Letter to the Editor

Response to "Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL): Why the Search for an Infectious Etiology May Be Irrelevant"

Aesthetic Surgery Journal
2017, Vol 37(9) NP122–NP128

DOI: 10.1093/asj/sjx133
www.aestheticsurgeryjournal.com
OXFORD UNIVERSITY PRESS

Anand K. Deva, BSc (Med), MBBS, MS, FRACS (Plast)

Editorial Decision date: June 29, 2017; online publish-ahead-of-print August 21, 2017.

"*Reasoning will never make a man correct an ill opinion, which by reasoning he never acquired*"[1]

I thank you for the opportunity to respond to Dr Swanson's letter.[2] It is the second time that I have had to take my pen to paper to answer a range of allegations and recriminations from him.[3] After years in private practice, he has more recently emerged as a frequent commentator of evidence-based practice,[4] the dangers of overcommercialisation in plastic surgery[5] (which I must admit I agree with), and allegations of industry involvement corrupting the truth in research.[6] It is easy to throw stones but they will fall short of the mark if you are not speaking from a position of scientific and/or professional credibility.

In summary, here are the allegations and assertions he has raised in his letter.

1. The downside of the 14-point plan including criticism of triple antibiotic irrigation.
2. The pledge site and its ramifications.
3. Conflict of interest as a motivation behind a defense of textured implants and in particular the role of Allergan and Allergan-sponsored research and authors in recent publications supporting the use of textured implants.
4. The lack of evidence behind infection as one of the factors that may contribute to breast implant associated anaplastic large cell lymphoma (BIA-ALCL) and publication bias.
5. The call for abandoning textured devices.
6. The irrelevance of further study to delineate underlying pathogenesis of BIA-ALCL.

I will now go through each of these and attempt to provide supporting arguments and published evidence as a contrary view to the one he has written. I make no apology in going through this in detail because as you will see, it is easy to skim through the surface of much of this information and form an erroneous opinion. Where relevant, I have included quick fact check boxes (Tables 1-4) to counter some of the glaring inaccuracies.

The 14-Point Plan

This group of perioperative strategies was first developed and published over the past decade[7] and codified and published in 2013.[8] It was formed by accumulating both clinical and laboratory studies at that time and with reference to the wider literature on device associated infection and the prevention of capsular contracture. Since its publication, more supportive evidence has come to light with respect to the use of sleeves[9] and the protective effect of pocket irrigation to reduce capsular contracture by a factor of 10.[10,11]

Professor Deva is Head of Plastic and Reconstructive Surgery and Co-Chair of the Surgical Infection Research Group, Macquarie University, Sydney, Australia.

Corresponding Author:
Prof. Anand K. Deva, Department of Plastic and Reconstructive Surgery, MQ Health, Macquarie University, Suite 301, Macquarie University Clinic, 2 Technology Place, Macquarie Park NSW 2109, Australia.
E-mail: anand.deva@mq.edu.au

Table 1. Fact Check 1

Swanson: "The other practice recommendations (nipple shields; introduction sleeve; new instruments, gloves, and drapes when handling the implant; minimizing time of implant opening; and minimizing repositioning) are not strongly supported by evidence."
Rebuttal: All of these steps are supported by clinical and/or laboratory evidence. For nipple shields, see Collis et al[12] and Wixtrom et al[13] for dual plane showing less contracture, see comparative clinical studies show advantage of muscular cover.[11,14-18] There is evidence to show that gown and glove contamination occur after about 1 hour of surgical operating time.[19,20] It lies in the wider literature in prevention of device-associated infection and I would encourage all surgeons using implants to familiarize themselves with advances in this area. Ward et al[19] have shown a fourfold higher level of baseline bacterial contamination (31% vs 7%) on the sleeve of surgical team members wearing cloth gowns. Twenty-six of these 27 gowns allowed bacterial transmission through the material. Surgeons retaining outer gloves 1 hour in to operating had a bacterial contamination rate of 23%. Beldame et al[20] have shown that over 50% of gloves are contaminated during routine sampling during prosthetic joint replacement with *S. epidermidis.* Interestingly, 16% of cultures were also positive for methicillin resistant *S. aureus.* The duration of surgery has been shown to significantly increase the risk of surgical infection.[21] Saito et al[22] have shown high levels of contamination of surgical instruments after being used in routine procedures. The highest level of contamination was for instruments used for a laparotomy with 31% of these instruments registering growth of microorganisms. The commonest contaminant was *S. epidermidis.*[22]

Table 2. Fact Check 2

Swanson: "If the cause of both conditions is a chronic bacterial infection, as proposed, one might expect to see more cases of breast implant associated anaplastic large cell lymphoma in patients with capsular contracture."
Rebuttal: This statement shows that he has not read or understood the threshold phenomenon and the various inflammatory/fibrosis vs transformational pathways that bacterial antigens can push T cells into.[24,25] Figure 1 shows that in most cases, with biofilm mitigation, bacterial contamination can be kept below threshold and live symbiotically with the host. In the setting of higher levels of contamination a host response is set up and this can be inflammatory leading to contracture or potentially transformative leading to cancer.

Table 3. Fact Check 3

Swanson: "The website promotes the 14-point plan to prevent capsular contracture and to reduce the incidence of BIAALCL to "infinitesimal," and to "prevent future issues with textured implants guaranteeing their use for many years to come."
Rebuttal: It is evident that Dr Swanson has not accessed or read the website closely. I encourage readers to scan the website for themselves as these words do not appear. On the webpage, he has cited as reference no. 5, the information states that the 14-point plan targets bacteria, which are a cause of contracture. The role of subclinical infection is supported by over 10 years of research and Koch's postulates have been satisfied from both laboratory and clinical research.[27] There does not appear to be any reference on the website promoting textured implants and any guarantee of outcomes related to textured implants as he has quoted in his letter.

Table 4. Fact Check 4

Swanson: "Deva's microbiological research laboratory is supported by funding from implant manufacturers."
Rebuttal: Readers are directed to a list of grants here that have funded our program into surgical infection (http://www.mq.edu.au/about_us/faculties_and_departments/faculty_of_medicine_and_health_sciences/research/research_groups/our_staff/associate_professor_anand_deva). This list is slightly out of date, as we have received further competitive government grant funding for our work into hospital-acquired infection. Industry grants form a small percentage of our funding total and these have been institutional or matched grants with government (Enterprise partnership grants). They are carefully regulated by compliance and institutional rules as to what the funding is used for and there are key timelines for delivery of research outcomes. It would be impossible to drive translational research outcomes to the bedside without engaging industry.

It is true that some of these steps are supported by stronger evidence than others and in time, with more research and debate, we may well add or subtract from these steps. The plan was never meant to be prescriptive or be used as a means of dividing us into those that use it and those that do not. These are evidence based and individuals can balance between evidence and experience to apply the steps as indicated in their own practice.

In terms of the solution for pocket irrigation, there is some evidence that the microbiome around BIA-ALCL samples have shifted towards Gram-negative organisms.[23] Our work on detecting bacteria in BIA-ALCL has achieved significant recognition for the validity of the scientific findings, including the recent award of the James Barrett Brown prize. I accept the limitations of the numbers of specimens in this paper but these are acknowledged in the discussion and are supported by valid statistical analysis.

We are continuing to analyze the microbiome prospectively from BIA-ALCL specimens (and nontumor controls) in Australia and will report these findings in the very near future. The predominance of Ralstonia Picketii in our published paper has prompted further in vitro analysis of the currently practiced pocket irrigation solutions with respect to both activity against these Gram-negative organisms and the presence of associated biological contamination eg, serum, blood, protein. We are in the process of analyzing these data but have already issued a statement favoring the use of betadine containing irrigation solutions in the interim on the saferbreastimplants.org website. The emerging patterns of microbial resistance will also require ongoing monitoring of the species of bacteria, fungi and other microorganisms that contaminate implants with appropriate adjustment of antiseptics and/or topical antibiotics in the future. I refer Dr Swanson and the readership to a

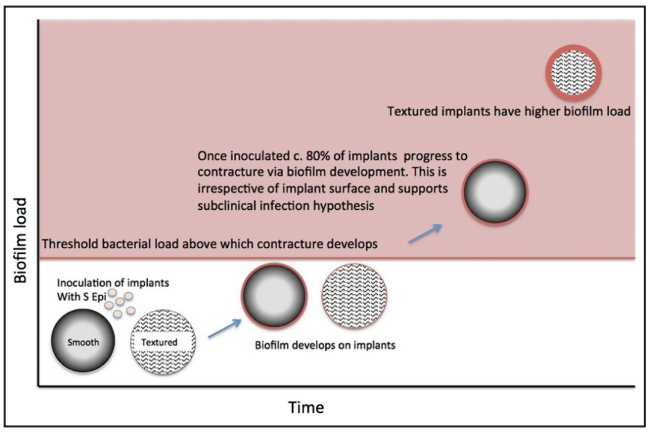

Figure 1. The threshold phenomenon and why textured implants do not necessarily result in a higher rate of contracture from infection. Reprinted with permission from Wolters Kluwer Health, Inc.[25]

commentary I published on the issue of microbial resistance in *ASJ* previously.[26]

The Pledge Site

The pledge is not to force surgeons to use the 14-point plan to the letter—some of us use drains, periareolar incisions, and subglandular pockets for example, and have great outcomes. The pledge is simply to state a public commitment to reducing bacterial contamination of breast implants. This is backed by a strong evidence base that supports bacterial biofilm as an important causative factor in capsular contracture and should therefore push all of us to become more aligned with preventing implant contamination. What we do as surgeons in the operating room when the implant goes in is key to ensuring a good long-term outcome for patients with breast implants.

Our orthopedic colleagues treat implant surgery with far more respect than we do and it pains me to say that we should learn from them. Even the most cynical of us cannot deny the motivation to improve standards of care based on evidence and research is a worthy goal to ascribe to. For surgeons who have taken the pledge, I thank you for seeing this for what it is rather than ascribing base motives and/or being concerned with legal ramifications. Our numbers continue to grow around the world and it gives me great comfort to know there are many of us that are like-minded and are willing to subscribe to a heightened level of awareness of the issue of breast implant infection. If Dr Swanson does not feel he should take a pledge to support this, that is entirely his decision.

Conflict of Interest (COI)

I have previously replied to Dr Swanson's allegations that any research that is partly funded by industry is automatically conflicted and thus is immediately called to question.[3] A recent issue of *JAMA* has further examined this growing issue in medicine.[28] Historically, science has been largely supported by private patronage and support from the church. This was not free of bias—just ask Galileo when he took on the church. The move to government (taxpayer) funding began in the 19th century but as the cost and scale of research rose, we now have to seek a variety of sources to support research programs. It is true that in the 1950s and 60s; industry funding was used strategically by companies for their own ends.[29] Work on the link between cigarette smoking, lung disease, and cancer is a classic case study of science being subverted by the powerful tobacco lobby.[30] In the last decade, as recognition of this bias, government, academia, and the wider community have called for checks and balances to be put into place.

A few take-home points for Dr Swanson (and readers) to consider.

1. Engagement with industry is now regulated through compliance and is transparent.[31] The quantum and nature of funding for each physician in the United States is now published and available here (https://openpaymentsdata.cms.gov) and here (https://projects.propublica.org/docdollars). Dr Swanson and others interested in seeing the flow of funding to any author publishing on breast implants or BIA-ALCL may simply search the name of the physician on these databases. The latest data for 2015 was uploaded this year. The issue of general payments is the one of most concern as these are made directly to the physician.[32]
2. Research into implants requires industry engagement as the impact of scientific findings will need to be translated to the manufacturers and drive better outcomes. Members and leaders of academic institutions are well placed to engage with industry as they are not directly funded by industry and have significant rules of engagement via their institutional legal and regulatory framework.[33]
3. Not all COIs are equal. There is little doubt of the existence of a conflict when the physician derives direct benefit from shares or license/royalty payments. For less obvious COI, the question then arises how much is enough and is there a "use-by" date for previous payments? I would put to readers that any personal payments used for marketing or recommending products to patients/colleagues is a much more serious level of conflict as compared with advisory boards, consulting reports, and/or contract research. In this instance, a direct financial transaction from industry was made to an individual to directly promote a product or sales of a device for the advantage of the company. The transaction involves a quid pro quo ie, you speak beneficially about our product and we will pay

you as this will result in increased profit/sales for our company. Physicians who are frequently engaged in this activity need to be called to account. I would, for example, be concerned about any physician that has received significant personal payment for the promotion of a product or device at any time in the past.[32]

4. There are also personal financial conflicts when we work in a for-profit private practice.[28] Advice given to patients to encourage them to a higher fee paying procedure, marketing to encourage patients to see you in your private practice, gaining attention through provocative media (and social media) are also means of competing for more patients and thus more private funding. Our professional code of ethics should act as a deterrent but there are certainly those who sail very close to the wind.[34]

A group of us led by Professor Rod Cooter are working on a conflict of interest scale (analogous to levels of evidence), which will stratify the various levels of COI (Cooter R, personal communication, 2017). It is clear that the type, level of financial remuneration and the time period will need to factor into a measure that will allow a true comparison of the complex nature of COIs between physicians and allow engagement with industry to be seen in its proper context.

The Lack of Evidence Behind Infection as One of the Factors That May Contribute to BIA-ALCL and Publication Bias

Our most recent publication has now formulated the unifying theory on the genesis of BIA-ALCL.[35] I am the first to acknowledge that the research now shows that it is not bacteria alone. In this fast-moving area, we are learning quickly through a global cooperative effort about the treatment, epidemiology, risk, and pathogenesis of this disease. Figure 2 summarizes the unifying hypothesis.

The cause of cancer is never unifactorial and so to simply focus on texture as the only cause is simplistic and most likely wrong. This working hypothesis negates much of what Dr Swanson has written in his letter about our claims that bacteria are the only factor in genesis of BIA-ALCL. He has failed to understand the science and has jumped to erroneous conclusions. We are not claiming it is bacteria alone but that higher levels of the wrong type of bacteria promoted by contact with high surface area texture, which supports greater bacterial growth in the setting of contamination, combined with genetic predilection for transformation over time that is the likely mechanism for genesis of BIA-ALCL.

The role of bacteria as one of the four main factors is particularly relevant as it is something we can target right now using proven bacterial mitigation strategies.

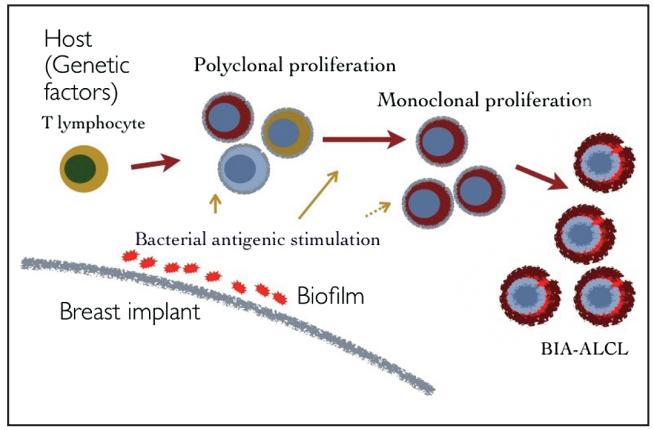

Figure 2. The unifying hypothesis for genesis of BIA-ALCL.[35]

Here is, once again, the cumulative evidence that points to bacteria as a source of inflammation and likely trigger for transformation in BIA-ACL.

1. Bacteria as a cause of lymphoma via inflammatory stimulation of lymphocytes.[36]
2. The role of bacterial superantigens in activating T cell receptors.[37,38]
3. The finding that high surface area implants are significantly associated with BIA-ALCL consistent with our findings that surface area is a determinant for higher growth of bacteria in patients[25] and higher stimulation of lymphocytes.[24]
4. Detection of a Gram-negative microbiome in BIA-ALCL.[23]
5. Cluster patterns of incidence from our latest study suggesting infection as a factor.[35]
6. The role of the microbiome in the genesis/potentiation of gastric cancer,[39] breast cancer,[40] oral cancer, hepatobililary cancer,[41] and colorectal cancer.[42,43]

We no longer view bacteria on our skin, gut, breast, and oral cavity as passive. They are interacting with our immune system every single moment of the day and can modulate our bodies' response to inflammation[44] and disease.[45,46] I would urge Dr Swanson to familiarize himself with this significant and growing body of research across many areas of both biology and medical science before he dismisses it all as "publication bias."

The Call for Abandoning Textured Devices

Our most recent paper has now shown a differential risk for different textures.[35] High surface area textures (Biocell and Silimed Polyurethane) are 10 to 14 times more likely to be associated with BIA-ALCL as compared with lower surface area textures (Siltex). Interestingly our study has shown the highest risk for Biocell (salt loss) texture at 1

in 3810 implants, analogous to the risk from the Allergan sponsored study at 1 in 4000 implants.[14] It is good to see consistency in this number across these two independent studies. Consistency is a sign that these data are correct. Interestingly, we also showed a high risk for polyurethane textured implants. These two unrelated textures have one thing in common—a very high surface area. This is further supportive evidence for the role of bacteria as one of the 4 key factors in pathogenesis of BIA-ALCL.

It no longer makes sense to quote a 1 in 30,000 risk overall for BIA-ALCL,[47] as the risk is significantly higher for some textures as compared to others. Furthermore, to advocate throwing out all textures just does not make sense particularly if there are some textures with proven advantages with tissue incorporation and form stability in the setting of a low risk of BIA-ALCL. I agree that these benefits will need to be further studied and proven through higher quality (and nonconflicted) clinical studies.

To rush to abandon texture will result in the same outcome of rushing to blame silicone for adjuvant disease and will create unnecessary panic, high cost for patients now wishing to have their textured implants removed for no good reason, and/or legal action. It took many years and great work by Garry Brody to delineate fact from fiction with regard to autoimmune disease and breast implants.[48] This time around, we now have sufficient data through our global cooperative effort to point to the real factors that are at play so let us act on these now. A slow and steady approach is called for rather than creating panic by banning texture or advocating change to smooth implants immediately, especially as this disease is rare and eminently treatable.

The Irrelevance of Further Study to Delineate Underlying Pathogenesis of BIA-ALCL

Swanson categorically states, "Once we stop using textured implants, there is no need to inquire further into the exact cause of BIA-ALCL." Is he really advocating stopping research into uncovering the underlying pathogenesis of BIA-ALCL? What would have happened if we simply decided that we have all the answers in medicine back in the 1500s based on the same mentality? I suspect we would still be using bloodletting and rebalancing humors as primary treatment for a range of diseases. The pursuit of understanding the etiology and pathogenesis of disease is one of the fundamental drivers for greater outcomes in medicine. It is through understanding how disease comes about that we are then able to prevent disease happening in the first place. Furthermore, the study of the human immune response to bacterial antigens on the surface of prosthetics and the underlying genetic risk factors that may point people to cancer has wider relevance to many other areas of medicine. Dr Swanson would have us shut this down completely as he now believes it is "irrelevant" or because he fears that the truth may put him a legal risk or blame for not adequately mitigating against infection.

One of the great loves that I have for science is that it speaks to you with the truth. The results of a well-designed experiment can either support or refute a hypothesis and it is this curiosity of challenging and proving or disproving ideas that drives us in research. I understand his concern that in breast implant research, that this truth has somehow been completely corrupted by conflicts, large amounts of cash payments to corrupt individuals who are now nothing but salesmen protecting big business. There may well be some instances of this but the behavior of a few should not tarnish the rest of us. I also believe that Dr Swanson's words belie a myopic and simplistic view formed from little understanding of the checks, balances, regulation, and transparency that now governs our engagement with industry. He should come and spend some time in our research program to see what it is really like! I would hope that before he decides to shoot his next broadside against me, or other researchers in this area, questioning the need for ongoing scientific pursuit and denouncing biofilm and microbiome research as "publication bias," that he takes a few moments to try to really understand the landscape with an open, less suspicious and accusatory mindset.

So there you have it. I have attempted to bring the debate back to solid ground and hope that it has been enough to bring both Dr Swanson and any other skeptical readers to a point of greater understanding and awareness. However, I never presume to be able to convince everyone with facts, logic, and evidence. I respect the right for individuals to hold a contrary opinion and enjoy the process of scientific debate. At some point, however, one should recognize that further engagement with closed minds that are intent on pushing their own ideas from a position of limited understanding is a waste of time and energy. For those of us who believe that improving outcomes through good practice, evidence, and research, I welcome you all to join us in trying to move aesthetics to where it should be—an outcome-driven profession based on science, objective evaluation with the patient, and his/her well being placed at front and center. For those who are like-minded and have taken the pledge, let us continue to build on an evidence base to improve outcomes in breast implant surgery for the sake of our patients.

Disclosures

Prof. Deva has previously coordinated research and been a consultant to Allergan (Irvine, CA), Mentor (Santa Barbara, CA), and KCI (San Antonio, TX).

Funding

The author received no financial support for the research, authorship, and publication of this article.

REFERENCES

1. Swift J. Letter to a young gentleman, lately enter'd into holy orders by a person of quality. *Writings on religion and the Church Vol 1*. Vol 1. Oxford Arms, London: J Roberts; 1720:27.
2. Swanson E. Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL): why the search for an infectious etiology may be irrelevant. *Aesthet Surg J*. 2017;37(9):NP118–NP121
3. Deva AK. Reply: Textured breast implants, anaplastic large-cell lymphoma, and conflict of interest. *Plast Reconstr Surg*. 2017;139(2):559e-560e.
4. Swanson E. Levels of evidence in cosmetic surgery: analysis and recommendations using a new CLEAR classification. *Plast Reconstr Surg Glob Open*. 2013;1(8):e66.
5. Swanson E. The commercialization of plastic surgery. *Aesthet Surg J*. 2013;33(7):1065-1068.
6. Swanson E. Textured breast implants, anaplastic large-cell lymphoma, and conflict of interest. *Plast Reconstr Surg*. 2017;139(2):558e-559e.
7. Adams WP Jr, Rios JL, Smith SJ. Enhancing patient outcomes in aesthetic and reconstructive breast surgery using triple antibiotic breast irrigation: six-year prospective clinical study. *Plast Reconstr Surg*. 2006;118(7 Suppl):46S-52S.
8. Deva AK, Adams WP Jr, Vickery K. The role of bacterial biofilms in device-associated infection. *Plast Reconstr Surg*. 2013;132(5):1319-1328.
9. Flugstad NA, Pozner JN, Baxter RA, et al. Does implant insertion with a funnel decrease capsular contracture? A preliminary report. *Aesthet Surg J*. 2016;36(5):550-556.
10. Giordano S, Peltoniemi H, Lilius P, Salmi A. Povidone-iodine combined with antibiotic topical irrigation to reduce capsular contracture in cosmetic breast augmentation: a comparative study. *Aesthet Surg J*. 2013;33(5):675-680.
11. Blount AL, Martin MD, Lineberry KD, Kettaneh N, Alfonso DR. Capsular contracture rate in a low-risk population after primary augmentation mammaplasty. *Aesthet Surg J*. 2013;33(4):516-521.
12. Collis N, Mirza S, Stanley PR, Campbell L, Sharpe DT. Reduction of potential contamination of breast implants by the use of 'nipple shields'. *Br J Plast Surg*. 1999;52(6):445-447.
13. Wixtrom RN, Stutman RL, Burke RM, Mahoney AK, Codner MA. Risk of breast implant bacterial contamination from endogenous breast flora, prevention with nipple shields, and implications for biofilm formation. *Aesthet Surg J*. 2012;32(8):956-963.
14. McGuire P, Reisman NR, Murphy DK. Risk factor analysis for capsular contracture, malposition, and late seroma in subjects receiving natrelle 410 form-stable silicone breast implants. *Plast Reconstr Surg*. 2017;139(1):1-9.
15. Vazquez B, Given KS, Houston GC. Breast augmentation: a review of subglandular and submuscular implantation. *Aesthetic Plast Surg*. 1987;11(2):101-105.
16. Puckett CL, Croll GH, Reichel CA, Concannon MJ. A critical look at capsule contracture in subglandular versus subpectoral mammary augmentation. *Aesthetic Plast Surg*. 1987;11(1):23-28.
17. Biggs TM, Yarish RS. Augmentation mammaplasty: a comparative analysis. *Plast Reconstr Surg*. 1990;85(3):368-372.
18. Egeberg A, Sørensen JA. The impact of breast implant location on the risk of capsular contraction. *Ann Plast Surg*. 2016;77(2):255-259.
19. Ward WG Sr, Cooper JM, Lippert D, Kablawi RO, Neiberg RH, Sherertz RJ. Glove and gown effects on intraoperative bacterial contamination. *Ann Surg*. 2014;259(3):591-597.
20. Beldame J, Lagrave B, Lievain L, Lefebvre B, Frebourg N, Dujardin F. Surgical glove bacterial contamination and perforation during total hip arthroplasty implantation: when gloves should be changed. *Orthop Traumatol Surg Res*. 2012;98(4):432-440.
21. Leong G, Wilson J, Charlett A. Duration of operation as a risk factor for surgical site infection: comparison of English and US data. *J Hosp Infect*. 2006;63(3): 255-262.
22. Saito Y, Kobayashi H, Uetera Y, Yasuhara H, Kajiura T, Okubo T. Microbial contamination of surgical instruments used for laparotomy. *Am J Infect Control*. 2014;42(1):43-47.
23. Hu H, Johani K, Almatroudi A, et al. Bacterial biofilm infection detected in breast implant-associated anaplastic large-cell lymphoma. *Plast Reconstr Surg*. 2016;137(6):1659-1669.
24. Hu H, Jacombs A, Vickery K, Merten SL, Pennington DG, Deva AK. Chronic biofilm infection in breast implants is associated with an increased T-cell lymphocytic infiltrate: implications for breast implant-associated lymphoma. *Plast Reconstr Surg*. 2015;135(2):319-329.
25. Jacombs A, Tahir S, Hu H, et al. In vitro and in vivo investigation of the influence of implant surface on the formation of bacterial biofilm in mammary implants. *Plast Reconstr Surg*. 2014;133(4):471e-480e.
26. Deva AK. Commentary on: Incidence of methicillin-resistant ***Staphylococcus aureus*** (MRSA) carrier status in patients undergoing post-mastectomy breast reconstruction. *Aesthet Surg J*. 2017;37(1):44-45.
27. Tamboto H, Vickery K, Deva AK. Subclinical (biofilm) infection causes capsular contracture in a porcine model following augmentation mammaplasty. *Plast Reconstr Surg*. 2010;126(3):835-842.
28. Fineberg HV. Conflict of interest: why does it matter? *JAMA*. 2017;317(17):1717-1718.
29. Brandt AM. Inventing conflicts of interest: a history of tobacco industry tactics. *Am J Public Health*. 2012;102(1):63-71.
30. Cummings KM, Brown A, O'Connor R. The cigarette controversy. *Cancer Epidemiol Biomarkers Prev*. 2007;16(6):1070-1076.

31. Ornstein C. Public disclosure of payments to physicians from industry. *JAMA*. 2017;317(17):1749-1750.
32. Lo B, Grady D. Payments to physicians: does the amount of money make a difference? *JAMA*. 2017;317(17): 1719-1720.
33. Pizzo PA, Lawley TJ, Rubenstein AH. Role of leaders in fostering meaningful collaborations between academic medical centers and industry while also managing individual and institutional conflicts of interest. *JAMA*. 2017;317(17):1729-1730.
34. Nissen SE. Conflicts of interest and professional medical associations: progress and remaining challenges. *JAMA*. 2017;317(17):1737-1738.
35. Loch-Wilkinson A, Beath K, Knight RJW, et al. Breast implant associated anaplastic large cell lymphoma in Australia and New Zealand—high surface area textured implants are associated with increased risk. *Plast Reconstr Surg*. 2017. doi: 10.1097/PRS.0000000000003654.
36. Brawner KM, Morrow CD, Smith PD. Gastric microbiome and gastric cancer. *Cancer J*. 2014;20(3):211-216.
37. Kadin ME, Deva A, Xu H, et al. Biomarkers provide clues to early events in the pathogenesis of breast implant-associated anaplastic large cell lymphoma. *Aesthet Surg J*. 2016;36(7):773-781.
38. Kadin ME, Morgan J, Xu H, Glicksman CA. CD30 + T cells in late seroma may not be diagnostic of breast implant-associated anaplastic large cell lymphoma. *Aesthet Surg J*. 2017;37(7):771-775.
39. Zhang C, Powell SE, Betel D, Shah MA. The gastric microbiome and its influence on gastric carcinogenesis: current knowledge and ongoing research. *Hematol Oncol Clin North Am*. 2017;31(3):389-408.
40. Yang J, Tan Q, Fu Q, et al. Gastrointestinal microbiome and breast cancer: correlations, mechanisms and potential clinical implications. *Breast Cancer*. 2017;24(2):220-228.
41. Mima K, Nakagawa S, Sawayama H, et al. The microbiome and hepatobiliary-pancreatic cancers. *Cancer Lett*. 2017;402:9-15. doi: 10.1016/j.canlet.2017.05.001.
42. Wang X, Yang Y, Huycke MM. Microbiome-driven carcinogenesis in colorectal cancer: models and mechanisms. *Free Radic Biol Med*. 2017;105:3-15.
43. Cho M, Carter J, Harari S, Pei Z. The interrelationships of the gut microbiome and inflammation in colorectal carcinogenesis. *Clin Lab Med*. 2014;34(4):699-710.
44. Slingerland AE, Schwabkey Z, Wiesnoski DH, Jenq RR. Clinical evidence for the microbiome in inflammatory diseases. *Front Immunol*. 2017;8:400.
45. Singh RK, Chang HW, Yan D, et al. Influence of diet on the gut microbiome and implications for human health. *J Transl Med*. 2017;15(1):73.
46. Thomas CL, Fernández-Peñas P. The microbiome and atopic eczema: more than skin deep. *Australas J Dermatol*. 2017;58(1):18-24.
47. Doren EL, Miranda RN, Selber JC, et al. U.S. epidemiology of breast implant-associated anaplastic large cell lymphoma. *Plast Reconstr Surg*. 2017;139(5):1042-1050.
48. Brody GS. The breast-implant controversy. *N Engl J Med*. 1993;328(10):732; author reply 734-732; author reply 735.