Prof. Dr. M. Hamdi comments on the preliminary opinion report of the SCHEER committee.

From: *European Master of surgical oncology, reconstructive and aesthetic breast surgery*

Vrij Universiteit Brussel (VUB) – Belgium

Universitat Autonoma de Barcelona, Spain

Dear members of the Scientific Committee on Health, Environmental and Emerging Risks (SCHEER),

First, I would like to thank you for the organization of such a discussion among different members involved in the field of breast implants.

When I initially read the preliminary opinion delivered by the SCHEER on the safety of breast implants in relation to anaplastic large cell lymphoma (ALCL), I was rather reserved on how the discussion would be conducted during the public hearing. However, I must admit that our dialogue was based on respect to scientific and common-sense principles. The discussion did not invoke any political views nor issues linked to conflict of interest. The moderation of Mr. de Jong was balanced and contributed strongly to the very satisfactory audit.

Concurrently, I read with utmost care the excellent comments submitted by my colleague Dr. Nava and I wholeheartedly agree with his statement.

Nevertheless, I felt obliged to emphasize some additional points:

> "The clinical indications for the use of a specific type of breast implant do not depend on the preoperative clinical conditions, but only on the clinician's and patient's preferences, and consequently on industry and/or media information."

- We totally disagree with this statement. It is not based on a well-founded resource but is rather an incorrect expectation of false information. It remains the clinician's responsibility to choose the right implants for his or her patient. As I mentioned in my presentation, implant choice is a fine balance between the patient's wishes and what is surgically possible with her tissue characteristics. In other words, patient desire could influence the choice of the implant, but standard of care should guide the surgeon to select the right implant based on the quality of the breast tissue (gland thickness/skin thickness and quality/previous treatment/future treatment? etc.) [1,2]
- Implant choice might also be influenced by the pharmaceutical industry and the implant manufacturers. It is true that surgeons may opt for a service provided by a company they trust, rather than this relationship being based on

financial remuneration. During the discussion, one of the panelists raised the issue of conflict of interest among some speakers and accused some of them as acting as a voice of implant companies! It is very important to distinguish between surgeons who are a part of a company, which may involve being on the payroll or having a share in the company, and another group of surgeons who have built up a long-term clinical experience using implants from a specific company after which they have published scientific works and presented their experience in a number of international meetings. The last group of surgeons are considered KEY OPINION LEADERS (KOL) and their impact is very important to evaluate any subject such as BIA-ALCL.

- The choice of experts should also be balanced. When the SCHEER committee selects such experts to write their report, the choice should be based on scientific criteria. Surgical experts should be those who are involved in BIA-ALCL groups but also who are KOL in breast surgery. I have the feeling that SCHEER's choice of surgical experts selection was partially inadequate and influenced the preliminary report directly and indirectly.

In section 4.3 Alternative to breast implants

"Alternatives to the use of breast implants include surgical techniques using autologous tissue that can be performed by various flap techniques (whole tissue transfers) or by autologous fat transplantation. The latter may need multiple procedures before an acceptable result is obtained."

-The report described widely the different options and techniques for breast reconstruction. We all agree that conservative breast treatment should be the first choice and that reconstruction should be performed by autologous tissue where possible (breast unit definition by EC). However, mastectomies are still oncologically indicated for breasts with large tumors or to prevent breast cancer in patients with genetic mutation [3]. Most of the risk-reducing mastectomies are indicated in young patients and many of these patients are not good candidates for flap surgery. Implant-based breast reconstruction is still the most used method worldwide. In Belgium, autologous breast reconstruction after mastectomy, has reached about 40% which is the highest in the world. Nonetheless, 60% of our Belgian patients are still treated by breast implants [4]. **As such, breast implants remain essential for breast reconstruction.**

-For aesthetic patients: flap surgery is not feasible, mostly technically, and their cost is unbearable by our patients. Fat grafting is not an option for most of these patients because they have low BMI, and their bodies have little donor fat. **So, breast implants remain nearly the only option for these patients.**

"There is a moderate[8] level of evidence for a causal relationship between textured breast implants and ALCL."

"Based on a moderate[9] weight of evidence, the SCHEER concludes that there is a causal relationship between textured breast implants and BIA-ALCL."

-We all agree that most of the reported cases of BIA-ALCL were linked to textured implants. However, I regret using different language when it comes to smooth implants. Our colleagues in North America still use statements such as "no *pure* smooth implants have been linked with BIA-ALCL". Yet with such a large number of unreported or even unknown information as stated in the last FDA report, such statements are not acceptable. No one is able to guarantee our patients the "zero percent" risk of BIA-ALCL being linked to any type of implants, including smooth implants.

-For statistic reasons, a difference should be made between BIA-ALCL primary cases (patient who only one implant history) and secondary cases (patients with multiple history of various implants with different textures/companies…). When it comes to secondary cases, the BIA-ALCL should be linked to the last implant used, but with a minimum period of follow-up (that should at least exceed the previous duration of time found in primary cases in the literature).

-Since surface texturation technologies are also different, it would be more accurate to report the BIA-ALCL cases related to technology and also to company (e.g. Biocells from Allergan versus textured Implants of Sebbin or Polyurethane from Silimed versus Polytech).

"A number of different systems have been proposed to classify implant surfaces:

- *ISO 14607:2018* is the most widely accepted and divides breast implants into Smooth (<10µm), Micro (10-50µm) or Macro (>50µm) textured surfaces based on the implant's average surface roughness. Average roughness is determined as a height parameter by integration of peaks and valleys around a lineal surface. [5]
- *Atlan et al.,* (2018) used an X-ray CT to determine the actual surface area of 10mm diameter discs, four from the anterior and four from the posterior implant shell as a proxy of texture, and divided breast implants into Smooth (80-100mm^2), Micro (100-200mm^2), Macro (200-300mm^2) and +Macro (>300mm^2) surfaces. [6]
- *Jones et al.,* (2018) measured the surface area and roughness of implants using scanning electron microscopy (SEM) and subjected the shells to an *in vitro* bacterial attachment assay with four bacterial pathogens studying their growth in relationship to the surface area and roughness. According to roughness (and propensity for bacterial growth) they classified implant surfaces into: Minimal (<25µm), Low (25-75µm), Intermediate (75-150µm) and High (>150µm) textured surfaces. [7]
- *Barr et al.,* (2017) used SEM and laser confocal microscopy (LCM) and classified implant surfaces based on roughness (peaks and valleys) into Nano (<5µm), Meso (<15µm), Micro (10-75µm), and Macro (>75µm), further dividing Macroand Micro categories into porous and non-porous. [8]

To date, none of the proposed surface texture classifications mentioned above have been validated in a clinical study to determine which classification best predicts the risk of BIA- ALCL."

I cannot agree more with SCHEER last statement from SCHEER which reflects the non-validity of any classification. As I mentioned above, the classification system is a static grading system which does not reflect the characteristics of the different implants per company and per shell manufacturing technology. More important, the classification system does not reflect the clinical behavior of these implants.

Most of my presentation was focused on polyurethane implants and their clinical superiority which was confirmed in several clinical studies. [9,10,11]

In conclusion, I would like to emphasize the following points:

- ALCL is extremely rare [12]

- we still need implants

- we still need anatomical implants [13]

- implant choice is essential for the surgeons and it is based on tissue characteristics mainly and not solely on patient wish or information provided by the implant company

- ISO texture classification is a bold static classification and does not reflect the characteristic of each texture/implant/company.

- importance of an implant registry

- importance of standard of care to avoid/reduce complications.

- when only smooth implants were used, a high number of complications was reported [14]

- when the right indication is made for implant choice, smooth implants can only be indicated in 1 out of 5 patients [14,15]

- when polyurethane or micro/textured implants are indicated, the benefit exceeds the risk[16]

References

1) Nava MB, Catanuto G, Rocco N. *A decision-making method for breast augmentation based on 25 years of practice. Arch Plast Surg.* 2018 Mar;45(2):196-203.
2) Martin del Yerro JL, Vegas MR, Fernández V, Moreno E, Sanz I, Puga S, Biggs TM. Selecting the implant Height in breast augmentation with anatomical prosthesis: The number Y. *Plast Reconstr Surg*. 2013 Jun;131(6):1404-1412.
3) Domchek SM.Risk-Reducing Mastectomy in BRCA1 and BRCA2 Mutation Carriers: A Complex Discussion.JAMA. 2019 Jan 1;321(1):27.
4) Sources:RIZIV.fgov.be
5) ISO International Organization for Standardization. *ISO 1460: 2018—Non-active surgical implants—Mammary implants—Particular requirements*. https://www.iso.org/ standard/63973.html. Accessed January 7, 2019.
6) Atlan et al. Breast implant surface texture impacts host tissue response. *J Mech Behav Biomed Mater*. 2018 Dec;88:377-385.
7) Jones P, Mempin M, Hu H, et al. The functional influence of breast implant outer shell morphology on bacterial attach- ment and growth. *Plast Reconstr Surg*. 2018;142:837–849.
8) Barr S, et al. Functional biocompatibility testing of silicone breast implants and a novel classification system based on surface roughness. *J Mech Behav Biomed Mater.* 2017 Nov;75:75-81.
9) Pompei S, Evangelidou D, Arelli F, et al. The modern polyurethane-coated implant in breast augmentation: long-term clinical experience. *Aesthetic Surg J* 2016;36:1124e9.
10) Pompei S, Arelli F, Labardi L, et al. Polyurethane implants in 2-stage breast reconstruction: 9-year clinical experience. *Aesthetic Surg J* 2017;37:171e6.
11) Loreti et al. Immediate Breast Reconstruction after mastectomy with polyurethane implants versus textured implants: A retrospective study with focus on capsular contracture. *The Breast.* 54 (2020) 127e132
12) Campanale A, Spagnoli A, Lispi L, Boldrini R, Marletta M. The crucial role os surgical treatment in BIA- ALCL prognosis in early and advanced stage patients. *Plast Reconstr Surg*. 2020. Nov 146(5):530e- 538e.
13) Montemurro P, Adams WP, Malluci P, De Vita R, Layt C, Calobrace MB, Brown MH, Nava MB, Teitelbaum S, Martin del Yerro JL, Bengtson B, Maxwell GP, Heden P. Why do we need anatomical implants? The Science and rationale for maintaining their availability and use in breast surgery. *Aesthetic Plast Surg*. 2020. Apr 44(2):253-263.
14) Montemurro P, Vincent K.S. Tay KSV. Transitioning From Conventional Textured to Nanotextured Breast Implants: Our Early Experience and Modifications for Optimal Breast Augmentation Outcomes. Aesthetic Surgery Journal 2020, online publish-ahead-of-print June 24, 2020.
15) Moustapha Hamdi. Nano-Surface Implants: Indications and Limitations Aesthetic Surgery Journal*, sjaa265, https://doi.org/10.1093/asj/sjaa265*
16) Moustapha Hamdi, MD, PhD. Association Between Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) Risk and Polyurethane Breast Implants: Clinical Evidence and European Perspective *Aesthetic Surgery Journal*, Volume 39, Issue Supplement_1, March 2019, Pages S49–S54,