

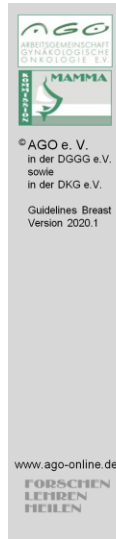


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Guidelines Breast
Version 2020.1

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HEILEN

Diagnosis and Treatment of Patients with early and advanced Breast Cancer

Oncoplastic and Reconstructive Surgery



Plastic-reconstructive aspects after mastectomy

- **Versions 2002–2019:**
Audretsch / Bauerfeind / Blohmer / Brunnert / Dall / Ditsch / Fersis / Friedrich / Gerber / Hanf / Kümmel / Lux / Nitz / Rezaei / Rody / Scharl / Solbach / Thomssen
- **Version 2020:**
Blohmer / Kühn

Pubmed 2003 - 2017

Cochrane data base (z.B. Cochrane Breast Cancer Specialised Register)

Suchbegriffe: breast reconstruction; ... AND random allocation, ... AND cohort study

Einteilung in EBM-Grade nach

Jeremy Howick, et al. "The 2011 Oxford CEBM Evidence Levels of Evidence (Introductory Document)". Oxford Centre for Evidence-Based Medicine. <http://www.cebm.net/index.aspx?o=5653>

Verwendete Guidelines zu Diagnostik und Therapie des Mammakarzinoms

National Institute of Health (NIH) – National Cancer Institute:
<http://www.cancer.gov/cancertopics/pdq/treatment/breast/HealthProfessional/>

American Association of Clinical Oncology (ASCO) and Technology Assessments:
<http://www.asco.org/portal/site/ASCO/menuitem>. (Practice Guidelines),

Canadian Medical Association (CMA): <http://www.cmaj.ca/cgi/content/full/158/3/DC1>

NCCN 2016

Regeln zur Überarbeitung der AGO Empfehlungsdias_Stand 01/ 2019

Definition of oncoplastic surgical procedures

Use of plastic surgical techniques at the time of tumor removal to enable safe resection margins and to preserve aesthetic breast contour.

Focus on favorable scar placement, adequate soft tissue formation, choice of proper reconstruction procedure (including in the context of radiation) and reconstruction of the contralateral side to achieve symmetric results.

1. Oncoplastic breast surgery: comprehensive review. Bertozzi N, et al. 2017; 21(11): 2572-2585.
2. Optimizing breast cancer adjuvant radiation and integration of breast and reconstructive surgery. Kuerer H, et al. ASCO Educational Book 2017

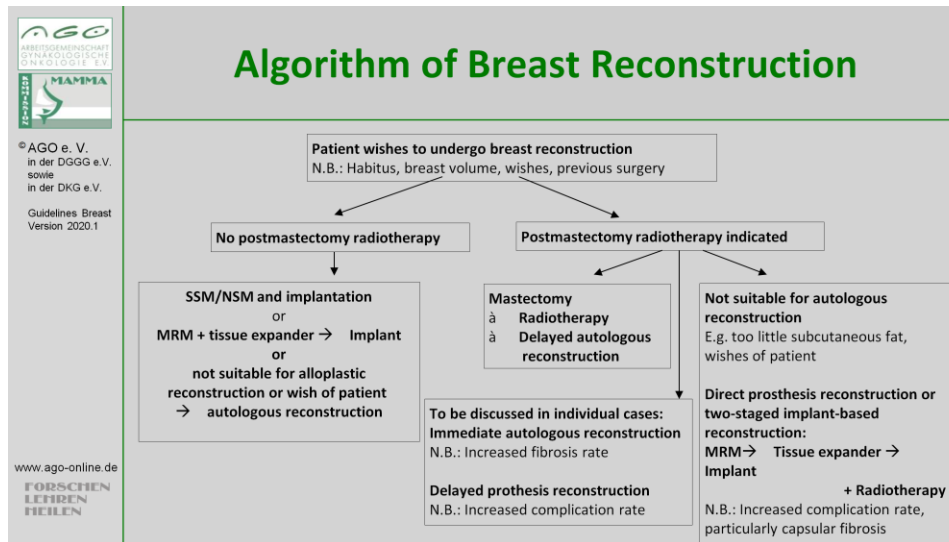
Oncoplastic Breast Conserving Surgery

- Tumor-adapted reduction mammaplasty
- Local flap techniques
- Partial mastectomy with tissue transfer

	Oxford		
	LoE	GR	AGO
2a	2a	B	+
2a	2a	B	+
3b	3b	B	+/-

1. Determinants for patient satisfaction regarding aesthetic outcome and skin sensitivity after breast-conserving surgery. Dahlbäck C, et al. World J Surg Oncol. 2016; 14(1):303.
2. Oncoplastic surgery combining abdominal advancement flaps with volume displacement techniques to breast-conserving surgery for small- to medium-sized breasts. Ogawa T, et al. Breast Cancer. 2016; 23(6):932-938.
3. The role of oncoplastic breast conserving treatment for locally advanced breast tumors. A matching case-control study. Vieira RA, et al. Ann Med Surg (Lond). 2016; 10:61-8.
4. Complications of Oncoplastic Breast Surgery Involving Soft Tissue Transfer Versus Breast-Conserving Surgery: An Analysis of the NSQIP Database. Cil TD, et al. Ann Surg Oncol. 2016; 23(10):3266-71.
5. Comparative study of oncoplastic versus non-oncoplastic breast conserving surgery in a group of 211 breast cancer patients. Calì Cassi L, et al. Eur Rev Med Pharmacol Sci. 2016; 20(14):2950-4.
6. Operative and Oncologic Outcomes in 9861 Patients with Operable Breast Cancer: Single-Institution Analysis of Breast Conservation with Oncoplastic Reconstruction. Carter SA, et al. Ann Surg Oncol. 2016; 23(10):3190-8.

7. Outcomes After Oncoplastic Breast-Conserving Surgery in Breast Cancer Patients: A Systematic Literature Review. De La Cruz L, et al. Ann Surg Oncol. 2016; 23(10):3247-58.
8. Oncoplastic breast conserving surgery and oncological outcome: Systematic review. Yiannakopoulou EC, et al. 2016; 42(5):625-30.
9. Oncoplastic reduction mammoplasty for breast cancer in women with macromastia: Oncological long-term outcomes. Emiroglu M, et al. Asian J Surg. 2017; 40(1):41-47.
10. Patient-reported cosmetic satisfaction and the long-term association with quality of life in irradiated breast cancer patients. M. C. T. Batenburg¹ · M. L. Gregorowitsch¹ · W. Maarse · et al. on behalf of the UMBRELLA study group. Breast Cancer Research and Treatment <https://doi.org/10.1007/s10549-019-05470-y>



1. Radiation and breast reconstruction: Algorithmic approach and evidence-based outcomes. El-Sabawi B, et al. J Surg Oncol. 2016; 113(8):906-12.
2. Breast Reconstruction Following Cancer Treatment. Gerber B, et al. Dtsch Arztebl Int. 2015; 112(35-36):593-600
3. Optimizing breast cancer adjuvant radiation and integration of breast and reconstructive surgery. Kuerer H, et al. ASCO Educational Book 2017; Memorial Sloan Kettering Cancer Center, Fig. 2 und 3
4. What is the optimum timing of postmastectomy radiotherapy in two-stage prosthetic reconstruction: radiation to the tissue expander or permanent implant? Cordeiro PG, et al. Plast Reconstr Surg. 2015

Breast Reconstruction Principles - AGO: ++

- Planning of reconstructive procedure by interdisciplinary tumor board before mastectomy
- Counseling regarding all surgical techniques, including advantages and disadvantages
- Offer second opinion
- Discussion of neoadjuvant treatment if unfavorable tumor-breast-relation
- Consideration of contralateral breast;
 - discuss possible alignment / sequencing surgical procedures to produce symmetry; usually after at least 3-6 months (Caveat: need for post-resections, consider effects of radiotherapy for affected side)
- Preference for less stressful surgical technique with stable long-term esthetic result (prefer BCS over mastectomy)
- Avoid delay of adjuvant therapy due to reconstruction
- Assessment of outcome (e.g. PROM)
- Oncologic safety is not impaired

1. AWMF Leitlinien: S3-LL. Brustrekonstruktion mit Eigengewebe. Registernummer 015 – 075, Stand: 01.04.2015 , gültig bis 31.03.2020
2. Oncoplastic breast surgery: comprehensive review. Bertozzi N, et al. Eur Rev Med Pharmacol Sci. 2017; 21(11):2572-2585.
3. Oncologic safety of nipple-sparing mastectomy in women with breast cancer. Smith BL, et al. J Am Coll Surg
4. Nipple-sparing mastectomy and direct to implant breast reconstruction. Colwell AS, et al. Plast Reconstr Surg. 2017; 140(5S Advances in Breast Reconstruction):44S-50S.
5. Impact of Breast Reconstruction on Time to Definitive Surgical Treatment, Adjuvant Therapy, and Breast Cancer Outcomes. Brice Jabo, Ann C. Lin, Mayada A. Aljehani et al.: [Ann Surg Oncol](#). 2018 Oct;25(10):3096-3105.
6. Patient reported outcome measures (PROMs) following mastectomy with breast reconstruction or without reconstruction: a systematic review Leonardo Z. Cordova, David J. Hunter-Smith, Warren M. Rozen. Gland Surg 2019;8(4):441-451

7. A Meta-analysis of Clinical, Patient-Reported Outcomes and Cost of DIEP versus Implant-based Breast Reconstruction. Ankur Khajuria, Max Prokopenko, Max Greenfield et al. *Plast Reconstr Surg Glob Open* 2019;7:e2486
8. The use of Patient Reported Outcome Measures in assessing patient outcomes when comparing autologous to alloplastic breast reconstruction: a systematic review. Robert Phan, David J. Hunter-Smith, Warren M. Rozen. *Gland Surg* 2019;8(4):452-460

Postmastectomy Reconstruction

	Oxford		
	LoE	GR	AGO
■ Use of silicone gel filled breast implants one step or two steps after expander	2a	B	+
■ Safety comparable to saline implants	2b	B	
■ Autologous tissue reconstruction	2a	B	+
■ Pedicled tissue reconstruction	2a	B	+
■ Free tissue reconstruction (including vascular anastomoses)	2a	B	+
■ Autologous tissue procedure plus implants	3a	C	+

Caveat: BMI >30, smoking status, diabetes, radiotherapy, age, bilateral mastectomy

1. Complications in Postmastectomy Breast Reconstruction: One-year Outcomes of the Mastectomy Reconstruction Outcomes Consortium (MROC) Study. Wilkins EG, et al. Ann Surg. 2016 [Epub ahead of print]
2. Comparison of subcutaneous versus submuscular expander placement in the first stage of immediate breast reconstruction. Zhu L, et al. J Plast Reconstr Aesthet Surg. 2016; 69(4):e77-86.
3. Five-Year Safety Data for More than 55,000 Subjects following Breast Implantation: Comparison of Rare Adverse Event Rates with Silicone Implants versus National Norms and Saline Implants. Singh N, et al. Plast Reconstr Surg. 2017; 140(4):666-679.
4. Short-term safety outcomes of mastectomy and immediate implant-based breast reconstruction with and without mesh (iBRA): a multicentre, prospective cohort study. Shelley Potter, Elizabeth J Conroy, Ramsey I Cutress, Paula R Williamson et al.: [Lancet Oncol.](#) 2019 Jan 9. pii: S1470-2045(18)30781-2.
5. Comparison of Saline Expanders and Air Expanders for Breast Reconstruction. Porter BE1, Vonu PM, Mast BA. Ann Plast Surg. 2019 Dec 19. doi: 10.1097/SAP.0000000000002154. [Epub ahead of print]

Timing of Reconstruction

	Oxford		
	LoE	GR	AGO
▪ Immediate Breast Reconstruction			
▪ Mandatory: SSM/NSM			
▪ Avoidance of a postmastectomy syndrome			
▪ Delayed Breast Reconstruction	3b	B	++
▪ No interference with adjuvant procedures (CHT, RT)			
▪ Disadvantage: loss of skin envelope			
▪ „Delayed-immediate“ Breast Reconstruction	3b	B	+/-

1. Complications After Mastectomy and Immediate Breast Reconstruction for Breast Cancer: A Claims-Based Analysis. Jagsi R, et al. Ann Surg. 2016; 263(2):219-27.
2. What Is the Optimum Timing of Postmastectomy Radiotherapy in Two-Stage Prosthetic Reconstruction: Radiation to the Tissue Expander or Permanent Implant? Maione L, et al. Plast Reconstr Surg. 2016; 138(1):150e-1e.
3. Comparison of Delayed and Immediate Tissue Expander Breast Reconstruction in the Setting of Postmastectomy Radiation Therapy. Ribuffo D, et al. Ann Plast Surg. 2016; 76(6):743-4.
4. Impact of bilateral versus unilateral mastectomy on short term outcomes and adjuvant therapy, 2003–2010: a report from the National Cancer Data Base. Sharpe SM, et al. Ann Surg Oncol. 2014; 21:2920–7.
5. A Comparison of Surgical Complications Between Immediate Breast Reconstruction and Mastectomy: The Impact on Delivery of Chemotherapy-An Analysis of 391 Procedures. Zhong T, et al. Ann Surg Oncol. 2012; 19(2):560-6.
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Cochrane Database Syst Rev. 2011; (7):CD008674.

7. Direct to implant versus two stage tissue expander/implant reconstruction: 2 year risks and patient reported outcomes from a prospective, multicenter study. Srinivasa DR, et al. *Plast Reconstr Surg*. 2017; 140(5):869-877.
8. Quality of life and patient satisfaction after one-stage implant-based breast reconstruction with an acellular dermal matrix versus two-stage breast reconstruction (BRIOS): primary outcome of a randomised, controlled trial. Vera Lidwina Negenborn, Danny Aschwin Young-Afat, Rieky Elise Gustina Dikmans et al: [Lancet Oncol](#). 2018 Sep;19(9):1205-1214.

Timing of implant Based Reconstruction and Radiotherapy

- **Implant Reconstruction (IR)**
 - IR without radiotherapy
 - IR prior to radiotherapy
 - IR following radiotherapy
 - IR following secondary mastectomy (after BCS* with radiotherapy)
 - Perioperative antibiotic prophylaxis (at least 24 hours)

Oxford		
LoE	GR	AGO
2a	B	+
2a	B	++
2a	B	+
2b	B	+/-
2a	B	+/-
2b	B	+


* BCS: Breast Conserving Surgery

1. Postmastectomy Radiation Therapy and Two-Stage Implant-Based Breast Reconstruction: Is There a Better Time to Irradiate? Santosa KB, et al. Plast Reconstr Surg. 2016; 138(4):761-9.
2. What Is the Optimum Timing of Postmastectomy Radiotherapy in Two-Stage Prosthetic Reconstruction: Radiation to the Tissue Expander or Permanent Implant? Maione L, et al. Plast Reconstr Surg. 2016; 138(1):150e-1e.
3. Radiation and breast reconstruction: Algorithmic approach and evidence-based outcomes. El-Sabawi B, et al. J Surg Oncol. 2016; 113(8):906-12.
4. Antibiotic Prophylaxis following Implant-Based Breast Reconstruction: What Is the Evidence? Phillips BT, Halvorson EG. Plast Reconstr Surg. 2016; 138(4):751-7.
5. Discussion: Antibiotic Prophylaxis following Implant-Based Breast Reconstruction: What Is the Evidence? Hunter JG. Plast Reconstr Surg. 2016; 138(4):758-9.
6. Are Prophylactic Postoperative Antibiotics Necessary for Immediate Breast Reconstruction? Results of a Prospective Randomized Clinical Trial. Phillips BT, et al. J Am Coll Surg. 2016; 222(6):1116-24.
7. Prosthetic breast reconstruction in previously irradiated breasts: A meta-analysis. Lee KT, Mun GH. J

Surg Oncol. 2015; 112(5):468-75.

8. A single pre-operative antibiotic dose is as effective as continued antibiotic prophylaxis in implant-based breast reconstruction: A matched cohort study. Townley WA, et al. J Plast Reconstr Aesthet Surg. 2015; 68(5):673-8.
9. Implant breast reconstruction and radiation: a multicenter analysis of long-term health-related quality of life and satisfaction. Albornoz CR, et al. Ann Surg Oncol. 2014; 21(7):2159-64.
10. Acellular dermal matrices and radiotherapy in breast reconstruction: a systematic review and meta-analysis of the literature. Valdatta L, et al. Plast Surg Int. 2014; 472604.
11. A systematic review of morbidity associated with autologous breast reconstruction before and after exposure to radiotherapy: are current practices ideal? Kelley BP, et al. Ann Surg Oncol. 2014; 21(5):1732-8.
12. Reconstruction: before or after postmastectomy radiotherapy? A systematic review of the literature. Berbers J, et al. Eur J Cancer. 2014; 50(16):2752-62.
13. Radiotherapy in implant-based immediate breast reconstruction: risk factors, surgical outcomes, and patient-reported outcome measures in a large Swedish multicenter cohort. Eriksson M, et al. Breast Cancer Res Treat. 2013; 142(3):591-601.
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15. Extended trimethoprim/sulfamethoxazole prophylaxis for implant reconstruction in the previously irradiated chest wall. Mirzabeigi MN, et al. Plast Reconstr Surg. 2012; 129(1):1e-7e.
16. Radiotherapy and breast reconstruction: a meta-analysis. Barry M, Kell MR. Breast Cancer Res Treat. 2011; 127(1):15-22.
17. Determining the outcomes of post-mastectomy radiation therapy delivered to the definitive implant in patients undergoing one- and two-stage implant-based breast reconstruction: A systematic review and meta-analysis. Magill LJ, et al. J Plast Reconstr Aesthet Surg. 2017; 70(10):1329-1335.
18. Impact of Radiotherapy on Complications and Patient-Reported Outcomes After Breast Reconstruction. Jagsi R, et al. J Natl Cancer Inst. 2018; 110(2).
19. Patient-reported cosmetic satisfaction and the long-term association with quality of life in irradiated breast cancer

patients M. C. T. Batenburg · M. L. Gregorowitsch · W. Maarse · A et al. behalf of the UMBRELLA study group. Breast Cancer Research and Treatment <https://doi.org/10.1007/s10549-019-05470-y>



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Radiotherapy and Implant-based Reconstruction

Caveat: High complication rate in combination with radiotherapy (capsular contracture, revision surgery, reconstruction failure, reduced cosmetic outcome and patient satisfaction)

Caveat: Lower patient satisfaction with implant-based reconstruction plus radiotherapy compared to autologous reconstruction plus radiotherapy

LoE 2b B

1. Determining the outcomes of post-mastectomy radiation therapy delivered to the definitive implant in patients undergoing one- and two-stage implant-based breast reconstruction: A systematic review and meta-analysis. Magill LJ, et al. J Plast Reconstr Aesthet Surg. 2017; 70(10):1329-1335.
2. Impact of Radiotherapy on Complications and Patient-Reported Outcomes After Breast Reconstruction. Jagsi R, et al. J Natl Cancer Inst. 2018; 110(2).
3. Impact of Postmastectomy Radiation Therapy in Prepectoral Versus Subpectoral Implant-Based Breast Reconstruction. Catherine J. Sinnott, Sarah M. Persing, Mary Pronovost et al.: [Ann Surg Oncol](#). 2018 Oct;25(10):2899-2908.



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Possible Associations between Implants and rare Diseases

- **US FDA Breast Implant Postapproval Studies (LPAS)**
Long-term Outcomes in 99,993 Patients
(Primary Augmentation: N= 71.937 / Primary Reconstruction: N= 9942)
 - 56% of implants were silicone implants
- **Possible Associations:**
 - Sjogren syndrome: (SIR*8.14)
 - scleroderma: (SIR 7.00)
 - rheumatoid arthritis: (SIR5.96)
 - stillbirth: (SIR4.50)
 - melanoma: (SIR3.71)
- At 7 years, reoperation rate is 11.7% for primary augmentation, and 25% for primary/revision reconstruction.
- One case of BI-ALCL

Associations need to be further analyzed with
patient-level data to provide conclusive evidence !

*Standardized incidence ratio

New Background slide

Statistical Analysis:

LPAS data is expressed relative to normative population rates using standardized incidence ratios (SIRs)

Systemic harm rates in the study population are calculated per 10,000 person-years.

Normative population rates for systemic harms, self-harm, and reproductive outcomes are obtained from the literature; rates reflect LPAS demographics for female sex, age, and race in the United States.

1. [Coroneos CJ](#)¹, [Selber JC](#), [Offodile AC](#) 2nd et al.: US FDA Breast Implant Postapproval Studies: Long-term Outcomes in 99,993 Patients. [Ann Surg.](#) 2019 Jan;269(1):30-36.

Possible Associations between Implants and rare Diseases							
Rare Systemic Harms Compared With the General Population:							
	Manufacturer	Study Events	Study Event Rate (Per 10,000 Person Yr)	General Population Event Rate (Per 10,000 Person Yr)	SIR	SIR 95% CI	P Value
Fibromyalgia	Allergan	9	1.8	112.8	0.02	0.01–0.03	<0.001
	Mentor	307	28.4	112.8	0.25	0.22–0.28	<0.001
Rheumatoid arthritis	Allergan	4	0.8	5.4	0.15	0.04–0.38	<0.001
	Mentor	349	32.2	5.4	5.96	5.35–6.62	<0.001
Scleroderma	Mentor	46	4.2	0.6	7.00	5.12–9.34	<0.001
Sjogren syndrome	Mentor	62	5.7	0.7	8.14	6.24–10.44	<0.001
Systemic lupus erythematosus	Allergan	3	0.6	5.4	0.11	0.02–0.32	<0.001
	Mentor	66	6.0	5.4	1.11	0.86–1.41	0.398
Cancer	Allergan	80	16.0	41.3	0.39	0.31–0.48	<0.001
	Mentor	532	63.8	41.3	1.54	1.42–1.68	<0.001
Breast cancer	Mentor	116	13.9	12.5	1.11	0.92–1.33	0.26
Lung cancer	Mentor	5	0.6	5.2	0.12	0.04–0.27	<0.001
Brain cancer	Mentor	3	0.4	0.6	0.67	0.14–1.95	0.639
Melanoma	Mentor	65	7.8	2.1	3.71	2.87–4.73	<0.001
Neurological disorder	Allergan	18	3.6	22.5	0.16	0.09–0.25	<0.001
	Mentor	394	35.8	22.5	1.59	1.44–1.76	<0.001
Multiple sclerosis	Mentor	47	4.3	2.5	1.72	1.26–2.29	0.001
Myositis	Mentor	17	1.5	0.8	1.88	1.09–3.00	0.018
Allergan follow-up 2 years Mentor follow-up 7 years							

New Background slide

1. [Coroneos CJ](#), [Selber JC](#), [Offodile AC 2nd](#) et al.: US FDA Breast Implant Postapproval Studies: Long-term Outcomes in 99,993 Patients. [Ann Surg.](#) 2019 Jan;269(1):30-36.

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

- Rare disease, 3 % of Non-Hodgkin Lymphomas, 0.04-0.5 % of all malignant breast diseases
- Estimated incidence 0.6-1.2 / 100.000 women with implants (median age: 54 y)
- Mainly associated with textured implants
- Interval to diagnosis: 8 years (median)
- Clinical symptoms
 - Swelling and seroma. (60 %)
 - Solid tumor (17 %)
 - Seroma and solid tumor (20 %)
- Histology: CD30+ / ALK-T-Cell Lymphoma
- Compulsory registration as SAE (§3 MPSV to BfArM)

Reviews

1. Kim, B., Predmore, Z. S., Mattke, S., et al. (2015). Breast Implant-associated Anaplastic Large Cell Lymphoma: Updated Results from a Structured Expert Consultation Process. Plastic and Reconstructive Surgery. Global Open, 3(1), e296. <http://doi.org/10.1097/GOX.0000000000000268>
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6. Brody, G. S., Deapen, D., Taylor, C. R., et al. (2015). Anaplastic large cell lymphoma occurring in women with breast implants: analysis of 173 cases. *Plast Reconstr Surg*, 135(3), 695–705. <http://doi.org/10.1097/PRS.0000000000001033>
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9. Leberfinger, A.N., Behar, B.J., Williams, N.C., et al. (2017). JAMA Surg.Breast Implant-Associated Anaplastic Large Cell Lymphoma: A Systematic Review. 152(12):1161-1168. doi: 10.1001/jamasurg.2017.4026.
10. Kricheldorf, J., Fallenberg, E.M., Solbach, C., et al. (2018). Breast Implant-Associated Lymphoma. *Dtsch Arztebl Int.*;115(38):628-635. doi: 10.3238/arztebl.2018.0628.

BIA-ALCL - Surfaces of Breast Implants

- The cause of BIA-ALCL is not established; however, it has been proposed that lymphomagenesis may be driven by a chronic inflammatory reaction induced by capsule contents or surface. **The risk for BIA-ALCL has been shown to be significantly higher for implants with grade 3 and 4 surfaces.**

Process	Polyurethane foam	Salt Loss (Biocell/Eurosilicone)	Gas Diffusion	Salt Loss (Nagotex)	Imprinting	Smooth/Nano
Surface Area	high	intermediate	intermediate	low	low	minimal
Roughness	high	intermediate	low	low	low	minimal
SURFACE TYPE	4	3	3	2	2	1

- Jones P, Mempin M, Hu H, et al. The functional influence of breast implant outer shell morphology on bacterial attachment and growth. *Plast Reconstr Surg.* 2018;142:837–849
- Collett DJ, Rakhorst H, Lennox P, et al.: Current Risk Estimate of Breast Implant-Associated Anaplastic Large Cell Lymphoma in Textured Breast Implants. *Plast Reconstr Surg.* 2019 Mar;143(3S A Review of Breast Implant-Associated Anaplastic Large Cell Lymphoma):30S-40S. doi: 10.1097/PRS.0000000000005567.
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- Breast Implant-Associated Anaplastic Large Cell Lymphoma in Australia: A Longitudinal Study of Implant and Other Related Risk Factors. Anand K Deva, BSc (Med), MBBS, MS, FRACS, Anna Loch-Wilkinson, MBBS, FRACS, H Miles Prince, MD, FRACP, FRACPA, ADRACMA, MACD et al. © 2019 The American Society for Aesthetic Plastic Surgery, Inc. Reprints and permission: journals.permissions@oup.com

BIA-ALCL– Diagnosis

	Oxford		
	LoE	GR	AGO
▪ Breast US (assessment of new seromas > 1 year after implant insert, solid lesion)	3a	D	++
▪ Mamma-MRT in confirmed cases	3a	D	++
▪ Staging (Imaging, e.g. CT, PET-CT)	3a	D	++
▪ Cytology of late seromas			
▪ - > 50 ml			
▪ - Complete assessment	3a	D	++
▪ - flow-cytology (T-cell clone)			
▪ - BIA-ALCL specific cytologic diagnostic (CD 30+)			
▪ Core needle biopsy in solid lesions	3a	D	++
▪ Lymphoma assessment of resected tissue and histologic staging			
▪ Documentation of the implant (manufacturer, size, volume, surface, Batch-number) and enter in registry	5	D	++

1. Clemens, M. W., Medeiros, L. J., Butler, C. E., et al. (2016). Complete Surgical Excision Is Essential for the Management of Patients With Breast Implant-Associated Anaplastic Large-Cell Lymphoma. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology*, 34(2), 160–168. <http://doi.org/10.1200/JCO.2015.63.3412>
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BIA-ALCL – Therapy

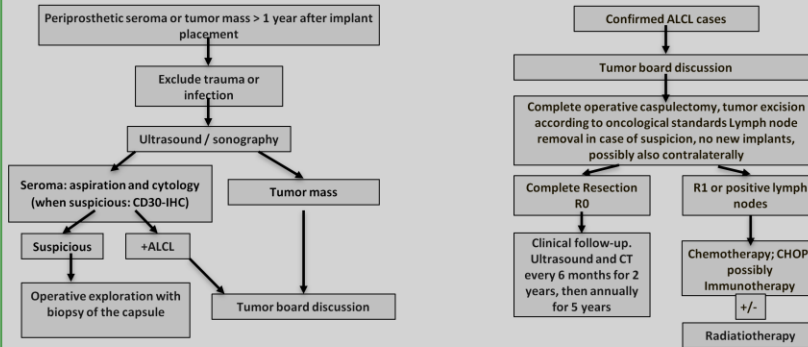
	Oxford		
	LoE	GR	AGO
▪ Implant resection and complete capsulectomy including tumorectomy	3a	C	++
▪ Resection of suspicious lymph nodes, no routine use of Sentinel-Node-Biopsy, no axillarx dissection	4	D	++
▪ Polychemotherapy (e.g. CHOP) in cases of extra capsular extension	4	D	+
▪ Radiotherapy in unresectable tumors	5	D	+/-
▪ Case discussion in an interdisciplinary tumor board in the presence of a specialist for lymphomas	5	D	++


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Breast Implant-Associated Anaplastic Large-Cell Lymphoma (BIA-ALCL) - Summary of the Management (acc. to Noah 2017) -





ARBEITSGEMEINSCHAFT
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Stage Adapted Therapy of BIA-ALCL


TNM	Description
T= tumor extent	
T1	Confined to effusion or a layer on luminal side of capsule
T2	Early capsule infiltration
T3	Cell aggregates or sheets infiltrating the capsule
T4	Lymphoma infiltrates beyond the capsule
N= lymph node	
N0	No lymph node involvement
N1	One regional lympho nodes positive
N2	Multiple regional lymph nodes positive
M= metastasis	
M0	No distant spread
M1	Spread to other organs /distant sides

IA-IC/(IIA): surgical **complete resection** of capsula, implant, suspected nodular lesions and, only if suspicious, regional lymph nodes
no indication for mastectomy, sentinel node extirpation or axillary dissection

IIA/IIB-IV: 2-18%

- surgical complet resection (see above)
- CHO(E)P** (Cyclophosphamide, Vincristin, Doxorubicin, Prednison) +/- Etoposid
- Brentuximab Vedotin** (Adcetris®)
antibody-drug-conjugate (ADC) containing monoclonal antibody against human CD30 antigen and 3-5 molecules of cytostatic drug Monomethylauristatin E
- CHT & stem cell transplantation**
and **radiotherapy** only in for patients with incomplete resection and advanced stages

Clemens MW et al., PRS 2018; https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf



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BIA-ALCL – EUSOMA-Recommendation

- **Despite an increase of BIA-ALCL in association with texture implants the use of textured implants is still permitted!**

„For the moment, textured implants can safely continue to be used with patient's fully informed consent, and that women that have these type of implants already in place don't need to remove or substitute them, which would undoubtedly cause harm to many tens of thousands of women, to prevent an exceptionally rare, largely curable and currently poorly understood disease.“

Cardoso MJ, Wyld L, Rubio IT, et al EUSOMA position regarding breast implant associated anaplastic large cell lymphoma (BIA-ALCL) and the use of textured implants.

Breast. 2019 Apr;44:90-93. doi: 10.1016/j.breast.2019.01.011. Epub 2019 Jan 26.

Tissue Replacement Techniques and Meshes (Details of Implant Reconstruction)

- Autologous tissue
(e.g. autodermal graft, TDAP[§], LDF *)
- Acellular dermal matrix (ADM)
- Synthetic meshes
- Pre- or subpectoral implant position comparable
(with or without meshes or ADM)

Oxford		
LoE	GR	AGO
3b	C	+
2a	B	+ [#]
2b	B	+ [#]
2b	B	+ [#]

§ Thoracodorsal Arteries Perforator flap

* Latissimus dorsi flap

[#] Participation in registry studies recommended

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Lipotransfer

- Lipotransfer following mastectomy and reconstruction
- Lipotransfer after BCS*
- Autologous adipose derived stem cells (ASCs)-enriched fat grafting

Oxford		
LoE	GR	AGO
2a	B	+
2a	B	+
4	C	-

*BCS: Breast Conserving Surgery

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Postmastectomy Pedicled Reconstruction

	Oxford		
	LoE	GR	AGO
Breast reconstruction (BR) with autologous tissue			
▪ TRAM, Latissimus-dorsi-flap (both can be performed as a muscle-sparing technique)	3b	C	+
▪ Delayed TRAM in patients at high-risk	3a	B	+
▪ Ipsilateral pedicled TRAM	3b	A	+
▪ Radiotherapy:			
▪ BR following radiotherapy	2a	B	+
▪ BR prior to radiotherapy	2a	B	+/-
▪ (higher rates of fibrosis, wound healing problems, liponecrosis and reduced aesthetic outcome)			

1. Comparison of Outcomes following Autologous Breast Reconstruction Using the DIEP and Pedicled TRAM Flaps: A 12-Year Clinical Retrospective Study and Literature Review. Knox AD, et al. Plast Reconstr Surg. 2016; 138(1):16-28.
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Free flaps for reconstruction

Type of free flap

- DIEP
- Free TRAM
- SIEA
- Glutealis flaps (SGAP- / IGAP, FCI)
- Free gracilis flap (TMG)

Advantages

- DIEP and free TRAM are potentially muscle-sparing procedures. DIEP has a lower rate of abdominal hernias.

Disadvantages

- Time- and personnel consuming microsurgical procedures
- Intensified postoperative monitoring
- Higher reoperation rate
- Pre-reconstruction radiotherapy increases rate of vascular complications

	Oxford		
	LoE	GR	AGO
2a		B	+
2a		B	+
3a		C	+/-
4		C	+/-
4		C	+/-

1. Effects of Obesity on Postoperative Complications After Breast Reconstruction Using Free Muscle-Sparing Transverse Rectus Abdominis Myocutaneous, Deep Inferior Epigastric Perforator, and Superficial Inferior Epigastric Artery Flap: A Systematic Review and Meta-analysis. Lee KT, Mun GH. Ann Plast Surg. 2016; 76(5):576-84.
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Pedicled versus free tissue transfer

Oxford		
LoE	GR	AGO
3a	A	++

- Muscle-sparing techniques and accuracy of abdominal wall closure lead to low rates of late donor site complications independent of method used
- Autologous abdominal-based reconstructions have highest satisfaction rates (PROM) in all patient groups
- Donor site morbidity (e.g. impaired muscle function) has to be taken into consideration with all flap techniques

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Flap-implant combination

LDF* + Implant

- IR following RT
- IR prior to RT

Additional flap techniques + implant

Advantages:

- TRAM: staged procedure preferable
- Improved implant coverage
- Suitable for irradiated tissue

Disadvantage:

- muscle contraction (LDF)

* LDF = Latissimus dorsi flap

Oxford		
LoE	GR	AGO
2b	C	+
3b	C	+
5	D	-
5	C	+/-

1. A Systematic Meta-analysis of Prosthetic-Based Breast Reconstruction in Irradiated Fields With or Without Autologous Muscle Flap Coverage. Fischer JP, et al. Ann Plast Surg. 2016; 77(1):129-34.
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Skin-/nipple-sparing Mastectomy (SSM/NSM) and Reconstruction

	Oxford		
	LoE	GR	AGO
▪ Skin-/nipple-sparing Mastectomy (SSM/NSM)			
▪ Safe (same recurrence rate as MX)	2b	B	++
▪ Higher QoL for patients	2b	B	++
▪ NAC can be preserved under special conditions	2b	B	++
▪ Feasible after mastopexy / reduction mammoplasty	4	C	++
▪ Use of ICG* to predict necrosis of the skin	1b	B	+
▪ Skin incisions - different possibilities:			
▪ Periareolar			
▪ Hemi-periareolar with/without medial/ lateral extension			
▪ Reduction pattern: „inverted-T“ or vertical			
▪ Inferior lateral approach, inframammary fold			
▪ Lowest incidence of complications	2b	B	+

* ICG = Indocyanine Green

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Risk-reducing bilateral mastectomy for healthy women (RRBM)

	Oxford		
	LoE	GR	AGO
▪ RRBM reduces breast cancer incidence	1b	A	++
▪ RRBM in deleterious BRCA1/2 mutation	2a	B	+*
▪ RRBM in high-risk situation without BRCA 1/2 mutation (individual decision depending on personal- family history and mutational status – e.g. high and moderate-risk genes, Hodgkin lymphoma)	4	D	+/-*
▪ High risk and no BRCA counselling in specialized centre*	5	D	--
▪ Non-directive counselling prior to RR-BM	2b	B	++*
▪ RR-BM should be considered with other risk-reducing surgical options incl. bilateral salpingoophorectomy (BSO) and in the context of pre-existing diseases	2a	A	++*
▪ Further need for education of physicians regarding possibilities and advantages of RRBM	1b	A	++

* Counselling, risk prediction, and follow-up in specialized centers recommended

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Surgical Prevention for Healthy Female *BRCA1/2* Mutation Carriers

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> ▪ Risk-reducing bilateral salpingo-oophorectomy (RR-BSO)** <ul style="list-style-type: none"> ▪ Reduces OvCa incidence and mortality ▪ Reduces overall mortality ▪ Risk-reducing bilateral mastectomy (RR-BM) <ul style="list-style-type: none"> ▪ Reduces BC incidence ▪ Reduces BC mortality in <i>BRCA1</i> mutation carriers*** 	2a	B	++* ++* +* +*

*study participation recommended

** The RRSO is recommended from about 35 years for *BRCA1* and from about 40 years for *BRCA2* mutation carriers, taking into account the age of ovarian cancer diagnosis in the family and the family planning status.

*** No reduction in mortality could be shown for *BRCA2* mutation carriers. RRM counselling should be individualised.

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12. Ye-Lei Xiao, Kang Wang, Qiang Liu, et al.: Risk Reduction and Survival Benefit of Risk-Reducing Salpingo-oophorectomy in Hereditary Breast Cancer: Meta-analysis and Systematic Review. *Clinical Breast Cancer*, Vol. 19, No. 1, e48-65
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Forms of risk-reducing (bilateral) mastectomy (RRBM)

	Oxford		
	LoE	GR	AGO
RRBM reduces breast cancer incidence;** bc-spec mortality also likely reduced			
▪ Simple mastectomy	2b	B	+
▪ RRBM by SSM*	2b	C	+
▪ RRBM by NSM* (NAC# sparing)	2b	C	+
▪ Contralateral prophylactic mastectomy	4	C	+/-

* SSM / NSM: Skin-/Nipple-Sparing Mastectomy

NAC: nipple-areola complex

** depending on prior illnesses, e. g. pre-existing ovarian cancer 1-2% (stage III-IV)

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