

## BIA-ALCL Safety Advisory

The following advisory represents a collaborative effort between ASPS and ASAPS to produce biannual updates on recent disease developments, government regulatory communications, and consensus recommendations.

Q: What is BIA-ALCL?

A: BIA-ALCL (Breast Implant-Associated Anaplastic Large Cell Lymphoma) is an uncommon lymphoma that has only been reported in patients with a history of a textured breast implant device. When caught early, it may be curable in most patients. BIA-ALCL is not a cancer of the breast tissue itself, but of the scar envelope that the body naturally forms around a breast implant – called the capsule. All government authorities and oncology organizations currently classify BIA-ALCL as a lymphoma.\* However, BIA-ALCL consists of a spectrum of disease that ranges from indolent CD30+ fluid collections within the capsule, to capsular tumors, to lymph node involvement and rarely distant metastases. Ongoing research continues to strive to better understand and define BIA-ALCL.

*\*Lymph cells are part of the body's immune system that helps to protect and rid the body from noxious agents. A lymphoma is cancer of the lymph system. Lymph nodes are glands in many locations in the body that are part of the lymph system. Indolent refers to a cancer that is slow to progress.*

Q: What are the symptoms of BIA-ALCL?

A: The most common presenting symptom of BIA-ALCL is a swelling of the breast that develops several years (average 8 years, range 2 to 28 years) after the insertion of textured breast implants. The disease can also present as a lump in the breast or the lymph node in the armpit.

Q: What is the risk of developing BIA-ALCL?

A: In March 2018, the FDA issued a report that it has received 414 adverse event reports of BIA-ALCL, and nine disease-related death reports. However, the FDA warns this data may have duplicates and unverified cases. The ASPS/FDA PROFILE Registry reports 230 unique U.S. cases to date. For a frame of reference, both the American Society of Plastic Surgeons and the American Society for Aesthetic Plastic Surgery report that approximately 300,000 breast augmentations and 150,000 breast reconstructions are performed annually in the United States. Approximately 12 percent of these patients receive textured implants.

The lifetime risk of developing BIA-ALCL, from previous epidemiological studies and implant sales data from the U.S., Canada, Netherlands, and Australia, ranges from 1:1000 to 1:30,000 people with textured implants. There appears to be some variability in risk depending on the type of texturing used on the implant. The risk is higher with textured implants that have greater surface area, such as the Biocell and polyurethane coating\*, compared to those that have less surface areas. However, BIA-ALCL has been identified in patients with all types/brands

of texturing. At this time there are no reported cases of a patient who has only had a smooth implant developing BIA-ALCL.

*\*Polyurethane sponge covered implants have not been available in the US since the early 1990's.*

Q: What did the latest FDA statement say in regards to BIA-ALCL?

A: The FDA's March 2018 statement recognizes BIA-ALCL is an uncommon and highly treatable condition and emphasized that most cases are in patients who have had textured implants. The FDA also acknowledged and agreed with the World Health Organization's classification of BIA-ALCL as a lymphoma, and the National Comprehensive Cancer Network (NCCN) treatment guidelines.\* The FDA noted surgical management for the majority of patients, and recommends all confirmed BIA-ALCL cases be reported to the PROFILE registry for detailed tracking of cases. The statement also affirmed that if a breast implant patient is not experiencing symptoms then there "is no need to change your routine medical care and follow-up."

In October 2017, the European Commission's Scientific Committee on Health, Environmental, and Emerging Risks (SCHEER) released a scientific advice report on BIA-ALCL where it stressed the importance of future research and reporting to prospective patient registries.

In June 2018, the French regulatory body National Agency for Medicines and Health Products Safety (ANSM) released a report on biocompatibility testing of textured implants, and recommended no changes to current device approval.

Both ASPS and ASAPS are funding research focused on determining the cause of this cancer and finding a solution to the disease.

*\*The National Comprehensive Cancer Network (NCCN) is an alliance of 27 cancer centers in the United States which establishes consensus diagnosis and treatment recommendations for the majority of known cancers. NCCN established evidence based guidelines for BIA-ALCL in 2016 which are updated annually.*

Q: Is BIA-ALCL a major concern?

A: All patients should be advised of the risk of BIA-ALCL. Although the incidence is uncommon, any procedure that may lead to the death of a patient must be considered a major concern, and patients should be made aware of it prior to undergoing breast implant surgery. As of July 30, 2018, the PROFILE registry\* has received 230 unique cases of BIA-ALCL in the U.S.: 56 percent had a history of cosmetic breast augmentation; 44 percent had a history of post-mastectomy reconstruction. Worldwide, 570 unique cases have been reported, which includes 16 disease-related deaths.

ASAPS and ASPS provide online patient education tools that help breast implant patients put this disease in perspective. The relative risk of capsular contracture versus BIA-ALCL is approximately 100 to 3000 times higher in any given patient. Though the risk is small, patient

safety is the primary focus of the plastic surgery community, and we strive to educate and inform our members and the public about the symptoms and risk of BIA-ALCL.

*\*The PROFILE registry was created in 2012 by ASPS, The PSF and the FDA to prospectively track confirmed BIA-ALCL patients in the United States. PROFILE data is regularly updated and available by contacting [www.thepsf.org/PROFILE](http://www.thepsf.org/PROFILE).*

Q: Can you explain the differences in implant texture and what role that factor plays in the research?

A: Although it is uncommon, BIA-ALCL appears to develop exclusively in women who have or have had textured implants. There is a higher incidence of BIA-ALCL in higher surface area/roughness devices. To date, there has not been a documented case of BIA-ALCL in a patient with only smooth implants. Suggested theories of the cause of BIA-ALCL include textured implant particulate, chronic allergic inflammation, and/or response to a biofilm. Research is ongoing in all these areas.

In both the US and the worldwide reported cases of BIA-ALCL, there does not appear to be a difference in risk in silicone versus saline filled implants, nor between and reconstructive or cosmetic use of breast implants.

Q: How does this impact those with breast implants?

A: ASPS, ASAPS, and the FDA advocate that all women, including those with breast implants follow their normal routine medical care and follow up, including mammography when appropriate. Patients should immediately contact their physician if they sense any abnormalities within the breast or notice any significant changes. There is no recommended BIA-ALCL screening for patients without symptoms. Fluid collections around implants within the implant capsules can occur and are usually not malignant. However, if the fluid collection around the implant is present one year or more after implantation, it should be considered suspicious and MUST be aspirated and the fluid tested with CD30\* immunohistochemistry and cytology.

*\*CD30 refers to a cell membrane protein that occurs normally on activated T-cell lymphocytes and abnormally in some lymphomas. CD30 immunohistochemistry is the screening test for BIA-ALCL and should be performed on all fluid collections developing more than one year after implantation. If CD30 is negative, BIA-ALCL is excluded. If CD30 is positive, it may or may not be BIA-ALCL and cell block cytology and flow cytometry are required to make the diagnosis.*

Q: What about those considering breast implants?

A: Physicians should include BIA-ALCL in breast-implant patient education materials and during the informed consent process, so that patients can determine the right procedure for them. Breast implants have established as well as ongoing long-term safety data available – and the incidence of BIA-ALCL is low.

Q. How is BIA-ALCL treated and what is the prognosis?

A. Diagnosis and treatment follow standardized guidelines established by the National Comprehensive Cancer Network (NCCN). (Algorithm available on ASPS and ASAPS websites). Current recommendations for the treatment of BIA-ALCL call for total capsulectomy, removal of the breast implant, as well as excision of any associated lumps or masses. Cases have been reported where both breasts are affected, and therefore surgeons may consider removing both implants and capsules. All cases of BIA-ALCL with disease limited to the scar tissue around the breast capsule and treated with complete surgical excision have been cured to date. The majority of early-stage patients treated with total capsulectomy require no additional treatment. Chemotherapy is required for unresectable disease, lymph node spread or distant metastases.

Q: Are some patients at greater risk than others?

A: It is not possible to predict who will develop BIA-ALCL. It has occurred in women who have a history of textured breast implants for both cosmetic and reconstructive purposes and has occurred in women with both saline and silicone implants. The following are the current risk factors for BIA-ALCL based on published data and research:

1. Device. Textured surface devices. There have been no reported cases in patients with only smooth-walled implants.
2. Genetics. There have been two published reports that there may be a genetic predisposition (germ line mutations in JAK1 and STAT3 genes). Further investigation is required.
3. Inflammation. Chronic inflammation triggered by an allergic response, bacteria, another as yet unknown factor, or some combination has been implicated.
4. Time. BIA-ALCL typically presents several years (average 8 years, range 2-28 years) after the implants were placed.

Q: Should healthy patients have their implants removed prophylactically?

A: The FDA does not suggest additional screening or removal of implants for women that are not having symptoms.

Q: Should women with breast implants be screened for BIA-ALCL?

A: The FDA advises that women without breast changes do not require more than routine follow-up. If a patient experiences a change in her breasts – especially if there is swelling or a lump – she should see her surgeon and undergo examination, imaging, and fluid testing if present.

Q: What causes BIA-ALCL?

A: The ASPS, PSF, ASAPS, ASERF and the FDA are studying BIA-ALCL.\* Bacterial contamination, long-term allergic inflammation and/or irritation from implant texturing, and genetic factors have been theorized and are undergoing further study. Research is ongoing and cases are being monitored. Concentrations of reported cases vary widely across the globe, with some geographic areas reporting very few cases. Ongoing data collection worldwide will help to determine any genetic propensities for this disease.

*\*American Society of Plastic Surgeons ASPS, Plastic Surgery Foundation PSF, American Society for Aesthetic Plastic Surgery ASAPS, The Aesthetic Surgery Education and Research Foundation ASERF, United States Food and Drug Administration FDA.*

Q: Does the FDA recommend against the use of textured implants?

A: The FDA confirms that all breast implants carry a reasonable assurance of safety when used as indicated. Best practice requires plastic surgeons to discuss the known risks and potential complications associated with any procedure. It is important for the patient and her surgeon to frankly discuss all treatment options available, along with the risks that include BIA-ALCL, capsular contracture, implant malposition, and rates of reoperation. The plastic surgeon must provide a frank and transparent discussion regarding the benefits and risks of implants, both smooth and textured. The patient must then make an informed decision, based upon her own assessment of her needs and the risks involved. If the surgeon's evaluation deems equivalent results from both a smooth or textured implant, the use of a smooth implant may prove prudent.

Q. Have there been any deaths due to BIA-ALCL?

A. There have been 16 confirmed deaths globally, which includes 5 U.S. cases, attributed to BIA-ALCL to date. Disease-related deaths have been reported in Australia, Brazil, France, Netherlands, New Zealand, Sweden, United Kingdom, and the U.S. In the 16 known deaths from the disease, all patients either received chemotherapy/XRT alone, died of the treatment itself, had incomplete capsule removal, or disease spread prior to treatment (metastatic disease). These reports emphasize the importance of disease recognition and proper treatment in a timely fashion.

Q. What is the recommended clinical response to a patient presenting with symptoms that could be attributable to BIA-ALCL?

A. Diagnosis of BIA-ALCL follows international recommendations by the National Comprehensive Cancer Network (NCCN).\* Following NCCN guidelines, a swollen breast can be evaluated with ultrasound for either a fluid collection, capsular mass, or lymph node swelling.

Fluid collections should be sampled with a needle through the skin (aspirated percutaneously).

A minimum 20ml and ideally as much fluid available should be sent for:

Fluid collections should be aspirated percutaneously.

Aspirate (minimum 25-50ml) should be sent for:

CD30 immunohistochemistry

2. Cell block cytology and flow cytometry evaluation and labelled to "rule out BIA-ALCL."

CD30 testing is critical to direct pathologists and efforts should be made to establish a diagnosis prior to any surgical intervention.

*. \*In July 2016, ASPS and ASAPS issued a joint "Tear Sheet" describing the recommended clinical treatment for patients presenting with symptoms that could be a sign of BIA-ALCL which ultimately was the framework for NCCN guidelines. For a copy of the ASPS/ASAPS Tear Sheet please go to: Joint ASPS-ASAPS Statement On Breast Implant-Associated ALCL. The document can also be accessed on the ASAPS website at:  
<http://www.surgery.org/professionals>*

Q: How is BIA-ALCL diagnosed?

A: Diagnosis should be made by fluid sampling (aspiration) in a clinic or by interventional radiology prior to any surgical intervention. Diagnosis requires very specific findings: large anaplastic cells on cytology, CD30+ immunohistochemistry, and clonal expansion on flow cytometry. Mammography is not useful in diagnosing BIA-ALCL. In confirmed cases, PET and CT scanning is performed to help stage the disease, evaluate for associated capsule masses, lymph node metastasis or organ metastasis. Once the diagnosis is confirmed, oncologic consultation should be obtained prior to any surgical intervention.

Q: Should patients that have textured implants in place be contacted about the risk of BIA-ALCL?

A: Physicians can provide preoperative disclosure and maintain adequate patient records and operative reports. Patient education resources are available to surgeon members from ASPS\*.

*\*Available at [www.plasticsurgery.org/alcl](http://www.plasticsurgery.org/alcl)*

Q: Should patients with implants in place be followed on a routine basis, i.e. annually?

A: There are no current screening recommendations for BIA-ALCL. The FDA recommends patients be screened post-operatively with MRI to diagnose implant rupture but this may or may not detect BIA-ALCL. Periodic clinical examination for implant patients is recommended, as one would do to screen for implant complications such as capsular contracture. Patients should also undergo age-appropriate breast cancer screening with mammography and be encouraged to perform monthly self-examination.

Q: Where can I find more information on BIA-ALCL?

A: Additional information, downloadable manuscripts, and resources on BIA-ALCL are available online at [www.theptf.org/PROFILE](http://www.theptf.org/PROFILE) and at [www.plasticsurgery.org/alcl](http://www.plasticsurgery.org/alcl) and in the Medical Professionals section of [www.surgery.org](http://www.surgery.org) as well as by searching "ALCL" on RADAR.

Reporters seeking information or plastic surgeons contacted by a member of the media are encouraged to forward inquiries to:

Adam Ross, ASPS integrated communications manager, at [aross@plasticsurgery.org](mailto:aross@plasticsurgery.org) or 847-228-3361.

Leigh Hope Fountain at [leigh@surgery.org](mailto:leigh@surgery.org) or Sarah Lebrum at [sarah@surgery.org](mailto:sarah@surgery.org) or 562-799-2356.