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Response to Comments on "Determination of Low Molecular Weight Silicones in Plasma and Blood of Women after Exposure to Silicone Breast Implants by GC/MS"

SIR: Generally, the comments by Dr. Smith imply that in our study, sample contamination and loss play a significant role (body text and remarks 1, 3, 4, and 7) and that the results obtained for those patients with LMW silicones in blood are erratic and inconsistent (body text and remarks 2, 5, and 6).

We agree with Dr. Smith that determination of LMW cyclic silicones is a challenging task. However, our method of detection (GC/MS using SIM mode) and our general approach is well-established. It is used in many analytical laboratories worldwide, and has been published by scientists from Dow Corning.[1−3] GC/MS is commonly regarded as the most sensitive and selective method to quantify silicone species[4,5] and is especially well-established for the quantification of cyclic siloxanes.[5] Moreover, it is quite obvious when analyzing traces of cyclic silicones in blood that one takes all the necessary precautions to avoid contamination. Our laboratory is very familiar with analyzing LMW cyclic siloxanes near the limits of detection,[6−8] and the senior author has significant expertise in the use of GC/MS methods for more than a decade.[9,10] In particular, our group had been involved in a silicone industry (CES)-funded special project regarding artifact formation during silicone analysis.

Among other precautions reported in the literature,[1−3] steps were taken to avoid contamination, including separate storage of samples and standards and performed blank evaluation. Here, no contamination with LMW silicones was observed (Figure 1). This figure, by the way, was initially included in the original manuscript, but had been omitted, since one of the reviewers found it to be redundant. Of course, articles in high-quality journals have to be condensed and cannot present detailed data like a PhD thesis.

Finally, procedural blanks and results on patients without implants confirmed the absence of PDMS and LMW silicones and, thus, the absence of any significant analytical procedure contamination, as suspected by Dr. Smith.

Our comments to the individual remarks 1−7:

1. Thermodynamic volatility data are of no value when considering the nature of the hydrophobic interaction of cyclic siloxanes with the blood matrix. Furthermore, spiking experiments are performed under laboratory conditions in open systems and, thus, they cannot realistically simulate siloxane transition into human blood. Therefore, siloxane spiking experiments in water and blood (see Table 2 of our paper, on page 609) show different silicone recovery rates.

2. Our results simply demonstrate the potential for the detection of siloxanes in blood. However, there is no simple relationship between LMW silicones in blood and implant status; for example, rupture of implants may be caused by their implantation.[11] Timing of intra-/extracapsular ruptures and of gel migration is not known. Gel bleeding can occur even with intact implants, and capsule calcification can accompany long-term implantation. To date, a number of papers exist dealing with the migration of silicone; the amount of silicone found in capsules formed around implants is independent of implantation time.[12] Migration of silicone into capsules is not dependent upon implant status and is decreased by capsule calcification.[13] Relative signal intensities of silicone detected in the liver of women with ruptured implants were not correlated with the implant status.[14] In addition, Peters et al. found no dependence on implantation time.[15]

3. Since our extraction efficiencies are comparable with those of Varaprath et al., we consider that our data will still be valid in the low concentration range.[16]

4. We decided not to perform statistical analysis of our data, since we considered the body of data to be too small to obtain meaningful results. However, in most similar papers that have been published, no such statistical analysis has, to our knowledge, been included.

Results of concentrations near the detection limit may be regarded as semiquantitative (∼30% SD). In particular, we chose a very conservative approach for the determination of our detection limit. The signal we observed upon injection of

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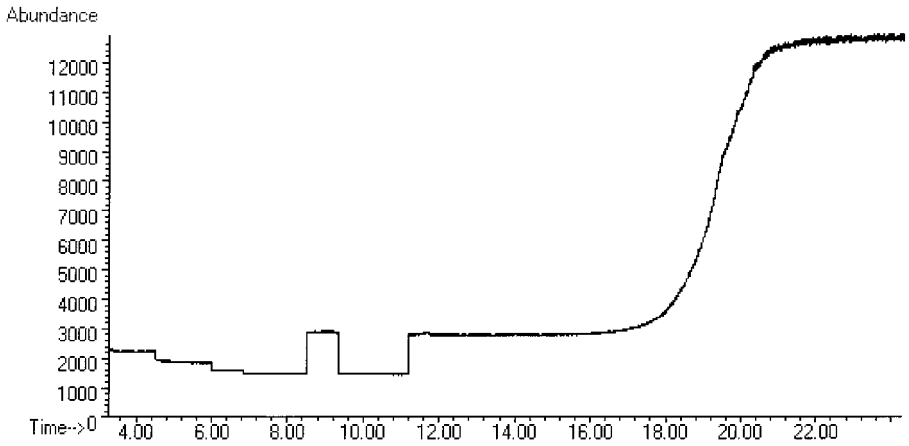

Figure 1. GC/MS chromatogram of hexane after passing the sample preparation in vials used for extraction and centrifugation.

2 pg/μL siloxane was clear and significantly higher than background noise level.

5. It is impossible for us to trace back origin and specifications of the implants used. The use of different implant materials will likely increase the "inconsistencies" listed above (2). In our study, we aimed to demonstrate the possible presence or absence of siloxanes in blood and plasma, a situation already described in 1979.[17] Silicone migration from implant into lung also needs blood as the transport vehicle.[18]

The private communication cited by Dr. Smith (ref 6) is not available to us, and we, therefore, can not judge if these results are reliable or not. It is known from literature that 1−2% of the silicone gel from implants (mostly cyclic siloxanes) can be analyzed by GC/MS.[19]

6. Most data are from plasma samples; only 4 were patients' whole blood samples. We agree that in further studies, more controls should be run.

To date, the detection of siloxanes in the blood of women without breast implants has not been reported. The citation of the Lugowski et al. paper by Dr. Smith is misleading, because total silicon, not silicones, were measured in the cited study. Contrary to statements of industrial scientists, silicon can never be a proxy for silicones in blood!

7. As pointed out before, the method of detection (SIM) and our approach are well-established and used in many analytical laboratories worldwide, as well as by scientists from Dow Corning, as a standard analytical technique.

To summarize, in using established instrumental techniques combined with careful sample handling and preparation, we were able to present a reliable method for the determination of LMW silicones in blood. On the basis of the analytical-quality parameters received (extraction efficiency, detection limit, blank level), LMW silicones could be analyzed in blood/plasma of several women having or having had silicone breast implants. To explain the concentrations found, however, is far beyond the task of this analytical paper, and will hopefully be the subject of many applied follow-up studies in medicine.

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