HSE NATIONAL CLINICAL GUIDELINE FOR THE DIAGNOSIS AND TREATMENT OF BREAST IMPLANT ASSOCIATED – ANAPLASTIC LARGE CELL LYMPHOMA (BIA-ALCL)

HSE

RCSI ROYAL COLLEGE OF SURGEONS IN IRELAND

NCPS NATIONAL CLINICAL PROGRAMME IN SURGERY

HSE NATIONAL CLINICAL GUIDELINE FOR THE DIAGNOSIS AND TREATMENT OF BREAST IMPLANT ASSOCIATED – ANAPLASTIC LARGE CELL LYMPHOMA (BIA-ALCL)

National Policy ☐	National Procedure ☐	National Protocol ☐	National Guideline ☐	National Clinical Guideline ☒

HSE National Clinical Guideline for the Diagnosis and Treatment of Breast Implant Associated – Anaplastic Large Cell Lymphoma (BIA-ALCL)

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Clinical Guideline for the Diagnosis and Treatment of Breast Implant Associated – Anaplastic Large Cell Lymphoma (BIA-ALCL)

NATIONAL GROUP:

NCPS in consultation with the BIA-ALCL Expert Advisory Group, Working Group and Contributors

SHORT SUMMARY:

This Clinical Guideline will support the diagnosis and treatment of individuals presenting with concerns or symptoms associated with BIA-ALCL.

DESCRIPTION:

This National Guideline sets out a standardised approach to the diagnosis, treatment and follow-up of BIA-ALCL. It provides the necessary information to support the identification of symptoms, manage an initial presentation, perform a clinical examination and summarises best practice for anyone presenting with the symptoms associated with BIA-ALCL.

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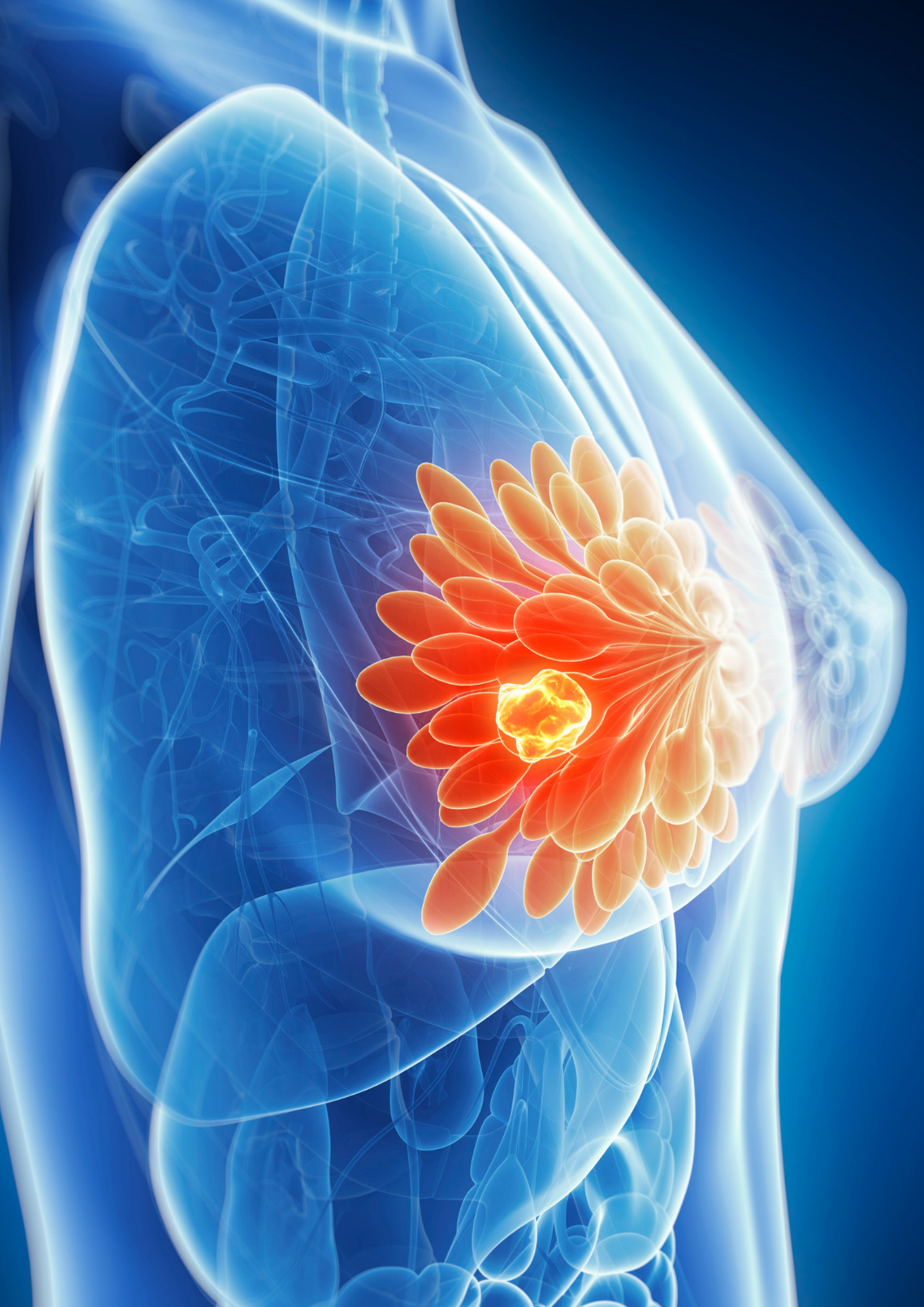

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1.0 Background

1.1 PURPOSE

In 2021, at the request of the National Clinical Advisor and Group Lead (NCAGL) for Acute Operations, the National Clinical Programme in Surgery (NCPS) established an expert advisory group to develop guidance on the diagnosis and management of Breast Implant Associated - Anaplastic Large Cell Lymphoma (BIA-ALCL).

1.2 SCOPE

This guidance is for use in primary care services, as well as by specialists in all relevant clinical areas, including Symptomatic Breast Disease Clinics, Plastic Surgery, and Radiology. These recommendations may be revised in line with emerging innovative imaging techniques, specific radiotracers, or if new evidence based research is published.

1.3 OBJECTIVE

The objective of this guideline is to support services caring for individuals presenting with concerns or symptoms associated with BIA-ALCL by providing standards for care in the diagnosis, treatment and follow-up of this newly classified, rare lymphoma[1].

1.4 OUTCOME

This guideline sets out a standardised approach to the diagnosis, treatment and follow-up of BIA-ALCL. It promotes teamwork and communication by defining a care pathway for all involved, resulting in seamless care and supporting earlier diagnosis in the management of this rare, complex, multifaceted condition. The guideline provides the necessary information to support the identification of symptoms, manage an initial presentation and perform a clinical examination, as part of a primary assessment for BIA-ALCL. It also summarises best practice in the use of diagnostic imaging, effusion and tissue biopsy, and in the subsequent associated histopathological investigations.

Guidance is given on the clinical management of negative, indeterminate and suspicious or confirmed findings, including recommendations regarding lymphoma work up, staging, surgical intervention and systemic treatment, where necessary. Advice is also provided on BIA-ALCL follow-up and monitoring, with reference to the HPRA and the Irish Breast Implant Registry.

1.5 GUIDELINE DEVELOPMENT GROUP

This guideline was developed in a multi-service collaboration between Plastic Surgery, Breast Surgery, Radiology, Radiation Oncology, Histopathology, Haematopathology, Haematology, HPRA, NOCA, NCCP and Acute Operations, as coordinated by the NCPS.
See Appendix I for membership of the Guideline Expert Advisory Group.
See Appendix II for membership of the Guideline Working Group and Contributors.

1.6 SUPPORTING EVIDENCE

This guideline was formulated following a comprehensive international literature review, with reference to existing national and international best practice recommendations, as listed in the References section below.

1.7 GLOSSARY OF TERMS

BIA-ALCL	Breast Implant Associated-Anaplastic Large Cell Lymphoma
CT	Computed Tomography
DBT	Digital Breast Tomosynthesis
FDG-PET	Fluoro-deoxy-glucose Positron Emission Tomography
GP	General Practitioner
HSE	Health Service Executive
NCPS	National Clinical Programme in Surgery
MDT	Multidisciplinary Team
MRI	Magnetic Resonance Imaging
RT	Radiation Therapy
TNM	Tumour-Node-Metastasis
US	Ultrasound

1. Note in September 2022, the FDA published a safety communication regarding reports of breast implant associated-squamous cell carcinoma (BIA-SCC) and other non-ALCL lymphomas seen in the scar tissue (capsule) formed around breast implants (FDA, 2022). On 8 March 2023, the FDA issued an update specifically regarding reports of BIA-SCC, and BIA-SCC related deaths, the cause, incidence and risk factors for which remain unknown (FDA, 2023b). While management recommendations for BIA-SCC are beyond the scope of this document, international updates regarding the condition will be kept under surveillance, and if necessary in the future this document will be updated to include the management of BIA-SCC.

2.0 Guidance on the Diagnosis and Treatment of BIA-ALCL

2.1 PATHOPHYSIOLOGY

Breast Implant Associated - Anaplastic Large Cell Lymphoma (BIA-ALCL) is a rare type of non-Hodgkin lymphoma, occurring in individuals who have synthetic breast implants. It was first described in 1997 and was given World Health Organisation (WHO) provisional recognition as a type of ALCL in 2016. Although several hypotheses have been suggested, the mechanisms underpinning BIA-ALCL's aetiology and pathogenesis are not yet fully understood. Additionally, the factors leading to disease progression have not yet been delineated (Swerdlow et al., 2016).

Two distinct subtypes of BIA-ALCL have been identified: "effusion-only" or "mass-forming" disease (Mehdi et al., 2022). BIA-ALCL is more commonly found near the breast implant, in the fluid surrounding the implant (seroma), and is contained within the fibrous scar capsule (FDA, 2023). See Figure 1 for a schematic illustration of BIA-ALCL, showing the septated effusion between the implant and the fibrous tissue surrounding the implant. The malignant cells are contained within this fluid and adhere to the fibrous capsule within a sero-fibrinous exudate, with no penetration into the breast parenchyma (FDA, 2023, Thompson, 2010).

While the aetiology of BIA-ALCL remains unknown, some current theories centre on triggers associated with biofilm formation and chronic infection, fragmentation of the implant shell and predisposing genetic factors (Mallucci and Bistoni, 2022, Marra et al., 2020). There is some evidence that BIA-ALCL is linked to *Li Fraumeni Syndrome* and *BRCA* gene mutations, and further investigations are necessary to determine whether a genetic predisposition for breast cancer is also a risk factor for BIA-ALCL (Turton et al., 2021).

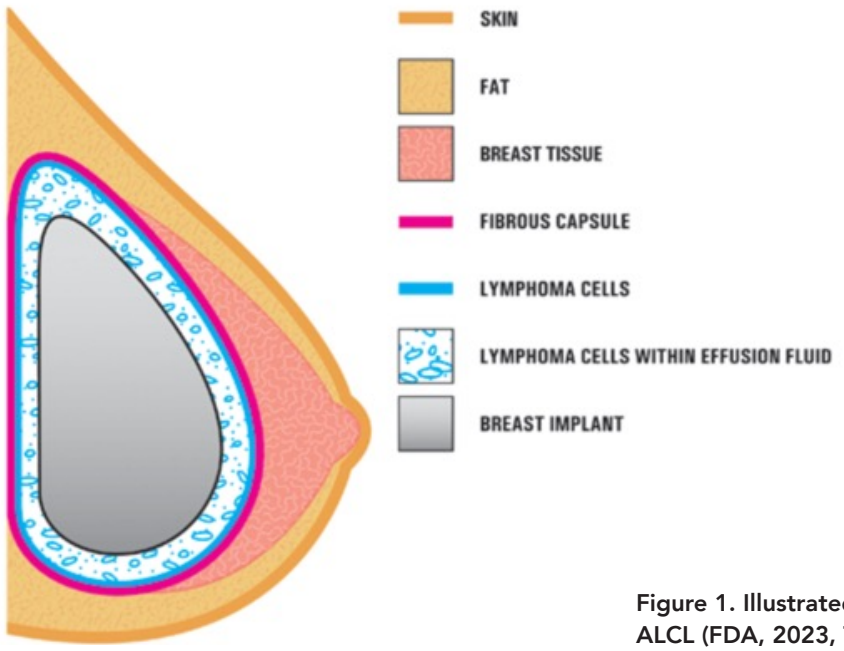

Figure 1. Illustrated anatomy of BIA-ALCL (FDA, 2023, Thompson, 2010)

BIA-ALCL is seen with both silicone gel and saline implants, whether positioned for cosmetic or reconstructive purposes (PROFILE, 2023, Brody et al., 2015).

There is a moderate weight of evidence for a causal relationship between textured breast implants and BIA-ALCL, particularly relating to implants with an intermediate to high surface roughness (De Jong et al., 2021). It is more commonly associated with textured implants, and in particular, with the *Biocell* surface of Allergan implants and *Silimed* polyurethane implants, which are no longer available on the market (Mallucci and Bistoni, 2022). There have been no reported cases of BIA-ALCL in individuals with a breast implant history that is confirmed to only include a smooth device (Turton et al., 2021).

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The majority of individuals with BIA-ALCL present with localised disease which can be treated with surgery alone (NCCN, 2023b). The incidence of distant disease appears to be very low, with the mass-forming subtype being a risk factor for distant involvement (Sharma et al., 2020). Research shows better event-free survival rates and overall survival rates for individuals with resectable BIA-ALCL confined to the fibrous capsule surrounding the implant compared to individuals with invasive BIA-ALCL that had spread beyond the capsule (Clemens et al., 2016). One long-term follow-up study reported a complete remission rate of 93% for individuals with disease confined to the fibrous capsule compared to 72% for those presenting with a tumour mass (Aladily et al., 2012). Another retrospective study reported 2-year overall survival rates of 100% and 53%, respectively, for in situ and infiltrative BIA-ALCL (Laurent et al., 2016).

Lymph node involvement was reported in 20% of patients, with regional axillary lymph nodes most frequently involved (93% of patients) (Ferrufino-Schmidt et al., 2018). BIA-ALCL beyond the capsule was associated with a higher risk of lymph node involvement (38% compared to 12% in patients with tumours confined by the capsule). The 5-year overall survival rates were 75% and 98%, respectively, for patients with and without lymph node involvement at presentation (Ferrufino-Schmidt et al., 2018).

2.2 INCIDENCE

Determining an exact figure for the incidence of BIA-ALCL is very challenging as it is dependent on the reported type of implant used and the time since implantation. The incidence is highest in individuals who have had textured implants for longer than 10 years (Nelson et al., 2020). The median time from implant placement to diagnosis has been reported as 8 to 10 years (Turton et al., 2021).

The reported absolute risk of developing BIA-ALCL is small and varies significantly depending on the study conducted and geographic location (Turton et al., 2021). In August 2020, the FDA was aware of 733 medical device reports and 36 deaths due to BIA-ALCL worldwide (NCCN, 2023b). In 2021, the estimated incidence of BIA-ALCL in the United States was 33 per 1 million persons with textured breast implants (Nelson et al., 2021). Additionally, that study estimated the lifetime prevalence of BIA-ALCL for individuals with textured breast implants at 1 in 3,000 (Nelson et al., 2021). A crude estimate of incidence in the UK is 1 per 15,000 implants sold (Allison and Gilmour, 2022).

While only broad overall estimates are available, the specific risk of BIA-ALCL associated with an individual manufacturer or product is often known. For example, the relative risks for *Silimed* polyurethane, *Biocell* and *Siltex* implants have been published (Magnusson et al., 2019). Allergan's *Biocell* textured implant is associated with the highest incidence of BIA-ALCL, and has not been used in Ireland since December 2018 (HSE, 2023). Where product specific BIA-ALCL risks are known, surgeons should quote these when seeking informed consent (Mallucci and Bistoni, 2022). Patients should also be fully informed of all elements of risk versus benefits in deciding on implant shape and texture, including re-operation risk (Mallucci and Bistoni, 2022).

In Ireland, the HPRA encourages healthcare professionals to report all cases of suspected or confirmed BIA-ALCL. Nationally, to date the HPRA have received a small number of incident reports[2] of suspected or confirmed cases of BIA-ALCL, associated with Allergan's *Biocell* textured implant. Additional information on BIA-ALCL associated with particular breast implants, as well as details on how to report, can be found on the HPRA website at https://www.hpra.ie/homepage/medical-devices/special-topics/breast-implant-associated---anaplastic-large-cell-lymphoma-(bia-alcl)).

2.3. SPECIALIST REFERRAL CENTRES

This care pathway standardises the assessment process, diagnosis and management of BIA-ALCL. Therefore, individuals with suspected BIA-ALCL can be managed by their local Symptomatic Breast Disease Clinic, if the service has access to all the resources necessary for the diagnosis and treatment of BIA-ALCL, as outlined in this care pathway (see clinic locations in Appendix III).

2.4. SYMPTOMS

The symptoms associated with BIA-ALCL are usually unilateral and associated with a peri-prosthetic fluid collection and/or a localised tumour mass. Most individuals with BIA-ALCL present with a delayed seroma and no systemic symptoms (Tevis et al., 2022). Table 1 lists the presenting symptoms most commonly associated with BIA-ALCL.

2 When the number is less than five, it is described as a 'small' number to avoid any potential inadvertent identification of the individuals concerned

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Table 1. Presenting Symptoms in BIA-ALCL

COMMON SYMPTOMS	LESS COMMON SYMPTOMS
Swelling in the area of the implant	Pain
Significant change in the size of the affected breast, which happens rapidly (over days or weeks) more than one year (median 8 to 10 years) after implantation	Hard lump beside or near implant
	Overlying skin rash
	Capsular contracture
Discomfort in the affected breast	Lumps in the armpit on the affected side

2.4.1. PERI-IMPLANT FLUID COLLECTION

Up to 80% of individuals with BIA-ALCL present with a large spontaneous, rapidly developing, persistent seroma or a peri-prosthetic effusion or seroma, that may be accompanied by breast swelling, asymmetry, or pain (Turton et al., 2021, Clemens et al., 2016, Mehta-Shah et al., 2018). This occurs a median of 8 to 10 years post implantation (Turton et al., 2021). Early occurrences have been reported and the diagnosis should, therefore, be considered in any cases where implants have been in situ for longer than 12 months (Turton et al., 2021).

The lymphoma develops from the luminal aspect of the peri-implant capsule (85%), resulting in distortion to the breast including breast swelling or new onset breast asymmetry (Turton et al., 2021).

While commonly only one breast is affected, rare bilateral cases have also been reported (Clemens et al., 2016, McCarthy et al., 2019).

Late seroma is a rare and usually benign complication seen in up to 0.1% of all breast implant procedures (Turton et al., 2021). However, in an individual with a textured breast implant presenting with a delayed seroma (> 1 year after implantation), the risk of BIA-ALCL is up to 10% (Clemens et al., 2016, Mehta-Shah et al., 2018).

2.4.2. TUMOUR MASS

A small subset of individuals (10–20%) develop a tumour mass with possible nodal involvement (Turton et al., 2021, Marra et al., 2020). Some of these present with a combination of effusion and mass (Turton et al., 2021).

2.4.3. OTHER CLINICAL MANIFESTATIONS OF BIA-ALCL

Approximately one third of individuals report pain and additional signs such as erythema (14%), or skin lesions/ulceration (8%) (Adrada et al., 2014, McCarthy et al., 2019). In a small proportion of cases, local dissemination presents with ipsilateral axillary, supraclavicular, internal mammary chain or mediastinal lymphadenopathy (Turton et al., 2021). In 9% of cases, systemic 'B' symptoms such as unexplained weight loss, fevers or night sweats, are observed (McCarthy et al., 2019). Additionally, BIA-ALCL may be an incidental finding on routine histology post capsulectomy for capsular contraction or implant rupture (Adrada et al., 2014, Miranda et al., 2014).

2.4.4. DIFFERENTIAL DIAGNOSES IN BIA-ALCL

There are several differential diagnoses to consider in individuals with breast implants who present with evidence of a seroma or tumour mass. These include silicone bleed, implant rupture, trauma, infection, idiopathic, haematoma as well as BIA-ALCL. Where there is evidence of a mass-forming lesion or lymphadenopathy, important differentials include reactions to silicone, primary breast cancer, other lymphoma subtypes, sarcoma and metastases from other primary malignancies such as melanoma, all of which occur at a significantly greater frequency than BIA-ALCL (Turton et al., 2021). Skin lesions in isolation may represent primary cutaneous ALCL, rather than BIA-ALCL (Turton et al., 2021).

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Up to 10% of individuals with breast implants who present with evidence of a seroma or tumour mass may have BIA-ALCL (Turton et al., 2021). Unlike other lymphomas of the breast, breast cancer or benign lesions of the breast, the parenchyma is usually not involved in BIA-ALCL, unless the malignancy extends through the implant capsule into the surrounding tissue (Turton et al., 2021). More subtle presentations of BIA-ALCL may be difficult to identify, particularly in the presence of pre-existing breast asymmetry.

2.5. MANAGING AN INITIAL PRESENTATION

Individuals with breast implants who have concerns regarding the risk of developing BIA-ALCL should contact their GP or the surgeon at the hospital or clinic where implant surgery took place. Alternatively, if they are participating in a 5-year cancer follow-up care plan, they should discuss their concerns with their cancer physician. If implant surgery was performed outside Ireland, they should also contact the health service attended to establish the type of implants used (HSE, 2023).

On presenting to their GP or surgeon, **asymptomatic individuals** can be reassured that there is no need for concern. Imaging surveillance is not indicated in asymptomatic individuals with breast implants (Turton et al., 2021). There is currently no evidence supporting the replacement of textured implants with smooth implants to reduce the risk for BIA-ALCL (Nelson et al., 2021). Individuals with concerns should be advised to continue to perform regular breast checks, and provided with information regarding the symptoms associated with BIA-ALCL (see Table 1 for details of usual symptoms seen). For useful advice and information, they should also be directed to the HSE website at https://www.hse.ie/eng/services/news/newsfeatures/advice-for-patients-textured-breast-implants-tissue-expanders/).

On presenting to their GP, all **symptomatic individuals** should be urgently referred either to the surgeon who performed the original implant surgery, or to the local Symptomatic Breast Disease Clinic (see clinic locations in Appendix III). Plastic surgeons who see **symptomatic individuals** should also urgently refer them directly to the local Symptomatic Breast Disease Clinic (see clinic locations in Appendix III). This will facilitate a multidisciplinary approach, improve the quality of assessment and reduce the risk of missed or late diagnosis (Turton et al., 2021). In some instances, it may be possible for the referring surgeon to be involved in the subsequent management of the individual, as part of the specialist MDT.

Symptomatic Breast Disease Clinics should ensure they have robust referral processes in place for individuals with suspected BIA-ALCL, and should follow this care pathway in its diagnosis and management.

2.6. PRIMARY ASSESSMENT PROCESS

Investigations to confirm a diagnosis of BIA-ALCL should be performed at a Symptomatic Breast Disease Clinic that is equipped with the appropriate diagnostic expertise, following the principle of Triple Assessment: Clinical Examination, Imaging and Biopsy (Turton et al., 2021). The assessment process is summarised in Figure 2.

2.6.1. CLINICAL EXAMINATION

A thorough clinical examination should be performed to look for suspicious symptoms as described in Table 1 and illustrated in Figure 1 (FDA, 2023, Thompson, 2010). Clinicians should also document a detailed medical history, including a personal and familial history of cancer (Turton et al., 2021), with reference to international guidance on the assessment of familial risk (NICE, 2019). National guidance on familial risk and an associated pathway is currently under development by the NCCP.

2.6.2. IMAGING

Imaging is essential to distinguish the many benign and malignant causes for breast implant-related symptoms. These include infection, haematoma, primary breast cancer, primary non-breast malignancy such as melanoma and metastatic cancer to the breast, all of which occur at higher incidence than BIA-ALCL (Turton et al., 2021).

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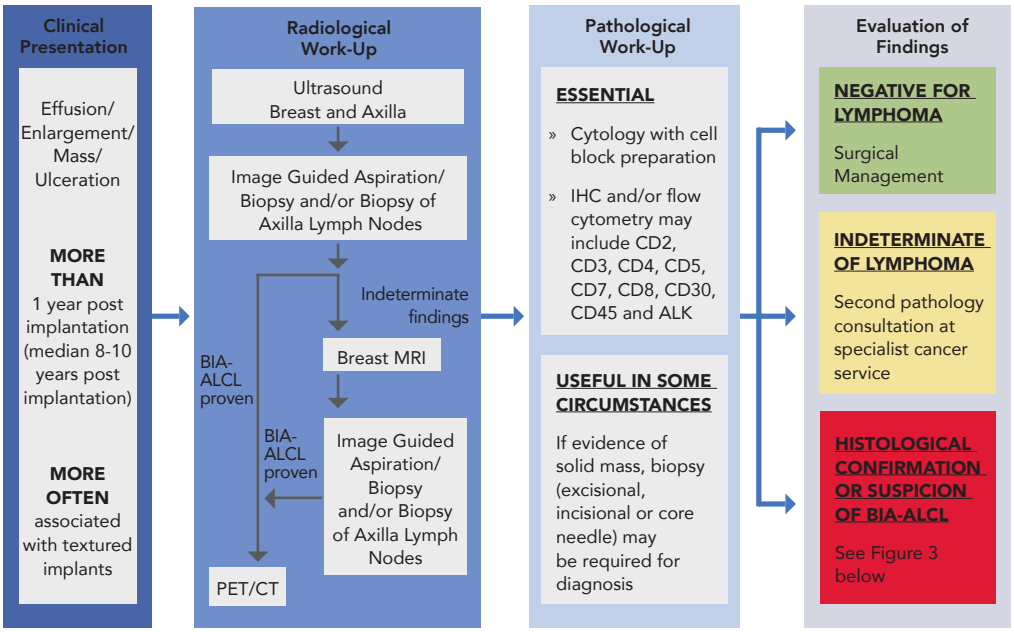
Figure 2. BIA-ALCL Diagnostic Algorithm



MRI, magnetic resonance imaging; PET, positron emission tomography; CT, computed tomography; IHC, immuno-histochemistry

Imaging guidelines for the diagnosis of this condition in the Irish context are formulated with reference to existing national and international best practice guidelines. Irish sources include the Health Products Regulatory Authority special topics information (HPRA, 2019), the National Breast Cancer GP referral guidelines (NCCP, 2021), National Clinical Guideline No. 7 (HSE, 2015) and the Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL); SIMT Report (Hamilton, 2019). International disease-specific guidelines included those from the EU (De Jong et al., 2021), the UK (Turton et al., 2021), the US (NCCN, 2023a) and Australia (GOV.AU, 2023).

Imaging surveillance in asymptomatic individuals with implants in the context of a normal clinical examination is not warranted. See Table 2 for a summary of the breast imaging modalities used in the diagnosis and staging of BIA-ALCL.

Table 2. Summary of role of Breast Imaging Modalities in BIA-ALCL

IMAGING MODALITY	UTILITY
Breast Ultrasound	Investigation of choice in diagnosis of BIA-ALCL Guided aspiration of all peri-implant fluid for cytopathology analysis Image guided biopsy of soft tissue masses and abnormal lymph nodes
Breast MRI	Evaluation of local disease and chest wall Evaluation of implant integrity Evaluation of parenchymal abnormalities in breast
FDG-PET/CT	Investigation of choice for loco-regional staging in proven BIA-ALCL

MRI = Magnetic Resonance Imaging; FDG-PET/CT = Fluoro-deoxy-glucose Positron Emission Tomography (FDG PET) and Computed Tomography (CT)

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2.6.2.1. ULTRASOUND (US) OF BREAST AND AXILLA

Breast ultrasound (US) is the imaging modality of choice to evaluate breast implants in the context of concerning signs and symptoms suggestive of BIA-ALCL. It has a high sensitivity rate (84%), but limited specificity (approximately 75%) (Turton et al., 2021).

The ultrasound examination should be performed in a Symptomatic Breast Disease Clinic which has access to breast MRI, expert breast histopathology and cytopathology services, in addition to a multi-disciplinary breast cancer and lymphoma team. The US examination should be performed by a suitably qualified Radiologist with a special interest in breast imaging. US equipment should be optimised for breast parenchymal and implant imaging. A high frequency, linear array probe should be used (Turton et al., 2021).

Prior knowledge of implant type is important in interpreting the images seen (Turton et al., 2021). Where possible, information regarding implant type, age of implant, primary breast cancer history, prior breast and axillary surgery and any relevant medical/surgical history should be provided by the referring clinician. Breast US should include an assessment for axillary lymphadenopathy, an evaluation of the contralateral implant, where present, and an examination of the entire implant membrane, capsule and material contents, along with the adjacent breast parenchyma (Turton et al., 2021). See Appendix IV for details of the information to be included in a Breast US Report.

2.6.2.1.1. EFFUSION

A small volume of peri-implant fluid (5-10 ml) is considered normal in implant imaging and aspiration of this is not warranted. Where there are moderate and large peri-implant effusions (i.e. a volume large enough to cause a significant difference in breast size), image-guided aspiration should be performed (De Jong et al., 2021).

All peri-implant fluid should be retrieved – at least 50 ml, through a single aspiration site, on a single occasion to minimise infection risk. A pathological review of the first aspirate is recommended, as serial aspirations may decrease or dilute tumour burden, making diagnosis more challenging (Jones et al., 2019). See Table 3 for details of the effusion specimens to be sent for analysis. All retrieved fluid should be sent for cytopathological analysis, requesting that the entire effusion sample should be analysed, stating that BIA-ALCL is suspected, as specific immunophenotyping markers may have to be tested to confirm its diagnosis (Turton et al., 2021).

Local procedures for the handling of fluid specimens and requirements for haematology and microbiology should be followed. Sterile samples for flow cytometry should be submerged in RPMI medium and stored at room temperature. Samples should be analysed within 24 hours of collection.

Table 3. Effusion Specimens for Analysis

	SAMPLE SIZE	SPECIMEN COLLECTION TUBE
Flow Cytometry	2 x 10mL samples	Send in RPMI
Microbiology	1 x 5-10mL	White top sterile universal container
Cytology*	Multiple samples to a total volume of 50mL-500mL (or more**)	White top sterile universal container

* Send fresh sample. Do not use CytoLyt®
** Send all remaining aspirate to Cytology for analysis

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2.6.2.1.2. MASS

A 14G ultrasound-guided biopsy of any peri-implant masses should be performed. When performed by experienced Radiologists, the risk to implant integrity is minimal.

2.6.2.1.3. AXILLA

Axillary masses and abnormal axillary lymph nodes should be sampled pre-operatively with standard biopsy/fine needle aspiration techniques. Abnormal axillary findings in the presence of implants may be due to inflammation or silicone lymphadenopathy. Surgical excision of lymph nodes should be considered in equivocal cases, following an MDT discussion.

2.6.2.1.4. CUTANEOUS LESIONS

Cutaneous lesions should be evaluated with a surgical punch biopsy or excision biopsy, as appropriate.

2.6.2.2. BREAST MAGNETIC RESONANCE IMAGING (MRI)

Breast MRI should be performed when there is a clinical or radiological concern for BIA-ALCL, in the context of a negative or inconclusive ultrasound examination (NCCN, 2023b, Sharma et al., 2020). It should also be performed to aid surgical planning. Breast MRI should be performed in a centre with appropriate equipment (e.g. 1.5T or 3T) and a dedicated breast coil and should be reported by an appropriately qualified Radiologist with a special interest in breast imaging.

The MRI breast examination should include sequences optimised for silicone evaluation to establish implant integrity, and gadolinium-contrast-enhanced sequences to evaluate for any underlying masses, malignancy or abnormal parenchymal enhancement. MRI may demonstrate masses and capsular changes not demonstrated on ultrasound, and contribute to T-staging assessment. It is standard practice that MRI breast abnormalities may be evaluated with second-look ultrasound, MRI-guided localisation or MRI-guided-biopsy, if appropriate and feasible. The MRI findings should be discussed at an MDT meeting. See Appendix V for details of the information to be included in a Breast MRI Report.

2.6.2.3 FLUORO-DEOXY-GLUCOSE POSITRON EMISSION TOMOGRAPHY (FDG PET) AND COMPUTED TOMOGRAPHY (CT)

FDG PET/CT should not be performed routinely to establish the diagnosis of BIA-ALCL. However, it is the imaging investigation of choice for staging in confirmed BIA-ALCL, and should be performed pre-operatively in all cases (Clemens et al., 2019). FDG PET/CT is the optimal examination for determining the extent of local and distant disease, allowing for surgical planning (Clemens et al., 2019), as it can detect distant sites of spread including lymph node or soft tissue involvement (Sharma et al., 2020).

Caution should be used in interpreting FDG-PET/CT findings, as they may be negative in the context of an effusion with low volume of cells, leading to a false-negative result. Caution is also advised in the interpretation of axillary lymph nodes which may be reactive, and US-guided sampling or surgical excision of these nodes should be considered (Turton et al., 2021). Post-operative and post-procedure sequelae and other factors such as infection/inflammatory change may also cause FDG avidity, contributing to false-positive findings.

Where BIA-ALCL is diagnosed incidentally, PET/CT may still be useful in the evaluation of distant and metastatic disease in order to complete staging. This should be performed approximately 6 - 8 weeks post-surgery to minimise false-positive findings (Turton et al., 2021).

As with other lymphoma types, serial PET/CT is useful in monitoring response to systemic treatment (Turton et al., 2021). There is no clear evidence to support a recommended frequency of PET/CT surveillance. However, in the standard lymphoma assessment, PET/CT is indicated 6 weeks after the last chemotherapy cycle.

All PET/CT results should be discussed at an MDT meeting.

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2.6.2.4 MAMMOGRAPHY, DIGITAL BREAST TOMOSYNTHESIS (DBT) & CONTRAST-ENHANCED MAMMOGRAPHY

Mammography is not a useful test to specifically diagnose BIA-ALCL. However, due to the common incidence of primary breast cancer, mammograms are recommended to exclude a primary breast carcinoma, where residual breast tissue is present in women aged over 35 years (DOHC, 2006, NCCP, 2021). If a woman has had a mastectomy and implant reconstruction, standard practice is not to perform a mammography on the side of the implant. However, where appropriate, the contralateral breast should be evaluated for co-existing breast abnormalities using mammography or DBT. Neither DBT nor contrast-enhanced mammography have a proven role in the diagnosis of BIA-ALCL.

2.6.3 PATHOLOGICAL WORK UP

BIA-ALCL can be characterised by evidence of a monoclonal population of large anaplastic cells, which are uniformly CD30-positive, anaplastic lymphoma kinase (ALK) negative and variably express T cell markers and EMA (Swerdlow et al., 2016, Miranda et al., 2014). The pathological work up involves an analysis of all samples collected from the peri-prosthetic effusion, tumour mass, affected nodes and skin lesions. Any additional pathology identified by breast imaging should also be followed up as part of this process. All biopsy and cytopathology results should be discussed at a breast-specialty MDT meeting or lymphoma MDT meeting, as appropriate.

The evaluation of any peri-prosthetic effusions or masses identified on imaging is done in two stages, as outlined in Table 4. Flow cytometry and immuno-histochemistry (IHC) are both necessary for the accurate diagnosis of BIA-ALCL (NCCN, 2023b). First, a morphological assessment is performed. If BIA-ALCL is suspected at this stage, a secondary assessment is then carried out by using immuno-histochemical markers to determine the haematopoietic origin of the suspicious cells (Turton et al., 2021). Samples taken from suspicious nodes or from skin lesions should also be investigated as part of this assessment process.

Fresh, unfixed seroma fluid should undergo cytocentrifugation and filtration, followed within 48 hours by air-drying and staining with Giemsa, Wright-Giemsa or another Romanowsky-type stain (Jaffe et al., 2020). Preparation of a cell block is desirable, as it allows haematoxylin and eosin staining and supports the immunohistochemical analysis of formalin-fixed, paraffin-embedded histologic sections (Jaffe et al., 2020). Cell block sections can also be used for polymerase chain reaction–based investigations of the T-cell receptor gene rearrangement to detect clonality (Jaffe et al., 2020). Capsulectomy specimens should be fixed and mapped to select multiple representative sections to assess for microscopic tumour involvement and capsular invasion (Jaffe et al., 2020).

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Table 4. Two Stage Histopathological Assessment

Stage 1: Morphological Assessment
• The characteristic morphological abnormalities seen on standard cytology are regarded as a gold standard pre-requisite for the diagnosis of BIA-ALCL (Turton et al., 2021). Although characterised by CD30-positive neoplastic cells, this finding must be interpreted with care, as it may result in false-positive diagnoses (Jones et al., 2019). • Tumour cells may be seen in both the effusion and the capsule mass, or may only be present in one or the other (Turton et al., 2021). Usually the total cellularity of the seroma fluid is made up of approximately 70% neoplastic cells, but in some cases only 10% atypical cells are seen (Di Napoli et al., 2017). • Where BIA-ALCL presents as a seroma, non-cohesive atypical neoplastic cells are confined to the luminal aspect of the capsule embedded in fibrinoid material, usually with sparse associated inflammatory infiltrate (Jones et al., 2019). • If a mass lesion is present, sheets of malignant cells infiltrate the capsule and surrounding tissue, often with areas of necrosis and a variable acute inflammatory infiltrate: prominent eosinophils may also be seen (Laurent et al., 2016). • Acellular samples and those composed of bland inflammatory cells are regarded as negative for BIA-ALCL and do not require further analysis. However, the cytologic assessment to detect BIA-ALCL has an approximate sensitivity of 78% (Adrada et al., 2014). Patients should be informed of this limitation and the possibility of false negative results (Turton et al., 2021). • If clinical or radiological evidence is suggestive of BIA-ALCL despite negative cytology, the patient should be referred for consideration by an MDT. A Stage 2 immuno-histochemistry assessment may also be considered (as outlined below) (Turton et al., 2021). • If no suspicion remains, the patient should be referred for surgical management, and followed up after three months to ensure that swelling has not recurred. Patients should also be advised to immediately report any recurring symptoms (Turton et al., 2021).
Stage 2: Immuno-histochemistry Assessment
• All diagnoses of suspected BIA-ALCL should be reviewed by a Histopathologist with a special interest in haematopathology, using immunohistochemistry markers to determine the haematopoietic origin of the suspicious cells (Turton et al., 2021). Multiple markers are explored as part of this process, including those listed in the diagnostic algorithm (see Figure 2).

2.7. MANAGEMENT OF AN INDETERMINATE BREAST ASSESSMENT

Although approximately 90% of chronic delayed seromas are not associated with malignancy (Turton et al., 2021), there is a significant risk of false-negative results due to the paucity of neoplastic cells. Therefore, all cases should undergo a cytological assessment. If reasonable suspicion persists despite negative cytology, see Table 5 for suggested next steps (Turton et al., 2021).

Decisions should be made carefully on a case-by-case basis, considering the degree of concern, differential diagnoses and the pros and cons associated with each intervention, e.g. en-bloc capsulectomy is associated with pneumothorax in up to 4% of cases, with the additional risks of chronic pain and significant cosmetic sequelae (Turton et al., 2021).

Table 5. Options in Suspected BIA-ALCL following a Negative or Inconclusive Primary Assessment

1. Referral for a specialist haematopathology review
2. Multidisciplinary Team (MDT) discussion
3. Repeat Ultrasound imaging (US)
4. Magnetic Resonance Imaging (MRI)
5. Repeat aspiration and cytology work up
6. Consider PET/CT pre-operatively
7. Diagnostic total en-bloc capsulectomy and explantation
8. Close monitoring

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2.8. CLINICAL MANAGEMENT OF HISTOLOGICALLY SUSPECTED OR CONFIRMED BIA-ALCL

BIA-ALCL's unique biology means it must be managed differently to other lymphomas (Sharma et al., 2020). Recommendations for its management follow best practice guidelines and evidence based on experience gained in the multidisciplinary management of known cases internationally (Turton et al., 2021). A suggested management algorithm is shown in Figure 3.

If BIA-ALCL is identified incidentally following a routine capsulectomy performed at implant exchange or explantation associated with capsule contracture, the patient should be referred to a Symptomatic Breast Disease Clinic, and follow the standard care pathway as outlined here (Turton et al., 2021).

An MDT meeting must take place for all confirmed cases of BIA-ALCL prior to any intervention, as early collaboration that establishes shared care is likely to improve patient outcomes (Turton et al., 2021, Sharma et al., 2020). This meeting must take place at a Symptomatic Breast Disease Clinic and have representatives from haemato-oncology, haemato-pathology, radiology, and breast surgery including plastic surgery (Turton et al., 2021). Consideration should also be given to the inclusion of radiation oncology and psycho-oncology in the core MDT.

The MDT discussion should include a review of the following (Turton et al., 2021):

- All imaging reports, including MRI and PET/CT.
- Routine pre-operative blood tests, including a full blood count (FBC), full metabolic panel including urea and electrolytes (U&E), liver function tests (LFTs), lactate dehydrogenase (LDH).
- Virology work up (Turton et al., 2021, Clemens et al., 2019), including Human T-lymphotropic viruses (HTLV) I & II (NCCN, 2023b).
- Echocardiogram or MUGA scan report, if an anthracycline-based regimen is indicated.
- A pregnancy test, if relevant, and chemotherapy or radiation therapy being considered.
- An assessment of bone marrow aspirate and trephine for the presence of marrow disease is also recommended prior to surgery, in cases where the disease is aggressive, defined as local-regional or distant lymph node involvement, or if there is unexplained cytopenia (Turton et al., 2021, Clemens et al., 2016, Verde, 2021).

A full physical examination should also be performed, including a complete skin examination, and a full medical history should be documented (NCCN, 2023b).

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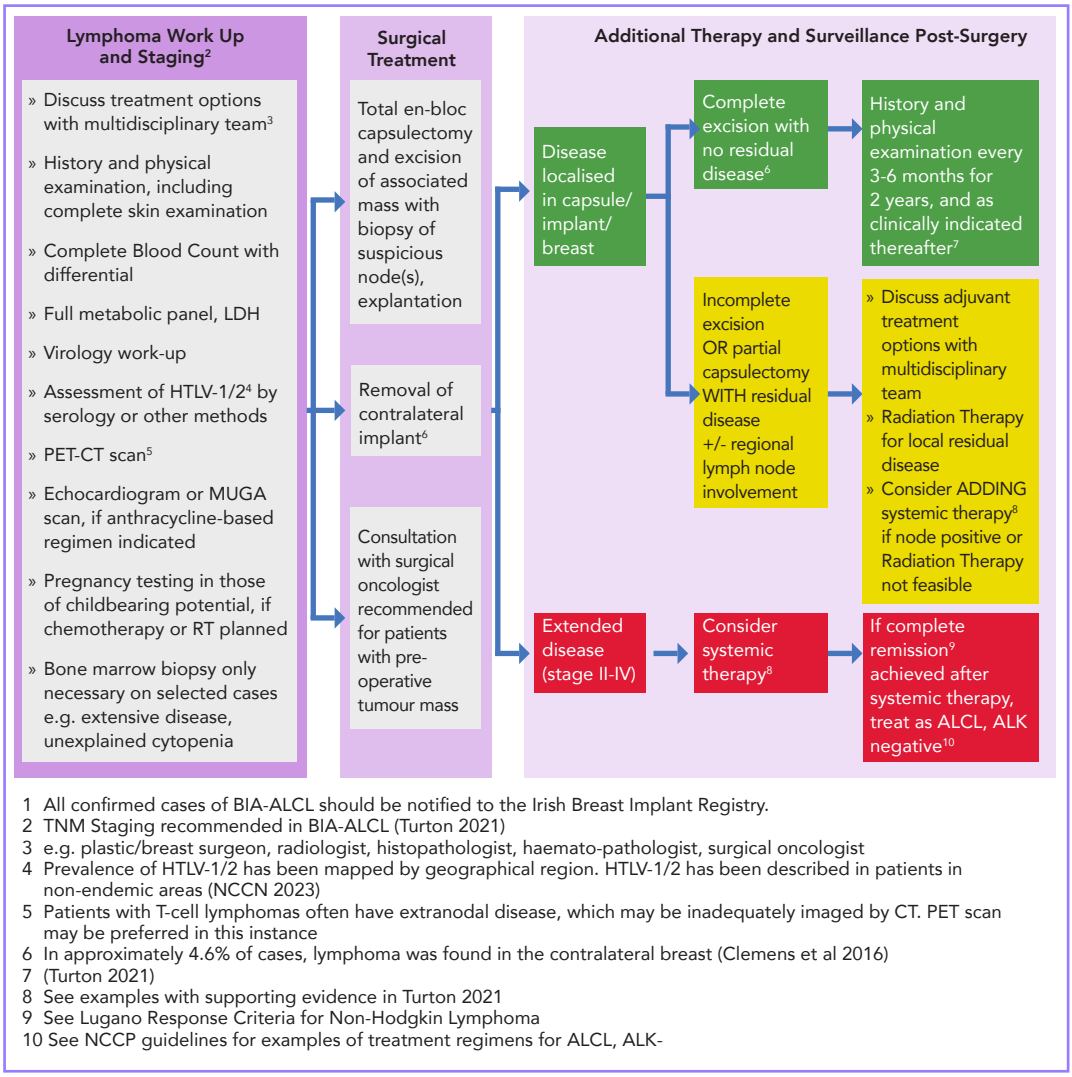
Figure 3. Management of Histologically Suspected or Confirmed BIA-ALCL[1]



1 All confirmed cases of BIA-ALCL should be notified to the Irish Breast Implant Registry.
2 TNM Staging recommended in BIA-ALCL (Turton 2021)
3 e.g. plastic/breast surgeon, radiologist, histopathologist, haemato-pathologist, surgical oncologist
4 Prevalence of HTLV-1/2 has been mapped by geographical region. HTLV-1/2 has been described in patients in non-endemic areas (NCCN 2023)
5 Patients with T-cell lymphomas often have extranodal disease, which may be inadequately imaged by CT. PET scan may be preferred in this instance
6 In approximately 4.6% of cases, lymphoma was found in the contralateral breast (Clemens et al 2016)
7 (Turton 2021)
8 See examples with supporting evidence in Turton 2021
9 See Lugano Response Criteria for Non-Hodgkin Lymphoma
10 See NCCP guidelines for examples of treatment regimens for ALCL, ALK-

2.8.1. SURGICAL INTERVENTION

Surgical excision is recommended as first-line (and curative) therapy in most cases of BIA-ALCL (Miranda et al., 2014, Adrada et al., 2014, Turton et al., 2021). Effusion-limited BIA-ALCL (presenting as an effusion or confined by the fibrous capsule) can generally be adequately treated with surgery alone with an excellent long-term survival (NCCN, 2023b). Infiltrative BIA-ALCL may have a more aggressive clinical course, but can still be amenable to surgical treatment if complete surgical excision is possible, although it may require additional treatment following removal of the implant (Laurent et al., 2016).

Complete surgical therapy includes en-bloc excision and explantation of (a) the breast implant with total capsulectomy and (b) any associated masses, with contralateral prophylactic breast implant removal (Sharma et al., 2020). Removal of the contralateral implant and total capsulectomy should be strongly considered in BIA-ALCL since bilateral breast involvement may be seen in 2 – 4.6% of cases (McCarthy et al., 2019, Clemens et al., 2016).

Surgery should be performed by an experienced member of the oncoplastic breast or plastic surgery team, familiar with performing implant-based surgery and with additional expertise in capsulectomy and tumour extirpation (Turton et al., 2021). Multiple systematic scar capsule biopsies may be required to identify early invasive disease and mass formation, which may have implications for prognosis (Lyapichev et al., 2020). All cases should be orientated to enable accurate T staging by the reviewing pathologist.

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Complete surgical excision alone is the optimal treatment for patients with localised disease (stage 1A-1C) who present with effusion, with or without a distinct breast mass (NCCN, 2023b). There is no role for mastectomy or sentinel lymph node biopsy in these cases, as BIA-ALCL is not a disease of the breast parenchyma (NCCN, 2023b). Local disease relapse may be amenable to re-excision surgery alone without requiring systemic therapies (NCCN, 2023b). In cases with evidence of BIA-ALCL beyond the capsule, any mass identified should be excised, with biopsy of any suspicious node(s) and explantation (NCCN, 2023b). Where there is incomplete surgical excision or partial capsulectomy with residual disease (with or without regional lymph node involvement) or where individuals present with an unresectable mass or extended disease (stage II-IV), additional therapy (systemic or radiation therapy) may be required (NCCN, 2023b). See details in Section 2.8.3.

The capsule should ideally be removed in one piece and correctly orientated. It should be inspected to identify areas of particular concern and submitted for histological analysis (Turton et al., 2021). A primary morphological assessment should be conducted by the breast pathology team, working very closely with the haematopathology team. If a double capsule is present, they should be separated and analysis undertaken on both layers. It is critical that multiple representative sections are taken for analysis to improve the detection rate (Turton et al., 2021). A minimum of 12 samples is recommended (De Jong et al., 2021).

All removed implants (or components thereof) should be retained, treated as biohazardous material, and stored in an appropriate manner, pending collection by the manufacturer as outlined in Section 3.2 below (Turton et al., 2021). Ideally, the explanted implant should be photographed post-operatively and details recorded in the patient notes. These should include visual details from the posterior "patch", carrying the manufacturer's name, implant style and batch number, to facilitate the identification of the implant (Turton et al., 2021).

Immediate or delayed reconstruction may be considered (NCCN, 2023b), although a delayed setting may be preferred (Sharma et al., 2020, Lamaris et al., 2019). Reconstructive options include autologous tissue or smooth surface breast implants (NCCN, 2023b, Lamaris et al., 2019).

2.8.2. STAGING

BIA-ALCL's unique behaviour means that current lymphoma staging and response guidelines are not easily applicable to this disease (Sharma et al., 2020). See Table 6 for details of differences in the recommended management of BIA-ALCL and other lymphomas. Both the NCCN and UK guidelines advocate the American Joint Committee (AJC) TNM system for staging for better prognostic classification (Turton et al., 2021, Clemens et al., 2019).

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Table 6. Differences between BIA-ALCL and other Lymphoma Histologic Subtypes

	Classic Hodgkin Lymphoma, High Grade Non-Hodgkin Lymphoma	Low-Grade Non-Hodgkin Lymphoma	BIA-ALCL
Biopsy method	Histologic (surgical excision biopsy or core biopsy)	» Histologic (surgical excision or core biopsy) » Haematologic assessment	» Cytologic for effusion subtype (Fine-needle aspirate and cell block) » Histologic for mass disease (core biopsy)
Staging system	Stages I-IV		TNM
PET*	Validated	Validated in proportion of histologic subtypes; research application or not applicable in others	Not validated
Deauville Criteria	Validated	Validated in proportion of histologic subtypes; research application or not applicable in others	Not validated
Response assessment guidelines	IWG criteria, Lugano Classification, LyRIC, RECIL	IWG criteria, Lugano Classification, RECIL	Not validated
Treatment	Systemic therapy, radiation therapy		Surgery (curative, first-line); systemic therapy for advanced-stage disease

*For staging, response assessment and prognostication. TNM = American Joint Committee Tumour-Node-Metastasis (TNM) staging system; IWG = International Working Group (Cheson et al., 1999); LyRIC = Lymphoma Response to Immunomodulatory Therapy Criteria (Cheson et al., 2016); RECIL = Response Evaluation Criteria in Lymphoma (Younes et al., 2017). Adapted from (Sharma et al., 2020).

BIA-ALCL should be staged as shown in Table 7 (Clemens et al., 2016). Bilateral BIA-ALCL is not to be included in this staging system, and needs careful consideration on a case-by-case basis (NCCN, 2023b). It is notable that research to date shows the majority (35-70%) of BIA-ALCL was detected at Stage IA (effusion only), with a predicted overall survival rate of 94% (Clemens et al., 2019). Distant disease is rare, as are "B" symptoms (Sharma et al., 2020).

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Table 7. Proposed TNM Staging for BIA-ALCL

Disease Extent		Description
T: Tumour extent	T1	Confined to effusion or a layer on luminal side of capsule
	T2	Early capsule infiltration
	T3	Cell aggregates or sheets penetrating the capsule
	T4	Cells infiltrate beyond the capsule
N: Lymph node	N0	No lymph node involvement
	N1	One regional lymph node (+)
	N2	More than one regional lymph node (+)
M: Metastasis	M0	No involvement of distant sites
	M1	Disease present at distant organs/ sites

Stage	Description
IA	T1 N0 M0
IB	T2 N0 M0
IC	T3 N0 M0
IIA	T4 N0 M0
IIB	T1-3 N1 M0
III	T4 N1-2 M0
IV	T1-4 N0-2 M1

Adapted from (Clemens et al., 2016)

2.8.3. RADIATION THERAPY AND SYSTEMIC TREATMENT

For Stage I BIA-ALCL where complete excision has been achieved and there is no residual disease, no further treatment is deemed necessary. The individual should be followed up as outlined in Section 4.0 below. For individuals with local residual disease, radiation therapy (RT) may be of value (Adrada et al., 2014, Clemens et al., 2016). If RT is necessary, modern general principles of Involved-site Radiation Therapy (ISRT) should be followed (NCCN, 2023b). If RT is not feasible, systemic chemotherapy may be considered, although there is little evidence to recommend an optimal approach here (Turton et al., 2021, Collins et al., 2019).

Individuals for which there has been incomplete excision or partial capsulectomy, who present with mass-forming or distant disease, or have relapsed or refractory disease generally have a more aggressive clinical course which may be fatal, justifying cytotoxic chemotherapy in addition to surgery (Adrada et al., 2014, Laurent et al., 2016, Turton et al., 2021, Sharma et al., 2020). Systemic treatment may be required for mass-forming or distant disease, or where there is lymph node involvement, and this is advocated for stage 2–4 disease (Turton et al., 2021).

Although chemotherapy is not always associated with better treatment outcomes in BIA-ALCL (Adrada et al., 2014, Clemens et al., 2016, Mehta-Shah et al., 2018), there is anecdotal support for the use of brentuximab vedotin (Alderuccio et al., 2018, Stack et al., 2020). An individualised approach to systemic treatment is recommended for more advanced cases, and there is published evidence available for some systemic adjuvant therapies (Turton et al., 2021).

3.0 Registration and Reporting of Confirmed or Suspected BIA-ALCL

3.1. IRISH BREAST IMPLANT REGISTRY

In late 2022, the National Office of Clinical Audit (NOCA) was granted funding to develop and implement a breast implant registry for Ireland. Its purpose is to record prospective data on breast implants, and capture any reported instances of breast implant-related disease, including BIA-ALCL. It is anticipated that this registry will undergo piloting in 2024, with a view to becoming operational in 2025. For up to date information, see www.noca.ie.

All those providing breast implant surgery, or otherwise involved in the diagnosis, treatment and follow-up of breast implant-associated disease in Ireland are expected to participate by registering their patients at this site.

Breast implant registries have been developed world-wide. The aim of these clinical, quality registries is to enhance the long-term safety and performance monitoring of implanted breast devices and improve patient outcomes. ICOBRA is the International Collaboration of Breast Registry Activities, and member countries include the UK, Netherlands, Australia, New Zealand, and the United States, as well as Ireland. ICOBRA was developed to establish an internationally agreed and comparable minimum dataset, made up of standardised and epidemiologically sound data that reflect global best practice, which each country develops and manages independently. This minimum data set includes data collection about BIA-ALCL.

A specific registry to retrospectively record cases of BIA-ALCL was established in the US in 2012 (PROFILE, Patient Registry and Outcomes for Breast Implants and Anaplastic Large Cell Lymphoma Etiology and Epidemiology).

3.2. INCIDENT REPORTING

The HPRA strongly encourages healthcare professionals to report any confirmed or suspected cases of BIA-ALCL through the HPRA's online reporting system* or by completing an online Medical Device Incident User Report Form or by emailing devices@hpra.ie. The HPRA will ensure that the manufacturer of the implant concerned is also informed of the report.

Clinicians may also report any confirmed or suspected cases of BIA-ALCL directly to the implant manufacturer, as these are serious incidents, which manufacturers are required to report to the HPRA. The manufacturer should be provided with appropriate assistance to facilitate completion of their investigation. Where possible, this may include access to the device for examination, and access to any other relevant information.

As part of any report, the following information in particular will assist the HPRA in its follow-up of these cases:

» Device details (manufacturer and model, surface texture of the implant, if known);
» Dates of implantation, revision, and explant removal, as applicable;
» Diagnostic specifics of BIA-ALCL (including CD30 and ALK status);
» Details of any previous implants;
» Clinical signs, symptoms, and management to date.

*For printing purposes: https://www.hpra.ie/homepage/about-us/report-an-issue/mdiur

4.0 Clinical Follow-up and Surveillance in BIA-ALCL

A clinical review should be performed every three to six months for 2 years following a diagnosis of BIA-ALCL, and thereafter as clinically indicated (Turton et al., 2021, NCCN, 2023a).

There is currently no consensus internationally on the role or frequency of imaging in BIA-ALCL surveillance. While the NCCN advocates the consideration of 6 monthly surveillance scans for 2 years, thereafter scanning only as clinically indicated (NCCN, 2023a), the UK guideline only recommends imaging for symptomatic individuals in follow-up (Turton et al., 2021).

Research has shown that routine imaging surveillance in other Non-Hodgkin lymphoma subtypes does not influence patient outcomes (Armitage, 2012, Thompson et al., 2014). It is also acknowledged that unnecessary examinations may result in harm through false-positive results and anxiety.

Therefore, in the context of an integrated MDT approach, and in line with the UK recommendations, this care pathway advocates imaging surveillance only for symptomatic individuals in BIA-ALCL follow-up (Turton et al., 2021). Widespread surveillance of asymptomatic individuals is not indicated (Turton et al., 2021).

An imaging surveillance plan, if deemed warranted, should be devised on a case-by-case basis, as part of the pre-treatment and post-treatment MDT discussion. CT or FDG-PET/CT may also be recommended following discussion.

Individuals who become symptomatic should be immediately re-referred to a Symptomatic Breast Disease Clinic for investigation (Turton et al., 2021).

5.0 Governance and Approval

Appendix I and II outline the membership of the Guideline Expert Advisory Group and Guideline Working Group respectively. This clinical guideline falls under level 4 of the CDI - Document Approval - Hierarchy of Compliance V02 and, as such, has been approved by the National Clinical Advisor and Group Lead (NCAGL) for Acute Operations and also by the HSE Clinical Forum. It has been further approved by the NCPS, RCSI's Committee of Surgical Affairs and RCSI Council.

6.0 Communication and Dissemination

6.1. PATIENT COMMUNICATION

Clear and accurate communication to individuals who have breast implants is essential, both to reassure those who are asymptomatic, and also to provide guidance to those who may be symptomatic or have concerns.

6.1.1 COMMUNICATION ACTIVITY TO DATE

In 2019, the Department of Health (DoH) requested a meeting with the Health Service Executive (HSE) and the Health Products Regulatory Authority (HPRA) when Allergan announced a global withdrawal of their *Biocell* macro-textured implants. Various actions were taken, which included the commissioning of this guidance and the issuing of a patient advisory document.

The advice recommended that all symptomatic breast patients should attend their GP for referral to a Symptomatic Breast Disease Clinic. It was agreed that using existing pathways was important, as individuals with such symptoms were more likely to have breast cancer than BIA-ALCL, if they had a subsequent cancer diagnosis.

6.0 Communication and Dissemination

Asymptomatic breast patients or those with symptoms not typically associated with breast cancer or BIA-ALCL were to be referred for an outpatient appointment with a plastic or breast surgeon if requested.

The patient advisory document* was binary:
- *Biocell* textured implant
- Other implant

In the absence of a breast implant registry (now under development), hospitals where people had received implants since 1997 were asked to generate and check a patient list and issue patient letters using the template given.

Each cancer centre was asked to nominate a co-ordinator to:
- Co-ordinate the issue of all letters
- Identify telephone helpline operators
- Establish a telephone helpline
- Maintain patients' lists in the event additional information was needed to be communicated as knowledge related to this condition became available over time

It was anticipated that this advisory would generate increased patient attendance at Symptomatic Breast Disease Clinics, as individuals were encouraged to self-examine and be breast aware. It was expected that some individuals might request the opportunity to discuss the condition with their implanting surgeon in an outpatient setting. In addition to HSE patients, there were also individuals who had implants inserted in a private healthcare setting who could require care in this context.

A third cohort who had implants in non-affiliated settings or overseas were contacted through the media; the HSE, HPRA and the Irish Association of Plastic Surgeons (IAPS) websites, informing them of the risks, advising them to be breast aware and to attend their GPs if they have concerns that they have symptoms or signs of breast disease.

6.1.2 COMMUNICATION ONGOING

Both the HPRA and HSE have developed patient information sites on their websites to support people who may have concerns about their breast implants, whether symptomatic or not.

All healthcare professionals who care for this population should be familiar with these sites and know how and when it is appropriate to refer patients.

HSE Website: Advice for patients with textured breast implants and tissue expanders
https://www.hse.ie/eng/services/news/newsfeatures/advice-for-patients-textured-breast-implants-tissue-expanders/

HPRA: Breast Implant Associated - Anaplastic Large Cell Lymphoma (BIA – ALCL)
https://www.hpra.ie/homepage/medical-devices/special-topics/breast-implant-associated---anaplastic-large-cell-lymphoma-(bia-alcl)

6.2 DISSEMINATION OF THIS GUIDANCE

This approved document will be placed on the HSE Central Repository. There will also be a link on the NCPS website in the RCSI domain. Notification of its availability will be circulated via the RCSI to all Fellows and Members with a focus on Plastic and Breast Surgeon colleagues. The document will be forwarded to professional organisations including the Irish Association of Plastic Surgery, the General Surgery Advisory Group and Faculty of Radiologists, RCSI. The guidance will also be issued to the NCAGL for Primary Care and to the Irish College of General Practitioners. The document will be forwarded to Hospital Group clinical directors for onward distribution. CDI and NCPS will also use their social media channels to promote the launch of the document.

*For printing purposes: https://www.hse.ie/eng/services/news/newsfeatures/advice-for-patients-textured-breast-implants-tissue-expanders/

7.0 Implementation

7.1 IMPLEMENTATION OF THIS GUIDELINE

This guideline outlines a standardised approach for care in the diagnosis, treatment and follow-up of Breast Implant Associated – Anaplastic Large Cell Lymphoma (BIA-ALCL). It supports teamwork and communication by defining a care pathway for all involved, and should be implemented in the context of a multidisciplinary approach.

Following its publication, this guidance will be disseminated as outlined in Section 6.2, and its recommendations should be adopted across primary, secondary and tertiary care. The NCPS will also request that this guidance is included as part of the surgical training curriculum.

7.2 IMPLEMENTATION OF THE IRISH BREAST IMPLANT REGISTRY

As outlined in Section 3.1, the National Office of Clinical Audit (NOCA) was granted funding to develop and implement a breast implant registry for Ireland. Its purpose is to record prospective data on breast implants, and capture any reported instances of breast implant-related disease, including BIA-ALCL. It is anticipated that this registry will undergo piloting in 2024, with a view to becoming operational in 2025. All those providing breast implant surgery, or otherwise involved in the diagnosis, treatment and follow-up of breast implant-associated disease in Ireland are expected to participate by registering their patients at this site.

8.0 Monitoring, Audit and Evaluation of this Guideline

8.1 REPORTING CASES OF BIA-ALCL TO THE HPRA

As part of its role of monitoring the safety of medical devices on the market in Ireland, the HPRA maintains a vigilance reporting system which receives reports from users, members of the public and manufacturers, in relation to medical device issues. It is important to report all cases of BIA-ALCL to the HPRA, to help make informed decisions on the safety of these devices. All cases of BIA-ALCL encountered should be reported along with the following data:

» Device details (Manufacturer and Model, Surface Texture of the implant)

» Implantation date details (Initial, Revision and Explantation if applicable)

» Diagnostic specifics of the ALCL (including CD30 and ALK status)

» Details of any previous implants

» Clinical Symptoms and Management to date

Please note, patient identifying information is not required.
The portal for reporting these cases, and any medical device incident, can be found on the HPRA website.

9.0 Revision/Update

This clinical guideline should be reviewed after three years unless evidence comes to light that requires a rapid update. In the event that this is required, the Guideline Working Group will be reconvened to review and decide on the appropriateness of any amendments before putting the document through the governance approval route. In the event that not all members are available, then representation will be sought from the relevant specialist area.

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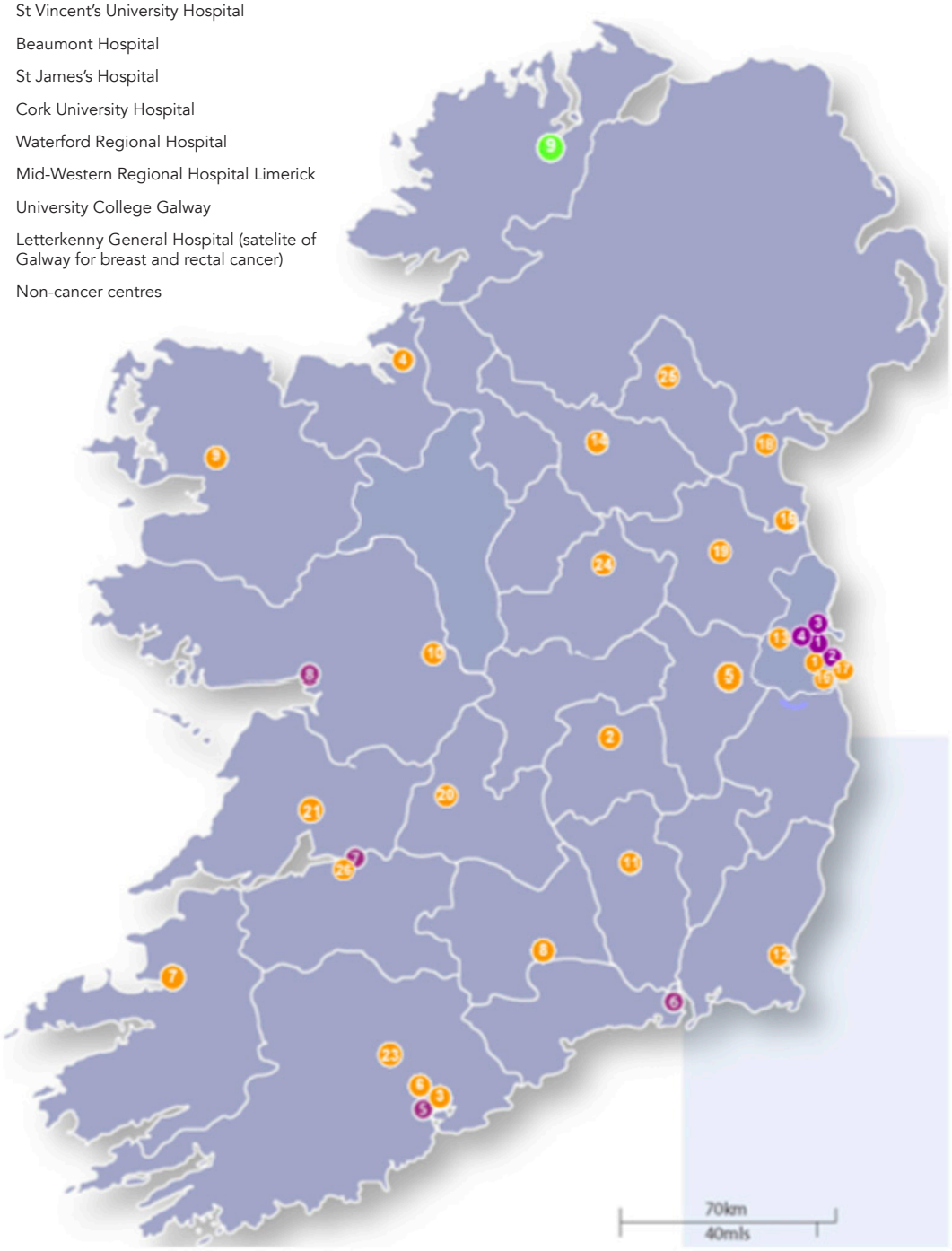
APPENDIX III. LOCATION OF SYMPTOMATIC BREAST DISEASE CLINICS IN IRELAND (HSE, 2015)

1. Mater Misericordiae Hospital
2. St Vincent's University Hospital
3. Beaumont Hospital
4. St James's Hospital
5. Cork University Hospital
6. Waterford Regional Hospital
7. Mid-Western Regional Hospital Limerick
8. University College Galway
9. Letterkenny General Hospital (satelite of Galway for breast and rectal cancer)
- Non-cancer centres



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APPENDIX IV. **BREAST ULTRASOUND REPORT**

The Breast Ultrasound report should document:

» Adequate visualisation of the implant surface
» Presence of peri-implant fluid / approximate estimate of volume (e.g. small (acceptable), moderate, large)
» Presence / absence of peri-implant masses
» Integrity of capsule / focal capsular thickening
» Appearance of the breast parenchyma / any ancillary findings
» Appearance of axillary lymph nodes if present / visualised
» Evaluation of contralateral breast implant

APPENDIX V. **BREAST MRI REPORT**

The Breast MRI report should document:

» Implant integrity / capsular integrity
» Presence of oedema
» Presence / location / approximate quantity of peri-implant fluid
» Location size and nature of any enhancing masses
» Chest wall involvement
» Axillary or internal thoracic lymphadenopathy
» Evaluation of contralateral breast / implant / axillary regions

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