A Conversation on BII and Its Breaking Research

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MH: Thank you so much, Pat and Caroline, for joining me today! I’d love to talk to you about the ‘big paper,’ the one that you two spearheaded and I was lucky enough just to contribute patients to. Let’s start from the beginning. What’s the background? Why did you decide now is the time we needed a breast implant illness paper, in particular a prospective data paper?

PM: I started seeing increasing numbers of patients around 2016, right when BIA-ALCL was recognized by the WHO as the fourth form of anaplastic large cell lymphoma. They weren’t just concerned about ALCL, they were also concerned about a variety of symptoms they had developed since they had implants placed. Increasingly they had specific requests they had developed since they had implants. They wanted pictures of the implants, pictures of the capsules, and they wanted pictures of the pocket to be sure the entire capsule had been removed. I was skeptical, but then after explanation, many of them got better. At the device hearings in March of 2019, we heard some very compelling testimony from these women. They had real symptoms and some of them got better when their implants were removed, so I started thinking ‘what are we missing?’ They say it’s the most studied medical device of all time, but then why do we still see this much distrust and concern?

MH: That concern worried me too. I was worried about increasing distrust of plastic surgeons, especially when I started to hear about some surgeons taking advantage of patients, having them spend incredible amounts of money, and saying that only select surgeons could perform capsulectomies correctly.

CG: We really needed to collect specimens on all the patients as the capsule was necessary for pathology, heavy metals testing, and testing of microbes. We needed enough specimens to be able to obtain statistically significant data, so we did not have a group of patients with no capsulectomy.

PM: More than just a tiny biopsy was required in order to do the heavy metals testing. The lab required approximately 10 grams of tissue to perform the metals analysis. Some of the capsules were very thin, so even the partial capsulectomy resulted in more than just a small piece of tissue removed, and was why all patients were at least a partial capsulectomy.

MH: You have presented this data in a lot of different formats to a lot of plastic surgeons. What are the biggest questions or comments that are you’re getting?

CG: The Aesthetic Society’s and ASERF’s presidents just came out with a joint position statement, an alert, reiterating the findings of this study which is that the type of capsulectomy makes no difference in symptom improvement. I’ve received a great deal of feedback from plastic surgeons, both in the United States and around the world, who had been waiting for data to address these issues with some surgeons in their communities who may be taking advantage of these women. What I’m hearing so far is an appreciation for this data so they can inform patients that they may not need such aggressive procedures to feel better. Now, we don’t yet completely understand why some patients get better, but they do not appear to need so much surgery that they’re left with unnecessary serious complications.

PM: The other question I received was whether there were enough patients to achieve statistical significance. Before we started, we knew these biospecimen analyses were going to be expensive: we did peripheral blood for CBC, thyroid function, vitamin D levels, we looked at 12 different cytokines, CRP, heavy metals testing, routine pathology, next-generation DNA sequencing... it was going to be expensive! So we needed

The next step was to design a study that would be prospective, blinded and include two cohorts of patients with breast implants, one that self-reported systemic symptoms that they attributed to their implants and a second cohort that had implants and systemic symptoms that they did not attribute to their implants as well as a control group that never had any implanted medical device. The study design included run in two parts. We wanted to look at biospecimens which included the capsules for the presence of bacteria, pathology, and to identify any heavy metals. We also took blood from all three cohorts on the day of surgery. For the second part of the study, we included a detailed psychosocial investigation. Many of the reported symptoms included anxiety, depression, cognitive impairment, sleep disturbances—that have not been fully studied prospectively. We also needed to collect enough specimens to be statistically significant. We knew this was required to answer questions the FDA, patients, and surgeons. Our first question was whether the type of capsulectomy performed at the time of implant removal made a difference in symptom improvement.

PM: Yes, I want to emphasize that point. The previous papers have been retrospective, had few case studies, had no control groups, and had no long-term follow-up. There was one that got a lot of press, but 48% of the patients were followed for less than 30 days and there was no control group. Our study is the first prospective, blinded study with controls.

MH: Why wasn’t there a group where there was no capsule taken at all? I have heard it asked ‘well why is it just partial capsulectomy or total capsulectomy?’

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to know the minimum number that we could analyze and reach statistical significance.
Prior to beginning the study we talked to an experienced biostatistician who told us with 50 subjects in each cohort we could achieve statistical significance. According to our statistician, this does reach statistical significance, even with multivariate analysis, the p-value could have been raised and we still would have reached statistical significance.

MH: Let’s talk about the funding, too, because unlike nearly every other big study done on breast implants, this had no industry funding. How did you get funding?

CG: This is an issue primarily for aesthetic plastic surgeons, largely in private practice. We need to make sure that our patients trust us. Our first thought when designing the study and creating the budget was to approach ASERF. When we submitted the grant application, the Scientific Research Committee came back asking us to include further analysis and offered even more funds which was really exciting. This was the largest grant ASERF ever awarded! We were so happy to complete this study, especially during a COVID year, thanks especially to all of our collaborating surgeons around the country. And remember, many laboratories had shut down to divert research to COVID. It’s very hard for private practice plastic surgeons to collect this level of data but we have the full support of the aesthetic community.

PM: We went back for additional funding to do an analysis that was beyond reproach. We used the statistician who’s been used on FDA studies, who knew what they were looking for, and that was not cheap to do. But it wasn’t just about the funding, it was about the support, encouragement, and ideas that pushed us across the finish line.

MH: So the study is out, we’ve seen the big bombshell that, number one, the patients do feel better after implant removal, and number two, it doesn’t matter what kind of capsulectomy, total or partial, is done. Give us an idea of what we can look forward to as this research progresses.

PM: The second paper will be on the heavy metals analysis of the capsule, which is one I believe everyone is looking forward to, and we’re in the process of writing. For example, we found heavy metals in the capsules, but we also found metals in breast tissue of women who never had any implanted medical device. So it will analyze the differences and potential sources and consequences of metals in tissue.

CG: Yes, I think it will be very interesting. We tracked everything from diets, to smoking, to tattoos, to cities for sources of drinking water. You have to remember that when we have a metals discussion we don’t live in a bubble, we have environmental toxins that we are exposed to over time, which is why we also took normal breast tissue from women who were never exposed to any medical device to compare whether or not heavy metals are present in the breast and how they got there.

The third paper will look at the capsule histology, the patient’s cytokines, and all of the peripheral blood work that was taken in the three cohorts. Specimens were also sent to Johns Hopkins for enterotoxin analysis looking to see if there is any evidence of possible superantigens. We tried to conduct a study that would address all past and recent theories related to the potential systemic effects of breast implants.

MH: I’ve heard about how multidisciplinary the analysis is in the upcoming papers. Could you talk a bit about who was included?

PM: Yes it is! We included Dr. Wixtrom, a PhD toxicologist, who’s as experienced as anybody with medical devices and potential toxicity. Dr Marshall Kadin is the pathologist who described cutaneous ALCL. He’s done a lot of work with breast implant-associated ALCL. He had theories on what he thought might be going on with these patients. He was the one who got us involved with Dr. Robert Hamilton who is a PhD immunologist at Johns Hopkins, which is where we sent the enterotoxin studies. Dr. James Sung, who’s a pathologist at Brown University, didn’t know a lot about breast implant illness, but now he’s completely fascinated by it and is excited to have been included. Also included was Jill Newby in New South Wales, who’s a clinical psychologist for our patient-reported outcome data from the PROMIS surveys. We’re not psychologists and we really needed someone with a PhD in psychology to interpret the data.

MH: That’s such good information, and a lot to digest! But I’m sure you have more on the horizon. Future studies: where do you see yourselves going from here?

PM: Of course there’s more! The next thing we’d like to study is removing implants without any capsulectomy to see if we have the same symptom improvement.

CG: There is also a new study being designed on the Aesthetic Society’s SETA platform which will be able to collect prospective breast implant data and Patient Reported Outcome Measures. We have the funding and are just putting the pieces in place. This study will collect data over a couple of years, looking at possible symptoms before and after surgery.

PM: One thing that also requires more study is the fact that we found significantly more anxiety and depression in our BII cohorts than our control groups, and it poses a chicken or egg question.

MH: How about the angle of saline implants? At least in the patients that I enrolled, there was a higher percentage of saline implants which, I believe, make up less than ten percent of total implants placed nationally. Yet saline implants seemed to be disproportionately represented in BII cases.

PM: 60% of our BII patients had saline implants and 90% were smooth, but what we have seen around the world is that the most common implant involved is the most common implant used in any geographical location. It’s important we saw predominantly saline implant patients and this shows it was not a dose response to silicone, which would have been higher in silicone gel implants. Also, the length of time the implants were in place was statistically the same between the BII and non-BII implant cohorts.

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MH: Were there any interesting findings in demographic data? I think I’ve heard you talk about smoking between BII and non-BII, or body surface area of tattoos, or any other specific things?

PM: Yes, the BII patients had statistically lower educational levels, were more likely to smoke tobacco or smoke marijuana, they were more likely to take non-steroidal anti-inflammatory agents, anti-anxiety and anti-depression medications.

CG: The patients in the BII cohort were seven times more likely to be on a gluten-free diet, which is predominantly rice-based with potentially considerable arsenic content. They also took more nutritional supplements. Some of these confounders may be in part due to the fact that we conducted our study during the COVID pandemic while patients were taking more supplements, like zinc for instance. Patients in the BII cohort also had a statistically higher number of tattoos. We looked at the colors of the tattoos because some have cadmium, chromium, zinc, arsenic, lead, and mercury in tattoos. Also, the non-BII cohort had a lower BMI than the other two cohorts.

MH: Anything I’ve missed? I think we’ve covered a lot of fascinating ground.

PM: The bottom line is that these women have real symptoms, they are not hypochondriacs, and their symptoms get better when their implants are removed. We don’t know why yet, but that’s why we’re continuing with this research.

“Impact of Capsulectomy Type on Post-Explantation Systemic Symptom Improvement: Findings From the ASERF Systemic Symptoms in Women-Biospecimen Analysis Study: Part 1” can be found in the December 2021 Aesthetic Surgery Journal.

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Capsulectomy can be performed for a variety of reasons after implant-based breast surgery. The heightened public attention around Breast Implant Illness (BII) has raised awareness of and increased the rates of capsulectomy in the US. Yet the literature around the safety of capsulectomies is quite limited. My fellow authors and I utilized the CosmetAssure database, a robust and powerful prospective dataset tool, to analyze the safety of the capsulectomy procedure among board-certified and board-eligible plastic surgeons from all types of plastic surgery practices and across all regions of the US over a 2½ year period, which included 76,128 patients in all. Our study defined major complications as those that required hospital admission, takeback to the OR, or ER visits within 45 days of the incident surgery.

We found capsulectomy, as compared to all other procedures, to have a higher rate of major complications. In fact, 2.8% of patients in this dataset undergoing capsulectomy had at least one major complication. Compared to patients who underwent only implant replacement without capsulectomy, the patients who had capsulectomy had a higher rate of any major complication (2.8% vs 1.9%, P<0.05), as well as nearly double the risk of a hematoma (1.6% vs 0.9%, p<0.05). A majority of the hematomas occurred on postoperative day 1 and 0 (46.9% vs 38.1%).

Complications within the capsulectomy group were found to be in descending order: hematoma, infection, suspected or confirmed VTE, and pulmonary dysfunction. ASA Classes III and IV predicted risk for any type of complication. Body Mass Indices (BMI) over 30, as well as procedures performed in Office-Based Surgical Suites, as compared to Ambulatory Surgery Centers and Hospitals, had a higher risk for major infectious complications.

In order to make an assessment of the possible influence of social media on capsulectomy rates, our study chose to compare capsulectomies performed before and after January 6, 2019—a date from Google and Twitter trend analyses performed by Adidharma et al. These authors found a spike in Google searches and trends for breast implant illness during the week of January 6, 2019, coinciding with a YouTube influencer’s public interview sharing her experience with breast implant illness. Similarly, within the CosmetAssure database, capsulectomy rates significantly rose and nearly doubled from an average of 2.7/day to 5.2/day from that January 6, 2019 date. A similar peak in Google trends for BII was observed the week of February 3, 2019 following an FDA letter raising awareness of BIA-ALCL. Unfortunately, some of the public appear to associate the two entities of BII and BIA-ALCL.

We are grateful to share our data on the safety of capsulectomy. When performed by board-certified/board-eligible plastic surgeons, the absolute rate of complications is relatively low. But severe complications can and do occur. Our data demonstrates the relative risk of complications is higher than other cosmetic procedures. As capsulectomies continue to increase, the overall incidence of complications can be expected to also increase, underscoring the importance of understanding and sharing the risks of capsulectomy so that patients can make a truly informed decision for treatment.


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