

PSF, ASPS and FDA efforts lead to BIA-ALCL registry, need your data

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The Patient Registry and Outcomes for Breast Implants and Anaplastic Large Cell Lymphoma Etiology and Epidemiology (PROFILE) registry – a partnership between The PSF, ASPS and the FDA – was launched in 2011 in response to reports of a possible link between women with breast implants and anaplastic large cell lymphoma (BIA-ALCL).

The goal of PROFILE, led by ASPS member and principal investigator Colleen McCarthy, MD, MS, is to increase the scientific data on BIA-ALCL in women with breast implants. The data that's being collected include patient demographics, potential risk factors, incidence of disease, characterization/staging, and management of BIA-ALCL.

Since the PROFILE registry launch, more than 70 cases of BIA-ALCL have been reported to the registry, with data being provided on more than 30 of these cases. ASPS/PSF has actively been working to promote the PROFILE registry – and the Society and The Foundation encourage all ASPS members who've treated a patient with BIA-ALCL to report their case to ALCL@plasticsurgery.org.

In addition to the PROFILE registry, ASPS and The PSF have further advanced their BIA-ALCL-related efforts through the formation of a BIA-ALCL Subcommittee of The PSF's Clinical Trials Network Committee. Chaired by ASPS member Mark Clemens, MD, the subcommittee is an integrated group of both physician volunteers and ASPS/PSF staff charged with monitoring and providing oversight of BIA-ALCL initiatives, and to recommend on an ongoing basis the strategic direction, organizational needs and oversight for BIA-ALCL-related initiatives.

One of the first activities with which The PSF President-elect Charles Butler, MD, charged the BIA-ALCL Subcommittee was the review and endorsement of a set of frequently asked questions that can be found later in this article. The BIA-ALCL Subcommittee will continue to review and amend this effort as new information is learned about the condition.

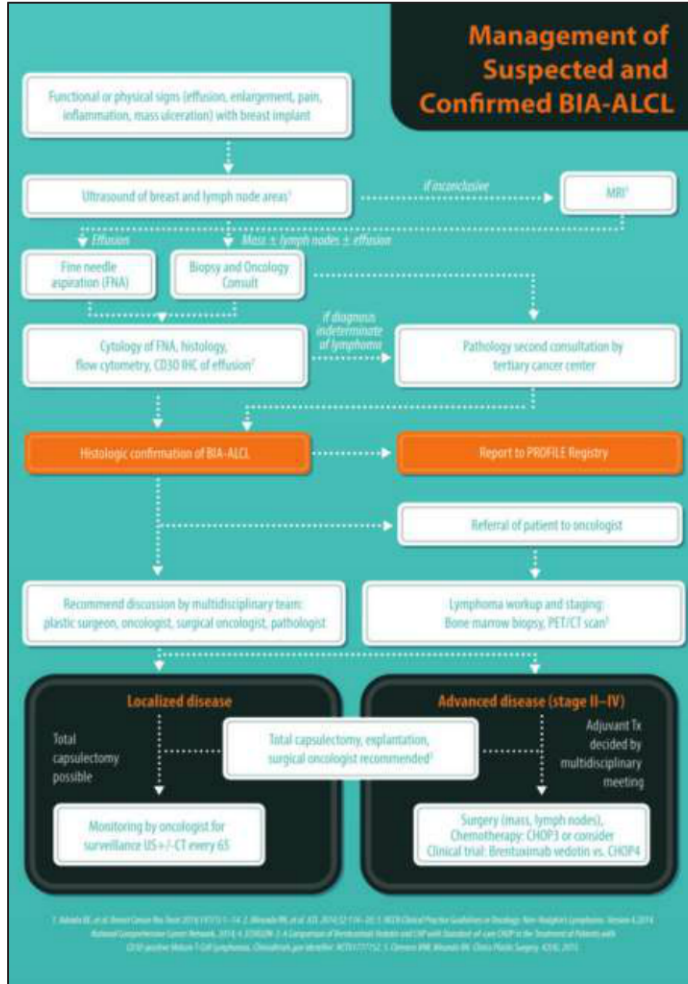
A guide to BIA-ALCL

BIA-ALCL is a rare cancer that can develop around breast implants. In January 2011, the FDA released a statement that women with breast implants "may have a very small but increased risk of developing" BIA-ALCL. Understandably, this has created concern among the plastic surgery community as well as among the patients treated by ASPS members. However, the FDA confirms that breast implants are considered safe devices.

Additional research is critical to identifying patients at risk of developing this disease; to characterize its early signs and symptoms; and to determine best practices for treatment. Physicians must be aware of this rare disease to ensure that patients are treated appropriately and in a timely manner. The following summary of frequently asked questions about BIA-ALCL serves as a starting point to facilitate a discussion in the plastic surgery community.

Q: What is breast implant-associated anaplastic large cell lymphoma (BIA-ALCL)?

A: It's a rare form of lymphoma, a cancer of the immune system developing from lymphocytes, and a malignancy of the blood. BIA-ALCL is a distinct type of ALCL involving the capsule or effusion surrounding a breast implant. On average, BIA-ALCL occurs at a mean of eight years following implantation. Some unique technical



ASPS thanks the members of the BIA-ALCL Subcommittee of The PSF's Clinical Trials Network Committee

Mark Clemens, MD, chair
Charles Butler, MD, The PSF president-elect

William P. Adams Jr., MD	Patrick Garvey, MD	Devinder Singh, MD
Anuja Antony, MD, MPH	Colleen McCarthy, MD	Keith Hume
Garry Brody, MD	Michael Olding, MD	Katie Sommers

characteristics include that it's most commonly a purely T-cell lymphoma; that it does not have an anaplastic lymphoma kinase-gene translocation (ALK-); and that it's CD30 receptor protein-positive on immunohistochemistry.

Q: How common is BIA-ALCL?

A: There are an estimated 10 million-11 million women worldwide with breast implants. While total numbers vary in the literature, 99 distinct cases have been reported; to date, MD Anderson Cancer Center recognizes 135 cases worldwide of pathologically confirmed BIA-ALCL from 14 countries. Fewer than 10 patients are diagnosed per year with this disease. The only epidemiological study demonstrating an association between breast implants and BIA-ALCL estimated an incidence of 1/300,000. However, determining the true incidence will be dependent upon improved physician awareness and reporting, as well as formal disease recognition.

Q: Should BIA-ALCL be included on surgical consent forms?

A: Following recommendations made by the FDA in 2011, implant manufacturers added language warning of the existence of

BIA-ALCL to all breast implant-package inserts within the United States and Canada. ASPS includes the risk of BIA-ALCL in the breast implant informed-consent documents it makes available for download or on CD at ShopASPS.org. Therefore, the recommendation is that surgeons should consider including BIA-ALCL in breast implant informed-consent discussions. Discussions with breast implant patients can include the existence of BIA-ALCL, common presenting symptoms such as a mass or delayed seroma/effusion, and directions to see their physician if these symptoms occur.

Symptoms

Q: How would I know if I've encountered a case of BIA-ALCL?

A: Patients receiving an implant should be aware of common presenting symptoms such as a spontaneous seroma or effusion after one year from implantation. Although common causes of a delayed seroma are infection or trauma, suspicious effusions should receive a fine-needle aspiration that's subsequently sent for pathologic review. A complete physical examination will help detect the one in eight cases that present with lymphadenopathy. Ideally, the diagnosis should be made

prior to surgical exploration to allow for proper oncologic workup.

Risk factors

Q: Are there any modifiable risk factors that make a patient more susceptible to BIA-ALCL?

A: At this time, there are no known modifiable risk factors or specific patient populations known to be at a higher risk of developing this disease. There's roughly an even number of aesthetic/cosmetic and reconstructive breast-implant patients, and both saline and silicone implants are involved, with a few reported polyurethane implants. However, the vast majority of known, involved devices have been in textured, rather than smooth, implants. Recent studies have demonstrated a possible pathogenic mechanism of chronic T-cell stimulation with local antigenic drive, ultimately leading to the development of lymphoma. Preliminary reports have hypothesized a role for chronic biofilm leading to malignant degeneration, and therefore standard of care precautions such as antibiotic prophylaxis, antibiotic irrigation, sterility, and skin preparation should all be maintained when placing an implant. The FDA does not recommend screening or prophylactic implant-removal for asymptomatic patients or for patients with familial susceptibility.

Q: What do I do if I encounter a suspected case of ALCL?

A: In suspicious cases, physicians should order an ultrasound evaluation for the patient, to confirm the presence and extent of an effusion; should determine if there is presence of a mass; and should evaluate regional lymph-node basins for lymphadenopathy. Fine-needle aspiration is performed of an effusion, which is sent to an experienced hematopathologist for culture, flow cytometry and cytology. It is critical to include a clinical history and to direct the pathologist to "rule out BIA-ALCL," as well as to perform CD30 surface protein immunohistochemistry. Ultrasound is an acceptable screening tool for the two-thirds of patients presenting with an effusion or the one-third with a mass. PET/CT and MRI are reserved for confirmed cases, and there does not appear to be a role for mammography.

Confirmed cases

Q: What are the essential studies performed for the preoperative evaluation after confirming a case?

A: Physicians are strongly encouraged to include a lymphoma oncologist for medical management and future disease surveillance. Preoperative evaluation includes a bone marrow biopsy to distinguish from other systemic forms of ALCL, which have a more aggressive clinical course and poor prognosis. Patients should also receive a preoperative PET/CT scan to evaluate for a baseline extent of disease, masses and involved lymph nodes. Physicians with confirmed cases have a responsibility to report their cases to the PROFILE registry at the-psf.org/PROFILE.

Treatment

Q: How should I manage a confirmed case of BIA-ALCL?

A: Definitive treatment for most patients is removal of the implants and total capsulectomy, which includes complete resection of any mass associated with the capsule (see box above). Physicians should consider the possible removal of contralateral breast implants with capsulectomy, as several bilateral cases have been detected incidentally. The implant, capsule and effusion should all be sent to pathology for evaluation. Suspicious

lymph nodes should also be excised. At this time, there does not appear to be a role for routine sentinel lymph-node biopsy or for full axillary dissection, if no clinically positive nodes are present.

Surgeons are strongly encouraged to include a surgical oncologist for resection of disease, as well as resection of the involved lymph nodes. Surgery should be performed with strict oncologic technique including use of specimen orientation sutures and placement of surgical clips within the tumor bed. Complete surgical resection may be sufficient treatment for the majority of patients. The role for further adjunctive therapy – such as chemotherapy (CHOP regimen: cyclophosphamide, doxorubicin, vincristine, prednisolone), clinical trials of targeted immunotherapy (Brentuximab vedotin), and chest wall radiation therapy for unresectable tumors or positive margins – is the subject of ongoing research.

Q: How should BIA-ALCL patients be reconstructed?

A: Ideal type and timing of reconstruction remains controversial. Replacement of textured implants is not advised in a patient who has already demonstrated a propensity for malignancy. Placement of smooth implants has been performed without reported progression or recurrence of disease; however, the safety of this strategy is still being investigated. Autologous reconstructions that do not require a breast implant are advisable. Reconstruction is suggested following a sufficient (one year) surveillance period to confirm complete eradication of the disease.

Prognosis

Q: What is the prognosis of patients diagnosed with BIA-ALCL?

A: The disease course is commonly indolent and the majority of patients may be adequately treated with complete capsulectomy and implant removal with rare recurrence. However, even if appropriately treated, aggressive variants have been reported that include lymph node metastases and death. The presence of a mass has a slightly higher but significant disease recurrence and progression.

Q: How are patients followed for surveillance of BIA-ALCL?

A: Confirmed cases of BIA-ALCL that have been adequately treated are followed with serial PET/CT scans and physical examination every six months for approximately two to four years. An experienced lymphoma oncologist ideally performs surveillance.

Further reading

Q: Where can I learn more about this rare cancer – and what can I do to help?

A: Many resources exist for oncologists and surgeons treating a BIA-ALCL patient, and a number of credible online resources are available – such as the FDA recommendations posted on the fda.gov website. Physician and patient resources can be found on the MD Anderson Cancer Center website at mdanderson.org to introduce BIA-ALCL patients to a supportive community where they may receive insights and potential leads on developing therapies.

Most importantly, physicians with confirmed cases of BIA-ALCL have a responsibility to report and share their cases with our national societies, as information gathered from every single case brings researchers closer to a cure. The PSF, ASPS and the FDA have created the PROFILE registry to increase the scientific data on BIA-ALCL, to support research characterizing BIA-ALCL, and to elucidate the role of breast implants in the etiology of the disease. Treating physicians are encouraged to report confirmed cases to the registry at thepsf.org/PROFILE.

Disclaimer

This information has been developed to assist physicians in clinical decision-making; it also was developed through a review of the scientific literature and the consideration of relevant clinical experience. It describes a range of generally acceptable approaches to diagnosis, management or prevention of specific diseases or conditions. This document attempts to define principles of practice that should generally meet the needs of most patients in most circumstances.

However, this document should not be

construed as a rule, nor should it be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the appropriate results. It is anticipated that it will be necessary to approach some patients' needs in different ways. The ultimate judgment regarding the care of a particular patient must be made by the physician in light of all the circumstances presented by the patient, the available diagnostic and treatment options, and the available resources.

This document is not intended to define

Atlanta Breast Surgery Symposium

SESPRS promises wide-ranging breast meeting

An outstanding program – and faculty – await attendees of the 32nd annual Atlanta Breast Surgery Symposium slated for Jan. 22-24, and organized by the Southeastern Society of Plastic and Reconstructive Surgeons (SESPRS).

The Intercontinental Hotel in Atlanta's Buckhead neighborhood will play host to this year's program, "Video Surgical Panels: Experience vs. Technique," which will feature renowned plastic surgeons who will share their knowledge, insight and experiences covering the full range of aesthetic and reconstructive breast surgery.

The meeting will include live surgery focusing on breast reduction by Dennis Hammond, MD; mastopexy by Brad Calobrace, MD; correction of capsular contracture with exchange of round to shaped implants by Mitch Brown, MD; and oncoplastic breast reconstruction by Bert Losken, MD.

"There's no other meeting that includes live surgical demonstrations with state-of-the-art techniques performed by world leaders in plastic surgery of the breast," says symposium Chair Mark Codner, MD. "This event is an opportunity for plastic surgeons to learn – from the best and the brightest – the newest and most advanced techniques being performed in the world."

Topics relevant to all plastic surgeons will be discussed, with emphasis placed upon practical solutions for common problems – with that process involving analysis,

treatment options and decision-making.

The focus of this year's live surgery program is a combination of aesthetic and reconstructive breast surgery. In keeping with the reconstructive tradition of the Atlanta Breast Surgery Symposium as well as with the innovative nature of its founder, Carl Hartrampf Jr., MD, this year's meeting will feature G. Patrick Maxwell, MD, as the Hartrampf Lecturer.

According to symposium Co-chair James Nannoum, MD, a number of new developments in aesthetic breast surgery have occurred over the past few years, with the introduction of shaped implants giving plastic surgeons many more options – and a lot more to think about.

Worldwide innovation

The meeting will also highlight innovations from around the world, including new incisionless and sutureless mastopexy, reverse abdominoplasty for breast reconstruction and fat grafting prior to breast augmentation. Roger Khouri, MD, will put forth a video presentation of alternative techniques for immediate breast reconstruction with local tissue and fat grafting.

The didactic sessions slated to begin Friday afternoon will focus on a full range of breast reconstruction topics. Presenters will include a video presentation of their techniques and share their experiences and outcomes. Challenges in autologous and prosthetic reconstruction, including the pros

and cons of acellular dermal matrix, as well as fat grafting for reconstructive breast surgery, will round-out Friday's afternoon session. Saturday sessions will provide panel discussions on aesthetic breast surgery with a thorough discussion of benefits and problems, including a thorough review of augmentation mastopexy, covering the full breadth of techniques, as well as breast reduction and revisional breast surgery. Oncoplastic surgery discussions will be offered Sunday, as well as panels on anaplastic large-cell lymphoma (ALCL) and DIEP flaps, along with the two-hour panel "Hot Topics in Breast Surgery and Breast Reduction."

As part of the SESPRS Foreign Scholarship Program, a group of deserving young surgeons from Poland will attend the meeting. This program, which is part of the Atlanta Breast Meeting legacy, will provide these deserving surgeons with useful information designed to improve patient care and surgical outcomes in their homeland.

"The Atlanta Breast Symposium has become an international meeting that embraces 15 countries – and it will reach many more through live Internet streaming," says Dr. Codner.

Registration information for the symposium is available at sesprs.org. (DVDs of previous meetings are also available for purchase.) To register online or learn more about the breast surgery symposium, go to the SESPRS website or call 435-901-2544. [P20](#)

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