

Breast Implant Associated – ALCL MD Anderson Cancer Center Experience

FDA Advisory Panel
March 25, 2019



Mark W. Clemens, MD, FACS
Associate Professor
MD Anderson Cancer Center

Disclosures

Mentor Corporation: Clinical investigator for Athena Trial

Establishment Labs: Clinical investigator for US Safety/Efficacy Trial

Allergan Corporation: Former Consultant 2012-2015, Travel expenses for an educational meeting

Committee Author, National Comprehensive Cancer Network (NCCN) Lymphoma Guidelines

Comparison of Databases



		US Only As of 3/5/2019 (n=101)	All MDR Reports as of 9/30/2018 (n=660)*	All MDR Reports (as of 9/30/2018 (n=457)*	US Only As of 3/20/2019 (n=152)
Age at time of diagnosis (yrs)	Mean	55	53	53	54
	Range	31-84	24-90	24-90	28-87
	Not specified	n/a	240 (36%)	111 (24%)	n/a
Time from the last Implant to ALCL Diagnosis (yrs)**	Mean	9.1	8.5	9	8.1
	Range	.08-27	0-44	0-34	0.8-28
	Not specified	4	231 (35%)	110 (24%)	n/a
Time from Any Implant to ALCL Diagnosis (yrs)	Mean	12.7	n/a	n/a	12.6
	Range	2.1-44	n/a	n/a	2.2-32
	Not specified	4	n/a	n/a	n/a

- Short time interval to development of disease is 2.2 years from implantation
- Average time to develop disease 8-10 years

Comparison of Databases



		US Only As of 3/5/2019 (n=101)		All MDR Reports as of 9/30/2018 (n=660)*		All MDR Reports (as of 9/30/2018 (n=457)*		US Only As of 3/20/2019 (n=152)	
Anaplastic lymphoma kinase (ALK)	Positive	0	0	0	0	0	0	0	0
	Negative	75	74	239	36	229	50	152	100
	Not specified	19	19	421	64	228	50	0	0
	Unknown	7	7	n/a	n/a	n/a	n/a	0	0
CD30 Status	Positive	83	82	239	36	215	47	152	100
	Negative	0	0	0	0	0	0	0	0
	Not Specified	15	15	421	64	242	53	0	0
	Unknown	3	3	n/a	n/a	n/a	n/a	0	0

- By WHO criteria, are all CD30+ ALK –
- CD30 is screening test, ALK differentiates from systemic ALCL

Comparison of Databases



		US Only As of 3/5/2019 (n=101)		All MDR Reports as of 9/30/2018 (n=660)*		All MDR Reports (as of 9/30/2018 (n=457)*		US Only As of 3/20/2019 (n=152)	
Clinical Presentation (breast)****	Seroma	81	80	350	53	266	58	98	64.5
	Breast swelling/pain	n/a	n/a	188	28	135	30	18	11.8
	Capsular contracture	33	33	75	11	69	15	14	9.2
	Peri-implant mass/lump	13	13	85	13	82	18	34	22.4
	Rupture	n/a	n/a	n/a	n/a	54	12	0	0
	Other	n/a	n/a	226	34	43	9	1	0.7
	Not specified	n/a	n/a	187	28	105	23	0	0

- Most common presentation delayed seroma (>1 year)
- No testing/screening of asymptomatic patients

Comparison of Databases



		US Only As of 3/5/2019 (n=101)		All MDR Reports as of 9/30/2018 (n=660)*		All MDR Reports (as of 9/30/2018 (n=457)*		US Only As of 3/20/2019 (n=152)	
		N	%	N	%	N	%	N	%
Implant Surface***	Textured	79	78	425	64	310	68	118	77.6
	Smooth	4	4	39	6	24	5	0	0
	Polyurethane	1	1	n/a	n/a	n/a	n/a	1	0.7
	Not specified	17	17	196	30	123	27	33	21.7
Implant Fill	Silicone	55	54	399	60	274	60	81	53.3
	Saline	41	41	260	39	183	40	61	40.1
	Saline/Silicone	1	1	n/a	n/a	n/a	n/a	0	0
	Not specified	4	4	1	0	0	0	10	6.6
Reason for Implant	Reconstruction	49	49	119	18	108	24	62	40.8
	Augmentation	50	50	125	19	104	23	90	59.2
	Not specified	1	1	416	63	245	54	0	0
	Unknown	1	1	n/a	n/a	n/a	n/a	0	0

- No only-smooth implant cases within PROFILE, MDACC, or case series
- Even mix of cosmetic/augmentation and silicone/saline

Smooth Implant-Only Cases?

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Medical Devices

Implant Surface ⁴	Textured	242	60
	Smooth	30	7
	Not specified	142	34

⁴ 5 of the 30 smooth cases had a reported history of prior implant(s), and the rest of them had not provided prior implant history.

Silicone Gel-Filled Breast Implants

Labeling for Approved Breast Implants

As of September 30, 2017, the FDA has received a total of 414 medical device reports (MDRs) of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), including 9 deaths¹. BIA-ALCL are counted for those with a confirmed pathology test, or ALK or CD30 biomarkers, or reported by health care professionals. There are 272 reports with data on surface information at the time of reporting. Of these, 242 were on textured implants and 30 smooth implants. There are 413 reports with data on implant fill type. Of these, 234 reported the use of silicone filled implants, and 179 reported the use of saline-filled implants.

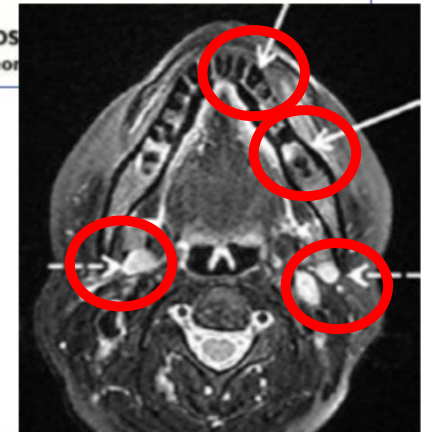
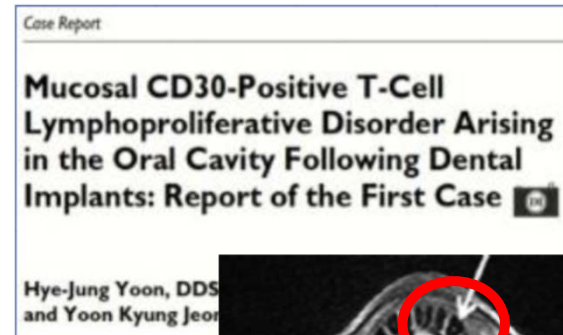
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Prosthesis-associated?

- Tibial Implant
- Dental implant ALCL²
- Chest port ALCL³
- Shoulder repair ALCL
- Lap Band ALCL
- Gluteal Implants x 2



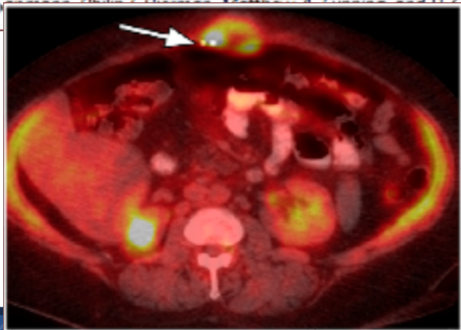
Tibial implant ALCL¹



Dental implant ALCL²

Bariatric Implant-Associated Anaplastic Large-Cell Lymphoma

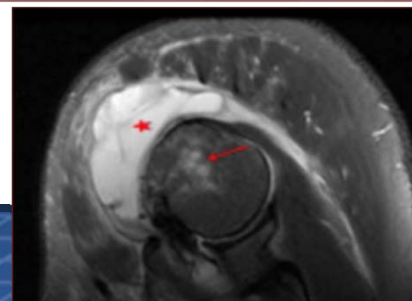
Jayadev Manikam Umakanthan, Corrigan L. McBride, Timothy Greiner, Ji Yuan, Jennifer S. ...



CASE REPORT

Anaplastic large cell lymphoma masquerading as osteomyelitis of the shoulder: an uncommon presentation

Matthew Tuck,^{1,2} Jane Lim,³ Jose Lucar,⁴ Debra Benator²



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Development of a Plaque Infiltrated With Large CD30+ T Cells Over a Silicone-Containing Device in a Patient With History of Sézary Syndrome

Anna K. Engberg, Christ ... Michael Girardi



Chest port ALCL³

1. Palraj B, et al. J Foot Ankle Surg 2010;49:561-4; 2. Yoon HJ, et al. Int J Surg Pathol 2015;23:656-61; 3. Engberg A, et al. J Clin Oncol 2013;31:e87-e89. 4. Kellogg B et al. Annals Plastic Surgery 2013; 73(4).

Comparison of Manufacturers

Adapted Brody
2015 - World²

Manufacturer	n	%
Unknown	61	35
Allergan/ Inamed/ McGhan	97	56
Mentor	3	1.7
Biocell	3	1.7
Eurosilicone	0	0
PIP	5	2.9
Sientra/Silimed	1	0.5
Total	170	

Biocell:
8.1x Vs. All Other
32x vs. Siltex

MAUDE FDA 2017 Database^{1,2}
85% US, 15% OUS*

Manufacturer	n	%
Unknown	22	9.6
Allergan/ Inamed/ McGhan	184	80.3
Mentor	20	8.7
CUI	1	0.4
Sientra	1	0.4
Total	228	

Biocell:
8.3x Vs. All Other
9.2x vs. Siltex

*Unverified, unconfirmed

MD Anderson
2019 Tracking - US¹

Manufacturer	n	%
Unknown	68	44.7
Allergan/ Inamed/ McGhan	78	51.3
Mentor	6	3.9
Bioplasty	1	0.6
Silimed PU	1	0.6
Sientra	3	2.0
Total	152	

Biocell:
7.1x Vs. All Other
13x vs. Siltex

Review Article

Understanding rare adverse sequelae of breast implants: anaplastic large-cell lymphoma, late seromas, and double capsules

Mark W. Clemens¹, Maurizio Bruno Nava², Nicola Rocco², Roberto N. Miranda²

Global Adverse Event Reports of Breast Implant-Associated ALCL: An International Review of 40 Government Authority Databases

Dhivy R. Seemabasa, M.D.
Roberto N. Miranda, M.D.
Armin K. Kaur, B.A.
Ashleigh M. Francis, M.D.
Antonella Campanale, M.D.
Rosaria Boldrini, M.D.
Janette Alexander, M.D.
Anand K. Deva, M.D.
Paula R. Gravina, M.D.
L. Jeffrey Medeiros, M.D.
Karen Nast, R.N.
Charles E. Butler, M.D.
Mark W. Clemens, M.D.

Background: Tracking world cases of breast implant-associated anaplastic large cell lymphoma (ALCL) is currently limited to patient registries at a few academic centers, dependent upon patient referral and case reports in the literature. The purpose of this study was to review and compare federal database adverse event reports of breast implant-associated ALCL encompassing the major breast implant markets worldwide.

Methods: Federal implantable device regulatory bodies were contacted and database queries were performed for 40 countries. Demographics, device characteristics, pathology, treatment modalities, and outcomes were assessed where available.

Results: For the countries queried, 363 unique cases were reported for breast implant-associated ALCL. Search terms "anaplastic" and "ALCL" were queried of the U.S. Manufacturer and User Facility Device Experience (MAUDE)

1. Clemens MW, et al. Gland Surgery 2016; doi: 10.21037/gs.2016.11.03; 2. Brody GS, et al. Plast Reconstr Surg 2015;135:695-705.

CA/CARE Style 410 (Biocell) Prospective Trial

- McGuire et al. 2017
 - 17,656 patients
 - 31,985 implants¹
- 8 BIA-ALCL²: 1:2207 (95%CI:1120,5112)

Risk Factor Analysis for Capsular Contracture, Malposition, and Late Seroma in Subjects Receiving Natrelle 410 Form-Stable Silicone Breast Implants

Patricia McGuire, M.D.
Neal R. Reisman, M.D., J.D.
Diane K. Murphy, M.B.A.
St. Louis, Mo.; Ho

Background: Natrelle 410 silicone breast implants are approved in the United States for breast augmentation, reconstruction, and revision.

Methods: In two ongoing prospective multicenter 10-year studies, 17,656 sub-augmentation

mass index, device size, style, or incision site. Four cases of breast implant-associated anaplastic large cell lymphoma were reported. One case each was reported in the augmentation, revision-augmentation, reconstruction, and revision-reconstruction cohorts. In these four subjects, breast implant-associated anaplastic large cell lymphoma was diagnosed from approximately 3.5 to 11.6 years after implantation.

1. McGuire P, et al. Plast Reconstr Surg 2017;139:1-9; 2. Clemens MW, McGuire P. Commentary on: Roberts JM et al. A Prospective Approach to Inform and Treat 1,340 Patients at Risk for BIA-ALCL. Plast Reconstr Surg 2019, In press

Biocell Recall

- November 21: ANSM recommends against textured implants
- December 17, 2018: CE mark withdrawal and voluntary recall for Biocell and Microcell products
- 38 countries: Europe, Israel, Brazil, Russia, Australia
- “Allergan cites an incomplete routine review and renewal of the file”



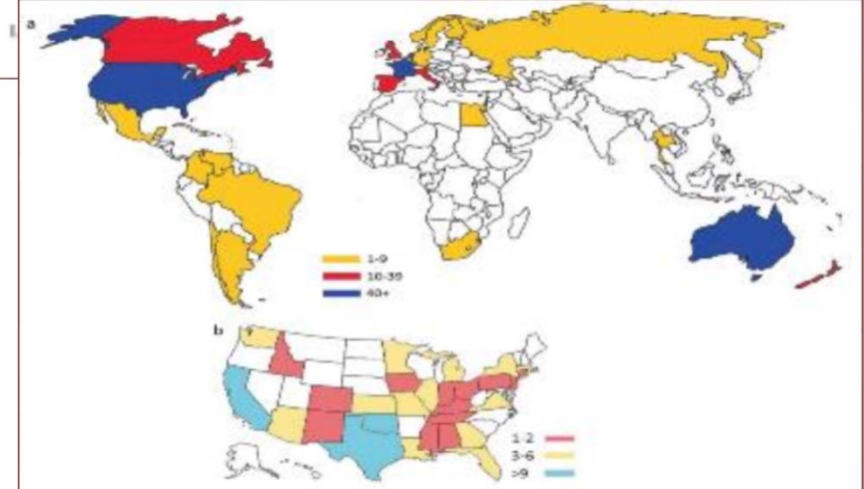
Global Risk Estimates

- US: 1:19,737 (152 cases, 2019)
 - Mixed market Allergan:Mentor
- Netherlands 1:6920 (40 cases)
 - Textured market
- Australia, New Zealand (95 cases)^{1,2} – Textured Market
 - Risk 1:1000-1:10,000?¹ for textured implants
 - Allergan Biocell (1:3345)
 - Silimed polyurethane (1:2832)
 - Mentor Siltex (1:86029)
 - 25.7 to 1 ratio of Biocell to Siltex BIA-ALCL risk

U.S. Epidemiology of Breast Implant–Associated Anaplastic Large Cell Lymphoma

Erin L. Doren, M.D.
Roberto N. Miranda, M.D.
Jesse C. Selber, M.D.,
M.P.H.
Patrick B. Garvey, M.D.

Background: Breast implant-associated anaplastic large cell lymphoma (ALCL) is a distinctive type of T-cell lymphoma that arises around breast implants. Although rare, all cases with adequate history have involved a textured breast implant. The objective of this study was to determine the U.S. incidence and



13:46

BREAST-IMPLANT ASSOCIATED ANAPLASTIC LARGE CELL LYMPHOMA (BIA-ALCL): RELATIVE AND ABSOLUTE RISK ASSESSMENT BASED ON 100% OF ALL NATIONAL CASES OF BIA-ALCL IN THE NETHERLANDS

Mintsje DE BOER, René DAN DER HULST, Floor VAN LEEUWEN,
Daphne DE JONG, Hinne RAKHORST
Maastricht University Medical Centre, Maastricht, The Netherlands

Australian Government
Department of Health
Therapeutic Goods Administration

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Breast implants

Expert advisory panel advice on association with anaplastic large cell lymphoma

20 December 2016

1. Therapeutic Goods Administration update, 20 December 2018; 2. Magnusson M, et al. The epidemiology of breast implant-associated anaplastic large cell lymphoma in Australia and New Zealand confirms the highest risk for grade 4 surface breast implants. *Plast Reconstr Surg.* 2019;143:

BIA-ALCL Global Network Roundtable

427 OUS World Cases,
Unique and pathology
confirmed

19 Deaths Worldwide



- ◆ 35 countries
- ◆ Argentina: 8 cases, 1 death
- ◆ Australia: 82 Cases, 3 deaths
- ◆ Belgium: 10 Cases
- ◆ Brazil: 12 Cases, 1 death
- ◆ Canada: 25 Cases
- ◆ Chile: 2 Cases
- ◆ China: 0
- ◆ Colombia: 6 Cases
- ◆ Czech Republic: 1 case
- ◆ Denmark: 7 Cases
- ◆ Egypt: 1 case
- ◆ Finland: 10 Case
- ◆ France: 59 Cases, 4 deaths
- ◆ Germany: 7 cases
- ◆ Ireland: 1 case
- ◆ Israel: 8 Cases
- ◆ Italy: 38 Cases
- ◆ Japan: 0
- ◆ Mexico: 4 Cases
- ◆ Netherlands: 40 c, 1 Death
- ◆ New Zealand: 13 c, 1 death
- ◆ Norway: 3 cases
- ◆ Romania: 0
- ◆ Russia: 2 cases
- ◆ Singapore: 0
- ◆ South Africa: 1 Case
- ◆ South Korea: 0
- ◆ Spain: 29 Cases
- ◆ Sweden: 6 Cases, 2 death
- ◆ Switzerland: 4 cases
- ◆ Taiwan: 0
- ◆ Thailand: 1 Case
- ◆ Venezuela: 2 cases
- ◆ United Kingdom: 45 Cases, 1 death
- ◆ United States: 152 cases, 5 deaths

Published This Month – March 2019



- Supplements in ASJ and PRS journals
- 55 authors, 16 peer-reviewed articles on BIA-ALCL

- | | | | |
|----------------------|-----------------------|------------------|--------------------|
| ◆ Garry Brody | ◆ Dennis Hammond | ◆ Andrea Pusic | ◆ Andrew Feldman |
| ◆ Mark W. Clemens | ◆ Steven Horwitz | ◆ Gayle Gordillo | ◆ Eric D. Jacobsen |
| ◆ Anand K. Deva | ◆ Meredith Collins | ◆ Hinne Rakhorst | ◆ Greg Lamaris |
| ◆ John A. Keech | ◆ L. Jeffrey Medeiros | ◆ Tony Connell | ◆ Ali Qureshi |
| ◆ Colleen McCarthy | ◆ Daphne deJong | ◆ Kelly Hunt | ◆ Ahmet Dogan |
| ◆ Roberto N. Miranda | ◆ Charles E. Butler | ◆ Suzanne Turner | |
| ◆ Mark Magnusson | ◆ Marshall Kadin | ◆ Miles Prince | |
| ◆ Arianna DiNapoli | ◆ Peter Lennox | ◆ Nadim Hallab | |

Patient Registry and Outcomes for Breast Implants and Anaplastic Large Cell Lymphoma Etiology and Epidemiology (PROFILE): Initial Report of Findings, 2012–2018

Colleen M. McGee, MD, MS
New York-Bronx, PhD

Al A. Qureshi, MD
John Miller
Tanya Goffin, MD
Andrew L. Davis, MD, MPH
Bella S. Adini, MD, MBA
Kara S. Gorman, MPH
Mark W. Clemens, MD

Background: In January of 2011, the US Food and Drug Administration initiated a safety communication regarding the potential association between

Molecular Drivers of Breast Implant–Associated Anaplastic Large Cell Lymphoma

Peter Blomberg, MBBS
Ellis R. Thompson, PhD
H. Miles Prince, MBBS
Pathologic and East Melbourne, Victoria, Australia

Summary: Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare T-cell lymphoproliferative disorder occurring in patients with breast implants. Genomic characterization performed in BIA-ALCL to date has demonstrated qualitatively similar molecular abnormalities to those seen in its more common counterpart [ALK-negative systemic anaplastic large cell lymphoma (sALCL)] including JAK/STAT activation and MYC/TP53 dysregulation. Despite these observed similarities at the molecular level, the outcomes of

Pioneers of Breast Implant–Associated Anaplastic Large Cell Lymphoma: History from Case Report to Global Recognition

Roberto N. Miranda, MD
L. Jeffrey Medeiros, MD
Maria C. Ferrufino-Schmidt, MD

John A. Keen, Jr, DO
Garry S. Brody, MD
Daphne de Jong, MD
Ahmet Dogan, MD
Mark W. Clemens, MD

Summary: The first case of breast implant-associated anaplastic large cell lymphoma (breast implant ALCL) was described by John Keen and the late Brevator Creech in 1997. In the following 2 decades, much research has led to acceptance of breast implant ALCL as a specific clinicopathologic entity, a process that we bring up to life through the memories of 6 persons who were involved in this progress, although we acknowledge that many others also have contributed to the current state of the art of this disease. Dr. Keen recalls the events that led him and Creech to first report the disease. Ahmet Dogan and colleagues at the Mayo Clinic described a series of 4 patients with breast implant ALCL and led to increased awareness of breast implant ALCL in

Characteristics and Treatment of Advanced Breast Implant–Associated Anaplastic Large Cell Lymphoma

Meredith S. Collins, MD
Roberto N. Miranda, MD
L. Jeffrey Medeiros, MD
Marcelo Pinheiro Silva de Meneses, MD
Srinivasan P. Iyer, MD
Charles E. Butler, MD, FACS
Jun Liu, PhD
Mark W. Clemens, MD, FACS

Background: Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) most commonly follows an indolent course; however, a subset of patients display more advanced disease marked by recurrent and disseminated growth refractory to treatment. This study evaluated outcomes of advanced disease, specifically bilateral disease, lymph node involvement, organ metastasis, and/or disease-related death.
Methods: Published cases of BIA-ALCL from 1997 to 2018 and unpublished cases at the authors' institution were retrospectively reviewed, and patients with advanced disease were selected. Treatment and outcomes were compared

Achieving Reliable Diagnosis in Late Breast Implant Seromas: From Reactive to Anaplastic Large Cell Lymphoma

Arianna Di Napoli, MD, PhD
Rome, Italy

Molecular Drivers of Breast Implant–Associated Anaplastic Large Cell Lymphoma

Peter Blomberg, MBBS
Ellis R. Thompson, PhD
H. Miles Prince, MBBS
Pathologic and East Melbourne, Victoria, Australia

Summary: Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare T-cell lymphoproliferative disorder occurring in patients with breast implants. Genomic characterization performed in BIA-ALCL to date has demonstrated qualitatively similar molecular abnormalities to those seen in its more common counterpart [ALK-negative systemic anaplastic large cell lymphoma (sALCL)] including JAK/STAT activation and MYC/TP53 dysregulation.

Theories of Etiopathogenesis of Breast Implant–Associated Anaplastic Large Cell Lymphoma

Pratik Rastogi, MBBS, GDAAD, MS
Edward Riordan, MBBS
David Moon, MBBS
Anand K. Deva, BSc(Med), MBBS, MS, FRACS

Summary: Breast implant-associated anaplastic large cell lymphoma is a malignant

Current Risk Estimate of Breast Implant–Associated Anaplastic Large Cell Lymphoma in Textured Breast Implants

David J. Coletti, MBBS
Linne Rakhov, MD, PhD
Peter Lamm, FRCSG
Mark Magnusson, MBBS, MS, FRACS
Rodney Carter, MBBS, FRACS

Background: With breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) now accepted as a unique (iatrogenic) subtype of ALCL directly associated with textured breast implants, we are now at a point where a sound epidemiologic profile and risk estimate are required. The aim of this article is to provide a comprehensive and up-to-date global review of the available epidemiologic data and literature relating to the incidence, risk, and prevalence of BIA-ALCL.

Breast Reconstruction Following Breast Implant–Associated Anaplastic Large Cell Lymphoma

Gregory A. Lamaris, MD, PhD
Charles E. Butler, MD, FACS
Anand K. Deva, BSc(Med), MBBS, MS, FRACS
Roberto N. Miranda, MD
Kelly K. Hunt, MD, FACS
Tony Connell, MD
Joan E. Lipa, MD
Mark W. Clemens, MD, FACS

Background: Standard of care treatment of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) involves surgical resection with implant removal and complete capsulectomy. We report a case series of BIA-ALCL reconstruction with proposals for timing and technique selection.
Methods: We retrospectively reviewed and prospectively enrolled all BIA-ALCL patients at 2 tertiary care centers and 1 private plastic surgery practice from 1998 to 2017. Demographics, treatment, reconstruction, pathology staging, patient satisfaction, and oncologic outcomes were reviewed.
Results: We treated 66 consecutive BIA-ALCL patients and 18 (27%) received reconstruction. Seven patients (39%) received immediate reconstruction, and

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2019 NCCN Consensus Guidelines on the Diagnosis and Treatment of Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)

Mark W. Clemens, MD, FACS; Eric D. Jacobsen, MD; and Steven M. Horwitz, MD

Aesthetic Surgery Journal
2019, Vol 39(51) S3–S13
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Mark Clemens

The Cellular Origins of Breast Implant–Associated Anaplastic Large Cell Lymphoma (BIA-ALCL): Implications for Immunogenesis

Suzanne Dawn Turner, PhD*



DOI: 10.1093/asj/sjy229
www.aestheticsurgeryjournal.com

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The Inflammatory Effects of Breast Implant Particulate Shedding: Comparison With Orthopedic Implants

Nadim James Hallab, PhD; Lauryn Samelko, PhD; and Dennis Hammond, MD

Aesthetic Surgery Journal
2019, Vol 39(51) S36–S48
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What Cytokines Can Tell Us About the Pathogenesis of Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)

Marshall E. Kadin, MD

Aesthetic Surgery Journal
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Association Between Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) Risk and Polyurethane Breast Implants: Clinical Evidence and European Perspective

Moustapha Hamdi, MD, PhD

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Genetics of Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)

Naoki Oishi, MD, PhD; Roberto N. Miranda, MD; and Andrew L. Feldman, MD*

The “Game of Implants”: A Perspective on the Crisis-Prone History of Breast Implants

Anand K. Deva, BSc (Med), MBBS (Hons), MS, FRACS;
Amanda Cuss, BMedSci (Hons), MBBS (Hons); Mark Magnusson,
MBBS, FRACS; and Rodney Cooter, MBBS, MD, FRACS

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NCCN Guidelines¹

- Internationally recognised algorithms for the diagnosis and treatment of cancer
- Utilized by the majority of oncologists
- Adopted by international societies



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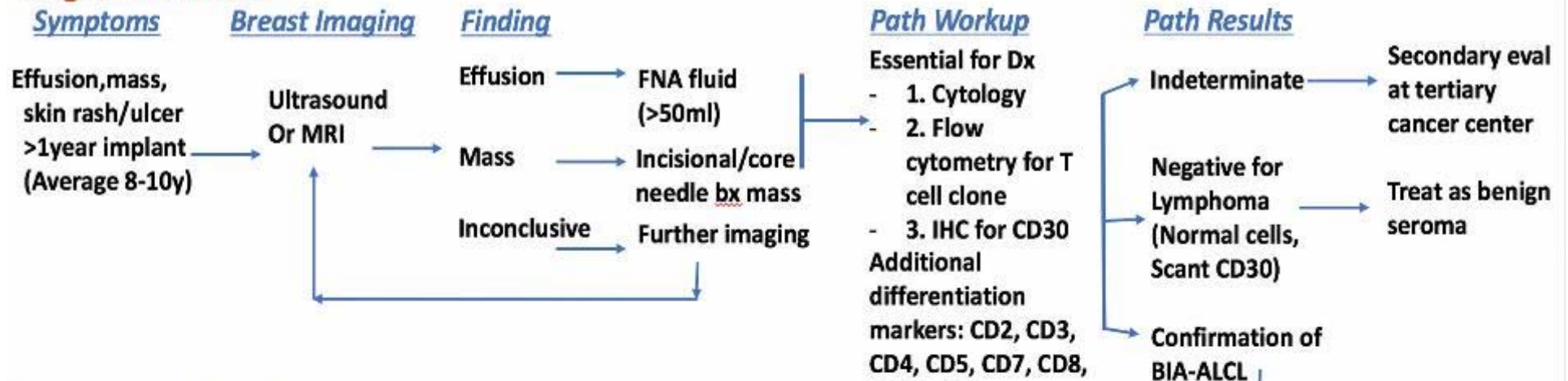
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2019 NCCN Consensus Guidelines on the
Diagnosis and Treatment of Breast
Implant-Associated Anaplastic Large
Cell Lymphoma (BIA-ALCL)

Mark W. Clemens, MD, FACS; Eric D. Jacobsen, MD; and
Steven M. Horwitz, MD

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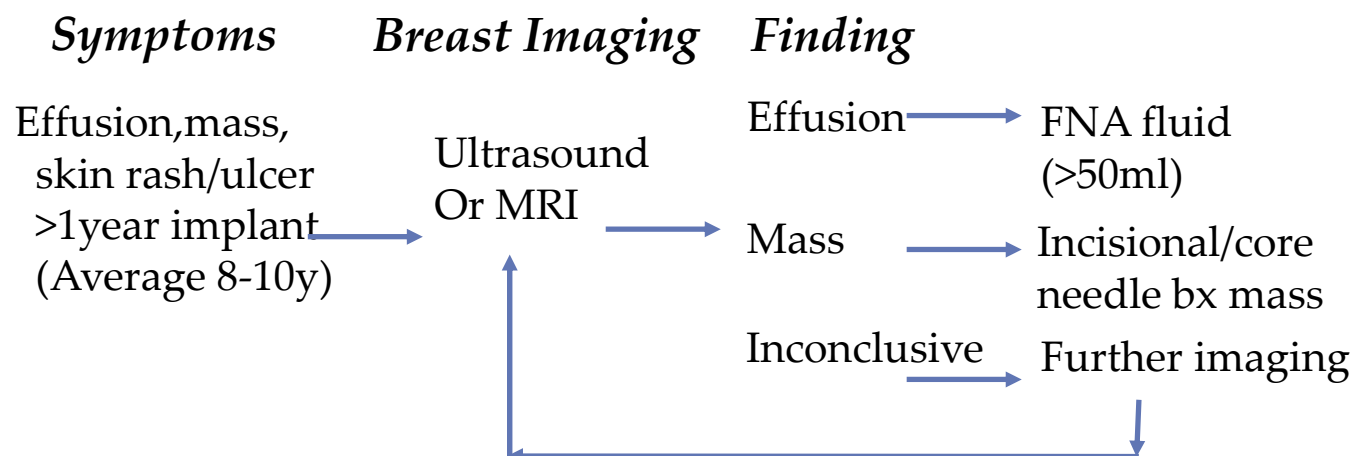
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Diagnosis BIA-ALCL

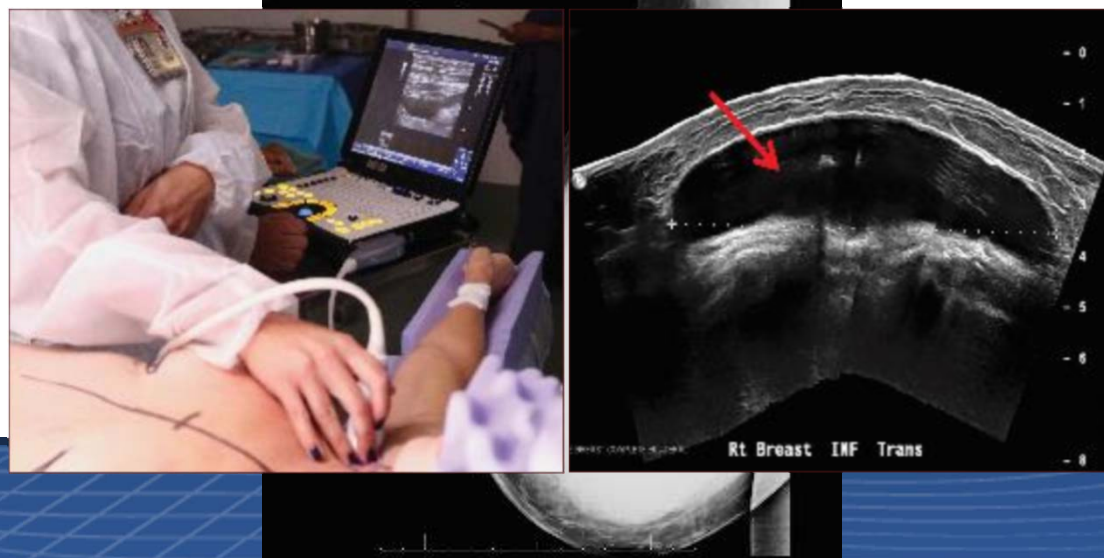
Abbreviations: MRI Magnetic Resonance Imaging, FNA Fine needle aspiration, Bx Biopsy, CBC Complete blood count, PET/CT Positron emission tomography, CMP Complete metabolic profile, LDH Lactate dehydrogenase, RT Radiation therapy, CHOP Cyclophosphamide Doxorubicin Vincristine Prednisone, Dose adjusted Etoposide



BIA-ALCL Diagnosis



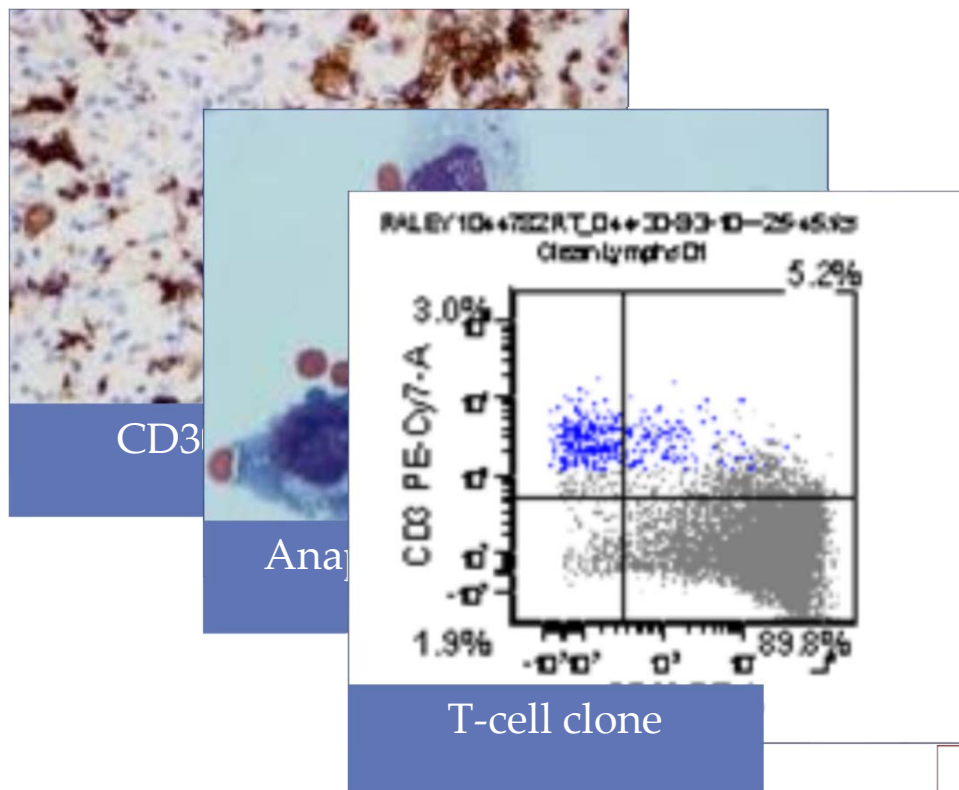
- Effusion 79.3%
- Mass 40%
- Capsular contracture 8%
- Skin rash 2%
- Lymphadenopathy 8%



Breast implant-associated anaplastic large cell lymphoma: sensitivity, specificity, and findings of imaging studies in 44 patients

Beatriz E. Adrada · Roberto N. Miranda · Gaiane Margishvili Rauch · Elisa Arribas · Rushmi Kanagal-Shamanna · Mark W. Clemens · Michelle Fanale · Nisreen Haidari · Ed Mustafa · John Larrinaga · Neal R. Reisman · Jesse Inso · M. James You · Ken H. Young · L. Jeffrey Medeiros · Wei Yung

Pathology Workup



Path Workup

Essential for Dx

- 1. Cytology
- 2. Flow cytometry for T cell clone
- 3. IHC for CD30

Additional differentiation markers: CD2, CD3, CD4, CD5, CD7, CD8, CD45, ALK

Path Results

Indeterminate

Negative for Lymphoma (Normal cells, Scant CD30)

Confirmation of BIA-ALCL

Modern Pathology
<https://doi.org/10.1038/s41379-018-0134-3>

USCAP

REVIEW ARTICLE

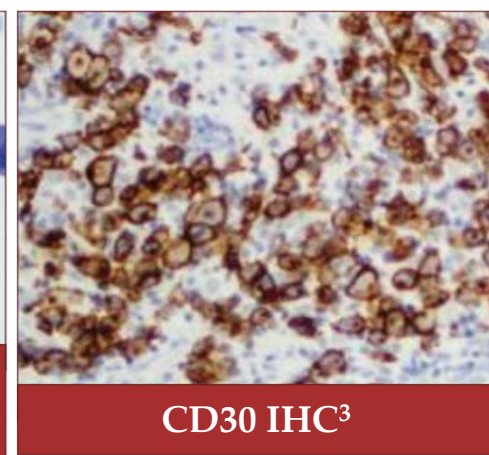
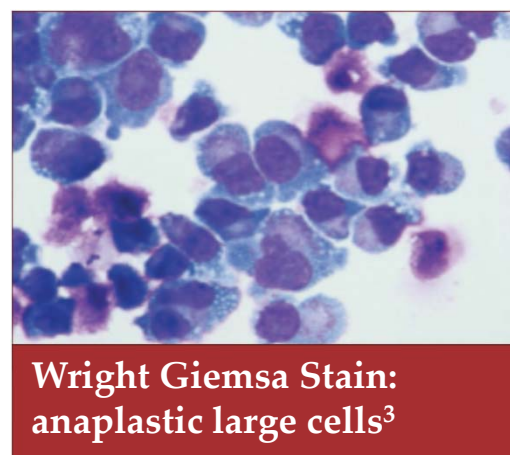
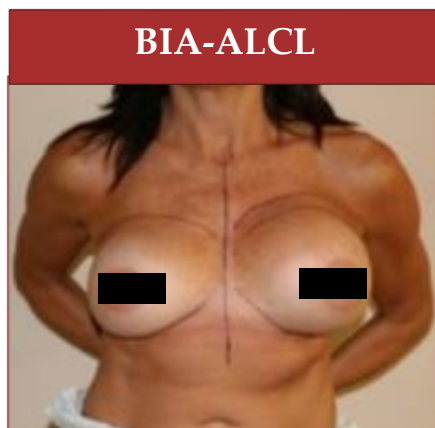
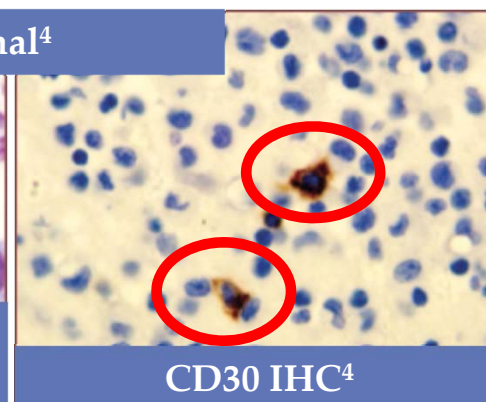
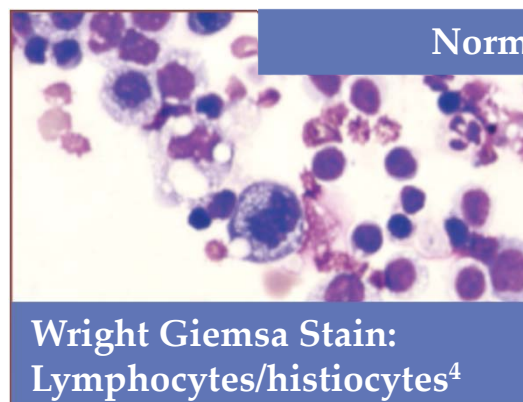
Breast implant-associated anaplastic large cell lymphoma: a review

Andrés E. Quesada¹ · L. Jeffrey Medeiros¹ · Mark W. Clemens² · Maria C. Ferrufino-Schmidt³ · Sergio Pina-Oviedo⁴ · Roberto N. Miranda¹

Received: 29 March 2018 / Revised: 31 May 2018 / Accepted: 2 June 2018
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Case study: Benign Seroma Vs. BIA-ALCL

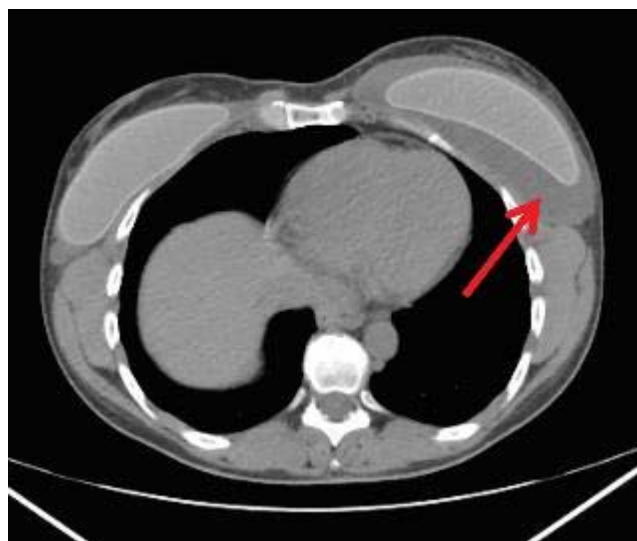
3



Images courtesy of Dr Mark Clemens.

1. Clemens MW, et al. Gland Surg 2017;6:169–84; 2. Personal communication, Dr Mark Clemens, May 2017. 3. NCCN Guidelines. Breast implant-associated ALCL Version 2.2017; 4. Clemens MW, Miranda RN. Aesthet Surg J 2017. doi: 10.1093/asj/sjx040; 4.

Disease Workup



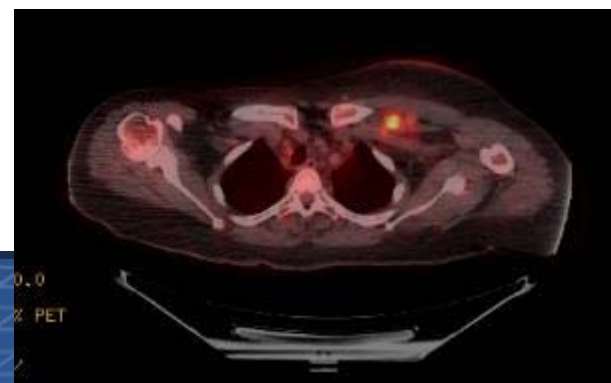
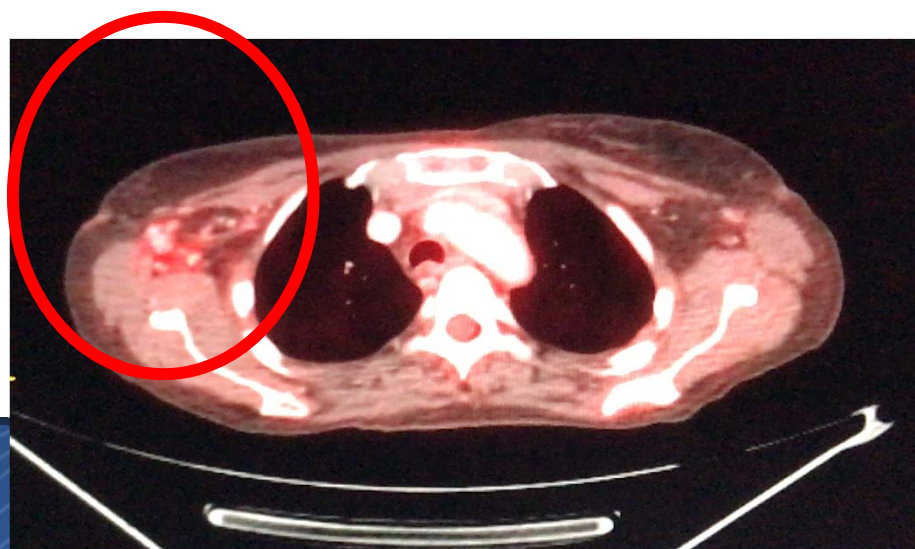
Treatment BIA-ALCL

Disease Workup

H&P
 Labs: CBC with diff
 CMP, LDH
 Imaging: PET/CT scan
 Recommend multidisc team
 Oncologist lymphoma
 Surgical oncologist
 Plastic Surgery
 Hemepathologist

Surgery

En bloc resection:
 Total capsulectomy
 Explantation
 Exc mass
 Exc biopsy node(s)
 Consider contralateral
 Consider delayed or
 immediate recon



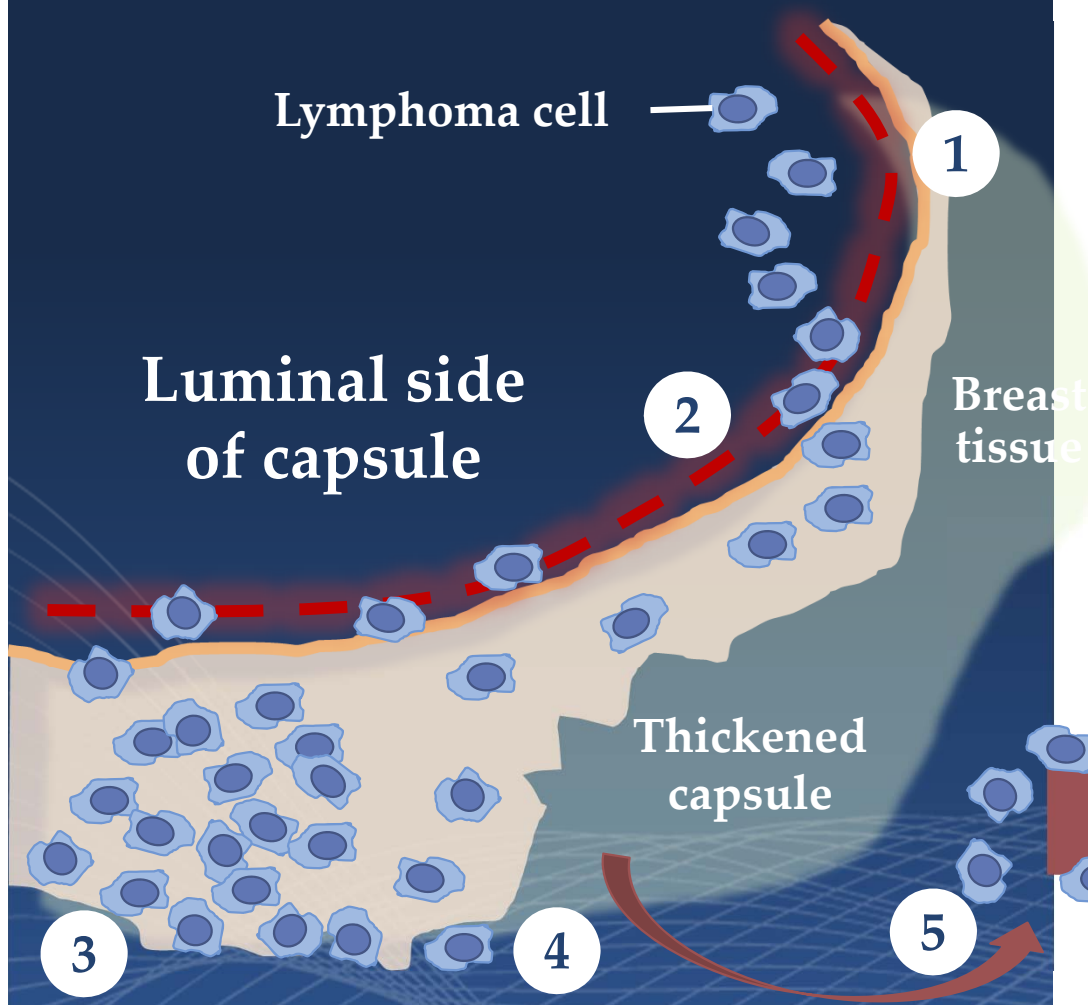
BIA-ALCL As Two Distinct Diseases?

- Laurent 2016
- Effusion-limited (in situ) versus massively infiltrative
- Based on pathology review 19 BIA-ALCL patients to Lymphopath

Breast implant-associated anaplastic large cell lymphoma: two distinct clinicopathological variants with different outcomes

C. Laurent^{1,2*}, A. Delas¹, P. Gaulard^{3,4}, C. Haioun^{4,5}, A. Moreau⁶, L. Xerri⁷, A. Traverse-Glehen⁸, T. Rousset⁹, I. Quintin-Roue¹⁰, T. Petrella¹¹, J. F. Emile¹², N. Amara¹, P. Rochaix¹, M. P. Chenard-Neu¹³, A. M. Tasei¹⁴, E. Menet¹⁵, H. Chomarat¹⁶, V. Costes⁹, L. Andrac-Meyer¹⁷, J. F. Michiels¹⁸, C. Chassagne-Clement¹⁹, L. de Leval²⁰, P. Brousset^{1,2}, G. Delsol^{1,2} & L. Lamant^{1,2}

Solid tumor progression



1

- 35% of cases

2

11%

3

13%

4

25%

5

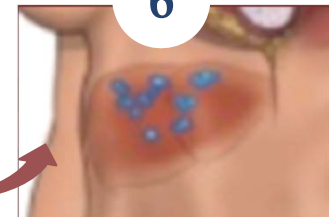
14%

6

3%

Lymph node invasion

6

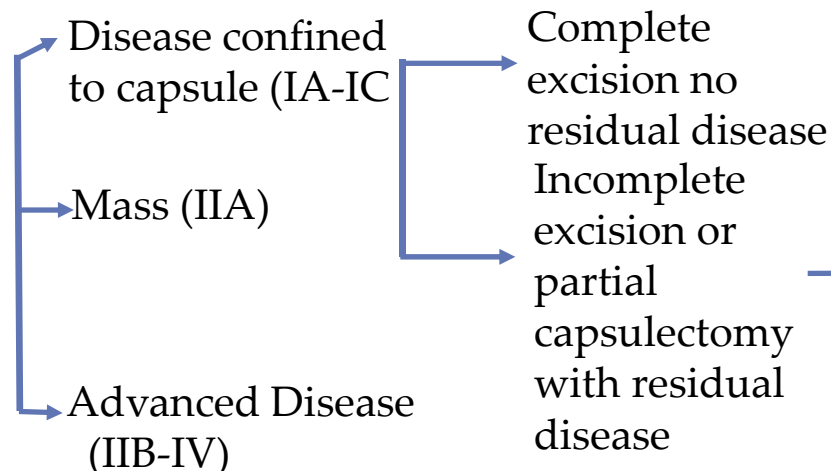


BIA-ALCL behaves like a SOLID tumour
(like lung or breast cancer) and therefore treated surgically¹

Treatment By Staging

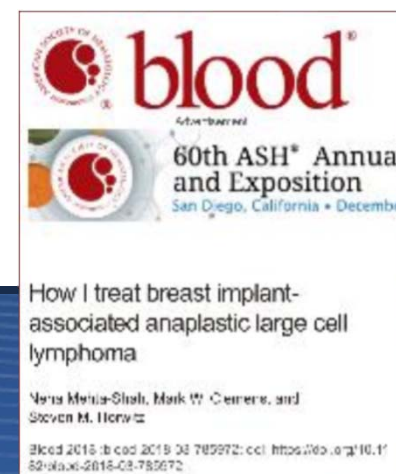
- En bloc resection
- Excision of suspicious lymph nodes
- Complete resection of capsule, including posterior wall

Staging



Adjuvant Treatment

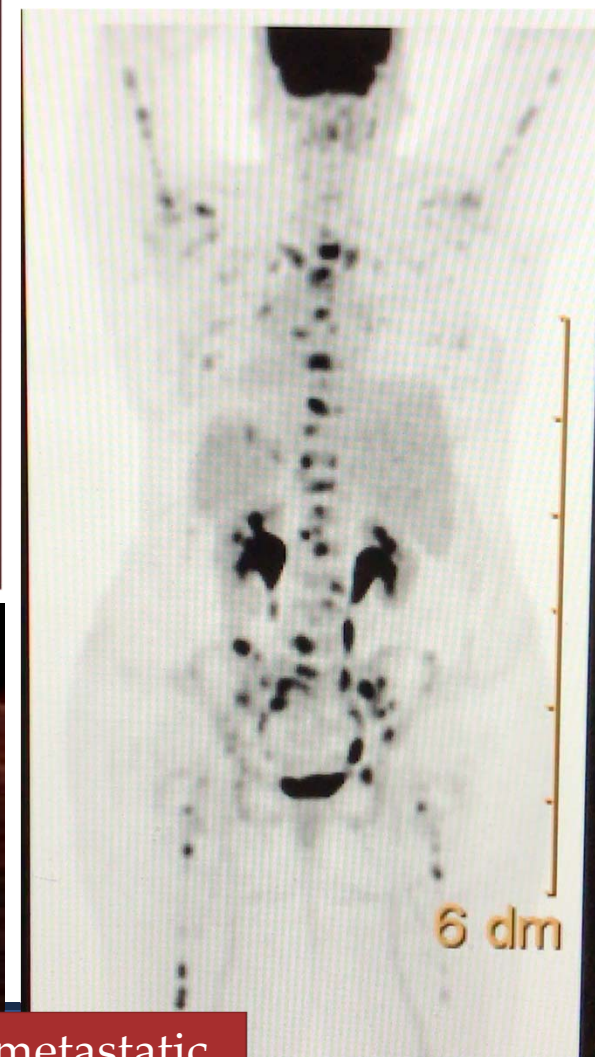
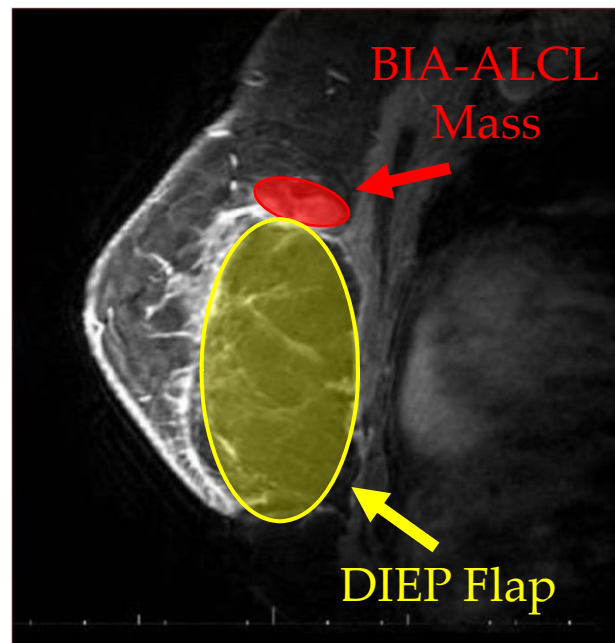
RT (24–36 Gy) local residual disease
 Systemic therapy
 Brentuximab vedotin
 Anthracycline-based systemic ALCL regimens (CHOP, daEPOCH)



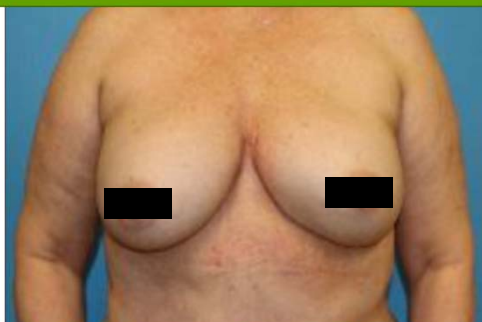
Complete Resection Critical



57yo 22y after cosmetic augmentation

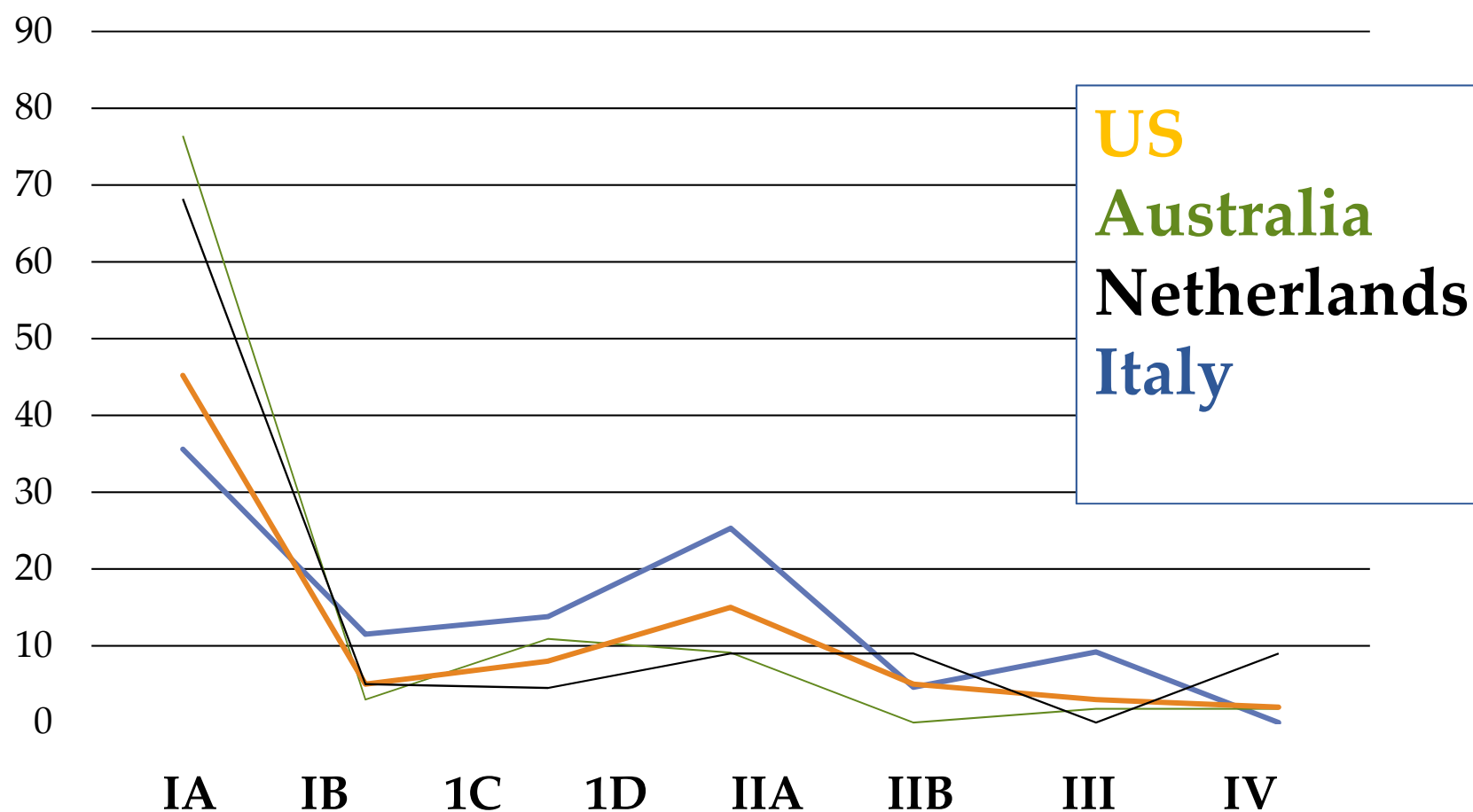


Widely metastatic
BIA-ALCL to bone

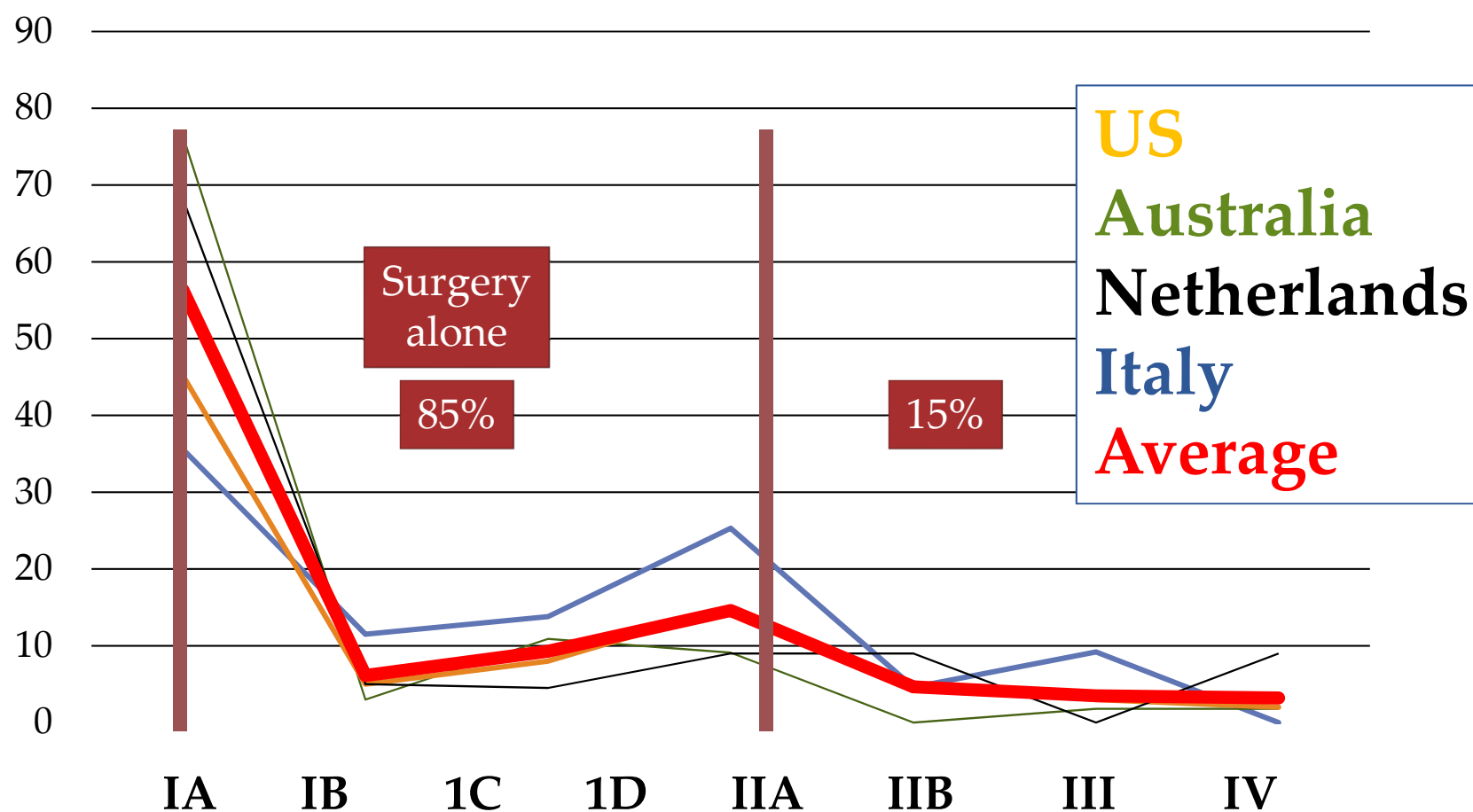


DIEP flap recon of BIA-ALCL

Staging of BIA-ALCL



Staging of BIA-ALCL



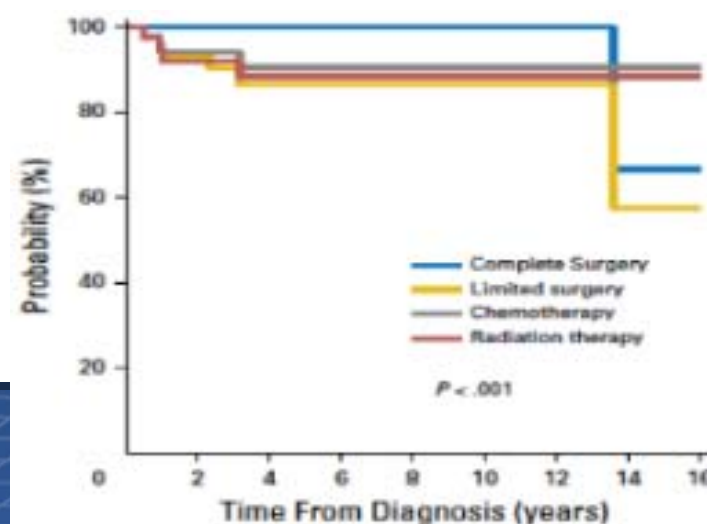
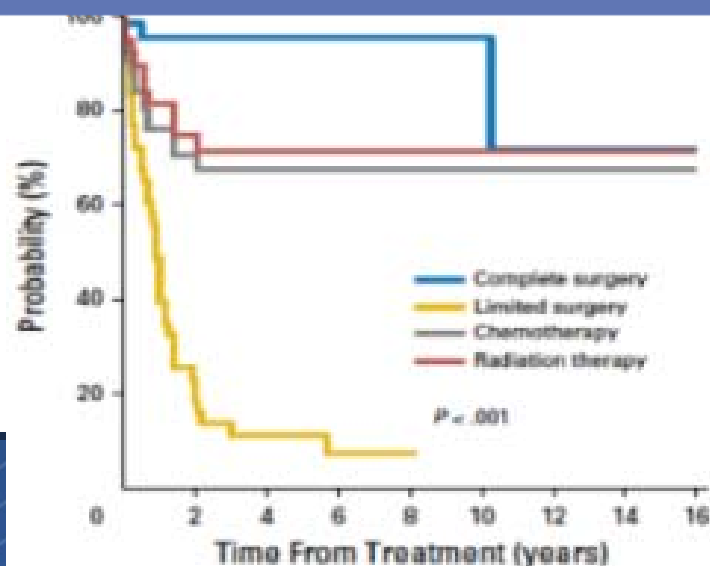
Surgery essential for cure

Treatment after diagnosis	Number	%
Limited surgery	43	52.9
Complete surgery	74	85.1
Radiation	39	44.8
Chemotherapy	51	58.6
ASCT	6	6.9
Immunotherapy	2	2.3

Patients can progress or up-stage if untreated

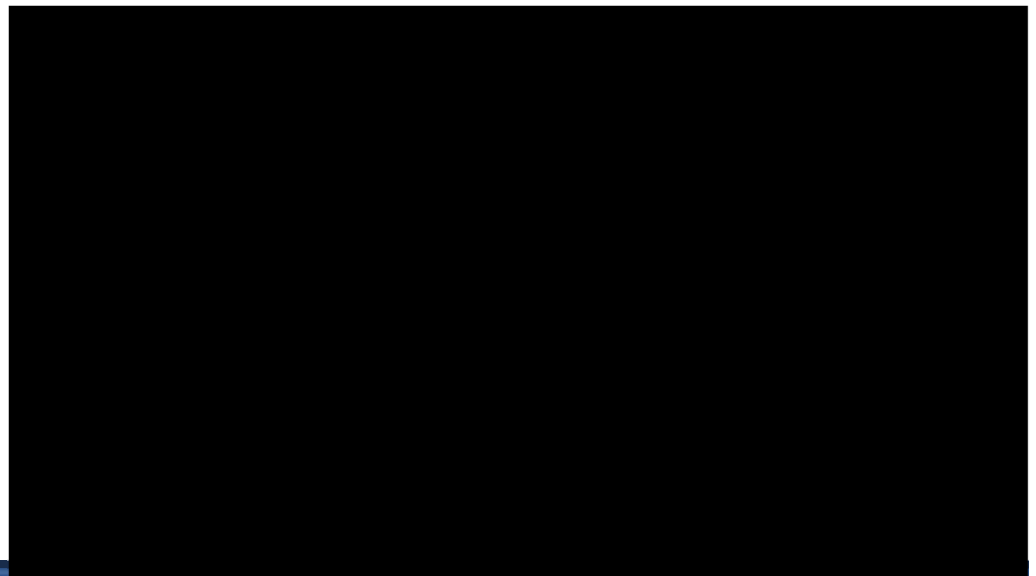
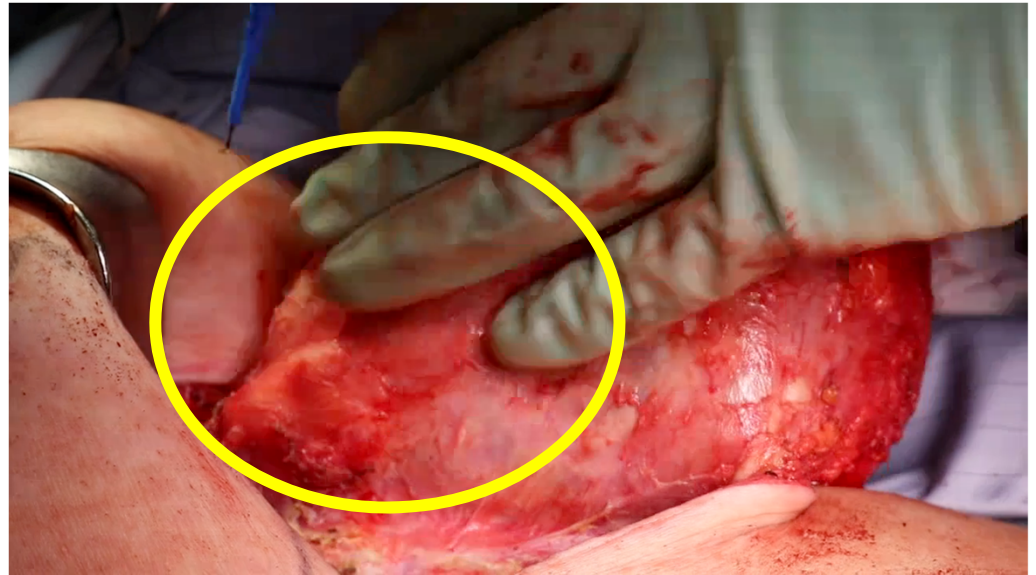
Treatment	1 year (%)	3 years (%)	5 years (%)
Overall	35	50.8	50.8
Limited surgery	60	89	89
Complete surgery	4	4	4
Radiation	18	28	28
Chemotherapy	24	32	32

Event-free survival



Total capsulectomy implant removal

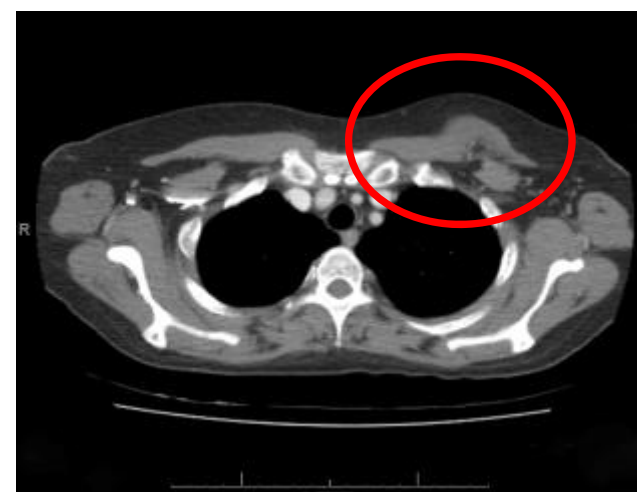
- Oncologic technique¹
- Complete resection of capsule, including posterior wall
- Excision biopsy of lymph nodes



1. NCCN Guidelines. Breast implant-associated ALCL Version 2.2017.

Targeted Immune Therapy - Brentuximab

- Anti-CD30 therapy¹
 - First line treatment of systemic and peripheral ALCL
 - “Preferred” in BIA-ALCL



Deaths rare, Good prognosis if treated

- 19 attributable deaths*^{1,2}
- Delay in treatment or under-treatment
- Deaths most commonly from invasion of chest wall



BREAST

Characteristics and Treatment of Advanced Breast Implant–Associated Anaplastic Large Cell Lymphoma

Meredith S. Collins, MD
Roberto N. Miranda, MD
L. Jeffrey Medeiros, MD
Marcelo Pinheiro Silva de
Meneses, MD
Swaminathan P. Iyer, MD
Charles E. Butler, MD, FACS
Jun Liu, PhD
Mark W. Clemens, MD, FACS

Background: Breast implant–associated anaplastic large cell lymphoma (BIA-ALCL) most commonly follows an indolent course; however, a subset of patients display more advanced disease marked by recurrent and disseminated growth refractory to treatment. This study evaluated outcomes of advanced disease, specifically bilateral disease, lymph node involvement, organ metastasis, and/or disease-related death.

Methods: Published cases of BIA-ALCL from 1997 to 2018 and unpublished cases at the authors' institution were retrospectively reviewed, and patients with advanced disease were selected. Treatment and outcomes were compared

BIA-ALCL US Centralized Tissue Repository



**BOSTON
UNIVERSITY**



UNIVERSITY OF
CAMBRIDGE



THE UNIVERSITY OF TEXAS
**MD Anderson
Cancer Center**

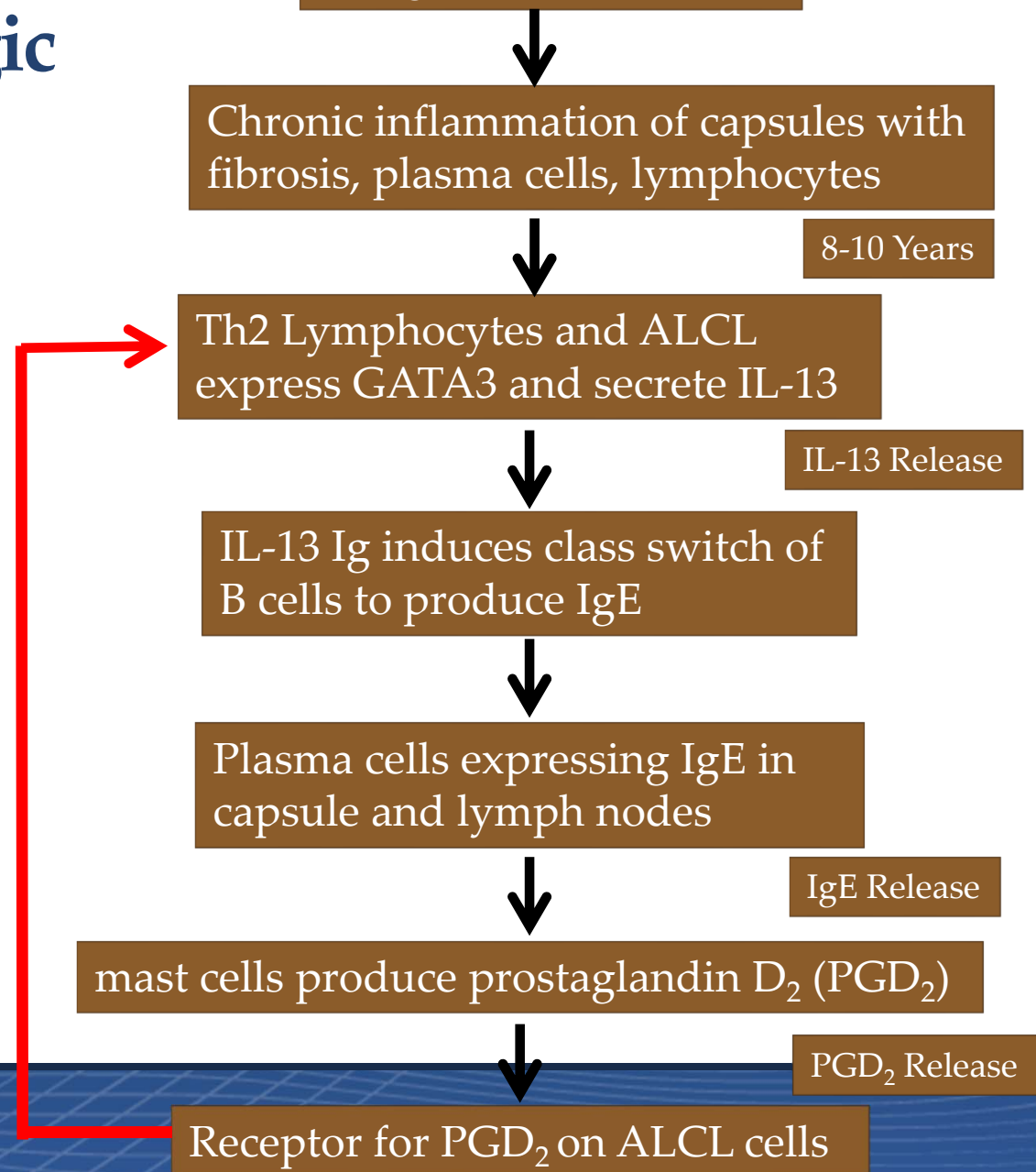


**MACQUARIE
University**

Anand Deva, MacQuarie University, Australia
Marshall Kadin, Boston University, USA
Andrew Feldman, Mayo Clinic, USA
Terence Myckatyn, Wash U, USA
Suzanne Turner, Cambridge University, UK

Mechanism of Allergic Inflammation

- IL-13 is the signature cytokine of allergic inflammation
- Th2 Lymphocytes and ALCL both express GATA3 (Th2 transcription factor) and both secrete IL-13
- Creates Feedback loop



**BOSTON
UNIVERSITY**

THE UNIVERSITY OF TEXAS
**MDAnderson
Cancer Center**

Genetic Predisposition BIA-ALCL

- JAK1/STAT3 Mutations implicated
 - Blombery 2016¹
 - Di Napoli 2016²

bjh correspondence

Targeted next generation sequencing of breast implant-associated anaplastic large cell lymphoma reveals mutations in JAK/STAT signalling pathway genes, *TP53* and *DNMT3A*

Breast implant-associated anaplastic large cell lymphoma (BI-ALCL) is an uncommon neoplasm occurring in women with either cosmetic or reconstructive breast implants (Clemens et al. 2016). Until now, most studies have focused on defining the clinico-pathological features of BI-ALCL, leading to its inclusion as a new provisional entity, a subtype of anaplastic lymphoma kinase (ALK)-negative ALCL, in the revised World Health Organization classification of lymphoid malignancies (Swerdlow et al. 2016). BI-ALCL is characterized by the presence of CD30⁺ large atypical lymphocytes frequently confined to the peri-implant serous fluid. Nevertheless, solid infiltrating masses and cases presenting as

prior literature, and two different prediction algorithms

Whole Exome Sequencing Reveals Activating *JAK1* And *STAT3* Mutations In Breast Implant-Associated Anaplastic Large Cell Lymphoma

Piers Blombery, Ella R. Thompson, Kate Jones, Gisela Mir Anau, Stephen Lade, John F. Markham, Jason Li, Anand Deva, Ricky W. Johnstone, Amit Khot, H. Miles Prince, David Westerman
Haematologica September 2016 101: e387-e390; doi:10.3324/haematol.2016.146118

- Feldman 2018
- 36 cases BIA-ALCL
- All cases triple negative
 - Significant homogeneity
- 100% STAT3 Expression
- STAT3 is mediated by JAK1/STAT3 mutations



Genetic subtyping of breast implant-associated anaplastic large cell lymphomas

Naoki Oishi^{a,b}, Garry Brody^c, Rhett P. Ketterling^a, Christopher A. Sattler^a, Rebecca L. Boddicker^d, Ellen D. McPhail^a, N. Nora Bannani^d, Cristin A. Harless^e, Kuldeep Singh^e, Mark W. Clemens^f, L. Jeffrey Medeiros^g, Roberto N. Miranda^{h*} and Andrew L. Feldman^{h*}

Genetic subtype

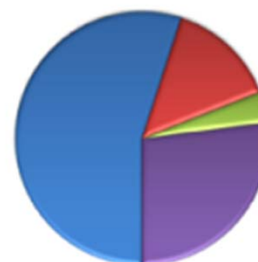
ALCL type

Systemic

Cutaneous

Breast implant-associated

■ ALK
■ DUSP22
■ TP63
■ -/-



Blombery P, et al. Haematologica 2016;10:e387-90;
2. Di Napoli A, et al. Br J Haematol 2016.

Gram Negative Biofilm Endotoxin¹



BREAST

Bacterial Biofilm Infection Detected in Breast Implant-Associated Anaplastic Large-Cell Lymphoma

Honghua Hu, Ph.D.
Khalid Johani
Ahmad Almatroudi
Karen Vickery, Ph.D.,
B.V.Sc.
Bruce Van Natta, M.D.
Marshall E. Kadin, M.D.
Garry Brody, M.D.
Mark Clemens, M.D.

Background: A recent association between breast implants and the development of anaplastic large-cell lymphoma (ALCL) has been observed. The purpose of this study was to identify whether bacterial biofilm is present in breast implant-associated ALCL and, if so, to compare the bacterial microbiome to nontumor capsule samples from breast implants with contracture.

Methods: Twenty-six breast implant-associated ALCL samples were analyzed for the presence of biofilm by real-time quantitative polymerase chain reaction, next-generation sequencing, fluorescent in situ hybridization, and scanning electron microscopy, and compared to 62 nontumor capsule specimens.

1. Hu H, et al. Plast Reconstr Surg 2015;135:319–29.

Shaped Versus Round

- MROC Outcomes, 11 centers
- 822 patients: Shaped vs round
- Similar PROs at two years
- 3x infection rate 6% vs. 2%, ($p=0.03$)

BREAST Outcomes Article

Shaped versus Round Implants in Breast Reconstruction: A Multi-Institutional Comparison of Surgical and Patient-Reported Outcomes

Nima Khavanin, M.D.
Mark W. Clemens, M.D.
Andrea L. Pusic, M.D.,
M.H.S.
Neil A. Fine, M.D.
Jennifer B. Hamill, M.P.H.
H. Myra Kim, Sc.D.
Ji Qi, M.S.
Edwin G. Wilkins, M.D.,
M.S.
John Y. S. Kim, M.D., M.A.

Baltimore, Md.; Houston, Texas;
New York, N.Y.; Chicago, Ill.; and
Ann Arbor, Mich.

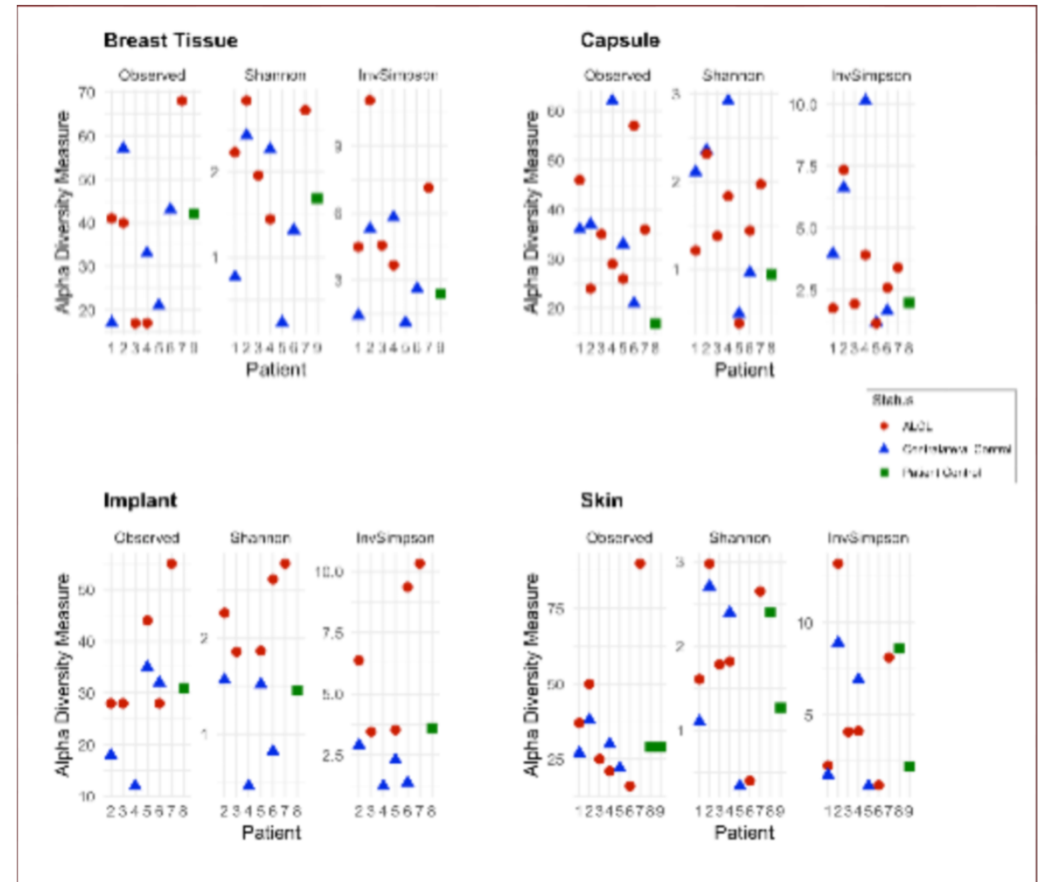
Background: Since the 2012 approval of shaped implants, their use in breast reconstruction has increased in the United States. However, large-scale comparisons of complications and patient-reported outcomes are lacking. The authors endeavored to compare surgical and patient-reported outcomes across implant types.

Methods: The Mastectomy Reconstruction Outcomes Consortium database was queried for expander/implant reconstructions with at least 1-year post-exchange follow-up (mean, 18.5 months). Outcomes of interest included postoperative complications, 1-year revisions, and patient-reported outcomes. Bivariate and mixed-effects regression analyses evaluated the effect of implant type on patient outcomes.

Results: Overall, 822 patients (73.5 percent) received round and 297 patients (26.5 percent) received shaped implants. Patients undergoing unilateral reconstructions with round implants underwent more contralateral symmetry procedures, including augmentations (round, 18.7 percent; shaped, 6.8 per-

Microbiome of BIA-ALCL

- Comparison BIA-ALCL vs. Cap con vs. control
- No distinct microbiome
- Propionibacterium and Staphylococcus spp. Most common in all specimens



1. Walker. Characterization of the Microbiome of Breast Implants and Periprosthetic Tissue in Breast Implant-Associated Anaplastic Large Cell Lymphoma. 2019.



Effect of Anti-Infective Technique on Risk?

- Betadine breast irrigation associated with decreased capsular contracture
- Antibiotic alone may select out resistant bacteria



Macrotextured Breast Implants with Defined Steps to Minimize Bacterial Contamination around the Device: Experience in 42,000 Implants

William P. Adams, Jr., M.D.
Eric J. Culbertson, M.D.
Anand K. Deva, F.R.A.C.S.
Mark R. Magnum, M.D.
J. Plastic Surg. 2013;132:1319-1328

Background: Bacteria/biofilm on breast implant surfaces has been implicated in capsular contracture and breast implant-associated anaplastic large-cell lymphoma (ALCL). Macrotextured breast implants have been shown to harbor more bacteria than smooth or microtextured implants. Recent reports also suggest that

PATIENTS AND METHODS

Eight plastic surgeons in five countries collected their prospective macrotextured implant

The overall experience is reported in Table 2.

A total of 42,035 Biocell implants were placed in 21,650 patients, with a mean follow-up of 11.7 years (range, 1 to 14 years). A total of 704 polyure-

The Role of Bacterial Biofilms in Device-Associated Infection

Anand K. Deva,
M.B.B.S.(Hons.), M.S.
William P. Adams, Jr., M.D.
Karen Vickery, B.V.Sc.
(Hons.), Ph.D.
Sydney, Australia; and Dallas, Texas

Summary: There is increasing evidence that bacterial biofilm is responsible for the failure of medical devices, leading to device-associated infection. As plastic surgeons, we are among the leading users of prostheses in surgery, and it is important that we are kept informed of this growing problem. This article summarizes the pathogenesis of device-associated infection, outlines the evidence for such infection in a number of medical devices, and outlines operative strategies aimed at reducing the risk of bacterial contamination at the time of device deployment. It also outlines strategies under investigation to combat the development of device-associated infection. (*Plast. Reconstr. Surg.* 132: 1319, 2013)

Breast Surgery

Special Topic

Betadine and Breast Implants

Mark L. Jewell, MD; and William P. Adams Jr., MD

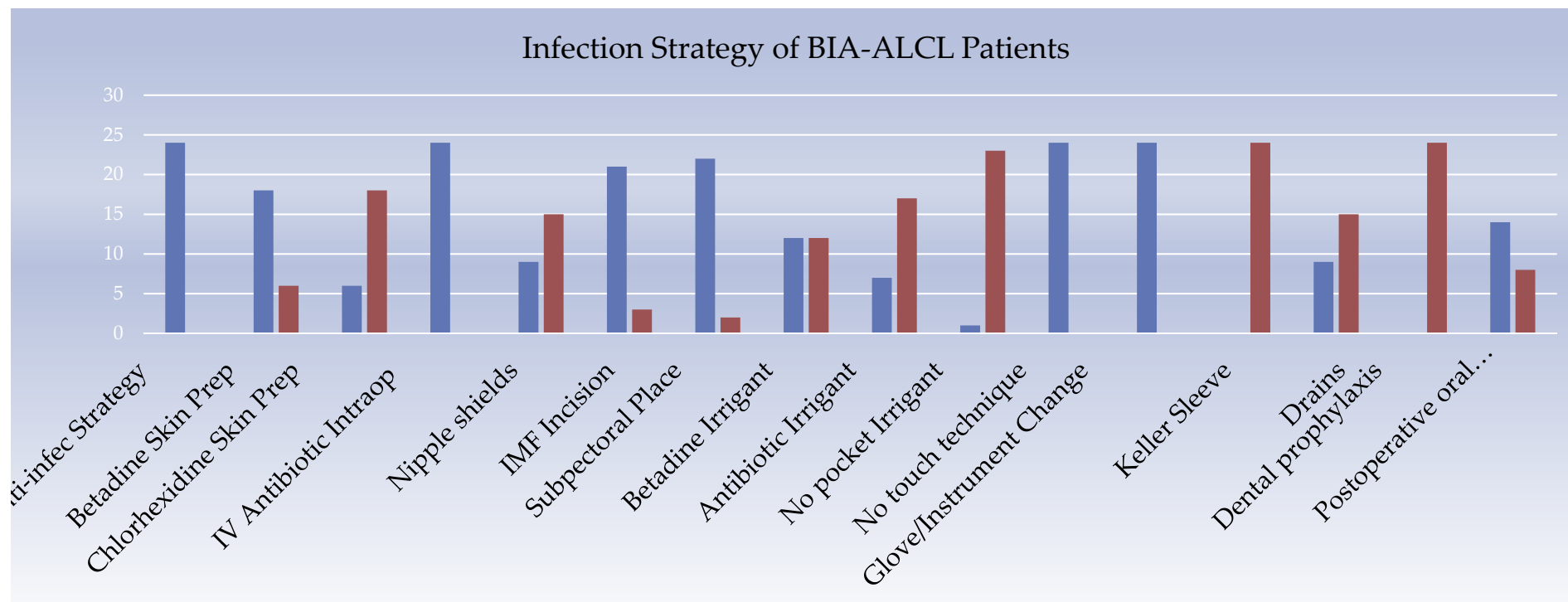
Aesthetic Surgery Journal
2018, Vol. 38(6) 623-626
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DOI: 10.1093/asj/sy044
www.aestheticsurgeryjournal.com

OXFORD
UNIVERSITY PRESS

Deva A, Adams Jr WP, Vickery K. *Plast Reconstr Surg* 2013; 132:1319-1328. Zhadan O, Becker H. Surgical site irrigation in plastic surgery. *Aesthet Surg J.* 2018;38:265-273.

Intraoperative Techniques in BIA-ALCL Patients

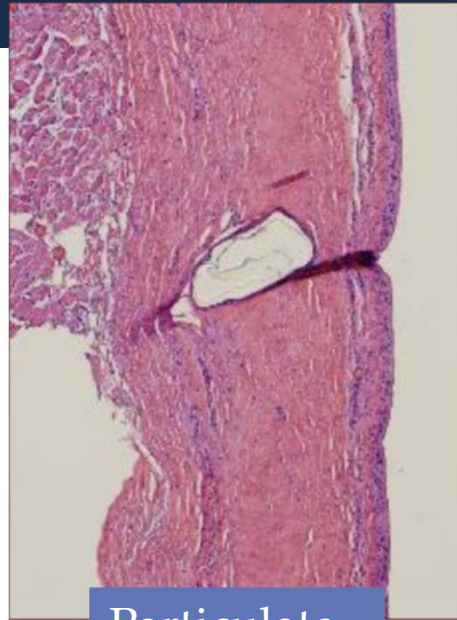
- ◆ If operative technique could affect risk, no strategies have yet been determined



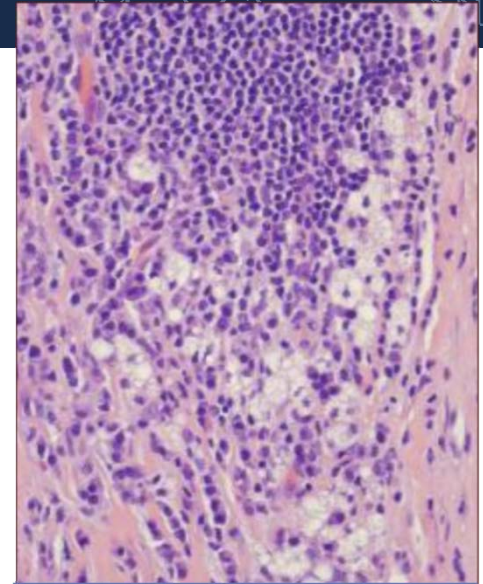
- ◆ N=24 patients
- ◆ Betadine Irrigant: 12 patients (No full strength, 6 50% Strength, 4 25% Strength, 2 “tea colored”)
- ◆ Antibiotic Irrigant: 7 patients (5 Baci/Cef/Gent, 2 Polymyx/Baci)

Macrophage Particulate Digestion

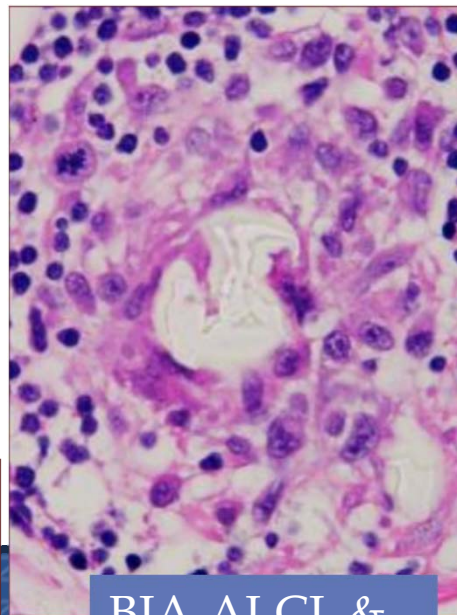
- Chronic macrophage engulfment of particulate
- Development of foamy cells
- Cytokine induced lymphocyte chemotaxis
- Synovitis rare sequelae of implant arthroplasties



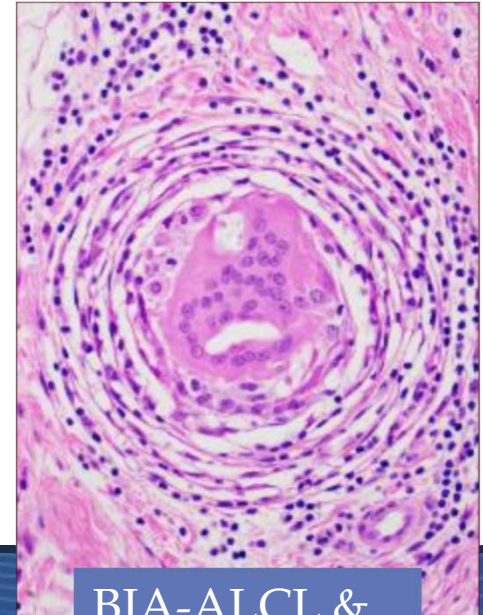
Particulate



Foamy macrophage



BIA-ALCL & particulate



BIA-ALCL & particulate

LONG-TERM RESULTS AFTER SILICONE PROSTHESIS
REPLACEMENT OF THE PROXIMAL POLE OF THE
SCAPHOID BONE IN ADVANCED SCAPHOID NON-UNION
P. HARRINGTON

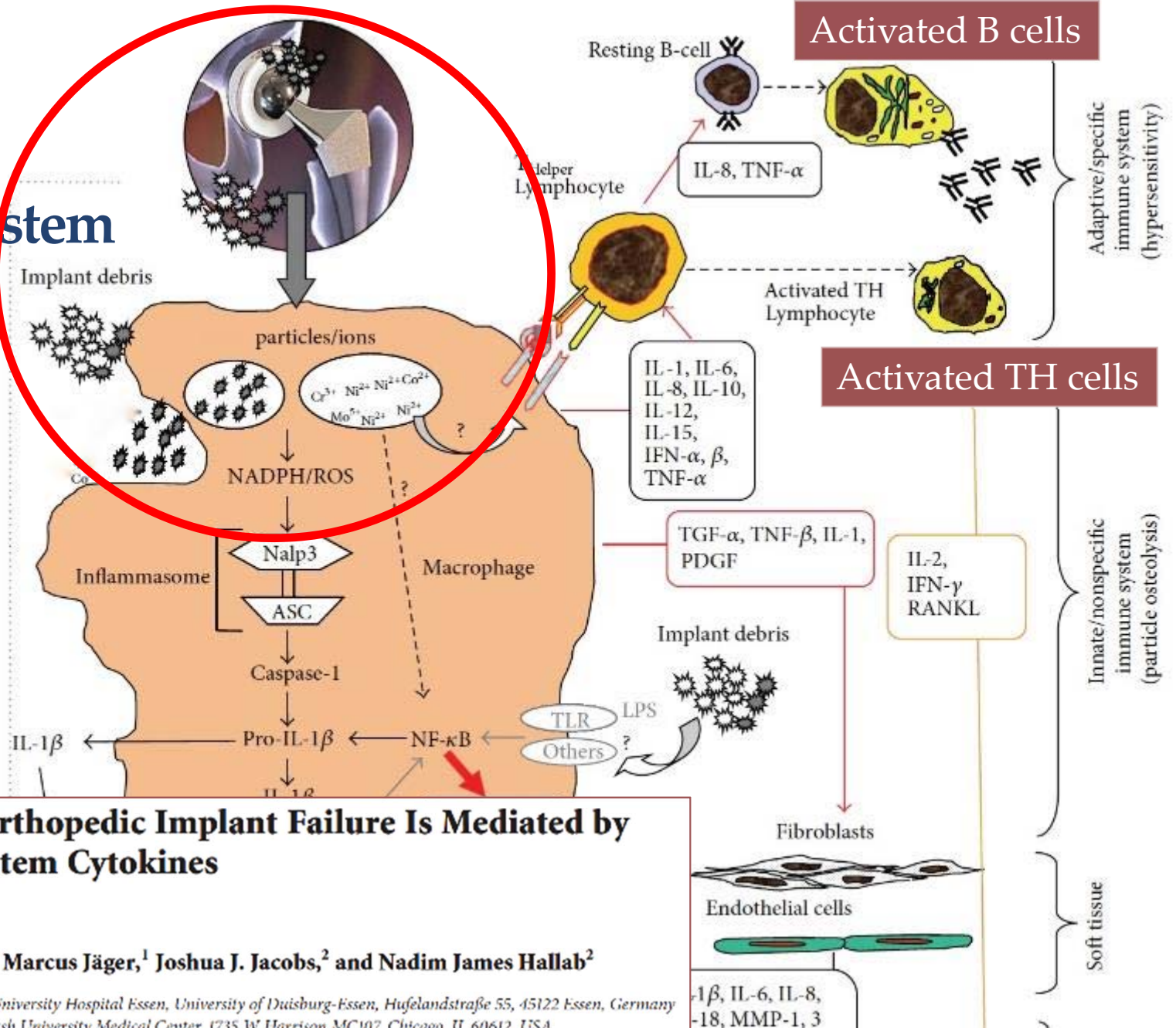
*Research in Arthroscopy, Prosthetics and Rehabilitation Group, Department for Maxillofacial
Plastic and Reconstructive Surgery, at the HAN-Klinik, Aachen, Germany*

Silicone Synovitis

Longer Term Outcome Data and Review of the Literature

David Pugliese, DO, David Bush, MD,† and Thomas Harrington, MD**

Particulate digestion stimulates immune system



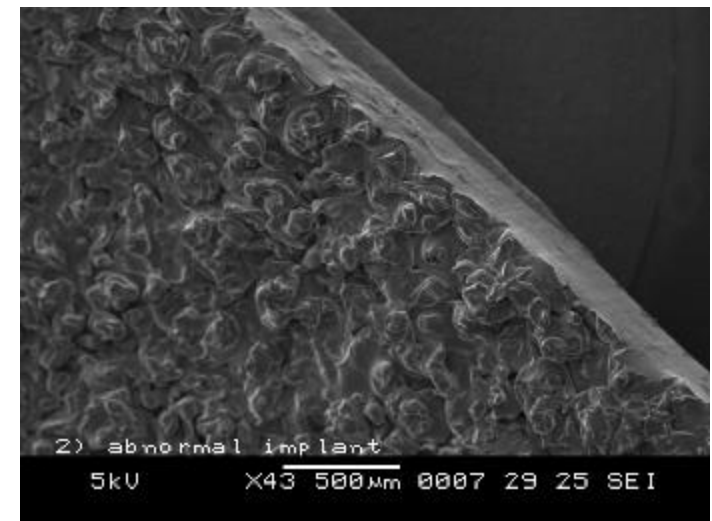
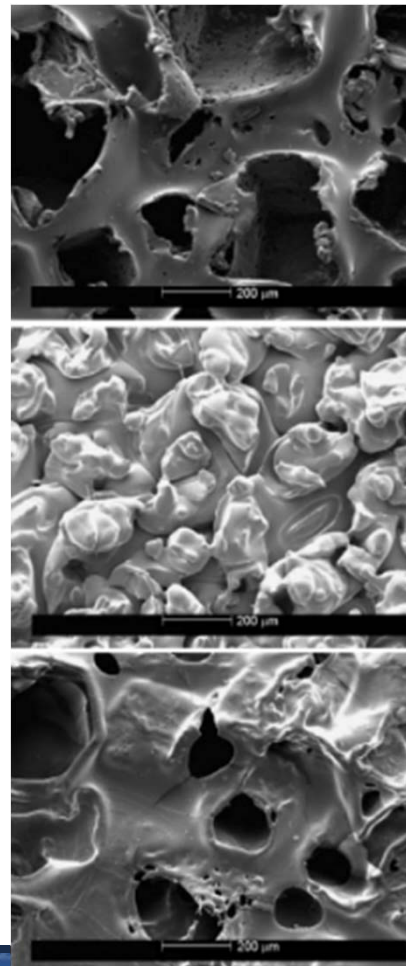
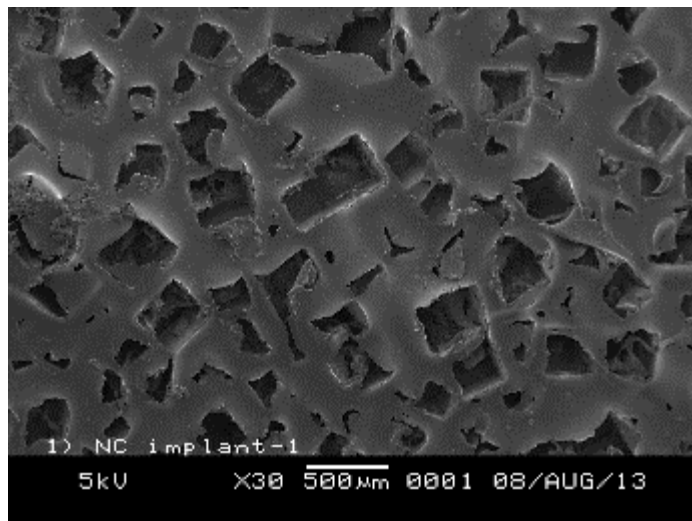
The Pathology of Orthopedic Implant Failure Is Mediated by Innate Immune System Cytokines

Stefan Landgraeber,^{1,2} Marcus Jäger,¹ Joshua J. Jacobs,² and Nadim James Hallab²

ⁱ Department of Orthopaedics, University Hospital Essen, University of Duisburg-Essen, Hufelandstraße 55, 45122 Essen, Germany

² Department of Ophthalmology, Rush University Medical Center, 1735 W. Harrison, MC107, Chicago, IL 60612, USA

Is type of texturing predictive for BIA-ALCL?



Semantics: How to Categorize Texture?

Macro

Aggressive

Mid-texture

Rough

Micro

Nano

Smooth

Biocompatibility Based on Roughness

- Macrophage reaction to texturing
- Significant difference in implant hydrophobicity ($P < 0.0001$)
- Certain surfaces promoted poor macrophage polarization (pro-inflammatory response)
- Hydrophilic less inflammatory and less bacterial adherence



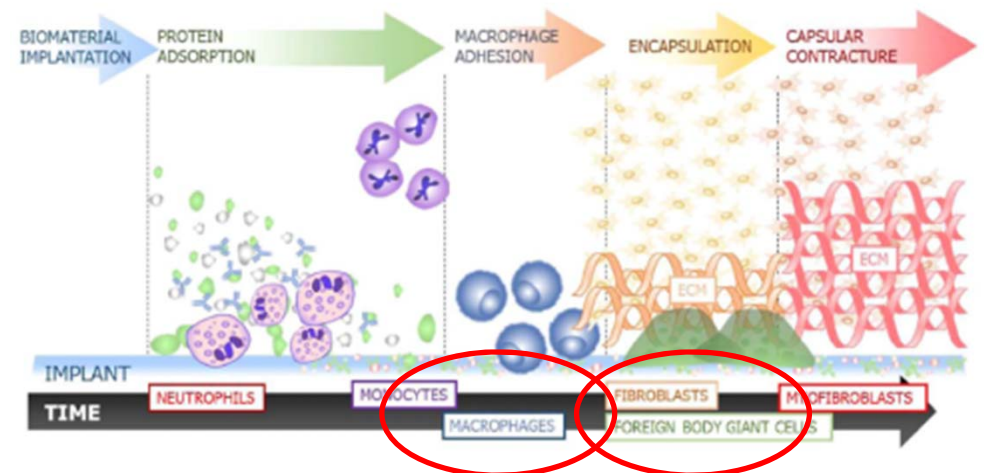
Contents lists available at ScienceDirect

Journal of the Mechanical Behavior of
Biomedical Materials

journal homepage: www.elsevier.com/locate/jmbbm

Functional biocompatibility testing of silicone breast implants and a novel classification system based on surface roughness

S. Barr^{a,b}, E.W. Hill^b, A. Bayat^{b,c,*}



Barr et al. Functional biocompatibility testing of silicone breast implants and a novel classification system based on surface roughness. J Mech Behav Biomed Materials, 2017.

Texture Grading Classifications

Summary of Smooth and Textured Implant Classifications¹

ISO 2018 Average roughness by SEM		ANSM 2018 Average roughness by SEM		Atlan 2018 Surface area by Xray CT		Jones/Deva 2018 SEM, Surface area/roughness by MicroCT		James/Kinney 2018 Bact adhes, Surface area/ roughness by profilometry	
Smooth <10 μm	All smooth, Motiva silk	Smooth	All smooth	Smooth/nanotexture 80-100mm2	All smooth, Motiva Silk and Velvet	1 Minimal	All smooth, Motiva Silk/Velvet	Smooth	All smooth, Motiva Silk/Velvet
Microtextured 10 to 50 μm	Motiva Velvet, B-Lite, Allergan Microcell/ BRST, Mentor Siltex, Sientra True	Microtextured	Arion Micro, Sebbin Micro, Motiva Silk/Velvet	Microtextured 100–200mm2	Mentor Siltex, Allergan Microcell/BRST	2 Low	Mentor Siltex, Nagor	Rough	Allergan Biocell, Mentor Siltex
Macrotextured over 50 μm	Allergan Biocell, Silimed PU, Polytech PU	Macrotextured	Allergan Microcell/Biocell, Mentor Siltex, Eurosilicone Micro, Nagor, Polytech, Silimed	Macrotextured 200–300mm2	Allergan Biocell, Sientra True, Eurosilicone	3 Intermed	Allergan Biocell, Eurosilicone		
				Macrotexture-Plus > 300mm2	Nagor, Polytech	4 High	Polytech PU, Surgitek PU Silimed PU		
Based upon ISO-14607:2018		By ANSM per ISO-14607:2007		Peer Reviewed Scientific Publications					

Abbreviations: mm² millimeters squared, SEM scanning electron microscopy, ISO the International Organization for Standardization, Bact adhes bacterial adhesion

Surface area is a measure of the total area that the outer surface topography of an implant occupies and that interfaces with the patient. Surface roughness is a measure of the average height of the peaks and valleys of an implant surface.

Reference 1: Clemens MW. Bridging the knowledge gap: Commentary on the epidemiology of Breast Implant Associated Large Cell Lymphoma in Australia and New Zealand. Plast Reconstr Surg. 2019.

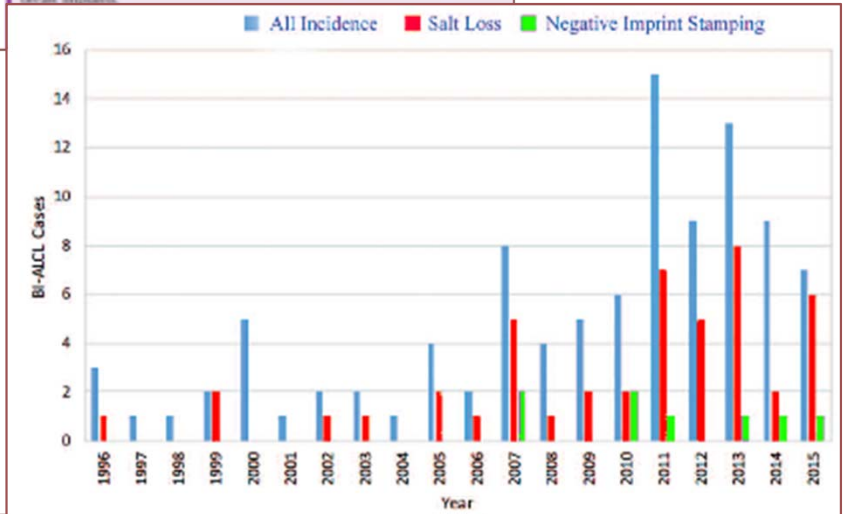
Is 'Macro-texturing' predictive for ALCL?

- Surface area predictive for BIA-ALCL
- Risk may be implant specific

U.S. Epidemiology of Breast Implant-Associated Anaplastic Large Cell Lymphoma

Eric L. Doren, M.D.
Roberto N. Miranda, M.D.
Jesse C. Selber, M.D.,
M.P.H.
Patrick B. Carvey, M.D.
Jun Liu, M.D.
L. Jeffrey Medeiros, M.D.
Charles E. Budetti, M.D.
Mark W. Clemens, M.D.

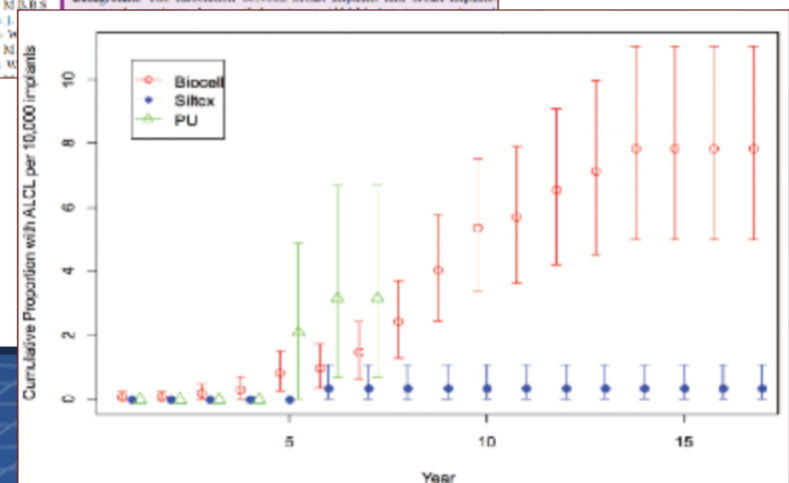
Background: Breast implant-associated anaplastic large cell lymphoma (ALCL) is a distinctive type of T-cell lymphoma that arises around breast implants. Although rare, all cases with adequate history have involved a textured breast implant. The objective of this study was to determine the U.S. incidence and lifetime prevalence of breast implant-associated ALCL in women with textured breast implants.



Breast Implant-Associated Anaplastic Large Cell Lymphoma in Australia and New Zealand: High-Surface-Area Textured Implants Are Associated with Increased Risk

Anna Loch-Wilkinson,
M.B.B.S.
Kenneth L.
Selbert, M.B.B.S.
Rugale, M.
William Tami, M.B.B.S.

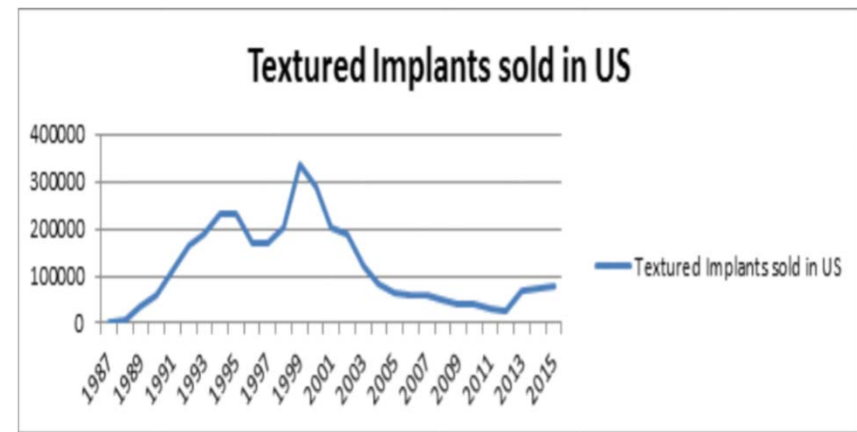
Background: The association between breast implants and breast implant-



Doren et al. PRS, 2017. Loch Wilkinson et al. PRS, 2017.

North America Predominantly Smooth Implants

- Smooth greater than 87% of implant market
- Trending toward smooth implants and TEs
- 3 million textured implants in US circulation



COSMETIC

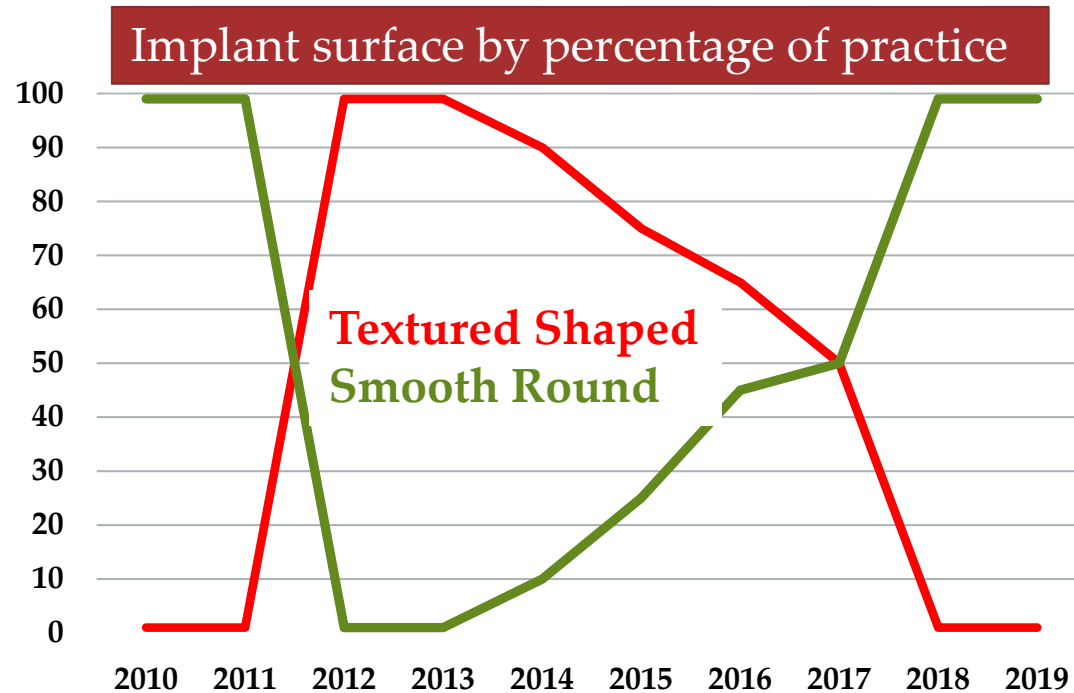
Evolving Trends in Textured Implant Use for Cosmetic Augmentation in the United States

Vickram J. Tandon, M.D.
Michael R. DeLong, M.D.
Tiffany N. Ballard, M.D.
Mark W. Clemens, M.D.

Background: Breast implants have evolved for decades. In 2011, the U.S. Food and Drug Administration identified an association between textured breast implants and breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). The purpose of this study was to identify the trends of textured implants.

My Practice

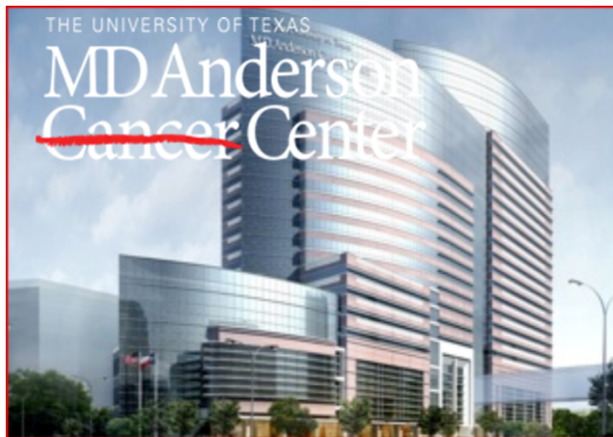
- 2010 – 2019
- 1112 Implant Patients
- 2017 smooth implants



- 64 Cases of BIA-ALCL treated at MDACC

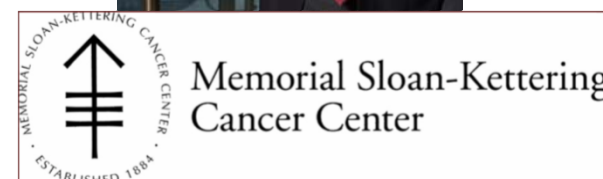
MD Anderson Practice

- 21 Surgeons
- ~960 Implants per year
- ~11,250 over 15 years
- Smooth implant use



MSK Single Surgeon - Cordeiro Experience

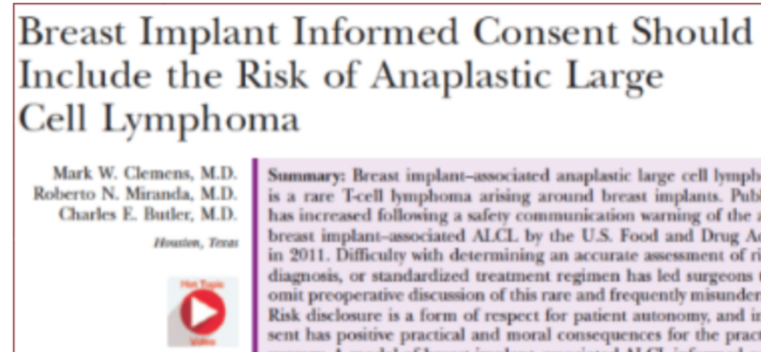
- 26+ Year practice
- 3680 patients, 5768 implants placed
- 5704 breast reconstructions
- 96% textured Biocell practice
- 8 Personal cases of BIA-ALCL (1:460)
- Now recommends smooth implants
 - Bilateral case revision, will replace both



Best practice: Surgery consent

Inform, not frighten¹

- Recommended as part of informed consent for all breast implants
- May include: CE Mark withdrawal and voluntary recall in 35 countries



“The FDA has found that women with breast implants have a very low but increased risk of developing anaplastic large cell lymphoma (ALCL), a rare form of lymphoma, a cancer of the immune system. The main symptoms of ALCL in women with breast implants were a delayed fluid collection around a breast implant, often years after implant placement. Notify your health care provider if you develop any unusual signs or symptoms of your breast implants.”¹

1. Clemens MW, et al. Plast Reconstr Surg 2016;137:1117–22.

Retroactive Notification of Past Patients

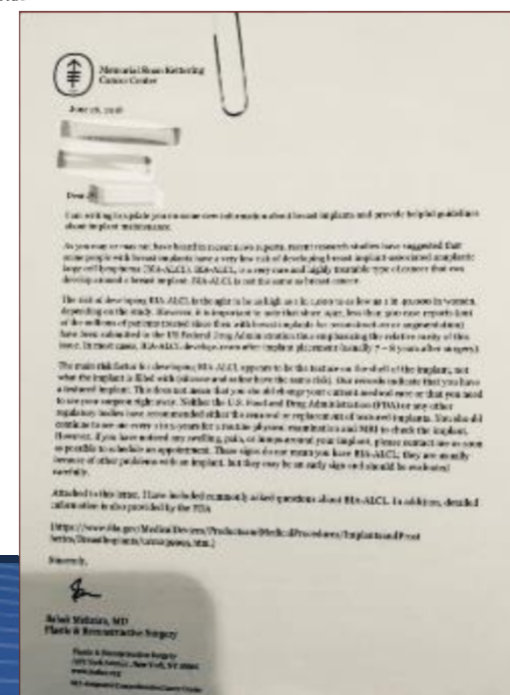
- Example forms available from ASPS
- Memorial Sloan Kettering
- Penn State
 - 1340 patients notified, 100 patients (7.4%) asked for evaluation, 9 (0.67%) requested implant exchange
- Pat McGuire Private Practice
 - 1000 patients notified, 34 (3.4%) asked for evaluation, 1 (0.1%) elective explantation with mastopexy



PennState
College of Medicine



Memorial Sloan-Kettering
Cancer Center



Clemens MW, McGuire PA. Commentary on: Roberts JM et al. A Prospective Approach to Inform and Treat 1,340 Patients at Risk for BIA-ALCL. *Plast Reconstr Surg.* 2019, In press.

Conclusions

- BIA-ALCL is a **lymphoma** based on pathology and clinical course
- NCCN guidelines are the **standard** for the diagnosis and management of BIA-ALCL
- Emerging risk stratification indicates the need for investigation of texture types



Thank you

THE UNIVERSITY OF TEXAS

Mark Clemens, MD

**MD Anderson
~~Cancer~~ Center**



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