What can we learn from sonication results of breast implants?

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Abstract: BACKGROUND Different research groups have identified microorganisms on breast implants by sonication with significant correlation to the rate of capsular contracture. This substantiated the hypothesis of an infectious etiology of capsular contracture. However, no clinical consequence has been drawn from these results yet. Aim of this study was to review sonication results from breast implants and to evaluate the current preoperative antibiotic regime for breast-implant surgery. METHODS We compared breast implant sonication culture results from published reports and our own database. Current perioperative antibiotic recommendations were compared with the susceptibility profile of the found organisms. RESULTS We found Coagulase-negative staphylococci and Propionibacteria to be the main group of microorganism found by sonication on explanted breast implants. Most guidelines recommend cephalosporins for preoperative antibacterial prophylaxis for breast-implant surgery. CONCLUSION There is a discrepancy between antibiotic activity of commonly used antibiotics for preoperative prophylaxis of surgical site infections, and microorganisms found by sonication on breast implants, suspected to trigger the formation of capsular contracture. A targeted antibiotic prophylaxis for breast implant surgery with glycopeptides (e.g. Vancomycin) should be considered for the prevention of capsular contracture.

DOI: https://doi.org/10.1371/journal.pone.0182267

Posted at the Zurich Open Repository and Archive, University of Zurich
ZORA URL: https://doi.org/10.5167/uzh-189970
Journal Article
Published Version

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Originally published at:
Reischies, Frederike M J; Krause, Robert; Holzer, Judith; Tiefenbacher, Fabian; Winter, Raimund; Eylert, Gertraud; Meikl, Tobias; Tuca, Alexandru; Köfer, Martin J; Kamolz, Lars P; Lumenta, David B (2017). What can we learn from sonication results of breast implants? PLoS ONE, 12(8):e0182267.

DOI: https://doi.org/10.1371/journal.pone.0182267
What can we learn from sonication results of breast implants?

Frederike M. J. Reischies1 *, Robert Krause2, Judith Holzer1, Fabian Tiefenbacher1, Raimund Winter1, Gertraud Eylert1, Alexandru Tuca1, Martin J. Köfer1, Lars P. Kamolz1, David B. Lumenta1

1 Department of Surgery, Division of Plastic, Aesthetic and Reconstructive Surgery, Medical University of Graz, Graz, Austria, 2 Department of Internal Medicine, Section of Infectious Diseases and Tropical Medicine, Medical University of Graz, Graz, Austria, 3 Department of Surgery, Landeskrankenhaus Feldbach/Fürstenfeld, Feldbach, Austria, 4 Institute for Hospital Hygiene and Microbiology, Medical University of Graz, Graz, Austria

* frederike.reischies@medunigraz.at

Abstract

Background
Different research groups have identified microorganisms on breast implants by sonication with significant correlation to the rate of capsular contracture. This substantiated the hypothesis of an infectious etiology of capsular contracture. However, no clinical consequence has been drawn from these results yet. Aim of this study was to review sonication results from breast implants and to evaluate the current preoperative antibiotic regime for breast-implant surgery.

Methods
We compared breast implant sonication culture results from published reports and our own database. Current perioperative antibiotic recommendations were compared with the susceptibility profile of the found organisms.

Results
We found Coagulase-negative staphylococci and Propionibacteria to be the main group of microorganism found by sonication on explanted breast implants. Most guidelines recommend cephalosporins for preoperative antibacterial prophylaxis for breast-implant surgery.

Conclusion
There is a discrepancy between antibiotic activity of commonly used antibiotics for preoperative prophylaxis of surgical site infections, and microorganisms found by sonication on breast implants, suspected to trigger the formation of capsular contracture. A targeted antibiotic prophylaxis for breast implant surgery with glycopeptides (e.g. Vancomycin) should be considered for the prevention of capsular contracture.
Introduction

Periprosthetic capsular contracture is one of the leading long term complications following reconstructive or aesthetic breast implant surgery. It has a reported incidence of 5–22% in the literature[1], depending on follow-up time and surgical indication for breast implantation. Capsular contracture of Baker grade 3 and 4[2] is a severe complication given the need for surgical revision due to malposition and pain. The etiology of capsular contracture, its treatment and prevention are not entirely understood. Many possible causative factors were discussed, e.g. immune mechanisms in foreign body reactions, postoperative haematoma or individual predisposition[1]. However, evidence-based support for these theories is lacking.

A chronic subclinical Infection, caused by biofilm forming bacteria (e.g. Coagulase-negative staphylococci (CNS) or Propionibacterium spp.) has already been suspected decades ago to play a role in the etiology of capsular contracture[3]. This hypothesis was supported by several studies, showing correlations between antiinfective measures preventing contamination of breast implants and lower rates of capsular contracture[4][5][6]. However, for a long time the consistent detection of microorganisms on explanted breast implant surfaces and its association to capsular contracture was not evident, possibly due to the lack of sensitivity of conventional culture methods.

Sonication of medical devices has been introduced as a valid tool to detect biofilms on various implant surfaces and to identify organisms by culturing the sonication fluid[7]. Implants are put into a bath, to which ultrasound is applied, breaking down any possible biofilm. This technique has significantly improved the detection of implant associated infections in orthopedic surgery[8]. Sonication of breast implants eventually allowed for the consistent detection of the same microorganism and significant correlation to capsular contracture[9][10][11], which strongly supports an infectious etiology of capsular contracture.

The use of systemic antibiotics for the prevention of capsular contracture has only a few proponents in the surgical literature, which reported no effect on the rate of capsular contracture using cephalosporins or penicillins [12][13]. 97% of plastic surgeons stated to use cefazolin as antibiotic prophylaxis for breast implantation surgery in breast reconstruction in a recent study[14]. Given that the detection and identification of microorganism on breast implants was reported by different groups with significant association between capsular contracture and sonication result, a more targeted antibiotic regimen for the prevention of capsular contracture should be considered.

To the best of our knowledge, this is the first paper comparing sonication results from different sources including our own data. Aim of this study was to evaluate the suitability of commonly used antibiotic prophylaxis against microorganisms detected by sonication of breast implants.

Methods

After revision of the proposed study protocol with a waiver for additional informed consent and final approval by the local ethical board (Medical University of Graz, vote # EK 28–626 ex 15/16), we retrospectively analyzed breast implant sonication data from otherwise asymptomatic patients, aged 18 years and above, who were carriers of uni- or bilateral breast implants and had an elective implant removal at the University Hospital Graz, Graz, Austria, between January 2015 and April 2016. Patients with signs of local infection in the breast region (e.g. redness, pain, swelling etc.) or systemic infection (e.g. elevated temperature, elevated leucocyte count, elevated c-reactive protein) were excluded. We compared these breast implant sonication results to sonication data of previously published papers. Studies on sonication for breast implants were reviewed, and compared for all retrieved data points.
Current recommendations for perioperative antibiotic prophylaxis for breast implant surgery were extracted from published guidelines, compared to actual antibiotic susceptibility of organisms found in sonication specimens, and profiled for their suitability in perioperative prophylaxis for surgery involving breast implants.

Patient data collection
Following ethical board approval, the following patient data were extracted from electronic patient records (SAP R/3, SAP Germany, Walldorf, Germany): Patient age, sex, reason for implantation, reason for explantation, indwelling time of implants, placement of implants, degree of capsular contracture, sonication culture result.

Degree of capsular contracture was classified according to Baker: grade IV—hard, painful contraction, contracted capsule visible, distorted shape or/and placement; grade III—breast harder than normal, implant visible and palpable, distortion of the implant; grade II—implant palpable, implant not visible, increased firmness of breast; grade I—normal soft breast.

Breast implant: Sonication and culture
Immediately after removal, implants were put in sterile 1000ml containers (Pathopack, Intelsius, York, UK) by the surgeon and covered with 500ml of sterile Ringer solution. The containers were transported to the Institute of Clinical Hygiene and Microbiology, Medical University of Graz for sonication analysis. The closed container was fist vortexed for 30 seconds at maximum speed. The container was then placed into the ultrasound bath and was sonicated for 5 minutes at a frequency of 40 kHz and 200 Watt power. The container was then again vortexed for 30 seconds to distribute detached biofilm components in the fluid homogeneously. The container was next opened in a laminar air-flow biosafety cabinet, to avoid contamination, and 20 ml was removed from the fluid. 10 ml were transferred in to an aerobic blood culture bottle and 10 ml were transferred into an anaerobic blood culture bottle. Blood culture bottles were incubated at 37˚C for 7 days. Conventional microbiological techniques were used to identify positive cultures.

Comparing results from other sonication publications
A systematic review of the literature was performed to identify studies that used sonication analysis for explanted breast implants. For identification of studies, we used the following search terms and search terms combination in the PubMed database: ("breast implants" OR "breast implant") AND ("sonication" OR "broth culture") AND ("capsular contracture" OR "capsular fibrosis"). Inclusion criteria for studies were as follows: Full text articles on breast implants explanted and swiftly analyzed by sonication without further processing. Exclusion criteria were: duplicate publication of data. Articles were included on the 15.12.2016. The systematic review was conducted by FMJR and JH. From included studies demographical data, clinical data as well as sonication results were copied from demographical and clinical data tables from full text articles (Table 1 and S1 Table) Case reports were excluded, and no further restriction on levels of evidence below that was applied. Accumulated data was compared using descriptive statistics.

Review of antibiotic agents recommended by guidelines for prophylactic use in surgery to prevent surgical site infection
Current guidelines for prevention of surgical side infection were collected and, if available, antibiotic recommendations specifically for breast implant surgery were reviewed.
Recommended antibacterial agents and microorganisms found by sonication analysis were evaluated for antibiotic suitability.

**Results**

We included 28 implants from 20 patients, all females, into our study of which 6 implants (21.4%) were excluded because of clinical infection (pain, redness, swelling of breast). Mean age at explantation was 48 (range 19–75) years. 22 implants were included into further analysis, of which 16 (72.7%) were implanted for aesthetic reasons, and 6 (27.3%) for reconstructive reasons. Mean implant indwelling time was 16.7 (1–34.4) years. Data on location of implants was available for 16 of 22 implants (72.7%), of which 10 (45.5%) were positioned subglandular, 5 (22.7%) subpectoral and 1 (4.5%) was positioned underneath a latissimus dorsi muscle flap. Implant surface details were available for 19 of 22 implants (86.4%), of which 13 (68.4%) were textured, 3 (15.8%) were smooth, and 2 (10.5%) had a polyurethane surface.

The main reason for explantation was capsular contracture, with 21 (95.5%) of 22 implants, of which 7 implants were also ruptured. 1 (4.5%) implant was explanted due to patient request. Of 22 analyzed implants 1 (4.5%) was explanted from a breast, showing no signs of capsular contracture (Baker grade 1) and 21 (95.5%) implants came from breasts, which showed considerable capsular contracture, with 17 (80.9%) implants from breasts classified Baker grade 3, and 4 (19%) implants from breasts classified Baker 4.

**Sonication results**

Culture results after sonication showed that out of 22 analyzed implants, 3 (13.6%) were culture negative, and 19 (86.4%) were culture positive, of which 1 (5.3%) with *Propionibacterium avidum* and 18 (81.8%) with Coagulase-negative staphylococci (CNS). 18 of 21 (85.7%) implants, which were explanted from breasts with capsular contracture (Baker 3/4) had positive sonication results. Since only one implant was explanted from a breast without signs of capsular contracture, a correlation analysis of positive culture results and rate of capsular contracture was not reasonable.
Sonication results from previously published paper

Seven studies matched our initial search, after further screening five papers were found reporting of breast implant sonication results, of which all were published after 2000, and two excluded from further analysis due to overlapping patient cohorts\(^1\)\(^2\)\(^3\), (Table 1).

Pajkos et al analyzed 21 implants and 27 capsule-pieces from 16 patients. Capsule material and, if available, implant material was analyzed after maceration by sonication. Of all sonication results in this study \(n = 48\), \(24(50\%)\) were positive, of which \(18/24 (75\%)\) grew CNS, with significant association of CNS positivity and the presence of Baker grade 3/4\(^4\). Del Pozo analyzed 45 implants from 29 women. There was a significant difference between implants explanted due to capsular contraction and implants explanted for other reasons, regarding positivity of sonication culture results \((p = 0.034)\). The main group of isolated bacteria found were CNS and Propionibacterium\(^5\)\(^6\). Rieger analyzed 121 breast implants from 84 patients of which nine were excluded because of clinical infection. There was a significant correlation between degree of capsular contracture and culture positivity after sonication. The main group of bacteria found were Propionibacteria\(^7\)\(^8\) and CNS\(^9\).

Antibiotic agents recommended by guidelines for perioperative prophylaxis

Despite some conflicting reports on antibiotic prophylaxis for breast implantation surgery\(^1\)\(^2\)\(^3\), all reviewed guidelines recommended the use of antibiotic prophylaxis for breast implant surgery. The Sanford guide to antimicrobial therapy recommends cefazolin, 1-2mg iv single-shot preoperatively for breast surgery\(^4\). ASHP therapeutic guidelines recommend antibiotic prophylaxis for breast implantation surgery, as they count the implant as a risk factor for infection\(^5\). Also according to SIGN guidelines (updated 2014), in breast surgery involving implants for reconstructive or aesthetic reasons antibiotic prophylaxis is recommended\(^6\). Systemic reviews also recommend the use of antibiotic prophylaxis in breast implantation surgery\(^7\)\(^8\). In all reviewed guidelines cephalosporins are most often recommended.

These recommendations are congruent with the recent report of 97% of plastic surgeons using cefazolin for this type of surgery\(^9\).

However, there is a discrepancy between optimal antibiotic efficacy of cephalosporines and microorganism found by sonication, which are high-profile suspects to trigger the formation of capsular contracture (Table 2).

Discussion

The detection and identification of microorganism on breast implants by sonication, explanted from breasts with capsular contracture, substantiated the hypothesis of an infectious etiology of capsular contracture. The strong link between these microorganisms and capsular contracture was supported by Tamboto et al, who has demonstrated a causal link between subclinical infection, biofilm formation, and capsular contracture in a porcine model\(^1\). Microorganism found by sonication form part of the skin flora, which are generally considered to have low virulence\(^2\). Fig 1 depicts possible sources of these microorganisms found on breast implants. Possible contamination of the implant during surgery may occur during contact with the skin flora (patient, surgeon, scrub personnel etc.)\(^3\)\(^4\). Contamination may also occur from microorganisms originating from breast ducts or glands, or result from asymptomatic bacteraemia of the patient\(^5\)\(^6\).

Studies which reported methods to reach lower rates of capsular contracture describe methods to improve prevention of contamination of breast implants. Manual pocket dissection
A no-touch technique was proposed to reduce the risk of capsular contracture, since Mladick 1993 published a contracture rate of 0.6 percent in 2863 patients with a 17 year follow-up[3]. The implantation of suction drains were reported to increase the risk of capsular contracture more than fourfold[30]. Implants placed under the pectoral muscle have been reported to be associated with a decreased capsular contracture rate[31]. In the case of a periareolar implantation, the incidence of capsular contracture was 9.5 compared to 0.59 in the case of an inframammary access[6]. All of which presumably reduced the risk of contamination by the natural microbial flora of the breast ducts, by avoiding opening of breast gland ducts and allowing for a larger distance between breast gland and the implant. A systematic review showed no reproducible data regarding the

Table 2. Antibiotic activity against different microorganism.

|                      | Gram positive | Gram negative |
|----------------------|---------------|---------------|
|                      | Staph aureus  | Staph epidermidis | Strep pneumoniae | Ecoli | Klebsiella spp | Pseudomonas aeruginosa |
| Penicillins          |               |               |                |       |               |                      |
| Benzylpenicillin     | -             | -             | +              | -     | -             | -                     |
| Ampicillin/          | -             | -             | +              | V     | V             | -                     |
| Amoxicillin          |               |               |                |       |               |                      |
| Co-amoxiclav         | +             | -             | +              | +     | +             | -                     |
| Cefuroxacin          | -             | -             | V              | +     | -             | -                     |
| Cefofoxacin          | +             | +             | +              | +     | V             | -                     |
| Ceftriaxone          | -             | -             | -              | +     | +             | -                     |
| Ceftazidime          | -             | -             | -              | +     | +             | +                     |
| Cefradine            | +             | -             | V              | +     | +             | V                     |
| Cefuroxime           | +             | -             | V              | +     | +             | -                     |
| Erythromycin         | +             | V             | -              | +     | -             | -                     |
| Clarithromycin       | +             | V             | -              | +     | -             | -                     |
| Clindamycin          | +             | V             | V              | -     | -             | -                     |
| Aminoglycosides      |               |               |                |       |               |                      |
| Gentamicin           | +             | +             | V              | -     | +             | +                     |
| Diaminopyrimidines   |               |               |                |       |               |                      |
| Trimethoprim         | +             | V             | -              | +     | +             | -                     |
| Quinolones           |               |               |                |       |               |                      |
| Ciprofloxacin        | +             | -             | -              | +     | +             | +                     |
| Levofoxacin          | +             | -             | -              | +     | +             | +                     |
| Glycopeptides        |               |               |                |       |               |                      |
| Vancomycin IV        | +             | +             | +              | +     | -             | -                     |
| Teicoplanin          | +             | +             | +              | +     | -             | -                     |
| Nitroimidazoles      |               |               |                |       |               |                      |
| Metronidazole        | -             | -             | -              | -     | -             | -                     |
| Tetracyclines        |               |               |                |       |               |                      |
| Doxycycline          | +             | +             | V              | +     | -             | -                     |

Table 2, showing ineligibility of cephalosporins against staphylococcus epidermidis (coagulase negative staphylococci—CNS) and suitability of glycopeptide antibiotics against staphylococcus epidermidis (coagulase negative staphylococci—CNS). From “Antibiotic prophylaxis in Surgery” Scottish Intercollegiate Guideline Network, updated 2014. V indicates variable antibiotic susceptibility according to local epidemiology.

https://doi.org/10.1371/journal.pone.0182267.t002
The successful identification of microorganisms on breast implants with capsular contracture in recent years should be used to apply targeted antibiotic prophylaxis against the detected microorganisms for the prevention of capsular contracture.

Gylden et al. reported no significant difference in capsular contracture between two groups of patients, one receiving penicillin antibiotic prophylaxis perioperatively for breast implant surgery[12]. These findings are in accordance with those of Mirzabeigi et al., who showed in a
large cohort of primary and secondary breast augmentations, that three days of postoperative administration of cephalosporins did not result in lower rates of complications such as infections or capsular contracture[33]. However, penicillin and cephalosporin antibiotics (beta-lactam antibiotics) do not provide suitable activity against microorganisms found on implants by sonication (Table 2)[34]. May et al reported 80% of CNS to be Oxacillin resistant in over 500,000 CNS isolates in the United States from 1999–2012, Oxacillin was tested as the antibiotic agent representative for beta-lactam antibiotics. Whereas, Vancomycin resistance in CNS isolates was not detected[34]. These results are in conjunction with reports from Asia and Europe where also very high rates of beta lactam antibiotic resistance (>70%–90%) in CNS isolates were reported[35][36]. We were unable to retrieve any other studies investigating systemic perioperative antibiotic prophylaxis for the prevention of capsular contracture.

Although many different microorganisms can cause infections, surgical site infections are usually caused by a small number of common pathogens like *staphylococcus aureus* and *beta-haemolytic streptococci*. Antibiotic prophylaxis in surgery focuses on elimination of pathogens commonly responsible for surgical site infections (Fig 2). Microorganisms, which are suspected to trigger capsular contracture are considered to be of low virulence, thus they are not mainly targeted by currently recommended perioperative antibiotic regimens.

Therefore, cephalosporins, which are mostly used[14], do not provide sufficient activity against organisms isolated from breast implants by sonication, suspected to trigger the formation of capsular contracture. Glycopeptide antibiotics are highly efficient against gram positive organisms[34], like *propionibacteria spp* and CNS, the most frequently found microorganisms by sonication on breast implants[11][10][9]. As a result, for an efficient prevention of capsular contraction, glycopeptide antibiotics (Vancomycin) in addition to cephalosporins should be considered for preoperative antibiotic prophylaxis in breast implant surgery.

The benefit of using the proposed single iv dose of Vancomycin additionally to the single shot of cephalosporin, prior to breast implant surgery, results from the reliable antibiotic coverage against these microorganisms found by sonication on breast implants and the microorganisms typically responsible for surgical site infections. Vancomycin used alone as antibiotic prophylaxis led to higher rates of surgical site infections due to methicillin-sensitive *staphylococcus aureus* (MSSA)[37]. Actually Vancomycin plays a limited role in perioperative antibiotic prophylaxis, is only used in settings with high incidence rates of MRSA infections[38], and for patients with allergies against beta-lactam antibiotics[19]. As a side effect, Vancomycin has been reported to cause acute kidney injury and after fast infusion of Vancomycin a rash, that can affect the whole body, known as the red-man syndrome[39][40]. Therefore, patients considered for the proposed dual antibiotic regimen should be screened for kidney function prior to its administration and Vancomycin should be injected slowly, over 60 min prior to surgery.

Ideally biofilm formation and capsular contracture can be prevented by this targeted antibiotic prophylaxis of a cephalosporin in combination with Vancomycin, at a relatively low cost. One dosage of iv Vancomycin amounts to under 3 Euro at our institution and kidney function tests cost under 3 Euro. An acceptable trade-off, compared to the costs of possible revision surgery in the case of high grade capsular contracture, with resultant capsulectomy and bilateral implant exchange.

Breast implant operations have a considerably high share among aesthetic procedures, which is small compared to the overall number of surgical procedures in general. Therefore, the recommendation of a single iv dose of Vancomycin, interests only a negligible proportion of all surgical procedures, has a well-defined indication, and is based on our as well as previously published data [41]. Vancomycin resistance especially in enterococci emerged after the use of Avoparcin, a glycopeptid used as a growth promoter in food animals. Vancomycin
resistant staphylococci in humans are still very rare despite Vancomycin being in place for almost 60 years [34][41].

Other antibiotic substances which can also be taken into consideration due to activity against CNS are Daptomycin and Trimethoprim/Sulfamethoxazole. Compared to Vancomycin, Daptomycin does not cause the red man syndrome (flush after injection) and shows no nephrotoxicity. However, one dose of Daptomycin costs about sixty times as much as one dose of Vancomycin. In our region Trimethoprim/Sulfamethoxazole has only weak activity against CNS with up to 30% resistance rates, and cannot be considered [35].

Local antibiotic solutions used during breast implant surgery such as local Gentamycin solution, do not provide reliable antibiotic activity against CNS, and cannot prevent the formation of a CNS biofilm around the implant—in our region resistance rates of CNS against Gentamycin reach up to 40%. There is also no official licensing for Gentamycin for local wound irrigation and the implants manufacturers do advice against the usage of any local wound solutions like betadine due to the possible interaction with the implant surface with unknown consequences.

Limitations include the retrospective design of our data review, and a possible non-exhaustive retrieval of additional publications (no records were identified through other sources on this topic as stated in the PRISM chart).

**Conclusion**

Antibiotic single-shot intraoperative prophylaxis for breast implant surgery should be focused on eradication of CNS and propionibacteria, which seem to play a causative role in the formation of capsular contracture. Conventionally used cephalosporines alone for preoperative prophylaxis predominantly applied for prevention of surgical site infections are not suitable to eliminate organisms found to be associated with capsular contracture. We suggest to add Vancomycin to this regimen prior to breast implant surgery to target microorganisms found to be associated with capsular contracture, and aim to analyze the future outcome in a prospective fashion.
Supporting information

S1 Table. Additional information on sonication results. S1 Table, showing additional information on sonication results from following publications: Pajkos 2003, Del Pozo 2009, Rieger 2013 and Reischies 2017.

S1 File. Systematic Review PRISMA flow chart.

S2 File. Systematic Review PRISMA checklist.

Author Contributions

Conceptualization: Frederike M. J. Reischies, Judith Holzer, Fabian Tiefenbacher, Raimund Winter, Martin J. Köfer, Lars P. Kamolz, David B. Lumenta.

Data curation: Frederike M. J. Reischies, Judith Holzer, Tobias Meikl, Martin J. Köfer.

Formal analysis: Robert Krause, Fabian Tiefenbacher, Gertraud Eylert, Lars P. Kamolz.

Investigation: Frederike M. J. Reischies, Fabian Tiefenbacher.

Methodology: Fabian Tiefenbacher, Raimund Winter, Gertraud Eylert, Tobias Meikl, Alexandru Tuca, Martin J. Köfer, David B. Lumenta.

Project administration: Robert Krause, Raimund Winter, Martin J. Köfer, Lars P. Kamolz.

Resources: Raimund Winter, Alexandru Tuca, Lars P. Kamolz.

Software: Judith Holzer, Raimund Winter, Gertraud Eylert, Tobias Meikl, Alexandru Tuca.

Supervision: Robert Krause, Lars P. Kamolz, David B. Lumenta.

Validation: Gertraud Eylert, Tobias Meikl, Alexandru Tuca.

Visualization: Judith Holzer, Fabian Tiefenbacher, Gertraud Eylert, Alexandru Tuca, Martin J. Köfer.

Writing – original draft: Frederike M. J. Reischies, David B. Lumenta.

Writing – review & editing: Frederike M. J. Reischies, Robert Krause, Raimund Winter, Gertraud Eylert, Tobias Meikl, Alexandru Tuca, Martin J. Köfer, Lars P. Kamolz, David B. Lumenta.

References

1. Wan D, Rohrich RJ. Revisiting the Management of Capsular Contracture in Breast Augmentation: A Systematic Review. Plast Reconstr Surg 2016; 137:826–41. https://doi.org/10.1097/01.prs.0000480095.23356.ae PMID: 26910663

2. Spear S, Baker JJ. Classification of capsular contracture after prosthetic breast reconstruction. Plast Reconstr Surg 1995; 96(5):1119–23. PMID: 7568488

3. Shah Z, Lehman JAJ, Tan J. Does infection play a role in breast capsular contracture? Plast Reconstr Surg 1981; 68:34–42. PMID: 7243998

4. Namnoum JD, Largent J, Kaplan HM, Oefelein MG, Brown MH. Primary breast augmentation clinical trial outcomes stratified by surgical incision, anatomical placement and implant device type. J Plast Reconstr Aesthet Surg 2013; 66:1165–72. https://doi.org/10.1016/j.bjps.2013.04.046 PMID: 23664574

5. Mladick RA. “No-touch” submuscular saline breast augmentation technique. Aesthetic Plast Surg 1993; 17:183–92. PMID: 8213311
6. Wiener TC. Relationship of Incision Choice to Capsular Contracture. Aesthetic Plast Surg 2008; 32:303–6. https://doi.org/10.1007/s00266-007-9061-2 PMID: 17994260

7. Trampuz A, Piper KE, Jacobson MJ, Hanssen AD, Unni KK, Osmen DR, et al. Sonication of Removed Hip and Knee Prostheses for Diagnosis of Infection. N Engl J Med 2007; 357:654–63. https://doi.org/10.1056/NEJMoa061588 PMID: 17699815

8. Ahmad SS, Shaker A, Saffarini M, Chen AF, Hirschmann MT, Kohl S. Accuracy of diagnostic tests for prosthetic joint infection: a systematic review. Knee Surg Sports Traumatol Arthrosc 2016:3064–74. https://doi.org/10.1007/s00167-016-4230-y PMID: 27377905

9. Pajkos ABS, Deva AKFRACS, Vickery K, Cope CFRACS, Cossart YEFRC (Path). Detection of Subclinical Infection in Significant Breast Implant Capsules. Plast Reconstr Surg 2003; 111:1605–11. https://doi.org/10.1097/01.PR.S.0000054768.14922.44 PMID: 12655204

10. Del Pozo JL, Tran NV, Petty PM, Johnson CH, Walsh MF, Bite U, et al. Pilot Study of Association of Bacteria on Breast Implants with Capsular Contracture. J Clin Microbiol 2009; 47:1333–7. https://doi.org/10.1128/JCM.00996-09 PMID: 19261794

11. Rieger UM, Mesina J, Kalbermatten DF, Haug M, Frey HP, Pico R, et al. Bacterial biofilms and capsular contracture in patients with breast implants: Breast capsular contracture and bacterial biofilm. Br J Surg 2013; 100:768–74. https://doi.org/10.1002/bjs.9084 PMID: 23468161

12. Gylbert L, Asplund O, Berggren A, Jurell G, Ransjö U, Ostrup L. Preoperative antibiotics and capsular contracture in augmentation mammoplasty. Plast Reconstr Surg 1990; 86:260–269.

13. Mirzabeigi MN, Sbitany H, Jandali S, Serletti JM. The role of postoperative antibiotics in reducing biofilm-related capsular contracture in augmentation mammoplasty. Plast Reconstr Surg 2011; 128:34e–5e. https://doi.org/10.1097/PRS.0b013e3182173fe5 PMID: 21701309

14. Gowda AU, Chopra K, Brown EN, Slezak S, Rasko Y. Preventing Breast Implant Contamination in Breast Reconstruction: A National Survey of Current Practice. Ann Plast Surg 2017:153–6. https://doi.org/10.1097/SAP.0000000000000822 PMID: 27464530

15. Rieger UM, Pierer G, Lüscher NJ, Trampuz A. Sonication of removed breast implants for improved detection of subclinical infection. Aesthetic Plast Surg 2009; 33:404–8. https://doi.org/10.1007/s00266-009-9333-0 PMID: 19322605

16. Rieger UM, Raschke GF, Frei R, Djedovic G, Pierer G, Trampuz A. Role of bacterial biofilms in patients after reconstructive and aesthetic breast implant surgery. J Long Term Eff Med Implants 2014; 24:131–8. PMID: 25272211

17. Ariyan S, Martin J, Lai A, Cheng D, Borah GL, Chung KC, et al. Antibiotic Prophylaxis for Preventing Surgical-Site Infection in Plastic Surgery: An Evidence-Based Consensus Conference Statement from the American Association of Plastic Surgeons. Plast Reconstr Surg 2015; 135:1723–39. https://doi.org/10.1097/PRS.0000000000000822 PMID: 25724064

18. Phillips BT, Halvorson EG. Antibiotic Prophylaxis Following Implant-Based Breast Reconstruction—What is the Evidence? Plast Reconstr Surg 2016. https://doi.org/10.1097/PRS.0000000000002530 PMID: 27307337

19. David N. Gilbert, Henry F. Chambers, George M. Eliopoulos, Michael S. Saag. The Sanford Guide To Antimicrobial Therapy 2016 n.d.;46th Edition.

20. Bratzler DW, Dellinger EP, Olsen KM. Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery 2013;Am J Health-Syst Pharm:195–283.

21. Scottish Intercollegiate Guidelines Network. Antibiotic prophylaxis in surgery. 2014.

22. Huang N, Liu M, Yu P, Wu J. Antibiotic prophylaxis in prosthesis-based mammoplasty: a systematic review. Int J Surg Lond Engl 2015; 15:31–7. https://doi.org/10.1016/j.ijsu.2015.01.020 PMID: 25638736

23. Hardwicke JT, Bechar J, Skillman JM. Are Systemic Antibiotics Indicated in Aesthetic Breast Surgery? A Systematic Review of the Literature: Plast Reconstr Surg 2013; 131:1395–403. https://doi.org/10.1097/PRS.0b013e31828bd752 PMID: 23416440

24. Tamboto H, Vickery K, Deva AK. Subclinical (Biofilm) Infection Causes Capsular Contracture in a Porcine Model following Augmentation Mammoplasty: Plast Reconstr Surg 2010; 126:835–42. https://doi.org/10.1097/PRS.0b013e3181e3b456 PMID: 20811216

25. Grice EA, Segre JA. The skin microbiome. Nat Rev Microbiol 2011; 9:244–53. https://doi.org/10.1038/nrmicro2353 PMID: 21407241

26. Wixtrom RN, Stutman RL, Burke RM, Mahoney AK, Codner MA. Risk of Breast Implant Bacterial Contamination From Endogenous Breast Flora, Prevention With Nipple Shields, and Implications for Biofilm Formation. Aesthet Surg J 2012; 32:956–63. https://doi.org/10.1177/1090820X12456841 PMID: 22964141
27. Jianu DM, Săndulescu O, Streinu-Cercel A, Berciu I, Biliau A, Filipescu M, et al. Microbiologic Safety of the Transareolar Approach in Breast Augmentation. Aesthet Surg J 2016; 36:51–7. https://doi.org/10.1093/asj/sjv106 PMID: 26590196

28. Becker K, Heilmann C, Peters G. Coagulase-negative staphylococci. Clin Microbiol Rev 2014; 27:870–926. https://doi.org/10.1128/CMR.00109-13 PMID: 25278577

29. Rahkonen M, Luttinen S, Koskela M, Hautala T. True bacteremias caused by coagulase negative Staphylococcus are difficult to distinguish from blood culture contaminants. Eur J Clin Microbiol Infect Dis Off Publ Eur Soc Clin Microbiol 2012; 31:2639–44. https://doi.org/10.1007/s10096-012-1607-9 PMID: 22466934

30. Araco A, Gravante G, Araco F, Delogu D, Cervelli V, Walgenbach K. A retrospective analysis of 3,000 primary aesthetic breast augmentations: postoperative complications and associated factors. Aesthetic Plast Surg 2007; 31:532–9. https://doi.org/10.1007/s00266-007-0162-8 PMID: 17659411

31. Henriksen TF, Fryzek JP, Hølmich LR, McLaughlin JK, Høyer AP, et al. Surgical intervention and capsular contracture after breast augmentation: a prospective study of risk factors. Ann Plast Surg 2005; 54:343–51. PMID: 15785269

32. Schaub TA, Ahmad J, Rohrich RJ. Capsular contracture with breast implants in the cosmetic patient: saline versus silicone—a systematic review of the literature. Plast Reconstr Surg 2010; 126:2140–9. https://doi.org/10.1097/PRS.0b013e3181fbb5a2 PMID: 20661169

33. Mirzabeigi M, Merici A, Ortlip T, Tuma G, Copit S, Fox J 4th, et al. Evaluating the role of postoperative prophylactic antibiotics in primary and secondary breast augmentation: a retrospective review. n.d.; Aesthet Surg J.:61–8. https://doi.org/10.1177/1090820X11430830 PMID: 22234264

34. May L, Klein EY, Rothman RE, Laxminarayan R. Trends in Antibiotic Resistance in Coagulase-Negative Staphylococci in the United States, 1999 to 2012. Antimicrob Agents Chemother 2014; 58:1404–9. https://doi.org/10.1128/AAC.00108-13 PMID: 24342646

35. John JF, Harvin AM. History and evolution of antibiotic resistance in coagulase-negative staphylococci: Susceptibility profiles of new anti-staphylococcal agents. Ther Clin Risk Manag 2007; 3:1143–52. PMID: 18516271

36. Xiao Xue M, En Hua W, Yong L, En Jie L. Antibiotic susceptibility of coagulase-negative staphylococci (CoNS): emergence of teicoplanin- non-susceptible CoNS strains with inducible resistance to vancomycin 2011; J Med Microbiol:1661–8. https://doi.org/10.1099/jmm.0.034066-0 PMID: 21799199

37. Bull AL, Worth LJ, Richards MJ. Impact of Vancomycin Surgical Antibiotic Prophylaxis on the Development of Methicillin-Sensitive Staphylococcus aureus Surgical Site Infections: Report From Australian Surveillance Data (VICNISS). Ann Surg 2012; 256:1089–92. https://doi.org/10.1097/SLA.0b013e31825fa398 PMID: 22824854

38. Weigelt JA, Lipsky BA, Tabak YP, Derby KG, Kim M, Gupta V. Surgical site infections: Causative pathogens and associated outcomes. Am J Infect Control 2010; 38:112–20. https://doi.org/10.1016/j.ajic.2009.06.010 PMID: 19889474

39. Sivagnanam S, Deleu D. Red man syndrome. Crit Care 2003; 7:119–20. https://doi.org/10.1186/cc1871 PMID: 12720556

40. Courtney PM, Melnic CM, Zimmer Z, Anari J, Lee G-C. Addition of Vancomycin to Cefazolin Prophylaxis Is Associated With Acute Kidney Injury After Primary Joint Arthroplasty. Clin Orthop Relat Res 2015; 473:2197–203. https://doi.org/10.1007/s11999-014-4062-3 PMID: 25421958

41. Cattor V, Leclercq R. Twenty-five years of shared life with vancomycin-resistant enterococci: is it time to divorce? J Antimicrob Chemother 2013; 68:731–742. https://doi.org/10.1093/jac/dks469 PMID: 23208830