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ORIGINAL PAPER

# The current UK perspective of breast surgeons on breast implant-associated anaplastic large cell lymphoma (BIA-ALCL)

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## Abstract

**Background** Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare type of T cell lymphoma associated with breast implants. Five hundred and twenty-one cases have been reported worldwide to date. The clinical presentation has two distinct subtypes: late seroma and, rarely, a distinct mass lesion. We wanted to determine the implications of this emerging disease on the current practice of breast surgeons in the United Kingdom (UK) and Ireland and whether they have changed their practice following growing reports of associations with BIA-ALCL in the literature.

**Methods** An 11-question survey was sent to four associations in the UK and Ireland: Association of Breast Surgery (ABS); British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS); British Association of Aesthetic Plastic Surgeons (BAAPS); and the Irish Association of Plastic Surgeons (IAPS). It was advertised in newsletters and also emailed to a list of consultant members of BAPRAS.

**Results** Seventy-two responses were from consultant surgeons throughout both the UK and Ireland. Ninety-seven percent of consultants discussed the risks and associations of breast implants and BIA-ALCL with their patients. Seventeen percent had a patient who was diagnosed with ALCL in their practice. Seventeen percent of consultants have already changed their practice, including a transition to using smooth implants or using micro- or nano-textured implants. A further 11% will consider changing their practice in the future depending on more information and recommendations from higher departments.

**Conclusions** BIA-ALCL is likely to be caused by a complex interplay of factors, allowing for the variation in clinical presentation and disease progression. Our survey has already shown a growing knowledge amongst breast surgeons in the UK and Ireland as well as a switch in practice in less than a third of consultants already.

Level of Evidence: not ratable

**Keywords** BIA-ALCL · Breast implant · Texture · Biofilm · Lymphoma · Late seroma

## Introduction

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a new and emerging neoplasia associated with breast implants. Currently, reports in the literature from around the world are increasing with more than 500 cases reported to date. The latest figures published by the American Society of Plastic Surgeons (ASPS) are 195 cases in the USA and 521 worldwide as of 21 March 2018 [1].

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With increasing numbers of patients being diagnosed with BIA-ALCL, information gathering and research into associated risk factors has begun. The real incidence and lifetime risk of BIA-ALCL remains unknown. Figures have been released internationally based on the information we know to date. The ASPS quote a lifetime risk of 1:3817–1:30,000 in women with textured implants [1].

Despite the rise in incidence and improvement in the diagnostic process, the underlying cause of BIA-ALCL development is still unknown. Two of the main factors reported in the literature to play a role in the development on BIA-ALCL include implant texturing and the role of a bacterial biofilm and subsequent chronic inflammatory process. Even though these associations have been widely reported, there remains insufficient scientific factual evidence. This has left some surgeons sceptical and reluctant to initiate a change in practice

until a direct link is scientifically proven and advice is given at a higher institutional level.

We wanted to determine the implications of this emerging disease on the current practice of breast surgeons in the United Kingdom (UK) and Ireland and whether they have changed their practice following growing reports of associations with BIA-ALCL in the literature.

## Methods

A questionnaire was developed to address the aims of the project. This included 11 questions covering subspecialty, location, breast surgery practice (cosmetic/reconstruction/National Health Service (NHS)/private) and questions directly relating to BIA-ALCL.

An electronic survey was produced, and this was sent to four associations in the UK and Ireland with members from both general and plastic surgery: Association of Breast Surgery (ABS); British Association of plastic, Reconstructive and Aesthetic Surgeons (BAPRAS); British Association of Aesthetic Plastic Surgeons (BAAPS); and the Irish Associations of Plastic Surgeons (IAPS).

Subsequently, it was advertised in the BAPRAS newsletter and on the ABS website. Following this, the questionnaire was then emailed to a list of consultant members of BAPRAS. The email was sent to a total of 241 consultants. Five consultants emailed to say they no longer do any breast implant surgery. Five emails failed to be delivered. One consultant replied to say he came across the email in his spam folder which may have been the case for other consultants emailed. The total response rate was 32%.

## Results

We received a total of 72 responses from consultant surgeons throughout both the UK and Ireland. Two surgeons worked across two of these areas: 86% England, 10% Scotland, 3% Wales, 3% Northern Ireland and 1% Ireland. The majority of respondents were plastic surgeons, with 68 plastic surgeons and four general surgeons.

With regard to breast surgery practice, the majority of surgeons, 86%, perform breast surgery as part of private practice and 58% perform breast surgery on the NHS in the UK. The majority of surgeons perform breast surgery for cosmetic purposes (81%) and 50% for breast reconstruction (Fig. 1). There is an overlap amongst surgeons who perform breast surgery in both the NHS and the private sector, and some surgeons perform a combination of both cosmetic and reconstructive procedures across different sites, which allows for the discrepancy in the total percentage.

Seventy-eight percent routinely use textured implants, 11% use a combination of implant types, 4% use smooth implants mainly and 7% use 'other' implant types (Fig. 2). Consultants were not specifically asked to define 'other' implant types but one consultant has discussed the use of polyurethane-coated silicone implants.

### Do you discuss the risk and associations of BIA-ALCL with patients? If so, what rate of BIA-ALCL risk do you quote?

Ninety-seven percent of consultants discussed the risks and associations of breast implants and BIA-ALCL with their patients. A variety of rates were quoted in the responses. Some consultants reported a single figure of risk, and others quoted risks which varied depending on implant type. Others described risk as 'rare', 'very rare' or 'very low'. Some consultants used analogies to help patients understand and described the risk of developing BIA-ALCL as, less than the risk of crashing a car or less than the risk of a general anaesthetic for capsular contracture.

### Do you explain the likely higher risk in textured implants? If so, do you offer the patient a choice of implant? Smooth vs textured

With regard to the potential higher risk of BIA-ALCL with textured implants, 64% (46) of consultants said they told

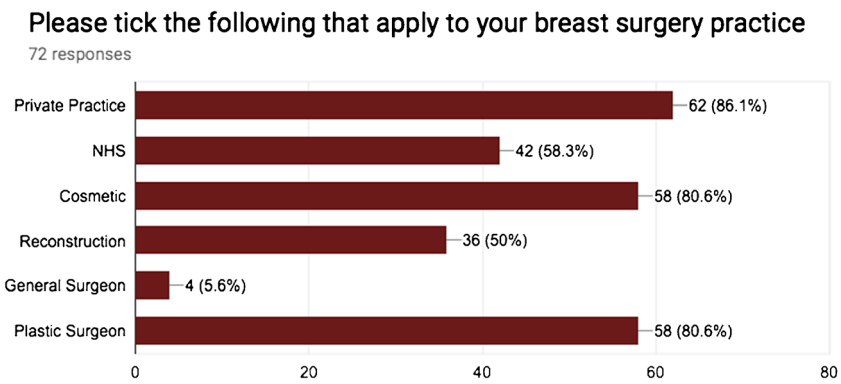


**Fig. 1** Graph showing breakdown of breast surgery practice

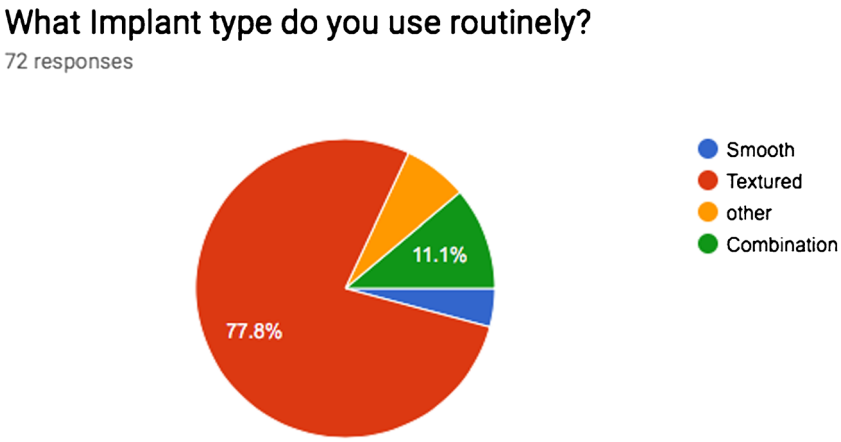


**Fig. 2** The breakdown of implant type used. (78% textured, 11% combination, 4% smooth, 7% 'other')

patients the risk might be higher with textured implants. In these cases, 67% (31) of these consultants then offer the patient a choice of implant following discussion.

Six consultants (8%) said they do not think there is sufficient evidence to tell patients about a potential link between textured implants and BIA-ALCL currently.

Two consultants stated they do not explain the potential higher risk in textured implants as they only use anatomical implants for reconstruction and there are no smooth anatomical implants available.

One consultant has changed to only using smooth implants and another has stopped using Allergan implants due to a potential higher risk with them.

### Have you had any cases of ALCL diagnosed?

Twelve of the 72 consultants (17%) had a patient who was diagnosed with ALCL in their practice. Fifty percent of consultants who had patients diagnosed with BIA-ALCL said they had no plans to change their practice. Four consultants (33%) have already changed their practice, and one consultant said they would consider changing their practice in the future. The 12th consultant is no longer working.

### Do you plan to change your practice in the future to only use smooth implants or offer patients the choice of implant?

This question was asked to all consultants regardless of whether they had a patient diagnosed with BIA-ALCL or not.

A total of 12 consultants (17%) surveyed have already changed their practice, including a transition to using smooth implants or using micro- or nano-textured implants.

A further eight (11%) will consider changing their practice in the future depending on more information and recommendations from higher departments.

Sixteen consultants (22%) already offer patients a choice of implant.

The majority of the rest, 44%, have no current plans to change their future practice.

### What do you think is the main contributing factor that increases ALCL risk? For example, biofilm, textured implant and debris

As part of the questionnaire, we suggested three possible responses as examples—these were biofilm, textured implants and debris. There was a box for free text, and consultants could write anything in the space provided. Many of the consultants listed multiple potential theories.

Thirty-five consultants (49%) attributed some of the risk to biofilm/chronic inflammatory process; 23 (32%) felt that textured implants played a role, whether that be due to surface characteristics or the chemicals used in the manufacturing process; and 20 consultants (28%) stated they either did not know or it was too early to tell with current research and evidence to date.

Only seven (10%) thought debris might play a role, and surprisingly, only two (3%) listed genetics as a contributory factor.

## Discussion

BIA-ALCL is a rare type of T cell lymphoma. The first reported case was in 1997, and now, over 500 cases have been diagnosed and reported worldwide after it was first recognised by the FDA in 2011 [2].

There are two distinct pathological entities. The most common presentation is a late peri-prosthetic seroma, and the second pathological type is a more aggressive infiltrating mass lesion, which thankfully is the less common of the two types [3].

Since 2014, guidelines have been available on the management of late seromas to help detect BIA-ALCL cases. Seromas developing more than 1 year after implant insertion

should be investigated with an ultrasound scan and aspiration of fluid for cytology and flow cytometry [4]. Pathways for the management of suspected BIA-ALCL have been released in both the USA and the UK, and more recently, Johnson et al. have developed a pathway for the UK. This takes into account the different infrastructure and National Health Service (NHS).

Importantly, a national database (Breast and Cosmetic Implant Registry (BCIR)) has been set up for all implants inserted in the UK. This will enable prospective follow-up and aim to help capture complications and, in particular, cases of BIA-ALCL in the future [2].

Diagnosis is made based on pathology results from either the seroma aspirate or a tissue biopsy. At least 20–50 ml of seroma fluid should be sent for histological and cytological analysis. Abnormal cells characteristically over express CD30 on the cell surface and will stain negatively for a second marker, known as anaplastic lymphoma kinase (ALK). This CD30 overexpression is said to be diagnostic [2, 5]. Following pathological diagnosis, the UK guidelines by Johnson et al. recommend discussion amongst a multi-disciplinary team and a PET-CT scan for staging.

There are several staging systems discussed in the literature based on the disease pathology (seroma vs tumour mass). The Ann Arbor staging system is used for the so-called liquid tumours: stage IE, disease confined to the breast and stage IIE, disease present in the breast and ipsilateral lymph nodes. In addition, there is a staging system used for solid tumours: the M. D. Anderson Tumour, Node, Metastases (TNM) classification with stage one through to four. Any stage of BIA-ALCL is currently classified as a lymphoma according to the World Health Organisation (WHO) [5].

Treatment of BIA-ALCL may vary slightly between countries worldwide, but in all cases, it depends on the stage of disease at diagnosis. The majority of patients present with localised disease: stage IE of the Ann Arbor staging and stage IA-IIB of the TNM staging. In these cases, surgical removal of the diseased tissue, the implant and total capsulectomy is usually the only treatment required [2, 5].

Up to 18% of patients will have advanced disease at presentation and may require adjuvant therapy. All cases should be discussed with oncologists and a targeted plan made. The current literature indicates systemic ALCL can be treated with anthracycline-based multi-agent chemotherapy regimes. There are phase II and phase III trials currently underway using anti-CD30 monoclonal antibody treatment called brentuximab vedotin, either as an alternative or in addition to current chemotherapy regimens. Preliminary outcome data comes from case reports due to the rare nature of this disease entity. Promising results have been published with brentuximab vedotin causing complete disease remission of both solid organ metastatic BIA-ALCL and progressive disease occurring despite chemotherapy treatment [2, 5].

In the UK, stage I disease is treated with implant removal and capsulectomy. Stage II and above diseases are treated with surgery as above and in addition adjuvant or neo-adjuvant chemotherapy ± consideration of brentuximab vedotin [2].

Our survey aimed to assess the current views of consultant surgeons in the UK and Ireland and to determine the impact of BIA-ALCL on current surgical practice and patient counselling. In addition, we wanted to see if new and rising evidence on the association of textured implants with BIA-ALCL has led to a change in the type of implant used routinely.

Informed consent is now a legal requirement and one of the duties of a doctor described by the General Medical Council (GMC) in the UK. All patients undergoing breast augmentation in the UK must be counselled regarding BIA-ALCL risk.

In our questionnaire, 97% of surgeons stated they counselled patients regarding the associations of breast implants and BIA-ALCL in the pre-operative consent process.

Worryingly, a larger scale questionnaire distributed to over 1300 surgeons throughout America, Australia and Europe revealed less than 27% of surgeons routinely counsel patients regarding BIA-ALCL. When this was broken down by region, there was a significant disparity between countries. Seventy-eight percent of Australian surgeons counselled patients pre-operatively on BIA-ALCL risk [4].

Surprisingly, in such a litigious country, the lowest rate was amongst American plastic surgeons, of whom only 24% of patients were counselled regarding BIA-ALCL during the consent process. In comparison to American surgeons, Australian, German and French plastic surgeons were five times more likely to include BIA-ALCL as part of the informed pre-operative consent process [4].

## Textured implants and BIA-ALCL risk

Reports from various countries throughout the world have elucidated potential factors associated with developing BIA-ALCL. The association of textured implants with BIA-ALCL development has been reported as statistically significant by several authors across the world.

A recent paper published in Plastic and Reconstructive Surgery (PRS) describes the incidence rate in the United States (US) and associated epidemiological factors. The paper by Doren et al. was a retrospective review of 100 confirmed cases of BIA-ALCL in the USA between 1996 and 2015. They have reported a statistically significant link with textured implants and have quoted a lifetime prevalence of 33 per one million people with textured implants [6].

Another paper published in PRS by Loch-Wilkinson et al. revealed a total of 55 cases between 2007 and 2016 across both Australia and New Zealand. Once again, the authors have reported a link with textured implants, stating all patients diagnosed with BIA-ALCL in their series had textured breast implants. In addition to this association, they carried out

further investigations to determine the surface area of the textured implants involved, with 85% of implants involved having a higher surface area. They concluded that there was a significant association between high surface area textured implants and the development of BIA-ALCL in Australia and New Zealand [7].

Loch-Wilkinson et al. did a further analysis to determine the risk associated with specific types of textured implant. In comparison to Siltex® textured implants, they have quoted a 14-fold increase in risk of developing BIA-ALCL in patients with Biocell® textured implants and an 11-fold increase in risk with polyurethane textured implants. This paper concluded that not only do textured implants increase the risk of BIA-ALCL development but the specific type and surface area of texturing appears to play a role in the pathogenesis of BIA-ALCL [7].

A review paper from the UK describes 23 cases of BIA-ALCL diagnosed between 2012 and 2016. All cases occurred in patients with textured implants or tissue expanders. The authors have advised caution with attributing BIA-ALCL to textured implants alone as the number of textured implants used throughout the world greatly outnumbers smooth implants [2].

The majority of surgeons we surveyed, almost 80%, use textured implants routinely, and a further 11% used a combination of implant types. In our survey, we specifically asked surgeons if they counselled patients that textured implants may increase the risk of developing BIA-ALCL. Interestingly, 64% of surgeons counselled patients about the higher risk of BIA-ALCL with textured implants and the majority then offered the patient a choice of smooth or textured implants.

Our survey has shown that just under a third of breast surgeons in the UK and Ireland have already changed their breast practice or would consider doing so in the future. This was either a change to using smooth implants only or at least offering the patient a choice of smooth or textured implant after pre-operative counselling. A further 22% stated they already offer patients a choice of implant at the time of survey. The senior author of this article has changed his breast practice. Currently, all patients are counselled regarding the potential higher risk of BIA-ALCL with textured implants and are subsequently offered a choice of either textured or smooth implants. Until there is more concrete evidence, the decision will remain with the patient; in the future, a change in practice to use smooth implants only may be warranted, but to date, there is insufficient evidence to support this.

### The biofilm theory of BIA-ALCL development

Textured implants have already been shown to allow colonisation by a higher number of bacteria due to their surface characteristics. The potential for this chronic infective and inflammatory process to drive lymphocyte proliferation and eventual malignant transformation has already been shown. According to a leading cancer website, infections are associated with up to 20% of malignancies throughout the world. A well known example is the role of *Helicobacter pylori* in gastric lymphoma. Other examples of infections which can lead to lymphoma formation include; hepatitis, herpes virus, Epstein-Barr virus, *Campylobacter jejuni* and *Borrelia burgdorferi* [8].

A recent paper by Hu et al. compared the biofilm present on 26 BIA-ALCL samples to 62 non-ALCL capsules. Despite a similar bacterial load in both samples, they found a significant difference in the type of bacteria present within the biofilm. In particular, there was a significant increase in gram-negative bacilli (similar to *Helicobacter pylori*) called *Ralstonia* spp. in the BIA-ALCL samples. The predominant bacterial species in non-ALCL capsules was *Staphylococcus* spp. [3].

Given the presence of different bacterial species in both ALCL capsules and non-ALCL capsules, it would suggest that bacterial infection alone is not the key-contributing step to disease development. The specific type of bacteria present appears to play a particular role in the pathogenesis of chronic inflammation leading to malignant transformation over time. This is in keeping with what we already know; the presence of specific bacterial species at certain body sites can lead to lymphomatous transformation as discussed above.

Hu et al. also comment on the timeline of lymphoma formation, which requires a lag time from the initial infective process. Given that textured implants were only introduced in the 1980s/1990s, and the average time from implant insertion to diagnosis is approximately 10 years, the authors feel this is further evidence for the contributory role of the biofilm and chronic inflammation in BIA-ALCL formation [3].

## Conclusion

BIA-ALCL is likely to be caused by a complex interplay of factors, allowing for the variation in clinical presentation and disease progression. Given that chronic infection and inflammation is well known to cause lymphocytic proliferation and ultimately lymphoma formation and surface characteristics of textured implants allow a higher bacterial load, it makes sense that these two main associations play a contributory role in BIA-ALCL development.

Our survey has already shown a growing knowledge amongst breast surgeons in the UK and Ireland as well as a switch in practice in just under a third of consultants already. Patients undergoing breast augmentation for either reconstruction or cosmetic purposes are being well educated during the consent process on both the risks and associations in the vast majority of cases.

Unfortunately, there is a limit to our current knowledge, but with increasing numbers of cases diagnosed worldwide, larger scale research and statistical analysis will hopefully provide us with new insights and determine if there is a true causal relationship. The key currently would appear to be informed consent with the most up to date information and risk levels until we discover more definitive evidence.

## Compliance with ethical standards

**Funding** No funding received.

**Conflict of interest** Serena Martin, Michael McBride and Khalid Khan declare that they have no conflict of interest.

**Ethical approval** Not required.

**Informed consent** Not required.

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