Views of the European Taskforce on Breast Implant Associated-ALCL for ANSM's Public Hearing on Breast Implants

1. Introduction into breast implants & BIA-ALCL

It may be helpful to provide a brief introduction on breast implants. Breast implants are available in different sizes (volume), shapes (round or anatomical), surface texture (smooth, micro textured, macro textured, polyurethane coated), and fill (silicone or saline).

Round implants are available in both smooth and textured surface finishes, but anatomical implants are only available in a textured surface finish.

There are various manufacturing methods for creating texture on the surface of implants, which lead to varying degrees of surface texture e.g. surface roughness, porosity.

Currently there is no consensus on a single classification system for surface texture. There is ongoing discussion internationally into the classification of textured implants. ANSM have produced a report with categories for smooth silicone implants, micro-textured silicone implants, macro-textured silicones implants, and polyurethane coated silicone implants. There is an ISO standard, and a group in Australia (Jones et al) has produced a paper with suggested categories. ICOBRA are considering the issues and trying to determine a harmonised system to be adopted by breast implant registries internationally.

Anaplastic Large Cell Lymphoma (ALCL) is a rare type of non-Hodgkin's lymphoma of which there are several sub-types. In 2016, the World Health Organisation (WHO) defined a specific type of ALCL called Breast Implant Associated Anaplastic Large Cell Lymphoma or BIA-ALCL. This has specific diagnostic criteria which includes expression of the marker CD30+ and negativity for ALK.

ALCL is not fatal for the majority of patients and if caught early is treatable with explantation and total capsulectomy alone.

Scientific proof of causal relationship has not been established and the cause and the mechanism for the development of BIA-ALCL is yet to be determined. International research in this area continues worldwide.

2. Experience of the BIA-ALCL Taskforce:

As BIA-ALCL is a rare disease, an EU Taskforce (TF) was formed to monitor cases of BIA-ALCL with the aim of getting a picture of the issue across Europe[1]. The TF pool the number of cases received per country to form a larger European dataset, this should help with identifying any trends or commonality in the types of reports received. However, collecting information about the reports has not been a straightforward task.

Between July 2014 and November 2018, 238 cases in the EU were reported to the Taskforce out of which 188 were confirmed cases of BIA-ALCL. Of the confirmed cases 147 were reported to be

[1] The EU Taskforce is composed by the competent authorities from DE, PT, NL, FR, BE, AT, UK, DK, IE, SL, IS, SE, IT and the Commission

textured implants at the time of diagnosis, including polyurethane coated, microtextured or macro-textured implants. We do not know the texture of the implants in the other reports.

The FDA's website says that some cases of BIA-ALCL in the US were associated with smooth breast implants at the time of diagnosis.

Although most of the reports of BIA-ALCL have been in patients with textured implants at the time of diagnosis, to date, no controlled clinical trials that compare homogenous samples of patients implanted with smooth or textured implants have been carried out. The investigation into BIA-ALCL is ongoing and, as with all issues, an evidence-based approach is being taken.

Consequently, considering the rarity of this emerging pathology, even if all European BIA-ALCL cases have been diagnosed with a textured surface at the time of diagnosis, this sample is still not representative and the pathogenesis of this disease has not been identified.

3. EU and International activity

SCHEER

The European Commission and its Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) has published scientific advice related to breast implants and health. According to the SCHEER expert advice "Scientific advice on the state of scientific knowledge regarding a possible connection between breast implants and anaplastic large cell lymphoma" of October 2017, there is currently insufficient scientific information available to establish a methodologically robust risk assessment to investigate a possible association of breast implants with ALCL development[2]. It was therefore seen as necessary to intensify research in the field of BIA-ALCL and to continue to devote greater attention to better understand this disease.

RIVM

On 19th November 2018, members of the EU Taskforce participated in the international workshop on BIA-ALCL organised by the Dutch National Institute of Public Health and the environment (RIVM) consisting of an expert group including regulators, manufacturers, public health authorities, medical specialists, epidemiologists, experts on implant registries, laboratory scientists and representatives of the clinical and scientific societies.

The first part of the meeting focused on sharing knowledge and experience gained internationally. The second part focused on identification of research questions, requirements for performing such research, types of studies suitable to answer the research questions, and how to organize future research in terms of parties involved, roles of each party, funding, and timeframes.

RIVM concluded that given the relatively low number of BIA-ALCL cases seen per country and the variety of factors to take into account, a coordinated international and multidisciplinary approach is necessary. Future research topics discussed include looking into the characteristics of the patient, implant and tumour, as well as biofilm formation around the implant. The participants who attended the meeting agreed to set up an international consortium with the task to prepare research proposals, and plan to meet again in the second half of 2019[3].

ICOBRA

[2] https://ec.europa.eu/health/sites/health/files/scientific_committees/scheer/docs/scheer_o_007.pdf
[3] https://www.rivm.nl/documenten/summary-international-expert-meeting-on-bia-alcl-november-19th-2018

The International Collaboration of Breast Registry Activities (ICOBRA) was developed to establish an internationally agreed and comparable minimum data set for breast implant registries. The PIP scandal identified the need for a high capture rate globally of standardised and epidemiologically sound data about breast implant procedures. ICOBRA facilitate the establishment of globally agreed definitions on a national level for breast implant registries. Contributing countries and organisations consist of national plastic and reconstructive surgery societies, national health services and national health regulatory agencies.

This work is important as breast implants are usually implanted for long periods of time, sometimes in excess of 10 years. Typically, details about the device's model, surface, or even manufacturer are not known at the time of reporting by healthcare professionals. Some individuals may have had their devices removed and replaced but, if a full capsulectomy was not conducted between implants, then the contribution of a previously implanted device cannot be ruled out as a contributor to the disease. Details of the patient's previous implants are rarely provided, and often the details of the original implanting surgeon are either unknown or cannot be obtained as the clinic where the procedure took place is no longer in operation. This highlights the need for information to be collected in a national device registry, which is independent from market factors such as changes in the availability of information from clinics or manufacturers.

Not all the surface textures of breast implants are manufactured in the same way and they appear to have different levels of risk. The TF welcomes the ongoing work to categorise the surface type by ICOBRA to ensure registries are using harmonised taxonomy, which will enable data sharing in the future.

Medical Device Regulation 2017 (MDR)

The changes in the medical devices regulatory system with the introduction of EU MDR 2017/745 will require implant cards to be provided to individuals and for healthcare institutions to keep and make available to individuals, the information about their procedures and implant details. These measures should help reduce the problems with future data collection. Also, MDR foresees the encouragement of the establishment of registers and databanks for specific types of devices, setting common principles to collect comparable information, and in this way it will contribute to the independent evaluation of the long-term safety and performance of devices.

4. Motivation/interest for the use of textured breast implants in the context of a cosmetic surgery (aesthetic results, patient characteristics, surgical practices, complications)

Based on preferred outcome, the individuals can opt to have a round breast implant or an anatomically shaped prosthesis. Clinically, the choice is determined by anatomical aspects of the chest wall, such as the thickness of the breast tissue and the thickness of the soft tissue.

Experience gained in Europe is that most individuals who have cosmetic breast augmentation would like to achieve a natural improvement of the chest wall. In other regions of the world, individuals may prefer to opt for a well-defined contour of the cleavage, and so they normally choose round implants.

From a safety perspective, the use of textured implants is preferred in most European countries to prevent the undesirable movement or rotation of the implants, and more importantly reduce the risk of capsular contracture around the implant which is cited as the most common cause of revision in smooth implants. Movement or rotation is particularly undesired in an anatomical implant, as the device is asymmetrical and could result in unacceptable aesthetic outcome, when the aim is to provide a natural looking augmentation.

5. Motivation/interest for the use of textured breast implants in the context of a reconstruction surgery (aesthetic results, patient characteristics, surgical practices, complications)

For women with breast cancer who undergo mastectomy, breast reconstruction offers improved psychological and cosmetic outcomes. The literature presents innumerable articles that support the notable psychological advantages for women who receive breast reconstruction. These women express an improved quality of life.

The options for reconstructive surgery include alloplastic material (implant-based) or autologous tissue transfer.

Considerations include whether the patient has already undergone or is planning to undergo radiation therapy as part of their treatment, lack of sufficient autologous donor tissue, operation and recovery time, and the potential for future procedures associated with implant complications and revision.

When a unilateral implant-based reconstruction is selected, the most popular choice is the anatomical implant, as a better symmetric outcome is achieved with the contralateral breast.

To date, removing textured devices from the market would by default also remove the option of anatomical implants, and therefore prevent a more natural breast reconstruction from being achieved.

6. Existing alternatives to textured breast implants in reconstruction and/or aesthetic indications

There are a limited number of alternatives to the use of textured implants, such as autologous fat transfer, smooth implants in association with synthetic or biological meshes (detailed below). However, all of them are associated with their own risks and contraindications.

When indicated, autologous breast reconstructions are better in terms of aesthetic and long-term results than the alloplastic procedures, however it is a longer procedure and carries additional intraoperative risks, with donor site morbidity, including potentially fatal lung embolism, and not all health care professionals are trained to perform autologous breast reconstructions. Additionally, not all women are suitable candidates for this type of surgery because of anatomical reasons or co-morbidity. In case of bilateral reconstruction only few women have enough tissue for autologous reconstruction of both breasts.

For the cosmetic surgery, there are individuals in which only the anatomical implant could provide good aesthetic results, and these are only available as textured implants.
In the past, some manufacturers have tried to produce smooth ***anatomical implants***. Unfortunately, it seemed that benefit/risk ratio was too low because of the high number of complications observed with this kind of device.

The experience of clinicians who conduct corrective or revision of aesthetic breast surgery involving smooth implants, indicate that a large number of the procedures are due to mal-position of the implants caused by post-operative movement. They often become displaced away from the breast (bottoming out and/or moving sideways) which require correction. If textured implants are not available, then the use of synthetic or biological meshes to control the position of a smooth implant, will increase in an attempt to correct the problems associated with smooth implants. This may result

in a new set of problems, as the risk of this type of procedure and the long-term performance of the combined use of meshes with smooth implants is unknown.

7. Acceptability of the risk of ALCL with textured breast implants

The acceptability of the risk of BIA-ALCL associated with textured implants should be evaluated taking into consideration that:

- To date, this is considered a rare disease. Approximately 600 cases of BIA-ALCL have been reported worldwide, and this should be viewed in the context of an estimated 10 million breast implants that have been implanted;
- It has not been proven that smooth implants are not involved in the pathogenesis of BIA-ALCL;
- An very large number of women have benefited from receiving a textured implant without reporting complications;
- In the vast majority of patients with BIA-ALCL, the prognosis is favourable when diagnosed and treated at the early stage.
- Other alternatives to the use of textured implants are also associated with risks and complications.
- Currently there is no single classification system for surface texture. Further research is needed to determine the exact level of risk before effective and targeted action can be taken.

8. Specific indications that could be identified for textured breast implants

Textured implants have well defined place in the clinical portfolio as they provide advantages both in terms of clinical and psychological outcome for the patient when compared to smooth implants. However it is vital, that the risks of using textured or smooth surfaced implants are fully discussed with all individuals before surgery so that they are able to make fully informed choices.

9. Any other useful element

A. Discussions at the RIVM meeting indicated that due to the rarity of BIA-ALCL a retrospective study involving patients already diagnosed with BIA-ALCL should be encouraged, in order to identify any genetic factors that might predispose an individual to developing BIA-ALCL, as this could provide useful information about indications and contraindications prior to implant surgery.

B. Research on device aspects should be promoted.

C. The awareness of physicians and patients of BIA-ALCL issue should be increased:
   - For the physicians, to discuss the risks with their patient pre-operatively, and to diagnose and treat the disease at the early stage, which has a favourable outcome.
   - For the patients, to increase awareness about the risks and benefits when they decide to undergo this type of surgery, be informed and vigilant of potential symptoms indicative of this condition and participate in the follow-up according to the clinician's request.

10 - Conclusion

In summary, the Taskforce's evaluation of BIA-ALCL is ongoing and as with all issues, we take an evidence-based approach. BIA-ALCL is a topic of significant concern and the data is continuing to emerge. Research into this area is yet to provide an answer to how BIA-ALCL develops, and research is ongoing. The choice of a particular type of breast implant for a patient should be made in view of this emerging evidence. The opinion of the majority of the Member States in the EU Taskforce to date is that there is insufficient scientific evidence to limit the use of textured breast implants as they provide positive clinical and psychological outcomes for patients. It is, however, vital that **the risks of having either textured or smooth-surfaced implants are fully discussed** with all individuals before surgery so that they can make fully informed choices.

The Taskforce will continue to evaluate the data as it emerges and our opinion may evolve as further evidence comes to light.

N.B. These views are shared by all members of the Taskforce with the exception of France.