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Diagnosis and Treatment of Patients with early and advanced Breast Cancer

Oncoplastic and Reconstructive Breast Surgery



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- **Versions 2002–2024:**
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- **Version 2025:**
Lux / Thill




Definition of Oncoplastic Surgery

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Use of plastic surgical techniques at the time of tumor removal to improve aesthetic and quality of life outcomes without compromising oncological safety.

Focus on favorable scar placement, adequate soft tissue formation, choice of a suitable reconstructive technique (taking radiation therapy into consideration) and contralateral symmetrization.

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AGOGEMEINSCHAFT
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REPERENZ
MAMMA

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Classifications


1. Hoffmann / Wallwiener (2009):
Classification by reconstructive surgery complexity with respect to breast conservation and mastectomy

2. Clough et al. (2010):
Oncoplastic classification for breast conservation according to relative resection volume:
Level 1: < 20% of breast volume resection („simple oncoplastic surgery“) and Level 2 > 20% of breast volume resection with quadrant per quadrant techniques of mastopexy

3. American Society of Society of Breast Surgeons (2019):
Level 1: < 20% breast tissue removed; Level 2: 20–50% of breast tissue removed; Volume replacement: > 50% of breast tissue removed

Hoffmann D et al., BMC 2009; Clough KB et al., Ann Surg Oncol 2010; Chatterjee A et al. Ann Surg Oncol 2019


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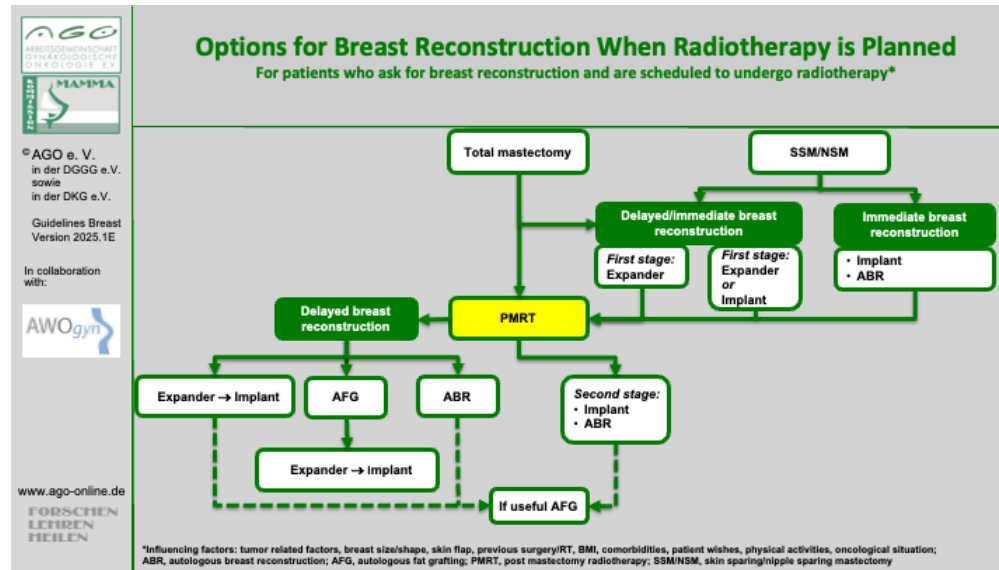
Oncoplastic Breast-Conserving Surgery (OPS)

| | Oxford | |
|---|----------|--------|
| | LoE | GR |
| <ul style="list-style-type: none"> ▪ OPS may replace mastectomy in selected patients <ul style="list-style-type: none"> ▪ also in case of multicentric / multifocal tumors | 2b 2b | B B |
| <ul style="list-style-type: none"> ▪ OPS and BCS have equivalent oncological safety | 2a | B |
| <ul style="list-style-type: none"> ▪ Complication rates of OPS and BCS are similar | 2a | B |
| <ul style="list-style-type: none"> ▪ In breast hypertrophy, tumor-adapted reduction before RT is associated with fewer complications than secondary reduction after RT; however, secondary reduction is still possible in terms of complication rate (major complications) | 3a | B |

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| | |
|---|---|
|  | <h2 style="color: green;">Breast Reconstruction Principles Good Clinical Practice</h2> |
| <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2025.1E</p> <p>In collaboration with:</p>  <p>www.ago-online.de FORSCHEN LEBEN HEILEN</p> | <p style="text-align: center; color: green; font-weight: bold;">AGO: ++</p> <ul style="list-style-type: none"> ▪ Planning of breast reconstruction by interdisciplinary tumor board before mastectomy ▪ Counseling regarding all surgical techniques, including advantages and disadvantages ▪ Preference for autologous reconstruction after radiotherapy or if radiotherapy is planned ▪ Offer second opinion ▪ Discussion of neoadjuvant treatment (if indicated based on tumor biology) in case of unfavorable breast-tumor relation ▪ Consideration of contralateral breast: <ul style="list-style-type: none"> ▪ Discuss symmetrization procedures ▪ Preference for less radical surgical technique with stable long-term aesthetic result (prefer BCS / OPS over mastectomy) ▪ Avoid delay of adjuvant therapy due to reconstruction ▪ Assessment of outcome, e.g. Patient Reported Outcome (PRO) ▪ Oncologic safety is not impaired |


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Mastectomy and Reconstruction Options

| | Oxford | | |
|---|--------|----|-----|
| | LoE | GR | AGO |
| ▪ Heterologous reconstruction* | 2a | B | + |
| ▪ Autologous reconstruction | 2a | B | + |
| ▪ Pedicled flap reconstruction | 2a | B | + |
| ▪ Free flap reconstruction (including vascular anastomoses) | 2a | B | + |
| ▪ Autologous reconstruction combined with implant placement | 3a | C | +/- |
| ▪ AFG prior expander / implant after mastectomy and radiotherapy | 2b | B | +/- |

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

* Documentation in implant registry

Germany: <https://www.bundesgesundheitsministerium.de/implantateregister-deutschland>
Mandatory documentation of breast implants in the Medical Implants Registry begins on 1st July 2024


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Prior reconstruction after mastectomy and radiotherapy


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Timing of Reconstruction

| | Oxford | | |
|---|-----------|----------|-----------|
| | LoE | GR | AGO |
| <ul style="list-style-type: none"> ▪ Immediate breast reconstruction <ul style="list-style-type: none"> ▪ Prevention of postmastectomy syndrome | 3b | B | ++ |
| <ul style="list-style-type: none"> ▪ Delayed breast reconstruction (2-step) <ul style="list-style-type: none"> ▪ No interference with adjuvant (CHT, RT) ▪ Disadvantage: loss of skin envelope | 3b | B | ++ |
| <ul style="list-style-type: none"> ▪ „Delayed-immediate“ breast reconstruction (placeholder before definitive reconstruction) | 3b | B | + |

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| | | Oxford | | |
|---|---|---------------|----|-----|
| | | LoE | GR | AGO |
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| | ▪ Implant reconstruction | | | |
| | ▪ without radiotherapy | 2a | B | ++ |
| | ▪ prior to radiotherapy | 2a | B | + |
| | ▪ following radiotherapy | 2b | B | +/- |
| | ▪ following secondary mastectomy after breast-conserving therapy | 2a | B | +/- |
| ▪ Moderately hypofractionated RT after mastectomy (total dose approx. 40 Gy in approx. 15-16 fractions in approx. 3 to 5 weeks) | 1a | A | ++ | |
| ▪ after breast reconstruction | 1b | B | ++ | |
| Cave: Risk of capsular fibrosis after radiation, especially in cases of prolonged wound healing, prolonged pain, seroma and swelling | | | | |

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| | Oxford | | |
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| | LoE | GR | AGO |
| Heterologous reconstruction: | | | |
| ▪ Perioperative antibiotic prophylaxis (max. 24 h) | 1a | A | + |
| ▪ Extended antibiotic prophylaxis (> 24 h) | 2a | B | + |
| ▪ Prophylactic antibiotic rinse intraoperatively | 2a | B | + |
| ▪ Antibiotic therapy after culture from drainage (week 2) | 3a | C | +/- |
| ▪ Changing gloves before implantation | 4 | C | + |
| ▪ Antiseptic rinse | 2a | B | + |
| Autologous reconstruction: | | | |
| ▪ Perioperative antibiotic prophylaxis (max. 24 h) | 2b | B | + |
| ▪ Extended antibiotic prophylaxis (> 24 h) | 2a | B | +/- |
| ▪ Extended antibiotic prophylaxis > 24 h in as part of AFG | 3b | B | - |

Implant-based reconstruction:

Meta-analyses:

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3. Klifto KM, Rydz AC, Hultmann CS et al. Evidence-Based Medicine: Systemic Perioperative Antibiotic Prophylaxis for Prevention of Surgical-Site Infections in Plastic and Reconstructive Surgery. *Plast Reconstr Surg* 2023 Dec 1;152(6):1154e-1182e.
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Randomized trials: Single-dose vs. 24 h (4 doses):

1. Gahm J, Konstantinidou AL, Lagergren J et al. Effectiveness of Single vs Multiple Doses of Prophylactic Intravenous Antibiotics in Implant-Based Breast Reconstruction. A Randomized Clinical Trial. JAMA Network Open. 2022;5(9):e2231583.

Randomized trials: 24 h vs. until drain removal (implant + ADM):

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Early Cultures and targeted antibiotics:

1. Moyer HR, Sisson KM. The Effect of Early Cultures and Dual-port Expanders on Two-stage, Prepectoral Breast Reconstruction: The 25/25 Study. Plast Reconstr Surg Glob Open. 2024 Jan 8;12(1):e5507. doi: 10.1097/GOX.0000000000005507. eCollection 2024 Jan.

Randomized trials: preoperative vs. no antibiotics:

1. Amland PF, Andenaes K, Samdal F et al. A prospective, double-blind, placebo-controlled trial of a single dose of azithromycin on postoperative wound infections in plastic surgery. Plast Reconstr Surg 1995 Nov;96(6):1378-83

Retrospective cohort studies:

1. Rothe K, Münster N, Hapfelmeier A et al. Does the Duration of Perioperative Antibiotic Prophylaxis Influence the Incidence of Postoperative Surgical-Site Infections in Implant-Based Breast Reconstruction in Women with Breast Cancer? A Retrospective Study. Plast Reconstr Surg 2022 Apr 1;149(4):617e-628e.
2. Ranganathan K, Sears ED, Zhong L et al. Antibiotic Prophylaxis after Immediate Breast Reconstruction: The Reality of Its Efficacy. Plast Reconstr Surg 2018 Apr;141(4):865-877.
3. Avashia YJ, Mohan R, Berhane C et al. Postoperative antibiotic prophylaxis for implant-based breast reconstruction with acellular dermal matrix. Plast Reconstr Surg 2013 Mar;131(3):453-461,
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Exchanging sterile gloves:

1. Perez A, Baumann DP, Viola GM. Reconstructive breast implant-related infections: Prevention, diagnosis, treatment, and pearls of wisdom. *J Infect*. 2024 Aug;89(2):106197. doi: 10.1016/j.jinf.2024.106197. Epub 2024 Jun 13.

Autologous reconstruction:

Meta-analyses:

1. Aldarragi A, Farah N, Warner CM et al. The Duration of Postoperative Antibiotics in Autologous Breast Reconstruction: A Systematic Review and Meta-Analysis. *Cureus* 2023 Jun 19;15(6):e40631
2. Klifto KM, Rydz AC, Hultmann CS et al. Evidence-Based Medicine: Systemic Perioperative Antibiotic Prophylaxis for Prevention of Surgical-Site Infections in Plastic and Reconstructive Surgery. *Plast Reconstr Surg* 2023 Dec 1;152(6):1154e-1182e.

Randomized trials:

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Retrospective cohort studies:

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Aesthetic surgery (reduction mammoplasty, augmentation), meta-analyses:

1. Hardwicke JT, Bechar J, Skillman JM. Are systemic antibiotics indicated in aesthetic breast surgery? A systematic review of the literature. *Plast Reconstr Surg* 2013 Jun;131(6):1395-1403.
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| Tranexamic Acid in Complex Breast Surgery | | | | |
|--|-----------------|---------------|-----------|------------|
| | | Oxford | | |
| | | LoE | GR | AGO |
| Prevention of: | | | | |
| ■ | Hematoma | 2a | B | +/- |
| ■ | Seroma | 2a | B | +/- |
| No increased risk for thromboembolic complications in patients without history of thromboembolic events | | 2a | B | + |
| CAVE: Dosage and application routes (local, i.v., oral) differ between studies, consider history of thromboembolic events | | | | |

Metaanalyses:

TXA topically and intravenously or both in breast surgery:

1. Huynh MNQ, Wong CR, McRae MC et al. The Effects of Tranexamic Acid in Breast Surgery: A Systematic Review and Meta-Analysis. *Plast Reconstr Surg.* 2023 Dec 1;152(6):993e-1004e.

TXA intravenously (breast-conserving surgery, mastectomy +/- reconstruction)

1. Liechti R, van de Wall BJM, Hug U et al. Tranexamic Acid Use in Breast Surgery: A Systematic Review and Meta-Analysis. *Plast Reconstr Surg.* 2023 May;151(5):949-957.

Prospective randomized studies:

Topical TXA / Nipple-sparing mastectomy:

1. Safran T, Vorstenbosch J, Viezel-Mathieu A et al. Topical Tranexamic Acid in Breast Reconstruction: A Double-Blind Randomized Controlled Trial. *Plast Reconstr Surg.* 2023 Oct 1;152(4):699-706.

Topical TXA / Reduction mammoplasty:

1. Plast Reconstr Surg. 2023, Yao A, Wang F, Benacquista T et al. Topical Tranexamic Acid Does Not Reduce The Incidence Of Hematoma In Reduction Mammoplasty: A Double-Blinded, Randomized Placebo-Controlled Trial. Plast Reconstr Surg. 2023 Jul 25. doi: 10.1097/PRS.0000000000010952.

Topical TXA / Mastectomy without reconstruction:

1. Ausen K, Hagen AI, Østbyhaug HS et al. Topical moistening of mastectomy wounds with diluted tranexamic acid to reduce bleeding: randomized clinical trial. BJS Open. 2020 Apr;4(2):216-224
2. Bae J, Lee DDU, Lee KT, et al. The early postoperative effects of rinsing the breast pocket with tranexamic acid in prepectoral prosthetic breast reconstruction. J Plast Reconstr Aesthet Surg. 2024 Feb;89:125-133. doi: 10.1016/j.bjps.2023.12.004. Epub 2023 Dec 11. PMID: 38181633


Systemic TXA / breast-conserving surgery and mastectomy:

1. Oertli D, Laffer U, Haberthuer F et al. Perioperative and postoperative tranexamic acid reduces the local wound complication rate after surgery for breast cancer. Br J Surg. 1994 Jun;81(6):856-9.
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Retrospective Cohort Studies:

1. Sipos K, Kämäräinen S, Kauhanen S. Topical tranexamic acid reduces postoperative hematomas in reduction mammoplasties. J Plast Reconstr Aesthet Surg. 2023 Aug;83:172-179.
2. Weissler JM, Banuelos J, Alsayed A et al. Topical Tranexamic Acid Safely Reduces Seroma and Time to Drain Removal Following Implant-Based Breast Reconstruction. Plast Reconstr Surg Glob Open. 2020 Oct 9;8(9 Suppl):9-10.

3. Weissler JM, Banuelos J, Jacobson SR et al. Intravenous Tranexamic Acid in Implant-Based Breast Reconstruction Safely Reduces Hematoma without Thromboembolic Events. *Plast Reconstr Surg.* 2020 Aug;146(2):238-245.



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Breast Implant-associated Diseases

BIA-ALCL = Breast implant-associated anaplastic large cell lymphoma

BIA-SCC = Breast implant-associated squamous cell carcinoma

SSBI = Systemic Symptoms Associated with Breast Implants
Synonyms:
Breast Implant Illness (BII); Autoimmune syndrome induced by adjuvants (ASIA);
Shoenfeld's syndrome; Silicone implant incompatibility syndrome (SIIS)

1. von Fritschen U, Kremer T, Prantl L et al Breast Implant-Associated Tumors. Geburtshilfe Frauenheilkd. 2023 Jun 6;83(6):686-693

BIA-ALCL

1. Santanelli di Pompeo F, Clemens MW, Paolini G et al. Epidemiology of Breast Implant–Associated Anaplastic Large Cell Lymphoma in the United States: A Systematic Review, *Aesthetic Surgery Journal* 2024 Jan, 44,1 January 2024, NP32–NP40,
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BIA-SCC

1. Niraula S, Katel A, Barua A et al. A Systematic Review of Breast Implant-Associated Squamous Cell Carcinoma. *Cancers (Basel)*. 2023 Sep 12;15(18):4516.
2. Möllhoff N, Ehrl D, Fuchs B et al. Brustimplantat assoziiertes Plattenepithelkarzinom (BIA-SCC) – eine systematische Literaturübersicht [Breast implant-associated squamous cell carcinoma: a systematic literature review]. *Handchir Mikrochir Plast Chir*. 2023 Aug;55(4):268-277.
3. Glasberg SB, Sommers CA, McClure GT. Breast Implant-associated Squamous Cell Carcinoma: Initial Review and Early Recommendations. *Plast Reconstr Surg Glob Open*. 2023 Jun 14;11(6):e5072.
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5. Yadav S, Yadav D, Zakalik D. Squamous cell carcinoma of the breast in the United States: incidence, demographics, tumor characteristics, and survival. *Breast Cancer Res Treat*. 2017 Jul;164(1):201-208.
6. Santanelli di Pompeo F, Firmani G, et al. Breast Implants and the Risk of Squamous Cell Carcinoma of the Breast: A Systematic Literature Review and Epidemiologic Study. *Aesthet Surg J*. 2024 Jun 14;44(7):757-768.

SSBI/BII

1. Cohen Tervaert JW, Martinez-Lavin M et al. Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) in 2023. *Autoimmun Rev*. 2023 May;22(5):103287.
2. McGuire P, Clauw DJ, Hammer J et al. A Practical Guide to Managing Patients With Systemic Symptoms and Breast Implants. *Aesthet Surg J*. 2022 Mar 15;42(4):397-407
3. Atiyeh B, Emsieh S. Breast Implant Illness (BII): Real Syndrome or a Social Media Phenomenon? A Narrative Review of the Literature. *Aesthetic Plast Surg*. 2022 Feb;46(1):43-57.
4. Magnusson MR, Cooter RD, Rakhorst H et al. Breast Implant Illness: A Way Forward. *Plast Reconstr Surg*. 2019 Mar;143(3S A Review of Breast Implant-Associated Anaplastic Large Cell Lymphoma):74S-81S
5. Kabir R, Stanton E, Sorenson TJ, et al. Breast Implant Illness as a Clinical Entity: A Systematic Review of the Literature. *Aesthet Surg J*. 2024 Aug 20;44(9):NP629-NP636
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|---|---|
| | <h2 style="color: green;">Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL)</h2> |
| <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2025.1E</p> <p>In collaboration with:</p> <p>www.ago-online.de FORSCHEN LEBEN HEILEN</p> | <ul style="list-style-type: none"> ▪ Peripheral non-Hodgkin's T-cell lymphoma arising around a textured breast implant or in a patient with a history of a textured surface device ▪ Number of global cases reported as MDR (medical device regulation) to the FDA by 30.06.2023: 1,264 with 63 deaths ▪ Number of global cases reported by the American Society of Plastic Surgeons (ASPS) by 25.11.2024: 1,593 ▪ Approximately 35,000,000 implant carriers worldwide (According to a survey by the International Society of Aesthetic Plastic Surgeons (ISAPS) 2023: 2,174,616 augmentations worldwide were performed) ▪ Prevalence and incidence vary greatly, as the number of women with implants can only be estimated <ul style="list-style-type: none"> ▪ 30.54/10,000 for textured implants (1 case per 3,274 implanted patients) and 6.70/100,000 for implants any type (1 case per 14,925 implanted patients) ▪ The current lifetime risk ranges between 1:355 and 1:86,029 patients with textured implants ▪ Time interval between last implantation and lymphoma diagnosis: 8 years (median) ▪ 5-year-OS 89-92% ▪ Clinical presentation <ul style="list-style-type: none"> • Frequently periprosthetic seroma, breast asymmetry • in rarer cases tumor, regional lymphadenopathy, skin rash and/or capsular contracture ▪ Tumor cells are CD30-positive / ALK-negative ▪ Obligation to notify the BfArM as SAE according to §3 MPSV* <p>* Germany: BfArM https://www.bfarm.de/SharedDocs/Formulare/DE/Medizinprodukte/BIA-ALCL-Meldung.html</p> |

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7. Correction to: Epidemiology of Breast Implant-Associated Anaplastic Large Cell Lymphoma in the United States: A Systematic Review. *Aesthet Surg J.* 2023 Oct 9:sjad324.

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Systematic review (prevalence)

1. Ward JA, Calderbank T, Tang CC, et al. Estimating the prevalence of Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) - a systematic review. *Plast Reconstr Surg.* 2024 Sep 23.

Meta-analysis

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| | | Oxford | | |
|---|--|---------------|-----------|------------|
| | | LoE | GR | AGO |
|  <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2025.1E</p> <p>In collaboration with:</p>  <p>www.ago-online.de FORSCHEN LEBEN HEILEN</p> | <ul style="list-style-type: none"> ▪ Breast ultrasound (assessment of new seromas > 1 year after implant placement, solid lesions, axillary lymph nodes) ▪ Cytology of late seromas <ul style="list-style-type: none"> ▪ Assessment of min. 50 ml ▪ Complete assessment incl. BIA-ALCL specific cytologic diagnostic (CD 30+) ▪ Flow cytometry (T-cell clone) ▪ Core needle biopsy of solid lesions ▪ Breast-MRI in confirmed cases ▪ Staging (PET-CT, alternatively: CT [neck, chest, abdomen, pelvis]) ▪ Lymphoma assessment in resected tissue and histologic staging ▪ Documentation of the implant in the Implant Registry * | 3a | D | ++ |
| | 3a | D | ++ | |
| | 3a | D | ++ | |
| | 3a | D | ++ | |
| | 3a | D | ++ | |
| | 3a | D | ++ | |
| | 5 | D | ++ | |

* Germany: <https://www.bfarm.de/SharedDocs/Formulare/DE/Medizinprodukte/BIA-ALCL-Meldung.html>

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Systematic review

1. Ward JA, Calderbank T, Tang CC, et al. Estimating the prevalence of Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) - a systematic review. *Plast Reconstr Surg*. 2024 Sep 23.

Meta-analysis

1. Elameen AM, AlMarakby MA, Atta TI, Dahy AA. The Risk of Breast Implant-Associated Anaplastic Large Cell Lymphoma; A Systematic Review and Meta-Analysis. *Aesthetic Plast Surg*. 2024 May 9. doi: 10.1007/s00266-024-03956-9. Online ahead of print. PMID: 38724638

| BIA-ALCL – Therapy | | | |
|--|---------------|-----------|------------|
| | Oxford | | |
| | LoE | GR | AGO |
| ▪ Case discussion in a multidisciplinary tumor board in the presence of a lymphoma specialist | 5 | D | ++ |
| ▪ Implant resection and complete capsulectomy including tumorectomy | 3a | C | ++ |
| ▪ Contralateral implant removal and capsulectomy in case of bilateral implants (4-6% bilateral BIA-ALCL) | 4 | D | +/- |
| ▪ Resection of suspicious lymph nodes, no routine use of sentinel node biopsy or axillary lymph node dissection | 4 | D | ++ |
| ▪ Systemic therapy depending on disease stage | 4 | D | + |
| ▪ Radiotherapy in unresectable tumors | 5 | D | +/- |

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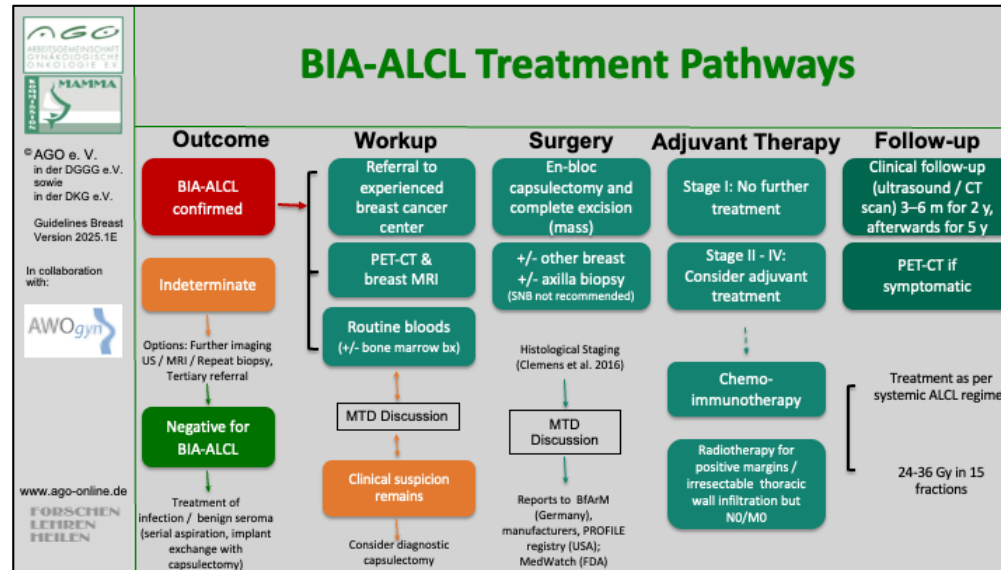
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| TNM Staging of BIA-ALCL | | | | | |
|------------------------------|---------------|--|-------|----------------|--|
| | TNM-Kategorie | Definition | Stage | Definition | |
| Tumor extent (cT/pT) | T1 | Confined to seroma or a layer on luminal side of capsule | IA | T1 N0 M0 | |
| | T2 | Early capsule infiltration | IB | T2 N0 M0 | |
| | T3 | Cell aggregates or sheets infiltrating the capsule | IC | T3 N0 M0 | |
| | T4 | Lymphoma infiltrates beyond the capsule | IIA | T4 N0 M0 | |
| Regional lymph nodes (cN/pN) | N0 | No lymph node involvement | IIB | T1-3 N1 M0 | |
| | N1 | One regional lymph node positive | III | T4 N1-2 M0 | |
| | N2 | Multiple regional lymph nodes positive | IV | T any N any M1 | |
| Metastasis (cM/pM) | M0 | No distant spread | | | |
| | M1 | Spread to other organs or distant sites | | | |



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Guidelines Breast
Version 2025.1E

In Zusammen-
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Breast Implant Capsule-Associated Squamous Cell Carcinoma


- **By March 22, 2023, the FDA had reported 19 cases of BIA-SCC; 30 cases were described up to 11/2023 (Aesthet Surg J. 2024;44(7):757-768)**
- **BIA-SCC occurred approximately 7 to 42 years after initial implant placement (median time 18 years) in aesthetic and reconstructive cases**
- **BIA-SCC was located in the capsule around the breast implant, often in the posterior aspect**
- **There is not a consistent type of implant (textured vs. smooth), content (silicone vs. saline), or location (subglandular vs. retropectoral) that is associated with BIA-SCC**
- **Prevalence 0,61/100,000, lifetime risk 1:164,884**
- **Periprosthetic fluid should be sent for CK5/6 and p63, should be rich in keratin and cytology should display abnormal squamous cells**
- **Initial presentation with breast pain, erythema and swelling**
- **Overall poorer prognosis**
 - **7/21 cases had recurrent cancer within 12 months after definitive resection**
 - **in a review of 18 cases the estimated 12-month mortality rate was 23.8% (calculated from 10 cases with survival data reported)**
- **In this limited cohort it is difficult to ascribe prognostic factors, but extracapsular extension does appear to be a concerning finding.**

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Systemic Symptoms Associated with Breast Implants = SSBI


Breast Implant Illness (BII); Autoimmune syndrome induced by adjuvants (ASIA); Shoenfeld's syndrome; Silicone implant incompatibility syndrome (SIIS);

- Summarize a variety of systemic symptoms that have been reported by some women following reconstruction or augmentation with breast implants, independent of the type of implant, filling, shape or surface characteristics, with an onset anywhere from immediately after implantation to years later
- The most frequent systemic symptoms reported in the FDA MDR database (sorted by frequency more to less common):


| | |
|--------|--|
| > 40% | Fatigue |
| > 30% | Joint pain |
| > 20% | Brain fog, Autoimmune diseases, Hair loss |
| 10-20% | Depression, Rash, Headache, Weight changes |
- Currently SSBI are not recognized as a formal medical diagnosis
- SSBI remain a diagnosis of exclusion, there are no specific tests or defined criteria to characterize it
- Any persistent symptoms reported by patients with breast implants should be evaluated for other medical diseases prior to consider implant removal surgery
- More patients with “cosmetic” vs “reconstructive” reasons (cosmetic, 3864/4109 [94.0%] vs. reconstruction, 245/4109 [5.96%]; $p < 0.001$) experience BII symptoms
- Breast implant explantation can show significant improvement of systemic complaints as well as improvement of overall quality of life

1. <https://www.fda.gov/medical-devices/breast-implants/things-consider-getting-breast-implants#:~:text=Although%20treatable%2C%20there%20is%20a,be%20categorized%20as%20a%20disease> (assessed 25.12.2024)
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3. Medical Device Reports for Systemic Symptoms in Women with Breast Implants <https://www.fda.gov/medical-devices/breast-implants/medical-device-reports-systemic-symptoms-women-breast-implants> (assessed 25.12.2024)
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Kabir R et al. Breast Implant Illness as a Clinical Entity: A Systematic Review of the Literature. *Aesthet Surg J.* 2024 Aug 20;44(9):NP629-NP636

Fifteen studies of 2572 patients reported implant explantation status, with 72.4% of the patients (1861/2572; 72.4%) choosing to remove their implants:


| Implant removal status and patient outcome | |
|--|-------------------------|
| Explantation status | |
| Implant removed | 1861 (1861/2572; 72.4%) |
| Implant removal with total capsulectomy | (1000/1861; 53.7%) |
| Symptom improvement | 658 (658/788; 83.5%) |
| Implant to explant time (years) | 13.1 (6.58) |

1. <https://www.fda.gov/medical-devices/breast-implants/things-consider-getting-breast-implants#:~:text=Although%20treatable%2C%20there%20is%20a,be%20categorized%20as%20a%20disease> (assessed 25.12.2024)
2. <https://www.vdaepc.de/vdaepc-asaps-joint-patient-safety-advisory-for-breast-implant-removal-and-capsulectomy/> (assessed 25.12.2024)
3. Medical Device Reports for Systemic Symptoms in Women with Breast Implants <https://www.fda.gov/medical-devices/breast-implants/medical-device-reports-systemic-symptoms-women-breast-implants> (assessed 25.12.2024)
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BIA-ALCL – EUSOMA-Recommendation

- **Despite an increase of BIA-ALCL in association with textured 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.“

1. Cardoso MJ 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.

| | Oxford | | |
|--|-----------|----------|-----|
| | LoE | GR | AGO |
| ▪ No significant difference between pre- and subpectoral implant position (complication rate) | 2b | B | |
| ▪ Acellular dermal matrix (ADM) | | | |
| ▪ subpectoral | 1b | A | +/- |
| ▪ prepectoral | 2b | B | +/- |
| ▪ Synthetic meshes | | | |
| ▪ subpectoral | 2a | B | +/- |
| ▪ prepectoral | 2b | B | +/- |

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| AFG (autologous fat grafting) | | | |
|--|---|---|---|
| | Oxford | | |
| | LoE | GR | AGO |
| <ul style="list-style-type: none"> ▪ AFG ▪ after mastectomy and radiation and prior reconstruction ▪ after mastectomy and reconstruction ▪ after breast conserving surgery ▪ after autologous reconstruction ▪ as the sole technique for breast reconstruction ▪ Autologous adipose derived stem cells (ASCs)-enriched fat grafting vs. without stem cells | <p>2b</p> <p>2a</p> <p>2a</p> <p>2a</p> <p>1b</p> <p>2a</p> | <p>B</p> <p>B</p> <p>B</p> <p>B</p> <p>B</p> <p>B</p> | <p>+/-</p> <p>+</p> <p>+</p> <p>+</p> <p>+</p> <p>+/-</p> |


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Piatkowski AA et al. Effect of total breast reconstruction with AFG using an expansion device vs. implants on quality of life among patients with breast cancer - a randomized controlled trial, JAMA Surg 2023

- BREAST trial - multicenter, randomized clinical trial with an active control including a 1:1 allocation ratio.
- n = 193, 11/2015 - 11/2021
- Patients receiving postmastectomy radiotherapy were excluded.
- The predefined primary outcome was QoL at 12 months after final surgery. This was measured by the BREAST-Q questionnaire
- 193 patients (mean [SD] age, 49.2 [10.6] years) 18 years or older who desired breast reconstruction were included, 91 patients in the AFG group and 80 in the immediate breast reconstruction (IBR) group received the allocated intervention. In total, 64 women in the AFG group and 68 women in the IBR group completed follow-up. The BREAST-Q scores were higher in the AFG group in all 5 domains and significantly higher in 3: satisfaction with breasts, physical well-being: chest, and satisfaction with outcome. QoL change over time was dependent on the treatment group in favor of AFG. No differences in oncological serious adverse events were found.
- Higher QoL and an increase in QoL scores over time in the AFT group compared with the IBR group. No evidence was found that AFT was unsafe.

Piatkowski AA et al., Effect of Total Breast Reconstruction With Autologous Fat Transfer Using an Expansion Device vs Implants on Quality of Life Among Patients With Breast Cancer - a randomized controlled trial, JAMA Surg 2023,158(5):456-464

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| Pediced Flap Reconstruction | | | |
|--|---------------|-----------|------------|
| | Oxford | | |
| | LoE | GR | AGO |
| ▪ TRAM, latissimus dorsi flap (both can be performed as muscle-sparing techniques) | 2a | C | + |
| ▪ Delayed TRAM in high-risk patients | 3a | B | + |
| ▪ Ipsilateral pediced TRAM | 2a | B | + |
| ▪ Omentum Flap (unilateral) | 3 | B | +/- |
| ▪ Radiotherapy: | | | |
| ▪ Breast reconstruction following radiotherapy | 2a | B | + |
| ▪ Breast reconstruction prior to radiotherapy | 2a | B | +/- |
| (higher rates of fibrosis, wound healing disorders, liponecrosis and reduced aesthetic outcome) | | | |

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Omentum flap

1. Smit JM, Plat VD, van Est MLQ et al. Clinical outcomes of breast reconstruction using omental flaps: A systematic review. *JPRAS Open.* 2024 Jul 31;42:10-21.

| <h2>Free Flaps for Reconstruction</h2> | | | |
|--|--------|----|-----|
| | Oxford | | |
| | LoE | GR | AGO |
| ▪ DIEP (deep inferior epigastric artery perforator) | 2a | B | + |
| ▪ Free TRAM (transverse rectus abdominis myocutaneous) | 2a | B | + |
| ▪ SIEA (superficial inferior epigastric artery) | 3a | C | +/- |
| ▪ Glutealis flaps (SGAP [superior gluteal artery perforator] / IGAP [inferior gluteal artery perforator], FCI [fasciocutaneous infragluteal]) | 4 | C | +/- |
| ▪ Free gracilis flap (TMG , transverse myocutaneous gracilis) | 4 | C | +/- |
| ▪ PAP (profunda artery perforator) | 2a | B | +/- |
| ▪ Omentum Flap | 3a | B | +/- |
| Use of ICG* to assess flap perfusion | 2a | B | + |
| Advantages | | | |
| ▪ DIEP and free TRAM are potentially muscle-sparing procedures. DIEP has a lower rate of abdominal hernias, especially in obese patients | | | |
| Disadvantages | | | |
| ▪ Time- and personnel consuming microsurgical procedures, intensified postoperative monitoring | | | |
| * ICG: indocyanin green | | | |

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DIEP

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PAP


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Omentum flap


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| 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)**
- **Donor site morbidity (e.g. impaired muscle function) has to be taken into consideration with all flap techniques**

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| Skin-/ Nipple-Sparing Mastectomy (SSM / NSM) and Reconstruction | | | |
|---|--------|----|-----|
| | Oxford | | |
| | LoE | GR | AGO |
| <ul style="list-style-type: none"> ▪ Skin-/nipple-sparing Mastectomy (SSM / NSM) <ul style="list-style-type: none"> ▪ Oncologically safe (equivalent recurrence rate as in total mastectomy in suitable patients) ▪ Higher QoL ▪ NAC can be preserved under special conditions <ul style="list-style-type: none"> ▪ Feasible after mastopexy / reduction mammoplasty ▪ Use of ICG* to predict skin necrosis ▪ Skin incisions → different possibilities: <ul style="list-style-type: none"> ▪ Periareolar ▪ Hemi-periareolar with / without medial / lateral extension ▪ Reduction pattern: „inverted-T“ or vertical ▪ Inferior lateral approach, inframammary fold <ul style="list-style-type: none"> ▪ Lowest incidence of complications | | | |
| | 2a | B | ++ |
| | 2b | B | ++ |
| | 2b | B | ++ |
| | 4 | C | ++ |
| | 1b | B | + |
| | 2b | B | + |

* ICG = Indocyanine Green


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Guidelines Breast
Version 2025.1E

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arbeit mit:



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Mastectomy + Reconstruction

Risk of complications with the addition of radiotherapy

| Autologous reconstruction | | Implant-based reconstruction | |
|---------------------------|---|------------------------------|---|
| Endpoint | Risk Ratio with addition of radiotherapy (95%-CI) | Endpoint | Risk Ratio with addition of radiotherapy (95%-CI) |
| Wound infection | 1.14 (NA) | Wound infection | 2.49 (1.43,4.35) |
| Secondary surgery | 1.62 (1.06, 2.48) | Secondary surgery | 1.64 (1.17-2.31) |
| Reconstructive failure | 0.80 (NA) | Reconstructive failure | 2.89 (1.30,6.39) |
| Volume loss | 8.16 (4.26,15.63) | | |
| Fat necrosis | 1.91 (1.45, 2.52) | | |
| | | Capsular contracture | 5.17 (1.93,13.80) |
| | | ME skin flap nekrosis | 1.62 (1.27, 2.08) |
| | | Implant extrusion | 3.44 (2.18, 5.43) |

Further risks of autologous reconstruction:
Distorsion of breast shape, fibrosis, vascular complications
Autologous reconstruction is favored in terms of patient satisfaction and and assessment of the aesthetic outcome.

NA: not available

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5;9(11):e3910

| | | Oxford | | |
|-------------------------------|--|--------|----|-----|
| | | LoE | GR | AGO |
| Prevention | | | | |
| ▪ | Textured implantats (Caveat: BIA-ALCL) | 1a | A | + |
| ▪ | Acellular Dermal Matrix (ADM) vs. nil | 2a | B | + |
| ▪ | Synthetic mesh vs. nil | 3a | C | + |
| ▪ | Preference of a prepectoral implant position (for post-mastectomy radiation) | 2a | B | + |
| ▪ | Topical antibiotics / antiseptics | 2a | B | + |
| ▪ | PVP (Povidone-Iodine) | 2a | B | +/- |
| ▪ | Leukotriene-antagonists | 2a | B | +/- |
| ▪ | Breast massage | 3a | C | - |
| Surgical interventions | | | | |
| ▪ | Capsulectomy | 2a | B | + |
| ▪ | Capsulotomy (Caveat: exclusion of BIA-ALCL) | 2a | B | + |

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Pre- vs. subpectoral implant position and post-mastectomy radiation:

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ADM:

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| | | Oxford | |
|---|---|--------|----|
| | | LoE | GR |
|  <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2025.1E</p> <p>In collaboration with:</p>  <p>www.ago-online.de FORSCHEN LEBEN HEILEN</p> | <h2 style="text-align: center;">Seroma after Implant-Based Reconstruction I</h2> | | |
| | <ul style="list-style-type: none"> Incidence: approx. 5-10% (2-50%) | 2a | B |
| | Influencing factors: | | |
| | <ul style="list-style-type: none"> History of radiation increases risk (RR approx. 3) | 2a | B |
| | <ul style="list-style-type: none"> Obesity increases risk (e.g. BMI > 30 vs. < 30; RR approx. 3) | 2a | B |
| | <ul style="list-style-type: none"> Use of ADM increases risk (RR approx. 3) | 2a | B |
| | <ul style="list-style-type: none"> Use of expander with smooth surface increases risk (RR approx. 5) | 3b | C |
| <ul style="list-style-type: none"> History of neoadj. chemotherapy does not appear to increase risk | 2a | B | |
| <ul style="list-style-type: none"> Prepectoral approach does not appear to increase risk | 2b | B | |
| * Participation in the SERMA study is recommended. | | | |

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| Seroma after Implant-Based Reconstruction II | | | |
|--|--------|----|-----|
| | Oxford | | |
| | LoE | GR | AGO |
| Prevention | | | |
| ▪ Drain | 3b | C | + |
| ▪ Drain removal at < 30 ml per 24 hours | 2b | B | + |
| ▪ Tranexamic acid | | | |
| ▪ i.v. / oral (if no contraindication) | 2a | B | + |
| ▪ Topic | 1b | B | + |
| Therapy | | | |
| ▪ Evacuation of seroma by FNA or re-insertion of drain | 4 | C | + |
| ▪ Pressure dressing | 5 | D | +/- |
| ▪ Revision surgery with capsulectomy (ultima ratio) | 5 | D | + |
| ▪ Revision surgery with implant removal (ultima ratio) | 5 | D | + |

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Systemic TXA:

1. Guggenheim L, Magni S, Catic A et al. The Effects of Systemic Tranexamic Acid Administration on Drainage Volume, Duration of Drain Placement, and Length of Hospital Stay in Skin- and Nipple-Sparing Mastectomies with Immediate Expander-Based Breast Reconstruction. *J Clin Med*. 2024 Oct 30;13(21):6507.
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Topic TXA / Nipple-sparing mastectomy:

1. Liechti R, van de Wall BJM, Hug U et al. Tranexamic Acid Use in Breast Surgery: A Systematic Review and Meta-Analysis. *Plast Reconstr Surg*. 2023 May;151(5):949-957.
2. Safran T, Vorstenbosch J, Viezel-Mathieu A et al. Topical Tranexamic Acid in Breast Reconstruction: A Double-Blind Randomized Controlled Trial. *Plast Reconstr Surg*. 2023 Oct 1;152(4):699-706.
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Tranexamic Acid (TXA) in Implant Surgery - Schedules, Dosage and Timing -

Topic tranexamic acid (Safran T et al., PRS 2023), prospective randomized, double-blind, n = 53, 106 breasts

- 3 g TXA in 100 ml sodium chloride solution for rinsing the implant cavity after NSM and prior implant insertion

Systemic TXA (Guggenheim L et al, J Clin Med 2024), retrospective, n = 132, 155 mastectomies

- First 24 hours:
 - 1 g at the beginning of the operation
 - Then 1 g every 8 hours i.v.
- Second 24 hours:
 - 1 g oral every 8 hours for the next 24 hours

Systemic:



1. Guggenheim L, Magni S, Catic A et al. The Effects of Systemic Tranexamic Acid Administration on Drainage Volume, Duration of Drain Placement, and Length of Hospital Stay in Skin- and Nipple-Sparing Mastectomies with Immediate Expander-Based Breast Reconstruction. J Clin Med. 2024 Oct 30;13(21):6507.

Topic:

1. Safran T, Vorstenbosch J, Viezel-Mathieu A et al. Topical Tranexamic Acid in Breast Reconstruction: A Double-Blind Randomized Controlled Trial. Plast Reconstr Surg. 2023 Oct 1;152(4):699-706

Meta-analysis:

1. Liechti R, van de Wall BJM, Hug U et al. Tranexamic Acid Use in Breast Surgery: A Systematic Review and Meta-Analysis. Plast Reconstr Surg. 2023 May;151(5):949-957

| Skin necrosis after mastectomy | | | |
|---|---------------|-----------|------------|
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| | LoE | GR | AGO |
| Prevention | | | |
| ▪ Local nitroglycerin * | 1a | A | + |
| ▪ Closed-incision negative pressure therapy (ciNPT) | 2a | B | +/- |
| ▪ Local dimethylsulfoxid | 2b | B | +/- |
| ▪ Oral cilostazol | 2b | B | +/- |
| ▪ Preoperative local heat preconditioning | 2b | B | +/- |
| ▪ Prostaglandin E1 | 2b | B | +/- |
| * Dose and regimen vary between studies, off-label | | | |

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2. Liew AN, Lim KY, Khoo JF. Closed Incision Negative Pressure Therapy vs Standard of Care Dressing in Breast Surgery: A Systematic Review. *Cureus.* 2022 Apr 26;14(4):e24499.
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Efficacy and safety of topical nitroglycerin in the prevention of mastectomy flap necrosis – a systematic review and meta-analysis


Wang P et al. Sci Rep 2020

- **7074 patients (3 randomized clinical trials, 2 retrospective cohort studies)**
- **Intervention: transdermal nitroglycerin treatment (ointment; 4.5-45 mg nitroglycerin, applied immediately after end of surgery and in some studies in the first postoperative period until day 6)**
- **Nitroglycerin significantly reduced the mastectomy flap necrosis rate (immediate breast reconstruction [IBR]: OR, 0.48, 95% CI, 0.33–0.70, p < 0.01)**
- **Full-thickness flap necrosis rate in patients receiving IBR was significantly lower in the nitroglycerin group than in the control group (OR, 0.42; 95% CI, 0.25–0.70; p < 0.01)**

1. Wang P, Gu L, Qin Z et al. Efficacy and safety of topical nitroglycerin in the prevention of mastectomy flap necrosis: a systematic review and meta-analysis. Sci Rep. 2020 Apr 21;10(1):6753



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Siliconomas

- In breast parenchyma or regional lymph nodes, rarely in distant organs (pleura, ribs, muscles)
- Incidence unclear
- May occur with or without implant rupture (“silicone bleeding”)
- Migration of silicone to the lymph nodes takes 6-10 years
- Risk of malignancy is not increased


| Oxford | | |
|--------|----|-----|
| LoE | GR | AGO |
| 2b | B | + |
| 2b | B | + |

- Asymptomatic siliconomas do not require removal
- Complete removal of implant and silicone gel (in capsule, if possible) in case of implant rupture


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Prevalence, clinical characteristics, and management of silicone lymphadenopathy: A systematic review of the literature

Pelegrina Perez TC et al., J Plast Reconstr Aesthet Surg 2024

- **279 cases of silicone lymphadenopathy and 107 with information on initial diagnosis, 35 (33%) were incidental.**
- **The most common symptom was painless lymphadenopathy, followed by painful lymphadenopathy.**
- **251 (95%) and 13 (5%) patients had silicone and saline implants, respectively, 149 (68%) patients had implant rupture.**
- **Axillary lymphadenopathy was the most affected region (136 cases, 72%), followed by internal mammary (40 cases, 21%), cervical/supraclavicular (36 cases, 19%), and mediastinal (24 cases, 13%) regions.**
- **25% of patients underwent fine-needle aspiration, 12% core needle biopsy, and 59% excisional biopsy. 32% of cases underwent explantation and/or implant exchange.**
- **The most common indication for surgery was implant rupture.**

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Surgical Prevention



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- **Risk-reducing unilateral or bilateral mastectomy (RRME) without the presence of clearly defined genetic risk factors**
- **Axillary dissection or Sentinel lymph node excision during RRME**

| Oxford | | |
|--------|----|-----|
| LoE | GR | AGO |
| 2a | B | - |
| 2a | B | -- |

RRME ohne gentisches Risiko

1. Kurian AW, Lichtensztajn DY, Keegan TH, et al. Use of and mortality after bilateral mastectomy compared with other surgical treatments for breast cancer in California, 1998-2011. JAMA. 2014;312(9):902-14.
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Sentinel-Lymphknoten Exzision bei RRME

1. Wong SM, Ferroum A, Apostolova C et al. Incidence of Occult Breast Cancer in Carriers of BRCA1/2 or Other High-Penetrance Pathogenic Variants Undergoing Prophylactic Mastectomy: When is Sentinel Lymph Node Biopsy Indicated? Ann Surg Oncol. 2022 Oct;29(11):6660-6668.

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 | 2a | B | ++* |
| <ul style="list-style-type: none"> ▪ Risk-reducing bilateral mastectomy (RR-BM) <ul style="list-style-type: none"> ▪ Reduces BC incidence ▪ Reduces BC mortality in <i>BRCA1</i> mutation carriers*** | 2b | B | +* |

* Study participation recommended
 ** The RR-BSO 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. RRBM counselling should be individualised.

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Risk-reducing Interventions for BRCA1/2 Female Mutation Carriers Affected by Breast Cancer

| | 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 (contradictory results for reduction of cl BC incidence) | 2b | B | +* |
| <ul style="list-style-type: none"> ▪ Prophylactic contralateral mastectomy (RR-CM)* <ul style="list-style-type: none"> ▪ Reduces BC incidence and mortality | 2b | B | +* |
| <ul style="list-style-type: none"> ▪ Tamoxifen (reduces contralateral BC incidence) | 2b | B | +/-* |
| <ul style="list-style-type: none"> ▪ Indication for RR-CM should consider age at onset of first breast cancer in affected gene | 2a | B | ++* |
| <ul style="list-style-type: none"> ▪ RR-BM after ovarian cancer | 4 | C | +/-** |

* Study participation recommended.
** Depends on tumor stage (FIGO I/II), recurrence free interval (≥ 5 yrs.), age.

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