypersensitivity in silicone breast implant recipients, and attributed the symptoms to platinum present in the silicone breast implants.[41,42] However, this case series was criticized due to a lack of providing causal evidence supporting their conclusion.[43]

Recently, a company in the Netherlands, named Hair Diagnostix, started offering a commercial platinum hair screening test to women with silicone gel-filled breast implants. Platinum levels have been found to be elevated in the hairs of a small group of women with silicone breast implants, when compared with women without breast implants.[12] Hair analysis is noninvasive, and the ability to investigate a range of several months ensures a large range of detection.[44] The company suggested that elevated levels of platinum in hair may be correlated with implant rupture or silicone leakage and this, in turn, might be associated with breast implant illness.[26]

Takeaways

Question: Recently, a new commercially available test for platinum measurement in hair has become available for women with breast implants to measure leakage from implants. Can we use this test clinically as a biomarker in women with silicone breast implants and suspected breast implant illness?

Findings: We compared three groups (women with silicone breast implants and suspected breast implant illness, women with silicone breast implants but no systemic symptoms, and women without breast implants) and found no difference in platinum level in the hair between the three groups.

Meaning: We do not recommend this test for clinical use in women with breast implants.

On that proposition, we hypothesized that women with breast implants and systemic complaints, possibly associated with silicone leakage from implant ruptures or gel-bleed, would have increased levels of platinum in their hair. Identifying a biomarker associated with gel-bleed or implant rupture will contribute to improving the diagnostic approach in patients with suspected silicone leakage and associated breast implant illness. This pilot study aims to investigate the possible associations between platinum levels in hair, in the presence or absence of silicone gel-filled breast implants and of breast implant illness, thereby evaluating whether this hair test could be used as a feasible diagnostic marker for breast implant illness.

METHODS

Patients were included from a specialized breast implant illness-outpatient clinic in the Amsterdam University Medical Centre, location VUmc, the Netherlands. A total of 30 female participants was included, divided over three groups. Group A consisted of women with silicone gel-filled breast implants and systemic symptoms, in accordance with the description of breast implant illness, as presented in Table 1. The criteria used to diagnose breast implant illness were based on extensive clinical experience from hundreds of women visiting the outpatient clinic, and prior studies.[2,9,13] Group B consisted of women with silicone gel-filled breast implants, but without the symptoms presented in Table 1. Group C, serving as a control group, consisted of female friends or relatives from group A and B without breast implants or systemic complaints. They were selected from the close environment from group

Table 1. Typical Pattern of Symptoms Suggested for Breast Implant Illness[2,9,13]

Major Criteria	Minor Criteria
• Chronic fatigue (unrefreshing sleep or sleep disturbances) • Myalgia (myositis or muscle weakness) • Joint pains/arthritis and/or morning stiffness >30 min • Cognitive impairment, memory loss • Neurological manifestations such as numbness or neuropathic pains in the extremities	• Sicca complaints (dry eyes, dry mouth) • Skin disorders (rashes) after silicone breast implantation • Night sweats • Generalized pruritus • Worsening of allergies • Alopecia

Breast implant illness: at least four major criteria with severe burden of disease, or three major criteria, and at least two minor criteria with severe burden of disease.

A and B to reduce the impact of possible environmental factors. This study was reviewed by the ethical review board of the Amsterdam UMC, VU University Medical Centre Amsterdam (reference number: 2020.0695). It was determined that the Medical Research Involving Human Subjects Act does not apply to this study, and written informed consent was obtained from all participants.

Inclusion criteria from group A and B included women above the age of 18 with 2 years or more of exposure to silicone gel-filled breast implants and a scalp hair length of 5 cm or longer. The exclusion criteria for all groups included any type of potential exposure to platinum, such as previous treatment with (cisplatin) chemotherapy (Table 2).[23,33,45,46] Upon their outpatient clinic visit, a detailed medical history was obtained. If the patient met the proposed criteria for breast implant illness, they were allocated to group A. When they presented with no systemic symptoms or only with symptoms that could be fully explained by other causes (eg, tingling sensation accompanied by a lumbar herniated disc), they were allocated to group B. Assessment of allocation was performed by two independent researchers. Routine physical examination and laboratory testing were performed to exclude an alternative explanation for the symptoms. All the patients in group A and B underwent radiological imaging (MRI or ultrasound) to identify possible ruptures or axillary node silicone depositions that could indicate silicone leakage. Data collection from medical records included demographics, medical history and implant details, including reason for implantation, implantation time, brand, date of placement, and number of implant revisions. Participants in group C were approached by telephone for participation. Baseline assessment for these participants included a questionnaire collecting data on medical history, demographics, comorbidities, smoking, and medication use. A total of nine scalp hairs longer than 5 cm was collected from each participant by hand. The sealed envelopes were sent for analysis to Hair Diagnostix, part of Dutch Screening Group in Maastricht, the Netherlands. The company was aware of our study, but was blinded to the study protocol and did not receive any participant-related information.

The platinum concentration in hair samples was measured using laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS). The LA-ICP-MS system consists of an HeIEx-II Fast-ARIS (G2 193 nm) laser ablation unit from Teledyne Technologies (Thousand Oaks, Calif.), coupled to a 7900 ICP-MS system from Agilent Technologies (Santa Clara, Calif.). Before testing, the scalp hair strands were decontaminated using a two-step dichloromethane wash, straightened out, and placed on a plastic slide using double sided tape. The concentration of platinum was reported as micrograms of platinum per kilograms of hair (µg/kg). A length of 3 cm of hair represents a 90-day period. To increase accuracy, the test was duplicated, and the highest platinum level was used for analysis.

Descriptive statistics included categorical variables reported as frequency counts and percentages. Normally distributed continuous variables were reported as mean and SD. ANOVA and independent sample t-tests were performed to evaluate differences in baseline characteristics. Median and range were used to present nonnormally distributed data.

Kruskal-Wallis H test and Mann-Whitney tests were performed to investigate the differences in median platinum measurements in hair samples (µg/kg). Analysis of covariance on ranks was performed whilst correcting for possible confounders. A P value less than 0.05 was set as threshold for statistical significance. Statistical analyses were performed using SPSS (version 27.0; IBM Corp., Armonk, N.Y.)

RESULTS

The participants from group A and B visited the outpatient clinic between March and May 2021. Participants from group C were included during the same period. Baseline characteristics are summarized in Table 3. There were no significant differences in the demographic data between the three groups. The number of smokers was comparable between the three groups; however, group A showed a higher number of total pack-years.

Women with silicone gel-filled breast implants and breast implant illness (group A) showed a median platinum concentration [interquartile range] of 0.09 µg per kg [IQR 0.04–0.15]. One women showed an outlying platinum concentration of 0.52 µg per kg, which was more than five times higher than the median. Women with silicone gel-filled breast implants and no breast implant illness (group B) showed a platinum concentration of 0.08 µg per kg [IQR

Table 2. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Group A and B • Women >18 years with >2 years of exposure to silicone gel-filled breast implants • A scalp hair length of at least 5 cm Group A • A typical pattern of combined symptoms fitting the description of breast implant illness (Table 1) Group B • Without systemic symptoms Group C • A female partner/friend/relative from group A or B without breast implants or systemic symptoms • A scalp hair length of at least 5 cm	• Any type of implant containing platinum (other than gel-filled silicone breast implants in group A and B) (eg, dental implants, pacemakers, vagus nerve stimulators, surgical pins and screws, copper intra-uterine device, implanon, intraocular lenses) • Platinum-containing jewelry • Usage of silicone gel on the skin • A history of chemotherapy or radiotherapy • Usage of platinum-containing medication • Occupational exposure to platinum (eg, hospital workers with exposure to chemotherapeutic agents containing platinum)

Table 3. Patient Demographics and Clinical Characteristics

Group	A (n = 10)	B (n = 10)	C (n = 10)
Age, mean ± SD, y	45.5 ± 8	46.2 ± 15	45.9 ± 19
BMI, mean ± SD	23.7 ± 3	21.5 ± 3	24.7 ± 4
Place of residence, n (%)			
City	8 (80%)	7 (70%)	10 (100%)
Countryside	2 (20%)	3 (30%)	0
Smoking, n (%)			
Never	4 (40%)	3 (30%)	4 (40%)
Current	2 (20%)	2 (20%)	1 (10%)
Former	4 (40%)	5 (50%)	5 (50%)
Pack-years, median (IQR), y	20 (12–29)	10 (2–22)	5 (3–19)
Alcohol, n (%)	6 (60%)	7 (70%)	7 (70%)
No. lasses per week, mean ± SD	2.7 ± 4	4.0 ± 5	3.7 ± 6
History of autoimmune disease,* n (%)	4 (40%)	2 (20%)	2 (20%)
Allergies, n (%)	7 (70%)	7 (70%)	3 (30%)
Nickel	4 (40%)	2 (20%)	0
Medicine	1 (10%)	4 (40%)	1 (10%)
Other	2 (10%)	1 (10%)	2 (20%)
Atopic constitution, n (%)	6 (60%)	4 (40%)	3 (30%)
Implantation time, mean ± SD, y	17.4 ± 7	15.2 ± 9	NA
Duration of symptoms, mean ± SD, y	8 ± 5	NA	NA
Symptom free period, mean ± SD, y	7.5 ± 7	NA	NA
Revisions, n of patients (%)	6 (60%)	4 (40%)	NA
Reason for revisions, n (%)			
Rupture	3 (30%)	0	NA
Contracture	3 (30%)	2 (20%)	NA
Other	0	2 (20%)	NA
Reason for implantation, n (%)			
Augmentation	10 (100%)	8 (80%)	NA
Reconstruction	0	2 (20%)	NA
MRI/US, n (%)			
Current rupture	1 (10%)	0	NA
Axillary silicone deposition	1 (10%)	0	NA
Axillary adenopathy	3 (30%)	0	NA
Implant brand, n (%)			
Mentor (siltex/perthese)	2 (20%)	0	NA
Eurosilicone	3 (40%)	2 (20%)	NA
Allergan	2 (20%)	2 (20%)	NA
McGhan	1 (10%)	1 (10%)	NA
Natrelle	0	1 (10%)	NA
Unknown	1 (10%)	4 (40%)	NA
Location, n (%)			
Submammary	3 (30%)	3 (30%)	NA
Subpectoral	6 (60%)	7 (70%)	NA
Missing	1 (10%)	0	NA

Group A, women with SBI and breast implant illness; Group B, women with SBI and no breast implant illness; Group C, control; BMI, Body Mass Index; IQR, interquartile range; n, frequency count; MRI, magnetic resonance imaging; US, ultrasound.
*Group A: Systemic lupus erythematosus-like disease, psoriasis, colitis ulcerosa, oral lichen planus. Group B: hypothyroidism (n = 2). Group C: hypothyroidism (n = 2).

0.04–0.12]. The control group (group C) showed a platinum concentration of 0.04 μg per kg [IQR 0.02–0.13]. No outliers were found in group B or C. We found no statistically significant difference in platinum concentration across the three groups (P = 0.43, SDC 1a). [**See figure, Supplemental Digital Content 1,** which displays the (a) individual median platinum concentration in women with silicone breast implants and breast implant illness (group A), in women with silicone breast implants and no breast implant illness (group B), and in controls (group C). Bar represents median. Error bars indicate interquartile range. P values indicate Kruskal-Wallis H and Mann-Whitney testing with levels of significance. (b) Individual median platinum concentration of women with current and previous ruptures in group A. Group A: women with silicone breast implants and breast implant illness. http://links.lww.com/PRSGO/C53.] Subsequently, no significant difference was found between all women with silicone breast implants (group A+B, median platinum concentration of 0.09 μg/kg [IQR 0.04–0.11]) when compared with women without breast implants (group C, 0.04 μg/kg [IQR 0.02–0.13], P = 0.21).

This remained unchanged after adjusting for BMI and smoking pack-years (P = 0.35, P = 0.66, respectively). Furthermore, adjustment for implantation time showed no significant effect on platinum concentration between group A and B (P = 0.77). Additionally, women from group A or B with one or more revisions of implants showed a platinum concentration of 0.06 μg per kg [IQR 0.03–0.12]. When compared with women without revisions with a corresponding median platinum concentration 0.09 μg per kg [IQR 0.06–0.14], no significant difference was found (P = 0.40).

Supplemental Digital Content 1b shows possible associations between platinum levels and radiological imaging. (**See figure, Supplemental Digital Content 1,** http://links.lww.com/PRSGO/C53.) An intracapsular implant rupture was observed by ultrasound in one patient from group A, 15 years after the breast implantation. The hair platinum concentration of this patient was 0.09 μg per kg. Furthermore, the medical histories of three women from group A reported one or more previous implant ruptures. One woman presented with bilateral axillary silicone

depositions from a previous rupture, with a corresponding platinum concentration of 0.02 µg per kg. Another woman reported three previous ruptures, with a platinum concentration of 0.04 µg per kg. Lastly, one woman, with a single previous rupture, showed a platinum concentration of 0.04 µg per kg. As shown in Supplemental Digital Content 1b, none of these current or previous ruptures were correlated with an elevated median platinum level.

DISCUSSION

This blinded pilot study aimed to investigate possible associations between platinum concentration measured in hair and presence of silicone gel-filled breast implants and breast implant illness, using LA-ICP-MS. We found no statistically significant difference in platinum levels between women with breast implants and breast implant illness, women with breast implants but no suspected breast implant illness, and women without breast implants. Furthermore, no correlation was found between platinum concentration and radiologically proven implant rupture or axillary silicone depositions from previous ruptures.

Only one previous study from Texas measured platinum concentration in hair samples of women with silicone gel-filled breast implants, using ion chromatography ICP-MS. The authors reported a mean platinum concentration (SD) of 2.3±2.98 µg per kg (range 0.6–10.0, n = 9), which is a hundredfold higher compared with our present findings.[12] The implantation time was the same as in the present study. The difference in platinum concentration is probably best explained by unknown differences in analytical techniques of platinum determination,[23] or because of our strict exclusion criteria regarding platinum exposure. Other potential explanations can be found in geographically differences in environmental exposure to platinum (eg, derived from food sources or automobile exhaust).[23]

We found three studies that examined platinum in hair samples from subjects without breast implants. The first study used adsorptive voltammetry to measure platinum levels in the hair of 21 Sydney residents, and reported an average of 3.84 µg per kg (range 0.87–18.31 µg/kg).[46] A second study from Tokyo, also using the LA-ICP-MS method, found a median platinum concentration of 2.17 µg per kg [IQR 1.62–2.85] in 15 office workers.[45] Lastly, a study performed in Sweden used double focusing sector field ICP-MS for elemental characterization of human hair, and reported a mean platinum level of 0.17 µg per kg ± 0.16.[47] The results of the abovementioned studies are remarkably similar to the reported platinum levels in hair of women with silicone gel-filled breast implants, and do not suggest that women with breast implants have significantly elevated platinum levels in their hair. To put these findings into perspective, a median platinum level of 213 µg per kg has been reported in patients receiving platinum-containing drugs, such as cisplatin.[45] However, given paucity of data, the different analytic methods and thereby discrepancies in platinum concentration between the studies, and the lack of adequate reference values for platinum in the normal population, it is difficult to draw conclusions.

Based on the premise that platinum accumulation in hair is caused by platinum leakage from silicone gel-filled breast implants, we expected women from our study with prolonged exposure to breast implants and/or previous implant ruptures, to present with increased levels of platinum. However, our data do not seem to support this premise. None of the women with one or more previous ruptures, a current intracapsular rupture, or axillary silicone depositions showed evidently higher platinum concentrations than women without radiologically proven silicone leakage. A possible explanation for these findings might be the analytical method, in which platinum levels are evaluated only for the past 90 days. Thereby, it is possible that earlier leakage or gel-bleed is not reflected in a platinum measurement in the hair strain of the last three months. Lastly, we need to take into consideration that there is currently insufficient data on whether or not every brand and type of implant contains platinum, and if so, how much.

Furthermore, no explanation was found for the 39-year-old woman from group A who presented with an outlying elevated platinum level. She underwent unilateral breast augmentation because of asymmetry, presented with a relatively high BMI of 25.34 kg per square meters, but no history of implant rupture or radiological signs of silicone leakage. Given the fact that the major route of platinum exposure is through diet, the difference might be explained by increased platinum intake.[33,46] However, additional adjustment in the statistical analysis for BMI did not show any different outcomes. In line, even though we found a higher number of total smoking pack-years in group A, no evidence in the literature indicates that this affects platinum levels, and adjustment during statistical analysis showed no different outcomes.

Although we focus on platinum in this article, other heavy metals have been detected in breast implants, such as cadmium and tin. According to toxicity tests performed by manufacturers, the small amounts of heavy metals are likely to be safe. The Food and Drug Administration, however, states that individual responses may vary and not all reactions can be predicted.[48]

One of the methodological strengths of the present study includes the use of LA-ICP-MS for platinum measurement in hair, which has multiple advantages over conventional techniques such as blood tests. Hair analysis allows for accurate measurement of platinum levels over time, is noninvasive, and can be easily performed and stored. Measurement of platinum concentration in hair, using LA-ICP-MS, has previously shown to be useful in the calibration of platinum based anti-cancer drugs, and monitoring of platinum exposure in healthcare workers.[45,49] Moreover, the addition of the control group allowed us to compare the platinum levels of women with breast implants with healthy women without breast implants.

The main limitation of this pilot study is the small sample size. Another limitation includes the lack of baseline levels of platinum, before breast augmentation. Because individual platinum levels are fluctuant, we cannot fully attribute increased platinum levels to silicone gel-filled breast implants, without a baseline value. Furthermore, we lacked

data on the size of the silicone gel-filled breast implants, because platinum concentrations may vary by implant size or brand. Lastly, despite independent examination by two experienced physicians, meticulous selection of patients, and exclusion of other causes for the symptoms, breast implant illness cannot be diagnosed with certainty yet and is mostly based on clinical assessment of subjective symptoms.

To our knowledge, this is the first study that evaluated this commercially available screening test in the Netherlands, to compare platinum concentrations in hair samples of women with silicone gel-filled breast implants, with or without breast implant illness, and a control group. Introduction of the hair test in the Netherlands led to widespread media attention, and consequently, drastic increase in referrals of concerned women to the specialized breast implant illness-outpatient clinic.

The results of this pilot study showed no statistically significant difference between median platinum hair levels in women with silicone gel-filled breast implants compared with women without breast implants. In addition, there was no difference in median platinum hair levels in women with breast implants and suspected breast implant illness, and women with breast implants but no suspected breast implant illness. Importantly, we found no correlation between radiologically proven implant ruptures or silicone leakage and elevated platinum levels.

Therefore, based on the present findings from this pilot study, we do not recommend the use of the hair test in the diagnostic workup of women with silicone gel-filled breast implants and suspected breast implant illness. However, this remains an interesting field of investigation. Given the small sample size from this pilot study, a larger study might be required to fully determine the usefulness of platinum tests in clinical practice.

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